Development of a core outcome set for adult traumatic brachial plexus injuries.

A thesis submitted for the degree of Doctor of Philosophy (PhD)

By

Caroline Miller

Faculty of Medicine and Health Sciences: School of Health Sciences

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Declaration

I certify that the work contained in this thesis for the degree of Doctor of Philosophy is my original work except where due reference is made to other authors and has not been previously submitted for a degree, diploma or any other qualification at any other university or institution.

Abstract

Background: A traumatic Brachial Plexus Injury (BPI) involves major trauma to the large nerves of the arm, resulting in partial or complete paralysis, loss of feeling and unremitting pain. Outcome reporting in BPI research is inconsistent hindering synthesis of evidence to inform best care. This research aimed to develop a Core Outcome Set (COS) for adult BPI.

Methods: Patient interviews and a systematic review of outcomes in BPI studies identified a long list of outcomes. Key stakeholders (surgeons, therapists and adults with a BPI) rated their importance in a 3 round international online Delphi on a 9-point Likert scale. During online patient and clinician consensus meetings the COS-BPI was determined. A systematic review was conducted to identify potential instruments available to measure the domains in the COS.

Results: Sixty -four outcomes were identified from the systematic review and interviews. Seventy-two participants (21 people with a BPI, 20 surgeons and 31 therapists) from nineteen countries rated the importance of these outcomes in the online Delphi. Thirty-eight participants voted on 33 outcomes in the consensus meetings (25 clinicians and researchers and 13 people with the injury). Pain, voluntary movement and carrying out daily routine outcomes were included in the COS-BPI. A systematic review identified that the Brachial Assessment Tool (BrAT) and the Brief Pain Inventory could potentially measure the carrying out daily routine and pain outcomes in the COS-BPI. No suitable instrument to measure voluntary movement was identified.

Conclusion: International consensus was reached on a COS for BPI which includes pain, voluntary movement and carrying out daily routine. The BrAT and Brief Pain Inventory can be used to measure the carrying out daily routine and pain domains. This will ensure that relevant outcomes are measured and reported and facilitate comparison across studies supporting BPI data synthesis to inform evidence-based practice.

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Publications and presentations

Publications

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Miller C, Cross J, O'Sullivan J, Power DM, Kyte D, Jerosch-Herold C. Outcome reporting in traumatic brachial plexus injury: an in-depth analysis to inform the development of a core outcome set: the COMBINE study. Biennial British Society of Surgery of the Hand (BSSH) and British Association of Hand Therapists (BAHT) conference, Swansea, UK, April 2019

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Miller C, Jerosch- Herold C, Cross J. Brachial Plexus Injury: Living with Uncertainty. Annual Physiotherapy UK conference, online, November 2021

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Abbreviations

BPI	Brachial Plexus Injury
BrAT	BRachial Assessment Tool
CAG	Clinical Advisory Group
CJH	Christina Jerosch-Herold (Primary supervisor)
ClinRO	Clinician Reported Outcome
COMBINE	Core Outcome Measures in Brachial plexus INjuriEs
COMET	Core Outcome Measures in Effectiveness Trials
COMS	Core Outcome Measurement Set
COS	Core Outcome Set
COSMIN	COnsensus-based Standards for the selection of health Measurement Instruments
COS-STAD	Core Outcome Set STAndards for Development
DASH	Disabilities of the Arm Shoulder and Hand
DP	Dominic Power (Clinical and academic supervisor)
HCP	Health Care Professional
ICF	International Classification of functioning, disability and health
ICHOM	International Consortium for Health Outcomes Measurement
IMBIQ	IMpact of Brachial plexus Injury Questionnaire
JC	Jane Cross (Academic supervisor)
JJ	Jack Jeffrey
JOS	Joel O Sullivan
MRC	Medical Research Council
NHS	National Health Service
OMERACT	Outcome Measures for Rheumatology Clinical Trials
OMI	Outcome Measurement Instrument
OBPI	Obstetric Brachial Plexus Injury
ORB	Outcome Reporting Bias
PAG	Patient Advisory Group
PerfO	Performance Outcome
PIS	Participant Information Sheet
PP	Proximal Phalanx
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
PRO	Patient-Reported Outcome
PROSPERO	Prospective Register of Systematic Reviews
PAG	Patient Advisory Group
RWD	Real World Data
USA	United States of America

Chapter 1 Introduction

1.1 Introduction

The focus and scope of the research presented in this thesis developed because of my role as a specialist physiotherapist in a tertiary brachial plexus and peripheral nerve injury service in the United Kingdom (UK). Traumatic brachial plexus injuries are complex and life-changing, and people with the injuries often have multiple surgeries followed by months of rehabilitation. After extensive interventions and rehabilitation many patients were still presenting to me with ongoing disability and limited physical improvements. I was unsure whether the interventions and rehabilitation were effective. It made me question how we were measuring the impact of these interventions. What outcomes were we measuring? Were we measuring outcomes important to patients and health professionals? How did this inform the evaluation of current and new treatments? These questions led to the development of this programme of research, which aimed to identify current gaps in outcome assessment in brachial plexus injury and develop a solution. The thesis will present the iterative steps involved in developing a core outcome set. This chapter will define what a brachial plexus injury is, how it is managed and explore current gaps in outcome assessment. It concludes by outlining the aims and objectives of the research in this thesis.

1.2 Brachial plexus injury

1.2.1 Anatomy of the brachial plexus

The brachial plexus is a group of nerves that arise in the spinal cord in the neck and supply motor, sensory and sympathetic input to the whole upper limb (Gregory et al., 2009). The brachial plexus consists of 5 parts: 5 roots, 3 trunks, 6 divisions, 3 cords and 5 terminal branches (Figure 1.1). The roots comprise of the anterior rami of the lower four cervical and first thoracic nerve root (Feigl et al., 2020). There are occasionally contributions from C4 (11% of plexuses) and T2 (1%) (Benes et al., 2021). The three trunks then form from the roots in the supraclavicular area (Uysal et al., 2003). The upper trunk is formed from C5 and C6 , C7 continues to become the middle trunk and

C8 and T1 form the lower trunk (Gregory et al., 2009; Johnson et al., 2006). Each of these trunks split into posterior and anterior divisions just above the clavicle (Uysal et al., 2003), which then merge to form cords. The posterior cord develops from the posterior divisions. Anterior divisions of the upper and middle trunks unite to form the lateral cord while the anterior division of the lower trunk forms the medial cord (McMinn and Hutchings, 1993). Lastly, the final subdivisions of the brachial plexus give rise to their terminal branches. The medial cord becomes the ulnar nerve and the lateral cord becomes the musculocutaneous nerve. Parts of the lateral and medial cords unite to form the median nerve. The posterior cord continues as the radial nerve. Additional nerves arise along the length of the brachial plexus, which innervate the proximal upper limb muscles.

Figure 1. 1 Anatomy of the brachial plexus

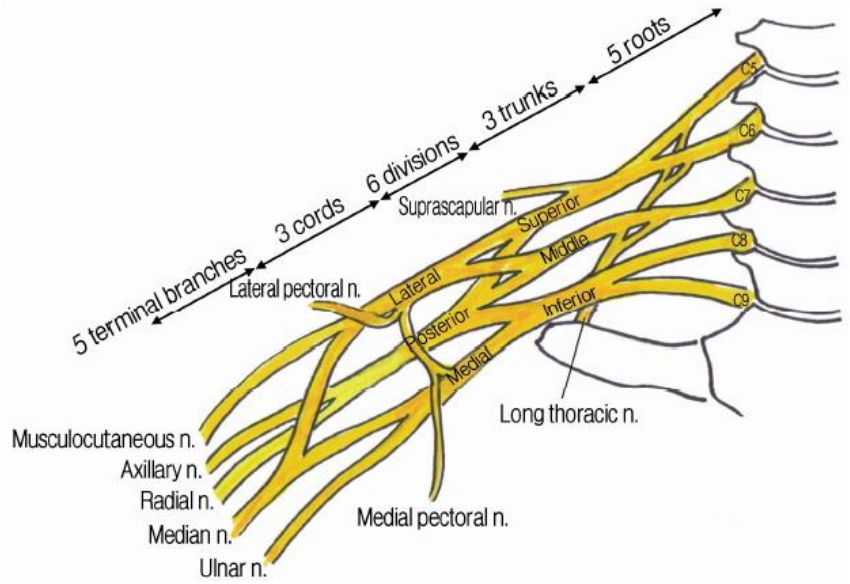


Illustration from Park et al., 2017 with permission

The complex anatomy of the brachial plexus means that the muscles and skin of the upper limb receive their sensory and motor innervation from several nerve roots (Medical Research Council, 1976). Table 1.1 presents the innervation of key upper limb muscles. Trauma to different sections of the plexus, i.e., brachial plexus injury (BPI), results in complicated combinations of motor and sensory deficits. These can be partial or can impact the whole arm. Some patterns of a BPI are more prevalent, for instance, injury to the whole brachial plexus or the upper or lower sections only. However, rarely will people appear with the same movement and sensory deficit based on the

anatomical site and extent of trauma to the plexus. Therefore, people presenting with a BPI are a heterogenous group and experience wide-ranging differences in how they can use their arm and hand.

Table 1. 1 Key upper limb muscle innervation by the brachial plexus

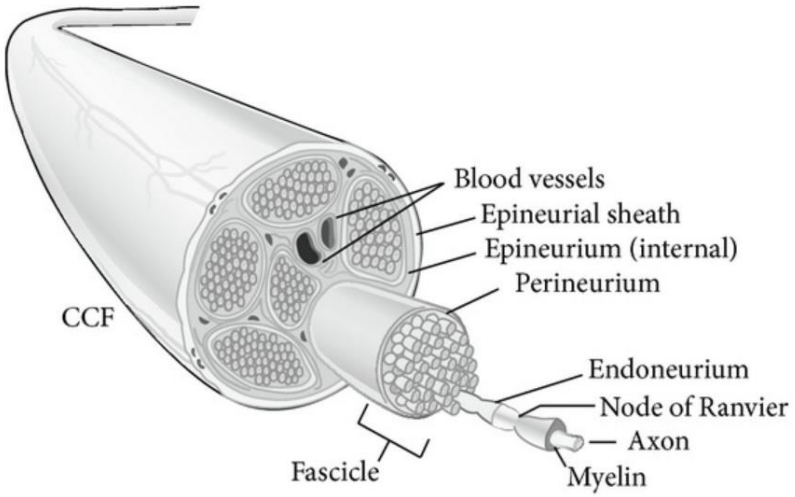
Joint	Muscle	Nerve root	Peripheral nerve	Main action
Shoulder	Deltoid	C5, C6	Axillary	Abduction
	Infraspinatus	C5, C6	Suprascapular	External rotation
	Serratus anterior	C5, C6, C7	Long thoracic	Scapular stabilisation
	Clavicular pectoralis major	C5, C6	Lateral pectoral	Horizontal adduction at 90
	Sternal pectoralis major	C6, C7, C8	Medial & lateral pectoral	Adduction
	Latissimus dorsi	C6, C7, C8	Thoracodorsal	Adduction & internal rotation
Elbow	Biceps/Brachialis	C5, C6	Musculocutaneous	Flexion (flex)
	Triceps	C6,7,8	Radial	Extension
	Brachioradialis	C5, C6	Radial	Flexion
Forearm	Supinator	C6, C7	Radial	Supination
	Pronator teres	C6, C7	Median	Pronation
Wrist	Extensor carpi radialis longus	C5, C6	Radial	Extension and radial deviation (dev)
	Flexor carpi ulnaris	C6, C8, T1	Ulnar	Flex and ulnar dev
	Flexor carpi radialis	C6, C7	Median	Flex and radial dev
	Extensor carpi ulnaris	C7, C8	PIN	Extension & ulnar dev
Fingers	Extensor digitorum	C7, C8	PIN	Extension of digits
	Flexor digitorum superficialis	C7, C8, T1		Flex proximal IPJ
	Flexor digitorum profundus	C7, C8, T1	Median I, II, ulnar III, IV	Flex distal IPJ
	Interossei	C8, T1	Ulnar	Abduction & adduction digits
	Lumbricals	C8, T1	Median I, II, ulnar III, IV	Extension proximal IPJ
Thumb	Flexor pollicis longus	C7, C8	AIN	Flex IPJ thumb
	Extensor pollicis longus	C7, C8	PIN	Extension IPJ
	Adductor pollicis	C8, T1	Ulnar	Adduction of thumb
	Opponens pollicis	C8, T1	Median	Opposition of thumb
	Abductor pollicis brevis	C8, T1	Median	Abduction PP thumb

PIN: posterior interosseous nerve, *AIN*: anterior interosseous nerve, *IPJ:* interphalangeal joint, *PP:* proximal phalanx

1.2.2 Functional anatomy of the brachial plexus and peripheral nervous system

An intact nervous system conducts impulses between the central and peripheral nervous systems. The roots (spinal nerves), brachial plexus and its terminal branches are all part of the peripheral nervous system. These peripheral nerve structures contain neurons (nerve cells) that are the structural and functional unit of the nervous system. Each neuron is made up of a cell body, dendrites, and an axon. Nerves in the body consist of thousands of neurons, which may be efferent (motor) or afferent (sensory) (Gregory et al., 2009). Motor axons arise from the cell bodies in the anterior horn of the spinal cord, and the dorsal root ganglia in the spinal cord host the cell bodies of the sensory neurons (Johnson et al., 2006). Endoneurium, a connective tissue, envelops the axons, grouping them together into fascicles (Stewart, 2003). Each fascicle is then surrounded by another layer of connective tissue called perineurium and the entire nerve is contained by a final layer of connective tissue called the epineurium (Gregory et al., 2009; Grinsell and Keating, 2014) (see Figure 1.2). Individual fascicles and whole nerves can consist completely of afferent or efferent neurons or be mixed in content (Johnson et al., 2006). This implies that injury to a nerve can impact motor or sensory functioning or both.

Figure 1.2 Fascicular structure of a nerve



1.2.3 Classification of brachial plexus injuries

The extent of intraneural damage experienced during a BPI impacts prognosis. There are three main classification systems for all nerve injuries that relate to intraneural damage. These include the Seddon (Seddon, 1942), Sunderland (Sunderland, 1951) and Mackinnon (Mackinnon, 2015) systems. The original Seddon system (Seddon, 1942) classified injuries from neurapraxia (temporary conduction block, likely to resolve spontaneously) and axonotmesis (axonal loss, variable potential for spontaneous recovery) to neurotmesis (nerve transected and surgery needed for repair). Sunderland (Sunderland, 1951) and later Mackinnon (Mackinnon, 2015) extended this classification system, introducing further subcategories. However, all the classification systems have limited clinical use, as within each of these subcategories there are variations and a BPI is aften a combination of total rupture, avulsion and stretched nerve fibres. It is often only through careful history taking and close monitoring of motor and sensory recovery that prognosis can be predicted.

BPIs are also categorised in relation to the location of injury. Supraclavicular nerve injuries are either pre-ganglionic or post-ganglionic (see Figure 1.3). Pre-ganglionic

injuries occur proximal to the cell body in the dorsal root ganglion (Park et al., 2017). In pre-ganglionic injuries, the nerve root detaches from the spinal cord, but the sensory cell bodies in the dorsal root ganglia remain intact. Regeneration is not possible for nerve injuries at this level (Carlstedt and Risling, 2019). Supraclavicular post-ganglionic injuries involve a rupture or traction injury to the brachial plexus distal to the ganglion and have better functional outcomes than pre-ganglionic injuries (Terzis et al., 1999), as surgical repair is possible for post-ganglionic ruptures (section 1.2.7) and traction injuries have the capacity to regenerate (section 1.2.4).

Figure 1.3 Cross-section of normal spinal cord and nerve root connection

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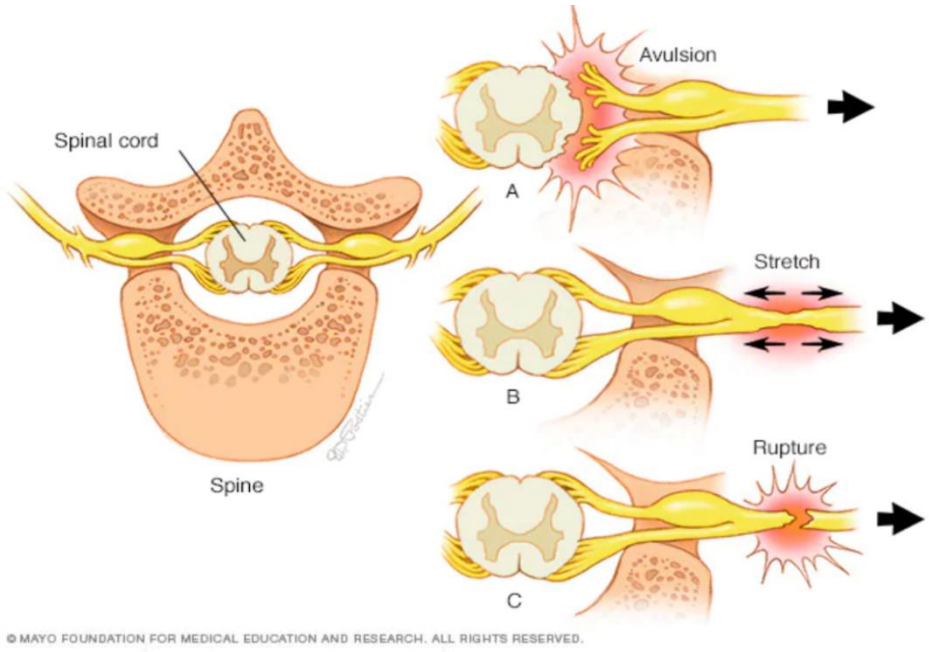

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An infraclavicular injury occurs at the distal parts of the brachial plexus or its terminal branches. People who experience infraclavicular injuries often have better prognosis than those who experience a pre- or post-ganglionic supraclavicular lesion (Hems and Mahmood, 2012). Data regarding patterns of infraclavicular injuries are scarce in the literature (Kaiser et al., 2018). However, the most common mechanism of injury for an isolated infraclavicular injury is an anterior glenohumeral (shoulder) dislocation (Hems and Mahmood, 2012).

Frequently, BPIs involve the supraclavicular region or a combination of supra with infraclavicular, with a prevalence of 90% compared to a 10% prevalence of isolated infraclavicular injuries (Kaiser et al., 2018). This conflicts with previous published findings by Narakas, who found a 70% prevalence of supraclavicular injuries in his 1,068 patients (Narakas, 1985). The difference may be as a result of the recent meta-analysis including higher number of surgical cases (Kaiser et al., 2018). Supraclavicular lesions are commonly associated with either an upper plexus syndrome (73%), impacting the shoulder or elbow, or a complete brachial plexus palsy (53%), impacting the whole upper limb.

1.2.4 Neurophysiological recovery of a brachial plexus injury

Once a neuron's cell body remains intact then the axon has potential to regenerate. In a pre-ganglionic avulsion injury, where the root avulses from the spinal cord, there is no potential for regeneration (Carlstedt and Risling, 2019).

For post-ganglionic injuries, trauma to the brachial plexus nerves initiates a sequence of events. Following axonal injury, a process called Wallerian degeneration begins (Allodi et al., 2012; Stoll et al., 2002). The axon distal to the injury site degenerates, accompanied by parallel fragmentation and shrinkage of its myelin sheath (Sulaiman and Gordon, 2013). This process begins approximately 36–44 hours after injury (Beirowski et al., 2005). By the 7th day following injury, macrophages are signalled by Schwann cells to clean up the axonal and myelin debris (Gaudet et al., 2011), preparing the area for outgrowing axonal stumps. New axons then sprout from the proximal nerve segment, secondary to neurochemical release (Gaudet et al., 2011). If axons find a corresponding endoneurial tube, then regrowth is possible, although recovery may be inconsistent. Following a neurotmesis, Wallerian degeneration also occurs, but regeneration does not commence as there is no conduit to guide the axons' regrowth. For these transection injuries microsurgical repair is necessary.

Although axons can regenerate, functional recovery is frequently inadequate for several reasons. Firstly, at the injury site, axons need to regenerate to the appropriate endoneurial tubes so that they reach their previous motor or sensory target organ. However, axonal misdirection is common, whether regeneration occurs naturally or

with surgery (Nguyen et al., 2002). This misdirection is linked with functional deficits (Alant et al., 2013; Sulaiman and Gordon, 2013) and central nervous system changes, with synaptic reorganisation of the somatosensory and motor cortex (Lundborg, 2000a; Lundborg and Rosén, 2007; Merzenich and Jenkins, 1993). Secondly, the distance from the injury to the target organ influences recovery. Axons regrow at a rate of approximately 1 to 2mm a day (Griffin et al., 2010; Grinsell and Keating, 2014; Lee and Wolfe, 2000), therefore recovery times for more proximal nerve injuries, innervating distal target organs (for example, small hand muscles), are much longer. After a BPI, regrowth of 1m might be necessary to reach the end organ and this could take two to three years (Choi et al., 1997). However, after this time the target organ may not be viable.

Reinnervation of muscles is time-dependent because denervated motor end plates degenerate over time (Gupta et al., 2020; Sulaiman and Gordon, 2013). Muscle fibres fibrose after 12-18 months of motor endplate denervation (Grinsell and Keating, 2014; Gupta et al., 2020). Therefore, reinnervation after this time is likely to fail (Terzis et al., 1999). Denervation also results in degeneration of sensory end organs in animal models (Dellon et al., 1975; English, 1977). However, there have been reports that protective sensation can return in adults after five years (Terzis et al., 1999). Finally, nerve regeneration will not occur if the cell body is damaged. In a BPI, neuronal cell body apoptosis occurs after 6 months, if distal regeneration does not occur (Adyaksa and Heri, 2021). Sensory nerve cell death starts soon after nerve rupture, with significant cell death in the dorsal root ganglia at 1 week if no repair is conducted (Groves et al., 1997; McKay Hart et al., 2002; Vestergaard et al., 1997). Therefore, for all these reasons, early reinnervation is important to optimise outcomes following nerve injuries (Martin et al., 2019; Pondaag et al., 2018).

1.2.5 Aetiology and epidemiology of brachial plexus injury

The aetiology of BPIs has changed over time. Historically these injuries were associated with open war wounds, whereas now most people present with closed injuries resulting from a traction force (Kaiser et al., 2018). The majority result from motor vehicle accidents (Ciaramitaro et al., 2010; Flores, 2006; Kouyoumdjian, 2006; Midha, 1997) and the most frequent mechanisms of injury are motorbike accidents (Kaiser et

al., 2018; Kazamel and Sorenson, 2016). Characteristically, a motorcyclist is thrown off their bike. The motorcyclist's head hits the road forcing the neck to side flex while the shoulder girdle is depressed in the opposing direction. The severe traction to the nerve(s) can result in nerve rupture, root avulsion from the spinal cord (see Fig 1.3) or a significant stretch injury to the nerve, although it remains intact (Songcharoen et al., 2005).

The location of the arm when the force is sustained can often predict the specific roots, trunks or cords affected (Hems, 2015a). Upper plexus injuries (C5, C6 ± C7) occur when the plexus is stretched while the arm is by the trunk (Barnes, 1949). This results in motor loss to the shoulder and elbow, with thumb and index finger sensory changes (Park et al., 2017). Lower plexus injuries occur when the arm is overhead and a traction force impacts the arm or trunk (Barnes, 1949). This causes motor and sensory loss to the wrist and hand (Park et al., 2017). A pan-plexus injury impacts innervation from C5-T1, and may result from a traction to the plexus while the arm is behind the trunk (Bonham and Greaves, 2017) and causes loss of motor and sensory function to the whole upper limb (Park et al., 2017).

The prevalence of a closed BPI in multi-trauma patients ranges from 1.2% in Canada (Midha, 1997) to 5.7% in Guatemala (González Lemus and Romero Prieto, 2021). The variation is linked to the use of motorbikes. In a systematic review including 3,032 international adults with BPI, Kaiser et al. (2018) identified that the most common cause of a closed injury was a motorcycle accident, with a 67% (95%, CI:49-82%) pooled prevalence. There is limited data on the incidence of BPIs in the UK. In 1992, Goldie and Coates (1992) surveyed UK orthopaedic surgeons and estimated 450-500 cases in a single year. More recently, Dy et al. (2020) estimate an annual incidence of surgically treated BPI of 0.89 per 100,000 general population in the USA. They also found that incidence increased from 2008 to 2014 (Dy et al., 2020). However, there are limitations with the study as it extrapolated incidence from people having surgery in a private insurance system only. Also, it does not include the incidence of BPIs that were treated non-surgically. Conversely, the incidence of a BPI in Brazil is estimated at 1.75 cases per 100,000 local population per year (Flores, 2006), which may be related to the increased use of motorbikes in this region. Finally, approximately 93% of those

suffering adult BPIs are young men in their twenties and early thirties (Ciaramitaro et al., 2010; Estrella, 2011; Flores, 2006; Jain et al., 2012; Kaiser et al., 2018; Kazamel and Sorenson, 2016).

1.2.6 Clinical presentation and impact of brachial plexus injuries

It is clear from the above sections that a BPI is heterogenous in its presentation, depending on the location and the extent of trauma to the plexus. People with pre-ganglionic avulsions of all roots present with complete sensory and motor loss in their arm, often complicated by shoulder subluxations secondary to loss of muscle tone (Choong and Shalimar, 2015). They may need long-term use of arm and shoulder supports. People who experience an avulsion of any root will experience partial paralysis and sensory loss. All individuals with brachial plexus pre-ganglionic avulsions report intractable neuropathic pain (Brown et al., 2018; Htut et al., 2006; Teixeira et al., 2015; Wellington, 2010; Zhou et al., 2017) that is resistant to pharmacological treatments (Teixeira et al., 2015) and increases with the number of roots avulsed (Htut et al., 2006). Functional use of the arm is limited (Brito et al., 2019; Franzblau et al., 2014) and direct nerve repair is not possible, as the root(s) have avulsed from the spinal cord and regeneration is not viable (Carlstedt and Risling, 2019).

With a post-ganglionic injury, outcomes vary. People can regain near-normal function or the arm can work as a passive stabiliser (Ochiai et al., 1996; Satbhai et al., 2016). This depends on the severity of the initial injury (number of roots, trunks, cords and classification of nerve injury). However, recovery of good forearm and hand function is rarely achieved due to long regeneration distances (Ochiai et al., 1996). People with a pan BPI usually have poor outcomes (Bertelli et al., 2011) with significant disability (Wali et al., 2017).

In addition to the physical impairments and pain suffered by people with a BPI, individuals also experience emotional and psychological distress despite progress in treatments (Hruby et al., 2020). Challenges with role and identity are frequently highlighted (Brito et al., 2019; McDonald and Pettigrew, 2014). Individuals discuss how their role in the family alters because of the injury, often impacting on relationships with partners (McDonald and Pettigrew, 2014). Some men with the injury report

feeling “less of a man” (McDonald and Pettigrew, 2014, p150) at home because of the disability, frustrations around letting people down, and difficulties asking for help. Additionally, people with the injury discuss struggling with loss of roles in leisure activities and how this impacts on friendships (Brito et al., 2019). However, over time some people develop and participate in new hobbies (Brito et al., 2019). Finally, people report significant challenges with returning to previous roles at work due to ongoing upper limb disability and pain (Brito et al., 2019; McDonald and Pettigrew, 2014; Wellington, 2010). Indeed, fewer than 50% of people return to any work regardless of the site or extent of injury (Kretschmer et al., 2009). These challenges with returning to employment exacerbate financial uncertainties (Brito et al., 2019).

Many people discuss needing time to come to terms with a BPI, both in terms of the disability but also body image (Brito et al., 2019). If a muscle loses its nerve innervation there is a loss of muscle bulk. Sometimes deformities in the upper limb develop because of stiffness in the joints or unopposed muscle actions. Issues surrounding body image are often related to social anxiety for people with a BPI (Franzblau and Chung, 2015; Verma et al., 2019; Wellington, 2010). People with the injury discuss attempting to cover their arm to avoid people asking questions or staring at the injured arm (McDonald and Pettigrew, 2014). It is clear this devastating injury has a considerable effect on both physical and mental health.

People with a BPI often need numerous surgical procedures, associated with long periods of rehabilitation with protracted time off work. This can result in considerable direct and indirect costs to the person and society. It is important to understand the economic impact of BPI, as it predominantly affects young people of working age whose most productive years are interrupted by the condition.. Although the injury is relatively rare, it is associated with a NHS cost of £35 million annually (National Audit Office, 2010). Recent research in the USA estimated that the indirect cost of a BPI for each patient averaged $1,113,962 over a lifetime (Hong et al., 2019). This included the cost of productivity loss and disability payments. Direct surgical costs are estimated at an additional $40,000 per patient (Lingampalli et al., 2020). Additionally, it is anticipated that the incidence and costs will increase with better survival following major trauma (Lecky et al., 2010; Lecky and Coats, 2015) and associated increase in

injury complexity (Dutton et al., 2010), causing substantial societal and economic burden.

1.2.7 Management of a traumatic brachial plexus injury

As explored in section 1.1.4, for successful regeneration after injury, nerves need a conduit to guide axonal growth. For all but a neurapraxia or a less severe axonotmesis, microsurgery may be required to reconstruct the internal neural architecture and support axonal regrowth (Mackinnon, 2015). Management is therefore often surgical, with supportive rehabilitation. To illustrate the different treatment pathways that exist for people with a BPI, I have presented three vignettes (Table 1.2). The interventions are discussed in more detail in sections 1.2.7.1 – 1.2.7.3 below.

Table 1. 2 Brachial plexus injury vignettes

	Vignette 1	Vignette 2	Vignette 3
Age	19	32	63
Mechanism of injury	High-speed motorbike accident	Hit by speeding car while on bicycle	Fall onto her outstretched hand
Sex	Male	Male	Female
Symptoms	Intractable upper limb pain, no movement or sensation	Intractable neuropathic pain in upper limb, no shoulder or elbow movement but good hand movement	Anterior humerus fracture dislocation with neuropathic upper limb pain and no active arm movement
Suspected hypothesis	Complete pre-ganglionic avulsion injury C5-T1	Supraclavicular injury to upper roots or trunks	Suspected infraclavicular BPI secondary to shoulder dislocation
Immediate intervention	Neuropathic pain medication, arm support and advice to maintain passive range of movement in whole upper limb	Neuropathic pain medication, arm support and advice on passive range of movement for upper limb	Closed reduction of dislocation Non-surgical management of fracture Neuropathic pain medication, arm support and advice to maintain passive range of movement elbow and hand
Early intervention	Two weeks: surgical exploration to identify extent of injury or confirm hypothesis. Diagnosis confirmed	Three weeks following injury: surgical exploration of brachial plexus (diagnosed upper trunk rupture)	Non-surgical therapy-led treatment
5-6 months	Surgery: free muscle transfer to upper limb to gain elbow flexion and finger flexion, followed by ongoing physiotherapy	Three surgical nerve transfers: -spinal accessory nerve to suprascapular nerve (aim to innervate rotator cuff) -radial nerve to axillary nerve (aim to innervate deltoid) -ulnar nerve to musculocutaneous nerve (aim to innervate biceps)	Non-surgical therapy-led treatment
12 months	Ongoing physiotherapy	Ongoing physiotherapy	1.Surgery released scarring around nerves 2. Fingers manipulated, as poor function in median and ulnar nerve and stiff fingers
18 months	Ongoing physiotherapy	Ongoing physiotherapy	Ongoing physiotherapy
3 years	Discussion regarding amputation of arm	Tendon transfer to improve lateral rotation	Tendon transfers for thumb and finger movement

1.2.7.1 History

For many centuries surgeons have tried to repair the brachial plexus, and the first successful repair was published in 1896 (Thorburn, 1900). However, it was not until the mid-20th century that brachial plexus surgery began and became reported in earnest (Barnes, 1949; Bonney, 1959; Leffert and Seddon, 1965; Narakas, 1978).

1.2.7.2 Primary surgical interventions

In the immediate and acute stage of a BPI, one (or a combination) of the following three primary surgical interventions are often used with the aim of optimising chances of axonal regeneration and ultimately end organ innervation. These are: (i) end-to-end primary repair (direct suture); (ii) nerve grafting; and (iii) nerve transfers.

Direct repair and nerve grafts: Early brachial plexus repair involved direct suturing of the epineurium of nerve ends (Raza et al., 2020). However, microsurgical techniques, including magnification loupes, developed in the 1970s so individual fascicles could be sutured together allowing for the matching of sensory and motor bundles (Millesi, 1979). Despite this progress, clinical outcomes following fascicular repair may not be any better than epineurial repair (Lundborg, 2000b). For nerve injuries where more than 10% elongation of the nerve is required for the gap to be bridged, a nerve graft is necessary (Trumble and McCallister, 2000). Further surgical innovation in 1970s resulted in the first description of fascicular nerve grafting techniques (Narakas, 1978). There are, however, disadvantages to using direct repair or nerve grafts in a BPI. Because a BPI is a proximal injury, it will take a substantial amount of time for axons to regenerate to reach their target organs. By the time nerves have regenerated to their end organs, motor endplate denervation and muscle atrophy, in addition to sensory end organ degeneration, can occur (see section 1.2.4). This will impact on functional outcome. For instance, Arnal et al. (2016) conducted a retrospective cohort study (n = 21) to evaluate motor recovery in the hand following nerve grafting of C5. They reported that only 40% of the cohort achieved anti-gravity finger flexion.

Nerve transfers: Although direct repair and nerve grafts are still used today, since the 1990s nerve transfers have been increasingly used to treat BPIs (Čebron et al., 2021; Domeshek et al., 2019; Oberlin et al., 1994). A nerve transfer is “the connection of a functioning nerve (of lesser functional importance) to a distal stump of an avulsed

nerve" (Tung and Mackinnon, 2010, p332). The advantages of nerve transfers include reducing the distance between healthy donor axons and the end target, in addition to decreased time in surgery, risk, and technical expertise (Hill et al., 2021).

The Oberlin nerve transfer is commonly used to improve elbow flexion in people with BPI (Oberlin et al., 1994). In a C5/C6 or upper trunk BPI, the surgeon dissects fascicles from the ulnar nerve (C7-T1), which normally innervate flexor carpi ulnaris (wrist flexor), and sutures them to the musculocutaneous nerve, which innervates the biceps. When innervation occurs then the patient initially flexes their wrist to start elbow flexion. Systematic reviews demonstrate that nerve transfers for these upper trunk injuries perform better than nerve grafting in terms of improving movement of the arm (Ali et al., 2015; Garg et al., 2011). Ali et al. (2015) found that nerve transfers led to significantly better movement in the elbow ($F = 82.82$, $p < 0.001$) and shoulder ($F = 5.53$, $p = 0.0044$) compared to nerve grafting. Success was defined as anti-gravity movement of the arm. Similarly, Garg et al. (2011) found that 83% (247/299) of people who had received nerve transfers achieved elbow flexion against resistance, compared to only 56% (32/57) of those who had received nerve grafts. The outcomes included in both these systematic reviews were clinician-rated evaluations of motor recovery from cohort studies, and therefore open to bias, so caution should be taken when interpreting the results.

Although researchers report improved motor outcomes following nerve transfers to the shoulder and elbow, limited motor and sensory recovery is reported when nerve transfers are used to reinnervate the small muscles of the hand (Gao et al., 2018; Hattori et al., 2009; Kawai et al., 1988). Gao et al. (2018) evaluated motor outcomes in the hand in a retrospective cohort study (n = 73) and reported that 68% of participants achieved "efficient" motor recovery. The efficient grading was reported to be equivalent to an anti-gravity movement. However, it is unclear whether improvement in this impairment-focused outcome equates to better function for the individual. In another retrospective cohort study, Hattori et al. (2009) evaluated sensory outcomes in the hand following nerve transfers in people with a BPI (n = 17). They reported that all participants recovered deep pressure sensation; however, 88% (15/17) did not achieve any protective sensation. The limited benefit of nerve transfers for the hand may be because long nerve grafts are often required, which can result in the loss of

some regenerating axons (Hoben et al., 2018). Additionally, there is often a mismatch in axon count at this level between the donor and recipient nerve. For example, the anterior interosseous nerve, sometimes used to innervate the ulnar nerve, has a much smaller axon count (506) compared to the ulnar nerve (1,523) (Brown et al., 2009). This can result in underpowered motor units and therefore limited force production to support function.

Despite their increased use in BPI, nerve transfers also have several limitations. Nerve transfers will result in loss of function in the donor nerve (Hems, 2011). Hems (2011) reports scapula winging and an unstable shoulder following the use of the spinal accessory nerve as the donor. Another potential limitation is that a prolonged period is needed for cortical plasticity to occur in the donor area of the brain to learn its new function (Amini et al., 2020; Dimou et al., 2013). For example, Mano et al.(1995) found that when intercostal nerves were used to innervate the ipsilateral biceps (for return of elbow flexion), the cortical motor area of the reinnervated biceps moved from the intercostal muscle area (initially) to the arm muscles area over 4-33 months from surgery. Sometimes, however, the inability to relearn a new movement can lead to co-contraction of the donor and newly innervated muscle (Hems, 2011). This results in an inability to move and use the arm functionally. Finally, for those people with injuries to all levels of the brachial plexus there may be a lack of donor nerves available to transfer, limiting the treatment's use and necessitating harvesting of donor nerves from outside the plexus and even the opposite limb (Li et al., 2016).

Free functioning muscle transfer: A free functioning muscle transfer is increasingly being used early following a BPI. A free functioning muscle transfer is used for people with complete avulsions of all nerves and where direct repair, grafts and nerve transfers are not possible (Doi et al., 1998). It involves transferring a muscle, usually the gracilis, from the leg to the upper limb to perform the lost function (often elbow flexion). The new muscle is innervated by a nerve from outside the brachial plexus, such as the intercostal nerve (Bishop, 2005; Dodakundi et al., 2013; Satbhai et al., 2016). A recent systematic review (including 364 patients) found that 87% of patients achieved anti-gravity elbow flexion and 65% achieved anti-gravity elbow flexion plus resistance following a free functioning muscle transfer, with a significant improvement in the patient-reported outcome measure called the Disabilities of the Arm Shoulder

and Hand (Yi Lee et al., 2019). Additionally, a retrospective observational study (n = 75) found that an isolated free muscle transfer was equally as effective in restoring muscle strength (measured using a clinician-rated motor grading system) as when free muscle transfers were combined with a nerve transfer (Maldonado et al., 2017). Despite first claims that the gracilis free muscle transfer could improve hand function (Doi et al., 1998), studies show that it results in a secure shoulder with some elbow bend but limited hand function (Fischer et al., 2013; Yi Lee et al., 2019). In conclusion, although free functioning muscle transfers are becoming more popular, they can result in limited functional improvements.

1.2.7.3 Secondary operative procedures

Finally, secondary procedures are used if people continue to present with functional limitations or present too late for primary options like direct repair or nerve transfers. Examples of secondary procedures are tendon transfers and joint fusions. A person with good intrinsic hand flexion function but no wrist extension may undergo a radial nerve tendon transfer (Kumar Vyas et al., 2020). The insertion point of a muscle, such as pronator teres, is detached and connected to the wrist extensors. This facilitates wrist extension (Kumar Vyas et al., 2020).

Although there has been progress with microsurgery and muscle and tendon transfer procedures for people with BPI, there is a paucity of well conducted research to support the effectiveness of developments. Historically and currently, published research focuses around non-randomised and mostly small series studies from single sites due to the relative rarity of the condition. The next section will discuss the issues surrounding outcome assessment in BPI.

1.3 Problems with outcome assessment in brachial plexus injury

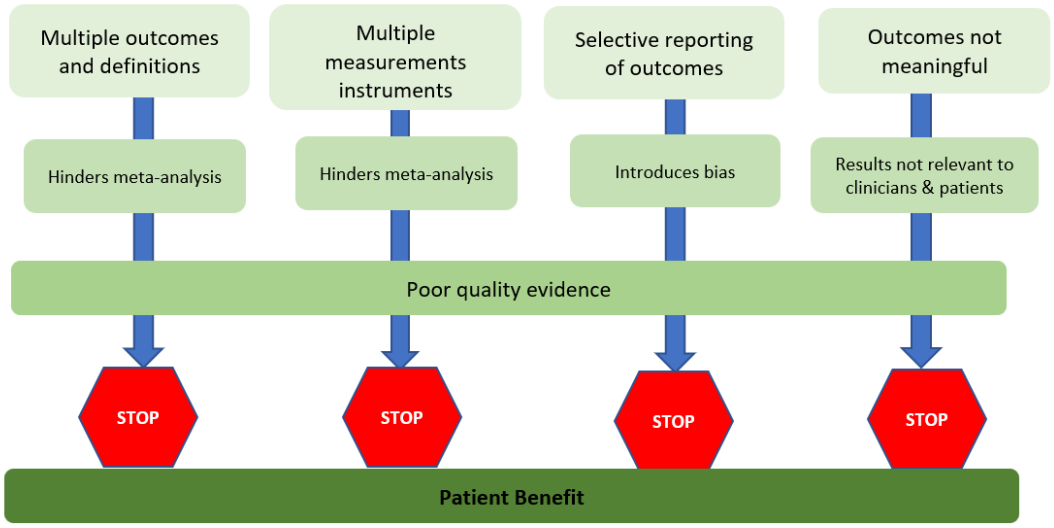
1.3.1 Outcome assessment in research and routine care

An outcome is defined as a measurement or observation used to capture and assess the effect of treatments, such as assessments of the benefits or harms of interventions (Williamson et al., 2017). Measuring health outcomes helps to inform evidence-based

practice in day-to-day clinical practice. In routine care, healthcare professionals use outcome measurement instruments to assess patients' progress, set new goals and inform decision-making regarding future treatment planning. In research, outcome assessment is used to evaluate the effectiveness of interventions informing evidence-based practice and future patient care. Traditionally, outcome selection has been based on the views of individual clinicians or researchers, or in research has been informed by statistical or regulatory recommendations (Gorst et al., 2016).

The outcomes selected for a study affect the relevance and the validity of the evidence generated and therefore its impact on clinical practice and policy. If appropriate outcomes are not selected, the translation of research findings to inform patient care is hindered in four ways: (i) using different outcomes and outcome definitions in the same health condition impedes comparison and combination of results in meta-analysis; (ii) using different outcome measurement instruments measuring the same outcome also hinders meta-analysis; (iii) outcomes that are selectively reported result in bias; and (iv) not assessing and reporting outcomes that are important to patients restricts the relevance of research findings informing evidence-based practice (see Figure 1.4).

Figure 1.4 Problems with outcome measurement and reporting



adapted from Fish (2018)

Outcome assessment in routine care should be aligned with outcome assessment in research. Recently, there has been increasing use of real-world data (RWD) in research and clinical practice (Zhangid et al., 2022). RWD are *"routinely collected data relating to a patient's health status or the delivery of health care from a variety of sources other than traditional clinical trials"*, such as electronic health records and patient registries (Cave et al., 2019, p36). The National Health Service (NHS) Long Term Plan prioritises digital transformation of the NHS with the linkage of data collected in routine care to the data needed for clinical research (Alderwick and Dixon, 2019). Routinely collected data is increasingly available, in line with information governance restrictions. However, there are many constraints when using these routine data to evaluate interventions. These include outcome-reporting heterogeneity, diverse measurements and issues of documentation standardisation across databases (Franklin and Schneeweiss, 2017; Khozin et al., 2017). If outcome data collected in routine practice through electronic health records are aligned with those chosen for research, it would facilitate effectiveness research and ultimately patient care.

1.3.2 Problems with outcome assessment in traumatic brachial plexus injury.

Outcome heterogeneity exists in BPI reporting, preventing the ability to synthesise results from studies and inform best evidence-based treatment. Ayhan et al. (2020) aimed to compare the effectiveness of elbow flexion reconstruction with nerve transfer or nerve grafting in a systematic review. However, they reported heterogeneity in outcome reporting, which meant that they could not complete a meta-analysis. In a recent systematic review evaluating patient-reported outcomes following nerve transfer surgery, outcome-reporting heterogeneity limited the authors' ability to combine data and perform subgroup analyses (Haldane et al., 2022). Even with outcomes which are commonly assessed, like muscle strength, there is variation in how this is measured. Donnelly et al. (2020) aimed to compare ulnar fascicular nerve transfers to a double ulnar and median fascicular nerve transfers for restoration of elbow flexion in their systematic review. They reported issues with the consistency of measuring muscle strength outcomes in a reliable manner and found that most studies used strength scores which depended on the healthcare

professional's subjective assessment (Donnelly et al., 2020). Additionally, Dy et al. (2015) found that muscle strength is measured with many modifications of the Medical Research Council muscle strength rating scale (Medical Research Council, 1976), making synthesis of outcomes between studies challenging.

Studies evaluating interventions in BPI surgery often measure and report short-term clinician-reported outcomes, such as early recovery of strength (Dolan et al., 2012; Dy et al., 2015; Estrella, 2011; Leechavengvongs et al., 2006; Teboul et al., 2004; Tung and Mackinnon, 2010). However, final outcome following an intervention for a BPI may not be seen for five years (Choi et al., 1997). Dy et al. (2015) assessed outcome reporting in BPI surgical reconstruction studies and found that 94% of included studies measured and reported post-operative motor function but 59% of studies did not include measurement of any other clinical outcomes (Dy et al., 2015). Furthermore, outcomes prioritised by patients, such as pain (Brown et al., 2018), social disability (Choi et al., 1997; McDonald and Pettigrew, 2014; Wellington, 2010) and return to work (Franzblau et al., 2014; Mancuso et al., 2015) were rarely measured (Dy et al., 2015), resulting in disparity between what outcomes patients reported as being important and those being measured and reported by researchers.

The heterogeneity of the outcomes in these studies and potential for outcome-reporting bias, combined with the limited inclusion of outcomes potentially important to patients, has impeded the availability of relevant, high-quality research to inform evidence-based practice for brachial plexus care.

1.3.3 Core outcome sets as a solution

One solution is to develop a core outcome set (COS) for adults with a BPI. A COS contains a minimum set of outcomes to be reported and measured in a health condition (Williamson et al., 2012a, 2012b). They can be developed for research, routine care or both (Gargon et al., 2021). A COS can improve the quality of evidence produced by research in a health condition by: (i) reducing outcome heterogeneity; (ii) increasing the relevance of research; and (iii) reducing the scope for outcome bias (Williamson et al., 2012a). COS are being increasingly developed for different clinical areas and are endorsed by national research funders, journal editors, policy and

reporting guidelines (Hughes et al., 2019; Chan et al., 2013; Tugwell et al., 2007). There has been successful implementation of a COS for rheumatoid arthritis (Kirkham et al., 2019, 2017a) resulting in an improvement in the quality and relevance of research in this area. COS methodology is constantly being developed and supported by the Core Outcome Measures in Effectiveness Trials (COMET) initiative (Williamson et al., 2011). There is currently no core outcome set for BPI published in the COMET database (http://www.comet-initiative.org/studies/search).

1.4 Core Outcome Measures in Brachial plexus INjuriEs (COMBINE) project: aims

The project name COMBINE (Core Outcome Measures in Brachial plexus INjuriEs) was selected as an appropriate acronym for the research as it aimed to *combine* the expert opinion of patients, healthcare professionals and researchers, to reach consensus on a COS for adults with a BPI. This research then aimed to identify existing validated outcome measurement instruments that could measure the COS in future research and routine care.

1.4.1 Objectives:

- to generate an exhaustive *long list* of outcomes reported in studies of adult BPI through a systematic review
- to identify outcomes relevant to patients through 1:1 interviews with patients
- to reach consensus between patients, healthcare professionals and researchers, through an international online Delphi and consensus meetings, on the outcomes to include in the COS-BPI
- to identify existing valid and reliable measurements that measure the domains in the COS-BPI through a systematic review.

1.5 Conclusion

This chapter has summarised the aetiology, pathophysiology and mechanisms of injury associated with an adult BPI. The evidence for modern treatments is reviewed. Issues surrounding outcome assessment have been identified and the development of a COS is proposed as a solution. The next chapter (Chapter 2) will review the guidance and methods available for developing a COS and justify the methodological approach taken in the COMBINE project.

Chapter 2 Methodological considerations and methods for the COMBINE research project

2.1 Introduction

In Chapter 1, issues surrounding outcome reporting were discussed and the rationale for the need for a core outcome set (COS) and core outcome measurement set (COMS) in adult brachial plexus injuries (BPIs) was justified. This chapter provides a review of COS and COMS development and approaches. Current methods are examined, and the approaches and rationale for methods used for the COMBINE (Core Outcome Measures in Brachial plexus INjuriEs) project are discussed. The protocol for this project was published in BMJ Open (Miller et al., 2019). Chapters 3 to 6 will include specific detail on the justification of approaches adopted within each stage of the COMBINE project.

2.2 Benefits of a COS and COMS

A COS is an agreed minimum set of important outcomes that should be measured and reported in a health condition (Williamson et al., 2012a, 2012b). A COMS is a list of outcome measurement instruments (OMIs) that measure the outcomes in the COS. These sets are, however, not restrictive, and researchers and healthcare professionals (HCPs) can include outcomes and OMIs pertinent to their own research or practice (Beaton et al., 2021a; Williamson et al., 2017).

A COS and COMS aim to address several issues related to outcome measurement and reporting in health. Firstly, a COS and COMS can reduce outcome heterogeneity. If there is widespread uptake by researchers in a healthcare area, this will result in the same outcomes being assessed with the same OMIs and increase the potential for evidence synthesis and meta-analysis. Secondly, if used universally in clinical care, it can support benchmarking of services and interventions locally, regionally and nationally, potentially driving up quality of care for patients. Thirdly, it can reduce outcome-reporting bias. Outcome-reporting bias involves selectively reporting a small number of the original outcomes based on the results (Hutton and Williamson, 2000), and is acknowledged as an issue in clinical trials and subsequent systematic reviews

(Kirkham et al., 2010). Outcomes that are statistically significant have higher odds of being reported compared to those that are non-significant (Chan and Altman, 2005). The results of systematic reviews can therefore be affected by missing data, potentially impacting on effect size estimates for interventions. However, if outcomes and OMIs are standardised then interventions can be fully evaluated while minimising outcome-reporting bias (Page et al., 2014). Finally, but most importantly, a COS development that involves all relevant stakeholders, including patients, will increase the measurement of outcomes important to them (Harman et al., 2015).

2.3 COS and COMS development methods

The methods used to develop a COS and their included OMIs will influence not only the final outcomes recommended for measurement but also potentially its uptake and implementation. To achieve the benefits discussed in the previous section, a COS and COMS must be used widely by both researchers and clinicians in that healthcare condition. Firstly, researchers and clinicians need to be aware that the COS and COMS exist to use it for outcome and OMI selection. Widespread presentations, publications and registration through the COMET website, where clinicians and researchers can search for them, can increase awareness. Secondly, it is likely that researchers and clinicians will use a COS if they have confidence that the included outcomes are representative of relevant stakeholder priorities. This confidence could be increased by using methods that promote inclusion of key stakeholders and minimise the potential for bias. Therefore, a priority for this COS and COMS development, to ensure its widespread implementation and maximise impact, was to include relevant stakeholders and minimise bias.

2.3.1 Developments in COS and COMS methods

There is no gold standard method for COS development. However, the concept of COS and its methodological developments have been driven primarily by two organisations: the OMERACT (Outcome Measures for Rheumatology Clinical Trials) group and the COMET (Core Outcome Measures in Effectiveness Trials) initiative. Both groups were originally focused on COS and COMS for trials. However, recently COMET has reported

an increase in published COS and COMS for research and routine care (Gargon et al., 2021).

OMERACT was established in 1992 (Kirwan et al., 2014) with the aim of improving outcome measurement in rheumatology (Tugwell et al., 1994). Initially OMERACT focused on the selection of OMIs and "how to measure" more than "what to measure" (Tugwell and Boers, 1993). Measures were endorsed by OMERACT if they met the criteria of truth (measures what it intends to measure), discrimination (discriminates between situations of interest) and feasibility (addresses whether the measure is pragmatic) (Tugwell et al., 2007). However, more recently OMERACT has also developed guidance on reaching consensus on "what to measure", with the recent OMERACT handbook including a chapter on core domain set selection prior to identifying measures (Beaton et al., 2021a). Originally, OMERACT did not include patients in outcome generation or consensus methods (Fried et al., 1993; Tugwell et al., 2007). However, lately there has been increasing acknowledgment of the importance of including patients throughout methods to generate and prioritise both outcomes and then OMIs (Beaton et al., 2021b). A range of methods are suggested to generate an outcome list, including 1:1 interviews, focus groups, and consensus methods including the Delphi method, nominal group technique and workshops (Beaton et al., 2021a).

The COMET initiative launched in 2010 and aims to bring together people interested in the generation and implementation of COS (COMET, 2022). As described by Tunis et al. (2016), the objectives of COMET are to:

I. raise awareness of current problems with outcomes in clinical trials

II. encourage COS development and uptake

III. promote patient and public involvement in COS development

IV. avoid unnecessary duplication of effort

V. encourage evidence-based COS development

The COMET initiative fosters rigorous consensus methods and promotes the inclusion of relevant stakeholders in COS development. COMET published a handbook in 2017, summarising the current knowledge in COS development and focusing on methods for selecting "what to measure" (Williamson et al., 2017). The handbook does not recommend specific methods for the development of a COS but explores the various options available, critiquing their benefits and challenges. The COMET handbook (Williamson et al., 2017) encourage researchers to consider the methodological issues linked to their own project. Additionally, COMET provides a searchable online international database of all studies linked to COS (COMET, 2022). An increasing number of studies have been added since its inception and the number of visits to the website has also increased (Gargon et al., 2017a). The growth in the use of the website evidences the growing use and need for COS.

In addition to the OMERACT group and the COMET initiative, other research groups have formed with the aim of developing COS in a variety of different health areas. These include groups with a focused interest in developing COS in areas such as maternal health (Khan, 2014), eczema (Schmitt et al., 2015) and pain (Dworkin et al., 2005). The COS generation methods used by these groups are usually underpinned by OMERACT or COMET guidance.

A further important initiative to consider is the International Consortium for Health Outcomes Measurement (ICHOM). The ICHOM was founded in 2012 and co-ordinates international teams of HCP experts, researchers and patients to agree standard outcome sets for use in routine clinical practice (ICHOM, 2022). ICHOM's mission is to support value-based healthcare (Porter, 2010) through the generation, measurement and reporting of standard outcome sets relevant to patients (ICHOM, 2022). ICHOM aims to provide a defined process to reaching agreement on routine healthcare outcomes to be reported, with the aim of comparing performance between competitive healthcare providers. An ICHOM standard set includes OMIs and timepoints to measure essential outcome domains. They also include case-mix variables (e.g., baseline demographics or variables describing health status). However, there are calls to increase the transparency of the methods used by ICHOM (MacLennan et al., 2015; Tunis et al., 2016). These include requests for more information on consensus methods used, increased reporting on how ICHOM decides

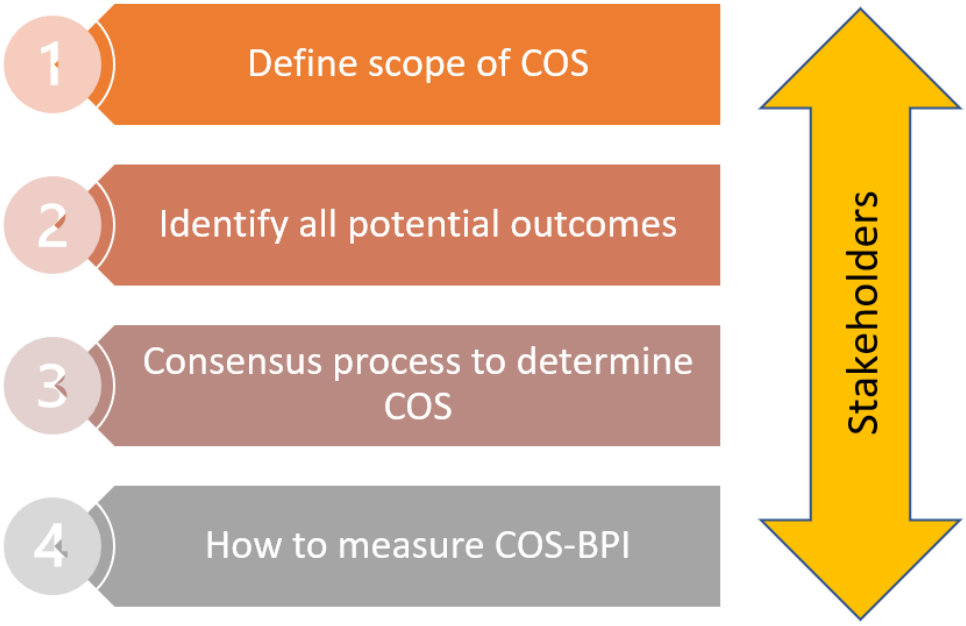
the number of patients included, and how patients are identified, selected and involved in the ICHOM process (MacLennan et al., 2015; Tunis et al., 2016).

2.4 Methodological considerations in COS development

Research to improve the methods used in COS and COMS development is ongoing. Both the OMERACT (Beaton et al., 2021a, 2021b, 2021c) and COMET handbooks (Williamson et al., 2017) provide some guidance. Additionally, the Core Outcome Set STAndards for Development (COS-STAD) project identified the minimum standards for designing a COS study through a global consensus process (Kirkham et al., 2017b). The COS-STAD recommendations are appropriate to all COS, irrespective of healthcare condition or whether the COS is designed for research or clinical care. They contain 11 standards that should be adhered to in all COS development projects (Kirkham et al., 2017b). The recommendations focus on three key issues: i) defining the scope of the COS; ii) deciding which stakeholders to involve and how to involve them; iii) achieving consensus on which outcomes are most important. There was no consensus on: iv) identifying potential outcomes; or v) development of the measurement set. Section 2.5 presents how the COMBINE project aims to meet the COS-STAD standards.

Both OMERACT and COMET agree on the sequence of events included in a COS development. First, key stakeholders need to reach consensus on "what" to measure (i.e., the core outcomes) and then on "how" to measure the outcomes (i.e., the instruments) (Prinsen et al., 2016). Initially the scope, including context and setting, are established and then a *long list* of relevant outcomes is identified (Beaton et al., 2021a; Williamson et al., 2017). Key stakeholders use this *long list* to reach consensus about which outcomes to include in the COS. Finally, a COMS is developed that identifies valid and reliable OMIs to measure the COS. Figure 2.1 illustrates the recommended COS development process. Methodological considerations across the different phases of COS development, including decision-making around stakeholders, will now be explored. Then COS and COMS development in this thesis will be presented and justified.

Figure 2.1 Recommended COS development process



2.4.1 Defining the scope of the core outcome set (COS)

It is recommended that the scope of a COS is specified in terms of four criteria: i) research or practice settings in which the COS is to be implemented; ii) health condition; iii) target population; and iv) relevant interventions (Kirkham et al., 2017b). There are no recommendations about whether the scope should be narrow or broad. COS developers must decide whether their COS is designed for effectiveness trials, all research, routine clinical care, registries, all or some. Similarly, the population needs to be determined either in terms of all persons with the condition, specific subgroups or age groups. Finally, COS developers need to define if the COS applies to all interventions for the health disorder or specific interventions. COS developers can reduce uncertainty surrounding the aim of the COS by defining the scope at the beginning of the project. Having a clear scope also supports potential users to decide whether the COS is relevant to their needs.

2.4.2 Stakeholder participation

In COS development, stakeholder participation is where stakeholders contribute information on which outcomes to prioritise: for example, through 1:1 interviews to identify important outcomes or scoring outcomes in Delphi studies. Stakeholders, in a COS for both research and routine care, should include those who would potentially use the COS in either of these contexts (patients, HCPs, researchers). There is increasing evidence which demonstrates that diverse stakeholders prioritise health outcomes and priorities differently (Hewlett, 2003; Reilly et al., 2017). These differences underscore the importance of facilitating contribution from different stakeholder groups in COS generation. Decisions about which stakeholders to include as participants are influenced by both the scope of the COS but also practical considerations. For instance, deciding who to include in a consensus meeting may be influenced by optimal participant numbers for a space to allow thorough discussion.

The COS-STAD standards identified that, as a minimum, HCPs, potential users of the COS in research and patients should be included in COS development (Kirkham et al., 2017b). Historically, participants of COS development projects comprised of HCPs and researchers (Gargon et al., 2014). However, patient participation has grown recently. Now 77% of published COS studies include patients or their representatives (Gargon et al., 2021). The following section presents a more thorough discussion of patient participation.

2.4.2.1 Patient participation

There is increasing evidence which highlights that outcomes important to patients may differ from those outcomes HCPs or researchers regard as important (Gonçalves et al., 2020; Kirwan et al., 2005; Sinha et al., 2012). Patients bring a distinct perspective, having a lived experience of the disease or injury. For example, the OMERACT research programme conducted focus groups with people with rheumatoid arthritis and found that relief of fatigue was especially important to them (Kirwan et al., 2005). However, HCPs had reported fatigue as less important (Kirwan et al., 2005). The results of the patient focus group led to fatigue being added to the rheumatology COS. Similarly, in a recent qualitative study, people living with dementia identified 10 new outcomes that had not previously been reported in published research (Gonçalves et al., 2020). These

findings suggest that some outcomes important to patients may not be regarded as important to measure and report by HCPs and researchers. Therefore, in a COS development project, eliciting outcomes important to people with the health condition is critical and recommended by the wider COS community (Gargon et al., 2014; Jones et al., 2017; Keeley et al., 2016; Williamson et al., 2017; Young and Bagley, 2016).

Although the benefits of patient participation in COS development studies are clear, if the integration of patients as stakeholders is not an established model in that healthcare area, it can be challenging. Qualitative work has identified that some COS developers 'problematise' patient participation, citing that patients find it difficult to comprehend the COS and prioritise outcomes (Gargon et al., 2017b). Some researchers commented that patients scored everything highly (Gargon et al., 2017b). However, by requesting patients to be part of COS projects, developers are asking patients to enter a research world (Young and Bagley, 2016). It is therefore the role of the COS developer to support meaningful patient participation to facilitate the insights they can provide.

2.4.3 Identifying outcomes to be considered for inclusion in a COS

Phase one of COS development involves identifying a long list of outcomes that are potentially relevant for inclusion in a COS. Identifying this exhaustive list ensures that all possible outcomes are considered. Potential outcomes may be identified through a range of sources, including literature reviews, reviews of qualitative research, analysis of outcomes in national health databases, and considering the views of individual stakeholders through qualitative work (Beaton et al., 2021a; Williamson et al., 2017). The methodological challenges associated with identification of outcomes for inclusion in a COS will now be discussed.

2.4.3.1 Reviews of outcome reporting

The main purpose of systematic reviews in COS development is the identification of an exhaustive list of outcomes reported in published studies about that health condition (Beaton et al., 2021a; Williamson et al., 2017). Additionally, a review can identify outcome heterogeneity, thus justifying the need for a COS in a specific health area. Indeed, systematic reviews are increasingly the preferred method used by developers

to identify potential outcomes for the COS (Gorst et al., 2016). To be inclusive with a search, limitations (such as time, language and study type) should be reduced. However, unlimited searches can lead to thousands of results for different interventions across a health condition. Therefore, it may be necessary to limit the search depending on the resources available for the study. When researchers use limitations, they need to consider how this may exclude outcomes and potentially introduce bias.

Some COS developers limit systematic reviews to include only recently published studies, with the justification that older outcomes are not relevant (Kim et al., 2021; Machin et al., 2021; Whistance et al., 2013). However, this introduces the COS developers' opinion into outcome selection at the beginning of the COS project, without justification as to why outcomes used in older studies might not be relevant. COS developers could minimise bias by undertaking an initial search with outcome identification, followed by a search with earlier time dates. If researchers do not identify any new outcomes in the earlier search, then further searches are not needed. Additionally, many developers limit searches to include only randomised controlled trials (Alkhaffaf et al., 2018; Young et al., 2019b) to identify studies for outcome extraction. However, outcomes measured in observational or cross-sectional studies may differ to those measured in randomised controlled trials (Hodgson et al., 2007). Therefore, COS developers need to consider how to balance the risk of potentially excluding relevant outcomes (because of study type limits) with the burden of reviewing an excessive number of studies.

There are challenges associated with identifying outcomes from existing published studies. Extracting outcomes from studies involves grouping verbatim outcomes into a list of outcomes that are unique and distinct from each other. However, the term 'unique outcome' is poorly defined (Young et al., 2019a). For instance, some reviewers may group all variations of a broader outcome under one phrase, with others categorising multiple diverse definitions as unique outcomes (Young et al., 2019a). 'Pain' could be defined as a unique outcome by some COS developers, whereas another researcher might separately categorise 'pain impact on functioning', 'pain frequency', 'pain impact on sleep', 'pain quality' and 'pain severity' as unique outcomes. Unique outcomes reported by COS developers range from 12 to 5,776

(Young et al., 2019a). This disparity may reflect the lack of guidance on what a unique outcome is and suggests that different COS developers extract a different number of outcomes from the same data source. COS developers need to consider how they will define a unique outcome prior to categorising outcomes from a systematic review. This may also be influenced by the consensus methods used at later stages and the burden on participants of prioritising long lists of outcomes. For instance, a long list of extremely specific outcomes will place more burden on participants prioritising the items and could lead to attrition (Gargon et al., 2019a).

Another consideration for COS developers is the categorisation of outcomes into a taxonomy. Health taxonomies or classification frameworks provide structure to the conceptualisation of outcome domains (Bakas et al., 2012). Historically, COS developers have provided little detail on how outcomes were grouped and categorised (Gargon et al., 2017a; Gorst et al., 2016). Several health classification systems exist, including the Wilson Cleary model (Wilson and Cleary, 1995) and the World Health Organization International Classification of Functioning, Disability and Health (ICF) (World Health Organization, 2001). The Wilson and Cleary Model of Health-Related Quality of Life (Wilson and Cleary, 1995) was developed in 1995 and includes a five-level classification of outcomes: biological and physiological factors, symptoms, functioning, general health perception and overall quality of life. These factors are set within the context of individual and environmental factors (Wilson and Cleary, 1995). The ICF (World Health Organization, 2001) includes health-related domains focusing on body functions and structure, activities, participation, environmental and personal factors. Although COS developers have used these frameworks to categorise outcomes (Dodd et al., 2018; Wallace et al., 2019) in the past, there are issues with them. The Wilson and Cleary Model (Wilson and Cleary, 1995) excludes outcomes such as adverse events and resource use. Similarly, the ICF (World Health Organization, 2001) provides a framework for understanding and describing health and disability. Focusing on functioning, however, does not intend to provide a comprehensive system for classifying all research outcomes. It does not include domains linked to delivery of care, resource use, adverse events or death.

Other models have been developed specifically with the aim of classifying outcomes within COS development (Dodd et al., 2018; Idzerda et al., 2014), including the

OMERACT Filter 2 (Boers et al., 2014b) and more recently the COMET taxonomy (Dodd et al., 2018). The OMERACT Filter 2 includes four broad core areas: death, life impact, resource use and pathophysiological manifestations (Boers et al., 2014b), and recommends that for the life impact core area, researchers consider domains included in the ICF (World Health Organization, 2001) and Wilson and Cleary models (Wilson and Cleary, 1995).

The COMET taxonomy is a 38-item classification system which, when piloted by the developers, successfully classified 16,525 outcomes from 3,515 Cochrane reviews, outcomes from 30 study protocols on a trials registry and outcomes from 299 COS on the COMET database (Dodd et al., 2018). The development process and testing demonstrated its general applicability for outcomes from COS, systematic reviews and recorded trials. Although the COMET taxonomy (Dodd et al., 2018) has undergone rigorous development and provides a moderately detailed classification, it is relatively new. Therefore, its use in a wide range of COS health conditions is yet to be evaluated.

The OMERACT Filter 2.0's taxonomy is popular and has been used by many COS developers. However, it is grounded in the setting of chronic rheumatological conditions. OMERACT recommends that at least one outcome domain must be specified for each of the four core areas when developing a COS (Beaton et al., 2021a). However, resource use is not mandatory. The OMERACT's core areas are broad and COS developers might find the structure not detailed enough to support categorisation of outcomes beyond them. COS developers need to consider which COS taxonomy may suit their individual project.

2.4.3.2 Qualitative research to identify important outcomes

Outcomes identified from a literature review will represent outcomes important to researchers and potentially HCPs. However, these outcomes may have been chosen because they were relatively easy to undertake and measure, rather than clinically relevant (Bursztajn, 2000). More importantly, outcomes identified may not be relevant to patients. Therefore, it is recommended that other methods are used in addition to systematic review of existing literature, including reviewing existing qualitative studies in the healthcare area or conducting qualitative work with relevant stakeholders if none exists (Beaton et al., 2021a; Williamson et al., 2017).

Primary qualitative research is frequently used to identify and explore outcomes important to stakeholders that may not be identified through reviews of quantitative or the qualitative literature (Biggane et al., 2018; Gargon et al., 2021; Young and Bagley, 2016). Qualitative research can offer an in-depth understanding of patients' and carers' perspectives (Ritchie et al., 2013). Therefore, these methods are appropriate to identify outcomes important to stakeholders and understand why they are important. Qualitative methods can also help to establish the scope of the outcomes, identify appropriate language for description of the outcomes in the follow-on consensus process, and finally to compare data from different stakeholders to understand areas of discordance (Keeley et al., 2016).

Despite the increasing use of qualitative methods in COS projects, there is no consensus on what qualitative methods should be used (Kirkham et al., 2017b). The most frequently used methods are interviews or focus groups (Jones et al., 2017). However, studies often do not report the underpinning methodological framework or information regarding data saturation and reflexiveness (Jones et al., 2017). COS developers need to consider the following issues when selecting which qualitative approach to use: how data will be collected, the topic and the study population (Keeley et al., 2016; Ritchie et al., 2013). The key qualitative methods (focus groups and interviews) used to explore outcomes with stakeholders in the literature will be explored next.

Focus groups bring together the views of various people and therefore benefit from the interaction between participants to generate data (Kitzinger, 1995). The within-group interaction between different people with varied views can create additional data that may not be produced in 1:1 interviews (Freeman, 2006; Kitzinger, 1995). Participants can support each other in discussing issues that are common to their group but which they consider differ from conventional culture (or the perceived culture of the researcher). This is especially important when investigating stigmatised or taboo experiences. Focus groups often involve 6-12 participants, with a mean of 8 participants, who are purposefully sampled to represent a wide range of variation in the phenomenon of interest (Carlsen and Glenton, 2011). However, the high number of participants in a time-limited focus group may result in a more superficial rather than in-depth understanding of the experiences. There is also a risk, when conducting

focus groups, that some participants will dominate and overly influence the discussion (Reed and Payton, 1997). With focus groups being time-limited, outcomes important to dominant participants may receive more attention and discussion time. This could result in others in the group feeling they did not have time to discuss outcomes important to them.

Individual interviews can provide a detailed, rich understanding of an individual's beliefs and attitudes linked to the research topic, with the opportunity for the researcher to build a rapport with the interviewee (Braun and Clarke, 2013). Interviews are often used when investigating topics important to vulnerable people, as the interview allows the participant to control the conversation to ensure all points are covered (Braun and Clarke, 2013; Ritchie et al., 2013). Finally, it is important to consider the setting when planning an interview, as relaxed and comfortable environments can help people feel at ease and lead to open conversations (Dicicco-Bloom and Crabtree, 2006).

With regards to COS development, Jones et al. (2017) compared interviews and focus groups in a COS development for burns and found that interviews generated more in-depth data. They recommended that, if time and resources allowed, interviews were the best method to use in COS development (Jones et al., 2017). For these reasons, in-depth, 1:1 semi-structured interviews may be more suitable for identifying and exploring outcomes important to patients.

2.4.4 Achieving consensus

Once the outcomes from the literature review and qualitative work (if used) are identified, they are combined into a long list of outcomes. It is recommended that consensus methods, including all relevant stakeholders, are used to prioritise the outcomes in the long list and develop the final COS (Beaton et al., 2021a; Williamson et al., 2017). A consensus process can deal with conflicting evidence or opinions, determining how much experts agree about a specific topic (Jones and Hunter, 1995). It can overcome the shortcomings often found with decision making in groups, including dominance by one person or people working together for a vested interest (Jones and Hunter, 1995). Key elements of a consensus process include: anonymity (to

avoid dominance), an iterative process, and controlled feedback with an aggregate of individual opinions (Dalkey and Helmer, 1963; Jones and Hunter, 1995). The three best known consensus methods used by COS developers are the Delphi process (Hopkins et al., 2015; Kuizenga-Wessel et al., 2017), the nominal group technique (Duffy et al., 2020) and the consensus meeting (Tugwell et al., 2007).

Single or combined methods of consensus can be used. Hutchings et al. (2006) suggest that conducting a survey followed by a consensus meeting could increase reliability, agreement and understanding of other stakeholders' opinions . Although there is no agreement on which consensus methods to use in COS development, there are recommendations on the transparency of the process (Kirkham et al., 2017b). These will be discussed in relation to the COMBINE project in section 2.5.3.2. Three consensus methods frequently used in COS development - the Delphi process, nominal group technique and consensus meetings - will now be discussed.

2.4.4.1 Nominal group technique

The nominal group technique originates from the United States in the 1960s and was originally adopted to resolve issues in social services, government and education. The technique involves hosting a structured face-to-face meeting with a group of experts (usually less than 15) to gather information about a given issue (Jones and Hunter, 1995). A chair with expertise in the topic usually facilitates a nominal group technique. The process includes at least two rounds where participants rank, discuss and re-rank a list of items (Murphy et al., 1998). It is thought that the face-to-face meetings in a nominal group technique can minimise misunderstandings and allow discussion of differences of opinion (Delbecq and Ven, 1971). COS developers may choose the nominal group technique when there is a dearth of evidence available to inform other survey type methods (Fisher et al., 2021). It is also chosen in COS development when survey or electronic methods of consensus are inaccessible to potential participants. For example, Fisher et al. (2021) used a nominal group technique with professionals and patients with severe disability after stroke. However, because of the small groups involved in nominal groups they may be unrepresentative and thus have the potential of arriving at unreliable judgements (Raine et al., 2005).

2.4.4.2 Delphi method

The Delphi method is commonly used to prioritise the inclusion of outcomes in a COS (Gargon et al., 2019b). Its name originates from the Delphic oracle's abilities of interpretation and foresight. The RAND Corporation originally developed the Delphi process with the aim of forecasting the impact of technology on warfare (Dalkey and Helmer, 1963). The classical Delphi involves development of a questionnaire, which is presented to a group of experts to seek their opinion on a topic (McKenna, 1994). Responses are analysed, and a new questionnaire designed, focused on the results of the initial survey. Participants receive the second questionnaire, in addition to feedback on other participants' responses. Participants are then asked to review their initial responses to the items in the questionnaire while considering other participants' responses. Multiple rounds of the process are conducted. The repetition and feedback aim to decrease the range of responses and achieve consensus. Criteria for including items in subsequent rounds should be pre-defined for transparency. There have been numerous modifications of the Delphi since its inception (McKenna, 1994). One modification popular in COS development is the adaptation of the "reactive Delphi". This involves asking participants, in the initial Delphi round, to respond to previously prepared information rather than requesting participants to generate lists of items (McKenna, 1994). However, frequently there is an option in this initial round for participants to suggest items to add to a predetermined questionnaire (Williamson et al., 2017).

The Delphi method offers anonymity and gives equal weight to all participants, therefore the likelihood of an individual or group of participants being overly dominant in the process is mitigated (Murphy et al., 1998). A benefit of the Delphi survey is that it can be applied electronically, facilitating the collection of a wide range of views from large numbers of experts from diverse, geographical populations (Hsu and Sandford, 2007). Participants can take part at their convenience and with shorter time commitments compared to alternative consensus approaches (Hsu and Sandford, 2007). However, numerous methodological issues need to be considered to ensure the Delphi is rigorously conducted.

One issue COS developers need to consider is panel constitution. When a Delphi includes multiple stakeholder groups, either all participant responses can be pooled into a single panel or each stakeholder group's views can be presented in separate panels for analysis and feedback. Separating stakeholder groups into different panels ensures that each group's views are equally represented, irrespective of panel size. Different panels may be beneficial if there is a potential that stakeholder groups have diverse opinions and would be interested in knowing the opinions of the other groups. Dividing results into stakeholder groups supports decision-making based on how others and their own group *have* scored each item, rather than guessing how they *might* score.

There is some research on the impact of separate panels on achieving consensus in a Delphi. Brookes et al. (2016) randomised patients and HCPs from three different Delphis (n = 164, 259, 252) to get feedback from their peer group only or feedback from each stakeholder group separately. They found that seeing other groups' opinions increased consensus (Brookes et al., 2016). Other COS developers (MacLennan et al., 2018) randomised participants in one Delphi (n = 158) to get peer-only, combined stakeholder or multiple separate stakeholder group feedback. A higher number of items did not reach consensus in the multiple combined group, but the difference was very low (2% difference between peer-only compared to multiple separate; 5% difference between peer-only versus multiple combined). This evidence concurs with findings from a qualitative study (Fish et al., 2020) where participants of a COS Delphi reported "trying to understand the outcome from the perspective of another participant" (Fish et al., 2020, p122). This was one of the most common reasons for participants revising their scores and particularly for HCPs. Despite growing evidence to support the use of separate panel feedback to improve consensus, a recent systematic review identified that almost 50% of COS Delphis did not document that participants received feedback by stakeholder group (Barrington et al., 2021). Instead, participants in the included studies frequently received feedback from their own stakeholder group or for all participants combined (Barrington et al., 2021). In summary, if participants in a Delphi do not receive feedback separately from each stakeholder group, then it could be more difficult to reach consensus across all the groups.

A further issue to consider when planning a Delphi is related to the number of rounds to include. OMERACT and COMET recommend including two to four rounds (Beaton et al., 2021a; Williamson et al., 2017) when designing a Delphi for COS development. A classical Delphi, which includes an initial round where participants generate items for subsequent iterations, may have a higher number of rounds (McKenna, 1994). However, if COS developers follow a rigorous process to identify an exhaustive long list of outcomes, then this removes the need for item generation in round 1. COS developers need to consider the potential benefits of multiple iterations, which provide participants with more feedback and opportunity to reach consensus, against the potential disadvantages, which include the burden on the project and participants and the potential for increased participant attrition.

One other issue to consider when organising a Delphi study surrounds decision making around item retention between rounds. A central feature of the Delphi is re-scoring items based on feedback from other participants. If an item is dropped between rounds, then participants are prevented from re-scoring them. If items are dropped between rounds 1 and 2, these items have been excluded without participants receiving any feedback. This is contradictory to the Delphi process philosophy. Nevertheless, if COS developers drop items between rounds it can reduce participant burden, which could be beneficial if the Delphi includes numerous outcomes from the outset. Other considerations of time and resources, in conjunction with number of rounds in the Delphi, will influence decision making around item retention.

