Juvenile Idiopathic Arthritis: Quality of Life and Parent Experiences of Giving Methotrexate Injections

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Thesis Portfolio Abstract

Background: Juvenile Idiopathic Arthritis (JIA) is a chronic autoimmune condition, that causes joint pain and inflammation in young people. A diagnosis of JIA brings with it a unique set of challenges including treatment regimes, parental stress, and physical limitations. Although there is no cure, it is typically managed with immunosuppressant medication, the most common being the medication Methotrexate (MTX). However, whilst MTX is the recommended gold standard treatment (NICE, 2014) it can be challenging to administer and the commonly associated side effects, such as significant nausea, can lead to emotional difficulties and have a negative impact on a young person's Quality of Life (QoL), however without it, there can be long term implications to health and QoL. The role of supporting a young person with these difficulties often lies with the parents, who play a crucial role in supporting a young person practically and emotionally. Despite this, little is known about the QoL for young people with JIA, the experiences of parents supporting their child with treatment, and how best clinicians could support them. This thesis was developed based on the experiences of clinical staff working within a JIA clinic, who were interested in these difficulties and how best to support these families.

Aims: First, this thesis aims to better understand the QoL for young people living with JIA through a systematic review of the evidence to date. Second, the thesis will explore the experiences of parents who administer MTX to their children as a treatment for JIA, with a view to better understanding the role of the parent in supporting the QoL of their child.

Methods: A systematic review was conducted, and 14 quantitative papers were synthesised using narrative synthesis. A further empirical paper used Interpretative Phenomenological Analysis to analyse nine parent interviews.

Results*:* The systematic review highlighted lower than optimal QoL in young people with JIA. These results should however be interpreted with caution as the review also identified significant limitations with poor reliability and validity of the tools used to measure QoL in this context. The empirical paper highlighted the adversarial nature of MTX as a treatment regimen for young people, and the challenges parents face in supporting their child to take this medication. Five major themes emerged from the qualitative study: including "The Parent-Carer"; "The Child at the Centre"; "The Role of the Hospital"; "Our Lives with Methotrexate"; and "Coping with Methotrexate". These themes demonstrate the high emotional demand placed on parents of children with JIA, and the difficulties families have coping with MTX. Clinical and research implications are discussed.

Conclusion: This thesis identifies several theoretical and practical challenges in assessing the QoL of young people with JIA. QoL appears to be negatively impacted, however the findings highlight a lack of reliable and valid measurement tools to assess this and as such clinicians need to be mindful of how best to assess and interpret this in their work with these families. Without treatment, young people may experience poorer JIA outcomes and a worse overall QoL. As MTX is the gold standard treatment for JIA, it's vital we understand these difficulties so appropriate support may be put in place. Parents of children taking MTX face a unique challenge in the difficulties they may experience, therefore thought must be given to the availability and timing of support and resources that are given to parents, and the crucial nature of this in supporting the family as they undergo their MTX journey.

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Chapter One: Thesis Portfolio Introduction

This Thesis Portfolio aims to explore the experiences of young people and their families, living with Juvenile Idiopathic Arthritis (JIA). Specifically, this work aims to better understand what is the Quality of Life (QoL) like, for a young person living with JIA, and further explores systemic influences on their QoL through the experiences of their parents who administer the effective but complicated medication, Methotrexate (MTX).

This introductory chapter sets the context for the systematic review and empirical paper that follows. Key terms that provide an introduction and wider context to the work presented here, are defined. The philosophical positioning of the work is also introduced here, to allow the reader to orient themselves to the positioning of this study.

Juvenile Idiopathic Arthritis

Juvenile idiopathic arthritis (JIA), or juvenile arthritis is a chronic autoimmune condition that affects one in 1000 young people under the age of 16 (Giacane et al, 2016; van der Meer, 2007), with a prevalence of 43.5 per 100 000 and incidence of 5.61 per 100 000 (Costello et al, 2022). JIA is the most common rheumatic disease in children and is currently of an unknown aetiology (Barut et al, 2017). It has no cure and affects the individual across the lifespan, although can be treated with a variety of approaches including immunosuppressants, tumour necrosis factor inhibitors, or biologics (Hashkes & Laxed 2005; Stoll & Cron 2014), all medications which aim to manage the illness and prevent further inflammation and long-term damage.

There are six subtypes of JIA: Oligoarthritis, affecting four of fewer larger joints; Polyarthritis, affecting five or more joints; Systemic arthritis, affecting the entire body including the skin and internal organs; Psoriatic arthritis, comprised of some joint symptoms and some skin symptoms; Enthesis related arthritis, where the muscles and ligaments are affected; and Undifferentiated arthritis, where inflammation is present in one or more joints (Arthritis Foundation, n.d).

JIA is considered a chronic condition. Whilst there is no single definition for chronic illness, (Goodman et al, 2013) the Centre for Disease Control and Prevention (CDC), defines this broadly as conditions that last a year or more, require ongoing medication or limit activities of daily living in some way (CDC, 2023). This definition is supported by Hwang et al (2004) who define a person as having a chronic condition if it is expected to last 12 months or more and leads to limitations in activities of daily living, and the need for ongoing care.

JIA typically causes pain and inflammation across various joints, (Arthritis Foundation, nd; Prakken et al, 2011). Whilst living with JIA, an individual may experience improving or worsening levels of inflammation at different time points. It is critical that JIA inflammation is treated, as without proper treatment, more prolonged damage can be caused to the bones and connective tissue. JIA can also impact the eyes, large organs such as the heart and lungs, intestinal system, skin, bones, and joints, leading to difficulties with pain and physical functioning. In addition to pain, young people with JIA commonly experience fatigue and loss of lower muscle strength, which can have a significant negative affect on a young persons' quality of life (QoL) over time (Weiss et al, 2007).

Impact of JIA on young people and the family system

The impact that chronic conditions have on QoL is well researched (Heath et al, 2011; Payot & Barrington, 2011; Sawyer et al, 2007). Whilst those with hearing impairments, psychiatric disorders and dermatologic conditions may experience a relatively positive QoL, when compared to other chronic conditions, those with musculoskeletal conditions experience the worst QoL (Sprangers et al, 2000), highlighting the need for better disorder specific understanding of QoL, and the specific needs of different populations (Ingerski et al, 2009).

JIA can have multifaceted impacts on the body, potentially also affecting the eyes, large organs such as the heart and lungs, intestinal system, skin, bones, and joints, leading to difficulties with pain and physical functioning. Subsequently, patients may experience difficulty with the physical impact of the condition, including functional limitations, increased pain, and fatigue (Arthritis Foundation, n.d). Comparative to other health conditions such as asthma, JIA may impact the whole body, with fluctuating severity and levels of disability over time (Packham & Hall, 2002). Further, young people with JIA are more likely to experience significantly lower scores on physical health subscales of QoL, when compared to other chronic conditions (Haverman et al, 2012). These ongoing physical challenges, can add to the emotional impact of living with JIA, contributing to a sense of feeling different, which can impact the young person's self-esteem and psychosocial wellbeing (Cartwright et al, 2014; Eyckmans et al, 2011).

Not only are these factors challenging for young people, but also for the wider family system, due to emotional, systemic, and economic influences such as missed work to attend appointments (Bernatsky et al, 2007; Waite-Jones & Madill et al, 2007). As family dysfunction is associated with poorer child resilience in JIA, the influencing systemic factors are important to understand, in order to best support families and young people (Hynes et al, 2019).

Research on family systems suggests that families can effectively adapt to the introduction of a new chronic condition, by flexibly utilising their skills and resources. Families that are able to face these fluctuating challenges, tend to have better outcomes for the young person (Patterson & Garwick, 1994). This idea has been referred to as "balanced coping" (Cohen, 1999), where the family is able to meet the demands of the illness whilst maintaining the overall wellbeing and functioning of the family. This idea positions the illness as a member of the family, with whom all members of the family must have a relationship with (Cohen, 1999).

However young people and their families may not be sufficiently resourced or prepared for this new relationship, sometimes leading to behavioural or emotional difficulties (Geist et al, 2003). Within this system, the siblings of an unwell child, are also an important factor to consider, due to the potential emotional impact on the sibling (O'Brian et al, 2009). A meta-analysis of siblings with chronic conditions found overall, siblings of those with a chronic condition experienced poorer levels of psychological functioning, compared to controls (Sharpe & Rossiter, 2002). Siblings may attempt to care for the sibling to receive attention from a parent (Ratcliffe, 2001), and express sensitivity to being treated differently (Waite-Jones & Madill, 2007). For siblings of those with JIA, they report a loss of normality, and a level of shared distress with their sibling when facing adverse illness-related experiences (Waite-Jones & Madill, 2007). This indicates there is a need to support the wider family with the emotional adjustment to the condition, rather than focussing the intervention simply on the young person, when experiencing illness related difficulties.

A growing body of research is now highlighting the importance of parent interventions in improving outcomes for young people, notably meeting the information needs of parents, providing social support and helping parents and young people to jointly manage the condition (Stinson et al, 2012; Barlow & Ellard, 2004). The concept of the triangle of care (Hannan et al, 2016) addresses this dynamic by equally involving carers alongside the service user and professionals in the management of a condition. Whilst it was originally developed for use in inpatient mental health services, the benefits of this approach may be far reaching across settings (Hannan, 2013). This approach is especially relevant when considering the role parents taking in helping the child to manage their condition.

Research has also explored integrated interventions for parents and siblings, which can lead to positive impacts on sibling knowledge, feelings of connectedness, and improvements in sibling behavioural difficulties (Lobato & Kao, 2002).

However, a significant variable in the management of JIA, is the role of medication in JIA. As noted by Eyckmans et al (2011) the long-term use of multiple medications can be wearing for young people,

but in particular the difficult side effects and lack of information may lead to poor treatment adherence, or for patients to seek alternatives, as discussed below. It is also important to note that the impact on QoL of the treatment regime can vary between conditions, for example QoL for children with chronic otisis significantly improves during treatment, whereas for those with JIA QoL may decrease with treatment (Janse et al, 2005). This highlights the importance of developing disorder specific understanding regarding treatment regimes and the impact on young people.

The Treatment of JIA with Methotrexate

MTX is considered a gold standard drug used in the treatment of JIA (NHS, 2020). MTX works through both anti-inflammatory and immunosuppressive mechanisms (Kremer, 2004). It is typically taken once a week, and can be taken subcutaneously, or in a liquid or tablet form. As taking it subcutaneously is more effective, this is the preferred method of delivery most often recommended by clinical teams. Children may administer MTX themselves via injection, or parents often administer this for them. In some instances, families struggle to complete the MTX injection at home, and may have the injection at the hospital, or have nurses visit at home to administer this.

As well as controlling the physical symptoms of JIA, MTX has been shown to improve Health related Quality of Life (HrQoL), notably in the physical domain (Céspedes-Cruz et al, 2008). Despite being a highly effective treatment, common side effects when taking MTX include: nausea; a loss of appetite; diarrhoea; headaches; feeling tired; and hair loss, among others (NHS, 2023). These side effects can lead to understandable difficulties with treatment adherence (Pelajo et al, 2012), with one study finding parents reported medication side effects in 67% of children, which negatively impact their child's QoL, and children with JIA describe these side effects as challenging (Mulligan et al, 2013). Qualitative research conducted by Khan et al (2019) identified themes of associative intolerance, the role of coping, and "working hard to live with MTX intolerance". These themes contribute to the picture that MTX is a complex and challenging medication to take, despite its medical benefits. As a result of the difficulties experienced with MTX, psychological side effects sometimes occur, which can include anticipatory anxiety and associated nausea, anticipatory pain, needle phobia, medication refusal and behavioural difficulties (Jacobse et al, 2019; Mulligan et al, 2013), all of which can be challenging for both parents, young people, and professionals alike (van der Meer et al, 2007). Therefore, the empirical paper in Chapter four aims to better understand this complex issue in order better understand how to support young people and families dealing with MTX related difficulties.

A note on Quality of Life and Health Related Quality of Life

The term “quality of life” (QoL) first appeared in medical literature in the 1960’s, in reference to thinking beyond “material mechanisms” of health to include “the wholeness of human life” (Post, 2014). This became more pertinent as medical advances meant patients were living longer, however not necessarily maintaining their premorbid activity levels and livelihoods (Karim & Brazier, 2016). The World Health Organisation (WHO) have since defined QoL as a “state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity” (WHO, 1948). However, the term “Health related quality of life” (HrQoL) has subsequently emerged. This revised term was proposed in response to the recognition that health could no longer simply be measured through rates of morbidity and functioning alone (Karimi & Brazier, 2016). HrQoL tries to conceptualise the holistic experience of patients experiencing health difficulties. Whilst proposed as distinct term to begin with, this term is now often used interchangeably with QoL, leading to sometimes unclear boundaries around the phenomena being observed. Torrance (1987) attempted to distinguish these two terms by stating “quality of life is an all-inclusive concept incorporating all factors that impact upon an individual’s life, whilst HrQoL includes only those factors that are part of an individual’s health” (Torrance, 1987). A more contemporary definition is offered from the by the Centre for Disease Control and Prevention, which defines health related quality of life as “an individual’s or groups perceived physical and mental health over time” (CDC, 2018).

For those with chronic conditions such as JIA, this is an important concept to measure. If a young person feels their QoL is poor this does not automatically mean they have a poor health status, likewise, a good Qol does not always indicate a good health status (Bradley, 2001). It is however acknowledged that a good QoL correlates with positive longer-term outcomes in JIA (Foster et al, 2003) and so this is important area to understand, with clear clinical relevance.

In young people and children, HrQoL is typically measured using self-report measures either by the patient, or by proxy-parent reports. Typically, generic measures such as the Short-Form 36 (Burholt, 2011) or the World Health Organization Quality of Life Scale (WHOQOL-BREF: WHO-QoL Group, 1998) are used to measure QoL in children and young people. However, several disorder specific measures are available which may provide a more valid assessment of QoL in children with a particular condition (Anderson and Meyers, 2000). There is a significant number of disorder specific measures available to measure QoL in children and young people. One review (Solans et al, 2008) found as many as 30 generic and 64 disease relevant measures available for use, however the psychometric properties of these measures are variable, with only 67% assessed for internal consistency and 44% reporting test-retest reliability. This indicates that the proposed measures may be unreliable therefore not accurately assessing the concept they intend to, which is clearly problematic. Within more generic measures of QoL, domains assessed commonly include physical functioning, psychological functioning, social functioning, and the persons environment, with many providing

both child and proxy assessment allowing for additional responses that may account for the cognitive level of the child.

The role of the parent

As introduced above, parents play a key role in supporting and treating their child with JIA, in that they are often the ones to administer the required medication. With this in mind, the experience of parenting a child with JIA can prove challenging. Parents report a mix of emotions such as guilt, anxiety, and anger, while attempting to manage the condition, and have reported a need for greater support and information to reduce parental stress (Barlow et al, 2016). Based on this, it is unsurprising perhaps that parents report greatest caregiving burden specifically in emotional domains as opposed to physical domains (Bruns et al, 2008).

Whilst QoL varies by JIA subtype it has been noted that as QoL decreases, parental stress increases, (Joseph et al, 2013) and moreover, poorer parental stress and coping is associated with worse QoL in JIA (Cavallo et al, 2009). This is important, due to the associations between poor QoL and higher rates of depression in young people with JIA (Fair et al, 2019; Stevanovic & Susic, 2013). Family resilience and adaptability are key in nurturing a supportive environment for the management of chronic conditions, and research focussing on how to foster this within families and parents is timely and important, in leading to improved QoL in families (Whitehead et al, 2017).

Outline of Thesis Portfolio

This thesis aims to pull together the overarching themes of QoL and the impact of treatment for JIA within the family system, with an aim to provide a fresh contribution to this research area. In the next chapter a systematic review will attempt to quantify what is the QoL for young people with JIA. A bridging chapter then introduces factors influencing QoL in JIA. This will link the systematic review to the empirical paper, which aims to illustrate the parental experience and impact of administering MTX to a child with JIA. The results of the empirical paper illustrate the parent experience and impact of giving the medication MTX.

The final chapter provides a synthesis of the body of work along with a discussion as to how the current work sits within the existing literature and what future research may build upon this.

Philosophical Positioning of the Thesis Portfolio.

This thesis takes a Constructionist position and an overview of this is provided below.

The question of how we gain knowledge about others' experiences remains a philosophical debate (Byrne et al, 2001). In attempting to understand others' experience, to gain knowledge, a researcher needs to be clear in their epistemological position, so that discerning interpretations about this can be made about the knowledge that has been "found". In the absence of being able to directly observe a phenomenon, this thesis employs a Constructionist epistemology, which proposes that knowledge about our world can be gained through a co-constructed interaction between the subject and "object" (Moon & Blackman, 2017).

With regard to the ontological dilemma, what is there for the researcher to discover, a critical realist ontology is used to attempt to understand the unobservable. Critical realism questions what do we mean about the nature of what is real, when it comes to others lived experiences? Within the frame of this research, it suggests that the knowledge we have about the world is constructed through the "observable" parts of the world, thus aligning with a constructionism stance in that reality can be observed through co-construction.

From a theoretical perspective, this thesis uses Phenomenology: the study of the way we "experience" our world-to understand the human experience. It is therefore important to consider the researcher's position to the work and this will be discussed further in Chapter 5, Reflections of the Researcher.

Therefore, whilst the realities explored in this body of work may not be directly observable, a level of knowledge may be gained regarding the lived truth of these families and proposes there is a knowable truth we can reach taking this critical realist approach.

Chapter Two

What is the quality of life of Children and young people under the age of 18 with Juvenile Idiopathic Arthritis: A Systematic Review

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Abstract

Background: A diagnosis of a chronic condition in childhood brings several unique challenges. For the child, treatment regimens, physical limitations, and illness burden, can all have a negative impact on quality of life (QoL). For the parent, parental stress, emotional burden and practical stresses can impact carer wellbeing. Current literature highlights the relationship between positive QoL and positive outcomes for young people, despite the concept QoL and its alternate terms, remaining nebulous concepts. For Juvenile Idiopathic Arthritis (JIA), research to date has focused on causal pathways to quality of life (QoL). There is currently no synthesis of the QoL data for this population.

Aims of review: This review aims to synthesise current research on quality of life in JIA. In doing this the review will attempt to quantify this for young people with JIA, whilst also addressing the wider issues of quality of life terminology and research methodology.

Methods: Papers were identified by searching the databases PubMed, CINAHL, Scopus and Psychinfo. A narrative synthesis was conducted, and quality appraisal was completed using the AMSTAR tool.

Results: Fourteen papers were identified and reviewed. Across these children and young people with JIA had a below optimal quality of life, and lower quality of life when compared to healthy controls. The most impacted subtype was those with Oligoarthritis, with a small proportion of results finding adolescents were more likely to have a worse QoL compared to younger populations of children with JIA.

Conclusion: Children with JIA were found to have consistently lower than optimal QoL, with the domains of physical health, motor functions, and school functioning, most impacted, as observed by using a variety of tools. However, variability was observed between ages, JIA subtype, with differences also observed between child and proxy parental reports. This review was not able to provide conclusions beyond the descriptive data provided, due to limitations in the tools and methods used to assess this, and these limitations are discussed in depth. In attempting to quantify the QoL for children with JIA, the multifaceted nature of QoL is illustrated. It is recommended that a tailored approach is needed when assessing QoL within clinical populations and the findings highlights the current lack of heterogeneity amongst quality-of-life research, making it difficult to draw wider conclusions across populations.

Keywords: *Juvenile Idiopathic arthritis, arthritis, chronic conditions, quality of life, health related quality of life, child, adolescent.*

Introduction

Chronic conditions are defined as conditions that last more than one year; that require ongoing attention and treatment; or those that impact an individual's daily activities and or living (Centre for Disease Control, 2022). In children, the incidence of common chronic conditions such as asthma, type 1 diabetes, cystic fibrosis, and epilepsy, are increasing (Perrin, 2014; Royal College of Paediatrics and Child Health, 2022) causing changeable demands to be placed upon health care providers, families, schools, and individuals.

The practical and psychological aspects of living with these conditions are complex. The strict treatment regimes, medication side effects and physical limitations a young person might experience as a result of their diagnosis can have far reaching consequences on development and wellbeing such as limiting activities, impacting school and family functioning, (Newacheck & Taylor, 1992; Sawyer et al, 2007), and can have negative impacts on mental health, with higher rates of depression and anxiety seen in this population (Fair et al, 2019; Margetić et al, 2005; Stevanovic & Susic, 2013).

Health care professionals have traditionally ascertained what life is like for families at home via anecdotal reports in the clinic room. However, the early 2000's saw a significant increase in health-related quality of life (HrQoL) research, providing an empirical foundation to the unique challenges brought about by these diagnoses (Zheng et al, 2021). Whereas research had previously focussed on the association between disease severity and quality of life (QoL), there was increasing recognition of the complex biopsychosocial relationships that impact QoL and how this might affect treatment adherence, and long-term outcomes for young people.

Although the role the medical team plays should not be understated, the day-to-day burden of managing a chronic condition in childhood is typically held within families (Litman, 1974; Toledano-Toledano & Domínguez-Guedea, 2019). Upon receiving a diagnosis, families face a steep learning curve, and upon returning him from the hospital must adjust to a new way of living, ultimately becoming their own experts by experience (Heath et al, 2017).

Juvenile Idiopathic Arthritis

This paper will focus on Juvenile Idiopathic Arthritis (JIA). JIA is the most common rheumatic disease observed in childhood (Giacane et al, 2016), with a prevalence of 43.5 per 100 000 and incidence of 5.61 per 100 000 (Costello et al, 2022). Symptoms typically present before the age of 16, with the child experiencing stiff and painful joints, typically in the knees, hands, feet, and ankles-

although symptoms vary dependent on disease subtype (Kim & Kim 2010). The International League of Associations for Rheumatology identifies there to be six subtypes of JIA, including oligoarticular (persistent or extended), polyarticular (RF-negative or RF-positive), systemic JIA, psoriatic arthritis and enthesitis-arthritis (Zaripova et al, 2021). The condition is commonly indicated to general practitioners through reduced mobility, fatigue, rashes and fevers, but is diagnosed through the exclusion of other potential diagnoses such as infection, leukaemia or autoinflammatory syndromes (Giacane et al, 2016). Additionally, children with JIA may experience eye inflammation, or inflammation of the eyes, referred to as JIA associated uveitis.

Although manageable, early detection and treatment are critical to improving prognosis (Marzan & Shaham 2012), and children are typically started on a rigorous course of steroids, immunosuppressants and anti-inflammatory medications shortly after diagnosis. Options for treatment typically include antirheumatic medications including disease-modifying antirheumatic drugs such as methotrexate (MTX), and nonsteroidal anti-inflammatory drugs and corticosteroids. However, these are not without side effects. One study found the incidence of side effects of these medications was as high as 67% in the first year after diagnosis (Chédeville et al, 2021). The gold standard for treating JIA is to use MTX, a medication that suppresses the immune system and is commonly administered orally or though subcutaneous injection (NICE, 2014). Although the medication can be painful to administer through injection, it is considered the most effective way to deliver MTX. Additionally, giving this medication may also accompanied by a range of unpleasant side effects, including fatigue, nausea, low appetite, vomiting, neutropoenia, headaches and diarrhoea. These side effects are commonly reported as distressing to health care practitioners for children and families (Mulligan et al, 2015).

Considering the physical and psychological aspects to living with JIA, it is easy to assume that young people with a chronic condition like JIA may experience a lower QoL when compared to “healthy” children, however the evidence base is developing. Studies have identified discrepancies between parent and child reports of QoL highlighting the subjective nature of QoL and the importance of not assuming individual experience (Hall et al, 2019).

Defining and Assessing Quality of life

As noted in Chapter One, there have been many attempts to quantify HrQoL across various populations over a number of years, yet the terms QoL or HrQoL remain nebulous, preventing a consistent understanding of this phenomena (Barcaccia, 2013; Feinstein, 1997). As health outcomes have moved beyond simply focussing on the biological status of an individual, to considering aspects such as life satisfaction and happiness (Ferrans et al, 2005) this is an important concept to understand

in order to not make erroneous assumptions and decisions about a person's health, care and wellbeing (Haraldstad et al, 2019).

