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TITLE PAGE

TITLE:

Interventions for reducing hospital-associated deconditioning: a systematic review and meta-analysis.

AUTHORS & AFFILIATIONS:

Toby O Smith PhD – Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, UK & Nuffield Department of Orthopaedics Rheumatology & Musculoskeletal Sciences, University of Oxford, UK. Email: toby.smith@uea.ac.uk

Ashwini Sreekanta MSc - Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, UK. Email: Ashwini.sreekanta@uea.ac.uk

Sarah Walkeden MSc - Physiotherapy Department, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK. Email: sarah.walkenden@nnuh.nhs.uk

Bridget Penhale MA - Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, UK. Email: bridget.penhale@uea.ac.uk

Sarah Hanson PhD - Faculty of Medicine and Health Sciences, University of East Anglia, Norwich, UK. Email: sarah.hanson@uea.ac.uk

CORRESPONDING AUTHOR: Dr Toby Smith, Queen's Building, School of Health Sciences, University of East Anglia, Norwich, NR4 7TJ, UK; T:+44 1603 591686; E: toby.smith@uea.ac.uk

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ABSTRACT

Purpose: To determine the effectiveness of hospital-based interventions designed to reduce Hospital-Associated Deconditioning (HAD) for people in inpatient hospital settings.

Materials & Methods: Systematic literature search of published and unpublished databases was conducted from (inception to 01 June 2020). Randomised and non-randomised controlled trials investigating the effectiveness of enhanced inpatient programmes aimed to reduce HAD in adults admitted to a hospital ward were included. Evidence was appraised using the Cochrane Risk of Bias tool and outcomes evaluated against the GRADE criteria. Where appropriate, data were pooled in meta-analyses and presented as risk difference (RD) or standardised mean difference with 95% confidence intervals (CI).

Results: Seven studies recruiting 12,597 participants (7864 enhanced programmes; 4349 usual care) were included. There was low-quality evidence for reduced risk of decline in physical performance for those in the enhanced programmes compared to usual care (RD: -0.04; 95% CI: -0.08 to -0.01; N=2085). There was low- or very-low quality evidence reporting no benefit of enhanced programmes for mobility on discharge, length of hospital stay, hospital readmission, and mortality within the first three-months post-admission ($p>0.05$). There was low-quality evidence that nursing home placement and mortality at 12-months was superior through enhanced inpatient programmes compared to usual care.

Conclusion: Enhanced inpatient programmes targeted at HAD may offer benefit over usual care for some outcomes. There remain uncertainty in relation to how applicable the findings are to non-North American countries, which elements of an enhanced programme are most important to reduce HAD, and longer-term sequelae.

Keywords: Inpatient; deconditioning; physical inactivity; bed-rest; frailty; ward intervention

HIGHLIGHTS

- Hospital-associated deconditioning (HAD) is a negative consequence of hospital stay, impacting on morbidity and mortality
- Older people who experience HAD are at greatest risk of poor health outcomes.
- Enhanced ward-based interventions targeting HAD may reduce declining physical performance and institutional care placement.
- Enhanced ward-based interventions targeting HAD may reduce mortality at 12-months for older people.
- The evidence is based on medical-ward settings and not post-surgical interventions.

1.0 INTRODUCTION

Hospital-associated deconditioning (HAD) is a complex negative consequence following hospitalisation. It is associated with prolonged periods of immobility. The cumulative impact of extended or complicated hospitalisation among older patients typically results in patients experiencing a decrease in muscle mass and significant functional decline due to a complex process of physiological changes that can affect multiple systems.[1-3] It has been estimated that 68% of patients are discharged from post-acute medical settings below their pre-admission level of function.[4] This means that post-hospitalisation, patients are not only recovering from their acute illness but also facing physiological stress[5-8] and susceptibility to complications not directly related to the cause of their admission.

HAD has a very concerning impact on well-being and quality of life of people after they leave the acute setting. It may result in delayed discharge, increased likelihood of re-admission and admission to community facilities (sub-acute, residential or nursing care) instead of a patient returning to their home. Patients who are discharged with poor physical function have three times greater risk of being readmitted within 30 days post-discharge compared to older adults with medically complex conditions but higher physical functioning.[9] This creates unnecessary costs (in wider terms) to health and care systems.

A number of factors have been identified which may place patients at greater risk of HAD. These include: increased age, delirium on admission, presence of multiple comorbidities, cognitive deficits, poor mobility/use of a gait aid, depression, deficits in basic or instrumental activities of daily living (ADL) at hospital admission/discharge, or both.[10-12] These may be exacerbated by: patients' fear of falling, causing them to limit their activity; tethering interventions (e.g. indwelling urinary catheters); healthcare staff prioritising patient safety, especially fear of falls, over patient activity.[6,7,10-13]

Whilst there is clear rationale for why HAD interventions would be beneficial, there remains uncertainty as to what these are, what the optimal ward environment would be, who delivers the intervention and how effective these are within health services. To the authors' knowledge, there have been no published systematic reviews to answer these questions for adults admitted to hospital for surgical or non-surgical interventions. The purpose of this study was to undertake such a review and determine the clinical and cost-effectiveness of hospital-based interventions designed to reduce HAD for people on hospital wards.

2.0 MATERIALS & METHODS

This systematic review was registered through the International Prospective Register of Systematic Reviews database (Reference: CRD42020169893). It has been reported following the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines.[14]

2.1 Search Strategy

The search was undertaken on 24th February 2020 and updated on 30 June 2020 by one reviewer (TS) using published and unpublished literature databases including CENTRAL, EMBASE, MEDLINE, CINAHL and PubMed. Searches were conducted from database inception to 01 June 2020. The search strategy for MEDLINE is presented in **Supplementary Table 1.** Searches were undertaken from database inception to the search date. This was modified for each database. We accessed clinical trial registries for unpublished or ongoing clinical trials including the WHO International Clinical Trial Registry and ClinicalTrials.gov registry. Reference lists of all potentially eligible studies were reviewed by two reviewers (TS, AS).