There are numerous limitations to Delphis that COS developers need to consider. One limitation of online Delphis is the need to access the internet and have a proficient reading ability to participate. This could limit the sample in terms of age and socio-economic background, potentially biasing the sample and reducing the generalisability of the results. Due to the larger sample size, the Delphi has a higher reliability than the nominal group technique (Hutchings et al., 2006). However, it may result in a lesser degree of consensus, perhaps because of the lack of face-to-face interactions (Hutchings et al., 2006). Hence, at the end of the Delphi, there may be a high number of items not reaching consensus criteria to move to the next stage (i.e., consensus meeting or add to the COS) or that did not meet consensus criteria to be excluded. COS developers need to plan how they will manage these items. Finally, attrition rates

have been reported as high in Delphi methods, with patient participants having higher drop-out rates in some studies (Duffy et al., 2020; Remus et al., 2021). High attrition rates can potentially result in response bias and may affect the final consensus results (Williamson et al., 2017). There seems to be an association between attrition and higher number of items (Gargon et al., 2019a). Therefore, OMERACT recommends including fewer than 70 items in Delphi questionnaires (Beaton et al., 2021a). COS developers need to consider all strategies to minimise attrition, and this is discussed in relation to COMBINE Delphi in Chapter 5.

2.4.4.3 Consensus meeting

Frequently, following a Delphi, too many outcomes reach consensus to be included in a COS or there may be outcomes which do not reach consensus on 'in' or 'out' criteria. These will need further discussion. A consensus meeting or a workshop is often needed to further discuss and prioritise which outcomes should be 'core'. COS developers need to consider the various methods available at this stage of COS development. Combining a consensus meeting with elements of a nominal group technique could be used to prioritise the outcomes. Other options include using card-sorting workshops (Beaton et al., 2021a), where participants use file cards to represent domains and position them on a wall or online in a Google jam board to prioritise the domain's position in a core set. Another alternative is where participants are allocated a set number of votes to endorse an outcome as 'core'. If voting is used, then it is frequently conducted anonymously.

Consideration of pre-defined consensus criteria is essential prior to the consensus meetings to minimise bias. There is no agreement on what these consensus criteria should be. However, generally greater than 70% agreement is supported for outcomes to be included in a COS (Beaton et al., 2021a; Williamson et al., 2017). Several factors might influence decision making around the consensus criteria. If few participants take part in the meeting, then a high consensus criterion might mean that one participant's vote could dictate whether an outcome is included or not. Too low a consensus criterion could result in too many outcomes included in a COS, which could hinder its uptake because of the high burden on patients and HCPs.

COS developers need to consider whether to host a joint patient and HCP meeting or separate ones. Some COS developers advocate separate meetings because of the power imbalance between clinicians and patients, which might influence patients' voting (Coulman et al., 2016a). The decision may be influenced by other factors, such as whether the meeting is hosted online or face-to-face. A face-to-face meeting might facilitate increased support, including non-verbal communication, for patients in a consensus process. Finally, a skilled facilitator should chair the meeting. However, this needs to be balanced with the need for the chair to have some knowledge of the health condition to facilitate discussion. Both OMERACT and the COMET initiative have developed resources with patients to support researchers improve the accessibility of consensus meetings (COMET, 2022; De Wit et al., 2013). These were used to support the consensus process in the COMBINE project.

2.4.5 Core outcome measurement set (COMS)

A two-stage process is recommended for COS and COMS development (Beaton et al., 2021a; Williamson et al., 2017). First, achieving consensus on the COS and then defining the COMS.

In the past, COS developers have used numerous methods to develop a COMS, including systematic reviews, meetings with experts and various consensus methods (Gorst et al., 2020). However, in 2016 a guideline recommending methods for selecting OMIs to be included in a COMS was published (Prinsen et al., 2016). This was based on the results of a Delphi study, methodology from the COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) initiative and recommendations from OMERACT (Boers et al., 2014b). Despite the guidance, COS developers will still need to consider certain methodological issues, as not all the guideline's criteria concur with other initiatives' recommendations. For example, OMERACT recommends that responsiveness is assessed before an OMI is included in a provisional core set (Beaton et al., 2021c), whereas Prinsen et al.'s guideline (2016) recommends that for an OMI to be included it should have at least high-quality evidence for content validity and internal consistency.

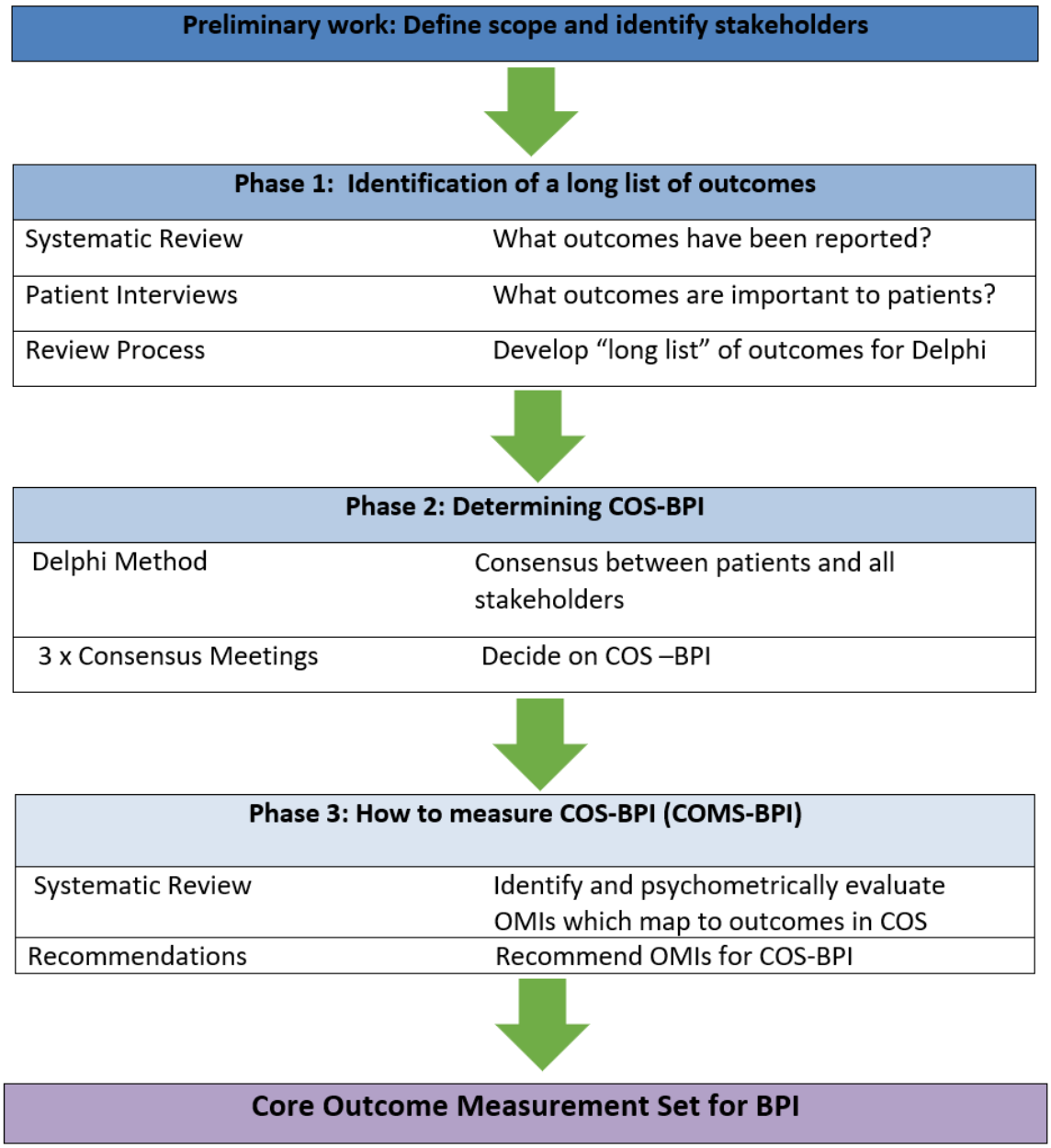
Developing a COMS is a rigorous and time-consuming process and can include outcome mapping of identified OMIs, systematic review(s), psychometric evaluation of OMIs mapped to the COS, and single or numerous consensus process(es) (Prinsen et al., 2016). Practical issues, such as timeframe and resources, will influence what is feasible within a COS and COMS project. COS developers need to bear in mind that to realise the benefits of COS, OMIs need to be recommended. If COS developers do not recommend OMIs for the COS, outcome measurement heterogeneity for the health condition will continue, limiting evidence synthesis and undermining the potential benefit of the COS.

The methodological considerations related to developing a COMS in this project are discussed in Chapter 6.

2.5 COS and COMS development in this thesis

The following section discusses the scope, stakeholder involvement, methods used to identify the outcomes long list, consensus methods and COMS methods used in this thesis. The rationale for the selected approach is detailed and linked to the corresponding COS-STAD (Kirkham et al., 2017b) recommendation (where appropriate). Figure 2.2 illustrates an overview of the project.

Figure 2.2 Overview of the COMBINE project



2.5.1 Scope of COMBINE project

2.5.1.1 Setting (COS-STAD 1)

Routine care and research settings:

The aim of the COMBINE project was to develop a COS for research and routine care in adults with a BPI (COS-BPI). As discussed previously, a BPI is a relatively rare injury and can be diverse in its presentation. Most research to date consists of single-site cohort studies led by clinicians in tertiary centres and as part of patients' routine care (Jerome, 2021; Suroto et al., 2021). These same outcomes collected in routine practice are frequently used to evidence the effectiveness of interventions. It was therefore decided to widen the scope of the setting to include research, routine care and registries. This aligns with results of a recent review of the COMET database, which has seen a 16% increase in COS being developed for both clinical research and routine clinical care (Gargon et al., 2021).

2.5.1.2 Health condition (COS-STAD 2)

Traumatic brachial plexus injury

The health condition this COS applies to is called a brachial plexus injury (BPI), which is described in Chapter 1.

2.5.1.3 Population (COS-STAD 3)

Adults ≥ 16 years of age

The population that this COS will be used for is adults aged 16 and over. A BPI very rarely occurs in people under the age of 16. Although obstetric brachial plexus injuries (OBPI) are common, acquired at birth, a COS for OBPI has already been developed (Pondaag and Malessy, 2018). The outcomes and OMIs that are important and appropriate to adults with a BPI are likely to be different to those important to children (Kalnins and Love, 1982; Sarac et al., 2013).

2.5.1.4 Types of interventions (COS-STAD 4)

Surgical and non-surgical interventions for a BPI

An adult with a BPI may undergo periods of non-surgical and surgical care, experiencing numerous interventions during their rehabilitation. It makes sense that the same minimum core set (important to all stakeholders) is used to evaluate these interventions, therefore facilitating direct comparison of their effectiveness. The use of the COS-BPI and the COMS should not preclude the addition of intervention-specific outcomes and OMIs if necessary.

2.5.2 Stakeholder involvement

2.5.2.1 Those who will use the COS in research (COS-STAD 5)

Healthcare professionals involved in research studies including adults with BPI

The COS-BPI and COMS will inform evidence-based practice in adult BPI care. Studies in adult BPIs are frequently led and co-ordinated by clinical academics, who conduct research while remaining practising clinicians. The stakeholder group, 'those who will use the COS in research', included clinical academics, a subcategory of the broader HCP group (both surgeons and therapists).

2.5.2.2 Healthcare professionals (COS-STAD 6)

Healthcare professionals involved in the management of adults with BPI

All members of the multidisciplinary team were invited to participate in the COMBINE project. This included HCPs from a range of clinical backgrounds, including surgeons, nurses, pain specialist doctors and therapists. Different professions may have alternative opinions on outcomes important to measure in adult BPI. It was therefore important to have an inclusive approach to ensure that different perspectives were represented. As the COS-BPI and COMS are intended to be used globally, the COMBINE project sought to recruit and include the views of international HCPs involved in the management of and research across the diversity of BPI presentations.

2.5.2.3 Patients who have experience of the condition (COS-STAD 7)

Adults with a BPI who experience any surgical or non-surgical intervention

Adults who experienced any surgical or non-surgical intervention for a BPI were included.

2.5.3 Consensus methods

The consensus methods for the COMBINE project included two phases: i) generation of a long list of outcomes - the long list was generated through a systematic review of studies evaluating interventions in BPI and through 1:1 interviews with patients; ii) an online Delphi, informed by outcomes identified in phase one, and online consensus meetings prioritised the long list of outcomes and finalised the COS-BPI. The COS-BPI should be relevant to international stakeholders (patients and HCPs); therefore it was anticipated that an online Delphi would be the most inclusive method to access a wide range of views from experts (patients and HCPs) from different geographical regions.

2.5.3.1 Phase 1. Outcome long list generation

The initial list of outcomes considered both healthcare professionals' and patients' views (COS-STAD 8).

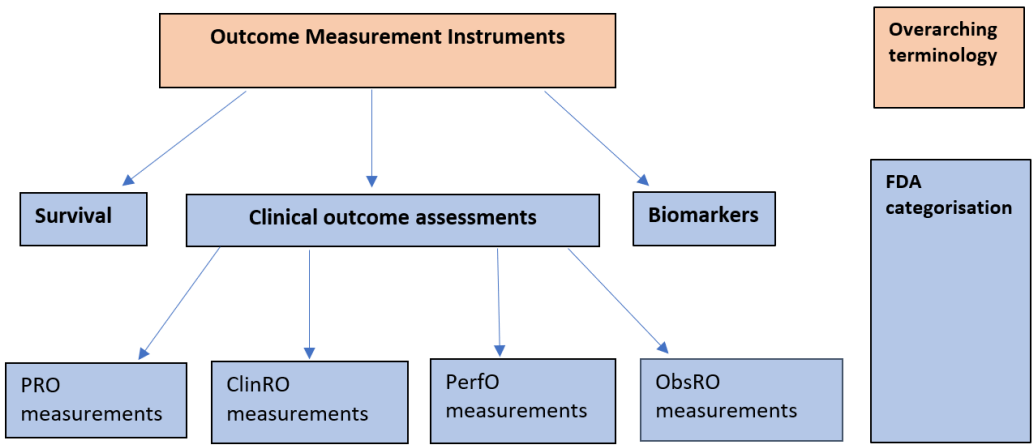
Systematic review: The long list of outcomes was generated by identifying outcomes through a systematic review of published BPI studies and though 1:1 interviews with patients. It is assumed that the outcomes extracted from the literature represented outcomes important to HCPs and researchers. The COMBINE project used guidance from Young et al. (2019a) to standardise unique outcome identification. The COMET taxonomy (Dodd et al., 2018) was used to facilitate categorisation of the outcomes identified because it was created specifically for classifying outcomes within COS development. As such it encompasses a wider range of core areas compared to traditional health classification systems (Wilson and Cleary, 1995; World Health Organization, 2001). These areas include resource use, death, and delivery of care, which could be important to measure in BPI research and routine care. Finally the COMET taxonomy (Dodd et al., 2018) was chosen over the OMERACT Filter 2.0 (Boers

et al., 2014b) because it was anticipated that its detailed 38-item taxonomy would support categorisation of outcomes compared to OMERACT's broader taxonomy.

In addition to categorising outcomes identified in the systematic review, OMIs also need to be categorised to facilitate identification of potential assessments to measure the COS-BPI in phase 3 (see section 2.5.4). The OMI term is used consistently in both COMET and OMERACT handbooks and literature (Beaton et al., 2021c; Prinsen et al., 2016; Williamson et al., 2017) and is defined as "any instruments, definitions, tools, procedures, etc., that are used to measure an outcome" (Gorst et al., 2020, p2). This definition is useful, but it is not sufficiently detailed to facilitate categorisation of diverse OMIs. It was necessary therefore to combine this overarching term (OMI) with a categorisation system to support accurate identification, consistent terminology and categorisation of potential OMIs to measure the domains in the COS-BPI.

The Federal Drug Administration (FDA) has completed comprehensive work defining different types of OMIs (FDA-NIH Biomarker Working Group, 2016) and this model was used to detail and expand the term 'OMI' to support categorisation of OMIs in the thesis (Figure 2.3). The FDA broadly categorises instruments into survival, clinical outcome assessment (COA) and biomarkers (Powers et al., 2017). It further categorises these as follows. A COA is any evaluation that can be influenced by human choices, judgment or motivation (FDA-NIH Biomarker Working Group, 2016). According to the FDA there are four types of COA: patient-reported outcome (PRO), clinician-reported outcome (ClinRO), observer-reported outcome (ObsRO), and performance outcome (PerfO) (FDA-NIH Biomarker Working Group, 2016). In addition to these, COAs can be combined. For example, the Constant-Murley (Conboy et al., 1996) contains ClinRO and PRO assessments within the instrument. These types of assessments are categorised as combined ClinRO and PRO assessments.

Figure 2.3 Outcome measurement instrument (OMI) terminology



PRO (Patient Reported Outcome); a measurement based on a report that comes directly from the patient about the status of their health condition without amendment or interpretation of the patient's response by a clinician or anyone else.
ClinRO (Clinician Reported Outcome); a measurement based on a report that comes from a trained health-care professional after observation of a patient's health condition
PerfO (Performance Outcome); a measurement based on standardized task(s) actively undertaken by a patient according to a set of instructions
ObsRO (Observer Reported Outcome); a measurement based on a report of observable signs, events or behaviours related to a patient's health condition by someone other than the patient or a health professional

1:1 patient interviews: Because of the limited number of high-quality qualitative studies in BPI (see scoping review in Chapter 4), semi-structured interviews with a purposeful sample of individuals with BPI were conducted, to identify outcomes important to them. The concept of a COS can be difficult to understand (Young and Bagley, 2016), so the interviews focused on patients' experiences from which outcomes important to them were explored. A full discussion of the qualitative methodology and methods chosen for the COMBINE project is detailed in Chapter 4. Methods used in the systematic review are presented in Chapter 3.

2.5.3.2 Phase 2. COMBINE Delphi and consensus meetings

The next section details the issues considered when planning the COMBINE online Delphi and consensus meeting. Chapter 5 will provide a comprehensive discussion of the Delphi and consensus methods, including scoring and a priori consensus criteria, in addition to criteria for retention and removing of items between rounds (COS-STAD 9 and 10).

2.5.3.2.1 COMBINE Delphi panels

Surgeons, other HCPs and patients were allocated to three separate panels in the COMBINE Delphi. This meant that participants received a summary of their own stakeholder group's scores and a summary for each of the other stakeholder groups. Having separate surgeons' and other HCPs' stakeholder panels facilitated analysis between the two groups, as previous COS developers identified that different HCPs prioritise different outcomes (Coulman et al., 2016b).

2.5.3.2.2 COMBINE Delphi rounds and item retention

A 3-round Delphi study was conducted for the COMBINE project. The reasons are numerous and detailed here.

Firstly, the patient interviews only included patients from the United Kingdom, therefore potentially the results (which informed the Delphi) may only represent outcomes important to patients in this geographic locality. An open-ended question was therefore included in round 1 of the Delphi to seek the opinion of all international participants (including patients) on what outcomes are important to them. All participants only saw and scored these outcomes for the first time in round 2, and therefore needed a third round to view and consider other participants' scores on these outcomes before re-scoring. Secondly, participants had the opportunity to reflect on their peers' viewpoint in round 2 before being invited to consider the viewpoint of their stakeholder group and that of the other stakeholder groups in round 3. This is recommended practice in COS Delphi studies (Brookes et al., 2016), as it is thought to improve agreement between stakeholder groups. Finally, a diversity of opinion was expected across BPI experts and patients, and therefore it was anticipated that more rounds might be needed to reach consensus.

No items were dropped between rounds 1 and 2, as participants did not have the opportunity to consider other stakeholder groups' scores, so it would undermine the Delphi philosophy to drop items at this stage. Items were dropped between rounds 2 and 3, according to pre-defined criteria (see Chapter 5), as participants had the opportunity to view their peers' scores and revise their rating. This also aimed to reduce the burden on the third round by decreasing the number of items.

2.5.3.2.3 COMBINE Delphi content

Numerous meetings were planned with the research team, patient advisory group, clinical advisory group and expert clinicians to discuss the long list of outcomes identified from the systematic review and interviews. The aim of these meetings was to ensure the outcomes were easy to understand and there was no duplication (COS-STAD 11). The long list of outcomes then informed the creation of the Delphi. Each outcome was presented in lay language, with more information in parenthesis. The Delphi was piloted with HCPs and patients with the aim of reviewing the presentation and wording of the questionnaire, refining labelling and descriptions of outcomes, and identifying best methods for feedback.

2.5.3.3 Consensus meeting

Three online consensus meetings were held to finalise the COS-BPI. This included a patient-only meeting, HCP-only meeting and a final combined HCP and patient meeting to ratify the final COS-BPI. Participants discussed the outcomes and then used anonymous electronic voting to finalise outcomes to include in the COS-BPI. Pre-defined criteria for consensus were established. Chapter 5 presents a comprehensive discussion of the consensus meeting's methods and the decision making around hosting separate patient and HCP meetings.

2.5.4 Phase 3. How to measure the COS-BPI?

The overarching consensus-based guideline (Prinsen et al., 2016) for identifying OMIs for COS was followed in the COMBINE project. However, limited time and project resources of this PhD prohibited complete adherence to the guideline. The project focused on identification and psychometric evaluation of condition-specific and domain-specific PRO measures that assessed the domains in the COS-BPI. It provided recommendations for a provisional COMS for BPI to realise the benefits of the COS-BPI. Chapter 6 provides full details of the decision making involved during this final phase.

2.6 Additional methodological considerations

2.6.1 Stakeholder research partners in the COMBINE project

To develop a COS and a COMS it is important to have a management team representative of relevant stakeholders, including members with experience of outcomes research (Schmitt et al., 2015). Additionally, where patients are research participants, project developers need to involve them in designing the study (Beaton et al., 2021b; Williamson et al., 2017). The COMBINE project included a core research team, a patient advisory group and a clinical advisory group who supported and guided the project from inception to dissemination. Appendix 2.1 presents more details on each of these groups and their role within the COMBINE project.

2.7 Conclusion

Chapter 2 has reported the methodological considerations associated with developing a COS and a corresponding COMS. It has also justified some of the decision making made in the COMBINE research project.

The next chapter will detail the first step in developing a COS for BPI by identifying and defining outcomes though a systematic review of outcome reporting in BPI literature.

Chapter 3 Outcome reporting in traumatic brachial plexus injuries: a systematic review

3.1 Introduction

In the previous chapter, core outcome set (COS) methods and justification for those methods in the Core Outcome Measures in Brachial plexus INjuriEs (COMBINE) research project were discussed. This chapter will present the first step in developing a COS for Brachial Plexus Injuries (COS-BPI) by identifying and defining outcomes through a systematic review of outcome reporting in BPI literature. The list of potentially relevant outcomes identified in this systematic review informed the development and content of the Delphi. Work from this chapter has been published in BMJOpen https://bmjopen.bmj.com/content/bmjopen/11/7/e044797.full.pdf.

3.2 Rationale for a systematic review

It is recommended that potentially relevant outcomes are identified from existing work to inform the consensus process (Beaton et al., 2021a; Williamson et al., 2017). The Core Outcome Measures in Effectiveness Trials (COMET) (Williamson et al., 2017) recommend that three data sources should be considered: systematic reviews of published studies or reviews of qualitative work; investigation into national audit data sets; and published qualitative work with stakeholders to understand their views on outcomes of importance. At the time of planning this study there were no reviews of BPI qualitative work or qualitative studies exploring what outcomes were important to adults with BPI. Furthermore, there were no national audit datasets. However, there was one previous systematic review of outcome reporting in adult BPI (Dy et al., 2015).

Dy et al. (2015) conducted a review of outcome reporting in brachial plexus surgical reconstruction only. The authors (Dy et al., 2015) performed a systematic search of English language literature using MEDLINE/EMBASE and Cochrane Central Register of Controlled Trials databases up to August 2013. Furthermore, the previous review (Dy et al., 2015) did not document all outcomes/outcome measurement instruments (OMIs) reported, nor extract outcomes from these measures. As the scope of this COS

included evaluation of surgical and non-surgical interventions, there was a need for another review including non-surgical interventions to ensure outcomes were not missed. Also, to ensure comprehensive identification of outcomes reported, all OMI names needed to be documented and outcomes extracted from these measures, in addition to extracting the standalone clinician-reported outcomes (ClinRO) in studies. Finally, it is important to review outcome reporting in contemporary BPI studies, due to significant advancements in treatments such microsurgery and robotics (Ayhan et al., 2020; Kubota et al., 2017).

The systematic review by Dy et al. (2015) identified significant issues with outcome reporting in studies evaluating surgical interventions for BPI, such as an emphasis on ClinROs, a focus on muscle strength and a paucity of patient-reported outcomes (PROs). The authors also identified substantial heterogeneity of muscle strength measurement, with numerous modifications of the Medical Research Council motor score (Medical Research Council, 1976) making synthesis of outcomes between studies challenging. Despite the publication of this study highlighting heterogeneity in 2015, evidence synthesis across studies evaluating surgical intervention in adult BPI continues to be challenging (as discussed in section 1.3.2).

There is a need to evaluate the full extent of this issue in contemporary studies evaluating surgical and non-surgical interventions. This systematic review was conducted to identify outcomes reported in adult BPI studies, measurement instruments used and their timing. The outcomes extracted informed the “long list” of outcomes (in addition to outcomes from interviews with people with BPI) to be prioritised in the Delphi study. The review’s objectives were to:

I. Identify what outcomes were assessed in published studies, evaluating surgical and non-surgical treatment for BPI.
II. Compare the definitions of outcomes and timepoints of outcomes assessed.
III. Identify how the outcomes were measured.
IV. Produce a preliminary list of outcomes to be considered for inclusion in the COS-BPI.
V. Categorise outcomes extracted into a taxonomy.

3.3 Methods

A systematic review using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) recommendations (Moher et al., 2015) was carried out. The review protocol was prospectively registered (CRD42018109843) on the International Prospective Register of Systematic Reviews (PROSPERO) website http://www.crd.york.ac.uk/PROSPERO. Deviations from the protocol are reported in Appendix 3.1.

3.3.1 Data sources and search strategy

A search strategy was developed to identify studies evaluating interventions in adults with a traumatic BPI published between January 2013 and September 2018. This period was chosen so that the outcomes extracted reflected those related to contemporary BPI care. It also expanded on work by Dy et al. (2015), who conducted a systematic review of outcome reporting for brachial plexus reconstruction, including publications up to July 2013. The following search terms were used to identify studies of interest: brachial plexus inj*, brachial plexus pals*, brachial plexus lesion*, brachial plexopathy*, brachial plexus traction*, brachial plexus avulsion*, limited to human and adult publications. Full details of the search strategy are presented in Appendix 3.2. The electronic databases MEDLINE (via Ovid), EMBASE (via OVID), AMED (via Ovid) and CINAHL (via EBSCO) were searched. The thesaurus vocabulary of each database was used to adapt search terms. Boolean operators (AND, OR) were used to narrow or widen the search and no language restrictions were applied. Additional references were searched for by examining the reference lists of retrieved studies. The search was not limited to studies published in English.

3.3.2 Eligibility criteria

Studies were included if they met the following criteria:

Study type: Any controlled or uncontrolled experimental and observational studies evaluating interventions in adult traumatic BPIs, including case reports, case series, case studies, prospective and retrospective cohort studies, randomised and non-randomised clinical trials. Conference proceedings and abstract-only publications were

excluded due to the potential of incomplete and duplication of data. Studies not involving human subjects were also excluded.

Participants: Studies reporting outcomes in individuals with BPI aged 16 years or over. A BPI was diagnosed as any traumatic injury or combination of injuries to the C5-T1 cervical roots, superior middle and inferior trunks, divisions or cords of the brachial plexus. Supraclavicular and infraclavicular injuries were included. Studies of patients with isolated peripheral nerve injuries and obstetric BPIs were excluded.

Interventions: Any surgical or non-surgical intervention for BPI.

Outcomes: All outcomes reported in the published abstract, methods or results. These included physiological and functional outcomes, adverse events and PROs either in the study or subsequently extracted from the PRO measurement instrument.

3.3.3 Screening

The reference management software Mendeley was used to compile the literature, and duplicates of titles and abstracts were removed. An abstract screening tool was created, using items that were single-barrelled and including yes/no/unclear answers (Polanin et al., 2019). Appendix 3.3 presents the screening sheet. Two reviewers (JOS, CM) piloted the screening sheet by screening the same 20 abstracts. They repeated the process for another 10 abstracts, at which point they reached consensus on the screening process. The same two reviewers (CM and JOS) then independently screened the remaining abstracts and discussed disagreements involving a third reviewer where necessary (CJH). CM retrieved full texts for studies appearing to meet the inclusion criteria, based on the titles and abstracts. The number of excluded papers and reasons for exclusion were noted at each stage.

3.3.4 Quality assessment

The aim of this review was to identify outcomes reported in studies, rather than synthesise data on intervention effectiveness. However, selective outcome-reporting can provide information on what outcomes authors prioritise. We used a modified version of Kirkham et al.'s (2010) matrix (Deshmukh et al., 2021) to assess outcome-reporting bias in prospective studies and randomised controlled trials (see outcome-

reporting bias instrument in Appendix 3.4). Two reviewers (JOS, CM) independently performed the assessment of outcome-reporting bias for all outcomes included in prospective observational studies and randomised controlled trials. Both reviewers met to discuss results from the independent categorisation of outcomes within the included studies. Any disagreements were resolved through discussion.

3.3.5 Data extraction

CM created data extraction templates in Microsoft Excel (see Appendix 3.5). CM's primary supervisor (CJH) reviewed the content of the data extraction sheet and amended it accordingly. Finally, JOS and CM piloted the data extraction sheet with five included studies. Consensus was reached on what modifications were necessary and additional drop-down tabs were added to criteria, including 'interventions'. A body region column was also added with drop-down tabs (e.g., shoulder, elbow, wrist, digits or not applicable), so if outcomes were specific to an anatomical area they could be recorded. The first Excel template reported study-specific information: authors, year of publication, title, country of study site, type of BPI, study design, number and sex of study patients, and study intervention. Drop-down options were available for study design, intervention, and type of BPI. A second Excel sheet focused on the details of outcomes reported and the following data were extracted: outcome name reported verbatim in the study, OMI name, type of outcome (patient-reported/clinician-reported/performance-based), area of body assessed (if relevant), adverse events reported and timepoints of all outcomes measured. Drop-down options were available for area of the body, type of outcome and timepoints measured. CM and JOS performed dual data extraction for the first 20% of included studies. At this stage the data extracted were compared and disagreements discussed and resolved through one-to-one debate or discussion with the primary supervisor (CJH). A further 10% of studies had data extracted by both JOS and CM. At this stage there were no further differences in data extracted and dual data extraction was stopped. CM continued to extract data for the remaining studies.

CM downloaded full copies of the PRO, ClinRO and PerfO measures that were used and composed of multiple items. Definitions of these different types of OMIs are described in Chapter 2 (section 2.5.3.1). The verbatim wording for each instrument and each

item in multi-item instruments were extracted by CM as recommended by Macefield et al. (2014). The OMIs were categorised as: (i) general health (generic use in any patient population); (ii) upper limb physical function (region-specific); (iii) symptom or domain-specific (to assess a single symptom, such as pain or domain, e.g. psychological distress); and (iv) condition or disease-specific. Timepoints at which outcomes were measured were also noted. Each item extracted from the OMI was mapped to an outcome name, using the International Classification of Functioning, Disability and Health (ICF) following standard linking rules (Cieza et al., 2005b).

3.3.6 Classification of outcomes into domains

All standalone outcomes (for example, shoulder flexion range of movement, biceps strength, wound infection) extracted from each study and outcomes from each OMI were input into one MS Excel sheet. Identically worded and spelled verbatim outcomes were removed at this stage. Identical outcomes measured over different timepoints were noted as one outcome. To classify and organise the long list of outcomes, it was necessary to categorise the outcomes into a taxonomy. Decision making around which taxonomy to use in the COMBINE project is presented in Chapter 2. Appendix 3.6 presents the outcome taxonomy used in the COMBINE project. CM piloted categorisation of some of the outcomes into the taxonomy and discussed this with supervisors. It was clear from this pilot that most outcomes from the systematic review would be categorised within the ‘musculoskeletal and connective tissue’ outcome domain. It was agreed that there would be a need for the development of subdomains within some of the domains to aid organisation of the outcomes.

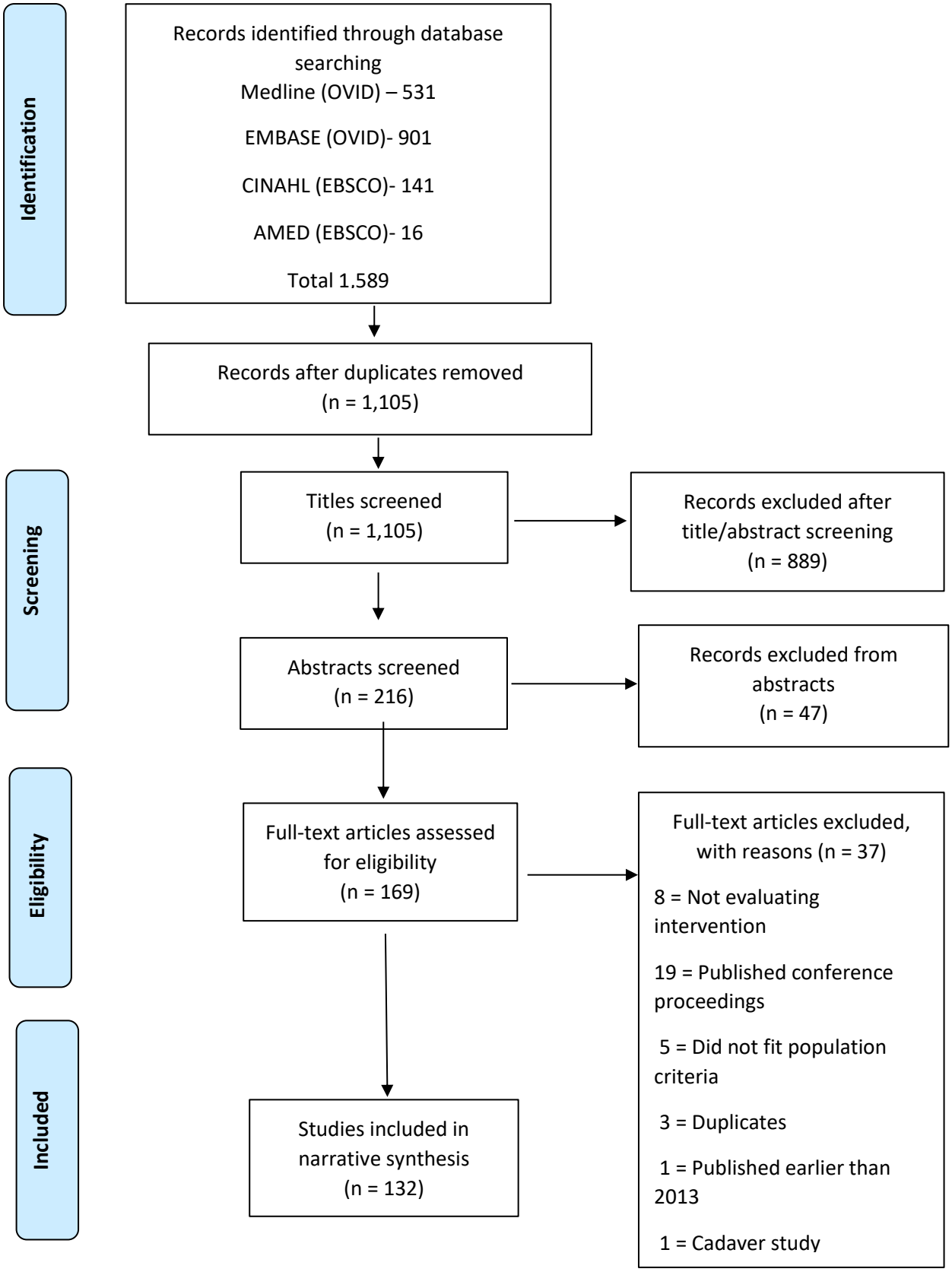
CM categorised all outcomes into the COMET taxonomy (Dodd et al., 2018). The long list of categorised outcomes were presented to supervisors at a face-to-face meeting, where the categorisation of outcomes into domains and subdomains was reviewed using the taxonomy. Due to the diversity in terminology used to report outcomes, similar outcomes were grouped within each subdomain and defined 'unique outcome' names. It is recommended that outcomes with different words, phrasing or spelling addressing the same concept should be categorised as a unique outcome (Young et al., 2019a). For example, *active range of motion of shoulder abduction* and *active goniometry of shoulder abduction* were named active shoulder abduction range, and *grasp strength* and *grip strength* were named as grip strength. Disagreements and uncertainty about categorisation and naming unique outcomes at this stage were discussed further during face-to-face meetings with subject experts. Neurophysiological outcomes were discussed with a neurophysiologist, adverse events with a peripheral nerve surgeon and psychological outcomes with a psychologist.

3.4 Results

3.4.1 Study selection

The search identified 1,589 studies, and after removing duplicates 1,105 studies remained. After reviewing titles and abstracts, 169 potentially relevant articles were identified. Of these, 37 studies were excluded as they did not meet the inclusion criteria (see PRISMA flow diagram, Figure 3.1). Appendix 3.7 presents a summary of all 132 included studies.

Figure 3. 1 PRISMA diagram for systematic review of outcome reporting



3.4.2 Study characteristics

A total of 3,201 participants were recruited into 132 studies spanning 32 countries across six continents (Table 3.1). Most participants were male (82%). Of the 132 studies, 87 (66%) were retrospective case series, with most studies published from Asia (n = 61, 46%). The most frequently studied surgical intervention was nerve transfers (n = 66, 57%).

Table 3. 1 Characteristics and demographics of included studies

	Study number	**%**
Number of retrospective studies	87/132	66
Number of prospective studies	20/132	15.1
Number of case studies	23/132	17.4
Randomised controlled trials	2/132	1.5
World region recruitment		
Asia	61/132	46.2
North America	20/132	15.1
South America	20/132	15.1
Europe	27/132	20.5
Africa	3/132	2.3
Australasia	1/132	0.8
Year published		
2013	25/132	19
2014	24/132	18
2015	15/132	11
2016	30/132	23
2017	27/132	20
2018	11/132	8.3
Gender (total 3,201)		
Male	2622/3201	82
Female	323/3201	10
Not stated	256/3201	7.9

	Study number	%
Site of plexus injury per study (n = 132)		
Upper trunk	26/132	20
Lower trunk	10/132	7.6
Pan plexus (all avulsed)	50/132	38
Infraclavicular	7/132	5.3
Mixture	32/132	24
Unclear	7/132	5.3
Interventions (n = 132)		
Surgical	115/132	87
Electrotherapy	2/132	1.5
Pain treatments	11/132	8.3
Rehabilitation	2/132	1.5
Orthotic	1/132	0.7
Stem cell	1/132	0.7
Types of surgical intervention (n = 115)		
Neurotisation	66/115	57
Tendon transfer	7/115	6.1
Free flap	16/115	14
Multiple surgeries	12/115	10
Contralateral C7	8/115	6.9
Other	6/115	5.2

3.4.3 Outcomes reported

Extraction of verbatim outcomes from each study (e.g. range of movement and muscle strength) and those extracted from measures composing of several items identified a total of 1,460 verbatim outcomes. After removing duplicates 157 different unique outcomes remained. These were categorised into 54 subdomains. No single outcome was reported across all 132 studies. Outcomes were categorised into four of the five core areas within the COMET outcome taxonomy (physiological/clinical, life impact, resource use, adverse event). No outcome was categorised into the core area of death. Outcomes were categorised to three outcome domains within the physiological/clinical core area, seven outcome domains within life impact and one domain in both resource use and adverse events. See Table 3.2.

Table 3. 2 Percentage of studies reporting outcomes by domain

Core areas	Domains (% of included studies reporting domain)
Physiological/clinical	Musculoskeletal and connective tissue (87%)
	Nervous system (35%)
	General symptoms (36%)
Life impact	Physical functioning (23%)
	Social functioning (23%)
	Role functioning (25%)
	Emotional functioning (22%)
	Global quality of life (0.8%)
	Perceived health status (4.5%)
	Delivery of care (8.3%)
Resource use	Hospital resources (0.76%)
Adverse event	Adverse events (33%)

Most reported outcomes were in the musculoskeletal and connective tissue domain. Studies also displayed a focus on reporting outcomes from the nervous system and general symptoms domains.

3.4.3.1 Physiological and clinical core area

Outcomes were categorised into three domains in the COMET physiological and clinical core area: musculoskeletal and connective tissue, nervous system and general outcomes/symptoms. Tables 3.3 and 3.4 present subdomains and unique outcomes within this core area. Musculoskeletal and connective tissue domains were reported in most studies (87%, n = 115/132). Six subdomains were developed within this category and 18 unique outcomes were identified. Nervous system outcome domains were reported in 35% (n = 46/132) of studies and included six subdomains and 15 unique outcomes. Outcomes within the symptoms/general outcomes domain were reported in 36% (n = 47/132) of studies and included 10 subdomains and 23 unique outcomes.

Table 3. 3 Physiological and clinical core area: subdomains and unique outcomes within musculoskeletal and nervous system outcome domains

Subdomains	Unique outcomes
Musculoskeletal and connective tissue outcome domain	
Muscle strength	Isometric muscle strength
	Concentric strength
	Eccentric strength
	Maximum strength
	Muscle flicker/contraction
	Anti-gravity muscle activity
	Muscle endurance
	Muscle fatigue
	Muscle torque
Active range of movement	Active range of movement
	Perception of movement
	Independent movement without donor
Passive movement	Passive movement
Control of movement/stability	Control of movement/stability
Muscle mass	Muscle mass
Bony structure and position	Bony union
	Joint position
	Joint stability
Nervous system outcome domain	
General sensory recovery	General sensory recovery
	Feeling of numbness
	Proprioception
Discriminative touch	Light touch
	2-point discrimination
	Vibration
	Object recognition
Protective touch	Pain
	Temperature
	Deep pressure
Peripheral nervous system structure	Brachial plexus structure
Reinnervation	Level of reinnervation
	Time to reinnervation
	Progression of reinnervation
Speed of motor/sensory conduction	Speed of motor/sensory conduction

Table 3. 4 Physiological and clinical core area: subdomains and unique outcomes within the general outcomes domain

Subdomain	Unique outcomes
General outcomes/ symptoms outcome domain	
Pain intensity/relief	Pain intensity
	Pain relief/reduction
Pain duration/frequency	Pain duration
	Pain frequency
Pain quality and interference with life	Pain quality
	Pain interference with walking
	Pain interference in mood
	Pain interference with work
	Pain interference in activities of daily living
	Pain interference with relationships
	Pain interference with enjoyment of life
	Pain interference with sleep
Pain when arm exposed to cold	Sensitivity to cold
Paraesthesia and itchiness	Paraesthesia
	Itchiness
Sensitivity to touch, pressure etc	Sensitivity to pressure
	Sensitivity to touch
Location of pain	Pain location
Pain medication use	Pain relief from medication
Stiffness	Stiffness
Impact on sleep	Impact on general sleep
	Impact on sleep on affected side
	Frequency sleep disturbed by injury

3.4.3.2 Life impact

In the life impact core area outcomes were categorised into seven outcome domains from the COMET taxonomy. These were: physical functioning, role functioning, social functioning, emotional functioning, global quality of life, perceived health status and delivery of care. The subdomains and unique outcomes for physical, role, social and emotional functioning domains are presented in Tables 3.5 and 3.6. Outcomes in the physical functioning and social functioning domains were reported in 23% (n = 30/132) of studies, outcomes in role functioning were reported in 25% (n = 33/132) of studies and 22% (n = 29/132) of studies reported outcomes within the emotional functioning domain.

Table 3. 5 Life impact core area: subdomains and unique outcomes within the physical and emotional functioning domains

Subdomains	Unique outcomes
Physical functioning domain	
Physical function non-specific	General physical function
	Patient-led functional outcome
Lower limb and non-upper limb function	Walking short distance
	Balance
	Running
	Climbing stairs
	Bending
	Kneeling
Reaching, pulling, pushing, carrying…	Reaching
	Pulling
	Pushing
	Carrying
	Throwing
	Lifting
	General function of arm
Turning twisting, gripping and releasing with the arm	Turning and twisting arm
	Grip and release
Fine hand movement	Pinching
	Fine hand movement (writing/buttons)
Emotional functioning domain	
Emotional distress/mood	Emotional impact on work
	Energy levels
	Emotional impact on ADL
	Happiness
	Impact on life enjoyment/satisfaction
	Emotional impact on relationships
	Anxiety
	Depression
Thoughts and beliefs	Acceptance/adjustment
	Coping with trauma
Self-esteem and confidence	Confidence
	Self-esteem
Body image	Body image

Table 3. 6 Life impact core area: subdomains and unique outcomes within the role and social functioning

Subdomains	Unique outcomes
Role functioning domain	
Impact on paid or unpaid work or role in education	Returning to work
	Ability to do work
	Usual time at work
	Type of work
	Usual school activities
Role function – patient-specific	General rating to perform a patient-specific activity
Carrying out daily routine	Impact on ADL (general)
	Return to ADL (general)
	Impact on food preparation and feeding
	Housework (washing, cleaning, ironing, folding, vacuuming)
	Gardening (includes indoor plants)
	Using a phone
Maintaining personal hygiene	Maintaining personal hygiene
Maintaining personal appearance	Maintaining personal appearance (grooming hair)
Dressing	Dressing
Transport needs	Transport needs (e.g. driving)
Impact on recreational activities and sport	Impact on normal hobbies
	Time doing normal hobbies
	Playing instrument in usual way
	Ability to play instrument
	Impact on time spent playing instrument
	Impact on time spent doing sport
	Impact on participation in sport
Social functioning domain	
Effect on relationship with family, friends, neighbours and groups	Social activities with friends
	Social activities with neighbours
	Social activities with family
	Social activities with groups
	Dependence on family and friends
	Appearance interferes with social activities
Effect on intimate relationships	Intimate relationships

The subdomains and unique outcomes for global quality of life, perceived health status and delivery of care domains are presented in Table 3.7. There was only one unique outcome within the global quality of life domain and it was measured in one study. Outcomes within the perceived health status domain were measured in 4.5% (n = 6/132) of studies and outcomes within the delivery of care domain was measured in 8.3% (n = 11/132) studies.

Table 3. 7 Life impact: subdomains and unique outcomes within the global quality of life, health status and delivery of care

Subdomains	Unique outcomes
Global quality of life domain	
Quality of life	Quality of life
Health status domain	
Perceived health status	Rating of health
Delivery of care domain	
Patient satisfaction	General patient satisfaction
	Satisfaction with appearance of arm
	Satisfaction with function
	Satisfaction with movement
	Satisfaction with strength
	Satisfaction with pain
	Satisfaction with colour
	Satisfaction with shape
	Satisfaction with feeling
	Satisfaction with procedure
Patient preference	Patient preference
Quality of intervention	Quality of intervention
Time to surgery	Time to surgery

3.4.3.3 Adverse events and resource use core areas

Within the adverse events core area, outcomes were categorised into six subdomains: donor site morbidity, musculoskeletal, respiratory, vascular, infection and general non-specified complications. Outcomes categorised to donor site morbidity were the most frequently reported outcomes within the included studies (24/132, 18%). Adverse events related to musculoskeletal outcomes were reported in 9% (n = 12/132) of studies, respiratory adverse events in 4.5% (n = 6/132) studies, vascular adverse events

5.3% (n = 7/132), infection 2.3% (n = 3/132) and non- specified in 1.5% (n = 2/132) of studies. Outcomes were categorised to one domain within the resource use core area and only one unique outcome was categorised to this outcome, which was measured in one study. See Table 3.8 for details of the unique outcomes categorised within the outcome domains of adverse events and resource use core areas.

Table 3. 8 Adverse events and resource use core areas subdomains and unique outcomes categorised to adverse events and resource use

Subdomains	Unique outcomes
Adverse events domain	
Donor site morbidity	Motor morbidity
	Sensory morbidity
	Pain
General complications	General complications
Respiratory complications	Pneumothorax
	Respiratory function
	Respiratory symptoms
	Pneumonia
Vascular complications	Arterial thrombosis
	Venous thrombosis
	Haematoma
	Venous spasm
	Iatrogenic vascular injury
	Vascularity of flap
	Swelling
Musculoskeletal complications	Fracture
	Passive range of motion loss
	Co-contraction
	Bowstringing
	Failure of tendon attachment
	Joint instability
	Scapula crepitus
Infection complications	Infection complications
Resource use domain	
Operation time	Operation time

3.4.5 Multi-item measurement instruments

In addition to extraction of standalone ClinROs and PROs such as muscle power, range or movement or return to work, outcomes were also extracted from individual items contained in a total of 30 different OMIs: PRO measures (n = 20), combined ClinRO and PRO OMIs (n = 3) and performance outcome (PerfO) OMIs (n = 7). See Tables 3.9 and 3.10.

These measures were reported 83 times in the included publications. Twenty-five of the 30 OMIs were reported in only one study in the review. The most frequently reported measures were the Disabilities of the Arm Shoulder and Hand (DASH) (Hudak et al., 1996) questionnaire (n =27 studies, 32%) and the Visual Analogue Scale for pain (n =18, 22%). The median number of items per instrument was 15, ranging from one (Numerical Rating Scale; Jensen et al., 1986) to 54 (Trinity amputation and prosthesis experience scales; Gallagher and MacLachlan, 2000). These individual items mapped to 34 different outcome domains.

Table 3. 9 PRO measurement instruments used in studies

	Number of items	Number of subscales	Frequency (n = 83)
Upper limb physical function measures (n=6)			
Disabilities of Arm Shoulder and Hand	38	3	27
Upper Extremity Functional Index	20	0	2
American Shoulder and Elbow Score	15	0	1
Modified American Shoulder and Elbow Score	13	0	1
Simple Shoulder test	12	0	1
Michigan Hand Questionnaire	37	0	1
Generic questionnaires (n =2)			
36 item short form survey (SF36)	36	8	5
Patient-specific functional score	4	0	1
Condition specific questionnaires (n =1)			
Trinity amputation and prosthesis scale	54	5	1
Domain specific questionnaires (n =11)			
Visual Analogue Scale (pain)	1	0	18
Numerical Rating Scale (pain)	1	0	6
Wong Baker Faces rating scale (pain)	1	0	1
Brief pain inventory	15	6	1
Neuropathic pain symptom inventory	10	5	1
University of Washington Neuropathic score	10	3	1
McGill Pain Questionnaire	28	3	1
McGill Pain Questionnaire SF	17	3	1
McGill Pain Questionnaire (Japanese version)	17	3	1
Self-rating anxiety scale	20	0	1
Zung self-rating depression scale	20	0	1

Table 3. 10 Performance and combined patient and clinician-reported measurement instruments used in studies

	Number of items	Number of subscales	Frequency (n = 83)
PRO & ClinRO measurement instruments (n = 3)			
University of California Los Angeles shoulder score	5	0	1
Constant-Murley	5	0	1
MAYO Performance Index	4	0	1
Performance measurement instruments (n = 7)			
Jebsen Taylor	7	0	1
University of New Brunswick Test of Prosthetic Function for Unilateral Amputees (UNB)	30	3	1
Upper Limb Module Questionnaire	22	3	1
Action Reach Arm Test	19	4	1
Southampton Hand Assessment Procedure	26	0	1
Purdue Peg test	3	0	1
Activities Measure for Upper Limb Amputees	24	0	1

Mapping of items within OMIs to subdomains and domains in the taxonomy is presented in the appendices. Appendix 3.8 presents mapping of items within PRO instruments. Appendix 3.9 presents mapping of items from combined ClinRO and PRO instruments, and Appendix 3.10 presents mapping of PerfO instruments.

3.4.6 Diversity in outcome definition and measurement

Many outcomes were not clearly defined, and different terms were frequently found for the same concept. For example, shoulder abduction strength was described in 11 different ways, including ‘deltoid strength’, ‘motor function of axillary nerve’, ‘motor recovery of shoulder abductors’, ‘muscle power supraspinatus’, ‘motor function of deltoid, and ‘motor function of supraspinatus’.

Measurement of both the standalone outcomes from the studies and those within the multi-item measurement instruments were diverse. This heterogeneity is presented in

tables 3.11 – 3.18. Muscle strength was the subdomain with the highest diversity/heterogeneity in measurement methods. Indeed, 62 different methods were used to evaluate muscle strength, including the British Medical Research Council motor score (Medical Research Council, 1976), 11 different modifications of the British Medical Council motor score, isokinetic, dynamometry and Constant-Murley score (Conboy et al., 1996). Active range of movement and the pain intensity subdomains were also measured by 15 different OMIs. Within the life impact core area, 14 different methods were used to measure "carrying out daily routine". In addition, it was often not clear which instrument was used for measurement of the outcomes. For example, the instrument used to measure active range of movement was not reported in 36% of studies (63/174) where the outcome was assessed. Finally, with regards to method of measurement, 55 studies employed a PRO instrument to evaluate the intervention.

Table 3. 11 Methods used to measure muscle strength subdomain in musculoskeletal and connective tissue domain

Measurement of muscle strength subdomain (number of studies)
DASH (n = 27), UEFI (n = 2), MHQ (n = 1); manual muscle testing undefined (n = 5); MRC muscle grading (n = 61, including UCLA); MRC muscle grading modified (n = 23) – see Appendix 3.11 for details
Other manual muscle tests (n = 3)
Kendall and McCreary testing procedure (n = 1), Oxford muscle testing (n = 1), modification of the Louisiana State University Medical Centre grading system (n = 1)
Time to (n = 12)
Contraction (n = 7), M2 (n =1), strength greater than or equal to M3 (n = 1), M3 (n = 1), greater than or equal to modified M3 (n = 1), time to improvement in MRC scale (n = 1)
Dynamometry (n = 23)
Dynamometry – isokinetic machine, undefined method (n = 1), grip strength JAMAR, undefined method (n = 4), hook grip – isokinetic machine, undefined method (n = 1), grip strength JAMAR mean of 3 trials (n = 2), grip strength PABLO system, undefined (n = 1), pinch grip JAMAR, undefined (n = 3), pinch grip JAMAR, mean 3 trials (n = 1), peak isometric, hand-held dynamometer (n = 2), isometric strength, hand-held dynamometer, best of 3 trials (n = 1), isometric strength, Kendall & Kendall positions, 3 trials mean value (n = 1), measurement on digital scales after 5 seconds (n = 1), concentric strength through range, isokinetics (n = 1), eccentric strength through range, isokinetics (n = 1), combined action of using elbow and hand on digital hanging scale (n = 1), Constant-Murley score: dynanometry 90 degrees abduction (n = 2)
Narakas score modified (n = 1)
Thoraco brachial grasp, elbow flexion with weight, elbow extension with weight, wrist flexion with weight, wrist extension with weight, fist power with weight, pinch power
ULM (n = 1)
Shoulder flexion to shoulder height with 500g, shoulder flexion above shoulder height with 500g, shoulder flexion above shoulder with 1kg, move weight on table (100g), move weight on table (500g), move weight on table (1kg) (n = 1)
SHAP (n = 1)
Grip strength, pinch strength, pinch grip (lateral), pinch grip (tip), grip strength (power), heavy extension, ability to lift weight, undefined, number of repetitions movement can be performed in 10 seconds, maximum weight sustained when flexing elbow
Unclear (n = 3)
Force recovery: cross-sectional area of the muscle under isometric contraction divided by cross-sectional area at rest (n = 1)

(B)MRC (British) Medical Research Council (motor scale), *DASH* Disabilities of the Arm Shoulder and Hand, *M* motor grade, *MHQ* Michigan Hand Questionnaire, *SHAP* Southampton Hand Assessment Procedure, *UCLA* University of California at Los Angeles (UCLA) Shoulder Score, *UEFI Upper* Extremity Functional Index, *ULM* Upper Limb Module

Table 3. 12 Methods used to measure movement subdomains in musculoskeletal and connective tissue domain other than muscle strength

Active movement
SST (n = 1) MHQ (n = 1), UCLA shoulder rating scale (n = 1), MPI (n = 2), Constant-Murley (n = 2) (2xPRO, 8x ClinRO), ARAT (PerfO, n = 1), ULM (PerfO, n = 2), goniometry (n = 48), visual assessment (n = 32), first web space in cm (n = 3), total active movement (n = 2), pulp to palm distance (n =2),months to full active movement (n = 1), months to anti-gravity movement (n = 3), months to initial movement (n = 1), months to independent movement without donor (n =1), not clear (n = 63)
Passive range of movement
Not clear (n = 7), goniometry (n = 6)
Movement control and stability
MPI (ClinRO, n = 1), ULM (PerfO, n = 1), not clear (n = 2)
Bone structure/position/healing
Not clear (n = 4)
Muscle mass
Not clear (n = 4)

ARAT Action Research Arm Test, *ClinRO* Clinician-Reported Outcome, *MHQ* Michigan Hand Questionnaire, *MPI* Mayo clinic Performance Index for the elbow, *PerfO* Performance Outcome, *PRO*-Patient Reported Outcome, *SST* Simple Shoulder Test, *UCLA* The University of California at Los Angeles (UCLA) Shoulder Score, *ULM* Upper Limb Module

Table 3. 13 Methods used to measure nervous system subdomains

Subdomains	Measurement instruments (no. of studies)
Nervous system	
General sensory recovery including proprioception	Sensory BMRC (n = 5), Modified Sensory BMRC (n = 2), Highet classification (n = 2), not clear (n =8), MHQ (n = 1)
Discriminative touch (light touch, 2-point discrimination, vibration, object recognition)	Cotton wool (n = 3), Semmes Weinstein Monofilaments (n = 4), 2-point discrimination (n = 2), tuning fork (n = 4), not clear (ClinRO, n = 1)
Protective touch (pain, temperature, deep pressure)	Blunt pin (n = 3), not clear (n = 7)
Structure of peripheral nervous system	MRI (n = 1)
Reinnervation (level of reinnervation, time to innervation)	2-point scale on EMG (n = 1), 4-point scale on EMG (n = 4), not clear EMG (n = 49)
Progression of regeneration	Tinel sign (n = 5)
Speed of motor and sensory conduction	EMG (n =9)

BMRC British Medical Research Council*, EMG* Electromyography*, MHQ* Michigan Hand Questionnaire

Table 3. 14 Methods used to measure subdomains in general outcomes

General outcomes /symptoms	
Pain intensity/relief	DASH (n = 27), ASES (n = 1), TAPES (n = 1), VAS (n = 18), NRS (n = 12), MHQ (n = 1) WBFRS (n = 1), BPI (n = 1), UNWNS (n = 1), McGill Pain Questionnaire SF (n = 2), McGill pain questionnaire (n = 1), MPI (n = 1), Constant-Murley (n = 2), 4-point scale (n =3); author-developed questionnaire (n = 1), not clear (n = 3)
Pain duration or frequency	SST (n = 1), SF36 (n = 5), MHQ (n = 1), TAPES (n = 1), NPSI (n = 1), BPI (n = 1), UCLA shoulder rating score (n = 1), not clear PRO (n = 1)
Pain quality	TAPES (n = 1), NPSI (n =1), UWNS (n = 1), McGill SF (n = 2), McGill (n = 1), not clear PRO (n = 1)
Pain when arm exposed to cold	NPSI (n = 1)
Paraesthesia	DASH (n = 27)
Sensitivity to touch, pressure, vibration etc	NPSI (n =1), UWNS (n = 1), NRS (n = 1)
Location of pain	BPI (n = 1)
Pain medication use	BPI (n = 1)
Stiffness	DASH (n = 27)
Impact on sleep	DASH (n = 27), UEFI (n = 3), ASES (n = 1), MHQ (n = 1), SST (n = 1), BPI (n =1), Constant-Murley (n = 2), not clear PRO (n = 1)

ASES American Shoulder and Elbow Surgeons Index*, BMRC* British Medical Research Council*, BPI* Brief Pain Inventory*, DASH* Disabilities of the Arm Shoulder and Hand, *EMG* Electromyography*, MHQ* Michigan Hand Questionnaire*, MPI* Mayo clinic Performance Index for the elbow, *MRI* Magnetic Resonance Imaging*, NPSI* Neuropathic Pain Symptom Inventory*, NRS* Numerical Rating Scale, *PRO* Patient-Reported Outcome, *SF36* Short Form 36 health survey, *SST* Simple Shoulder Test*, TAPES* The Trinity Amputation and Prosthesis Experience Scales, *UCLA* The University of California at Los Angeles (UCLA) Shoulder Score, *UEFI* Upper Extremity Functional Index, *UNWNS* University of Washington Neuropathic pain score*, VAS* Visual Analogue Scale, *WBFRS* Wong Baker Faces Rating Scale

Table 3. 15 Methods used to measure physical and emotional functioning subdomains

Subdomains	Measurement instruments (no. of studies)
Physical functioning	
Physical function non-specific	PSFS (n = 1), TAPES (n = 1)
Lower limb and non-upper limb function (walking, running, climbing stairs etc)	SF36 (n = 5), TAPES (n = 1), BPI (n = 1) Not described PRO (n = 1)
Reaching, pulling, pushing, carrying, throwing, lifting	DASH (n = 27), UEFI (n = 2), MHQ (n = 1), ASES (n = 1), SST (n = 1), SF36 (n = 5), ARAT (n =1), AMULA (n =1) UNBtP (n = 1)
Turning twisting, gripping and releasing with the arm	DASH (n = 27), UEFI (n = 2), MHQ (n = 1), ARAT (n = 1), SHAP (n = 1), JHFT (n = 1), AMULA (n = 1), UNBtP (n = 1), not clear (n = 1)
Fine hand movement (including writing)	DASH (n = 27), UEFI (n = 2), MHQ (n = 1), ARAT (n = 1), SHAP (n = 1), JHFT (n =1), Purdue Peg test (n = 1), AMULA (n = 1), UNBtP (n = 1)
Emotional functioning	
Emotional distress/mood	SF36 (n = 5), TAPES (n = 1), BPI (n = 1), UWNS (n = 1), self-rated anxiety scale (n = 1), self-rated depression scale (n = 1), MHQ (n = 1)
Thoughts and beliefs (acceptance and adjustment)	TAPES (n = 1)
Self-esteem and self-confidence	DASH (n = 27), TAPES (n = 1)
Body image	MHQ (n = 2), not described (n =1)

AMULA American Measures for Upper Limb Amputees*, ARAT* Action Research Arm Test*, ASES* American Shoulder and Elbow Surgeons Index, *BPI* Brief Pain Inventory, *DASH* Disabilities of the Arm Shoulder and Hand, *JHFT* Jebsen Hand Function Test, *MHQ* Michigan Hand Questionnaire*, PSFS* Pain Specific Functional Scale, *SF36* Short Form 36 health survey, *SHAP* Southampton Hand Assessment Procedure, *TAPES* The Trinity Amputation and Prosthesis Experience Scales, *UEFI* Upper Extremity Functional Index*, SST* Simple Shoulder Test, *UNBtP* University of New Brunswick test of Prosthetics function

Table 3. 16 Methods used to measure role and social functioning subdomains

AMULA American Measures for Upper Limb Amputees, *ASES* American Shoulder and Elbow Surgeons Index, *BPI*

Subdomains	Measurement instruments (no. of studies)
Role functioning	
Impact on return to work	DASH (n = 27), UEFI (n = 2), MHQ (n = 1), ASES (n = 1), SST (n = 1), SF36 (n = 5), TAPES (n = 1), MPI (n = 1) No description PRO (n = 1), questionnaire no data (n = 1)
Role function patient-specific	PSFS (n = 1)
Carrying out daily routine (including food preparation, housework, garden, plants)	DASH (n = 27), UEFI (n = 2), MHQ (n = 1), TAPES (n = 1), BPI (n = 1), UCLA (n =1), SHAP (n = 1), Jebsen (n =1), ULM (n =1) Questionnaire not defined (n =2), not clear PRO (n = 1), AMULA (n = 1), UNBtP (n = 1), unclear ClinRO (n = 1)
Maintaining personal hygiene	DASH (n = 27), ASES (n =1), SST (n = 1), SF36(n = 5), MHQ (n = 1) AMULA (n =1), UNBtP (n = 1)
Maintaining personal appearance	UEFI (n = 2), ASES (n = 1), AMULA (n = 1)
Dressing	DASH (n = 27), UEFI (n = 2), MHQ (n = 1), ASES (n = 1), SST (n =1), AMULA (n = 1) SHAP (n = 1)
Transport needs	DASH (n = 27), UEFI (n = 2),
Impact on recreational activities and sport	DASH (n = 27), UEFI (n = 2), ASES (n = 1), TAPES (n = 1), Constant-Murley (n =2), not clear PRO (n =1)
Social functioning	
Effect on relationship with family, friends, neighbours and groups	DASH (n = 27), SF36 (n = 5), TAPES (n = 1), MHQ (n =1)
Effect on intimate relationships	DASH (n = 27)

Brief Pain Inventory, *ClinRO* Clinician-Reported Outcome, *DASH* Disabilities of the Arm Shoulder and Hand, *MHQ* Michigan Hand Questionnaire, *MPI* Mayo clinic Performance Index for the elbow, *PerfO* Performance Outcome, *PRO* Patient-Reported Outcome, *SF36* Short Form 36 health survey, *SHAP* Southampton Hand Assessment Procedure, *SST* Simple Shoulder Test, *TAPES* The Trinity Amputation and Prosthesis Experience Scales, *UCLA* The University of California at Los Angeles (UCLA) Shoulder Score, *UEFI* Upper Extremity Functional Index, *ULM* Upper Limb Module, *UNBtP* University of New Brunswick test of Prosthetics function

Table 3. 17 Methods used to measure general quality of life, perceived health status and delivery of care subdomains

Subdomains	Measurement instruments (no. of studies)
Global quality of life	
General quality of life	Not described PRO (n = 1)
Health status	
Perceived health status	SF36 (n = 5), TAPES (n = 1)
Delivery of care	
Patient satisfaction	TAPES (n = 1), UCLA (n = 1), MHQ (n = 1), 10-point scale (n = 1) 4-point scale (n = 2), 3-point Likert scale (n = 1), questionnaire not described (n = 1), not defined PRO (n = 2)
Patient preference for treatment	Not described (n = 1)
Accessibility, quality and adequacy of intervention	4-point scale (n = 1)
Resource use	
Operation time	Not described (n = 1)

MHQ Michigan Hand Questionnaire, *PRO* Patient-Reported Outcome, *SF36* Short Form 36 health survey, *TAPES* The Trinity Amputation and Prosthesis Experience Scales, *UCLA* The University of California at Los Angeles (UCLA) Shoulder Score

Table 3. 18 Methods used to measure adverse events subdomains domain.

Subdomains	Measurement instruments (no. of studies)
Adverse events	
Donor site motor morbidity to include weakness	BMRC motor score (n =7), BMRC motor score modified (n = 2), dynamometry (n = 8), EMG (n = 1) Not clear (n = 19)
Donor site sensory morbidity	10-point scale PRO (n = 1) Not defined (n = 4), 2-point discrimination (n = 2), monofilaments (n = 1)
Donor site morbidity - pain	Not defined PRO (n = 3)
General complications	Unclear (n = 2)
Respiratory complications	4-point scale PRO (n = 1), x-ray (n =2), FEV (n = 1), TLC (n = 1), MVV (n = 1), not defined (n = 4)
Vascular complications	Not defined (n =13), visual assessment (n =1), USS (n =1)
Musculoskeletal complications	Not defined ClinRO (n = 2), unclear (n = 19)
Infection complications	Not defined ClinRO (n = 1), unclear (n = 2)

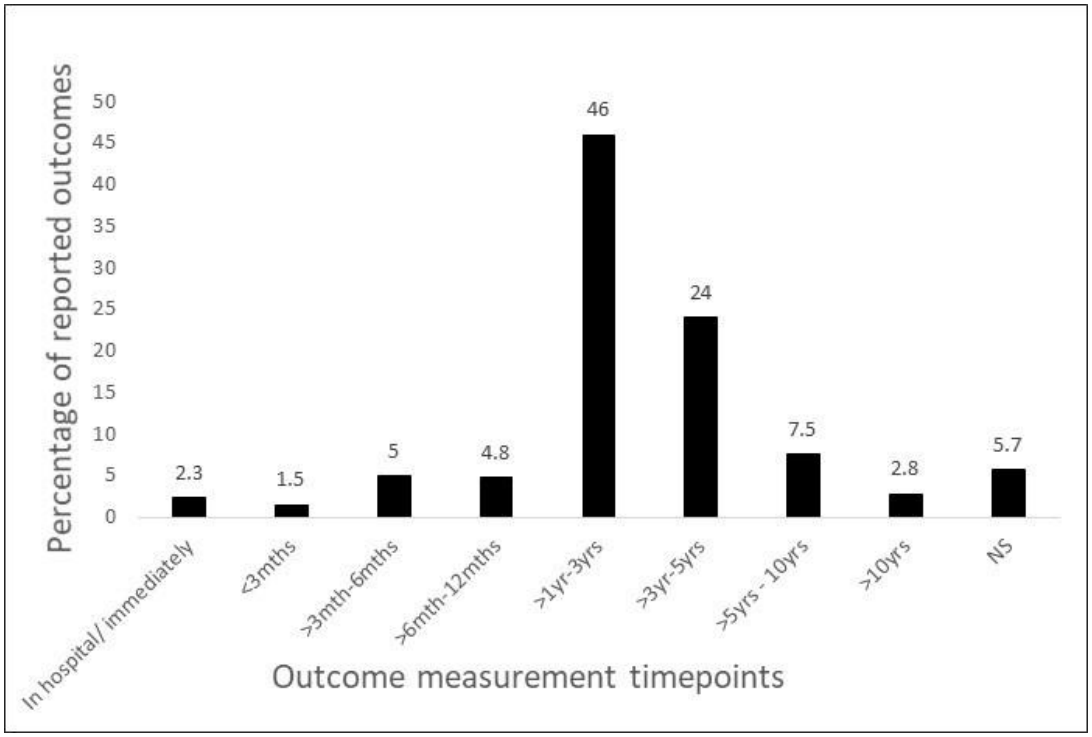
BMRC British Medical Research Council, EMG Electromyography, *FEV* Forced Expiratory Volume, *MVV* maximal voluntary ventilation, *TLC* Tidal Lung Capacity

3.4.7 Timing of outcome reporting

Outcomes were measured at various stages of patients' care and recovery, with some measurements being taken immediately after treatments and others up to 10 years post-intervention. Figure 3.2 demonstrates the variation in the timeframe of outcome reporting.

Of the 1,460 verbatim outcomes, 672 (46%) were measured between 1- and 3-years following intervention. Early/immediate outcomes were less frequently measured, with only 1.5% (22/1,460) of outcomes being reported within 3 months of an intervention. A small selection of outcomes (n =83; 5.7%) reported did not have a timeframe allocated to their measurement.

Figure 3. 2 Outcome measurement timepoints

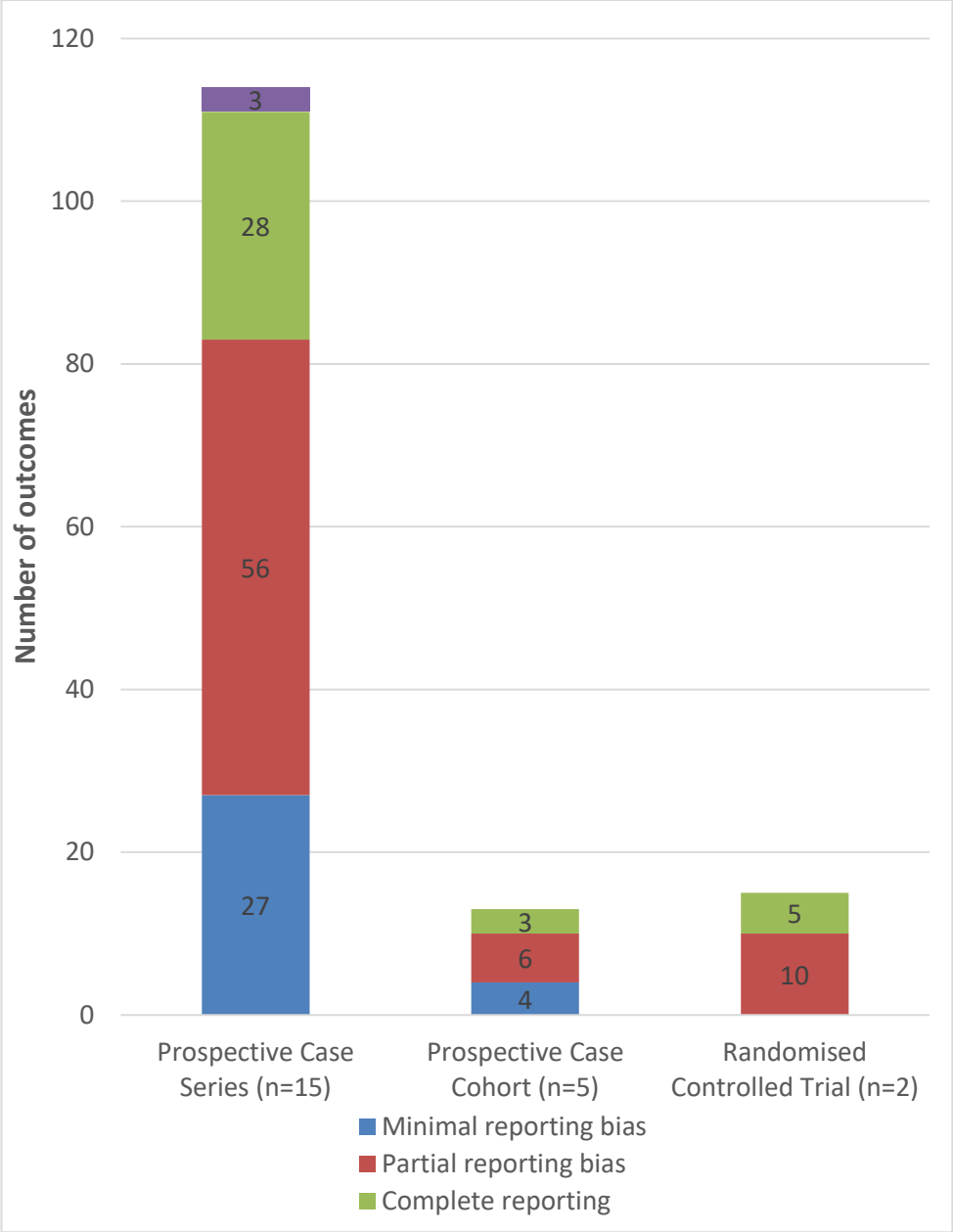


NS not stated; *yr(s)*- year(s); *mth(s)* month(s)

3.4.8 Outcome reporting bias

Figure 3.3 illustrates the reporting status of outcomes (n = 142) across the included prospective case series (n = 15), cohort (n = 5) and randomised controlled studies (n = 2). None of the studies were prospectively registered. Fewer than one quarter of the outcomes in the prospective case series and cohort studies and half of outcomes in randomised controlled studies were “completely” reported.

Figure 3. 3 Outcome-reporting bias bar chart



n = number of studies

3.5 Discussion

This review aimed to identify what outcomes and OMIs are assessed in adult BPI research, compare definitions of outcomes and timepoints assessed, and produce and categorise an outcome long list to be considered for inclusion in the COS-BPI. The review demonstrated heterogeneity and inconsistencies in outcome reporting in studies evaluating interventions in adult BPI. It found a focus on impairment domains and that PROs are rarely measured. There was also evidence of outcome-reporting bias.

3.5.1 Heterogeneity in what and how outcomes were reported

From the results, 1,460 verbatim outcome names were identified, which were reduced to 157 unique outcome names. This, and the fact that the reporting of these outcomes is sporadic across studies, implies high heterogeneity. Comparison of interventions can be problematic because of the inconsistencies in outcome reporting (Clarke, 2007; Williamson et al., 2012a). In addition to heterogeneity in what outcomes were reported, there was also diversity in how they were measured. Researchers assessed many outcomes, using a variety of different measures. Muscle strength was the most frequently assessed outcome, measured using 62 different OMIs, and 10 studies did not report what they used or how they assessed muscle strength. Similarly, active range of movement was frequently measured, but 63 studies did not define how they evaluated it. Variation in definitions and measurement of outcomes has been found within other areas of healthcare. Outcome heterogeneity is found in the reporting of outcomes relating to burn care, (Young et al., 2019b), breast reconstruction (Potter et al., 2011) and spinal cord injury (Watzlawick et al., 2019), among others. A recent review of outcome reporting within burns illustrated that wound healing was defined in 166 different ways across 147 studies (Young et al., 2019b).

The heterogeneity in the outcomes measured and methods of measurement causes a problem for decision makers (e.g. patients, clinicians, guideline developers), who rely on systematic reviews for evidence-based practice (Luckmann, 2001). A frequent reason for non-conduct of meta-analysis in these reviews is that studies report different outcomes or assess the same outcomes using different methods (Kirkham et

al., 2013b). In a recent evaluation of 175 systematic reviews, 41% of the studies could not conduct a meta-analysis because fewer than two studies measured the same outcomes or OMIs were inconsistent (Saldanha et al., 2020). Indeed, two recently completed reviews evaluating interventions in BPI have also listed this as a factor, preventing synthesis of data from included studies (Ayhan et al., 2020; Donnelly et al., 2020). Ayhan et al. (2020) were unable to complete multivariate analysis because of heterogeneity in outcome reporting in studies comparing effectiveness of interventions aiming to reconstruct elbow flexion. Donnelly et al. (2020) reported that a lack of consistency in outcome measurements impeded their analysis.

Additionally, the inability to synthesise the evidence from different studies results in research waste (Chalmers and Glasziou, 2009), as the data which was resource-intense in study planning to publication has little value (Chalmers and Glasziou, 2009). The production of the COS-BPI should increase comparability in outcomes across studies, facilitating formal synthesis in systematic reviews and development of clinical practice guidelines. In addition, patients and HCPs would be better able to compare more directly the effectiveness of treatment options. This would ultimately improve patient care by facilitating evidence-based care for patients with a BPI.

3.5.2 Impairment focus

There is clear evidence within the literature that individuals with a BPI suffer emotional and psychological issues (Brito et al., 2019; McDonald and Pettigrew, 2014). However, although all relevant domains within the COMET taxonomy were represented, the vast majority were related to the musculoskeletal domain. Researchers infrequently measured emotional and psychological consequences. Emotional functioning was measured in 29/132 studies. In 27 of these studies the emotional functioning outcome was mapped to a single item, on confidence and capability, in the DASH. This highlights, perhaps, how little importance emotional functioning is given by researchers in this area. There was also limited measurement of physical, social and role functioning domains within the included studies, and when identified they were also related strongly to items in the DASH. While the inclusion of outcomes such as these is encouraging and should be recognised, their use is infrequent and gives a narrow reflection of the wide-ranging impact of a BPI or its treatments on patients.

