Long-term clinical and socio-economic outcomes following wrist fracture: A systematic review and meta-analysis.

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Abstract

Purpose: To summarise and appraise evidence on the prognosis and long-term clinical and socio-economic outcomes following wrist fracture among adults aged 50 years and over.

Methods: Five databases (MEDLINE, EMBASE, AMED, CINAHL-P and PsycINFO) were comprehensively searched (supplemented by a grey-literature search) from inception till June 2021 for prospective/retrospective cohort studies of patients (≥50 years) with a history of wrist fracture and reporting long-term (≥6 months) outcomes. Peer study selection, data extraction and risk of bias assessment were conducted. A random effects meta-analysis was used to summarise estimates of pain and function outcomes.

Results: 78 studies (n=688,041 patients) were included. Patients report persistent moderate to severe pain (range: 7.5%-62%) and functional limitations (range: 5.5-78%) up to 12-months or later after wrist fracture. Mean Patient-Rated Wrist Evaluation (PRWE) score for pain and function (9 studies, n=1759 patients) was 15.23 (95%CI 12.77, 17.69) at 6-months to 13-years follow-up. Mean disabilities of the arm, shoulder and hand (DASH) score (9 studies, n=1346 patients) was 13.82 (95%CI 12.71, 14.93)(at 6- to 17-months follow-up. A 10-20% increase in healthcare encounters in the first 12-months after fracture was observed. Twelve prognostic factors were associated with poor long-term outcomes.

Conclusion: Evidence shows that a high proportion of people aged over 50 years with wrist fracture experience pain and functional limitation >6months after fracture. This is associated with increased healthcare costs, and reduced quality of life. Exploratory evidence was found for several candidate prognostic factors. Their predictive performance needs to be investigated further.

(PROSPERO: **CRD42018116478**).

Keywords: ***wrist fracture, long-term pain, functional limitation, healthcare utilisation, prognosis***

Mini Abstract

A comprehensive review of studies shows that patients with wrist fracture, aged over 50 years, experience pain and functional limitation long after fracture. This is associated with increased healthcare costs, and reduced quality of life. Understanding factors that predict poor outcomes is important for future healthcare policy and planning.

Introduction

Wrist fractures account for 25% of all fractures among adults aged 50 and over [1-4] and are one of the most common reasons for attending emergency departments, with fragility fractures in total costing the NHS up to £4.4 billion/year [5-7]. Recent research has identified that, partly due to their sheer volume, non-hip and non-vertebral fractures result in significantly more healthcare resource use than hip fractures [8]. Many of these fractures occur in individuals who are functionally independent, active, and with good health-related quality of life [9-12]. However, following such injuries, and as a result of pain, disability, and a fear of falling, a transition to a less physically active lifestyle has been theorised, particularly in previously fit and active individuals. This inactivity results in reduced general strength, bone health, balance and coordination followed by general functional decline [13-16]. Studies investigating people aged 65 years and over have shown that having a wrist fracture increased the risk of functional decline by 50%, and in 15% this contributed to a progressive, clinically important functional decline at 3 years post fracture [9,11]. Furthermore, up to 34% of fragility wrist fractures occur in a working, 50 to 64-year-old age group [2] and long-term socio-economic consequences, such as impact on work, are unknown in this group.

In terms of patient-oriented clinical outcomes, studies have highlighted consequences of wrist fracture and have shown that, whilst many patients regain good wrist function [11,13, 17-18], 63% still have pain (11% severe), and 15% develop long-term hand/wrist disability [18, 19-22]. Wrist fractures have also been associated with complications including persistent neuropathies in the hand and complex regional pain syndrome [23-27]. Whilst the immediate consequences and impact of wrist fracture have been reported in the literature, the personal consequences and detrimental effect on activities of daily living (work, self-care, meal preparation, mobility) and quality of life in the long term are less well known.

In addition to understanding the extent and burden of long-term consequences of wrist fracture, it is important for clinicians and healthcare planners to know how best to identify subgroups of patients with wrist fracture who are likely to benefit from early, targeted intervention. A scoping review suggested a wide range of candidate prognostic factors in the short term but there is, as yet no consensus on key predictors that can identify patients with wrist fracture at high risk of long-term functional decline and increased healthcare needs [12-13, 28-35]. No systematic review has summarised long-term functional or healthcare-utilisation outcomes after wrist fracture or their related prognostic factors. The aim of this systematic review, therefore, was to summarize evidence from existing cohort studies regarding the long-term socio-economic (healthcare utilisation, work absence) and clinical outcomes (pain, functional disability, complications, quality of life, mortality) after wrist fracture. The review also aims to identify characteristics (prognostic factors) associated with long-term outcomes for patients with wrist fractures aged 50 years and over.

Methods

An a priori protocol was developed. The title and protocol for this systematic review and meta-analysis was registered on PROSPERO, ID: CRD42018116478. The review was conducted in consultation with a Patient and Public Involvement and Engagement (PPIE) group, including people with lived experience of a wrist fracture

and/or care of someone with a wrist fracture, referred to as public contributors. Public contributors informed the refining of the review question, specification of study eligibility criteria, outcomes, and interpretation of findings. This systematic review has been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Searching (information sources, search strategy) and selection of potentially eligible studies

Comprehensive literature searches for primary studies (prospective/retrospective longitudinal cohort studies) investigating long-term outcomes (≥6 months) of wrist fractures were conducted in five electronic databases including MEDLINE, EMBASE, AMED, CINAHL-P and PsycINFO. Electronic databases were searched initially from inception to June 2021 using a structured search strategy developed by an information specialist with input from the team (Supplementary file S1). Grey literature was sought (e.g., from The Networked Digital Library of Theses and Dissertations [NDLTD], Open Grey databases) and additional relevant publications were identified by screening reference lists of seminal articles identified as eligible for inclusion in the review. Studies were included if they reflected all presentations of wrist fracture in people over 50 years; studies including only those receiving a specific treatment (e.g., surgical interventions) or with a specific type/complexity of fracture were excluded. Search results were initially uploaded to the Rayyan review platform (https://www.rayyan.ai/). To establish agreement and shared understanding of eligibility criteria, the first stage (title screening) was initially piloted on a random selection of citations (n=200) by pairs of reviewers (OB, MB, ZP, CB, DvdW) and completed by single reviewers to exclude clearly irrelevant papers. Using Covidence (systematic review software: www.covidence.org), screening of potentially eligible abstracts and full texts was performed independently by two reviewers (OB, ZP, CB, NC, JF, DvdW), and disagreements were resolved via discussion. Detailed eligibility criteria are presented in Box 1.

	Inclusion criteria	**Exclusion criteria**
Study design	Retrospective or prospective longitudinal cohort studies	Randomised controlled/clinical trials, qualitative studies, case studies, and abstract-only reports from conference proceedings and without full results data
Participants/conditions of interest	Population: Adults, 50 years and older who have suffered fracture of the wrist.	* Studies among populations with 'red flag' diagnoses (e.g., suspected cancer) * Studies focusing on patients with high-impact trauma-related conditions. * Studies in specific populations: e.g., those with inflammatory conditions, or receiving specific fracture treatment. * Malunion & complications of prior treatments
Interventions/exposures	Different treatment options (conservative/surgical). Placebo, medications	Imaging studies; studies comparing surgical techniques (wire A vs B), bone grafts.
Comparisons / control groups	Placebo/ Usual care / Active treatment comparison groups.	

Outcomes of interest	* Clinical/ patient-oriented outcomes: pain, functional decline, complications, quality of life. * Socio-economic outcomes: healthcare utilisation, work absence. * Exclusive to long term outcome reports (>6 months)	
Settings	Any settings	

Data extraction and methodological appraisal

A customised data extraction instrument was developed for the review, and pilot-tested by the team. Data were extracted regarding study design; healthcare setting; characteristics of the study population; details (type, duration, intensity, frequency of sessions) of treatments received for wrist fracture; potential prognostic factors; outcome measures; follow-up time points; and follow-up rates (response and attrition rate at each time point). Concurrently with data extraction, risk of bias in the included studies was appraised using the Quality in Prognosis Studies' (QUIPS) tool [36]. The quality appraisal process included consideration of risk of bias in six domains related to representativeness of study population, follow-up and attrition, prognostic factor measurement (where applicable), outcome measurement, measurement and adjustment for confounding, and statistical analyses and data presentation. Similar to criteria (slightly amended) proposed by Grooten et al,[37], each study was subsequently assessed as having: overall low risk of bias if all domains were classified as having low risk of bias, or up to 2 having moderate risk of bias; high risk of bias if more than one domain was classified as having high risk of bias, or > 3 having moderate risk of bias; and moderate risk of bias for papers which met neither low or high risk of bias classifications. Data extraction and risk of bias appraisal for each included study were conducted by one reviewer (OB, ZP, CB, JF, DvdW) and checked for accuracy and consistency by a second reviewer (OB, MB). Conflicts regarding extracted data were resolved via discussion between reviewers.

Evidence synthesis & data analysis

Extracted data were coded and classified into meaningful groups where feasible. Data regarding associations of prognostic factors with outcome following wrist fracture were grouped as comorbidities, lifestyles, sex, age, and other. However, the definitions were too heterogeneous, both in terms of specific prognostic factors' definitions as well as outcomes examined, to provide enough relevant papers to enable quantitative pooling of the reported associations. For overall prognosis following wrist fracture, outcomes were classified into pain, function, quality of life, clinical socio-economic and complications categories. Where follow-up outcome summary was reported in terms of median (range or interquartile range), these were converted into means (standard deviation, SD) [38,39]. Many studies reported summary measures separately for different subgroups, such as sex or operative group, and these were merged via inverse variance pooling before entering a random effects meta-analysis of the means. We required there to be four or more studies reporting the same outcome for meta-analysis to be considered; the five outcomes which were reported with this frequency were: pain/function measured by the Patient-Rated Wrist Evaluation (PRWE), PRWE pain subscale, Disabilities of the Arm, Shoulder and Hand (DASH), SF 12/36 Physical Component Scale (PCS) and SF 12/36 Physical Component Scale (MCS). The Cochran Q statistics was derived to assess the presence of heterogeneity in studies reporting the same outcome at

follow-up. A small number of studies considered each outcome, hence we assumed heterogeneity up to a two-sided P-value of 0.05. Furthermore, the I^2 statistics were computed, representing the proportion of total variation in study results that is accounted for by heterogeneity. Random effects meta-analyses, based on the approach by DerSimonian and Laird [40], were employed. Sensitivity analyses were planned to explore the potential impact of risk of bias by repeating the analyses but excluding data from studies considered to be at high risk of bias, but this was not possible due to the limited amount of data available for meta-analysis.

As meta-analysis of long-term outcomes was only possible for a small subset of studies and not feasible for associations of prognostic factors with outcomes, a best-evidence synthesis was conducted to summarise evidence for patient and socio-economic outcomes. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) method as adapted for prognosis research was used to rate the overall quality of evidence across studies for overall prognosis (outcomes post-fracture) and prognostic factor-outcome associations. The modified GRADE approach used in this study considered four factors that may decrease confidence in the evidence: risk of bias, inconsistency, indirectness, and imprecision, partly based on recommendations proposed by Huguet et al. 2013, Lorio et al. 2015 and Foroutan et al. 2020 [41-43].

Briefly, evidence from more than one well-conducted cohort study with sufficient sample size and consistent findings was deemed to constitute high-quality evidence on overall prognosis or prognostic factors. Evidence was then downgraded for risk of bias when there were less than 2 cohorts at low risk of bias, or >50% of the cohorts were considered high risk of bias. Evidence was downgraded for inconsistency when studies showed clear clinical or methodological heterogeneity (e.g., retrospective design based on health records versus prospective bespoke cohort design; use of very different outcome measures or length of follow-up) and/or estimates of the prognostic factor association with the outcome vary in direction (for example, some effects appear protective whereas others show risk). Judgement on overall precision was based on the number of studies and sample size (downgraded if fewer than 2 cohorts and/or the majority of studies (>50% had sample size smaller than 200). Downgrading the quality of evidence for indirectness was considered appropriate when: the results considered for the outcome across included studies relates only to a subset of the population of interest (e.g., subsets of total sample with complex fractures).

Summary estimates of pain and function outcomes after wrist fracture were presented to describe overall prognosis, and individual study conclusions on the strength of association between individual prognostic factors and outcomes were noted. However, confidence in the quality of evidence for prognostic factors was not upgraded based on the strength of associations, given the wide heterogeneity in prognostic factor and outcome definitions, and data presentation. This meant meta-analysis was not feasible, and interpretation of the strength of associations was difficult. Finally, contributory evidence for each prognostic factor was assessed based on the phase of investigation (exploratory or confirmatory) [42]. Exploratory evidence was defined as generated from studies aiming to identify prognostic factors/pathways, or from studies that preliminarily tested associations between prognostic factors and patient-related outcomes. Evidence was considered as confirmatory when this emerged from cohort studies that tested prognostic factors based on a fully developed a priori hypothesis, previous empirical evidence for the prognostic factor(s) and/or conceptual framework.

Results

Study flow and characteristics of included studies

In total, 11,319 unique records were initially identified through database searching and other sources. After titles screening, 3249 potentially eligible abstracts were reviewed. Subsequently, 434 full texts were further examined on the basis of pre-specified inclusion and exclusion criteria. This led to 99 articles being subjected to data extraction and quality appraisal. A further 21 studies were excluded during data extraction and as a result, 78 full texts met the eligibility criteria and were included in the review (see Fig.1 for the study flow diagram).

Data were published between 1982 and 2021 from studies mostly conducted in European countries (51%). Six were conducted in the UK [8, 44-48]. Included studies were cohort studies, which were either retrospective (n=43) or prospective (n=35) in design. Many studies were based on data from health records using hospital/outpatient data (n=23), health insurance, or population-based samples (n=26). Only two studies were conducted in primary care settings. For studies reporting mean age (61 papers), mean age of participants across studies ranged between 52.6 (SD not reported) [49] and 80 years (SD 8.2) [50]. Sample size varied from <30 participants from one clinical cohort [51] to over 157,000 [52] from one general population study. The majority of included studies (~80%) did not conduct a formal assessment of prognostic factors that may be potentially associated with clinical or patient outcomes after wrist fracture. Summary characteristics of included studies are presented in Table 1 and detailed characteristics per study is presented in supplementary file S1.