2.2 Selection Criteria

Inclusion criteria:

- Studies recruiting adults (aged 18 years and over) admitted to a hospital ward (acute or rehabilitation settings) for elective or non-elective hospital procedures (surgical and non-surgical).
- Patients who have been specifically identified as those with existing or at risk of HAD or where interventions have been delivered to specifically address HAD.
- Randomised (RCT) and non-randomised (non-RCTs) comparative studies where one intervention was a ward-based intervention, strategies or pathways designed to prevent or treat HAD in people admitted to hospital wards. This may have included: exercise programmes; changes to ward environments; training for staff members; or provision of patient contacts (with health professionals, other patients or visitors) in alternative locations. This could have included: supplementary interventions including follow-up telephone calls/video messaging, online resources and/or paper-based reading materials.
- Studies where a comparative group was either usual care provision or comparison to alternative interventions, strategies or pathways.
- Studies which reported one or more of the following outcomes: physical activity performance (level and/or quantity); physical function, health-related quality of life (HRQOL), cost-effectiveness or health resource use, complications and adverse events or psychological measures.

Exclusion criteria:

- Participants admitted to acute mental health wards or high-dependency/critical care wards.
- Specific rehabilitation interventions or pathways for patients admitted to hospital wards where HAD was not the target or aim of the intervention i.e. generic elderly rehabilitation or post-operative rehabilitation strategies.

One reviewer independently reviewed all titles and abstracts from the search results (TS), and independently verified by a second reviewer (AS or SH). Full-text papers for all potentially eligible studies were independently reviewed by each reviewer to determine final inclusion. Disagreements between the two reviewers were resolved through discussion, with an adjudicator available to address any disagreements.

2.3 Data Extraction

Data were extracted onto a pre-defined data extraction form by one reviewer (TS) and verified by two reviewers independently (AS, SH). Where the same study was reported across two or more papers, these were classified as a single study to avoid multiple/duplicate counting.

Data extracted from each eligible paper included: country of origin, year of study conduct, number and characteristics of participants including data on: age, gender, medical morbidities, reason for hospital admission, intervention strategies tested (control and experimental) which included the underpinning theory and principles, the description of the ward environment and who was delivering the intervention, timing of data collection (acute or rehabilitation hospital), and outcomes for the intervention versus control groups. Disagreements in data extraction between the reviewers were resolved through discussion to gain agreement/consensus.

2.4 Outcome Measures

The primary outcome measure was physical activity performance (level and quantity) performed three-months post-discharge. Secondary outcome measures included: health-related quality of life, economic measures (e.g. re-admission rates and hospital length of stay), complications and adverse events, and psychological outcomes (e.g. anxiety, depression, self-efficacy).

The primary endpoint was three months post-hospital discharge. Secondary outcome endpoints included: at discharge (short-term), three to nine months (mid-term) and 12 months and longer (long-term) follow-up points.

2.5 Assessment of Methodological Quality of Studies Included for Review

One reviewer (TS) independently critically appraised each included study using the Cochrane Risk of Bias tool for RCTs.[15] This was then verified by two reviewers independently (AS, SH). Disagreements in scoring between the reviewers were resolved through discussion.

2.6 Data Analysis

Data extraction tables were reviewed for study heterogeneity. Through this, between-study variability in participant characteristics (patients and staff), interventions and study design were assessed. Where heterogeneous, a narrative analysis of the results was presented. Where homogeneous, data were pooled for those outcomes using a Mantel-Haenszel method meta-analysis.[16] All analyses used a random-effect model as there was variability in normal international health-service provision across trials. If there was evidence of substantial variability for any analysis, a narrative analysis was undertaken. For continuous outcomes, when trials use the same outcome instrument to assess an outcome domain, mean difference (MD) and 95% confidence intervals (CI) were presented. When trials used different outcome instruments for an outcome domain, standardised mean difference (SMD) and 95% CIs were reported. For dichotomous outcomes, risk difference (RD) and 95% CIs were presented. For each meta-analysis, statistical heterogeneity was assessed using the I^2 statistic. Corresponding authors were contacted to gain clarification on missing data.

Small sample size publication was planned to be assessed using funnel plots when there was a minimum of 10 studies for a specific outcome.[15]

Planned subgroup analyses were:

- Type of hospital ward (i.e. acute hospital versus rehabilitation hospital)
- Clinical sub-speciality of patient group (i.e. surgical versus medical)
- Type of intervention (i.e. education of ward staff vs. environmental adaptations vs. combined ward staff training and environmental adaptations)

All analyses were conducted by one reviewer (TS) using RevMan (Review Manager (RevMan) [Computer program]; Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.)

2.7 Assessment of GRADE

We assessed the quality of evidence for each outcome using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) criteria.[17] Through this, two reviewers (TS, AS) assessed outcomes by: (1) methodological limitations through the assessment of risk of bias using the Cochrane Risk of Bias tool[15]; (2) indirectness relating to similarity to clinical practice; (3) imprecision

relating to the number of participants and events; (4) inconsistency in effect estimates across the studies for a given analysis; and (5) likelihood of publication bias.[17]

3.0 RESULTS

3.1 Search Results

A summary of the search results is presented in **Figure 1**. In total, 283 papers were identified from the search strategies. Of these, 38 were deemed potentially eligible. On full-text review, seven satisfied the eligibility criteria and were included.

3.2 Characteristics of Included Studies

A summary of the characteristics of included studies is presented in **Table 1**. Of the seven studies included, five were RCTs,[18-22] two were non-RCTs.[23,24] In total 12,597 participants were recruited. Of those 7864 recruited to enhanced programmes, this included 4349 females (55.3%), with a mean age of 79.2 years. Those 4733 recruited to usual care comparisons included 2603 females (54.9%), with a mean age of 78.5 years. Three studies reported the patient's living situation prior to admission.[18,19,24] Follow-up periods ranged from discharge in one study,[22] mid-term (three to nine months) in five studies,[19-21,23,24]and to 12 months in one trial.[18]

All seven studies were undertaken in North America. Five studies were based in USA,[18-20,22,23] two in Canada.[21,24] Hospital settings were acute medical wards in all seven studies. No surgical wards or surgical patients were recruited.

