# Independent factors associated with long-term functional outcomes in patients with a proximal femoral fracture: A systematic review

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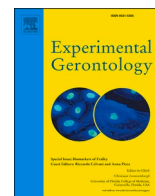
Review

# Independent factors associated with long-term functional outcomes in patients with a proximal femoral fracture: A systematic review

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A B S T R A C T

*Introduction:* The current understanding of prognostic factors of functional recovery after a proximal femoral fracture is limited, and enhancements could improve the prognostic accuracy and target subgroups for additional care strategies. This systematic review aims to identify all studied factors with an independent prognostic value for the long-term functional recovery of patients with a proximal femoral fracture.
*Materials and methods:* Observational studies with multivariate analyses on prognostic factors of long-term functional outcome after proximal femoral fractures were obtained through an electronic search performed on November 9, 2018.
*Results:* In the 31 included articles, thirteen prognostic factors were studied by at least two independent studies and an additional ten by only one study. Age, comorbidity, functionality and cognition were factors for which the majority of studies indicated a significant effect. The majority of studies which included sex as a factor found no significant effect. The level of evidence for the remaining factors was deemed too low to be conclusive on their relevance for long-term functional outcome.
*Conclusion:* The identified factors showed overlap with prognostic factors of short-term functional outcomes and mortality. The validity and applicability of prognostic models based on these factors may be of interest for future research.

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## 1. Introduction

Proximal femoral fractures in older patients are a major cause of impaired mobility, institutionalization and mortality (Vochteloo et al., 2013). Although the overall quality of emergency medicine, surgical procedures and post-acute care has improved in recent decades, the functional prognosis of this population is still poor (Ouellet and Cooney Jr., 2017). The high risk for adverse outcomes coincides with the high fracture risk associated with age: a combination of acute and chronic geriatric syndromes often referred to as frailty. Adverse functional outcomes are also associated with permanent institutionalization in a nursing home and consequently have a major socioeconomic impact.

Current prognostic models on the outcomes of patients with a low-energetic proximal femoral fracture show a limited accuracy, which in turn limits individualized decision-making for specific treatments and rehabilitation strategies. Insufficient prognostic accuracy and consequent reservations regarding the use of such models in clinical settings, can be attributed to the enormous heterogeneity in vitality of these patients.

Constructing an accurate predictive model requires the inclusion of all relevant factors, and demands a good understanding of the mutual relationships of these factors. A recent review by Sheehan et al. identified 25 prognostic factors (Sheehan et al., 2018). However, only one modifiable factor (anemia) and one immutable factor (cognition) were sufficiently substantiated by the available literature. The review included studies with short-term assessments of functional outcome (until the moment of acute care discharge) only, while functional recovery after a proximal femoral fracture is slow and may continue for up

to one year after surgery (Magaziner et al., 2000). Additional or different results may be expected when studying the long-term functional outcomes.

A meticulous summary of all available primary research on this topic will improve our understanding of the associations of patient characteristics and functional outcomes after a proximal femoral fracture. This systematic review aims to facilitate improvements of prognostic accuracy regarding the functional outcomes of individual patients upon admission. Better prognostic models may help to target specific patient subgroups for cost-effective additional care. This type of integrated care strategy has been shown to improve outcomes in older patients (Tarazona-Santabalbina et al., 2016). Furthermore, it may also uncover novel underlying mechanisms and mediators among previously studied factors, and thus facilitate the identification of poorly understood or poorly studied prognostic characteristics of interest for future studies.

To summarize, the goal of this systematic review is to identify factors with an independent prognostic value for the long-term functional recovery of patients with a proximal femoral fracture.

## 2. Materials and methods

The study protocol was registered in the international prospective register of systematic reviews (PROSPERO, registration number 132061, 12-04-2019). The review was performed according to the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) statement guidelines (Moher et al., 2009).

### 2.1. Search strategy and selection procedure

Online databases (PubMed, Embase, Web of Science, Cochrane Library, Emcare and Academic Search Premier) were searched for published studies that identified factors associated with functional recovery. Search terms were developed by a professional medical librarian (JWS) and adjusted for each database. The terms included MeSH terms and keywords for proximal femoral fractures, functional outcomes and multivariate analyses (Appendix A). The reference lists of the included articles were screened for any additional relevant articles missed by the electronic search.

All identified studies were screened by two independent reviewers (MPL, MVE) for eligibility based on the inclusion- and exclusion criteria. Any discrepancies in the article selection were resolved through discussion, when necessary, with a third reviewer (WA).

For methodological reasons, only studies on independent factors associated with long-term (6 months or longer) functional outcomes were included. The multivariate analyses had to be designed to find associations of demographics and assessments of any kind (registered during admission up to 1 week after surgery), with functional outcomes. Studies including any other factors (such as rehabilitation strategies or function later than one week after surgery) were excluded because these data are not available in the acute phase of fracture treatment and interfere with the predictive value of other variables.

As dependent variable, any assessment of functional outcome registered at or later than six months after surgery was applicable. To reduce inclusion bias, only inception cohort studies (meaning patient selection no later than the time of hospital admission for acute care) were included. Studies on absolute functional outcome were included, as well as studies on patient-specific recovery to their individual prefracture level of function.

The following exclusion criteria were applied in the study selection process:

- Studies including patients with non-traumatic and elective hip surgeries.
- Studies on specific subgroups: patients with specific comorbidities, a mean age <65 years or >90 or solely inclusion of specific fracture types or causes other than low-energy traumas.

- Studies without long-term functional outcomes.
- Studies without original data.
- Meeting abstracts, editorials, commentaries, case reports and case series.
- Studies only available in languages other than English.

When two or more eligible studies reported on the same dataset, both were included if they individually presented original outcomes. If not, the methodologically most applicable one was selected.

### 2.2. Data extraction

The study characteristics collected from the selected articles included the first author, year of publication, study period and country, sample size, sample size (and fraction) of patients included in the multivariate analysis, design, patient inclusion- and exclusion criteria, age and sex. The extracted outcome data included the functional outcome assessment(s), the outcome stratification method (if no continuous outcome was used) and percentage of patients classified as 'successfully recovered', the type of multivariate analysis used, all prognostic factors studied, and the effect estimates. If multiple multivariate analyses were performed in the same study using different outcome assessments, stratification methods or follow-up periods, each was individually included for this review. If multiple varieties of the same multivariate analysis were presented in an article, only the most appropriate version was selected.

### 2.3. Outcomes

When possible, corresponding factors from different studies were grouped into the following domains: demographic (including age, sex, living situation and ethnicity), function (including functionality, cognition and psychological), biological (including comorbidity, nutritional status and vitamin D status) and treatment-related factors (including fracture type, delayed surgery and complications). An independent association between the factor and the functional outcome with a 2-sided $p$-value $< 0.05$ was considered statistically significant (unless stated otherwise).

Factors included in the multivariate analysis, for which the effect was not reported (for example in stepwise regression analyses) were not assumed to have no significant effect, but were disregarded in our analyses. If a factor was studied in multiple multivariate analyses within the same study, but the effects were contradictory, the outcome was regarded as significant but mixed (and reported as such).

### 2.4. Quality assessment

The methodological quality of all included studies was independently assessed by two reviewers (MPL, WHT) using the Quality in Prognosis Studies (QUIPS) tool (Hayden et al., 2006, 2013). The QUIPS tool rates the risk of bias (ROB) in six domains as either high (+), moderate (+/−) or low (−). Studies were assigned an overall high ROB if one or more domains were considered high risk. Conflicts were resolved through discussion, if necessary, with a third reviewer (MVE).

## 3. Results

A total of 3008 references were identified. After removal of 1781 duplicates and 237 meeting abstracts, 990 records remained. A total of 911 articles were excluded based on title and abstract, and 48 articles after full-text assessment. Predominant reasons for exclusion were no applicable functional outcomes and the inclusion of non-acute factors in the multivariate analysis (such as the type of rehabilitation program or functional assessments more than one week after discharge). A total of 31 articles were eligible for inclusion. No additional articles were obtained from the reference lists of the selected articles (Fig. 1).
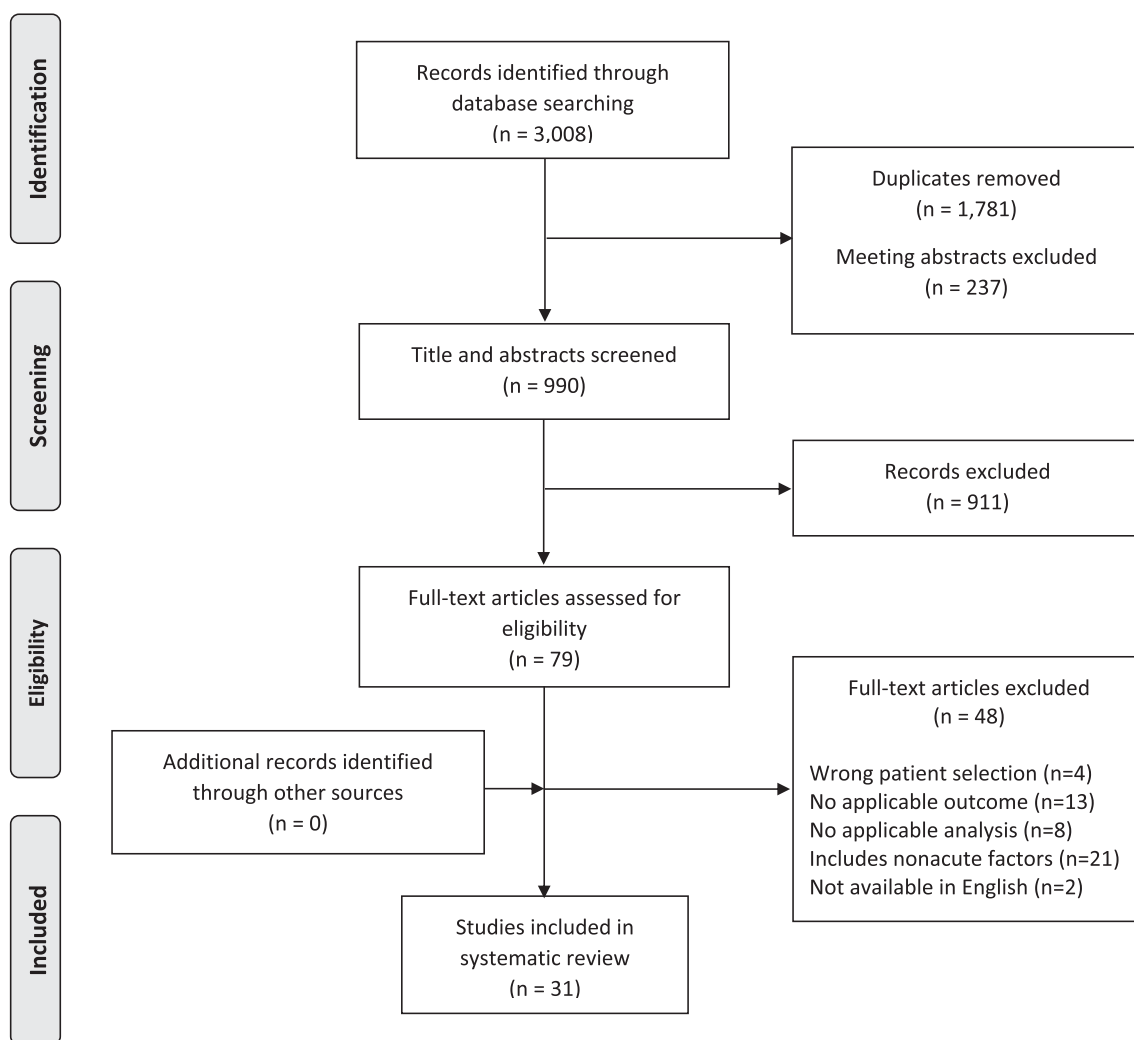
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┌─────────────────────────────────┐
│  Records identified through     │
│     database searching          │
│        (n = 3,008)              │
└─────────────────────────────────┘
```

**Identification**

```
┌─────────────────────────────────┐
│   Duplicates removed            │
│      (n = 1,781)                │
│                                 │
│  Meeting abstracts excluded     │
│       (n = 237)                 │
└─────────────────────────────────┘
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┌─────────────────────────────────┐
│  Title and abstracts screened   │
│         (n = 990)               │
└─────────────────────────────────┘
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**Screening**

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┌─────────────────────────────────┐
│    Records excluded             │
│       (n = 911)                 │
└─────────────────────────────────┘
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┌─────────────────────────────────┐
│  Full-text articles assessed for│
│         eligibility             │
│          (n = 79)               │
└─────────────────────────────────┘
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**Eligibility**

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┌─────────────────────────────────┐
│  Full-text articles excluded    │
│          (n = 48)               │
│                                 │
│  Wrong patient selection (n=4)  │
│  No applicable outcome (n=13)   │
│  No applicable analysis (n=8)   │
│  Includes nonacute factors (n=21)│
│  Not available in English (n=2) │
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┌─────────────────────────────────┐
│  Additional records identified  │
│   through other sources         │
│         (n = 0)                 │
└─────────────────────────────────┘
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**Included**

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┌─────────────────────────────────┐
│   Studies included in           │
│    systematic review            │
│         (n = 31)                │
└─────────────────────────────────┘
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**Fig. 1.** Flow diagram of the study selection process.

### 3.1. Study characteristics

The 31 selected studies included one cohort from a randomized controlled trial (RCT) (Givens et al., 2008) and 30 observational cohort studies, of which 26 were prospective (POC) and four retrospective (RCS) (Beloosesky et al., 2010; Gatot et al., 2016; Osnes et al., 2004; Tarazona-Santabalbina et al., 2015). The studies were performed between 1982 and 2018, in fourteen different countries, and included a total of 12,643 patients (range: 55 (Fortinsky et al., 2002) to 2692 (Penrod et al., 2008)). Some prevalent patient exclusion criteria were high-energy traumas (HET), pathological fractures, cognitive impairments (Beloosesky et al., 2010; Iaboni et al., 2017; Ingemarsson et al., 2003; Koval et al., 1998a,b), non-ambulatory status(Helminen et al., 2017; Iaboni et al., 2017; Koval et al., 1998a,b; Pajulammi et al., 2015; Savino et al., 2013), nursing home residence(Fortinsky et al., 2002; Kim et al., 2012; Koval et al., 1998a,b; Marottoli et al., 1994) or lost to follow-up (including mortality) (Corcoles-Jimenez et al., 2015; Hannan et al., 2001; Helminen et al., 2017; Ingemarsson et al., 2003; Koval et al., 1998b; Lin and Chang, 2004; Osnes et al., 2004; Pajulammi et al., 2015; Shyu et al., 2010; Tarazona-Santabalbina et al., 2015). Most studies included older patients only, but with different lower age limits. The mean age of the patients ranged from 75 (Kim et al., 2012) to 87 (Pareja et al., 2017), and 45% (Lin and Chang, 2004) to 91% (Pioli et al., 2016) were female. However, not all patients included and described in each study were also included in the multivariate analysis (range: 7.9%

(Hannan et al., 2001) to 100%). The follow-up period varied between 6 months and 2 years after admission or surgery (Table 1).

Variance among the included studies was observed in the type of analyses performed (linear, logistic, repeated measure and cox regression analyses) and methods used (unconditionally, forward and backward conditional) (Table 2).