Methodological appraisal of included studies

The results of risk of bias assessment for the 78 included studies are presented in Fig. 2-3. High risk of bias was considered present most frequently for study attrition (40%, 31 studies) and confounding (27%, 21 studies). Many studies lacked a description of the sampling frame, loss to follow-up, methods used to measure or account for confounding, and/or missing data, and were classified as having moderate/unclear risk of bias related to selection (41%), confounding (34%), and statistical analysis and presentation of data (41%). Outcome measures were mostly well defined and measured using valid and reliable instruments with up to 49 out of the 78 (62%) studies assessed as having low risk of bias in this domain.

Long-term outcomes

Table 2(a-c) presents a detailed summary of individual results for studies reporting pain, function and QoL outcomes after wrist fracture. Fig.4 shows forest plots of meta-analyses for pain, function and QoL outcomes. A summary of findings for each of the outcomes presented in this study, including socio-economic outcomes, is presented in Table 3.

Long-term outcomes of pain, function and health related Quality of Life (QoL)

Of the 78 included studies, 20 (n=4,300) presented data on long-term (6 months to 10 years) pain post wrist fracture [14, 46-49, 53-67]. Assessment of pain was patient reported for all studies, mostly involving the use of the PRWE assessing pain and functional limitation during activities of daily living or a visual analogue scale (VAS). Most studies reported that a proportion of patients still experienced moderate to severe wrist pain more than 6 months after the fracture, although estimates varied widely (range 7.5 to 62% [56, 60]). For example, after

a 10-year follow-up period, one UK cohort [46] reported that only 56% of wrist fracture patients were pain free and for those who had pain, patients experienced discomfort of at least 30 on a 0-100 VAS. Nine studies (n=1949 patients) [54, 55, 57-59, 62-64, 66] provided suitable data for meta-analysis, yielding a summary mean estimate for total PRWE (scale 0-100) of 15.23 (95%CI 12.77, 17.69) at 6 months to 13 years follow-up after wrist fracture. Five studies reported suitable data on the pain subscale of PRWE [55, 57, 59, 63, 67], with a pooled mean estimate 10.04 (95%CI 8.27, 11.81). About half of the studies were at high risk of bias. Estimates of prognosis varied widely between studies but most studies consistently reported significant proportion of patients experience long-term pain post wrist fracture. Overall confidence in the evidence for pain was therefore graded as moderate.

Twenty-four studies (n=4,574) presented data on functional outcomes using a range of measures (Gartland and Werley score, DASH score, PRWE, grip strength or the Barthel Index) at 6 months to 12 years follow-up [9, 14, 44, 46-49, 51, 53, 55-57, 59-63, 68-74]. As with pain outcomes, most of the studies (n=20) reported limitation in function at long-term follow-up (6 months or more after wrist fracture). Only one study [48], reported no clinically or statistically significant difference in function between patients with and without history of wrist fracture at one-year follow-up. Nine studies [9,14, 44, 46, 47, 56, 60, 71, 72] presented the proportion of participants with long-term functional decline, with results indicating between 5.5% -78% [60, 72] of patients with wrist fracture reported problems with activity performance, and functional limitations at 12 months post-fracture. On a scale of 0-100 (DASH score), summary estimate, mean functional limitation for patients with wrist fracture was estimated at 13.83 (95%CI 12.71, 14.93) based on 9 studies (n=1346) at 6 months to 17 months follow-up [49, 53, 57, 59, 60, 62, 68, 73, 74]. Eight out of the 24 studies contributing to evidence on functional limitation after wrist fracture were assessed as having high risk of bias. In addition, only a small sample of participants (as low as 5%) across included studies reported being without any functional disability after 1 year. Overall confidence in the evidence for functional limitation subsequent-to wrist fracture was assessed as moderate.

Sixteen studies (n=4,432) [46, 49, 55, 57, 59, 60, 63, 66, 69, 73-79] assessed the long-term impact of wrist fracture on health related QoL using the Short-Form (SF) 36 (n=4), SF 12 (n=4) and EuroQol-5D instruments (n=5) at 6 months to 12 years follow-up. Studies generally showed a gradual decline in QoL over 18 months after wrist fracture, though four studies [49, 55, 75, 78] found no statistically significant differences compared to people without a fracture. Mean summary estimate for the SF 12/36 Physical Component Scale (PCS) (n=2187, 8 studies [49, 55, 57, 59, 63, 70, 73, 74]) was 52.66 (47.85, 57.46) at 6 months to 1 year follow-up. Mean summary estimate for the SF 12/36 Mental Component Scale (PCS) (n=1387, 5 studies [55, 59, 73, 74, 77]) was 53.12 (95%CI 52.32, 53.91) at 6 months to 1 year follow-up.
Five studies out of 16 have an overall high risk of bias. Findings were consistent across primary studies and overall estimates of decline in QoL were low. Overall confidence in the evidence for decline in QoL following wrist fracture was assessed as moderate.

Complications and mortality
Twenty-eight studies (n=367,431) [46, 47, 51, 52, 55, 57, 58, 60, 61, 70, 73, 80-87, 88-96] reported data regarding mortality (13 studies); re-fracture/ fracture at other sites (11 studies); or complications after wrist fracture, such as Complex Regional Pain Syndrome (CRPS) (6 studies), nerve compression including carpal tunnel

syndrome/algodystrophy (7 studies), or other complications e.g., stiffness, tendon rupture or trigger finger (5 studies). Studies mostly presented data on proportions without measures of dispersion or indication of statistical significance. Two studies, providing data on severity of complications, reported that up to 38% (range 3-38% [46, 58]) of patients developed moderate to severe complications within the first 12 months post fracture. In one other study, incidence of subsequent osteoporotic fractures of the hip and other sites was significantly increased in the first year following wrist fracture for patients aged 60 years and over with the hazard ratio estimated at 3.45 (95% CI 2.59, 4.61) [57].

Six studies [80, 81, 84, 85, 91, 94] reported that up to 7% of patients died within 1 year of sustaining a wrist fracture (range: 1.3% - 7.42%; [84, 94]). Only three [83, 86, 87] out of 13 studies reported mortality compared to an age- and sex-standardised control group with two reporting non-significant differences. Standardised mortality rates, reported in two studies, were estimated at 0.75 (95% CI 0.50,1.08) and 1.8 (95% CI 0.5,2.7) [83, 87]. The third study [86] reported an increased risk of mortality (RR 1.5; 95% CI 1.2–1.9) in men (but not in women) in the first-year post-fracture. Impact of wrist fracture on mortality varied between studies showing inconsistency in terms of the direction of effect across studies and effect estimates were generally not statistically significant. Overall confidence in the evidence for risk of death and other complications in the first-year post wrist fracture was assessed as low.

Socio-economic outcomes

Eleven studies (n=82,346) [8, 75, 76, 86, 97-103] provided data on socio-economic outcomes. Data on healthcare utilisation (9 studies) showed wide variability between studies in terms of design and the type of data provided but reported up to 3 days of acute in-hospital stays [97], and up to 18 days of nursing home care [8]. Medication use (often osteoporosis medication) was reported to increase by 30-40% [98, 99], and the number of healthcare encounters by 10-20% [8, 99]. Total mean healthcare costs in the first year after the fracture (provided by 3 studies) were estimated at £1,680 in the USA in 2003 [100], £1,460 in Sweden in 2004 [76], and £1,151 in the Netherlands in 2008 [101]. The only study comparing healthcare costs to an age/sex-matched control group reported median incremental costs of £330 for women and £496 for men in Canada in 2006 [99]. One study, providing information on indirect costs due to work absence, was based on a very small cohort in the Netherlands (23 participants with complete data), reporting annual costs per patient of £2,060 (95% CI 652-7,328) in 2008 [101]. Though there was variability in estimated socio-economic costs of wrist fractures across study settings and countries, indicative costs were substantial, and this was consistent across studies. Only one study out of 11 was assessed as having high risk of bias. Overall confidence in the evidence for the long-term socio-economic implications of wrist fracture was assessed as moderate.

Prognostic factors

In total, 34 studies [9, 11, 45, 47, 50, ,52, 53, 61, 62, 64, 66-69, 73-75, 77, 80, 83-87, 91, 95, 104-111] explored possible association between some prognostic factors and poor outcome (functional disability, subsequent falls/fracture, QoL, and mortality) following wrist fracture (Table 4). Statistical analysis to estimate strength and significance of association with outcome, was reported for 12 distinctive prognostic factors. These included age, sex, presence of comorbidities, previous history of fragility fractures, body mass index (BMI), QoL at baseline,

level of pain and functional disability at baseline, fracture characteristics (degree of trauma/complicated fractures), surgical treatment for wrist fracture, emergency department visit and complications within 6 months after fracture, affected side (dominant), and sociodemographic factors (employment, income, living in urban/rural region). Given wide heterogeneity in terms of the methods used to measure prognostic factors, follow-up time points, types of outcome measures and data presentation, it was not possible to use meta-analysis to provide summary estimates of the strength of association. A summary of the evidence for each prognostic factor is presented in Table 4 using the adapted GRADE method as previously described. For both pain and function outcomes, factors significantly associated with long-term prognosis after wrist fracture included sex (being female), age (being 65 years and older), presence of comorbidities, previous history of fragility fractures, fracture characteristics (e.g., degree of trauma/complicated fractures); surgical treatment; and emergency department visit and complications within 6 months after fracture. A detailed summary of individual results of studies, presenting evidence of association between age and sex (most reported prognostic factors) and pain/function outcomes, are presented in supplementary file 1 (Table S1-S2). The affected side and other sociodemographic factors such as employment, income, living in urban/rural region were not significantly associated with poor outcome following wrist fracture. As none of the primary studies included in this review tested a fully developed a priori hypothesis and conceptual framework for any of the prognostic factors, overall evidence for each of the highlighted prognostic factors did not constitute high level confirmatory evidence and are therefore classed as exploratory in nature.

Discussion

Summary of main findings

This is the first systematic review of evidence for long-term patient-reported and socio-economic outcomes of wrist fracture in people aged 50 years and over. It also summarised evidence for prognostic factors associated with risk of poor outcome at 6 months and over. Although many patients with wrist fracture do improve in the short term, up to 62% and 78% report persistent pain or some functional limitations, respectively at one-year follow-up. Our findings show that pain, functional disability, and increased healthcare utilisation can persist over a longer term (up to 12 years) for many people who have experienced a wrist fracture. This has implications for clinical practice and healthcare planning.

Despite the high degree of heterogeneity in study design and analysis, certain generic prognostic factors have consistently emerged from available data. Being female and older than 65 years, the presence of comorbidities, and previous history of fragility fractures were all associated with risk of poor outcome (i.e., functional disability, subsequent falls and fracture, low QoL and risk of death) for more than 6 months after wrist fracture. Age and previous fragility fractures are well established risk factors for future fracture, and future fracture might contribute to poor outcome. However, there may be other mechanisms by which the presence of comorbidities and age affect healing and functional recovery post fracture. Other prognostic indicators identified by the review across multiple studies included high BMI (>30 kg/m^2), reduced QoL at baseline, and characteristics of the fracture (including degree of trauma/complicated fractures, surgical treatment, and complications within 6 months after fracture).

Findings of the current review are in line with previous studies, which studied prognostic factors for other specific outcomes (e.g., subsequent hip fractures [112] and complications [113]). Our study presented consistent evidence

for older age and being female, as predictors of poor outcome after wrist fracture. The current study did not find any association between socio-economic status, level of education or living in urban areas and a risk of poor outcome. Though based mostly on exploratory evidence, without confirmatory evidence of independent associations between these prognostic factors and the stated outcomes, the evidence for many of the identified prognostic factors is consistent across included studies.

Strengths and limitations of the study

This systematic review included 78 articles, over half of these being based on retrospective data from population and health insurance databases. It is the first to summarise overall long-term prognosis in terms of patient-reported and socio-economic outcomes after wrist fracture. We have identified some prognostic indicators of poor outcomes (e.g., being females, older, having comorbidities) but the contribution of these factors to predicting future outcome in individual patients has not yet been determined. Individual outcome prediction would require prognostic model studies, which was outside the scope of the present systematic review. Future high-quality cohorts are needed to replicate the analysis of candidate prognostic factors and provide confirmatory evidence of prognostic factors before they can be confidently and reliably used in the identification of high-risk subgroups or used in the development of prognostic models that will support individual risk prediction.

There was substantial heterogeneity in how prognostic factors were defined across studies. Therefore, we felt meta-analysis was not appropriate to pool the reported associations of identified prognostic factors with stated outcomes. Our narrative approach using the modified GRADE for prognosis research provides a transparent approach to summarising currently available evidence, taking into account risk of bias, consistency, directness, and precision of findings across studies. The list of prognostic factors identified from our review cannot be taken to be comprehensive nor exhaustive. For instance, psychosocial factors were conspicuously absent from our list of prognostic factors. This may be due to the exclusion of studies with less than 6 months of follow-up from this review, but evidence for the potential role of psychological and social factors is emerging. A recent study demonstrated that being retired, using opioids or antidepressants, having greater pain interference, and greater pain catastrophizing explained most variability in upper-extremity function in 364 people following fracture, with fear of movement and self-efficacy predicting limitations in physical function and general health [114].

Reporting bias is common in prognosis research, where non-significant associations, especially in studies with small sample size, tend not to be reported [115]. As part of this systematic review, a formal assessment of small study bias including the use of funnel plots would not have been informative as most studies included in the analyses had low sample sizes. However, in our QUIPS assessment, the signalling item looking at selective reporting was scored as negative in only 13% of all included studies. We have ensured a comprehensive search of the body of literature in order to identify relevant studies. The search strategy for this review included several bibliographic databases and our search strategy was comprehensive, having been informed by expert researchers and clinicians in the field and search for grey literature. The review also included all eligible studies irrespective of their methodological quality, whilst accounting for this in our syntheses.

Implications for future research and clinical practice

This systematic review is a necessary first step in addressing clinical and research questions regarding long-term prognosis subsequent to wrist fractures and potential prognostic factors associated with long-term outcome and has shown evidence for considerable pain and functional limitation persisting beyond 1 year following wrist fracture. It has also presented likely indicators of poor outcome, which in future, once their predictive performance has been established, may help in identifying and targeting individuals for early intervention.