All seven HAD programmes aimed to increase ward-based physical activity through education, change in healthcare practice and in some instances, ward environment. Increased education and allocation of staffing for physical activity promotion was demonstrated in two studies.[18,24] Greater education was also provided for caregivers and patients in three studies.[21-23] Timmer et al[21] and Lenze et al[22] studies focused interventions on pacing-based and goal-setting education for patients. Lenze et al[22] alone aimed to increase the intensity of activities. Ward-based environmental changes including seating and changes in space usage for eating and socialising away from the bed-space was tried in two studies.[18,20] Enhanced rehabilitation staff time for physical activity was adopted in two studies[18,20] and increased and earlier assessment for barriers such as medication review was adopted in three enhanced rehabilitation interventions.[18,19,23] Interventions were delivered by multi-disciplinary teams,[24] with an Occupational Therapy focus,[21] or nurse-led.[19,20,22] Hastings et al[23] utilised a dedicated walks assistant and Liu et al[24] used a 'local champion'. The environment was altered as part of the intervention in two studies.[18,19] There was some description of strategies known to support behaviour change, such as goal-setting, feedback and self-monitoring. The Health Action Process Approach and Motivational interviewing underpinned the work by Lenze et al[22] and Liu et al[24] mapped barriers and facilitators to behaviour change theory. Hastings et al[23] listed the barriers to mobility outside of the supervised episodes of walking. A detailed description of the experimental intervention and underlying programme theories, is presented in **Supplementary Table 2**.

The comparator in the seven studies was usual care in an acute hospital setting. This consisted of standard hospital care in typical ward settings within the USA and Canadian health models.

3.3 Critical Appraisal

A summary of the risk of bias assessment results is presented in **Table 2**. All but two studies demonstrated low risk of bias for sequence generation.[23,24] However only two studies clearly demonstrated low risk of bias for selection bias through allocation concealment.[18,21] There was a high risk of bias for performance bias, where all but Timmer et al[21] demonstrated high risk of bias by not blinding participants or personnel. Similarly, there was high risk of detection bias for all but two studies.[21,22] There was low risk of attrition bias for all studies except Counsell et al[18] which demonstrated high risk of bias, and Mundy et al[20] where this was unclear. All studies except Lenze et al [22] and Timmer et al [21] reported high risk of reporting bias.

3.4 Meta-Analysis

The results of the meta-analysis are presented in **Table 3**.

3.4.1 Primary outcome: Physical activity performance

Physical activity performance was assessed by activity of daily living (ADL) performance and mobility in four studies.[18,19,21,22] No studies reported physical activity performance at the primary endpoint of three months. All outcomes reported were short-term (i.e. to discharge).

When assessed by change in ADL score from baseline to discharge (at discharge), there was low-quality evidence (due to risk of bias and imprecision) for no difference between the enhanced programme and usual care (SMD: 0.09; 95% CI: -0.13 to 0.30; N=1657: Figure 2). However when assessed categorically by the number of participants to demonstrated decline in ADL performance from baseline to discharge, there was low-quality evidence (downgraded two levels due to risk of bias) for reduced risk of decline for those in the enhanced programmes compared to usual care (RD: -0.04; 95% CI: -0.08 to -0.01; N=2085; Figure 3).

There was low-quality evidence (downgraded two levels for risk of bias) of no benefit of enhanced programmes over usual care for the risk of mobility decline from baseline to discharge (RD: -0.01; 95% CI: -0.04 to 0.02; N=2085; Figure 3). Similarly, there was low-quality evidence (due to imprecision and risk of bias) of no benefit of enhanced programmes over usual care for mobility score on discharge (SMD: 0.40; 95% CI: -0.30 to 1.11; N=1508; Figure 2).

3.4.2 Secondary Outcomes: health-related quality of life

No studies reported health-related quality of life as an outcome.

3.4.3 Secondary outcome: economic measures

Health utilisation costs were assessed by hospital length of stay,[20-22] hospital re-admission,[19-21,23] and nursing home placement.[18,19,24]

There was moderate-quality evidence (downgraded by risk of bias) of no benefit of enhanced programmes of usual care for hospital length of stay (MD: -0.59; 95% -1.64 to 0.46; N=574). There was very low (downgraded two levels due to risk of bias) and low (downgraded one level due to risk of bias and imprecision) that enhanced programmes do not benefit reduced risk of nursing home residence in the short or longer term (short: RD: -0.03; 95% CI: -0.07 to 0.01; N=11,123; longer-term: RD: -0.0; 95% CI: -0.03 to 0.02; N=1488). There was low-quality evidence (downgraded due to risk of bias and imprecision), that enhanced programmes reduced the risk of nursing home placement in the mid-term (RD: -0.08; 95% CI: -0.15 to -0.01; N=603).

3.4.4 Secondary outcome: complications and adverse events

Mortality was the only adverse event reported from the four studies which reported this.[18,20,21,24] In the short-term and mid-term there was very low-quality evidence (downgraded two levels due to

risk of bias, and one level due to imprecision) of no benefit of enhanced programmes over usual care (short-term: RD: 0.00, 95% CI: -0.02 to 0.01; N=10,978; mid-term: RD: 0.03; 95% CI: -0.02 to 0.08; N=558). There was low-quality evidence (downgraded due to risk of bias and imprecision) for a reduced risk of mortality in the enhanced programme over usual care in the longer-term (12-month) assessment (RD: -0.23; 95% CI: -0.27 to -0.19; N=1482).

3.4.5 Secondary outcome: psychological outcomes

One study reported patient depression levels as an outcome.[18] This provided low-quality evidence (downgraded due to risk of bias and imprecision) of a benefit of usual care over enhanced programmes for the risk of reporting depression on hospital discharge (RD: 0.11, 95% CI: 0.02, 0.21; N=346).