Fourteen studies followed the recovery of patients to their individual level of prefracture function (Corcoles-Jimenez et al., 2015; Gatot et al., 2016; Givens et al., 2008; Helminen et al., 2017; Iaboni et al., 2017; Kim et al., 2012; Koval et al., 1998a,b; Moerman et al., 2018; Pajulammi et al., 2015; Pioli et al., 2016; Savino et al., 2013; Shyu et al., 2010; Vergara et al., 2014). The other studies investigated some absolute form of functional outcome, either by categorizing patients with a favorable or unfavorable outcome, or as a continuous outcome. There was considerable diversity regarding the assessment used to rate functional outcome. The most prevalent assessments used were the Functional Independence Measure (score, Barthel Index (BI) and walking ability, but with various modifications. Studies with a categorical outcome used a wide variety of definitions for 'successful' and/or 'unsuccessful' recovery. The percentage of patients classified as 'successfully recovered' based on the study's own criteria ranged from 16% (Ingemarsson et al., 2003) to 87% (Penrod et al., 2008). These data were deemed too heterogeneous to pool. Some ROB was present in most studies, but eighteen studies were assigned an overall low ROB (Appendix B). Major reasons for a high ROB rating were a disproportionate number of included

**Table 1**

Characteristics of the included studies.

| Author[†] | Publication year | Study period | Country[‡] | Sample size N (n;%) [§] | Design | In/exclusion criteria | Mean age (y) | Sex (%f) |
|---|---|---|---|---|---|---|---|---|
| Aigner (Aigner et al., 2017) | 2017 | 2009–2011 | DEU | 402 (312; 77.6) | POC | In: ≥60y. Ex: pathologic #, polytraumas, incomplete follow-up. | 81.0 (SD ± 8) | 72.9* |
| Beloosesky (Beloosesky et al., 2010) | 2010 | 2003–2004 | ISR | 93 (93; 100) | RCS | In: completed follow-up. Ex: terminal illness, polytraumas, demented patients. | 81.2 (SD ± 7.2) | 69.5 |
| Carpintero (Carpintero et al., 2006) | 2006 | 2002 | ESP | 109 (107; 98.2) | POC | In: >65y, osteoporotic fractures. Ex: HET, pathologic #, liver/kidney disease. | 81.4 (SD ± 7.2) | 79.8* |
| Corcoles (Corcoles-Jimenez et al., 2015) | 2015 | 2005–2006 | ESP | 205 (165; 80.5) | POC | In: >65y. EX: dependence for ADLs, cognitive impairment, mortality. | 25.4% 65–75, 48.3% 75–85, 19.5% 85–95, 6.8% > 95 | 74.1 |
| Cornwall (Cornwall et al., 2004) | 2004 | 1997–1998 | USA | 537 (na) | POC | In: >50y, acute fractures. Ex: bilateral #, pathologic #, concomitant injuries, previous ipsilateral #/surgery, pelvis/subtrochanteric #, operation contraindicated. | 81.9 (SD ± 8.9*) | 81.7* |
| Fortinsky (Fortinsky et al., 2002) | 2002 | 1999–2000 | USA | 55 (24; 43.6) | POC | In: community dwelling, ambulatory, English-speaking. Ex: polytrauma, pathologic #. | 82 (SD ± 6), 79[c] (SD ± 6*) | 82 |
| Gatot (Gatot et al., 2016) | 2016 | 2011–2013 | SGP | 153 (na) | RCS | In: complete 1y follow-up, surgical treatment. | 77.0 (SD ± 7.4) | 67.3 |
| Givens (Givens et al., 2008) | 2008 | <1997* | USA | 126 (na) | RCT | In: ≥65y, surgical treatment. Ex: pathologic #, life expectancy <6 m. | 79 (SD ± 8) | 78.6 |
| Gumieiro (1) (Gumieiro et al., 2013b) | 2013 | 2010 | BRA | 86 (na) | POC | In: >65y. Ex: pathologic #. | 80.2 (SD ± 7.3) | 76.7 |
| Gumieiro (2) (Gumieiro et al., 2013a) | 2013 | 2010 | BRA | 82 (82; 100) | POC | In: >65y. Ex: pathologic #, pressure ulcers before admission. | 80.4 (SD ± 7.3) | 75.6 |
| Gumieiro (Gumieiro et al., 2015) | 2015 | 2011 | BRA | 86 (na) | POC | In: ≥65y, EX: pathologic #, conservative treatment. | 80.2 (SD ± 7.3) | 76.7* |
| Hannan (Hannan et al., 2001) | 2001 | 1997–1998 | USA | 571 (45; 7.9) | POC | Ex: <50y, inpatient #, transferred patients, concurrent #/injury, pathologic #, subtrochanteric #, bilateral #, prior ipsilateral #/surgery, mortality. | 18.6% < 75, 38.2% 75–84, 43.3% ≥ 85 | 81.4 |
| Helminen (Helminen et al., 2017) | 2017 | 2011–2014 | FIN | 594 (154; 25.9) | POC | Ex: pathologic #, periprosthetic #, prefracture inability to walk, mortality. | 85 (range 65–100)* | 71.5* |
| Iaboni (Iaboni et al., 2017) | 2017 | 2008–2012 | CAN | 477 (na) | POC | In: ≥60y, surgical treatment. Ex: non-ambulatory, cognitive impaired, pathologic #, interferon treatment, sensory impairment, non-English. | 78.4 (SD ± 8.8*) | 75.5* |
| Ingemarsson (Ingemarsson et al., 2003) | 2003 | – | SWE | 157 (57; 36.3) | POC | Ex: severe illness, severe dementia, mortality. | 80.9 (SD ± 9.5) | 70.7 |
| Kim (Kim et al., 2012) | 2012 | 2005–2009 | KOR | 415 (415; 100) | POC | In: >60y, noninstitutionalized, LET, surgically treated, no previous #. Ex: pathologic # | 75.13 (SD ± 9.32) | 68.2 |
| Koval (1) (Koval et al., 1998a) | 1998 | 1987–1995 | USA | 631 (531; 84.2) | POC | In: ≥65y, ambulatory and home dwelling, nonpathological #. Ex: moderate/severe dementia, medically predetermined anesthetic technique. | 79.6 (SD na) | 80.0 |
| Koval (2) (Koval et al., 1998b) | 1998 | 1988–1990 | USA | 398 (310*; 77.9) | POC | In: ≥65y, acute fracture, nonpathological, no severe dementia, ambulatory and home dwelling. Ex: mortality/loss to follow-up | 27% ≥ 85 | 79 |
| Lin (Lin and Chang, 2004) | 2004 | 2000–2001 | TWN | 103 (61; 59.2) | POC | In: >65y. Ex: pathologic #, mortality/loss to follow-up. | 78.3 (SD ± 5.8) | 45.6 |
| Marottoli (Marottoli et al., 1992) | 1992 | 1982–1988 | USA | 62 (45–83) | POC | In: ≥65y, non-institutionalized. Ex: Insufficient data | 78.2* (SD na) | 72.0* |
| Moerman (Moerman et al., 2018) | 2018 | 2008–2009 | NLD | 480 (364; 75.8) | POC | In: >50y. Ex: HET, pathologic #, conservative treatment. | 82.6 (range 50–101) | 71 |
| Osnes (Osnes et al., 2004) | 2004 | 1996–1997 | NOR | 593 (420; 70.8) | RCS | In: ≥50y. Ex: pathologic #, mortality. | 79.8 (range 50.2–101.4) | 79.3 |
| Pajulammi (Pajulammi et al., 2015) | 2015 | 2007–2012 | FIN | 611 (611; 100) | POC | In: ≥65y, first #. Ex: pathologic #, periprosthetic #, prefracture inability to walk, mortality. | 83* | 78.4* |
| Pareja (Pareja et al., 2017) | 2017 | 2014–2015 | ESP | 130 (na) | POC | In: >75y, osteoporotic #. Ex: pathologic #, HET, iron deposit disorders, intolerant to ferro therapy. | 87 (IIC 83–91) | 81 |
| Penrod (Penrod et al., 2008) | 2008 | 1987–2001 | USA | 2692 (2012–2041) | POC | In: ≥50y. | 20.0% < 75; 43.0% 75–84; 37.0% ≥ 85 | 78.9 |

**Table 1** (*continued*)

| Author† | Publication year | Study period | Country‡ | Sample size N (n;%) § | Design | In/exclusion criteria | Mean age (y) | Sex (%f) |
|---------|-----------------|--------------|----------|----------------------|--------|----------------------|-------------|----------|
| Pioli (Pioli et al., 2016) | 2016 | 2008–2009 | ITA | 774 (604; 78.0) | POC | In: ≥75y, fragility #, mobile outdoors/indoors/ with help. Ex: pathologic #, major trauma. | 85.8 (SD ± 5.5*) | 90.8* |
| Savino (Savino et al., 2013) | 2013 | 2008–2009 | ITA | 504 (437; 86.7) | POC | In: ≥70y, fragility #, walk independently, surgically treated. Ex: pathologic #, major trauma, previous ipsilateral #. | 85.3 (SD ± 5.5) | 76.1 |
| Tarazona (Tarazona-Santabalbina et al., 2015) | 2015 | 2004–2008 | ESP | 1258 (na) | RCS | In: >69y. Ex: pathologic #, life expectancy <6 m, mortality. | 83.8 (SD ± 6.0) | 76.2 |
| Vergara (Vergara et al., 2014) | 2014 | – | ESP | 557 (557; 100) | POC | In: ≥65y. Ex: severe impairments, syncope, pathologic #, loss to follow-up. | 83.2 (SD ± 7.2) | 84.4* |
| Jones (Jones et al., 2017) | 2017 | – | CAN | 383 (na) | POC | In: ≥65y. Ex: pathologic #, refractures within 5y, HET, non-English, conservative treatment. | 81.3 (SD ± 7.3*) | 70.0* |
| Shyu (Shyu et al., 2010) | 2010 | 2002–2005 | TWN | 155 (119; 76.7) | POC | In: ≥60y, surgical treatment, no cognitive impairment. Ex: mortality/loss to follow-up. | 77.9 (SD ± 7.78) | 68.4 |

* Calculated or derived from article data. † multiple articles with the same first author and published in the same year are distinguished with a number between brackets. ‡ ISO 3166-1 alpha-3 country codes, § number of patients described (number of patients included for the analysis; percentage of patients included in the analysis), y years of age, f female, POC prospective observational cohort study, RCS retrospective cohort study, RCT randomized controlled trial, In inclusion criteria, Ex exclusion criteria, # fractures, HET high energy trauma, ᶜ Patients included in the multivariate analysis only.

patients analyzed in the multivariate analysis (study attrition bias), and unknown covariates included in the multivariate analysis (study confounding bias and statistical analysis and reporting bias). The prognostic factors identified from all studies were pooled into thirteen different domains (Table 3).

### 3.2. Demographic

Age was analyzed in nineteen studies (Beloosesky et al., 2010; Corcoles-Jimenez et al., 2015; Cornwall et al., 2004; Gatot et al., 2016; Hannan et al., 2001; Iaboni et al., 2017; Ingemarsson et al., 2003; Jones et al., 2017; Kim et al., 2012; Koval et al., 1998b; Marottoli et al., 1992; Moerman et al., 2018; Osnes et al., 2004; Pajulammi et al., 2015; Penrod et al., 2008; Pioli et al., 2016; Savino et al., 2013; Tarazona-Santabalbina, 2015; Vergara et al., 2014) and was included as either a continuous or categorical factor, with large heterogeneity in the categorical cut-off values for the age groups (Appendix Table D.1). Ten of the twelve studies with a low ROB found a statistically significant negative association between a favorable functional outcome and higher age (Appendix Fig. C.1) (Beloosesky et al., 2010; Corcoles-Jimenez et al., 2015; Cornwall et al., 2004; Hannan et al., 2001; Iaboni et al., 2017; Kim et al., 2012; Moerman et al., 2018; Osnes et al., 2004; Pajulammi et al., 2015; Vergara et al., 2014). Two of these had mixed results (Penrod et al., 2008; Pioli et al., 2016). Some studies with categorized age-groups found age to be a significant factor only when patient groups with wide age differences were compared (Gatot et al., 2016; Jones et al., 2017; Penrod et al., 2008; Pioli et al., 2016).

Sex was included by eight studies with a low ROB (Jones et al., 2017; Osnes et al., 2004; Pajulammi et al., 2015; Penrod et al., 2008; Pioli et al., 2016; Savino et al., 2013; Tarazona-Santabalbina et al., 2015; Vergara et al., 2014). Two found significant associations, although one was mixed (Appendix Fig. C.2) (Pioli et al., 2016; Savino et al., 2013). Whereas Savino et al. found male sex to be associated with a worse functional outcome (OR 0.50, 95% CI 0.27–0.92; p = s), the opposite was reported by Pioli et al. (for patients with a prefracture outdoor mobility only, HR 2.59, 95% CI 1.18–5.65; $p = 0.017$) (Appendix Table D.2).

Seven low ROB studies included premorbid residence (Jones et al., 2017; Moerman et al., 2018; Osnes et al., 2004; Pajulammi et al., 2015), caregiver support (Savino et al., 2013; Vergara et al., 2014), or discharge location (Pareja et al., 2017) (Appendix Table D.3). One study found no significant associations (Moerman et al., 2018), and one found positive associations (with social support and living with relatives in some of the analyses) (Vergara et al., 2014). The other five studies reported an association between a more dependent form of living and worse functional outcomes (Appendix Fig. C.3).

Ethnicity was included by two low ROB studies (Appendix Table D.4) (Iaboni et al., 2017; Penrod et al., 2008). Only one indicated a significant association between non-Caucasian ethnicity and a worse functional outcome (Appendix Fig. C.4) (Iaboni et al., 2017).

### 3.3. Function

Seventeen studies included prefracture function (Beloosesky et al., 2010; Cornwall et al., 2004; Fortinsky et al., 2002; Hannan et al., 2001; Iaboni et al., 2017; Ingemarsson et al., 2003; Jones et al., 2017; Koval et al., 1998b; Lin and Chang, 2004; Marottoli et al., 1992; Moerman et al., 2018; Pajulammi et al., 2015; Pareja et al., 2017; Pioli et al., 2016; Savino et al., 2013; Tarazona-Santabalbina et al., 2015; Vergara et al., 2014). Many different assessments and variations thereof were used to assess prefracture functionality. These included the Katz ADL (Pioli et al., 2016), BI (Lin and Chang, 2004; Pareja et al., 2017; Savino et al., 2013), IADL (Lin and Chang, 2004; Moerman et al., 2018; Pioli et al., 2016), FIM scores (Cornwall et al., 2004; Fortinsky et al., 2002; Jones et al., 2017), the Disabilities of the Arm, Shoulder and Hand (DASH) (Beloosesky et al., 2010), the Physical component score of the 12-Item Short Form Survey (PCS SF-12) (Vergara et al., 2014), Western Ontario and McMaster Universities Arthritis Index (WOMAC) (Vergara et al., 2014) and various assessments of mobility (Appendix Table D.5) (Ingemarsson et al., 2003; Lin and Chang, 2004; Moerman et al., 2018; Pajulammi et al., 2015). Of the ten low ROB studies, those by Pioli et al. (which grouped patients according to their prefracture mobility before the analyses) and Vegara et al. had mixed outcomes (Pioli et al., 2016; Vergara et al., 2014). Eight other studies found significant positive associations between favorable prefracture functionality and favorable functional outcomes (Appendix Fig. C.5a).

Two studies included an assessment of functionality registered after surgery, at the moment of hospital discharge (Beloosesky et al., 2010; Ingemarsson et al., 2003). Only one had a low ROB and found a significant (positive) association with better postoperative FIM scores and Handgrip Strength (HGS) (Appendix Fig. C.5b) (Beloosesky et al., 2010).

Psychological status, rating depressive symptoms, was included in three studies with a low ROB (Appendix Table D.6) (Givens et al., 2008; Savino et al., 2013; Vergara et al., 2014). Only one study found a significant association, with worse functional outcome (Appendix Fig. C.6) (Vergara et al., 2014). A similar effect was observed by Givens et al., albeit borderline significant, which may have been due to an underpowered analysis.