For the purposes of this review, QoL and its associated terms broadly refer to the "wholeness of human life" (Post, 2014), and considers the aspects of being that exist beyond the purely biological. Tension exists between the use of the terms QoL and HrQoL, though they are often used interchangeably in the literature. To this end, this thesis refers primarily to the term QoL, however the terms may be used interchangeably where appropriate.

JIA and Quality of Life

Several studies attempt to understand QoL for young people with JIA, though the problems described above such as poor reliability are also seen in this domain of illness. Research has identified physical disability and pain are important predictors of HrQoL, with coping strategies identified as predictors independent to pain (Haverman et al, 2012; Sawyer et al, 2004). Further, a study by Tarkiainen et al, (2019) identified that improvement in the physical health domain of HrQoL improved psychosocial domains (Tarkiainen, 2019).

Whilst understanding predictors of HrQoL is pertinent, the lived experience of young people living with JIA has not been fully explored for example, does JIA subtype, or duration since diagnosis impact on the state of a young person's HrQoL? Which domains of HrQoL might be most affected by this diagnosis? Two similar reviews of this nature exist: one for adults, and a qualitative synthesis for children with JIA. Grazziotin et al, (2018) found few studies examined differences in HrQoL across JIA diagnoses; the over reliance on generic rather than disease specific HrQoL measures, and limitations in how the data could be used to inform lifetime models of HrQoL (Grazziotin et al, 2018). Tong et al, (2012) completed a synthesis of qualitative studies examining experiences of living with JIA and found themes such as "aversion to being different"; "managing treatment"; "striving for normality" and stigma and misunderstanding were all relevant factors in impacting young people and impacting their capacity for social participation, factors thought to be relevant to HrQoL. Despite these earlier studies, there is currently no review summarising papers that specifically examine the state of HrQoL for children and young people under the age of 18 with JIA.

This question has clear clinical relevance, as a better understanding of the HrQoL of children with JIA, will allow researchers and clinicians to develop a more specific picture of the needs of this population, and provide more tailored interventions to support QoL as required.

Review Aims

This review aims to answer the question: “What is the quality of life for children and young people with JIA?”. The review will examine quantitative results, alongside ascertaining the components of QoL that are most affected.

The research question was developed following a scoping search for similar papers and a review of the current PROPSPERO database. The sample is young people under the age of 18 and their parents, and the phenomenon of interest if their quality of life or health related quality of life. Data extracted was exclusively quantitative, and a narrative synthesis methodology is used to answer the review question.

As discussed in the introduction, the terms QoL and HrQoL are often used interchangeably, therefore this review has used both terms in a similar manner where appropriate.

Methods

Framework and Prospero

A scoping search identified no current systematic review answering the research question, and therefore, this paper aims to synthesise the current research in this area. Of note there is no one valid method for using a narrative synthesis approach for quantitative data, therefore a narrative synthesis approach was used, with adapted guidance from Popay et al, (2006) and the Synthesis Without Meta-analysis (SWiM) guidelines (Campbell et al, 2020).

The systematic review was registered with PROPSERO, (registration number: CRD42022310425). To ensure transparency of methods, the review used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist (PRISMA, Moher et al., 2009).

Inclusion and Exclusion Criteria

The search aimed to identify papers that specifically quantified QoL for this population. Papers were included if they pertained directly to assessing the QoL for children and young people with JIA. These included both cross sectional and longitudinal studies. Intervention studies and studies assessing development and validity of measurement tools were excluded.

The review only included English language articles due to the limitations on translation services but did not exclude papers from non-English speaking countries. Original research articles and related systematic reviews are included.

Throughout the review process several papers were identified that examined causal pathways to quality of life, however these were considered beyond the scope of the review question and the decision was made to exclude these.

Search Strategy

This search was conducted using Pubmed, CINAHL, Scopus and Psychinfo electronic databases. The initial search was completed in February 2022 with an updated search conducted in February 2023. Based on other reviews conducted within this topic area, search terms included “juvenile idiopathic arthritis”; “quality of life”; “health related quality of life”; and “child” or “adolescent” and the variants of these words.

Table 2.1

Final Search terms used across databases

Term One	***Term Two***	***Term Three***
Relevant to Juvenile Idiopathic Arthritis and it’s subtypes	*Relevant to Quality of life*	*Relevant to ages 0-18 years.*
“Juvenile Idiopathic Arthr*” or JIA or “rheumatoid arthr*” or polyarthritis or “rheumatoid disease*”	“quality of life” or "health related quality of life or hrqol or qol	Child* or adolescen* or pediatric or paediatric
Final Search Terms		
(juvenile idiopathic athr* OR jia OR rheumatoid athr* OR polyarthritis OR rheumatoid disease* OR rheumatic disease*) AND (quality of life OR hrqol OR qol) AND (child* OR adolescen* OR pediatric OR paediatric)		

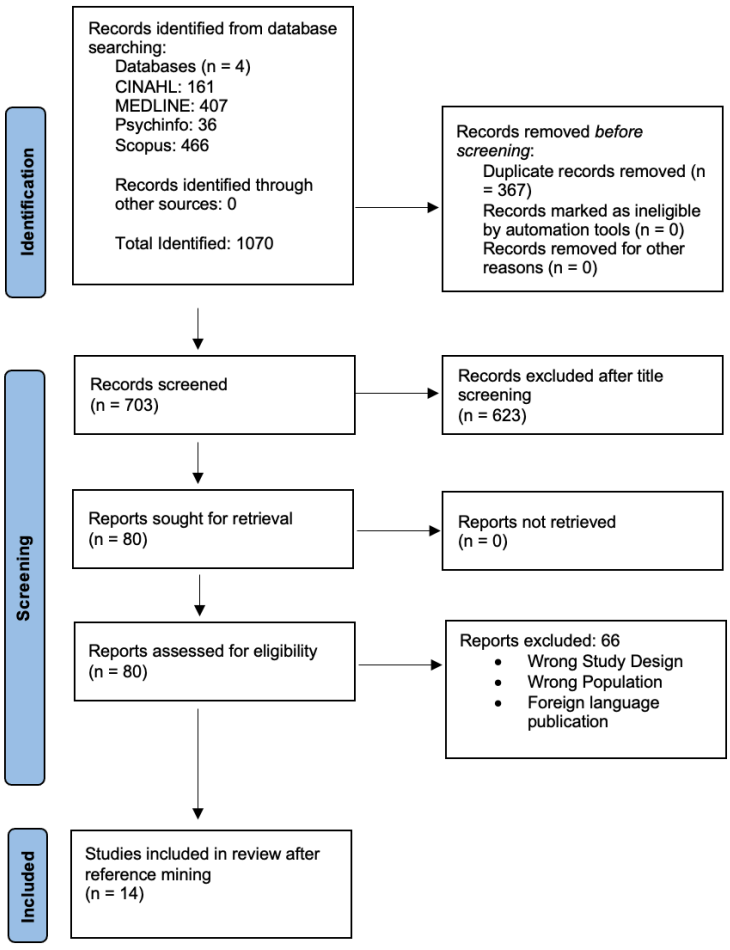
Identification of studies and study selection

An initial search identified 1070 potential studies. Screening was conducted using the Rayaan online platform. 703 studies remained after duplicates were removed. After titles were screened for eligibility, 80 remained with 53 "maybe". To ensure inter-rater reliability, a sample of 30% (217) studies were sent to an external reviewer to screen based on titles, and there were no discrepancies. Of note, the external reviewer involved in this process was an assistant psychologist working within a healthcare setting, but without prior knowledge of the study area, accounting for potential bias when screening the study titles.

After abstracts were screened, 40 remained and 13 were identified for final inclusion based on full text read through. Additional reference mining was completed which identified a further one study, leaving a final number of included studies at fourteen. This process is illustrated further in Figure 2.2.

Figure 2.2

Prisma flow diagram



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

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

Quality assessment

Studies were compared against the Appraisal tool for Cross-Sectional Studies (AXIS, Downes et al, 2016) a 20-item quality appraisal tool. This tool was selected due to the cross-sectional nature of most studies identified. Although this tool has no formal guidelines for an overall quality rating, a score out of 20 is transformed into a percentage and used as indication of quality, with higher percentage scores indicating a greater study quality.

To ensure validity of the quality assessment a sample of 30% (five papers) was sent to the external reviewer (as described above) to ensure there were no discrepancies in quality assessment. There was one discrepancy noted across two papers which were discussed, and a conclusion was reached about the quality of this paper.

Data extraction

Complete data extraction can be found in Appendix A and includes the following categories: Author; Year/Country; Participant No; Age Range & Gender; Diagnosis; Mean age of onset/Disease Duration; Study Design & Analysis; Measure of HR-QoL; Inclusion/ Exclusion Criteria; Key Findings Relevant to the Systematic Review Question.

Data analysis

Narrative synthesis was completed using guidance from Popay et al (2006) & the SWiM guidelines (Campbell et al, 2020), who state that the usefulness of the synthesis lies in how "trustworthy" this process is (Popay et al, 2006; Campbell et al, 2018). These guidelines are not intended to be followed in a linear manner but may be adapted to account for different methodologies. To provide a transparent account of the process followed the following steps were taken in completing the analysis:

- Data was extracted and a preliminary synthesis performed. Study results were tabulated into Appendix A.

- Data was then assessed for quality using a quality assessment framework (please see Appendix C for assessment framework and Figure 2.3 for summary of quality assessment findings).

- Results were synthesised and summarised according to appropriate domains.

- The information was then summarised and discussed in terms of the overall implications

Results

Study Characteristics

The 14 papers included in this review originated from 14 different countries, which indicates the findings may have good generalisability. One paper stated their data was from "Europe" with another indicating the data was sourced from 32 countries (please see Appendix A). Publication date ranged from 2006 to 2021. At the time of completing this review, there were no papers identified before the year 2006. The age of participants ranged from two to 18 years old. 12 papers used a cross sectional methodology, with two using a longitudinal design.

Quality Assessment Summary

All studies were compared against the AXIS quality appraisal tool for cross sectional research (Downes et al, 2016), a summary of which can be seen in Figure 2.3 below. A sample of 30% (4 papers) were randomly selected and sent to the external reviewer for quality assurance. Any differences were agreed upon jointly and resolved.

As the AXIS uses 20 items to score quality, this was transformed into a percentage as a benchmark for quality. For allow for better interpretation, for the purposes of this paper anything above 80% was considered high quality, and anything below 20% was considered low quality. Between 20-80% was considered moderate quality. All but one study was considered to be of moderate quality, with one achieving high quality status (Haverman et al, 2013).

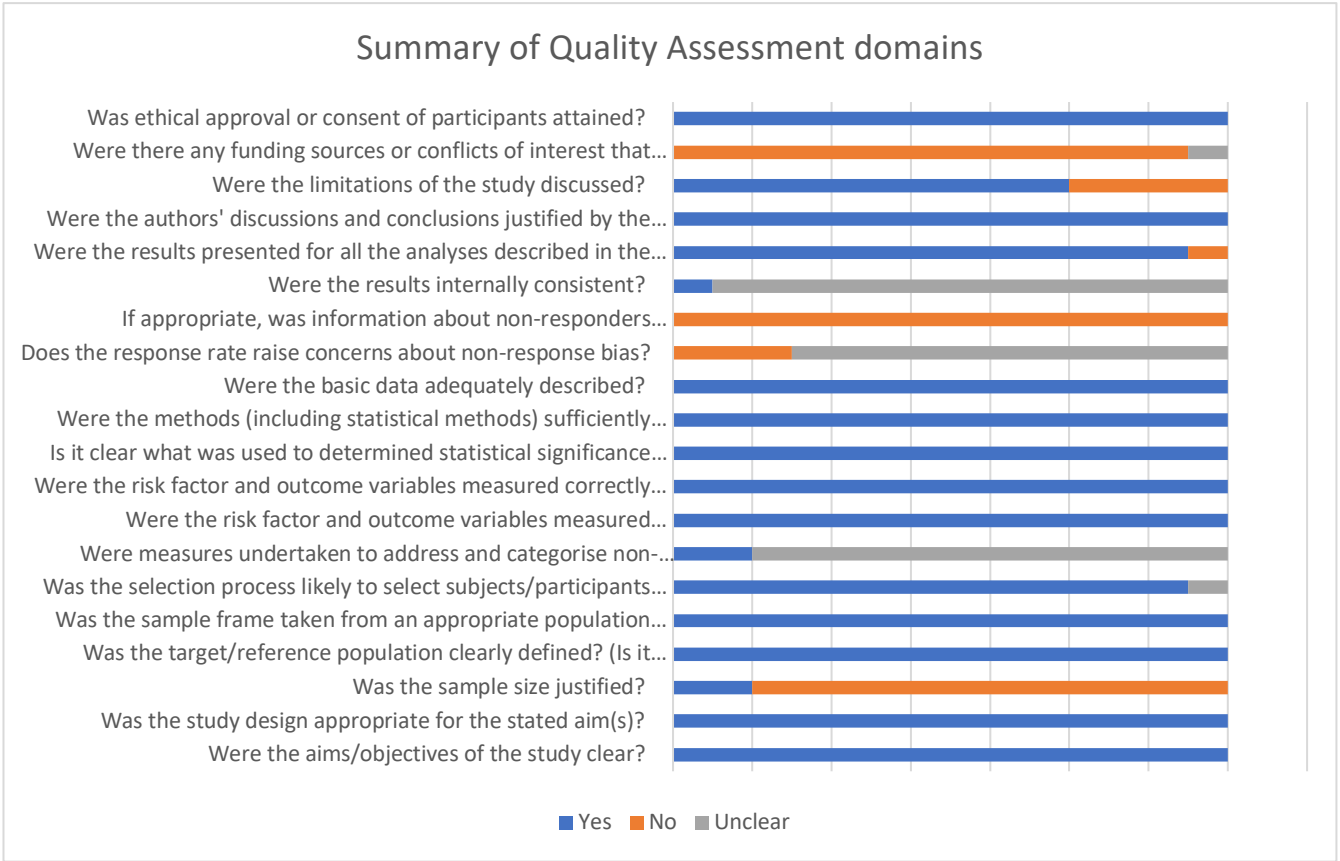
Of the papers appraised, all papers provided a clear description of their rationale, population, and sampling methods, and had a good study design suitable for studying what the intended cohort. The samples were almost exclusively taken from pre-existing populations such as those with a diagnosis of JIA, registered under the recruiting clinic. Therefore, papers mostly were likely to select subject's representative of the target population. Only one papers justified their sample size (Haverman et al, 2013), which is important as this may mean some studies are underpowered and conclusions drawn may be inaccurate.

Where papers actively recruited participants (i.e., did not use a pre-existing data set) only two papers addressed the risk of non-response bias (Haverman et al, 2013; Ringold et al, 2009). This indicates the possibility that a proportion of the population have not been represented in the research compromising the generalisability of findings. All papers reported adequate basic data, and methodology allowing for possible replication of their research. Overall studies included made fair conclusions based on their data. However, 28% (N=4) did not report any limitations of their research.

All papers reported that ethical consent was sought, and that there were no conflicts of interest. In summary, the quality of the papers included in this review was generally moderate, with improvements possible in describing the sampling and recruitment of participants, risk of response bias and discussion on the limitations of their research.

Figure 2.3

Summary of Quality Assessment Domains



Synthesis and Appraisal of Data

Measures used in assessing Quality of Life

As discussed above, the imprecise definition of QoL and its interchangeable nature with HrQoL has led to the development of an array of measures, both generic and JIA specific. The variability in measures used and the overall quality of these means synthesising this data beyond the descriptive is difficult. Within the results of this review, five individual measures of QoL were used, as seen in Table 2.4 below.

Table 2.4

Summary of measures used

Measure Used	**Authors**	**Number**	**JIA/Arthritis validated?**
PEDSQL 4.0 Generic Core Scales *English version* *Thai version* *German version* *Chinese version* *Dutch version*	Varni et al, 2002	8	Yes
PEDS-QL 3.0 Multidimensional fatigue scale *English version*	Varni et al, 2004	1	n/a
PEDS QL 3.0 Rheumatology module *English version* *Chinese version*	Varni et al, 2004	2	Yes
Juvenile arthritis quality of life questionnaire (JAQQ)	Duffy et al, 1997	3	Yes
Child Health Questionnaire	Landgraf et al, 2020	2	No
Kidscreen 52	Ravens-Sieberer et al, 2014	1	No
Quality of my Life Questionnaire	Gong et al, 2007	1	No

Of the measures identified, two measures were validated for use in JIA populations, and another specifically for “arthritis” (Weiss et al, 2013) meaning these measures are better suited to assess QoL concepts specifically for this population. Others were generic measures of QoL in young people, of varying length and content, from more lengthy questionnaires encompassing several domains of QoL, weighted differently between measures, to three item measures that use a visual scale to help young people to self-report. This difference means there may be varying results in terms of what QoL concepts are assessed. Furthermore, considering the phenomenological variation in chronic conditions, generic measures may be less able to capture the nuanced experiences of young people

with JIA. Therefore, the conclusions drawn may be erroneous due to a lack of internal reliability within measurement.

The most commonly used measure in this review, was the Paediatric Quality of Life Inventory (PEDS-QL 4.0 Core: Varni et al, 2004), a generic measure of QoL. Eight papers in total used versions of this measure, with four using the validated translated language versions. The PEDS-QL 4.0 Core includes a total score, and additional physical, emotional, social, and school domain scores. A physical and psychosocial health summary score are also available. Although not JIA specific, the PEDS-QL 4.0 is considered a valid and reliable measure able to distinguish healthy from target populations (Młyńczyk et al, 2021) with adequate psychometric properties. The PEDS-QL 4.0 uses a modular approach to assessing QoL, with optional units available. The PEDS-QL 3.0 rheumatology module (including its translated Chinese version) is used in two studies, and the PEDS-QL 3.0 multidimensional fatigue scale is used in one study. Higher scores on the PEDS-QL core, indicate a better QoL, with scores ranging from 0-100.

Other non-JIA specific measures identified included the Kidscreen 52 (Ravens-Sieberer et al, 2014) and Quality of my Life (QoML; Gong et al, 2007) which were used once each respectively. The Kidscreen 52 was developed to measure the HrQoL of children and adolescents. It includes 52 questions, assessing ten domains including physical well-being, psychological well-being, moods and emotions, self-perception, autonomy, parent relation and home life, financial resources, social support and peers, school environment, and social acceptance. The higher the score, the greater the QoL. In contrast, the Quality of My Life measure is a three-item generic measure that uses a visual analogue rating and single statement response to ascertain HrQoL in individuals since their last clinic visit. Whilst the briefer measure may hold greater clinical utility and may prove more accessible for younger patients, it omits some of the more in-depth assessment of social factors as seen in the Kidscreen 52. The significant difference in these two measures, highlights the wide variability seen in QoL measures.

The second most used measure in this review was the Juvenile arthritis quality of life questionnaire (JAQQ; Duffy et al, 1997). Three papers used this measure. The JAQQ is a JIA specific measure that consists of 74 questions grouped into four domains including gross motor function, fine motor function, psychosocial function, and systemic symptoms. Scores on the JAQQ can range from one to seven, with a higher score such as seven, representing a lower QoL. The use of this measure allows for tailored assessment of factors relevant to JIA and QoL for example motor function, which may be a less important consideration for other chronic conditions, such as Type 1 diabetes, where motor function is not typically impaired.

The Child Health Questionnaire (CHQ) (Landgraf et al, 1996) was used twice. It is typically a parent report measure, used to assess the emotional, physical, and social elements of "health status" of children. It includes 15 domains including global health, physical functioning, role/social limitations, emotional/behavioural, physical, bodily pain/discomfort, behaviour, general behaviour, mental health self-esteem, general health perception, change in health, parent impact-emotional, parent impact-time, family activities and family cohesion. There are also summary scores for physical and psychosocial domains. The advantage of parent measures lies in their ability to provide an alternative viewpoint on the child's QoL, not reliant on the level of language or development of the child, however similar research in oncology patients has identified negative correlations between parental distress and parent reported child QoL (Houtzager et al, 2005). There is then the possibility that parents are more likely to focus on certain aspects of their child QoL as opposed to what is most important for the child, highlighting the importance that the child's voice is heard.

Of note, the Childhood Health Assessment Questionnaire (CHAQ) was used alongside QoL measures in four instances. The measure includes assessment of disability, discomfort and focusses on aspects of daily living. Although there is arguably overlap between QoL constructs, it is typically used as a measure of functional status and thus to avoid confounding of variables, the CHAQ is not used in the synthesis of QoL results.

Descriptive synthesis of overall QoL scores

All fourteen papers included in this review found that on average children and adolescents with JIA had a lower than optimal QoL, and lower QoL than healthy peers, where a comparison was made. This is concerning given the impact of poor QoL in childhood and the implications for longer-term impacts into adulthood (Foster et al, 2003).

Five studies quantified QoL with a percentage, with a range of between 45-59% of children with JIA experiencing lower than optimal QoL (Charuvanij & Chaiyadech, 2018; Haverman et al, 2013), compared with the 16% of the general population (Haverman et al, 2013). Listing et al, (2018) found that when measured at baseline children with JIA experienced a poor QoL, however 76% of patients with JIA were able to obtain a favourable HrQoL above the clinical cut off of 79.3 at the three year follow up. These results imply that QoL is not a fixed concept and may be influenced by shifting factors during the child's development.

Summary of the Paediatric Quality of Life Inventory (PEDS QL 4.0 Core) and PEDS-QL 3.0 Rheumatology and Fatigue modules

A summary of PEDS-QL core domain scores can be found in Table 2.5. Of the eight papers to use the English language, or language variant of the PEDS-QL 4.0 Core, mean overall scores ranged from 70.26 to 87.12, indicating a lower than optimal QoL. One study reported a median (as opposed to the mean) of 80.7 with a range of 36.9-100. The lowest QoL was identified in children with JIA ages 6-7 on the emotional functioning subscale (Haverman et al, 2013). This may in part be explained by time passed between receiving a diagnosis and being assessed at study baseline. It is possible that children at this age are experiencing higher levels of pain as their JIA may not yet be managed. In addition, younger children may have a lower level of understanding and communication regarding their illness, leading to greater distress and lower QoL. However, this was only commented on by one paper. The highest QoL was identified for children with the diagnosis of Oligoarticular JIA (Wu et al, 2021). This JIA subtype affects four joints or less, as opposed to other subtypes of JIA, and has positive treatment outcomes, possibly accounting for the comparatively positive QoL.

Table 2.5

PEDS-QL 4.0 Core and Domain Scores

PEDS-QL Core	**Total**	**Physical functioning/Summary score**	**Psychosocial Summary score**	**Emotional Functioning**	**Social functioning**	**School functioning.**	**Proxy?**
Bomba et al, 2021	**Mean** 73.77 ± 12.85	75.92 ± 12.69	67.32 ± 20.53	72.73 ± 16.92	84.09 ± 15.28	70.97 ± 19.38	No
Charuvanij & Chaiyadech 2018	**Median** 80.7 (36.9–100)	78.1 (34.4-100)	Not stated	85 (35-100)	90 (30-100)	80 (25-100)	Yes
Listing et al, 2018	**Mean** 71.5 ± 18.4,	66 ± 24.6	74.8 ± 17.4	68.9 ±22.1	82 ± 19.1	72.9 ± 20.9	No
Lundberg et al, 2012	**Mean** 75.06 ± 16.28	Male62.5 ± 25.72 Female: 70.82 c 17.98	78.66 ± 16.88.	Male 76.48 ± 23.78 Female 79.86 ± 21.06	Male 79.37 ± 19.91 Female 86.69 ± 14.51	Male:75 ± 18.07 Female: 71.65 ± 21.03	Yes
Haverman et al, 2013	**Mean** **6-7:** 70.26 ± 23.02 **8-12**: 71.67 ± 14.06 **13-18:** 71.91 ± 17.36	71.9± 13.9	71.9±17.36	69.84±20.32	76.98±15.07	68.89±17.04	Yes

Ringold et al, 2009	**Mean** 83.54	82.27 ± 17.40	82.77±14.48	81.14± 16.85	90.55± 13.39	77.18± 19.76	Yes
Weizman et al, 2018	**Mean** 76.7 ±18.2.	76.2± 22	76.9±17.9	Not stated	Not stated	Not stated	No
Wu et al, 2021	Mean 82.85 ± 14.82 Systemic: 77.05±19.11 : 84.33±12.46 Oligoarticular: 87.12 ± 10.23	Systemic: 76.83±23.67 Polyarticular: 84.38±20.4 Oligoarticular: 86.88±15.11	Not stated	Systemic: 87.28±18.76 Polyarticular: 87.70±14.12 Oligoarticular: 92.65±12.02	Systemic: 81.34 ±21.33 Polyarticular: 89.17±15.88 Oligoarticular: 92.97±11.98	Systemic: 67.64±18.83 Polyarticular: 77.03±14.02 Oligoarticular: 77.28±13.99	No

PEDS-QL Core physical function/physical summary scale, scores ranged from 62.5 to 86.88 On the psychosocial summary score, scores ranged from 67.32 to 82.77. Two studies did not report the psychosocial summary score. On the Emotional Functioning domain, scores ranged from 68.9 to 92.65. On the Social functioning domain, scores ranged from 79.37 to 92.97, and on the school functioning domain, scores ranged from 67.64 to 77.28. These results illustrate the lowest scores in the domain of school functioning, and greatest variability in the domain of social functioning. Whilst the physical impact of JIA may explain scores on the physical function/physical summary scale, the impact on school and emotional functioning may be harder to interpret without context. However, the perspective provided by the rheumatology and the multidimension fatigue modules indicate the influencing roles of more JIA specific subscales such as pain, fatigue, and treatment. These results indicate pain, cognitive fatigue, worry and treatment factors as additional impactful variables and the results are contextually congruent with the observed lower QoL observed on school and emotional functioning, as these are likely to be affected by factors such as pain and fatigue.