The focus on impairment outcomes concurs with findings in a previous systematic review in brachial plexus reconstruction (Dy et al., 2015). Dy et al. (2015) similarly found that in the 88 studies included in their review, 83 (94%) measured motor function. Furthermore, 49 (59%) of those studies measuring motor function did not measure any other outcomes. This previous study differs from the current review as Dy et al. (2015) did not examine the diversity within the measurement instruments and they did not extract outcomes from OMIs identified within the study. Furthermore, this current review included studies evaluating any intervention in the adult BPI population, whereas Dy et al. (2015) specifically included studies evaluating BPI surgical reconstruction. Nevertheless, the findings are similar and indeed concerning because of the lack of progression with outcome reporting in this complex, devastating condition.

One plausible explanation for the choice of impairment outcomes extends from the model of illness adopted by society/clinicians/researchers. Cultural and professional models of illness will influence decisions on the individual patient's care and delivery of healthcare (Farre and Rapley, 2017). Hence, a 'narrow definition' of the purpose of medical care in terms of disease, strictly concerned with organ malfunction, will result in treatments exclusively concerned with the physical aspects of illness. The high prevalence of impairment-focused outcomes, in this review, highlights the biomedical focus in the assessment and treatment of BPI. Despite their importance, models of illness are rarely explicitly discussed or defined. The often criticised but nevertheless dominant 20th-century biomedical model originates from Virchow's conclusion that all disease results from cellular abnormalities (Rocca and Anjum, 2020), that health is the absence of disease or physiological abnormality, and that mental phenomena such as emotional functioning are separate and unrelated to physical dysfunction.

Recognising the weaknesses with the biomedical model, Engel proposed an alternative popular biopsychosocial model (Engel, 1977). The biopsychosocial approach expands the biomedical model to include the psychosocial without sacrificing the advantages of the biomedical approach (Engel, 1980), so that '*patients would continue to be cared for from a disease standpoint but, additionally, psychological and social information would be given equal standing in the care process'* (Smith et al., 2013, p266). In doing so, a healthcare professional should be able to evaluate all the factors contributing to

illness, rather than focusing solely on biological aspects (Engel, 1980). Over the last 40 years the biopsychosocial model has evolved and the basic model has been combined with the International Classification of Disability Functioning and Health (ICF), developed by the World Health Organization (World Health Organization, 2001) to clarify the different concepts of health to be measured. However, it is thought that despite biopsychosocial concepts being used in some areas of healthcare (rehabilitation, chronic pain services, palliative care), its use in areas such as acute medical and surgical services is almost unknown (Wade and Halligan, 2017).

Clinical decisions about the care of patients are made on the basis of outcomes assessed, so if outcome measurement is impairment-focused in BPI then biopsychosocial care may be lacking. This is despite evidence that individuals who experience a BPI suffer significant emotional and psychological distress (Brito et al., 2019; C. Verma et al., 2019; Wellington, 2010). The impairment focus identified in this review suggests that the emotional and psychological distress raised by patients in qualitative studies is not assessed and therefore not explored in overall management. This reductionist approach to BPI assessment and management is concerning. Including patients in both the outcome generation and as equal partners in the COS-BPI consensus process aimed to support an inclusive approach to its development. This maximised the potential that outcomes relevant to patients were included in the COS-BPI and aimed to support a biopsychosocial approach to assessment of outcomes in the future.

3.5.3 Patient-reported and clinician-reported outcomes

Linking with the impairment focus, only 42% (55/132) of studies measured a PRO when evaluating an intervention in BPI. Most studies measured ClinROs. Comparing the prevalence of the use of PRO instruments to other similar traumatic injury cohorts, PRO instruments are frequently used in traumatic brain injury, spinal cord injury and within burn care (Rosenberg et al., 2018). However, within general polytrauma, as with BPI, PRO instrument use is low (Dy et al., 2015; Rosenberg et al., 2018). This is a problem for two reasons. Firstly, it may underestimate the burden of a BPI and secondly, it can be biased. This following section explores these issues.

In this review the ClinROs primarily focused on a clinician's assessment of muscle recovery, including strength and active range of movement. Although important in the context of innervation of muscles following the injury, if used in isolation they do not capture the patient's perspective of their own health (Basch et al., 2016; Pakhomov et al., 2008). Evidence suggests that relying on ClinRO instruments alone may underestimate the impact of a condition (Calvert and Freemantle, 2003). It could be argued that these concepts reflect an injury viewed from opposite ends: by the clinician (who makes treatment decisions based primarily on nerve innervation) and the patient (whose primary concern is the impact of the injury on function and quality of life). All outcomes are interrelated but the relationship between them is complex. For example, the loss of motor power is associated with worsening patient-reported function, but the relationship is not necessarily direct and the correlation not perfect (Foldvari et al., 2000).

Another issue associated with the high use of ClinRO instruments in this review is bias. The most frequently measured outcome was muscle strength, a ClinRO. Muscle strength was most commonly measured using the Medical Research Council (MRC) motor scale (Medical Research Council, 1976). This involves a subjective assessment by the HCP of the patient's ability to generate strength with their muscles. It is based on a 6-point rating scale, where 0 is no muscle activity seen (by HCP) and 5 is normal strength (compared to the patient's other side). As most studies were retrospective or prospective case series and measurements were not conducted by blinded assessors, the risk of bias is inherent. A PRO measured through a PRO instrument is directly reported by the patient without interpretation of the patient's response by a clinician or researcher (Black, 2013). Using PRO instruments can reduce the bias that is otherwise seen where results are based on ClinROs collected in unblinded case series studies.

3.5.4 Outcome-reporting bias

Only two studies included in this review were randomised controlled trials (Martins et al., 2013; Tu et al., 2014). However, despite prospective trial registration on a public registry being a condition of publication (De Angelis et al., 2004), none of the randomised trials on BPI were registered. There was also selective outcome reporting

in the included prospective and randomised BPI studies. Most outcomes were only partially reported, frequently lacking specific detail about the outcome result or time of measurement, omitting certain outcomes or lacking the statistical details needed for meta-analysis. This outcome-reporting bias identified in current BPI literature threatens the validity of evidence-based practice in BPI, because it potentially overestimates the effect of treatments or distorts results of studies (Kirkham et al., 2010). This contributes to research waste and, critically, delays advancement of care for patients (Glasziou and Chalmers, 2018). Developing a COS for BPI will minimise the risk of outcome-reporting bias in the future, as the minimum set of outcomes should be assessed and reported in all studies.

3.5.5 Strengths and limitations

One potential limitation is that this study focused on outcomes from studies evaluating interventions in adult BPI over a recent 5-year period. Older studies were excluded to ensure we identified outcomes relevant to contemporary BPI care. Furthermore, a previous systematic review (Dy et al., 2015) of outcome reporting within BPI reconstruction included studies to 2013. On comparing results of both studies, no extra outcomes were identified. However, there is still a potential that some outcomes and OMIs used prior to 2013 were excluded due to the time limits on the search.

Another potential limitation is that we included all study designs within our systematic review, including retrospective and prospective cohort studies. This resulted in the inclusion of low-quality studies, where outcomes were often poorly defined with limited detail on their measurements. Although it may be reflective of the research in BPI, the limited detail on some of the outcomes and OMIs may have led to errors in their categorisation.

The strengths of this review are that the protocol was prospectively registered to ensure transparency. The screening and data extraction form were pre-specified and piloted. The review was supported by an extensive systematic search, including four databases. International and non-English publications were included to reduce the risk of selection bias.

To account for multidisciplinary perspectives, researchers and clinicians were involved

in categorising outcomes into domains. The review details the scale of outcome heterogeneity in BPI research using a systematic method.

3.5.6 Next steps

A list of potentially relevant outcomes has been identified and categorised into a clear taxonomy for COS development. The outcomes identified in this review were combined with outcomes identified in face-to-face patient interviews (Chapter 4) to inform a long list of outcomes. This long list informed the development of an online Delphi (Chapter 5) to reach consensus on the COS-BPI. The next chapter will identify outcomes important to people with a BPI.

Chapter 4: Exploring outcomes important to individuals with a traumatic brachial plexus injury: a qualitative study

4.1 Overview

The previous chapter identified a list of potentially relevant outcomes to be included in a core outcome set (COS) for brachial plexus injury (BPI) through a systematic review of the literature. Chapter 4 presents a qualitative study which sought to identify the outcomes which matter to individuals with a BPI. The rationale for the methodological approach taken, methods of data collection and findings are also discussed.

4.2 Introduction

It is essential that the final COS includes outcomes relevant to people with a BPI. Outcomes that are identified solely through a systematic review of published studies may reflect only those which clinicians and researchers deem as important. This is because patients historically have had little say in what outcomes are measured in studies. Patients' views may therefore be overlooked if systematic reviews alone are used to inform the COS. This has been evidenced by a number of COS studies (Gonçalves et al., 2020; Kirwan et al., 2005) where new outcomes, not reported in the literature, were identified through qualitative work with patients and carers. As discussed in Chapter 2, to identify potentially eligible outcomes for COS, views from stakeholder groups not encompassed by the systematic review of published literature should be elicited (Beaton et al., 2021a; Williamson et al., 2017). Methods such as interviews, focus groups or review of previously published qualitative studies on outcomes are recommended (Beaton et al., 2021a; Williamson et al., 2017).

A review of the research literature demonstrated that little effort had been expended to determine what outcomes are truly important to people who have experienced a BPI (Appendix 4.1). A scoping review of existing published qualitative literature identified seven studies (Brito et al., 2019; Brown et al., 2018; Franzblau and Chung, 2015; Mancuso et al., 2015; McDonald and Pettigrew, 2014; Verma et al., 2019; Wellington, 2010). Several focused only on exploring psychosocial experiences (Franzblau and Chung, 2015; McDonald and Pettigrew, 2014; Wellington, 2010), with

two studies exploring patient experiences linked to specific interventions, including nerve transfer to improve elbow flexion (Brown et al., 2018) or free muscle transfers (Brito et al., 2019). Five of the seven studies (Brito et al., 2019; Franzblau et al., 2014; McDonald and Pettigrew, 2014; C. Verma et al., 2019; Wellington, 2010) included only male participants. Brown et al. (2018) included one female participant and Mancuso's study (Mancuso et al., 2015) included four female participants. Because of the limited sampling and narrow scope of the available qualitative studies in BPI, there is a risk that identifying outcomes from this research may not be representative of the wider BPI community.

No previous studies were found with the specific aim of identifying and exploring outcomes important to patients with a BPI. One previous qualitative study, set in the United States of America (USA), explored expectations of 10 patients who were about to have BPI surgery (Mancuso et al., 2015). Expectations identified through the semi-structured interviews included pain, movement, self-care, interaction with family, work, sports and global function (Mancuso et al., 2015). However, the study focused only on surgical interventions, so expectations are likely to be related to the specific intervention and to people at a specific stage in their condition (i.e. considering surgery). As the scope of this COS includes patients having both surgical and non-surgical treatment, identifying outcomes solely from previous qualitative studies (focusing on surgical interventions) to inform the COS would not be sufficient and would likely miss outcomes important to patients undergoing other treatments for BPI.

This qualitative study, therefore, sought to identify all potential outcomes relevant to patients; help understand why particular outcomes are important; and also to explore the language used by patients when referring to these outcomes, to support subsequent phases in the COS development (Jones et al., 2017). By gaining an in-depth understanding of outcomes, more meaningful outcomes can be taken forward to the Delphi study. For example, in the PARTNERS2 study (Keeley et al., 2016), which aimed to identify a COS for use in bipolar trials, literature review and interviews identified that employment was an important outcome. However, the qualitative research identified that suitable employment, related to security and belonging, was more important than just being employed. This meant that a more specific outcome was

taken forwards to the Delphi, with informed descriptions to support people to interpret the outcomes.

4.2.1 Aims and objectives

The aim of this qualitative study was to investigate and gain an understanding of outcomes important to patients with a traumatic BPI.

Objectives

i) To identify any outcomes that are important to individuals with traumatic BPIs, contributing to a 'long list' of outcomes.

ii) To explore the language that participants used to describe outcomes to inform the next phase.

iii) To elucidate why these outcomes are important.

4.3 Methodology

4.3.1 Qualitative research

Qualitative research methods were chosen to provide an exploratory approach to understand what outcomes are important to patients with a BPI. Qualitative research deals with meaning, capturing aspects of a participant's social and psychological world, recording the messiness of real life and interpreting it (Braun and Clarke, 2013). Qualitative research can be an interpretative approach to explore phenomena "from the interior" (Flick, 2018). The diverse range of source data (text, images, observations and audio recordings) used in qualitative research are in contrast to quantitative research, which uses numbers, frequently analysed statistically (Braun and Clarke, 2013; Ritchie et al., 2013). Qualitative research is therefore the ideal method to explore not only what outcomes are important to people with a BPI but also why those outcomes are important, and the words people use to describe them.

4.3.2 Qualitative methodologies

Methodology is described as the theory, including the description, explanation and justification of methods used in research but not the methods themselves (Braun and Clarke, 2013; Carter and Little, 2007; Kaplan, 1964). In order to make an informed decision about this study's design, an appreciation of the underlying principles, similarities and differences of qualitative methodologies was essential (Ritchie et al., 2013). Details on some of the most common qualitative methodologies are presented in Table 4.1. Following reflection on the underpinning theoretical perspectives of phenomenology, ethnography, grounded theory and others, a decision was made that adopting one of these approaches would not be appropriate in terms of achieving my aims and objectives. The methodology of interpretative description (Hunt, 2009; Smith et al., 2011; Thorne et al., 1997), which falls under the umbrella of generic qualitative research (Caelli et al., 2003; Kahlke, 2014), was chosen for this study. A generic qualitative research approach has been suggested as appropriate to use in qualitative studies developing core outcome sets (Jones et al., 2017). A detailed account of interpretative description is presented in section 4.3.2.1

Table 4.1 Summary of frequently used qualitative approaches

Methodology	Description	Relevance to this research
Grounded theory	The discovery and development of a theory about a phenomenon from the data.	Origins are based in sociology with aims to predict and explain behaviour. It seeks to generate a theory from the data. This research aimed to understand and explore outcomes important to patients. Generating a theory about outcomes was not the aim of the study.
Phenomenology	Phenomenology aims to look in detail at how someone makes sense of life experience, and to give detailed interpretation of the account to understand the experience.	It originates from philosophies aiming to understand human existence with a detailed and systemic analysis of consciousness. This study's aim was to identify outcomes important to patients with a BPI to inform a consensus process. Because of the pragmatic nature of the research, this approach was inappropriate. If a more in-depth exploration of the lived experience of a patient with a BPI was the aim of the study, then a phenomenological approach would have been appropriate.
Ethnography	Ethnography focuses on gaining a deep understanding the culture, conventions and social dynamics of a group. This results in the production of a rich description of the culture of the group.	It originated from the field of anthropology with an emphasis on understanding culture. It was therefore not relevant to the aim of this research.

Methodology	Description	Relevance to this research
Narrative, life histories	Focuses on an experience in a person's life. Produces rich detailed stories.	These are a family of approaches with an underlying philosophy that people are story tellers and that the stories themselves become the raw data. Although this approach could have been appropriate to this study, the pragmatic nature of the generic qualitative approach matched the aims and objectives of the study.
Case study	An investigation and analysis of a single case intended to capture the complexity of a phenomenon. Case studies are designed to suit the case and research question, and multiple data collection methods and analysis may be used.	The focus of the case study as an in-depth exploration of one case meant that the approach was inappropriate for this study. Due to the diversity in presentation of patients with a BPI, a maximum variation sample was needed to ensure all important characteristics were represented.

Frank, 2002; Glaser and Strauss, 1967; Hagemaster, 1992; Hyett et al., 2014; Pope, 2005; Ritchie et al., 2013; Tuffour, 2017

4.3.2.1 Generic qualitative research

A generic qualitative approach seeks to understand how people interpret, construct, or make meaning from their world and their experiences (Kahlke, 2014). However generic qualitative research is not guided by an explicit or established set of philosophical assumptions. Caelli et al. (2003) suggest that there are two types of generic qualitative approaches: one which blends established methodological approaches and another which claims no formal methodological framework at all. Although generic qualitative approaches are not bounded by or defined by specific methodologies, this does not mean that they lack credibility (Caelli et al., 2003; Kahlke, 2014). Indeed, justification of methods, the need for rigour and consideration of the researcher's analytical lens on the study design are imperative (Caelli et al., 2003).

Interpretative description is an established example of a generic qualitative approach (Hunt, 2009; Thorne et al., 1997). It originates from the nursing field, with the aim of developing knowledge to inform practice (Thorne et al., 1997). Knowledge is developed through describing or interpreting a health or illness phenomenon from the perspective of those who live it (Thorne et al., 1997). Interpretative description is aligned to constructivist enquiry (Hunt, 2009). This means that interactions between the researcher and the participants influence each other and together co-construct meaning (Thorne et al., 2005). The interpretative description also acknowledges the researcher's sociological biography, experience, and the practical and theoretical knowledge they bring to the study, and recommends that these factors are made explicit (Hunt, 2009; Thorne et al., 1997). This was important in the COMBINE (Core Outcome Measures in Brachial plexus INjuriEs) project. As discussed in Chapter 1, I have over 15 years of experience treating people with a BPI, in addition to previous involvement in research in the area. Section 4.4.5.3 discusses my sociological biography and its potential influence on the data co-constructed. This existing knowledge and experience inform the design of the study (Hunt, 2009), and reflecting on its influence aims to bring credibility to the study's findings. Finally, findings from interpretative descriptive studies can be triangulated with other data sources, including literature reviews or other quantitative research, to increase the depth and breadth of knowledge (Hunt, 2009; Thorne et al., 1997).

Reflecting the pragmatic aims and objectives of this study, I felt that the generic interpretative descriptive approach was appropriate to elicit outcomes important to patients with BPI, to understand why they are important and determine the scope and language used for the outcomes. Furthermore, the COMBINE project aimed to combine results from different data sources (interviews and systematic review) to inform the long list of potential outcomes. This method of using data from a range of sources aligns with the interpretative descriptive approach. In summary, the interpretative descriptive approach best suited the research question, rather than trying to fit the question to a particular philosophical stance (Caelli et al., 2003; Patton, 2014; Ritchie et al., 2013).

4.4 Methods

The data collection methods used for this study were face-to-face semi-structured interviews. Although there have been developments in patient and carer involvement in COS in recent years, there is no consensus on the most appropriate methods of identifying outcomes important to them (Kirkham et al., 2017b). Chapter 2 presents a full discussion on the different qualitative methods used in COS development and the methodological considerations associated with them. I chose face-to-face semi-structured interviews, as the open questions provided participants with the opportunity to answer in their own words. I wanted to use these words to name and describe the outcomes going forward to the Delphi, and hoped that this would improve clarity and understanding of the outcomes (Williamson et al., 2017; Young and Bagley, 2016). I also thought that using semi-structured interviews would help to access in-depth information about the outcomes important to patients, improving our understanding of the value patients place on them. Finally, I chose interviews over focus groups, as interviewing participants with a BPI may require discussing sensitive topics, which can be a deeply personal experience, and a focus group would not provide enough privacy. One-to-one interviews can facilitate open discussion, offering the opportunity for participants to reveal more deeply held beliefs.

4.4.1 Ethical considerations

The study was conducted in line with the Principles of Good Clinical Practice (GCP), the Department of Health Research Governance Framework, the Declaration of Helsinki and the University of East Anglia's Code of Practice for Research (NHS Health Research Authority, 2017; WMA, 2018). See section 4.4.5 for more details on consent. Solihull Research Ethics Committee granted a favourable opinion for all three phases of the COMBINE project: 18/WM/0297 (Appendix 4.2). Research governance approval for the COMBINE project was given by University Hospitals Birmingham Foundation Trusts (Reference number RRK 6535) (Appendix 4.3).

4.4.1.1 Patient safety and wellbeing

As the research required discussing potentially sensitive topics, it was important to ensure the safety and wellbeing of participants. Although unlikely, it was possible for participants to experience distress during the interviews. I placed specific attention on issues such as sensitive and open questioning, researcher self-disclosure and a comfortable interviewing environment. I am an experienced physiotherapist in the peripheral nerve service and had completed in-depth interview training prior to undertaking the interviews. The training helped increase my awareness of and put into practice skills such as active listening, open questioning, probing and designing topic guides. I encouraged participants to bring a family member with them to the interview if they felt they needed this support. The interviews were conducted in a location of the participant's choice, including their home. This lessened the burden of travel and expense of parking. Costs of travel and car parking were reimbursed if participants chose to have their interview at the trust.

A plan was put in place to support a participant if they became distressed. This included stopping the interview, offering support and signposting to relevant support groups, such as the national Traumatic Brachial Plexus Charity and Healthy Minds, or a clinical nurse specialist within the peripheral nerve injury service. During the interviews, three participants became distressed at their homes. If the distress was minor, then I reconfirmed consent prior to continuing the interview. If major distress was experienced, then the interview was stopped completely, and the patient signposted to support. I supported participants with signposting to relevant services

and through active listening. I offered to discontinue all three interviews. However, all participants wanted to continue with the interviews. One participant sought solace with a family member. On reflection, perhaps those interviews which took place in the participant's home were more in-depth, with participants feeling more comfortable to discuss their experiences in an open and honest manner. This may influence the choice of interview settings offered to participants with BPI in the future, to ensure open discussions.

4.4.1.2 Researcher safety

The safety and wellbeing of the researcher was an important consideration. The lone working directive from the University of East Anglia was consulted (https://my.uea.ac.uk/divisions/health-and-safety-department/health-and-safety-requirements/lone-working). This included scheduling interviews within office hours, informing a member of the clinical team at the Queen Elizabeth Hospital Birmingham of the location of the interview, and contacting the team on arrival and after completion of the interview.

4.4.1.3 Data protection and confidentiality

Data were collected and retained in accordance with GDPR 2018 (GOV, 2018) and GCP guidelines (NHS Health Research Authority, 2017). Recorded transcriptions were held on an encrypted device until downloaded on a password-protected computer. Transcripts were coded and depersonalised, with the participant's identifying information replaced by a pseudonym and categories for age and time since injury, ensuring no data were traceable to an individual participant. All patient-based data (paper and electronic) were securely stored in a locked filing cabinet and password-protected computers at the Queen Elizabeth Hospital Birmingham. As lead researcher, only I had access to personal data as necessary for quality control, audit and analysis. Only depersonalised data were accessible by other members of the research team.

4.4.2 Recruitment

The study took place between February and November 2019 in a peripheral nerve injury unit in an acute NHS trust in the United Kingdom (UK), where I was a clinical specialist physiotherapist. Participants for the study were recruited through two routes (clinic or database screening).

4.4.2.1 In-clinic identification

Potential participants having treatment for their BPI and attending the peripheral nerve injury clinic (Queen Elizabeth Hospital Birmingham) were identified and introduced to the study by several members of the peripheral nerve injury clinical team (i.e., the site physiotherapy lead, surgeons, specialist occupational therapist and specialist nurse). Potential participants were given a Participant Information Sheet (PIS), see Appendix 4.4, and the study was explained. If a patient was interested in being involved, they were asked permission to be contacted. I contacted the interested patients at least 24 hours after being given the PIS. It was hoped that this allowed the potential participants time to consider their participation and also to discuss it with their family.

4.4.2.2 Database identification

I screened the Peripheral Nerve Injury database (n = 205 BPI) for any patients who had been treated for a BPI at the Queen Elizabeth Hospital Birmingham in the last 10 years. Potential participants were sent a PIS (Appendix 4.5), asking them to contact me either via phone or email if they were interested in taking part.

If contact was made following either clinic or database identification, I discussed any questions by potential participants regarding the study. If at this stage a potential participant wished to proceed with an interview, I arranged a convenient time and place.

4.4.3 Inclusion and exclusion criteria

Participants were eligible for inclusion if they were 16 years or over with a BPI, had capacity and were competent to give consent. They were excluded if they had any other significant co-morbidities that could overshadow the BPI, e.g., traumatic brain

injury or other central or peripheral nervous system dysfunction affecting the upper limbs. Finally, they were also excluded if they were unable to communicate in English.

4.4.4 Sample

4.4.4.1 Sampling

A patient's experience of a BPI will vary greatly depending on a range of internal and external factors, such as age, sex, type of BPI, type of interventions received and time since injury. To ensure the breadth and diversity was captured, a purposive, "maximum variation sample" was sought (Coyne, 1997; Patton, 2014). This was important if the outcomes generated from the interview were to cover the spectrum of dysfunction associated with a BPI. A sampling framework (see Table 4.2) was constructed to reflect characteristics I thought were important, informed by carrying out a literature review exploring the epidemiology of a BPI (Faglioni et al., 2014; Flores, 2006; Jain et al., 2012). This served as a guide when I was recruiting participants for the study, and I used it to identify and approach participants who represented particular characteristics from the sample frame that were missing in participants recruited to date. This helped to generate a sample that encompassed most/all the characteristic identified from the epidemiology data.

Table 4.2 Maximum variation sampling table

	Sex		Site of injury			Management		Time since injury		Age		
	M	F	C5/C6	C8/T1	All	Sx*	Cons*	Short < 12 mths	Long > 12 mths	Young	Middle	Old
1	x				x	x			x	x		
2		x			x	x			x	x		
3	x				x	x		x		x		
4	x		x			x		x				x
5	x			x			x		x		x	
6	x			x		x			x	x		
7	x		x				x		x	x		
8	x		x			x			x		x	
9		x			x	x			x	x		
10		x		x		x			x		x	
11		x		x		x			x	x		
12	x				x	x			x		x	
13	x		x			x			x	x		

M = Male; F = Female; C5,6,7,8 = Cervical roots C5,6,7,8; T1= Thoracic nerve root 1; Sx = treated surgically, Cons = treated conservatively; Mths = months: Young = 16-40: Middle = 41-65: Old = 66 and over

4.4.4.2 Sample size

In both qualitative and quantitative research, sample sizes can affect the credibility of the results. Data saturation was used as the criterion for determining the sample size in this study, and when saturation was reached data collection was discontinued and analysis was stopped. The term saturation is a concept that was developed from grounded theory (Bowen, 2008; Glaser and Strauss, 1967) and refers to the point when further data collection fails to generate new information (Sandelowski, 2000). Although its origins lie in grounded theory (Glaser and Strauss, 1967), data saturation is used across a range of approaches to qualitative research (Saunders et al., 2018). The achievement of data saturation is an informed but nevertheless subjective decision made by the individual researcher or the research team. The nature of the topic, quality of the data and study design all influence when data saturation is reached (Morse, 2000). For example, if a topic is clear and in-depth data are collected through interviews or focus groups, then saturation may be achieved quickly (Morse, 2000). I undertook data analysis concurrently with data collection to facilitate the identification of data saturation and to inform future interviews. I identified data saturation when no new outcomes arose after coding the interviews completed to date.

4.4.5 Data collection

4.4.5.1 Interview process

At the interview, I reviewed with the participant, the purpose of the interview, intended used of the data and measures taken to protect confidentiality. Full informed consent (Appendix 4.6) was taken, and I reminded participants that they could withdraw at any time and that participation would not affect their usual care.

Interviews were conducted in private where possible to ensure openness. I was aware that my dual role as a PhD student and physiotherapist may have caused undue influence or a power imbalance during the interview. To minimise issues with this dual role, I didn't wear a clinical uniform for the interviews but clearly introduced myself as a PhD student conducting a research project. Participants may have been concerned that information would be relayed to the clinical team or included in their medical

notes, so I addressed these concerns and reassured participants that all information would be kept confidential and anonymous. As an active participant in the discussion and story being told, I provided whatever extra information was asked for, whether this pertained to disability income, advice on driving or on orthotics such as slings. Reciprocity and attempts to minimise power imbalances are characteristics of qualitative research methods (Oakley, 1981). I aimed to create a relaxed and comfortable conversation, engaging the participant with general, everyday conversation and asking a few background questions first, such as asking the participant their age and what they like to do with their time. These aimed to serve as 'warm up' questions as they are easy to answer. I informed the interviewee that there was no right or wrong answer, aiming to increase free speech. I took notes, documenting reactions by patients such as voice tones, facial expression and other non -recordable reactions, like tearful eyes or antalgic positions.

4.4.5.2 Interview topic guide

The COS literature acknowledges that it can be difficult for participants to understand the concept of outcomes (Biggane et al., 2019; Jones et al., 2017; Mathers et al., 2015; Williamson et al., 2017; Young and Bagley, 2016). Consequently, we agreed within the research team that the interview should focus on the experience of patients from which outcomes could be interpreted, as opposed to asking direct questions about outcomes. This is a method used previously in both COS (Keeley et al., 2016; Sanderson et al., 2010) and PRO measurement development (Ashwood et al., 2018).

I used a semi-structured approach, with questions directed by a topic guide (Appendix 4.7). The topic guide was informed by published research with a similar focus (Fish et al., 2017; Sanderson et al., 2010) and themes identified from a scoping review of published qualitative studies (Franzblau and Chung, 2015; Mancuso et al., 2015; McDonald and Pettigrew, 2014). Two members of the patient advisory group (PAG) also assisted with question development and piloted the interviews to ensure questions were clear and appropriate. See Appendix 4.8 for changes made following pilot interviews.

The interviews sought to gain a full picture of the patient's experience, so I asked patients about their life prior to the injury, the injury itself and their experience in

hospital. Once a better understanding of the context was developed, we discussed post-injury experiences, expectations of treatments and goals for the future.

Example questions included:

"How does the injury affect your normal day to day activities?"

"What were your expectations/goals with this treatment/s?"

"Why were these important?"

I explored specific outcomes with more direct questions and probes. Where possible, transcription and initial reading of previous interviews took place before the next interview. This allowed me to reflect on the interview technique and adapt the topic guide. My reflection on the interview technique helped to ensure future interviews were conducted more effectively.

4.4.5.3 Reflexivity

Qualitative data are a product of the relationship between researcher and participants (Berger, 2015). Reflexivity refers to the critical examination of the position of the researcher, including the role of prior assumptions and experience within the research (Finlay, 2002; Pope and Mays, 2013). Biographical positions, such as gender, ethnicity, class, race, sexual orientation, age, religion, (dis)ability, professional status, education and other dimensions of social differentiation of the researcher, will affect the interviewer-interviewee relationship and the nature of the data collected (Hammell and Carpenter, 2004). Depending on the research topic a researcher may be regarded as an "insider" or an "outsider" (Le Gallais, 2008). We have "insider" status when we share some aspect of the participant's identity, such as gender, or an "outsider" when we do not share identities with a participant. Researchers will often share both insider and outsider identities with a participant (Dwyer and Buckle, 2009). For example, I am an insider as I have many years' experience of treating patients with a BPI and have a deep knowledge of the injury from a clinician's perspective. This may influence my data collection, as participants may assume that I have knowledge that is not present. My experience of treating patients with BPI should, however, have helped to improve rapport and helped me to empathise. However, I am also an "outsider" as I have never

experienced a BPI and I am a middle-aged female, which is not the usual demographic for an individual with a BPI. This may influence the data co-created with young male participants, as what they might share with me would be possibly different to what they would share with a young male of a similar age in a different setting. This is because meanings are negotiated within particular social contexts and other researchers are likely to unfold different stories (Finlay, 2002). A brief biography is presented in Appendix 4.9.

To develop self-awareness of these intersubjective dynamics, it is recommended that researchers engage in reflexivity (Finlay and Ballinger, 2006). Practising reflexivity involves self-reflection on how the researcher's social background, assumptions, positioning and behaviour affect the research process (Finlay and Ballinger, 2006). Reflexivity does not just relate to data collection, but to the whole research process and can include keeping reflexive diaries throughout the process (Mays and Pope, 2000). This can make personal and intellectual biases clear at the outset of the research and enhance the credibility of the researcher's findings (Mays and Pope, 2000). Following each interview, I made notes on my thoughts and impressions on the discussion in a diary. I also used the diary during the analysis of the interviews. This helped me identify and reflect on biases and make changes. On a personal level I was aware that this research question had been developed because of my clinical experience with patients with a BPI. From this experience and from the literature, I understood that musculoskeletal and physical issues were being prioritised in the treatment of patients with a BPI. I had, however, had the experience of treating patients with emotional and psychological consequences from the injury. I recognised that I may have therefore prioritised the emotional experiences described by participants and tended to focus on them in interview discussions and analysis. However, discussions with supervisors, my reflections on the interviews and using the topic guide helped to minimise this bias.

4.4.6 Analysis

Analysis aims to interpret the data in relation to the research questions (Braun and Clarke, 2013), transforming data into findings (Patton, 2014). There are multiple different qualitative analytical approaches and the overarching methodology can dictate the analysis approach to be taken (Braun and Clarke, 2013; Patton, 2014).

The recommended methods for developing a COS are outlined by both the Core Outcome Measures for Effectiveness Trials (COMET) and OMERACT (Outcome Measures in Rheumatology) handbooks (Beaton et al., 2021a; Williamson et al., 2017) and are discussed in Chapter 2. Outcome domains are defined as broad concepts that group similar individual outcomes together. There are no existing guidelines on the best methods to identify outcomes or outcome domains from qualitative data. It is therefore the decision of the research team which analysis method suits the research question and study design (Beaton et al., 2021a; Williamson et al., 2017). For this study the definition of an outcome was something that was important to patients because of the BPI or its treatment. Outcomes from the COMBINE project were identified through thematic analysis, where the themes identified were linked to the research objective, which was to identify outcomes that are important to individuals with traumatic BPI. As such the themes identified were 'outcome domains' important to participants who had experienced a BPI.

Inductive thematic analysis (Clarke and Braun, 2018; Elo and Kyngäs, 2008) is compatible with interpretative descriptive methodology (Caelli et al., 2003; Kahlke, 2014; Thorne et al., 1997). Thematic analysis is a method for identifying, analysing and reporting patterns (themes) within the data (Braun and Clarke, 2019, 2013, 2006). Thematic analysis is also theoretically flexible, so it can be aligned with any qualitative methodology and is commonly used by researchers (Braun and Clarke, 2019, 2006; Clarke and Braun, 2018). A six-step approach is recommended for conducting thematic analysis (Braun and Clarke, 2013, 2006). These are presented in Table 4.3.

Table 4.3 Stages of thematic analysis

Phase		**Description of the process**
1	Familiarisation with data	Transcribing (if necessary), reading and re-reading the data, noting initial ideas
2.	Generating initial codes	Coding interesting features across the whole data set. Collate data relevant to each code
3.	Searching for themes	Collating codes into potential themes. Gathering all data relevant to that particular theme
4.	Reviewing themes	Checking if themes work in relation to the coded extracts and the entire data set
5.	Defining and naming themes	Ongoing analysis to refine the themes and overall story the analysis tells. Generating definitions and names for themes
6.	Producing the report	Selection of vivid and compelling data extracts, with final analysis of the extracts relating back to the research question and literature.

Taken from Braun and Clarke (2006)

Thematic analysis was conducted in the recommended stages. This analysis occurred concurrently with data collection. Initially, I familiarised myself with the data by actively reading the transcripts, trying to make sense of it. Each line was coded. Initially coding was semantic, identifying codes with obvious or superficial meanings. After the first three interviews I met with the research team (CJH and JC) and discussed coding in these initial transcripts. There was agreement that I needed to ensure that the analysis was in sufficient depth and latent codes were also captured. A latent code is one which is developed around implicit ideas (Braun and Clarke, 2019). Reading the transcripts, CJH and JC recognised that there may be assumed knowledge which was not explored because of my role as a physiotherapist, and there were potentially power imbalances at play which could be influencing the co-creation of the data. Reflecting on the interactions there were times when participants continued to see me as the 'health expert', perhaps by virtue of my training and experience. Some answers

were short, with phrases like “you know”. Perhaps participants assumed I had the ‘knowledge’. I too may have unconsciously taken on the ‘health expert’ role, assuming I had knowledge, which was evident through a lack of probing in early interviews. This discussion with the research team led to changes in future interviews where I was explicit about my role, and also I tried to become more aware of ‘assuming knowledge’ and probing appropriately.

The initial three transcripts were coded again and this time I made sure that semantic and latent codes were captured. Codes are a specific, single idea linked to a segment of data and consist of labels identifying what is of interest (Braun and Clarke, 2013). Some of these initial codes included ‘finger movement’, ‘straightening wrist’, ‘returning to work’, ‘doing hair’, ‘opening jars’, ‘the way the arm looks’, and ‘intensity of pain’. Transcript data related to each code were collated. After refinement, the codes were sorted into initial themes. Themes and associated codes were discussed with the supervisory team, finalised, and checked for appropriateness and their relationship to the research objectives.

4.5 Results

The results are described in relation to objectives: i) to identify outcomes important to individuals with traumatic BPIs; ii) to explore the language participants used to inform the next stage, and iii) to facilitate an understanding of why these outcomes are important.

Understanding the experience of living with a BPI is crucial to this research, and participants were generous with their stories. A recurring theme in the participants' narratives was around uncertainty. To pay sufficient regard to this narrative, a separate analysis was conducted, focusing on uncertainty, which led to a paper that was published in Disability and Rehabilitation in 2022 (Miller et al., 2022).

4.5.1 Recruitment

Invitation letters were sent to 32 potential participants from searching databases and past clinics. Five people were interested in taking part and contacted me following receipt of the letter. Of these five, all were eligible, but one decided not to continue with a face-to-face interview due to work commitments. A further 20 potential participants were approached in the peripheral nerve injury clinics by members of the clinical team. Nine registered their interest and were eligible to participate.

4.5.2 Study population

Of the 24 eligible patients, 13 consented to and participated in face-to-face interviews. Interviews lasted between 45 and 97 minutes. Eight participants chose to have their interview in their home and five interviews took place in a pre-booked room at the Queen Elizabeth Hospital Birmingham. Participant characteristics are summarised in Table 4.4.

Table 4. 4 Demographics of interview participants

Pseudonym	**Sex**	**Age category (years)**	**Interview timing (months)**	**BPI (supraclavicular infraclavicular)**	**Upper/lower/pan plexus**	**Surgeries**	**Mechanism of injury**
Jake	M	21-30	37-59	Supraclavicular	C5, C6, C7, C8 avulsion T1 in continuity lesion	Nerve transfer x2, FMT x1, Wrist arthrodesis	Motorbike
Amy	F	21-30	37-59	Supraclavicular	Pan plexus	Nerve grafts x2, Nerve transfer x2, FMT x 1	Car accident
Alan	M	31-39	< 12	Supraclavicular	C567 rupture C7, T1 avulsions	Neurolysis	Motorbike
Henry	M	71-80	< 12	Infraclavicular	Medial and lateral cord	Neurolysis	Shoulder surgery
Maurice	M	51-60	12-36	Infraclavicular	Posterior cord	No operation at time of interview	Dislocation
James	M	31-40	12-36	Supraclavicular	C8/T1 avulsions	Nerve transfer x1, Tendon transfer x1 MCP capsulodesis	Motorbike
Colin	M	31- 40	12-36	Supraclavicular	C5, C6, C7 avulsions	No operation at time of interview	Motorbike
Peter	M	41-50	12-36	Supraclavicular	C5/6/7 (upper)	Nerve transfers x5	Motorbike
Emma	F		12-36	Infraclavicular	Pan plexus (lateral and posterior cord)	Neurolysis x1, Nerve graft x1, Nerve transfer x1	Work accident

Pseudonym	Sex	Age category (years)	Interview timing (months)	BPI (supraclavicular /infraclavicular)	Upper/lower/pan plexus	Surgeries	Mechanism of injury
Valerie	F	51-60	37-59	Infraclavicular	Pan (posterior)	Tendon transfer x1	Dislocation
Sue	F	21-30	12-36	Supraclavicular	C8/T1 (lower)	Nerve transfers x3, Tendon transfer x1	Car accident
George	M	21-30	37-59	Supraclavicular	Pan plexus	Nerve graft x1	Motorbike
William	M	31-40	12-36	Supraclavicular	C5/6 (upper)	Nerve transfers x4	Pedestrian hit by car

4.5.3 Outcome domains identified (Objective 1)

Objective 1: To identify outcomes that are important to individuals with traumatic BPI

There were commonalities between the stories alongside components unique to each participant's story. From the patients' narratives, the following outcome domains were identified: physical symptoms, arm appearance, mobility and physical function, emotional and psychological wellbeing, returning to normal life and access to treatment. These outcome domains are described in Table 4.5.

Table 4. 5 Descriptions of interview outcome domains

Outcome domain	**Description**
Symptoms	Symptoms associated with the injury, such as pain and pins and needles. What participants hoped the treatment of these symptoms could achieve. Participant's perceived success or failure of the treatment.
Arm appearance	The appearance of their arm, for example the bulk of the muscles. What participants hoped treatment would achieve.
Mobility and physical function	Movement in the injured arm. How their injury also impacted on their physical function and ability to carry out everyday activities and tasks.
Emotional and psychological wellbeing	The emotional and psychological effects following a BPI.
Returning to normal life	The things participants described as important to them to return to a sense of normality.
Access to treatment	The experience of accessing treatment for their BPI.

4.5.4 Outcomes identified informed by patient language (Objective1& 2)

The outcomes identified within each domain are presented in Table 4.6, in the language used by participants where possible. Outcome descriptions in *italics* are taken verbatim from patient transcripts.

Table 4.6 Outcomes within each interview domain

Symptoms	**Arm appearance**	**Movement strength and physical function**	**Emotional and psychological wellbeing**	**Returning to normal life**	**Access and cost of treatment**
Pain	*Colour and position of arm*	*Movement*	Loss of identity	Driving	Information about treatment
Pins and needles	*Muscle bulk*	Physical function	*Self-confidence*	*Back to my work*	Waiting time for treatment
Lack of feeling		*Strength*	*Depression*	*Hobbies* and pastimes	Cost of attending treatment
Coldness of arm			Grief	*Looking after children*	
Sensitivity			*Stress*	*Money worries*	
Pulling and dragging			*Anxiety*	*Going out with friends*	
			Guilt/self-blame	Effect on wider family	
			Anger	Back to studying	
			Addiction		
			Hopes		

Outcomes in italics are taken verbatim from interview transcripts

4.5.5 Facilitate an understanding of why these outcomes are important (Objective 3)

The following sections describe the outcomes identified and interpreted from the data that facilitate an understanding of why these outcomes are important. The outcomes, in each domain, are highlighted in the text in **bold** and supported with illustrative quotes.

4.5.5.1 Symptoms

Many participants discussed how easing the **pain** was their main priority of treatment. However, at the same time they realised that complete removal of pain may not be achievable:

> *"Yeah, I would probably say the pain relief was the main thing ...but I don't know, I don't know whether, you see you don't know whether they can do anything for it. I mean they have given me the pills now, they just say keep taking them maybe up the dose. It is not an expectation that they can completely get rid of the pain, if anything I think just, you know just to keep it down a bit."* (Maurice)

In addition to pain, other symptoms such as **pins and needles** were often described and related to an increase in **sensitivity** (symptoms) in the arm. This may affect social interaction, such as shaking hands as described by Henry:

> *"It is like a very bad pins and needles you couldn't touch it, that is why when I shook your hand I always say 'do it gently' I have told you that one anyway because it hurts so bad."* (Henry)

Although most participants described neurogenic-type pain, which is related to injury to the nerves of the brachial plexus or avulsion of the nerve roots from the spinal cord, some patients also described a **pulling or dragging** pain. This pain was described as related to the heaviness of an arm that didn't have innervated muscles in the upper limb which would help to support the weight of the arm. The **pulling and dragging** pain was important to participants and taken into consideration when choosing treatments. In the extract below, Alan discusses how he rationalises choosing an amputation for his BPI, but also understands that this may not relieve the neurogenic symptoms:

> *"…. the right arm is pulling on the muscles and tendons and that kind of thing, so an amputation would halve my arm, halve the weight, that is how I see it as and probably lessen the pulling on my arm…. I don't know I don't think it would help with me feeling the pain in my wrist or my arm or anything like that or being cold umm but I think it would be that if it was chopped off it would help with the weight and pulling."* (Alan)

Pain was often linked with other outcome domains. Often participants discussed how the pain affected their everyday physical function and impacted on their identity within the family (returning to normal life):

> *"I am still doing nappy changing, I am still doing a little bit around the house but probably I could do more of it because it is, I get to a certain point of it and the pain just takes over what I am doing, its, I know it is kind of like trying to get your mind out of the situation that you are sitting there thinking about your arm but when you do something sometimes the pain goes and it will come back in like fifteen twenty minutes, sometimes it is five minutes, it depends, it is finding out..* "(Alan)

In addition, there were links between experiencing the pain and its effect on people's mental health (emotional and psychological wellbeing) – how it wore people down. Here James describes how the pain can get him emotionally:

> *"so I had taken tablets already, I can't take no more, the pain was that bad I actually got out of my bed and I started crying. I had to cry and my wife she woke up with me and she said 'James, what's wrong' I goes 'I can't, the pain is too much, the pain is too much."* (James)

Participants frequently discussed how **coldness** (symptoms) affected the pain in the injured upper limb and tried different methods to ease the impact of the cold. George discusses how he mitigates the effects of cold:

> *"Umm if it is the coldness it is kind of trying to warm it up, put it next to your body, sitting on it umm lying against it on the settee umm anything just to kind of warm the blood into the arm a little bit ….obviously I wear jumpers a lot, I have got biker sleeves, the push biker sleeves….It is like, I don't know it kind of just keeps it warm, it is like your underlay, you know the underlay for push bikers, where instead of just the chest bit, it is just the arm."* (George)

As a BPI affects the nerves that provide the sensation to the arm, many participants discussed how the **lack of feeling** (symptoms) was important to them. Valerie discusses below how the lack of feeling often resulted in injuries such as burns or cuts:

> *"….umm and as I say I mean I was at work, I was helping in the kitchen peeling the veg for Sunday lunch, we do it on Saturday and it wasn't until I looked and the blood was on the side and on the floor and I looked and I thought 'God' .But I didn't know I had done it, I didn't feel it whereas normally if you do that and it was quite a deep cut umm I mean it hasn't closed up yet and I have had plasters on it all weekend umm normally you would feel any cut with a sharp knife, you know straightaway so."* (Valerie)

4.5.5.2 Arm appearance

In this domain, participants described the look of their arm and their hopes and perceived success/failure of treatments in relation to appearance. Almost all the participants talked about the **muscle bulk** and how they would like treatments to improve this. They often used disparaging terms when referring to the muscle wasting in the arm, such as "piece of meat", "deformed", "dead" and "withered":

> *"Yeah so pretty much its mad, this, this from halfway up my forearm to my shoulder looks normal and then from the rest to my hand it all looks like bone, well skin and bone, it looks like I haven't been eating!"* (William)

Others discussed the **position of the arm** and how it didn't look like it could move. Some had accepted that they may not achieve active range of movement in the arm, but it was still important that the arm looked like it could move. Many hoped treatments would help with how the arm looked:

> "*Yeah the way it looks when I walk, that bothers me and I think as soon as the wrist bolt is straight it's not going to look so bad because it just naturally hangs like that. Yeah it just curls over like this yeah."* (Peter)

The arm appearance was a visible reminder of the accident and that participants had moved from able-bodied to disabled, a reminder of what they had lost since the accident and how their life had changed. Maurice discusses how it affected him emotionally (emotional and psychological wellbeing)*:*

> *"And the way it looks as well, like it just doesn't look right to me, to me I feel like I am an invalid, I really do I feel like I'm like an invalid I can't, it is hard. Can you imagine because I am a fit person, I am fit... you don't know how much it is frightening me and then I look at my hand and I look at my arm, especially why my hand is deformed [SOBBING] my hand is deformed."* (Maurice)

To many the general appearance of the arm could affect an individual's self-confidence (emotional and psychological wellbeing). Participants discussed how the general appearance made them less confident to go out in public and how they tried to hide their arm when they went out. Similarly, other participants discussed how intimate relationships were affected and they spoke about keeping parts of the upper limb covered up:

> *"Yeah it is not very nice watching your arm slowly rot away basically, it is not the nicest of things at all, and aesthetically the shoulder and things like that you know with err, obviously with girls and stuff it's, I don't like people seeing it to be honest (Peter)*

> *"Right, so do you do anything to cover it up, have you changed the way you dress?" (interviewer)*

> *"Well, I leave my T-shirt on to have sex!"* (Peter)

4.5.5.3 Movement, strength and physical function

Participants used the terms **movement, strength and function** interchangeably. The following definitions apply for the purpose of this analysis: i) movement – range of movement in the joints; ii) strength – the ability of the muscle to generate enough force to work against gravity, resistance or with repetition, and iii) physical function – the ability to carry out everyday activities and tasks.

The loss of neural innervation to upper limb muscles associated with a BPI has a direct influence on **movement, strength and function** and this in turn can affect return to normal life. Having **movement** was important to participants and often participants explained that it was important even if function was not improved:

> *"I would love yeah to have that, hand movement, even if I can't use it like before just any kind of movement I think."* (Amy)

But often the link between movement, strength and function was clear, as William describes it here:

> *"now there's an option for another operation which I am really hopeful about… because I think it will you know, because lifting my arm up it gets stuck down here, having that motion to be able to move it that way I will be able to reach higher up, you know I can reach the lowest shelf on the wall cupboards in the kitchen."* (William)

The functional limitations were focused to the upper limb, as would be expected with individuals who have experienced a BPI. Most participants discussed challenges with cooking and preparing food.

> *"I used to cook before, I used to cook yeah, I can't cook now. It is impossible for me to cook now, I tried, I will be honest with you, I have fried an egg."* (Henry)

Strength was important and often linked to grip and the ability to pick something up:

> *"Yeah, I can but they have got to be like a grippable thing like I can't, like I can grip something and hold it but if it's a big enough item I can pick it up with my hand but if it's a small item I can't literally like trying to pick it up, it just slips because I ain't got my strength."* (Sue)

Return of **movement** or **function** was a turning point in participants' recovery, which William discusses below:

> *"Because they're, you know it took a while before my bicep did come back, which it has now so and you know that was really the turning point when I could, when I could move my arm around a bit more and obviously by that time I'd got more practised at using my left-hand."* (William)

The lack of **physical function** often meant that participants relied on others to support them for a while with everyday activities. Valerie discusses how her daughter had to support her with daily tasks early after the injury:

> *"Umm she [daughter] came in every day, a couple of times a day, she would help me get washed and dressed, she would shower me if I wanted a shower, wash my hair, dry my hair, do my housework, change my bed, do my washing, do my ironing and get my evening meals ready."* (Valerie)

There was also a link between the emotional and psychological wellbeing and the loss of **function** experienced. Here, Peter discussed how frustrated (emotional and psychological wellbeing) he got when trying to complete a small task:

> *"I certainly wasn't the easiest person to be around after the injury, frustration is one of the biggest things and you are going out and you try and do the zip up on your coat and it can be infuriating until you get the hang of things."* (Peter)

Improving **strength** was also seen as important for other reasons. There was a recognition by some participants that getting stronger generally, not specific to the

affected limb, would help them return to normal and Peter discussed how he felt it would impact his emotional and psychological wellbeing:

> *"obviously if I couldn't find an office job for six months or whatever then obviously try and build myself back up to do the manual stuff umm it is a possibility, I used to keep myself fit, as I say kick boxing, Martial arts and stuff and err I need to get back a healthy body, healthy mind isn't it?"* (Peter)

Many participants viewed exercise as the key, alongside other treatments, to regain movement, strength and function and some were keen to expedite this part of their recovery:

> *"I do physio every week and they have given me some exercises that I have to do here and every morning I get up and I do them, yeah I think that is what has made this arm a bit stronger*" (Maurice)

In the main, participants felt that treatments (nerve transfers and surgery and physiotherapy) helped to improve their physical function, strength and movement:

> *"because before I had the nerve transplant my shoulder was, I couldn't do much because I would have to be carrying it all the time whereas I am now back at the gym now and that is brilliant." (Amy)*

4.5.5.4 Emotional and psychological wellbeing

Overall, most of the emotional and psychological wellbeing outcomes interpreted were negative feelings or emotions, such as a **loss of identity.** Some participants who were parents talked about the role reversal when their child had to start looking after them and when the impact of the injury meant their role supporting the family had changed:

> *" I had to be reliant on my daughter and you know I am so grateful she did everything for me that she did but at the time I kept thinking 'she shouldn't have to be doing this' you know, so it did make me look at it slightly different, I'm okay I'm over it all now umm but to have to ask for help constantly whoever it be I found it really hard, I don't like to ask for help I never have done in the past, I have always done everything for myself."* (Valerie)

Parents with younger children also felt the impact on their **role** and described the guilt they felt when unable to help with day-to-day parenting tasks:

> *"and I went to pick him up and I couldn't pick him up and it got to me because he is just, because that is something that I was doing that and then we went in the garden to play and I couldn't play with him, I couldn't play with him properly even though he was there."* (Maurice)

Some participants described how the injury had changed their whole being and it was difficult to come to terms with or understand who they were now. This loss of identity challenged their **confidence**:

> *"Umm well it's just made me more cautious of everything. It's really affected my umm, my confidence, it has sort of really, well I don't feel like me anymore. It's like the person I was before the accident they have gone. It's a constant sort of struggle now so I don't know, I don't know how, it's difficult for me being within myself, I can't judge do you know".* (William)

There was link between **self-confidence/vulnerability** (psychological and emotional wellbeing) and a participant's view of their arm appearance. They described how they felt susceptible to stares and comments from others, and how this frequently impacted on their confidence with going out and therefore returning to normal life was challenging:

> *"everyone would comment on it, I would have random people asking me about it and then they would ask about the arm so then that stops you wanting to go out, it makes you feel really low. I think the way it looks is really big and it is more for other people than you because when people come up to you and start asking it is hard, so I had plastic surgery done twice."* (Amy)

Some participants talked about suffering from **depression** and **feeling low** (psychological and emotional wellbeing) since the accident and the mental implications caused by thinking about what happened and what the future holds. For some, the depression manifested itself in suicidal thoughts. Peter described how he got so low that he attempted suicide:

> *"No you can't err the mental side of it was probably bigger than the physical side if I'm honest…. err yeah the mental health aspect is a very big part of it to the point where, to the point where one night I was in a hotel and I actually tried to hang myself with my jacket. A very dark place, I am okay now, I'm fine now and I am so glad it (the suicide attempt) didn't work, the arm, it ripped the arm off my jacket but err yeah it can take you to a bad place, and the mornings were the hardest I used to wake up and just cry because in your dreams you have got two arms and then you wake up and you realise."* (Peter)

Participants often used adjectives associated with death to describe their arm. One participant used the term dead to describe the arm, referencing that a part of his body had died. The **grief** experienced was discussed when people talked about their arm and what they felt they had lost:

> *"because it's kind of like you have kind of lost a part of your body, it is kind of losing yourself a little, it is like kind of, it is not a death but it is kind of one of them things where it feels like it, it is like a part of your body where you can't move it or do anything with it, it is like, so it is kind of hard, it is, I don't know it is one of them things, it is, as I say it is finding a way and then just go on with it."* (Alan)

Some people had experienced **stress** and **anxiety** since the accident. As most of the injuries were related to road traffic accidents, some participants' psychological effects were associated with being back in a car or on a bike again. Maurice discusses his anxieties when travelling now:

> *"Yeah it has been hard psychologically because especially on the road like if I am travelling somewhere and I see brake lights in front of me I get anxious like I literally have to be probably about ten cars away from the car in front of me for me not to be scared if you know what I mean because every time, and especially if I see a little white van in front of me that's, I just, it gives me flashbacks to when the accident happened because that is all I had seen was this guy pull out in front of me and then brake lights and then I sort of tried to dodge him and then…"* (Maurice)

Emma's psychological effects, including **anxiety** were crippling and limited her ability to return to normal life:

> *"I think everything scares me now, I don't want to ever get hurt again do you know what I mean so I can't walk into a lift because I am scared that I am going to get stuck in the lift or the door is going to close on me and trap me, do you know what I mean, I don't even want to be like that. If I'm in the car I feel like a lorry next to me is going to fall and crush us, so I overthink every situation now and then I will just shut myself off. You know I would rather stay in my room where I know I am not going to get hurt than go out and have a laugh."* (Emma)

A few participants talked about their **anger**. This was often directed at the BPI and why it happened to them, or its impact on their day-to-day life, as Maurice discusses here:

> *"you feel cheated don't you, it's like why me? I am an active guy in my forties and why take my arm off me? When you get these heroin addicts who just sit around doing nothing all day apart from going mmm, why not take their arm? You feel a bit like that you know but I don't know."* (Maurice)

4.5.5.5 Returning to normal life

Returning to a normal life was important to all participants. Normal life varied by participant, as did the extent to which they thought they could achieve it. Linked to this domain were the other domains of, symptoms, arm appearance, movement, strength and physical function and emotional and psychological wellbeing. Without improvement in these domains, it might be difficult for a participant to accept that they are able to lead a life as close to their pre-accident life as they would like. The ability to return to their **hobbies and pastimes** (returning to normal life) and often the resumption of **driving** again following the accident represented return of independence:

> *"No it's fourteen or fifteen months now since I have been able to drive. Err its, yeah it's a bit of a nightmare because I have always, since I was seventeen I have always driven, as soon as I was seventeen I passed my test, I have always driven and that's one of the things that did hit me quite hard to start with you know, having to rely on other people to take me places.* If *I can just get back to driving then I can be independent."* (Peter)

Participants talked about how the lack of physical function stopped them from returning to their **hobbies and pastimes**, and this affected them emotionally and psychologically:

> "It gets me down… It's the not being able to do stuff because up until my accident I loved doing things with my hands, that's what my thing was, doing things like building things." (James)

Participants frequently discussed their hesitance about **going out** because of their lack of confidence (emotional and psychological wellbeing) or because of feeling stigmatised because of other people's stares or intrusive questioning. However, for some like Alan, this got easier after the initial injury period:

> "*it probably did (stop me going out) in the first couple of months, because it is like 'how is people going to look at it and react to it.' Nowadays I just, if they ask they get told what I have done kind of thing or I just laugh and shrug it off because I can see someone kind of looking at me and I am like 'oh look all you want I am still me' kind of thing it is, it is society isn't it, they are just curious I think."* (Alan)

Returning to work or **education** had a positive influence on returning to normal life. Unfortunately, for many of the participants it had been challenging. Other outcomes identified in the thesis could hamper return to work or education. For example, participants discussed how physical function (movement, strength and physical function) could hinder the physical aspects of their job or individual did not feel psychologically able to return to work or education:

> *"I did electrical engineering and that's what we were doing, was building sector boards with solder and everything so I used to be able to do it and then obviously I couldn't do it and now it's just, I don't know it made me burst out into tears when I tried to do it so I just chucked it away."* (James)

One of the most talked about aspects of **returning to work** (returning to normal life) in the interviews was the lack of employer support and understanding. Participants felt at the behest of employers and the participant's choice of employment choice was restricted by other people's analysis of their ability:

> *"So I worked on a site where you know I couldn't maintain equipment, or big machinery, cranes and stuff like that, so obviously I couldn't go back and do that, so when I went back to work they had me on just ordering spare parts and doing all the paperwork side of things and then it was around this time last year they called me in and said 'well we have had Occupational Health out here you are not going to get better any time soon, we have found you a new role to do for work, you either do this or you walk."* (Jake)

Returning to work was very important to many participants and prioritised because they felt that the routine would help their emotional and psychological wellbeing. The social aspect of being at work was also acknowledged, as discussed by Jake:

> *"Yeah, yeah getting back to work, having had lots of banter with some of the blokes and that do you know what I mean it's -? Being normal and just being around to talk with them, what you are used to. That's what I miss."* (Jake)

Many participants had not been able to return to their previous role at work and this affected them psychologically. Peter discussed how the inability to 'return to work' resulted in isolation which affected his mental health (emotional and psychological wellbeing):

> *"since this injury I do drink a lot and most of that is boredom I think, when you are used to working 50 hours a week and I get, and I would go mental if I am sat in this flat for too long on my own I will go mental you know."* (Peter)

4.5.5.6 Access to treatment

Overall, participants had quite negative experiences regarding their immediate care and diagnosis following their injury. They often struggled to access clear **information** about diagnosis and treatment. This was frequently down to staff's inexperience and lack of knowledge regarding appropriate care following a BPI and was apparent across disciplines. When meeting non-specialist healthcare professionals, many participants noted their lack of knowledge about BPI and the participant's needs:

> "*Yeah I was taken to [name of hospital] first umm but they wasn't, they wasn't very clued up and they thought that I had just got breaks."* (Emma)

Similarly, Peter discusses how his GP did not have appropriate knowledge of the injury to support him:

> *"I don't think my GP even knows what it is, they haven't got a clue, I talk to them about it and you know I say about working and they are like 'and you could answer phones, use a keyboard' so, I'm in constant pain all the time you know, you are not getting up for work when you are lying in bed all night trying to sleep."* (Peter)

Sometimes, although participants were seen by specialist clinicians, clear **information** was not accessible to them. Alan explained how he couldn't understand what the health professionals were talking about:

> *"It is just confusing, there is so much, you hear all these words bounced around…They are not the words I understand! You know I didn't understand it, the err the extent of the injury, I think that could have been explained a little bit better to me to be honest, but apart from that all the care I received there was top notch."* (Alan)

Because participants struggled to access clear **information about diagnosis and treatment** from health professionals, they often sought health information themselves through online resources or other avenues:

> *"Umm I was pretty much in the dark as to how much it would help umm I knew it would give me a little bit of movement but not too much umm but yeah it was kind of, I was still kind of like in the dark at the time, it was, and still quite new so it was like researching, doing stuff but obviously there was nothing coming up."* (Alan)

This lack of information sometimes led to assumptions by the participants that there would be no recovery and that drastic treatments such as amputations should be considered:

> *"… there was a period I think after about the second month when there was no, still nothing, umm I actually considered 'if it is not going to get better I might as well have it taken off'."* (Valerie)

Some participants also talked about how they **waited for treatments** for a long time and found it difficult to access the right treatments:

> *"Yeah I think I was feeling quite low about it all and then, so I went to my GP but I was told I had to wait about 12 weeks for that and then I had a phone assessment, then I had to wait another few weeks but she said she wanted me to wait because he was really good but there is quite a wait isn't there?"* (Amy)

4.6 Discussion

The objectives of this study were to i) identify outcomes that were important to individuals with a BPI, ii) explore the language participants used to inform the next stage and iii) facilitate an understanding of why these outcomes are important. We identified 32 outcomes important to participants. These were grouped into six outcome domains: a) symptoms, b) arm appearance, c) movement, strength and function, d) emotional and psychological wellbeing, e) return to normal life and f) access to treatment. As the analysis progressed it became clear that there was overlap and connections between many of the outcome domains and outcomes. For example, there was a clear link between the appearance of the arm and psychological wellbeing, such as self-confidence. In the following section each domain will be discussed in the context of the literature and to facilitate a deeper understanding about why each domain is important to people with a BPI. I will then discuss the use of patient language to inform the outcomes, and finally consider the strengths and limitations of the study.

4.6.1 Symptoms

In the symptom's domain, pain was frequently discussed as an important outcome for patients. This is recognised within much of the BPI literature (Brown et al., 2018; Htut et al., 2006). The causes of pain are varied and it is common for patients to describe both neurogenic and nociceptive pain (Brown et al., 2018; Franzblau and Chung, 2015; Wellington, 2010). Neuropathic pain is often linked to nerve root avulsion (Htut et al., 2006). However, all participants in this qualitative study experienced pain irrespective of whether a nerve root was avulsed or not. Participants spoke about how pain "just takes over" and interferes with everyday activities. They discussed the impact pain had on mental health and described how it got them "down". This link between neuropathic pain (including paraesthesia) and anxiety and mood disorders is well established in the literature (Radat et al., 2013). Similarly, the pain may be a reminder of the traumatic incident and contribute to post-traumatic stress (Soberg et al., 2015), which was also described by some participants. This qualitative study's findings underline the wide-ranging impact of pain on people with a BPI, illustrating its multidimensional nature and helping us understand why it is important. Despite this,

only 36% of included studies in the systematic review (Chapter 3) measured and reported pain, highlighting perhaps that researchers and clinicians do not prioritise it as important to measure. It was important, therefore, that this outcome and its multidimensional aspects were reflected in the long list which informs the Delphi.

4.6.2 Arm appearance

How the arm looked was important to all of the participants. Participants discussed how they would like the arm to look “normal” or to look “like it moved”. The upper limbs, and specifically the hands, are a significant part of perceived body image contributing to communication and function (Hannah, 2011; Lundborg and Rosén, 2007). Traumatic peripheral nerve injuries, including BPIs, can result in long-term cosmetic changes (Grunert et al., 1988). In this study participants frequently talked about “hiding” their arm when in public places to avoid “stares” and unwanted “comments”. Patients also discussed how because of their self-consciousness, they purposefully avoided social and professional public situations. This has been found in other BPI qualitative studies (Franzblau and Chung, 2015; Verma et al., 2019). Brito et al. (2019) also identified how self-consciousness can affect social relationships and particularly a person’s confidence. Despite this outcome frequently being highlighted by patients in lived experience studies, the appearance of the arm or muscle wastage is very rarely measured in BPI studies (Dy et al., 2015; Miller et al., 2021). It is clear from these wide-ranging effects that the appearance of the arm is important to participants and should inform the ‘long list’.

4.6.3 Movement, strength and physical function

Movement, strength and physical function were important to all participants and discussion of these outcomes were present across all the interviews. A BPI involves a disruption to the nerves that provide movement, strength and function to the upper limb, often resulting in paralysis or semi-paralysis, so this finding was not surprising and often the reason cited for seeking treatment. However, there were variations in the types of movement and functional limitations important to participants. This may be attributed to several factors, such as the type of injury experienced (those experiencing a more severe injury will have less motor recovery), variation in time

from injury to interview, or perhaps the impact of interventions. Most of the discussion around movement and strength were related to functional tasks, and participants rarely talked about strength in isolation. This is similar to findings in a recent focus study including adults with BPI (Brown et al., 2018). Most participants cited activities related to gross movement of the arm and essential activities such as self-care and preparing food as those which impacted their life. This echoes findings by McDonald and Pettigrew (2014) during interviews of 10 male participants with a BPI. They generated a theme called 'all the little things', relating to dressing, washing and eating. In concordance with this study, dependence on others because of functional limitations was also highlighted in a phenomenological study with five Australian men with a BPI (Brito et al., 2019). Participants in both Brito et al.'s (2019) and this study reported how the inability to complete simple self-care tasks meant dependence on others and a feeling that they had taken a "backward step in life". It is suggested in other trauma literature (Johnson et al., 2016) that this dependency can make patients revert back to a child/parent relationship, unable to make their own decisions, and with diminished self-efficacy (Franzblau and Chung, 2015). Although range of movement and strength are measured frequently in studies evaluating interventions in adult BPI, only 23% of studies measured physical functioning (Chapter 3). Physical function was very important to participants because of its impact on routine everyday tasks but also its impact on their roles, whether at home or in wider society. The significant impact of physical dysfunction on a patient with a BPI made it undoubtedly an important outcome domain.

4.6.4 Emotional and psychological wellbeing

Psychological symptoms can have a big impact on other BPI outcomes and vice versa. All patients cited effects of the BPI on their mental health, with a spectrum of depressive, anxiety and anger symptoms. Some participants discussed how they considered suicide. Due to the nature of the BPI injury and the feelings of uncertainty about the future, it is not uncommon for patients with BPI to experience depression or other psychological symptoms (Brito et al., 2019; Franzblau et al., 2014; McDonald and Pettigrew, 2014; Wellington, 2010). This is also evident in the wider upper limb peripheral nerve injury literature (Ashwood et al., 2019; Chemnitz et al., 2013). Indeed,

over one third of patients with a BPI report symptoms of depression (Franzblau and Chung, 2015). Similarly high levels of psychological distress are seen in patients who experience major trauma from road traffic accidents (Soberg et al., 2010). These psychological effects were important to participants, as they impacted on their ability to return to everyday life. The symptoms affected their ability to leave the house, go out in public and their interactions with others, such as family and friends. Despite this, only 29/132 (22%) of BPI studies in the systematic review (Chapter 3) evaluated any emotional or psychological outcome. This evidences perhaps the difference between clinician and patient priorities. It was important, therefore, that the patients' voices from this study were carried forward to the long list, to include the scope of the domain reflected by the different psychological and emotional outcomes identified in this qualitative analysis.

4.6.5 Returning to normal life

Patients discussed challenges with returning to normal life. All participants had expectations related to work and returning to hobbies, which were key to rehabilitation and resuming normal life. The findings that some patients returned to the job they had had before the accident and some to different jobs is supported by research by Brito et al. (2019) and Franzblau and Chung (2015). A return to work may be dependent on the patient's physical ability, psychological health and the support of employers. The latter cannot be underestimated and a lack of support can mean the difference between a patient returning to work or not (Brito et al., 2019). Some participants talked about discrimination based on their physical abilities, and this was echoed in work done with BPI patients in Ireland (McDonald and Pettigrew, 2014). The issue of employment is an important one, as patients diagnosed with a BPI are usually of working age. The fact that the injury is more commonly associated with men can also affect the type of work they may wish to take. The capacity to work is important to a person's self-esteem, provides a sense of control, financial independence, and also a structure for the day (Johansson and Tham, 2006). Participants in this study echoed this sentiment, discussing how work was more than just a job to go back to. They talked about how the social relationships at work were very important. This concurs with experiences of people following traumatic brain injury (Johansson and

Tham, 2006). Returning to work and leading a "normal life" were cited as very important goals for individuals with a BPI. However, in the systematic review in Chapter 3 only 25% of studies measured any aspect of role functioning. Again, it highlights, perhaps, the disparity between patient and clinician priorities.

4.6.6 Access and cost of treatment

Participants in this study highlighted how important it was to have access to treatment. Participants discussed how they were frustrated with delays in diagnosis, confused about ongoing loss of movement, persistent pain and "words" they didn't understand. Lack of awareness of this rare injury by non-specialist healthcare professionals, or the presence of other major injuries masking the BPI, may have contributed to the lack of information, leaving patients feeling "in the dark". Participants sometimes said that if they had been seen or referred quicker, they would have had better outcomes. They also found that the delays led to unnecessary "stress" and "worry". This is consistent with previous research (Brito et al., 2019; McDonald and Pettigrew, 2014) in Australia and Ireland, where participants with a BPI identified that concomitant injuries were prioritised. Delays or missed injuries in polytrauma are recognised as a challenge (Pfeifer and Pape, 2008), and for patients with a BPI delays in diagnosis and onward referral results in poorer functional outcomes (Hems, 2015b; Martin et al., 2019). Wider research in other rare diseases identifies that delays in diagnosis contribute to uncertainty for patients (Nutt and Limb, 2011). It is important to minimise these delays if services are to improve both clinical outcomes and reduce uncertainty for those with BPI. The systematic review in Chapter 3 did not identify any study measuring any outcome in this domain. It was important, therefore, that the outcomes identified here, such as access to and cost of treatment, were taken forwards to the long list.

4.6.7 Using patient language to inform wording of outcomes for the Delphi

I aimed to use words from the patient interview transcripts to inform the wording of outcomes for the Delphi. Although the language from patient transcripts informed the wording of many outcomes, for others it did not. For the outcome 'sensitivity', no participant used this word. However, one participant discussed how "you couldn't

touch my hand … because it hurt so much". This was interpreted as sensitivity. Participants frequently used metaphors to describe the outcomes and how they impacted on them. For example, when one participant talked about not having access to information, they talked about "feeling in the dark". When participants talked about the arm appearance, they often spoke using very negative language, with one participant describing their arm as a "piece of meat" and others using words like "dead" or "deformed". The language was emotionally laden and illustrates the impact on an individual of muscle wasting, lack of function, and limited access to information and treatment. However, there was a need to interpret some of these phrases into language that would be more appropriate to inform the long list for an international Delphi. More information on how the long list was developed is presented in Chapter 5.

4.6.8 Strengths and limitations

One of the strengths of this study is the use and reporting of an underpinning qualitative methodological approach, which can help the reader to understand how the research aims and questions were explored (Tong et al., 2007). The decision to use interviews to elicit outcomes, which gave participants time and opportunities to give detailed information about their injuries and how they impacted their life, is a strength of the study. The elicitation of the rich data co-created here would have been unlikely with other methods, such as focus groups. It is acknowledged in the COS literature that it can be difficult for participants to understand the concept of outcome (Jones et al., 2017; Keeley et al., 2016; Young and Bagley, 2016). Other COS developers incorporating qualitative work advocate the benefit of asking experiential questions for which outcomes can be interpreted, as opposed to direct questions about outcomes (Keeley et al., 2016; Sanderson et al., 2010). For the COMBINE project the topic guide was designed with members of the patient advisory group to encourage an experiential narrative from the participants.

One limitation is that the study was conducted in one tertiary specialist centre for BPI in the UK, and this may not be representative of patients from other geographical areas or those being treated in other settings. A possible limitation of using one semi-structured interview is that participants' priorities may have changed as time

progressed. It was difficult to elicit evidence for a temporal shift in the outcomes that mattered using one interview at a single time point. My lack of previous experience as a qualitative interviewer may have affected the data produced. However, by attending interview training, and discussing and reviewing interview transcripts with my supervisors, I hope to have compensated for my lack of experience. Indeed, after the first three interviews, the transcripts were discussed with my supervisors and at this stage there was evidence that prompting was limited because of assumed knowledge between the researcher and the interviewee. Following this meeting I became more aware of this issue and prompted participants to elaborate and thus create richer data.

4.7 Conclusion

The findings of this qualitative study highlight the outcome domains and outcomes that are important to adults with a BPI. The outcome domains and outcomes were used to inform the development of the COS-BPI.

In addition to identifying the outcomes important to adults with a BPI, the qualitative study explored why these outcomes were important and determined the scope of outcome domains to ensure breadth was taken forwards to the Delphi. Appropriate language used by participants in the interviews was used to inform wording of the outcomes in the subsequent consensus process.

The next chapter will present how the outcomes from the systematic review and the interviews were merged into a long list of outcomes, informing the development of the online Delphi. It will also present the methods, results and discussion of the international online Delphi study.

Chapter 5 Consensus development to inform an international core outcome set in adult traumatic brachial plexus injury

5.1 Introduction

In this chapter outcomes from the systematic review (Chapter 3) and patient interviews (Chapter 4) will be brought together to inform the content of a Delphi. This chapter details the methods, results and discussion of an online 3-round modified Delphi, and final consensus meetings to develop a core outcome set (COS) for adults with a traumatic brachial plexus injury (BPI). The methods reported here also highlight any deviations from the published protocol (Miller et al., 2019).

5.1.1 Aim and objectives

This phase sought to achieve consensus on a COS for use in clinical practice and research for adults with BPI.

Specific objectives were to:

i) create a comprehensive 'long list' of outcomes to inform an international online Delphi (step 1)

ii) prioritise these outcomes from the perspectives of patients, healthcare professionals (HCP) and researchers (step 2)

iii) obtain consensus on a minimum set of the most important and relevant outcomes for evaluating and reporting in adult BPI research and routine care (step 3).

5.2 Methods

The consensus process involved three steps. Step 1 involved the development of a survey questionnaire including a long list of outcomes. In step 2, international HCPs, researchers and patients prioritised outcomes in terms of importance in a 3-round Delphi. Finally, step 3 involved consensus meetings to agree on the most important outcomes and the final COS-BPI. The following sections detail the methods of each of these steps.

5.2.1 Step 1: Creating a long list of outcomes

The subdomains identified in the systematic review (n = 54) and outcomes from the interviews (n = 32) were combined to make a long list of outcomes. I categorised the long list of outcomes into a taxonomy developed to support COS generation (Dodd et al., 2018) and presented it to JC and CJH during a face-to-face meeting. The team then reviewed all outcomes in each of the taxonomy's domains. Where outcomes were similar, they were combined to be taken forward into the Delphi questionnaire as an item. Categorisation completed at this meeting included all domains except 'adverse events/ complications', 'nervous system' and 'emotional functioning'. I met separately with a neurophysiologist, a peripheral nerve surgeon and a psychologist to support the categorisation of outcomes in the neurophysiology, adverse events/ complications and emotional functioning domains respectively.

One challenge I encountered during this step was deciding on the "granularity" of the subdomains. Outcome domain "granularity" concerns how broad or narrow a researcher defines the domains (Williamson et al., 2017; Young et al., 2019a). For example, one researcher may include all definitions of a specific outcome under one term (for example, pain), while others seek a narrower and more specific categorisation into pain intensity, pain frequency, pain duration, interference with work, interference with sleep and interference with mood. In Delphi surveys, too many subdomains (items) result in the list becoming too long, which has been shown to reduce the number of completed surveys (Gargon et al., 2019a). On the other hand, a very restrictive method may exclude key outcomes. In the absence of guidance on how narrow or broad the outcomes should be, I aimed for this Delphi to be inclusive of

subdomains but to limit the items to fewer than 100, in line with other COS (Fish et al., 2018; Retzer et al., 2020).

5.2.2 Step 2: Delphi survey

5.2.2.1 Ethics

Solihull Research Ethics Committee and the Health Research Agency had previously granted a favourable opinion for the whole Core Outcome Measures in Brachial plexus INjuriEs (COMBINE) project, including this phase; 18/WM/0297 (Appendix 4.2). Participants received an anonymous identifier number (e.g., study ID COMBINE001) once registered. The study ID code linked to participants' responses. Only the Chief Investigator had access to the data that linked the stakeholder to their responses. The data were kept in a password-protected PC on an NHS (National Health Service) computer at the Queen Elizabeth Hospital Birmingham.

5.2.2.2 Question generation

The final subdomains became the questionnaire items. The questions and items were designed following reviews of previous Delphi studies (Coulman et al., 2016a; Retzer et al., 2020) and with advice from the COMBINE patient advisory and clinician advisory groups and research supervisory team. Where possible, I used lay wording, using language from interview transcripts. The corresponding medical terminology was included in parentheses. Combining plain language and medical terminology is recommended to improve the accuracy of item interpretation and content validity in questionnaires including HCPs and patients (Macefield et al., 2019). Three patients reviewed early drafts of the items for the questionnaire and guided revision of the language. The neurophysiology domains (reinnervation) were challenging to define in lay language, and with patient feedback, I used: "The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm". However, patients also wanted to include "nerve/electrical tests", as they felt the measurement of this outcome was easier to understand. As the objective of the Delphi was to prioritise outcomes and not outcome measurement instruments, we compromised and used 'nerve tests' in parenthesis to make it clearer to all participants. Therapists also

commented that having lay language clarified the outcome for them, illustrating the benefit of using lay terms in everyday communication in BPI care and research.