3.5 Subgroup Analyses & Publication Bias

There were insufficient data to perform the *a priori* subgroup analyses or publication bias assessments.

4.0 DISCUSSION

The findings of this study indicate that enhanced in-patient programmes to reduce HAD reduced the risk of declining ADL ability by 4% at discharge, reduced nursing home residence by 8% at one to three months post-discharge and reduced one-month mortality by 23%. However enhanced programmes were reported to increase the risk of depression at discharge by 11%. These outcomes are based on low-quality evidence and therefore should be interpreted with caution. All other measures of clinical outcomes and economic markers including hospital length of stay demonstrated no difference between enhanced programmes and usual care.

The findings reported a substantial decrease in risk of mortality at 12 months (23%) and nursing home residence at one to three months (8%) for those randomised to receive an enhanced inpatient care programme aimed to reduce HAD compared to usual care. Whilst we acknowledge that this is based on low- and very-low quality evidence respectively, this provides an important signal that such programmes may have longer-term benefits. What remains unclear is what aspect of these interventions may have contributed most to these outcomes. No identified study had performed mediation analyses for their complex intervention. Such analyses can be valuable to better understand the inter-relationship(s) between the components of enhanced programmes,[25] and to identify which elements had the most impact on outcome.[26] Given the multi-factorial nature of the interventions identified, and potential challenges which some health services may have in being able to provide all elements, notably around infrastructure, space and staff resource, understanding which elements had the most impact on outcome, is desirable and recommend for future study.

The results indicated that people allocated to an enhanced programme had an 11% greater risk of experiencing depression on hospital discharge compared to those allocated to usual care. This is a concerning finding, on current evidence which is difficult to interpret. Given that physical activity and being more physically active is associated with improving mood[27] the findings appear contradictory. One hypothesis is that being more active may change an individual's expectations of their own ability post-recovery.[28] Those who are discharged and are more active may place greater expectation on being able to self-manage post-discharge, which may represent as reduced psychological status with increased burden[29] or equally a treatment-effect through improved self-efficacy from HAD interventions.[30] Alternatively, this may be a spurious result, reflecting the small number of studies which investigated this outcome. Nonetheless, given this surprising outcome, further study to assess psychological status such as resilience, burden, anxiety and not just depression, is warranted in future trials.

Enhanced programmes may offer no benefit in changing ADL and mobility scores at discharge, and hospital length of stay. Whilst the intervention may propose people being more active, or change their perception of activity during hospital stay, the specific measures of ADL capability or mobility may not reflect functional change in the domains modified through interventions. Alternatively, people discharged from hospital may be expected to be at a similar functional and mobility status irrespective of group allocation. People under a threshold of capability are not able to be discharged from health institutions. Likewise, as this time-point assessment is variable dependent on discharge capability, people who are functionally more able may have been expected to be discharged earlier. However, our analysis indicated no substantial difference between the groups for length of hospital stay. This questions this interpretation. Given these, there may be considerable strengths to investigating which component of enhanced programmes have the greatest impact on physical capability.

There were limited data reported on longer-term outcomes. Whilst the inpatient interventions delivered may be anticipated to have the largest effect early post-discharge, there was a signal of a difference between the groups for mortality. No intervention provided a within-community outreach element. Such post-discharge interventions may have important value for re-enforcing earlier learning on physical activity engagement, but also provide opportunity for individuals to develop problem-solving and pacing/behaviour modification approaches which may have value. Timmer et al[21] and Lenze et al[22] both included such elements within their inpatient intervention. Further implementation within the post-discharge setting may have provided further clinical effectiveness for these skill-based elements. Considering friends and family as informal caregivers with appropriate skill-training may have particularly important benefits for those with an expected long recovery with long-term physical disabilities or cognitive impairment, where skills acquisition are valuable in self-management processes.[31] If such interventions were to be assessed, both the fidelity of intervention uptake post-discharge and longer-term clinical and economic outcomes should be considered for both patient and informal caregiver.

This systematic review presented with two key limitations which should be considered. Firstly, the search strategy focused on reducing HAD specifically in increasing inpatient mobility and physical activity programmes. Interventions exploring wider care pathways *per se*, such as comprehensive geriatric assessment models were not included. This was justified as the purpose of this analysis was to determine the effectiveness of interventions designed specifically to promote physical activity participation. Nonetheless this acknowledges that experimental intervention arms should therefore consider such 'good care' pathways plus physical activity promotion strategies over 'good care pathways' alone. Secondly, the evidence was based in North America (USA and Canada). No studies were identified from Europe, Australia, Asia, Africa or South America. There therefore remains uncertainty as to whether this is because the interventions under investigation in this systematic review have not been published because they are standard practice in these countries, or the healthcare services are not sufficiently flexible to be able to deliver such models. Whilst both suggestions are mere hypotheses, generalisability of the interventions both of their implementation and also on the impact of society and the populations from other non-North American countries, should be considered when interpreting these findings.

5.0 CONCLUSION

There is low quality evidence that for some outcomes, notably nursing home placement and mortality, enhanced inpatient care to reduce HAD may benefit patients admitted to hospitals with acute medical illnesses. No studies have investigated the effectiveness of such interventions for those on surgical care pathways. There remain a number of uncertainties to this, including how applicable the findings are to non-North American countries, which elements of an enhanced programme are most important

to reduce HAD and to promote physical activity, and the longer-term outcomes of this. These are research priorities to identify appropriate interventions to manage the consequences of HAD.

DECLARATIONS

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Ethical Approvals: No ethical approvals were required for this study design.

FIGURE AND TABLE LEGENDS

Figure 1: PRISMA flow-chart summarising search strategy results

Figure 2: Forest plot illustrating the standard mean difference of ADL and mobility score at hospital discharge for enhanced programmes versus usual care to assess physical function.

Figure 3: Forest plot illustrating the risk difference of decline in ADL and mobility from hospital admission to hospital discharge for enhanced programmes versus usual care to assess physical function.

Table 1: Summary of the characteristics of included studies.