Of note, the use of clinical cut offs is not common practice in QoL research, however there may be utility of this, for both clinical and research purposes. There have been several attempts to establish meaningful cut offs for the PEDS-QL. Seid et al, (2009) suggested that a suboptimal QoL might be anything below a total mean scale score of 78.6. However, Huang et al, (2009) established a score of over 78 for children over eight and 82 for children under eight could be considered a good QoL. This sample included a variety of chronic conditions, signifying there is a need for condition specific meaningful cut off scores allowing for. It is also important to consider that cognitive development may play a role in the self-report assessment of QoL, as a certain level of cognition is required to effectively provide self-report information, and children in younger age brackets may lack the meta

cognition required to accurately report their QoL status (Bevans et al, 2020). The existence of more than one suggested cut off, potentially reduces the ability to generalise these ranges to broader populations. However, using a clinical cut off at 78.6 as defined by Seid et al, (2009), in general, overall scores on the PEDS-QL indicate a lower than optimal HrQoL. Although two papers identified a HrQoL score above this cut off (notably for the Polyarticular and Oligoarticular sub types) these scores were significantly lower when compared to healthy controls (Ringold et al, 2009; Wu et al, 2021). Of note, there are no clinical cut offs for the Rheumatology and Fatigue modules, however they were used to establish a worse HrQoL for those experiencing active Systemic JIA (Ringold et al, 2009; Wu et al, 2021). This is problematic, as in the absence of clinical cut offs, it may be difficult to use these measures to make a conclusion about the level of a young person's QoL without additional information.

The Juvenile Arthritis Quality of Life Questionnaire (JAQQ)

Of the three papers that used the JAQQ, average scores ranged from 2.6 to 2.7, with one paper reporting a median score of 2.7 (Shaw et al, 2006). These scores indicate a lower than optimal QoL, although as above, there are no published cut offs to specify this. One paper identified there were significant differences between age groups, with worse global, disability and pain specific scores for adolescents (Amine et al, 2008). Another paper identified the highest level of difficulty was in gross motor function, with no differences between age groups. Least difficulty was found in fine motor function, results which are apt within the context of large joint inflammation in JIA (Shaw et al, 2006). Interestingly, in this study, one third of young people reported that frustration was a significant problem for them, which is pertinent to mention given frustration is not a commonly assessed domain in HrQoL (Shaw et al, 2006). As the JAQQ is a JIA specific measure, the inclusion of frustration in QoL assessment in JIA, further emphasises the importance of condition specific measures that capture the nature of living with JIA and explicitly considers emotions.

Table 2.6

Summary of JAQQ scores

	Mean score	**Gross motor**	**Fine motor**	**Psychosocial function**	**Systemic problems**
Amine et al	2.6 +/- 1.3 (1-6)	2.6 (1-5.95)	2.79 (1-6.4)	2.82 (1-6.4)	2.36 (1-5.5)
Oen et al, 2017	2.7 (1.9-4)	Not stated	Not stated	Not stated	Not stated
Shaw et al, 2006	2.7	Not stated	Not stated	Not stated	Not stated

Other Measures

Other papers included in the review used the Kidscreen 52 (Ravens-Sieberer et al, 2014), Child Health Questionnaire (CHQ; Landgraf et al, 1996), and Quality of my Life Questionnaire (QoML; Feldman et al, 2000).

Using the CHQ, Gutierrez-Suarez et al, (2007) identified that, compared with healthy children, those with JIA had lower values in all subscales of the CHQ. Most impacted subdomains were physical functioning, bodily pain/discomfort, global health, and general health perceptions, with these two standard deviations below the means of the control group of health children. These results are similar to those observed with other measures.

One paper used the Kidscreen 52 and identified lower HrQoL than healthy peers in a European reference group, in four out of 10 domains: physical well-being, psychological well-being, autonomy and social support & peers. In comparison with Polish children, these values were lower in one domain only: physical well-being, whereas in 3 domains, moods & emotions, parent relations & home life and financial resources, JIA values were higher than Polish reference values (Manczak et all, 2016). Of note, only one other paper commented on cultural differences, identifying that that non-white-and/or Hispanic youth had lower levels of physical HRQOL than did white non-Hispanic youth (Weizman et al, 2018). The absence of cultural variety in QoL assessment may mean a proportion of young people with JIA are currently omitted from QoL research and indicates the need for culturally sensitive measures of QoL due to variances in the overall QoL of young people between countries.

Appraisal of Study Designs

Of the 14 papers included, 12 included a cross sectional design, investigating HrQoL at one point in time. This study design provides a clear snapshot of QoL that can allow for comparison with different population groups. Seven studies used a control group of healthy children to compare HrQoL. The other five studies provided descriptive group data and compared against other JIA subtypes. Whilst informative, the studies that are without control group comparison, limit the conclusions that can be drawn about how QoL is affected, and whether this is specifically by JIA or another unknown variable.

Of the 12 cross sectional studies, two compared differences between age groups, and one compared difference between genders. Additionally, two studies included a longitudinal analysis of how HrQoL changed over time, and one compared children with active JIA vs JIA in remission. A further one

study compared differences between cultural backgrounds, and one study compared differences between JIA diagnoses. Two papers employed a longitudinal design to see how HrQoL might change over time. Listing et al, (2018) found no significant differences in HrQoL between children with JIA and the healthy control group, 3 years after their baseline assessment- commenting that 76% of patients with JIA had a good QoL. Oen et al (2017) commented that a proportion of patients continued to follow troubling trajectories, with 8-14% of patients maintaining a poor HrQoL. Specifically, Oen et al, (2017) identified one trajectory that suggests the young person will show improvement in HrQoL by around the two-year mark, with another showing ongoing moderate impairment. The use of longitudinal research is key in chronic conditions, to understand how this my change over the lifespan, but also what factors may keep a young person on a concerning trajectories. If the aim of QoL research is to ultimately provide intervention, it is important to understand where and at what time points these interventions may be most timely.

Appraisal of Study Results

Subtypes and Disease Status

Three papers noted differences between JIA subtypes. All three papers noted that Oligoarthritis had the least impact on HrQoL (Amine et al, 2008; Oen et al, 2017; Oliviera et al, 2007), with reported better gross motor function and less psychosocial impact, and as noted above this may in part be due to the lower levels of physical impact associated with this subtype. Further, Wu et al, (2001) identified that compared to healthy peers, those in an active period and diagnosed as systemic type were undergoing worst QoL than the polyarticular and oligoarticular subtypes also in an active period.

A further two papers commented on differences between young people with active JIA vs JIA in remission. Children with active disease reported lower scores in all domains of the PedsQL 4.0 Core Scales than did the children with inactive disease, the largest difference found in emotional functioning and lower scores on each domain of the PedsQL Multidimensional Fatigue Scale than children with inactive disease (Ringold et al, 2009). This suggests a greater importance in understanding the emotional experience of this population of young people. They also identified children with active disease reported lower scores on each of the domains of the PedsQL 3.0 Rheumatology Module than the children with inactive disease, with the exception of the communication domain, on which they reported higher mean scores. This domain assesses how hard young people find it to communicate with others about their illness, and this finding suggests generally young people feel able to communicate with others, including health care professionals about their illness, contributing positively to QoL. Children with inactive disease in this cohort and their parents reported scores that were similar to, or higher than, those of the healthy controls for the

majority of domains of the PedsQL 4.0 Core Scales, which suggests that a good QoL can be achieved for young people with treated JIA and emphasises the importance of maintaining good adherence to treatment.

Age and Gender differences

In one study that looked at differences between age groups, both the 6-7-, and 13–18-year-old age groups reported lower HrQoL than the healthy control group, however there were no reported differences in HrQoL between age groups (Haverman, 2013). Two papers identified that adolescents were more likely than younger children to have a worse quality of life (Amine et al, 2008; Shaw et al, 2006). The period of adolescence can be a troubling time of physical and emotional change (Kelsey & Simons, 2014). As JIA demands a degree of consistency and responsibility sometimes incongruent with the tasks of adolescence, this may in part explain the poorer QoL observed in adolescence, difficulties that are observed in other chronic conditions (Klein-Gitelman & Curran, 2015).

With regards to gender, one paper reported that there were no gender differences found in the children's self-report. However, there were significant differences between self and parent-report, primarily evident among girls, where scores across all domains were reported significantly lower by parents (Lundberg et al, 2012). Of note, differences were also observed between parent and child reports in four out of five of the papers that utilised proxy reports. This represents an ongoing discrepancy between child and parent repots in JIA (Lal et al, 2011). Given the importance of child self-report in QoL assessment (Bomba et al, 2012) it's important to understand what might be driving these variations.

Parent report and differences with young person reports

Five studies included both child and parent reports and one study used parent reports only. Papers did not justify why those chose to omit a parent proxy report, however given the variability in cognitive development through childhood, without proxy data, it is possible the child's QoL is not fully and accurately captured, as highlighted by the four studies that identified discrepancies between young person and parent reports. Globally, parents tended to report lower HrQoL across all domains, (Ringold et al, 2009; Lundberg et al, 2012), however these findings were not replicated across all papers with another paper finding no significant differences between child and parent reports (Bomba et al 2021). Two papers found parents reported physical functioning to be lowest (Gutierrez-Suarez et al, 2007; Lundberg et al, 2012), which may represent the concerns. of the parent who has a more observational role in assessing QoL. One paper reported parents reported school functioning as the lowest domain (Charuvanij & Chaiyadech 2018). The differences observed may be in part due to

differences in priorities between parent and child, however, also may represent measurement error in using tools that are not JIA specific.

Narrative Summary of Analysis and Robustness of Synthesis

Across the fourteen papers identified for this review, all papers identified that on average young people with JIA had a lower than optimal quality of life, with a range of 45-59% of children with JIA experiencing this. This was notable within the seven papers that included comparisons with "healthy peers," although the cross-sectional design provides only a "snapshot", meaning conclusions are limited. Two papers employed a longitudinal design which illustrated that HrQoL can change over time, however although demographic information pertaining to age, gender, and subtype was commonly available, not all studies chose to use these variables consistently in their analysis.

There was also great deal of variation in the type and quality of measures used to assess QoL, with the PEDS-QL 4.0 Core (and additional fatigue and rheumatology modules) and JAQQ the most used. The results of the domain specific findings, suggest areas of Physical health and School domains are most impacted- although there was discrepancy between parent and child reports. In general, parents tend to view their child's QoL as lower than compared to the child's self-report. There were also some differences noted between the subtypes of JIA, with Oligoarticular JIA found to have better HrQoL than notably systemic JIA. Some differences were also observed between age groups, with adolescents identified as having a worse HrQoL. Considering this variability, the review has identified a possibly lack of consistency in what is being measured. Therefore, any conclusions drawn may be erroneous as they may not have fully and accurately captured the QoL for this population.

To assess the robustness of this synthesis, this paper uses the "A MeaSurement Tool to Assess systematic Reviews" (AMSTAR) tool (Shea et al, 2009), as found in Table 2.7 below.

Table 2.7

A MeaSurement Tool to Assess systematic Reviews (AMSTAR) tool

	Response: Yes/No/Can't Answer/Not Applicable
Reviewer name	Rachael Mellor
Was an a priori design provided?	Not applicable
Was there duplicate study design and data extraction?	Yes
Was a comprehensive literature search performed?	Yes

Was the status of publication used as an inclusion criteria? (e.g., grey literature?)	No
Was a list of studies (included and excluded provided?)	Included, yes Excluded, available on request
Was the scientific quality of the included studies assessed and documented?	Yes
Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes
Were the methods used to combine the findings of studies appropriate?	Yes
Was the likelihood of publication bias assessed?	No
Was the conflict of interest included?	Yes

Discussion

This paper set out to answer the question "what is the QoL for young people with JIA?". To answer this, fourteen papers directly pertaining to this question were identified and reviewed. In terms of answering the review question, it appears QoL for young people with JIA is lower than optimal, and notably is significantly lower when compared to healthy peers. Although this finding was consistent across the studies, overall research was scarce, with variability in the methods used to ascertain these results. Different results may arise due to the use of these multiple different methods of assessing QoL (Macků & Barvíř, 2022) and was something observed within this review, for example one paper by Manczak et al (2016) identified that children with JIA were impacted on the physical wellbeing domain only, when compared to healthy Polish children. However, many papers identified deficits in QoL compared to healthy peers. Variation observed between JIA diagnoses may be accounted for differences in pain and functional ability, but subtle differences between cultural groups may be harder to explain without additional contextual information.

Importantly however, in aiming to answer this question, this review identified several pitfalls related to measurement of this construct, which means that despite lower observed QoL in groups with JIA, concrete conclusions are difficult to draw. Notably, research pertaining directly to QoL in JIA, has identified variation in whether studies measure QoL, HrQoL or a mixture, thus suggesting poor face validity in what is being assessed (Adunuri & Feldman, 2014). The lack of homogeneity in assessment means broad conclusions may be drawn, and the variability in assessment and results means generalisability is low. The variation observed also suggests that there are potential influences on QoL that are not currently captured by the measures used. Given these methodological problems, results should be interpreted cautiously due to limitations in the measurement and the validity of pooling these studies to draw conclusions.

Given the subjective nature of QoL, it is possible some measures used may not be sensitive enough to account for relevant factors such as cultural differences, the impact of socio-economic status (Didsbury et al, 2016) or differences in how families support a young person based on cultural norms. It is also important to consider how these measures might then be used in clinical practice. In the absence of defined cut offs, a child's QoL may be assessed primarily using clinician judgement, a practice potentially then open to risk of bias. This represents a common trade-off between clinical and academic utility of QoL measures (Higginson & Carr, 2001), whereby the current tools are too lengthy to use within the clinic room, and therefore QoL is often judged based on clinician experience, thus lacking generalisability.

Strengths and Limitations and Implications for Future research

In terms of strengths, this review contributes to the current evidence base in that it summarises the current state of QoL research and highlights the current limitations in measurement and understanding of QoL for this population. It highlights a lack of consensus on the phenomena's of QoL and HrQoL, and how this is translated into the way this is measured in young people. With the data available, this review concludes that QoL is lower for children with JIA, when compared to healthy peers, with variations observed in which domains and which young people might be most affected. However, papers included came from a wide variety of geographical locations, suggesting these results are not limited to Western-centric locales.

In terms of limitations, much in the same way QoL remains an ill-defined term, the main aim of this review perhaps was restricted by its own remit. This review aimed to quantify what is the quality of life for young people with JIA, however the capacity to answer this question definitively is limited, in part due to the limitations of the tools used. An in-depth review of the measures typically used to measure QoL in JIA, is beyond the scope of this review, however alternative papers such as those by Adunuri & Feldman (2014) are able to provide a critique of these measures- notably finding in a review of 50 measures, none were able to meet the face validity set out in the standards by Gill & Feinstein (1994). It has been suggested that due to the highly individual perceptions of QoL, quantitative assessment should be supplemented with patient reports and qualitative data (Gill & Feinstein, 1994).

Study quality was generally adequate, however it was noted there was a risk of selection bias due to the purposive nature of the sampling for most papers. Therefore, the conclusions drawn in this review are severely limited by the quality of the data brought forward through inadequate measurement tools.

Further limitations include the inability of this review to consider the mediating roles of depression and anxiety in the QoL of young people with JIA. As highlighted by previous research (Fair et al, 2019; Margetić et al, 2005) rates of depression and anxiety are higher within this population. No papers stated that young people were screened for these diagnoses and excluded, leading to possible confounding variables. Additionally, several papers did exclude young people with associated conditions, such as uveitis. Therefore, it is possible there is a proportion of young people with JIA whose experience is not currently captured by the QoL research.

In carrying out this review, several interesting papers were excluded that pertained to causal pathways to quality of life, and in doing so excluded some interesting themes in this narrative, for example the roles of disease activity and treatment (Oen et al, 2021). Further research might also focus on the "temporal order" of these factors and how they might impact QoL as the young person grows up (Seid et al, 2012) for example what role does the impact on social domains play on QoL in younger children vs adolescents for example. Currently, limited research exists on how QoL might change across the lifespan and therefore there is a need for further longitudinal research in this area. Most studies reported age of onset/disease duration, however the relevance of this was not routinely discussed.

In terms of implications for future research, this review has clearly highlighted a need for improvements in the way QoL is measured. The array of measures used with varying validity means not only are the results difficult to pool in a meaningful way, but they also vary in the results that are produced. Future research might focus on the development of more JIA sensitive measures of QoL that might be able to account for associated conditions such as uveitis.

With regard to clinical implications, the results of this review would suggest clinicians should monitor quality of life of young people with JIA based on the universal experience of most young people, but notably to consider children whose QoL may be on a worrying trajectory (Oen et al, 2017) due to the population of adolescents with JIA who seem to persevere with a poor QoL. However as suggested by Gill & Feinstein (1994) it's important to hear the young person's voice alongside quantitative measures of QoL, to better understand how individual variations may impact a young person's quality of life and how clinicians may be able to intervene to improve this. These voices may be harnessed in the co creation of meaningful quality of life measures that may show greater reliability within this population.

Conclusion

This review aimed to quantify what is the quality of life for young people with JIA. The results of this review suggest that on average, QoL for those with JIA is lower than their healthy peers, however

there is significant variability in this. Whilst some young people with JIA are either less impacted, be it due to the sub type of JIA, or are able to obtain a good HrQoL by adolescence, others continue to have a poor HrQoL into adolescence, with their physical functioning, and educational functioning most impacted. Considering the wide variability in research conducted, the findings of this review indicate more rigorous assessment of quality of life and disease impact across populations and ages is needed. Although this review was not without its imitations, it's clear that HrQoL is low in this group.

Conflict of interest statement

The author would like to declare there is no conflict of interest in completing this systematic review.

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Appendices

Appendix A: Summary Table of Study Characteristics

Author Year	Country	Participant No.	Age Range & Gender	Diagnosis	Mean age of onset/Disease Duration	Study Design & Analysis	Measure of HR-QoL	Inclusion/ Exclusion Criteria	Key Findings Relevant to the Systematic Review Question
Amine et al, 2008	Morocco	N=80	**Mean age:** 10.85± 2.95 (6-17) **Gender:** Female: 47% Male: 53%	**JIA subtypes:** Systemic N=21 (26%) Polyarticular N= 25 (31.6%) Extended Oligoarticular N= 4 (5%) Persistent Oligoarticular N= 30 (37.5%)	**Mean disease duration:** (years) 3±1.93 (1-8)	Cross Sectional, between groups Between two groups ANOVA	Juvenile arthritis quality of life questionnaire (JAQQ). Childhood Health Assessment Questionnaire (CHAQ) Child report only.	**Inclusion:** Children and adolescents with a diagnosis of JIA aged less than 18 years. **Exclusion:** Patients with psoriatic and enthesitis related arthritis.	In general, children and adolescents with JIA had a poorer HRQL as measured by the JAQQ. **The mean global score** of JAQQ was 2.6±1.3 (1-6) There were significant differences between the age groups, with worse scores for adolescents, and greater disability and pain for adolescents. The most affected health concepts were psychosocial and motor function. ***Subscales:*** Gross motor: 2.6 (1-5.95) Fine motor: 2.79 (1-6.4) Psychosocial function: 2.82 (1-6.4) Systemic problems: 2.36 (1-5.5) Overall scores were better for the oligoarticular subtype with better gross motor function, better motor function, less psychosocial impact, and less symptoms than other subtypes.
Bomba et al, 2021	Italy	JIA group N=39 Control group N=80	**Mean age:** *With JIA* 11.43±2.1 *Control* 11.53±1.5 *Age range* 5-16 **Gender:** Female: 69% Male: 31%	**JIA subtypes:** Systemic JIA N=2 (5.1%) Oligoarticular JIA N= 24 (61.5%) Polyarticular JIA N=11 (28.2%) Arthritis with enthesitis N=1 (2.6%) Psoriatic arthritis N= 1 (2.6%)	**Mean disease duration:** (months) 37.79±32 .45	Cross sectional, between groups Nonparametric Mann–Whitney U	PEDSQL 4.0 Generic Core Scales Child report + Parent report (Varni et al, 2002)	**Inclusion:** Diagnosis of JIA **Exclusion:** Comorbid diseases or mental illness. **Control group** 80 healthy children recruited from primary and secondary schools and matched.	Those with JIA had lower quality of life scores across all areas of functioning compared to the controls. There was no difference was observed on PEDSQ 4.0 Core Scale scores when comparing the proxy reports obtained in the two groups. **The PEDS-QL Total QoL mean score** for subjects with JIA was 73.77 ± 12.85 For healthy subjects it was 86.81 ± 9.45 ***Subscales for children with JIA*** Psychosocial health: 67.32 ± 20.53 Physical health: 75.92 ± 12.69 Emotions: 72.73 ± 16.92 Sociability: 84.09 ± 15.28 School: 70.97 ± 19.38 ***Subscales for healthy subjects*** Psychosocial health: 86.81± 9.45 Physical health: 75.92 ± 12.69 Emotions: 72.73±16.96 Sociability: 87.92± 12.72 School: 79.86±21.36

Charuvanij & Chaiyadech 2018	Thailand	N=65	**Median age:** 9.6 (6.4-12.3) **Gender** Female: N=33 (50.77%) Male: N=32 (49%)	**JIA subtypes:** Systemic JIA: N=26 (40%) ERA: N=14 (21.5%) Oligoarticular JIA: N=12 (18.5%) Polyarticular JIA RF-: N=6 (9.2%) Polyarticular JIA, RF+: N=5 (7.7%) Undifferentiated JIA N=2 (3.1%)	**Mean disease duration :** (years) 1.1 (0.2-2.2)	Cross sectional Mann–Whitney U test Pearson's chi-square test.	PedsQL 4.0 generic core scales *Validated Thai version* Parent and Child report.	**Inclusion:** Children with JIA aged 2-18 and their parents. **Exclusion:** Children/parents unable to complete the questionnaire	45.4% children were classified as having suboptimal HRQOL. **The PEDS-QL Total QoL median score** for children with JIA was 80.7 (36.9–100), and by parents was 71 (33.3–100). The median (range) parent-reported HRQOL subscale scores were lower than the child-reported scores for all subscales. Physical health had the lowest subscale score for children. Social functioning had the highest subscale score for children. Parents reported school functioning domain lowest. Social functioning highest for parents. ***Subscales for children with JIA*** Physical health: 78.1 (34.4-100) Emotional functioning: 85 (35-100) Social functioning:: 90 (30-100) School functioning: 80 (25-100) ***Subscales reports from parents*** Physical health: 75 (0-100) Emotional functioning: 80 (40-100) Social functioning: 85 (25-100) School functioning: 60 (25-100)
Gutierrez-Suarez et al, 2007	Western Europe Eastern Europe Latin America	N=6290 JIA N=3167 Healthy control N=3123	**Mean age:** 10.0 ± 4.3	**JIA subtypes:** Systemic: N=613 (19.4%) Polyarticular: N=1069 (33.7%) Extended oligoarticular: N=567 (17.9%) Persistent oligoarticular: N=918 (29%)	**Mean disease duration :** 4.1 ± 3.5 (years)	Cross sectional, Between groups One way ANOVA	Parent's administered 50-item version of the CHQ (also called CHQ-PF 50) *Regional translation* Parent report only.	**Inclusion:** Those with a diagnosis of JIA. Healthy children <18 years of age. **Exclusion:** Children with psoriatic and enthesitis arthritis.	Compared with healthy children, JIA patients had lower values in all subscales of the CHQ. The most impaired domains (<2 S.D. of the means of healthy children in one or more geographic areas) being Physical Functioning, Bodily Pain/Discomfort, Global Health and General Health Perceptions. Statistically significant differences between patients and health controls were found among the three geographic regions for the following CHQ subscales: Bodily pain, Global health, General Health, Change in health. with respect to the previous year, Self-esteem, and Family cohesion. Parent reported more impact on physical wellbeing than psychosocial, with no differences across origins.
Listing et al, 2018	Germany	N=1444 JIA: N=953 Control: N=491	**Mean age:** With JIA: 7.9 ± 4.8 Controls 8.4 ± 4.6	**JIA subtypes:** Oligoarthritis: N=441 (46.3%) Persistent oligoarthritis: N=250 (26.2%) Extended oligoarthritis,: N=0	**Mean age of diagnosis** 7.7 years ± 4.8.	Longitudinal cohort study, between groups Logistical regression	PedsQL 4.0 generic core scales *Validated German version* Children with JIA and healthy peers.	**Inclusion:** Diagnosis of JIA For less than 12 months **Exclusion:** Not stated	Baseline characteristics of both groups differed significantly. Compared with the healthy peers, the HRQoL in JIA patients was impaired in both physical and psychosocial health. **The PEDS-QL Total QoL mean score** for children with JIA was 71.5 ± 18.4, and for healthy peers was 89.9 ± 7.7. ***Subscales for children with JIA*** Physical health: 66 ± 24.6 Emotional functioning: 68.9 ±22.1 Social functioning: 82 ± 19.1