5.2.2.3 Response scale and rounds

The type of rating scale used in a Delphi can influence the results (Krosnick and Presser, 2009). Some studies have reported increases in reliability from 2 to 7 response options (Komorita and Graham, 2016; Preston and Colman, 2000; Simms et al., 2019). Indeed Alwin and Koswick (1991) identified that 9-point scales demonstrate maximal reliability. There is also evidence that respondents prefer 7- and 9-point response options (Preston and Colman, 2000). However test-retest reliability reduces when there are more than 10 response options available (Preston and Colman, 2000). In Delphis for COS development, qualitative work has identified that although some patients prefer the 9 response options, others struggled with it (Biggane et al., 2019). This evidence is generally supportive of the scale chosen in the current study. However, ultimately the 9-point scale was chosen because it is recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group to assess the importance of evidence (Guyatt et al., 2008). It is also the scale used in Delphi Manager, a web-based system designed by the Core Outcome Measures in Effectiveness Trials (COMET) Initiative (Williamson et al., 2012a) for facilitating and managing e-Delphi surveys https://www.comet-initiative.org/delphimanager/.

In each of the three rounds, participants rated the importance of each outcome on a 1 to 9 scale, described as: not important (1-3); important but not critical (4-6); and critical (7-9). An 'unable to score' option was provided for participants to indicate if they did not have an opinion about an outcome. This may be because the outcome is unknown to them, for example, if a HCP had not come across it in their practice. Some studies report that infrequently occurring items can be omitted to keep the Delphi list manageable (Green et al., 1999; Whitman, 1990). However, this goes against the basic tenets of the Delphi technique (Hasson et al., 2000). Participants themselves should judge items in terms of importance, not the researchers.

The number of Delphi rounds varies across different COS development studies. Usually, COS studies contain two (Fish et al., 2018; Retzer et al., 2020; Tyler et al.,

2020) or three rounds (Damhuis et al., 2020; Evangelidis et al., 2017; Smaïl-Faugeron et al., 2013; Taylor et al., 2008). However, wider Delphi literature suggests that three rounds are needed to achieve consensus (Brooks, 1979; Cyphert and Grant, 1971; Ludwig, 1997). I chose a 3-round Delphi to give participants the chance to first reflect on their peers' viewpoints in round 2, before being invited to consider the viewpoint of their stakeholder group and that of the other stakeholder groups in round 3. This is recommended practice in COS Delphi studies (Brookes et al., 2016), as it is thought to improve agreement between stakeholder groups. I anticipated a diversity of opinions across BPI experts, as was seen in previous COS Delphi studies, where subgroups of HCPs and patients prioritised different outcomes (Coulman et al., 2016b; Fish et al., 2018; Potter et al., 2011). Time to reflect and "trying to understand the importance of an outcome from the perspective of another participant" are important drivers of score change (Fish et al., 2020, p119). Indeed, there is evidence that HCPs are highly influenced by patient scores in Delphi feedback and frequently change their ratings as a result (Fish et al., 2020). Taking all of this into account, I therefore chose three rounds to maximise the likelihood of reaching consensus. Figure 5.1 illustrates the layout of the questionnaire for one domain page.

Figure 5. 1 Example page from electronic Delphi questionnaire

Questions on physical signs

Please do not use the browser's back button.

You have answered: 0 out of 68 Outcomes **Page 1 of 17**

This page lists physical signs that may be affected before and after a treatment for a traumatic brachial plexus injury.

Some of these signs may get better after treatment. Some may get worse or remain the same. Please note these are only possibilities and do not occur in everyone. If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the *'feedback'* box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Outcome	Not important			Important but not critical			Critical				
	1	2	3	4	5	6	7	8	9	Unable to score	Provide Feedback
Physical signs (movement, strength and ability)											
Voluntary movement of the arm	○	○	○	○	○	○	○	○	○	●	☐
Passive/ assisted movement of the arm	○	○	○	○	○	○	○	○	○	●	☐
Strength of muscles in the arm	○	○	○	○	○	○	○	○	○	●	☐
The physical appearance of the arm	○	○	○	○	○	○	○	○	○	●	☐
Reaching, pulling, pushing, turning or twisting with the arm	○	○	○	○	○	○	○	○	○	●	☐
Carrying and lifting objects	○	○	○	○	○	○	○	○	○	●	☐
Fine hand movement	○	○	○	○	○	○	○	○	○	●	☐

Please note: You will only be able to save/move to the next page if you have answered ALL the questions on this page.

Save and exit

Next Page

5.2.2.4 Piloting the questionnaire

Delphi studies should be piloted (Jairath and Weinstein, 1994; Williamson et al., 2017), but few general Delphi or COS Delphi researchers report undertaking piloting (Barrington et al., 2021; Clibbens et al., 2012; Keeney et al., 2001). Delphi piloting was necessary for this study as people with a BPI and HCPs were the participants and it was important that the information in and design of the Delphi were accessible and enabled views of all stakeholders (Hui and Stickley, 2007). Pilot studies can ensure greater rigour in the design of first-round questions (Mead and Moseley, 2001), which is particularly important as the questions in the first round are the basis for subsequent rounds. Specifically for COS development, Williamson et al. (2017) suggest piloting can help refine outcome labels and explanations. Finally, the choice of feedback is also important to pilot, as there is no clear guidance on the best methods to present results between Delphi rounds to stakeholders (Barrington et al., 2021; Fish et al., 2020).

The aims of this pilot were to:

i) review presentation of the questionnaire and wording and order of questions

ii) refine labelling and descriptions of outcomes

iii) identify the best method of between-round feedback.

The questionnaire was piloted in two stages:

i) Think-aloud interviews

One patient (patient advisory group member), surgeon and therapist (clinical advisory group member) were invited to take part in individual “think-aloud” interviews (Collins, 2003). Think-aloud interviews are frequently used by survey researchers to test questions and identify areas not understandable by the respondent population (Collins, 2003; Drennan, 2003). During a think-aloud interview, the respondent verbalises his/her thoughts in response to each question while completing the

questionnaire. The findings can give insight into whether the questionnaire makes sense to the user and can inform changes, such as rephrasing instructions, questions or items, or removing items (Collins, 2003; Drennan, 2003).

I recorded the interviews and asked each participant to read the questionnaire and verbalise their thoughts on the structure, the wording and their understanding of each section. Each participant was also provided with an example of two feedback methods: percentage of stakeholders allocating an outcome a certain rating (1-9) or a histogram of the range of votes for each outcome (per stakeholder group) and asked if they understood these and which they preferred.

ii) Piloting of the Delphi

The approach in the pilot study used elements of purposive and convenience sampling. The sample was purposive in that the volunteers all met the predefined criteria of the full study. It was convenient because each expert participant was already in contact with the researcher. This resulted in one occupational therapist, one specialist nurse, two brachial plexus surgeons and two individuals with a BPI agreeing to take part. The six participants were emailed the link to the Delphi with the invitation letter on 6th February 2020.

Each pilot participant completed the registration page and rated each of the outcomes within round 1 of the Delphi. They could also add comments or any extra outcomes that they felt were important to be included in the Delphi. Attached to the invitation to join the pilot Delphi was a Word document with a form to review the Delphi (Appendix 5.1). Feedback on the introduction and registration page, each domain page, the time taken to complete it and other comments were collated. Appendix 5.2 gives full details of results and any changes made after the pilot.

5.2.2.5 Participants

The composition of panels in Delphi studies can influence ratings (Campbell et al., 1999; Macefield et al., 2013) and heterogeneity is preferred to homogeneity to ensure different opinions are included on a topic (Black et al., 1999; Hong et al., 2010). Good practice standards (Kirkham et al., 2017b) for COS development highlight the importance of including representative stakeholders throughout the COS development

process. Chapter 2 discusses the importance of the patient voice in COS development in detail. It was important that people with a BPI participated in this Delphi, otherwise there was a risk that outcomes important to them would be overlooked.

It is anticipated that the COS-BPI will be used in future national and international BPI studies and clinical practice, therefore the target population for participation included three distinct international stakeholder groups:

- adults (over 16) with a BPI
- nurses and therapists involved in their care/research
- BPI surgeons and researchers.

The surgeons, therapists and nurses were clinicians working with patients with adult BPI at any point along their care pathway. Having separate stakeholder groups for surgeons and therapists/nurses facilitated analysis between the two groups, as previous COS developers identified that different HCPs prioritise different outcomes (Coulman et al., 2016b). All participants needed to be able to read English and have access to the internet to complete the Delphi.

5.2.2.6 Sampling

There is no standard sample size for COS Delphi surveys (Sinha et al., 2011; Williamson et al., 2017). Sample size is not based on statistical power (Powell, 2003), but is often dependent on the number of patients or experts available within the scope of the COS being developed (Williamson et al., 2017). A minimum of 10-18 participants per expert group has been suggested (Brookes et al., 2016; Okoli and Pawlowski, 2004). However, the more participants representing each stakeholder group, the better in terms of reliability and accuracy (Dalkey and Helmer, 1963). Larger Delphi sample sizes also increase the generalisability of results to future patients and could convince stakeholders of the COS's value (Williamson et al., 2017). Retention rates need to be considered when deciding on sample size. Retention rates are variable between different international COS Delphi, ranging from 19.5 to 87.1% (Hall et al., 2018). High attrition can result in attrition bias, which occurs when the participants who do not respond in subsequent rounds have different views from their stakeholder peers who

continue to participate. If a participant receives feedback suggesting they are in the minority regarding their scoring, they are more likely to drop out, leading to over-estimation of the degree of consensus (Bardecki, 1984; Humphrey-Murto and de Wit, 2019). BPI is a rare injury, with HCPs and people with the injury invested in the management of this rare condition. Therefore, despite some international Delphis reporting high attrition rates, I anticipated that the attrition rate in the COMBINE Delphi would be less than 20%, similar to Delphis in other rare conditions (Allin et al., 2019).

For this study, the sample size was therefore based on sample sizes in other similar Delphi studies (Allin et al., 2019; Sinha et al., 2012), guidance from the COMET handbook (Williamson et al., 2017) and a reflection that BPI is a specialist area. The study aimed to recruit 20-25 participants per stakeholder group. This included over-recruitment by 10-20% to allow for some attrition between the Delphi rounds.

5.2.2.7 Recruitment

People with the injury: Originally, I had ethics approval to recruit people with the injury from both a tertiary NHS centre and through online social media and support groups. Evidence suggests that recruiting patients through treatment centres improves retention rates in COS Delphis (Barrington et al., 2021). However, the Delphi launch coincided with COVID-19 in Spring 2020. NHS Research & Development departments prioritised COVID-19 studies and I was unable to recruit from the trust. I therefore focused the recruitment of people with the injury through online methods. I set up a closed Facebook site to promote the study, as I had identified 14 international BPI community groups on Facebook. I contacted the administrator for each of the groups, national charities and forums (Appendix 5.3) and asked permission to promote the study using a plain English video. I conceived and designed the video in collaboration with the patient advisory group and a specialist medical illustrator: https://www.youtube.com/watch?v=7k6MYpugvRk.

People contacted me if they were interested in participating, and at this stage I checked eligibility. If an individual was eligible then I emailed them a Participant Information Sheet (PIS) (Appendix 5.4) and a link to the Delphi registration.

Surgeons and therapists and nurses were recruited by direct email, with an electronic PIS attached (Appendix 5.5) sent to international authors (n = 22), lead clinicians in tertiary BPI international centres (n = 24) and attendees of an international BPI conference (NARAKAS 2019) who had registered interest in participating in the study and consented to communication (n = 47 therapists and nurses; 52 surgeons). The NARAKAS group also promoted the study through its distribution list. Finally, I set up a Twitter site to promote the study. The snowball method was used, where professionals were asked to forward invitation letters to others who they thought were eligible and might be interested in participating (Griffiths, 2011). Although snowball sampling has been criticised for non-probability sampling (Sadler et al., 2010), it is particularly useful for recruitment of hard-to-reach groups and identifying large convenience samples through networks (Wagner and Lee, 2014). Therefore, for this international COMBINE Delphi, where potential participants are hard to reach, I felt it was appropriate to use this approach.

5.2.2.8 Delphi process

When respondents clicked on the link in the invitation email or electronic PIS, they were taken to the home page of the COMBINE Delphi study hosted on Delphi Manager https://www.comet-initiative.org/delphimanager/. The requirement to complete all rounds of the study was emphasised in the PIS, to reduce drop out (Sinha et al., 2012). The 3-round Delphi ran between July and December 2020. Rounds were open to respondents to complete for 5, 6 and 4 weeks respectively. Reminder emails were sent for all rounds at 2 weeks, 1 week and 1 day before each survey closed.

Round 1: Respondents were invited to rate all outcomes and they could not progress to the next page unless all previous outcomes were rated. In round 1, respondents had the option to suggest new outcomes that they felt were missing. These suggestions were reviewed by the research team (CM, CJH, and JC) and any outcome not already represented was added to round 2.

Round 2: Respondents who rated more than 75% of items in round 1 were invited to participate in round 2. There are different methods of providing feedback on the results from round 1 of Delphi studies to stakeholders. Frequently, central tendencies (means, medians and modes) and level of dispersion (standard deviation, range)

provide information about collected opinions (Hasson et al., 2000). However, a recent qualitative study with 8 patient participants of a COS Delphi (anal cancer) identified that none of the patient participants understood the term 'median' and many had issues with understanding averages (Fish, 2018). The patient participants understood and liked seeing other participants' ratings (expressed as percentages) of each outcome (Fish, 2018). However, as this study included only 8 patient participants, it may not be representative of patient participants of COS more generally. Participants in the COMBINE study were shown the score they gave each outcome in the previous round, together with the distribution of scores from other participants within their own stakeholder group. By viewing these scores, participants were able to see their response relative to that of the group (Hasson et al., 2000). Participants were asked to reflect on the similarities and differences observed before proceeding to re-score each outcome. Additional outcomes added from round 1 were scored as before without reflection.

Round 3: Items from round 2 continued to round 3 if they were rated between 7 and 9 (important) by 50% or over and between 1 and 3 (not important) by less than 15% in any stakeholder group. Participants were shown the score they gave each outcome in the previous round, together with the distribution of scores from participants in their own and each stakeholder group separately. Participants were invited to reflect on the information and re-scored each outcome again.

5.2.2.9 Data extraction and analysis

Extraction: Demographic information for HCPs collected in round 1 included profession, country of practice and the average number of adults with BPI seen per month. Demographics collected for people with a BPI included sex, the country where the injury occurred, time since injury, and whether the participant had surgery. The user score and demographic data were extracted and downloaded into Microsoft Excel. Figure 5.2 shows an example of the scores data extraction.

Figure 5. 2 Example of a scores data extract

	A	B	C	D	E	F
1	UserID	StakeholderGro	StudyRour	Domain	Outcome	Score
2	COMBI00001	Therapists/Nurs	1	Physical signs (movement; stre	Voluntary movement of the arm	9
3	COMBI00001	Therapists/Nurs	2	Physical signs (movement; stre	Voluntary movement of the arm	9
4	COMBI00001	Therapists/Nurs	3	Physical signs (movement; stre	Voluntary movement of the arm	9
5	COMBI00001	Therapists/Nurs	1	Physical signs (movement; stre	Passive/ assisted movement of the arm	9
6	COMBI00001	Therapists/Nurs	2	Physical signs (movement; stre	Passive/ assisted movement of the arm	9
7	COMBI00001	Therapists/Nurs	3	Physical signs (movement; stre	Passive/ assisted movement of the arm	4
8	COMBI00001	Therapists/Nurs	1	Physical signs (movement; stre	Strength of muscles in the arm	9
9	COMBI00001	Therapists/Nurs	2	Physical signs (movement; stre	Strength of muscles in the arm	9
10	COMBI00001	Therapists/Nurs	3	Physical signs (movement; stre	Strength of muscles in the arm	9
11	COMBI00001	Therapists/Nurs	1	Physical signs (movement; stre	The physical appearance of the arm	4
12	COMBI00001	Therapists/Nurs	2	Physical signs (movement; stre	The physical appearance of the arm	4
13	COMBI00001	Therapists/Nurs	3	Physical signs (movement; stre	The physical appearance of the arm	4
14	COMBI00001	Therapists/Nurs	1	Physical signs (movement; stre	Reaching; pulling; pushing; turning or twistin	6
15	COMBI00001	Therapists/Nurs	2	Physical signs (movement; stre	Reaching; pulling; pushing; turning or twistin	8
16	COMBI00001	Therapists/Nurs	3	Physical signs (movement; stre	Reaching; pulling; pushing; turning or twistin	4

Analysis:

Qualitative analysis round 1: All new potential outcomes suggested in round 1 were documented or reviewed. Qualitative data were then analysed by grouping similar suggestions/outcomes together (Hasson et al., 2000) and categorising them under existing domains in the Delphi (for example, 'physical signs'). If new suggestions did not fit under existing domains, they were documented separately. The new suggestions, and where they potentially fitted in the domain framework, were presented to the research group (CJH and JC) during an online meeting. The research group reached consensus on whether the suggestions were one of the following: new outcome, an outcome instrument, duplicating an existing outcome, or necessitated rewording of the existing outcome. New outcomes were added with appropriate 'help text' and existing outcomes reworded where necessary.

Quantitative analysis all rounds: In any round where participants had started the survey but did not rate > 75% of items, their scores were removed. For each stakeholder group and for the whole sample, the percentage of score distributions across the subsections of the GRADE scale were calculated to determine whether a predefined consensus of critical or limited importance had been achieved. Where an item was rated 'unable to score' these data were excluded from the analysis.

Attrition between rounds: As discussed in section 5.2.2.6, attrition rates are important to calculate. The number of participants completing each round was calculated.

Overall and per stakeholder group percentage attrition per round and over the whole three rounds were calculated.

5.2.2.10 Selection of items for the final consensus meeting

Definitions of consensus vary widely and are poorly reported in the general Delphi literature (Diamond et al., 2014). COMET and OMERACT (Outcome Measures in Rheumatology) recommend a threshold of ≥70% participant agreement that an outcome is of sufficient importance to be included in a draft COS (Maxwell et al., 2019; Williamson et al., 2012a). The rationale for this split is to ensure that the majority of participants think the outcome should be in the COS, with only a minority considering it to have little or no importance (Williamson et al., 2017). The original protocol stated that an outcome reaching consensus criteria (see Figure 5.3) in any stakeholder group would be discussed at the consensus meeting (Miller et al., 2019). However, at the end of the Delphi, a large number of outcomes reached consensus and it would have been unfeasible to take all of them to the consensus meetings. Therefore, more stringent criteria were applied for the selection of outcomes to carry through to the final consensus meetings. This was a deviation from the published protocol, agreed by the research team. Instead of items reaching consensus criteria in *any* group being taken forwards, items rated 7-9 by at least 70% of participants in *all* groups were discussed at the consensus meeting, as recommended by OMERACT in their updated guidelines (Beaton et al., 2021a).

Figure 5. 3 Consensus criteria

Consensus *IN* (Consensus that outcome should be included in the COS) 70% or more participants scoring an outcome as critically important (7-9) AND < 15% or fewer participants rate the outcome as limited importance (1-3)

Consensus *OUT* (Consensus that outcome should not be included in the COS) 70% or more participants scoring an outcome as limited importance (1-3) AND < 15% of participants scoring an outcome as very important (7-9)

NO Consensus (Uncertainty about importance of outcome) Anything else

5.2.3 Step 3: Consensus meetings

Originally, I planned for one combined face-to-face meeting with patients and clinicians. However, due to the COVID-19 pandemic, this was no longer feasible, and participants attended online meetings. On reflection, conducting the meetings online was more inclusive for an international and partly physically disabled population. The following sections discuss the decision making regarding separate and combined consensus meetings, the aims of the consensus meeting and the methods used.

5.2.3.1 Decision making regarding separate or combined consensus meetings

There is no agreement on how to best to host consensus meetings to inform COS development. Some COS developers recommend that face-to-face consensus meetings are held separately for patients and professionals to allow patients' views to be heard without contamination from other parties (McNair et al., 2016; Potter et al., 2015). Other groups have brought patients and professionals together to discuss their views alongside evidence arising from a Delphi survey (Harman et al., 2015) and to make recommendations about a COS. Previous COS patient participants recommend consensus methods should suit the preference of a particular patient group whose input is being sought and the sensitivity of the topic (Young and Bagley, 2016).

For the COMBINE project certain issues needed to be considered to inform whether separate or combined meetings should be conducted. The clinician group involved in the specialist care of adults with a BPI is relatively small, and it was likely that at a combined consensus meeting many patient participants would know the clinicians. I needed to consider the potential impact this would have on patient participants. I felt that a large online meeting with people with BPI and surgeons and therapists may have inhibited open and honest discussion by patients. They may have been discouraged to discuss issues about their treatment and outcomes important to them, if their current or past clinician was in the same online space. Patients' lack of openness may be driven by a fear of negative repercussions on future treatment decisions made by these clinicians (Bell et al., 2018; Frosch et al., 2012), a fear of appearing not to understand the concepts discussed (Bell et al., 2018), and a perception of low status compared to the clinicians (Bell et al., 2018). Indeed, a recent COS development team hosted a combined patient and HCP consensus meeting, and then needed to host a separate patient meeting following patient feedback (Blackwood et al., 2019). Patients told the developers that they did not understand some of the research-focused discussions on outcome selection (Blackwood et al., 2019). I felt, therefore, that two separate consensus meetings (one separate patient meeting and one separate HCP meeting), followed by a combined meeting, would provide the best opportunity for all stakeholders' views to be heard but still reach consensus. Hence, three online consensus meetings were hosted.

At the time of conducting these meetings, there was little guidance on best practice for online consensus meetings. I contacted COMET for guidance and they put me in touch with Alison Tong, who had recently convened four international online consensus meetings when developing a COS for COVID-19 (Tong et al., 2020). Alison Tong advised (via email) on the use of a detailed run sheet to avoid technical hitches. Although Tong et al. (2020) did not use voting in their consensus meeting, she advised me on the polling option on the online platform Zoom and that it may be useful. I used both of these methods to support the consensus meetings.

5.2.3.2 Aim of consensus meetings

The objective of each consensus meeting was to discuss the full list of outcomes that were rated 'critically important' by all three stakeholder groups in round 3 of the Delphi study and to agree on the most important outcomes (Williamson et al., 2017) that would make up the COS-BPI.

5.2.3.3 Ethical considerations

The Solihull Ethics Committee (REC number 8/WM/0297) approved a substantial amendment on 6th January 2021 (see Appendix 5.6) based on a change of location, number of consensus meetings, and amended invitation letters. Zoom was used to host all three consensus meetings online. It is recommended that support is provided for patient participants in COS development so that they are in a position to give meaningful and credible input (Young and Bagley, 2016). I arranged a trial online Zoom meeting with each patient attendee individually before the meeting, to ensure they were comfortable logging on and using the online platform. I explained the plan for the meeting and their role. I verbally reminded them that their data would be anonymous but results from the consensus meeting would be published. Attendance at the consensus meeting was taken as implicit consent for participation with no additional written consent provided.

There are issues of power when multiple stakeholders work together to seek agreement. Power is a relational, co-constructed process and represents a potential to exert influence (Drinka and Ray, 1986). The nature of clinician-patient relationships mean they are unequal. This asymmetrical relationship is a result of HCPs possessing expert power (Beisecker, 2009) and patients being reliant on HCPs to provide the healthcare they need. In consensus meetings the spoken language and non-verbal communication used can exclude or subtly undermine patient participants (Williamson et al., 2017). To minimise the impact of HCP power on the consensus process and support open and honest patient involvement, separate online consensus meetings were held. Further justification for this is presented in section 5.2.1.1.

5.2.3.4 Participants

Adults with a BPI, therapists and surgeons who had participated in and completed all three Delphi rounds were eligible to attend the consensus meetings.

5.2.3.5 Sample size

COS developers report a range of participant numbers in online consensus meetings. This ranges from 36 participants (including 5 patients) for the development of a COS for tennis elbow (Bateman et al., 2022) to 16 participants (including 2 patients) in an online consensus meeting for evaluation of outcomes for participants who lack capacity (Shepherd et al., 2021). Finally, researchers developing a COS for COVID-19 included 96 participants (17 people with experience of COVID-19) in their online consensus meetings (Tong et al., 2020).

I aimed for 30-35 consensus meeting attendees, with equal representation from the three stakeholder groups (people with the injury, surgeons, and non-surgical HCPs). Guidance from OMERACT suggests that 10% of the total consensus group should be patient participants (Boers et al., 2014a). However, more recent COS developers have increased proportions of patient representatives (Fish et al., 2018; MacLennan et al., 2017) to approximately one-third. I aimed for 10-15 patient participants at the online consensus meeting to ensure individuals could get their voice heard and increase the diversity in terms of geography and injury type across patient-participants.

5.2.3.6 Recruitment

Personalised emails with invitation letters were sent to all patient (n = 20) and surgeon participants (n = 20). Fifty per cent more therapists completed all Delphi rounds compared to surgeons and patients. As I sought for equal representation from each stakeholder group, I purposively sampled 20 therapists by geographic location to ensure international representation. If occupational therapists and physiotherapists from the same centre took part in the Delphi, a representative from each professional group from the centre was invited, to account for any difference in opinions between the professions. Members of the core research team (CJH, JC and DP) were invited to all meetings to support the consensus process but did not vote. Appendices 5.7 and 5.8 present the consensus invitation letters.

5.2.3.7 Consensus process

This section describes the preparation for the COMBINE consensus meetings.

5.2.3.7.1 Consensus meeting preparation

Good facilitation is recognised as crucial to ensuring the smooth running of a consensus meeting and that the patient voice is heard (De Wit et al., 2013; Williamson et al., 2017). Williamson et al. (2017) also recommend consideration of whether the facilitator needs relevant clinical experience. In this case, the research team agreed that having relevant clinical experience was important, as BPI was a rare injury and knowledge may be needed by the facilitator to support and direct the discussions. Therefore, as I had over 15 years of clinical experience in adults with a BPI, I facilitated each of the meetings with the support of the research team (CJH, DP) and Jack Jeffrey (JJ), a clinical academic colleague who assisted with the vote percentage calculation and presented overall online voting results in PowerPoint.

To prepare for the consensus meetings, I met regularly with CJH and JC to plan the content and voting process. I met with JJ to trial the voting and presentation of the results on the Zoom platform. I reviewed the content of the meeting and the polling process with a member of the patient advisory group. Finally, I piloted the online consensus meeting with six colleagues at the Queen Elizabeth Hospital Birmingham who treated patients with BPI on 11th February 2021. At this meeting, the online polling system and different methods of presenting the outcomes were tested.

Both patient and HCP meetings were identical in structure. Results from round 3 of the Delphi were emailed to the attendees in advance of the meeting. Furthermore, participants were also emailed a word version of all outcomes to be voted on at the meeting (see Appendix 5.9). Outcome wording was shortened and simplified for the consensus meetings for easy reading on the Microsoft PowerPoint slides, with verbal clarification as needed. Participants were asked to review this outcome list in advance of the meeting and print it out if possible. The email also documented that voting was restricted to a maximum of 10 outcomes, to ensure that participants voted for outcomes they viewed as essential in clinical practice and research. There are several reasons why participants were restricted with their votes. Firstly, there is some

evidence that COS with a large number of outcomes may hinder uptake and implementation (Williamson et al., 2020). Secondly, OMERACT suggest a COS should contain up to seven outcomes and to support this recommend that participants (in consensus meetings) choose up to 10 outcomes as their top or most important (Beaton et al., 2021a). Finally, the Cochrane summary of findings tables allows the inclusion of seven outcome domains (Langendam et al., 2013), therefore inclusion of more than seven in a COS may result in research waste, as these extra outcomes cannot be included in the meta-analysis of a Cochrane review.

5.2.3.7.2 Patient-only and health professional-only consensus meetings (consensus meetings 1 and 2):

Separate consensus meetings were held for patients and HCP meetings at 19.00 (GMT) on 25th February and 4th March 2021 respectively. Meetings were recorded and transcribed. Participants were welcomed and reminded of the aims of the meeting, the purpose of a COS, and that the meeting would be recorded. A short presentation of the results of the final round of the Delphi were presented, with an opportunity for questions. The list of outcomes to be discussed and voted on was presented on PowerPoint.

Participants discussed groups of outcomes within their domains and then voted 'yes' (this outcome should be included in the COS) or 'no' (this outcome should not be included), using the anonymous polling system on Zoom. Voting results (in percentage voted ***IN*** and voted ***OUT***) for the group of outcomes were presented immediately after everyone had voted. Using the literature of other COS developments (Damhuis et al., 2020) as guidance, outcomes voted ***IN*** by 85% or more participants were taken forwards to the final ratification meeting for inclusion in the COS-BPI. Outcomes voted ***IN*** by 70%-84% of the participants were discussed and re-voted on. Outcomes receiving 69% or fewer votes were removed, in keeping with other COS consensus meetings (McNair et al., 2016). Discussion and further rounds of voting were undertaken until consensus was reached on all outcomes.

Outcomes reaching consensus ***IN*** at either meeting were taken forwards to the ratification meeting with patient and HCP representation. Any outcome not reaching consensus ***IN*** or ***OUT*** was also taken forwards for discussion at the final ratification

meeting. Data were collected on participant demographics in terms of profession for HCPs and country of origin for all participants. Transcribed data from the meeting were reviewed and categorised into themes where there was discordance or concern regarding consensus meeting results.

5.2.3.8 Ratification meeting

A final ratification online meeting was held on Zoom following the separate patient and HCP consensus meetings. Previous COS with separate patient and HCP consensus meetings have identified large numbers of outcomes (Coulman et al., 2016a; McNair et al., 2016; Potter et al., 2015). A COS for breast reconstruction identified 11 outcomes (Potter et al., 2015) and a COS for bariatric surgery initially identified 12 outcomes, which were reduced to 9 following the merging of outcomes after the meetings (Coulman et al., 2016a). Similarly, a COS for colorectal surgery included 12 outcomes after separate patient and HCP meetings, as different outcomes were prioritised at each meeting (McNair et al., 2016). The aim for the COS-BPI was to include 3-7 outcomes in line with recommendations from OMERACT (Beaton et al., 2021a), to improve the implementation and uptake of the COS (Williamson et al., 2020). Based on previous research using separate patient and HCP meetings, I anticipated a large number of outcomes might be included in the COS-BPI. So, I planned a ratification meeting with patient and HCP representatives to discuss the results from both meetings, and if necessary, come to a consensus and ratify a final, feasible COS.

Participants: A therapist and two patient representatives who had completed the Delphi and attended the consensus meeting were invited to the final consensus meeting. The therapist invited, who was from Australia, had experience treating and researching adults with a BPI. The patient representatives invited were both from the UK but differed in the time and type of BPI. They were also active in the UK BPI charity and could speak for a broader group of adults with BPI. The surgeon invited was from the Birmingham peripheral nerve injury unit and experienced in treating patients with a BPI and was also part of the supervisory team. CJH and JC attended the meeting as part of the research team.

Meeting plan: Table 5.1 presents the agenda for the ratification meeting.

Table 5. 1 Agenda for ratification meeting

Item no.	Topic	Who
1.	Welcome and introductions and plan of meeting	CM
2.	Present results of separate patient and HCP meetings	CM
3.	Review outcomes voted ***IN*** at both meeting and confirm scope and discuss if merging needed	All
4.	Review and discuss outcomes voted ***IN*** at either patient or HCP meetings. CM present a summary of the discussion around those outcomes voted in by only one group	All
5.	Discuss outcomes that did not reach consensus ***IN*** or ***OUT***	All
6.	Agree final COS-BPI	All

5.3 Results

These following sections present the results related to the three objectives of the study in this chapter.

i) create a comprehensive 'long list' of outcomes to inform an international online Delphi (step 1)

ii) prioritise these outcomes from the perspectives of patients, HCPs and researchers (step 2 - Delphi)

iii) obtain consensus on a minimum set of the most important and relevant outcomes for evaluating and reporting in adult BPI research and routine care (step 3 - consensus meetings)

5.3.1 Step 1: Outcome long list generation and questionnaire creation

The outcome long list consisted of clinician-reported and patient-reported outcomes identified in the systematic review and outcomes explored in the patient interviews. The systematic review identified 54 subdomains, as described in Chapter 3. An additional 12 subdomains were identified from interviews with patients, which were added to the list. In total there were 66 subdomains. Table 5.2 presents the subdomains and their source.

The 66 subdomains were converted into a 64-item questionnaire. The decision making about the items moved forward into the Delphi is presented in Appendix 5.10. The 64 items were grouped into 10 categories linked to the domains in the COMET taxonomy (Dodd et al., 2018) (physical signs, sensation and pain, neurophysiology and structure of the nervous system, activities of daily living, social wellbeing, emotional wellbeing, sleep and overall health, delivery of care**,** costs of care and complications). Each category (domain) became a page in the online Delphi. See Appendix 5.11 for blueprint of round 1 of the online Delphi.

Table 5. 2 Final subdomains associated with source identified

Subdomains (n = 66)	Systematic review	Interview
Muscle strength	X	
Active range of movement	X	
Passive movement	X	
Control of movement/stability	X	
Muscle mass	X	
Bony structure and position	X	
General sensory recovery	X	
Discriminative touch	X	
Protective touch	X	
Peripheral nervous system structure	X	
Reinnervation	X	
Speed of motor/sensory conduction	X	
Pain intensity/relief	X	
Pain duration/frequency	X	
Pain quality and interference with life	X	
Pain when arm exposed to cold	X	
Paraesthesia and itchiness	X	
Sensitivity to touch, pressure, etc	X	
Location of pain	X	
Pain medication use	X	
Stiffness	X	
Impact on sleep	X	
Physical function non-specific	X	
Lower limb and non-upper limb function	X	
Reaching, pulling, pushing, carrying	X	
Turning twisting, gripping, and releasing with the arm	X	
Fine hand movement	X	
Emotional distress/mood	X	
Thoughts and beliefs	X	
Self-esteem and confidence	X	
Body image	X	
Impact on paid or unpaid work or role in education	X	
Role function -patient-specific	X	
Carrying out daily routine	X	
Maintaining personal hygiene	X	
Maintaining personal appearance	X	
Dressing	X	
Transport needs	X	
Impact on recreational activities and sport	X	

Subdomains	Systematic review	Interview
Effect on relationship with family, friends, neighbours, and groups	X	
Effect on intimate relationships	X	
Quality of life	X	
Perceived health status	X	
Patient satisfaction	X	
Patient preference	X	
Quality and adequacy of intervention	X	
Time to surgery	X	
Donor site morbidity	X	
General complications	X	
Respiratory complications	X	
Vascular complications	X	
Musculoskeletal complications	X	
Infection complications	X	
Operation time	X	
Cost of attending for care		X
Money worries		X
Hopes		X
Addiction		X
Looking after the children		X
Pulling and dragging		X
Arm appearance		X
Access to treatment		X
Effect on wider family		X
Going out with friends		X
Back to my work		X
Back to studying		X

Italics: patients' words

5.3.2 Step 2: Delphi results

5.3.2.1 Demographic results

Response rate: In round 1, 114 participants registered and 99 (86%) completed the round. From a total of 36 adults with BPI who started the survey, 30 (83%) completed round 1. Of the 39 surgeons who started the survey, 33 (85%) completed round 1. The non-surgeon HCP stakeholder group were all physiotherapists and occupational therapists, and this group will be named *therapists* from here onwards. Of the 39 therapists who started the survey, 36 (92%) completed round 1. The 15 participants who did not complete the survey rated less than 75% of the items, so their data were excluded from the results. Participants for the Delphi were recruited via a snowballing approach, so it was not possible to calculate the total number of potential participants who were contacted.

Participants from 21 countries, 11 of which were low- and middle-income countries, took part in round 1 of the Delphi. In round 1, participating surgeons originated from 16 countries and 5 continents. Of these, 42% (n = 14) were from low- and middle-income countries. Therapists originated from 9 countries and 4 continents. Of these 8% (n = 3) came from low- and middle-income countries. Finally, adults with BPI originated from 10 countries and 6 continents with 10% (n = 3) participating from low- and middle-income countries. Tables 5.3, 5.4 and 5.5 present the Delphi demographic data.

Table 5. 3 Demographic information for healthcare professionals, rounds 1-3 Delphi

	Round 1 survey n = 69		Round 2 survey n = 54		Round 3 survey n = 51	
	n	%	n	%	n	%
Healthcare professional occupation						
Therapist	36	52.2%	31	57%	31	61%
Surgeon	33	47.8%	23	43%	20	39%
No. of new patients with BPI seen per month						
One or less	13	18.8%	10	18.5%	9	17.6%
2-3	13	18.8%	10	18.5%	9	17.6%
4-5	16	23.2%	13	24%	12	23.5%
6-10	10	14.5%	8	14.8%	8	15.7%
More than 10	13	18.8%	10	18.5%	10	19.6%
Not stated	4	5.8%	3	5.5%	3	5.8%

Table 5. 4 Demographic information for adults with BPI, rounds 1-3 Delphi

		Round 1 survey n = 30		**Round 2 survey n = 24**		**Round 3 survey n = 20**	
		n	**%**	**n**	**%**	**n**	**%**
Sex							
	Male	26	86.6	20	83.3	17	85
	Female	4	13.3	4	16.7	3	15
Age							
	Under-30	3	10	3	12.5	2	10
	31-50	17	56.6	12	50	11	55
	51 and over	10	33.3	9	37.5	7	35
Time since diagnosis							
	Less than 6 months	0	0	0	0	0	0
	7-12 months	2	6.6	2	8.3	1	5
	1-2 years	7	23.3	5	20.8	4	20
	3-5 years	5	16.6	4	16.6	4	20
	More than 5 years	15	50	12	50	10	50
	No response	1	3.3	1	4.2	1	5
Had surgery							
	Yes	27	90	23	95.8	19	95
	No	3	10	1	4.2	1	5

Table 5. 5 Distribution of countries of practice or residence of round 1 participants

Continent	Country	People with BPI (n = 30)	Therapists (n = 36)	Surgeons (n = 33)	Total % of all participants
Europe (50.3%)	UK	14	11	9	34.3%
	Denmark		3		3%
	Netherlands		1	2	3%
	Sweden	1	6	2	9%
	Switzerland		1		1%
North America (17.1%)	USA	4	2	4	10.1%
	Guatemala*			1	1%
	Canada	3	2		5%
	Jamaica*	1			1%
Asia (7%)	Philippines*			1	1%
	Indonesia*			1	1%
	Pakistan*			1	1%
	Thailand*			1	1%
	Israel			1	1%
	India*	1		1	2%
Oceania (12.1%)	Australia	5	7		12.1%
Africa (3%)	South Africa*			2	2%
	Egypt*			1	1%
South America (10.1%)	Brazil *	1	3	3	7.1%
	Argentina*			2	2%
	Chile			1	1%

*Low- and middle-income countries (from Organisation for Economic Co-Operation and Development) dated Dec 2021

5.3.2.2 Round 1 Delphi results

See Tables 5.6 and 5.7 for voting responses by stakeholder group separately and the whole sample.

Table 5. 6 Round 1 Delphi results: outcomes rated 7-9 by 70% or more of whole sample

Questionnaire items	Whole sample n = 99	Patients n = 30	Therapists n = 36	Surgeons n = 33
Pain intensity	92.6%	86.6%	97.2%	93.9%
Voluntary movement of the arm	91.8%	86.6%	88.8%	100%
Strength of muscles in the arm	87.6%	76.6%	86.1%	100%
Maintaining personal hygiene	90.8%	90%	91.6%	90.9%
Pain duration and frequency	87.7%	86.6%	88.8%	87.8%
Loss of voluntary (active) movement	86.4%	76.6%	88.8%	93.9%
Damage to other nerves during the surgery	86.2%	70%	91.6%	96.9%
Worsening of existing pain/pins and needles	85.7%	83.3%	86.1%	87.8%
Emotional distress	85.6%	83.3%	91.6%	81.8%
Appropriateness of treatment	85.8%	83.3%	83.3%	90.9%
Carrying out a daily routine	84.6%	83.3%	91.6%	78.8%
Ability to feel to protect the arm from injury	84.2%	73.3%	94.4%	84.8%
Fine hand movement	82.2%	73.3%	91.6%	81.8%
Failure of the surgical join of the nerves	82.2%	66.6%	86.1%	93.9%
Carrying and lifting objects	81.6%	76.6%	83.3%	84.8%
Breathing problems	81.3%	70%	86.1%	87.8%
Access to treatment	80.8%	80%	77.7%	84.8%
The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm	78.9%	80%	75%	81.8%
Failure of the surgical join of the artery/vein	78.2%	66.6%	86.1%	81.8%
Reaching, pulling, pushing, turning, or twisting with the arm	78.1%	80%	69.4%	84.8%
Effect on relationship with and or ability to care for, children	77.7%	83.3%	86.1%	63.6%
A nerve join results in the formation of a bundle of painful nerves	77.4%	70%	83.3%	78.8%
Loss of assisted range of motion (stiffness)	77.2%	60%	77.7%	93.9%
Putting on and taking off clothes	76.8%	60%	88.8%	81.8%
Infection in the body part that was operated on	76.1%	70%	91.6%	66.6%
Description of the pain (quality and interference)	74.3%	66.6%	80.5%	75.7%
Development of a blood clot	73.3%	66.6%	77.7%	75.7%
Intentions and goals	73.2%	70%	86.1%	63.6%
Ability to feel with the arm	75.6%	53.3%	91.6%	81.8%
Problems with the wound such as infection, failure to heal properly	71.1%	66.6%	86.1%	60.6%
Self-esteem and self-confidence	71.1%	63.3%	83.3%	66.6%
Failure of the bone to unite following bone surgery	71.0%	56.6%	77.7%	78.8%
Overall quality of sleep	70.3%	66.6%	77.7%	66.6%

Table 5. 7 Round 1 Delphi results: outcomes rated 7-9 by 69.9% or less of whole sample

Questionnaire items	Whole sample n = 99	Patients n = 30	Therapists n = 36	Surgeons n = 33
Development of pain/pins and needles in a new area of the body	69.6%	66.6%	66.6%	75.7%
Overall health	69.4%	63.3%	72.2%	72.7%
Return to any other paid/non-paid previous role	68.9%	56.6%	80.5%	69.7%
Effect on relationship with partner/spouse	68.3%	66.6%	77.7%	60.6%
Patient satisfaction with health care received	68.3%	56.6%	69.4%	78.8%
Passive/assisted movement of the arm	68.0%	56.6%	75%	72.3%
Return to full duties at previous role in paid employment	66.3%	60%	72.2%	66.6%
Thoughts and beliefs	66.2%	60%	75%	63.6%
Chest infection	65.3%	60%	69.4%	66.6%
Effects on intimate relationships	64.9%	73.3%	63.8%	57.6%
Injury to an artery or vein resulting in bleeding where the operation takes place	64.1%	56.6%	75%	60.6%
Addictive behaviours (e.g., alcohol, medication drugs)	62.8%	60.6%	72.2%	55.6%
Costs to the patient from long term loss of individual/family income	63.1%	73.3%	58.3%	57.6%
Maintaining personal appearance	59.2%	53.3%	66.6%	57.6%
Transport needs	59.6%	60%	58.3%	60.6%
Bone uniting in the wrong position	58.8%	50%	75%	51.5%
The structure of brachial plexus using MRI or other techniques	57.4%	80%	52.7%	39.4%
Return to previous recreational activities	55.7%	60%	55.5%	51.5%
Effect on relationship with other family members	55.4%	56.6%	61.1%	48.5%
Return to or begin role in education	53.6%	46.6%	50.5%	63.6%
Body Image	52.9%	43.3%	63.8%	51.5%
Pain when the arm is exposed to cold	52.8%	53.3%	44.4%	60.6%
Bleeding from the wound	49.4%	46.6%	50%	51.5%
Effect on relationships with friends and neighbours	48.7%	40%	63.8%	42.4%
Pins and needles or tingling in the arm	48.4%	46.6%	50%	48.5%
Costs to uninsured private paying patients, insurance, or other third-party payers (includes national health services) for all outpatient and in-patient care received for a brachial plexus injury including medication	42.5%	43.3%	38.8%	45.5%
Out of pocket costs to the patient for outpatient appointments and inpatient care	40.5%	40%	36.1%	45.5%
Increased sensitivity of the scar	40.7%	26.6%	47.2%	48.5%
A measure of the activity in the movement and sensation areas of the brain	37.8%	56.6%	35.5%	21.2%
The physical appearance of the arm	30.1%	26%	25%	39.4%
A sensation of heaviness in the arm	28.9%	33.3%	11.1%	42.4%

5.3.2.3 New outcome suggestions and wording changes after round 1 Delphi

Participants added 68 comments about potential additional outcomes. I reviewed all suggestions with my supervisors (CJH and JC). Appendix 5.12 presents an audit trail of this decision making. Following this, a further six new outcomes were added to round 2 (see Table 5.8) and wording for seven existing outcomes revised (see Table 5.9). Of the remaining comments, more than one third duplicated concepts in the original list (38%), while others considered items that had been excluded at the stage of preparing the long list because they were multidomain concepts (12%), described co-morbidity (12%), or were related to how an outcome may be assessed (12%).

Table 5. 8 New outcomes added to round 2 Delphi

Domain	New outcome proposed wording	Hover wording[1]
Physical signs	Muscle fatigue or endurance	The ability of the muscle to sustain force over time
	Development of musculoskeletal problems in other parts of the body	Development of other musculoskeletal problems in other parts of the body secondary to traumatic brachial plexus injury
Emotional wellbeing	Expectations of treatment	To include expectations of benefit and side effects of treatments
	Ability to cope	Coping strategies to include self-efficacy (an individual's belief and confidence that they can exert control over their life)
Activities of daily living	Ability to eat using utensils or hand	To include the manipulation of utensils (knife and fork, chopsticks, etc) or using their fingers to eat in a socially and culturally appropriate way
Complications (muscle or bone)	Limited voluntary movement because of the inability to co-ordinate muscles at the same time (co-contraction)	Co-contraction or poor muscle coordination leads to a lack of voluntary movement.

[1] When a participant **hovers** over an outcome in the Delphi, a more detailed explanation of the outcome appears in a text box by the outcome.

Table 5. 9 Revised wording of seven outcomes from feedback in round 1 Delphi

Domain	Existing outcome	Proposed wording for the outcome	Proposed new wording for 'hover' function[1]	Rationale
Physical signs	Strength of muscles in the arm	No change Strength of muscles in the arm	The ability of the muscle to generate enough force to work against gravity or resistance.	Several participants suggested that fatigue should be a separate outcome, so we removed it from the 'strength' outcome and made a new outcome
Sensation and pain in the arm	Ability to feel with the arm	Ability to feel with the arm including the hands and fingers	No change For example, the ability to feel touch, texture, shape, and weight	Some participants commented and suggested the hand and fingers should be included as the sensation was more important in the hand than in the arm
Activities of Daily Living	Return to previous recreational activities	No change Return to previous recreational activities	Including sports, gardening, and hobbies	Two participants suggested sports needed to be included
	Transport needs	Transport needs, including driving cars and riding motorbikes and bicycles	The ability to use transport including driving cars, riding motorbikes and bicycles	A comment suggested that riding bicycles were particularly important in certain parts of the world where these injuries occur. It was decided to move 'ride a bicycle' into the main outcome

[1] *When a participant **hovers** over an outcome in the Delphi, a more detailed explanation of the outcome appears in a text box by the outcome.*

Domain	Existing outcome	Proposed wording for the outcome	Proposed new wording for hover[1] function	Rationale
Emotional wellbeing	Emotional distress	Emotional distress including anxiety, depression, post-traumatic stress	To also include low mood, suicidal thoughts, flashbacks, and nightmares	Many comments suggested that we should be measuring depression, anxiety and PTSD. These were always included in the hover so we moved them to the outcome title
	Thoughts and beliefs	Thoughts and beliefs	Including acceptance of injury	Remove expectations of treatment, as becoming a new outcome
	Access to and quality of treatment	Access to (waiting times, distance from, ease of referral) and quality of treatment	Including distance to centres, waiting times, and information regarding treatment	Many comments that ease of access to specific centres was important and needed to be a main outcome, not only in explanation.

When a participant ***hovers*** over an outcome in the Delphi, a more detailed explanation of the outcome appears in a text box by the outcome.

5.3.2.4 Round 2 Delphi results

Items for voting and responses: These consisted of those outcomes carried forward from round 1, plus 6 additional outcomes added after round 1 (n = 70). Tables 5.10 and 5.11 present voting as a percentage of respondents in each stakeholder group and the whole sample.

Response rate: Of those participating in round 1, 78 (78.8%) took part in round 2.

Demographic characteristics of participants: Of all participants, 24 were people with BPI (80% of those completing round 1), 31 were therapists (86% of those completing round 1) and 23 were surgeons (70% of surgeons completing round 1). The overall attrition was 21% (21/99). Tables 5.3 and 5.4 present the demographic data.

In round 2, at least 50% of the respondents rated 62 of the 70 outcomes as very important (7-9), and these were carried forward to round 3. One outcome, 'sensation of heaviness in the arm', met the criteria for removal (50% or fewer participants in each group voting an item 7-9). Thus 69 outcomes were carried through to round 3.

Table 5. 10 Round 2 Delphi results: outcomes rated 7-9 by 80% or more of whole sample

Questionnaire items (n = 70)	Whole sample n = 78	Patients n = 24	Therapists n = 31	Surgeons n = 23
Appropriateness of treatment	100%	100%	100%	100%
Pain duration and frequency	98.5%	95.6%	100%	100%
Maintaining personal hygiene	98.5%	95.6%	100%	100%
Pain intensity	98.5%	95.6%	100%	100%
Emotional distress	98.5%	100%	100%	95.6%
Carrying out a daily routine	98.5%	100%	100%	95.6%
Voluntary movement of the arm	97.5%	95.8%	96.7%	100%
Strength of muscles in the arm	97.2%	91.6%	100%	100%
Failure of the surgical join of the nerves	96.2%	95.2%	93.5%	100%
Worsening of existing pain/pins and needles	96.4%	100%	93.5%	95.6%
Carrying and lifting objects	96.1%	96%	96.7%	95.6%
The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm	94.9%	95.6%	93.5%	95.6%
Breathing problems	94.3%	95.3%	96.7%	90.9%
Loss of voluntary (active) movement	93.3%	87.5%	96.7%	95.6%
Damage to other nerves during the surgery	93.3%	83.3%	96.7%	100%
Fine hand movement	91.5%	83.3%	100%	91.3%
Access to and quality of treatment	91.2%	83.3%	90.3%	100%
A nerve join, results in a formation of bundle of painful nerves	92.3%	95.3%	90.3%	91.3%
Effect on relationship with and or ability to care for, children	90.2%	95.6%	96.7%	78.2%
Putting on and taking off clothes	89.9%	74%	100%	95.6%
Failure of the surgical join of the artery/vein	91.2%	95%	96.7%	81.8%
Limited voluntary movement because of the inability to co-ordinate muscles at the same time*	89.1%	91.3%	93.5%	82.6%
Description of the pain (quality and interference)	89.9%	81.8%	96.7%	91.3%
Ability to cope*	89.1%	100%	93.5%	73.9%
Intentions and goals	88.6%	83.3%	100%	82.6%
Ability to feel to protect the arm from injury	88.4%	78.3%	100%	87%
Ability to eat using utensils or hand*	88.4%	82.6%	87.1%	95.6%
Reaching, pulling, pushing, turning, or twisting the arm	88.2%	91.6%	77.4%	95.6%
Expectations of treatment*	87.6%	79.2%	96.7%	87%
Loss of assisted range of motion (stiffness)	87.6%	83.3%	83.8%	95.6%
Failure of the bone to unite following bone surgery	86.4%	77.7%	90.3%	91.3%
Overall health	86.8%	82.6%	90.3%	87%
Infection in the body part that was operated on	86.6%	90.5%	96.7%	72.7%
Ability to feel with the arm	85.8%	69.5%	96.7%	91.3%
Development of a blood clot	85.6%	78.2%	96.7%	81.8%
Self-esteem and self-confidence	82.6%	79.2%	90.3%	78.2%
Problems with the wound (infection, failure to heal)	82.3%	91%	96.7%	59.1%
Development of pain/pins and needles in new area of the body	81.4%	87.4%	61.3%	95.6%
Patient satisfaction with health care received	80.7%	66.6%	80.1%	95.6%
Addictive behaviours (e.g., alcohol, medication drugs)	81%	87.5%	90.3%	65.2%
Thoughts and beliefs	80.5%	66.6%	96.6%	78.2%
Effects on intimate relationships	80.8%	82.6%	90.3%	69.5%
Return to any other paid/nonpaid previous role	80.8%	72.7%	87.1%	82.6%

Additional outcomes added after participants' suggestions in round 1

Table 5. 11 Round 2 Delphi results: outcomes rated 7-9 by 79.9% or less of whole sample

Questionnaire items n = 70	Whole sample n = 79	Patients n = 24	Therapists n = 31	Surgeons n = 23
Injury to an artery or vein resulting in bleeding where the operation takes place	79.8%	85.7%	90%	63.6%
Overall quality of sleep	79.4%	74%	90.3%	73.9%
Chest infection	80.6%	91%	87.1%	63.6%
Effect on relationship with partner/spouse	79.4%	78.2%	90.3%	69.6%
Passive/assisted movement of the arm	76.3%	62.5%	83.9%	82.6%
Maintaining personal appearance	78.3%	69.5%	87.1%	78.2%
Transport needs	78%	74%	77.4%	82.6%
Costs to the patient from long term loss of individual/ family income	76.2%	91.3%	67.7%	69.5%
Bone uniting in the wrong position	75.6%	83.3%	87.1%	56.5%
Effect on relationship with other family members	75.4%	78.3%	87.1%	60.8%
Return to full duties at previous role in paid employment	76.1%	68.2%	77.4%	82.6%
Return to or begin role in education	71.2%	59.1%	80.6%	73.9 %
Body Image	67.8%	58.3%	80.1%	65.2%
Return to previous recreational activities	66.4%	74%	60%	65.2%
The structure of brachial plexus using MRI or other techniques	64.4%	95.6%	58.6%	39.1 %
Muscle fatigue or endurance*	60%	66.6%	61.3%	52.2%
Bleeding from the wound	59.7%	63.6%	56.6%	59.1%
Pain when the arm is exposed to cold	57.8%	65.2%	38.7%	69.6%
Effect on relationships with friends and neighbours	56.3%	47.8%	77.4%	43.5%
Costs to uninsured private paying patients, insurance, or other third-party payers (includes national health services) for all outpatient and in-patient care received for a brachial plexus injury including medication	46.2%	62%	28.6%	47.8 %
Development of musculoskeletal problems in other parts of the body*	43.7%	70.8%	38.7%	21.7%
Increased sensitivity of the scar	43.9%	29.2%	41.9%	60.8%
A measure of the activity in the movement and sensation areas of the brain	42.2%	90%	15%	21.7%
Pins and needles or tingling in the arm	40.8%	52.2%	35.5%	34.7%
Out of pocket costs to the patient for outpatient appointments and inpatient care	41.9%	34.7%	34.5%	56.5%
The physical appearance of the arm	36.2%	20.8%	22.6%	65.2%
Sensation of heaviness in the arm	36.1%	47.8 %	25.8%	34.7%

**Additional outcomes added after participants' suggestions in round 1*

Shading: outcome which reached criteria to be removed for round 3

5.3.2.5 Round 3 Delphi results

Items for voting and responses: They consisted of 69 items carried forward from round 2. Tables 5.12 and 5.13 summarise the percentage of respondents voting an outcome very important (7-9).

Response rate: Of those participating in round 2, 71/78 (91%) took part in round 3.

Demographic characteristics of participants: Of all participants, 20 were people with a BPI (80% of those completing round 2), 31 were therapists (100% of those completing round 2) and 20 were surgeons (87% of surgeons completing round 2). The overall attrition for all three rounds was 28% (78/99). Tables 5.3 and 5.4 summarise the demographic data.

Table 5. 12 Round 3 Delphi results: outcomes rated 7-9 by 80% or more of whole sample

Questionnaire items	Whole sample n = 71	Patients n = 20	Therapists n = 31	Surgeons n = 20
Emotional distress	98%	95%	100%	100%
Voluntary movement of the arm	97%	95%	97%	100%
Carrying out a daily routine	97%	100%	97%	95%
Worsening of existing pain/pins and needles	95%	95%	90%	100%
Appropriateness of treatment	94%	95%	93%	95%
Pain intensity	93%	95%	93%	90%
Loss of voluntary (active) movement	94%	90%	93%	100%
Maintaining personal hygiene	93%	85%	93%	100%
The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm	93%	90%	93.1%	95%
Damage to other nerves during the surgery	92%	80%	97%	100%
Ability to feel to protect the arm from injury	91%	85%	87%	100%
Pain duration and frequency	91%	90%	93%	90%
Failure of the surgical join of the nerves	91%	84.2%	90%	100%
Strength of muscles in the arm	90%	95%	74%	100%
Ability to eat using utensils or hand	89%	80%	86%	100%
Failure of the surgical join of the artery/vein	89%	88.8%	89.6%	90%
Ability to cope	88%	90%	90%	85%
Effect on relationship with and or ability to care for, children	85%	85%	90%	80%
Fine hand movement	85%	75%	84%	95%
Ability to feel with the arm	86%	70%	87%	100%
Breathing problems	86%	84.2%	89.7%	85%
Overall health	85%	75%	84%	95%
A nerve join, results in a formation of bundle of painful nerves	85%	84.2%	80%	90%
Carrying and lifting objects	84%	85%	77%	90%
Loss of assisted range of motion (stiffness)	84%	75%	81%	95%
Expectations of treatment	83%	70%	90%	90%
Limited voluntary movement because of the inability to co-ordinate muscles at the same time (co-contraction)	82%	80%	86.6%	80%
Failure of the bone to unite following bone surgery	82%	68.7%	76.6%	100%
Description of the pain (quality and interference)	82%	75%	81%	90%
Putting on and taking off clothes	81%	70%	84%	90%
Access to and quality of treatment	80%	75%	74%	90%

Shading: item not reaching consensus criteria to be carried to the consensus meeting

Table 5. 13 Round 3 Delphi results: outcomes rated 7-9 by 79% or less of whole sample

Questionnaire items	Whole sample n = 71	Patients n = 20	Therapists n = 31	Surgeons n = 20
Bone uniting in the wrong position	77%	81.3%	69.3%	75%
Intentions and goals	77%	69.4%	86%	75%
Self-esteem and self-confidence*	77%	80%	81%	70%
Infection in the body part that was operated on	77%	68.4%	86.6%	75%
Problems with the wound such as infection, failure to heal properly	76%	65%	86.6%	75%
Reaching, pulling, pushing, turning, or twisting with the arm	75%	80%	64%	80%
Overall quality of sleep	74%	65%	81%	75%
Patient satisfaction with health care received	74%	60%	71%	90%
Injury to an artery or vein resulting in bleeding where the operation takes place*	73%	73.7%	75.9%	70%
Effect on relationship with partner/spouse	73%	65%	84%	70%
Development of a blood clot*	72%	70%	75.8%	70%
Addictive behaviours (e.g., alcohol, medication drugs)	71%	75%	64%	75%
Development of pain/pins and needles in a new area of the body	70%	65%	55%	90%
Passive/assisted movement of the arm	69%	50%	71%	85%
Return to any other paid/non-paid previous role	69%	63.1%	65%	80%
Effects on intimate relationships	68%	70%	74%	60%
Transport needs	68%	70%	55%	80%
Thoughts and beliefs	66%	60%	74%	65%
Maintaining personal appearance	66%	65%	58%	75%
Return to full duties at previous role in paid employment	65%	52.6%	58%	85%
Effect on relationship with other family members	65%	60%	74%	60%
Chest infection	64%	68.4%	62.1%	60%
Return to previous recreational activities	64%	68.4%	58%	65%
Body Image	64%	55%	61%	75%
Return to or begin role in education	61%	42.1%	65%	75%
Costs to the patient from long term loss of individual/family income	58%	73.7%	46.6%	55%
Bleeding from the wound	50%	55%	44.8%	50%
Effect on relationships with friends and neighbours	48%	35%	58%	50%
The structure of brachial plexus using MRI or other techniques	47%	63.2%	41.4%	35%
Muscle fatigue or endurance	42%	42.1%	55%	30%
Pain when the arm is exposed to cold	41%	50%	23%	50%
Development of musculoskeletal problems in other parts of the body	32%	40%	23%	0%
A measure of the activity in the movement and sensation areas of the brain	31%	61.1%	10.4%	20%
Pins and needles or tingling in the arm	29%	35%	16%	35%
Costs to uninsured private paying patients, insurance, or other third-party payers (includes national health services) for all outpatient and in-patient care received for a brachial plexus injury including medication	27%	27.8%	14.3%	40%
Out of pocket costs to the patient for outpatient appointments and inpatient care	25%	20%	10.7%	45%
Increased sensitivity of the scar	25%	20%	10%	45%
The physical appearance of the arm	20%	15%	6%	40%

**Additional items carried through to consensus meeting*

Voting responses: 33 outcomes reached the criteria to be carried through to the consensus meeting and Table 5.14 presents these.

Table 5. 14 Results round 3 Delphi: outcomes rated 7-9 by at least 70% in all groups

Outcome	Combined % rating 7-9	Outcome	Combined % rating 7-9
Voluntary movement of the arm	97%	Expectations of treatment	83%
Strength of the arm	90%	Overall health	85%
Carrying and lifting	84%	Access to treatment	80%
Fine hand movement	85%	Appropriateness of treatment	94%
Ability to feel with the arm	86%	Loss of voluntary (active) movement	94%
Ability to feel to protect the arm from injury	91%	Loss of assisted range of movement (stiffness)	84%
Pain intensity	93%	Limited voluntary movement because of the inability to co-ordinate muscles at the same time	82%
Pain duration and frequency	91%	Damage to other nerves during surgery	92%
Pain description (quality and interference)	82%	Worsening existing pain/pins and needles	95%
The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm	93%	A nerve join results in the formation of a bundle of painful nerves	85%
Carrying out a daily routine	97%	Failure of the surgical join of the artery/vein	89%
Ability to eat using utensils/hands	89%	Injury to an artery or vein resulting in bleeding where the operation takes place	73%
Maintaining personal hygiene	93%	Development of a blood clot	72%
Putting on and taking off clothes	81%	Breathing problems	86%
Effect on relationship with and or ability to care for, children	85%	Failure of a surgical join of the nerve	88%
Emotional distress	98%		
Self-esteem and self-confidence	77%		
Ability to cope	88%		

5.3.2.6 Attrition over the Delphi rounds

The overall attrition between rounds 1-3 was 29 %, with the highest attrition for surgeons (see Table 5.15).

Table 5. 15 Attrition rates between rounds

Stakeholder Group	Registered n (% total registrants)	Completed R1 (% of registered)	Completed R2 (% of round 1 completers)	Completed R3 (% of round 1 completers)
People with the injury	36 (32)	30 (83)	24 (80)	20 (66)
Surgeons	39 (34)	33 (85)	23 (70)	20 (61)
Therapists	39 (34)	36 (92)	31 (86)	31 (86)
Total	114	99	78 (79)	71 (71)

5.3.2.7 Difference between stakeholder group ratings

At the end of round 3 of the Delphi, surgeons reached consensus that 51 outcomes were 'critical' to be included in the COS-BPI. Patients rated 39 outcomes 'critical' to be included and therapists agreed 44 should be included in a COS-BPI. Six outcomes which patients rated as "critical" did not proceed to the consensus meetings. These included bone uniting in the wrong position; reaching, pulling, pushing, turning, or twisting with the arm; addictive behaviours, effect on intimate relationships, transport needs and costs to the patient from long term loss of individual/family income. The differences between the groups are detailed in Appendix 5.13.

5.3.3 Consensus meetings

5.3.3.1 Consensus meetings demographics

In total 38 participants attended two consensus meetings. This included 25 clinicians and 13 patients. Figures 5.4, 5.5, and Table 5.16 present details of the consensus meeting attendees.

Figure 5. 4 Geographical distribution of consensus meeting attendees

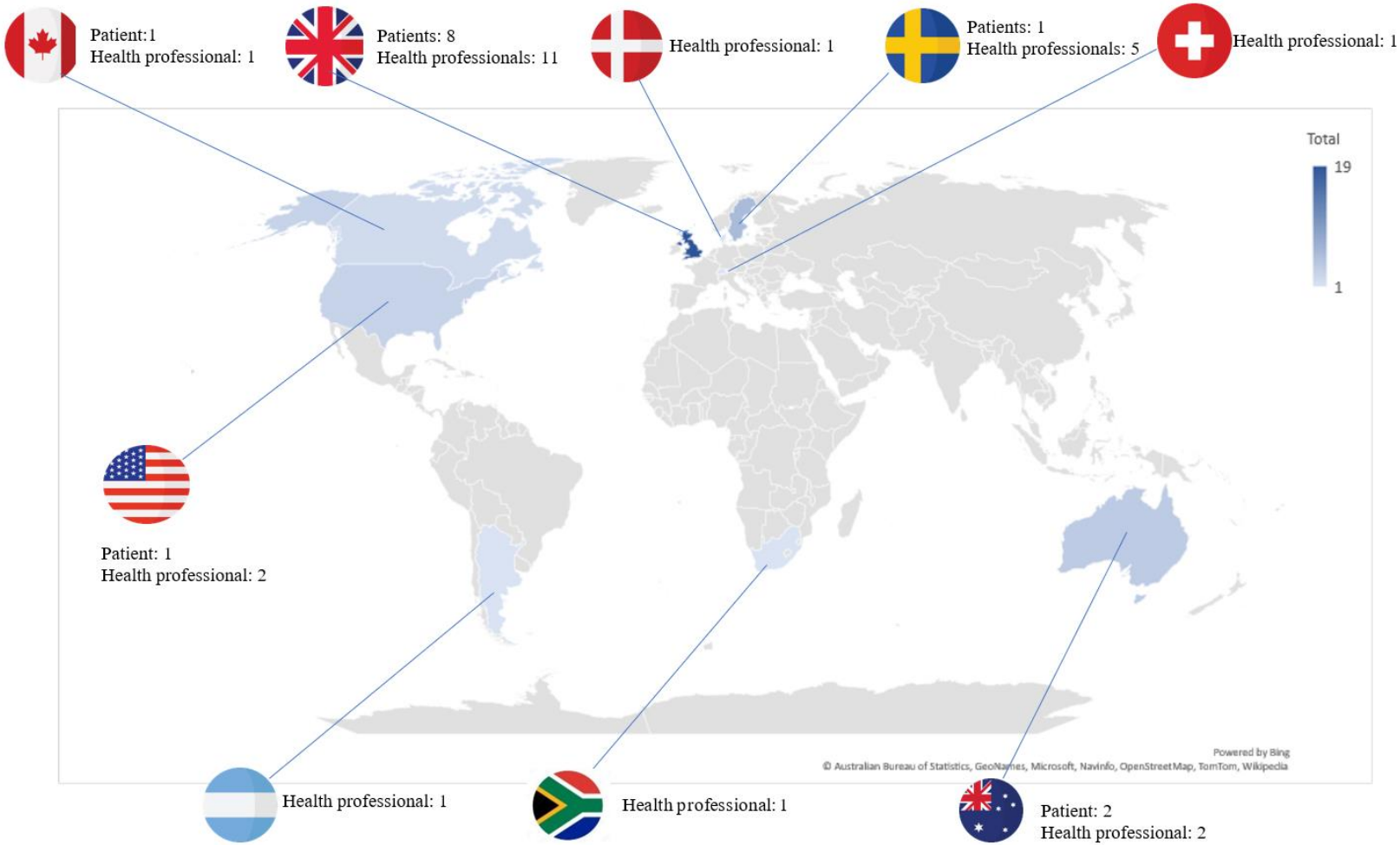
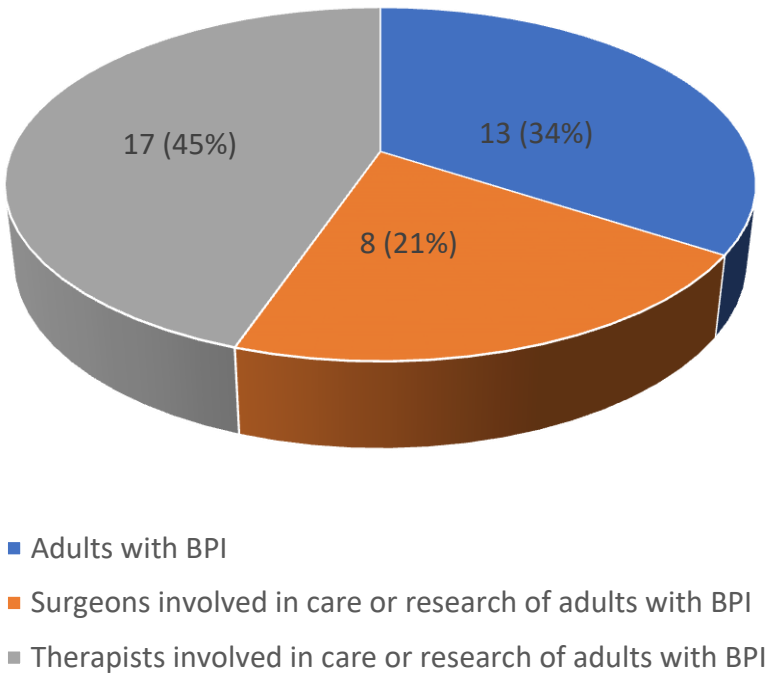


Table 5. 16 Consensus meetings: participant type and country

Country of participant	Patient n (%)	Clinician n (%)	Total n (%)
United Kingdom	8 (61.5%)	11 (44%)	19 (50%)
Australia	2 (15.4%)	2 (8%)	4 (10.5%)
US	1 (7.7%)	2 (8%)	3 (7.9%)
Canada	1 (7.7%)	1 (4%)	2 (5.4%)
Sweden	1 (7.7%)	5 (20%)	6 (15.8%)
Argentina	0	1 (4%)	1 (2.6%)
South Africa	0	1 (4%)	1 (2.6%)
Switzerland	0	1 (4%)	1 (2.6%)
Denmark	0	1 (4%)	1 (2.6%)

Figure 5. 5 Stakeholder representation at consensus meetings



5.3.3.2 Patient consensus meeting results

All participants (n = 13) took part in voting for each of the outcomes. Tables 5.17 and 5.18 summarises the voting results for the general and complication outcomes. Only two outcomes were re-voted on in round 2 as they did not reach the consensus threshold of 85%, but 70% or more participants voted to include them.

Table 5. 17 Percentage voting for general outcomes at the patient consensus meeting

Outcomes (n=22)	**Include % (n)**	**Exclude % (n)**	**Revote-include**	**Revote exclude**
Voluntary movement of the arm	100% (13)	0% (0)		
Strength of the arm	54% (7)	46% (6)		
Carrying and lifting	15% (2)	85% (11)		
Fine hand movement	54% (7)	46% (5)		
Ability to feel with the arm	31% (4)	69% (9)		
Ability to feel to protect the arm from injury	54% (7)	46% (6)		
Pain intensity	85% (11)	15% (2)		
Pain duration	69% (9)	31% (4)		
Pain description	23% (3)	77% (10)		
Overall health	46% (6)	54% (7)		
Access to treatment	77% (10)	23% (3)	100% (13)	0
Appropriateness of treatment	85% (11)	15% (2)		
The ability of the brachial plexus to send signals to the skin and muscles of the arm	54% (7)	46% (6)		
Carrying out daily routine	85% (11)	15% (2)		
Maintaining personal hygiene	46% (6)	54 % (7)		
Putting on and taking off clothes	38% (5)	62% (8)		
Ability to eat using utensils /hands	38% (5)	62% (8)		
Effect on relationship with or ability to care for children	46% (6)	54% (7)		
Emotional distress	15% (2)	85% (11)		
Self-esteem and self-confidence	23% (3)	77% (10)		
Ability to cope	69% (9)	31% (4)		
Expectations of treatment	62% (8)	46% (5)		

*Shading = outcomes reaching consensus **IN***

Table 5. 18 Percentage voting for complication outcomes at the patient consensus meeting

Outcomes (n= 11)	**Include**	**Exclude**	**Re-vote include**	**Re-vote exclude**
Loss of voluntary movement	100 % (13)	0		
Loss of assisted movement (passive)	31% (4)	69% (9)		
Limited voluntary movement because of inability to co-ordinate muscles at the same time	54% (7)	46% (6)		
Nerve forms a painful bundle of nerves (neuroma)	54% (7)	46% (6)		
Damage to other nerves during the surgery	54% (7)	46% (6)		
Worsening of existing pain or pins and needles	100% (13)	0		
Failure of a surgical join of the nerve*	77% (10)	23% (3)	77% (10)	23% (3)
Failure of a surgical join of an artery of a vein	31% (4)	69% (9)		
Injury to an artery or vein resulting in bleeding where the operation takes place	23% (3)	77% (10)		
Development of a blood clot	31% (4)	69% (9)		
Breathing problems	54% (7)	46% (6)		

*Shading = outcomes reaching consensus **IN***

***Outcome not reaching consensus IN or OUT*

Patients voted seven of the 33 outcomes into the COS. Following the voting, there was discussion about two of the outcomes 'access to treatment' and 'appropriateness of treatment'. Following this discussion, patients decided to merge these two outcomes into one called 'access to appropriate treatment'. Therefore, the following six outcomes were prioritised by patients for inclusion in the COS-BPI:

- Voluntary movement
- Pain intensity
- Access to appropriate treatment
- Carrying out daily routine
- Loss of voluntary movement
- Worsening of existing pain or pins and needles (complication)

One outcome did not reach the criteria for inclusion or exclusion even with re-voting. This outcome was 'failure of a surgical join of the nerve'. The research team decided to carry this outcome forward to be discussed at the ratification meeting with patients and HCPs.

5.3.3.3 Healthcare professional consensus meeting results

All participants (n = 25) took part in voting for each of the outcomes. Tables 5.19 and 5.20 summarise the voting results for the general and complication outcomes respectively. The three pain outcomes (pain intensity, duration and frequency, and description) did not reach consensus. Participants expressed concern about this and felt that the votes had been split between the separate pain outcomes and considered it important to be part of the COS. Participants asked and agreed to re-vote on pain as a whole (including pain intensity, duration and frequency, and description). In total, participants re-voted on six outcomes that had not reached consensus ***IN*** or ***OUT*** in round 1.

Table 5. 19 Percentage voting for general outcomes at the HCP consensus meeting

Outcomes (n=22)	**Include**	**Exclude**	**Re-vote include**	**Re-vote exclude**
Voluntary movement of the arm	79% (19)	21% (5)	92% (23)	8% (2)
Strength of the arm	62% (15)	38% (9)		
Carrying and lifting	46% (11)	54% (13)		
Fine hand movement	79% (19)	21% (5)	88% (22)	12% (3)
Ability to feel with the arm	72% (18)	28% (7)	96% (24)	4% (1)
Ability to feel to protect the arm from injury	16% (4)	84% (21)		
Pain intensity	64% (16)	36% (9)		
Pain duration and frequency	20% (5)	80% (20)		
Pain description (quality and interference)	28% (7)	72% (18)		
Overall health	36% (9)	64% (16)		
Access to treatment	40% (10)	60% (15)		
Appropriateness of treatment	24% (6)	76% (19)		
The ability of the brachial plexus to send signals to the skin and muscles of the arm	28% (7)	72% (18)		
Carrying out daily routine	92% (22)	8% (2)		
Maintaining personal hygiene	25% (6)	75% (18)		
Putting on and taking off clothes	17% (4)	83% (20)		
Ability to eat using utensils/hands	29% (7)	71% (17)		
Effect on relationship with or ability to care for children	24% (6)	76% (19)		
Emotional distress	56% (14)	44% (11)		
Self-esteem and self-confidence	36% (9)	64% (16)		
Ability to cope	60% (15)	40% (10)		
Expectations of treatment	36% (9)	64% (16)		
Pain (combining intensity, duration and frequency, and description)	----------	----------	100% (25)	0%

Shading = outcomes reaching consensus in

Table 5. 20 Percentage voting for complication outcomes at the HCP consensus meeting

Outcomes (n=11)	Include	Exclude	Revote include	Revote exclude
Loss of voluntary movement	76% (19)	24% (6)	100% (24)	0% (0)
Loss of assisted movement (passive)	44% (11)	56% (14)		
Limited voluntary movement because of inability to co-ordinate muscles at the same time	44% (11)	56% (14)		
Nerve forms a painful bundle of nerves (neuroma)	48% (12)	52% (13)		
Damage to other nerves during the surgery	60% (15)	40% (10)		
Worsening of existing pain or pins and needles	60% (15)	40% (10)		
Failure of a surgical join of the nerve (n = 24 then 25) *	79% (19)	21% (5)	76% (19)	24% (6)
Failure of a surgical join of an artery of a vein	25% (6)	75% (18)		
Injury to an artery or vein resulting in bleeding where the operation takes place	25% (6)	75% (18)		
Development of a blood clot	33% (8)	67% (16)		
Breathing problems	38% (9)	62% (15)		

*Shading = outcomes reaching consensus **IN***

Outcome not reaching consensus IN or OUT

Healthcare professionals voted six outcomes into the COS. These were:

- Voluntary movement
- Fine hand movement
- Ability to feel with the arm
- Carrying out daily routine
- Pain (including intensity, duration and frequency, and description)
- Surgical complications: loss of voluntary movement (donor or affected limb)

One outcome did not reach the criteria for inclusion (85% or more voting it ***IN***) or exclusion (69% or less voting it ***IN***), even with re-voting. This outcome was 'failure of a surgical join of the nerve'. The research team decided to carry this outcome forward to be discussed at the ratification meeting with patients and HCPs. There was general concern at the end of the clinicians' consensus meeting that none of the emotional wellbeing outcomes had been voted into the core outcome set. Therapists and surgeons discussed how they felt that the emotional wellbeing outcomes significantly impacted on a patient's recovery and that measuring them was important. One therapist said:

> *"More to say that this is very important, this is a very debilitating injury, a life-changing injury and we definitely need some way to pick it up." (P11)*

Another therapist said emotional wellbeing could change with time:

> *"Their [people with a BPI] set of expectations on day one or even on month one / two is vastly different than in year two and that's what makes it hard to also quantify their coping ability changes, their psychosocial ability changes/ adapt with time…. it is not like other types of injuries that you see for 6 weeks/ 2 months and then they are gone" (P4)*

Finally, a surgeon reiterated that negative psychological impact was common and can be a barrier to recovery:

> *"It's just that none of the psychological outcomes went through yet, every single patient I treat with a plexus injury it is certainly a huge component that can be a barrier to their recovery" (P6)*

There was concern that, as with the pain outcomes, the number of outcomes relating to psychological status had split votes, hence none had reached consensus:

> *"I think we just got a little bit deluded because there was so many options kind of like with pain. So, is there a way to get that included because I think that is really important too?" (P11)*

Some therapists asked for all the outcomes within the emotional wellbeing domain to be merged and then re-voted on, as had been done with pain. However, the emotional wellbeing outcomes (emotional distress, expectations of treatment, ability to cope, and self-esteem and self-confidence) were quite different and thus not feasible to merge. A compromise was agreed, whereby the distribution of votes should be analysed by the research team and presented and reviewed at the final ratification meeting.

