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#### SYSTEMATIC REVIEW

# Perioperative interventions to improve early mobilisation and physical function after hip fracture: a systematic review and meta-analysis

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#### **Abstract**

**Background:** Perioperative interventions could enhance early mobilisation and physical function after hip fracture surgery. **Objective:** Determine the effectiveness of perioperative interventions on early mobilisation and physical function after hip fracture.

**Methods:** Ovid MEDLINE, CINAHL, Embase, Scopus and Web of Science were searched from January 2000 to March 2022. English language experimental and quasi-experimental studies were included if patients were hospitalised for a fractured proximal femur with a mean age 65 years or older and reported measures of early mobilisation and physical function during the acute hospital admission. Data were pooled using a random effect meta-analysis.

**Results:** Twenty-eight studies were included from 1,327 citations. Studies were conducted in 26 countries on 8,192 participants with a mean age of 80 years. Pathways and models of care may provide a small increase in early mobilisation (standardised mean difference [SMD]: 0.20, 95% confidence interval [CI]: 0.01–0.39,  $I^2 = 73\%$ ) and physical function (SMD: 0.07, 95% CI 0.00 to 0.15,  $I^2 = 0\%$ ) and transcutaneous electrical nerve stimulation analgesia may provide a moderate improvement in function (SMD: 0.65, 95% CI: 0.24–1.05,  $I^2 = 96\%$ ). The benefit of pre-operative mobilisation, multidisciplinary rehabilitation, recumbent cycling and clinical supervision on mobilisation and function remains uncertain. Evidence of no effect on mobilisation or function was identified for pre-emptive analgesia, intraoperative periarticular injections, continuous postoperative epidural infusion analgesia, occupational therapy training or nutritional supplements.

**Conclusions:** Perioperative interventions may improve early mobilisation and physical function after hip fracture surgery. Future studies are needed to model the causal mechanisms of perioperative interventions on mobilisation and function after hip fracture.

**Keywords:** surgery, pre-operative, post-operative, model of care, analgesia, systematic review, older people

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#### **Key Points**

- The primary goal of hip fracture surgery is to optimise health-related quality of life by alleviating pain and restoring physical function.
- The effect of perioperative interventions on the ability to mobilise early postoperatively and restoration of physical function is relatively unknown.
- Pathways, models of care and analgesia interventions may improve early mobilisation and physical function.

#### Introduction

Hip fracture is a life changing injury for older people that is associated with considerable morbidity, mortality, loss of independence and reduced health-related quality of life (HRQoL) [1–3]. Approximately 25% of hip fracture patients die within 12 months of injury; [4] of those who survive, around 40–70% fail to regain their previous level of physical function and 10–20% require new residential aged care facility accommodation [5]. By 2050, hip fractures are expected to affect 4.5 million people per year, representing considerable personal, health and societal cost from hospitalisation, rehabilitation and long-term support [6, 7].

The primary goal of treatment is to optimise HRQoL by alleviating pain and restoring physical function. For most hip fracture patients, this is best achieved with surgery followed by early mobilisation and rehabilitation [8, 9]. Early mobilisation is recommended in clinical practice guidelines usually by day 1 postoperatively [10, 11]. However, despite best efforts, only 20–50% of patients achieve first day walking and less than half receive physiotherapy for greater than two hours in the first 7 days after surgery [11, 12]. Factors thought to contribute to delay in first day walking include postoperative delirium, haemodynamic instability, pain, restricted weight bearing instructions, post-operative anaemia and patient expectations, [13] all of which are potentially amenable to interventions in the perioperative care period.

Perioperative interventions, such as analgesia regimens, timing of surgery and type of anaesthesia are recommended in clinical practice guidelines to address barriers to early mobilisation and optimise physical function outcomes [14–16]. However, the delivery of these perioperative interventions varies substantially between hospital sites and their impact on the ability to mobilise early postoperatively and restoration of physical function is not yet well understood. The aim of this systematic review is to determine the effectiveness of perioperative interventions on achieving early mobilisation and improving physical function after hip fracture.

#### Methods

A systematic review was undertaken and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses statement (PRISMA) [17]. The

protocol was registered with Prospero (CRD42022313693) [18].