				RF-negative polyarthritis: N=250 (26.2%) RF-positive polyarthritis: N= 16 (1.7%) Enthesitis-related arthritis: N= 100 (10.5%) Psoriatic arthritis: N=40 (4.2%) Systemic-onset JIA: N=35 (3.7%) Undifferentiated arthritis: N=71 (7.5%)				Psychosocial functioning: 74.8 ± 17.4 School functioning: 72.9 ± 20.9 ***Subscales for healthy subjects*** Physical health: 89.9 ± 7.7 Emotional functioning: 80.4 ± 13.8 Social functioning: 92.7 ± 10 Psychosocial functioning: 87.1 ± 9.5 School functioning:88.1 ±12.1 **At 3 year follow up** There was no statistically significant (p = 0.44) difference in HRQoL between the groups at the 3-year FU. Using the PedsQL data of the peers to define a favourable HRQoL (score ≥ 79.3), we found that 76% of patients with JIA attained this HRQoL, with a mean PedsQL total value of 93.6 ± 6.3.
Lundberg et al, 2012	Sweden	N=53	**Mean age:** Females 14 (8-18) Males 14 (10-18)	Oligoarthritis: N=19 (36%) Polyarticular arthritis RF-positive: N=9 (17%) Enthesetis-related arthritis: N=8 (15%) Unspecified arthritis: N=7 (13%) Psoriatic arthritis: N=6 (11%) Polyarticular arthritis RF-negative: N=2 (4%), Systemic arthritis: N=2 (4%)	**Disease Duration:** Female median: 5 (0-16) Male median: 2 (0-13) (years)	Cross-Sectional Mann Whitney U Wilcoxon signed-rank	Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL) Parent and child reports.	**Inclusion:** Children aged 8 to 18 years with JIA **Exclusion:** Not stated	More than half of the children experienced suboptimal HRQOL, based on both self- and parent-reports- by 29 of the children (55%) and 31 of the parents (59%). No gender differences were found in the children's self- reports. There were significant differences between self- and parent-reports, primarily evident among girls. Children and parents rated physical functioning the worst, and social functioning the best, was comparable to results found in an earlier psychometric study. **The PEDS-QL Total QoL mean score** of 75.06 ± 16.28. Physical health mean scores= 68.31 ± 20.72; psychosocial health mean score of 78.66 ± 16.88. The total parental mean score was 71.14 ±18.66. The physical health was 66.01 ±20.49. Psychosocial health mean score was 73.83 ±19.54. ***Subscales for females-child report*** Physical health: 70.82 c 17.98 Emotional functioning: 79.86 ± 21.06 Social functioning: 86.69 ± 14.51 Psychosocial functioning: 79.4 ± 15.91 School functioning: 71.65 ± 21.03 ***Subscales for females- parent reports*** Physical health: 65.49 ± 20.73 Emotional functioning: 71.59 ± 22.78 Social functioning: 76.76 ± 18.49 Psychosocial functioning: 72.06 ± 18.9 School functioning: 67.89 ± 22.6 ***Subscales for males- child report*** Physical health: 62.5 ± 25.72 Emotional functioning: 76.48 ± 23.78 Social functioning: 79.37 ± 19.91 Psychosocial functioning: 76.94 ± 19.37 School functioning: 75 ± 18.07 ***Subscales for males- parent reports*** Physical health: 67.21 ± 20.52 Emotional functioning: 74.37 ± 25.02 Social functioning: 85.94 ± 19.25 Psychosocial functioning: 77.92 ± 20.99 School functioning: 73.44 ± 23.57
Manczak et all, 2016	Poland	N=173 Children: N=89 Parents: N=84	**Median age:** 14 years (11-16)	JIA Otherwise not stated	**Disease Duration:** "No longer	Cross sectional, between groups	KIDSCREEN-52 questionnaire	**Inclusion:** 8-18 years, JIA longer than 1 year.	Children's HRQoL was lower than in healthy children from the European reference group, in 4 out of 10 domains: physical well-being, psychological well-being, autonomy and social support & peers. In comparison with reference values for Polish children, these values were lower in one domain only: physical well-being, whereas in 3 domains – moods & emotions, parent relations & home life and financial resources, JIA values were higher than Polish reference values.

			Female: N=55 (62%) Male: N=34 (38%)		than one year".	Cohen's d effect size coefficient	Child and Parent reports.		Lowest quality of life values compared with the healthy population of children from the reference group, were observed in the physical well-being dimension. QoL of JIA children in comparison with European data is lower in other dimensions: autonomy, social support and peers and school environment. ***Child report subscale means:*** Physical wellbeing: 42.23 ±9.28 Psychological wellbeing: 46.78 ±11.66 Moods and emotions: 51.43 ±10.72 Self-perception: 49.34±9.77 Autonomy: 46.37±8.44 Parent relation and home life: 49.85±10.24 Financial resources: 48.41±9.43 Social support and Peers: 44.09±10.61 School environment: 47.75±10.25 Bullying: 51.918±8.98 ***Parent Report subscale means:*** Physical wellbeing: 32.70 ±7.76 Psychological wellbeing: 44.79 ±12.47 Moods and emotions 51.19 ±11.63 Self-perception: 47.33±9.06 Autonomy: 47.82±10.86 Parent relation and home life: 51.17±11.6 Financial resources: 47.01±9.48 Social support and Peers: 41.76±10.33 School environment: 46.11±9.47 Bullying: 51.08±9.44
Haverman,2013	Netherlands	Children with JIA: N=152 Parents: N=139	**Mean age:** 13.03 ±3.4 (6-18) Female: N=102 (67%) Male: N=50 (33%)	**JIA Subtype:** Oligoarticular JIA, persistent: N=30 (19%) Oligoarticular JIA, extended: N= 21 (13.8%) Poly articular JIA, RF negative: N= 66 (43.4%) Poly articular JIA, RF positive (7 (4.6%) Systemic JIA: N=3 (2%) Enthesitis related arthritis: N=15 (9.9%) Undifferentiated JIA: n=8 (5.2%) Chronic arthritis with other autoimmune	**Disease duration:** 8.61±4.4 (years)	Cross Sectional, between groups. t-tests Mann-Whitney tests.	Paediatric Quality of Life Inventory 4.0 (PedsQL) *Validated Dutch version* Childhood Health Assessment Questionnaire (CHAQ) *Dutch version*	**Inclusion:** Children aged 6-18 years with JIA **Exclusion:** Those who did not respond.	**The PEDS-QL Total QoL mean score** for children with JIA ages 6-7 was 70.26 ± 23.02, and for healthy peers was 86.07 ± 8.29. **The PEDS-QL Total QoL mean score** for children with JIA ages 8-12 was 71.67 ± 14.06, and for healthy peers was 82.31 ± 8.83. **The PEDS-QL Total QoL mean score** for children with JIA ages 13-18 was 71.91 ± 17.36, and for healthy peers was 83.14± 8.99. There was significant Impairment in HrQoL in those with JIA in nearly all domains, independent of disease activity. Both the child age group (6-7 years) and the adolescent age group (13-18 years) reported lower HRQOL compared to their healthy peers. Almost half the children (47-57%) had an impaired HrQoL, as opposed to 16% of the general population. Scores were equal compared to those with other chronic conditions. Most impacted areas seemed to be physical and psychosocial functioning. Emotional functioning is less affected. ***Proxy reported subscales for children with JIA ages 6-7*** Psychosocial functioning: 72.98±18.75 Physical health: 65.18 ±32.22 Emotional functioning: 69.29± 22.09 Social functioning: 76.79± 20.06 School functioning: 72.86± 19.88 ***Proxy reported subscales for norm population ages 6-7*** Psychosocial functioning: 86.07±8.29 Physical health: 88.83±9.43 Emotional functioning: 78.44± 12.77 Social functioning: 89.02±11.21 School functioning: 86.31±10.80

				inflammatory disease: N= 2 (1.3%)					***Child with JIA reported subscales ages 8-12*** Psychosocial functioning: 71.9±17.36 Physical health: 71.9± 13.9 Emotional functioning: 69.84±20.32 Social functioning: 76.98±15.07 School functioning: 68.89±17.04 ***Child with JIA reported subscales ages 13-18*** Psychosocial functioning: 74.38± 15.99 Physical health: 67.29±23.92 Emotional functioning: 72.60±23.07 Social functioning: 83.27± 13.89 School functioning: 67.27± 20.46	***Norm population reported subscales ages 8-12*** Psychosocial functioning: 80.75±10.34 Physical health: 85.25±8.85 Emotional functioning: 76.85±13.76 Social functioning: 86.51±12.24 School functioning: 78.88±11.90 ***Norm population reported subscales ages 13-18*** Psychosocial functioning: 81.21±10.22 Physical health: 86.76±9.21 Emotional functioning: 77.53±15.01 Social functioning: 90.14±11.37 School functioning: 75.95±12.68
Oen et al, 2017	Canada	N=1,249	Mean age not stated. Female: N=785 (64.1%) Male: N= 464 (36%)	**JIA Subtype** Systemic: N=76 (6.1%) Persistent Oligoarticular: N=422 (33.8%) Extended Oligoarticular: N=77 (6.2%) RF-negative Polyarthritis: N=249 (19.9%) RF-positive polyarthritis: N=47 (3.8%) Psoriatic arthritis: n=74 (5.9%) Enthesitis related arthritis: N=176 (14.1%) Undifferentiated arthritis: N=128 (10.2%)	**Mean age *at diagnosis*** 9.6 ± 3.9 (years)	Longitudinal Between groups Mann-Whitney U test; Kruskal-Wallis test, or chi-square test.	Juvenile Arthritis Quality of life Questionnaire (JAQQ) Quality of My Life questionnaire (QoML)	**Inclusion:** Enrolled in Research Within 6 months of diagnosis At least 1 recorded value of HRQoL. **Exclusion:** Not within enrolment window, those without a confirmed diagnosis and those with a changed diagnosis after enrolment.	In total, 8–14% of patients followed worrisome trajectories of persistently poor HRQoL. There was substantial heterogeneity in HRQoL scores across subjects within a JIA category. Median JAQQ and HRQoML scores were worst at enrolment and gradually improved over time. Values were statistically different across JIA categories up to visit 6 (37 months after diagnosis). Persistent Oligoarthritis had the least impact on HRQoL. Children in this subgroup had median values near the best possible scores by 25 months. Median HRQoML values of children with systemic arthritis also came near the best possible scores by this time. Many subjects followed minimal impairment trajectories, which quickly reached near best possible values or mild impairment trajectories with moderate initial impairment that improved For both measures, the analysis identified 2 trajectories of major impairment: one characterized by persistent major impairment in HRQoL and another with transient major impairment that started with poor HRQoL but improved substantially by 2 years. The remaining JAQQ trajectory was characterized by persistent moderate impairment ***Mean JAQQ scores 2 weeks post diagnosis*** Total: 2.7 (1.9-4) Systemic: 3 (1.7-4.6) Persistent Oligoarticular: 2.4 (1.6-3.1) Extended Oligoarticular: 3 (2.1-4.2) RF-negative Polyarthritis: 3.3 (2-4.5) RF-positive polyarthritis: 3.9 (2.4-4.7) Psoriatic arthritis: 3 (2.3-4) Enthesitis related arthritis: 3 (2.3-4) Undifferentiated arthritis: 2.9 (2-3.2) ***Mean HRQoML scores 2 weeks post diagnosis*** Total: 7.8 (5.2-9.3) Systemic: 7.6 (4.7-9.3) Persistent Oligoarticular: 8.8 (6.9-9.8) Extended Oligoarticular: 8 (5.4-8.8) RF-negative Polyarthritis: 7.3 (5.1-9) RF-positive polyarthritis: 6.4 (3.7-8) Psoriatic arthritis: 7.8 (5.3-9.1) Enthesitis related arthritis: 6.3 (4.6-8.5) Undifferentiated arthritis: 7.1 (4.6-9.4)
Olivier a et al, 2007	Brazil Spans 32 countries	N=6639 With JIA N=3,324	Mean age With JIA: 10.0 ± 4.4	Not stated	***Disease Duration :*** 5.9 ± 3.9	Cross sectional, between groups	CHQ proxy report	**Inclusion**: Diagnosis of JIA Under 18 years of age at the	On average, patients with JIA have a poorer HRQOL as compared with healthy peers in both physical and psychosocial domains, with physical health being more affected.	

		Healthy control N=3,315	Female: N= 2,250 (68%) Male: N=4389 (32%)			Descriptive statistics t-test Mann-Whitney U test 1 way ANOVA		time of the evaluation. **Exclusion:** Patients with psoriatic arthritis and enthesitis-related arthritis due to too small numbers.	The areas of HRQOL most affected by JIA (<2 SDs of the mean of healthy children) were global health, physical functioning, role social limitation (physical), and bodily pain/discomfort. The mean + SD Physical Summary score of the CHQ was significantly lower in patients with JIA than in the sample of healthy children (44.5 ± 10.6 and 54.6 ± 4.0, respectively). Likewise, the mean Psychological Summary score of the CHQ was significantly lower in patients with JIA than in healthy children (47.6 ± 8.7 and 51.9 ± 7.52, respectively). Patients with persistent oligoarthritis showed better levels of HRQOL in all CHQ subscales and in both summary measures compared with patients with the other subtypes. The level of HRQOL in all CHQ domains was similar across patients with systemic arthritis, polyarthritis, and extended oligoarthritis; in these 3 subtypes the most impaired CHQ health concepts were global health, physical functioning, role social limitation (physical), and bodily pain/discomfort.
Ringold et al, 2009	USA	N=60	**Mean age** 8.4±9.4 (1.3-15) Female: N=50 (83%) Male: N=10 (17%)	Not specified	Not stated	Cross sectional, between groups Unpaired t-tests and Pearson correlations.	Paediatric Quality of Life Inventory (PedsQL) Generic Core Scales PedsQL Rheumatology Module PedsQL Multidimensional Fatigue Scale Childhood Health Assessment Questionnaire (CHAQ)	***Inclusion:*** Dx and treated for JIA between January 1, 2000, and December 31, 2006. Minimum of 2 visits to the rheumatology clinic, ***Exclusion:*** Guardian not present; non-English speaking; recent foster care placement.	**The PEDS-QL Total QoL mean score** for children with JIA was 83.54. Compared to healthy controls, children with JIA and their parents reported lower scores in the majority of domains of the PedsQL Generic Core Set. Children with inactive disease in this cohort and their parents reported scores that were similar to, or higher than, those of the healthy controls for the majority of domains of the PedsQL Generic Core Scales. Children with active disease reported lower scores in all domains of the PedsQL Generic Core Scales than did the children with inactive disease, the largest difference in emotional functioning. The parents of children with active disease also reported lower scores in all domains of this measure than did the parents of children with inactive disease, with the largest difference in the physical health domain Children with active disease reported lower scores on each of the domains of the PedsQL Rheumatology Module than the children with inactive disease, with the exception of the communication domain, on which they reported higher mean scores. On the PedsQL Multidimensional Fatigue Scale, children in this cohort and their parents/proxies reported lower scores on all domains of the Multidimensional Fatigue Scale than the healthy controls, regardless of disease activity status. Similarly, children with active disease also reported lower scores on each domain of the PedsQL Multidimensional Fatigue Scale than children with inactive disease. ***Child with JIA self-report*** Psychosocial functioning: 82.77±14.48 Physical health: 82.27 ± 17.40 Emotional functioning: 81.14± 16.85 Social functioning: 90.55± 13.39 School functioning: 77.18± 19.76 ***Health Control self-report*** Psychosocial functioning: 81.83±13.97 Physical health: 87.77±13.21 Emotional functioning: 79.21± 18.02 Social functioning: 84.97±16.71 School functioning: 81.31±16.09 ***Parent of JIA proxy report*** Psychosocial functioning: 82.13±16.74 Physical health: 82.06± 18.10 Emotional functioning: 81.41±20.18 ***Parent non-JIA proxy report*** Psychosocial functioning: 81.24±15.34 Physical health: 84.08±15.34 Emotional functioning: 81.20±16.40

								Social functioning: 88.80±15.05 School functioning: 78.70±21.01 ***Child with JIA Rheumatology module self-report*** Pain and Hurt: 74.52± 23.48 Daily Activities: 94. 31 ±9.90 Treatment: 78.04±16.70 Worry: 75.33± 26.77 Communication: 81.63 ± 20.93 ***Child with JIA fatigue self-report*** Total Fatigue: 78.92±15.45 General Fatigue: 83.01±16.22 Sleep/rest fatigue: 73.35±20.32 Cognitive Fatigue: 79.90± 20.57	Social functioning: 83.05±19.66 School functioning: 78.27±19.64 ***Parent proxy report Rheumatology module*** Pain and Hurt: 73.15± 23.83 Daily Activities: 88±17.19 Treatment: 73.68±23.09 Worry: 78.71±26.85 Communication: 73.14± 31.38 ***Parent proxy report Fatigue module*** Total Fatigue: 81.08± 18.40 General Fatigue: 81.08±18.40 Sleep/rest fatigue: 80.60±23.03 Cognitive Fatigue: 81.52±23.93
Shaw et al, 2006	UK	N=308	***Mean age:*** 14.2 (10.9–18.0) Male to female ratio: 1:1.5	***JIA subtype:*** Oligoarthritis persistent: N=60 (19.5%)	**Disease duration:** 5.7 (0.0–16.3) (years)	Cross sectional Nonparametric inferential statistics. Chi-square, Mann-Whitney, Kruskal-Wallis.	Juvenile Arthritis Quality of life Questionnaire (JAQQ)	***Inclusion:*** Dx of JIA Under care for next 6 months ***Exclusion:***	HRQOL of adolescents with JIA was less than optimal, particularly in the domains of gross motor and systemic functioning The median JAQQ score for the entire sample was 2.7 with no significant differences between the age groups. Across the domains, the highest level of problems were reported in the area of gross motor function. Least problems were reported in fine motor function. The domain scores did not differ between age groups. The results indicate that the HRQOL of adolescents with JIA is less than optimal, particularly in the domains of gross motor and systemic functioning and has significant and independent relation- ships with pain, disease activity, and functional disability. One-third of participants reported frustration among their biggest problems. Adolescents with JIA are faced with symptoms that can be difficult to relieve, activities they cannot perform, and the uncertainty of daily fluctuations and long-term prognosis.
Weizman et al, 2018	America	N=203	***Mean age*** 11.8±3.6 Female N=138 (76.7%) Male: N=42 (23.3%)	***JIA subtype:*** Not stated	**Disease duration:** 7.7±3.5 (years)	Cross sectional Descriptive statistics Wilcoxon rank-sum or Chi Square tests	Paediatric Quality of Life Inventory (PedsQL) Generic Core Scales	***Inclusion:*** Children with JIA enrolled in the CARRA Registry ***Exclusion:*** Not stated	**The PEDS-QL Total QoL mean score** for children with JIA was 76.7 ±18.2. ***Child with JIA reported subscales*** Psychosocial functioning: 76.9±17.9 Physical health: 76.2± 22 Average HRQOL among the cohort was suboptimal. Non-white-and/or Hispanic youth had lower levels of physical HRQOL than did white non-Hispanic youth. Among those taking methotrexate, a greater proportion of females compared to males reported symptoms of intolerance. This view highlights the importance of evaluating both treatment experiences and disease burden when measuring outcomes. For youth with JIA, HRQOL is multidimensional, reflecting disease as well as treatment factors. Adverse treatment experiences undermine HRQOL even after accounting for disease symptoms and disease activity and should be assessed routinely to improve wellbeing.

Wu et al, 2021	China	N=180	***Mean age*** 10.47±2.66 (8-18.22) (102 boys and 78 girls)	***JIA subtype:*** JIA Systemic JIA: N=60 Polyarticular: N =70 Oligoarticular: N=38	***Disease Duration :*** 6.81 ± 3.10 (years)	Cross sectional Pearson correlation coefficients	PedsQL4.0 Generic Core PedsQL3.0 Rheumatology Module scale *Chinese versions*	***Inclusion*** Dx with JIA Longer than 3 months Families understand JIA ***Exclusion criteria*** Other diseases that affect QoL. Do not understand/cannot answer items.	**The PEDS-QL Total QoL mean score** for children with JIA was 82.85 ± 14.82. In the active period was 72.05 ± 15.29, in remission period was 89.77 ± 9.23. The QoL score of systemic, polyarticular and oligoarticular JIA patients were 77.05 ± 19.11, 84.33 ± 12.46 and 87.12 ± 10.23. The mean score of PedsQL3.0 Rheumatology Module scale on 180 patients was 91.22 ± 9.45, for these in active period was 84.70 ± 11.37, in remission period was 95.43 ± 4.48. The QoL score of systemic, polyarticular and oligoarticular JIA patients were 89.41 ± 11.54, 89.38 ± 10.08 and 93.71 ± 6.92. The QoL of Chinese JIA children is worse than their healthy peers, these in active period and diagnosed as systemic type were undergoing worst quality of life. The reliability and validity of PedsQL 4.0 Generic Core and PedsQL3.0 Rheumatology Module scale in Chinese JIA children are satisfactory, and can be used in clinical and scientific researches. ***Systemic JIA self-report*** Total: 77.05±19.11 Physical functioning: 76.83±23.67 Emotional functioning: 87.28±18.76 Social functioning: 81.34 ±21.33 School functioning: 67.64±18.83 ***Polyarticular JIA self-report*** Total: 84.33±12.46 Physical functioning: 84.38±20.4 Emotional functioning: 87.70±14.12 Social functioning: 89.17±15.88 School functioning: 77.03±14.02 ***Oligoarticular JIA Self-report*** Total: 87.12 ± 10.23 Physical functioning: 86.88±15.11 Emotional functioning: 92.65±12.02 Social functioning: 92.97±11.98 School functioning: 77.28±13.99 **Rheumatology module** ***Systemic JIA self-report*** Total: 89.41±11.54 Pain and Hurt: 82.73±20.55 Daily Activities: 97.50±10.85 Treatment: 88.69± 12.60 Worry: 91.82±13 Communication: 85.03±21.80 **Rheumatology module** ***Polyarticular JIA self-report*** Total:89.38 ± 10.08 Pain and Hurt: 82.73±19.89 Daily Activities: 97.50±9.98 Treatment: 88.72±12.85 Worry: 88.86±13.77 Communication: 85.98±15.87 **Rheumatology module** ***Oligoarticular JIA Self-report*** Total: 93.71±6.92 Pain and Hurt: 90.07±13.92 Daily Activities: 99.41±3.29 Treatment: 93.64± 7.16 Worry: 93.75±12.06 Communication: 91.41±12.86

Appendix C: AXIS Tool for Appraisal of Cross-Sectional Studies

	Question	Yes	No	Don't know/ Comment
Introduction				
1	Were the aims/objectives of the study clear?			
Methods				
2	Was the study design appropriate for the stated aim(s)?			
3	Was the sample size justified?			
4	Was the target/reference population clearly defined? (Is it clear who the research was about?)			
5	Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?			
6	Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?			
7	Were measures undertaken to address and categorise non-responders?			
8	Were the risk factor and outcome variables measured appropriate to the aims of the study?			
9	Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?			
10	Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)			
11	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?			
Results				
12	Were the basic data adequately described?			
13	Does the response rate raise concerns about non-response bias?			
14	If appropriate, was information about non-responders described?			
15	Were the results internally consistent?			
16	Were the results presented for all the analyses described in the methods?			
Discussion				
17	Were the authors' discussions and conclusions justified by the results?			
18	Were the limitations of the study discussed?			
Other				
19	Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?			
20	Was ethical approval or consent of participants attained?			