Comparison of outcomes voted in at patient and HCP meeting: Table 5.21 compares the outcomes voted in at the patient and HCPs consensus meeting.

Table 5. 21 Comparison of outcomes reaching consensus at patient and HCP meeting

Outcomes	Both patient and HCP meetings	Patient only	HCP only
Voluntary movement of the arm	**X**		
Carrying out daily routine	**X**		
Loss of voluntary movement (donor complication)	**X**		
Pain intensity		**X**	
Pain (including intensity, duration and frequency, and description)			**X**
Access to appropriate treatment		**X**	
Worsening of existing pain or pins and needles (donor complication)		**X**	
Fine hand movement			**X**
Ability to feel with the arm			**X**

5.3.3.4 Ratification meeting

The research team (CM, CJH, JC), two patient representatives, one therapist and one surgeon attended the online final ratification meeting on 20th April 2021.

All outcomes voted ***IN*** at both meetings were included in the final COS. Attendees agreed to include fine hand movement within the 'voluntary movement of the arm' outcome. Attendees agreed it was appropriate to include a larger pain domain (including intensity, duration and description). The patient representatives at the ratification meeting felt that if a larger pain domain had been presented for voting at the patient meeting, it would have been voted through. Attendees discussed the merits of having several tiers, similar to other COS (Tong et al., 2020) and as OMERACT recommends (Beaton et al., 2021a). Tier 1 would include outcomes that *all* stakeholders agreed as important to include. Tier 2 would include outcomes which *one* stakeholder group agreed were critically important. Tier 1 outcomes would always be measured and reported in clinical practice and research, while Tier 2 outcomes are important but optional to measure.

Attendees discussed the outcomes within the emotional wellbeing domain, as there were concerns at both consensus meetings that these outcomes did not reach consensus. CM presented the distribution of votes across the different emotional wellbeing outcomes (emotional distress, self-esteem and confidence, expectations of treatment, ability to cope). At least one of the outcomes from the domain 'emotional wellbeing' had been selected for inclusion by every participant in the clinician meeting. However, the votes were split between multiple outcomes and no single one reached the required consensus threshold. At the patient meeting, 10/13 (76%) participants voted to include at least one emotional wellbeing outcome. Emotional distress and ability to cope were the highest-rated outcomes (in the 'emotional wellbeing' domain) in both meetings. After a lengthy discussion, all attendees at the ratification meeting agreed that emotional distress and ability to cope should therefore be included in Tier 2 of the COS-BPI.

Finally, the two surgical complications outcomes were discussed. Loss of voluntary movement was voted ***IN*** at both meetings. However, 'worsening of existing pain or pins and needles' was only voted ***IN*** by the patient group. There was general

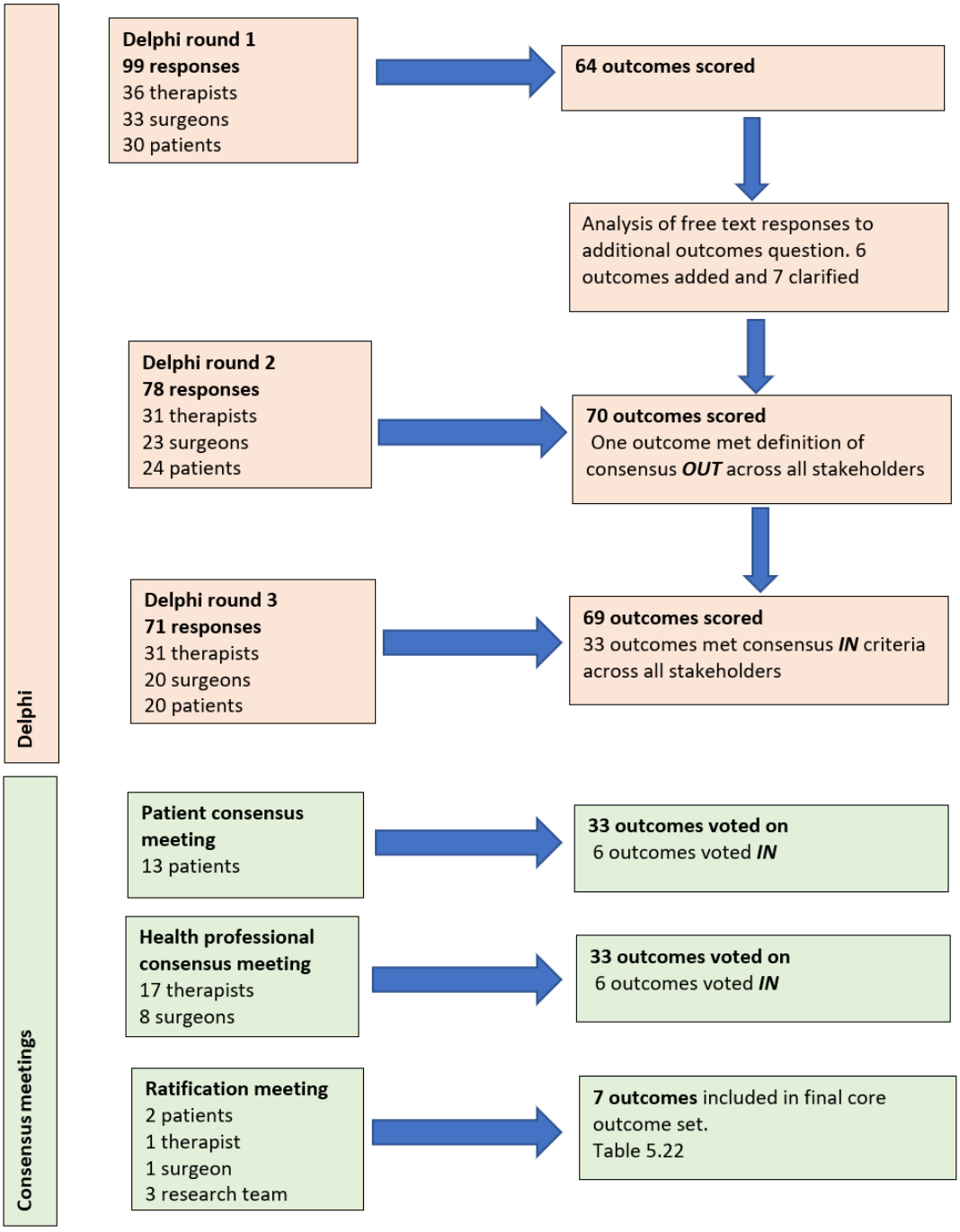
agreement that 'worsening of existing pain or pins and needles' would not be appropriate to fit into Tier 2 where it would be optional, as it was felt an important outcome in donor morbidity. Also, there was discussion about having one complication in Tier 1 and another in Tier 2 may be confusing for future COS users. It was agreed therefore that these two surgical complication outcomes, associated with donor morbidity, should be always measured and reported in surgical cases where donor tissue is used. Table 5.22 presents the final COS-BPI. Figure 5.6 presents an overview of the development of the COS-BPI.

Table 5. 22 Final COS-BPI

Tier	Outcome	Definition
Tier 1	**Voluntary movement**	To include all active movement of the whole upper limb, shoulder, elbow, wrist, and hand.
	Pain	The experience of pain including pain intensity, duration and frequency, and description (quality and interference).
	Carrying out daily routine	Daily routine to include housework, taking care of plants indoors and outdoors, preparing meals (expanded at consensus meeting to include maintaining personal hygiene, personal appearance, dressing, and ability to carry out routine at work and with hobbies).
	Loss of voluntary movement	In previously unaffected donor muscles not already denervated from original BPI.
	Worsening of pain or pins and needles	In the distribution of the affected BPI nerves or donor sites.
Tier 2	**Emotional distress**	The emotional impact on life (including work, ADL, and relationships), energy levels, mood and anxiety, and depression.
	Ability to feel with the arm	To include both the ability to feel and the ability to feel to protect.
	Ability to cope	The ability to cope.
	Access to appropriate treatment	Access to appropriate treatment.

Red text *= complications of surgery and will not apply to all*

Figure 5. 6 Overview of COS-BPI development



5.4 Discussion

The objectives of this study were to develop a long list of clinical outcomes relevant to adults with a BPI, prioritise these outcomes and finally achieve consensus on the most important outcomes for evaluating and reporting in BPI research and care. A Delphi questionnaire (including the long list of clinical outcomes) was developed from the results of the previous interviews and systematic review. It underwent piloting and think-aloud interviews before being used in a 3-round international Delphi to prioritise the outcomes. In a final virtual meeting with international patients and HCPs, a final COS-BPI was agreed.

Consensus was reached on the inclusion of three outcomes in the COS-BPI: voluntary movement, carrying out a daily routine, and pain. At least, 85% of international patients, surgeons and therapists identified these outcomes as critically important. It is recommended that as a minimum these three outcomes should be measured and reported in clinical care and research in adults with a BPI. Two complications of surgery (loss of voluntary movement AND worsening of pain or pins and needles) are complications specific to donor morbidity (see Chapter 1). These complications are critical to measure in surgical studies or in patients undergoing surgery using donors. Four further outcomes were included in Tier 2, which were critically important to some but not all stakeholders and are important but optional outcomes to be measured and reported. The COS was prioritised from an initial total of 64 outcomes (plus six added in round 2).

5.4.1 In the context of other literature

No other published COS for BPI has been identified. Hill et al. (2015a) previously stated the need for consensus on a core outcome measurement set, but they recommended this be conducted involving clinicians and without the direct input of patients. In contrast, both patients and a broad range of HCPs have been involved in every stage of the development of this COS.

The results of the COMBINE consensus process highlighted differences between the outcomes reported in current BPI studies (Chapter 3) and those prioritised as important by HCP and patient stakeholder groups in this study. Strength is measured

and reported in approximately 90% of studies including patients with a BPI (Dy et al., 2015; Miller et al., 2021). However, strength did not achieve consensus in the COMBINE study. Only 25% of BPI studies measure and report voluntary movement and pain (Dy et al., 2015; Miller et al., 2021), but both reached a consensus in the current study. Finally, BPI studies infrequently report "carrying out daily routine" (Dy et al., 2015; Miller et al., 2021) but the COS-BPI includes it. Regarding strength being omitted from this COS, participants discussed extensively in both meetings that there was overlap in the outcomes presented. It is plausible that participants used a strategy of voting for the broader domains, which would include outcomes. For example, to achieve 'voluntary movement' and 'carrying out daily routine', an individual needs 'strength' in their upper limb. Additionally the included core outcome 'access to treatment' was not identified at all in the systematic review in Chapter 3 (Miller et al., 2021), but was identified through interviews with patients (Chapter 4). Access to treatment was consistently rated highly by all stakeholders throughout the Delphi but in the consensus meetings, only the patient stakeholder group voted it critical to be included in the COS. The inclusion of 'access to appropriate treatment' in the COS indicates the value of including the patient voice throughout this COS development. If patients had not been included in the COS development from the beginning, then it is unlikely that 'access to appropriate treatment', an outcome critically important to them, would be included.

Outcomes chosen are similar in type and number to those agreed in other trauma COS. However, definitions of these similar domains vary. In a hip fracture COS, the outcomes chosen included mortality, mobility, pain, activities of daily living, and health-related quality of life (Haywood et al., 2014). A COS for distal radius fractures included pain and function as the core outcomes (Goldhahn et al., 2014). Finally, a COS developed for shoulder disorders includes four outcomes (pain, physical functioning, global assessment of treatment success, and health-related quality of life) with two additional outcomes (sleep functioning and psychological functioning) meeting inclusion for some but not all stakeholders (Page et al., 2016). Outcomes in the COS-BPI overlap with many of these other COS, implying that core outcomes may be similar across different areas of clinical care and research. However, despite similarities in broad domains, there are differences in definitions or included outcomes within each

domain. Goldhahn et al. (2014) included pain intensity and frequency within their domain of pain, but included pain quality, impact, pain catastrophising, and interference as optional attributes. Haywood et al. (2014) also included pain in their hip fracture COS, but it was specific to pain sensations. During the development of a COS for shoulder disorders, eight different pain outcomes were merged between rounds 1 and 2 of the Delphi, and pain as a single domain was included in round 2 (Page et al., 2016). This domain was included in the final COS for shoulder disorders and defined as "how much a person's shoulder hurts, reflecting the overall magnitude of the pain experience (rest, during and after activity, at night)". In the COS-BPI, the HCPs wanted all pain outcomes merged into one larger domain, as they believed that votes were being split between intensity, duration and frequency, and description. This is similar to what happened in other COS in trauma (Goldhahn et al., 2014; Page et al., 2016), where during these development processes, pain outcomes were merged. Although this supported inclusion of pain in the COS, the multidimensional nature of pain in this COS and others makes measurement of this domain more challenging and may impact on implementation if numerous measures are needed to measure one domain.

Although there was an overlap of some outcome priorities by professionals and patients, there were also some notable differences. At the end of the consensus meetings, nine outcomes were prioritised by either patients and/or HCPs. Five outcomes were prioritised by both groups (voluntary movement, carrying daily routine, two pain outcomes and the complication, loss of voluntary movement); the remaining four were prioritised by one group only (Table 5.21). The 'ability to feel with the arm' and 'fine hand movement' reached consensus for inclusion in the COS by the HCPs only, whereas 'access to appropriate treatment' and 'worsening of pain or pins and needles' reached consensus in the patient-only group. Differences in patient and professional views are common in COS development and have been seen in other disease areas (Blazeby et al., 2015; Coulman et al., 2016b; Fish et al., 2018; Potter et al., 2015). During the development of a breast reconstruction COS, professionals prioritised operation-specific complications that patients did not, whereas patients prioritised "self-esteem", "emotional wellbeing" and "physical wellbeing", which professionals did not (Potter et al., 2015). Similarly, patients rated the longer-term

quality of life outcomes more highly than shorter-term clinical outcomes during the development of a core information set for oesophageal cancer (Blazeby et al., 2015). In contrast, patients in the COMBINE consensus process did not rate the emotional wellbeing outcomes highly in the consensus meetings. This may be because people with a BPI and the patient participants in the COMBINE consensus process are generally young men of working age, a very different demographic to the patient participants in the other studies, which focused on cancer and included older participants. Voluntary movement and the ability to carry out a daily routine, complications and access to treatment were rated highly by our patient participants. The results of the COMBINE consensus process suggest that patients do rate some outcomes differently to HCPs. However, those outcomes are not always related to a certain "type" of outcome as posited by Blazeby et al. (2015), but specific to the health condition and perhaps demographic of the patient participants. This further supports the inclusion of patients in COS development to ensure that outcomes are relevant to them.

5.4.2 Achieving consensus

At the end of the COMBINE Delphi process, a large number of outcomes reached the consensus criteria to be taken to the consensus meeting. If the original protocol had been adhered to (any outcome in either stakeholder group where 70% or more participants voted it very important (7-9)), then 55 outcomes would have been taken forwards for discussion and voting at the consensus meetings. This was too many outcomes to discuss at the meetings. Therefore, the consensus criteria were changed so only outcomes rated very important across all three stakeholder groups were included. High consensus rates after Delphis are common (Coulman et al., 2016a; Retzer et al., 2020) and previous COS developers have used different methods, such as merging outcomes (Retzer et al., 2020) or raising the consensus criteria to 90% of participants voting an outcome "very important" (Coulman et al., 2016a). Further methodological work is needed to explore the impact of rating scales and other methods in outcome selection in COS development.

5.4.3 Decision making

Decision-making in the COMBINE consensus process was sometimes influenced by how outcomes could feasibly be measured. Following COS development guidance (Beaton et al., 2021a; Williamson et al., 2017), the COMBINE project sought to identify "what" to measure before exploring "how" these outcomes should be measured. This was emphasised in the Delphi and consensus meetings, where it was explained that the selection of instruments would be considered once the most important outcomes had been selected. However, particularly in the HCP consensus meeting, decisions around 'what' outcomes were important to measure were influenced by issues surrounding 'how' these outcomes would be measured, such as availability of instruments, feasibility and cost. For example, some outcomes such as 'access to appropriate treatment' were quickly dismissed during initial discussions in the HCP consensus meetings, because they were considered too difficult to measure. This was challenging for me as chair, and I and other members of the research team frequently reminded the HCPs that the focus should be on 'what' outcomes and not 'how' they would be measured. To facilitate the discussion, I revisited the aims of the meeting and I also reiterated that the next stage would identify 'how" these outcomes would be measured. This issue is not unique to the COMBINE project. In the development of a COS for hand osteoarthritis (Kloppenburg et al., 2015), Health-Related Quality of Life was removed from the mandatory COS at a consensus meeting as there was no instrument to measure it. The influence of these factors (available instruments, feasibility and cost) in guiding decisions in COS development consensus meetings need to be further evaluated in future research.

On the other hand, in the patient consensus meeting, patients were less interested in how outcomes would be measured and focused more on whether they were important to them. On reflection, having separate patient and HCP meetings was important, as it lessened the influence of "how" to measure outcomes and ensured that outcomes important to patients were protected, despite not knowing how these might be measured in the future.

5.4.4 Impact of separate consensus meetings

Although there is consensus regarding patient inclusion in COS development, there is no agreement on the best methods to use when conducting consensus meetings. The COMBINE consensus process used separate online patient and HCP meetings. Sections 5.2.3.1 and 5.2.3.3 present the decision making around hosting separate patient and HCP meetings, which included factors such as clinician power and the fact that BPI specialist care is a small area and therefore many patient participants would have potentially known or been treated by the HCPs. This could have impacted on open and honest discussions. Many COS developers, however, have hosted combined meetings (Evangelidis et al., 2017; Harman et al., 2015; Tong et al., 2020). Others, frequently in the surgical area of healthcare, endorse and have hosted separate meetings (McNair et al., 2016; Potter et al., 2015). Having separate patient and HCP consensus meetings potentially influenced the outcomes included in the COS-BPI. The 'access to appropriate treatment' outcome may not have been included in the final COS-BPI. It was not rated as critically important in the HCP consensus meeting, and potentially discussions (held in the HCP meeting) regarding the inability to measure it and relevance to these HCPs' practice could have influenced the patient vote. The importance of 'access to appropriate treatment' to patients would then have been lost. Similarly, HCPs felt 'ability to feel with the arm' was critically important but patients didn't, and a combined meeting may have resulted in this difference in opinion not being identified. However, the merits of a combined patient and HCP consensus meeting cannot be dismissed. Its unique strength is bringing together patients and HCPs to enable each group to hear the other's opinions on why the outcomes are important to them, facilitating open discussion. Potentially, more outcomes would have been included in Tier 1 (must measure and report) of the COS-BPI if patients and HCPs had had the opportunity to listen and discuss why outcomes were important to each stakeholder group. With such mixed views on how consensus meetings for COS development are hosted, there is a need for research into this aspect of the consensus process.

5.4.5 Outcomes or contextual factors

Within the COMBINE consensus process, there was debate among the research team and some HCP participants whether some of the outcomes were contextual factors or modifiers rather than outcomes. The outcomes in the COMBINE consensus development process were categorised using a taxonomy designed specifically for categorisation of health outcomes in research and COS development (Dodd et al., 2018). The categories include 38 domains in five core areas (death, physiological/clinical, life impact, resource use, and adverse events). The delivery of care domain, in the life impact core area, included outcomes such as patient satisfaction, access to health systems, and quality of care. Patients consistently highlighted the outcome 'access to appropriate treatment' during interviews and subsequently rated it highly in the Delphi. It reached a consensus to be included in COS in the patient consensus meeting. 'Access to appropriate treatment' is an example of an outcome that matters greatly to patients. However, if this COS had been designed using the OMERACT or ICHOM framework, 'access to appropriate treatment' may not have been included in the COS and could have been categorised as a "contextual factor" (Kloppenburg et al., 2015). Additionally, despite contextual factors being frequently included in wider COS development (ICHOM and OMERACT), there is no consensus on their definition and role in research and COS development (Nielsen et al., 2021). Future research should consider how contextual factors intersect with the COMET COS taxonomy (Dodd et al., 2018) to improve consistency in future COS development. Further research should also evaluate whether there is parity in definitions of outcomes and contextual factors across COS frameworks.

5.4.6 Strengths and limitations

The COMBINE consensus process has several strengths. The methods adhered to recommendations from international consensus (Kirkham et al., 2017b) and were defined a priori in a protocol (Miller et al., 2019). The inclusion of both patients and HCPs at every stage ensured the outcomes in the final COS were representative of their shared priorities. The views of different stakeholder groups were represented equally, despite a difference in the number of participants. The comprehensive and

rigorous long-listing process ensured that outcomes across all COMET domains were considered in the consensus process.

There were also limitations to the consensus process. Retention of each stakeholder group in the COMBINE Delphi ranged from 61-86% over the three rounds, with surgeons having the highest attrition rates. There is no recommendation on acceptable response rates for Delphis. However, Williamson et al. (2017) suggest that 80% retention for each stakeholder is satisfactory, concurring with a recent review of average response rates in round 2 Delphis for COS (Gargon et al., 2019a). This reflects the response rate in round 2 of the COMBINE Delphi, which was 79%; however, this did drop to an overall rate of 71% by round 3. Keeping participants fully engaged once recruited, so that there is low attrition, is one of the challenges of conducting a 3-round Delphi survey (Hsu and Sandford, 2007). Attrition of participants could mean that people with minority opinions drop out of the Delphi study, leading to an overestimation of consensus thus affecting the validity of the results (Hasson et al., 2000).

The COMBINE Delphi was conducted over the summer period and during the COVID-19 pandemic in 2021. This may have affected retention rates for the Delphi in round 3 and particularly the surgeons, some of whom contacted the study team to let them know of their redeployment to frontline clinical duties over this time. A variety of methods were used to maintain participants' engagement, including regular emails, newsletters and social media updates about study progress and announcements of next round dates, so participants were not caught unaware. Personalised reminder emails were sent to thank participants for their contribution to the study, encouraging completion of each round and emphasising that their views mattered. Using a personalised approach is also a common strategy used in other studies (Allin et al., 2019; Benstoem et al., 2017; Chiarotto et al., 2015) with high response rates and are an effective method of retaining participants between rounds (Gargon et al., 2019a; Hall et al., 2018).

There is evidence that studies recruiting through treatment centres have less attrition than studies recruiting through patient organisations (Barrington et al., 2021; Fish et al., 2018). Although the COMBINE Delphi had ethical approval to recruit through an

NHS trust, during this period non-COVID studies were paused in the NHS. Therefore, I recruited only through patient organisations and online support groups. This may have affected the attrition of patient-participants. Finally, if patients from the NHS had been recruited, the COMBINE consensus process would have potentially included more patients at an earlier phase in their injury. This could have influenced outcome inclusion in the final COS-BPI.

In the future, a "Real-Time Delphi" process may offer benefits in the development of COS and improve retention rates. In a Real-Time Delphi, participants have access to an online questionnaire portal for a time-restricted period. Participants can see all their and other participants' anonymised responses in real-time (Aengenheyster et al., 2017). This type of Delphi provides simultaneous feedback and participants are not tied into distinct time-bound rounds (Quirke et al., 2021). Each participant can change their opinion as often as they like within the set timeframe. The Real-Time Delphi method could improve the speed and efficiency of gathering opinions of experts and making decisions (Gordon and Pease, 2006). The roundless structure of a Real-Time Delphi (Gordon and Pease, 2006) may therefore improve retention rates for Delphis in COS. This is currently being evaluated in a randomised trial, recruiting participants into both a traditional and Real-Time Delphi (Quirke et al., 2021).

A strength of this study was the international representation of views from many low- and middle-income countries, particularly in the surgeon stakeholder group. This is often a limitation common to many COS Delphis, and currently only 20% of COS include participants from low- and middle-income countries (Karumbi et al., 2021). However, a limitation of the COMBINE Delphi was that it was developed for completion by participants who could read and understand English proficiently. Although efforts were made to advertise the Delphi in support groups internationally, patient participation from low- and middle-income countries was low. Furthermore, for non-native English speakers there could have been differences in how they understood and then prioritised the outcomes. BPI is an injury that is not exclusive to certain geographical locations, indeed published cohort studies frequently originate from Asia (Miller et al., 2021). This is likely to reflect the high use of motorbikes or mopeds as a mode of transport and BPI being a consequence of motorbike accidents. Care, therefore, needs to be taken when interpreting the results of the COS-BPI, as the

priorities may reflect high-income country perspectives. Future research is needed to explore whether the current COS reflects the priorities of individuals with BPI from non-western countries. Additionally, further research needs to be conducted by COS methodologists on how to enable initiation of COS development and improve public participation from non-western and low- and middle-income countries.

5.5 Conclusion

An international consensus process was used to agree on a minimum set of core outcomes to be measured and reported when evaluating adult BPI interventions. The outcomes included in the COS-BPI represent the consensus opinion of an international group of patients, therapists and surgeons. It is recommended that future studies and routine care of adults with BPI include the measurement of these core outcomes. This will enable consistent reporting and effective data synthesis to support evidence-based healthcare for patients with BPI. Implementation of the COS-BPI will enhance the relevance of study findings and treatments to patients, HCPs and researchers

Chapter 6 Identification of instruments which measure the core outcome domains and evaluation of their psychometric properties

6.1 Introduction

A 3-round online international Delphi process and consensus meetings, detailed in the previous chapter, generated a core outcome set (COS) for adults with a traumatic brachial plexus injury (BPI). This focused on *what* to measure. However, knowledge of *how* to measure these outcomes is crucial to enhance uptake and realise the benefits of the COS development. This chapter presents the methods used to identify instruments which measure the outcome domains in the COS, including a systematic review of development and validation studies of those currently available outcome measurement instruments (OMI) for assessing the three core outcome domains and an evaluation of their psychometric properties. It concludes with recommendations on the current best evidence on how to measure the COS-BPI.

6.2 Background

Three outcomes should always be measured in BPI studies and clinical practice. These are: carrying out daily routine, pain and voluntary movement. A further four outcomes (Chapter 5, table 5.22) were considered as critically important by some but not all stakeholder groups and are optional but important to measure and report.

While a COS is an important step in determining *what* domains should be measured, it does not describe *how* the key outcome domains should be assessed. The next step in improving the quality and consistency of outcome reporting in BPI studies is to identify the OMIs for the domains included in the COS (Boers et al., 2014b; Gorst et al., 2020). One systematic review on COS uptake in rheumatoid arthritis trials identified that although there was consistency in the outcomes assessed, there was persistent heterogeneity in the ways these outcomes were measured (Kirkham et al., 2013a). Several OMIs can exist for each outcome in the COS-BPI. For example, the systematic review in Chapter 3 identified that 'carrying out daily routine' was assessed using 14 different OMIs. Therefore, if research does not identify how outcomes are measured,

evidence synthesis will continue to be hampered by incomparable scores from these different instruments. This could potentially undermine the COS efforts.

The quality of available OMIs may vary considerably (Tunis et al., 2016) and it is often not clear if the most reliable and valid instrument has been used for a given outcome. In clinical practice, instrument scores influence clinical management, and in research, results influence evidence-based practice. If OMIs are used with questionable psychometric qualities, there is a risk of imprecise or biased results.

Finally, while many COS developers do not proceed to identify measurement sets, there is evidence that the absence of recommendations on which instruments should be used can limit the uptake and implementation of a COS (Boric et al., 2018b; Hughes et al., 2021; Palominos et al., 2012). To tackle uncertainty around instruments and measures, the COMET (Core Outcome Measures in Effectiveness Trials) initiative (Hughes et al., 2021) recommends that COS developers focus on determining *how* to measure the outcomes in the COS once consensus has been reached on *what* to measure. To aid COS developers with this process, a guideline recommending methods for selecting OMIs to measure COS domains was published in 2016 (Prinsen et al., 2016). This was based on the results of a Delphi study, methodology from the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative and recommendations from Outcome Measures in Rheumatology (OMERACT) (Boers et al., 2014b).

6.2.1 Aim and objectives

The aim of this work package was to identify OMIs with the strongest psychometric properties to assess the core outcome domains in the COS-BPI.

The specific objectives were to:

i) define the scope of each domain

ii) identify potential OMIs for each of the domains in the COS-BPI

iii) critically appraise, compare and summarise the quality of studies reporting the development and measurement properties of each OMI using the COSMIN guidelines

iv) make recommendations on the selection of OMIs for the COS-BPI.

6.3 Methods

Over the last decade, knowledge about measurement instrument assessment has evolved. The COSMIN initiative (http://www.cosmin.nl/) aims to improve the selection of OMI for clinical practice and research. This was developed with a focus on patient-reported (PRO) instruments, but recently it has expanded to include guidelines and recommendations on clinician-reported outcome (ClinRO) instruments and other OMIs (De Vet et al., 2011).

There are now numerous guidelines on the selection of OMIs for COS. In 2016 a collaboration between the COSMIN initiative and the COMET initiative developed a consensus-based guideline on how to select OMIs for outcomes included in a COS (Prinsen et al., 2016). The OMERACT initiative, which promotes standardised outcome measures in rheumatology (Maxwell et al., 2019), has also developed guidance on how to select OMIs for a COS (Beaton et al., 2021c). Finally, the Harmonizing Outcome Measures for Eczema (HOME) initiative (Schmitt and Williams, 2010) developed the HOME roadmap (Schmitt et al., 2015) as a methodological framework that has been adopted in several COS projects in dermatology.

To identify the most psychometrically robust OMIs for the COS-BPI, the COMET and OMERACT guidance were reviewed because the first has an overarching position on COS development and the second has pioneered COS research (Beaton et al., 2021a; Maxwell et al., 2019; Williamson et al., 2017). The HOME initiative applies the OMERACT guidance to determine which instruments have sufficient quality to be included in a COS (Schmitt and Williams, 2010).

All initiatives agree that there are four steps to select the appropriate OMIs for the COS. The procedure recommended by COSMIN (Mokkink et al., 2016) and guidance from Prinsen et al. (2016) was used here:

Step 1. Define the scope of the outcome domains.

Step 2. Identify (and categorise) existing OMIs.

Step 3. Quality assessment of OMIs.

Step 4. Generic recommendations on the selection of OMIs for the COS-BPI.

The following section describes the methods used to complete the four steps.

6.3.1 Define the scope of outcome domains (Step 1)

COMET, OMERACT and the HOME road pathway recommend defining the scope of each domain prior to identifying the OMIs (Beaton et al., 2021c; Prinsen et al., 2016; Schmitt et al., 2015). The COS-BPI has three core outcome domains: voluntary movement, pain, and carrying out daily routine. The discussions in the consensus meetings with patients, healthcare professionals and the research team (see Chapter 5) had already informed the definition and scope of each domain (Table 6.1).

Table 6.1 Scope of the outcome domains in COS-BPI

Outcome domain	Scope
Voluntary movement	To include all active movement of the upper limb, shoulder, elbow, wrist and hand
Pain	The experience of pain to include pain intensity, duration and frequency, and description
Carrying out daily routine	Daily routine to include housework, taking care of plants indoors and outdoors, preparing meals (expanded at consensus meeting to include maintaining personal hygiene, personal appearance, dressing and ability to carry out routine at work and with hobbies)

6.3.2 Identify outcome measurement instruments (Step 2)

Both OMERACT and the COSMIN and COMET guidelines suggest using systematic review methods to identify all potentially eligible OMIs for selection in a COS (Beaton et al., 2019; Beaton 2021c; Prinsen et al., 2016). Additionally, these guidelines (Beaton et al., 2019; Beaton 2021c; Prinsen et al., 2016) recommend that developers review reference lists of included studies and also use additional sources, such as expert panels, to ensure no OMIs are missed. To ensure comprehensiveness in identifying all possible OMIs, this study followed these recommendations and used the following methods to identify all existing OMIs measuring the core outcome domains:

i) A systematic review (including Medline and Embase) to identify OMIs currently used in studies evaluating interventions in BPI (search 1).
ii) A separate systematic review to identify newly developed OMIs in BPI and measures psychometrically evaluated in the BPI population (search 2).
iii) Identification from other resources, including expert opinion, online databases, book chapters and conference proceedings and protocols (search 3).

These steps are documented in sections 6.3.2.1 (search 1); 6.3.2.2 (search 2) and 6.3.2.3 (search 3).

6.3.2.1 Systematic review to identify measures currently used in BPI studies (search 1)

Chapter 3 details a systematic review which identified OMIs currently used in studies. The OMIs were categorised to aid comparison and organisation of all assessments. Previously, categorisation of assessments has focused on PRO assessments (Fitzpatrick et al., 1998; Valderas and Alonso, 2008). Although work has been completed to similarly categorise ClinRO assessments (Powers et al., 2017), there is no system which categorises both ClinRO and PRO assessments. As this review included all OMIs, I adapted (in discussion with my supervisors) previous categorisations. Similar to PRO assessments (Fitzpatrick et al., 1998), all the OMIs in this review were categorised into generic, condition-specific, region-specific and individualised measures. Table 6.2 displays the adapted categorisation of all measures.

Table 6.2 Categorisation of outcome measurement instruments in the review

Categorisation	**OMI**	**Description**
Domain-specific	PRO, ClinRO, PerfO	Evaluates one aspect of health, e.g., neuropathic pain symptom inventory (domain-specific PRO assessment); pulp to palm distance (domain-specific ClinRO assessment).
Region-specific	PRO, ClinRO, PerfO	Evaluates health problems on a specific part of the body, e.g., Action Reach Arm Test (region-specific PerfO assessment).
Condition-specific	PRO, ClinRO	Evaluates the impact of a specific disease/ condition on the individual, e.g., Brachial Assessment Tool (condition-specific PRO assessment).
Individualised measures	PRO	Reports issues or concerns which are important to the individual patient. Items are not predetermined, e.g., Patient Specific Functional Scale.
Generic	PRO	Captures a broad range of health conditions and can be used with many conditions, e.g., EQ5D.

OMI: Outcome Measurement Instrument, *PRO:* Patient Reported Outcome, *ClinRO*: Clinician Reported Outcome, *PerfO*: Performance Outcome

The review in Chapter 3 identified 30 OMIs. This included 20 PRO assessments, 3 combined PRO and ClinRO assessments, and 7 Performance Outcome (PerfO) assessments (Table 6.3)**.** The long list of ClinRO outcome assessments is detailed in Chapter 3 (Tables 3.11-3.13).

Table 6.3 Original long list of multi-item measurement instruments identified in literature

Instruments	PRO	PerfO	Combined PRO and ClinRO
Region-specific (whole upper limb)			
Disabilities of Arm Shoulder and Hand	X		
Upper Extremity Functional Index	X		
American Shoulder and Elbow Score	X		
Modified American Shoulder and Elbow Score	X		
Upper limb module questionnaire		X	
Action Reach Arm Test		X	
Region-specific (shoulder only)			
Simple Shoulder test	X		
University of California Los Angeles shoulder score			X
Constant-Murley			X
Region-specific (elbow only)			
MAYO Elbow Performance Index			X
Region-specific (hand and wrist only)			
Michigan Hand Questionnaire	X		
Jebsen Taylor		X	
Southampton Hand Assessment Procedure		X	
Purdue Peg test		X	
Generic			
36 item short form survey (SF36)	X		
Patient Specific Functional Score	X		
The WHOQOL BREF	X		
Condition-specific			
Trinity Amputation and Prosthesis scale	X		
University of New Brunswick Test of Prosthetic Function for Unilateral Amputees (UNB)		X	
Activities Measure for Upper Limb Amputees		X	
Domain-specific			
Visual Analogue Scale (pain)	X		
Numerical Rating Scale (pain)	X		
Wong Baker Faces rating scale (pain)	X		
Brief pain inventory	X		
Neuropathic pain symptom inventory	X		

Instruments	PRO	PerfO	Combined PRO and ClinRO
University of Washington Neuropathic score	X		
McGill Pain Questionnaire	X		
McGill Pain Questionnaire SF	X		
McGill Pain Questionnaire (Japanese version)	X		
Self-rating anxiety scale	X		
Zung self-rating depression scale	X		

6.3.2.1.1 Mapping outcomes in measurement instruments to COS

There are differences in the literature about how identified OMIs are mapped to the domains in the COS. OMERACT recommends surveying working group members and patients about the content and domain match of the instruments (Beaton et al., 2019; Beaton et al., 2021c). Although this method may be ideal, time constraints within this PhD prohibited further surveys and analysis. COSMIN and COMET (Prinsen et al., 2016) were unable to reach consensus on how to map domains to OMIs, but previously Macefield et al. (2014) developed methods to extract and map domains from items in PRO measures. These methods (Macefield et al., 2014) were used to map the COS-BPI domains to multi-item PRO and PerfO, ClinRO instruments. The primary supervisor (CJH) reviewed the long list (PRO, PerfO, ClinRO measures) and discrepancies between mapping were discussed and resolved.

Chapter 3 describes how items and scales from the OMIs were mapped to outcomes. To identify OMIs which map to one of the three outcomes in the COS (voluntary movement, pain, carrying out daily routine), only OMIs that included items assessing at least one of the domains were taken forwards. Two multi-item PRO assessments were excluded at this stage, as none of the items within the instrument mapped to any of the domains in the COS (self-rating anxiety scale and self-rating depression scale). Table 6.4 presents the ClinRO assessments which mapped to one or more of the outcome domains in the COS.

Table 6.4 ClinRO assessments that map to one or more core outcomes

Clinician assessed outcome measures	Core outcome mapped to
Region-specific (whole upper limb)	
Goniometry	Voluntary movement
Visual assessment face to face	Voluntary movement
Domain- and region-specific (hand and wrist only)	
First web space in centimetres	Voluntary movement
Total active movement	Voluntary movement
Pulp to palm distance	Voluntary movement

6.3.2.1.2 Data extraction of outcome assessments previously identified

All OMIs mapping to any of the three domains were reviewed to assess suitability for inclusion in the core outcome measurement set (COMS) for BPI. I retrieved each OMI and any instructions (if available) via Google searches. Data extracted for each OMI included (where available) original author, mode of administration, items, subscales, cost, equipment needed, accessibility and translations. I then searched for studies reporting the populations used in the initial development and content validation of the measures, looking for evidence that BPI patients were included in the study samples. If the development or subsequent content validity studies included ≥ 75% people with a BPI, then the OMIs were taken forwards and the other measurement properties evaluated, as documented in section 6.3.4.

6.3.2.2 Identify newly developed measures and measures psychometrically evaluated in the BPI population mapping to at least one of the domains (search 2)

A systematic review was conducted to i) identify newly developed OMIs that are not yet in published studies and ii) identify studies evaluating the psychometric properties of OMIs measuring one of the domains in the BPI population. The systematic review was registered on the PROSPERO international register of systematic reviews (CRD42022307564).

6.3.2.2.1 Data sources and search strategy

Embase (OVID), Medline (OVID), CINAHL (EBSCO), the networked digital library of theses and dissertation (NDLTD) and Open Access Theses and Dissertations (n = 202 titles) were searched from inception to 22nd October 2021. Thesis databases were searched to ensure identification of newly developed measures. There was no restriction on language. The search strategy was informed by COSMIN and COMET guidelines (Prinsen et al., 2018, 2016), using "outcome" AND "population" AND "type of OMI" and "measurement property" to identify all OMIs. A scoping search with the above broad search terms was conducted initially and very few articles were retrieved. Therefore the "measurement property" search term was removed, as there was a possibility that some studies evaluating psychometric properties in OMIs in the BPI population were being missed. Three searches were conducted within each database, to search for instruments measuring either voluntary movement, pain or carrying out daily routine. See Table 6.5. Full details of the search terms can be seen in Appendix 6.1. A review of all citations of the included full texts was also conducted. In addition, abstracts from two BPI-specific conferences, Narakas 2019 and 2016, were searched.

Table 6.5 Search strategies used to identify measurement instruments measuring COS

Population		**Outcomes**		**Instrument**
Brachial plexus (+synonyms)	AND	Pain	AND	"outcome measure" OR "instrument" OR "measurement" OR "patient reported outcome measure" or "tool" or "questionnaire"
Brachial plexus (+synonyms)	AND	movement OR range of movement OR mobility	AND	"outcome measure" OR "instrument" OR "measurement" OR "patient reported outcome measure" or "tool" or "questionnaire"
Brachial plexus (+synonyms)	AND	carrying out daily routine OR activities of daily living OR function	AND	"outcome measure" OR "instrument" OR "measurement" OR "patient reported outcome measure" or "tool" or "questionnaire"

6.3.2.2.2 Study selection

OMERACT (Beaton et al., 2019, Beaton et al., 2021c) and the COSMIN and COMET guidance (Prinsen et al., 2016) prioritise different psychometric properties when selecting an OMI for a COS. COSMIN and COMET guidelines (Prinsen et al., 2016) recommend evaluating nine measurement properties (content validity, structural validity, internal consistency, cross-cultural validity, reliability, measurement error, criterion validity, hypothesis testing (for construct validity) and responsiveness). The OMERACT group (Beaton et al., 2019; Beaton et al 2021c) recommends including studies of construct validity, inter-method reliability, test-retest reliability and long construct validity and also studies on clinical trial discrimination and thresholds of meaning. For this project, a study was included if it assessed at least one of the 9 measurement properties identified by the COSMIN taxonomy (Prinsen et al., 2018). Studies on clinical trial discrimination were not included as this was not viewed as appropriate in this population due to the low number of trials in BPI.

Any study presenting the development of an OMI in the adult BPI population intending to measure at least one of the COS domains was included to facilitate the assessment of content validity (Terwee et al., 2018b). Studies in populations that included patients other than those with a BPI were eligible only if ≥ 75% of the total sample was classified as having a BPI or if the results were presented separately for this population. Original OMI studies cited within the included articles were retrieved to evaluate content validity.

JJ and I independently applied the inclusion criteria (using a standardised proforma based on inclusion criteria) to the retrieved titles and abstracts. In cases of uncertainty, full text papers were reviewed. Consensus on inclusion was sought between reviewers, and in case of disagreement, a third reviewer (CJH).

6.3.2.3 Identification of measures from other sources (search 3)

An international online meeting via MS Teams was arranged for 30th September 2021. This was part of an existing regular biannual meeting of healthcare professionals interested in improving care for people with BPI. I chaired part of this and presented the progress of the COS to date and the three core outcomes that had reached

consensus. Participants were asked what OMIs they used to measure each outcome. Participants suggested OMIs verbally or entered suggestions in the chat function. The meeting was recorded. I transcribed suggestions from the meeting recording and included suggestions from the chat. I then cross-checked participants' suggestions with the existing long list of OMIs. If participants suggested OMIs not previously identified, then these were firstly reviewed with regards to the inclusion of the adult BPI population in the original development study, and secondly, reviewed for any subsequent studies evaluating the OMI's psychometric properties in a BPI population. Studies identified that met inclusion criteria for systematic review were added to the PRISMA diagrams (Figures 6.2, 6.3 and 6.4) and systematic review results.

6.3.3 Data extraction

I extracted data onto a standardised proforma, which included: i) characteristics of the OMI, including name of OMI, outcome domain(s) assessed, aim of study, country of study, recall period (if appropriate) and measurement properties evaluated; ii) characteristics of the included studies of OMIs assessing outcomes in adults with BPI, including study author, year, mean age and target population, and iii) results of the psychometric properties of the OMIs. If the newly identified OMI was a multi-item instrument, it was electronically downloaded, and items were examined to see if they mapped onto any of the three COS domains.

6.3.4 Quality assessment of measurement instruments (step 3)

COSMIN and COMET guidelines (Prinsen et al., 2016) recommend evaluating nine measurement properties (Table 6.6), with content validity being rated (in a consensus process) the most important to be assessed (Prinsen et al., 2016). Although OMERACT, and COSMIN and COMET guidelines recommend evaluating content validity initially prior to moving on to the evaluation of other psychometric properties, different methods are used to evaluate content validity.

6.3.4.1 Content validity

Content validity refers to whether the content of the OMI appropriately reflects the construct to be measured for a stated audience and context (Lasch et al., 2010; MacDermid, 2021; Mokkink et al., 2010; Rothman et al., 2009). For multi-item instruments, content refers to the themes or subjects addressed in the instrument, the wording and format of items, tasks, or questions in an instrument as well as the guidelines for administration and scoring (Rothman et al., 2009). The appropriateness of the content is related to the specific inferences to be made from the instrument scores (Rothman et al., 2009). For PRO instruments, qualitative methods involving a diverse sample from the target population are essential to ensure sufficient content validity (Fda, 2009; MacDermid, 2021; Patrick et al., 2011). Focus groups or 1:1 interviews with patients should be used to generate items for the instrument, ensuring *relevance* of content to the patient experience (Magasi et al., 2012; Terwee et al., 2018b). Additionally, a conceptual framework detailing the relationship between the domains and items and their relationship to the underlying construct in any OMI can also evidence content validity (Patrick et al., 2011; Rothman et al., 2009, 2007). This framework provides the initial skeleton for the instrument based on the existing information (Patrick et al., 2011).

For ClinRO and PerfO assessments, important components of content validity include evidence of a literature review relevant to the concept of interest, concept elicitation with clinicians, comprehensibility of instructions with clinicians and patients, and comprehensiveness of the OMI (Powers et al., 2017). For example, in a magnetic resonance imaging (MRI) procedure or new laboratory test, the materials, methods, procedures and scoring must be described in a way that enables researchers in that field to repeat it (De Vet et al., 2011).

Content validity is a fundamental requirement of all OMIs (MacDermid, 2021; Powers et al., 2017; Prinsen et al., 2016; Rothman et al., 2009) and affects all other measurement properties (MacDermid, 2021; Powers et al., 2017; Terwee et al., 2018a). It was, therefore, assessed thoroughly in this project before proceeding to further psychometric evaluations. Assessing psychometric properties of OMIs which don’t have adequate content validity is problematic. In PRO measures, items with poor

clarity can result in random error, limiting reliability and making it difficult to detect true changes (responsiveness) or real relationships between variables (construct validity) (MacDermid, 2021). However, high reliability or responsiveness does not imply that all items are relevant or that no important concepts are missing (Terwee et al., 2018a). Irrelevant items may decrease internal consistency, structural validity and interpretability of the PRO measure (Terwee et al., 2018a). Indeed, inadequate content validity means that clinicians and researchers can measure an incomplete or incorrect construct very reliably, and a real change in the construct of interest may be over- or under-estimated due to irrelevant or missing concepts. Thus, a failure to establish content validity can have negative consequences for everyday healthcare decisions and conclusions in health research, as poor content validity undermines the validity of all conclusions.

Qualitative and/or quantitative methods can be used to evaluate the content validity of existing OMIs (MacDermid, 2021; Terwee et al., 2018a) and it is likely that multiple methods are needed to determine whether the OMI represents the spectrum, context and features of the intended construct. Cognitive interviewing is frequently used to evaluate content validity in PRO measures (Ashwood et al., 2018; Packham et al., 2012; Patrick et al., 2011). Cognitive interviews use semi-structured qualitative interviews with think-aloud and probing approaches to explore *comprehensibility* and *comprehension* of instructions and items in a PRO measure (Patrick et al., 2011; Wright et al., 2019). Content validity indices use survey methods and percentage indicators to summarise how respondents rate the *relevance* of items (Bobos et al., 2020; Polit and Beck, 2006; Wynd et al., 2003). Clinimetric methods consider importance and frequency ratings as indicators of relevance (Bellamy et al., 2002; Wright and Feinsten, 1992). International Classification of Functioning Disability and Health (ICF) linking is also frequently used to assess relevance of a PRO assessment (MacDermid, 2021), with commonly multiple raters performing the linking procedures from ICF guidelines (Cieza et al., 2019, 2005a). ICF core sets (where they exist) are also commonly used as reference standards for this evaluation (MacDermid, 2021).

OMERACT, COSMIN and COMET guidelines differ in their recommendations for the evaluation of content validity. The OMERACT initiative recommends that surveys of OMERACT panel members and surveys of patients are conducted to evaluate content

validity (Beaton et al., 2019) and whether the content reflects the domain(s). The combined COSMIN and COMET guideline (Prinsen et al., 2016) suggests that 10 criteria are evaluated for content validity: 5 are allocated to relevance, one to comprehensiveness and 4 for comprehensibility (Terwee et al., 2018b). COSMIN (Terwee et al., 2018a) includes evaluation of OMI development, qualitative and quantitative content validity studies in its overall grading and review of the content validity.

To inform the approach taken in this study, the following issues were considered. If content validity was already evaluated through adequate development and content validity studies, then a patient and expert panel survey (as recommended by OMERACT) may have been redundant and COSMIN and COMET guidelines would be more appropriate to review the existing literature. However, the OMERACT method may be appropriate and practical to use with OMIs that have little or no evidence surrounding development and validation in the target population. The OMIs used in BPI (identified in Chapter 3) are a range of ClinRO, PerfO and PRO measures. Although it is likely that many of the ClinROs have little evidence to support their use in BPI, time constraints precluded further survey development and analysis, which would also have required further ethical approval. The COSMIN updated guidelines include a rigorous, systematic and wide-scoping evaluation of all components of content validity (Terwee et al., 2018a) and these were used to evaluate the content validity of OMIs in this study.

It is recommended that only OMIs with adequate content validity should have other measurement properties evaluated (Powers et al., 2017; Terwee et al., 2018a) in Phase 2 (Figure 6.1). Within content validity, there must be evidence that items in the PRO assessments are *relevant*, *comprehensive* and *comprehensible* with respect to the construct of interest and target population (Mokkink et al., 2018). Relevance is the most important criterion within content validity (Terwee et al., 2018a). Due to the limited number of OMIs developed within the BPI population, it was decided (in discussion with my supervisors) that PRO assessments with at least adequate relevance (in the content validity criteria) would be taken forwards for further evaluation of other psychometric properties. In that way, future research

recommendations could be made in relation to all psychometric properties, and not only content validity.

6.3.4.2 Other psychometric properties

The international guidelines (Prinsen et al., 2016) recommend that OMIs with adequate content validity should have the following 8 psychometric properties evaluated: structural validity, cross-cultural and criterion validity, hypothesis testing for construct validity, internal consistency, reliability, measurement error and responsiveness. This study adhered to the international guidelines, as it was anticipated that there would be few OMIs which would pass the strict content criteria recommended by COSMIN process (Terwee et al., 2018b). Therefore, the burden to evaluate the other eight properties would be low. Table 6.6 provides definitions of content validity and the 8 other psychometric properties evaluated. Figure 6.1 illustrates the process adopted to select clinical outcome assessments (COAs) for full psychometric property evaluation in this study.

Figure 6. 1 Selecting COAs for full psychometric property evaluation (phases 1 and 2).

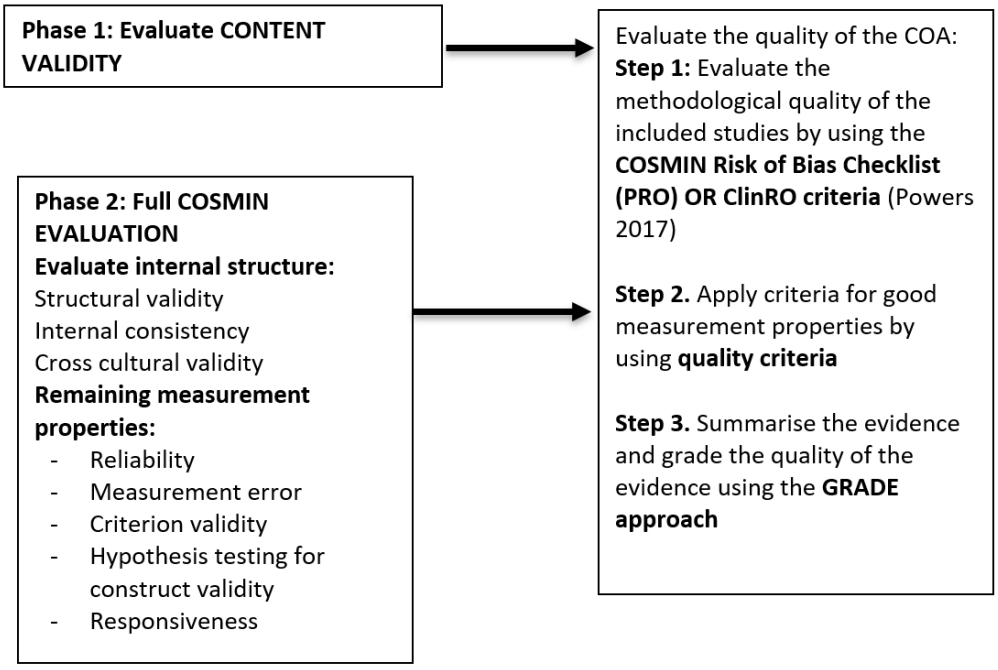


Figure adapted from Mokkink et al. (2018)

Table 6.6 Definitions of measurement properties of instruments assessed by COSMIN

Measurement property	Definition
Content validity	The degree to which the content of a PROM is an adequate reflection of the construct to be measured
Relevance	*All items in a PROM are relevant for the construct of interest within a specific population and context of use*
Comprehensive	*No key aspects of the construct should be missing*
Comprehensibility	*Items are understood by patients as intended*
Internal consistency	The degree of the interrelatedness among the items
Reliability	The proportion of the total variance in the measurements which is due to 'true' differences between patients
Measurement error	The systematic and random error of a patient's score that is not attributed to true changes in the construct to be measured
Structural validity	The degree to which the scores of a PROM are an adequate reflection of the dimensionality of the construct to be measured
Hypothesis testing for construct validity	The degree to which the scores of a PROM are consistent with hypotheses (for instance, with regards to internal relationships, relationships to scores of other instruments, or differences between relevant groups) based on the assumption that the PROM validly measures the construct to be measured
Cross-cultural validity	The degree to which the performance of the items on a translated or culturally adapted PROM are an adequate reflection of the performance of the items of the original version of the PROM
Criterion validity	The degree to which the scores of a PROM are an adequate reflection of a 'gold standard'
Responsiveness	The ability of a PROM to detect change over time in the construct to be measured

Definitions as described in COSMIN guidelines manual version 1.0, 2018 (Mokkink et al., 2018)

6.3.4.3 Feasibility

The COMET/COSMIN and OMERACT guidelines recommend that COS developers take feasibility aspects into consideration before considering selection for a COS (Beaton et al., 2019; Beaton et al 2021c; Prinsen et al., 2016). Feasibility is a practical assessment of the burden of use, where the burden could be cost, time, equipment, personal burden for the respondent (e.g. language, health literacy) or the administrator (required training), the interpretability of scores and other similar considerations (Auger et al., 2007). OMERACT recommends surveying working group members and then patients and other stakeholders regarding feasibility, with a final consensus process involving the working group deciding whether the OMI is feasible (Beaton et al., 2019; Beaton et al 2021c). This process is rigorous and systematic. However, due to time and resource constraints an alternative method was followed in this study.

JJ and I independently evaluated the following feasibility aspects as recommended by COSMIN and COMET (Prinsen et al., 2016): comprehensibility, completion time, patients' required mental and physical ability level, ease of standardisation, ease of score calculation, copyright, cost of using the instrument, required equipment and any regulatory approvals needed. I contacted developers and authors if extra information was needed to complete data extraction and inform decision making. JJ and I then came to a consensus on each feasibility aspect.

OMERACT recommends removing OMIs which aren't feasible before assessing psychometric properties. They recommend this method for time efficiency, so that the detailed process of psychometric evaluation is only conducted on feasible OMIs (Beaton et al., 2019; Beaton et al 2021c). This recommendation was adhered to for assessment of the ClinROs in the systematic review, and any ClinROs that were not deemed feasible in routine care or in research were not evaluated any further.

The COSMIN/COMET guideline (Prinsen et al., 2016) recommends evaluating feasibility after full psychometric property evaluation has been completed. This study followed the COSMIN and COMET recommendations for PRO instruments, as clinical experience in the area and previous reviews suggested that there were few PRO instruments (Haldane et al., 2022; Hill et al., 2011) evaluated in the BPI population.

6.3.4.4 Evaluating quality of the OMIs in the COMBINE study

Both COSMIN/COMET and OMERACT guidelines (Beaton et al., 2019; Beaton et al 2021c; Prinsen et al., 2016) recommend using COSMIN criteria on measurement properties (Prinsen et al., 2018) to evaluate the quality of psychometric property studies. Quality assessment consisted of three steps (see Figure 6.1), JJ and I scored the items independently. We reached consensus over three video conference meetings, with uncertainties and disagreements resolved by discussion with the third reviewer (CJH).

6.3.4.4.1 COSMIN Risk of Bias checklist (step 1)

The COSMIN Risk of Bias checklist (Mokkink et al., 2017; Prinsen et al., 2018; Terwee et al., 2018b) was used to evaluate the methodological quality of each single study. A Microsoft Excel document containing the checklist was downloaded from the COSMIN website. Both reviewers used the COSMIN user guide manuals (Mokkink et al., 2018; Terwee et al., 2018a) to support scoring. The COSMIN checklist consists of nine measurement properties, together with feasibility and interpretability of each instrument. The risk of bias for each study was rated using a four-point scale as either *very good*, *adequate*, *doubtful* or *inadequate quality*, and determined by taking the lowest rating of any items ("worst score counts") within each measurement property.

6.3.4.4.2 Applying criteria for good measurement properties by using quality criteria (step 2)

PRO assessments content validity: Each single study on PRO assessment development and content validity was rated against the 10 criteria for good content validity (Terwee et al., 2018b). The results of all available studies were qualitatively summarised to determine whether the overall relevance, comprehensiveness and comprehensibility, and overall content validity were sufficient (+), insufficient (-) or indeterminate (?). OMIs assessed as having insufficient relevance following this assessment were excluded from further evaluation in the systematic review, as these could not be recommended for use.

ClinRO and PerfO assessments content validity: Each single study on ClinRO and PerfO assessment development and content validity was reviewed against criteria set by

Powers et al. (2017). JJ and I independently decided whether the COAs had sufficient content validity to continue for further evaluation of psychometric properties.

Remaining Measurement Properties. For COAs assessed as having sufficient content validity (at minimum relevance), the results of each study for the remaining measurement properties were rated against the criteria for good measurement properties (Prinsen et al., 2018, 2016). Each result was rated as sufficient (+), insufficient (-), or indeterminate (?).

6.3.4.4.3 Summary of evidence and grading of quality of evidence (step 3)

The overall ratings determined in steps 1 and 2 were also accompanied by a grading for the quality of evidence using a modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for systematic reviews of clinical trials (GRADE working group, 2013) (scored as high, moderate, low or very low). The GRADE approach uses five factors to determine quality of evidence: risk of bias, inconsistency, indirectness, imprecision and publication bias (GRADE working group, 2013).

6.3.5 Final recommendations for COS-BPI core outcome measurement set

This stage concerns the final decision making on including an OMI in a COS. Prinsen et al. (2016) recommend that only one OMI is selected for each outcome in a COS. However, a complex outcome (like pain), which consists of multiple aspects, may need to be measured by different OMIs (Prinsen et al., 2016). It is also recommended that COS developers consider whether different subpopulations may need their own OMIs to measure the same outcome (Prinsen et al., 2016). This is relevant for this project, as BPI can have diverse presentations dependent on severity and location of the injury in addition to other factors (Chapter 1). An upper plexus injury can result in a loss of function in the shoulder and elbow, whereas a lower plexus injury may result in hand dysfunction only. A full plexus can lead to complete paralysis of the entire limb. Although measurement of pain may be relevant to all subgroups as it is domain-specific, how voluntary movement is measured is likely to differ according to the region of the upper limb affected.

Ideally an OMI included in a COS has high-quality evidence for all measurement properties. However, in practice there is often a lack of or (very) low-quality evidence for some measurement properties. COMET and COSMIN guidelines (Prinsen et al., 2016) recommend that an OMI can be provisionally included in a COS if there is at least high-quality evidence for good[1] content validity and for good[3] internal consistency (if applicable), and if the OMI seems feasible. Conversely there should be no high-quality evidence that one or more other measurement properties are poor[2]. OMERACT (Beaton et al., 2019; Beaton et al., 2021c) recommend conducting a red, amber and green rating on each measurement property evaluated (domain match, construct validity, test-retest reliability, responsiveness, clinical trial discrimination, threshold of meaning). The instrument then receives an overall either green (endorsed) or amber (provisionally endorsed) rating. A mixture of amber and green ratings mean that the instrument provisionally passes the OMERACT filter 2.2. OMERACT/COSMIN and COMET recommend a clearly defined research agenda of the additional research needed for those OMIs that lack evidence.

Prinsen et al. (2016) and OMERACT (Beaton et al., 2019; Beaton et al 2021c) recommend that COS developers use consensus procedures, including relevant stakeholders, to get final agreement on the selected OMIs included in a COS. Group discussions and a plenary discussion plus voting during a face-to-face meeting among a group of stakeholders can be used to achieve consensus on the final core set of OMIs. If the evidence is of sufficient quality then the results are presented at a consensus meeting, where it is recommended that 70% agreement by the OMERACT community will be considered support for endorsement and inclusion in a COS (Beaton et al., 2019; Beaton et al 2021c).

For this project OMIs that met the criteria set by the COSMIN and COMET guidelines (high-quality evidence for good[1] content validity and for good[3] internal consistency) were recommended for provisional inclusion in the COMS (Prinsen et al., 2016). If

[2] 'Poor' is defined as a "-" rating according to the criteria for good measurement properties
[3] 'Good' is defined as a "+" rating according to the criteria for good measurement properties

more than one OMI met the criteria for an outcome domain in the COS, then a consensus process would be required to decide the best OMI. Where an OMI lacked evidence on one or more measurement properties, a research agenda was proposed for further validation studies.

6.4 Results

6.4.1 Selection of studies

6.4.1.1 Search 1

Thirty-six OMIs (21 PRO, 7 PerfO, 5 ClinRO, and 3 combined PRO and ClinRO assessments) were identified. Only two OMIs had studies describing the development of the OMIs including a BPI population or relevant health professionals or evaluating psychometric properties within the BPI population. Appendix 6.2 presents data extraction for all included OMIs from search 1.

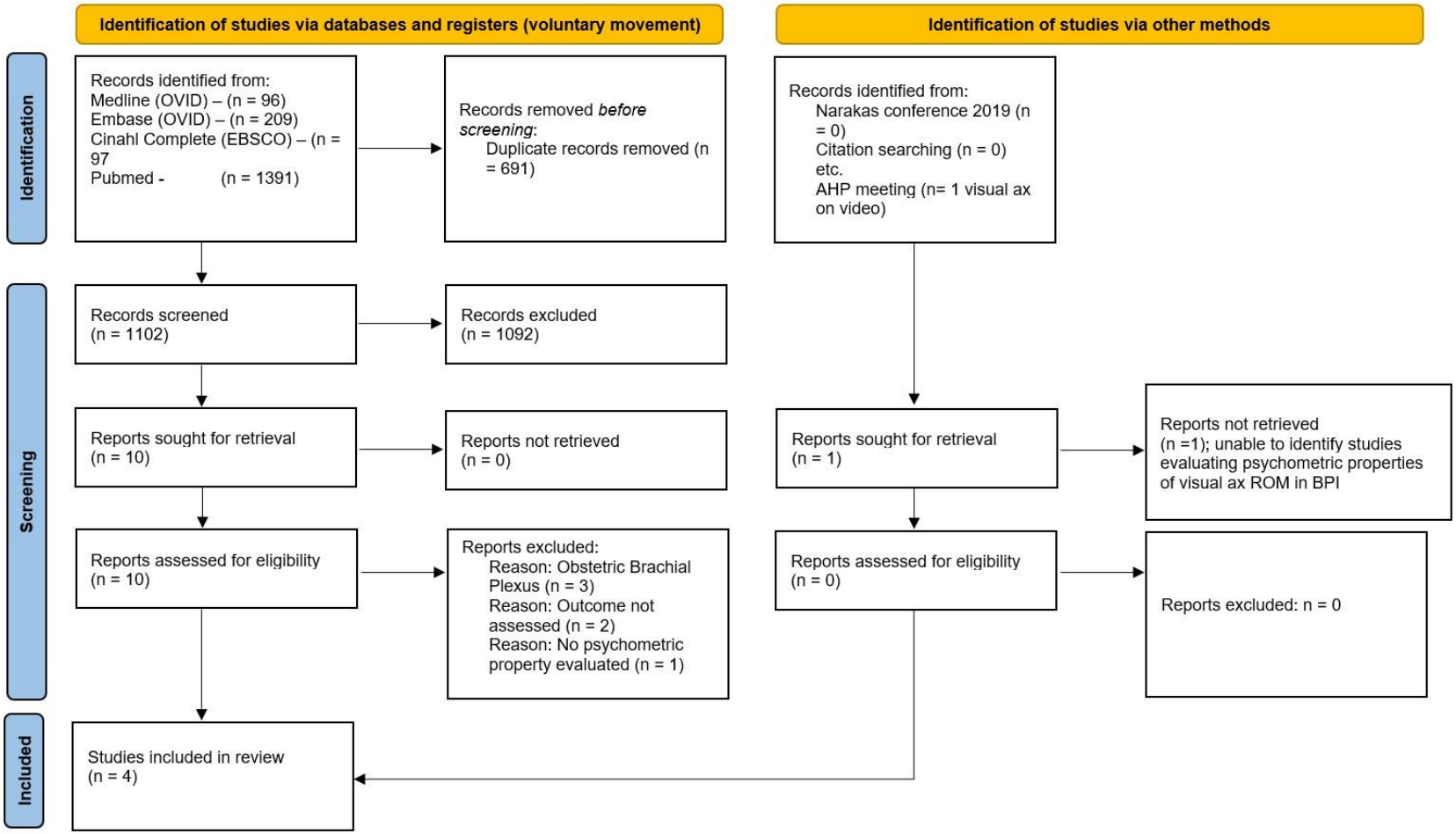
6.4.1.2 Search 2

After removal of duplicates, JJ and I screened 6,841 titles and abstracts. For full text review, based on title and abstract review, 31 articles were selected. Of these, 13 were excluded from the review for the following reasons: obstetric brachial plexus injury (n = 6); other populations (n = 4); COS domain not assessed (n = 2), no psychometric property evaluated (n = 1). A further three papers were identified from citation searching. Eighteen articles describing 5 PRO assessments and 4 ClinRO assessments were included in the review (see PRISMA diagrams in Figures 6.2, 6.3 and 6.4).

6.4.1.3 Search 3

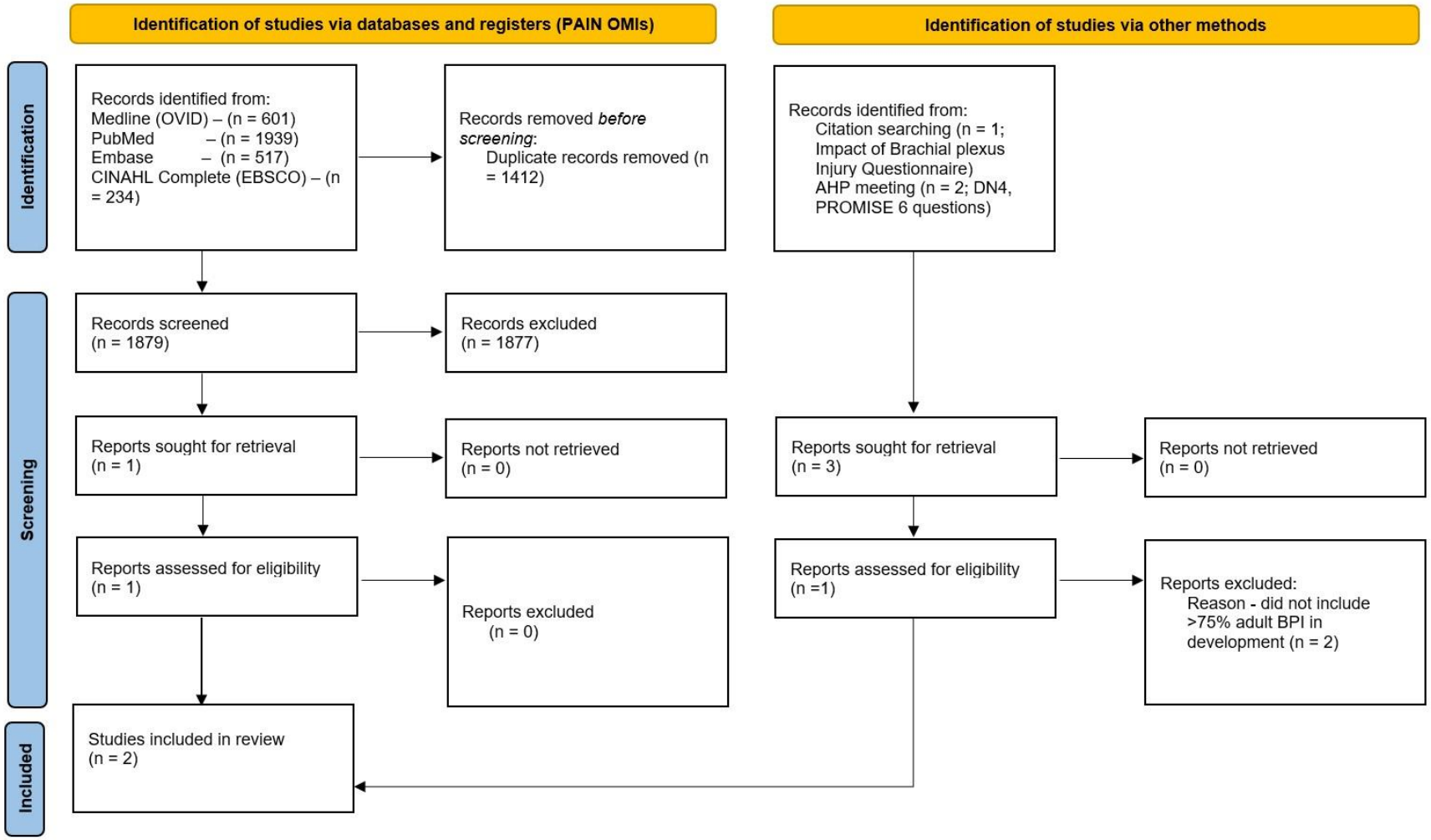
Participants at the health professionals meeting (n = 22) included occupational therapists and physiotherapists who treat people with BPI. Attendees were from England, Wales, Scotland, Sweden, Denmark, Ireland and Australia. Participants identified 10 additional COAs. None of the identified OMIs were developed with a BPI population or had psychometric properties evaluated later within this population. Appendix 6.3 details results from the meeting.

Figure 6. 2 PRISMA flowchart for studies evaluating psychometric properties of voluntary movement OMIs



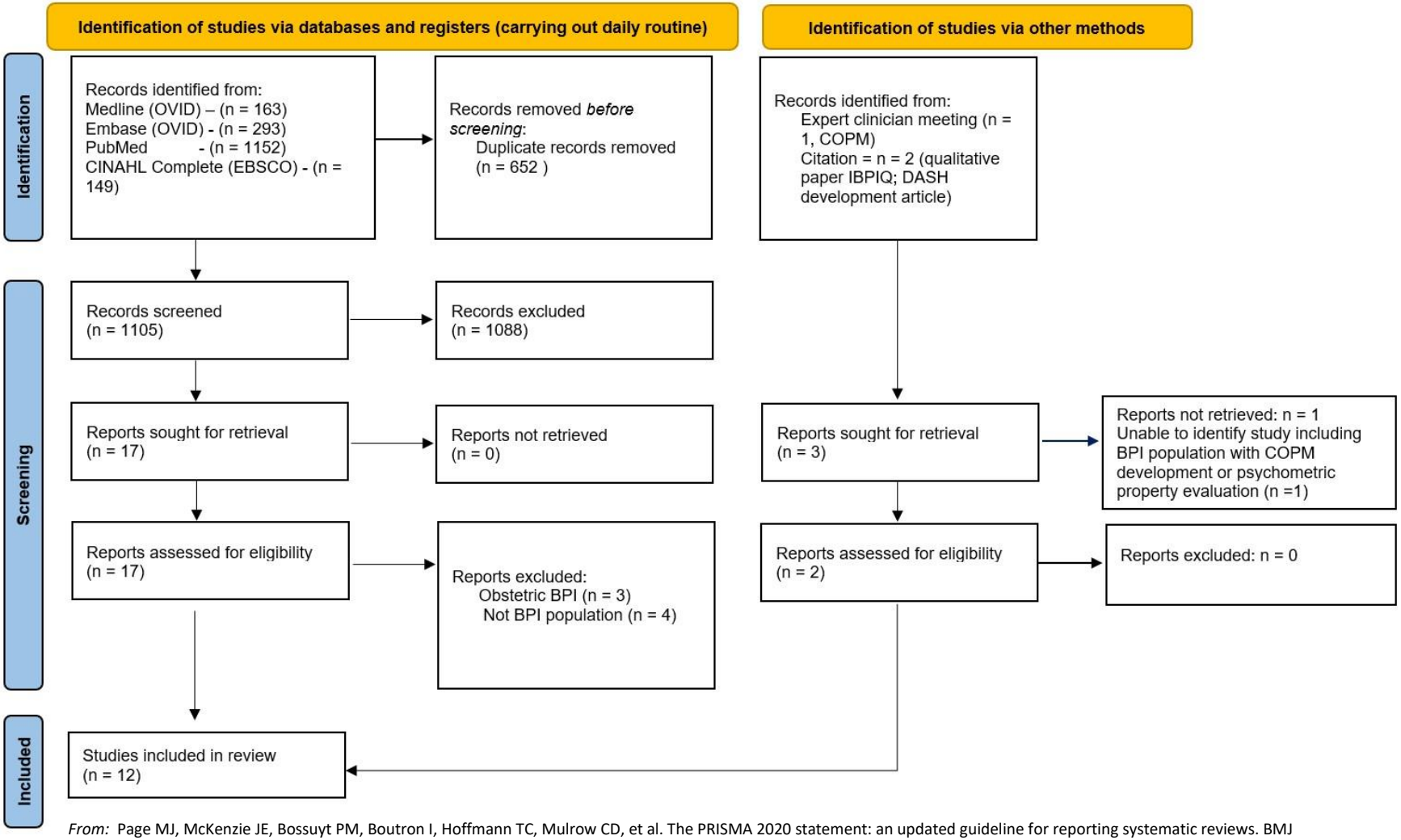
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information

Figure 6. 3 PRISMA flowchart for studies evaluating psychometric properties of pain OMIs



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information

Figure 6. 4 PRISMA flowchart for studies evaluating psychometric properties of carrying out daily routine OMIs



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information

6.4.2 Characteristics of included clinical outcome assessments

6.4.2.1 Characteristics of PRO instruments[4]

The five PRO instruments identified were the Brachial Assessment Tool (BrAT), (Hill et al., 2018a), the IMpact of Brachial Plexus Injury Questionnaire (IMBPIQ) (Mancuso et al., 2018), the DASH (Disabilities of Arm, Shoulder and Hand) (Hudak et al., 1996), the Patient Specific Functional Scale (PSFS) (Stratford et al., 2009) and the Brachial Plexus Pain Scale (Bonilla et al., 2011). All OMIs were developed for use in English-speaking patients. Three of the instruments were patient-reported (BrAT, IMBPIQ and DASH) and two were completed via interview by a clinician (Brachial Plexus Pain Scale, PSFS). All questionnaires had one version except the IMBPIQ (Mancuso et al., 2018), which has pre- and post-treatment questionnaires. Items within the IMBPIQ pre- and post-treatment questionnaires are the same, but the questions differ slightly to account for expectations pre-treatment (pre-operative version) and improvement achieved in the post-operative version.

Outcome domains measured in the identified PRO instruments included: carrying out a daily routine, pain intensity and frequency, social and emotional wellbeing, expectations and satisfaction with treatment, general health, return to work or school, and voluntary movement. The IMBPIQ (Mancuso et al., 2018) includes items which measure all three core domains. The DASH (Hudak et al., 1996) includes items measuring two core domains: carrying out daily routine and pain (intensity). The BrAT (Hill et al., 2018a) and the PSFS (Stratford et al., 2009) include items relating to carrying out daily routine only. Finally, the Brachial Plexus Pain Scale (Bonilla et al., 2011) measures pain intensity and frequency only. None of the identified instruments had items that mapped to pain duration or description of pain. Table 6.7 presents details of the included PRO instruments.

4 PRO assessments were all multi-item instruments so will be called instruments from now on.

6.4.2.2 Characteristics of clinician-reported outcome instruments

The four ClinRO assessments included were the Evaluation of Function in the Flail Upper Limb (EFFUL) (Eggers and Mennen, 2001, 1997), dynamic radiography (Shimoe et al., 2017) and accelerometery (Smith et al., 2019), and inertial measurement units (Nazarahari et al., 2021). Voluntary movement was measured by all four ClinROs, and in addition the EFFUL measured carrying out daily routine. Table 6.8 presents characteristics of the ClinRO assessments.

Table 6.7 Characteristics of included PRO instruments

PRO/ instruments (original reference)	**Core outcome domain** (number of items)	**Target population**	**Mode of administration**	**Recall period**	**Country (language which questionnaire evaluated)**	**Subscale (number of items)**	**Range of scores**	**Original language**	**Translations**
BrAT (Hill et al., 2018a)	**Carrying out daily routine** (31)	Adult BPI	Self-report	Now	Australia (English)	3 (31)	0-93	English	0
IMBPIQ (Mancuso et al., 2018)	**Carrying out daily routine** (9) **Pain intensity** (5) **Voluntary movement** (1)	Adult BPI undergoing surgery	Self-report	Past week & since surgery & since injury	North America (English)	4 (43)	43-172	English	0
DASH (Hudak et al., 1996)	**Carrying out daily routine** (16) **Pain intensity** (4)	Populations with upper extremity musculoskeletal conditions	Self-report	Past week	Canada (English)	1 (30) Optional work and sport modules (8)	0-100	English	54 at time of writing
Brachial Plexus pain scale (Bonilla et al., 2011)	**Pain intensity** (2) **Pain frequency** (1)	Adults with BPI avulsion injuries	Interview-based	ND	Argentina (English)	1 (6)	0-37	Unclear	0
PSFS (Stratford et al., 2009)	**Carrying out daily routine** (5)	Adults with back, knee and upper extremity problems	Interview-based	Now	Canada (English)	1(5)	0-50	English	0

BrAT: Brachial Assessment Tool; IMBPIQ: IMpact of Brachial Plexus Injury Questionnaire; DASH: Disabilities of Arm Shoulder and Hand; PSFS; Patient Specific Functional Scale; BPI: Traumatic Brachial Plexus Injury; PRO: Patient Reported Outcome

Table 6.8 Characteristics of included ClinRO assessments

Other outcome measurement assessments	Core outcome domain assessed	Target population	Mode of administration	Outcome measurement categorisation	Equipment needed	Anatomical focus	Measure(s)	Description/instructions
EFFUL	**Carrying out daily routine and voluntary movement**	BPI	Face to face	Condition-specific, rating scale	EMG biofeedback, goniometer, dynamometer, pinch gauge, various weights to measure strength of wrist, shoulder and elbow.	NA	NA	The health professional rates (0-10), the ability of patient to complete observed functional tasks in addition to strength, sensation and neurophysiological assessments.
Accelerometery	**Voluntary movement**	General population	Remote, body-worn sensor technology	Domain-specific reading scale	Remote sensor device	Shoulder and elbow	Total time motion detected; intensity of activity	The participants wear the accelerometery device on their wrist to perform everyday activities during every waking hour.
Inertial measurement units (IMU)	**Voluntary movement**	General population	Body worn sensor technology	Domain-specific, reading scale	Sensor device used in clinical setting or laboratory	Shoulder	Velocity, elevation angle, power score	The participants wear three IMUs on both upper arms and on the sternum. They then carry out activities as instructed by health professional/ researcher.
Dynamic Radiography	**Voluntary movement**	BPI	X-ray machine	Domain-specific reading scale	X-ray machine	Shoulder (abduction)	Between the line of the humerus and the vertical.	Anteroposterior plain radiographs in frontal plane are taken in neutral and maximal abduction (standing position)

6.4.3 Characteristics of included studies from the systematic review

6.4.3.1 Studies evaluating psychometric properties in patient-reported outcome instruments

Table 6.9 presents the characteristics of the 13 studies evaluating the five PRO instruments included in the review. Most studies were conducted in North America or Canada (n = 6), with no studies based in Europe. The sample sizes ranged from 21 to 106 with an age range of 28 to 41 years. Individual studies evaluated different measurement properties and not all measurement properties were assessed for each PRO instrument.