Table 2: Summary of the critical appraisal results (Cochrane Risk of Bias Tool)

Table 3: Summary of the meta-analysis clinical outcomes

Supplementary Table 1: Example search strategy (MEDLINE)

Supplementary Table 2: Detailed information regarding intervention, its underpinning theory and the ward setting trials were undertaken within.

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Figure 1: PRISMA flow-chart summarising search strategy results

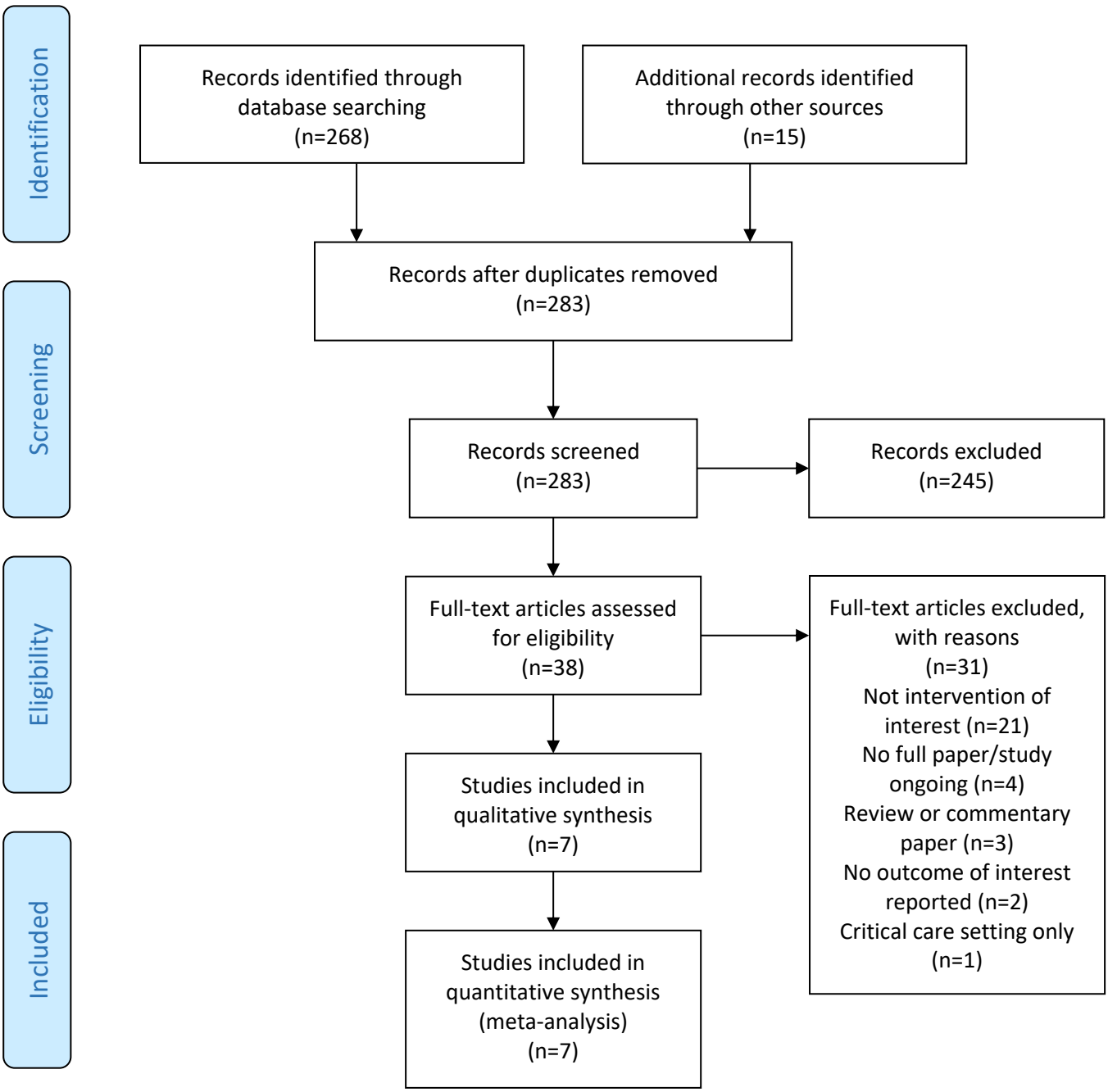

Figure 2: Forest plot illustrating the standard mean difference of ADL and mobility score at hospital discharge for enhanced programmes versus usual care to assess physical function.

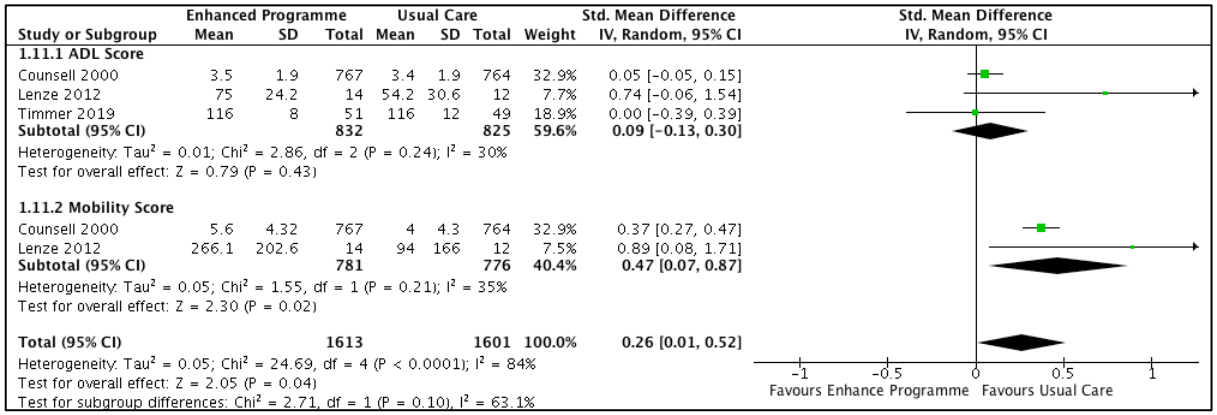

Figure 3: Forest plot illustrating the risk difference of decline in ADL and mobility from hospital admission to hospital discharge for enhanced programmes versus usual care to assess physical function.