#### Search strategy and selection criteria

Five academic databases (Ovid MEDLINE, CINAHL, Embase, Scopus and Web of Science) were searched for peer-reviewed English language articles published between 1 January 2000 and 4 March 2022. Searches were supplemented by snowballing the reference lists of included articles, and relevant reviews and protocols identified, as well as forward citation tracking of articles citing those included in the review. The search strategy was created in collaboration with a medical librarian (Supplementary 1).

#### Study selection

Four reviewers (LT, SS, AC and NR) independently assessed the eligibility of title/abstract and full text articles for inclusion in pairs using Rayyan [19]. The inclusion criteria for the review are presented in Box 1. Any disagreements during screening were discussed and a third independent reviewer was consulted for the final decision where consensus could not be achieved (MS). Authors of studies where relevant data could not be obtained were contacted and excluded if no response was received.

### **Box 1.** Systematic review inclusion criteria

#### **Participants**

Mean age of 65 years and older and admitted to hospital with a fractured proximal femur.

#### Intervention

Perioperative interventions were defined as those delivered in preparation for surgery and during the operative period to recovery. This excluded the operation or procedure performed. Where one of the perioperative interventions also included early mobilisation, we considered the protocolised early mobilisation as the intervention, and whether it was achieved as the outcome.

#### Control

Any control conditions, including usual care or alternative interventions or exposures.

#### Outcome

Measures of both early mobilisation and physical function were included, considering the potential

relationship between perioperative interventions on the ability to mobilise early and then improve eventual physical function outcomes.

- Early mobilisation: Timing of commencement, proportion of patients mobilised early, or total amount of early postoperative mobilisation activity achieved postoperatively during the acute hospital admission.
- Physical function: Any measure of function collected postoperatively during the acute hospital admission, including functional outcome assessments, distance walked and achievement of functional tasks, and level of independence during ambulation.

#### Types of study

Experimental and quasi-experimental studies.

#### Date of publication

Published between 1 January 2000 and 4 March 2022.

#### Language

English.

#### **Data extraction**

Data relating to study characteristics, interventions and outcomes were independently extracted to a customised Excel spreadsheet by reviewers in pairs (LT, SS, AC and NR), which was piloted before use. Risk of bias was assessed using the JBI Checklist for Randomised controlled trials (RCTs) or Checklist for Quasi-Experimental Studies (Supplement 2) [20]. Disagreements were resolved by discussion and a third independent reviewer was consulted for the final decision where consensus was not achieved (MS). Authors were contacted to request additional data as needed.

#### **Data synthesis**

Random effect meta-analysis was conducted where data were available for the same intervention and outcomes in two or more studies. Standardised mean difference (SMD) effect size was used for measures of early mobilisation and physical function with different scales and was interpreted according to Cohen's d (0.2 = small, 0.5 = moderate and 0.8 = large) [21]. The mean and standard deviation were estimated for studies reporting medians and ranges, [22-26] using methods described by Wan et al. [27]. Dichotomous and continuous outcomes were combined using methods described by the Cochrane Handbook for Systematic Reviews of Interventions, which involved re-expressing odds ratios as SMDs [28]. Effect size directions were transformed to standardise positive effects as favouring the intervention and negative effects favouring the control. The I-squared statistic ( $I^2$ ) was used to represent heterogeneity in the study findings, with >50% considered substantial [29]. A leaveone-out sensitivity analysis was undertaken where overall heterogeneity levels were above 50% to further explore how each individual study affected the overall estimate of the rest of the studies. Analysis was performed using STATA Version 18 [30].

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Early mobilisation: In studies where multiple measures of mobilisation were evaluated, time to first mobilisation was prioritised for the mobilisation outcome meta-analysis. Where not reported, number of patients mobilised on the earliest reported postoperative day (e.g. day 1) was used. Where activity during admission was reported, the number of mobilisation events was used instead of time spent mobilising.

Physical function: For studies with multiple functional outcomes assessed, the cumulated ambulation score (CAS) was prioritised as the functional outcome assessment for the meta-analysis. Totals or averages of functional outcomes over multiple inpatient days were used where reported; otherwise, the latest follow-up period was used (e.g. day of discharge). Distance walked was selected over achievement of tasks (e.g. walking beyond bedside chair) and ability to walk independently was selected over ability to walk with assistance. Ambulation capability over multiple distance categories were pooled to greater than 10 metres. The functional independence measure (FIM) motor function score was used over the locomotion sub-score.