Currently, approximately 78,000 people in the UK aged 50 and over experience a wrist fracture each year, accounting for 25% of all fragility fractures in this group. As the population ages, this figure is expected to rise [6,7]. Whilst immediate post-fracture care is well defined [116], guidelines lack the prognostic evidence necessary to guide post-fracture care over the longer term. As shown in a previous Cochrane review [117], current interventions and treatment pathways have often failed or at best resulted in modest improvement in patient-oriented outcomes in the short (≤6 months) and medium term (6-12 months). Early identification and targeted support for subgroups of wrist fracture population who may be at risk of persistent pain and disability may aid clinical management across healthcare settings. There is currently no consensus regarding the optimal pathway or treatment for these groups of patients despite the high costs, functional decline and reduced QoL following wrist fracture. Further research is warranted, particularly with regards to accurate prediction of the likely future course of wrist fracture and identification of high-risk groups.

Conclusions

This systematic review has summarised evidence for the long-term patient-reported and socio-economic outcomes of wrist fracture in people aged 50 years and over. Evidence from high quality, large, bespoke prospective cohorts is very limited. Although many patients with wrist fracture do improve in the short term, a high proportion of patients (>50%) report persistent pain or functional limitations at one-year follow-up or experience moderate to severe complications in the first year. Confirmatory evidence regarding candidate prognostic factors, potentially associated with poor functional recovery, may constitute a next step towards identification of vulnerable subgroups and the generation of protocols for wrist fracture rehabilitation aiming to prevent the health and socio-economic burden associated with wrist fracture in people aged 50 years and over.

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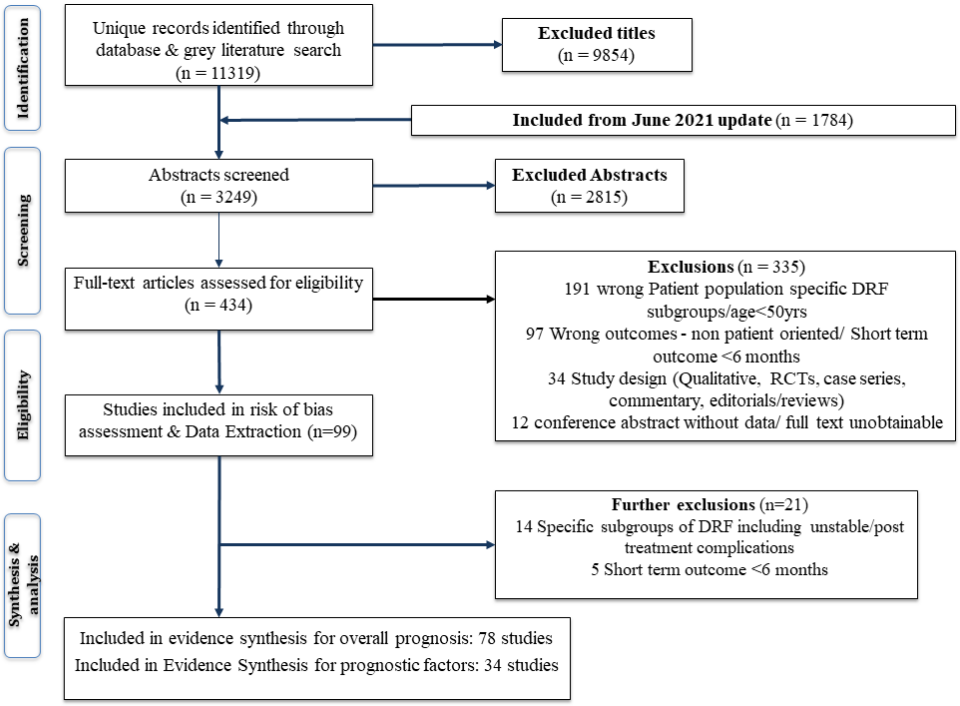


Figure 1

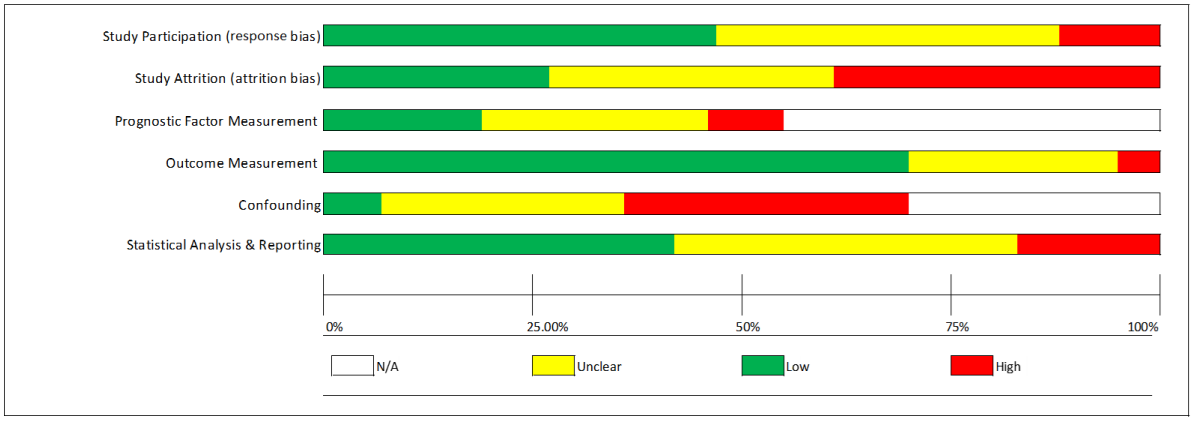


Figure 2

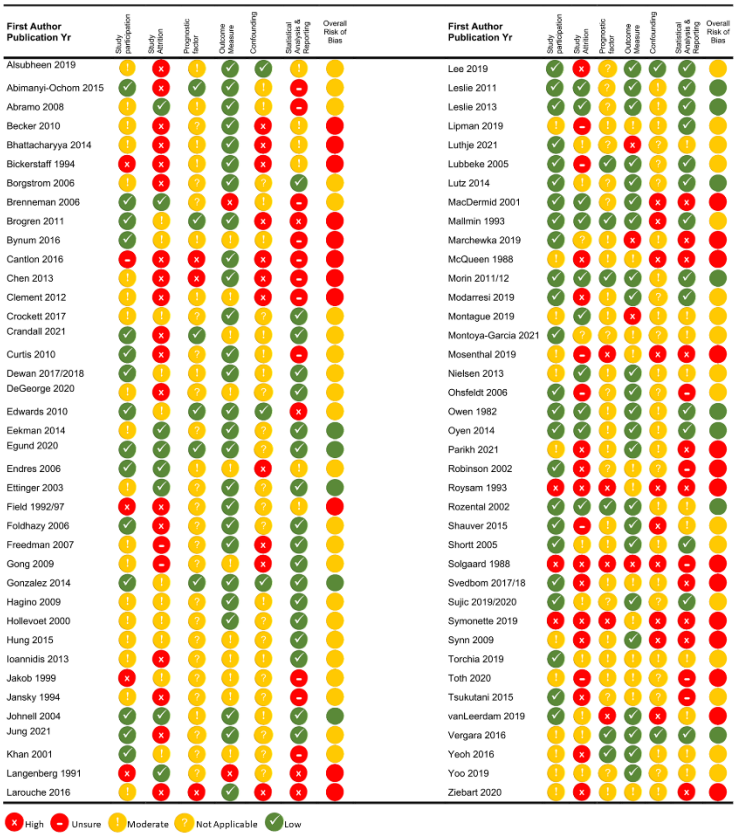
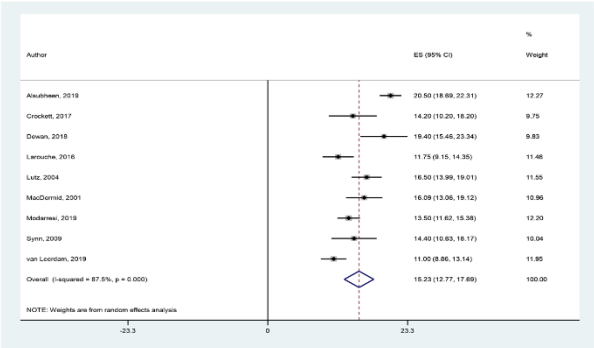
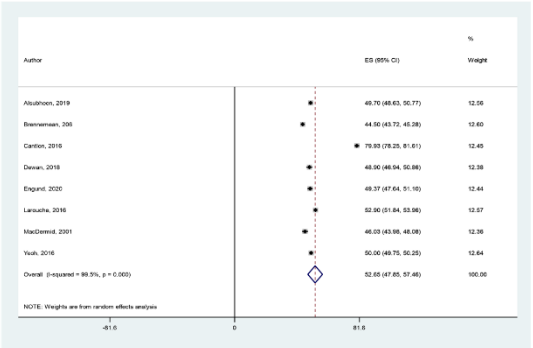


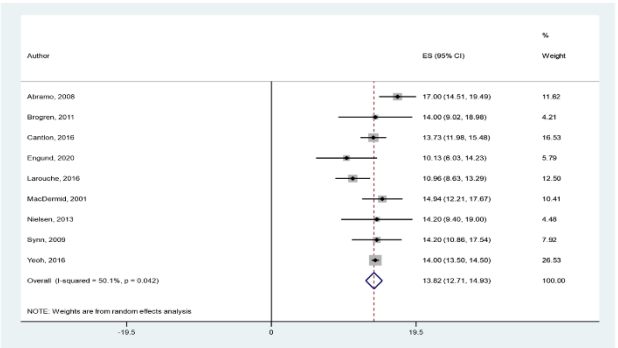
Figure 3



Pain - Total PRWE (9 studies)
Pooled estimate: Mean Total PRWE at follow-up 15.23 (95%CI 12.77, 17.69)
Heterogeneity chi-squared=63.77 (p<0.001); I-squared=87.5% (p<0.001)



QoL – SF 12/36 PCS (8 studies)
Pooled estimate: Mean SF12/36 PCS at follow-up 52.66 (95%CI 47.85, 57.46)
Heterogeneity chi-squared=16.03 (p<0.042); I-squared=50.1% (p<0.001)



Function – DASH 0-100 (9 studies)
Pooled estimate: Mean DASH at follow-up 13.82 (12.71, 14.93)
Heterogeneity chi-squared=16.03 (p<0.042); I-squared=50.1% (p<0.001)

Figure 4

Table 1: Summary characteristics of included studies

Summary Characteristics	No of studies	%
Continents		
Asia	8	10.2%
America	28	35.9%
Australia	2	2.5%
Europe	40	51.2%
Year of publication (>10yrs old)	29	50.9%
Study setting		
Population databases	7	12.3%
Health records (insurance)	9	15.8 %
Primary care	2	3.5%
Hospital/Rehabilitation/outpatient	18	31.6%
Secondary care	19	33.3%
Unclear/others	2	3.5%
Proportion Females*		
Reported	55	95.5%
Not reported	2	3.5%
Work status reported^	1	1.75%
Proportion with small sample sizes n<200	18	31.6%
Outcome measures (pain)~		
VAS	4	
PRWE	6	
Outcome measures (function)~		
DASH	10	

Table 2a: Summary of studies reporting pain outcomes after wrist fracture

First author, year of publication	Definition of outcome measure	Relevant sample size	Length of follow-up	Summary and dispersion statistics	Results details
Alsubheen, 2019	PRWE total (0/no pain or disability - 100/worst pain or disability)	479	1 year	Mean score (SD) at follow-up	With diabetes 25 (22); Without diabetes 12 (11)
Brogren, 2011	Pain VAS (0-100 NRS); reported separately for: at rest, light-activity and heavy-activity	49	1 year; 2-4 years (mean 3.3 years)	% with pain VAS>0 at follow-up; Median (IQR) pain VAS at follow-up	<u>1 year follow-up</u> Pain at rest: 18% with VAS>0; Median 10 Light-activity pain: 43% with VAS>0; Median 0 (IQR 1-24) Heavy-activity pain: 69% with VAS>0; Median 22 (IQR 0-80) <u>2-4 year follow-up</u> Pain at rest: 16% with VAS>0, Median=15 Light-activity pain: 25% with VAS>0; Median 0 (IQR 0-4) Heavy-activity pain: 41% with VAS>0; Median 0 (IQR 0-30)
Crockett, 2017	PRWE total (0/no pain or disability - 100/worst pain or disability)	63	1 year	Mean score (SD) at follow-up	Mean 14.2 (SD 16.2)
Cantlon, 2016	Pain VAS (0-10 NRS); reported separately for the following 3 groups: Group 1: normal radiograph at 6 week follow-up Group 2: unacceptable radiograph parameter Group 3: 2+ unacceptable radiograph parameters	Group 1: 303 Group 2: 63 Group 3: 16 Total 382	1 year	Mean (SD) VAS at follow-up	Group 1: Mean 1.54 (SD 2.08) Group 2: Mean 1.95 (SD 2.77) Group 3: Mean 1.18 (SD 2.40) Calculated overall: Mean 1.59 (SD 2.22)
Dewan, 2018	PRWE pain (0/no pain - 50/worst pain) PRWE total (0/no pain or disability - 100/worst pain or disability)	PRWE pain: n=69 PRWE total: n=65	6 months; 4 years	Mean (SD) PRWE at follow-up	<u>6-month follow-up</u> PRWE pain: Mean 11.7 (SD 8.9) PRWE total: Mean 19.4 (SD 16.2) <u>4 year follow-up</u> PRWE pain: Mean 6.3 (SD 9.6) PRWE total: Mean 9.03 (SD 15.2)
Field, 1992/1997	Pain VAS (0-100 NRS)	55	10 years	% with pain VAS=0 and pain VAS>30 at follow-up	31 (56%) reported pain VAS=0 3 (7%) reported pain VAS >30
Foldhazy, 2007	GOBC pain score Pain VAS (0-100 NRS); reported separately for: at rest, light-activity and heavy-activity	39 (elderly group)	11 years	Median (IQR) pain VAS at follow-up (estimated from a box plot)	Pain at rest: Median 3 (IQR 2-4) Light-activity pain: 5 (IQR 2-6) Heavy-activity pain: 5 (2-16)
Langenberg, 1991	Pain during activity	200	1 year	% with pain	n=15 (7.5%)