**Table 2**

Functional outcome assessments, analyses and prognostic factors of the included studies.

| Article author and year[a] | Functional assessment | Outcome stratification | Successful recovery (%) | Follow-up (mo) | Statistical analysis | Factors[b] |
|---|---|---|---|---|---|---|
| **Functional recovery** | | | | | | |
| Corcoles 2015 | BI | Regain of prefracture BI score | 48 | 12 | MLoR (stepwise) | Age, residence, no complications during admission, (unknown) |
| Gatot 2016 | Montebello Rehabilitation Factor Score | RFG ≥ 0.5 | NA | 12 | MLoR | Age-group, arthritis, hypercholesterolemia |
| Givens 2008 (1.1) | Katz ADL | ≤1 point decline | 47 | 6 (or last FU) | MLoR | Depressive symptoms/cognitive impairment/delirium/ cognitive and mood disorders combined; (age, sex, ethnicity, intervention status, number of comorbidities) |
| Givens 2008 (1.2) | Ambulatory status | Regained ability to walk 15 ft | 28 | | | |
| Helminen 2017 (1.1) | Mobility | Unchanged vs impaired | 80 | 12 | MLoR | MNA-SF; (age, sex, ASA, # type) |
| Helminen 2017 (1.2) | | | | | | MNA-LF; (age, sex, ASA, # type) |
| Helminen 2017 (1.3) | | | | | | Albumin; (age, sex, ASA, # type) |
| Iaboni 2017 | FRS | Recovery to ≥95% of prefracture score | 49 | 12 | CPH | Use of PIM/age/ethnicity/CIRS-G score/pain/FRS; (sex, marital status, ethnicity, education, MADRS, SBT score, smoking status, drinking status, social support, number of medications) |
| Kim 2012 | Kitamura's classification (modified) | Recovered to prefracture ability | 39 | 24 | CPH (stepwise) | Age, delay in surgery, cancer, operation type, previous #, # type |
| Koval 1998 (1.11) | Ambulatory status | Recovered to prefracture ability | 38 | 6 | MLoR (stepwise) | Anesthesia type, (unknown) |
| Koval 1998 (1.12) | | | 47 | 12 | | Anesthesia type, (unknown) |
| Koval 1998 (1.21) | FRS | | 86 | 6 | | Anesthesia type, (unknown) |
| Koval 1998 (1.22) | | | 86 | 12 | | Anesthesia type, (unknown) |
| Koval 1998 (2.11) | Katz ADL subscale | Recovered to prefracture score | 71 | 6 | MLoR (stepwise) | Age, ASA, no comorbidities, # type, dependence in less than one IADL, dependent in no basic ADL, lived with spouse, no previous hip # |
| Koval 1998 (2.12) | | | 73 | 12 | | Age, independent living, ASA, (unknown) |
| Koval 1998 (2.21) | Adapted IADL | | 42 | 6 | | Instrumental activities of daily living, ASA, (unknown) |
| Koval 1998 (2.22) | | | 48 | 12 | | Age, instrumental activities of daily living independence, (unknown) |
| Moerman 2018 | Groningen Activity Restriction Scale | Recovered IADL (GARS) | 29 | 12 | MLoR | Age, ASA, living situation, walking aids, anesthesia type, length of hospital stay, complications, prefracture IADL |
| Pajulammi 2015 | Mobility | Same/improved mobility vs decreased | 62 | 12 | MLoR | Age, sex, BMI, ASA, memory disorder, mobility level, living arrangement, # type, time to surgery, catheter removed |
| Pioli 2016 (1.1) | Walking recovery | Recovered outdoor walking ability | 44 | 6 | MLoR | Age, sex, cognitive impairment, CCI, APS, ADL, IADL, Walking device, albumin at admission, delirium, surgery <48 h |
| Pioli 2016 (1.2) | | | 47 | | | |
| Pioli 2016 (1.3) | | | 67 | | | |
| Savino 2013 | Persistent walking | Recovered walking independently | NA | 12 | MLoR | Age/sex/HGS/cognitive impairment/depressive symptoms/ BADL/caregiver assistance/CCI/vitamin D/time to surgery/ early rehabilitation; (age, sex, medical center, pre- admission BADL, cognitive decline, and depressive symptoms, CCI, caregiver assistance, time before surgery, type of surgery, early rehabilitation, vitamin D) |
| Vergara 2014 (1.1) | BI | ≥90 points and no decrease >10% | 29 | 6 | MLoR | Age, sex, cerebrovascular disease, SF-12 PCS, SF-12 MCS, LCF of womac, living status |
| Vergara 2014 (1.2) | IADL | ≥5 and no pre-post Δ-score of ≥2 points. | 25 | | | Age, sex, SF-12 MCS, LCF of womac, living status |
| Vergara 2014 (1.3) | BI and IADL combined | | NA | | | Age, sex, SF-12 MCS, LCF of womac, living status |
| Shyu 2010 (1.1) | BI subscale | Recovered to prefracture score | 73 | 6 | GEE | Follow-up medical services/caregiving related healthcare information/social services/support group; (postdischarge period, self-care ability, length of hospital stay, concomitant diseases) |
| Shyu 2010 (1.2) | IADL | Recovered to prefracture score | 29 | | | |
| Shyu 2010 (1.3) | BI | Recovered to prefracture score | 50 | | | |
| **Functional outcome (absolute)** | | | | | | |
| Aigner 2017 (1.11) | BI | Continuous | – | 6 | MLiR | Hospitalization within 3 m before #; (age, Sex, ASA) |

*(continued on next page)*

**Table 2** (*continued*)

| Article author and year[a] | Functional assessment | Outcome stratification | Successful recovery (%) | Follow-up (mo) | Statistical analysis | Factors[b] |
|---|---|---|---|---|---|---|
| Aigner 2017 (1.12) | | | | 12 | | |
| Aigner 2017 (1.21) | TT | Continuous | – | 6 | | |
| Aigner 2017 (1.22) | | | | 12 | | |
| Beloosesky 2010 | FIM self-care and motor subscale | Continuous | – | 6 | MLiR (stepwise) | Sex, age, cognitive state, DASH, FIM, HGS |
| Carpintero 2006 | Functional level categories | Able to walk vs unable to walk | 17 | 12 | MLoR | 1,25-dihydroxycholecalciferol, 25-hydroxycholecalciferol; (unknown) |
| Cornwall 2004 (1.1) | FIM score | Continuous | – | 6 | MLiR | Age, # type, preinjury FIM; (unknown) |
| Cornwall 2004 (1.2) | FIM locomotion subscale | | | | | Age, preinjury FIM, preinjury locomotion FIM, # type; (unknown) |
| Cornwall 2004 (1.3) | FIM transfer subscale | | | | | Age, preinjury FIM, # type; (unknown) |
| Cornwall 2004 (1.4) | FIM self-care subscale | | | | | Age, preinjury FIM, # type; (unknown) |
| Fortinsky 2002 | FIM lower body subscale | Recovered to prefracture scores | 33 | 6 | MLoR | Rehabilitation therapy self-efficacy, prefracture locomotion, depressive symptoms |
| Gumieiro 2013 (1.1) | Gait status | Ambulators vs non-ambulators | 70 | 6 (or last FU) | MLoR | NRS 2002; (age, sex, time to surgery, CRP) |
| Gumieiro 2013 (1.2) | | | | | | ASA; (age, sex, time to surgery, CRP) |
| Gumieiro 2013 (1.3) | | | | | | MNA; (age, sex, time to surgery, CRP) |
| Gumieiro 2013 (2.1) | Gait status | Ambulators vs non-ambulators | 70 | 6 (or last FU) | MLoR | 225 kDa homodimer pro-MMP 9; (age, sex, length of hospital stay, CRP) |
| Gumieiro 2013 (2.2) | | | | | | 130 kDa pro-MMP 9 + NGAL; (age, sex, length of hospital stay, CRP) |
| Gumieiro 2013 (2.3) | | | | | | 92 kDa pro-MMP 9; (age, sex, length of hospital stay, CRP) |
| Gumieiro 2013 (2.4) | | | | | | 72 kDa pro-MMP 2; (age, sex, length of hospital stay, CRP) |
| Hannan 2001 | FIM locomotion subscale | Continuous | – | 6 | MLiR | Age, sex, nursing home residence, paid homecare, modified RAND, modified APACHE, dementia, prefracture locomotion |
| Ingemarsson 2003 (1.11) | Walking ability | Good vs moderate/poor | 16 | 12 | MLoR (stepwise) | Prefracture outdoor walking, balance TUG; (age, prefracture independent walking, prefracture walking aids indoors, prefracture walking aids outdoors, bed to chair, walking 10 m independence, walking 10 m self-selected speed, standing balance, HGS, peak expiratory flow, motivation) |
| Ingemarsson 2003 (1.12) | | Good vs moderate/poor | 31 | | | |
| Ingemarsson 2003 (1.21) | Activity level | High vs moderate/low | 17 | | | Balance TUG; (age, prefracture outdoor walking, prefracture independent walking, prefracture walking aids indoors, prefracture walking aids outdoors, bed to chair, walking 10 m independence, walking 10 m, standing balance, grip strength, peak expiratory flow, BMD grams, BMD t-score, motivation) |
| Ingemarsson 2003 (1.22) | | High vs moderate/low | 29 | | | |
| Jones 2017 | FIM score | Continuous | – | 6 | LMM | Age, sex, residence, cognition, # type, chronic conditions, proxy respondent, baseline FIM |
| Lin 2004 (1.1) | BI | Continuous | – | 12 | MLiR (stepwise) | Ability to walk outdoors; (age, marital status, sex, residence, ADL, IADL, physiological function, eyesight, hearing ability, walking status, use of walking aid, history of falling down, disease and medication history) |
| Lin 2004 (1.2) | IADL | Continuous | – | | | Ability to do housework, marriage, use of walking aid; (age, sex, residence, ADL, IADL, physiological function, eyesight, hearing ability, walking status, history of falling down, disease and medication history) |
| Marottoli 1992 | Physical function score | Continuous | – | 6 | MLiR | Age, baseline physical function, SPMSQ, Emotional support, CES-D |
| Osnes 2004 (1.1) | Ability to perform ADL | No walking aid vs walking aid or not walking | 56 | 12 (mean, range 184–548) | MLoR | Residence/health status/site of accident/HET/previous/later #; age, sex |
| Osnes 2004 (1.2) | | Walking independently vs not independently | na | | | Age, sex |
| Osnes 2004 (1.3) | | Walking outdoors vs not outdoors independently | na | | | Age, sex |
| Pareja 2017 | BI | Continuous | – | 6 | MLiR (stepwise) | BI, cognitive impairment, supplements on discharge, social status on discharge |

**Table 2** (*continued*)

| Article author and year[a] | Functional assessment | Outcome stratification | Successful recovery (%) | Follow-up (mo) | Statistical analysis | Factors[b] |
|---|---|---|---|---|---|---|
| Penrod 2008 (1.11) | Mobility | Independent/ dependent (vs unable) | 66 | 6 | MLoR | Age/sex/ethnicity/dementia/hypertension/arrythmia/ diabetes/cancer/COPD/heart failure/angina pectoris/ myocardial ischemia/stroke/Parkinson; (# type, independent walking, ADL limitations, cohort, admission year) |
| Penrod 2008 (1.12) | | Independent (vs dependent/unable) | 31 | | | |
| Penrod 2008 (1.21) | Katz ADL subscale | Independent in ≥1 criterium vs 0 | 87 | | | |
| Penrod 2008 (1.22) | | Independent in ≥3 criteria vs ≤2 | 63 | | | |
| Tarazona 2015 | Walking ability | Walk 5 m | 56 | 6 | MLoR | Age, sex, BI, CCI, delirium, dementia |

mo months, MLiR multiple linear regression, MLoR multiple logistic regression, GEE generalized estimating equation, CPH Cox proportional hazard, LMM linear mixed model, na not available, FU follow-up moment.

[a] Multiple applicable multivariate analyses performed in one study are described separately and distinguished with a decimal number.

[b] The effects of each factor can be found in Appendix D. Factors included in the model, but with no reported effect, are placed between brackets. If a series of factors was only adjusted for a fixed set of other factors, they are separated by a forward slash (/), and separated from the fixed set of other factors by a semicolon (;).

Cognition was rated using a wide array of assessments. Both continuous and categorical scores were used for different diagnostic tools, including the Mini–Mental State Examination test (MMSE) (Givens et al., 2008; Jones et al., 2017), Short Portable Mental Status Questionnaire (SPMSQ) (Marottoli et al., 1992; Pioli et al., 2016; Savino et al., 2013), Blessed Dementia Rating Scale (BDRS) (Givens et al., 2008), Global Deterioration Scale (GDS) (Pareja et al., 2017; Tarazona-Santabalbina et al., 2015) and previously diagnosed disorders (dementia (Hannan et al., 2001; Penrod et al., 2008) and memory disorders (Pajulammi et al., 2015)) (Appendix Table D.7). Of the eight studies with a low ROB (Givens et al., 2008; Jones et al., 2017; Pajulammi et al., 2015; Pareja et al., 2017; Penrod et al., 2008; Pioli et al., 2016; Savino et al., 2013; Tarazona-Santabalbina et al., 2015), six found significant negative associations of cognition with functional outcomes, of which one had mixed outcomes (Pioli et al., 2016) and two studies showed no significant associations (Givens et al., 2008; Savino et al., 2013) (Appendix Fig. C.7).

### 3.4. Biological

Eleven studies included an assessment of general health or a comorbidity score, and an additional six studies included semi-specific comorbidities only. Validated tools or variants thereof included the Acute Physiology, Age, Chronic Health Evaluation score (APACHE) (Hannan et al., 2001; Pioli et al., 2016), American Society of Anesthesiologists (ASA) Classification (Aigner et al., 2017; Gumieiro et al., 2013b; Koval et al., 1998b), Cumulative Illness Rating Scale – Geriatric (CIRS-G) (Iaboni et al., 2017), (modified) RAND score (Hannan et al., 2001) and Charlson Comorbidity Index (CCI) (Pioli et al., 2016; Savino et al., 2013; Tarazona-Santabalbina et al., 2015). Some studies used less conventional methods (Jones et al., 2017; Koval et al., 1998b; Osnes et al., 2004) or specific comorbidities only (Gatot et al., 2016; Penrod et al., 2008; Vergara et al., 2014) (Appendix Table D.8). Six low ROB studies that included general health or comorbidity assessments showed a significant association (Aigner et al., 2017; Iaboni et al., 2017; Jones et al., 2017; Moerman et al., 2018; Osnes et al., 2004; Pioli et al., 2016) of which one was mixed (Pioli et al., 2016) (Appendix Fig. C.8).

Assessments of nutritional status were included in five studies using the Nutrition Risk Screening (NRS) (Gumieiro et al., 2013b), Mini Nutritional Assessment (MNA) (Gumieiro et al., 2013b; Helminen et al., 2017), albumin levels (Helminen et al., 2017; Pioli et al., 2016), Body Mass Index (BMI) (Pajulammi et al., 2015) and 'treatment with nutritional supplements at discharge' (Pareja et al., 2017) (Appendix Table D.9). Two low ROB studies found a significant association between poor nutritional status and a worse functional outcome (Appendix Fig. C.9) (Gumieiro et al., 2013b; Pioli et al., 2016).

Vitamin D was included as a factor by three studies with a low ROB. One found a significant association with unfavorable functional outcomes (Savino et al., 2013), one reported mixed outcomes (Pioli et al., 2016) and one observed no association (Gumieiro et al., 2015) (Appendix Fig. C.10, Appendix Table D.10).