A formal meta-regression was not planned, as it was anticipated that a small number of the included studies could be included in meta-analyses. A narrative synthesis was used to describe the data for the remaining studies.

#### Results

#### Study flow and characteristics of included studies

Twenty-eight studies were included in the review, from 1,327 identified citations (Figure 1). Eighteen studies were RCTs, five were non-randomised trials and five were controlled before and after studies. Studies were conducted in Sweden (n = 4), USA (n = 2), Australia (n = 3), China (n = 2), Denmark (n = 2), Japan (n = 2), Norway (n = 2), UK (n = 2), Korea (n = 1), Israel (n = 1), Italy (n = 1), Russia (n = 1), Spain (n = 1), Taiwan (n = 1), Ukraine (n = 1) and multinational (n = 2). Studies were conducted at a single (n = 22) or multiple hospital sites (n = 6). There were 8,192 participants across the included studies (range 41-781) with a mean age of 80 years. Interventions were grouped into six categories: analgesia, pathways and models of care, rehabilitation delivery modes, surgical protocols, nutritional supplements and clinical supervision. Early mobilisation outcomes were collected between postoperative days 1 and 7 or upon discharge. Physical function outcomes were collected between days 1 and 14 or upon discharge. Risk of bias assessment is reported in Supplement 2. Characteristics of the included studies are presented in Supplement 3, and the outcomes of perioperative interventions on early mobilisation and physical function after hip fracture surgery are presented in Supplement 4.

#### **Analgesia**

Ten RCTs (n = 843) and one non-RCT (n = 103) reporting the effects of analgesia interventions in the perioperative period were identified. Six studies (n = 705) [22, 31–36]

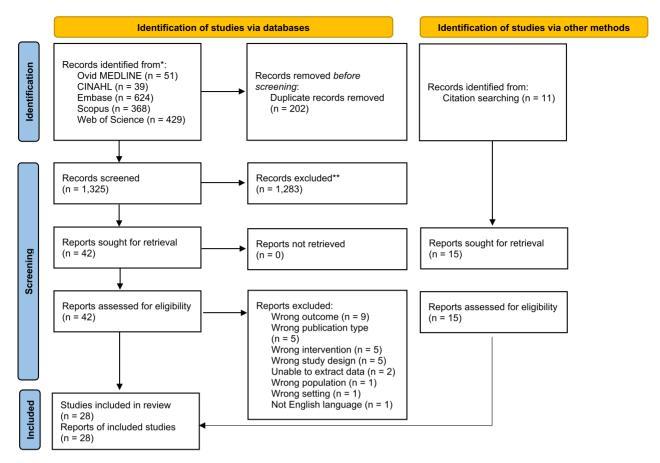


Figure 1. PRISMA flow diagram of studies in the review.

compared ultrasound guided peripheral nerve blocks to conventional pain management. Two studies (n = 104) [37, 38] compared active TENS to a sham device. One study (n = 82) [39] compared pre-emptive analysis medication and intraoperative periarticular injections to standard care and another study (n = 55, 40) compared continuous postoperative epidural infusion to a placebo. Analgesia interventions had no clear overall effect on early mobilisation (SMD: 0.39, 95% CI: -0.35 to 1.13,  $I^2 = 84\%$ ; Figure 2) or physical function (SMD: 0.64, 95% CI: -0.07 to 1.35,  $I^2 = 96\%$ ; Figure 3). Subgroup analysis showed that TENS provided a moderate improvement in physical function (SMD: 0.65, 95% CI: 0.24–1.05,  $I^2 = 96\%$ ; Figure 3). Leave-one-out sensitivity analysis suggested the absence of an effect persists irrespective of the omission of any one trial, with the exception of Foss et al. [40], where removed there was a large beneficial effect of analgesia interventions on physical function (Supplement 5-A and B).