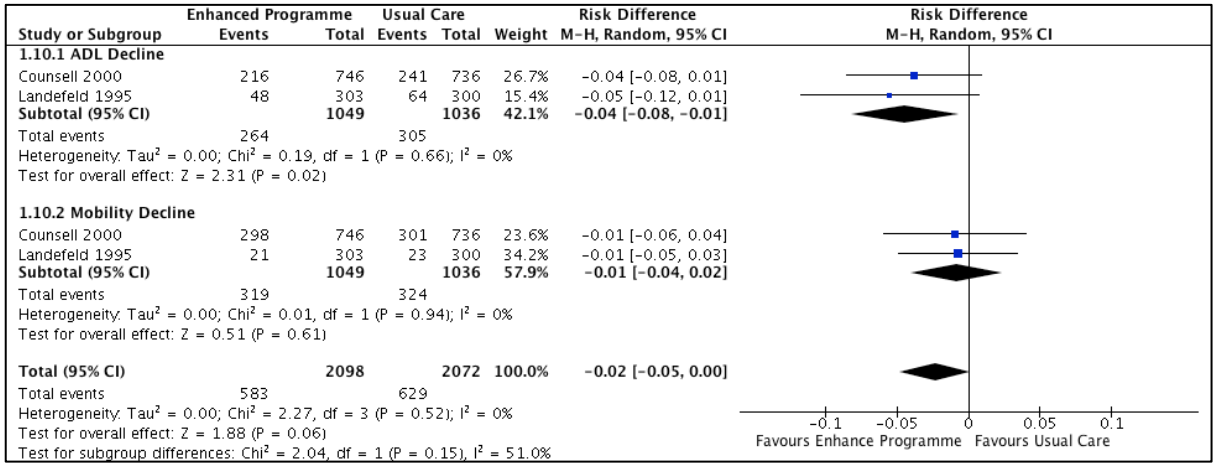

Table 1: Summary of the characteristics of included studies.

Study & Country	Study design	N	Mean age	Gender (female)	Medical Diagnosis	Intervention	Control	Follow-up Period
Counsell et al [18](USA)	RCT	Exp: 767 Control: 764	Exp: 80 (SD: 7) Control: 79 (SD: 7)	Exp: 462 (60%) Control: 464 (61%)	Acute medical illness	Ward setting with room for physical therapy, seating for eating and visiting family; physical and psychosocial assessment daily; nursing plan for wider health needs assessment; medication review to minimise non-required pharmacological interventions	Usual care without enhanced programme	12 months post-discharge
Hastings et al [23] (USA)	nRCT	Exp: 92 Control: 35	Exp: 74 Control: 75	Exp: 3 (3.3) Control: 0	Acute medical illness for military veterans	Early assessment, supervised ambulation, with walk assistant, uptake of activity programmes and education on daily ambulation for them and caregivers	Usual care	1 month
Landefeld et al[19] (USA)	RCT	Exp: 327 Control: 324	Exp: 80.2 (SD: 6.9) Control: 80.1 (SD: 6.6)	Exp: 223(68%) Control: 212(65%)	Acute medical illness	Great rehabilitation staff time and contact; patient's needs assessment by nurse on re-enablement	Usual care	Three months post-discharge.
Lenze et al[22] (USA)	RCT	Exp: 14 Control: 12	Exp: 80.8 (7.2) Control: 75.7 (8.96)	Exp: 69.2% Control: 83.3%	Following acute hospital admission for medical illness	Early mobility intervention based on models of motivation and behaviour change. Physiotherapy and OT intervention to increase patient engagement and intensity, with the goal of improving functional	Usual care	Discharge

						outcome, through: (1) a patient-directed, interactive approach, (2) increased rehabilitation intensity, and (3) frequent feedback to patients on their effort and progress		
Liu et al[24] (Canada)	nRCT	Exp: 6386 Control: 3318	Exp: 79.9 (SD: 8.37) Control: 80.0 (SD: 8.2)	Exp: 3490 (54.7%) Control: 1749 (52.7%)	Acute medical illness	Early mobilisation consisting of promotion of time out of bed and being active within the ward environment.	Pre-intervention usual care (time-interrupted analysis)	20 weeks
Mundy et al[20] (USA)	RCT	Exp: 227 Control: 231	Not stated	Exp: 127 (56%) Control: 129 (56%)	Community acquired pneumonia	Early mobilisation (out of bed for a minimum 20 minutes within first 24 hrs) including meals, mobility, toileting	Usual care	3 months
Timmer et al[21] (Canada)	RCT	Exp: 51 Control: 49	Exp: 80 (SD: 8) Control: 81 (SD: 7)	Exp: 35 (28%) Control: 39 (25%)	Acute medical admission	Usual care PLUS individual pacing activities review with OT and review sessions to initiative these. Group sessions to increase activities with other patients	Usual care	3 months post-discharge

Exp – Experimental; ICU – intensive care unit; IMCU – intermediate care unit; N – number of participants; nRCT – non-randomised controlled trial; OT-occupational therapy; RCT – randomised controlled trial; SD – standard deviation; USA - United States of America

Table 2: Summary of the critical appraisal results (Cochrane Risk of Bias Tool)

	Random sequence generation (selection bias)	**Allocation concealment (selection bias)**	**Blinding participants and personnel (performance bias)**	**Blinding outcome assessment (detection bias)**	**Incomplete outcome data (attrition bias)**	**Selective outcome reporting (reporting bias)**
Counsell [18]	Low risk	Low risk	High risk	High risk	High risk	High risk
Hastings [23]	High risk	High risk	High risk	High risk	Low risk	High risk
Landefeld [19]	Low risk	High risk	High risk	High risk	Low risk	High risk
Lenze [22]	Low risk	Unclear	High risk	Low risk	Low risk	Low risk
Liu [24]	High risk	High risk	High risk	High risk	Low risk	High risk
Mundy [20]	Low risk	Unclear risk	High risk	High risk	Unclear risk	High risk
Timmer [21]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Table 3: Summary of the meta-analysis clinical outcomes