Larouche, 2016	PRWE pain (0/no pain - 50/worst pain) PRWE total (0/no pain or disability - 100/worst pain or disability); reported separately for operative and casting groups	129 (operative group 71 (55%); casting group 58)	1 year	Mean (SD) PRWE at follow-up	<u>Operative group</u>: PRWE pain: Mean 7.85 (SD 8.53) PRWE total: Mean 12.37 (SD 15.85) <u>Casting group:</u> PRWE pain: Mean 6.95 (SD 8.43) PRWE total: Mean 10.98 (SD 14.14) <u>Calculated overall:</u> PRWE pain: Mean 7.45 (SD 52.72) PRWE total: Mean 11.75 (SD 15.06)
Lutz, 2014	PRWE total (0/no pain or disability - 100/worst pain or disability); reported by operative/nonsurgical group	Operative group: n=129 Nonsurgical group: n=129	Operative group: Mean 11.3 years (SD 9.3 months); Nonsurgical Group: 14.9 years (SD 8.9 months) Calculated overall: Mean 13.1 years	Mean (SD) score at follow-up	Operative group: Mean 17 (SD 23) Nonsurgical group: Mean 16 (SD 18) Calculated overall: Mean 16.5 (SD 20.6)
MacDermid, 2001	PRWE pain (0/no pain - 50/worst pain) PRWE total (0/no pain or disability - 100/worst pain or disability); reported separately age, gender and secondary compensation status (SC Vs No SC)	Males 51-65 SC: n=2 Males 51-65 no SC: n=19 Females 51-65 SC: n=6 Females 51-65: no SC: n=45 Males >65 SC: n=0 Males >65 no SC: n=4 Females >65 SC: n=2 Females >65 no SC: n=44	1 year	Mean (SD) PRWE at follow-up	<u>PRWE pain</u> Males 51-65 SC: Mean 24 (SD not reported, assume 13 as for females) Males 51-65 no SC: Mean 11 (SD 8) Females 51-65 SC: Mean 30 (SD 13) Females 51-65: no SC: Mean 7 (SD 8) Males >65 SC: NA Males >65 no SC: Mean 2 (SD 2) Females >65 SC: Mean 23 (SD 27) Females >65 no SC: Mean 7 (SD 11) Calculated overall: Mean 9.13 (SD 11.15) <u>PRWE total</u> Males 51-65 SC: Mean 39 (SD not reported, assume 12 as for females) Males 51-65 no SC: Mean 19 (SD 15) Females 51-65 SC: Mean 54 (SD 12) Females 51-65: no SC: Mean 12 (SD 4) Males >65 SC: NA Males >65 no SC: n=Mean 5 (SD 5) Females >65 SC: Mean 34 (SD 43) Females >65 no SC: Mean 13 (SD 19) Calculated overall: Mean 16.09 (SD 17.06)

McQueen, 1988	Pain measured by analogue scale and dichotomised into mild, moderate and severe categories, and reported by radiographic groups: group 1: fractures unite with ≤10° dorsal angulation and ≤2mm radial shift; group 2: 12°-34° dorsal angulation and >2mm radial shift	Group 1: 17 Group 2: 13	5.08 years	n(%) complaining of mild, moderate, severe pain	Group 1: 1 (6%) mild pain; 1 (6%) moderate pain Group 2: 1 (8%) mild pain; 1 (8%) moderate pain; 3 (23%) severe pain
Modarresi, 2019	Patient-Rated Wrist Evaluation (PRWE) scale. The maximum score on this scale is 100, with a higher number indicating higher pain or functional limitation	n=318	3, 6 and 12 months	Mean (SD)	Baseline total PRWE mean=66.5 (SD 21.2) – Month 6 mean=19.8 (SD 18.2) – Year 1 mean=13.5 (SD 17.1)
Nielsen, 2013	Pain frequency and influence via 5-point verbal scale (never, seldom, sometimes, often, all the time)	37	1 year	n(%) reporting pain sometimes/often; n(%) reporting moderate/severe pain	Pain sometimes/often: n=23 (62%) Moderate/severe pain: n=22 (59%)
Roysam, 1993	Pain	170	1 year	n(%) reporting pain	n=67 (39%) *note this results is for 6-week follow-up however authors state that results at 6 months and 1 year were similar*
Solgaard, 1988	Pain (Gartland and Werley scoring): no pain/slight/occasional/restrictive pain; reported by type of fracture	Fracture type 1: 63 Fracture type 2: 50 Fracture type 3: 22 Fracture type 4: 19	3.5 years	Mean (SD)	Fracture type 1: Mean 0.8 (SD 1.2) Fracture type 2: Mean 1.3 (SD 1.6) Fracture type 3: Mean 1.4 (SD 1.5) Fracture type 4: Mean 1.5 (SD 1.6) Overall calculated: Mean 1.13 (SD 1.45)
Synn, 2009	PRWE total (0/no pain or disability - 100/worst pain or disability); reported by radiographic displacement	Nondisplaced: n=27 Displaced: n=26	Mean 17 months	Mean (SD) score at follow-up	Nondisplaced: Mean 12.8 (12.9) Displaced: Mean 16.0 (SD 15.1) Calculated overall: Mean 14.4 (SD 14.0)
Symonette 2019	PRWE - threshold 25 considered poor	190	1 year		PRWE 1 year after injury (good/poor) (%) overall 83/17; 84.4/15.6 for non-surgical; 79.1/20.9 for surgical (n=44 treated surgically, non-significant difference)
Van Leerdam, 2019	PRWE total 1-100	272	3rs 10mo	mean (SD)	The mean PRWE score was 11 (SD 18, range 0–96).
Ziebart,2020	pain scale of PRWE	1508	2 yrs	mean (se)	baseline 29.7/50 (0.5); mo 6 12.7 (0.5); yr 1 9.7 (0.5); yr 2 7.6 (0.6)

Table 2b Summary of studies reporting function outcomes after wrist fracture

First author, year of publication	Definition of outcome measure	Relevant sample size	Length of follow-up	Summary and dispersion statistics	Results details
Alsubheen 2019	Grip strength (assessed using NeK DIGIT-Grip device using a standard protocol with established reliability)	550	1 year	Mean score (SD) at follow-up	With diabetes 24 (10) Without diabetes 24 (10)
Abramo, 2008	DASH (0/no disability - 100/worst disability); Quick DASH; reported for osteoporotic age group	248	1 year	Mean score (SD) at follow-up	DASH: Mean 17 (SD 20) Quick DASH: Mean 18 (21)
Bhattacharyy, 2014	ADL; reported by number of instability markers (≤3/>3) and by treatment group (immobilisation, manipulation and surgery)	Instability markers ≤3 and immobilisation: n=82; Instability markers ≤3 and manipulation: n=23; Instability markers ≤3 and surgery: n=14; Instability markers>3 and immobilisation: n=18; Instability markers>3 and manipulation: n=38; Instability markers>3 and surgery: n=29	n(%) with poor outcome at follow-up	Instability markers ≤3 and immobilisation: 4 (5%) Instability markers ≤3 and manipulation: 4 (17%) Instability markers ≤3 and surgery: 3 (21%) Instability markers>3 and immobilisation: n=5 (28%) Instability markers>3 and manipulation: 16 (42%) Instability markers>3 and surgery: 6 (21%) Calculated overall: 38 (18%)	
Brogren, 2011	DASH (0/no disability - 100/worst disability)	49	1 year; 2-4 years (mean 3.3 years)	Median (IQR) DASH at follow-up	1 year follow-up: Median: 14 (IQR 3-27) 2-4-year follow-up: Median: 8 (2-22)
Cantlon, 2016	DASH (0/no disability - 100/worst disability) Reported by radiographic alignment: group 1 (normal), group 2 (1 abnormal measurement), group 3 (2+ abnormal measurements)	Group 1: 303 Group 2: 63 Group 3: 16 Total 382	1 year	Mean (SD) DASH at follow-up	Group 1: Mean 12.89 (15.96) Group 2: Mean 18.17 (SD 22.73) Group 3: Mean 12.12 (SD 18.49) Calculated overall: Mean 13.73 (SD 17.42)
Dewan, 2018	PRWE disability (0/no disability - 50/worst disability) RAPA (can you include worst/best score range) MFES (0/not confident at all - 140/completely confident)	PRWE function: 66 RAPA: 67 MFES: 70	6 months; 4 years	Mean (SD) PRWE at follow-up	<u>6 month follow-up</u> PRWE function: Mean 7.6 (SD 8.4) RAPA: Mean 7.1 (2.0) MFES: Mean 9.8 (SD 0.5) <u>4 year follow-up</u> PRWE function: Mean 3.0 (SD 6.2) RAPA: 6.7 (2.3) MFES: Mean 9.7 (SD 0.9)
Edwards, 2010	Functional decline: presence/absence of a clinically important functional decline	268	Mean 6.3 years (range 1-9.5)	n(%) with functional decline at follow-up	41 (15%)
Egund, 2020	DASH : dichotomized DASH scores good (< 15) or poor (≥15)	133	1 year	Number, mean, median, IQR	No displacement <65 year: n=65 5, 2 (0;7) No displacement >=65 years: n= 17, 14, 10 (1;22) Displacement < 65 years: n= 5, 23,38 (1;39) Displacement >=65 years: n=10, 31, 18 (1; 73)
Field 1992/1997	Overall Gartland and Werley score (can you include worst/best score range)	55	5 weeks; 12 weeks; 10 years	% with excellent/good score at follow-up	<u>5 week follow-up</u> Excellent/good score: 12 (22%) <u>12 week follow-up</u> Excellent/good score: 49 (89%) <u>10 year follow-up</u> Excellent/good score: 47 (85%)
Foldhazy, 2007	Function VAS (0-100 NRS); reported separately for: light-activity and heavy-activity GOBC function score	39 (function VAS elderly group) 29 (GOBC score elderly group without contralateral wrist fracture)	11 years	Function VAS: median (IQR) at follow-up (estimated from a box plot); elderly group GOBC score: % reporting excellent/good at follow-up; elderly	<u>Function VAS</u> Light-activity function: 4 (IQR 2-7) Heavy-activity function: 6 (4-34) <u>GOBC score</u> Elderly group: 21 (72%) reported excellent/good outcome Total group: 52 (79%) reported excellent/good outcome

				and total group	
Gonzalez, 2014	Quick DASH (0/no disability - 100/worst disability) Barthell index (0/totally dependent - 100/completely independent)	Males 106 Females 854	6 months	Mean change between baseline and 6 months	Quick DASH Males: -13.46 (2.23) Females: -22.31 (0.78) Barthel index Males: -3.53 (1.45) Females: -4.71 (0.52)
Hollevoet, 2000	Gartland and Werley	27	Mean 23 months (range 12-69)	Mean (range) score	Mean 2.6 (range 0-8)
Hung, 2015	Quick DASH (0/no disability - 100/worst disability); reported by locking plate fixation/immobilisation	Locking plate fixation: n=26 Immobilisation: n=31	Mean 1 year	Median score at follow-up	Locking plate fixation: Mean 4.5 Immobilisation: Mean 13.6 Calculated overall: Mean 9.45
Jakob, 1999	Subjective parameter - % reporting results as very good/good, unsatisfied and moderately satisfied	102	Mean 8 years	% in each group	Very good/good: 82% Moderately satisfied: 15% Unsatisfied: 3%
Jansky, 1994	Clinical measure (unspecified): good/moderate/poor	361	Mean 10.5	% in each group	Good: 69.6% Moderate: 24.9% Poor: 5.5%
Langenberg, 1991	Loss of strength (self-reported) Functional results Overall perceived recovery	200	1 year	Loss of strength at follow-up: n(%) Functional result: n(%) good/very good Overall perceived recovery: n(%) very good/good/moderate/poor	Loss of strength: 23 (11.5%) Functional result (good/very good): 167 (83.5%) Overall perceived recovery: very good n=91 (45.5%); good n=96 (48%); moderate n=13 (6.5%); poor: 0
Larouche, 2016	DASH (0/no disability - 100/worst disability); reported separately for operative and casting groups	129 (operative group 71 (55%); casting group 58)	1 year	Mean (SD) DASH at follow-up	Operative group: Mean 10.90 (SD 14.79) Casting group: Mean 11.03 (SD 11.93) Calculated overall: Mean 10.96 (SD 13.53)
MacDermid, 2001	DASH (0/no disability - 100/worst disability); reported separately age, gender and secondary compensation status (SC Vs No SC)	Males 51-65 SC: n=2 Males 51-65 no SC: n=19 Females 51-65 SC: n=6 Females 51-65: no SC: n=45 Males >65 SC: n=0 Males >65 no SC: n=4 Females >65 SC: n=2 Females >65 no SC: n=44	1 year	Mean (SD) DASH at follow-up	Males 51-65 SC: Mean 21 (SD not reported, assume 7 as for females) Males 51-65 no SC: Mean 14 (SD 12) Females 51-65 SC: Mean 45 (SD 7) Females 51-65: no SC: Mean 11 (SD 13) Males >65 SC: NA Males >65 no SC: Mean 4 (SD 2) Females >65 SC: Not reported (exclude from calculated overall) Females >65 no SC: Mean 16 (SD 16) Calculated overall: Mean 14.94 (SD 15.36)
McQueen, 1988	Activities of daily living (e.g. lifting weights, turning keys, using scissors etc); reported by radiographic groups: group 1: fractures unite with ≤10° dorsal angulation and ≤2mm radial shift; group 2: 12°-34° dorsal angulation and >2mm radial shift	Group 1: 17 Group 2: 13	5.08 years	n(%) with or without difficulty	Group 1: 1 (6%) with difficulty Group 2: 5 (38%) with difficulty Calculated overall: 6 (20%). NB: Counts: 7 out of 30 had difficulty with ADL, 2 in good anatomy grp, 5 in mal-union grp
Nielsen, 2013	DASH; categorised into no disability (0), minimal (1-20), mild (21-40), moderate (41-60) and severe disability (81-100) COMP (performance of tasks, activities, and occupations)	37	1 year	Median (range)DASF score at follow-up; n(%) in mild-severe DASH categories at follow-up; COMP: Median (Range) score at follow-up; COMP: n(%) reporting performance problems at follow-up	DASH Median (range): 14.2 (0-9.5) DASH Mild/moderate disability: n=13 (35%) COMP Median (range): 8.6 (5.8-10) COMP performance problems: n=29 (78%)
Roysam, 1993	Grip strength; reported by DRUJ involvement	81 (with DRUJ involvement); 89 (without DRUJ involvement)	1 year	Mean score	DRUJ involvement: Mean =2.3 No DRUJ involvement: Mean=0.36 Calculated overall: Mean=1.28