#### Pathways and models of care

Six RCTs (n = 1,210) [23, 41–45], one non-RCT (n = 244) [46] and two controlled before and after studies (n = 1,262) [47, 48] reporting the effects of perioperative pathways and models of care were identified. Four studies (n = 840) [23, 41, 42, 46] compared orthogeriatric models of care to conventional care. Five studies (n = 881) [43–45, 47, 48]

compared Enhanced Recovery After Surgery (ERAS) care pathways to conventional postoperative care. Perioperative pathways and models of care produced a small positive effect on early mobilisation (SMD: 0.20, 95% CI: 0.01–0.39,  $I^2$  = 73%; Figure 4) and physical function (SMD: 0.07, 95% CI: 0.00–0.15,  $I^2$  = 0%; Figure 5). Leave-one-out sensitivity analysis suggested the small effect noted persisted following the removal of Gonzalez-Montalvo [46], Kang [43], Roberts [47] or Panella [45]. The effect did not persist following removal of remaining three studies (Supplement 5-C).

#### Rehabilitation delivery modes

One RCT (n = 100) [49] compared patients receiving occupational therapy training to those receiving conventional nursing care only, finding no significant difference in early mobilisation physical function. One RCT (n = 51) [24] compared recumbent cycling to usual care reporting similar between group function. One non-RCT (n = 150) [50] compared a preoperative mobilisation program with usual care finding significant improvements in physical function using the modified Barthel Index on admission day 3 and at discharge. One controlled before and after study (n = 155) [51] examined the effect of a multidisciplinary rehabilitation program compared to usual care, reporting significantly earlier ability to mobilise and less mobility decline (relative to pre-fracture mobility status).

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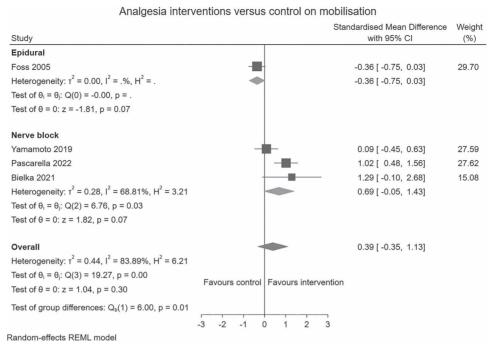


Figure 2. Forest plot of comparison: analgesia interventions versus control on mobilisation.

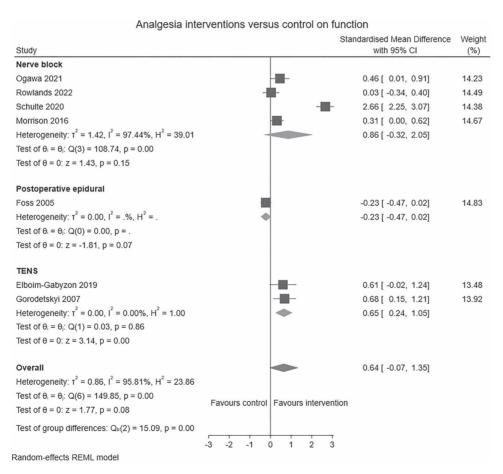


Figure 3. Forest plot of comparison: analgesia interventions versus control on function.

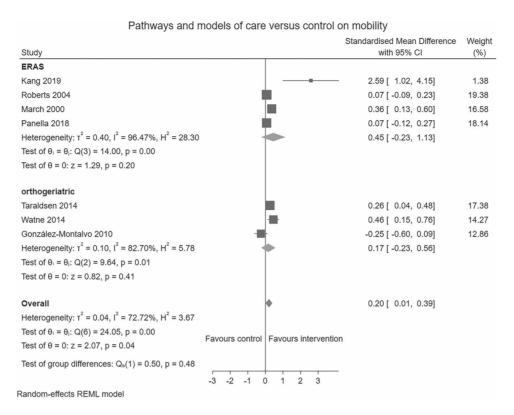


Figure 4. Forest plot of comparison: pathways and models of care versus control on mobilisation.

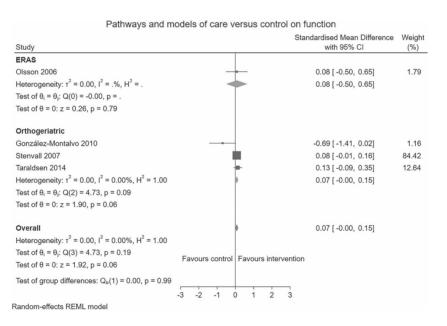


Figure 5. Forest plot of comparison: pathways and models of care versus control on function.