### 3.5. Treatment

The fracture type was included by five studies of which three had a low ROB (Appendix Table D.11) (Cornwall et al., 2004; Jones et al., 2017; Kim et al., 2012; Koval et al., 1998b; Pajulammi et al., 2015). Of these, only Jones et al. reported that femoral neck fractures are more favorable than per- and subtrochanteric fractures (Appendix Fig. C.11).

A delay in surgery defined as more than two days, was included by three studies (Appendix Table D.12), none of which found a significant association (Appendix Fig. C.12) (Kim et al., 2012; Pioli et al., 2016; Savino et al., 2013).

Five studies examined complications. Two included all complications pooled (Corcoles-Jimenez et al., 2015; Moerman et al., 2018) and three at delirium during admission (Givens et al., 2008; Pioli et al., 2016; Tarazona-Santabalbina et al., 2015) (Appendix Table D.13). Of the three studies with a low ROB, only Moerman et al. (postoperative complications pooled) found a significant negative association with functional outcome (Moerman et al., 2018). The other two, studying delirium, found no significant association (Appendix Fig. C.13).

Additional significantly associated factors which were included in only one study (and which didn't fit any of the previous domains), were length of hospital stay (Moerman et al., 2018), serum metalloproteinases 72 kDa (pro-MMP 2) (Gumieiro et al., 2013a), use of 'potentially inappropriate medication (PIM)' (Iaboni et al., 2017), postoperative pain (Iaboni et al., 2017), site of the accident (outdoors versus indoors) (Osnes et al., 2004) and whether the urinary catheter was removed during the hospital stay (Pajulammi et al., 2015) (Appendix Table D.14).

### 4. Discussion

The aim of this systematic review was to identify factors associated with the long-term functional outcome of patients with a low-energetic proximal femoral fracture. Out of 31 studies included, thirteen factors (grouped into four domains) were described in at least two independent studies and an additional ten factors in only one study. Age, comorbidity, functionality and cognition were found to have a significant effect in the majority of studies. Most studies that included sex as a factor found no significant effect. The level of evidence for the remaining factors (including residence and social status, ethnicity, psychological status, nutritional status, vitamin D, ethnicity fracture type, delay in

**Table 3**
Overview of the associations of study factors with functional outcome.

| Study author (year) | Demographic | | | | Function | | | Biological | | | Treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age (high) | Sex (male) | Residence and social | Ethnicity (non-Caucasian) | Functionality (good) | Psychological | Cognition (poor) | Comorbidity (poor) | Nutritional status (poor) | Vitamin D (poor) | Fracture type | Delay in surgery | Complications |
| **Low ROB studies** | | | | | | | | | | | | | |
| Aigner 2017 | | | | | | | | −* | | | | | |
| Beloosesky 2010 | − | | | | + | | | | | | | | |
| Givens 2008 | | | | | | − | +/− | | | | | | +/− |
| Gumieiro 2013 (1) | | | | | | | | +/− | −* | | | | |
| Gumieiro 2013 (2) | | | | | | | | | | | | | |
| Gumieiro 2015 | | | | | | | | | | +/− | | | |
| Iaboni 2017 | − | | | + | + | | | − | | | | | |
| Jones 2017 | −* | +/− | − | | + | | − | − | | | − | | |
| Kim 2012 | − | | | | | | | | | | +/− | +/− | |
| Moerman 2018 | − | | +/− | | + | | | − | | | | | − |
| Osnes 2004 | − | +/− | −* | | | | | − | | | | | |
| Pajulammi 2015 | − | +/− | | | + | | − | | +/− | | +/− | | |
| Pareja 2017 | | | | | + | | − | | +/− | | | | |
| Penrod 2008 | −* | +/− | | +/− | | | − | | | | | | |
| Pioli 2016 | −* | +* | | | +* | | − | −* | −* | −* | | +/− | +/− |
| Savino 2013 | +/− | − | − | | + | +/− | +/− | +/− | | − | | +/− | |
| Tarazona 2015 | +/− | +/− | | | + | | −* | +/− | | | | | +/− |
| Vergara 2014 | − | +/− | +* | | +* | − | | | | | | | |
| **High ROB studies** | | | | | | | | | | | | | |
| Carpintero 2006 | | | | | | | | | | − | | | |
| Corcoles 2015 | − | | − | | | | | | | | | | − |
| Cornwall 2004 | − | | | | − | | | | | | +/− | | |
| Fortinsky 2002 | | | | | +/− | +/− | | | | | | | |
| Gatot 2016 | −* | | | | | | | | | | | | |
| Hannan 2001 | | +/− | − | | − | | +/− | +/− | | | | | |
| Helminen 2017 | | | | | | | | | +/− | | | | |
| Ingemarsson 2003 | − | | | | +/−* | +/− | | | | | | | |
| Koval 1998 (1) | | | | | | | | | | | | | |
| Koval 1998 (2) | −* | | +/− | | −* | | | −* | | | +/− | | |
| Lin 2004 | | | *− | | − | | | | | | | | |
| Marottoli 1992 | +/− | | | | − | −* | +/− | | | | | | |
| Shyu 2010 | | | +/−* | | | | | | | | | | |
| Positive | 0/12 | 1/8 | 1/5 | 1/2 | 10/10 | 0/3 | 0/8 | 0/9 | 0/4 | 0/3 | 0/3 | 0/3 | 0/4 |
| No effect (ns) | 2/12 | 6/8 | 1/5 | 1/2 | 0/10 | 1/3 | 2/8 | 3/9 | 2/4 | 1/3 | 2/3 | 3/3 | 3/4 |
| Negative | 10/12 | 1/8 | 3/5 | 0/2 | 0/10 | 2/3 | 6/8 | 6/9 | 2/4 | 2/3 | 1/3 | 0/3 | 1/4 |

+ significant positive association, +/− no significant association (no effect), − significant negative association, *mixed outcome because the factor was included in multiple multivariate analyses within the same study (see Table 2 and Appendix D). Factors with more than two categories (for instance: age < 50 as a reference, and age 50–75 and > 75 as tested categories) were regarded significant if at least one category had a significant effect.

surgery and complications) was deemed too low to be conclusive regarding their relevance for long-term functional outcomes.

Considerable overlap was observed with the factors included in the short-term functional outcome studies described in a review by Sheehan et al. (2018). Herein, cognition was also identified as a prognostic factor supported by a sufficient level of evidence. Prognostic factors for mortality in proximal femoral fracture patients have been examined in many more studies, and the pooling of data on this unambiguous outcome is less problematic. Comprehensive reviews by Hu et al. (2012) and Smith et al. (2014) indicated that age, comorbidity (high ASA grade and high CCI), cognitive impairment and pre-fracture functionality were relevant factors for mortality, in addition to male gender, residence in a care institution and intra-capsular proximal femoral fractures (Hu et al., 2012; Smith et al., 2014). The prognostic factors for short-term functional outcome, long-term functional outcome and mortality seem very comparable.

The identification of a relevant set of prognostic factors could enhance the accuracy of prognostic models based on those factors. Developing a well-validated prognostic model of functional outcome may help to select patients for cost-effective care strategies, that might include interventions in nutrition, varying the intensity and frequency of physiotherapy or anticipating and organizing care for ADL. However, an accurate prognostic model of the functional recovery of patients with a proximal femoral fracture remains elusive. No such model has been extensively validated or widely implemented for routine use. The advanced age of the patient population, and the wide variety of comorbidities and severities found in this group, makes development of a model extremely challenging. Using the factors identified in this and previous reviews is one approach to investigate and construct such a model (Hu et al., 2012; Sheehan et al., 2018; Smith et al., 2014). A better understanding of the relationships of all independent variables and the dependent variable, with some acting as potential mediators and confounders, might also help to improve the model. These relationships are still poorly addressed in available studies (Sheehan et al., 2018).

In any population-based study, age is regarded as one of the most important prognostic factors. Age itself, however, is simply a proxy for biological age. In an effort to improve prognostic value relative to chronological age, biological age can be determined using various combinations of physical and biological assessments. However, these models (often including biomarkers) have so far not been proven superior to chronological age in general population studies (Jackson et al., 2003; Jylhava et al., 2017). In a more homogenous population, adequate assessment of comorbidities, their severity, and their impact on pre-morbid function may suffice. Interestingly, those studies that used the CCI to adjust for comorbidity found no association between age and functional outcome in at least some of the analysis performed (Pioli et al., 2016; Savino et al., 2013; Tarazona-Santabalbina et al., 2015). However, of these studies only Pioli et al. found a significantly negative association with worse CCI (Pioli et al., 2016).

Besides the CCI, many other assessments were used to rate patients' comorbidity or general health status, indicating that little consensus exists and that comorbidity remains a poorly defined concept. The assessments used to rate comorbidity tend to overlap with other factors such as cognition, functionality and nutritional status. While comorbidities themselves may impair or interfere with a patients' rehabilitation capacity, premorbid functionality is probably a major mediator in many studies (Feng et al., 2009; Idjadi et al., 2005; Regan et al., 2013). Extensively validated assessments of comorbidity (including the ASA, APACHE and CCI) are designed to represent the patients' mortality risk rather than the functional prognosis. However, mortality could also be categorized as failure to (functionally) recover. Some studies adopt this strategy (Kim et al., 2016), but many studies actually excluded all mortality cases, which could lead to variation in outcomes.

Prefracture functionality could be regarded as a mediator of co-morbidity, but also as a construct of more fundamental biological factors such as physical fitness, which in turn might be a construct of muscle mass, muscle strength, cardiopulmonary capacity and functional impairments (neuromuscular comorbidities, joint pathology) and motivational or cognitive problems (Beloosesky et al., 2010; Ingemarsson et al., 2003; Savino et al., 2013). These individual factors are still poorly understood, and could be an interesting focus for future studies.

While the inclusion of more fundamental biological factors (such as biomarkers) may be one way to enhance prognostic accuracy, these factors often require intensive or impractical assessments and can complicate a model substantially. Alternatively, effective methods to assess more practical factors, or practical factors in more effective combinations, could also improve a prognostic model. Most studies included in this review, however, aimed to assess the relevance of one specific factor, rather than to design an effective prognostic model for routine clinical purposes. Systematic reviews evaluating clinical prediction models of mortality and function are available for patients with ischemic strokes, but not yet for proximal femoral fractures (Fahey et al., 2018). Some of these predictive models have been comprehensively externally validated, and routinely collected data such as age, sex, disease characteristics (severity, subtype) and comorbidities have consistently been identified as the most suitable predictive factors of functional outcome and mortality (Fahey et al., 2018).

### 4.1. Study limitations

Most studies on prognostic factors are observational, an approach that potentially opens a measured effect to the influence of confounders (Hanley, 1983). However, multivariate analyses can adjust for the effect of confounders (Hanley, 1983). Only studies that undertook multivariate analyses were included in this systematic review. Some studies may have been omitted due to the limitations in the search strategy. However, no additional studies were identified by screening the reference lists of included studies. Only studies written in English were included, but additional relevant information on this topic may be available in other languages.

A high ROB was observed for a substantial number of studies, which were consequently largely excluded from the discussions and conclusions of this review. The majority of studies gave a poor description of the routine in-hospital care and rehabilitation strategy and no relevant effect due to these potential variations was assumed.

Substantial heterogeneity was observed in the methods used to assess patient functionality and prognostic factors (such as comorbidity, cognition and nutritional status). In addition, every individual factor included in a multivariate analysis potentially influences the effect measure of every other included factor, and the studies analyzed in this review did not include a collective of identical factors. Consequently, pooled data or summary effect measures could not be synthesized.

The included studies also showed heterogeneity in patient selection. Thirteen excluded all deceased patients or those with an incomplete follow-up (Aigner et al., 2017; Beloosesky et al., 2010; Corcoles-Jimenez et al., 2015; Gatot et al., 2016; Hannan et al., 2001; Ingemarsson et al., 2003; Koval et al., 1998b; Lin and Chang, 2004; Osnes et al., 2004; Pajulammi et al., 2015; Shyu et al., 2010; Tarazona-Santabalbina et al., 2015; Vergara et al., 2014). These studies focused on the long-term functional outcome of surviving patients only. However, studies that include deceased patients and regard this as an unfavorable functional outcome may be regarded as more useful for clinical prognostic purposes. Some studies excluded all cognitively impaired (Beloosesky et al., 2010; Iaboni et al., 2017; Ingemarsson et al., 2003; Koval et al., 1998a, b), non-ambulatory (Helminen et al., 2017; Iaboni et al., 2017; Koval et al., 1998a,b; Pajulammi et al., 2015; Savino et al., 2013) and/or non-community dwelling patients (Fortinsky et al., 2002; Kim et al., 2012; Koval et al., 1998a,b; Marottoli et al., 1992). This may have influenced the detectable effects of prognostic factors. No separate review after selections of these studies was performed.

Studies that focused on one or more specific prognostic factors, rather than a prognostic model, are suspect in terms of publication bias

for positive outcomes (Aigner et al., 2017; Carpintero et al., 2006; Gumieiro et al., 2015; Iaboni et al., 2017; Koval et al., 1998a). Studies withholding the effects of specific or unknown factors included in their models are suspect for selective reporting (Aigner et al., 2017; Carpintero et al., 2006; Corcoles-Jimenez et al., 2015; Cornwall et al., 2004; Gumieiro et al., 2013a,b; Helminen et al., 2017; Iaboni et al., 2017; Ingemarsson et al., 2003; Koval et al., 1998a,b; Lin and Chang, 2004). Studies on associations between factors and absolute functional outcome, and studies of recovery to individual prefracture levels of function were both included. No major differences were observed between the outcomes of these two types of studies.

This review can also provide assistance in the choice of appropriate tools and outcome assessments for future studies on the functional recovery of patients with a proximal femoral fracture. Selecting more widely used assessments improves the comparability of outcomes, and we plead against the use of new and unique assessments as a primary outcome, without proper validation or clear indications for new insights.

## 5. Conclusions

The 23 factors identified in the 31 included studies were evaluated for prognostic value in determining the functional recovery of patients with a proximal femoral fracture. Of these factors, only age, comorbidity, cognition and prefracture functionality were supported by a substantial level of evidence and thus relevant to prognostic models of routine care data.

## Funding sources

## Declaration of competing interest

The authors have no competing interests to declare.