Synn, 2009	DASH (0/no disability - 100/worst disability); Gartland and Werley; MASS07; reported by radiographic displacement	Nondisplaced: n=27 Displaced: n=26	Mean 17 months	Mean (SD) score at follow-up	DASH Nondisplaced: Mean 14.3 (SD 13.1) Displaced: Mean 14.0 (SD 11.9) Calculated overall: Mean 14.2 (SD 12.4) Gartland and Werley Nondisplaced: Mean 3.1 (SD 3.5) Displaced: Mean 4.0 (SD 2.8) Calculated overall: Mean 3.5 (SD 3.2) MASS07 Nondisplaced: Mean 5.8 (SD 9.0) Displaced: Mean 7.6 (SD 10.2) Calculated overall: Mean 6.7 (SD 9.6)
Yeoh, 2016	DASH (0/no disability - 100/worst disability); reported by CES-D score at baseline (≥16/<16)	CES-D ≥16 at baseline: 25% (i.e. n=57) CES-D <16 at baseline: 171	1 year	Mean (SD) score at follow-up	CES-D ≥16 at baseline: Mean 20 (SD 2.3) CES-D <16 at baseline: Mean 12 (SD 1.3) Calculated overall: Mean 14 (SD 3.82)

Table 2c: Summary of studies reporting long term (>6months) Quality of Life (QoL) outcomes after wrist fracture

First author, year of publication	Definition of outcome measure	Relevant sample size	Length of follow-up	Summary and dispersion statistics	Results details
Alsubheen, 2019	SF-12 PCS, SF-12 MCS; normalized to the general US population and transformed to have mean 50 and SD 10 (lower score=reduced quality of life)	n = 289	1 year	Mean score (SD) at follow-up	With diabetes 45 (12) Without diabetes 50 (9)
Abimanyi-Ochom, 2015	EuroQol (EQ-5D): utility score (anchor points: "perfect health"=1, "death"=0)	n=308	1 year, 1.5 years	Mean score (SD) at follow-up % from baseline to follow-up	1 year follow-up Mean score: 0.88 (0.18) % change from baseline: -2.2% 1.5 years follow up Mean score:0.90 (0.17) % change from baseline: 0%
Borgstrom, 2006	EuroQol (EQ-5D): utility score (anchor points: "perfect health"=1, "death"=0)	n=276	1 year	Mean score (95% CI) at follow-up	0.86 (0.84, 0.88)
Brenneman, 2006	SF-12 PCS, SF-12 MCS; normalized to the general US population and transformed mean of 50 and SD 10 (lower score=reduced quality of life)	n=835	Approx. 1 year	Mean score (SD) at follow-up	SF-12 PCS: Mean 44.5 (SD 11.5) SF-12 MCS: Mean 52.6 (SD 8.7)
Cantlon, 2016	SF36 (0/worst QoL - 100/best QoL)	Group 1: 303 Group 2: 63 Group 3: 16 Total: 382	1 year	Mean score (SD) at follow-up	Group 1: Mean 80.44 (SD 15.42) Group 2: Mean 77.36 (SD 21.40) Group 3: Mean 80.45 (SD 21.25) Calculated overall: Mean 79.93 (SD 16.80)
Dewan, 2018	SF-12 PCS (0/worst QoL - 100/best QoL); SF-12 MCS (0/worst QoL - 100/best QoL)	SF-12 PCS n=69; SF-12 MCS n=69	6 months; 4 years	Mean (SD) score at follow-up	6 month follow-up SF-12 PCS Mean=48.9 (SD 8.3) SF-12 MCS Mean=55.2 (SD 6.3) 4 year follow-up SF-12 PCS Mean=50.1 (8.3) SF-12 MCS Mean=51.9 (SD 8.8)
Egund, 2020	SF-36 (Physical component scale) SF-36 (Mental component scale)	n=133	1 year	Mean score (SD) min-max	<65 years 52 (8); 28-62 >=65 years 42 (12); 15-57 <65 years 52(8) 14-65 >= 65 years 50 (12); 27-65
Gonzalez, 2014/2016	SF-12 PCS (0/worst QoL - 100/best QoL); SF-12 MCS (0/worst QoL - 100/best QoL); reported by gender	Males 106 Females 854	6 months	Mean change between baseline and 6 months	SF-12 PCS Males: -4.84 (1.07) Females: -7.79 (0.38) SF-12 MCS

					Males: -0.71 (1.11) Females: -2.32 (0.40)
Hagino, 2009	EuroQol (EQ-5D): utility score (anchor points: "perfect health"=1, "death"=0)	n=50	6 months, 1 year	Mean (SD) score at follow-up Mean change (SD) from baseline to follow-up	6-month follow-up Mean score: 0.873 (SD 0.15) Mean change from baseline: -5.9 (SD 18.2) 1 year follow up Mean score: 0.881 (SD 0.148) Mean change from baseline: -5.8 (SD 15.9)
Larouche, 2016	SF36 PCS (0/worst QoL - 100/best QoL); reported separately for operative and casting groups	129 (operative group 71 (55%); casting group 58)	1 year	Mean score (SD) at follow-up	Operative group: Mean 53.64 (SD 6.14) Casting group: Mean 51.99 (6.13) Calculated overall: Mean 52.90 (SD 6.17)
Lee 2019	Mortaltiy ratio	n=13,164	57.8 months (mean)	Hazard ratio (compatred with no fracture)	Unadjusted: 1.03 (0.97–1.10) Adjusted: 1.04 (0.98–1.11) Males Unadjusted: 1.17 (1.04–1.33) Adjusted: 1.19 (1.05–1.35) Females Unadjusted: 0.99 (0.92–1.07) Adjsuted: 0.99 (0.92–1.07) 50-59 years Unadjsuted: 1.18 (0.95–1.47) Adjusted: 1.17 (0.94–1.45) 60-69 Unadjusted: 1.01 (0.88–1.17) Adjusted: 1.00 (0.87–1.16) >70 Unadjusted: 1.03 (0.95–1.11) Adjusted: 1.03 (0.96–1.11) Adjusted for: age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, and stroke histories

MacDermid, 2001	SF36 PCS (0/worst QoL - 100/best QoL); SF36 MCS (0/worst QoL - 100/best QoL) reported separately age, gender and secondary compensation status (SC Vs No SC)	Males 51-65 SC: n=2 Males 51-65 no SC: n=19 Females 51-65 SC: n=6 Females 51-65: no SC: n=45 Males >65 SC: n=0 Males >65 no SC: n=4 Females >65 SC: n=2 Females >65 no SC: n=44	1 year	Mean score (SD) at follow-up	Males 51-65 SC: PCS Mean 38 (SD not reported, assume 12 as for females); MCS Mean 51 (SD not reported, assume 12 as for females Males 51-65 no SC: PCS Mean 47 (SD 9); MCS Mean 51 (SD 12) Females 51-65 SC: PCS Mean 33 (SD 12); MCS Mean 47 (SD 12) Females 51-65: no SC: PCS Mean 49 (SD 11); MCS Mean 55 (SD 6) Males >65 SC: PCS, MCS NA Males >65 no SC: PCS Mean 54 (SD 4); MCS Mean 58 (SD 3) Females >65 SC: PCS, MCS Not reported (exclude from calculated overall) Females >65 no SC: PCS Mean 44 (SD 12); MCS Mean 53 (SD 11) Calculated overall: PCS Mean 46.03 (SD 11.55) Calculated overall: MCS Mean 53.27 (SD 9.54)
Nielsen, 2013	SF-36 general health	n=37	1 year	n (%) reporting good/very good/excellent health at follow-up	33 (89%)
Tsukutani, 2015	Death, impairment of ambulatory ability, occurrence of new fracture, osteoporosis therapy	n=141	1 year	n at follow-up	Death: 0 Impairment of ambulatory ability: 2 Subsequent fracture (hip/vertebral/NHNV): 9 Osteoporosis therapy: 6
Van Leerdam, 2019	EQ5D EQVAS	272	3yrs 10 mo	mean score (SD)	The mean EQ-5D score after follow-up was 0.88 (0.2). 80(15)
Yeoh, 2016	SF36 PCS (0/worst QoL - 100/best QoL) SF36 MCS (0/worst QoL - 100/best QoL) reported by CES-D score at baseline (≥16/<16)	CES-D ≥16 at baseline: 25% (i.e. n=57) CES-D <16 at baseline: 171	1 year	Mean (SD) score at follow-up	<u>SF-36 PCS</u> CES-D ≥16 at baseline: Mean 47 (SD 1.3) CES-D <16 at baseline: Mean 51 (SD 0.74) Calculated overall: Mean 50 (SD 1.96) <u>SF-36 MCS</u> CES-D ≥16 at baseline: Mean 48 (SD 1.2) CES-D <16 at baseline: Mean 55 (0.71) Calculated overall: Mean 53.25 (SD 3.16)

Table 3: Summary of findings per outcome

	Evidence base No of studies; relevant sample size	Magnitude of effects	Quality of studies (risk of bias) for this outcome	Inconsistency	*Indirectness	Imprecision	Strength of evidence (Modified Grade)
Pain (overall)	20 studies (10 prospective, 13 retrospective; n=4 300)	Meta-analysis: 9 studies (n=1949 patients) Mean PRWE 15.23 (95%CI 12.77, 17.69) at 6 months -13 years follow-up after wrist fracture.	✖ 10 studies have overall high risk of bias. 4 had a low risk of bias	✓ Consistently studies reported few participants (as low as 7%) who are pain free after 1 year	✓	✓	⊕⊕⊕◯ Moderate
Function	24 studies (16 prospective, 8 retrospective; n = 4574)	Meta-analysis: 9 studies (n= 1346 patients) Mean DASH score 13.83 (95%CI 12.71, 14.93) at 6 months to 17 months follow-up	✓ 8 studies have overall high risk of bias. 3 had overall low risk of bias	✓ Consistently studies reported few participants (as low as 5%) without any functional disability after 1 year	✓	✓	⊕⊕⊕◯ Moderate
QoL	16 studies (13 prospective, 3 retrospective; n=4432)	Meta-analysis: 8 studies (n=2187 patients) Mean SF 12/36 PCS 52.66 (47.85, 57.46) at 6 months to 1 year follow-up. 5 studies (n= 1387 patients) Mean SF 12/36 MCS 53.12 (95%CI 52.32, 53.91) at 6 months to 1-year follow-up.	✖ 5 studies have overall high risk of bias. 3 had overall low risk of bias	✓ fairly similar outcome measures, study designs and direction of results	✓	✓	⊕⊕⊕◯ Moderate
Complications and mortality	28 studies (n=367 431). No meta-analysis could be conducted	6 studies Average proportion of patients who died within one year of sustaining a wrist fracture (~7%; Range: 1.3% - 7.42%). Standardised mortality rates range 0.75 (95% CI 0.50-1.08) to 1.8 (95% CI 0.5-2.7).	✓ 10 studies have overall high risk of bias. 6 had overall low risk of bias	✖ Inconsistencies across studies in direction of effect, and outcome measures	✓	✓	⊕⊕◯◯ Low
Socio-economic factors	Eleven studies (2 prospective, 9 retrospective; n=82346) No meta-analysis could be conducted.	Variable: Total mean healthcare costs in the first year after the fracture (average of 3 studies from USA, Sweden & Netherlands) estimated at £1430. Indirect costs due to work absence (1 study, n=23 patients) estimated at £2,060 (95% CI 652-7,328) per patient per annum.	✓ Only 1 study have overall high risk of bias. 3 had overall low risk of bias	✖ Evidence limited to Europe and 1 USA study Variable across health settings	✓	✓	⊕⊕⊕◯ Moderate

*Comments on generalisability: outcome results represented whole cohorts in most studies. Overall prognosis for outcomes were not downgraded in relation to in directedness as the inclusion of all wrist fracture was required as part of review's eligibility criteria.

Conceptualization: Quality of evidence across studies

⊕⊕⊕⊕ High = Further research is very unlikely to change our confidence in the estimate of effect.

⊕⊕⊕◯ Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

⊕⊕◯◯ Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

⊕◯◯◯ Very low = Any estimate of effect is very uncertain

Table 4: Summary of findings for prognostic factors

Outcome: Function

Prognostic factors	Number of studies/references	Relevant sample size	Phase of investigation [design & analysis]	∞effect size	risk of bias/ effect of risk of bias on GRADE	Inconsistency	Imprecision	Overall quality
Age>65 years	N=13: [9, 11, 50, 62, 64, 66-68, 70, 73, 74, 84, 105	7454	Mix of exploratory evidence identifying and preliminary testing to confirm associations	+	✓ 🟢🟢🟢🟡🟡🟡🟡🟡🟡🔴🔴🔴	✓	✓	⊕⊕⊕◯ Moderate
Gender (female)	N=12: [2,11, 50, 62, 64, 66-68, 70, 73, 99, 105]	19258	Mix of exploratory evidence identifying and preliminary testing to confirm associations	+	✓ 🟢🟢🟢🟡🟡🟡🟡🟡🔴🔴🔴	✓	✓	⊕⊕⊕◯ Moderate
presence of comorbidities	N=3: [9, 11, 73]	1176	Exploratory evidence from phase 2 studies testing to confirm associations		× 🟢🟡🟡	✓	✓	⊕⊕⊕◯ Moderate
previous history of fragility fractures	N=2: [9, 11]	948	Exploratory evidence from phase 2 studies testing to confirm associations	+	× 🟢🟡	✓	✓	⊕⊕⊕◯ Moderate
high BMI	N=1: [9]	268	Only 1 exploratory evidence identifying and preliminary testing to confirm associations		× 🟡	?	?	⊕◯◯◯ Very Low
low QoL at baseline	N= 1: [107]	589	Only 1 exploratory evidence identifying and preliminary testing to confirm associations		× 🔴	?	?	⊕◯◯◯ Very Low
Fracture characteristics [degree of trauma/ complicated fractures]	N= 5: [9, 50, 53, 61, 70]	2098	Mix of exploratory evidence identifying and preliminary testing to confirm associations	+	× 🟢🟡🟡🔴🔴	×	✓	⊕⊕◯◯ Low
Surgical treatment	N=: 3: [11, 50, 73]	1575	Mix of exploratory evidence identifying and preliminary testing to confirm associations		× 🟢🟡🟡	×	✓	⊕⊕◯◯ Low
Emergency department visit & complications within 6 months after fracture	N= 4: [45, 47, 68, 73]	780	Mostly exploratory evidence identifying association and preliminary testing to confirm associations		× 🟡🟡🔴🔴	×	✓	⊕⊕◯◯ Low
affected side [dominant]	N= 3: [45, 68, 70]	1462	Mostly exploratory evidence identifying association and preliminary testing to confirm associations		× 🟢🟡🔴	×	✓	⊕⊕◯◯ Low
Sociodemographic factors [employment, income, living in urban/rural region]	N= 1: [11];	680	Only 1 exploratory evidence identifying and preliminary testing to confirm associations		× 🟢	?	?	⊕◯◯◯ Very Low