Four of the included full text articles reported information on the development and the validation of the BrAT (Hill et al., 2018a, 2018b, 2016, 2015b). Two studies detailed the development of the IMBPIQ (Mancuso et al., 2018, 2015). Four studies assessed the development of the DASH and its psychometric properties in the BPI population (Estrella et al., 2019; Hudak et al., 1996; Jianmongkol et al., 2011; Novak et al., 2019). Two studies detailed the development of the PSFS and its psychometric properties in the BPI population (Novak et al., 2013; Stratford et al., 2009). The development of a pain scale specific to the BPI population was detailed in another study (Bonilla et al., 2011).

6.4.3.2 Studies evaluating psychometric properties in clinician-reported outcome instruments

Table 6.10 presents the characteristics of five published articles discussing the development or evaluation of psychometric properties of ClinRO assessments. Two articles originated from North America, two from South Africa and one from Japan. Again, no studies were conducted in Europe. Sample sizes ranged from 5 to 103 participants. All the included articles discussed or evaluated only one psychometric measurement property in the BPI population. Two out of the five studies evaluated construct validity of the ClinRO assessments (Nazarahari et al., 2021; Smith et al., 2019), one evaluated reliability (Shimoe et al., 2017) and two papers discussed the development (content validity) of the EFFUL (Eggers and Mennen, 2001, 1997).

Smith et al. (2019) evaluated the construct validity of accelerometery, correlating results to six different PRO assessments: Douleur Neuropathique 4 (DN4) questionnaire, the Shoulder Pain and Disability Index (SPADI), shortened version of the Disabilities of the Arm, Shoulder, and Hand (QuickDASH), ABILHAND, International Physical Activity Questionnaire (IPAQ) and PROMIS. An inertial measurement unit (IMU) was evaluated for construct validity by Nazarahari et al. (2021). An IMU is an instrument combining several triaxial sensors, in most cases an accelerometer, a gyroscope and/or a magnetometer (O'Reilly et al., 2018). The researchers (Nazarahari et al., 2021) evaluated correlations between the asymmetry indexes (associated with velocity, power, moment and range of movement scores) obtained from the IMU and the Simple Shoulder Test and the DASH. The reliability of dynamic radiography was evaluated by Shimoe et al. (2017).

Table 6.9 Characteristics of included studies evaluating PRO instruments

		BPI patient characteristics					Instrument administration		
Instrument	**Reference**	**N**	**Male %**	**Age, Mean (SD/range)**	**Mean time from injury/surgery (range)**	**Study Design**	**Country**	**Language**	**COSMIN measurement properties evaluated**
BrAT	(Hill et al., 2018a)	29	100%	ND	2 years since surgery	Prospective cohort	Australia	English	**Construct validity Responsiveness**
	(Hill et al., 2015b)	21	90%	38	129 weeks since injury (36-306)	Nominal group technique AND Interviews	Australia	English	**Content validity**
	(Hill et al., 2016)	106	ND	40 (18-82)	124 weeks (10-740) injury	Cross-sectional	Australia	English	**Structural validity**
	(Hill et al., 2018b)	43	89%	42 (19-82)	214 weeks (SD 155.15)	Prospective repeated measure design	Australia	English	**Reliability (test-retest) Internal consistency**
Brachial Plexus Pain Scale	(Bonilla et al., 2011)	28	93%	27.6 (mean) No range available	3 months since surgery	Prospective cohort study	Argentina	English	**Content validity**

		BPI patient characteristics					Instrument administration		
Instrument	**Reference**	**N**	**Male %**	**Age**		**Study Design**	**Country**	**Language**	**Measurement property**
DASH	(Hudak et al., 1996)	N/A	N/A	N/A	N/A	Literature review Consensus methods Field testing-patients	Canada	English	**Content validity**
	(Estrella et al., 2019)	35	97%	30.5 (17-69)	31 months since injury (7-74)	Prospective repeated measure design	Philippines	Filipino	**Internal consistency, test-retest reliability, construct validity**
	(Jianmongkol et al., 2011)	34	97%	28.6 (16-50)	ND	Prospective repeated measure design	Thailand	Thai	**Internal consistency, test-retest reliability, construct validity**
	(Novak et al., 2019)	88	ND	ND	ND	Cross-sectional	Canada	English	**Structural validity**
PSFS	(Stratford et al., 2009)	N/A	N/A	N/A	N/A	Cross-sectional	Canada	English	**Content validity**
	(Novak et al., 2013)	62	ND	ND	ND	Cross-sectional	Canada	English	**Construct validity**
IMBPIQ	(Mancuso et al., 2018)	50	88%	41 (20-84)	5 months (injury) 57 months (surgery)	Prospective repeated measure design	America (New York)	English	**Content validity** **Test-retest reliability** **Internal consistency** **Construct validity**
	(Mancuso et al., 2015)	23	83%	37 (19-63)	7±3 months (injury)	Qualitative interviews	America (New York)	English	**Content validity**

Table 6.10 Characteristics of included studies evaluating ClinRO assessments

		BPI patient characteristics					Instrument administration	
Instrument	**Reference**	**N**	**Male %**	**Age, Mean (SD/range)**	**Mean time (yrs) from injury/ surgery (SD/range)**	**Study design**	**Country**	**COSMIN measurement properties evaluated**
EFFUL	(Eggers and Mennen, 2001)	103	82%	31	NR	Prospective cohort study	South Africa	Content validity
	(Eggers and Mennen, 1997)	N/A	N/A	N/A	N/A	Descriptive paper on design of measure	South Africa	Content validity
Accelerometery	(Smith et al., 2019)	5	100%	41(± 17)	2 (±1)	Prospective cohort study	United States of America (Michigan)	Construct validity
Inertial Measurement Units	(Nazarahari et al., 2021)	15	80%	54(±16)	NR	Prospective cohort study	Canada	Construct validity
Dynamic radiography	(Shimoe et al., 2017)	69	N/A	30 (±12)	4(±3)	Prospective repeated measure design	Japan	Reliability (test-retest)

6.4.4 Outcome measurement instruments selection for full psychometric evaluation

6.4.4.1 Patient-reported outcome instruments

Of the five identified PRO instruments only two, the BrAT (Hill et al., 2018a, 2018b, 2016, 2015b) and the IMBPIQ (Mancuso et al., 2018, 2015), were considered to have sufficient content validity to proceed for full COSMIN evaluation of all psychometric properties. Of the remaining PRO instruments the Brachial Plexus Pain Questionnaire (Bonilla et al., 2011) included a specific item set for the evaluation of pain in adults with a BPI, using input from the authors alone. There was no patient input into item generation or item reduction, therefore this questionnaire was considered to have insufficient content validity and was excluded from further COSMIN evaluation.

The PSFS (Stratford et al., 2009) was also developed using only input from the authors alone. Furthermore, the PSFS is an individualised PRO instrument, making comparison difficult between patients, whether in clinical practice and research, because for each patient the items will be different. Due to the lack of content validity and categorisation of the PSFS as an individualised PRO instrument, it was also excluded from further COSMIN evaluation.

Finally, the DASH (Hudak et al., 1996) had originally been developed to evaluate symptoms and function in populations with musculoskeletal upper limb disorders. Developers did not include patients in the initial item generation of this PRO instrument, but patients were involved in item reduction of the long form of the questionnaire (Hudak et al., 1996; Marx et al., 1999). Members of the BPI population or those with similar traumatic nerve injury populations were not included in this stage (Marx et al., 1999). Although authors had subsequently evaluated some of their psychometric properties in a BPI population (Novak et al., 2019), no studies on content validity in a BPI population have been conducted. The questionnaire was therefore considered to have insufficient content validity for further COSMIN evaluation.

6.4.4.2 Clinician-reported outcome instruments

Of the four ClinRO measures, three were deemed not feasible for use in routine care and research. These included dynamic radiography (Shimoe et al., 2017), accelerometry (Smith et al., 2019) and inertial measurement units (Nazarahari et al., 2021). None of the ClinRO assessments were considered to have sufficient content validity to proceed for further evaluation of their psychometric properties. The EFFUL was the only ClinRO assessment which described its development with a specific focus on the BPI population (Eggers and Mennen, 2001, 1997). However, the EFFUL rating scale was designed by a single developer with no evidence of contribution from other clinical experts or literature. It therefore does not meet the criteria set by Powers et al. (2017) for good measurement practices in ClinRO assessment development and evaluation.

6.4.5 Overall rating and grading of quality of evidence per measurement property for each PRO instrument

Table 6.11 presents a summary of the analysis and grading of measurement properties for the two PRO instruments (BrAT and IMBPIQ) included for full COSMIN evaluation. This includes the overall rating and grading of the quality of evidence assigned to each of the measurement properties that were measured. The overall ratings and quality of evidence for each measurement property assessed for both PRO instruments are presented in Table 6.12 for ease of comparison between the instruments. Cross-cultural validity, measurement invariance measurement error and criterion validity were not assessed for either of the two included PRO instruments and thus not included in Table 6.12.

6.4.5.1 Content validity

The following section describes the evaluation of the content validity of the BrAT and the IMBPIQ. This included evaluation of *relevance, comprehensiveness* and *comprehensibility*, in addition to the quality of the PRO instrument development. The overall quality of evidence for content validity for both the BrAT and the IMBPIQ was rated as “moderate”, as only development studies were available to review the

content validity and no independent separate content validity studies were identified (Terwee et al., 2018a).

6.4.5.1.1 PRO instrument design and relevance

For a PRO instrument to have sufficient *relevance*, all items need to be relevant for the construct of interest within a specific population and context of use (Terwee et al., 2018b). The BrAT developers (Hill et al., 2016) provide a clear description of the domain to be measured (activity) and the target population (adults with BPI). The ICF (World Health Organization, 2001) was used as a conceptual framework. The authors of the BrAT used robust item generation and item reduction methods. Item generation was derived from 1:1 patient interviews and nominal group sessions (n = 21), with additional input from clinical experts (n = 30) and a literature review (Hill et al., 2015b, 2011). Item reduction consisted of a patient survey, where participants rated the importance of each item. The literature review focused on the identification of upper limb questionnaires that assessed activity in the BPI literature (Hill et al., 2011).

The IMBPIQ developers (Mancuso et al., 2018) also provided a clear description of the domains to be measured and the target population (adults with BPI undergoing treatment). Item generation was gained through 1:1 interviews with 10 pre-operative patients and 13 post-operative patients with a BPI (Mancuso et al., 2015). Interviews were based on an interview guide and skilled interviewers conducted the interviews (Mancuso et al., 2015). Data from interviews were analysed inductively using grounded theory (Mancuso et al., 2015).

6.4.5.1.2 Comprehensiveness and comprehensibility

For a PRO instrument to have sufficient *comprehensiveness,* no key aspect of the construct should be missing (Terwee et al., 2018a), and to ensure *comprehensibility* the items should be understood by patients as intended (Terwee et al., 2018a). COSMIN guidelines suggest that a cognitive interview or other field testing should be performed to test the comprehensiveness and comprehensibility of a PRO instrument, either during development or in a separate content validity study (Terwee et al., 2018a). Neither the BrAT or IMBPIQ developers conducted cognitive interviews or field testing to evaluate comprehensibility (Hill et al., 2015b; Mancuso et al., 2015). With

regards to comprehensiveness, the concept elicitation stage was well performed in both PRO instruments, so there is less likelihood that important concepts have been missed (Terwee et al., 2018a). However, as no cognitive interviews were conducted the rating for this property was downgraded.

6.4.5.2 Structural validity

Only the BrAT showed evidence of structural validity. The BrAT was graded "moderate" for the quality of the evidence, as the sample size was at the lower bounds of the minimum required for Rasch analysis (n = 106). Results from the Rasch analysis showed that for 35 items there was no deviation from the Rasch model, with non-significant chi-squared values (p=0.30 Bonferroni adjusted), no violation of unidimensionality, and no local dependency (Hill et al., 2016).

6.4.5.3 Internal consistency

Both PRO instruments evaluated internal consistency, and both scored "moderate" for the quality of the evidence. The BrAT demonstrated excellent interrelatedness among subscale items, with Cronbach's alpha(s) ≥ 0.90 for each of the three subscales and 0.97 for the summed items (Hill et al., 2018b). The Cronbach alphas for the pre-operative IMBPIQ Disability and Improvement subscales were 0.91 and 0.86 respectively and 0.64 and 0.94 for the post-operative version (Mancuso et al., 2018). As the disability items in the post-operative version of the IMBPIQ are below the acceptable threshold for internal consistency and there is no structural validity study, it scored an overall "insufficient" rating for internal consistency.

6.4.5.4 Reliability

Test-retest reliability was assessed in both PRO instruments. The quality of the evidence was variable with the BrAT scoring as "moderate" and the IMBIQ scoring "very low". Quality of evidence for the BrAT was downgraded due to a low sample size (n = 43) and the IMBPIQ was downgraded because of a high risk of bias and a low sample size (Hill et al., 2018b; Mancuso et al., 2018). The intra-class correlation coefficient (ICC) was reported across both PRO instruments. All three subscales in the BrAT achieved an ICC ≥ 0.90 and an ICC of 0.97 for the summed score (Hill et al., 2018b). They also demonstrated high Cronbach's α values (≥ 0.90). Test-retest

reliability for all four subscales of both versions of the IMBIQ was also excellent, with ICC showing excellent agreement (ICC ≥ 0.85) (Mancuso et al., 2018).

6.4.5.5 Hypothesis testing for construct validity

Hypothesis testing for construct validity was assessed across both PRO instruments evaluating and demonstrating positive supporting evidence. The overall quality of evidence was "moderate" for the BrAT, downgraded because of a low sample size (n = 29), and was "low" for the IMBPIQ because of a low sample size and an adequate score on risk of bias. The BrAT was compared with the DASH and the Upper Extremity Functional Index (UEFI), and hypotheses relating to correlations between the BrAT and the DASH and UEFI were supported. An a priori hypothesis of low to moderate association between the BrAT and the DASH was accepted (because they measure dissimilar activity constructs), with correlations ranging from 0.48-0.69 (Hill et al., 2018a). A moderate association was predicted and confirmed between the BrAT and the UEFI summed scores, with Pearson's correlations of r=0.78, r=0.78 and r=0.81 at 0, 9 and 18 months respectively, indicating they were measuring similar constructs (Hill et al., 2018a). The IMBPIQ pre-op and post-op versions were compared with the DASH and the physical and mental health sections in the SF-36 (Mancuso et al., 2018). Worse symptoms and limitations scores in the IMBPIQ were associated with worse DASH and SF-36 physical health scores.

6.4.5.6 Responsiveness

Of the two PRO instruments, only the BrAT evaluated this property. The BrAT scored an overall sufficient rating and "moderate" score for quality of evidence, due to a low sample size (n = 29) (Hill et al., 2018a). Changes in summed scores from baseline to 18 months were statistically significant ($p < 0.05$). The magnitude of change as measured by effect size was larger for the BrAT than the DASH or the UEFI, with moderate effect sizes for the three separate subscales of 0.4, 0.4 and 0.52 respectively (Hill et al., 2018a).

Table 6.11 Summary of findings per measurement property (PRO instruments with "sufficient" relevance in content validity only)

COSMIN	BrAT			IMBPIQ		
Measurement property	**Summary of results**	**Overall rating**	**Quality of evidence**	**Summary of results**	**Overall rating**	**Quality of evidence**
Content validity	Content validity		Moderate	Content validity		Moderate
	Relevance	Sufficient (+)	Moderate	Relevance	Sufficient (+)	Moderate
	Comprehensiveness		Moderate	Comprehensiveness		Moderate
	Comprehensibility	Insufficient (-)	Moderate	Comprehensibility	Insufficient (-)	Moderate
Structural validity	Fit to Rasch model was good, no violation of unidimensionality, no violation of independence (Hill et al., 2016)	Sufficient (+)	Moderate	No information available	N/A	N/A
Internal consistency	Cronbach's α: 0.90 - 0.98 (Hill et al., 2018b)	Sufficient (+)	Moderate	Cronbach's α: 0.64-0.94 (Mancuso et al., 2018)	Insufficient (-)	Low
Cross-cultural validity/ measurement invariance	No information available	N/A	N/A	No information available	N/A	N/A
Reliability	ICC = ≥ 0.90 (Hill et al., 2018b)	Sufficient (+)	Moderate	ICC ≥ 0.85 (Mancuso et al., 2018)	Sufficient (+)	Very low
Measurement error	No information available	N/A	N/A	No information available	N/A	N/A
Criterion validity	No information available	N/A	N/A	No information available	N/A	N/A

COSMIN	BrAT			IMBPIQ		
Measurement property	**Summary of results**	**Overall rating**	**Quality of evidence**	**Summary of results**	**Overall rating**	**Quality of evidence**
Hypothesis testing (for construct validity)	The result was in accordance with the hypothesis	Sufficient (+)	Moderate	The result was in accordance with the hypothesis	Sufficient (+)	Low
Responsiveness	The result in accordance with the hypothesis	Sufficient (+)	Moderate	No information available	N/A	N/A

Table 6.12 Quality of evidence for measurement properties for PRO instruments

Measurement property	**BrAT**		**IMBPIQ**	
	OVERALL RATING + / - / ?	QUALITY OF EVIDENCE High, moderate, low, very low	OVERALL RATING + / - / ?	QUALITY OF EVIDENCE High, moderate, low, very low
Content validity				
Relevance	+	moderate	+	moderate
Comprehensiveness	+	moderate	+	moderate
Comprehensibility	-	moderate	-	moderate
Structural validity	+	moderate	NA	NA
Internal consistency	+	moderate	-	low
Reliability	+	moderate	+	very low
Construct validity	+	moderate	+	low
Responsiveness	+	moderate	NA	NA

[a] Cross-cultural validity, measurement invariance, measurement error and criterion validity are not listed as these measurement properties were not assessed in any of the two PRO instruments (BRAT or IMBPIQ); NA not assessed/not applicable

6.4.6 Feasibility of patient-reported outcome instruments

Table 6.13 summarises the different aspects of feasibility (Prinsen et al., 2016) evaluated for each PRO instrument. Both instruments are free to use and had regulatory approval for development. The BrAT takes only 5-6 minutes to complete, the IMBPIQ takes 12 minutes. No studies have evaluated patient comprehensibility in either PRO instruments or evaluated their reading levels. The BrAT is straightforward to score, with totals of columns summed (per scale and total) and presented as a value from the maximum total available. The IMBPIQ is more difficult to score. Each of the responses for items within the four subscales need to be reassigned a different number (one less) to calculate the score. Each subscale total then needs to be transformed to a range between 0-100. To calculate the total disability score, a mean score from the symptom, limitations and emotions subscales is calculated and divided by 3 (Mancuso et al., 2018).

Table 6.13 Feasibility aspects of PRO instruments: BrAT and IMBPIQ

Feasibility aspects	**BrAT**	**IMBPIQ**
Patient comprehensibility	Not clear, but in thesis (Hill 2017) reports that "*Clinicians and adults with BPI have reported that the instructions are simple and appear to be easily understood"*	Not clear but via email correspondence, developers noted that during piloting "*there was no need to paraphrase questions and no missing items"*
Completion time	5-6 minutes	12 minutes
Patient's required mental and physical ability level Ease of standardisation	Not clear	Not clear
Ease of score calculation	Easy	Difficult
Copyright	Freely available to use	2017 Hospital for Special Surgery, New York
Cost of instrument	None	None
Regulatory agency's requirement for approval	Received full ethics approval from the University of Western Sydney, Australia (H8616)	Approved by the Institutional Review Board at the Hospital for Special Surgery, New York
No. of studies citing/using instrument	None	None
Timeframe for use	Prior to intervention OR once discharged home and living in community for at least 3-4 weeks	Pre-operative version: Prior to operation/intervention Post-operative version: No timescale provided for post-intervention

6.4.7 Recommendations

Based on the results of this systematic review and evaluation of the psychometric properties of existing OMIs, provisional recommendations for measurement of outcomes in the COS-BPI can be made (Table 6.14). This includes the BrAT to measure 'carrying out daily routine' and the Brief Pain Inventory (Cleeland, 1989) to measure 'pain intensity' and 'pain quality' respectively. No recommendation can be made for OMIs to measure voluntary movement and pain frequency at present.

Table 6.14 Provisional COMS for adult traumatic brachial plexus injury

Core outcome domain	**Instrument**	**Free of Charge**	**Availability**
Carrying out daily routine	BrAT	Yes	Freely available
Pain intensity	Brief pain inventory	Yes	Permission routinely given for free use
Pain quality and interference	Brief pain inventory	Yes	As above
Pain frequency	Unable to make recommendation	N/A	N/A
Voluntary movement	Unable to make recommendation	N/A	N/A

BrAT: Brachial plexus Assessment Tool

The BrAT (Appendix 6.4) was the only OMI which met the criteria of the COSMIN and COMET guidelines (Prinsen et al., 2016) and therefore is recommended for *provisional inclusion in the core outcome measurement set*. It is a free OMI, easily accessible (https://www.brachialplexus.scot.nhs.uk/documents/BrAT%20Assessment%20Form.pdf).

Although no pain-specific OMIs have been evaluated in the BPI population, a provisional recommendation has been made to limit measurement variability for this domain. The Brief Pain Inventory was recommended by experts in the clinical advisory group (see Appendix 6.3). The Brief Pain Inventory (see Appendix 6.5) evaluates pain intensity, and quality and interference of pain on daily activity (Cleeland, 1989; Tan et al., 2004), thus measuring two of the pain outcomes in the COS-BPI. It was originally developed to assess cancer pain, but has been shown to be valid in chronic and neuropathic pain (Tan et al., 2004), with acceptable internal consistency (Cronbach α 0.85 intensity and 0.88 for interference), a stable 2-factor structure, and sensitivity to change with treatment. It has been recommended for the COMS for chronic pain (Dworkin et al., 2005), so is appropriate for measurement of the chronic intractable pain suffered by people with a BPI. Finally, it has recently been included in a COMS for children and adolescents with obstetric brachial plexus injury (Pondaag, 2022). These patients are frequently treated in the same tertiary units and by the same health professionals who treat adults with BPI. It is therefore pragmatic and may help uptake if the same measure for pain is provisionally recommended for the adult population.

The Brief Pain Inventory has been validated in the following languages: Arabic, Cebuano, Chinese (Simplified), Chinese (Traditional), Croatian, Czech, English, Filipino, French, German, Greek, Hebrew, Hindi, Italian, Japanese, Korean, Malay, Norwegian, Russian, Slovak, Slovenian, Spanish, Spanish (Spain) and Thai. The University of Texas M.D. Anderson Cancer Center holds the copyright, and permission to use the tool can be sought by filling in an online form https://www4.mdanderson.org/symptomresearch/index.cfm. Permission is routinely granted at no cost but no amendments are permitted.

Measures of the temporal aspects of pain, including frequency, have not received sufficient attention in pain research (Dworkin et al., 2005) and there was limited evidence available to support recommendation for assessment of this outcome.

No recommendations can be made for measurement of voluntary movement. Voluntary movement assessment is very heterogeneous in BPI because of the different presentations associated with the injury. For example, upper, lower, infra-clavicular

and pan plexus injuries will each necessitate voluntary movement assessments of different groups of muscles and joints.

No specific recommendations were made regarding timeframes of outcome assessment in research and routine practice. Timeframes should match the specific goals and feasibility of each study and routine clinical practice.

6.5 Discussion

The objectives of this study were to identify OMIs measuring any of the three domains in the COS-BPI and to evaluate their psychometric properties. In total 18 articles describing the development or evaluation of psychometric properties of nine OMIs (five PROs and four ClinROs) were included in the review. All instruments were assessed for content validity, with two PRO instruments, the IMBPIQ and the BrAT, considered eligible for full measurement property assessment. The following provisional COMS for use in adult BPI research and routine practice (Table 6.14) is recommended. The BrAT for 'carrying out daily routine' and the Brief Pain Inventory for 'pain' (intensity, pain quality and interference). No current OMIs had sufficient psychometric properties to be recommended for voluntary movement. The following sections discusses the results in the context of other literature, highlight methodological challenges encountered, and then present the strengths and the limitations of the work.

6.5.1 Content validity

Content validity is considered the first and most important measurement property to consider when selecting an instrument for a COS (Prinsen et al., 2016), clinical practice or research (Powers et al., 2017; Rothman et al., 2009). Most of the included OMIs in this systematic review did not include patients in their development or evaluate the content validity in a BPI population. Only two condition-specific PRO measures were identified which included people with a BPI in their development. This is also surprising, considering the devasting impact a BPI has on a person. This concurs with

findings from the systematic review (Chapter 3), that the focus of treatment is on impairment-based outcomes and highlights the lack of patient-centred research in BPI.

Only the BrAT and the IMBPIQ included patients in the development of their instruments, in well conducted studies ensuring both PRO instruments had "relevance". This is not surprising as they are condition-specific PRO instruments. However, neither PRO instrument met the criteria for "adequate" comprehensiveness and comprehensibility, as developers did not conduct cognitive interviewing or similar pilot testing of the near-final versions of the instruments. The critical appraisal in this study was undertaken using the updated COSMIN guidance for content validity (Terwee et al., 2018a), which requires that the developers report detailed methods for development and validation of their instruments. Both the BrAT and IMBPIQ were developed prior to the introduction of the new guidelines, which might explain how they did not reach threshold for adequate comprehensiveness and comprehensibility.

The DASH is the most frequently used PRO instrument in BPI studies (Dy et al., 2015; Haldane et al., 2022; Miller et al., 2021). However, despite its common use, no studies were found evaluating its content validity in a BPI population. In contrast the BrAT and the IMBPIQ were not identified in any reviews of BPI studies (Dy et al., 2015; Haldane et al., 2022; Miller et al., 2021). This may be due to their more recent development, with both instruments published in 2018 (Hill et al., 2018a; Mancuso et al., 2018). Although the DASH may be valid for a range of upper limb disorder populations, its use with new populations such as BPI should be supported with new content validity studies. Otherwise, the ongoing use of the DASH could result in inaccurate inferences, as the content of the instrument may not be relevant, comprehensive or comprehensible to BPI patients. With the development of these two new BPI-specific PROs, there is potential that the use of the DASH will decline in the future.

There is a consensus that the minimum requirement to include an OMI in a COMS is that it has high-quality evidence for sufficient content validity (Prinsen et al., 2016), but this systematic review found that no instrument met this criterion for pain (intensity, quality and frequency) or voluntary movement. Despite this, I am recommending the Brief Pain Inventory to measure pain. The rationale for this decision

was that I felt that the absence of high-quality evidence did not equate to insufficient content validity. Furthermore, not endorsing any instrument may perpetuate heterogeneity of measurement in BPI research and clinical practice and may result in the persistent use of OMIs not relevant to stakeholders. Finally, data on psychometric properties of OMIs are constantly evolving and so in this respect, recommendations are always provisional. Taking into consideration all these points it was still important to make recommendations on the best available instruments.

6.5.2 Evaluating clinician-reported and performance outcome instruments

Although there are well established guidelines for measuring PRO instruments (Mokkink et al., 2018), there is no consensus on how to evaluate measurement properties of ClinRO and PerfO instruments. This study aimed to evaluate all OMIs mapping to the domains in the COS-BPI. The identified measures were a combination of patient- and clinician-reported outcome measures. In the past researchers have used a variety of methods to evaluate clinimetric properties of ClinRO instruments. Reynaud et al. (2020) reviewed instruments for a COMS for total knee arthroplasty and used guidance by Bombardier and Tugwell (1987), rating categories including time to administer, ease of scoring, internal consistency, construct validity, reliability, responsiveness and interpretability as either positive, negative or doubtful. The criteria for assigning these categories are, however, not transparent. A review of clinimetric properties of timed ‘up and go’ tests (Hafsteinsdóttir et al., 2014) in a stroke population identified 14 studies and included those measuring any psychometric property in the population. However, their evaluation did not exclude instruments with insufficient content validity. The variation in methods used to evaluate clinimetric properties, and the lack of clear guidance, is an issue for COS developers aiming to maximise the benefit of the COS development by identifying appropriate measures.

This study followed an international guideline developed for selecting any OMIs (PROs and ClinROs, PerfOs) for inclusion in a COS (Prinsen et al., 2016). Many of the steps, however, focus on evaluation of psychometric properties in PROs (Prinsen et al., 2016), aligning with COSMIN’s recommendations (Mokkink et al., 2018). The first property to evaluate for all OMIs is content validity. However, for ClinROs and PerfOs there are few

developed methods published to support this endeavour. Powers et al. (2017) developed broad categories for evaluating content validity of ClinRO instruments for inclusion in clinical trials, including i) summary of concept elicitation methods, ii) literature review, iii) understandability of instructions to perform assessment, iv) understandability of patient instructions (if appropriate), and v) integrity of measure in population. Although these are useful general principles, no methods on how to rigorously examine them have been provided. OMERACT (Beaton et al., 2021c) recommend assessing content validity and feasibility initially before any other properties are reviewed. They (Beaton et al., 2021c) suggest surveying members of the OMERACT workgroup, patient partners and other key stakeholders on whether the OMI has sufficient content validity and matches the domain. On reflection, the OMERACT recommendations are potentially more relevant for assessing ClinRO instruments. However, due to the time constraints on this project, further surveys were not feasible. In the end, only three ClinRO instruments met the inclusion criteria for the review. These were all unfeasible to carry out in routine care or even pragmatic research settings and were excluded at an early stage. To facilitate the selection of relevant and robust OMIs for future COS, research needs to be conducted on the best methods to evaluate content validity of OMIs that are not PRO instruments.

6.5.3 Methods to identify a Core Outcome Measurement Set

International guidelines recommend that when selecting OMIs for a COS, there should be another consensus process (Prinsen et al., 2016). COMET and OMERACT (Beaton et al., 2021a; Williamson et al., 2017) recommend that a two-step process is needed: first to identify “what to measure” (COS) and then to identify “how” (COMS) to measure it. The COMBINE project focused on step 1, identifying what to measure. Rigorously focusing on step 1 and adhering to the recommendations, however, limited the capacity to complete step 2 within the timeframe of a PhD. Because of this I was unable to conduct the recommended consensus process in the second stage. Yet, different methods which potentially combine these two steps are frequently used to accelerate COS and COMS development and realise their benefits. Gorst et al. (2020) reviewed 118 COS studies that had identified a COMS. The majority, 87/118, had used

one single process to identify the COS and the instruments. There needs to be further innovation in methods used for developing COS and COMS. The current recommendations for a two-step process may potentially lead to many successful COS being developed but without the identification of the OMIs to measure them.

6.5.4 Strengths and limitations

This study is not without its limitations. A key limitation of this study was not including a consensus process (e.g., consensus meeting) to achieve final agreement on the selected OMIs with relevant stakeholders. This is recommended by both the COMET/ COSMIN and OMERACT guidelines (Beaton et al., 2019; Beaton et al 2021c; Prinsen et al., 2016). For 'carrying out daily routine' only one disorder-specific OMI (BrAT) met the criteria to be included in a provisional COMS, thus a consensus meeting would probably not be necessary. However, numerous OMIs exist to measure pain (intensity and quality), which researchers have not psychometrically evaluated in the BPI population. Ideally, these OMIs should have been discussed and decided through a consensus process.

Another limitation of this review is the assumption that, if validation studies of BPI OMIs were not identified in the search, then these had not been conducted. For the two included condition-specific PRO instruments the authors were contacted. However, for other instruments the possibility of publication bias cannot be excluded. Additionally, this review focused on OMIs developed in a BPI population. However, there may be other OMIs with value in this group that were not considered because they were not developed or validated in the BPI population. However, generic measures have been shown to be less responsive than disease-specific instruments in several clinical trials (Laupacis et al., 1991; Ware et al., 2016). Therefore, disease-specific instruments may be necessary to improve understanding of the impact of a BPI and interventions on it.

Finally, it was not possible to make recommendations for OMIs to measure voluntary movement. This was due to several reasons. First, there is heterogeneity in the presentation of voluntary movement loss in subgroups of people presenting with a BPI.

Secondly, I was unable to identify any feasible OMIs that had been evaluated in the BPI population. There are numerous published studies evaluating the validity and reliability of goniometry to assess range of motion in the upper limb, but these could not be included as they were not conducted in the BPI population. A robust consensus process is needed to agree the best available OMIs to measure this domain and it is likely that subpopulations (upper, lower and pan plexus injuries) may need their own OMIs.

This study also has strengths. It prospectively published its protocol on the PROSPERO website aiming to reduce bias. The updated COSMIN guidelines for evaluating psychometric properties in PRO instruments was followed (Mokkink et al., 2018; Terwee et al., 2018b). It used several sources to identify all studies on potential instruments for the COMS (Prinsen et al., 2016). Two reviewers independently assessed the quality of each study (with disagreements or uncertainty discussed with a third reviewer), as recommended by COSMIN. The two independent reviewers evaluating psychometric properties were experienced clinicians in the BPI field and discussed uncertainties with a third reviewer, who is experienced in outcome measurement development and validation.

6.5.5 Recommendations for future research

This study followed a recommended systematic process to identify and review measurement properties for potential OMIs (Beaton et al., 2021c; Beaton et al 2019; Prinsen et al., 2016). The COMS remains provisional because high-quality evidence is lacking for the PRO measures and new evidence may emerge. Although all but one measurement property in the BrAT were rated sufficient (+) with moderate-quality evidence, none had high-quality evidence. The BrAT was rated insufficient (-) for comprehensibility with moderate evidence. Future work is needed to evaluate the comprehensibility of the BrAT and further studies with larger sample sizes are necessary to strengthen the evidence for the other psychometric properties for this OMI. Additionally, there is a need to evaluate and compare content validity, structural validity, reliability and responsiveness of the Brief Pain Inventory in the BPI population. Finally, it is recommended that future consensus work is completed to support a

recommendation for an OMI(s) for voluntary movement. This may involve subgrouping the BPI population into upper, lower and pan plexus, because of the heterogeneity of movement loss.

Cross-cultural validity is important for PRO measures recommended in a COMs. This measurement property assesses whether the performance of the items in a translated or culturally adapted PRO measure adequately reflects the performance of the original version (De Vet et al., 2011). Cross-cultural validity has not been investigated for any recommended instruments. Future cross-cultural validity studies would indicate whether it is appropriate to pool data from the same PRO measure from different countries.

6.6 Conclusion

This study has identified and evaluated psychometric properties of OMIs relevant for measuring the COS-BPI. It created a provisional COMS, specifying instruments which should be used in future routine clinical practice and research with patients with BPI. This will facilitate BPI evidence synthesis by reducing measurement heterogeneity in future research and routine care. These recommendations will be updated as further evidence of the psychometric properties of recommended and alternative instruments become available.

Chapter 7: Conclusions and implications

7.1 Overview

This chapter gives a synthesis of key findings and discussion points arising from the research. It discusses how the research contributes to knowledge and its implications for clinical and research practice, in addition to its implementation.

7.2 Introduction

I embarked on this PhD fellowship as a physiotherapist frustrated by the slow progress in the treatments offered to adults with a brachial plexus injury (BPI). I treated patients with these devastating and life-changing injuries, yet I was unclear what to measure and if what I and the team (in a peripheral nerve injury tertiary NHS centre) were measuring was relevant to patients with the injury. Similarly, the literature appeared focused on clinician-reported impairment outcomes. I was uncomfortable with this because people with a BPI told me that the impact was wide-ranging, encompassing much more than just physical consequences. Even within this relatively narrow focus on measurement of physical impairment, there was large variation. As a result, reviewers have been unable to synthesise the evidence in systematic reviews to inform evidence-based practice. In clinical practice, this variation in outcome measurement in national and international specialist healthcare centres also hindered combining routine collected data or benchmarking interventions to inform practice for this relatively rare injury.

To address this problem, I set out to i) develop a core outcome set (COS), with a range of relevant stakeholders, for adults with a traumatic BPI and ii) identify existing validated measurement instruments that could measure the COS in future research and routine care. The following section synthesises the key findings from the research conducted.

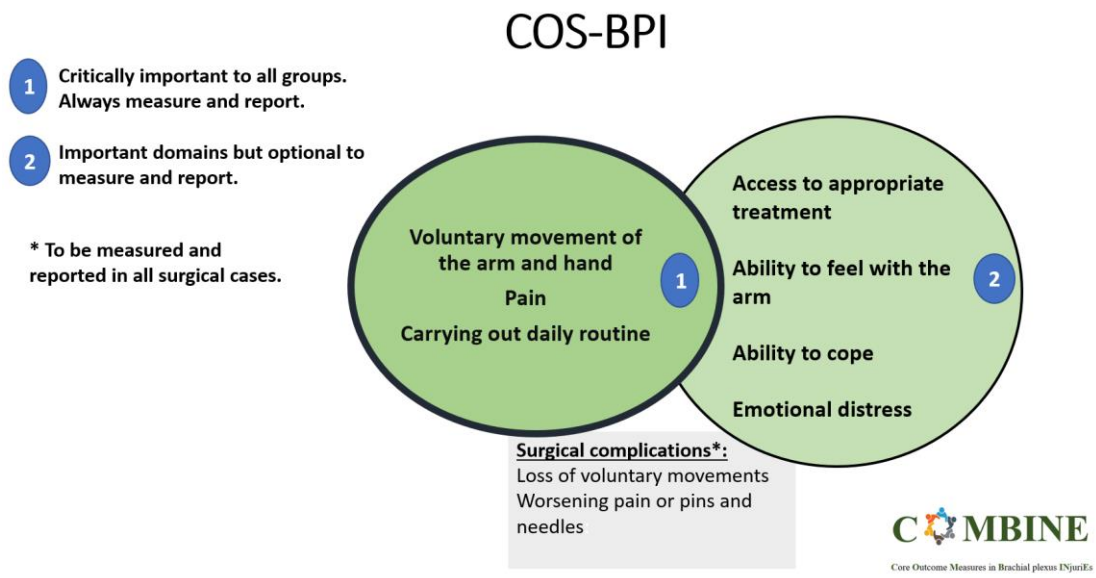
7.3 Key findings

First, I identified (through a systematic review) a long list of 157 different unique outcomes from 132 BPI studies, in addition to a long list of measurement instruments used in BPI (Chapter 3). Following this, I categorised the long list of outcomes into the COMET taxonomy framework, which facilitated the development of the COS-BPI.

I then interviewed a diverse sample of 13 adult patients with a BPI and identified 26 individual outcomes important to them (Chapter 4). When I compared the outcomes explored in the patient interviews to those identified in the review, most of the outcomes prioritised by patients were infrequently reported in the included studies. Indeed, the interview participants identified twelve outcomes that were not reported in the systematic review at all.

I combined the systematic review and interview outcomes into a long list and then used this list to generate an online Delphi questionnaire (Chapter 5). Seventy-one international participants (31 therapists/researchers, 20 patients, and 20 surgeons) completed a 3-round Delphi. Thirty-eight participants (including 25 healthcare professionals and 13 patients) from nine countries attended one of two online consensus meetings. I facilitated both meetings. Group discussions and anonymous voting, followed by a ratification meeting, resulted in consensus on seven core outcome domains (Figure 7.1). Three outcomes should be measured in all future studies and clinical care of adults with a traumatic brachial plexus injury. Four outcomes in tier two are important but optional to measure and report.

Figure 7. 1 COS-BPI



Finally, I conducted a systematic review (Chapter 6) and identified nine outcome assessments (five patient-reported assessments; four clinician-reported assessments) that had been psychometrically evaluated for use in adult brachial plexus injuries and which mapped to the COS developed in Chapter 5. Overall, the BrAT was the most rigorously evaluated outcome measurement instrument in the brachial plexus population for measuring the domain of carrying out a daily routine. The Brief Pain Inventory was mapped to the pain domain and was validated in populations with similar chronic neuropathic pain. Although there are many instruments which measure voluntary movement in the upper limb, I was unable to find any that were validated in the BPI population.

Additional research contribution: *Exploration of uncertainty in people with a traumatic BPI*

To fully explore outcomes which mattered to patients with a BPI, I designed an interview guide which focused on their lived experiences and from which outcomes could be interpreted.

However, these in-depth interviews revealed much more than the outcomes which mattered to people with the injury. Participants raised the feeling of uncertainty

throughout their narratives. Further analysis of the qualitative data identified how adults with a traumatic BPI face uncertainty in initial diagnosis, future outcomes from injury, and their role identity. People with the injury discussed how health professionals and maintaining hope can support them through this uncertainty. Following a presentation of the qualitative findings to my peripheral nerve injury team at the Queen Elizabeth Hospital Birmingham, they want to implement and evaluate shared decision-making instruments to enhance the care of patients with BPI to support uncertainty. The paper was accepted for publication in Disability and Rehabilitation (Miller et al., 2022)

7.4 Strengths

To ensure the COS-BPI was relevant to key stakeholders, it needed to represent the views of patients, surgeons and therapists. This project included several methods to ensure that this happened. Firstly, outcomes important to patients were elicited through patient interviews, and outcomes relevant to clinicians and researchers were identified through a systematic review. The difference between these outcomes showed that the priorities of healthcare professionals and patients do not always align. If either group had been excluded in the long listing process (systematic reviews and patient interviews), potentially important outcomes could have been missed. Secondly, the Delphi included separate patient and healthcare professional panels, thus allowing each group to reach consensus in their group before reviewing the other group's scores. Despite unequal participant numbers in the stakeholder groups in the Delphi, 70% of participants in each of the groups needed to identify an outcome as critically important for it to be included in the consensus meetings. Lastly, in separate patient and health professional consensus meetings, all outcomes voted ***IN*** by 85% or more in either group were taken forward to the ratification meeting and included in the final COS. Thus, those outcomes thought to be important by each stakeholder group were protected.

Another strength of the project was embedding patient and public involvement throughout the project. People with a BPI were involved in the planning, design, conduct and analysis of the COMBINE project. To support this involvement, guidance

from OMERACT (De Wit et al., 2013) and more recent guidance from the COMET group (Biggane et al., 2019; Young and Bagley, 2016) were followed. Patient and public involvement in the COMBINE study supported the development of patient-facing documents, the interview topic guide, language, and questions in the Delphi questionnaire. Patient and public members also co-developed an online video to promote the online Delphi internationally. Members of the patient and public involvement group piloted the 1:1 patient interview and early drafts of the online Delphi. In terms of analysis, two members were involved in the final ratification meeting to decide the structure of the final COS-BPI. One example of impact from members of the patient and public involvement group was the feedback I received from the design of a promotional poster to recruit people with the injury to the Delphi. On viewing the poster, one member of the patient and public group said:

> *"I immediately felt drawn to it because of the picture of the arm but it made me think I can't get my arm in this position*".

On discussion with this member, it was clear that many people with a BPI could not position their arm as illustrated on the poster and that a promotional poster using this image could have been demoralising for potential participants. It could also reduce trust in the project if an image which many potential participants could not relate to was used. Therefore, I changed the image on the poster to a neutral position of the arm by the trunk. Another instance of impact was feedback on the interview topic guide. Initially, it included a question "What did you hope these treatments would achieve?" Feedback from patients and public members was that often they hope to return to full function with minimal pain and that I should change the question to what did you "expect". I changed the question on the interview topic guide to reflect the feedback.

A final strength of this COS project is the identification of measures that could potentially assess the outcomes of the COS. Many COS developers stop at the development of the COS. However, this has been reported as potentially hindering uptake and implementation (Hughes et al., 2021).

7.5 Limitations

There are, however, several limitations to this programme of research. One limitation of the project was that the face-to-face interviews (which informed outcomes included in the consensus process) included a small group of BPI patients having treatment at a tertiary peripheral nerve centre in the Midlands in the United Kingdom. A patient's experience of healthcare and rehabilitation may differ between regions, countries, cultures and healthcare systems. However, people from outside the UK with the injury did have the opportunity to submit additional outcomes important to them in the first round of the Delphi. Unfortunately, due to the time and funding constraints of this PhD, the online Delphi was only available in English. The absence of translations into other languages potentially impacted patient participation from other countries, especially low- and middle-income countries where English is not widely spoken. Additionally, the development of an international working group at set up (even without translation of the Delphi) might have increased international participation through use of wider international networks. Care, therefore, needs to be taken when interpreting the results of the COS-BPI, as the priorities may reflect high-income countries' perspectives.

A further limitation is that the COMBINE project may not have included all relevant stakeholders. Williamson et al. (2017) suggest including additional stakeholders, including regulators, industry representatives and policy-makers. This project included people with the injury, surgeons, therapists and researchers. On reflection, specific recruitment of other stakeholders recommended above could have been targeted. However, some healthcare professionals may have had several roles in the field of brachial plexus healthcare. These may have included positions on funding panels, journal editorial boards, and roles in healthcare management and developing clinical guidelines. A limitation of the Delphi software was the inability to capture this diversity of roles among the stakeholders.

The scope of the COS-BPI was broad, including all interventions for adult BPI. This broad remit may neglect important outcomes for patients with a traumatic BPI undergoing specific treatments. Many of the COS domains cross all brachial plexus

interventions and include musculoskeletal outcomes such as voluntary movement, a symptom domain of pain, and the life impact domain of carrying out a daily routine. However, patients have distinct experiences following different interventions for a traumatic BPI. Problems with breathing may be associated with intercostal nerve transfer, or lower limb mobility problems experienced with a free functioning muscle transfer of gracilis. Nevertheless, participants' feedback suggests the outcomes included in the COS-BPI are important to measure in all BPI studies and routine care. Ultimately, the COS does not prevent the addition of other intervention-specific outcomes.

The number of “must measure” outcomes in this COS is three, with two surgery-specific complications, and this may be considered to be low. However, an evaluation of the uptake of a COS for pain in paediatrics found that some systematic reviewers felt six domains were too many (Boric et al., 2018a). A COS with a high number of outcomes may hinder implementation, as researchers and healthcare professionals perceive this increases the burden on patients (Dosenovic et al., 2019). It has recently been recommended that COS developers could restrict the outcomes considered “core” (Hughes et al., 2021) because of these fears.

7.6 Implementation for research

A COS is only useful if implemented. It means that in research, studies should universally use the COS, limiting outcome reporting bias and facilitating comparative effectiveness research (Williamson et al., 2012a). However, recent reviews have identified a low level of uptake for COS (Hughes et al., 2021; Williamson et al., 2022). For example, a COS for lower limb osteoarthritis had low uptake by researchers (45%), which decreased over time (Smith et al., 2019). Smith et al. (2019) noted contradictions in different regulators’ recommendations, which potentially influenced its implementation. The COS for rheumatoid arthritis is, however, an exception. The rheumatoid arthritis COS demonstrates high uptake, with 60%-82% of randomised controlled trials measuring it (Kirkham et al., 2019, 2017a, 2013a). Kirkham et al. (2017a) posited that the uptake may have improved because of endorsements by drug regulatory agencies. Endorsements seem to influence COS use in research. Various

government research funders in the UK now endorse the use of COS in submissions to their awards (http://www.comet-initiative.org/COSEndorsement). Hughes et al. (2019) evaluated the influence of the National Institute for Health Research Health Technology Assessment's (NIHR HTA) COS recommendations. They (Hughes et al.2019) identified that 38% of applicants submitting bids for funding between 2012 and 2015 looked for a COS (Hughes et al., 2019). Future research needs to explore which types of endorsements improve COS uptake and why.

From the beginning of this project, steps were taken to enhance the uptake of the COS-BPI. It was registered on the COMET database and this is linked to the published protocol (Miller et al., 2019). Intended users of the COS-BPI were engaged through newsletters and social media updates throughout the project to increase awareness and promote trust in the COS. The Narakas group is the international collaboration of surgeons and therapists interested in improving care for people with BPI. They run a four-yearly conference. I presented and promoted the project at its inception at the 2018 Narakas meeting and invited attendees to take part in the Delphi. The final COS-BPI and measurement instruments will be disseminated to the Narakas group, and the COS-BPI was presented at a specific brachial plexus session at the Joint Congress of the International Federation of Societies for Surgery of the Hand (IFSSH) and International Federation of Societies for Hand Therapy (IFSHT) in June 2022.

7.7 Implications for research

The COS-BPI aims to standardise outcome reporting and ensure that outcomes important to patients, healthcare professionals and researchers are measured and reported. If used by BPI researchers, it will improve evidence synthesis, increasing evidence-based practice for BPI interventions, therefore improving care and treatment of people with the injury. Furthermore, if implemented, the outcomes reported in the literature will be more relevant to patients, thus focusing treatments on what's important to them. Several of the life impact, physical functioning and delivery of care domains present in the COS-BPI represent priorities for patients, identified in the interviews (emotional distress, physical function, pain, access to treatment), yet studies seldom reported them. Implementation of the COS-BPI, therefore, could

improve the measurement and reporting of outcomes relevant to people with a BPI. This will increase the availability of relevant evidence to support evidence-based practice.

7.8 Implementation of COS in routine practice

Uptake and implementation of the COS-BPI by healthcare professionals will be essential to realise the benefits of the COS. However, there are challenges to implementing a COS for routine practice. Unlike COS for research, where many funders, registration bodies and journals now endorse their use, there are no similar incentives in routine care. Knowledge regarding the benefits of COS for routine care may be limited among clinicians. Developers of the cleft palate core set (Arora and Haj, 2016) found that education of team members, patients and facilitation of staff culture change were critical to the implementation of their set. However, the use of COS in routine care needs to have value to the individual healthcare professional. Ideally, real-time reporting is important, so healthcare professionals have access to patient outcomes in clinical consultations. This information can support clinical decision-making and planning for future treatment. Indeed, some systems are now implementing prediction models based on “average patient outcomes”, so they can be used in individual consultations (Selles et al., 2020). However, further research is needed to evaluate how healthcare professionals use a routine COS in clinical practice.

Implementing a COS into routine care may require a combination of clinician- and patient-reported outcomes being used, dependent on the measures included in the COS. Clinician-reported outcomes will need to be assessed at a consultation between the health professional and the clinician and then entered into an appropriate database, hence taking valuable clinical time. Patient-reported outcomes can be collected in a clinic or remotely by the patient. Research on routine care COS implementation has focused on online databases. There may need to be flexibility in methods of data collection to support the inclusion of underserved patient groups with limited internet access. I believe, however, that data collection, entry and extraction based on paper-based forms (which is time-consuming and costly) will hinder the

implementation of the COS-BPI, as evidenced in recent routine COS for OA (Ackerman et al., 2018).

A challenge for healthcare professionals is the assessment and entry of the results of the COS data in busy outpatient trauma and orthopaedic clinics (Ackerman et al., 2018). Similarly, patients might find it difficult to complete COS data in a time-restricted clinical appointment. In the case of a hand surgery COS for routine practice, therapists and nurses drove its implementation at one site (Arner, 2017). There is evidence, however, that implementation of COS in routine practice requires personnel resources (Ackerman et al., 2018) to support data collection, entry and extraction, in addition to resources for information technology development. Indeed, the value of high-quality databases with health professional and patient reminder systems has been emphasised in several studies (Ackerman et al., 2018; Arora and Haj, 2016; Selles et al., 2020).

7.9 Future implementation of COS-BPI in routine practice

To facilitate the implementation of the COS-BPI in routine practice in the UK, we aim to host an online database through collaboration with other tertiary specialist peripheral nerve centres. We already have support from four national centres and are investigating an ethics application. Measurement time points will be agreed by a consensus process between the clinical academics across all UK BPI units. Data will be collected digitally, using GemsTracker electronic data capture tools (Gemstracker, 2022). GemsTracker is a secure, open-source, web-based application for the dissemination of questionnaires and forms for healthcare research and quality improvement. It has been successfully used to collect outcome data for 52,000 people with hand and wrist disorders in the Netherlands and Switzerland (Duraku et al., 2022; Selles et al., 2020; Wouters et al., 2021). Completion of emailed questionnaires to routine hand surgery patients in the Netherlands is 73% at baseline and 62% at 12 months (Selles et al., 2020). When a patient is registered on the system, baseline questionnaires can be distributed via email, and then follow-up questionnaires at agreed timepoints. This aims to minimise patient measurement burden. The system calculates PRO instrument scores and displays instruments which have been answered,

yet to be answered, and omitted. If a measure is completed several times, then score progression is illustrated. If PRO data are missing, the healthcare professional can ask the patient to complete those specific questionnaires.

We will establish a COMBINE steering committee, including a small number of clinical academic healthcare professionals working in the UK BPI area, representing each tertiary peripheral nerve injury centre. Incentives will include co-authorship on studies and, through ethics applications, access to the adult BPI online database. The goal will be to drive collaborative inter-regional electronic outcome collection in BPI care. In the future, we aim to integrate the COS-BPI into trusts' electronic patient records, which will minimise the burden of data collection.

Measurement of outcomes in routine healthcare is a fundamental aspect of value-based and patient-centred care (Porter, 2010). Healthcare professionals can benchmark treatment outcomes against their peers, between tertiary centres and geographical areas (Arora and Travella, 2017). This can support identification and learning from best practices, providing opportunities to improve the quality of care (Arora and Travella, 2017; Porter, 2010). Benchmarking treatment outcomes can also help establish priorities for resource allocation. Therapists and surgeons can use measurements to assess progress and establish new goals. In online databases similar to Gemstracker (Gemstracker, 2022), people with the injury can see their progress over time, compared to the average outcome from former patients (Selles et al., 2020). Similarly, healthcare professionals can compare outcomes of individual patients to the average outcome for that particular treatment, from the larger dataset (Selles et al., 2020).

The National Health Service (NHS) Long Term plan prioritises digital transformation of the NHS with the linkage of data collected in routine care and provision of these data for research (Alderwick and Dixon, 2019; NHS, 2019). As a BPI is a relatively rare injury, national and international collaboration using routine or audit data is essential to create larger datasets to draw evidence from. The UK currently has no formalised BPI research collaborative links and there is no requirement to report outcomes following BPI interventions. However, the COS-BPI now provides a mechanism for longitudinal

data collection, generating large data sets for use in research. The collection of the COS-BPI in routine practice, reporting into this database, will serve two functions. Firstly, it will monitor the safety and quality of BPI interventions. It will detect interventions with poor outcomes at an early stage and prevent their widespread use. It can also identify interventions with improved outcomes and accelerate their implementation. Secondly, it will facilitate pragmatic prospective observational research (Ackerman et al., 2018) to evaluate brachial plexus care with a standardised group of outcomes relevant to patients and healthcare professionals.

In summary, the data collected in large registries with the COS-BPI can potentially extend knowledge on treatment effectiveness, identify predictors of outcome and support psychometric evaluation of OMIs. In the future, outcome data collected can be linked to treatment cost, informing quality of care from a value-based health care perspective (Porter, 2010).

7.10 Dissemination

I aim to disseminate the COS-BPI widely to maximise awareness amongst healthcare professionals and researchers. Dissemination will include further presentations at national and international conferences, publications in high-impact journals, and active social media engagement (Twitter @studyCOMBINE). I will disseminate the results through my professional networks and those of the wider research team. I will communicate links to the publication and a plain English summary to study participants (interviews, Delphi, and consensus meetings via email with consent) and via the charity groups involved in the study.

7.11 Future work

The research in this thesis defined a COS to be measured and reported in research and routine care of adults with a traumatic brachial plexus injury. An evaluation of psychometric properties of measurement instruments, mapped to the COS, identified the BrAT (Hill et al., 2018a) as the most rigorously developed and evaluated instrument to evaluate “carrying out daily routine”. Future research is needed to assess the

comprehensibility of the BrAT in the adult brachial plexus population. COSMIN (Terwee et al., 2018b) recommends that cognitive interview studies should be conducted to evaluate comprehensibility.

Further research is needed on measures to evaluate pain in the brachial plexus population. No pain instrument developed or tested in the BPI population had sufficient psychometric properties (Terwee et al., 2018b). Chapter 6 identified one potential OMI with excellent psychometric properties in other populations, mapping to the domain of pain – the Brief Pain Inventory. A future study using cognitive interviews could evaluate the content validity and a future prospective multi-centre study could assess the responsiveness of the Brief Pain Inventory in adults with a BPI. The systematic review in Chapter 6 did not identify any instrument measuring voluntary movement that had been psychometrically evaluated in the brachial plexus population. Further consensus work will need to be conducted to identify how to measure voluntary movements across the different subgroups of brachial plexus (upper, lower, and pan plexus). In the future, the instruments recommended in the provisional core outcome measurement set may need to be updated as and when new evidence emerges on the psychometric properties of current and future OMIs.

International healthcare professionals and patients collaborated to reach consensus on the COS-BPI. Although there was participation from low- and middle-income countries, this was low. Due to the relative rarity of brachial plexus injury, multi-centre and international recruitment is needed for adequate sample sizes to establish the evidence needed to support brachial plexus care. Future research to establish the international applicability of the COS-BPI is important. This is essential if the COS-BPI is to have the intended benefit of standardising cross-study outcome measurement and enabling data synthesis.

It will be necessary to review the COS-BPI periodically, to assess whether the outcomes remain important to stakeholders and relevant to brachial plexus care. New outcomes may need to be added or existing outcomes removed. Finally, uptake of the COS-BPI and enablers and barriers to its uptake in research and routine care will need to be

assessed and addressed. Surveys and qualitative research could potentially explore the implementation, sustainability and impact of the COS-BPI in routine care and research.

7.12 Conclusion

I started this project frustrated with outcome measurement in adult BPI and wanted to find out what we should be measuring and reporting to improve care for patients. I believe I have achieved this. The project aimed to develop a COS for adult traumatic BPIs for use in routine care and research and to identify existing measures that could measure the COS. Patients, healthcare professionals and researchers reached consensus on three core outcomes that should be measured in all BPI research and routine care. These include carrying out daily routine, voluntary movement, and pain. A systematic review and psychometric evaluation of existing instruments identified that the BrAT (an existing patient-reported outcome measure) has the potential to measure the 'carrying out daily routine' domain. The Brief Pain Inventory was mapped to the pain domain but would need validating in the brachial plexus population. The review did not identify any instruments with sufficient psychometric properties to measure voluntary movement in the brachial plexus population.

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Appendices

Appendix 2. 1 Research group, patient advisory group and clinical advisory group

For the COMBINE project a multidisciplinary team, representing all relevant stakeholders, was established. The group oversaw the design and management of the study and consisted of three smaller groups:

1) Core team: Caroline Miller (PhD student), Dr Jane Cross (supervisor), Professor Christina Jerosch-Herold (supervisor) and Mr Dominic Power (clinical supervisor and surgeon representative).
2) Patient advisory group
3) Clinical advisory group

CM led the study and generated key ideas for the COMBINE study, informed by current literature, clinical experience, and consultation with the core team, patient partners and the international clinical advisory group.

Patient advisory group

When patients or lay people are involved in designing and overseeing a research study, such as a COS generation, it is described as 'patient involvement'. Patient and public involvement (PPI) has been defined as research that is carried out "with" or "by" members of the public rather than "to", "about" or "for" them (NIHR, 2019). OMERACT recommends that patient involvement in COS development is a fundamental (Beaton et al., 2021b), although roles and tasks undertaken may vary depending on the stage or content of the research project (Beaton et al., 2021b). Williamson et al. (2017) states that involving the public or patients in both the design and oversight of the COS development study may have the potential to:

- inform discussions about ethical aspects of the study
- facilitate the design of appropriate study information

- promote the development of more relevant materials to promote the study
- enable ongoing troubleshooting opportunities for patient participation issues during the study, e.g. recruitment and retention issues of study participants
- inform the development of a dissemination strategy of COS study results for patient participants and the wider patient population
- ensure that the COS is relevant to patients and, crucially, that patients see it to be relevant and can trust that the development process has genuinely taken account of the patient perspective.

OMERACT recommends that each COS working group should involve as a minimum two patient partners, who should be identified based on their "lived experience" knowledge and personal interest (Beaton et al., 2021b).

There are multiple methods to involve public partners in designing and overseeing a COS. The following section will discuss how the COMBINE project involved public partners.

Three adults with a traumatic brachial plexus injury (BPI), including two males (ages 29, 32) with upper BPIs and one female (age 24) with a pan plexus injury, were involved in the COMBINE project from inception to dissemination. They have been involved in designing and reviewing patient information sheets, lay summaries, interview topic guide, lay video to promote the COS, and wording and layout of the Delphi. Two members were involved in the final meeting to ratify the final COS-BPI with the core team and a member of the clinical advisory group. Engagement with this team of patient advisors occurred face to face prior to the COVID pandemic (see figure 1) and thereafter has occurred via virtual meetings and email correspondence. More details of the patient and public involvement will be discussed in the relevant chapters.

Additionally, the wider UK Traumatic Brachial Plexus Injury charity committee supported and promoted the COMBINE project throughout. Prior to development of the project, the UK TBPI charity was contacted with the research idea, which was discussed at its annual general meeting in 2016. At that meeting there was overall support for the project and discussion

around how the charity could support its promotion and update progress on its website. Every August since 2016 I have attended the UK TBPI charity AGM, where the COS has been a standing item on the agenda. The meeting is held in a marquee at the back of a bikers' café in Yorkshire and it is attended by individuals with a BPI from around the UK – usually numbering 30-40 attendees (see figures 2 and 3). Issues discussed have included recruitment to the interview and e-Delphi studies and promotion of the various studies in the project.

Figure 1 PPI meetings and annual meetings in Squires biker's cafe

Clinical advisory group

The clinical advisory group (n=18) included occupational therapists (n = 6), physiotherapists (n = 11) and a nurse (n = 1), who were healthcare professionals or clinical academics involved in

the treatment and research of adults with BPI. They represented clinicians from nine countries (England, Wales, Scotland, Australia, Sweden, Denmark, Norway, Wales and Ireland) and were selected based on their clinical expertise or research with adults with BPI. The group was convened during development of the project and prior to submission of the PhD project for funding. In addition to supporting this project, the group also served as a networking group to share knowledge and combine efforts across this unique area of healthcare. Engagement with the steering group took place initially twice-yearly, alternating face to face meetings with virtual events. The initial meeting was held in Birmingham, with follow-up meetings in Scotland and London. Post-COVID-19 (March 2020) all meetings went virtual but continued twice yearly. Email correspondence was used between the meetings. Representatives from the clinical advisory group supported development of lay summaries, participant information sheets, the lay video and also wording for the online Delphi. Members piloted the online Delphi and fed back on initial versions. They promoted the Delphi internationally, particularly highlighting it to patient charity groups in their countries and their medical colleagues. One representative from the group sat on the ratification panel to agree the final COS after the consensus meetings. They reviewed existing outcome measurement instruments and identified any that were missed. It is hoped that the development of the clinical advisory group and their involvement throughout the study will also support implementation of the COS. Clinical advisory group involvement will be detailed in the relevant chapters.

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Appendix 3. 1 Deviations from systematic review registered protocol

Deviations from study protocol

Protocol method	**Deviation from protocol method with justification**
We planned to hand search Journal of Hand Surgery (Eur) and The Journal of Hand Surgery (American).	We did not hand search these journals as they were all indexed for MEDLINE.
We planned to include studies with participants aged 18 and over within the review.	We reduced the age of 'include' participants to 16 or over, as many studies included older teenagers with adults in their studies. On discussion with the research team, we concluded that there was no difference between treatments of those aged 16 and over versus those aged 18. If we had excluded these studies, many outcomes used across these age ranges would have been lost.

Appendix 3. 2 Search strategy outcome reporting systematic review

Search strategy 10/09/2018 COMBINE systematic review

MEDLINE (OVID)

1. (brachial plexus adj3 injur*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

2. (brachial plexus adj3 pals*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3. (brachial plexus adj3 lesion*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4. (brachial plexopath*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

5. (brachial plexus adj3 traction*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

6. (brachial plexus adj3 avulsion*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

7. Brachial Plexus/in, su, tr [Injuries, Surgery, Transplantation]

8. 1 or 2 or 3 or 4 or 5 or 6 or 7

9. limit 8 to (humans and "all adult (19 plus years)")

10. limit 9 to yr= “2013-current”

Appendix 3. 3 COMBINE Systematic review screening form help sheet

1. Is this an animal research study?
Yes (stop)
No/ unclear

2. What is the age group of the research participants?
Under 18 years (stop)
Mixed adult and children/ unclear then keep in

3. Is the research on brachial plexus anaesthetic injections?
Yes (stop)
No/ unclear

4. Narrative /descriptive review
Yes (stop)
No/ unclear

5. Oncology population with brachial plexus
Yes (stop)
No/ unclear

6. Diagnostic study on tests/instruments in participants with traumatic brachial plexus injury
Yes (stop)
No/ unclear

7. Cross-sectional study without a specific intervention
Yes (stop)
No/ unclear

8. Does the research assess the outcome of an intervention in a traumatic brachial plexus population (case study, case series, trial)?
NO (stop)
YES – Include

Appendix 3. 4 Outcome Reporting Bias assessment instrument

Outcome Reporting Bias assessment instrument (adapted from Deshmukh et al 2021)

Study ID	**Author**	**Registered**	**No clear reporting of outcome through description/table/figure**	**Outcome only by summary comment (e.g., there was no significant difference), no numerical values provided, lack of information so that reporting not meaningful (outcomes but no time points)**	**Outcome reported but not at all time points; lacks detail to be included in review**	**Outcome reported at all time points (methods, results)**	**Outcome not specified in registration or prior to results**
			NOT DONE	MIMIMAL	PARTIAL	COMPLETE	UNEXPECTED

Deshmukh SR, Mousoulis C, Marson BA et al. Developing a core outcome set for hand fractures and joint injuries in adults: a systematic review. Journal of Hand Surgery (Eur) 2021; 46(5):488-495

Appendix 3. 5 Data extraction template for outcome reporting systematic review

Study specific data extraction form

	Authors	Year published	Study title	Country study conducted	Type of BPI	Study design	Intervention	Intervention if surgical	No. of participants	Male	Female
Drop down options					Infraclavicular/ supraclavicular	Prospective /retrospective/ randomised clinical trial/ nonrandomised clinical trial/ case study	Pain/surgical / therapy/ electrotherapy/ other	Free muscle flap/ tendon transfer/ neurotisation/ neurolysis/ contralateral C7/ multiple/ other			

Outcome reporting data extraction

	Outcome name reported verbatim	Outcome region	Outcome measurement instrument	Outcome type	Time points measured	Adverse events reported
Drop down options		All/shoulder/ elbow/wrist/ hand/not specified/ not applicable/		Clinician reported outcome/ Performance reported outcome/ Observation reported outcome/ Patient reported outcome/ Biomarkers/ combination of PRO and ClinRO/ resource use	Immediately/ 0-3mths/ 4-6mths/7-12mths/ 1-3 years/ 3-5yrs/ 5-10yrs/> 10years	

Appendix 3. 6 Outcome taxonomy used in the COMBINE study

COMET outcome taxonomy - adapted from Dodd et al. (2018)

Core area	Outcome domain
Death	1. Mortality/survival
Physiological/clinical	2. Blood and lymphatic system outcomes
	3. Cardiac outcomes
	4. Congenital, familial and genetic outcomes
	5. Endocrine outcomes
	6. Ear and labyrinth outcomes
	7. Eye outcomes
	8. Gastrointestinal outcomes
	9. General outcomes
	10. Hepatobiliary outcomes
	11. Immune system outcomes
	12. Infection and infestation outcomes
	13. Injury and poisoning outcomes
	14. Metabolism and nutrition outcomes
	15. Musculoskeletal and connective tissue outcomes
	16. Outcomes, relating to neoplasms: benign, malignant and unspecified (including cysts and polyps)
	17. Nervous system outcomes
	18. Pregnancy, puerperium, and perinatal outcomes
	19. Renal and urinary outcomes
	20. Reproductive system and breast outcomes
	21. Psychiatric outcomes
	22. Respiratory, thoracic and mediastinal outcomes
	23. Skin and subcutaneous tissue outcomes
	24. Vascular outcomes
Life impact	**Functioning**
	25. Physical functioning
	26. Social functioning
	27. Role functioning
	28. Emotional functioning/wellbeing
	29. Cognitive functioning
	30. Global quality of life
	31. Perceived health status
	32. Delivery of care
	33. Personal circumstances
Resource use	**Resource use**
	34. Economic
	35. Hospital
	36. Need for further intervention
	37. Societal/carer burden
Adverse events	38. Adverse events/effects

Dodd S, Clarke M, Becker L et al. A taxonomy has been developed for outcomes in medical research to help improve knowledge discovery. *J Clin Epidemiol*. 2018; 96:84-92.