## Appendix A. Search strategy and term (PubMed)

(("Hip Fractures"[majr] OR "Femoral Neck Fractures"[majr] OR "hip fracture"[ti] OR "proximal femoral fracture"[ti] OR "proximal femur fracture"[ti] OR "femoral neck fracture"[ti] OR "femur neck fracture"[ti] OR "trochanteric fracture"[ti] OR "collum fracture"[ti] OR "intertrochanteric fracture"[ti] OR "collum femoris fracture"[ti] OR "hip fractures"[ti] OR "proximal femoral fractures"[ti] OR "proximal femur fractures"[ti] OR "femoral neck fractures"[ti] OR "femur neck fractures"[ti] OR "trochanteric fractures"[ti] OR "collum fractures"[ti] OR "intertrochanteric fractures"[ti] OR "collum femoris fractures"[ti] OR (("hip"[ti] OR "hips"[ti] OR "Femoral Neck"[ti] OR "proximal femoral"[ti] OR "proximal femur"[ti] OR "femur neck"[ti] OR "trochanteric"[ti] OR "collum"[ti] OR "intertrochanteric"[ti] OR "collum femoris"[ti]) AND ("fractures"[ti] OR "fracture"[ti] OR fractur*[ti]))) AND ("functional outcome"[ti] OR "functional outcomes"[ti] OR "Predictive"[ti] OR "prediction"[ti] OR predict*[ti] OR "Prognosis"[majr] OR "prognostic"[ti] OR "prognosis"[ti] OR "prognosticator"[ti] OR "prognosticators"[ti] OR "Risk Factors"[majr] OR "risk factors"[ti] OR "risk factor"[ti] OR "Recovery of Function"[majr] OR "recovery"[ti] OR "recover"[ti] OR "Rehabilitation"[majr] OR "rehabilitation"[ti] OR rehabilitat*[ti] OR "function"[ti] OR "functionality"[ti] OR "Activities of Daily Living"[majr] OR "daily living"[ti] OR "ambulation"[ti] OR "ambulant"[ti] OR "ambulatory"[ti] OR "mobility"[ti] OR "Walking"[majr] OR "walking"[ti] OR "dependence"[ti] OR "dependent"[ti] OR "independency"[ti] OR "independent"[ti] OR "Gait"[mesh] OR "gait"[ti] OR "Postural Balance"[mesh] OR "balance"[ti]) AND ("Multivariate Analysis"[Mesh] OR "multivariate analyses"[tw] OR "multivariate analysis"[tw] OR "Logistic Models"[Mesh] OR "logistic regression"[tw] OR "logistic regressions"[tw] OR "logistic model"[tw] OR "logit models"[tw] OR "logit model"[tw] OR "hazard ratios"[tw] OR "hazard ratio"[tw] OR "Odds Ratio"[Mesh] OR "odds ratios"[tw] OR "odds ratio"[tw] OR "odds ratios"[tw] OR "cross product ratio"[tw] OR "cross-product ratios"[tw] OR "relative odds"[tw] OR "risk ratio"[tw] OR "risk ratios"[tw] OR "Analysis of Variance"[mesh] OR "analysis of variance"[tw] OR "analyses of variance"[tw] OR "ANOVA"[tw] OR "variance analyses"[tw] OR "variance analysis"[tw]) AND (english[la] OR dutch[la]).

## Appendix B

**Appendix Table B.1**
Methodological risk of bias assessment of the included studies.

| Study author and year | QUIPS tool biases | | | | | | |
|---|---|---|---|---|---|---|---|
| | Study participation | Study attrition | Prognostic factor measurement | Outcome measurement | Study confounding | Statistical analysis and reporting | Overall |
| Aigner 2017 | − | − | +/− | − | +/− | +/− | Low |
| Beloosesky 2010 | +/− | +/− | +/− | +/− | +/− | +/− | Low |
| Carpintero 2006 | − | − | − | − | + | +/− | High |
| Corcoles 2015 | − | − | − | − | + | +/− | High |
| Cornwall 2004 | − | +/− | − | − | + | + | High |
| Fortinsky 2002 | − | + | − | − | + | + | High |
| Gatot 2016 | − | − | +/− | − | + | +/− | High |
| Givens 2008 | +/− | − | − | − | − | − | Low |
| Gumieiro 2013) (1) | − | +/− | − | +/− | +/− | +/− | Low |
| Gumieiro 2013 (2) | − | + | − | +/− | − | − | Low |
| Gumieiro 2015 | − | +/− | − | +/− | +/− | +/− | Low |
| Hannan 2001 | − | + | − | + | − | + | High |
| Helminen 2017 | − | + | − | − | +/− | +/− | High |
| Iaboni 2017 | − | +/− | − | − | − | − | Low |
| Ingemarsson 2003 | + | + | − | +/− | + | + | High |
| Jones 2017 | +/− | − | − | − | − | +/− | Low |
| Kim 2012 | − | − | − | − | − | − | Low |
| Koval 1998 (1) | − | − | +/− | +/− | + | + | High |
| Koval 1998 (2) | − | − | − | − | + | + | High |
| Lin 2004 | − | + | +/− | +/− | + | + | High |
| Marottoli 1992 | − | − | − | − | − | + | High |
| Moerman 2018 | − | +/− | − | − | +/− | − | Low |

*(continued on next page)*

**Appendix Table B.1** (*continued*)

| Study author and year | QUIPS tool biases | | | | | | |
|---|---|---|---|---|---|---|---|
| | Study participation | Study attrition | Prognostic factor measurement | Outcome measurement | Study confounding | Statistical analysis and reporting | Overall |
| Osnes 2004 | − | +/− | − | − | +/− | +/− | Low |
| Pajulammi 2015 | − | − | − | − | − | − | Low |
| Pareja 2017 | − | +/− | +/− | +/− | +/− | +/− | Low |
| Penrod 2008 | +/− | +/− | − | − | − | − | Low |
| Pioli 2016 | − | +/− | − | − | − | +/− | Low |
| Savino 2013 | − | +/− | − | − | − | − | Low |
| Shyu 2010 | − | +/− | +/− | +/− | + | − | High |
| Tarazona 2015 | − | +/− | − | − | − | − | Low |
| Vergara 2014 | − | − | − | − | − | − | Low |

+ high risk of bias, +/− moderate risk of bias, − low risk of bias.

## Appendix C
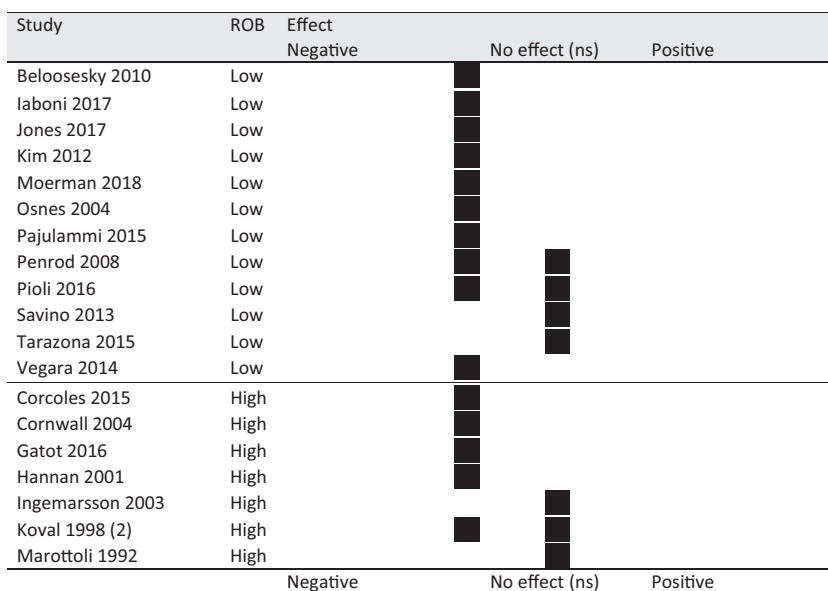


**Appendix Fig. C.1.** The association between higher age and functional outcome.
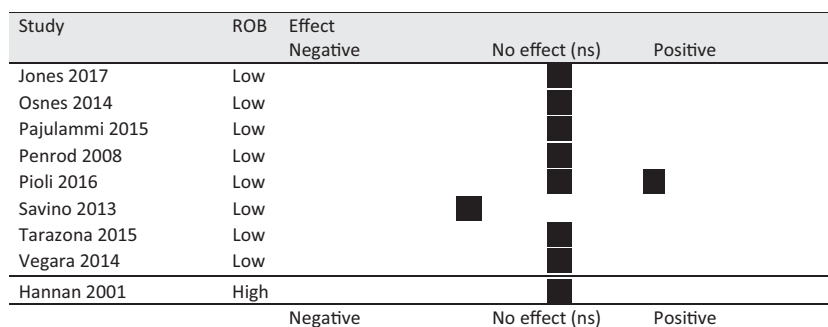


**Appendix Fig. C.2.** The association between male sex and functional outcome.

| Study | ROB | Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Jones 2017 | Low | ■ | | |
| Moerman 2018 | Low | | ■ | |
| Osnes 2004 | Low | ■ | ■ | |
| Pajulammi | Low | ■ | | |
| Pareja 2017 | Low | ■ | | |
| Savino 2013 | Low | ■ | | |
| Vergara 2014 | Low | | | ■ |
| Corcolez 2015 | High | ■ | | |
| Hannan 2001 | High | ■ | | |
| Koval 1998 (2) | High | | ■ | |
| Lin 2004 | High | ■ | ■ | |
| Shyu 2010 | High | ■ | ■ | ■ |

**Appendix Fig. C.3.** The association between residence or social status and functional outcome.

| Study | ROB | Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Iaboni 2017 | Low | ■ | | |
| Penrod 2008 | Low | | ■ | |

**Appendix Fig. C.4.** The association between ethnicity (non-Caucasian) and functional outcome.

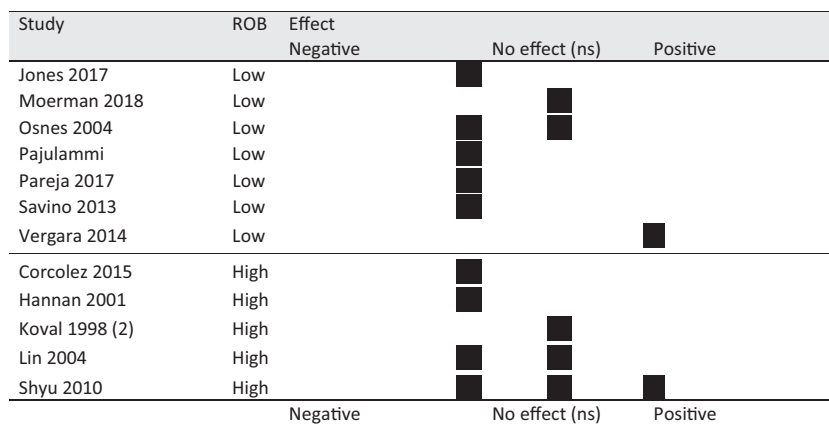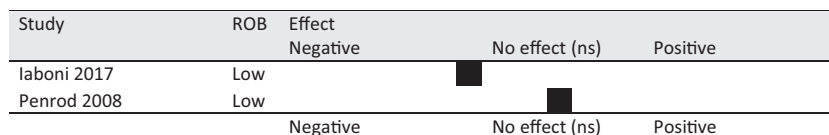| Study | ROB | Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Beloosesky 2010 | Low | | | ■ |
| Iaboni 2017 | Low | | | ■ |
| Jones 2017 | Low | | | ■ |
| Moerman 2018 | Low | | | ■ |
| Pajulammi 2015 | Low | | | ■ |
| Pareja 2017 | Low | | | ■ |
| Pioli 2016 | Low | | ■ | ■ |
| Savino 2013 | Low | | | ■ |
| Tarazona 2015 | Low | | | ■ |
| Vegara 2014 | Low | | ■ | ■ |
| Cornwall 2004 | High | | | ■ |
| Fortinsky 2002 | High | | ■ | |
| Hannan 2001 | High | | | ■ |
| Ingemarsson 2003 | High | | | ■ |
| Koval 1998 (2) | High | | ■ | |
| Lin 2004 | High | | | ■ |
| Marottoli 1992 | High | | | ■ |
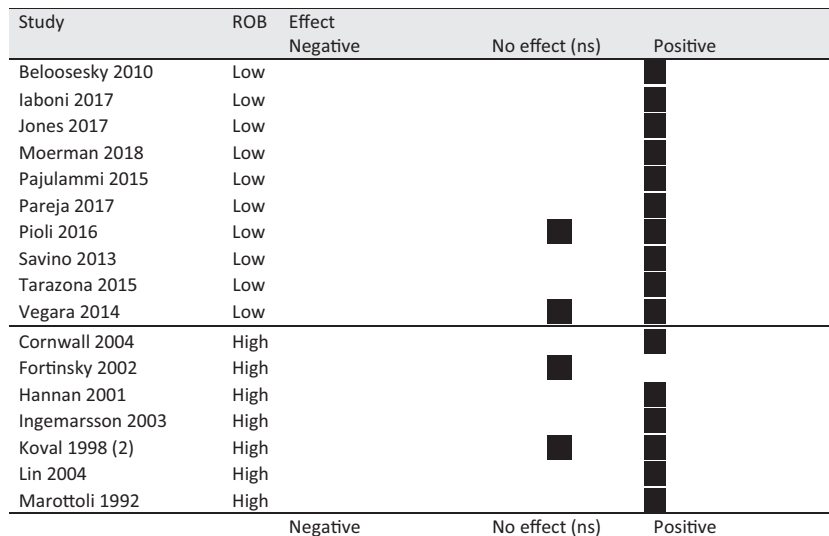
**Appendix Fig. C.5a.** The association between good prefracture functionality and functional outcome.

| Study | ROB | Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Beloosesky 2010 | Low | | | ■ |
| Ingemarsson 2003 | High | | ■ | ■ |
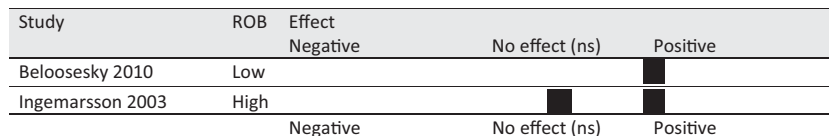
**Appendix Fig. C.5b.** The association between functionality at discharge and functional outcome.

| Study | ROB | Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Givens 2008 | High | | ■ | |
| Savino 2013 | Low | | ■ | |
| Vergara 2014 | Low | ■ | | |
| Fortinsky 2002 | High | | ■ | |
| Ingemarsson 2003 | High | | ■ | |
| Marottoli 1992 | High | ■ | ■ | |
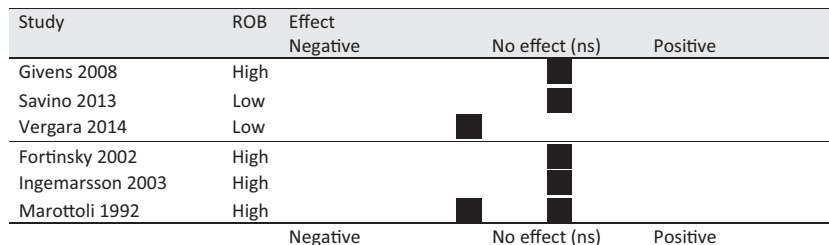
**Appendix Fig. C.6.** The association between (worse) psychological status and functional outcome.

| Study | ROB | Effect Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Jones 2017 | Low | ■ | | |
| Givens 2008 | | | ■ | |
| Pajulammi 2015 | Low | ■ | | |
| Pareja 2017 | Low | ■ | | |
| Penrod 2008 | Low | ■ | | |
| Pioli 2016 | Low | ■ | ■ | |
| Savino 2013 | Low | | ■ | |
| Tarazona 2015 | Low | ■ | | |
| Hannan 2001 | High | | ■ | |
| Marottoli 1992 | High | | ■ | |
| | | Negative | No effect (ns) | Positive |
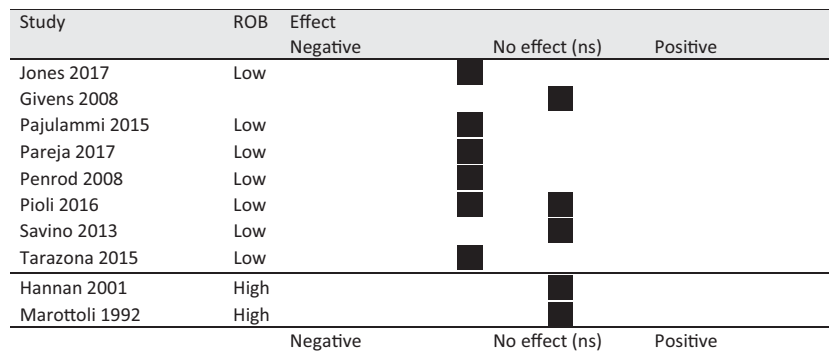
**Appendix Fig. C.7.** The association between cognitive impairment and functional outcome.