Outcome: QoL

Age>65 years	N=2 [75, 77]	1143	Mix of exploratory evidence identifying and preliminary testing to confirm associations		× 🟡🟡	✓	✓	⊕⊕⊕◯ Moderate
Gender female	N=2 [66, 75]	580	Exploratory evidence identifying associations. Only 1 preliminary testing to confirm associations C1		× 🟡🔴	?	?	⊕◯◯◯ Very Low
presence of comorbidities	N=1 [75]	308	Only 1 exploratory evidence identifying associations		× 🟡	?	?	⊕◯◯◯ Very Low
previous history of fragility fractures	N=1 [75]	308	Only 1 exploratory evidence identifying associations		× 🟡	?	?	⊕◯◯◯ Very Low
high BMI	N=1 [75]	308	Only 1 exploratory evidence identifying associations		× 🟡	?	?	⊕◯◯◯ Very Low
low QoL at baseline	N= 1 [75]	308	Only 1 exploratory evidence identifying associations		× 🟡	?	?	⊕◯◯◯ Very Low
Sociodemographic factors [employment, income, living in urban/rural region]	N=1 [75]	308	Only 1 exploratory evidence identifying associations		× 🟡	?	?	⊕◯◯◯ Very Low

Outcome: Mortality							
Age>65 years	N=8 [80, 84-87, 91, 106, 108]	107575	Mix of exploratory evidence identifying and preliminary testing to confirm associations	+	✓ 🟢🟢🟢🟢🟡🟡🟡🔴	✓	✓	⊕⊕⊕⊕ High
Gender female	N=8 [45, 80, 85-87, 91, 106, 108]	105818	Mix of exploratory evidence identifying and preliminary testing to confirm associations	+	✓ 🟢🟢🟢🟢🟡🟡🔴🔴	✓	✓	⊕⊕⊕⊕ High
presence of comorbidities	N=4 [9, 80, 86, 106]	95746	Exploratory evidence mostly preliminary testing of associations	+	✓ 🟢🟢🟡🟡	×	✓	⊕⊕⊕◯ Moderate
Fracture characteristics [degree of trauma/complicated fractures]	N= 1 [83]	44	Only 1 exploratory evidence identifying associations		× 🔴	?	?	⊕◯◯◯ Very Low
Surgical treatment	N=1 [80]	81568	Only 1 exploratory evidence identifying and preliminary testing associations		× 🟡	?	?	⊕◯◯◯ Very Low
Outcome: Subsequent falls and fractures							
Age>65 years	N=6 [52, 55, 81, 82, 95, 104]	105,839	Mostly exploratory evidence identifying associations. Only 1 preliminary testing to confirm associations	+	× 🟡🟡🟡🔴🔴🔴	×	✓	⊕⊕◯◯ Low
Gender female	N=3 [55, 81, 82]	84622	Mostly exploratory evidence identifying associations. Only 1 preliminary testing to confirm associations		× 🟡🔴🔴	×	✓	⊕⊕◯◯ Low
previous history of fragility fractures	N=1 [55]	94	Only 1 exploratory evidence identifying and preliminary testing associations		× 🟡	?	?	⊕◯◯◯ Very Low
Fracture characteristics [degree of trauma/complicated fractures]	N= 1 [105]	394	Only 1 exploratory evidence identifying and preliminary testing associations		× 🟢	?	?	⊕◯◯◯ Very Low
Sociodemographic factors [employment, income, living in urban/rural region]	N= 1 [82]	9986	Only 1 exploratory evidence identifying and preliminary testing associations		× 🔴	?	?	⊕◯◯◯ Very Low

Conceptualization: Quality of evidence for prognostic factors

⊕⊕⊕⊕ High = We are very confident that the true prognosis (probability of future events) lies close to that of the estimate.

⊕⊕⊕◯ Moderate = We are moderately confident that the true prognosis (probability of future events) is likely to be close to the estimate, but there is a possibility that it is substantially different.

⊕⊕◯◯ Low = Our confidence in the estimate is limited: the true prognosis (probability of future events) may be substantially different from the estimate.

⊕◯◯◯ Very low = We have very little confidence in the estimate: the true prognosis (probability of future events) is likely to be substantially different from the estimate

🔴 a study with overall high risk of bias, 🟢 a study with overall low risk of bias 🟡 a study with overall moderate risk of bias

× domain downgraded due to serious limitations (or not present for moderate/large effect size, dose effect); ✓ domain evidence unchanged/upgraded as there was no serious limitation.**?** unclear, domain unrateable based on available information.
NB:
Indirectedness: evidence was not downgraded for any prognostic factor in this domain as we are satisfied that contributing studies presented information for relevant wrist fracture population and/or in comparison with other fractures or age-matched nonfracture population. As in table 3, generalisability and evidence non-selective wrist fracture samples was required as part of review's eligibility criteria.
∞ As no meta-analysis was conducted, this domain was not used to upgrade evidence but was indicated (+) only if moderate association is reported in two or more studies indicating that the relationship between the prognostic factor and respective outcome probably exists.

FILTER: Prognosis of wrist fracture Search Strategy

Sources: Prognosis – developed from McKibbon PDQ Evidence-based principles and practice book

MEDLINE (Ovid; run 16.11.18) Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily, and Versions(R) 1946 to November, 2018

1 exp Fractures, Bone/
2 fracture$.ti,ab,kw.
3 exp Wrist Joint/
4 Wrist Injuries/
5 Wrist/
6 (radius/ or ulna/ or forearm/ or forearm injuries/) and distal.ti,ab,kw.
7 (wrist or colles$1 or smith$).ti,ab,kw.
8 ((radius or radial or ulna$ or forearm$) adj5 distal).ti,ab,kw.
9 1 and (or/3-8)
10 (1 or 2) and (or/3-6)
11 Colles' Fracture/
12 ((wrist or colles$1 or smith$) adj5 fracture$).ti,ab,kw.
13 Ulna Fractures/ and distal.ti,ab,kw.
14 radius fracture/ and distal.ti,ab,kw.
15 ((radius or radial or ulna$ or forearm$) adj5 fracture$ adj5 distal).ti,ab,kw.
16 ((non-hip or nonhip) adj5 fracture$).ti,ab,kw.
17 or/9-16
18 prognosis/
19 exp cohort studies/
20 "natural history".ti,ab,kw.
21 cohort$.ti,ab,kw.
22 predict$.ti,ab,kw.
23 prognos$.ti,ab,kw.
24 course$.ti,ab,kw.
25 or/18-24
26 17 and 25
27 animals/ not humans/
28 26 not 27

Table 1: Characteristics of Included Studies - detailed

First Author, Year of publication	Country (where study was conducted)	Study design	Study setting	Sample size, age and gender distribution	Length of follow-up	Outcomes considered	Prognostic factors considered
Abimanyi-Ochom, 2015	Australia	Pro-cohort	Hospital /rehabilitation	n=308; Age: mean 66.6 (SD 10.3); 84% Females	4 months, 1 year, 1.5 years	EQ-5D-3L	Age, gender, previous fracture, hospitalisation, income, education,
Abramo, 2008	Sweden	Pro-cohort	Hospital/rehabilitation	n=518; Age: mean 60 (range 19-93); 77% Females	3 months, 1 year	DASH, QuickDASH	
Alsubheen 2019	Canada	prospective cohort study	tertiary care referral cente	n=479 (completing primary outcome measure); Age 55 +- 14 (18-87 y); 74.5% female	baseline, 3 months, 1 year	PWRE; SF-12; Grip strength was assessed using NeK DIGIT-Grip device; wrist and forearm range of movement	
Becker, 2010	USA	Pro-cohort	Health records (insurance)	n=20373; Age: mean 78.9 (SD 7.4); 87% Females	6 months	Acute and postacute inpatient stay; home health care	
Bhattachary, 2014	UK	Retro-cohort	Hospital/rehabilitation	n=207; Age: mean 60 (range 19-96); 78% Females	Unclear	ROM; ADL; Radiographic outcomes	
Bickerstaff, 1994	UK	Pro-cohort	Secondary care	n=270; Age: mean 65 years (estimated from authour data); 82% Females	6 months	Post traumatic algodystrophy	age, gender, fracture type, number of manipulations, type of anaesthesia
Borgstrom, 2006	Sweden	Pro-cohort	Hospital/rehabilitation	n=276; Age: mean 69.5 (range 50-92); 91% Females	4, 12 and 18 months	Healthcare utilisation (transfer to lon-term care institution, inpatient care, primary care visits, outpatient care, fracture related medication use)	
Brenneman, 2006	USA	Pro-cohort	Primary care	n=835; Age: mean 66.7 (SD 9.3); 100% Females	Approximately 1 year	SF-12 PCS, SF-12 MCS	
Brogren, 2011	Sweden	Pro-cohort	Secondary care	n=49; Age: mean 67 (SD 6); 100% Females	1 year; 2-4 years (mean 3.3 years)	Pain VAS; Disability (DASH); Grip strength	
Bynum, 2016	USA	Retro-cohort	Health records (insurance)	n=74,542; Age: mean 78.76 (SD 7.64); 86% Females	1 year	Second fracture	Gender
Cantlon, 2016	Sweden	Pro-cohort	Secondary care	n=382; Age: mean 52.6; gender information unavailable	1 year	Pain VAS; Disability (DASH); QoL (SF36)	
Chen, 2013	Taiwan	Retro-cohort	Population based	n=9986; Age: range 30-60+; 62% Females	1 year	Hip fracture	Gender, age, occupation, urbanization, income, wrist fracture, osteoporosis
Clement, 2012	Scotland	Pro-cohort	Secondary care	n=468; Age: mean 78.9 (range 65-102); 77% Females	1 year	Mortality,	Multiple fractures by age
Crandall 2021	US	prospective cohort study	general population	Total cohort n=157,282; Age mean 63.1 (SD 7.20); 100% female; 47,126 experienced an incident fracture (9873 were wrist or lower arm)	Entire cohort (mean follow-up duration was 15.4 years (SD 6.2, median 18.5,	Subsequent fracture	

					interquartile range 9.0 - 20.9 years)		
Crockett, 2017	Canada	Pro-cohort	Secondary care	n=63; Age: mean 63 (SD 8.4); 100% females	3/9/12/26 weeks, 1 year	BBS, PASE, ABC, PRWE	
Curtis, 2010	USA	Retro-cohort	Population based	n=7635; Age: mean 78.9 (range 65-85+); 88% Females	5 years	Mortality, 2nd fracture	Gender, ethnicity, comorbidity
Dewan, 2018/2018	Canada	Pro-cohort	Secondary care	n=94; Age: mean 62.6 (SD 7.7); 87% Females	6 months; 4 years	PRWE, SF-12 PCS, SF-12 MCS, falls and fractures	Age, history of falls, balance, PRWE, T-score TH
DeGeorge 2020	US	retro-cohort	insurance data	n=13,713; Age mean 75.4 (SD 6.7); 85.6%	1 year	Complications; stiffness	
Eekman, 2014	Netherlands	Pro-cohort	Hospital/rehabilitation	n=23; Age: 50+; Approx 80% Females	3, 6, 9, 2 months	Direct and indirect medical and non-medical costs	
Edwards, 2010	USA	Pro-cohort	Population based	n=268; Age: mean 71.2 (SD 4.6); 100% Females	Mean 6.3 years (range 1-9.5)	Functional decline	Age, basline functional status, subsequent wrist fracture, hip fracture, comorbidities, previous falls, overall health, neuromuscular measures
Egund 2020	Sweden	prospective cohort study	Hospital	n=133; Age mean 54 (SD 18); 100% males	1 year	DASH, SF-36	
Endres, 2006	Germany	Pro-cohort	Population based	n=2031; Age: mean 67.6 (estimated from authors'data); 82% Females	Up to 1.5 years	Mortality	Age, gender
Ettinger, 2003	USA	Retro-cohort	Health records (insurance)	n=925; Age: range 60-90+; 0% Females	Mean 2.4 years	Subsequent fracture	
Field, 1992/1997	UK	Retro-cohort	Hospital/rehabilitation	n=100; Age: mean 68.8 (range 26-90); gender information unavailable	5 weeks; 12 weeks; 10 years	Pain (VAS), function (Gartland and Werley score), grip strength, algodystrophy, cosmetic deformity	
Foldhazy, 2007	Sweden	Pro-cohort	Hospital/rehabilitation	n=87; Age: mean 55 (range 19-78); 84% Females	Mean 11 (range 9-13) years	Pain; function; mobility; grip strength; wrist ROM; radiography	
Freedman, 2007	USA	Retro-cohort	Health records (insurance)	n=111; Age: mean 67.4(estimated from authors'data); 70% Females	1 year	Healthcare utilisation (number of consultations, prescriptions and referrals)	
Gong, 2009	South Korea	Retro-cohort	Health records (insurance)	n=61234; Age: range 50+; 100% Females	Unclear	Healthcare utilisation (bone density examination, osteoporosis medication)	
Gonzalez, 2014/2016	Spain	Pro-cohort	Hospital/rehabilitation	n=960; Age: mean 76.3 (SD 6.9); 89% Females	6 months, 18 months	SF-12 (PCS and MCS), QuickDASH, Barthel Index, Lawton & Brody index	Age, gender, fractured hand dominance