Appendix D: Prisma Statement (Moher et al, 2009).

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta- Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097
For more information, visit: **www.prisma-statement.org**.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	11
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	12
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	15
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	15
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	16
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	16
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	16

Section and Topic	Item #	Checklist item	Location where item is reported
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	17-18
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	17-18
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	17-18
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	17-18
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	18
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	n/a
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	18
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	18
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	18
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	18

Section and Topic	Item #	Checklist item	Location where item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	n/a
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	n/a
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	n/a
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	18
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	21
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	n/a
Study characteristics	17	Cite each included study and present its characteristics.	48
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	24
Results of individual	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	48

Section and Topic	Item #	Checklist item	Location where item is reported
studies			
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	23-35
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	n/a
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	23-35
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	n/a
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	n/a
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	23-35
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	35-37
	23b	Discuss any limitations of the evidence included in the review.	36
	23c	Discuss any limitations of the review processes used.	36
	23d	Discuss implications of the results for practice, policy, and future research.	36-37

Section and Topic	Item #	Checklist item	Location where item is reported
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	19
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	19
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	n/a
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	13
Competing interests	26	Declare any competing interests of review authors.	38
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	19-23

Chapter Three: Bridging Chapter

The systematic review presented in Chapter One attempted to answer the question "What is the Quality of Life (QoL) for young people with Juvenile Idiopathic Arthritis (JIA?)". The results of the review highlighted that whilst QoL for young people with JIA is lower than optimal, there is variation across gender, age, and geographical locales. The review also illustrated significant variation in the quality and type of tools used to assess QoL, meaning inferences made may be erroneous and the ability to draw valid conclusions is limited. From the review, a key finding was that discrepancies were observed between parent and child reports of QoL, and thus questions arise pertaining to the parent experience of having a child with JIA.

Although beyond the scope of the systematic review, several influencing variables on QoL for children with JIA were noted, including the role of medication, strict treatment regimens, and procedural distress (Eyckmans et al, 2011; Guerriero et al, 2022; Chédeville et al, 2022; Montag et al, 2022) associated with the subcutaneous administration of MTX.

Within these variables, the role of the parent is apparent. In the treatment of JIA, parental figures are key in the delivery of treatment to ensure the child's physical, medical and mental wellbeing in the long term.

As discussed in Chapter One, the role of the parent in managing the child's medication and subsequent treatment adherence, is significant (Guerriero et al, 2022) and yet parents of children with JIA are at an increased risk of psychological distress, in part due to the demands of the long-term management of the condition (Manuel, 2001). This is an important consideration as positive parental coping is associated with better outcomes in JIA (Gerhardt et al, 2003) and parents play an integral role in managing their child's treatment. Furthermore, the ability to manage pain and medication early on can help with longer term management and improve QoL over time (Cavallo et al, 2009; Stinson et al, 2012). Although research in this area is still in its infancy, consideration should be given to the unique role of the parent in their child's care, to better understand these relationships.

The qualitative empirical paper presented in the next chapter examines this dynamic in detail. The stories of nine unique families, who are interviewed about their experiences of managing MTX treatment for their child are presented. The themes arising illustrate the impact Methotrexate (MTX) can have on their child's QoL and its impact on parents themselves and their families. In doing so, the results illustrate the role MTX plays in aiding and complicating life with JIA, and the themes relevant for families coping with MTX.

This research emerged from the clinic room, where professionals have long been aware of the difficulties sometimes associated with MTX. Whilst the professionals working with these families have an array of expertise and experience to share, questions remained over how best to help these families, and the reality of living with MTX beyond what was heard in the hospital appointments.

This paper will aim to explore and furnish those gaps with additional knowledge specifically pertaining to parent's experiences, as understanding this experience will help teams support families and young people, leading to better child outcomes (Waite-Jones et al, 2020)

Whilst the size of the sample may not allow for wide generalisability, the emergent themes provide sigificant insight into what life with JIA is like for parents and families and concludes with some recommendations for future research and clinical implications for professionals working with these families.

Chapter Four

Empirical Paper: Parent experiences of giving their child Methotrexate injections

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Prepared for: Health Psychology Review (author guidelines in Appendix A).

Word count, excluding titles, tables and references: 8171

Word count including titles, tables/figures: 8638

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Abstract

Background: Childhood chronic conditions are on the rise (Perrin et al, 2014; Royal College of Paediatrics and Child Health (RCPCH), 2020; van Cleave et al, 2010). Management of these conditions is often complex, the burden of which often falls to parents to manage (Jerrett, 1994; Wickwar et al, 2013; Woo, 2006). One such condition is Juvenile Idiopathic Arthritis (JIA), an autoimmune condition, causing inflammation and pain across joints, and subsequent loss of lower muscle strength, fatigue and can have a negative impact on a young person Quality of Life (Weiss et al, 2007). The condition is commonly treated using an immunosuppressant medication, Methotrexate. However, it is often accompanied by a range of unpleasant side effects such as fatigue, nausea and lack of appetite. These side effects may lead to a range of psychological side effects, which can be challenging for both young people and their families.

Objective: This research aimed to explore the experiences of parents who administer this medication, with a view to understanding the emotional and practical burden on them, and how systematically this may then impact the young person. The research aimed to provide recommendations as to how clinicians may best support parents, to ensure better overall Quality of Life for young people with JIA and their families.

Method: Nine qualitative interviews were held with parents of children with JIA who took Methotrexate and had been experiencing related difficulties with this. These interviews were analysed using Interpretative Phenomenological Analysis.

Results: The results highlight the adversarial nature of Methotrexate, and the challenges parents and young people face in taking this medication. Five major themes emerged, including “The Parent-Carer”; “the Child at the Centre”; “The Role of the Hospital”; “Our Lives with Methotrexate”; and “Coping with Methotrexate”. These are discussed and the research and clinical implications are commented on.

Conclusion: Parents of children taking Methotrexate face a unique challenge in the difficulties they may face. Thought must be given to the availability and timing of support and resources that are given to parents, and the crucial nature of this in supporting the family as they undergo their Methotrexate journey.

Keywords: Juvenile Idiopathic arthritis, arthritis, chronic conditions, quality of life, health related quality of life, child, adolescent, parents, parenting, methotrexate, immunosuppressant

Introduction

Childhood chronic conditions such as asthma, type 1 diabetes, and cystic fibrosis, are on the rise (RCPCH, 2020; Perrin et al, 2014; van Cleave et al, 2010), in part due to the increase in survival rates and improvements in medical management. One such condition is juvenile idiopathic arthritis (JIA), or juvenile arthritis. Affecting one in 1000 young people under the age of 16 (van der Meer, 2007), JIA is an autoimmune condition with no cure, which remains with the individual across their lifespan. The condition typically causes pain and inflammation across various joints, (Prakken et al, 2011; arthritis.org), fatigue, and loss of lower muscle strength, all of which can have a significant negative impact on a young persons' quality of life (QoL) over time (Weiss et al, 2007).

Improvements in prognosis have in part been due to the development of drugs able to reduce the overactivity of the immune system (Ravelli & Martini, 2007; Klein-Wieringa et al, 2020). Such advances allow for better clinical management, however, influences on QoL are less well understood. For those with JIA, factors such as ongoing chronic pain, disease activity and medication burden all impact QoL (Ezzahri et al, 2014; Haverman et al, 2012), with chronic pain mediating the relationship between QoL and comorbid depression or anxiety (Fair et al; 2019; Krause et al, 2017; Stevanovic & Susic, 2013; Weizman et al, 2018). The presence and influence of medication side effects on JIA is important to understand. Medication side effects were reported in two-thirds of children with JIA and may lead to lower levels of QoL and lower levels of treatment adherence (Chédeville et al, 2021).

A significant variable in the management of JIA, is treatment by the immunosuppressant medication, Methotrexate (MTX) (Bechard et al, 2014). Typically administered weekly, MTX is considered the gold standard drug recommended by NICE (2014) for managing this condition, with outcomes including reduction in swelling and improvement in joint mobility, and disease remission (Takken et al, 1996;). Although MTX allows young people regain some of the physical function lost due to JIA, not only is the medication often painful to administer, it is also often accompanied by a range of unpleasant side effects including fatigue, nausea, low appetite, vomiting, neutropoenia, headaches and diarrhoea (Ramanan et al, 2003; Zachariae, 1990) with one study finding as many as 40% of patients experiencing MTX intolerance (Salim et al, 2013).

As a result of this psychological side effects are often reported by children receiving MTX as a treatment for JIA. Side effects are defined as a reaction secondary to the intended effect, that occur subsequent to giving a medication or procedure (APA, 2023). To this end, psychological side effects are psychological effects that can occur as a result of taking a medication or procedure. For MTX, these can include anticipatory anxiety and associated nausea, anticipatory pain, needle phobia,

medication refusal and behavioural difficulties (Jacobse et al, 2018; Mulligan et al, 2013). All of which can be challenging for both parents, young people and professionals alike (van der Meer et al, 2007). Anticipatory nausea and anxiety are typically amplified by the level of pain experienced (Bechard et al, 2014) with one study finding children experienced associative intolerance in merely talking about the injection (Khan et al, 2019). Of note, children must start on a regime of MTX for a minimum of 12 weeks in order to assess their tolerance and inform further decisions about alternative therapies (NICE, 2014).

Behavioural and Cognitive difficulties associated with MTX

Over time, children with JIA may develop a number of behavioural and cognitive strategies to cope with the difficulties associated with MTX treatment. Avoidance, behavioural distress, and internalizing and catastrophizing are often observed and can further contribute to the anxiety and nausea experienced (Kyvsgaard et al, 2020).

Van der Meer (2007) conducted a study looking at behavioural interventions to help manage the MTX associated psychological difficulties, and found cognitive behavioural therapy, utilising relaxation and desensitization, reduced side effects in five children, and reduced severity of nausea in a further two out of 19 (Van der Meer 2007). Of note however this study included a small sample of five, meaning conclusions drawn were limited. Eye movement desensitization reprogramming (EMDR) also has preliminary support in reducing MTX intolerance, finding effects four months after treatment concluded (Höfel et al, 2018).

In understanding how to support young people with this process, the role of the parent is also crucial. Parents may provide a variety of support to children with JIA, however little is understood about parents' experience of giving MTX to their children, particularly bearing in mind the challenges associated with administration and side effects of this treatment.

The Role of the Parent

The introduction of a long-term condition into a family may impact relationships, development, parental coping, and family functioning (Coffey, 2006; Hamlet et al, 1992; Patterson & Garwick 1994) and as children are typically diagnosed with JIA before the age of 16, parents play a key role in supporting a child with a complex long-term condition (Giacane et al, 2016; Kim & Kim 2010; Prakken et al, 2016; Smith et al, 2015).

Parenting a child with taking a MTX treatment regimen can require the administration of painful ongoing treatment (Jerrett, 1994; Wickwar et al, 2013; Woo, 2006), and the parent must provide both practical and emotional support and demonstrate resilience to their child (Beekman et al, 2019; Stinson et al, 2012). Yuwen et al, (2017) reported that parents described this experience as "struggling in the dark" due to the relentless demands of the condition, and its effects on the wider family (Bruns et al, 2008). Parents describe a "roller coaster" of emotions, such as admiration for their child, sympathy, frustration, and powerlessness (Gomez-Ramirez et al, 2016) along with the perception of their child as "vulnerable" (Haverman et al, 2014). Parents also describe experiencing ongoing uncertainty in the face of JIA, in relation to diagnosis, cause and prognosis, but also in relation to ongoing medical management and information available. This highlights the difficulties parents have managing the multiple sides of JIA.

Research exploring the lived experiences of parents administering MTX to their child is lacking. Jerret (1994) described the unexpected stress of suddenly having a chronically ill child, and the adjustment needed to cope with the demand placed on the parents. Specifically in relation to MTX, Barlow et al (2002) identified medication side effects as a significant cause of maternal stress, with maternal wellbeing found to be a mediating factor in the child's physical functioning. Gomez-Ramirez et al (2016) reported a turbulent emotional experience for parents acknowledging the difficulties in watching their child with JIA experience chronic pain.

However, research specifically into the lived experience of parents delivering the MTX injections, is lacking. Understanding these difficulties in greater depth would allow for development of more targeted interventions to support families living with JIA.

Research Questions/Aim

This qualitative research aimed to better understand how parents experience difficulties with their child's MTX injection treatment. Through the process of completing interviews with parents of children with JIA, it aimed to better understand this phenomenon, with a view to better supporting families experiencing specific MTX related difficulties. The study aimed to understand the impact on parents of delivering this medication and contributes to the knowledge base on how to support parents and families. Additional information including duration and frequency of treatment and care giver quality of life provides a broader depiction of parent experiences. Overall, this research aimed to help support parents and inform the potential for interventions for specific difficulties.

Method

Design

The research used a qualitative design; an approach commonly used to explore the depth of patient experience in health care research (Smith, 1996), to gain a rich description of the lived experience of parents experiencing difficulties with their child's MTX injection. The analysis used Interpretative Phenomenology Analysis (IPA) as its methodology. Grounded in critical realism (Easton 2010), IPA is often used in health psychology (Smith et al, 1999) as the field gives greater acknowledgement of "the constructed nature of illness". IPA aims to "give voice to" and make sense of an individual's experience (Larkin et al, 2006), making it an appropriate methodology to understand parental experience without imposing own beliefs and motivations on any potential interventions.

Participants

Inclusion criteria were parents of children up to the age of 18, who had a diagnosis of JIA. Further inclusion criteria were that the children were prescribed and either currently taking MTX by subcutaneous injection or had done so and stopped within the last 12 months, and had experienced difficulties either with physical side effects or wider psychological or behavioural side effects related to taking the medication.

Participants (further details are provided in Table 4.1) were recruited from two main teaching hospital sites, within the UK. Participants were initially recruited via gatekeepers; clinicians working directly within the service, who provided an information sheet and consent to contact form. The researcher then contacted to confirm their inclusion and gain consent for participation.

An initial 20 families of children with JIA were contacted after gaining consent to contact via gatekeepers. 11 parents decided not to participate in the study, leaving a final sample of nine participants. There is debate over what is considered an appropriate sample size for IPA. One suggestion exists, that a single participant may be considered a sample should the data provided be rich enough (Smith, 2004). However, Clarke (2010) suggested an appropriate sample size for IPA is between 4-10 participants. Therefore, recruitment was ongoing until a sufficient sample size of 9 was achieved, at which point the recruitment window had closed. Although the information sheet called for the primary caregiver to take part, this was exclusively female respondents, with one couple taking part in the interview. Two parents/carers were grandparents of the child with JIA, however for the purpose of this research they will also be referred to as parent/carers in recognition of the parental role they have.

Table 4.1

Participant characteristics

Participant No.	***Gender of main carer***	***Gender of child***	***Marital status***	***Employment status***	***Number of children***	***Number of children with JIA***	***Years with JIA***	***Approximate No. of injections****
1	F	M	Living Apart	Part Time	1	1	2	39
2	F	F	Married	Full Time	2	1	9	228
3	F	F	Married	Full Time	1	1	3	52
4	F	F	Living with Partner	Home maker	2	1	6 months	24
5	F	F	Married	Part Time	3	1	6	40
6	F	M	Living with Partner	Full Time	1	1	2	94
7	F	F	Married	Full Time	1	1	2	104
8	F	M	Married	Part Time	1	1	1 year 5 months	27
9	F	F	Married	Full Time	2	1	2 years	74

**As injections were given once per week, this figure was calculated based on number of weeks since MTX treatment commenced, minus any gaps in treatment declared by parents.*

Materials

An initial topic guide for interview was developed by a co-researcher and was co-created with parent involvement and hospital rheumatology team involvement (please see Appendix A). Information sheets, consent to contact, interview consent forms and debrief sheets can be found in Appendices B-E).

Alongside the qualitative interview, a six-item caregiver QoL measure, the Carer Experience Scale (Al- Janabi et al, 2008; Goranitis et al, 2014) was also administered to provide reliable contextual data on caregiver wellbeing and stress (see Appendix F). The CES assessed the domains of activities; support; assistance; fulfilment; control; and getting on (with the care recipient). This measure is considered a valid measure to gather data pertaining to quality of life in populations of long-term unpaid carers within the United Kingdom (Goranitis et al, 2014). Of note the descriptive results of this are discussed in Chapter 8. The decision was made to present these results separately as although they

provide important contextual information, the discussion detracted from the core qualitative findings that better meet the aims of the research.

Procedure

Letters of access and ethical approval were gained (Please see Appendix G & H) and participants were contacted via "gatekeepers". Gatekeepers were members of the rheumatology teams, who support families who are experiencing difficulties with the methotrexate injection via routine clinical contact. Gatekeepers initially explained the purpose of the study to potential participants and sought consent to contact. Following this, the researcher contacted potential participants to explain the study and consent process. If consent was provided then interviews were arranged and held with participants via Microsoft Teams.

Interviews were unstructured but were guided by a co-constructed topic guide, developed with clinicians and parents of children with JIA (Appendix A). Demographic information and the CES questionnaire were completed at the onset of the interview, and participants were offered breaks as required. Interviews lasted approximately one hour. At the end of the interview, participants were thanked for their time and debriefed (see Appendix F for information provided) and were given a £5 Amazon voucher as a token of appreciation for taking part in the research.

Interviews were automatically transcribed by Microsoft Teams and reviewed for accuracy by the researcher. Analysis was then conducted, by following the guidelines for IPA analysis as detailed by Smith et al, (2022). Following this procedure, a sample of two transcripts were coded by a secondary reviewer to ensure validity of themes. This reviewer was an assistant psychologist, working within a healthcare setting, but who was not associated with the research in any way, and had no prior knowledge of the research area, to minimise bias. All participants indicated they would like a summary of findings and will receive this once the study is fully complete.

Ethics

The research and its subsequent amendments were reviewed and granted ethical approval from NHS ethics (please see Appendices G & H). Personal information and data were kept on a secure database, and data was transcribed and anonymized by the researcher, in line with university and GDPR policies. Confidentiality and the limits of this were discussed at the outset of the interview. The process of recording and their right to withdraw was also explained to participants before commencement. It was made clear that their child's care would not be affected in any way should they take part or decline to take part in the research. Due to the emotive nature of conducting the

interviews, consideration was given to potential risk and distress management. Levels of distress were monitored throughout the interview, and participants were given the option to pause or stop the interview. Participants were provided with sources of support in the debrief sheet.

Results

A detailed description of the steps taken to complete the IPA analysis can be found in Chapter 7. Once the analysis was complete five major themes and their subthemes emerged. These are detailed in Table 4.2 below.

Table 2

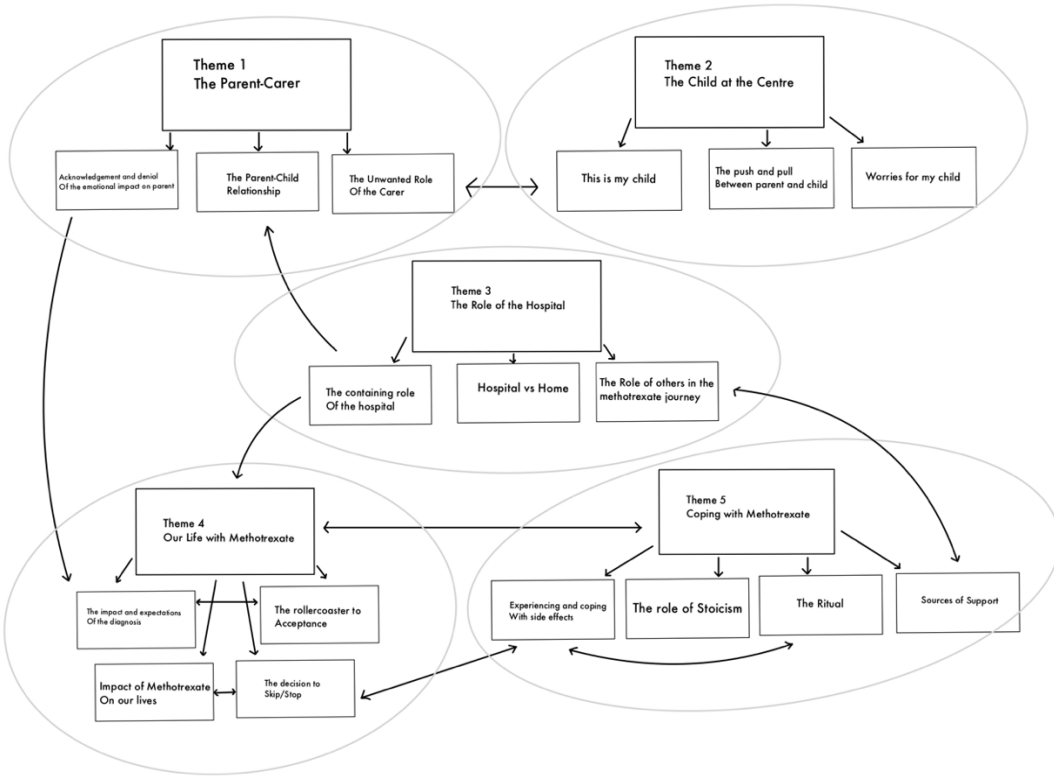
Summary of Themes

Major Theme	***Subthemes***	***Example Codes***
Theme 1-The Parent-Carer:	The Acknowledgement and Denial of the emotional impact of MTX on the parent.	*Heart-breaking* *Shouldering* *Watching child struggle*
	The parent-child relationship	*I let her down* *Questioning*
	The Unwanted Role of the Carer.	*Resentment* *Reaching out* *Parent monitoring own feelings* *Denial of own feelings* *Rejection of parent*
Theme 2- The Child at the Centre	This is my child	*Am I doing the right thing?* Admiration
	The push and pull between parent and child	*That's my daughter* *Child goes into self* *Trying to enter world of the child*
	Worries for my child.	*Grow up faster* *Sense of loss* *Mental vs physical health* *Clinical vs personal impact* *Behavioural issues* *Control vs giving that up* *Control for child* *Future vs hope* *Fear for emotional wellbeing*
Theme 3: The integral Role of the Hospital	The containing role of the hospital	*Seeking information* *Home vs hospital environment*
	Hospital vs home	*Reassurance- I'm not alone* *Too much vs too little information*
	The Role of Others in the MTX journey	*Hospital as parent figure to give control* *Valued explanation* *Sense that struggle is accepted*

Theme 4: Our Life with MTX	The impact and expectations of the diagnosis	*Normal but different* *\surprised to find it hard*
		Trapped taking MTX
	The roller coaster to acceptance	*Acceptance to anger*
		Hope for an end point
	The impact of MTX on our lives	*Processing enormity*
		A battle
	The decision to skip/stop.	*Enemy we've said goodbye to.*
Theme 5: Coping with MTX	Experiencing and coping with side effects	*This will help*
		What gets your through
		Idea of something going into body
	The role of stoicism	*Performance vs ritual*
		Sickness part of ritual
	The ritual	*Anticipation/dread*
		Relief when it's over
	Sources of support.	*Lasting associations*
		Something that has to be done

Figure 4.1

Thematic map illustrating relationships between themes



Theme 1-The Parent Carer:

The first major theme to arise from the analysis was that of the *Parent-Carer*, which refers to the dual nature in which the two roles (the parent and the carer) merge into one role. This major theme is comprised of three subthemes: *The Acknowledgement and Denial of the emotional impact of MTX on the parent; the Parent-Child relationship; and the Unwanted Role of the Carer.*

The first subtheme, *The Acknowledgement and Denial of the emotional impact of MTX on the parent,* arose as the emotional impact of taking MTX and the associated difficulties was prominent through all interviews, however parents often reported the need to suppress or deny these emotions to protect their child. Parents described watching their child in distress and how "horrendous and heart-breaking" this could be at times. Across the interviews, there was a strong sense of guilt, and the sense that the parent was inflicting something upon their child, connected with the subtheme "This is my child" (please see map of themes in Figure 1). Parents described feeling that they were the ones "putting their child through this" and that "*you feel like the worst person in the world*". The sense that this was a real weight for parents was profound, with one parent describing that they felt "emotionally broken" watching their child in such distress.