| Study | ROB | Effect Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Aigner 2017 | Low | ■ | | |
| Gumieiro 2013 (1) | Low | | ■ | |
| Iaboni 2017 | Low | ■ | | |
| Jones 2017 | Low | ■ | | |
| Moerman 2018 | Low | ■ | | |
| Osnes 2004 | Low | ■ | | |
| Pioli 2016 | Low | ■ | ■ | |
| Savino 2013 | Low | | ■ | |
| Tarazona 2015 | Low | | ■ | |
| Hannan 2001 | High | | ■ | |
| Koval 1998 (2) | High | ■ | ■ | |
| | | Negative | No effect (ns) | Positive |
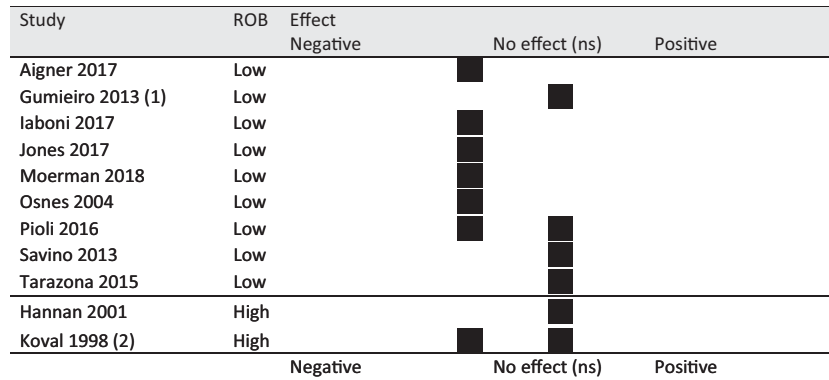
**Appendix Fig. C.8.** The association between comorbidity or worse health status and functional outcome.

| Study | ROB | Effect Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Gumieiro 2013 (1) | Low | ■ | ■ | |
| Pioli 2016 | Low | ■ | ■ | |
| Pareja 2017 | Low | | ■ | |
| Pajulammi 2015 | Low | | ■ | |
| Helminen 2017 | High | ■ | ■ | |
| | | Negative | No effect (ns) | Positive |
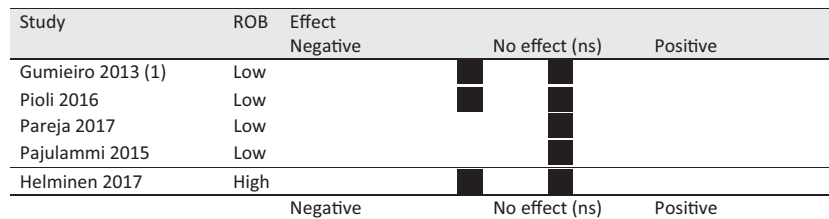
**Appendix Fig. C.9.** The association between poor nutritional status age and functional outcome.

| Study | ROB | Effect Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Gumieiro 2015 | Low | | ■ | |
| Pioli 2016 | Low | | ■ | ■ |
| Savino 2013 | Low | | ■ | |
| Carpentero 2006 | High | | ■ | |
| | | Negative | No effect (ns) | Positive |
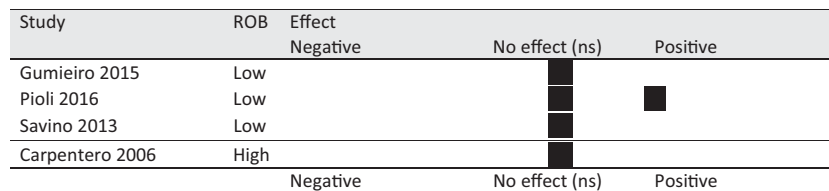
**Appendix Fig. C.10.** The association between vitamin D status and functional outcome.

| Study | ROB | Effect Negative | No effect (ns) | Positive |
|---|---|---|---|---|
| Jones 2017 | Low | | | ■ |
| Kim 2012 | Low | | ■ | |
| Pajulammi 2015 | Low | | ■ | |
| Cornwall 2004 | High | | ■ | |
| Koval 1998 (2) | High | | ■ | |
| | | Negative | No effect (ns) | Positive |
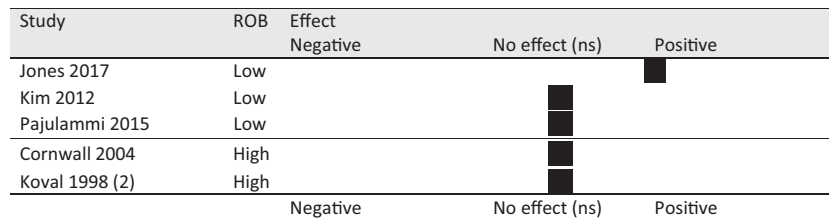
**Appendix Fig. C.11.** The association between fracture type (femoral neck fracture) and functional outcome.

| Study | ROB | Effect | | |
|---|---|---|---|---|
| | | Negative | No effect (ns) | Positive |
| Kim 2012 | Low | | ■ | |
| Pioli 2016 | Low | | ■ | |
| Savino 2013 | Low | | ■ | |
| | | Negative | No effect (ns) | Positive |
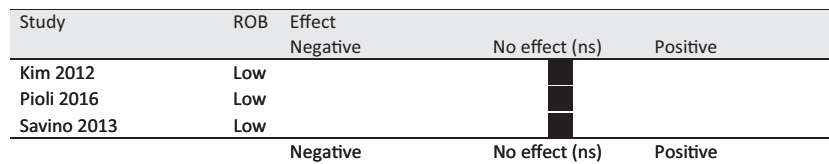
**Appendix Fig. C.12.** The association between a delay in surgery and functional outcome.

| Study | ROB | Effect | | |
|---|---|---|---|---|
| | | Negative | No effect (ns) | Positive |
| Moerman 2018 | Low | ■ | | |
| Pioli 2016 | Low | | ■ | |
| Tarazona 2015 | Low | | ■ | |
| Corcolez 2015 | High | ■ | | |
| Givens 2008 | High | | ■ | |
| | | Negative | No effect (ns) | Positive |
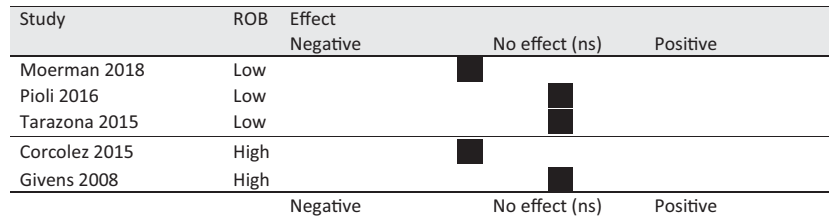
**Appendix Fig. C.13.** The association between complications during admission and functional outcome.

## Appendix D

**Appendix Table D.1**

Raw extracted data on age as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Beloosesky 2010 | Age | | Beta 0.134, p = 0.036 |
| Iaboni 2017 | Age | | Coef −0.047, Exp(Coef) 0.954, SE(Coef) 0.008, Z −5.67, pr > z 0.000 |
| Jones 2017 | Age | 67–74 | Ref |
| | | 75–84 | Coef −2.14 (95% CI -0.41-0.14) p = 0.066 |
| | | ≥85 | Coef −4.61 (95% CI -7.17;-2.06) p < 0.001 |
| Kim 2012 | Age | ≥80 | HR 0.77 (95% CI 0.41–1.23) p = 0.035 |
| Moerman 2018 | Age | | B 0.20 beta 0.11 T 3.22 p = 0.001 |
| Osnes 2004 (1.1) | Age | 50–74 | Ref |
| | | 75–79 | OR 2.57 (95% CI 1.43–4.65) p = s |
| | | 80–84 | OR 6.02 (95% CI 3.37–10.8) p = s |
| | | ≥85 | OR 11.3 (95% CI 5.94–21.5) p = s |
| Osnes 2004 (1.2) | Age | 50–74 | Ref |
| | | 75–79 | OR 2.15 (95% CI 0.93–4.96) p = s |
| | | 80–84 | OR 10.6 (95% CI 3.85–29.0) p = s |
| | | ≥85 | OR 17.8 (95% CI 3.78–83.7) p = s |
| Osnes 2004 (1.3) | Age | 50–74 | Ref |
| | | 75–79 | OR 3.59 (95% CI 1.95–6.63) p = s |
| | | 8 ≥ 5 | OR 5.25 (95% CI 2.90–9.49) p = s |
| | | ≥85 | OR 7.45 (95% CI 4.02–13.8) p = s |
| Pajulammi 2015 | Age | | OR 1.06 (95% CI 1.02–1.09) p = s |
| Penrod 2008 (1.11) | Age | <75 | Ref |
| | | 75–85 | OR 0.76 (95% CI 0.52–1.09) p = 0.13 |
| | | ≥85 | OR 0.69 (95% CI 0.46–1.03) p = 0.07 |
| Penrod 2008 (1.12) | Age | <75 | Ref |
| | | 75–85 | OR 0.54 (95% CI 0.40–0.70) p < 0.0001 |
| | | ≥85 | OR 0.46 (95% CI 0.40–0.70) p < 0.0001 |
| Penrod 2008 (1.21) | Age | <75 | Ref |
| | | 75–85 | OR 0.65 (95% CI 0.40–1.06) p = 0.08 |
| | | ≥85 | 85 OR 0.64 (95% CI 0.39–1.08) p = 0.10 |
| Penrod 2008 (1.22) | Age | <75 | Ref |
| | | 75–85 | OR 0.59 (95% CI 0.43–0.83) p < 0.001 |
| | | ≥85 | OR 0.38 (95% CI 0.27–0.53) p < 0.0001 |
| Pioli 2016 (1.1) | Age | Continuous | p = 0.000 |
| | Age | <80 | Ref |
| | | 80–84 | HR 0.84 (95% CI 0.40–1.74) p = 0.635 |
| | | 85–89 | HR 0.23 (95% CI 0.09–0.55) p = 0.001 |
| | | ≥90 | HR 0.07 (95% CI 0.01–0.36) p = 0.001 |
| Pioli 2016 (1.2) | Age | Continuous | p = 0.518 |
| | Age | <80 | Ref |
| | | 80–84 | HR 1.90 (95% CI 0.71–5.09) p = 0.201 |
| | | 85–89 | HR 1.10 (95% CI 0.40–3.06) p = 0.850 |
| | | ≥90 | HR 1.03 (95% CI 0.37–2.84) p = 0.958 |
| Pioli 2016 (1.3) | Age | Continuous | p = 0.673 |
| | Age | <80 | Ref |
| | | 80–84 | HR 1.13 (95% CI 0.27–4.80) p = 0.869 |
| | | 85–89 | HR 0.87 (95% CI 0.17–4.44) p = 0.862 |
| | | ≥90 | HR 2.08 (95% CI 0.47–9.25) p = 0.335 |
| Savino 2013 | Age | | OR 0.98 (95% CI 0.93–1.03) p = ns |

**Appendix Table D.1** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Tarazona 2015 | Age | | OR 0.971 95%CI (0.941–1.003) p = 0.078 |
| Vegara 2014 (1.1) | Age | | OR 1.10 (95% CI 1.07–1.14) p < 0.0001 |
| Vegara 2014 (1.2) | | | OR 1.16 (95% CI 1.12–1.20) p < 0.0001 |
| Vegara 2014 (1.3) | | | OR 1.15 (95% CI 1.11–1.20) p < 0.0001 |
| Corcoles 2015 | Age | >85 | B 0.089 Exp(B) 1.093 (95% CI 1.037–1.152) p = 0.001 |
| Cornwall 2004 (1.1) | Age | | p = 0.004 |
| Cornwall 2004 (1.2) | | | p = 0.010 |
| Cornwall 2004 (1.3) | | | p = 0.005 |
| Cornwall 2004 (1.4) | | | p = 0.009 |
| Gatot 2016 | Age | 60–69 | Ref |
| | | 70–79 | B −0.667; OR 0.513 (95% CI 0.201–1.310) p = 0.163 |
| | | 80–89 | B −1.269; OR 0.281 (95% CI 0.100–0.790) p = 0.016 |
| | | ≥90 | B −0.785; OR 0.456 (95% CI 0.067–3.083) p = 0.421 |
| Hannan 2001 | Age | | Parameter estimate −0.044, p = 0.02 |
| Ingemarsson 2003 (1.11) | Age | | p = ns |
| Ingemarsson 2003 (1.12) | | | p = ns |
| Ingemarsson 2003 (1.21) | | | p = ns |
| Ingemarsson 2003 (1.22) | | | p = ns |
| Koval 1998 (2.11) | Age | ≥85 | p < 0.001 |
| Koval 1998 (2.12) | | | p < 0.001 |
| Koval 1998 (2.21) | | | p = ns |
| Koval 1998 (2.22) | | | p = 0.021 |
| Marottoli 1992 | Age | | Estimate −0.015 SE 0.018 p = 0.399 |

Ref reference.

**Appendix Table D.2**
Raw extracted data on sex as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Jones 2017 | Sex | Male | Coef −0.87 (95% CI −2.84–1.10) p = 0.387 |
| Osnes 2004 (1.1) | Sex | Male | OR 0.99 (95%CI 0.58–1.70) p = ns |
| Osnes 2004 (1.2) | | | OR 0.56 (95% CI 0.25–1.25) p = ns |
| Osnes 2004 (1.3) | | | OR 0.88 (95% CI 0.53–1.46) p = ns |
| Pajulammi 2015 | Sex | Female | OR 0.88 (95% CI 0.55–1.38) p = ns |
| Penrod 2008 (1.22) | | | OR 1.01 (95% CI 0.76–1.34) p = 0.94 |
| Penrod 2008 (1.11) | Sex | Male | OR 1.01 (95% CI 0.76–1.44) p = 0.85 |
| Penrod 2008 (1.12) | | | OR 0.93 (95% CI 0.71–1.21) p = 0.58 |
| Penrod 2008 (1.21) | | | OR 0.94 (95% CI 0.63–1.41) p = 0.77 |
| Pioli 2016 (1.1) | Sex | Male | HR 2.59 (95% CI 1.18–5.65) p = 0.017 |
| Pioli 2016 (1.2) | | | HR 0.81 (95% CI 0.30–2.21) p = 0.679 |
| Pioli 2016 (1.3) | | | HR 0.27 (95% CI 0.06–1.30) p = 0.102 |
| Savino 2013 | Sex | Male | OR 0.50 (95% CI 0.27–0.92) p = s |
| Tarazona 2015 | Sex | Male | OR 1.088 (95% CI 0.665–1.778) p = 0.737 |
| Vegara 2014 (1.1) | Sex | Male | OR 1.09 (95% CI 0.57–2.06) p = 0.801 |
| Vegara 2014 (1.2) | | | OR 0.87 (95% CI 0.44–1.7) p = 0.675 |
| Vegara 2014 (1.3) | | | OR 1.24 (95% CI 0.60–2.59) p = 0.445 |
| Hannan 2001 | Sex | Male | Parameter estimate −0.371, p = 0.36 |