#### **Surgical protocols**

One RCT (n = 2,970) [26] compared accelerated surgery (goal of surgery within 6 hours of diagnosis) to standard care, reporting reduced time to first mobilisation following surgery and no difference in physical function, time to first standing and weight bearing. One RCT (n = 162) [25] compared liberal transfusion thresholds

to restrictive transfusion thresholds finding no significant difference in physical function on days 1–3.

#### **Nutritional supplements**

One controlled before and after study (n = 209) [52] compared nutritional supplements with usual care finding no

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significant improvement in walking assistance levels measured at day 5.

#### **Clinical supervision**

One controlled before and after study (n = 290) [53] compared the addition of direct face to face supervision of physiotherapists by an experienced orthopaedic physiotherapist external to the department to an existing reflective clinical supervision program. Patients receiving care from physiotherapists under the direct supervision program were more likely to mobilise day 1 and by day 2 postoperatively, and walked further day 5 with less assistance.

#### Discussion

This systematic review identified perioperative interventions that improved postoperative early mobilisation and physical function for hip fracture patients. TENS analgesia may provide a moderate improvement to physical function, and pathways and models of care may provide a small improvement in function, particularly orthogeriatric models. One study was identified supporting pre-operative mobilisation compared to bed rest for post-operative physical function when surgery was delayed beyond 48 hours. However, the average pre-operative waiting time in this study was greater than 6 days, limiting the generalisability to settings where operative waiting time is usually less than 48 hours. Other single studies supported improved early mobilisation for multidisciplinary rehabilitation delivery modes compared to usual care and direct clinical supervision of physiotherapists compared to usual reflective supervision. Multiple studies indicated less clear results for peripheral nerve blocks, and ERAS care pathways on early mobilisation and physical function, and orthogeriatric models and recumbent bike cycling on function. Single studies evaluating pre-emptive analgesia and intraoperative periarticular injections, continuous postoperative epidural infusion analgesia, indicated benefits for postoperative mobilisation and function. No improvement in physical function was identified from occupational therapy training rehabilitation delivery modes and nutritional supplements.

The proportion of patients achieving early mobilisation has been relatively resistant to improvement in the UK, Australia and New Zealand, despite increases in the proportion of hip fracture patients offered the opportunity to mobilise day 1 postoperatively [12, 54]. Several factors contribute to the inability to mobilise early, including the presence of delirium, low levels of pre-morbid mobility, older age, more days with a fever, urinary catheter or incontinence and non-use of anti-decubitus mattresses [13, 55]. Further barriers have been identified by treating physiotherapists, such as manual handling risks, patient declining rehabilitation, hypotension and pain [13]. Increasing opportunities for hip fracture patients to mobilise is important but other perioperative interventions are needed to overcome these barriers to improving physical function through early and ongoing rehabilitation in the acute phase postoperatively.

Peripheral nerve blocks and TENS analgesia interventions are thought to work by reducing reliance on opioids, which may avoid complications impacting the ability to mobilise including confusion, nausea, hemodynamic instability and chest infection [56, 57]. This mechanism is supported by Guay et al. who reported peripheral nerve blocks reduce pain, risk of acute confusion and probably reduce the risk of chest infection and time to first mobilisation [58]. There is a close bidirectional relationship between delirium and physical function [59], as immobility can be both a risk factor and a direct consequence of delirium [60–63]. Therefore, perioperative interventions that reduce the risk of delirium could also deliver dividends through earlier mobilisation and improved physical function.

Pathways and models of care may help to reduce variation by systematising the delivery of care [64]. Cooperation between orthopaedic surgeons, geriatricians and other multidisciplinary team members can lead to early identification of hip fracture patients for discharge planning and rehabilitation regimes [65]. Identifying and addressing comorbidities early is thought to optimise medical stability [66]; thereby reducing the risk of postoperative complications [67]. A study by Van Heghe et al. suggests that while there is evidence that orthogeriatric models of care reduce mortality and delirium and may reduce complications, the effect on functional outcome is inconsistent [68]. There is no ideal model identified to improve early postoperative mobilisation and physical function that is generalisable across different hospital sites with different contextual circumstances. The study by Snowdon et al. [53] evaluating clinical supervision of physiotherapists by an external senior orthopaedic physiotherapist could point to a potential mechanism for multidisciplinary team models improving mobility outcomes in an Australian context.