There was a sense of resentment, frustration, and unfairness, and that there was no release from these feelings. In recalling their experiences, parents described a desperation, and the mental battle of not knowing if they were doing the right thing for their child, given how much they were struggling. Also of note, was that for the main carer who took part in the interview there was the sense that they shouldered a greater burden, than the second parent who perhaps struggled more with a sense of frustration that their child could not simply do the injection.

Parents capacity to acknowledge these feelings seemed dependent on their temporal proximity to the distress. In the moment, parents described they would try to protect their children from their expressed emotions by monitoring and supressing their own distress.

"*Yeah…I was try…trying not to cry in front of him, but yeh, sometimes I did."*

"*…I didn't really have a choice…so actually, yeah, just felt really bad…and yeah…just tried not to think about it all the time, and I managed to do it…because if I do worry all the time, I wouldn't be my best as a parent….so…I just have to kind of cope with it I suppose".*

Parents recalled that they would often discredit their own feelings, stating "*this isn't about me*" and "*I don't give those thoughts much oxygen*". However, within the interview space, parents were able to acknowledge the impact the injections and the emotional labour had on their own lives- "everything is a bit harder" and this was clearly expressed. This seemed to be mediated by prior experience either in

a caring profession, having a health condition, or directly with MTX, given its use in the treatment of other conditions. In managing these feelings there was the sense that parents were reaching out for help, either literally or metaphorically for help, however as one parent acknowledged: "*The help needed to come to me*".

In discussing how parents were either drawn closer or rejected as part of the injection process, the subtheme of *The Parent-Child relationship* emerged. A child would sometimes want the parent close, however for some parents despite having a close relationship to the child, they found themselves entirely rejected as part of the injection process, which brought with it a unique sense of hurt for the parent. Commonly, parents also discussed using their physicality in some way. This was typically to provide comfort the child by remaining close or providing hugs.

It arose across the interviews, that restraint was not commonly used, seemingly related to the later theme of the child's autonomy and choice (see Figure 1). However, whilst many parents commented on how their relationship with the child became stronger, it was also acknowledged that the parent-child dynamic could be affected by the parent taking on the role of a carer.

There was a strong subtheme that taking on the role of a carer was an *Unwanted Role* for the parent. At least two parents really wrestled with this role, wishing that the hospital to take on this clinical role. There was the sense that they wanted to preserve the role of "Mum" and how desperate they were to distance themselves from the tasks of being a carer: "I never wanted to be her carer". This was in part achieved through removing things like clinical blue gloves and trying to maintain as much normality as possible.

"Yeh and I think from definitely from a carers point of view…I never wanted to be her carer…and I work in healthcare…and yeah…I think it was really those emotions deep down for me as well".

Theme 2- The Child at the Centre

A major theme, "*The Child at the Centre*" emerged from the sense that the parent was experiencing their child as an individual, with a unique personality, the desire for autonomy and experiencing the impact of this medication. Three subthemes comprise this major theme: *This is my child; the push and pull between parent and child; and worries for my child."*

Across the interviews a strong subtheme emerged that "*This is my child*". Throughout the interviews parents gave warm and heartening examples of the individuality of their child, however this was juxtaposed with the reality of living with MTX.

"..you really need to have a look cause I'm sure there's some glitter in that blood, because I'm sure you're half princess…"

Parents reported a strong sense of pride and admiration in watching their child cope with the MTX injections. At times during the interviews, a strong sense of "why us" or "why me" also arose, with the sense that something unwanted is happening to their child yet parents felt hopeless to do anything to help.

"*Yeh…I don't want this for my child…"*

"yeah…just trying to be calm and detach myself, but it's actually my daughter…I'm doing it for…and fighting that emotion, and actually yes, it's my daughter".

Parents would express a sense of struggle in weighing up, am I doing the right thing, whilst holding the knowledge that the MTX allowed the child to live a relatively normal life. However the sense that there was a lost innocence for the child came through, with the feeling that children taking MTX had to grow up faster, and there was a sadness to this.

"*...yeah the whole procedure is horrendous and I wouldn't wish it on my worst enemy to go through it, but certainly the pros for us outweighs all the you know…the cons."*

"…You know, no one wants to give their child injections. No one wants to see their child being sick in the sink to the point where they're red in the face…"

In the subtheme "*The push and pull between parent and child*", more than one parent discussed the sense of reaching out desperately to their child and wanting to enter their world, and yet in the face of the MTX injection the young person would often turn inwards to themselves, sometimes entirely rejecting the parent physically and emotionally. It was reflected perhaps that this was because both child and parent were "*dealing with the same thing, but differently*".

The importance of control and autonomy for the child was acknowledged, whilst commenting on the balance between validating their child's feelings and providing the firm message that the MTX must be done. This was mediated by their developmental stage and ability to understand and communicate but also the difficulty in balancing their own agendas, the desire to get the injection done, and the balance between overcompensation and providing choice, and not doing enough to ease the process for the child. One parent also talked about the importance of having the courage to take a step back

and the importance of trusting their child with the injection process, however there was the real sense that it was hard for parents to give up control.

"*You can't…when it comes to a child injecting herself…you know that because she was doing it herself, she was the one in control of it. And I felt like I had no control…because she wouldn't let me do it, I had to trust her to do it.*

Finally, the subtheme "*Worries for my child*" emerged through parents discussing their wider worries about the impact of MTX on their child. There emerged the sense that the young people were dealing with the impact of taking MTX alongside the typical struggles of growing up, and therefore parents worried about potential impact on their physical development, the impact on their school performance and social development, and predominantly worried about their child's mental health. Parents often expressed their struggle in knowing when to prioritise mental over physical health, due to the relentless strain of taking MTX on the child's wellbeing- however these worries were often tempered with a sense of hope for the future, and the role MTX could play in helping their child.

"*Because when she's on Methotrexate…she leads a normal, happy life and she is just a normal child, and it's and it's that in the back of your mind that gives you strength. To do that injection, knowing it's gonna make her sick".*

Theme 3: The Role of the Hospital

The role of the hospital comprised of three key subthemes: *the containing role of the hospital; hospital vs home; and role of the wider system.*

The hospital seemed to play a distinctive role for families, taking on an almost parental role for families, with one parent describing the wish that the hospital took the caring responsibilities from them, and other describing the reassurance and validation they received from the hospital.

"*…so I know when we started on Methotrexate we were given like a card where every time she had her bloods done, the results on it…I wasn't really…I didn't really wanna know that because I know they're dealing with that so I don't need to know that…yeah I think it was really, it was about me becoming her mum rather than…the healthcare medical side of it….so yeh it was me trying to get away from that."*

The subtheme *the containing role of the hospital* illustrates that the hospital provided this role for parents, whilst at times this could also be unhelpful. There emerged the sense that these difficulties

had become normalised by health care professionals, and yet for families there was the perception that the difficulties they were experiencing were far from normal. One parent commented:

"*They're not in the house with you, are they? Don't see that you're telling them over the phone when you've, you know, it's calmer. But I think I used to think, if you could be in the room with us when we're having to do it, or if you could be on the school run with me when she's crying her eyes out because she doesn't want to go in and she's heaving…I think it's difficult maybe for the professionals to see it".*

"*You go home and this is and I think…ok, that they're making it sound like…it's…I should be able to do it".*

"…we kept going with it, because that's what the nurses were telling us to do…"

As a result of this dynamic, parents would question whether what they were experiencing was normal, leading them to seek information and validation from other sources. However, it was highlighted that parents could easily be overwhelmed by the information they were provided by the hospital, and information they found online. As a result, parents described a sense of gratitude to the recruiting hospitals, expressing how valuable it was to receive information and direct support in a timely manner.

A final point that was raised was that parents wondered if some more realistic expectations about taking MTX might be helpful for parents. It was reported as validating for parents to find out that it wasn't "only my child" who experienced these difficulties and wondered if it might have been helpful to have this information sooner.

" *I wouldn't have liked for another parent to say to me, what do you think about Methotrexate? I don't think I could answer them honestly because I wouldn't want to bias….but I would just like to run 100 miles from it".*

Crucially, parents talked about the distinction between the hospital and home, and how the transition from receiving education within the hospital setting, to doing the injection at home was perhaps a much bigger transition than health care professionals realise. There was described the sense of home being a safe place and bringing the clinical responsibility of giving MTX into the home environment led to having to adjust to a new normal for families. For some families, this transition may initially work well, and the sense of novelty could make the young person feel special. However, for others they might have valued a slower progression from hospital to home.

"I could feel from what I could see it was completely different for her in that environment than it was for her being at home, and for me to be doing it…as soon as it was my face in the picture with the injections it was…just a complete horror on her face…"

Notably, parents also talked about *the Role of Others in the MTX journey*. Parents felt dismayed at the amount of education they were responsible for, from educating schools about how MTX might impact their child, to the difficulty they had receiving MTX from couriers. More than one parent also described failings of the healthcare systems when it came to their child's diagnosis, contributing to a sense of responsibility on the families to manage this. Parents described the sense that others, notably friends around the families, failed to truly understand the impact of MTX on their lives, in part due to the sense that this was an invisible illness.

"*I suppose I found it difficult because you know, unless somebody sees it, they really don't know it. It was only really close close family that know what an ordeal it was for her".*

Theme 4: Our Life with MTX

The fourth major theme to arise is comprised of four subthemes: *The impact and expectations after diagnosis; the roller coaster of acceptance; the impact of MTX on our lives; the decision to skip/stop.*

The impact and expectations after diagnosis was often talked about at the start of the interviews. Parents talked about the need to process the "enormity" of it and how unexpected their reactions were. Parents described feeling that they should have coped better. The subtheme "Impact of MTX on our lives encompasses

This is closely linked to the theme of *The rollercoaster of acceptance*. Parents talked about how they would fluctuate between a temporary acceptance of MTX and feeling trapped by the process of taking it.

"I support…do you get used to it? So I don't know if you actually ever get used to it, but you get used to dealing with it".

In discussing this, the wider impact MTX had on children's and family lives emerged. Holidays frequently came up as a difficult time for children to manage MTX, either due to difficulties with injection administration, or the sense that this might ruin the holiday. There emerged the sense that

living with MTX meant families had to adjust to a new normal with new routines, whilst strongly feeling that this is "not normal", and a desire for normality.

"Yeh, the school work started to suffer, things like that. And she had no interest in doing the things. And she's always been quite academic. She loved spellings and everything…but yeah all that fell away. She just said, oh just don't want to do it. I'm not in the mood…"

This relates to the next subtheme: *the decision to skip/stop*- which emphasises the decisions parents would sometimes make to skip a week, or to stop altogether. Whilst skipping weeks was not a common occurrence, parents who had made the decision described the sense that it was in their child's best interests to do this and that they valued being able to do so. One parent described MTX as "*an enemy we said goodbye to"* with the acknowledgement that they would not feel able to revisit that closed chapter of their lives, however others saw it as a positive force despite the difficulties, due to the life it had given back to their child.

"*It's a very important joint, but you feel like…having a sore ankle was better than having, you know…not happy at school, not attending. "*

"Where do we put the…put the mental health above the physical health, and it's you know, you want them both don't you?

Theme 5: Coping with MTX

The final theme encompasses the difficulties parents described with MTX and how they coped with these. Four subthemes contribute to this major theme: *the ritual; experiencing and coping with side effects; the role of stoicism; and sources of support.*

In terms of side effects, anxiety related nausea was commonly reported, with subsequent avoidance and for some children behavioural issues. Related to the nausea, it emerged that for more than one child, one incident of actually being sick as opposed to simply feeling nauseous seemed to heighten this anxiety for children. It was clear that parents felt the nausea was anxiety related and was associated with the process of the injection itself and not a side effect of the medication.

"…as she got older, she had horrendous, and I mean horrendous anxiety sickness…and it wasn't because she'd had the medicine. It literally was just the whole anxiety of knowing that she…and we tried the buzzy, uhm we tried the is it Emla cream? …we tried every sort of thing, and I don't even think it was the fact that it hurt. It was just the pure thought of that injection."

"It got to the point where she…I can't do it Mum, I can't do it. It's just the thought of…because it makes a funny noise, she said as well, the liquid sort of…you can hear it going in and I think that was part of it as well, played on her mind.

A strong sense of avoidance was described, and parents described a sense of dread and build up to having the injection that could take up a substantial portion of the evening- however there was described a strong sense of relief as soon as the injection was done.

"*Just upsetting really. You know, we knew what was coming. It's that….and the fear of you know, having to put her in that position again…"*

The child could then engage in distraction activities. Of note however, during the build-up it was clear that parents were trying every possible strategy to distract and calm their children, with some parents commenting that comically they had pretended to faint to distract their child from feeling sick. Parents described attempting a number of coping skills such as distraction or the use of reward, however there was also the sense that the side effects could be unpredictable, and some weeks were worse than others. There was a sense of hopelessness that nothing seemed to work or make things easier.

"*and I thought right in my brain, I though ohh pretend I fell down the stairs, because then she'll that will distract her…this is what you think of to do things! And she goes, so what are you doing? I said I'm trying to take your mind off it".*

"*…Oh god I feel horrible, horrible, that was horrible because you come out of that waiting room and she's howling in the waiting room going Mum, I don't want to do it anymore, and there's nothing you can do for her".*

In the face of this, a strong sense of stoicism emerged- parents reported knowing the medication worked and allowed their child to do the things they loved again- and this was what helped them to keep going in tough times. However, the reality of living with the side effects could at times make this difficult. Interestingly, parents would commonly report comparisons with other chronic conditions, or would compare their situation with a younger or older child. It was felt this was a way of keeping a perspective on the difficulties and helped families to keep going despite their struggles.

"*You just learn to deal with it, no matter how hard you, you just take it as part of her treatment and everything else I guess"*

"And she is one of the lucky ones I guess, who, her condition is treated solely by Methotrexate"

When it came to the injection process, parents described the ritual of preparing the injection, and its paraphernalia- however this ritual was different for each family and bordered on performative for some children. It was described as ritualistic for the child to engage in preparing themselves with a bowl, not talking to the parent, and for one child the process of being sick was seen as a sort of "purge" post injection. However, the process of preparing the injection seemed important for the parents too.

"So he had just kind of a routine. Just taking, getting ready the bowl, then doing the injection and start vomiting straight away…he just wanted to make sure that he's like…everything is all clear. He vomited everything. So it just feels alright, and I think…he's very used to vomiting".

"There was the sick bowl, and it was almost like, you know, the procedure that we had for doing this injection".

A component of coping with MTX is also the sources of support available, and this was for both parents and the young people. There was the sense of both children and parents at times pulling together for support, with the presence of family members and being physically present an important factor.

"But we manage, we can, I mean, my husband, we'd always do it together. And you know, he'd cuddle her and I'd do the nasty bit. And (sister) also played a big part in it because she was always, you know, really supportive. So…I didn't ever feel that I couldn't do it…"

"Yes, they argue like cat and dog. They are absolutely horrendous as sisters. But when it comes to…when it came to sort of the Methotrexate, she would always be there to support us and we do it together as a family…"

Parents also described reaching out for support to parent groups online and to the hospital, and the help they received was invaluable.

Discussion

This study aimed to understand what the experiences were of parents of children with JIA, who had to give them the MTX injection. Through the process of conducting this research and analysing the transcripts, a new understanding has emerged, of families who are faced with an unexpected and

unwanted challenge, and yet find ways to pull together with a sense of stoicism in the face of this unpredictable adversary.

Using IPA, the key emerging themes highlight that parents are faced with an unwanted role for which there is great variety in how prepared they may be. Although appearing at first to be a straightforward process, there was the sense that parents were unprepared for the emotional burden MTX would bring into their lives, feeling at times they should be coping better than they perceived themselves to be. This at times could be isolating, as parents reported a rapid deterioration in coping and the sense that nothing was working, and nobody could help. These results highlight the importance of the hospital in actively providing validation and reassurance to parents. There also exists the argument that parents need clear expectations about the potential for there to be difficulties when taking MTX, as this might provide parents with realistic expectations for MTX treatment. Clinically however there is concern over the potential for this information to prime families to have difficulties, and so there is uncertainty over how much to share with parents and when. Current research on shared decision making in medication, suggests there are both challenges and benefits to shared decision making (Charles et al, 1997; Bomhof-Roordink et al, 2019), however it's clear that relationship with the hospital and limited alternative options available play a key role in how this information is communicated (Boland et al, 2019). It could be argued that an honest and practical approach to sharing this information might allow parents to be better prepared to put strategies in place before serious emotional and behavioural difficulties develop. It may also allow parents to feel validated in their experiences when difficulties occur, instead of searching for answers feeling it is somehow their fault. Of note, of the parents who took part in the research, only two people reported a prior knowledge of MTX and it's associated side effects. Of those who were not aware of the potential for such challenging difficulties, they reported finding reassurance in the fact this research was being conducted as it provided a validity and reassurance to their experience that they were not alone in these struggles.

It's clear parents understand the reality of JIA and the benefits MTX brings into their and their child's life, however this knowledge does not diminish how difficult it is for parents to bring the clinical procedure of giving MTX into the home environment. Through the emergence of the themes "The Parent-Carer" and "The child at the Centre," a strong sense appears that parents felt they were "doing something to their child" and attacking them in some way, a difficult realisation that contributed to the emotional impact on the parents.

Further, MTX related difficulties are clearly something that affects the whole family system. In conducting these interviews, the main carer was exclusively the mother, and there existed the tendency to not acknowledge their own experiences and feelings in giving this medication. The sense of stoic resolve, whilst clearly holding practical importance, diminishes the high level of parent grief

experienced when witnessing their child in emotional distress. The emotional burden of this experience should not be understood with words such as “horrendous” and “heart-breaking” clearly illustrating the need for greater support for parents, potentially as form of peer support where parents are able to discuss these difficulties together.

It is also apparent that the secondary parent was also affected by feelings of upset and frustration. Siblings are often present, and it was heartening to hear how families will often pull together in these difficult times and find ways to cope together, for example providing unique methods of distraction and comfort.

However, throughout the interviews it emerged that families reached a point where simply nothing worked. Parents described a sense of desperation as their child would go into themselves and there was the sense of parents desperately reaching out, both to their withdrawn child and to wider systems for support. There existed the sense that they felt trapped into taking the MTX due to the role of NICE guidelines (2014) highlighting its preferential status compared to other treatments. At this point families at times felt stuck weighing up child autonomy, their child’s mental health, and the need to get the injection done, feeding into a wide array of worries about their child’s health and future.

Thus the role of the hospital, almost as a parental figure in managing these families, became apparent. Whilst the hospital provided comfort and reassurance at times, at times they might act as a disciplinary parent, in making the role of the guidelines clear to families, and families feeling they might get caught out should they decide to skip a week of the injection. However much in the same way a parent may trust their child to take on a level of responsibility, the hospital seemed to trust parents to make the correct decision for their child. Fundamentally, some parents reported a sense of wanting to reject this role and responsibility. This might suggest perhaps the hospital has a role in assessing parent readiness to take on this role at home.

Currently little is known about which families and young people experience MTX related difficulties however the role of parent anxiety and experience is apparent. For most families experiencing MTX related difficulties there is the sense that they reach a point where nothing seems to help their child, and the strategies suggested become futile. For these families, the burden, both emotional and practical, on parents and young people can lead to struggles experienced at home and at school, a loss of childhood and childhood experience, and questions remain over how the healthcare system and the hospital can help families to navigate these difficult experiences.

Strengths and Limitations

A key strength of this study lies in the face validity of themes to emerge through conducting the interviews. The rigorous and reflective process of analysis has brought to light the experiences that may have been shared individually in the clinic room and yet the research to corroborating these experiences to date has been lacking. As such there are some initial practical and clinical recommendations for staff working with these families that are discussed below.

The findings of this research are also congruent with previous research commenting on some of the emotional difficulties experienced by both mothers and fathers, and as such provides further evidence that there is a growing and pressing need for parental support when treating a child with MTX (McNeill, 2004; Mulligan et al, 2009; Mulligan et al, 2013).

Some limitations of the study have been identified and the findings should be considered within this context. In terms of homogeneity of participants, one participant described their child as not actually having difficulties with MTX but with another medication to treat JIA. However, after discussion with the research team, the decision was taken to include this participant in the research for the following reasons. The child involved was taking both MTX and an additional medication at the same time, and they experienced emotional and behavioural difficulties around the time of giving the injections, much in the same way as the other participants involved. As such, it could not be confirmed from which medication the side effects emerged, and as the interview continued, the parent described making the link with MTX during the interview, as many of the difficulties were similar.

The sample of participants was also recruited from the East of England and whilst the sample was representative of this predominantly white population, diverse generalisations may not be appropriate. Finally, the main care givers for this population were exclusively female, and predominantly married or cohabiting, with one exception. As research suggests there may be differences in experiences between caregivers (McNeill, 2004; Mulligan et al, 2009) this implies there is a population of caregivers who have not been accounted for by this research, and so caution should be employed when applying these findings to other groups.

Clinical Implications

This research emerged from discussions within the hospital setting, on how best to support these families seen in the JIA clinic, who were struggling with difficulties administering MTX treatment, and this is clearly a multifaced and challenging area for both families and the clinicians who care for

them. Thought must be given not only to how to support young people and families, but what guidance clinicians need, on how and when to assess for these difficulties.

In terms of clinical implications, the themes above clearly communicate that the hospital plays a critical and greatly valued role in supporting these families. Both parents and young people valued the opportunity to ask questions and take an active and engaged role in their care. This approach supports the importance of providing patient centred care, and research shows providing information and choice is key in developing a person-centred approach to care (Kuluski, 2020). However, the question does arise, what information is important for families to receive and when. As MTX is the gold standard treatment for JIA, NICE standards (2014) exist stating children must have been on MTX for 12 weeks before they are eligible to try alternative treatments. However, it was expressed that the families may have wanted to be prewarned about the extent of the difficulties they might experience. There was also the sense that they may receive either too much or too little information at various time points, bringing the question of what information is important to receive and when. The research has highlighted the importance for young people to feel in control of their treatment, however it is also clear that for children experiencing MTX related difficulties, the burden this places upon parents is immense. Given the key role of the relationship between the parent and child, more attention must be given to parent wellbeing and how this can be managed to best support children experiencing these difficulties.

In terms of what clinicians should be mindful of, previous research suggests that there is currently a disconnect between parent and clinician views on a child's QoL (Janse, 2005). This suggests there is perhaps a lack of clinician understanding regarding QoL, and more regular and thorough assessment of QoL is essential. Whilst measures to assess QoL do exist, these vary in their validity and utility, as evidenced by the results of the systematic review in Chapter 2. However, clinicians may be able to lean into their core clinical skills to provide some assessment of this. The importance of listening and asking questions, providing person centred care and choice should not be understated, with the understanding that no two families are the same and may require different levels and times of support at different times.

Research Implications

This research has contributed to the knowledge base by illuminating some of the key themes relevant to parents administering this medication to children. However, questions remain as to which families are more likely to struggle with this medication, treatment adherence for families than remain on MTX long-term, and what influences the final decision to stop treatment. Whilst this research is congruent with previous research in this area, future research might also replicate this research in

different populations with more diverse family structures to gain a wider understanding of parental difficulties. Moving forwards, a more robust way of assessing parental difficulties feels required. This may take the form of guidelines, indicating regular assessment of parental and wellbeing and coping may be considered best practice.

Conclusion

MTX is a gold standard treatment for JIA, however this medication poses unique challenges to children and families. This study highlights how the parent-carer may struggle in managing their role in administering MTX to their child due to the high emotional demand unexpectedly placed upon them in delivering a complex and often unpleasant treatment to their child to try and manage JIA . Although MTX allows young people to regain some of the function lost to JIA, for parents the balance between mental and physical health can be difficult to obtain. The hospital and specialist clinical teams play a key role in supporting parents, however it is clearly also important to hear the experiences of parents and young people to understand their unique journeys with MTX and consider how best to support families as they embark on this.