**Appendix Table D.3**
Raw extracted data on the residence and social status as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Jones 2017 | Living situation | Home (ref) | Coef −3.81 (95% CI −5.87; −1.74) p < 0.001 |
| Moerman 2018 | Living situation | Independent | B 2.92 beta 0.07 T 1.77 p = 0.078 |
| Osnes 2004 (1.1) | Living situation | Alone (ref) | OR 0.91 (95% CI 0.55–1.51) p = ns |
| Pajulammi 2015 | Living arrangement | Other than home | OR 2.14 (95% CI 1.33–3.44) p = s |
| Pareja 2017 | Social status on discharge | Nursing home | B −6.496 (95% CI −11.172 to −1.820) p = 0.007 |
| Savino 2013 | Caregiver assistance | | OR 0.34 (95% CI 0.18–0.63) p = s |
| Vergara 2014 (1.1) | Living status | Alone | Ref |
| | | Social support | na (p = ns) |
| | | With relative | na (p = ns) |
| Vergara 2014 (1.2) | | Alone | Ref |
| | | Social support | OR 2.44 (95% CI 0.87–6.86) p = 0.091 |
| | | With relative | OR 3.29 (95% CI 1.23–8.83) p = 0.018 |
| Vergara 2014 (1.3) | | Alone | Ref |
| | | Social support | OR 3.79 (95% CI 1.28–11.21) p = 0.023 |
| | | With relative | OR 3.92 (95% CI 1.42–10.79) p = 0.013 |
| Corcoles 2015 | Residence | Own home | B −2.857 Exp(B) 0.057 (95% CI 0.007–0.483) p = 0.009 |
| Koval 1998 (2.11) | Living with spouse | | na, p = ns |
| Koval 1998 (2.12) | | | na, p = ns |

**Appendix Table D.3** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Koval 1998 (2.21) | | | na, p = ns |
| Koval 1998 (2.22) | | | na, p = ns |
| Hannan 2001 | Dependent living | None | Ref |
| | | Homecare | Estimate −0.602 p = 0.10 |
| | | Nursing home | Estimate −1.406 p = 0.02 |
| Lin 2004 (1.1) | Marriage | | p = ns |
| Lin 2004 (1.2) | Marriage | | B -2.184 SE 0.796 Beta −0.291 R^2 0.485 p < 0.0001 |
| Shyu 2010 (1) | Follow-up medical services | | OR 1.10 p = 0.736 |
| | Caregiving related healthcare information | | OR 0.38 p = 0.009 |
| | Social services | | OR 0.57 p = 0.12 |
| | support group | | OR 1.93 p = 0.027 |
| Shyu 2010 (2) | Follow-up medical services | | OR 1.05 p = 0.825 |
| | Caregiving related healthcare information | | OR 1.91 p = 0.058 |
| | Social services | | OR 0.40 p = 0.035 |
| | support group | | OR 0.29 p = 0.02 |
| Shyu 2010 (3) | Follow-up medical services | | OR 1.13 p = 0.746 |
| | Caregiving related healthcare information | | OR 1.70 p = 0.186 |
| | Social services | | OR 0.41 p = 0.076 |
| | support group | | OR 0.96 p = 0.939 |

**Appendix Table D.4**
Raw extracted data on ethnicity as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Iaboni 2017 | Ethnicity | Other (non-white/Caucasian) | Coef −0.755, Exp(Coef) (HR) 0.470, SE Coef 0.310, z −2.43, pr > z 0.010 |
| Penrod 2008 (1.11) | Ethnicity | White | OR 1.54 (95% CI 1.01–2.37) p = 0.05 |
| Penrod 2008 (1.12) | | | OR 0.95 (95% CI 0.64–1.40) p = 0.77 |
| Penrod 2008 (1.21) | | | OR 1.52 (95% CI 0.89, 2.62) p = 0.13 |
| Penrod 2008 (1.22) | | | OR 1.20 (95% Ci 0.79, 1.82) p = 0.40 |

**Appendix Table D.5a**
Raw extracted data on prefracture function as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Pioli 2016 (1.1) | Katz ADL | | HR 1.06 (95% CI 0.61–1.84) p = 0.834 |
| | Lawton-Brody IADL | | HR 1.24 (95% CI 1.01–1.53) p = 0.042 |
| | Walking device | | HR 0.35 (95% CI 0.15–0.83) p = 0.016 |
| Pioli 2016 (1.2) | Katz ADL | | HR 1.46 (95% CI 1.07–2.00) p = 0.017 |
| | Lawton-Brody IADL | | HR 1.03 (95% CI 0.82–1.29) p = 0.824 |
| | Walking device | | HR 0.76 (95% CI 0.38–1.54) p = 0.449 |
| Pioli 2016 (1.3) | Katz ADL | | HR 1.54 (95% CI 1.03–2.32) p = 0.037 |
| | Lawton-Brody IADL | | HR 1.37 (95% CI 0.77–2.42) p = 0.289 |
| | Walking device | | HR 2.42 (95% CI 0.77–7.63) p = 0.130 |
| Cornwall 2004 (1.1) | Preinjury overall FIM score | | p < 0.001 |
| Cornwall 2004 (1.2) | Preinjury overall FIM score | | p < 0.001 |
| Cornwall 2004 (1.3) | Preinjury overall FIM score | | p < 0.001 |
| Cornwall 2004 (1.4) | Preinjury overall FIM score | | p < 0.001 |
| | Preinjury locomotion FIM | | p < 0.001 |
| Hannan 2001 | Locomotion FIM | | OR 0.498 p < 0.001 |
| Iaboni 2017 | FRS | | Coef −0.045, Exp(coef) 0.956, se Coef 0.009, z −4.81, pr > z 0.000 |
| Marottoli 1992 | Physical function score | (0–5) | Estimate 0.237 (SE 0.086) p = 0.008 |
| Fortinsky 2002 | locomotion FIM | | OR 0.66 (95% CI 0.24–1.84) p = ns |
| Ingemarsson 2003 (1.11) | Prefracture outdoor walking | | Regression −1.38, SE 0.60, OR 0.25 (95% CI 0.08–0.81) p = 0.020 |
| Ingemarsson 2003 (1.12) | | | Regression −0.39, SE 0.19, OR 0.68 (95% CI 0.47–0.98) p = 0.037 |
| Ingemarsson 2003 (1.22) | Prefracture independent walking | | Regression −2.07, SE 0.72, OR 0.13 (95% CI 0.03–0.52) p = 0.004 |
| Pajulammi 2015 | Mobility level (n, %) | Outdoors unassisted | Ref |
| | | Outdoor assisted | OR 0.47 (95% CI 0.30–0.75) p = s |
| | | Indoor assisted | OR 0.25 (95% CI 0.09–0.72) p = s |
| Beloosesky 2010 | DASH scores | | B 0.255 p = 0.005 |
| Moerman 2018 | Prefracture use of walking aids | | B 3.91 beta 0.11 T 2.39 p = 0.017 |
| | prefracture IADL (GARS) | | B 0.60 beta 0.56 t 10.74 p = 0.000 |
| Koval 1998 (2.11) | IADL | | p < 0.001 |
| Koval 1998 (2.12) | IADL | | p = ns |
| Koval 1998 (2.22) | IADL | | p = ns |
| Savino 2013 | BI difficulty | | OR 0.42 (95% CI 0.24–0.76) p = s |
| | HGS | Tertiles, lowest | Ref |
| | | Intermediate | OR 2.40 (95% CI 1.24–4.62) p = s |
| | | Highest | OR 2.46 (95% CI 1.11–5.44) p = s |

**Appendix Table D.5a** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Pareja 2017 | BI | | B 0.596 (95% CI 0.409–0.782) p < 0.001 |
| Tarazona 2015 | BI | | OR 1.022 (95% CI 1.014–1.030) p < 0.001 |
| Lin 2004 (1.1) | BI | ability to walk outdoors before fracture | B 40.004, SE 7.603 Beta 0.635 R^2 0.397 F 27.65 p < 0.0001 |
| Lin 2004 (1.2) | IADL Ability to do housework | | B 4.706 SE 0.796 -beta 0.291 R^2 0.485 F? p < 0.0001 |
| | Use of walking aid | | B -2.400, SE 0.912 Beta −0.290 R^2 0.561 p < 0.0001 |
| Vergara 2014 (1.1) | LCF WOMAC | | OR 1.36 (95% CI 1.2–1.55) p < 0.0001 |
| | SF-12 (PCS) | | OR 0.69 (95% CI 0.52–0.92) p = 0.010 |
| Vergara 2014 (1.2) | LCF WOMAC | | OR 1.36 (95% CI 1.23–1.51) p < 0.0001 |
| | SF-12 (PCS) | | p = ns |
| Vergara 2014 (1.3) | LCF WOMAC | | OR 1.47 (95% CI 1.30–1.67) p < 0.0001 |
| | SF-12 (PCS) | | p = ns |
| Jones 2017 | Baseline function (FIM) | | Coef 0.89 (95% CI 0.83–0.95) p < 0.001 |

**Appendix Table D.5b**
Raw extracted data on the functionality at discharge as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Beloosesky 2010 | Handgrip strength | | beta 0.497 p = 0.001 |
| | FIM score | | beta 0.261 p = 0.001 |
| Ingemarsson 2003 (1.11) | Balance (TUG) | | Regression −0.053 SE 0.023 OR 0.95 (95% CI 0.91–0.99) p = 0.019 |
| Ingemarsson 2003 (1.12) | | | Regression −0.022 SE 0.011 OR 0.98 (95% CI 0.96–1.000) p = 0.054 |
| Ingemarsson 2003 (1.21) | | | Regression −0.054 SE 0.020 OR 0.95 (95% CI 0.91–0.99) p = 0.009 |
| Ingemarsson 2003 (1.22) | | | Regression −0.023 SE 0.013 OR 0.97 (95% CI 0.95–1.003) p = 0.087 |

**Appendix Table D.6**
Raw extracted data on the psychological status as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Givens 2008 (1.1) | | Depressive symptoms (Geriatric Depression Scale) | OR 0.34 p = 0.08 |
| Givens 2008 (1.2) | | | OR 0.30 p = 0.07 |
| Savino (2013) | | Depressive symptoms (Geriatric Depression Scale) | OR 0.60 (95% CI 0.35–1.03) p = ns |
| Vergara 2014 (1.1) | | SF-12 mental component summary score (MCS) | OR 0.75 (95% CI 0.60–0.94) p = 0.012 |
| Vergara 2014 (1.2) | | SF-12 mental component summary score (MCS) | OR 0.66 (95% CI 0.52–0.84) p = 0.001 |
| Vergara 2014 (1.3) | | SF-12 mental component summary score (MCS) | OR 0.70 (95% CI 0.54–0.92) p = 0.011 |
| Fortinsky 2002 | | Rehabilitation therapy self-efficacy | OR 1.18 (95% CI 0.99–1.42) p = 0.07 |
| Ingemarsson 2003 (1.11) | | Motivation | na (p = ns) |
| Ingemarsson 2003 (1.12) | | | na (p = ns) |
| Ingemarsson 2003 (1.21) | | | na (p = ns) |
| Ingemarsson 2003 (1.22) | | | na (p = ns) |
| Marottoli 1992 | | Emotional support | Estimate −0.396 SE 0.204 p = 0.057 |
| | | Depression (CES-D) | Estimate 0.035 SE 0.015 p = 0.022 |

**Appendix Table D.7**
Raw extracted data on cognition as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Pajulammi 2015 | Memory disorder | | OR 1.89 (95% CI 1.19–3.00) p = s |
| Pioli 2016 (1.1) | SPMSQ | Continuous | p = 0.159 |
| | | No | Ref |
| | | Mild-moderate | HR 1.12 (95% CI 0.53-na) p = 0.762 |
| | | Severe | NA |
| Pioli 2016 (1.2) | | Continuous | p = 0.100 |
| | | No | Ref |
| | | Mild-moderate | HR 0.67 (95% CI 0.29–1.58) p = 0.635 |
| Pioli 2016 (1.3) | | Severe | HR 0.27 (95% CI 0.08–0.90) p = 0.033 |
| | | Continuous | p = 0.932 |
| | | Mild-moderate | Ref |
| | | Severe | HR 0.43 (95% CI 0.03–5.79) p = 0.754 |
| | | | HR 0.38 (95% CI 0.02–6.35) p = 0.963 |
| Savino 2013 | Cognitive impairment | SPMSQ <8 | OR 0.99 (95% CI 0.56–1.73) p = ns |
| Penrod 2008 (1.11) | Dementia | | OR 0.43 (95% CI 0.30–0.60) p < 0.0001 |
| Penrod 2008 (1.12) | | | OR 0.65 (95% CI 0.47–0.93) p = 0.02 |
| Penrod 2008 (1.21) | | | OR 0.25 (95% CI 0.17–0.36) p < 0.0001 |
| Penrod 2008 (1.22) | | | OR 0.26 (95% CI 0.18–0.39) p < 0.0001 |
| Pareja 2017 | GDS | | B −3.543 (95% CI −6.384, −0.702) p = 0.015 |
| Givens 2008 (1.1) | Cognitive impairment | BDRS ≥ 4 and MMSE < 27 | OR 1.11 p = 0.84 |

**Appendix Table D.7** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| | Cognitive and mood disorders (combined) | | OR 1.01 p = 0.96 |
| Givens 2008 (1.2) | Cognitive impairment | | OR 1.20 p = 0.72 |
| | Cognitive and mood disorders (combined) | | OR 0.93 p = 0.79 |
| Marottoli 1992 | SPMSQ | 0–10 | Estimate −0.097 SE 0.05 p = 0.056 |
| Jones 2017 | MMSE | ≥18 (ref) | Coef −4.78 (95% CI −8.47; −1.09) p = 0.011 |
| Hannan 2001 | Dementia | | Parameter estimate −0.739, p = 0.09 |
| Tarazona 2015 | GDS | Normal | Ref |
| | | Mild | OR 0.751 (95% CI 0.433–1.301) p = 0.307 |
| | | Moderate | OR 0.487 (95% CI 0.251–0.945) p = 0.033 |
| | | severe | OR 0.439 (95% CI 0.197–0.919) p = 0.044 |