Outcomes	**Timescale**	**Effect Estimate MD/SMD/RD (95% CI)**	**I^2 (%)**	**N**	**Study**	**GRADE**
Physical Function: ADL score	Discharge	SMD: 0.09 (-0.13, 0.30)	30	1657	18,21,22	Low Quality
Physical Function: ADL decline from baseline	Discharge	RD: -0.04 (-0.08,-0.01)	0	2085	18,19	Low Quality
Physical Function: mobility score	Discharge	SMD: 0.40 (-0.30, 1.11)	69	1508	18,22	Low Quality
Physical Function: mobility decline from baseline	Discharge	RD: -0.01 (-0.04, 0.02)	0	2085	18,19	Low Quality
Depression: categorical	Discharge	RD: 0.11 (0.02, 0.21)	NE	346	18	Low Quality
Health utilisation: hospital LOS	Discharge	MD: -0.59 (-1.64, 0.46)	76	574	20-22	Moderate Quality
Health utilisation: nursing home residence	Discharge	RD: -0.03 (-0.07, 0.01)	76	11,123	18,19,24	Very Low Quality
Health utilisation: nursing home residence	3 months	RD: -0.08 (-0.15, -0.01)	NE	603	19	Low Quality
Health utilisation: nursing home residence	12 months	RD: -0.00 (-0.03, 0.02)	NE	1488	18	Low Quality
Health utilisation: hospital re-admission	3 months	RD: -0.01 (-0.05, 0.04)	0	1278	19-21,23	Low Quality
Mortality	Discharge	RD: 0.00 (-0.02, 0.01)	54	10,978	18,20,24	Very Low Quality
Mortality	3 months	RD: 0.03 (-0.02, 0.08)	19	558	20,21	Low Quality
Mortality	12 months	RD: -0.23 (-0.27, -0.19)	NE	1482	18	Very Low Quality

Supplementary Table 1: Example search strategy (MEDLINE)

1. exp Exercise-Therapy/
2. exp Exercise/
3. exp Physical-Fitness/
4. exp Weight-Lifting/
5. exp Physical-Medicine/
6. exp Physical-Therapy-Modalities/
7. (rehabilitation adj3 (Exercise or Physical)).mp.
8. (Exercise or Physiatrics or Physiatry or Physiotherapy or mobili?ation).ti,ab.
9. Activit*.ti.
10. (movement adj3 (Active or Whole body)).mp.
11. (Exercise adj3 (training* or Progressive or therapy or intervention)).mp.
12. (training adj3 (Aerobic or endurance or Strength or resistance or weight or Fitness or Interval or Circuit)).mp.
13. (Physical therapy).mp. or (Weight lifting).mp.
14. MeSH descriptor Environment Design explode all trees
15. (environment near controlled)
16. ((multisensory or multi-sensory or sensory or therapeutic or restorative or healing) adj
17. environment* or design))
18. ((environmental or ambient) adj2 (design or feature$ or stimuli))
19. Atrophy/
20. Weakness/
21. Deconditioning.tw.
22. Sleep/
23. Nutrition/
24. Feeding/
25. (Food or nutrition) adj2 (supplement)
26. Eating.tw.
27. Hydration/
28. Drinking.tw.
29. (fluid*) adj2 (oral or intake)
30. Reablement.tw.
31. (activities of daily living)
32. ADL.tw.
33. (Instrumented or instrumental)
34. IADL.tw.
35. (tether* or restrict*) adj3 (catheter or line or intravenous or IV)
36. BEDS single term (MeSH)
37. (bed* or bedside*)
38. ((side* next rail*) or (safety next rail*) or (security next rail*))
39. (bedrail* or siderail* or cotside*)
40. HOSPITALS explode tree 1 (MeSH)
41. HOSPITALIZATION single tem (MeSH)
42. INSTITUTIONALIZATION single tem (MeSH)
43. (ward or hospital or bed or corridor) adj2 (space or environment or design)
44. CLINICAL-TRIAL.pt.
45. randomized.ab.
46. placebo.ab.
47. (clinical trials).sh.
48. randomly.ab.
49. trial.ti.
50. (animals not (humans and animals)).sh
51. 48 not 49

Supplementary Table 2: Detailed information regarding intervention, its underpinning theory and the ward setting trials were undertaken within.

Author	Underpinning principles and theory	Participant (patient) profile	Ward environment	Detailed description of intervention
Counsel [18]	Principles of quality improvement and comprehensive geriatric assessment. Four key elements: a specially designed environment; patient-centred care; discharge planning with the goal of returning the patient to their home; and review of medical care. To measure "process" variables and estimate the quantity or "dose" of interventions received by patients and the impact that the process has on professional caregivers' perceptions of the intervention	Aged >70. Admitted from the community. Non-elective. Length of stay > 2 days.	34-bed unit that was renovated to include a room for physical therapy and a room for dining and family visits	Nursing care plans for fall risk assessment, mobility, self-care, skin integrity, nutrition, continence, confusion, depression, and anxiety. Medications of potential risk to older patients (e.g., sedative-hypnotic agents) were identified by the medical director, who recommended alternative treatments, including non-pharmacologic interventions. Nursing staff-to-patient ratios were similar on the intervention and usual care units For most patients (67%) on all study units, the attending physician was the patient's physician in the outpatient setting as well
Hastings [23]	To optimise physical function of older veterans by increasing the amount of time spent out of bed. Three feature: early assessment (within 24 hrs of admission), supervised ambulation (for safety and ensure uptake of activities) and education on the importance of ambulation for the patient and their family.	Aged > 65 with a medical illness	271-bed tertiary care facility	Multi-disciplinary approach. Gait and balance assessment by Physical therapist on day 1. Assistive devices provided as needed, and safety recommendations given to the walks assistant. Daily walks supervised by a dedicated walks assistant (WA) for the duration of the hospital stay, up to 20 minutes daily. WAs followed protocols for offering rest breaks and monitoring vital signs. They worked closely with each participant's nurse to determine the best timing for the walk.