Appendix 3. 7 Included studies in outcome reporting systematic reviews

	Study title	First author	Year of publication
1	Effectiveness and safety of home-based muscle electrical stimulator in brachial plexus Injury patient (Limthongthang et al., 2014)	Limthongthang	2014
2	Elbow proprioception sense in total arm -type brachial plexus injured patients after neurotisation: a preliminary study (Homsreprasert et al., 2014)	Homreprasert	2014
3	Comparison between the anterior and posterior approach for transfer of the spinal accessory nerve to the suprascapular nerve in late traumatic brachial plexus injuries (Souza et al., 2014)	Souza	2014
4	Ultrasound-guided peripheral nerve stimulation for neuropathic pain after brachial plexus injury: two case reports (Kim et al., 2017)	Kim	2017
5	Contralateral lower trapezius transfer for restoration of shoulder external rotation in traumatic brachial plexus palsy: preliminary report and literature review(Satbhai et al., 2014)	Satbhai	2014
6	Restoration of shoulder abduction in brachial plexus avulsion injuries with double neurotization from the spinal accessory nerve: a report of 13 cases (Huan et al., 2017)	Huan	2017
7	Transfer of the musculocutaneous nerve branch to the brachialis muscle to the triceps for elbow extension: anatomical study and report of five cases (Bertelli et al., 2017)	Bertelli	2017
8	Posterior approach for accessory to suprascapular nerve transfer: an electrophysiological outcomes study (Rui et al., 2013)	Rui	2013
9	Reliability of functioning free muscle transfer and vascularized ulnar nerve grafting for elbow flexion in complete brachial plexus palsy (Potter and Ferris, 2017)	Potter	2017
10	Management of infraclavicular (Chuang Level IV) brachial plexus injuries: A single surgeon experience with 75 cases (Lam et al., 2015)	Lam	2015
11	Functioning free muscle transfer for the restoration of elbow flexion in brachial plexus injury patients (Estrella and Montales, 2016)	Estrella	2016
12	Radial to axillary nerve transfers: A combined case series(Desai et al., 2016)	Desai	2016
13	Thalamic deep brain stimulation for neuropathic pain after amputation or brachial plexus avulsion (Pereira et al., 2013)	Pereira	2013
14	Nerve transfers for shoulder function for traumatic brachial plexus injuries	Estrella	2014
15	Results of operative treatment of brachial plexus injury resulting from shoulder dislocation: A study with a long-term follow-up (Gutkowska et al., 2017)	Gutkowska	2017
16	Surgical treatment of brachial plexus posterior cord lesion: A combination of nerve and tendon transfers, about nine patients (Oberlin et al., 2013)	Oberlin	2013
17	The medial cord to musculocutaneous (MCMc) nerve transfer: a new method to reanimate elbow flexion after C5-C6-C7-(C8) avulsive injuries of the brachial plexus—technique and results (Ferraresi et al., 2014)	Ferraresi	2014
18	Transfer of a terminal motor branch nerve to the flexor carpi ulnaris for triceps reinnervation: anatomical study and clinical cases (Bertelli et al., 2015)	Bertelli	2015
19	Free functioning gracilis muscle transfer with and without simultaneous intercostal nerve transfer to musculocutaneous nerve for restoration of elbow flexion after traumatic adult brachial pan-plexus injury (Maldonado et al., 2017a)	Maldonado	2017
20	Isolated latissimus dorsi transfer to restore shoulder external rotation in adults with brachial plexus injury (Ghosh et al., 2013)	Ghosh	2013

21	Functional outcome and quality of life after traumatic total brachial plexus injury treated by nerve transfer or single/double free muscle transfers (Satbhai et al., 2016)	Satbhai	2016
22	Successful graded mirror therapy in a patient with chronic deafferentation pain in whom traditional mirror therapy was ineffective: A case report (Mibu et al., 2016)	Mibu	2016
23	Bipolar Transfer of Latissimus Dorsi Myocutaneous Flap for Restoration of Elbow Flexion in Late Traumatic Brachial Plexus Injury: Evaluation of 13 Cases (Azab and Alsabbahi, 2017)	Azab	2017
24	Comparison of objective muscle strength in C5-C6 and C5-C7 brachial plexus injury patients after double nerve transfer (Tsai et al., 2015)	Tsai	2014
25	Phantom remodelling effect of dorsal root entry zone lesioning in phantom limb pain caused by brachial plexus avulsion (Son and Ha, 2015)	Son	2015
26	Comparison of surgical strategies between proximal nerve graft and/or nerve transfer and distal nerve transfer based on functional restoration of elbow flexion: A retrospective review of 147 patients (Hu et al., 2018)	Hu	2018
27	Reconstruction of shoulder abduction by multiple nerve fascicle transfer through posterior approach (Ren et al., 2013)	Ren	2013
28	Intercostal nerve transfer to neurotise the musculocutaneous nerve after traumatic brachial plexus avulsion: A comparison of two, three, and four nerve transfers (Xiao et al., 2014)	Xiao	2014
29	Use of the DEKA Arm for amputees with brachial plexus injury: A case series (Resnik et al., 2017)	Resnik	2017
30	Polyester tape scapulopexy for chronic upper extremity brachial plexus injury (Leechavengvongs et al., 2015)	Leechavengvongs	2015
31	Contralateral C7 nerve transfer with direct coaptation to restore lower trunk function after traumatic brachial plexus avulsion (Wang et al., 2013)	Wang	2013
32	Outcome of surgical reconstruction after traumatic total brachial plexus palsy (Dodakundi et al., 2013)	Dodakundi	2013
33	Bionic reconstruction to restore hand function after brachial plexus injury: a case series of three patients (Aszmann et al., 2015)	Aszmann	2015
34	Surgical treatment of the plexus brachialis injury using long-lasting electrostimulation (Tsymbaliuk and Tretiak, 2013)	Tsymbalyuk	2013
35	Phrenic nerve transfer for reconstruction of elbow extension in severe brachial plexus injuries (Flores and Socolovsky, 2016)	Flores	2016
36	Direct coaptation of the phrenic nerve with the posterior division of the lower trunk to restore finger and elbow extension function in patients with total brachial plexus injuries (S. Wang et al., 2016)	Wang	2016
37	A prospective study comparing single and double fascicular transfer to restore elbow flexion after brachial plexus injury(Martins et al., 2013)	Martins	2013
38	Chronic post-traumatic neuropathic pain of brachial plexus and upper limb: a new technique of peripheral nerve stimulation (Stevanato et al., 2014)	Stevanato	2014
39	Effectiveness of contralateral C7 nerve root and multiple nerve transfer for treatment of brachial plexus root avulsion (Wei et al., 2014)	Wei	2014
40	Combined proximal nerve graft and distal nerve transfer for a posterior cord brachial plexus injury (Plate et al., 2013)	Plate	2013
41	The role of elective amputation in patients with traumatic brachial plexus injury (Maldonado et al., 2016a)	Maldonado	2016
42	Early microsurgical management of clavicular fracture combined with brachial plexus injury (Yafei Liu et al., 2014)	Liu	2014

43	Contralateral trapezius transfer to restore shoulder external rotation following adult brachial plexus injury (Elhassan et al., 2016)	Elhassan	2016
44	Comparative study of phrenic nerve transfers with and without nerve graft for elbow flexion after global brachial plexus injury (Yuzhou Liu et al., 2014)	Liu	2014
45	Shoulder and elbow recovery at 2 and 11 years following brachial plexus reconstruction (J.-P. Wang et al., 2016)	Wang	2016
46	Functional outcomes after treatment of traumatic brachial plexus injuries: clinical study (Aras et al., 2013)	Aras	2013
47	Free gracilis transfer reinnervated by the nerve to the supinator for the reconstruction of finger and thumb extension in longstanding C7-T1 brachial plexus root avulsion (Soldado et al., 2013)	Soldado	2013
48	Restoration of hand function in C7–T1 brachial plexus palsies using a staged approach with nerve and tendon transfer (Zhang et al., 2014)	Zhang	2014
49	Neurotization to innervate the deltoid and biceps: 3 cases (Dy et al., 2013)	Dy	2013
50	Arthroscopic arthrodesis of the shoulder in brachial plexus palsy (Lenoir et al., 2017)	Lenoir	2017
51	Outcome of contralateral C7 nerve transferring to median nerve (Kai-ming Gao et al., 2013)	Gao	2013
52	Intercostal nerve transfer to the biceps motor branch in complete traumatic brachial plexus injuries (Cho et al., 2015)	Cho	2015
53	Tactile feedback for relief of deafferentation pain using virtual reality system: a pilot study (Sano et al., 2016)	Sano	2016
54	Functioning free gracilis transfer to reconstruct elbow flexion and quality of life in global brachial plexus injured patients (Yang et al., 2016)	Yang	2016
55	Evaluation of infraspinatus reinnervation and function following spinal accessory nerve to suprascapular nerve transfer in adult traumatic brachial plexus injuries (Baltzer et al., 2017)	Baltzer	2017
56	Anatomic study of the intercostal nerve transfer to the suprascapular nerve and a case report (Hu et al., 2014)	Hu	2014
57	Shoulder abduction and external rotation restoration with nerve transfer(Kostas-Agnantis et al., 2013)	Kostas-Agnantis	2013
58	Contralateral C-7 transfer: is direct repair really superior to grafting? (Bhatia et al., 2017)	Bhatia	2017
59	Impact of phrenic nerve paralysis on the surgical outcome of intercostal nerve transfer (Kita et al., 2015)	Kita	2015
60	Flow-through anastomosis using a T-shaped vascular pedicle for gracilis functioning free muscle transplantation in brachial plexus injury (Hou et al., 2015)	Hou	2015
61	Free functional muscle transfer tendon insertion secondary advancement procedure to improve elbow flexion (Sechachalam et al., 2017)	Sechachalam	2017
62	Dual nerve transfers for restoration of shoulder function after brachial plexus avulsion injury (Chu et al., 2016)	Chu	2016
63	Cortical plasticity after brachial plexus injury and repair: a resting-state functional MRI study (Bhat et al., 2017)	Bhat	2017
64	Results of spinal accessory to suprascapular nerve transfer in 110 patients with complete palsy of the brachial plexus (Bertelli et al., 2016a)	Bertelli	2016
65	Magnetic resonance neurographic and clinical long-term results after Oberlin's transfer for adult brachial plexus injuries (Frueh et al., 2017)	Frueh	2017
66	Free functioning gracilis muscle transfer versus intercostal nerve transfer to musculocutaneous nerve for restoration of elbow flexion after traumatic adult brachial pan-plexus injury (Maldonado et al., 2016b)	Maldonado	2016

67	Results of wrist extension reconstruction in C5–8 brachial plexus palsy by transferring the pronator quadratus motor branch to the extensor carpi radialis brevis muscle (Bertelli et al., 2016b)	Bertelli	2016
68	Donor nerve sources in free functional gracilis muscle transfer for elbow flexion in adult brachial plexus injury (Nicoson et al., 2017)	Nicoson	2017
69	Use of contralateral spinal accessory nerve for ipsilateral suprascapular neurotization in global brachial plexus injury: a new technique (Bhandari and Deb, 2016)	Bhandari	2016
70	Objective evaluation of elbow flexion strength and fatigability after nerve transfer in adult traumatic brachial plexus injuries (Maricq et al., 2014)	Maricq	2014
71	Outcomes of muscle brachialis transfer to restore finger flexion in brachial plexus palsy (DeGeorge et al., 2017)	DeGeorge	2017
72	Functional outcome of nerve transfers for traumatic global brachial plexus Avulsion (Liu et al., 2013)	Liu	2013
73	Transfer of a flexor digitorum superficialis motor branch for wrist extension reconstruction in C5-C8 root injuries of the brachial plexus: a case series (Bertelli and Ghizoni, 2013)	Bertelli	2013
74	Outcome after transfer of intercostal nerves to the nerve of triceps long head in 25 adult patients with total plexus root avulsion injury (Gao et al., 2013)	Gao	2013
75	Good sensory recovery of the hand in brachial plexus surgery using the intercostobrachial nerve as the donor (Foroni et al., 2017)	Foroni	2017
76	The phrenic nerve as a donor for brachial plexus injuries: is it safe and effective? Case series and literature analysis (Socolovsky et al., 2015)	Socolovsky	2015
77	Complete avulsion of brachial plexus with associated vascular trauma: Feasibility of reconstruction using the double free muscle technique (Hattori et al., 2013)	Hattori	2013
78	Long-term outcome of brachial plexus re-implantation after complete brachial plexus avulsion injury (Kachramanoglou et al., 2017)	Kachramanoglou	2017
79	Force recovery assessment of functioning free muscle transfers using ultrasonography (Kodama et al., 2014)	Kodama	2014
80	Rhomboid nerve transfer to the suprascapular nerve for shoulder reanimation in brachial plexus palsy: A clinical report (Goubier and Teboul, 2016)	Goubier	2016
81	Outcome of contralateral C7 transfer to two recipient nerves in 22 patients with the total brachial plexus avulsion injury (Gao et al., 2013)	Gao	2013
82	Comparative study of phrenic and intercostal nerve transfers for elbow flexion after global brachial plexus injury (Yuzhou Liu et al., 2015)	Liu	2015
83	Donor-side morbidity after contralateral C-7 nerve transfer: results at a minimum of 6 months after surgery (X.-M. Li et al., 2016)	Li	2016
84	Outcome after brachial plexus injury surgery and impact on quality of life (Rasulic et al., 2017)	Rasulić	2017
85	Pronator teres branch transfer to the anterior interosseous nerve for treating C8T1 brachial plexus avulsion: An anatomic study and case report (Yang et al., 2014)	Yang	2014
86	Operative treatment with nerve repair can restore function in patients with traction injuries in the brachial plexus (Stiasny and Birkeland, 2015)	Stiasny	2015
87	Thoracodorsal nerve transfer for triceps reinnervation in partial brachial plexus injuries (Soldado et al., 2016)	Soldado	2016
88	Co-infusion of autologous adipose tissue derived neuronal differentiated mesenchymal stem cells and bone marrow derived hematopoietic stem cells,	Thakkar	2014

	a viable therapy for post-traumatic brachial plexus injury: a case report (Thakkar et al., 2014)		
89	Long-term clinical outcomes of spinal accessory nerve transfer to the suprascapular nerve in patients with brachial plexus palsy (Emamhadi et al., 2016)	Emamhadi	2016
90	Surgical treatment for total root avulsion type brachial plexus injuries by neurotisation: a prospective comparison study between total and hemi contralateral C7 nerve root transfer (Tu et al., 2014)	Tu	2014
91	Deactivation of distant pain-related regions induced by 20-day rTMS: a case study of one-week pain relief for long-term intractable deafferentation pain (Qiu et al., 2014)	Qiu	2014
92	End-to-side neurorrhaphy in brachial plexus reconstruction (Haninec et al., 2013)	Haninec	2013
93	Reanimation of elbow extension with medial pectoral nerve transfer in partial injuries to the brachial plexus (Flores, 2013)	Flores	2013
94	Early post-operative results after repair of traumatic brachial plexus palsy (Mohammad-Reda, 2013)	Mohammad-Reda	2013
95	Satisfied patients after shoulder arthrodesis for brachial plexus lesions even after 20 years of follow-up (Van der Lingen et al., 2018)	van der Lingen	2018
96	Posterior branch of the axillary nerve transfer to the lateral triceps branch for restoration of elbow extension: case report (Klika et al., 2013)	Kilka	2013
97	Clinical analysis of repairing the whole brachial plexus nerve root avulsion by transferring C7 nerve root from the uninjured side (J. Liu et al., 2014)	Liu	2014
98	Bipolar transfer of the pectoralis major muscle for restoration of elbow flexion in 29 cases (Cambon-Binder et al., 2018)	Cambon-Binder	2018
99	Thoracodorsal nerve transfer for elbow flexion reconstruction in infraclavicular brachial plexus injuries (Soldado et al., 2014)	Soldado	2014
100	Median nerve fascicle transfer versus ulnar nerve fascicle transfer to the biceps motor branch in C5-C6 and C5-C7 brachial plexus injuries: nonrandomised prospective study of 23 consecutive patients (Cho et al., 2014)	Cho	2014
101	Free functional muscle transplantation of an anomalous femoral adductor with a very large muscle belly: a case report (Kaizawa et al., 2013)	Kaizawa	2013
102	Selective neurotisation of the radial nerve in the axilla using the intercostal nerve to treat complete brachial plexus palsy (Tuohuti et al., 2016)	Tuohuti	2016
103	Objective predictors of functional recovery associated with intercostal nerves transfer for triceps reinnervation in global brachial plexus palsy (Flores, 2016)	Flores	2016
104	Nerve transfer to relieve pain in upper brachial plexus injuries: does it work? (Emamhadi, 2017)	Emamhadi	2017
105	Phrenic nerve transfer versus intercostal nerve transfer for the repair of brachial plexus root avulsion injuries (Abdixbir et al., 2016)	Abdixbir	2016
106	End-to-side neurorrhaphy to restore elbow flexion in brachial plexus injury (Limthongthang et al., 2016)	Limthongthang	2016
107	Chordata method combined with electrotherapy in functional recovery after brachial plexus injury: report of three clinical cases (De Oliveira et al., 2016)	De Oliveira	2016
108	Clinical outcome following transfer of the supinator motor branch to the posterior interosseous nerve in patients with C7-T1 brachial plexus palsy (Xu et al., 2015)	Xu	2015
109	Transposition of branches of radial nerve innervating supinator to posterior interosseous nerve for functional reconstruction of finger and thumb	Wu	2017

	extension in 4 patients with middle and lower trunk root avulsion injuries of brachial plexus (Wu et al., 2017)		
110	Electromyographic findings in gracilis muscle grafts used to augment elbow flexion in traumatic brachial plexopathy (Kazamel and Sorenson, 2016)	Kazamel	2016
111	Double distal intraneural fascicular nerve transfers for lower brachial plexus injuries (Z. Li et al., 2016)	Li	2016
112	Restoration of elbow and hand function in total brachial plexus palsy with intercostal nerves and C5 root neurotisation. Results in 21 patients (Arnal et al., 2016)	Amal	2016
113	The phrenic nerve transfer in the treatment of a septuagenarian with brachial plexus avulsion injury: a case study (Jiang and Lao, 2018)	Jiang	2018
114	Outcomes of transferring a healthy motor fascicle from the radial nerve to a branch for the triceps to recover elbow extension in partial brachial plexus palsy (Flores, 2017)	Flores	2017
115	Successful nerve transfers for traumatic brachial plexus palsy in a septuagenarian (Johnsen and Wolfe, 2016)	Johnsen	2016
116	Free functioning gracilis muscle transfer for elbow flexion reconstruction after traumatic brachial pan-plexus injury: Where is the optimal distal tendon attachment for elbow flexion? (Maldonado et al., 2017b)	Maldonado	2017
117	Results of distal nerve transfers in restoration of shoulder function in C5 and C6 root avulsion injury to the brachial plexus (Bhandari, 2017)	Bhandari	2017
118	Bipolar dual-lead spinal cord stimulation between two electrodes on the ventral and dorsal sides of the spinal cord: consideration of putative mechanisms (Watanabe et al., 2018)	Watanabe	2018
119	Triceps nerve to deltoid nerve transfer after an unsatisfactory intra-plexus neurotisation of the posterior division of the upper trunk (Al-Qattan et al., 2017)	Al-Qattan	2017
120	Trapezius muscle transfer for restoration of elbow extension in a traumatic brachial plexus injury (Alrabai et al., 2018)	Alrabai	2018
121	Transfer of the radial nerve branch to the extensor carpi radialis brevis to the anterior interosseous nerve to reconstruct thumb and finger flexion (Bertelli, 2015)	Bertelli	2015
122	Ultrasound-guided pulse-dose radiofrequency: treatment of neuropathic pain after brachial plexus lesion and arm vascularisation (Magistroni et al., 2014)	Magistroni	2014
123	Phrenic nerve transfer to the musculocutaneous nerve for the repair of brachial plexus injury: electrophysiological characteristics (Y Liu et al., 2015)	Liu	2015
124	Postoperative motor deficits following elbow flexion reanimation by nerve transfer (Le Hanneur et al., 2018)	Hanneur	2018
125	Comparative study of phrenic and partial ulnar nerve transfers for elbow flexion after upper brachial plexus avulsion-a retrospective clinical analysis (Liu et al., 2018)	Liu	2018
126	Contralateral medial pectoral nerve transfer with free gracilis muscle transfer in old brachial plexus injury (Yavari et al., 2018)	Yavari	2018
127	MEG-BMI to control phantom limb pain(Yanagisawa et al., 2018)	Yanagisawa	2018
128	Complete brachial plexus injury- an amputation dilemma, A case report (Choong and Shalimar, 2015)	Choong	2015
129	Reversal of phantom pain and hand-to-face remapping after brachial plexus avulsion (Tsao and Finn, 2016)	Tsao	2016
130	A newly developed upper limb single-joint HAL in a patient with elbow flexion reconstruction after traumatic brachial plexus injury: A case report (Kubota et al., 2017)	Kubota	2017

131	Free reverse gracilis muscle combined with Steindler flexorplasty for elbow flexion reconstruction after failed primary repair of extended upper-type paralysis of the brachial plexus (Bertelli, 2018)	Bertelli	2018
132	Multiple nerve and tendon transfers – a new strategy for restoring hand function in a patient with C7-T1 brachial plexus avulsions (Xu et al., 2017)	Xu	2017

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Appendix 3. 7 Included studies

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Appendix 3. 8 Mapping items in PRO instruments to domains

	Number of items in PRO instruments mapped to subdomains																		
PRO domain /subdomains	**DASH**	**MHQ**	**UEFI**	**ASES**	**SST**	**SF36**	**PSFS**	**TAPS**	**VAS**	**NRS**	**WBFRS**	**NPSI**	**BPI**	**UWNS**	**McGill (SF)**	**McGil (+ Jap)**	**SR anxiety scale**	**SR depression scale**	**CRIS-CAT**
Physiological /clinical																			
Muscle strength	1	1	1																
Active movement		1			1														
Passive range of movement (stiffness)	1																		
Physical functioning																			
Physical function non-specific							2	2											
Lower limb and non-upper limb function (walking, running, climbing stairs etc)						6		6					1						1
Reaching, pulling, pushing, carrying, throwing, lifting	5	1	5	3	6	3													
Turning twisting with the arm	3	1	1																
Fine hand movement (including writing)	2	4	1																
Sensation and pain domains																			
Discriminative feeling		1																	
Pain intensity/relief	2	1		5				3	1	1	1		5	1	2	7			
Pain duration or frequency		1			1	2		5				2	1						
Pain quality								1				5		7	15	21			
Pain when arm exposed to cold												1							
Paraesthesia	1																		
Sensitivity to touch, pressure, vibration etc												2		1					
Location of pain													1						
Pain medication use													1						

Appendix 3.8 Items mapped from PRO instruments to domains

PRO domain /subdomains	DASH	MHQ	UEFI	ASES	SST	SF36	PSFS	TAPS	VAS	NRS	WBFRS	NPSI	BPI	UWNS	McGill (SF)	McGil (+ lan)	SR anxiety scale	SR depression	CRIS-CAT
Role functioning																			
Role function patient-specific							2												
Carrying out daily routine (including food preparation, housework, garden, plants)	4	6	4					1					2						1
Maintaining personal hygiene	2	1		2	1	1													1
Maintaining personal appearance			1	1															1
Putting on and taking off clothes	1	2	2	1	1														1
Transport needs	1		1																1
Impact on role in employment or education	4	5	1	1	1	4		4											1
Impact on recreational activities	7		2	1				2											1
Social functioning																			
Effect on relationship with family, friends, neighbours and groups	1	1				1		3					1						1
Effect on intimate relationships	1																		1
Emotional functioning																			
Emotional distress/mood		1				13		2					2	1			20	20	
Thoughts and beliefs (acceptance and adjustment)								5											
Body image		2																	
Self-esteem and self confidence	1							3											
Sleep and overall health																			
Overall quality of sleep	1	1	1	1	1								1						
Overall health						6		8											
Patient satisfaction with outcome of treatment		7						9											
Total items	38	37	20	15	12	36	4	54	1	1	1	10	15	10	17	28	20	20	302

Appendix 3. 9 Mapping items in combined ClinRO and PRO instruments to domains

	No. of items in instrument mapped		
PRO domain /subdomains	**UCLA**	**Constant Murley**	**Mayo**
Physiological/clinical			
Muscle strength	1	1	
Active movement	1	4	1
Passive range of movement (stiffness)			1
Physical functioning			
Physical function non-specific			
Lower limb and non-upper limb function (walking, running, climbing …)			
Reaching, pulling, pushing, carrying, throwing, lifting			
Turning twisting with the arm			
Fine hand movement (including writing)			
Sensation and pain domains			
Discriminative feeling			
Pain intensity/relief		1	1
Pain duration or frequency	1		
Pain quality			
Pain when arm exposed to cold			
Paraesthesia			
Sensitivity to touch, pressure, vibration etc			
Location of pain			
Pain medication use			
Role functioning			
Role function patient-specific			1
Carrying out daily routine (including food preparation, housework, garden, plants)	1	1	
Maintaining personal hygiene	1		
Maintaining personal appearance	1		
Putting on and taking off clothes			
Transport needs			
Impact on role in employment or education			
Impact on recreational activities		1	
Social functioning			
Effect on relationship with family, friends, neighbours and groups			
Effect on intimate relationships			
Emotional functioning			
Emotional distress/mood			
Thoughts and beliefs (acceptance and adjustment)			
Body image			
Self-esteem and self-confidence			
Sleep and overall health			
Overall quality of sleep		1	
Overall health			
Patient satisfaction with outcome of treatment	1		
Total items	7	9	4

UCLA, University of California Los Angeles score (UCLA); Mayo, The Mayo Performance Index.

Appendix 3. 10 Mapping items in PerfO instruments to domains

	No. of items mapped to instruments						
PRO domain /subdomains	**ARAT**	**SHAP**	**JHFT**	**AMULA**	**UNBTP**	**ULM**	**PPT**
Physiological/clinical							
Muscle strength		15				7	
Active movement	3					8	
Passive range of movement (stiffness)							
Physical functioning							
Physical function non-specific							
Lower limb and non-upper limb function (walking, running….)							
Reaching, pulling, pushing, carrying, throwing, lifting	5	2	3	3			
Turning twisting with the arm		1		2		1	
Fine hand movement (including writing)	3	11	3	4	12	2	3
Sensation and pain domains							
Discriminative feeling							
Pain intensity/relief							
Pain duration or frequency							
Pain quality							
Pain when arm exposed to cold							
Paraesthesia							
Sensitivity to touch, pressure, vibration etc							
Location of pain							
Pain medication use							
Role functioning							
Role function patient specific					17		
Carrying out daily routine (including food preparation, housework)		5	1	7		4	
Maintaining personal hygiene				2	1		
Maintaining personal appearance		2		6			
Putting on and taking off clothes							
Transport needs							
Impact on role in employment or education							
Impact on recreational activities							
Social functioning							
Effect on relationship with family, friends, neighbours and groups							
Effect on intimate relationships							
Emotional functioning							
Emotional distress/mood							
Thoughts and beliefs (acceptance and adjustment)							
Body image							
Self-esteem and self-confidence							
Sleep and overall health							
Overall quality of sleep							
Overall health							
Patient satisfaction with outcome of treatment							
Total items	11	36	7	24	30	22	3

ARAT, Action Research Arm Test; SHAP, Southampton Hand Assessment Procedure; JHFT, Jebsen Hand Function Test; AMULA, Activities Measure for Upper Limb Amputee; UNBTP, University of New Brunswick test of prosthetics; ULM, Upper Limb Module; PPT, Purdue Peg Tes

Appendix 3. 11 Modifications of MRC manual muscle strength assessments reported

Types of MRC modification reported in studies

Type of modification	Number of studies using modification
Unclear how	5
Grade 3 active must equal passive	2
Grade 2 active must equal passive movement	2
M3+ contraction with resistance against a finger for less than 30 seconds,	1
M4 contraction of resistance against a finger against a finger for more than 30 seconds	1
M0, M1+, M1, M1+, M2-, M2, M2+, M3-, M3, M3+, M4-, M4, M4+, M5-, M5	6
Finger flexion tested with wrist extended 20-30 degrees	1
Addition of M4.5	1
Graded two muscles together	1
Finger extension tested with wrist extension at 20-30 degrees	1
Summated muscle score	1
Flexor Digitorum Superficialis tested by stabilising little finger and index finger to table and testing middle and ring finger interphalangeal flexion	1

Appendix 4. 1 Reviews of qualitative studies

Author	Method	No	Aim	Types of injury	Female	World	Outcomes / themes	Issues
Franzblau (2015)	Interview	12	Aims: to describe psychosocial outcomes, identify sources of stress and examine the use of coping strategies among patients to better understand the relationship between outcomes, coping and psychosocial adjustment after complete avulsion BPI	Avulsion injuries	0	USA	Anger, depression, hope, shrinking social circle, lack of peer understanding and shifting self-image	Only male
Wellington (2009)	1:1 interview	5	**Aim: To identify quality of life issues for** adult patients following traumatic brachial plexus injuries.	Mixture	0	Scotland	Employment, Pain, body image, self worth and external relationships, sexuality emotions internal relationships, future plans and goals	Only male, small numbers
Brito (2019)	1:1 interview	5	This study aimed to explore patients' experiences following free-functioning muscle transfer reconstructive surgery for the management of traumatic, pan-brachial plexus injury.	Avulsion and free muscle transfer	0	Australia	1.**Experience of health care systems** • Injury and early health care experience • Experience of rehab • Compensation 2. **Psychosocial considerations** • Emotional responses • Personal relationships • Processing and acceptance of injury 3. **Creating a new self-identity** • Coming to terms with a changed arm • Getting on with it • Participation: things will never be the same	Only participants after free muscle transfer, **all male** At least 5 years since injury
Brown et al (2018)	Focus groups	6	The purpose of this study was to give an account through the voice of patients who have **undergone surgery with successful restoration of ability to flex the elbow against resistance**	C5/6 or MCN injury	1	England	Pain, patience and positive thought, functionality and positive thought, Functionality and daily lifestyle	5 male 1 female Years since injury? 2.5 years since surgery
Mancuso et al (2015)	1:1 interview	23	Ascertain their **expectations of surgery** and their **experiences with BPI**, particularly the impact of BPI on quality of life and functional status.	13 partial injuries 10 complete injuries	?	USA	**Mental Health** Compensation Emotions Time to recuperate Coping Appearance in public Global view **Symptoms and physical limitations** Pain Sensation Movement Essential activities Work/school Sports	Mean time since injury- 33 months
Verma (2019)	1:1 interview	13	gain insight into patients' perception after traumatic BPI6 and thus	9 global and 4 upper	?0	India	Overarching theme of **Patient perception** **11 subthemes**	Unsure male to female

			help us consider these factors which are often missed in our holistic rehabilitation	plexus			Mental trauma, guilt, future worries, negative thoughts, social disconnect, interaction with doctors, interaction with fellow participants, curiosity, public appearance, body image and compensation for basic adl	ratio
McDonald and Pettigrew (2014)	1:1 interview	10	what it means to live with a diagnosis of TBPI, and what could be learned from people's lived experience in order to enhance the quality of the occupational therapy service provided.	undefined	0	Ireland	Six themes Role and identity Ups and downs All the little things Experience of health service Employment The survivor	At least 18 months since injury All male

Appendix 4. 2 Ethics approval for the COMBINE study

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Mrs Caroline Miller
Physiotherapy Department
Queen Elizabeth Hospital Birmingham
Birmingham
B15 2WB

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

10 December 2018

Dear Mrs Miller

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Improving the quality and relevance of outcome measurement for individuals with a Traumatic Brachial Plexus Injury. Development of an International Core Outcome Set**
IRAS project ID:	**248940**
Protocol number:	**R204919**
REC reference:	**18/WM/0297**
Sponsor	**University of East Anglia**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

IRAS project ID	248940

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Mr Graham Horne
Email: g.horne@uea.ac.uk

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **248940**. Please quote this on all correspondence.

IRAS project ID	248940

Yours sincerely

Thomas Fairman
HRA Assessor

Email: hra.approval@nhs.net

Copy to: *Mr Graham Horne, University of East Anglia, (Sponsor Contact)*
Dr Chris Counsell, Research and Development, (Lead NHS R&D Contact)

IRAS project ID	248940

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Delphi poster NHS patients]	1.0	29 August 2018
Covering letter on headed paper [Cover letter]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [sponsor insurance letter]		04 September 2018
GP/consultant information sheets or letters [GP letter interview study]	1.0	29 August 2018
HRA Schedule of Events	1.0	19 September 2018
HRA Statement of Activities	1.0	19 September 2018
Interview schedules or topic guides for participants [Interview topic guide]	1.0	29 August 2018
IRAS Application Form [IRAS_Form_05092018]		05 September 2018
Letter from funder [contract letter]		05 April 2018
Letter from sponsor [Cover letter from sponsor]		04 September 2018
Letters of invitation to participant [Delphi invitation health professionals]	1.0	29 August 2018
Participant consent form [consent interviews]	1.0	29 August 2018
Participant information sheet (PIS) [PIS Interview(clinic)]	1.0	29 August 2018
Participant information sheet (PIS) [PIS Interview (database)]	1.0	29 August 2018
Participant information sheet (PIS) [PIS Delphi NHS patients]	1.0	29 August 2018
Participant information sheet (PIS) [PIS Delphi non NHS patients]	1.0	29 August 2018
Research protocol or project proposal [Study protocol]	1.0	29 August 2018
Summary CV for Chief Investigator (CI) [Research CV CI]		01 June 2018
Summary CV for student [research CV student]		30 June 2018
Summary CV for supervisor (student research) [research CV supervisor]		19 July 2018
Summary CV for supervisor (student research) [Research CV supervisor]		27 March 2017
Summary CV for supervisor (student research) [Research CV supervisor]		01 March 2018
Summary, synopsis or diagram (flowchart) of protocol in non technical language [flow chart for study]	0.1	19 July 2018

IRAS project ID	248940

Summary of assessment

The following information provides assurance to you, the sponsor and the NHS in England and Wales that the study, as assessed for HRA and HCRW Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England and Wales to assist in assessing, arranging and confirming capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	The research team have confirmed that the questionnaire and the online registration/consent are not yet written, as these depend on the outcome of the study interviews. They confirmed that these would be submitted as a substantial amendment when ready.
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	The sponsor has submitted the HRA Statement of Activities and intends for this to form the agreement between the sponsor and study sites. The sponsor is not requesting, and does not require any additional contracts with study sites.
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study
4.3	Financial arrangements assessed	Yes	External study funding has been secured from the National Institute of Health Research.

IRAS project ID	248940

Section	Assessment Criteria	Compliant with Standards	Comments
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

All participating NHS organisations will undertake the same study activities. There is therefore only one study site 'type' involved in the research.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS or on the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net, or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

IRAS project ID	248940

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A Local Collaborator should be appointed at study sites. GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
As a non-commercial study undertaken by local staff, it is unlikely that letters of access or honorary research contracts will be applicable. Where arrangements are not already in place, researchers undertaking any of the research activities listed in A18 of the IRAS form would be expected to obtain a Letter of Access. This would be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm DBS checks and occupational health clearance.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.
The applicant has indicated that they do intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix 4. 3 Research governance approval for the COMBINE study

R&D Governance Office University Hospitals Birmingham NHS
NHS Foundation Trust

(RPAv45)

Mr Dominic Power
T&O Consultant Hand & Peripheral Nerve Surgeon
Trauma & Orthopaedics
Room 13H
Level 6
Nuffield House
QEH
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham B15 2WB

UHB Research Governance Office
1st Floor, Institute of Translational Medicine
Heritage Building
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham B15 2TH
Tel. 0121 371 4185

Research Project Authorisation

Project reference:**RRK 6535**

Main Ethics Committee Reference	18/WM/0297
IRAS Project ID	248940

3 January 2019

Dear Mr Power

Improving the quality and relevance of outcome measurement for individuals with a Traumatic Brachial Plexus Injury. Development of an International Core Outcome Set

Thank you for submitting details of your proposed research project, which I am happy to authorise on behalf of University Hospitals Birmingham; this includes confirmation of Capacity and Capability under the HRA Approval process.

Approval covers the following site(s) only: **Queen Elizabeth Hospital Birmingham**

The following main document versions were reviewed (note this is not a complete list of all documents submitted):

Protocol - version: V1.0 29/08/18
Participant information sheet (main) - version: V2.0 08/11/18
Participant consent form (main) - version: V1.0 29/08/18

Acv1/18

Sponsorship
University of East Anglia has agreed to act as sponsor for this study.

Indemnity arrangements.
Researchers who hold substantive or honorary contracts with University Hospital Birmingham (UHBT) will be covered against claims of negligence by patients of UHBT under the Clinical Negligence Scheme for Trusts (CNST). This scheme does not cover 'no fault' compensation and the Trust is precluded from taking out separate insurance to cover this. Any patient or volunteer taking part in the study is entitled to know that if they suffered injury as a result of participating in the study they would first have to prove negligence in a court of law before they could gain compensation.

R&D Office
Head of R&D Governance: Dr Christopher Counsell
Head of R&D Operations: Joanne Plumb
R&D Office, 1st Floor, ITM, Heritage Building, Queen Elizabeth Hospital Birmingham, Edgbaston Birmingham B15 2WG
Tel: 0121 371 4185 *Fax*:0121 371 4204 *Email:* R&D@uhb.nhs.uk
Website: www.research.uhb.nhs.uk
Projects database: //uhb/userdata/R & D/R&D database/distributed database 2002.mdb

that this is promptly recorded on PICS. If you have any queries about how to do this please contact the PICS training team (PICSTrainingTeam@uhb.nhs.uk). The consented date and recruitment date may be different if screening procedures are required after consenting to confirm eligibility for a study.

The R&D Governance Office will use anonymised records from PICS to update central recruitment records on the UKCRN Portfolio. From April 2017 this will be the only way of recording recruitment on portfolio studies so it is essential that PICS records are accurate.

You should separately keep accurate records on the study file of recruitment and participation in your study. There should be a record, with dates, of patients approached, consented, screened, recruited, completed, and dropped out as appropriate.

Annual Reports
The R&D Office will request information about progress with the study in 6 months, 12 months and annually thereafter. Approval for this study may be withdrawn if you do not complete and return reports when requested.

Protocol Breaches
Serious protocol breaches must be reported to the R&D office as soon as possible and must be notified to the Chief Investigator and Sponsor immediately you become aware of them. If you are the Chief Investigator you must notify the Ethics Committee within 7 days and, for CTIMP studies, you must notify the MHRA within 7 days. A serious breach is one that is likely to affect to a significant degree the mental or physical integrity of the research participants or the scientific value of the study. A report of a serious breach should identify measures taken to correct the consequences of the breach and measures to prevent future similar breaches (a so-called 'CAPA' log). Minor protocol breaches should be recorded in your study file.

Urgent Safety Measure
If necessary, appropriate urgent safety measure to protect clinical trial subjects from any immediate hazard to their health and safety can be taken immediately without waiting for Ethics Committee, Regulatory Authority or R&D approval. However you must inform the R&D Office, Chief Investigator, Sponsor, Ethics Committee and MHRA, as appropriate, in writing within 3 days.

Protocol Amendments
Trust approval will usually automatically cover minor protocol amendments but you must send details to the R&D office for information. Details of all substantial amendments must be sent to the R&D Office for authorisation together with copies of the ethics approval and/or regulatory approval for the amendments and any revised documentation. The R&D office will acknowledge all amendments. A substantial amendment is defined by NRES (the National Research Ethics Service) and would include any change that could affect the safety, conduct or the resource implications of the study.

Duration
It is expected that the study will begin at University Hospital Birmingham within 12 months of Trust authorisation. If there is a long delay in starting the study, the Trust may consider withdrawing authorisation for the study. Unless explicitly withdrawn, Trust approval lasts for as long as the study has valid ethics committee and regulatory approval.

End of Study
According to information you have provided, this study is expected to end in **March 2021** and the minimum recruitment target is **12**. The R&D Office will request a final report shortly after this date. If the study ends for any reason before this date you must notify the R&D Office. Note that the Chief Investigator for the whole study is required to provide an end of study report to the main research ethics committee and regulatory authorities.

Archiving

R&D Office
Head of R&D Governance: Dr Christopher Counsell
Head of R&D Operations: Joanne Plumb
R&D Office, 1st Floor, ITM, Heritage Building, Queen Elizabeth Hospital Birmingham, Edgbaston Birmingham B15 2WG
Tel: 0121 371 4185 *Fax*:0121 371 4204 *Email:* R&D@uhb.nhs.uk
Website: www.research.uhb.nhs.uk
Projects database: //uhb/userdata/R & D/R&D database/distributed database 2002.mdb

R&D Governance Office University Hospitals Birmingham NHS
NHS Foundation Trust

RRK6535

For studies designated as a Clinical Trial of an Investigational Medicinal Product (CTIMP), it is a **legal** requirement to retain essential documents for at least **5 years** after the declared end of the study. The sponsor or regulatory authorities may insist on a longer retention period for a particular study. For all other types of study there are no statutory requirements but generally accepted good practice guidelines recommend that documents are retained for at least 5 years. Documents must be archived in a way such that they can be readily accessed (24 hours notice) if required for audits or regulatory purposes. The costs of archiving is borne by the Principal or Lead Investigator and should be taken into account when applying for research grants or seeking other forms of funding. For CTIMPs, there must be a named archivist, approved by the sponsor, who is responsible for setting up and controlling the archive.

Health Records Labelling
The Health Records of study subjects are retained according to the Trust's "Health Records Management Policy"; for patients in research studies the retention period is 15 years after the last treatment or consultation related to the study. The Principal Investigator must ensure that all records for patients involved in a study are clearly labelled to ensure that the retention policy can be followed.

Cover for absence
If the Principal Investigator is likely to be absent and out of contact for a prolonged period (> 2 weeks), the PI must either explicitly suspend patient recruitment and patient-related activity in the study, or explicitly delegate the responsibilities of Principal Investigator to a named deputy. The PI must be satisfied that their deputy is sufficiently qualified through education, training and experience to take on the role of PI. These periods of absence and delegation must be recorded in the study file.

Website entry
Basic details of your study will be made available on the Trust's website at
http://www.research.uhb.nhs.uk/trials/RRK6535

Guidance Tool
The Trust R&D Office has developed a Powerpoint-based tool summarising some of the regulations relevant to clinical research. This is available at \\uhb\userdata\R & D\R&D Shared Docs\Guide to Responsibilities\Guide to Investigator Responsibilities.ppsx (requires access to the Trust's network)

Yours sincerely,
03 January 2019

Dr Christopher Counsell
Head of R&D Governance

Enclosed: Sample study file layout
Incident Reporting & Serious Adverse Event Form

Copies to:
Relevant Service Departments
Division D Manager, Robin Snead

R&D Office

Appendix 4. 4 Participant Information Sheet interview study (in clinic patient)

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

COMBINE

Core **O**utcome **M**easures in **B**rachial plexus **IN**juri**E**s

Your invitation to take part in a research study. Can you help?

Study title: What is important to measure in a Traumatic Brachial Plexus Injury?

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read through the information sheet carefully and discuss it with your family and friends. Please ask if anything is not clear or if you would like more information.

What is the purpose of the study?

Many individuals with a traumatic brachial plexus injury undergo surgery and rehabilitation in an attempt to restore some movement and function of the arm.

To help patients, doctors and health professionals make decisions about treatments for a traumatic brachial plexus injury we need evidence about what works best. To do this we look at the effects of treatments on patients. These effects are called "outcomes" which might be muscle strength or quality of life measured after treatments. At the moment different studies measure different outcomes. For example, Study A might measure pain and Study B might measure movement. When the studies are finished, we cannot combine or compare the results because they use different outcomes. Also, outcomes chosen in a study may not be relevant to patients. This is problematic as we then struggle to work out if a treatment is effective and really helps patients.

We can solve this problem by using the same important outcomes to decide whether treatments work. This is called a Core Outcome Set. This study will find out what outcomes are important to patients. The results will be used to help design the Core Outcome Set for Traumatic Brachial Plexus Injury. All studies and clinicians will then use this Core Outcome Set and it will help to bring together all the studies and get a better understanding of what treatments work best.

Appendix 4.4 Interview participant information sheet in clinic patient

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

Why have I been invited?

You have been invited because you have a Traumatic Brachial Plexus Injury and have had treatment at the Queen Elizabeth Hospital (QEH) Birmingham NHS Foundation Trust. We will invite between 15 and 20 patients to participate in the study. You will have as long as you like to consider taking part.

Do I have to take part?

No, it is entirely up to you to decide whether to take part. If you wish to take part, then please keep this information sheet. Consent to take part in the study will be taken immediately before your interview. You can withdraw from the study at any time, without giving a reason and this will not affect any treatment you receive.

What will happen to me if I wish to take part?

You will be invited to take part in an interview to find out about what is important to individuals with a traumatic brachial plexus injury. We will conduct the interview at a time convenient to you, either at your home or in a quiet location at the QEH, whichever you prefer. We will reimburse any travel and parking expenses incurred if you chose to do the interview in the hospital.

The interview will be conducted by a researcher who is a Specialist Physiotherapist and who has worked with the peripheral nerve injury team for over 10 years. She will ask you about your experience including how the injury has affected your day-to-day life. We are also interested in what you hope different treatments and rehabilitation might achieve and why these are important to you.

The interview will last approximately 45 -60 minutes. This is entirely voluntary and the interview can be stopped at any point if you want to. The researcher will take notes throughout the interview and record it on a secure data recorder. This will be used to produce a written version of the interview.

What are the possible disadvantages of taking part?

There is minimum risk to taking part in the study. A potential risk is that you might find talking about your experiences upsetting. If this happens, we will stop the interview. You can also contact the traumatic brachial plexus injury charity and on http://tbpi-group.org/ for further support.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

What are the possible benefits of taking part?

We cannot promise that taking part in the study will help you, but some people find that talking about their experience helpful. The information you provide will help patients like you in the future.

What if there is a problem?

It is unlikely that there will be any problems during the study however if you are concerned about any aspect of the way that you have been approached or treated, you should speak to the Chief Investigator, Caroline Miller, who will do her best to answer any questions (contact details at the end of the sheet). You can also seek advice from Mr. Dominic Power, Nuffield House, Queen Elizabeth Hospital Birmingham, B15 2WB. Telephone no. (0121) 3714992.

In the unlikely event that you are harmed whilst participating in this study, there are no special compensation arrangements, but if this is due to someone's negligence then you may have grounds for legal action. The University of East Anglia is indemnifying the researchers for any such claims. The normal National Health Service complaints mechanism will still be available to you, if appropriate. You may obtain advice from the Patient Services Teams (contact details at the end of this information sheet).

Will my taking part in the study be kept confidential?

The study is sponsored by the University of East Anglia (UEA). The Queen Elizabeth Hospital Birmingham will keep your name, NHS number and contact details confidential and will not pass this information to the UEA. The Queen Elizabeth hospital will use this information as needed to contact you about the research study and to make sure that relevant information is recorded for your care and to oversee the quality of the study. Certain individuals from the UEA and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The UEA will only receive this information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Your name or contact details will not be used in any report or publication. All information will be identified by a participant code (not your name) and will be stored in a locked filing cabinet at the Queen Elizabeth Hospital Birmingham and password protected computers. Only members of the research team will have access to the data. Only annonymised data will be kept for three years.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

Will my GP be informed of my involvement in the study?

With your written consent, your GP will be notified of your participation in this study.

Who is organising and funding this study?

This study is being led by Caroline Miller, a clinical specialist physiotherapist at the QEH, Birmingham who is studying for a doctoral degree at the University of East Anglia. Caroline's doctoral degree has been funded by the National Institute for Health Research (the research arm of the NHS). She is being supervised by Professor Christina Jerosch-Herold, and Dr Jane Cross at the University of East Anglia, Norwich, and Mr. Dominic Power a consultant at the Queen Elizabeth Hospital.

Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee, to protect your interests and those of the researchers. This study has been reviewed and given favourable opinion by the West Midlands -Solihull Research Ethics Committee and the Research and Development Directorates at the Queen Elizabeth Hospital Birmingham NHS Trust.

Contact for further information or any questions about this study:

Caroline Miller, Chief Investigator, University of East Anglia

Tel: 07743501508

E mail: caroline.miller@uea.ac.uk

Peripheral nerve injury admin (0121) 3714992

Contact details if you wish to seek advice from the Patient Services Teams at The Queen Elizabeth Hospital NHS Foundation Trust, Birmingham:

Patient Advice and Liaison Service (PALS) on 0121 371 3280 or PALS@uhb.nhs.uk

Thank you for reading this information sheet, which is yours to keep

Appendix 4. 5 Participant information sheet interview study (clinic lists)

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

COMBINE
Core **O**utcome **M**easures in **B**rachial plexus **IN**juri**E**s

Your invitation to take part in a research study. Can you help?

Study title: What is important to measure in a Traumatic Brachial Plexus Injury?

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read through the information sheet carefully and discuss it with your family and friends. Please ask if anything is not clear or if you would like more information.

What is the purpose of the study?

Many individuals with a traumatic brachial plexus injury undergo surgery and rehabilitation in an attempt to restore some movement and improve the function of the arm.

To help patients, doctors and health professionals make decisions about treatments for a traumatic brachial plexus injury we need evidence about what works best. To do this we look at the effects of treatments on patients. These effects are called "outcomes" which might be muscle strength or quality of life measured after treatments. At the moment different studies measure different outcomes. For example, Study A might measure pain and Study B might measure movement. When the studies are finished we cannot combine or compare the results because they use different outcomes. Also, outcomes chosen in a study may not be relevant to patients. This is a problem as we then struggle to work out if a treatment is effective.

We can solve this problem by using the same important outcomes to decide whether treatments work. This is called a Core Outcome Set. This study will find out what outcomes are important to patients. The results will be used to help design the Core Outcome Set for Traumatic Brachial Plexus Injury. All studies and clinicians will use this Core Outcome Set and it will help to bring together all the studies and get a better understanding of what treatments work best.

Why have I been invited?

You have been invited because you have a Traumatic Brachial Plexus Injury and are having or had treatment at the Queen Elizabeth Hospital (QEH) Birmingham NHS Foundation Trust. We aim to invite between 15 and 20 patients to participate in the study.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute fo Health Researcl

What will happen to me if I agree to take part?

You need to contact the study coordinator (Caroline Miller) via e mail or telephone. Details are at the end of this information leaflet. Caroline will answer any questions you may have about the study.

You will be invited to participate in an interview to find out more about what is important to individuals with a traumatic brachial plexus injury. We will offer to conduct the interview at a time which is convenient to you, either at your home or in a quiet location at the QEH, whichever you prefer. We will reimburse any travel and parking expenses incurred if you chose to attend for an interview at the hospital.

The interview will be conducted by a researcher who is a Specialist Physiotherapist and who has been working with the peripheral nerve injury team for over 10 years. She will ask you about your actual experience including how the injury has impacted on your day to day life. We are also interested to understand what you hope different treatments and rehabilitation can achieve and why these results are important to you.

We predict that the interview will last approximately 45 -60 minutes. The interviewer will spend time before and after the interviews chatting with you about the study. Participation in the interview is entirely voluntary and the interview can be stopped at your request at any point. The researcher will take notes throughout the interview. The interview will be audio recorded using a secure data recorder and transcribed using your own words.

Do I have to take part?

No, it is entirely up to you to decide whether or not to take part and you can take as long as you like to consider taking part. If you wish to take part, then please keep this information sheet. Consent to participate in the study will be taken immediately prior to beginning the study. You are free to withdraw from the study at any time, without giving a reason. This would not affect the normal treatment that you would receive.

What are the possible disadvantages of taking part?

There are no known risks of taking part in the study. A potential disadvantage is that some people find talking about their experiences upsetting If this happens we will stop the interview. You can also contact the traumatic brachial plexus injury charity and on http://tbpi-group.org/ for further support.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

What are the possible benefits of taking part?

We cannot promise that taking part in the study will help you, but some people find that talking about their experience helpful. The information you provide will help patients like you in the future.

What if there is a problem?

It is unlikely that there will be any problems during the study. If you have a concern about any aspect of the way that you have been approached or treated during the course of this study, you should speak to the Chief Investigator, Caroline Miller, who will do her best to answer any questions (contact details at the end of the leaflet). You can also seek advice from Mr. Dominic Power, Nuffield House, Queen Elizabeth Hospital Birmingham, B15 2WB. Telephone no. (0121) 3714992.

If you remain unhappy and wish to complain formally, you can do this by following the National Health Service complaints procedure. You may obtain advice from the Patient Services Teams at the hospital (contact details below).

In the unlikely event that you are harmed whilst participating in this study, there are no special compensation arrangements, but if this is due to someone's negligence then you may have grounds for legal action. The University of East Anglia is indemnifying the researchers for any such claims.

Will my taking part in the study be kept confidential?

The study is sponsored by the University of East Anglia (UEA). The Queen Elizabeth Hospital Birmingham will keep your name, NHS number and contact details confidential and will not pass this information to the UEA. The Queen Elizabeth hospital will use this information as needed to contact you about the research study and to make sure that relevant information is recorded for your care and to oversee the quality of the study. Certain individuals from the UEA and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The UEA will only receive this information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Your name or contact details will not be used in any report or publication. All information will be identified by a participant code (not your name) and will be stored in a locked filing cabinet at the Queen Elizabeth Hospital Birmingham and password protected computers. Only members of the research team will have access to the data. Only annonymised data will be kept for three years.

Will my GP be informed of my involvement in the study?

With your written consent, your GP will be notified of your participation in this study.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

Who is organising and funding this study?

This study is being led by Caroline Miller, a clinical specialist physiotherapist at the QEH, Birmingham, studying for a doctoral degree at the University of East Anglia. Caroline's doctoral degree has been funded by the NHS National Institute for Health Research (the research arm of the NHS). She is being supervised by Professor Christina Jerosch-Herold, and Dr Jane Cross at the University of East Anglia, Norwich and Mr. Dominic Power a consultant at the Queen Elizabeth Hospital Birmingham.

Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee, to protect your interests and those of the researchers. This study has been reviewed and given a favourable opinion by the West Midlands – Solihull Research Ethics Committee and the Research and Development Directorates at the Queen Elizabeth Hospital Birmingham NHS Trust.

Yes, I would like to take part in the study – what do I need to do now?

Please contact Caroline Miller (study coordinator) to organise a convenient time for an interview

Email: caroline.miller@uea.ac.uk or Tel: 07743501508

No, I do not wish to take part in the study – what do I need to do now?

You do not need to do anything.

Contact for further information or any questions about this study:

Caroline Miller, Chief Investigator, University of East Anglia
Tel: 07743501508
E mail: caroline.miller@uea.ac.uk
Peripheral nerve injury admin (0121) 3714992

Contact details if you wish to seek advice from the Patient Services Teams at The Queen Elizabeth Hospital NHS Foundation Trust, Birmingham:

Patient Advice and Liaison Service (PALS) on 0121 371 3280 or PALS@uhb.nhs.uk

Thank you for reading this information sheet, which is yours to keep

Appendix 4. 6 Informed consent for interview study

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

CONSENT FORM

Study: What is important to measure in a Traumatic Brachial Plexus Injury?

Participant ID: .....

Please initial each box	Initial
I confirm that I have read the information sheet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
I understand that all data will be confidential and securely stored. I understand that if I withdraw from the study my data up to the point of withdrawal will be used in the analysis	☐
I consent to the use of audio-taping, with possible use of verbatim quotation.	☐
I agree to my General Practitioner being informed of my participation in the study.	☐
I agree to take part in the above study.	☐

Signatures:

Participant: ..... Date: .....

Consenting researcher..... Date.....

Appendix 4. 7 Interview topic guide

COMBINE

Core Outcome Measures in Brachial plexus INjuriEs

Interview guide COMBINE

Topic guide

1. Thank you for agreeing to take part in the interview
2. The interview aims to understand what you think/feel is important to you following a brachial plexus injury and what are your expectations for treatments
3. It will take about 45 -60 minutes to complete

Before we start

- As we go through the interview please let me know if you don't understand any questions
- There are no right or wrong answers – so please respond feely and honestly
- If there is a question that you don't want to answer we can move onto the next questions
- You can stop at any time without giving a reason
- The interview will be recorded but the data will be kept securely and deleted after analysis
- Your answers and any quotes will remain anonymous and not be reproduced in any way to reveal your identity
- Do you have any questions/ concerns regarding the interview?
- Are you still happy for it to be recorded (even though written consent will have been received)?

The interview will cover two main areas, how the injury has affected your life and day to day routines and what expectations you have of treatments for the injury.

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Background

- *Can you tell me a little bit about how you injured your arm?*

Impact of the injury

- *How has this injury impacted on your life?*
  - *How does the injury affect your normal day to day activities?*
  - *Does the conditions affect your mental health in any way? (such as anxiety/low mood, ability to concentrate?)*
  - *Has the injury affected your relationship with your family and friends?*

- Has this injury changed what you see as important to you now and in the future?

Discussions of treatments received – expectations and ideal outcomes

thinking about the different treatments and rehabilitation you have had

- What were your expectations/ goals with this treatment/s?
  - Symptoms
  - Family life
  - Activities
  - Work
  - Were expectations and goals discussed with anyone?
  - **Why were these important?**
  - Were there any drawbacks to treatments and rehabilitation?
  - What worries you now about the future?

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In latter interviews (in addition to the previous questions) the scope and lay language of outcomes identified in previous interviews will be explored to take forward to the Delphi.

- *In earlier interviews individuals identified ..... as important.*
    - *Is this important to you? Why?*
    - *Is this how you would describe it ..... or would you use different words to describe it?*

End Question

- *Is there anything else that you want to say about your experiences of treatment for your brachial plexus injury that we haven't already covered?*

Probes

Probes may include

- *Can you give me an example of that?*
- *What did you mean when you said……?*
- *Tell me more about…?*

Silence will also be used as a probe as an encouragement for participants to continue.

Appendix 4. 8 Changes made following pilot interviews

i) I changed my opening conversation and introduction to the study.

I felt I needed to make it clear that I was here as researcher and not in a clinical role. I added more detail that the study was part of research I was doing at the university and would not influence their care in any way. I thought that after the first interview I was not clear with the definition of my new role. I felt this was particularly important, as many of the participants knew me in my clinical role. They might have assumed I already had knowledge of their experience. This may have limited the depth of the interview. Also, although I offered to interview all the participants in their home or a location of their choice, both participants in the pilot interviews chose to attend the hospital. Conducting the interview in the hospital may have influenced their answers, as they may have connected the interview with any ongoing treatment. I needed to be careful not to wear a clinical uniform and to conduct the interview in an area completely different to where participants had their clinical treatment.

ii) I also realised after the first two pilot interviews that I needed to re-structure how I asked the questions. I felt that I needed to enquire about all the treatments that participants had had or would consider in the future. Get a timeline of these treatments /proposed treatments and then discuss each one in isolation to explore what the participant's expectations and aims were of these treatments. Also, to review whether they had had any side effects for each of the treatments. Initially this was not clear in the topic guide. I also needed to prompt for specific treatments which may not have been at the forefront of the participant's mind, as most participants consider surgery as the main treatment. For example, "Have you seen an orthotist or been provided with any supports for the arm?", "Have you seen a pain management specialist or had your medications reviewed by anyone?", "Physiotherapy/ Occupational therapy/ Hand therapy?", "Have you had any psychological support?

Appendix 4. 9 Brief biography of Caroline Miller

Biography

I will summarise a brief biography of my life experiences and how they may impact on my position as an insider researcher for this thesis.

I come from an Irish white working-class background, where opportunities were limited. My supportive family and the presence of an Irish educational grant system provided me with the opportunity to attend university. I trained as a Physiotherapist in Dublin, Ireland, and to my surprise but not to those closest to me I achieved my goal and came away with a 2:1 honours degree in Physiotherapy. I moved to Birmingham UK for work, as jobs were scarce in Ireland in the 1990s. I thoroughly enjoy being a Physiotherapist and went on to secure funding from a Black Country Consortium to complete a Masters.

As a Physiotherapist I specialised in working with patients with upper limb disorders, and soon worked with a consultant in the hand service in Birmingham to set up a brachial plexus unit. I come into this research with questions around what outcomes should we measure for patients with a brachial plexus injury? These questions have developed from my experience in clinical practice. Our team and other national teams were unclear on what we should be measuring. It was also driven by my knowledge that most outcomes measured (clinically and in the literature) are musculoskeletal, despite my experience of treating patient suffering with emotional and psychological consequences.

I acknowledge that I bring this bias to the research, which stems from my experience treating patients with a TBPI. However, this has been clear from the start and discussions with supervisors who are aware of this bias help to keep it in check, as well as keeping reflective diaries.

Appendix 4.9 biography

My research involved interaction with participants who have gone through the traumatic experience of a BPI and now live with a disability. I am able-bodied and unable to relate to this particular experience (my outsider perspective), as I have not experienced the injury. However, I feel I can have empathy due to my years of experience treating patients with the injury and my extensive knowledge of the injury. BPI is a very rare injury and having this clinical experience gives me some "insider status". On the other hand, I am a middle-aged, now middle-class female and the majority of participants interviewed for this study were young, working class and mostly male. I understand that the qualitative data co-created in these interactions will be different to data co-created perhaps with a young male interviewer who rides motorbikes. There may have been issues or outcomes that were important to these participants which they would not have shared with me.

Braun and Clarke recommend disclosing your insider/outsider position to research participants. I disclosed to research participants that I had many years of experience treating individuals with a TBPI in Birmingham. However, I also made it clear that this would not impact any ongoing or future treatment and reassured them that all data would be anonymised. My outsider status as a middle -aged, able-bodied, female was clear and I did not dwell on it.

Appendix 5. 1 Pilot Delphi evaluation form

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Core Outcome Measures in Brachial plexus INjuriEs

Pilot Delphi evaluation form

Name:

Questions

1. **Did you understand the introduction page?**
   a. Did it make the aim of the study clear?
   b. Any changes you would make?
   c. Any repetitions?
   d. Anything you would add?
   e. Was there language/ terminology that you didn't understand that we could change?

2. **Registration page**
   a. Was the registration easy/ difficult to follow?
   b. Anything you would add or remove?

3. **Outcomes pages (x 14)**

For each page

Can you read the **instructions** and let me know if you can understand them and if they are clear

Each outcome – can you let me know if there are any you don't understand or that are confusing / overlap with others

Feedback (if any) on physical signs page

Feedback (if any) on sensation and pain page

Feedback (if any) on neurophysiology page

Feedback (if any) on emotional well-being page

Feedback (if any) on activities of daily living page

Feedback (if any) on sleep and overall health page

Feedback (if any) on social well – being page

Feedback (if any) on delivery of care page

Feedback (if any) on costs of care page

Feedback (if any) on complications page 11

Feedback (if any) on complications page 12

Feedback (if any) on complications page 13

Feedback (if any) on complications page 14

How long do you think it would take you to do?

Any other comments

Thanks for helping

Caroline

Appendix 5. 2 Pilot Delphi method, results and changes made

Methods: Six participants were invited on 6th February 2020 (via email) to pilot the first round of the online Delphi. This included 2 surgeons, one nurse, one occupational therapist and two individuals with BPI from the charity. They all met the inclusion criteria for the online Delphi. They were asked to complete the online Delphi as it was and to provide feedback.

The Delphi

When the online Delphi was accessed, it consisted of an introduction page, registration page and 13 pages of outcomes, grouped into outcome domains in each page.

Physical signs (n = 7), Sensation and pain in the arm (n = 8), Neurophysiology and structure of the nervous system (n = 3), Activities of daily living and work (n = 9), Social wellbeing (n = 5), Emotional wellbeing (n = 6), Sleep and overall health (n = 2), Delivery of care (n = 3), Costs of care (n = 7), Complications (muscle and bone) (n = 4), Complications (nerve related) (n = 6), Complications (problems with surgical joins and infection) (n = 5), Complications (bleeding and breathing problems) (n = 7)

In the invitation email I attached a review proforma in Word (Appendix 5.1) and asked participants to fill this out. By 12th February, 5 participants had completed the pilot Delphi. All but the nurse completed the questionnaire. Only two participants filled in the word proforma attached to the email. The rest provided ad hoc comments via email.

Each volunteer was required to participate in the whole round, complete the registration page and rate each of the outcomes within the Delphi. They could also add comments or any extra outcomes which they felt were important to be included in the Delphi.

Responses to questions and comments in emails are presented in Table 1, including actions which I took in response to the comments.

Table 1. Pilot Delphi comments and action taken

Comments	Actions
Introduction page	
Patient A: *More detail on timeline of next stages* **Therapist***: Yes the aim of the study was clear.* *My only comment in the patient information leaflet section survey 2 and 3 you number the rounds 1 and 2 and then round 3 you spell three instead of using number (line 7)*	I added "The three surveys will be conducted over a 5-month period and each survey will be open for 4 weeks" I changed three to number 3
Registration page	
Patient A: *Full name or first and second name* **Therapist:** *Easy to fill in and follow*	I asked the software developer if we could change this but unfortunately this was unable to be changed.
Language (general comments)	
Patient A: *Nothing I would change*	Nothing to change
Outcomes (general comments)	
Patient A*: Yes, all clear, however the instructions at start of each question page could be formatted so that this sentence:* ***"This page lists how sleep and overall health can be affected by having a traumatic brachial plexus injury"*** *is separate, as it's too easy to assume the paragraph is repeated on each page and therefore simply skip it, while this short summary is actually quite important to read, as it makes the questions clearer.* **Therapist:** *All clear Very useful having the added information when you hover over the sentence*	Discussed with supervisor (CJH) and I underlined this sentence and separated from rest of paragraph
Physical signs	
No comments from participants	
Sensation and pain	
Surgeon A: *question 2 - pain intensity How important is it?.....this needs rephrasing. having pain of intensity which doesn't interfere with the chosen lifestyle description of pain - you have options of not important / important etc.... - answers options do not fit the question Have you thought about separating pain and sensation to two different pages?*	I discussed this with my supervisors and decided to leave this as when we read back again we could not see the issue with these sentences I have merged sensation and pain to decrease the burden on the participant of the length of the questionnaire. I therefore did not separate them out again as it would increase the burden on the participant.
Neurophysiology and structure of Brachial Plexus	
Surgeon A: *What do you mean by structure of the BP - how important is it in what context*	I added structure of the brachial plexus using MRIs or other techniques.

Comments	Actions
Activities of Daily Living	
No comments	
Social well being	
No comments	
Emotional well being	
Surgeon A: *motives - for what...a bit of clarification*	Agree – need to change Changed to intentions and goals
Overall Heath	
No comments	
Delivery of care	
No comments	
Costs of care	
Patient A: *I wasn't sure how to interpret some of these. It took a while to work out if I should answer them from a personal viewpoint or how it affected the NHS, as some could go both ways. I feel most are probably aimed at the "non patients" and I'm guessing they may not be around for the second round of questions.*	I changed this as it was confusing to differentiate patient versus healthcare costs - Out of pocket costs to the patient for outpatient appointments and inpatient care - Costs to the patient from long term loss of individual/ family income - Costs to the patient from long term loss of individual/ family income
Complications (general)	
Patient A: *These are quite specific questions; I think they have value in the survey but a lot of it went over my head and I only have knowledge due to my talking with so many BPI patients. Also, hovering the mouse over the question doesn't give a laymen's explanation, just the medical terminology.*	I think that the hover button made it difficult here as the hover writing is quite big and obliterates the writing on the Delphi therefore, I have reiterated lay language in the hover and put medical language at the end
Length of questionnaire	
Patient A: *30 minutes a good estimate* **Surgeon B**: *5-10 mins*	Nothing to do

Comments	Actions
Other comments	
Patient A: *On the review page, you can alter answers, but you can't view/edit or add any comments. It could be useful to include.* **Patient B:** *I thought it was very thorough and some good questions. No issues with it from me.* **Occupational Therapist:** *When I got to the end of the survey I did want to go back again. I can't remember if there is a part that tells you once you click off the page with all the filled parts then you can't go back. It does say not to click the back arrow.* *It reads really well and will be exciting to see the results.* **Surgeon B:** *Done - it reads well* *Looking forward to see the surgeon-therapist-patient disparities!*	I changed the review page *Please review your ratings for all the outcomes below. You can change them at this stage, if you wish, before submitting. Once you click NEXT PAGE below you will NOT have the opportunity to change your ratings again. If you want to review previous comments/ feedback you will need to select the appropriate page below and select "Go to". This will direct you to previous pages to amend feedback. Once you are ready click on NEXT PAGE at the bottom of this page. You will have an opportunity to add additional outcomes on the next page.*

Limitations to the pilot

Limitation with this pilot is that it was limited to the first round, which failed to test the complex processes of analysis and measurement occurring later in the Delphi research process.

I could have piloted each round before the onset of the real round in the Delphi. While this may have improved rigour, managing a pilot sample alongside a live Delphi could have been complex and risked between-round delays and attrition of the full study sample.

Appendix 5. 3 Promotion of the COMBINE Delphi to adults with BPI

Each of these facebook sites and support groups were contacted to ask permission to advertise the COMBINE international Delphi

Facebook sites for people with TBPI (followers/ members)
Brachial Plexus Injury Asia (530 members)
Brachial Plexus Injury Awareness & Support Group (732 followers)
Brachial Plexus Injury (page 117 followers)
Brachial Plexus Canada (2.4K members)
Brachial Plexus Injury Awareness (3,720 members)
Brachial plexus and peripheral nerve injuries Asia (200 followers)
United brachial plexus nerve injury and erbs palsy support group (American) UBPN (4,000 members American)
Plexus brachial France (101 members)
Brachial plexus support group Singapore (14 members)
Brachial Plexus Injury South Africa (108 members)
Traumatic brachial plexus injury America (1.1K members)
Brachial plexus Australia (506 followers)
TBPI UK (300 followers)
Brachial Plexus Philippines (187 members)

On agreement from **facebook/ forum** administrator the following wording was used with a link to the youtube video https://www.youtube.com/watch?v=7k6MYpugvRk to promote the study.

Hi all, I am a brachial plexus researcher in the UK. If you have a traumatic brachial plexus injury, would you consider signing up to our international online research study. We want to find out what is important to people with the injury. This will help us be more specific with our treatments and tests. Hopefully, help us develop better treatments in the future. It is free and voluntary. Leave a message below or email me on combinebrachialplexus@gmail.com if interested.

On **twitter**, the following wording was used:

Would you be interested in learning more about our brachial plexus online study? Help us develop better treatments in the future. It is free and voluntary. DM or email me on combinebrachialplexus@gmail.com

Appendix 5. 4 Participant Information Sheet Delphi - adult with a BPI

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

COMBINE

Core **O**utcome **M**easures in **B**rachial plexus **IN**juri**E**s

Your invitation to take part in a research study. Can you help?

Study title: Reaching agreement on what to measure in a Traumatic Brachial Plexus Injury

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve for you. Please take time to read through the information sheet carefully and discuss it with your family and friends. Please ask (Caroline Miller, contact information is at the end of the leaflet) if anything is not clear or if you would like more information.

What is the purpose of the study?

Many individuals with a traumatic brachial plexus injury undergo surgery and rehabilitation to restore some movement and function of the arm.

To help patients, doctors and health professionals make decisions about treatments for a traumatic brachial plexus injury we need evidence about what works best. To do this we look at the effects of treatments on patients. These effects are called "outcomes" which might be muscle strength or quality of life measured after treatments. At the moment different studies measure different outcomes. For example, Study A might measure pain and Study B might measure movement. When the studies are finished, we cannot combine or compare the results because they use different outcomes. Also, outcomes chosen in a study may not be relevant to patients. This is problematic as we then struggle to work out if a treatment is effective and really helps patients.

We can solve this problem by using the same important outcomes to decide whether treatments work. This is called a Core Outcome Set. To decide which outcomes are important we need to get everyone's opinion and try to reach agreement, or 'consensus' on the most important outcomes. We will ask individuals with a Traumatic Brachial Plexus Injury, health care professionals and academics their opinions on what they consider to be the most important outcomes. To reach agreement, we will use three

consecutive on-line surveys in which each participant is given a list of possible outcomes and asked to rate how important it is to them.

Can I take part?

You can complete our surveys if you:

- Have had a traumatic brachial plexus injury
- Are aged 16 or over
- Can complete questionnaires in English

It is important that individuals who have had this injury are involved when we develop the core outcome set as we need to know which outcomes are most important to you. There will be no direct benefit to you from being involved however your involvement may help to improve the care of patients with a traumatic brachial plexus injury. There are no risks involved in participating in this project however if you are affected emotionally by the questionnaire, you can contact Caroline Miller on 0044(0)7743501508 or the traumatic brachial plexus injury support group on http://tbpi-group.org/

What will it involve?

To get "agreement" on what are the most important outcomes to measure we want patients and health care professionals to rate how important each outcome is to them. This will involve completing an online survey on three separate occasions. Each survey will be sent to you separately and you will have 4 weeks to complete it. Each survey will take up to 30 minutes to complete and can be completed over the internet at home, work or on the go. You can request a paper version of the survey if you wish.

Survey 1:

You will be presented with a list of outcomes and asked to rate the importance of each (for example pain or arm movement). You will also have the chance to add other important outcomes you feel we have missed from the list.

Surveys 2 and 3:

In round 2 we will present you with the same list of outcomes as before and remind you of how important you rated each one. You will also be presented with an average rating for the whole group. Based on this information you will be asked again to rate the importance of each outcome. After round 2 the lowest rated outcomes will be removed and in round three you will only rate those outcomes with the highest

rating again with the information how you last scored them and the average rating for the rest of the group.

Do I have to take part?

No. It is up to you to decide whether you would like to take part in this survey. You will have the option to withdraw at any point however any information we have collected up to that point will still be used.

Will my results be kept confidential?

University of East Anglia is the sponsor for this study based in the United Kingdom. Each participant will be issued with a unique ID number to be used by the facilitator and within the survey software. All questionnaire responses will be anonymous. Any names addresses and e-mail addresses will be held securely by the chief investigator on a password protected computer. We will be using information from you to undertake this study and will act as data controller. This means that we are responsible for looking after your information and using it properly. Anonymised data will be stored securely after the completion of the project and be kept for 3 years before being destroyed.

Your rights to access, change or move information are limited, as we need to manage your information in specific ways for research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained.

What happens after the surveys?

Following the surveys, there will be an optional group meeting to discuss and agree on the list of important outcomes to be included in the Core Outcome Set based on the survey results. The meeting will be held in Birmingham in the United Kingdom. There will be an opportunity to register your interest when completing the third round of the survey. Reasonable travel expenses will be reimbursed for this meeting.

What if there is a problem?

If you are concerned about any aspect of the way that you have been approached or treated during the study, you should speak to the Chief Investigator, Caroline Miller, who will do her best to answer any questions. You can also seek advice from

Professor Christina Jerosch Herold, Queens Building 2.19, School of Health Sciences, University of East Anglia, Norwich, NR4 7TJ. Telephone no. +44(0)1603593316

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

In the unlikely event that you are harmed whilst participating in this study, there are no special compensation arrangements, but if this is due to someone's negligence then you may have grounds for legal action. The University of East Anglia is indemnifying the researchers for any such claims.

Who is organising and funding this study?

This study is being led by Caroline Miller, a clinical specialist physiotherapist at the QEH, Birmingham. She is studying for a doctoral degree at the University of East Anglia. Caroline's doctoral degree has been funded by the National Institute for Health Research (the research arm of the NHS). She is being supervised by Professor Christina Jerosch-Herold, and Dr Jane Cross at the University of East Anglia, Norwich and Dominic Power, Trauma and Orthopaedic Consultant at University Hospitals Birmingham

Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee, to protect your interests and those of the researchers. This study has been reviewed and given favourable opinion by the West Midlands-Solihull Ethics Committee and the Research and Development Directorates at the Queen Elizabeth Hospital Birmingham NHS Trust.

What do I need to do now?

If you do decide to take part, then register online at …. *(Url to be added once set up*). You will consent to take part by agreeing to the statements during registration.

Contact for further information or any questions about this study:

Caroline Miller, Chief Investigator,
Physiotherapy Department
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
B15 2WB
Tel: 07743501508
E mail: caroline.miller@uea.ac.uk

Thank you for reading this information sheet, which is yours to keep

Appendix 5. 5 Participant Information Sheet Delphi - healthcare professional

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Queen Elizabeth Hospital Birmingham NHS
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NHS National Institute for Health Research

COMBINE

Core Outcome Measures in Brachial plexus INjuriEs

Developing consensus on a core outcome set for adult traumatic brachial plexus injuries

Dear [insert name]

You are invited to participate in an international effort to develop consensus on a core outcome set for adult traumatic brachial plexus injuries. Please take time to read through this information. If you have any questions, please do not hesitate to contact me (Caroline Miller- my contact details are provided at the end of the letter).

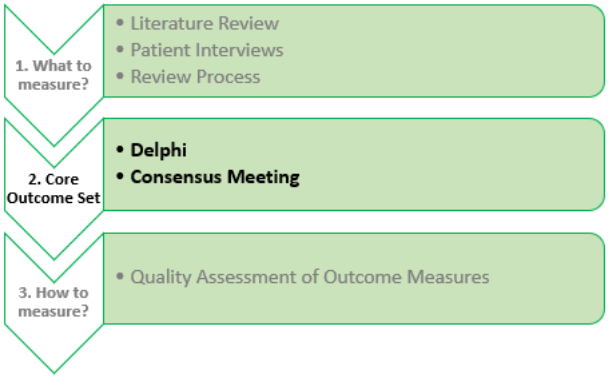
What is the purpose of the study?

The Core Outcome Measures in Brachial plexus INjuriEs (COMBINE) study aims to establish a set of core outcomes for routine care and future studies in traumatic brachial plexus injury. A core outcome set is the minimum set of outcomes which should be measured in an area of health care. With advances in treatments, including microsurgery, there has been an increase in research evaluating the outcomes of interventions for traumatic brachial plexus injuries. However, studies often focus on short term outcomes, outcomes which are important to clinicians but not to patients and by reporting different outcomes it is impossible to compare and combine the results.

Establishing an international Core Outcome Set in adult Traumatic Brachial Plexus Injuries will mean that the same outcomes which matter to patients and healthcare professionals will be consistently measured and reported in future studies and used in routine care. The Core Outcome Set will be developed over three phases (See Figure 1). Phase 1 has been completed and has identified a "long list" of outcomes important in adult traumatic brachial plexus injury through a systematic review of studies and patient interviews. The long list of outcomes has been turned into a survey.

You are invited to take part in phase 2 – the Delphi study. The purpose of this Delphi study is to gain consensus on what are the most important outcome domains to measure in adults with a traumatic brachial plexus injury. A Delphi study uses a structured method of sequential surveys with a group of experts to achieve agreement within the group.

Figure 1:



Can I take part?

You can take part if you are a health care professional (surgeon, therapist, nurse, or pain consultant) who regularly treat adults with a Traumatic Brachial Plexus Injury. You will need access to the internet, once over each of the four-week periods to complete the survey.

What will it involve?

We want health care professionals and patients to rate how important each outcome is to them. This will involve completing an online survey on three separate occasions over a 5-month period. Each survey will take up to 30 minutes to complete. Each survey will be open for 4 weeks and you can complete it at a time which is convenient to you using a personal computer, laptop, tablet, or mobile phone connected to the internet.

Survey 1:

You will be presented with a list of outcomes and asked to rate the importance of each (for example pain or arm movement). You will also have the chance to add other important outcomes if you feel we have missed any from the list.

Surveys 2 and 3:

In round 2 we will present you with the same list of outcomes as before and remind you of how important you rated each one. You will also be presented with an average rating for other groups (patients and other healthcare professionals). Based on this information you will be asked to rate the importance of each outcome again. After round 2 the lowest rated outcomes will be removed and in round 3 you will only rate those outcomes with the highest rating, again with the information how you last scored them and the average rating from each of the other groups. It is important that you can commit to completing all three rounds before taking part as dropping out before the end will affect the reliability of the results.

Will my taking part in the study be kept confidential?

University of East Anglia is the sponsor for this study based in the United Kingdom. Each participant will be issued with a unique ID number to be used by the facilitator and within the survey software. All questionnaire responses will be anonymous. Any names addresses and e-mail addresses will be held securely by the chief investigator on a password protected computer. We will be using information from you to undertake this study and will act as data controller. This means that we are responsible for looking after your information and using it properly. Anonymised data will be stored securely after the completion of the project and be kept for 3 years before being destroyed.

Your rights to access, change or move information are limited, as we need to manage your information in specific ways in order for research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained.

The results of the final Core Outcome Set will be published and participants completing all three rounds of the Delphi will be named on the publication as part of the TBPI (Traumatic Brachial Plexus Injury) collaboration group.

What happens after the Delphi study?

Following the three surveys, there will be a consensus meeting to agree on the final list of important outcomes to be included in the Core Outcome Set based on the survey results. This meeting will be held in Birmingham in the United Kingdom and will include healthcare professionals, researchers and patients. We are looking for healthcare professionals who are interested to join this meeting and there will be an opportunity to register your interest when completing the third round of the survey. Reasonable travel expenses can be reimbursed for this meeting.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

What do I need to do now?

If you do decide to take part in the survey, then register online at *(URL to be added once set up*). You will be asked to consent to take part by agreeing to the statements during registration before completing the survey

Who has reviewed the study?

This study has been reviewed and given favourable opinion by the West Midlands- Solihull Research Ethics Committee and the Research and Development Directorates at the Queen Elizabeth Hospital Birmingham NHS Trust.

Who is organising and funding this study?

Caroline Miller is leading this study a physiotherapist and undertaking this study as part of a 4-year Clinical Doctoral Research Fellowship (PhD) at the University of East Anglia and University Hospital Birmingham. She is being supervised by Professor Christina Jerosch-Herold, Dr Jane Cross, and Mr Dominic Power. The fellowship is funded by the National Institute of Health Research (NIHR) in the UK.

What if there is a problem?

If you have a concern about any aspect of this study, you should speak to the lead researcher Caroline Miller (see contact details below) who will do her best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting the study supervisor Christina Jerosch-Herold at the University of East Anglia (01603 593316).

Contact details for further information or any questions about the study:

Caroline Miller, Chief Investigator,
Physiotherapy Department
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
B15 2WB
Tel.: (044)7743501508
E mail: caroline.miller@uea.ac.uk

Appendix 5. 6 Ethics approval for consensus location substantial amendment

NHS
Health Research Authority

West Midlands - Solihull Research Ethics Committee

The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

27 January 2021

Mrs Caroline Miller
Physiotherapy Department
Queen Elizabeth Hospital Birmingham
Birmingham B15 2WB

Dear Mrs Miller

Study title:	**Improving the quality and relevance of outcome measurement for individuals with a Traumatic Brachial Plexus Injury. Development of an International Core Outcome Set**
REC reference:	**18/WM/0297**
Protocol number:	**R204919**
Amendment number:	**Substantial amendment COMBINE 2**
Amendment date:	**06 January 2021**
IRAS project ID:	**248940**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [248940_Substantial amendment COMBINE 2]	2	06 January 2021
Covering letter on headed paper [Cover letter amendment COMBINE 07 jan]	1.0	07 January 2021
Letters of invitation to participant [consensus invitation letter version 1.0 08 December]	1	08 December 2020
Research protocol or project proposal [COMBINE protocol version 1 28 08 2018 final]	1	29 August 2018

Research protocol or project proposal [Combine protocol version 2 08 Dec 2020]	2	08 December 2020

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS Project ID - 248940: **Please quote this number on all correspondence**

Yours sincerely

PP - Dr Rex J Polson
Chair

E-mail: solihull.rec@hra.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Mrs Caroline Miller*

West Midlands - Solihull Research Ethics Committee

Attendance at Sub-Committee of the REC meeting

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mrs Theresa Hyde	Retired Head Teacher	Yes	
Dr Rex J Polson	Consultant Physician - Chair	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mr Wai Yeung	Approvals Administrator

Appendix 5. 7 Consensus invitation letter- adult with BPI

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

COMBINE
Core Outcome Measures in Brachial plexus INjuriEs

Invitation to participate in final consensus meeting

Thank you for taking part in the recent COMBINE Brachial Plexus Delphi study. At the end of the study **22 outcomes** were rated as "very important" to be included in the core outcome set, by all three groups (people with the injury, surgeons, and therapists). In addition, there were **11 complications outcomes** which reached agreement. It is important that the core outcome set is practical, so the outcomes need to be further discussed and reduced. An online meeting has been arranged with the aim of discussing these remaining outcomes and voting on a final set of the most critical outcomes that should be assessed during treatment and in studies of people with a brachial plexus injury.

We are inviting you to participate in this meeting as a patient representative. You will be part of a group of 10-15 people who will all have the injury.

The meeting will be held virtually using an online meeting platform called ZOOM. This will enable us to abide by any restrictions imposed by the COVID-19 pandemic as well as allow people to participate who would not be able to travel long distances. The consensus meeting will take no more than two and half hours. There will be a break in the middle of the session.

At the start of the meeting, I will present the results of the study and the outcomes which were rated "very important" by all three groups in the Delphi study. There will be an opportunity to then discuss these outcomes and you will be invited to vote on whether an outcome should be included in the final core outcome set. The voting will happen via ZOOM and will be anonymous.

The consensus meeting will be video recorded. These recordings will be used to form a collective summary of the discussions and will not be linked to a specific individual. In this way the summaries of the discussions will be anonymous.

I will be sending out the results of the Delphi study, two weeks before the meeting. Information about how to join on ZOOM and use it will also be provided and I will offer a practice session on the zoom platform to anyone who would like that. To take part in the virtual meeting you will need a PC/laptop or tablet which has a camera and enables video and audio. Following participation, I will send you a report of the meeting and ask if you would consent to your participation being acknowledged in publications.

Information on confidentiality, ethics, management and funding has been previously sent to you when you participated in the Delphi study. Please let me know you require this information again.

The date of the online meeting is 25/02/2021 at 19.00 GMT.

We feel your knowledge/ experience with the injury would be extremely beneficial to help decide the outcome set. If you would like to take part, then please let me know via email. Please do not hesitate to contact us if you require further information.

Yours sincerely

Caroline Miller

On behalf of the COMBINE team

Queen Elizabeth Hospital Birmingham

Mindelsohn Way,

B15 2WB

Tel: 07743501508 Email: caroline.miller@uea.ac.uk

Appendix 5. 8 Consensus invitation letter- healthcare professional

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

COMBINE
Core **O**utcome **M**easures in **B**rachial plexus **IN**juri**E**s

Invitation to participate in final consensus meeting

Thank you for taking part in the recent COMBINE Brachial Plexus Delphi study. At the end of the study **22 outcomes** were rated as "critical" to be included in the core outcome set, by all three groups (people with the injury, surgeons, and therapists). In addition, there were **11 complications outcomes** rated critical. It is important that the core outcome set is practical, so the outcomes need to be further discussed and reduced. An online meeting has been arranged with the aim of discussing these remaining outcomes and voting on a final set of the most important outcomes that should be assessed during treatment and in studies of people with a brachial plexus injury.

We are inviting you to participate in this meeting as a healthcare professional representative. You will be part of a group of 20-25 people who will all be health professionals.

The meeting will be held virtually using an online meeting platform called ZOOM. This will enable us to abide by any restrictions imposed by the COVID-19 pandemic as well as allow people to participate who would not be able to travel long distances. The consensus meeting will take no more than two and half hours. There will be a break in the middle of the session.

At the start of the meeting, I will present the results of the study and the outcomes which were rated "critical" by all three groups in the Delphi study. There will be an opportunity to then discuss these outcomes and you will be invited to vote on whether an outcome should be included in the final core outcome set. The voting will happen via ZOOM and will be anonymous.