**Appendix Table D.8**
Raw extracted data on comorbidities as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Koval 1998 (2.11) | Number of comorbidities | | p < 0.05 |
| | ASA | Ref: <2 | p = ns |
| Koval 1998 (2.12) | Number of comorbidities | | p = ns |
| | ASA | Ref: <2 | p = ns |
| Koval 1998 (2.21) | Number of comorbidities | | p = ns |
| | ASA | Ref: <2 | p = ns |
| Koval 1998 (2.22) | Number of comorbidities | | p = ns |
| | ASA | Ref: <2 | p = ns |
| Osnes 2004 (1.1) | Health status | Excellent | Ref |
| | | Good | OR 1.76 (95% CI 0.99–3.14) p = s |
| | | Fair | OR 2.15 (95% CI 1.14–4.04) p = s |
| | | Poor | OR 2.84 (95% CI 1.03–7.85) p = s |
| Gumieiro 2013 (1.2) | ASA | | OR 1.684 (95% CI 0.830–3.416) p = 0.15 |
| Moerman 2018 | ASA | | B 2.69 beta 0.06 T 1.99 p = 0.048 |
| Hannan 2001 | Modified APACHE | | Estimate −0.090 p = 0.23 |
| | Modified RAND | | Estimate −0.080 p = 0.18 |
| Pioli 2016 (1.1) | APS of APACHE II | | HR 0.88 (95% CI 0.73–1.05) p = 0.162 |
| | CCI | | HR 0.69 (95% CI 0.54–0.87) p = 0.002 |
| Pioli 2016 (1.2) | APS of APACHE II | | HR 0.97 (95% CI 0.84–1.13) p = 0.723 |
| | CCI | | HR 1.01 (95% CI 0.82–1.25) p = 0.914 |
| Pioli 2016 (1.3) | APS of APACHE II | | HR 1.06 (95% CI 0.82–1.38) p = 0.647 |
| | CCI | | HR 0.86 (95% CI 0.66–1.12) p = 0.270 |
| Iaboni 2017 | Baseline CIRS-G score | | Coef −0.056 Exp(Coef) 0.946 SE Coef 0.022 z −2.59 pr > z 0.010 |
| Tarazona 2015 | CCI | | OR 1.012 (95% CI 0.915–1.118) p = 0.817 |
| Savino 2013 | CCI | 0 | Ref |
| | | 1 | OR 0.92 (95% CI 0.42–2.01) p = ns |
| | | 2 | OR 0.57 (95% CI 0.26–1.25) p = ns |
| | | >2 | OR 0.85 (95% CI 90.40–1.78) p = ns |
| Jones 2017 | Chronic conditions | | Coef −3.36 (95% CI −5.30; −1.41) p < 0.001 |
| Aigner 2017 (1.11) | Admission 3 m prior | | B −9.918 â −0.124 (95% CI −19.001; −0.835) p = 0.032 |
| Aigner 2017 (1.12) | | | B −10.025 â −0.117 (95%CI −20.958; 0.909) p = 0.072 |
| Aigner 2017 (1.21) | | | B −2.914 â −0.121 (95% CI −1.992; −0.047) p = 0.047 |
| Aigner 2017 (2.22) | | | B −4.680 â −0.179 (95% CI −8.042; −1.319) p = 0.007 |
| Specific comorbidities | | | |
| Beloosesky 2010 | DASH | | Beta −0.255 p = 0.005 |
| Gatot 2016 | Arthritis | | B 1.855 OR 6.389 (95% CI 0.658–62.014) p = 0.110 |
| | hypercholesterolemia | | B 0.990 OR 2.692 (95% CI 1.323–5.479) p = 0.006 |
| Koval 1998 (2.11) | Previous hip fracture | | p = ns |
| Koval 1998 (2.12) | | | p = ns |
| Koval 1998 (2.21) | | | p = ns |
| Koval 1998 (2.22) | | | p = ns |
| Osnes 2004 (1.1) | Previous/later fracture hip | | OR 2.45 (95% CI 1.12–5.36) p = s |
| Kim 2012 | Previous fracture | | HR 0.58 (95% CI 0.26–0.97) p = 0.018 |
| Kim 2012 | Cancer | | HR 3.29 (95% CI 1.64–6.34) p < 0.001 |
| Penrod 2008 (1.11) | Cancer | | OR 0.91 (95% CI 0.62–1.35) p = 0.66 |
| Penrod 2008 (1.12) | | | OR 0.92 (95% CI 0.67–1.26) p = 0.61 |
| Penrod 2008 (1.21) | | | OR 1.07 (95% CI 0.65–1.73) p = 0.19 |
| Penrod 2008 (1.22) | | | OR 1.02 (95% CI 0.73–1.42) p = 0.91 |
| Penrod 2008 (1.11) | Hypertension | | OR 0.99 (95% CI 0.76–1.28) p = 0.85 |
| Penrod 2008 (1.12) | | | OR 1.02 (95% CI 0.83–1.27) p = 0.92 |
| Penrod 2008 (1.21) | | | OR 1.01 (95% CI 0.73, 1.40) p = 0.13 |
| Penrod 2008 (1.22) | | | OR 0.89 (95% CI 0.71–1.10) p = 0.30 |
| Penrod 2008 (1.11) | COPD/Asthma | | OR 0.72 (95% CI 0.50–1.04) p = 0.08 |
| Penrod 2008 (1.12) | | | OR 0.95 (95% CI 0.69–1.31) p = 0.75 |
| Penrod 2008 (1.21) | | | OR 1.45 (95% CI 0.85–2.48) p = 0.17 |
| Penrod 2008 (1.22) | | | OR 0.81 (95% CI 0.58–1.14) p = 0.18 |
| Penrod 2008 (1.11) | DM | | OR 0.84 (95% CI 0.59–1.18) p = 0.32 |

**Appendix Table D.8** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Penrod 2008 (1.12) | | | OR 0.98 (95% CI 0.72–1.33) p = 0.88 |
| Penrod 2008 (1.21) | | | OR 0.89 (95% CI 0.58–1.37) p = 0.60 |
| Penrod 2008 (1.22) | | | OR 0.88 (95% CI 0.63–1.22) p = 0.45 |
| Penrod 2008 (1.11) | Parkinson | | OR 1.00 (95% CI 0.58–1.73) p = 0.99 |
| Penrod 2008 (1.12) | | | OR 0.37 (95% CI 0.22–0.66) p = 0.001 |
| Penrod 2008 (1.21) | | | OR 0.79 (95% CI 0.43–1.47) p = 0.46 |
| Penrod 2008 (1.22) | | | OR 0.65 (95% CI 0.39–1.09) p = 0.10 |
| Penrod 2008 (1.11) | Arrythmia | | OR 0.86 (95% CI 0.61–1.19) p = 0.33 |
| Penrod 2008 (1.12) | | | OR 0.71 (95% CI 0.52–0.98) p = 0.04 |
| Penrod 2008 (1.21) | | | OR 0.83 (95% CI 0.50–1.28) p = 0.39 |
| Penrod 2008 (1.22) | | | OR 0.85 (95% CI 0.60–1.18) p = 0.33 |
| Penrod 2008 (1.11) | Angina pec | | OR 0.92 (95% CI 0.59–1.41) p = 0.73 |
| Penrod 2008 (1.12) | | | OR 0.73 (95% CI 0.49–1.06) p = 0.10 |
| Penrod 2008 (1.21) | | | OR 1.09 (95% CI 0.61–2.00) p = 0.30 |
| Penrod 2008 (1.22) | | | OR 0.92 (95% CI 0.64–1.35) p = 0.74 |
| Penrod 2008 (1.11) | Heart failure | | OR 0.95 (95% CI 0.63–1.42) p = 0.79 |
| Penrod 2008 (1.12) | | | OR 1.06 (95% CI 0.73–1.55) p = 0.76 |
| Penrod 2008 (1.21) | | | OR 1.04 (95% CI 0.64–1.71) p = 0.17 |
| Penrod 2008 (1.22) | | | OR 0.87 (95% CI 0.59–1.29) p = 0.50 |
| Penrod 2008 (1.11) | CVA/Stroke | | OR 0.73 (95% CI 0.49–1.07) p = 0.10 |
| Penrod 2008 (1.12) | | | OR 0.78 (95% CI 0.54–1.13) p = 0.54 |
| Penrod 2008 (1.21) | | | OR 1.09 (95% CI 0.67–1.80) p = 0.72 |
| Penrod 2008 (1.22) | | | OR 0.48 (95% CI 0.33–0.72) p < 0.0001 |
| Penrod 2008 (1.11) | Myocardial ischemia | | OR 1.11 (95% CI 0.72–1.72) p = 0.64 |
| Penrod 2008 (1.12) | | | OR 1.22 (95% CI 0.86–1.78) p = 0.25 |
| Penrod 2008 (1.21) | | | OR 1.45 (95% CI 0.82–2.60) p = 0.20 |
| Penrod 2008 (1.22) | | | OR 0.97 (95% CI 0.67–1.41) p = 0.88 |
| Vergara 2014 (1.1) | Cerebrovascular disease | | OR 3.04 (95% CI 1.11–8.34) p = 0.031 |
| Vergara 2014 (1.2) | | | p = ns |
| Vergara 2014 (1.3) | | | p = ns |

**Appendix Table D.9**
Raw extracted data on the nutritional status as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Gumieiro 2013 (1.1) | NRS 2002 | | OR 1.429 (95% CI 0.686–2.275) p = 0.47 |
| Gumieiro 2013 (1.3) | MNA | | OR 0.773 (95% CI 0.663–0.901) p = 0.001 |
| Pioli 2016 (1.1) | Albumin | <3.2 g/dl (ref) | HR 0.47 (95% CI 0.22–0.99) p = 0.049 |
| Pioli 2016 (1.2) | | | HR 0.82 (95% CI 0.36–1.86) p = 0.635 |
| Pioli 2016 (1.3) | | | HR 0.81 (95% CI 0.29–2.36) p = 0.703 |
| Pareja 2017 | nutritional supplements at discharge | | B 9.611 (95% CI 1.497, −17.724) p = 0.21 |
| Pajulammi 2015 | BMI | 23–28 | Ref |
| | | <23 | OR 1.35 (95% CI 0.87–2.10) p = ns |
| | | >28 | OR 1.08 (95% CI 0.71–1.63) p = ns |
| Helminen 2017 (1.1) | MNA-SF | Normal | Ref |
| | | At risk | HR 1.81 (95% CI 1.17–2.80) p < 0.10 |
| | | Malnourished | HR 2.37 (95% CI 0.88–6.38) p < 0.10 |
| Helminen 2017 (1.2) | | Normal | Ref |
| | | At risk | HR 1.88 (95% CI 1.18–2.99) p < 0.10 |
| | | Malnourished | HR 3.28 (95% CI 0.97–11.0) p < 0.10 |
| Helminen 2017 (1.3) | Albumin | 34-45 g/l | Ref |
| | | 28-33 g/l | HR 1.16 (95% CI 0.72–3.86) p ≥ 0.10 |
| | | <28 g/l | HR 1.52 (95% CI 0.60–3.86) p ≥ 0.10 |

**Appendix Table D.10**
Raw extracted data on the vitamin D status as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Gumieiro 2015 | Calcifediol | <20 ng/ml | HR 1.463 (0.524–4.088) p = 0.469 |
| Savino (2013) | Calcifediol | Lowest tertile | Ref |
| | | Intermediate | OR 1.89 (95% CI 1.01–3.54) p = s |
| | | Highest | OR 2.29 (95% CI 1.22–4.28) p = s |
| Pioli 2016 (1.1) | Calcifediol | <6 ng/ml ref | Ref |
| | | 6–11 ng/ml | HR 1.81 (95% CI 0.76–4.28) p = 0.180 |
| | | >11 ng/ml | HR 2.9 (95% CI 1.23–6.85) p = 0.015 |
| Pioli 2016 (1.2) | | <6 ng/ml | Ref |
| | | 6–11 ng/ml | HR 2.81 (95% CI 1.21–6.51) p = 0.016 |
| | | >11 ng/ml | HR 3.66 (95% CI 1.47–9.11) p = 0.005 |
| Pioli 2016 (1.3) | | <6 ng/ml | Ref |

**Appendix Table D.10** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| | | 6–11 ng/ml | HR 0.81 (95% CI 0.22–3.05) p = 0.523 |
| | | >11 ng/ml | HR 1.03 (95% CI 0.27–3.90) p = 0.496 |
| Carpintero 2006 | Calcifediol | 25–113 nmol/l | OR 2.7 (95% CI -0.7-9.9) p = 0.13 |
| Carpintero 2006 | Calcitriol | 48–110 pmol/l | OR 6.97 (95% CI -1.7–27.4) p = 0.005 |

**Appendix Table D.11**
Raw extracted data on the fracture type as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Jones 2017 | Fracture type | FNF | Ref |
| | | Intertrochanteric | Coef −2.08 (95% CI −3.82; −0.34) p = 0.019 |
| | | Subtrochanteric/combination | Coef −7.67 (95% CI −11.84; −3.49) p < 0.001 |
| Kim 2012 | Fracture type | FNF (ref) | HR 1.11 (95% CI 0.63–1.55) p = 0.742 |
| Pajulammi 2015 | Fracture type | FNF | Ref |
| | | Intertrochanteric | 1.46 (0.996–2.15) p = ns |
| | | Subtrochanteric | 1.00 (0.45–2.22) p = ns |
| Cornwall 2004 (1.3) | | | p = ns |
| Cornwall 2004 (1.4) | | | p = ns |
| Koval 1998 (2.11) | Fracture type | FNF (ref) | na (p = ns) |
| Koval 1998 (2.12) | | | na (p = ns) |
| Koval 1998 (2.21) | | | na (p = ns) |
| Koval 1998 (2.22) | | | na (p = ns) |

**Appendix Table D.12**
Raw extracted data on the delay in surgery as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Kim 2012 | | Delay in surgery >2 days | HR 1.49 (95% CI 0.94–2.32) p = 0.039 |
| Pioli 2016 (1.1) | | Surgery <48 h (ref) | HR 0.95 (95% CI 0.49–1.84) p = 0.870 |
| Pioli 2016 (1.2) | | | HR 1.07 (95% CI 0.52–2.21) p = 0.860 |
| Pioli 2016 (1.3) | | | HR 1.53 (95% CI 0.48–4.84) p = 0.468 |
| Savino 2013 | Time to surgery | Lowest (tertile) | Ref |
| | | | Intermediate OR 1.72 (95% CI 0.98–3.02) p = ns |
| | | | Highest OR 1.35 (95% CI 0.61–2.96) p = ns |

**Appendix Table D.13**
Raw extracted data on complications as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Moerman 2018 | Postoperative complications | | B 3.53 beta 0.10 T 2.83 p = 0.005 |
| Pioli 2016 (1.1) | Delirium | | HR 0.48 (95% CI 0.21–1.10) p = 0.084 |
| Pioli 2016 (1.2) | | | HR 0.99 (95% CI 0.43–2.29) p = 0.978 |
| Pioli 2016 (1.3) | | | HR 0.36 (95% CI 0.11–1.22) p = 0.100 |
| Tarazona 2015 | Delirium | | HR 0.692 (95% CI 0.433–1.107) p = 0.125 |
| Corcoles 2015 | Without complications after discharge | | B −1.205 Exp(B) 0.3 (95% CI 0.133–0.674) p = 0.004 |
| Givens 2008 (1.1) | Delirium | | OR 2.35 p = 0.07 |
| Givens 2008 (1.2) | | | OR 2.10 p = 0.12 |

**Appendix Table D.14**
Raw extracted data on the remaining factors as a prognostic factor of functional outcome.

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Osnes 2004 (1.1) | Site of accident | Indoor | Ref |
| | | Outdoor | OR 0.44 (95% CI 0.27–0.72) p = s |
| | | In traffic | OR 0.49 (95% CI 0.15–1.66) p = ns |
| | | Unrecorded | OR 0.61 (95% CI 0.32–1.18) p = ns |
| | Trauma mechanism | HET (ref) | OR 1.24 (95% CI 0.59–2.60) p = ns |
| Koval 1998 (1.11) | Anesthesia type | General | na, p = ns |
| Koval 1998 (1.12) | | | na, p = ns |
| Koval 1998 (1.21) | | | na, p = ns |
| Koval 1998 (1.22) | | | na, p = ns |
| Moerman 2018 | Length of hospital stay | | B 0.26 beta 0.12 T 3.70 p = 0.000 |

**Appendix Table D.14** (*continued*)

| Study | Factor | Category | Coefficients, p-values |
|---|---|---|---|
| Savino 2013 | Early rehabilitation | | OR 2.38 (95% CI 0.92–6.16) p = ns |
| Gumieiro 2013 | 225 kDa (homodimer pro-MMP 9) | | OR 1.03 (95% CI 0.94–1.12) p = 0.55 |
| Gumieiro 2013 | 72 kDa (pro-MMP 2) | | OR 1.21 (95% CI 1.03–1.43) p = 0.02 |
| Gumieiro 2013 | 92 kDa (pro-MMP 9) | | OR 0.97 (95% CI 0.90–1.04) p = 0.34 |
| Gumieiro 2013 | 130 kDa (pro-MMP 9 + NGAL) | | OR 0.98 (95% CI 0.92–1.05) p = 0.52 |
| Ingemarsson 2003 (1.11) | Peak expiratory flow | | na, p = ns |
| Ingemarsson 2003 (1.12) | | | na, p = ns |
| Ingemarsson 2003 (1.21) | | | na, p = ns |
| Ingemarsson 2003 (1.22) | | | na, p = ns |
| Iaboni 2017 | Potentially inappropriate medication (PIM) user | | Coef −0.371 Exp coef 0.690 SE coef 0.147 z −2.52 p > z 0.012 |
| Iaboni 2017 | Postoperative pain | | Coef −0.092 Exp coef 0.913 SE coef 0.028 z −3.32 pr > z 0.001 |
| Pajulammi 2015 | Urinary catheter removed during hospital stay | | OR 0.45 (95% CI 0.29–0.70) p = s |

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