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Appendices

Appendix A: Topic Guide

Giving the injections

- Can you talk me through the process of giving the injections to your child – how does it feel? What is it like? Prompt for detail.
- During administration – can you tell me about this experience? What is this like for you? Thoughts? Feelings (which are)? How does this experience affect your child? How do you think they experience the administration? Other family members? Their thoughts/feelings? How do you feel about this?
- Practicalities – thoughts and feelings about handling the medication? Giving the injection? How confident do you feel with this? What makes this less/more difficult? Experience of health care professionals/consultations/teams? Experience on the training you have received – explore.
- Do you ever avoid giving the injections? Explore reasons for this and how this feels.

Experience before giving the injections

- Experience immediately before….
- Hours before….
- The night before….
- Can you tell me about this experience? Thoughts? Feelings? Impact on your child and how that feels for you, impact on family activities, work, routines etc. Their thoughts/feelings? How do you feel about this? Other family members?

Experience after giving the injections

- Experience after MTX administration – your experience after MTX has just been injected. How do you feel? Impact on your child? impact on family activities, work, routines etc. Their thoughts/feelings? How do you feel about this? Other family members?

Side effects of MTX and influences on life

- What are your experiences of the side effects? How does that make you feel? Does it influence compliance with MTX? Relationship with child?
- How MTX influences your life? Explore.
- How MTX influences your child's life? Explore. What is your child's understanding of MTX and side effects? Explore.
- MTX injections and parent and child relationship – attachment, changes before and after? Any difficulties within the relationship – strains, arguments, positives? Noticed any changes in this relationship over time?
- Does MTX influence your family's life? Specific member's experiences and feelings about this. Impacts relationships within your family?
- Does MTX influence activities? General life – holidays, work, day-to-day activities, mealtimes, bedtimes, school routine, important routines etc.

Managing difficulties

- What are your experiences in managing the difficulties with MTX? What has been helpful/unhelpful?
- Times that difficulties are manageable? Explore.
- Has your experience changed overtime? How? Feelings towards this? Looking forward – what are your thoughts/feelings about the future? Explore.
- Where do you gain support? Family? Friends? Shared experience? Elsewhere?

Positive Elements

- What has been helpful in managing this?
- What has the role of the hospital been in managing this?
- What would be helpful?
- Can you give examples of positive experiences?

Anything that we have missed?

Appendix B: Participant Information Sheet

Participant Information Sheet

Study Title

Exploring Parents' Experience of Difficulties with Their Child's Methotrexate Injection Treatment for Arthritis.

Researchers

Chief investigator (Trainee Clinical Psychologist): Rachael Mellor.

Research supervisors: Dr Amy Carroll and Kiki Mastroyannopoulou.

Sponsor Organisation

The University of East Anglia (UEA).

UEA Data Protection Officer

Ellen Paterson: Email dataprotection@uea.ac.uk Tel: 01603 592431 Address: The Library, University of East Anglia, Norwich Research Park, Norwich NR4 7TJ

Invitation and Brief Summary

The aim of the study is to gain a deeper understanding of parents' experience of difficulties with their child's methotrexate injection treatment for arthritis.

Purpose of and background to the research and invitation

We are carrying out this research, because methotrexate (MTX) is the first-choice treatment for juvenile idiopathic arthritis (JIA), and we know that many families experience difficulties with this treatment. Common difficulties with MTX injections are children becoming distressed or fearful when thinking about or having the injection and refusing to have it, which sometimes results in the

medication needing to be administered by hospital staff which can prove disrupting for the child's life. Despite this, there has yet to be any research to explore what these difficulties are like for families. Therefore, we aim to recruit parents who administer their child's MTX injection treatment, or have done so in the last 12 months, and who have had difficulties with it for at least a two-month period within the last year. This is so we can hear about their experience.

What would taking part involve?

If you agree, taking part will involve meeting with a Trainee Clinical Psychologist for an informed consent meeting and then an interview to discuss your experiences of having difficulties with your child's MTX injections. This meeting will last for approximately two hours. During this meeting, you will also be asked to fill in a form to provide some demographic information about you and your child and additional information about your child's JIA and either current or previous MTX treatment. However, if there are any questions in this form that you do not wish to answer you do not have to. The interview will be held via Microsoft Teams. A link to the meeting will be sent to your email address an hour before the interview time. The interviews will take approximately two hours and you will be given the option to take a break in the middle should you need. The interviews will be recorded for research purposes only and you will be given a number which will be used in recordings instead of your name. You will be asked not to use names during the interview. The interviews will be transcribed once complete and you will be asked to give yourself a fake name, which will be used in the transcript.

However, if you do not wish to take part this will not impact the care you or your child receive in any way. Also, if you decide to take part and then change your mind you can withdraw at any point during the interview and any data will be destroyed and will not be used in any research. You will also be given seven days to withdraw from the study after your interview has finished. If you withdraw at this time, then any data will be destroyed and will not be used in any research. You will be given the option to check the accuracy of your transcript after the interview. Your anonymised transcript will be emailed to you after the interview and you will be given 14 days to make any changes to this that you wish. When reviewing your transcript, you can request for specific quotes not be used in any publications and these will not be used. However, the data will still be used to generate themes overall.

Once all of the interviews have taken place and transcripts have been checked for accuracy, we will look for patterns and themes between them.

What are the possible benefits of taking part?

There is no financial or personal gain for taking part in the research and we unfortunately will not be offering you any solutions for the difficulties you are experiencing. However, the findings have the potential to be important in gaining understanding of how these difficulties are experienced. The findings will also be presented to your child's rheumatology team. As a thank you to you if you wish to take part you will be given a £5 Amazon voucher. You will also be sent a summary of the findings once this is available.

What are the possible disadvantages and risks of taking part?

As the study will take place remotely, we ask that you try and find a confidential space in your home for the interview to take place.

It is possible that the interviews could touch on some difficult or distressing topics for you. However, you do not have to answer any questions you do not feel comfortable answering and you are able to stop the interview at any time. You will be provided with some additional resources after the interview around ways you could obtain additional support or information. Furthermore, if you say anything in the interview which concerns us about your safety or that of anyone else, we have a duty of care to pass this on to the Clinical Psychologist who works within the rheumatology service. However, this will be discussed with you first.

A fake name will be used for you throughout the study and any identifiable information will be kept in locked cabinets on University East Anglia (UEA) or NHS premises, which only the study team will have access to. Finally, it is important that your family members, including any children, cannot overhear the interview. This is to protect your confidentiality and ensure that the interview is not interrupted. This is important to consider as the interview will take place via Microsoft Teams. This may be difficult for you should you need to get childcare arranged, so is an important factor to take into account when considering whether to take part.

How will we use information about you?

We will need to use information from you for this research project.

This information will include your name and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

If you decide to take part and then change your mind you can withdraw at any point during the interview and any data will be destroyed and will not be used in any research. You will also be given seven days to withdraw from the study after your interview has finished. If you withdraw at this time, any data will be destroyed and will not be used in any research. You will be given the option to check the accuracy of your transcript after the interview. Your anonymised transcript will be emailed to you after the interview and you will be given 14 days to make any changes to this that you wish. When reviewing your transcript, you can request for specific quotes not be used in any publications and these will not be used. However, the data will still be used to generate themes overall.

What happens to your data at the end of the study?

After the study has ended, your data will be archived and stored securely at the UEA and any paper data will be securely achieved via the UEA arching process. Consent forms will be archived separately from raw data so that this data remains anonymised. After ten years, all data will be destroyed, in order to comply with GDPR.

Where can you find out more about how your information is used?

You can find out more about how we use your information at https://www.hra.nhs.uk/information-about-patients/, viewing the leaflet available from www.hra.nhs.uk/patientdataandresearch or by contacting one of the research team.

Who can I contact if I have any questions?

Rachael Mellor (Chief Investigator): Email R.Mellor@uea.ac.uk Address: Department of Clinical Psychology and Psychological Therapies, Norwich Medical School, University of East Anglia, Norwich, NR4 7TJ.

Dr Amy Carroll (Supervisor): Email: amy.carroll@uea.ac.uk Address: As above.

Kiki Mastroyannopoulou (Supervisor): Email: K.Mastroyannopoulou@uea.ac.uk Address: As above.

Who can I contact if I have a complaint?

Professor Niall Broomfield (Programme Director and Head of Department): Email: N.Broomfield@uea.ac.uk Address: As Above.

Are there any other details I need to consider?

This is research project involving parents discussing their experience of managing their child's current or past methotrexate injection treatment. As we are not speaking directly to your children or accessing their health records, we do not need to obtain consent from them to interview you. However, if you are a parent of an older child you may want to involve them in decisions made about your involvement in the research. Therefore, if you wish to invite your child to the start of your meeting with the researcher then this can be arranged. However, children cannot be present for the interview.

The findings of the study will be written up for a Trainee Clinical Psychologist's doctoral thesis and will be marked by examiners at the UEA. The findings will be presented to your child's rheumatology team. It is also hoped that the findings will be published in an academic journal. All findings will be anonymised.

Appendix C: Consent to Contact

Consent to Contact for Research Purposes

TITLE: Exploring Parents' Experience of Difficulties with Their Child's Methotrexate Injection Treatment for Arthritis

SPONSOR: University of East Anglia

INVESTIGATORS: Rachael Mellor, Dr Amy Carroll, and Kiki Mastroyannopoulou

You are being invited to give consent for Rachael Mellor, or a member of the study team to contact you at some time in the future to invite you to participate in a research study.

Are you willing to learn more about the 'Exploring Parents' Experience of Difficulties With Their Child's Methotrexate Injection Treatment for Arthritis' (Circle one)

YES NO

If yes, you will be contacted at a later date. Please include your contact information below.

☐ **[Specify, e.g., Telephone]:** _____

☐ **[Specify, e.g., E-mail]:** _____

You have been made aware of the reasons why the contact information is needed and the risks and benefits of consenting or refusing to consent.

This consent is effective immediately. Your consent to be contacted can be revoked by you at any time.

Your Signature: _____

Date: _____

Clinician's Name: _____

Appendix D: Consent Form

Consent Form

Title of Project: Exploring Parents' Experience of Difficulties with Their Child's Methotrexate Injection Treatment for Arthritis

Name of Researcher: Rachael Mellor

Please initial box

- I confirm that I have read the information sheet dated 22nd June 2022 (version 2.2) 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 up to seven days after my interview without giving any reason, without mine or my child's medical care or legal rights being affected. ☐
- I understand that if I disclose anything which concerns the researcher about my safety or anyone else's that they may have to pass this onto other services. I know that they will try and discuss this with me before this is passed on. ☐
- I know that my personal information (such as my name) will not appear on any transcripts or be shared outside of the study team or published in any final report(s) ☐
- I agree to be audio recorded and for my anonymised quotes to be used within publications ☐
- I agree to take part in the above study ☐

Name of Participant	Date	Signature
Name of Person taking consent	Date	Signature

Appendix E: Debrief Sheet

Debrief Form

Thank you for participating in the study. Your time and efforts are much appreciated. If you have any questions about the study, please do ask me now or at a later date via telephone or email. You now have seven days to fully withdraw from the study. If you wish to do this, please let me know. If you do decide to withdraw, your data will be destroyed, and this will not affect your child's treatment in any way. You have the option to review your anonymised interview transcript, which will be emailed to you once written, and you will have 14 days to make any changes to this. If, when reading this, you do not wish for specific quotes to be used in any publications, please highlight these sections to make us aware. These quotes will not be used, but your data will still be used to produce overall themes as part of the findings.

The aim of the study was to gain a deeper understanding of parents' experiences of difficulties with their child's methotrexate injection treatment for arthritis. Once all interviews have been conducted patterns, themes, similarities and differences between parents' experiences of these difficulties will be explored.

If you have any concerns about your psychological health or that of those following the interview, please contact your GP or your child's rheumatology team or use the sources of support given below.

We aim to send you a summary of the findings via email once all interviews have been conducted and analysed. If you wish to not be contacted any further, please let me know.

Sources of Support

When people take part in research projects sometimes, they are interested in finding out more information around dealing with psychological difficulties, either for themselves or others. The first step in getting help or advice is to discuss the problem with your GP. They can signpost you to local resources or refer you onto an appropriate service is appropriate.

Additional resources:

Norfolk and Suffolk (including Ipswich and Great Yarmouth):

- **The Wellbeing service in Norfolk & Suffolk** offer different types of emotional support, such as self-help, group and individual talking therapies. Tel: 0300 123 1503 (lines open Monday

to Friday [excluding Bank Holidays] 8am to 8pm) or visit https://www.wellbeingnands.co.uk/norfolk/contact/. You can make a self-referral via the online form at https://www.wellbeingnands.co.uk/norfolk/get-support/register-with-our-services/

- **Mind Norfolk** and Waveney provide person-centred support and guidance for individuals with mental health difficulties and their families. Call 0300 330 5488 between 4pm and midnight, Monday to Friday and 10am until midnight on weekends.

Cambridge and Peterborough:

- **CPSL MIND -** CPSL (Cambridgeshire, Peterborough and South Lincolnshire) Mind is a mental health charity that offers lots of helpful advice and services for all Mental Health Challenges. Visit https://www.cpslmind.org.uk/contact-us/ or call 0300 303 4363 between 9:30-5:30pm.
- **Insight** – Insight Healthcare provides talking therapies nationwide, predominantly commissioned by the NHS and local authorities, as part of the IAPT (Improving Access to Psychological Therapies) programme. Call 0300 123 4502.

Essex (Colchester and Basildon):

- **Adult Mental Health and Wellbeing Team at Essex** offers support for people experiencing low level mental health difficulties. Call 0333 032 2958 (available Monday to Friday, between 10am and 4pm) or visit https://www.livingwellessex.org/health-and-well-being/mental-health/adult-mental-health-and-wellbeing-team-at-ecc/
- **Mid and North East Essex Mind** offers support for people experiencing mental health challenges. Contact them Monday to Friday, 9am to 5pm, on 01206 764600 or email enquiries@mnessexmind.org.

National Support

- **The Samaritans** offer confidential and non-judgemental support 24 hours a day, seven days a week, 365 days a year. Call 116 123.
- **ChildLine** offers counselling services for children and young people. You can also contact ChildLine if you are an adult worried about a child. Call 0800 1111.
- For more information for mental health hotlines, visit the NHS website: https://www.nhs.uk/conditions/stress-anxiety-depression/mental-health-helplines/

Appendix F The Carer Experience Scale (Al- Janabi et al, 2008).

Carer Experience Scale

PLEASE TICK ONE BOX FOR EACH GROUP to indicate which statement best describes your current caring situation.

1.Activities outside caring *(Socialising, physical activity and spending time on hobbies, leisure or study)*

You can do most of the other things you want to do outside caring ..... ☐1
You can do some of the other things you want to do outside caring ..... ☐2
You can do few of the other things you want to do outside caring ..... ☐3

2. Support from family and friends (*Personal help in caring and/or emotional support from family, friends, neighbours or work colleagues)*

You get a lot of support from family and friends ..... ☐1
You get some support from family and friends ..... ☐2
You get little support from family and friends ..... ☐3

3. Assistance from organisations and the Government *(Help from public, private or voluntary groups in terms of benefits, respite and practical information)*

You get a lot of assistance from organisations and the Government ..... ☐1
You get some assistance from organisations and the Government ..... ☐2
You get little assistance from organisations and the Government ..... ☐3

4. Fulfilment from caring *(Positive feelings from providing care, which may come from: making the person you care for happy, maintaining their dignity, being appreciated, fulfilling your responsibility, gaining new skills or contributing to the care of the person you look after)*

You mostly find caring fulfilling ..... ☐1
You sometimes find caring fulfilling ..... ☐2
You rarely find caring fulfilling ..... ☐3

5. Control over the caring *(Your ability to influence the overall care of the person you look after)*

You are in control of most aspects of the caring ..... ☐1
You are in control of some aspects of the caring ..... ☐2
You are in control of few aspects of the caring ..... ☐3

6. Getting on with the person you care for *(Being able to talk with the person you look after, and discuss things without arguing)*

You mostly get on with the person you care for ..... ☐1
You sometimes get on with the person you care for ..... ☐2
You rarely get on with the person you care for ..... ☐3

Appendix G Letters of Access from two recruiting sites

NIHR | Cambridge Biomedical Research Centre

Cambridge University Hospitals NHS Foundation Trust
Research and Development Department
Box 277
Cambridge Biomedical Campus
Hills Road
Cambridge CB2 0QQ

Direct Dial:
Switchboard: 01223 245151
E-mail:
jonathan.alvarezolieff@addenbrookes.nhs.uk
research@addenbrookes.nhs.uk
www.cuh.nhs.uk

14/04/2022

R&D ref: A095513
Dr Philippa Lewington
Cambridge University Hospitals
NHS Foundation Trust
Department of Paediatric Psychology –
Children Services

Dear Dr Lewington,

IRAS ID:	**266130**
REC Ref:	**20/EM/0007**
Short Title:	**Exploring difficulties with methotrexate injection treatment**
Title:	**Exploring Parents' Experience of Difficulties With Their Child's Methotrexate Injection Treatment for Arthritis: An Interpretative Phenomenological Analysis**

Thank you for sending details of the above named study.

The R&D department has received the HRA Approval letter and reviewed the study documents. The project has been allocated the internal R&D reference number of **A095513**. Please quote this in all future correspondence regarding this study.

Capacity and capability to conduct this study at Cambridge University Hospitals NHS Foundation Trust is confirmed. Any amendments that have been submitted whilst the project was in set up have been incorporated into our local confirmation of capacity and capability. Recruitment can commence at this site from the date of this letter; though this may change in light of further developments dictated by the Trust and or by Public Health England. Please note that whilst each required supporting department has given authorisation for the study, the capacity of the supporting departments is subject to change during the pandemic. At all times the safety of study participants who are continuing or discontinuing on the study protocol is a priority.

We would like to take this opportunity to remind you of your responsibilities under the terms of the UK Policy Framework for Health and Social Care Research, applicable to Researchers, Chief Investigators, Principal Investigators and Research Sponsors. We would also like to remind you of the requirement to:

- ✓ Notify R&D of any amendments to the protocol, changes in funding, personnel or end date. Amendments should be submitted in accordance with guidance in IRAS.
- ✓ Inform us of any research-related adverse events.
- ✓ Ensure that any staff working on this study at this site have been issued with a contract with CUH (honorary, substantive or bank) or a letter of access before they commence work on the study at this site.
- ✓ Maintain an Investigator Site File and/or Trial Master Files, ensure up to date GCP certification and Register the study on a publically accessible database (Clinical Trials only).
- ✓ Forward Annual Progress Reports and send copies of End of Study Reports to R&D as soon as they are available so that the study can be closed and archived.

Please remember that each recruited patient to your study should be logged on to our e-hospital to associate the patient's EHR to this study. Additionally, all recruitment figures for portfolio studies must be uploaded to the EDGE database on a regular basis and confirmed. R&D are able to provide EDGE and

NIHR | Cambridge Biomedical Research Centre

GCP training. Please note it is a Department of Health aim to enable fast patient access to research and as such we aim to consent the first patient within 30 days of study start.

The Trust is require to report regularly on its research activity and we request that you insert the following phrase into the acknowledgement section of any subsequent publication from this study: **This research was supported by the NIHR Cambridge Biomedical Centre (BRC 1215 20014)**. While this study may not have received funding from the Cambridge BRC, it will have been supported by campus infrastructure funded by it. We are very grateful for your help with this.

I wish you every success with this study. We are keen to support good research at Cambridge University Hospitals NHS Foundation Trust and are pleased that you have decided to conduct your project here.

Yours sincerely

TAssari

Tracy Assari
Research Governance Lead

Our Vision
To provide every patient with the care we want for those we love the most

NHS
Norfolk and Norwich University Hospitals
NHS Foundation Trust

Miss Rachael J Mellor
Trainee Clinical Psychologist
University of East Anglia
Via email to: R.Mellor@uea.ac.uk

Research and Development Department
Research Operations Office (NNUH)
Quadram Institute
Rosalind Franklin Road
Norwich
NR4 7UQ

e-mail: rdoffice@nnuh.nhs.uk
Telephone : 01603 286611
Website: www.nnuh.nhs.uk

13 April 2022

Dear Miss Mellor,

Re: 266130 (158-09-19) DIFFICULTIES WITH METHOTREXATE INJECTION TREATMENT
Letter of access for research

In accepting this letter, **Norfolk & Norwich University Hospitals NHS Foundation Trust** confirms your right of access to conduct research through this organisation for the purpose and on the terms and conditions set out below. This right of access commences on **13 April 2022** and ends on **1st March 2023** unless terminated earlier in accordance with the clauses below.

As an existing NHS employee you do not require an additional honorary research contract with the participating organisation. The organisation is satisfied that the research activities that you will undertake in the organisation are commensurate with the activities you undertake for your employer. Your employer is fully responsible for ensuring such checks as are necessary have been carried out. Your employer has confirmed in writing to this organisation that the necessary pre-engagement checks are in place in accordance with the role you plan to carry out in this organisation. Evidence of checks should be available on request to **Norfolk & Norwich University Hospitals NHS Foundation Trust**.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from **Norfolk & Norwich University Hospitals NHS Foundation Trust**. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving the organisation permission to conduct the project.

You are considered to be a legal visitor to **Norfolk & Norwich University Hospitals NHS Foundation Trust** premises. You are not entitled to any form of payment or access to other benefits provided by this organisation to employees and this letter does not give rise to any other relationship between you and **Norfolk & Norwich University Hospitals NHS Foundation Trust** or this NHS organisation, in particular that of an employee.

While undertaking research through **Norfolk & Norwich University Hospitals NHS Foundation Trust**, you will remain accountable to your employer **Cambridgeshire and Peterborough NHS Foundation Trust** but you are required to follow the reasonable instructions of your nominated manager **Kiki Mastroyannopoulou** in this organisation or those given on her behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by **Norfolk & Norwich University Hospitals NHS Foundation Trust** or this organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with **Norfolk & Norwich University Hospitals NHS Foundation Trust** policies and procedures, which are available to you upon request, and the UK Policy Framework for Health and Social Care Research.

You are required to co-operate with **Norfolk & Norwich University Hospitals NHS Foundation Trust** in discharging its duties under the Health and Safety at Work Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on **Norfolk & Norwich University Hospitals NHS Foundation Trust** premises. Although you are not a contract holder, you must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of a contract holder and you must act appropriately, responsibly and professionally at all times.

If you have a physical or mental health condition or disability which may affect your research role and which might require special adjustments to your role, if you have not already done so, you must notify your employer and each participating organisation prior to commencing your research role at each site.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice and the Data Protection Act 2018. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

The organisation will not indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 2018. Any breach of the Data Protection Act 2018 may result in legal action against you and/or your substantive employer.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that the organisation accept no responsibility for damage to or loss of personal property.

This letter may be revoked and your right to attend the organisation terminated at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of the organisation or if you are convicted of any criminal offence. You must not undertake regulated activity if you are barred from such work. If you are barred from working with adults or children this letter of access is immediately terminated. Your employer will immediately withdraw you from undertaking this or any other regulated activity and you MUST stop undertaking any regulated activity immediately.

Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

Our Vision
To provide every patient with the care we want for those we love the most

Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

If your circumstances change in relation to your health, criminal record, professional registration or suitability to work with adults or children, or any other aspect that may impact on your suitability to conduct research, or your role in research changes, you must inform the organisation that employs you through its normal procedures. You must also inform the nominated manager in each participating organisation.

Yours sincerely

Julie Dawson
Research Services Manager

cc: Cambridgeshire & Peterborough NHS Foundation Trust - nick.oliver@cpft.nhs.uk

Appendix H: NHS Ethical Amendment Approval

NHS
Health Research Authority

East Midlands - Derby Research Ethics Committee

Equinox House
City Link
Nottingham
NG2 4LA
Tel: 020 7104 8170

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.