University of East Anglia

Queen Elizabeth Hospital Birmingham NHS
Part of University Hospitals Birmingham NHS Foundation Trust

NHS National Institute for Health Research

The consensus meeting will be video recorded. These recordings will be used to form a collective summary of the discussions and will not be linked to a specific individual. In this way the summaries of the discussions will be anonymous.

I will be sending out the agenda and the results of the Delphi study, two weeks before the meeting. Information about how to join on ZOOM and use it will also be provided and I will offer a practice session on the zoom platform to anyone who would like that. To take part in the virtual meeting you will need a PC/laptop or tablet which has a camera and enables video and audio. Following participation, I will send you a report of the meeting and ask if you would consent to your participation being acknowledged in publications.

Information on confidentiality, ethics, management, and funding has been previously sent to you when you participated in the Delphi study. Please let me know you require this information again.

The date of the online meeting is 04/03/2021 at 19.00 GMT.

We feel your knowledge/ experience with the injury would be extremely beneficial to help decide the outcome set. **If you would like to take part, then please let me know via email.** Please do not hesitate to contact us if you require further information.

Yours sincerely

Caroline Miller

On behalf of the COMBINE team

Queen Elizabeth Hospital Birmingham

Mindelsohn Way,

B15 2WB

Tel: 07743501508 Email: caroline.miller@uea.ac.uk

Appendix 5. 9 Outcomes voted on at consensus meetings

Outcomes for voting at consensus meeting (print if possible)

General outcomes

Voluntary movement	Appropriateness of treatment
Strength of the arm	The ability of the brachial plexus nerves to send signals to the skin and muscles of the arm
Carrying and lifting	Carrying out daily routine
Fine hand movement	Maintaining personal hygiene
Ability to feel with the arm	Putting on and taking off clothes
Ability to feel to protect the arm from injury	Ability to eat using the utensils/ hands
Pain intensity	Effect on relationship with or ability to care for children
Pain duration	Emotional distress
Pain description	Self -confidence
Overall health	Ability to cope
Access to treatment	Expectations of treatment

1

Outcomes for voting at consensus meeting (print if possible)

Complication Outcomes

Loss of voluntary movement	Failure of a surgical join of the nerve
Loss of assisted movement (passive)	Failure of a surgical join of an artery of a vein
Limited voluntary movement because of inability to co-ordinate muscles at the same time	Injury to an artery or vein resulting in bleeding where the operation takes place
Nerve forms a painful bundle of nerves (neuroma)	Development of a blood clot
Damage to other nerves during the surgery	Breathing problems
Worsening of existing pain or pins and needles	

Appendix 5. 10 Decision making regarding items to include in Delphi

On 5th November 2019 there was a face-to-face meeting with supervisors (CJH and JC) where CM presented the outcomes identified from the systematic review and the interview study.

Categories: Categories were discussed to group the outcomes (items for the Delphi). The categories were in line with the original COMET taxonomy but reworded slightly for ease of understanding in a survey. The wording and content of the categories were also reviewed with patient and clinical advisers on 15th January 2020 during another face-to-face meeting. This meeting included two patient advisors and two clinicians (surgeon and physiotherapist). Decision making around items and wording of items for Delphi is discussed below and presented in Table 1.

Physical signs: At both meetings there was agreement that most of the outcomes in the physical signs category were easy to understand and should be included in the Delphi. One outcome from the systematic review (*control of movement/stability*) was excluded, as supervisors and clinicians felt it was already included in items 1,2 and 3. The outcome *muscle mass* was merged with appearance, as it was thought by participants of the meetings that appearance encompassed mass. A patient and surgeon debated whether patients would understand the term "passive" movement. It was agreed to change the term to passive or assisted movement of the arm, to assist with understanding and clarity.

Sensation and pain in the arm: Three sensory outcomes were identified in the systematic review (general sensory recovery, discriminative touch and protective touch). It was agreed in both meetings that these terms were not easy to understand and CJH suggested that the items were reworded to *ability to feel with the arm (merger of general sensory recovery and discriminative touch)* and *ability to feel to protect the arm from injury (protective touch).* Patients found these terms easy to understand at the subsequent patient and clinician meeting (15th January 2020). Sensitivity to touch pressure and paraesthesia and itchiness (outcomes from systematic review) were merged to form one Delphi item: *pins and needles or tingling in the hand*. There were seven separate outcomes relating to pain. It was felt that this was too many, so at the initial supervisors' meeting two outcomes, location of pain, pain quality and interference with life were merged to form one Delphi item: *pain description (quality and interference).* The outcome 'pain medication use' was removed as it was felt that it was encompassed more broadly by the other pain items in the Delphi.

Neurophysiology and structure of nervous system: At both meetings it was felt that the outcomes in this category were relevant, but they needed rewording to make it easy to understand for all participants. The surgeon at the clinician and patient meeting on 15th January 2020 felt that these were items that patients would not understand and should not vote on. The patients, however, felt it was important that they had the ability to vote although it needed to be clear what the outcome meant. Patients in this meeting helped to reword and develop explanations for these outcomes. The outcomes were reworded as displayed in table 1. The outcome 'reinnervation' was merged with 'speed of motor/sensory conduction' to form the item *the ability of the brachial plexus nerves to send signals to the skin and muscles in the arm.*

Activities of daily living: In this category it was felt that most outcomes from review or interviews were easily transferrable to the Delphi as items, and only minor changes were made to the wording of the outcomes. Two outcomes from the systematic review were felt to be too ambiguous and were removed from the long list. These were physical functioning (non-specific) and lower limb function.

Social wellbeing: Five outcomes from the interview study and systematic review were included in the Delphi and reworded for ease of understanding. See Table 1. One outcome from the systematic review (role function patient specific) was felt to be too ambiguous and was removed from the long list.

Emotional wellbeing: All outcomes identified in this category from the systematic review and interviews (n = 6) were included in the Delphi as items. Outcomes were slightly reworded to improve understandability.

Sleep and overall health: Both outcomes in this category were included in the Delphi.

Delivery of care: Three outcomes identified in this category were included in the Delphi with only slight rewording. Operation time was excluded, as patient advisors, the surgeon and supervisors were unclear of its value. The outcome 'patient preference' was excluded, as patient advisors and supervisors thought it was not specific enough. The outcomes 'time to surgery' and 'access to treatment' were merged to create the *access to treatment* Delphi item.

Costs of care: The two outcomes identified from patient interviews (money worries and costs of attending for treatment) were included in the Delphi as items but reworded as displayed in Table 1. These were reworded following feedback from the pilot Delphi (Appendix 5.2). As the Delphi was international, my supervisors (CJH and JC) felt it was important to reflect this with an item in the Delphi related to costs which may be incurred by uninsured private paying patients. This new item is displayed in Table 1.

Complications: These outcomes were discussed with two peripheral nerve surgeons (DP and ST) to help ensure accuracy and also relevance. DP felt that the outcomes identified in this category (from systematic review and interviews) were very broad and ambiguous, and would be difficult to rank in a Delphi process. Therefore, additional specific complication items were added during discussions with the surgeons. One additional item was included in the *complications (muscle and bone)* category. Four additional items were included in the *complications (nerve)* category. Three additional items were included in the *complications (problems with surgical joins and infection)* category. Four additional items were added to the *complications (breathing and bleeding problems)* category. See Table 1 for details.

Appendix 5.10 Decision making regarding items to include in Delphi

Table 1. Justification of items included in round 1 Delphi

Categories	**Systematic review** (outcomes)	**Interviews** (outcomes)	**Decision making**	**Round 1 Delphi** (items)
Physical signs				
1	Active range of movement		Include	Voluntary movement of the arm
2	Passive range of movement		Include	Passive or assisted movement of the arm
3	Muscle strength		Include	Strength of muscles in arm
4		Arm appearance	Include	Physical appearance of the arm
5	Reaching pulling pushing carrying		Include	Reaching, pulling, pushing,
6	Turning twisting, gripping and releasing, lifting		Include	Carrying and lifting objects
7	Fine hand movement		Include	Fine hand movement
	Control of movement / stability		Exclude: Felt to be included in 1,2 &3	
	Muscle mass		Merged with appearance	
Sensation and pain in the arm				
8	General sensory recovery		Include	Ability to feel with the arm
9	Protective touch		Include	Ability to feel to protect the arm from injury
	Discriminative touch		Merged with 8	
10		Pulling and dragging	Include	A sensation of heaviness
11	Paraesthesia and itchiness		Include	Pins and needles or tingling in the arm
12	Pain intensity/relief		Include	Pain intensity
13	Pain duration/frequency		Include	Pain duration and frequency
14	Pain quality and interference with life		Include	Pain description (quality and interference)
15	Pain when arm exposed to cold		Include	Pain when arm exposed to cold
	Sensitivity to touch pressure		Merged with 11	
	Location of pain		Merged with 14	
	Pain medication use		Decided with supervisors to remove as felt other pain outcomes encompassed this	

Categories	**Systematic review** (outcomes)	**Interviews** (outcomes)	**Decision making**	**Round 1 Delphi** (items)
Neurophysiology and structure of nervous system				
16	Speed of motor / sensory conduction		Include	The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm
17	Peripheral nervous system structure		Include	The structure of the brachial plexus using MRI or other techniques
	Reinnervation		Merged with 16	
18			Subcategory in systematic review	A measure of the activity in the movement and sensation areas of the brain
Activities of daily living				
19	Carrying out daily routine		Include	Carrying out daily routine
20	Maintaining personal hygiene		Include	Maintaining personal hygiene
21	Maintaining personal appearance		Include	Maintaining personal appearance
22	Dressing		Include	Putting on and taking off clothes
23	Transport		Include	Transport
24		Back to my work	Include	Return to full duties at previous role in paid employment
25		Back to studying	Include	Return to or begin education
26	Impact on paid or unpaid work or role in education		Include	Return to paid or nonpaid role
	Physical functioning nonspecific		Exclude: Supervisors and patient advisors felt too vague (would be covered by specific upper limb function)	
	Lower limb function		Exclude: Supervisors and patient advisors felt not specific enough to include	
27	Impact on recreational activities and sport		Include	Return to previous recreational activities

Categories	**Systematic review** (outcomes)	**Interviews** (outcomes)	**Decision making**	**Round 1 Delphi** (items)
Social well-being				
28	Effect on family, friends, neighbours and groups		Include	Effect on relationship with partner or spouse
29		Looking after children	Include	Effect on relationship with and or ability to care for, children
30		Effect on wider family	Include	Effect on relationship with other family members
31		Going out with friends	Include	Effect on friends neighbours and groups
32	Effect on intimate relationships		Include	Effect on intimate relationships
	Role function patient specific		Exclude: Felt to be too vague	
Emotional well-being				
33	Emotional distress, mood		Include	Emotional distress
34	Thoughts and beliefs		Include	Thoughts and beliefs
35		Intentions and goals	Include	Intentions and goals
36		Addiction	Include	Addictive behaviours (e.g., alcohol, medication drugs)
37	Body image		Include	Body image
38	Self-esteem and confidence		Include	Self-esteem and self confidence
Sleep and overall health				
	Quality of Life		Exclude: felt already included in more specific outcomes	
39	Impact on sleep		Include	Overall quality of sleep
40	Perceived health		Include	Overall health

Appendix 5.10 Decision making regarding items to include in Delphi

Categories	**Systematic review** (outcomes)	**Interviews** (outcomes)	**Decision making**	**Final round 1 Delphi** (items)
Delivery of care				
41	Patient satisfaction		Include	Patient satisfaction with healthcare received
42		Access to treatment	Include	Access to treatment
43	Quality of intervention		Include	Appropriateness of treatment
	Operation time		Exclude: Patient advisors, professionals and supervisors unclear of value	
	Patient preference		Exclude: Patient advisors and supervisors agreed this should not be included as not specific enough	
	Time to surgery		Include within 42 (access to treatment)	
Costs of care				
44		Cost of attending for treatment	Include	Out of pocket costs to the patient for outpatient appointments and inpatient care
45		Money worries	Include	Costs to the patient from long-term loss of income
46			Include: supervisors suggested because of international survey	Costs to uninsured private paying patients, insurance, or other third-party payers (includes national health services) for all outpatient and in-patient care received for a brachial plexus injury including meds.
Complications (muscle and bone)				
47	Musculoskeletal complications		Include	Loss of voluntary active movement (donor)
48	Stiffness		Include	Loss of assisted range of motion (stiffness)
49	Bony structure and position		Include	Bone uniting in wrong position
50			Surgeon and supervisors felt it was a subcategory of musculoskeletal complications	Failure of bone to unit following bone surgery

Appendix 5.10 Decision making regarding items to include in Delphi

Categories	**Systematic review** (outcomes)	**Interviews** (outcomes)	**Decision making**	**Final round 1 Delphi** (items)
Complications (nerve related)				
51			Discussion with nerve surgeons	Damage to other nerves during surgery
52			Discussion with patient advisors and surgeons	Worsening of existing pain/ pins and needles
53			Subcategory of nerve related complications	Development of pins and needles or pain in new part of body (donor)
54			Subcategory of nerve complications	Increased sensitivity of the scar
Complications (problems with surgical joins and infection)				
55			Discussion with nerve surgeons	A nerve join results in the formation of a bundle of painful nerves
56	Vascular complications		Include	Failure of surgical join of artery or vein
57			Discussion with nerve surgeons	Failure of surgical join of the nerve
58	Infections		Include	Infection in the body part that was operated on
59			Discussion with nerve surgeon. Subcategory of infection complication	Problems with the wound such as infection, failure to heal properly
Complications (breathing and bleeding problems)				
60			Subcategory of vascular complications	Injury to an artery or vein resulting in bleeding where the operation takes place
61			Subcategory of complications	Bleeding from wound
62			Discussion with nerve surgeon. Subcategory of vascular	Development of blood clot

Categories	**Systematic review** (outcomes)	**Interviews** (outcomes)	**Decision making**	**Final round 1 Delphi** (items)
63	Respiratory complications		Include	Breathing problems
64			Subcategory of infection complication	Chest infection
	Donor site morbidity		Subcategories developed (see 47, 53)	
	General complications		Subcategories developed (see 51-61)	

Appendix 5. 11 Blueprint for online Delphi round 1

REGISTRATION PAGE

STAKEHOLDERS

1. **INDIVIDUALS WITH A TRAUMATIC BRACHIAL PLEXUS INJURY**
2. **SURGEONS (CLINICIANS AND/OR RESEARCHERS)**
3. **THERAPISTS/NURSES/NON-SURGICAL DOCTORS (CLINICIANS AND/ RESEARCHERS)**

What country have you had treatment for your brachial plexus injury or as a health care professional provide treatments for individuals with traumatic brachial plexus injuries?

(TEXT)

If you are someone with a traumatic brachial plexus injury what age group do you fall into?

DROP DOWN

30 OR UNDER

31-50

51-70

>71

If you are someone with a traumatic brachial plexus injury when were you diagnosed?

DROP DOWN

LESS THAN 6 MONTHS AGO

7-12 MONTHS AGO

1-2 YEARS AGO

3-5 YEARS AGO

MORE THAN 5 YEARS AGO

If you are someone with a traumatic brachial plexus injury, have you had surgery?

RADIO BUTTON

If you are a HEALTH PROFESSIONAL how many new patients with a traumatic brachial plexus injury do you see on average a month

(RADIO)

ONE OR LESS

2-3

4-5

6-10

MORE THAN 10

INTRODUCTION PAGE

Thank you for participating in our survey

The study is relevant to you if you

a. Have been diagnosed with a traumatic brachial plexus injury

OR

b. Are a healthcare professional involved in care /management of individuals with a traumatic brachial plexus injury

As part of the study, you are expected to complete three on-line surveys on three different occasions regarding the importance you give to the different outcomes (impact treatment has on adults with a traumatic brachial plexus injury). **This will be conducted over a 5-month period and each survey will be open for 4 weeks.**

You will be asked to rate each outcome on a scale from 1(limited importance) to 9 (critical importance)

Our aim is to create a **"Core Outcome Set"** – the **minimum** group of outcomes that should be measured in future clinical treatments and studies of traumatic brachial plexus injury. By rating a particular outcome as "very important" this means that you think it is very important that in the future clinical treatment and studies of treatments in adults with a traumatic brachial plexus injury that particular outcome is measured.

Important note regarding a Traumatic Brachial Plexus

It is recognised that a traumatic brachial plexus injury is a complex injury which can vary in severity. The injury can range from a total rupture (tearing of the nerves) of some or all nerve roots to just stretching of the nerves after a shoulder dislocation. Because different types of injuries will have a different impact on which and how many muscles are affected we are not aiming to rank the importance of specific movements and muscles.

The aim of this study is to agree on the very **minimum outcomes** which should be measured for each adult with a traumatic brachial plexus injury treated in clinical practice or in research studies. Other specific outcomes can be added to these depending on the individuals' needs or the studies' aims.

This is round 1 of 3

It is very important that you complete the questionnaires in each round. The reliability of the results could be compromised if people drop out of the study before it is completed. If people drop out because they feel their opinions are in the minority then the final result will overestimate how many participants agree on the topic.

All responses will be anonymous. Only the principal investigator will be aware of your responses as this is needed as part of the Delphi process.

You will have the opportunity to add other outcomes (not listed in the survey) if you feel they are important. The research team will review all new outcomes suggested and if it is agreed that they are new and within the scope of the study then they will be added for everyone to review and rate in the second round.

Please answer all the questions yourself. This should take you a maximum 30 minutes. Don't spend too long on the questions; we are looking for your immediate feelings. The information you provide will remain anonymous. Thank you very much for your time and help with this survey which will help us with future research.

Physical signs (movement, strength, ability) (page 2)

This page lists physical signs that may be affected before and after a treatment for a traumatic brachial plexus injury.

Some of these signs may get better after treatment. Some may get worse or remain the same. Please note these are only possibilities and do not occur in everyone. If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback***' box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Sensation and pain (page 3)

This page lists symptoms that some people may experience before and after a treatment for a traumatic brachial plexus injury.

Some of these symptoms may get better after treatment. Some may get worse or remain the same. Please note these are only possibilities and do not occur in everyone. If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following signs are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback***' box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Neurophysiology and structure of the nervous system (page 4)

This page lists some neurophysiological changes that may occur before and after a treatment for a traumatic brachial plexus injury.

Some of these changes may get better after treatment. Some may get worse or remain the same. Please note these are only possibilities and do not occur in everyone. If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in

studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Activities of Daily Living (page 5)

This page lists activities that can be affected by having a traumatic brachial plexus injury.

If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following activities are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Social well-being (page 6)

This page lists other areas of life that can be affected by having a traumatic brachial plexus injury.

If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Emotional well-being (page 7)

This page lists other areas of life that can be affected by having a traumatic brachial plexus injury.

If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Sleep and overall health (page 8)

This page lists how sleep and overall health can be affected by having a traumatic brachial plexus injury.

If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the

items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Delivery of care (page 9)

This page lists how some aspects of care are delivered for an individual with a traumatic brachial plexus injury.

If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Costs of care (page 10)

This page lists how treatment for a traumatic brachial plexus injury may impact personal and healthcare resources and finances.

If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following outcomes are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Complications (page 11 -14)

This page lists events that may occur during or after treatment for a traumatic brachial plexus injury.

Please note, these are only possibilities and do not occur for everyone. Some of these events are extremely rare. If you have a traumatic brachial plexus injury or treat people with a brachial plexus injury please rate how important you think it is that the following events are assessed during treatment or in studies for traumatic brachial plexus injuries. Select a number between 1 and 9. 1=not important, 9=extremely important. If you feel unable to rate or don't understand what the items refer to then please use the unable to rate column and add your comments in the '***feedback'*** box to tell us why. More information and the medical terminology about each outcome can be obtained by hovering the mouse over each outcome.

Review Ratings (page 15)

Please review your ratings for all the outcomes below. You can change them at this stage, if you wish, before submitting. Once you click NEXT PAGE below you will NOT have the opportunity to change you ratings again. If you want to review previous comments/ feedback you will need to select the appropriate page below and select " Go to". This will direct you to previous pages to amend feedback. Once you are ready click on NEXT PAGE at the bottom of this page. You will have an opportunity to add additional outcomes on the next page.

Additional Outcomes (page 16)

Please add any additional outcomes which you think are important to be assessed during clinical treatment or in studies for a traumatic brachial plexus injury which we have not already included.

Comments (page 17)

Please leave any comments below.

Thank you (page 18)

Thank you for your contribution to this round of the survey. This survey will close on the *date to be inserted*. The research team will analyse the results and feedback to you a summary of yours and other participants scores. Additional outcomes may be added. This will be returned to you within 4 weeks after the close of this survey. You will then have time to review your scores and make changes if you wish.

Please contact the research team on **combinebrachialplexus@gmail.com** if you have any queries.

Appendix 5. 12 Decision making regarding suggested new outcomes Delphi round 1

Outcome name	Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/2020
Physical signs (movement, strength and ability)			
1. Voluntary movement of the arm	To include all active movement of the upper limb, shoulder, elbow, wrist and hand	Active goniometry (therapist)	**Instrument – not outcome**
2. Passive/ assisted movement of the arm	To include all passive movement (by assistance of someone else or other arm) of the upper limb, shoulder, elbow, wrist and hand		
3. Strength of muscles in the arm	The ability of the muscle to generate enough force to work against gravity or resistance or with repetition. For example, torque, endurance or muscle fatigue	Manual muscle test by dynamometer (therapist) Fatiguability of the arm (surgeon)	**Instrument- not outcome** **Duplicate- fatigue already in the hover**
4. The physical appearance of the arm	To include appearance of the muscle in terms of mass/ bulk, appearance of scar and deformities or positions of the arm		
5. Reaching, pulling, pushing, turning or twisting with the arm	For example, pushing a door, opening a jar		
6. Carrying and lifting objects	Lifting, carrying and putting objects down.		
7. Fine hand movement	Picking up, manipulating and releasing with the fingers and thumb. For example, picking up a coins / writing	Ability to write (therapist) Ability to manipulate wallet and manually handle money (therapist)	**Duplicate**

Outcome name		Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/discussion or justification with supervisors (CJH & JC) 07/08/2020
Sensation and pain in the arm				
8.	Ability to feel with the arm	For example, the ability to feel touch, texture, shape and weight	Sensation of the digits (therapist) Sensation in the hand (or maybe it is under sensation in the arm?) (therapist)	**Revise wording of outcome to "Ability to feel with the arm including the hand and fingers"**
9.	Ability to feel in order to protect the arm from injury	The ability to feel to protect the arm from injury from excessive heat, cold or pressure		
10.	Sensation of heaviness in the arm	This includes pulling/dragging of the arm and on the neck		
11.	Pins and needles or tingling in the arm	Paraesthesia		
12.	Pain intensity	How severe the pain is		
13.	Pain duration and frequency	How often pain is present and for how long		
14.	Description of the pain	Pain quality examples include stabbing, piercing, dull etc		
15.	Pain when the arm is exposed to cold	For example, pain in the arm when washing hands in cold water/ going out in cold weather	Cold tolerance symptoms (therapist)	**Duplicate - already an outcome**

	Outcome name	Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/2020
Neurophysiology and structure of nervous system				
16.	The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm.		EMG/method for numerical outcome data in nerve surgery (surgeon) Presence or absence of Tinel (surgeon) A measurement of the functioning and regeneration of the brachial plexus motor and sensory nerves (for example using neurophysiology tests or clinical tests such as Tinels) Advancing Tinel (surgeon)	Already an outcome within the hover- **Duplicate** **Duplicate** **Duplicate**
17.	The structure of brachial plexus using MRI or other techniques	Using imaging such as MRIs to view the structure of the brachial plexus		
18.	A measure of the activity in the movement and sensation areas of the brain.	Integrity and functional representation of the cortical map		
Activities of daily living and work				
19.	Carrying out a daily routine	Include housework, taking care of plants indoors and outdoors, preparing meals	Preparing food and cooking (patient) Ability to cut food (therapist) Ability to prepare meals (surgeon) Ability to make a meal (therapist)	**Duplicate** **Duplicate** **Duplicate** **Duplicate**
20.	Maintaining personal hygiene	Washing, bathing, including use of toilet and sanitary products		
21.	Maintaining personal appearance	For example: Doing hair, doing make up, cutting nails		

Outcome name		Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/2020
Activities of daily living and work				
22.	Putting on and taking off clothes	Including managing fastenings – zips and buttons		
23.	Transport needs	Transport including return to driving cars and motorbikes and others. Includes cycling also		
24.	Return to full duties at previous role in paid employment	Being able to accomplish work tasks		
25.	Return to or begin role in education	Return or begin role as a student in education		
26.	Return to any other paid/non-paid previous role	Includes caring for others, voluntary work		
27.	Return to previous recreational activities	Includes gym, gardening or hobbies	Sports practice (therapist) Sports practising (surgeon)	**Revise wording to include sports, comprehensive wording to include sports**
Social well-being				
28.	Effect on relationship with partner/ spouse	Effect on emotional relationship with partner or spouse		
29.	Effect on relationship with and or ability to care for, children	Effect on emotional relationship and ability to care for children		
30.	Effect on relationship with other family members	Effect on relationship with other family members		
31.	Effect on relationships with friends and neighbours	Effect on relationships with friends and neighbours		
32.	Effects on intimate relationships	For example, interest in and enjoyment of sex, ability to physically participate in sex and sexual confidence	You mentioned intimacy but this should be expanded - sexual acts/ intercourse etc (therapist)	**Duplicate**

Outcome name	Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/2020
Emotional well-being			
33. Emotional distress	Low mood, depression, feelings of anxiety, suicidal thoughts, flashbacks and nightmares	Depression/anxiety particularly in the young (therapist) Anxiety (therapist) Stress (therapist) Depression (therapist) Mood, depression (therapist) Depressive symptoms (surgeon) Mental health monitoring during initial recovery (patient) Screening for depression (therapist) Anxiety/posttraumatic stress (therapist) Psychological state/ PTSD (therapist) Assessment of suicidal ideas (surgeon)	**Revise wording of this section, although anxiety and depression is included within the hover section of the text** **Explain on the page that anxiety and depression included in this**
34. Thoughts and beliefs	Examples include acceptance of injury or outcome, expectations of treatment	Expecting your injured extremity to return to normal (surgeons) Failure to meet expectations/ goals (therapist) Recovery expectations of Clinician/patient (patient)	Expand 34 (thoughts and beliefs) to include expectations as a separate entity
35. Intentions and goals	Examples include: purpose in life, life goals, needs, Intention for physical activity	Client's self-efficacy/motivation (therapist)	**Revise wording to include**

Outcome name		Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/2020
Emotional well-being				
36.	Addictive behaviours (e.g alcohol, medication drugs)	Addictions to include, dependence on medication, alcohol and drugs	Patient's ability to cope with and adapt to the injury (therapist) Coping strategies (esp with pain) (surgeon) Sense of coherence (SOC) (therapist)	**Revise wording to include coping** **Revise wording** **Revise wording**
37.	Body image	Feeling satisfied and confident with one's body	Cortical representation (does the person consider their arm as part of them?) (therapist)	**Duplicate - already included in neurophysiology**
38.	Self-esteem and self-confidence	How someone perceives themselves		
Sleep and overall health				
39.	Overall quality of sleep	To include quality of sleep, ability to sleep and tiredness during the day		
40.	Overall health	Overall health including health related quality of life	Did/does the nerve transfer surgery provide meaningful benefit to quality of life (surgeon)	**Duplicate**

Outcome name		Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/ 2020
Delivery of care				
41.	Patient satisfaction with health care received	Overall patient satisfaction with health care to include provision of information and communication	Clients view of function ability and satisfaction (therapist)	**Duplicate**
42.	Access to and quality of treatment	e.g distance from centre, waiting times, information regarding treatments	Early and correct diagnosis (patient)	**Duplicate**
			Baseline understanding of biological processes (surgeon)	**Duplicate**
			Time of injury more than 6 months without any treatment (surgeon)	**Duplicate**
			Ability of GP/ Dr to refer patient to Specialist quickly (patient)	**Duplicate**
			Access to rehab services following any treatment (patient)	**Duplicate**
			Finding a capable provider early after injury (patient)	
43.	Appropriateness of treatment	Choice of treatment and timing of intervention		
Costs of care				
44.	Out of pocket costs to the patient for outpatient appointments and inpatient care	To include loss of earnings for time taken off work, travel and parking expenses and childcare costs incurred for attending appointments and receiving inpatient treatment		
45.	Costs to the patient from long term loss of individual/ family income	Financial implications on individual/ family income from loss of income from paid work, retraining or studying as a consequence of the brachial plexus injury		

Outcome name		Help text	Suggested additional outcomes by participants in round 1 (stakeholder)	To keep or not to keep/ discussion or justification with supervisors (CJH & JC) 07/08/ 2020
Costs of Care				
46.	Costs to uninsured private paying patients, insurance or other third-party payer (includes national health services) for all out-patient and in-patient care received for a brachial plexus injury including medication	Includes number of admissions to hospital (inpatient or day case) and number of nights stayed		
Complications (muscle and bone)				
47.	Loss of voluntary (active) movement	To include loss of voluntary movement because use of a donor nerve/tendon has resulted in muscle weakness (donor morbidity)	Co contraction limiting movements (therapist) Loss of donor strength post op (therapist) Co-ordination/independence of function of repaired nerves (surgeon)	**Revise wording to more comprehensive outcome at the beginning under voluntary movement to include co-ordination and quality** *"Quality of movement – co-ordination and co contraction "*
48.	Loss of assisted range of motion (stiffness)	To include loss of passive range of movement because of loss of glide of the tendon (tendon tether) or other reasons		
49.	Failure of the bone to unite following bone surgery	Non-union		
50.	Bone uniting in the wrong position	Mal-union		

There were no further suggestions for other complication domains (nerve related, problems with surgical joins and infection or bleeding and breathing)

Appendix 5. 13 Differences between stakeholders' ratings round 3 Delphi

Consensus within groups

Surgeons

51 outcomes reached Consensus ***IN*** 70% or greater rated outcome "critically important" (7-9) AND 15% or fewer rated it as "limited importance" (1-3)

Therapists

44 outcomes reached Consensus ***IN*** 70% or greater rated outcome "critically important" AND 15% or fewer rated it as "limited importance" (1-3)

People with the injury

39 outcomes reached Consensus ***IN*** 70% or greater rated outcome "critically important" AND 15% or fewer rated it as "limited importance" (1-3)

Table 1: Difference in outcomes reaching consensus *IN (end of round 3 Delphi)* between stakeholders

Outcome name	Patients	Surgeons	Therapists
Physical signs (movement, strength and ability)			
Voluntary movement of the arm	✓	✓	✓
Passive/assisted movement of the arm	X	✓	✓
Strength of muscles in the arm	✓	✓	✓
The physical appearance of the arm	X	X	X
Reaching, pulling, pushing, turning or twisting with the arm	✓	✓	X
Carrying and lifting objects	✓	✓	✓
Fine hand movement	✓	✓	✓
Muscle fatigue or endurance	X	X	X
Development of musculoskeletal problems in other parts of the body	X	X	X

Table 1: Difference in outcomes reaching consensus *IN (end of round 3 Delphi)* between stakeholders

	Patients	Surgeons	Therapists
Sensation and pain in the arm			
Ability to feel with the arm	✓	✓	✓
Ability to feel in order to protect the arm from injury	✓	✓	✓
Sensation of heaviness in	REMOVED after ROUND 2		
Pins and needles	X	X	X
Pain intensity	✓	✓	✓
Pain duration and frequency	✓	✓	✓
Description of the pain	✓	✓	✓
Pain when the arm is exposed to cold	X	X	x
Neurophysiology and structure of nervous system			
The ability of the brachial plexus nerves to send signals to the skin and muscles in the arm.	✓	✓	✓
The structure of brachial plexus using MRI or other techniques	X	X	x
A measure of the activity in the movement and sensation areas of the brain.	X	X	x

Table 1: Difference in outcomes reaching consensus *IN (end of round 3 Delphi)* between stakeholders

	Patients	Surgeons	Therapists
Activities of daily living and work			
Carrying out a daily routine	✓	✓	✓
Maintaining personal hygiene	✓	✓	✓
Maintaining personal appearance	X	✓	X
Putting on and taking off clothes	✓	✓	✓
Transport needs	✓	✓	x
Return to full duties at previous role in paid employment	X	✓	x
Return to or begin role in education	X	✓	x
Return to any other paid/non-paid previous role	X	✓	x
Return to previous recreational activities	X	X	x
Ability to eat using utensils/hands	✓	✓	✓
Social wellbeing			
Effect on relationship with partner/spouse	X	✓	✓
Effect on relationship with and or ability to care for, children	✓	✓	✓
Effect on relationship with other family members	X	X	✓
Effect on relationships with friends and neighbours	X	X	x
Effects on intimate relationships	✓	X	✓

Table 1: Difference in outcomes reaching consensus *IN (end of round 3 Delphi)* between stakeholders

	Patients	Surgeons	Therapists
Emotional wellbeing			
Emotional distress	✓	✓	✓
Thoughts and beliefs	X	X	✓
Intentions and goals	X	✓	✓
Addictive behaviours (e.g alcohol, medication drugs)	✓	✓	x
Body Image	X	✓	x
Self-esteem and self-confidence	✓	✓	✓
Ability to cope	✓	✓	✓
Expectations of treatment	✓	✓	✓
Sleep and overall health			
Overall quality of sleep	X	✓	✓
Overall health	✓	✓	✓
Delivery of care			
Patient satisfaction with health care received	X	✓	✓
Access to and quality of treatment	✓	✓	✓
Appropriateness of treatment	✓	✓	✓
Costs of care			
Out of pocket costs to the patient for outpatient appointments and inpatient care	X	X	x
Costs to the patient from long term loss of individual/family income	✓	X	x
Costs to uninsured private patients ……	X	X	X

	Patients	Surgeons	Therapists
Complications (muscle and bone)			
Loss of voluntary (active) movement	✓	✓	✓
Loss of assisted range of motion (stiffness)	✓	✓	✓
Failure of the bone to unite following bone surgery	X	✓	✓
Bone uniting in the wrong position	✓	✓	x
Limited voluntary movement because of the inability to co-ordinate muscles at the same time (co-contraction)	✓	✓	✓
Complications (nerve related)			
Damage to other nerves during the surgery	✓	✓	✓
Worsening of existing pain/pins and needles	✓	✓	✓
Development of pain/pins and needles in a new area of the body	X	✓	x
Increased sensitivity of the scar	X	X	x
Complications (problems with surgical joins and infection)			
A nerve join results in a formation of bundle of painful nerves	✓	✓	✓
Failure of the surgical join of the nerves	✓	✓	✓
Failure of the surgical join of the artery/ vein	✓	✓	✓
Infection in the body part that was operated on	X	✓	✓
Problems with the wound such as infection, failure to heal properly	X	✓	✓
Complications (bleeding and breathing problems)			
Injury to an artery or vein resulting in bleeding where the operation takes place	✓	✓	✓
Bleeding from the wound	X	X	x
Development of a blood clot	✓	✓	✓
Breathing problems	✓	✓	✓
Chest infection	X	X	x

Appendix 6. 1 Search terms MEDLINE (OVID) for systematic review to identify studies evaluating psychometric properties of OMIs mapped to COS-BPI

MEDLINE (OVID) (brachial plexus adj3 injur*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

2 (brachial plexus adj3 pals*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3 (brachial plexus adj3 lesion*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4 brachial plexopath*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

5 (brachial plexus adj3 traction*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

6 (brachial plexus adj3 avulsion*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

AND

7. **Construct carrying out daily routine**: activities of daily living OR function OR daily routine

   Construct pain: pain

   Construct voluntary movement: movement or range of movement or mobility or active movement

AND

8. outcome measurement OR instrument OR patient reported outcome measure OR questionnaire OR patient reported outcome measure (added device for voluntary movement)

Appendix 6. 2 Data extraction for instruments identified in in search 1 (Chapter 3)

Summary of outcome measures categorised in accordance with the ISPROR guidelines (Walton et al., 2015)

1. **Region-specific patient-reported outcome measures**

Five regions specific patient reported outcome measures were identified. They included the Disabilities of the Arm Shoulder and Hand, Upper Extremity Functional Index and the American Shoulder and Elbow score. The ABILHAND is an interview-based questionnaire. Summaries are presented below.

Outcome Measurement Instrument	**Disabilities of the Arm Shoulder and Hand (DASH)**
Authors	Coenen et al. (2013), Hudak et al. (1996)
Type of outcome measure	Region-specific patient-reported outcome measure (whole upper limb)
Mode of administration	Paper-based; Tablet-based app: Telephone not recommended: Not available for smartphone
Items	Thirty- plus two optional modules: work n = 4; sport n = 4
Subscales	Three subscales (Franchignoni et al., 2010) carrying out daily routine; work and sport
Core outcome(s) measured	Carrying our daily routine and pain
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	Novak et al. (2019) evaluated the validity of the factor structure of the DASH questionnaire to assess upper extremity disability in patients with upper extremity nerve injury including people with a BPI (n = 88). A three-factor structure explained the highest variance (60.7 percent), and there was no overlap of items between factors. They categorised each domain with labels related to: (1) light effort tasks (six items); (2) greater effort tasks (15 items); and (3) work/social activity limitations and pain (nine items).
Psychometric properties evaluated in other populations	Yes in numerous different conditions. A recent systematic review of psychometric properties of upper limb instruments concluded that the DASH had adequate validity and reliability in hand , arm and shoulder conditions (Wiitavaara and Florin, 2021). However it lacked evidence of content validity (Wiitavaara and Florin, 2021).
Accessibility and translations	Freely available to download on website, available as app on iPad. Translated into 54 different languages (at time of writing 05/01/22). See website for current list https://dash.iwh.on.ca/available-translations

Outcome Measurement Instrument	**Upper Extremity Functional Index (UEFI)**
Authors	Stratford et al. (2001)
Type of outcome measure	Region-specific patient-reported outcome measure (whole upper limb)
Mode of administration	Paper-based.
Items	Fifteen or 20 questions on a 5-point rating scale (UEFI 15 item and UEFI 20 item)
Subscales	None
Core outcome(s) measured	Carrying out daily routine
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	Hill et al. (2018) the UEFI to evaluate construct validity of the BrAT (BPI condition specific outcome measure). These authors (Hill et al., 2018a) established convergent validity between the BPI condition specific instrument and the UEFI. Correlations between the BPI condition specific measure (BrAT) and UEFI were large (range, 0.6 -0.8), indicating they measure similar constructs (Hill et al., 2018a). The condition -specific measurement (BrAT), but is more responsive to change in the BPI cohort (Zukowski et al., 2017) This study (Hill et al., 2018a) was conducted by the author of the BrAT and also on a small sample (n = 29) of participants with BPI therefore caution is recommended when interpreting the results.
Psychometric properties evaluated in other populations	Test -retest reliability, cross sectional and longitudinal validity has been established in patients with upper extremity dysfunction attending Physiotherapy study (Chesworth et al., 2014). In a group of participants with pre and post op breast cancer surgery (n = 53) Test- retest reliability was high, and the cross-sectional and longitudinal validity coefficients were consistent with expectations related to the extent to which the comparison measures were homogeneous and relevant to activity limitations (Binkley et al., 2018).
Accessibility and translations	Translated from English to Turkish, French Canadian and Spanish.

Outcome Measurement Instrument	**ABILHAND**
Authors	Penta et al. (1998)
Type of outcome measure	Region-specific interview-based questionnaire (whole upper limb)
Mode of administration	Interview-based
Items	Fifty-six items – each rated 1 (very difficult), 2 (difficult) and 3 (easy)
Subscales	None
Core outcome(s) measured	Carrying out daily routine.
BPI patients involved in development	No

Psychometric properties evaluated in BPI population	Hill et al. (2015) assessed whether domains measured by ABILHAND mapped to outcomes adult BPI patients think are important. A range of activities reported by adults with a BPI as limited following injury are under-represented in the ABILHAND (Hill et al., 2015).
Psychometric properties evaluated in other populations	The ABILHAND has been validated in populations with rheumatoid arthritis (Durez et al., 2007) , chronic stroke (Penta et al., 2001), paediatric cerebral palsy (Arnould et al., 2004), systemic sclerosis (Vanthuyne et al., 2009) and neuromuscular diseases (Vandervelde et al., 2010). There are currently versions specifically validated for chronic stroke, rheumatoid arthritis, systemic sclerosis, hand surgery
Accessibility and translations:	Free to download from website http://rssandbox.iescagilly.be/abilhand.html. Available in English, French, Dutch, Italian, Swedish, Brazilian-Portuguese, Chinese, Canadian English, Canadian French, Czech, Hungarian, Polish, Russian, Serbian, Spanish, UK English, Spanish USA, Bulgarian, Austrian German, Swiss German, Swiss-French, Norwegian, Slovak, Argentinian Spanish, Mexican Spanish.

Outcome Measurement Instrument	**American shoulder and elbow surgeons standardised shoulder assessment scale**
Authors	Richards et al. (1994)
Type of outcome measure	Region-specific patient-reported outcome measure (shoulder)
Mode of administration	Paper- based
Items	15
Subscales	3, activities of daily living, pain, instability
Core outcome(s) measured	Carrying our daily routine and pain
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Yes. Psychometric properties of the ASES found acceptable in shoulder instability, rotator cuff and shoulder arthritis populations. (Angst et al., 2008; Bot et al., 2004; Kocher et al., 2005; Oh et al., 2009)
Accessibility and translations	Free. Translated worldwide – translated into Greek and Finnish and numerous other languages

Outcome Measurement instrument	**Modified -American shoulder and elbow surgeons M-ASES questionnaire**
Authors	Beaton and Richards (1998)
Type of outcome measure	Region-specific patient-reported outcome measure (whole upper limb) – The ASES was modified to improve relevance to patients with distal extremity impairments
Mode of administration	Paper-based
Items	15
Subscales	2, activities of daily living and pain
Core outcome(s) measured	Carrying our daily routine and pain
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Yes. The M-ASES demonstrated acceptable responsiveness and reliability when tested with respondents with shoulder dysfunction (Beaton and Richards, 1998). Factor analysis demonstrated multidimensionality (wrist, hand and shoulder dysfunction). Most items demonstrated excellent discrimination (Cook et al., 2008).
Accessibility and translations	Free. Translated worldwide – translated into Greek and Finnish and numerous other languages

Outcome Measurement Instrument	**Simple Shoulder Test (SST)**
Authors	Lippitt (1993)
Type of outcome measure	Region-specific patient-reported outcome measure (shoulder)
Mode of administration	Paper-based
Items	12 item
Subscales	Pain (n = 2), function (n = 7) and motion (n = 3)
Core outcome(s) measured	Voluntary movement, carrying out daily routine, pain
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Excellent convergent validity between the SPADI and the SST in a shoulder disorder population (Roddey et al., 2000) population. Roddey et al. (2000) established that the SST had internal consistency in shoulder instability and rotator cuff injury populations. The SST has excellent construct validity and responsiveness in the shoulder arthroplasty, shoulder instability and rotator cuff population (Godfrey et al., 2007; Roy et al., 2010a).
Accessibility and translations	Free and translated into Spanish, Portuguese, Persian

Outcome Measurement Instrument	**Michigan Hand Questionnaire**
Authors	Chung et al. (1998)
Type of outcome measure	Region-specific patient-reported measure (hand only)
Mode of administration	Paper-based
Items	37
Subscales	6 (satisfaction, pain, daily living, work, function and aesthetics)
Core outcome(s) measured	Pain (intensity), carrying out daily routine, voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	The function and work domains show excellent fit to the Rasch model in people with rheumatoid arthritis (Jayaram et al., 2021). A systematic review of papers (Shauver and Chung, 2013). evaluating its psychometric properties identified the Michigan Hand Questionnaire has high test-retest reliability (all papers report >0.85 for ICC) ad high internal consistency (average of 0.89 with minimum value of 0.8). Correlations between test scores and patients report of improvement and other tests are always high (Shauver and Chung, 2013) Much higher responsiveness for acute conditions with quick changes and low responsiveness for long-term conditions (Shauver and Chung, 2013).
Accessibility and translations	The Michigan Hand Outcomes Questionnaire is copyright owned and can be licensed or used with permission from the University of Michigan.

Outcome Measurement Instrument	**University of California Los Angeles shoulder score**
Authors	Amstutz et al. (1981)
Type of outcome measure	Region-specific combined patient-reported, and clinician-assessed measure (shoulder only)
Mode of administration	Online, tablet or paper-based
Items	5 items
Subscales	0
Core outcome(s) measured	Pain and carrying out daily routine
BPI patients involved in development	No methods described in development and not patients included
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Minimal studies on psychometric properties
Equipment needed	Goniometer
Accessibility and translations	Freely available

Outcome Measurement Instrument	**Constant-Murley sore (CMS)**
Authors	Conboy et al. (1996)
Type of outcome measure	Region-specific combined patient-reported, and clinician-assessed measure (shoulder only)
Mode of administration	Paper-based
Items:	10
Subscales	Four (Pain, activities of daily living, strength and range of movement)
Core outcome(s) measured	Pain, carrying out daily routine and voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Several studies confirmed a good reproducibility, responsiveness and construct validity of the scor es (Hirschmann et al., 2010). The Constant-Murley score correlates strongly with shoulder specific questionnaires (Roy et al., 2010b)
Equipment needed	The score needs a specific method to measure strength with spring balance attached to distal forearm
Accessibility and translations	The Constant-Murley score is used in almost every language without official translations. In French, a validated translation has been published. The time needed to complete the Constant-Murley test is between 5 to 7 minutes.

Outcome Measurement Instrument	**MAYO Elbow Performance Index**
Authors	Longo et al. (2008)
Type of outcome measure	Region-specific combined patient-reported, and clinician-assessed measure (elbow only)
Mode of administration	Paper-based
Items:	4
Subscales	4 (Pain, daily function, range of motion, stability)
Core outcome(s) measured	Pain (intensity), carrying out daily routine, voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Few studies conducted on psychometric properties and none in BPI
Equipment needed	Goniometer
Accessibility and translations	Easy to conduct.

2. Region-specific performance-based outcome measures

Outcome Measurement Instrument	Upper limb module questionnaire (ULM)
Authors	Mazzone et al. (2011)
Type of outcome measure	Region-specific performance-based outcome measure (whole upper limb)
Items	22
Subscales	0
Core outcome(s) measured	Voluntary movement, carrying out daily routine
BPI patients involved in development	No
Psychometric properties evaluated	Evaluated and developed within the spinal muscular atrophy population
Equipment needed	200g, 500g and 1kg weights, pencil, paper, buttons and cup
Accessibility and feasibility	Freely available

Outcome Measurement Instrument	Action Reach Arm Test (ARAT)
Authors	Lyle, (1981)
Type of outcome measure	Region-specific performance-based (whole upper limb)
Items	19
Subscales	4 (grasp, grip, pinch and gross movement)
Core outcome(s) measured	Voluntary movement, carrying out daily routine
BPI patients involved in development	No. Developed for stroke, brain injury and multiple sclerosis populations. Aged 13 and over
Psychometric properties evaluated	Inter rater reliability in Parkinson's, concurrent and predictive validity and responsiveness in stroke (studies not reviewed for quality)
Equipment needed	Chair, table, wooden blocks, ball, sharpening stone, washer and bolts, glasses, marbles, ball hearings, tin lid.
Accessibility and feasibility	Lengthy to carry out

Outcome Measurement Instrument	Jebsen-Taylor Hand Function Test
Authors	Jebsen et al. (1969)
Type of outcome measure	Region-specific performance-based outcome measure (hand only)
Items:	7 items
Subscales	0
Core outcome(s) measured	Carrying out daily routine
BPI patients involved in development	No
Psychometric properties evaluated	Yes, in numerous hand conditions but not BPI
Equipment needed	Stopwatch, chair, desk, paper, clipboard, can, paper clips, bottle caps, coins, kidney beans, wooden checkers. A test kit including all items can be purchased.
Accessibility and feasibility	Takes 15-45 minutes. Shorter times indicate better performance. Readily available materials

Outcome Measurement Instrument	Southampton Hand Assessment Procedure
Authors	Light et al. (2002)
Type of outcome measure	Region-specific performance-based outcome measure (hand only)
Items	26
Subscales	0
Core outcome(s) measured	Carrying out daily routine
BPI patients involved in development	No
Psychometric properties evaluated	Few studies have evaluated psychometric studies
Equipment needed	The SHAP test kit
Accessibility and feasibility	Expensive equipment (£2,500 plus package and shipping)

Outcome Measurement Instrument	Purdue Peg test
Authors	Tiffin and Asher, (1948)
Type of outcome measure:	Region-specific performance-based outcome measure (hand only) – measures manual dexterity
Items	N/A
Subscales	0
Core outcome(s) measured	0
BPI patients involved in development	No
Psychometric properties evaluated	Not in BPI population Studies conducted evaluating reliability and validity in patients with stroke, brain injury, Parkinsons
Equipment needed	The Purdue Peg test kit.
Accessibility and feasibility	Cost £188.56 as of 01/11/21 Quick and easy to conduct

Condition-specific patient-reported outcome measures

Outcome Measurement Instrument	Trinity Amputation and Prosthesis scale
Authors	Gallagher and MacLachlan (2000)
Type of outcome measure	Patient-reported condition-specific outcome measure (upper limb amputation)
Mode of administration	Self- administered
Items	23
Subscales	9 (3 psychosocial subscales: general adjustment, social adjustment, and adjustment to limitation plus 3 activity restriction subscales: functional activity restriction, social activity restriction, and athletic activity restriction plus there are 3 additional subscales that assess satisfaction with the prosthesis)
Core outcome(s) measured	Pain, carrying out daily routine
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No. The factor structure was evaluated in adults with upper limb amputations. It was not specific to a BPI (Desmond and MacLachlan, 2005)

Psychometric properties evaluated in other populations	Yes, only in the upper and lower limb amputation population (Desmond and MacLachlan, 2005; Gallagher and MacLachlan, 2000)
Accessibility and translations	Freely available from authors on request.

Outcome Measurement Instrument	**The Brachial Assessment Tool (BrAT)**
Authors	(Hill et al., 2016)
Type of outcome measure	Patient-reported condition-specific outcome measure (BPI).
Mode of administration	Self-administered, paper-based.
Items	31
Subscales	3 subscales; Dressing and grooming (8 items); Arm and Hand items (16); No hand items (6)
Core outcome(s) measured	Carrying out daily routine
BPI patients involved in development	Yes
Psychometric properties evaluated in BPI population	Construct validity and responsiveness in BPI population (Hill et al., 2018b) Internal construct validity and unidimensionality in BPI population (Hill et al., 2016) Reproducibility (Hill et al., 2018b)
Psychometric properties evaluated in other populations	No
Accessibility and translations	Freely available – need to let author know it is being used.

Outcome Measurement Instrument	**The Impact of Brachial Plexus Injury Questionnaire (IMBPIQ)**
Authors	Mancuso et al. (2018)
Type of outcome measure	Patient-reported condition-specific measure (BPI)? also population specific as pre and post op.
Mode of administration	Self- administered, paper-based.
Items	43 items
Subscales	*Symptoms, limitations, emotion and improvement.* A score can be generated for each subscale according to the scoring instructions. An overall disability domain score also can be calculated as the mean of symptoms, limitations and emotion subscales.
Core outcome(s) measured	Pain, carrying out daily routine, (plus one from level 2 emotions).
BPI patients involved in development	Yes, qualitative study with patients exploring expectations following a BPI (Mancuso et al., 2015) This included 23 participants, 10 preoperative patients and 13 post-operative patients. Themes from qualitative study became items for the draft questionnaire and phrased using patient's terminology.
Psychometric properties evaluated in BPI population	To establish **test-retest reliability**, patients completed the same version of the questionnaire twice, several days apart (Mancuso et al., 2018). In most cases, the first administration occurred during an in-person interview and the second, during a

	telephone interview. To address external validity, patients also completed the DASH, the RAND-36, and the global "delighted-terrible" question at the time of the first interview. A sample size of 50 (23 pre-operative and 27 post-operative).
Psychometric properties evaluated in other populations	No
Accessibility and translations	Freely available to use. Not yet translated.

Condition-specific performance-based outcome measures

Outcome Measurement Instrument	**University of New Brunswick Test of Prosthetic Function for Unilateral Amputees (UNB)**
Authors	Sanderson and Scott (1985)
Type of outcome measure	Performance-based condition-specific measure (upper limb amputation).
Items	30
Subscales	3
Core outcome(s) measured	Carrying out daily routine
BPI patients involved in development	Originally validated in a population aged 11-1. It has been validated in adults with amputations (Resnik et al., 2013b)
Psychometric properties evaluated	Not in BPI
Equipment needed	Paper, tape, scissors, thread, button, needle, knife and fork, floor brush, dish cloth, jar, box of matches, paper punch, binder folder, can with metal pull.
Accessibility and feasibility	Freely available from https://limbclinic.com/unb-prosthetic-test.php. Lengthy to conduct, may require training

Outcome Measurement Instrument	**Activities Measure for Upper Limb Amputees**
Authors	(Resnik et al., 2013a)
Type of outcome measure	Performance-based condition-specific measure (upper limb amputation)
Items	18
Subscales	0
Core outcome(s) measured	Carrying out daily routine
BPI patients involved in development	No, no patients involved in development. Authors acknowledge lack of content validity
Psychometric properties evaluated	Original development included evaluation of internal consistency, interrater reliability, test-retest reliability and convergent validity.
Equipment needed	Hairbrush, shoes, cup, fork, spoon, bottle with fluid in, pencil, paper, scissors, phone, hammer, towel.
Accessibility and feasibility	Freely available, lengthy to conduct.

Condition specific clinician-reported outcome measures

Outcome Measurement Instrument	The EFFUL (Evaluation of Function in the Flail Upper Limb)
Authors	Eggers and Mennen (1997)
Type of outcome measure	Clinician-assessed condition-specific outcome measure (BPI)
Items	7
Subscales	0
Core outcome(s) measured	Carrying out daily routine, voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated	Developed in 1997 by Eggers & Mennen (1997) in South Africa as a system to measure improvement after reconstructive surgery for people with a BPI. The EFFUL system attempts to classify upper limb function. The evaluation by the EFFUL system uses everyday tasks in the testing procedure (Eggers and Mennen, 2001). Unable to identify any
Equipment needed	EMG biofeedback instrument, goniometer, dynamometer, pinch gauge, weights.
Accessibility and feasibility	Available in original papers (Eggers and Mennen, 2001, 1997)

Domain-specific patient-reported outcome measures

Outcome Measurement Instrument	**Visual Analogue Scale (pain)**
Authors	VAS was first been used to assess pain by Woodforde and Merksey (1972)
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Self-administered, paper-based or electronic
Items	1
Subscales	0
Core outcome(s) measured	Pain (intensity)
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Psychometric properties have been assessed in a variety of rheumatic conditions but not BPI. As the distance between 'no pain' and the patient-made mark has to be measured, scoring is more time-consuming and susceptible to measurement errors than a rating scale
Accessibility and translations	Freely available at no cost. Takes less than a minute to complete. No training required.

Outcome Measurement Instrument	**Numerical Pain Rating Scale**
Authors	Unclear
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Self-administered, paper-based or electronic. It can also be administered verbally and used in telephone interviews.
Items	1 (The numerical pain rating scale (NPRS) is a 21-point horizontal scale ranging from 0 to 10 in increments of 0.5, with higher numbers indicating greater severity (Jensen et al., 1994, 1986)
Subscales	0
Core outcome(s) measured	Pain
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Numerical Rating Scales have shown high correlations with other pain-assessment tools in several studies (Haefeli and Elfering, 2006). Compared to the VAS, it is simpler to complete, faster to score and less susceptible to measurement error (Hjermstad et al., 2011; Van Tubergen et al., 2002). Has high correlations with other pain-assessment tools in several studies (Haefeli and Elfering, 2006). Compared to the VAS, it is simpler to complete, faster to score and less susceptible to measurement error (Hjermstad et al., 2011; Van Tubergen et al., 2002). There is evidence in other pain conditions that its measurement properties are satisfactory (Hawker et al., 2011; Hjermstad et al., 2011).There is also some evidence that patients prefer the NRS (Ye et al., 2020).
Accessibility and translations	Takes less than a minute to complete. Easy to score. The feasibility of its use and good compliance have also been proven (Haefeli and Elfering, 2006). However, results cannot be treated as ratio data as in VAS/GRS (Haefeli and Elfering, 2006).

Outcome Measurement Instrument	**Wong Baker Faces rating scale (pain)**
Authors	Baker and Wong (1987)
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
	Self-administered on paper or electronically.
Items	1
Subscales	0
Core outcome(s) measured	Pain (intensity)
BPI patients involved in development	0
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Originally developed for children. Recently amendments have been made and cross-cultural validity has been examined for adults (Atisook et al.,

	2021)
Accessibility and translations	Licencing fee for healthcare organisations

Outcome Measurement Instrument	**Brief pain inventory short form (BPI-SF)**
Authors	Cleeland (1989)
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Paper -based , self -administered
Items	9
Subscales	0
Core outcome(s) measured	Pain (intensity/severity)
BPI patients involved in development	No (667 patients with cancer and 32 patients with rheumatoid arthritis)
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated	The psychometric properties of the tool have been analysed in a range of populations with cancer and non-cancer related pain, including nociceptive and neuropathic pain. See section 6.4.7 in Chapter 6 for more detail
Accessibility and translations	Permission routinely given for free use

Outcome Measurement Instrument	**Neuropathic pain symptom inventory**
Authors	Bouhassira et al. (2004)
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Self – administered paper or electronic based
Items	12
Subscales	5
Core outcome(s) measured	Pain (quality, duration, frequency, sensitivity to touch, sensitivity to cold)
BPI patients involved in development	No but has been validated in people with spinal cord Injuries and other people with neuropathic pain
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Validated in over 50 different languages (Bouhassira et al., 2004; Haanpää et al., 2011)
Accessibility and translations	Need to register to use, licenced and there may be a fee

Outcome Measurement instrument	**University of Washington Neuropathic score**
Authors	Unclear
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Paper or electronic based
Items	10
Subscales	0

Core outcome(s) measured	Pain (neuropathic pain intensity)
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Unable to find any studies on psychometric properties
Accessibility and translations	Unclear

Outcome Measurement Instrument	**McGill Pain Questionnaire**
Authors	Melzack (1975)
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Self -administered, paper or electronic -based.
Items:	20. The sensory intensity, the emotional impact and the cognitive evaluation of pain. Patients are presented with 78 adjectives in 20 groups and are instructed to select one from each group for the particular groups that most closely match their own pain experience. An overall score for each major dimension is obtained from the sum of either weighted scores or the ranks of the chosen word within the group.
Subscales	3 (sensory intensity, emotional impact and cognitive evaluation of pain)
Core outcome(s) measured	Pain (quality and intensity)
BPI patients involved in development	0
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations:	Validated for patients with cancer, chronic pelvic pain, fibromyalgia, headaches, herniated intervertebral discs, ischemic muscular pain, low back pain, lumbago-sciatica, orthodontics/dental pain, post-operative complications, rheumatic pain, trigeminal neuralgia and atypical facial pain, vulvar pain
Accessibility and translations	Fees may apply to funded academic users and healthcare organisations. Easy to score adding values associated with words. Takes up to 30 minutes to complete.

Outcome Measurement Instrument	**McGill Pain Questionnaire (short form version 2)**
Authors	Dworkin et al. (2009), Melzack, (1987, 1975)
Type of outcome measure	Domain-specific patient-reported outcome (pain intensity)
Mode of administration	Paper or electronic
Items	16
Subscales	3 (Sensory subscale with 11 words, and Affective subscale with 4 words from the original MPQ and pain intensity VAS)
Core outcome(s) measured	Pain (intensity, quality)
BPI patients involved in development	0

Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated	The test-retest reliability of the questionnaire has been evaluated in populations with a variety of conditions, such as osteoarthritis and musculoskeletal pain. Its validity and responsiveness has also been evaluated.
Accessibility and translations	The SF-MPQ has been translated into 53 languages. The use of the McGill Short Form Questionnaire-2 is administered by the MAPI Research Trust.

Domain-specific clinician-reported outcome measures

Outcome Measurement Instrument	**Goniometry**
Authors	Unclear
Type of outcome measure	Clinician-reported domain-specific outcome measure
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	0
Psychometric properties evaluated	Yes, in several upper limb joints (Reese and Bandy, 2016)
Equipment needed	Goniometer
Accessibility and feasibility	Easily accessible and cheap to purchase. Little training needed.

Outcome Measurement Instrument	**Estimation of range of movement**
Authors	Unclear
Type of outcome measure	Clinician-reported domain-specific outcome measure
Items	N/A
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	0
Psychometric properties evaluated	Yes, in several upper limb joints (Reese and Bandy, 2016)
Equipment needed	None
Accessibility and feasibility	Easily accessible and cheap to purchase. Little training needed.

Outcome Measurement Instrument	**First web space in centimeters**
Authors	Unclear
Type of outcome measure	Clinician-reported domain-specific outcome measure (voluntary movement)
Items	N/A
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	0
Psychometric properties evaluated	Reliability evaluated against other measurements (Murugkar et al., 2004)

Equipment needed	Tape measure
Accessibility	Easily accessible and cheap to purchase. Little training needed.

Outcome Measurement Instrument	**Total active movement**
Authors	Unclear
Type of outcome measure	Clinician-reported domain-specific outcome measure (voluntary movement)
Items	N/A
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	0
Psychometric properties evaluated	Unable to identify any studies
Equipment needed	Goniometer
Accessibility and feasibility	Easily accessible and cheap to purchase. Little training needed.

Outcome Measurement Instrument	**Pulp to palm distance**
Authors	Unclear
Type of outcome measure	Clinician-reported domain-specific outcome measure (voluntary movement)
Items	N/A
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	0
Psychometric properties evaluated	Macdermid et al. (2001) evaluated the validity of pulp to palm measurements in patients (n = 50) with finger dysfunction and found that goniometry measurement had a stronger correlation with upper limb disability. However, both types of range of motion measurements were able to discriminate between minimal and substantial upper extremity disability. Further methodological evaluation is required to support the use of pulp-to-palm distance measures as an outcome indicator.
Equipment needed	Tape measure
Accessibility and feasibility	Easily accessible and cheap to purchase. Little training needed.

Outcome Measurement Instrument	**3D motion capture in lab**
Authors	Webber et al. (2019)
Type of outcome measure	Domain-specific clinician-reported/biomarker (voluntary movement)
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated	No
Equipment needed	Expensive lab equipment needed
Accessibility and feasibility	Expensive and extensive training needed to conduct and analyse the results.

Outcome Measurement Instrument	Dynamic shoulder radiographic analysis
Authors	Shimoe et al. (2017)
Type of outcome measure	Domain-specific clinician-reported (voluntary movement)
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated in the BPI population	Adequate test retest, intra-examiner and inter-examiner reliability (n = 20)
Equipment needed	X-Ray machine
Accessibility and feasibility	Expensive machinery needed, extensive training needed to conduct, not feasible in everyday clinical practice and risk of radiation.

Outcome Measurement Instrument	Accelerometery
Authors	Nazarahari et al. (2021)
Type of outcome measure	Biomarker domain-specific (voluntary movement)
Core outcome(s) measured	Voluntary movement
BPI patients involved in development	No
Psychometric properties evaluated in the BPI population	Nazarahari et al. (2021) accelerometery had adequate convergent validity. They compared the kinematic scores obtained by inertial measurement units (IMUs) by comparing them against patient reported outcome measures (i.e. SST and DASH) (n=15).
Equipment needed	Accelerometery equipment
Accessibility and feasibility	Costly to invest as would need individual accelerometery equipment for each patient. Training, time and software needed to analyse the results.

Domain-specific patient-reported outcome measures

Outcome Measurement Instrument	PROMIS 5 item neuropathic pain questionnaire
Authors	Askew et al. (2016)
Type of outcome measure	Patient-reported domain-specific outcome measure (pain)
Mode of administration	Paper or electronic based surveys, computer adaptive testing (CAT)
Items	5
Core outcome(s) measured	Pain (quality)
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Yes, validated in diabetic neuropathy, chemotherapy induced neuropathy, osteoarthritis, rheumatoid arthritis (Askew et al., 2016)
Accessibility and translations	Freely available to use in a paper-based form http://healthmeasures.org/. Electronic interfaces are needed to deliver CATs in clinical environment or patient home. Available in Bengali, Czech, Georgian, Hindi, Nepali, Odia, Punjabi, Romanian, Sinhala and Xhosa

Outcome Measurement Instrument	DN4 (Douleur Neuropathique 4)
Authors	Bouhassira et al. (2005)
Type of outcome measure	Combined patient and clinician-reported domain specific
Mode of administration	Clinician administered questionnaire
Items	10 (items pain quality, 3 items clinician assessed sensation
Core outcome(s) measured	Pain (and sensation)
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Not in BPI population
Accessibility and translations	Translated in 85 different languages. Freely available use for clinical use by healthcare professionals.

Outcome Measurement Instrument	Brachial Plexus Pain scale
Authors	Bonilla et al. (2011)
Type of outcome measure	Clinician-administered questionnaire (interview) domain specific (pain)
Mode of administration	Paper based
Items	6
Core outcome(s) measured	Pain
BPI patients involved in development	No
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	No
Accessibility and translations	Available in original paper (Bonilla et al., 2011)

Generic patient-reported outcome measures

Outcome Measurement Instrument	36 item short form survey (SF36)
Authors	Ware and Sherbourne (1992)
Type of outcome measure	Patient-reported generic outcome measure
Mode of administration	Paper-based
Items	36
Subscales	2 (physical and mental)
Core outcome(s) measured	Carrying out daily routine, pain
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Reliable in people with schizophrenia and long-term survivors of childhood cancer. Valid in the following populations: schizophrenia, stroke, community dwelling elderly, mobility disability, COPD

Accessibility and translations	The SF-36; it is both licensed (Optum) and available freely online (Rand). Available in multiple languages

Outcome Measurement Instrument	**Patient Specific Functional Score**
Authors	Stratford et al. (2009)
Type of outcome measure	Patient-reported generic outcome measure
Mode of administration	Interview-based
Items	5
Scale (subscales)	1
Core outcome(s) measured	Carrying out daily routine
Psychometric properties evaluated in BPI population	Novak et al. (2013) evaluated the validity of the Patient Specific Functional Scale (PSFS) in patients with upper extremity nerve injury (n=157). A small number of patients with BPI (39%) were included in the study. The study provided evidence of construct validity in the upper limb nerve injury population.
Psychometric properties evaluated in other populations	The validity, reliability, and responsiveness of the PSFS has been examined for patients with back, neck, knee and upper extremity problems. It has also been shown to have a high test-retest reliability in both generic lower back pain and knee dysfunction issues. It is also clinically responsive to changes over time with chronic pain patients. The quality of these studies has not been examined.
Accessibility and translations	Quick to complete. Relatively easy for patients to complete

Outcome Measurement Instrument	**Canadian Occupational Performance Measure**
Authors	Law et al. (1990)
Type of outcome measure	Patient-reported generic outcome measure
Mode of administration	Clinician- administered
Items	5
Subscales	2 (Performance and satisfaction)
Core outcome(s) measured	Carrying out daily routine
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	The psychometric properties of the COPM have been widely tested. In a literature review including 19 methodological studies conducted on various target groups, the authors conclude that the COPM is a valid, reliable (test–retest), responsive, and feasible instrument (Carswell et al., 2004)
Accessibility and translations	Licenced and needs funding to use. Quick to complete and little training needed.

Outcome Measurement Instrument	**The WHOQoL -bref**
Authors	Harper et al. (1998)
Type of outcome measure	Patient-reported generic outcome measure

Mode of administration	Self -administered but can be interview -assisted or interview administered.
Items	26
Subscales	Physical health, psychological, social relationships and environment, overall quality of life and general health.
Core outcome(s) measured	Carrying out daily routine
Psychometric properties evaluated in BPI population	No
Psychometric properties evaluated in other populations	Evaluation of psychometric properties report satisfactory validity and reliability and in a wide variety of health conditions (Skevington et al., 2004)
Accessibility and translations	Raw scores need to be converted to transformed scores to calculate overall score. Over 100 culturally adapted translations are available.

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Appendix 6. 3 Results from meeting with Clinical Advisory Group regarding OMIs used

Participants at the health professional meeting (n=22) included occupational therapists and physiotherapists who treat people with BPI.

Measures identified from international therapy meeting

Voluntary movement:

The following measures were discussed as measures currently used: visual estimation, goniometry, myrin goniometry for the hand

Measurement suggested	Downloaded	Evidence of BPI involvement in development or later psychometric ax in population
Digit flexion measuring with tape (in cm) tip of worst finger to palm for general hand flexion	Unclear about where original documentation	None found
Measuring web space: measuring with tape in cm distal nail bed of thumb to distal nail bed of index finger	Unclear about where original documentation	None found
Video assessment (used by several centres) particularly since COVID	Previously identified in original review	None found

Several members of the meeting signposted to two books used to support their practice and to ensure standardised measurement of voluntary movement. These included the American Society of Hand Therapists (ASHT) published measurement in the hand. A similar version in Sweden and “Fundamentals of musculoskeletal assessment techniques” by Palmer, Epler.

Pain

The group discussed what they used to measure pain. The following instruments were noted as measures used. The most frequently used instrument was the Brief Pain Inventory which many agreed was easy to use, score and they reported patients found it easy to complete in the clinic.

Measurement suggested	Downloaded	Evidence of BPI involvement in development or later psychometric ax in population
Brief pain inventory	Previously identified in original literature review	No
DN4	Yes	No
5 item PROMIS questionnaire	Yes	No
Short McGill and long McGill	Previously identified in literature review	No

Numerical rating scale	Previously identified in literature review	No

DN4: *Douleur Neuropathique 4*

Carrying out daily routine

The BrAT and the DASH/Quick DASH were used by most people in the meeting. The Canadian Occupational Performance Measure (COPM) and Patient Specific Functional Scale were also being used. The COPM was added to the inventory of outcome measures identified.

Appendix 6. 4 The Brachial Assessment Tool

Patient label

The Brachial Assessment Tool (BrAT)

Date:

We are interested to know how you are using your arm/hand to do the activities listed below.

Please provide an answer for all activities by marking the number under the appropriate response. Your clinician will explain which items to answer.

Subscale 1: Dressing and grooming items

	Activity	Cannot do now	Very hard to do now	A little hard to do now	Easy to do now
1	Use both arms to put on a T-shirt	0	1	2	3
2	Use both arms to put on a pair of trousers	0	1	2	3
3	Use both hands to put on socks	0	1	2	3
4	Use both hands to put toothpaste on a toothbrush	0	1	2	3
5	Use both hands to do up belt buckle	0	1	2	3
6	Tuck your shirt in using your **affected** hand	0	1	2	3
7	Use both hands to do up shirt buttons	0	1	2	3
8	Use both hands to do up tight trouser buttons e.g. jeans	0	1	2	3
	Column Totals:				
				Subscale 1 Total	

Subscale 2: Arm and hand items

	Activity	Cannot do now	Very hard to do now	A little hard to do now	Easy to do now
9	Wash both hands at same time	0	1	2	3
10	Use both hands to push a pram, lawnmower or shopping trolley	0	1	2	3
11	Use both hands to do up zip including putting ends together	0	1	2	3
12	Use both hands to spread butter or jam on a piece of bread	0	1	2	3
13	Use both hands to tie up a rubbish bag and put in the bin	0	1	2	3
14	Use both hands to tie up shoe laces	0	1	2	3
15	Use a knife and fork at the same time	0	1	2	3
16	Carry an object only using your **affected** arm so your other arm/hand is free to do another task	0	1	2	3
17	Pick up a small object with the fingers of your **affected** hand eg a tablet, coin or pen	0	1	2	3
18	Hold a pot of food with 1 hand and stir it with the other	0	1	2	3
19	Use both arms/hands to change the sheet on a bed	0	1	2	3
20	Use both hands to wash your face	0	1	2	3
21	Use both arms to peg clothes on the washing line	0	1	2	3
22	Use both hands to type on a keyboard	0	1	2	3
23	Turn on a light switch using only your **affected** arm	0	1	2	3
24	Use your **affected** hand to wash your other armpit	0	1	2	3
25	Use both arms to lift a box or bag onto a shelf at eye level	0	1	2	3
	Column Totals:				
				Subscale 2 Total	

PLEASE TURN PAGE OVER

Subscale 3: No hand items

	Activity	Cannot do now	Very hard to do now	A little hard to do now	Easy to do now
26	Maintain control of your **affected** arm so you don't need to wear a sling	0	1	2	3
27	Hold an object between your **affected** upper arm and your chest wall, e.g. a book	0	1	2	3
28	Hold an object draped over your **affected** forearm, e.g. an article of clothing	0	1	2	3
29	Stabilize an object with your **affected** arm while you manipulate it with your other hand	0	1	2	3
30	Lift your **affected** arm to put it through the sleeve of a shirt	0	1	2	3
31	Roll over when sleeping without having to wake to move your **affected** arm	0	1	2	3
	Column Totals:				
				Subscale 3 Total	

Clinician. Scores can be generated as one summed total or 3 separate subscales:

Subscale 1 Dressing items: Sum column totals items 1 – 8: __/24

Subscale 2 Arm and hand items: Sum column totals items 9 – 25: __/51

Subscale 3 No hand items: Sum column totals items 26 – 31: __/18

Summed score: Sum all column totals for a raw score: __/93

Complete this section only if you injured your writing arm (DO NOT ADD to summed score)

Using **only your affected arm / hand** how easy or hard is it for you to perform these day-to-day activities.

Activity	Cannot do now	Very hard to do now	A little hard to do now	Easy to do now
Brush your teeth with your **affected** arm	0	1	2	3
Write with a pen or pencil with your **affected** arm	0	1	2	3
Use a computer mouse with your **affected** hand	0	1	2	3
Wipe yourself after going to the toilet with your **affected** arm	0	1	2	3
Column Totals:				

The BrAT is freely available for use; however, to enable ongoing evaluation we request that you please notify Bridget Hill at bridget.hill@epworth.org.au if you are using this tool so that dissemination and uptake can be tracked.

Appendix 6. 5 The Brief Pain Inventory

STUDY ID #:_____ DO NOT WRITE ABOVE THIS LINE HOSPITAL #:_____

Brief Pain Inventory (Short Form)

Date: ____/____/____ Time: _____

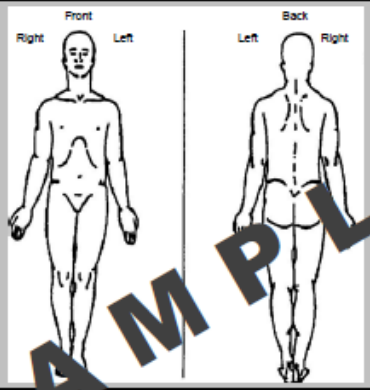
Name: _____ _____ _____

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these every-day kinds of pain today?

1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain at its least in the last 24 hours.

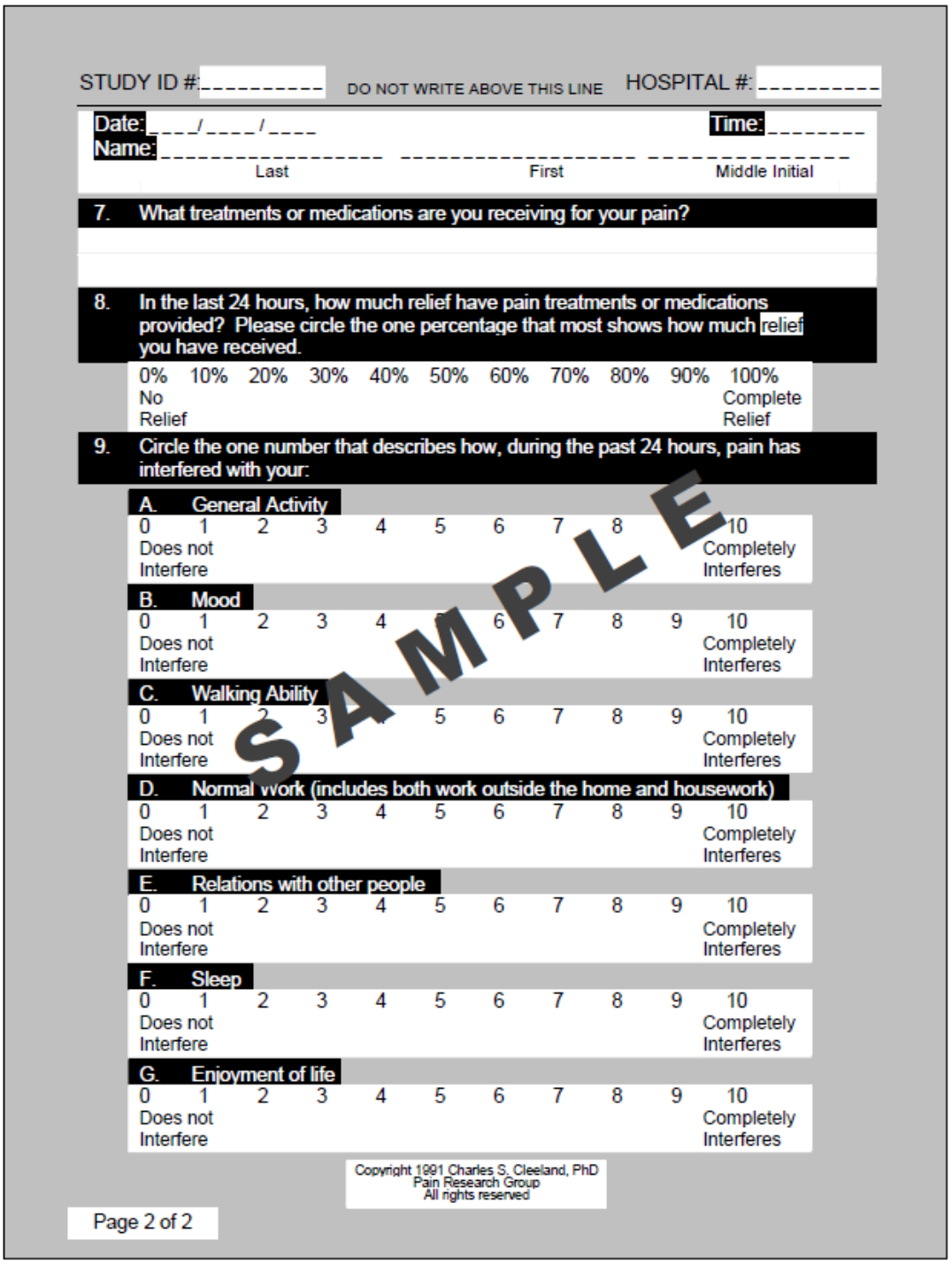
0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine



STUDY ID #:_____ DO NOT WRITE ABOVE THIS LINE HOSPITAL #:_____

Date: ___/___/____ Time: _____

Name: _____ _____ _____

Last First Middle Initial

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% No Relief 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% Complete Relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

B. Mood

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

C. Walking Ability

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

E. Relations with other people

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

F. Sleep

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

G. Enjoyment of life

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

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