				The WA also educated the patient and family members about the importance of out-of-bed activities, reviewed activity goals, and provided motivation and encouragement to contextualize walking as a normal activity
Landefeld [19]	Principles of quality improvement and comprehensive geriatric assessment: A specially designed environment, patient-centred care, planning for discharge, and review of medical care.	Aged > 70 admitted for general medical care	Single 14-bed unit: Specially prepared environment with uncluttered hallways, large clocks and calendars, handrails and raised toilet seats and door handles.	Patient-centred care emphasizing independence, including specific protocols to improve self-care, continence, nutrition, mobility, sleep, skin care, mood, cognition (implemented by the primary nurse and based on the daily assessment). The primary nurse assigned to each patient in the intervention group was responsible for assessing the patient's specific needs daily and implementing protocols for the prevention of disability and for rehabilitation. Discharge planning with the goal of returning the patient their home. Intensive review of medical care to minimize the adverse effects of procedures and medications.
Lenze [22]	Based on premise that post-acute rehabilitation is not of high enough intensity and that patients not sufficiently engaged (e.g. by using patient-directed therapy and frequent feedback).	Aged > 60 years.	USA Three units of a skilled nursing facility (SNF). Patients with all impairments were included (e.g., not solely hip fracture), because it was expected that patients' reasons for	EMR is a "how" intervention, not a "what" intervention. It is a set of behavioural skills for therapists to integrate into their OT/PT practice to increase the intensity of, and the patient's engagement in, all therapeutic sessions.

	Based on theories of behaviour change for engagement to better motivate patients – Health Action Process Approach and Motivational interviewing. The group developed Enhanced Medical Rehabilitation (EMR): PT and OT which focuses on engaging patients in their therapy sessions to increase patient engagement and intensity, with the goal of improving functional outcome, through: (1) a patient-directed, interactive approach, (2) increased rehabilitation intensity, and (3) frequent feedback to patients on their effort and progress.		admission would be varied and multiple.	EMR was developed for real-world rehabilitation to be done with their therapy with frail and deconditioned individuals. Training developed for therapists which included: a) providing and reviewing together the study manual and also a one-page checklist version of the manual for daily reminder; b) weekly 30-minute supervision meetings which included collaborative review of videotapes of therapy sessions c) one-on-one observation and feedback after each therapy session
Liu [24]	Targeted to staff to promote tailored early mobilisation in older hospitalised patients in medical wards. Intervention adapted to local context. Implementation in a 'real world' setting, reflecting constraints in resources, aligning with hospital initiatives, and facilitating sustainability. Barriers and facilitators mapped to behaviour change theory*. Underpinned by theoretical domains framework.	Medical patients aged > 65.	Canada In-patient medical units. 14 Academic hospitals in Ontario. Ward environment not described.	Multi-component, inter-professional early mobilisation initiative, tailored to local context, including local champions, online and/or in-person educational interventions for healthcare providers and patients, printed education materials, implementation coaching Patients assessed for mobilisation status within 24h of admission Mobilisation at least three times a day Mobility was progressive, scaled and tailored to the patient's abilities. The mobilisation messages targeting staff were multi-component and tailored to local context. All hospitals were required to provide inter-professional education and educational tools;

				additional strategies were selected based on appropriateness and context (e.g. reminders, local opinion leaders, patient/caregiver education materials). Hospitals were provided resources (e.g. education modules, checklists, mobility algorithms) to implement the intervention and invited to use or adapt these, or develop new materials. All hospitals received implementation coaching, had access to an online community of practice, and collaborated in monthly teleconferences. Coaches worked with each local implementation team to select intervention strategies mapped to identified barriers and facilitators, collected through focus groups with inter-professional care staff and using the theoretical domains framework * States that no new resources used.
Mundy [20]	Early mobilisation to shorten length of stay without adverse events.	Patients with community acquired pneumonia. Aged > 18 years.	Three sites: Urban hospital (1,287 beds). Community suburban hospital (473 beds). Community suburban hospital (494 beds). Ward environments not described.	Intervention delivered by nurses. Instead of prescribed bedrest, with physician permission nurses used the following script: 'Even though you have just been admitted with pneumonia, I would like to help you get of bed today. We think this may improve your recovery."
Timmer [21]	Multidisciplinary rehabilitation program to reduce the effects of the deconditioning that had occurred as a	Aged > 65 years admitted into sub-acute care for a reconditioning	Australia. Private rehabilitation hospital.	Occupational therapists (OTs). Individual or group, daily OT and twice daily physiotherapy five days a week.

	result of the older adult's admission to acute care. Activity Pacing (energy conservation, work simplification, and activity management) as an active self-management strategy to learn techniques such as self-monitoring, balancing rest and activity, prioritising and delegating activity, maintaining and increasing activity and to modify how and when activity is completed.	programme following an acute admission. Usual length of stay was 14 days. Patients were living independently prior to their acute admission.		An individual activity pacing education session (30 mins), participation in an activity pacing group (5 x 45 min sessions) and an individual activity pacing review session (30 mins). The individual sessions were conducted by the treating OT and the group sessions were conducted by an OT and an allied health assistant trained to provide the group intervention. Booklets and handouts were given to reinforce learning and as a future reference. Further details in the paper.

* Further information on the intervention available in the protocol paper. Liu et al (2013) Implementation Science https://link.springer.com/content/pdf/10.1186/1748-5908-8-76.pdf and mapping to Behaviour Change Theory Moore et al (20014) Implementation Science https://link.springer.com/content/pdf/10.1186/s13012-014-0160-6.pdf

** Details of the training, supervision, and treatment fidelity monitoring techniques are published https://www.ncbi.nlm.nih.gov/pubmed/22377824 Hildebrand et al. (2012) AmJ Phys Med Rehab