21 June 2022

Miss Kelsey Odgers
Department of Clinical Psychology and Psychological Therapies
Norwich Medical School
University of East Anglia, Norwich
NR4 7TJ

Dear Miss Odgers

Study title:	**Exploring Parents' Experience of Difficulties With Their Child's Methotrexate Injection Treatment for Arthritis: An Interpretative Phenomenological Analysis**
REC reference:	**20/EM/0007**
Protocol number:	**N/A**
Amendment number:	**Substantial amendment 2**
Amendment date:	**01 June 2022**
IRAS project ID:	**266130**

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 [Completed Amendment Tool]	1.6	01 June 2022
Participant consent form [RM_Consent Form Version 2.2.docx]	2.2	20 June 2022

Participant information sheet (PIS) [RM_Participant Information Sheet Version 2.2.docx]	2.2	20 June 2022
Research protocol or project proposal [Updated Protocol: Exploring Parents' Experience of Difficulties with Their Child's Methotrexate Injection Treatment for Arthritis: An Interpretative Phenomenological Analysis]	2.1	01 June 2022

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 - 266130:	**Please quote this number on all correspondence**

Yours sincerely,

Mrs Janet Mallett
Chair

E-mail: derby.rec@hra.nhs.uk

East Midlands - Derby Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 30 June 2022

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Johanna Cornwell	Retired General Practitioner	Yes	
Mrs Janet Mallett	Retired Nurse	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Ellie Gibbon	Approvals Administrator

Chapter 5: Personal Reflections of the Researcher

As introduced in Chapter one, the epistemological position of this research is that knowledge can be gained through co-constructed interactions. With this in mind the transparency and openness of the researcher, who is one part of this co-construction of knowledge, is paramount.

This chapter is a personal reflection of the work. Different to the other chapters of the Thesis Portfolio, the section below is written in the first person, representing a shift in tense, in order to allow the researcher to address this directly.

As someone with a chronic condition, albeit not JIA, I gave some time to thinking about how my bias and personal experience and reflections may influence the co-construction of this reality.

Reflections from the researcher

As someone with my own experience of chronic illness, it was a great honour to enter the realities of these families, if only for a time. In completing these interviews, it was incredibly important to me to be aware of my emotional reactions and manage any potential biases that arose in completing the analysis. It is also worth stating that at the time of conducting the interviews, I was completing a placement in paediatric rheumatology and sitting within the recruiting team. Although this allowed me an in-depth perspective into the medical aspects of the condition, I had to remain mindful when meeting with the parents, not to slip into the role of the clinician, who may be looking to assess or provide an intervention. Whilst I was able to keep the roles separate to a degree, it did bring a new depth to both my clinical and research work, and it was a potential vulnerability and strength that I kept in mind throughout the interview and analysis processes.

Having a chronic condition myself, gave me pause to reflect on my own family experience of being faced with an unexpected adversary we were not prepared for. Whilst I found this more emotive when completing the analysis, I found I was able to remain in the moment with the participant when completing the interviews, and I do not feel this influenced the direction of the questioning. In part this was because the semi-structured interview schedule allowed for guidance when navigating this tricky landscape. It should also be considered that the interview schedule itself, represents a form of co construction with the hospital as this was developed in part with paediatric rheumatology clinicians. On considering this, it felt as though the “reality” I was aiming to observe fell somewhere between the individual, the hospital and myself.

I was mindful to remain as impartial as possible, and yet was able to feel a great deal of empathy for the parents. In doing this, I believe our reality can only be co-constructed as humans, not robots, and as such to feel empathy in this process is to co-construct reality. I was aware of the possible risk that I may overidentify and thus prioritise certain themes I may over relate to, and thus the importance of the second reviewer was key.

In summary, whilst my epistemological position demands transparency of the position of the researcher, I can only feel this was a strength, providing an empathy that hopefully facilitated the availability of knowledge in this research.

Chapter 6: Discussion and Critical Evaluation

Overall Discussion

This final chapter synthesises the entire thesis, providing a summary of the findings of both the systematic review and empirical paper, and discusses the strengths and limitations of this body of work. Overall clinical recommendations are made, and suggestions for future research will be outlined.

The thesis focussed firstly on the Quality of Life (QoL) of young people with JIA, with a systematic review exploring the current state of the literature on this. To date, there has been no systematic review of this topic prior to the one presented here. Two similarly titled publications exist: first, a piece of research pertaining to contributing variables on QoL (Sur et al, 2021); and second, a further brief review in adults with JIA, but not children or young people (Fiorillo, 2022). As neither answer the wider question presented here, the systematic review offers a novel contribution to the literature at this point.

In the Systematic Review, 14 papers were identified, all of which were quantitative in nature. Overall, it was clear young people with JIA experience a lower than optimal QoL, and a lower QoL than their matched peers. However due to the variability in quantity and quality of measures, the question "what is the QoL for young people with JIA" proved difficult to succinctly answer.

Predominantly, the review identified key issues in the way QoL is assessed, namely a wide variability in the measures used, making synthesis of data difficult. Notably, the most used measure was the PEDS-QL (Varni et al, 2004), a generic measure of HrQoL for those with and without chronic conditions. However as noted by Quittner et al, (2019) more generic measures may not capture the unique symptoms experienced with a specific illness such as JIA. This potentially may indicate the QoL assessment is missing out on some nuanced aspects of that condition such as the impact of specific medication regimes such as MTX, that may negatively affect QoL. For those with JIA, understanding QoL early on might allow for better intervention or support leading to more positive long-term health and wellbeing outcomes. Whilst rheumatology teams have clinical psychology embedded within them, further work may be done on understanding the factors relevant to QoL in JIA, and supporting families in promoting these.

Variation in QoL was observed across ages, gender, and subtypes, therefore possibly suggesting a missing element in the assessment of QoL for this population. It is also interesting to note that the

review identified that not all areas of quality of life are impacted equally. Discrepancies between parent and child reports indicate differing priorities concerning QoL. Whereas parents were more likely to report lower education related QoL, young people were more likely to have poorer QoL in the domains of pain and physical functioning, potentially reflecting different priorities between parent and child.

With the above considered, although QoL is a nebulous term, it is a timely and important concept to explore. Links have been found between QoL and longer-term outcomes in JIA (Foster et al, 2003) possibly mediated by better medication adherence (April et al, 2022) and subsequent improved longer-term outcomes. MTX is considered a highly effective yet sometimes challenging immunosuppressant medication, and therefore, the empirical paper aimed to better understanding how Methotrexate (MTX) contributed to this picture, specifically through the experience of the parent. Clinically, health care teams have long been aware of the negative impact of MTX side effects on young people. Whilst the clinical benefits for JIA activity are clear (Ramanan et al, 2003), this is often balanced against the difficult side effects such as nausea, anxiety, avoidance and distress often experienced by the child (Falvey et al, 2017; Mulligan et al, 2013;). These experiences have a substantial negative impact on HrQoL, however little is currently understood about what interventions may be more beneficial (Mulligan et al, 2013). With this in mind, the empirical paper attempted to further develop the understanding of MTX in the family environment, using a constructionist position to mutually understand the parent experience.

The arising themes offer an impactful depiction of families faced with a difficult situation, and parents having to take on the "unwanted role of the carer." The trade-off between the clinical need of adherence to MTX, and the impact this had on their child's wellbeing was apparent. This concept of medication related burden is increasingly being represented in the literature with an acknowledgement that clinical management of a condition can often come at great detriment to QoL (Krska et al, 2013; Mohammed et al, 2016).

The major theme "Our Life with Methotrexate" reflects this, encompassing the idea that parents were on what felt like a "roller coaster to acceptance" in dealing with MTX, affected by both the positive and negative aspects of the treatment regime. This is concurrent with previous research exploring parent experiences of having a child with JIA, which highlighted the wide variety of emotions experienced, whilst struggling to remain in control of their child's illness (Gómez-Ramírez et al, 2016; Yuwen et al, 2017).

Overwhelmingly, parents described the emotional impact of watching their child struggle with MTX, however with the caveat that they often did not allow themselves to acknowledge their own emotional

responses in this process. This is parried with the great pride parents felt of their children, whilst acknowledging MTX was stealing away at least a part of their childhood or innocence. It is accepted that parents of children with chronic conditions have their own support needs (Smith et al, 2010) however the reality of this provision within the NHS system may be variable. Clinicians working in teams are able to offer support and guidance when requested or indicated. As such the provision of psychology with paediatric rheumatology teams (in line with NICE guidelines) represents a positive offering for families, however it may be that more work is needed to understand the timing and type of support that is offered to parents, to prevent serious difficulties from arising. The systemic approach may open alternative avenues to support the family system, and some intervention research has begun to focus on mindfulness and compassion-based approaches, in supporting parents develop adaptive coping and resilience (Cousineau et al, 2019). Further, Panicker (2013) found parent support, education and open communication were key in supporting the development of parent resilience and empowerment.

In summary, MTX is clearly a considerable variable in the lives of the young people who have to take it. Whilst anecdotally clinicians have been aware of the impact on parents, research illustrating the lived experience of this population has been sparce. The systematic review identified a lower than optimal quality of life, however with variation in assessment tools and outcome. The empirical paper honours the parent experience and brings to light the unique and difficult role of a parent administering MTX to their child.

Strengths and Limitations

The wider strengths and limitations of the thesis portfolio will be discussed here. Individual strengths and limitations of the SR and EP have been discussed in the respective chapters above and are not repeated here.

This thesis aimed to contribute to gaps in the current literature pertaining to QoL in young people with JIA and the role of parents who administer MTX.

This body of work presented here has highlighted not only the key role parents play in moderating and maintaining the QoL of their young people, but also the unique struggles demanded of these families in the face of a difficult adversary. Thus, a strength of this paper is its in-depth analysis of parent experience using Interpretative Phenomenological Analysis (IPA). This approach allowed for a much more detailed understanding of the reality of life at home with MTX. Although this approach may not be replicable, the themes which emerged show good face validity, allowing clinicians an

insight into familial experiences with treatments they prescribe potential interventions and ways to tailor support for families.

Although varying in methodology, both the systematic review and empirical paper provided a thorough and transparent methodology. Both began with a clear aim and question, and a transparent methodology for achieving this. The strengths of this thesis lie in its attempt to provide a unique contribution to an underrepresented area of research, however, its weakness lies in its subject matter, in that as QoL remains a difficult term to fully capture and reliably measure in this group Whilst the quantitative methodology used in the Systematic review provides easily summarised data, a further limitation is that beyond the descriptive, a limited attempt can be made to synthesis scores by means of a meta-analysis. Therefore, the thesis is limited in the conclusions that can be drawn about QoL.

Clinical Implications

It is clear through completion of the systematic review, that the issue of QoL is a nebulous one. When assessing the QoL of a young person with JIA, clinicians must be mindful of the tools and methods used. A more commonly used, but general tool such as the PEDS-QL (Varni et al, 2002) may provide a valid overview, however, may miss out on some of the more nuanced themes relevant to QoL in JIA. These nuances are important to understand, to provide a level of person-centred care that can effectively support young people and their families and promote positive QoL and positive longer-term outcomes. Clinicians however are in a challenging situation if they wish to measure QoL more specifically for children with JIA as the validity of specific measures is poor and may not be accurately assessing the true QoL of young people with specifically JIA. However more general measures may be even more limited. It is apparent clinicians must take an individualised approach, leaning on their expertise and considering the variables specifically relevant to QoL and JIA in the specific family presenting to their clinic.

Medication is such a relevant factor in the QoL of young people with JIA (Céspedes-Cruz et al, 2008; Mulligan et al, 2013) however parents reported varying relationships with it. The role of information seems critical, and clinicians should not underestimate the importance of their role in containing and reassuring the families. However, this is a relationship that must remain flexible, due to the risk over removing choice and autonomy from the family and young person, indeed, as commented by one parent, the clinician does not go home with the family. In this revelation, it is key for the clinician to remain mindful of the potentially limited information made available to them by the family, and to ask pertinent questions pertaining to the wider impacts of MTX on the young person. Whilst the clinical psychologist may be best placed to ask these questions, their time and remit is often limited. An increase in this resource may allow for the psychologist to be used to support families at multiple

levels, for example through individual assessment to supporting the team to understand and support a families difficulties.

Some research has suggested clinicians may be reluctant at times to open conversations regarding pain (Lee et al, 2019), potentially due to personal beliefs of prior experience. However, the importance of asking questions to families is apparent in the results discussed above. Therefore, clinicians might consider the guidelines available for communicating with young people, about their chronic condition (NICE, Babies, Children and young people's experience of healthcare, 2021).

Clinicians should be aware of the great resilience and sacrifice put upon families and young people in the taking of MTX. What may be routine or expected from a clinical point of view, represents a great disruptor into the family system. It is with compassion, curiosity, and empathy the clinician must assess the wellbeing of the young person and family, and to at times resist the urge to "fix the unfixable"- as evidenced by the fact so many families stated the strategies suggested did not work.

Research Implications

It is clear further research is needed into the development and validation of QoL measures for JIA. In relation to MTX, tools may be devised that are able to assess MTX distress, and research exploring how this distress impacts the wider impact on the child. This should be compared again valid tools for depression and anxiety in young people, to gain a deeper understanding of the impact of this medication.

With regard to the empirical paper, there is scope for a number of additional research projects that would contribute to the current evidence based. There is currently little quantitative literature on parental wellbeing for the population with JIA, and considering the links with childhood QoL, it seems research must focus on understanding the needs of this population better, so that tailored interventions may support families from a systemic perspective.

Future research should also further explore experiences across populations, as the current study was limited in its recruitment sample. Given the variety in familial coping strategies across cultures, we may not be able to make wider generalisations based on current findings (McCubbin et al, 1993.)

Overall Conclusion

In conclusion, in attempting to quantify quality of life for young people with JIA and understand the parent experience of coping with a medication that is sometimes difficult to administer, a picture has emerged of the journey families and young people with JIA face with MTX. Whilst it has contributed to the evidence based in a number of areas, questions remain pertaining to the nature of "Quality of life", its influences for this specific population, and how to support parents, young people and families who must face this adversary. It is clear this is a timely and relevant piece of work, and whilst the clinical teams bring a huge amount of compassion, expertise, and curiosity to the families they work with, their role in truly understanding the lived experience of these families should not be understated.

Chapter 7: Additional Qualitative Methodology

This chapter includes an in-depth description of the methodology used to complete the qualitative analysis completed in Chapter Four. The research used Interpretive phenomenological Analysis, following the steps laid out by Smith et al, (2009). Below are detailed the steps taken in analysing these interviews.

As all transcripts were automatically transcribed by Microsoft teams, all transcripts were first reviewed for accuracy and clarity. All names of participants, family members, recruiting hospitals and professionals were anonymised. In completing this step, the researcher was able to review all interviews and became familiar and immersed in the data before analysis.

Each transcript was then read through more than once. Initial codes were noted beside the transcript in the margins, of emerging thoughts or themes. As this process was completed, ideas developed, and a code was given to these emerging codes. The links between codes also were sometimes apparent. These links were kept note of in a separate notebook to return to at a later stage in the analysis.

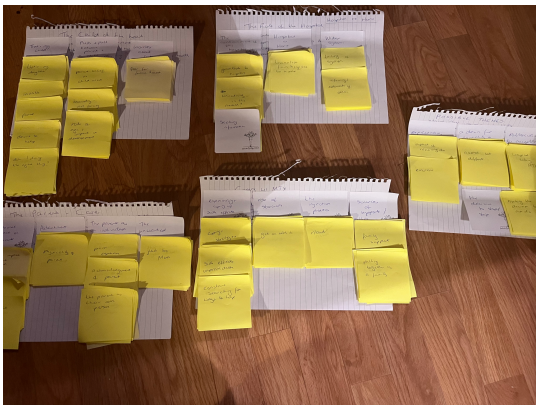
The next stage was to look at the codes and note how these may relate to potential themes and to write these on to sticky notes. Of note, the process of analysis was done by hand as opposed to using a computer programme such as NVivo. This process allowed the researcher to become fully immersed in the process and enable the researcher to easily move and manipulate themes manually to see what fit best. This process was done for each transcript until a stack of uncategorised notes was produced.

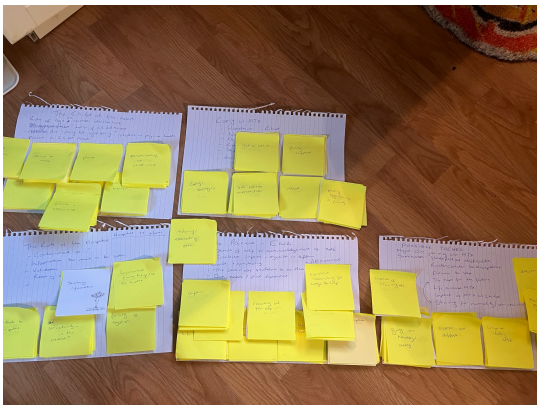
Figure 7.1
Illustrative Picture of Development of themes using IPA

Following this stage, the notes were arranged into groupings which represented potential themes. These themes were then given a title which best represented the codes held within.

Figure 7.2

Illustrative Pictures of arranging themes in IPA





The next step was to group these subthemes and see if larger emergent themes were apparent. This process was repeated several times. Similar subthemes were then reflected on and amalgamated into one theme.

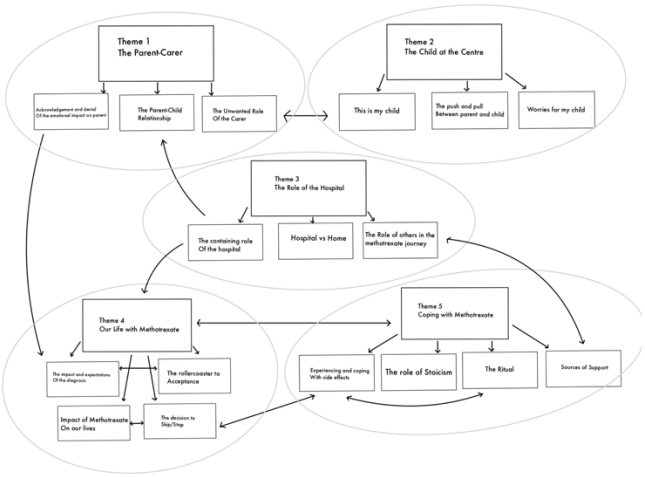
Table 7.1

Example arrangement of themes in table and corresponding codes

Major Theme	***Subthemes***	***Example Codes***
Theme 1-The Parent Carer:	The Acknowledgement and Denial of the emotional impact of MTX on the parent.	*Heart-breaking* *Shouldering* *Watching child struggle*
	The parent-child relationship	*I let her down* *Questioning*
	The Unwanted Role of the Carer.	*Resentment* *Reaching out* *Parent monitoring own feelings* *Denial of own feelings* *Rejection of parent*

The final major themes and subthemes were then arranged and drawn into a thematic diagram as seen below. The links between these themes were then drawn out and commented on in the results section of Chapter Four.

Figure 7.3 Thematic Map illustrating themes and their links



The themes were then systematically applied to each transcript for clarity and to ensure these themes had validity. A second reviewer was invited to complete the same process with a sample of two transcripts to ensure reliability. There were no queries between the transcripts, as themes were decided to be the same between first and second reviewer.

A master table of themes and subthemes can also be seen in Chapter Four.

Chapter 8: Descriptive Results of the Carer Experience Questionnaire

The Carer Experience Questionnaire (Al-Janabi et al, 2008) was administered pre interview, in an aim to gain additional qualitative data pertaining to the parent-carer experience. The CES is a measure of carer experience that focusses on "care related quality of life" and encompasses factors relevant to the role of the "unpaid carer". It includes questions pertaining to Activities, Support (from family and friends); Assistance (from organisations and the government); Fulfilment; Control (of the caring) and Getting On (with the care recipient). The CES has good construct validity, with 73% of the constructs showing significance indicating it measures what it purports to (Goranitis et al, 2014).

The rationale to include this in the study was that the results may provide additional contextual information to the parent stories. However, the decision was taken not to include this in the qualitative paper as it was felt the results, whilst relevant, would detract from the qualitative results presented in

Chapter four. An overall score is not provided here as it does not contribute, however the individual responses provide context to the participants, and are illustrated in Figures 8.1-8.6 below.

Key observations include that generally parents felt able to do most of the things they wanted to do outside of caring. In terms of support parents received support from family and friends, although less in terms of assistance from organisations and the government- of note, some parents interpreted this to mean support from the hospital, and indicated they get a lot of assistance from the hospital. Most parents indicated they sometimes find caring fulfilling, with one parent indicating they rarely find it fulfilling. Generally, parents also feel they are in control of the caring and do get on with the person they care for.

Whilst these results are not intended to form conclusions, they provide some context to the stories heard through the qualitative interviews.

Figure 8.1

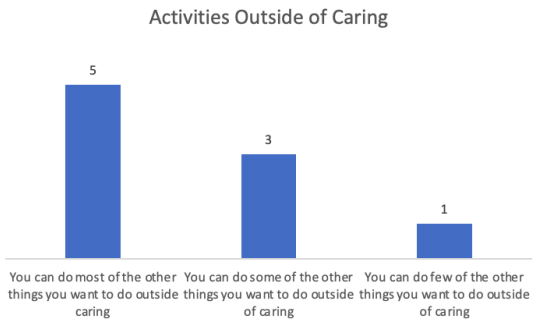


Figure 8.2

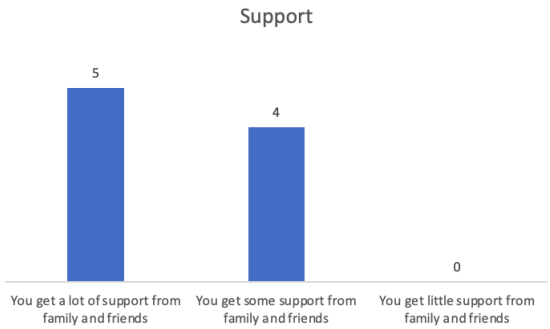


Figure 8.3

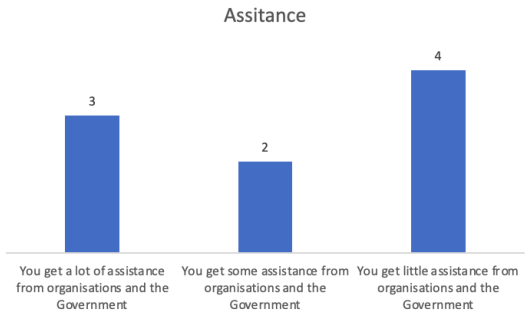


Figure 8.4

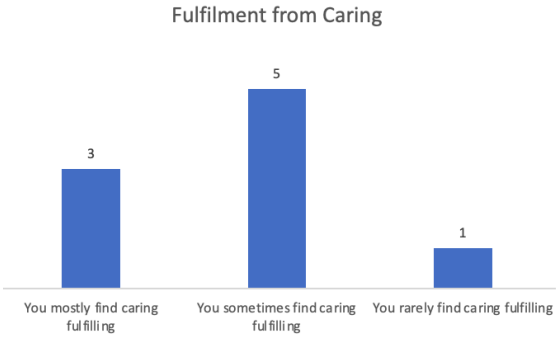
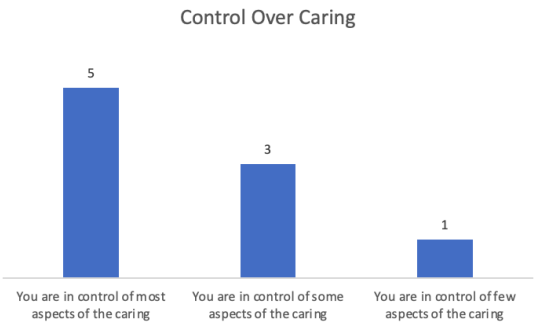
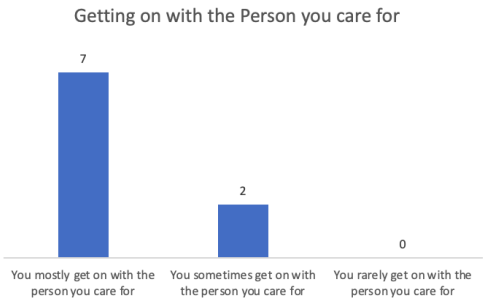


Figure 8.5

Figure 8.6


Control Over Caring
5
3
1
You are in control of most aspects of the caring
You are in control of some aspects of the caring
You are in control of few aspects of the caring


Getting on with the Person you care for
7
2
0
You mostly get on with the person you care for
You sometimes get on with the person you care for
You rarely get on with the person you care for

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Appendices

Appendix A: Author Guidelines for Submission To Health Psychology Review

Health Psychology Review

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