Mobilising hip fracture patients postoperatively can be resource intensive, often requiring two health professionals. Recumbent cycling offers an additional alternative mode to exercise that could be less resource intensive for therapists. However, the benefits on physical function were mixed, with the study authors suggesting benefits might not be expected to occur in the acute postoperative period and recommended a fully powered follow up trial [24]. Multidisciplinary rehabilitation programs were posited to offer more opportunities for early rehabilitation via nursing staff in addition to physiotherapists. Collaboration between members of the multidisciplinary team has been shown to result in fewer cases of death or loss of ability to live independently, although there is lower certainty of reductions in poorer functional outcomes at 12 months [69]. Pre-operative mobilisation targeted a different mechanism for improved post-operative early mobilisation, by preventing deconditioning and complications due to immobility while awaiting surgery. Immobilisation after fracture is a substantial contributor to poor prognosis and therefore efforts should be directed to improving time to surgery [70]. However, it is not uncommon for hip fracture patients to wait more than 48 hours for surgery [71]. Mobilisation during this pre-operative period could prevent functional deterioration, counter impaired ventilation and

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impaired cough reflex to reduce risk of pneumonia [72, 73], and prevent delirium and sleep disorders by helping to create a day and night routine [74].

Accelerated surgery reduces delirium, urinary tract infection and moderate to severe pain, which are closely related to early mobilisation [26]. However, the direction of this association between early mobilisation and these complications in the context of accelerated surgery is unclear. It is possible that early mobilisation itself reduces these complications rather than the absence of complications being a facilitator of early mobilisation. Foss et al. demonstrated that liberal transfusion thresholds did not affect physical function. Previous research has shown associations between postoperative anaemia and decreased mobilisation postoperatively [75–77]; however, correction via red blood cell transfusion has not previously been shown to improve rehabilitation outcomes [78].

#### Strengths and limitations

This review included only experimental and quasi-experimental study designs according to Cochrane Effective Practice and Organisation of Care study design criteria [79]. Most identified studies were RCTs, limiting the risk of confounding variables influencing the study findings. To ensure the capture of articles, forward and backward citation tracking snowballing of both included articles and other potentially relevant articles identified in the screening process was conducted. The included studies provided a relatively diverse sample (n = 8,192) from 26 countries and allowed comparisons across multiple studies evaluating similar perioperative interventions. However, the heterogeneity between methods, interventions and outcomes constrained our ability to examine pooled estimates across all included studies. Inclusive definitions of compared interventions and outcomes may have contributed to high levels of heterogeneity in our meta-analysis. Furthermore, some of the included studies did not restrict their inclusion criteria to older patient cohorts and reported on all patients over 18 years. These studies did not appear to have a younger average sample when compared to those with inclusion criteria selective of older age groups, but we were unable to examine the potential effect of age on the outcomes of interest. It is difficult to provided definitive recommendations for perioperative interventions with uncertain findings within and between studies, as well as those with only one study identified.

For analyses of analgesic approach, leave-one-out sensitivity analysis suggested the absence of an effect persists irrespective of the omission of any one trial. In contrast, the results of analyses of pathways and models of care varied with the omission of individual studies, but this did not appear to be related to underlying study quality.

#### **Conclusion**

The effect of several perioperative interventions on early mobilisation and physical function after hip fracture were

identified in this systematic review. TENS, and orthogeriatric models and ERAS care pathways may improve physical function after hip fracture surgery. The benefit of peripheral nerve blocks, pre-operative mobilisation, multidisciplinary rehabilitation, recumbent cycling and clinical supervision is less certain. No improvement was identified for pre-emptive analgesia and intraoperative periarticular injections, continuous postoperative epidural infusion analgesia, occupational therapy training and nutritional supplements. Many barriers to early mobilisation are potential amenable to perioperative interventions. Yet, despite the importance of achieving early mobilisation and restoring physical function after hip fracture surgery, relatively few studies were identified. There is a lack of standardisation in outcome measurement and reporting practices that limits the ability to synthesise findings across studies. Future aetiologic studies are required to understand and model the causal mechanisms by which early mobilisation and physical function after hip fracture can be improved by perioperative interventions.

**Supplementary Data:** Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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#### Declaration of Conflicts of Interest: None.

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**Data Availability Statement:** Data is available from the corresponding author upon reasonable request.

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