Hagino, 2009	Japan	Pro-cohort	Outpatient	n=50; Age: mean 68.6 (SD 10.3); 100% Females	2 weeks, 3 months, 6 months, 1 year	EuroQol (EQ-5D)	
Hollevoet, 2000	Belgium	Retro-cohort	Hospital/rehabilitation	n=27; Age: mean 67 (range 51-78); 100% Females	Mean 23 months (range 12-69)	BMD, Gartland and Werley score, grip strength, ROM	
Hung, 2015	Hong Kong, China	Retro-cohort	Hospital/rehabilitation	n=57; Age: range 61-80; 79% Females	Range 9-12 months	Radiographic parameters, ROM, grip strength, QuickDASH	
Ioannidis, 2013	Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, UK, and USA	Retro-cohort	Unclear	n=419; Age: mean 70 (SD 9); 100% Females	1 year	Healthcare utilisation (length of stay in hospital/rehab.nursing home, surgery)	
Jakob, 1999	GErmany	Pro-cohort	Hospital/rehabilitation	n=102; Age: mean 76; 83% Females	Mean 8 months (range 6-12)	Radiological measures, ROM, Katz index for ADL function, subjective parameters	
Jansky, 1994	Germany	Pro-cohort	Hospital/rehabilitation	n=361; Age: mean 60.1 (range 16-92); 80% Females	Mean 10.5 months; (up to 14 months)	Clinical and radiological measures	
Johnell, 2004	Sweden	Retro-cohort	Hospital/rehabilitation	n=473; Age: mean 72.9 (SD 11.0); 87% Females	1, 2, 3, 4, 5 years	Mortality	
Jung 2021	South Korea	retro-cohort	insurance data	n=41,417; 82% female. Age presented in bands only	4 years	subsequent osteoporotic fracture; mortality	
Khan, 2001	USA	Retro-cohort	Health records (primary care)	n=112; Age: mean 64 (SD 13); 83% Females	Range 6 months to 3 years	Healthcare utilisation (osteoporosis management, HRT/bisphosphonate use; calcium/Vit D use)	
Langenberg, 1991	Germany	Retro-cohort	Hospital/rehabilitation	n=205; Age: median 58.8 (range 14-95); 76% Females	Mean 1 year	Range of symptoms, perceived recovery, functional recovery	
Larouche, 2016	Canada	Pro-cohort	Hospital/rehabilitation	n=129; Age: Mean 64.6 (SD 7.6); 90% Females	6 weeks; 12 weeks; 1 year	PRWE, DASH, SF-36 PCS	
Lee 2019	South Korea	retro-cohort	insurance data	n=13,164; 81.2% female. Age presented in bands	56.8 months (SD 40.3)	mortality	
Leslie, 2011/2013	Canada	Retro-cohort	Population based	n=6295; Age: range 50+; 79% Females	1, 2, 3, 4, 5 years	Healthcare costs (according to drug, physician, hospital, nursing home, care home); Mortality	Gender
Lipman 2019	USA	Cohort, retro	Insurance databse	n=50 147 with distal radial fracture and fibromyalgia syndrome 10% male and 90% female, n=80 039 controls with distal radial fracture (no FMS) 17% male and 82% female.	3, 6, 9, and 12 months from injury	Complex regional pain syndrome (CRPS); Fibromyalgia as a prognostic factor	
Lubbeke, 2005	Switzerland	Retro-cohort	Hospital/rehabilitation	n=667; Age: Mean 80 n(SD 8.2); 86.4% Females	2 years	Rehabilitation	Age, gender, previous residence, type of injury, fracture site, treatment

Luthje 2021	Finland	Cohort, retro	Hospital	Wrist fracture total n= 150, mean age 70.4 (SD 10.8), of which n=135 women, mean age 69.9 (11.0) and n=15 men mean age 74.7 (7.2)	4 years	Fracture liaison service costs, mortality/survival, use of Ca + vit D, use of anti-osteoporotic treatment.	
Lutz, 2014	Canada	Pro-cohort	Hospital/rehabilitation	n=258; Age: mean 74 (SD 5); 92% Females	Operative group: Mean 11.3 years (SD 9.3 months); Nonsurgical group: 14.9 years (SD 8.9 months)	PRWE, complications	
MacDermid, 2001	Canada	Pro-cohort	Secondary care	n=250; Age: range 18 - 65+; 66% Female	2/3/6/ months; 1 year	PRWE, DASH, SF-36 PCS	
Mallmin, 1993	Sweden	Retro-cohort	health records (secondary care)	1338; Age: mean 62.3 (SD 10.8); 84% Females	Up to 24 years	Hip fracture	
Marchewka 2019	Poland	Cohort, retro	Hospital	n=256 men (19.6%) with mean age 66 ± 12 yr and 1052 women (80.4%) with mean age 74 ± 12 yr.	3, 6, 9 and 12 months	Standardized mortality ratios	
McQueen, 1988	UK	Retro-cohort	Secondary care (health records)	n=30; Age: mean 69 (range 56-86); 97% Females	Mean 5.08 years (range 4-6.75 years)	Pain, functional (activities of daily living), grip strength	
Modarresi 2019	Canada	Cohort, retro	Existing database	n=318 (80.5% female), age 59.6 (11.9) but range was 20–87 years. Mean age of females 60.6 years and males 55.4 years	3, 6 and 12 months	Recovery using Patient-Rated Wrist Evaluation (PRWE) scale, Self-Administered Comorbidity Questionnaire (extracted info on depression),	
Montague 2019	USA	Cohort, retro	Not reported (Hospital records data?)	130 patients (132 wrists, 51 classified as simple and 81 classified as complex). Average age 57 years (range 18-98 years), 77% female, and average BMI was 28.2 kg/m2. 50 patients completed the QuickDASH, 58 years (range, 34-83 years), 82% female with an average BMI of 29.3 kg/m2	Mean of 4.6 years, range 22-73 months	QuickDASH, with BMI as a predictor of complex fracture, and failure of nonoperative treatment	
Montoya-Garcia 2021	Spain	Cohort, retro	Hospital	n = 1369 in total, of which n=506 were wrist fractures	Mean of 2.3 years	Imminent risk of a subsequent fracture and mortality	
Mosenthal 2019	USA	retro-cohort	National insurance database	n=155353; age mean not given range 18+, mode 50-59; 72.6% female	1 year	Posttreatment complications exam ined included ICD-9 codes related to wound complication, infection, neurovascular injuries, tendon rupture, malunion, nonunion, and stiffness	
Morin, 2011/2012	Canada	Retro-cohort	Population based	n=13585; Age: Mean 68.7(estimated from authors 'data); 81% Females	1 year	Institutionalisation, mortality	Gender
Nielsen, 2013	Denmark	Pro-cohort	Health records (insurance)	n=37; Age: mean 67 (SD 14.5); 100% Females	3 months, 1 year	Pain, DASH	
Ohsfeldt, 2006	USA	Retro-cohort	Health records (insurance)	n=1652; Age: mean 70 (range 45+); 73% Females	1 year	Healthcare utilisation (hospital stay, physician services, long-term care); Direct medical costs	Gender, age

Owen, 1981	USA	Retro-cohort	Population based	n=394; Age: range 35+; 89% Females	Unclear	Hip fracture	Age, gender, degree of trauma
Oyen, 2014	Norway	Retro-cohort	Health records (insurance)	n=799; Age: mean 70; 85% Females	1 year, 5 years	Mortality	Gender
Parikh 2021	USA	retro-cohort	Insurance databse	n= 37,473; Age not specified but >85% were aged 65+years; 77% females	6 yrs	BMD testing, subsequent hip/vertebral fractures	
Robinson, 2002	Scotland	Pro-cohort	Secondary care	n=8119; Age: median 74 (IQR 63, 83); 87% Females	Median 3.65 years (IQR 1.29, 6.65 years)	Re-fracture	
Roysam, 1993	UK	Pro-cohort	Secondary care	n=170; Age mean 62.7 (SD 7); gender information unavailable	6 weeks, 6 months, 1 year	Pain, Function (Gartland and Werley), Grip strength	
Rozental, 2002	USA	Retro-cohort	Secondary care	n=325; Age: mean 77.37 (SD 8.16); Females 80%	7 years (max)	Mortality	Gender, comorbidity
Shauver, 2015	USA	Retro-cohort	Health records (insurance)	n=81568; Age: range 65+; 86% Females	5 years	Mortality	Age, gender, race, comorbidity, fracture treatment
Shortt, 2005	Scotland	Retro-cohort	Secondary care	n=7486; Age: 86.8% aged 55+; 88% Females	Median 46 months (IQR 16-82)	Mortality	Age, gender, mobility
Solgaard, 1988	Denmark	Pro-cohort	Secondary care	n=154; Age: mean 58 (SD 4); 77% Females	3.5 years	Arthrosis, Function (Gartland and Werley), ROM, grip strength	
Svedbom, 2017/2018	Multinational	Retro-cohort	Secondary care	n=589; Age: mean 65 (SD 9); 88% Females	4, 12, 18 months	Quality of life loss (EQ-VAS, EQ-5D-3L)	
Synn, 2009	USA	Retro-cohort	Secondary care	n=53; Age mean 69 (range 55-90); 87% Females	Mean 17 months (range 6-45 months)	DASH, PRWE, MASS07, Gartland and Werley score, Jebsen-Taylor hand function test	
Sujic 2019 and 2020	Canada	pro-cohort	FLS	n=2372; Age not specified >50 yrs; ~80% females	5 yrs	re-fracture, mortality	
Symonette 2019	Canada	pro-cohort	tertiary hospital	n=190; mean age 71.8+/- 5 yrs; 90% female	1 year	malunion as predictor of poor outcome measured by PRWE	
Torchia 2019	USA	retro-chort	Naional insurance database	n= 34385; mean age 78.95 (+/- 7.48 yrs); 88.75% female	1 year	Opioid use	
Toth 2020	sweden	retro-chort	national patient regsiter	n=35146 female 73.8 years (range, 55 to 90 years). 10,006 wrist fractures specifically	2 years	re-fracture	
Tsukutani, 2015	Japan	Other	Secondary care	n=141; Age: range 50+; 87% Females	1 year	Death, impairment of ambulatory ability, occurrence of new fracture, osteoporosis therapy	
Van Leerdam 2019	netherlands	retro-cohort	hospital records	n= 285, mean age (SD) 62 (16); 75% female	3.8 yrs (mean)	PRWE and EQ5D	
Vergara, 2016	Spain	Pro-cohort	Secondary care	n=680; Age: mean 76.5 (SD 7.0); 89% Females	6 months	BADL performance, IADL performance	Age, gender, cardiovascular disease, baseline HRQoL, previous falls

Yeoh, 2016	Canada	Pro-cohort	Secondary care	n=228; Age: mean 67 (SD 0.59); 89% Females	3 months, 1 year	Depression (CES-D), DASH, SF-36, complications and symptoms	Age, gender, surgery, Katz Comorbidity Index score, complication, depression at baseline
Yoo 2019	KOREA	RETRO-COHORT	NATionaal insurance database	n = 6243 with wrist fracture; distribution given, but not mean age (range 50+); 83.3% female	3.1 yrs (median)	refracture and morality	
Ziebart 2020	canada	retro-cohort	hospital/tertiary centre	1508; 53.5 yr old (SD = 16.3; range 18–91 yr). 70.1% female	2 yrs	prwe pain subscale	

Table 2: Summary of results for Prognostic factors: Age & Gender

Predictor - Age: 21 papers								
First author, year of publication	**Predictor**	**Definition of outcome measure**	**Relevant sample size**	**Length of follow-up**	**Statistical model**	**Measure of association**	**Adjustment**	**Results details**
Abimanyi-Ochom, 2015	Continuous age	QALY loss (from EQ-5D-3L)	Adjusted analysis: 247	1 year	Multivariable regression analysis	Beta (95% CI)	Gender, previous fracture, hospitalisation, income, education,	-0.0005 (-0.003, 0.002)
Abramo, 2008	Non-osteoporotic age group Osteoporotic age group	DASH (0/no disability - 100/worst disability)	360 (with available follow-up data)	1 year	Comparison of means at follow-up	p-value for difference in mean outcome value at 1 year	Unadjusted	Non-osteoporotic age group: mean 13 (SD 18) Osteoporotic age group: mean 17 (SD 20) p-value=0.02
Bickerstaff, 1994	Continuous age	Algodystrophy	270	6 months	Two-sample t-test	Mean (SE)	Unadjusted	Algodystrophy: n=64.7 (1.3) Borderline algodystrophy: 64.5 (1.1) No algodystrophy: 63.7 (1.1) p-value: non-significant
Brenneman, 2006	Age-specific results given: 50-64 years 65-99 years	SF-12 PCS, SF-12 MCS	n=835	Approx 1 year	Unclear	p-values	Unadjusted	p-values<0.001
Bynum, 2016	Age-specific results given: 66-74 years 75-84 years 85+ years	Second fracture	Total: 74542 Females: 63879 Males: 10663	1 year	Cox regression	Rate (per 100,000 person-years) (SE) Predicted probability (estimated from graphs)	Unadjusted	Figures to be taken from table 2 (for index fracture type) and combined for ages 66-74, 75-84 and 85+ years
Chen, 2013	40-49 years 50-59 years 60+ years 30-39 years (reference)	Hip fracture	9986	1 year	Univariable and multivariable Cox regression	Crude and adjusted HR	Gender, occupation, urbanization, income, wrist fracture, osteoporosis	Crude HR: 40-49 years: 1.74 (0.82, 3.68) 50-59 years: 2.87 (1.37, 6.00) 60+ years: 18.1 (9.8, 33.3) Adjusted HR: 40-49 years: 1.58 (0.75, 3.35) 50-59 years: 1.94 (0.92, 4.10) 60+ years: 8.67 (4.51, 16.7) NB: Includes data from other fragility fractures
Crandall 2021	Age 50-59	subsequent fracture	9873	unclear (entire cohort was mean 15.4 years)	Cox proportional hazards models	unadjusted HR with 95% CI, crude number (%)		Subsequent fracture 50-59: HR:6.45 (5.87,7.08) crude 593 (1.34%); 60-69: HR: 6.04 (5.64,6.47) crude 1116 (1.75%); 70-79: HR 4.99 (4.55, 5.49) crude 584 (2.26%). The risk of subsequent fracture after initial lower arm or wrist fracture, was significantly higher even among the youngest women aged 50-59 years.
Dewan, 2018	50-64 years (reference) 65-80 years	Subsequnt falls and fractures	Crude analyses: 94 Adjusted analyses: 69	4 years	Univariable and multivariable logistic regression	OR (95% CI)	Gender, history of falls, balance, PRWE, T-score TH	Falls: Crude OR: 0.7 (0.3, 1.8) Adjusted OR: 1.1 (0.3, 3.9) Fractures: Crude OR: 0.7 (0.3, 2.0) Adjusted OR: 0.7 (0.1, 3.7)

Edwards, 2010	Continuous age	Functional decline: presence/absence of a clinically important functional decline	268	Mean 6.3 years (range 1-9.5)	Multivariable logistic regression	OR (95% CI)	Basline functional status, subsequent wrist fracture, hip fracture, comorbidities, previous falls, overall health, neuromuscular measures	Age (per year): 1.06 (1.05, 1.08)
Egund, 2020	<65 years vs >= 65 years	DASH SF-36 (PCS) SF-36 (MCS)	133	1 year	Mann-Whitney	P<0.05	Unadjusted.	DASH Not displaced younger men < 65 Median (IQR): 1 (0; 7); Older men ≥ 65 years 10 (1; 22) p =0.008 DASH displaced younger men < 65 Median (IQR): 38 (1; 39); Older men ≥ 65 years 18 (1; 73), p=0.951 PCS younger men < 65: 52 ± 8; older men >65: 42 ± 12 < 0.001. MCS younger men < 65: 52 ± 8; older men >65: 50 ± 12 < 0.789. Disability was higher in older men (DASHmedian 10 vs 2; p = 0.002); a clinically meaningful difference (DASH = 10, p = 0.017) remained after adjustment for displacement, fracture classification and treatment method. Almost 50% of older men vs 14% in younger had poor outcome, p < 0.001. Older men with a displaced fracture at initial presentation had greater disability (DASHmedian, IQR 45, 14;73) and risk of fracture (FRAXmajor osteoporotic 14, 8;21).
Endres, 2006	Continuous age	Mortality	2031	Up to 1.5 years	Unclear	p-value	Unadjusted	p-value=0.08
Gonzalez, 2014	75-79 years 80+ years 65-74 years (reference)	Quick DASH (0-100); SF-12 PCS (0-100); SF-12 MCS (0-100); Barthel Index (0-100); Lawton & Brody index	960	6 months	Hierarchical linear mixed model	Beta (SE)	Baseline outcome score, gender, fractured hand dominance	Quick DASH: 75-79: -4.39 (1.98) 80+: -8.25 (1.95) SF-12 PCS: 75-79: -2.83 (0.92) -4.69 (0.91) SG-12 MCS 75-79: -2.41 (0.97) 80+: -1.13 (0.94) Barthel Index: 75-79: -1.18 (1.30) 80+: -8.08 (1.25) LWTON & Brody Index: 75-79: -4.69 (1.60) -12.93 (1.63)
Johnell, 2004	60 years 80 years	Mortality	473	1 year	Poisson regression	Relative risk	Unadjusted	Age 60: Males 1.1, Females 1.8 Age 80: Males 0.9, Females 1.3. NB: Relative risks are in relation to general population
Lipman 2019	Age	Complex regional pain syndrome (CRPS)	n=50 147 with fibromyalgia syndrome, n=803 039 control	1 year	Bivariate logistic and multivariable logistic regression	OR and covariate	Multivariable analyses	Too much to report here as broken into groups for age and only OP, regression coefficient and p-value presented. Results (OR and p-value) presented for 6 age categories, using 65-69 years as the reference category. Older age groups significantly more at risk of developing CRPC after DRF
Lubbeke, 2005	80+ years <80 years (reference)	Rehabilitation required	667 (crude analysis); 570 (adjusted analysis)	2 years	Univariable and multivariable logistic regression	Frequencies (%s) Crude and adjusted OR (95% CI)	Gender, previous residence, fracture site, treatment	<80 years: 28.2% of 323 80+ years: 45.6% of 344 Crude OR: 2.14 (1.55, 2.95) Adjusted OR: 3.29 (2.20, 4.93)

Mallmin, 1993	Continuous age (40+)	Hip fracture	2252 (1338 wrist fracture)	Up to 24 years	Cox regression	HR (95%CI)	Unadjusted	Females: 1.54 (1.24, 1.93) Males: 2.27 (1.15, 4.5). NB: HRs are given in relation to controls (non-wrist group)
Marchewka 2019	Age	Risk of mortality	n=256 men and 1052 women	1 year	Kaplan-Meier estimator and log-rank tests with univariate and multivariate Cox proportional hazards model	Hazard ratios (HR)	None	Cox proportional hazards model analysis: age was associated with higher risk of mortality (HR: 1.08, 95%CI: 1.07-1.10, p<0.000001))
Modarresi 2019	Age	Recovery based on Patient-Rated Wrist Evaluation (PRWE) scale	n=318	3, 6 and 12 months	Latent growth curve analysis (LGCA) was used to identify the recovery trajectories. Comparisons of proportion between the emergent classes were then conducted using chi-square and Kruskal-Wallis tests	%	n/a	The LGCA revealed three distinct trajectories (rapid-recovery: (69%), slow-recovery: (23%), and nonrecovery: (8%) as the best fit to the data. Mean age was similar between the three groups: 60 (12.2); 60 (10.6); 55 (12.8) years
Mosenthal 2019	categorical age	complication	no for this analysis not specifically reported	12 months	multivariate poisson regression model	IRR and 95% CI	adjusted for other factors in model	age 18-44 IRR1.00 age 45-54 IRR 1.13 1.10-1.15 <.0001 age 55-64 IRR 1.10 1.07-1.12 <.0001 age 65-74 IRR 1.06 1.04-1.08 <.0001 age 75+ IRR 1.04 1.02-1.06 .0004
Morin, 2011/2012	50-59 years (reference) 60-69 yeas 70-79 years 80-89 years 90+ years	Institutinalization, mortality	13,585 (2575 males; 11010 females)	1 year	Mortality: Poisson regression	Mnortality: RR (95%CI) Institutionalization: %s	Unadjusted	Mortality (females): 60-69 years: 4.0 (1.3, 12.4) 70-79 years: 8.5 (3.2, 23.0) 80-89 years: 15.1 (5.6, 41.2) 90+ years: 24.2 (8.3, 70.4) Mortality (males): 60-69 years: 3.5 (1.4, 8.4) 70-79 years: 8.8 (3.5, 22.0) 80-89 years: 11.5 (4.7, 28.3) 90+ years: 19.0 (6.4, 56.6) NB: For mortality, RRs are given in relation to controls (non-wrist group) Institutionalization:figures from table 1 could be pooled across gender and fiscal year but corresponding frequencies are not given (just %s)
Owen, 1982	35-49 years 50-59 years 60-69 years 70-79 years 80+ years	Hip fracture	Females: 35-49 years: 60 50-59 years: 119 60-69 years: 109 70-79 years: 45 80+ years: 17 Males 44 (no age-specific sample sizes given)	Unclear	Descriptive statistics	Frequencies (%)	Unadjusted	Females: 35-49 years: 1 out of 60 50-59 years: 13 out of 119 60-69 years: 16 out of 109 70-79 years: 14 out of 45 80+ years: 3 out of 17 Males 7 out of 44 (no age-specific sample sizes given)
Oyen, 2014	50-70 years >70 years	Mortality	799	1 year	SMRs based on mortality risk of the standard Norwegian population	Mortality rates, SMR	Unadjusted	50-70 years: mortality rate 1.0% >70 years: mortality rate 5.6 years Males 50-70 years: SMR 1.6 (-1.5, 4.7). NB: SMRs are given in relation to general population. Males >70 years: SMR 1.6 (0.4, 2.8) Females 50-70 years: SMR 1.5 (-0.2, 3.2) Females >70 years: SMR 0.8 (0.4, 1.2)
Rozental, 2002	Continuous age	Mortality	325	7 years (max)	Unclear	Unclear	Unclear - perhaps mean difference with 95% CI	6.14 (3.71, 8.56)

Shauver, 2015	65-69 years (reference) 70-74 years 75-79 years 80+ years	Mortality	81568	5 years	Unclear	HR (95% CI)	Unadjusted	70-74 years: 1.40 (1.33, 1.47) 75-79 years: 2.01 (1.91, 2.10) 80+ years: 4.22 (4.05, 4.40)
Shortt, 2005	Continuous age	Mortality	7486	Median 46 months (IQR 16-82)	Multivariable Cox regression	HR (95% CI)	Gender, mobility	HR 1.086 (1.079, 1.093)
torchia	categorical age; 66-74 reference	opioid use	no for this analysis not specifically reported	12 months	mutlivariate model	OR and p value	age, sex, race, Charlson co-morbidity index, month post-fracture, and treatment type (surgical vs. non-surgical)	age 75-84 OR 0.80 p < 0.01; age >85 OR 0.67, p < 0.1. NO CI given
toth	categorical age	refracture	10006	24 months		none, descriptive anlayses only		34% to 46% of index hip or clinical vertebral fractures in women ≥70 years were not their first fracture.Cumulative incidence of subsequent fracture within 12 and 24 months increased as a function of age
van leerdam	age <65 compared with 65 or above	PRWE	272	3 yr 10 mo	PRWE and EQ-5D scores were compared between patient groups (sex, treatment, dominant hand fractured, AO classification) using t Students' t-test or 1-way ANOVA. Multiple linear regression analysis to identify which patient and fracture charac teristics (age, sex, fracture type, dominance of the fractured hand, treatment) were associated with the PRWE score.	p value for difference in mean	no adjustment	10 (16) vs 12 (20) p = 0.2. Older people poorer outcomes, but not statistically significant.
Yeoh, 2016	Continuous age	DASH Score (0-100)	228	1 year	Multivariable linear regression	Beta (95% CI)	Gender, surgery, Katz Comorbidity Index score, complication, depression at baseline	0.079 (-0.17, 0.33)
ziebart	categorical age	pain PRWE EQ5D EQVAS	1503 272	2 yrs 3 yr 10 mo	Mixed-Effects Hierarchical Model including Interaction Terms	b coeffeicent (95% CI) p value for difference in mean	other variables in in model no adjustment	Unstandardized B coefficient (SE)for age 51-65 : 5.4 (1.9); Z statisctic :2.83; p value: 0.005; 95% CI: 1.6 to 9.1 0.9 (0.2) vs 0.85 (0.2) p = 0.09 82 (15) vs 78 (16) p= 0.04

Predictor - Gender: 20 papers

First author, year of publication	Predictor	Definition of outcome measure	Relevant sample size	Length of follow-up	Statistical model	Measure of association	Adjustment	Results details
Abimanyi-Ochom, 2015	Male (reference female)	QALY loss (from EQ-5D-3L)	Adjusted analysis: 247	1 year	Multivariable regression analysis	Beta (95% CI)	Age, previous fracture, hospitalisation, income, education,	-0.028 (-0.074, 0.018)
Abramo, 2008	Male Vs female	DASH (0/no disability - 100/worst disability)	360 (with available follow-up data)	1 year	Comparison of means at follow-up	p-value for difference in mean outcome value at 1 year	Unadjusted	Females DASH: mean (SD): 17 (19) Males DASH: mean 14 (19) p-value=0.07
Bickerstaff, 1994	Gender-specific results given	Algodystrophy	270	6 months	Chi-square test	Frequencies	Unadjusted	Females Algodystrophy: n=62 Borderline algodystrophy: n=60 No algodystrophy: n=99 Males Algodystrophy: n=11 Borderline algodystrophy: n=12 No algodystrophy: n=26 p-value: non-significant
Bynum, 2016	Gender-specific results given	Second fracture	Total: 74542 Females: 63879 Males: 10663	1 year	Cox regression	Rate (per 100,000 person-years) (SE) Predicted probability	Unadjusted	Females: 5590 (98) Males: 4475 (217) NB:Predicted probability results graphical - unable to depict individual values
Chen, 2013	Female (reference male)	Hip fracture	9986	1 year	Univariable and multivariable Cox regression	Crude and adjusted HR	Age, occupation, urbanization, income, wrist fracture, osteoporosis	Crude HR: 1.61 (1.22, 2.14) Adjusted HR: 0.95 (0.70, 1.30) NB: data not exclusive to patients with wrist fractrue only
Curtis, 2010	Gender-specific results given, by age group	Mortality, 2nd fracture	2635 (Males 951, Females 6684)	5 years	Unclear	%s	Unadjusted	Risk of death Males 65-74 years: 17.3% Males 75-84 years: 32.6% Males 85+ years: 60.4% Females 65-74 years: 12.3% Females 75-84 years: 22.6% Females 85+ years: 43.3% Risk of 2nd fracture Males 65-74 years: 17.6% Males 75-84 years: 18.7% Males 85+ years: 23.1% Females 65-74 years: 21.1% Females 75-84 years: 31.4% Females 85+ years: 33.5%

Dewan, 2018	Female (reference male)	Subsequnt falls and fractures	Crude analyses: 94 Adjusted analyses: 69	4 years	Univariable and multivariable logistic regression	OR (95% CI)	Age, history of falls, balance, PRWE, T-score TH	Falls: Crude OR: 4.2 (0.5, 34.0) Adjusted OR: result unavailable Fractures: Crude OR: 3.0 (0.4, 24.4) Adjusted OR: 0.3 (0.02, 3.9)
Endres, 2006	Gender-specific results given	Mortality	Total: 2031 Females: 1658 Males: 373	Up to 1.5 years	Chi-square test	Frequencies (%s)	Unadjusted	Females: n=54 (3.3%) Males: n=6 (1.6%)
Gonzalez, 2014	Female (reference male)	Quick DASH (0-100); SF-12 PCS (0-100); SF-12 MCS (0-100); Barthel Index (0-100); Lawton & Brody index	960	6 months	Hierarchical linear mixed model	Beta (SE)	Baseline outcome score, age, fractured hand dominance	Quick DASH: -8.78 (2.54) SF-12 PCS: -3.11 (1.17) SG-12 MCS -1.27 (1.24) Barthel Index: -1.19 (1.60) LWTON & Brody Index: 1.70 (2.11)
Johnell, 2004	Male/female wrist fracture Vs male/female non-wrist fracture	Mortality	473	1 year	Poisson regression	Relative risk	Unadjusted	Males (age 80): 0.9 Females (age 80): 1.3. NB: Relative risks are in relation to general population
Leslie, 2013	Gender-specific results given	Mortality	6295	5 years	Descriptive statistics	Frequencies (%)	Unadjusted	% alive at 5 years: 80% (males), 86% (females)
Lipman 2019	male vs female	Complex regional pain syndrome (CRPS)	n=50 147 with fibromyalgia syndrome, n=803 039 control	1 year	Bivariate logistic and multivariable logistic regression	OR and coefficient	Multivariable analyses include age, gender, intervention (surgery or reduction), and comorbidities (list of 9 lifestyle factors and morbidities including FMS)	Bivariate: Male OR=0.775 coefficient=−0.255; Female OR=1.290, coefficient=0.255 Multivariable: Male OR=0.593 coefficient=–0.523; Female OR=1.687, coefficient=0.523. Higher incidence of CRPS in women
Lubbeke, 2005	Female (reference male)	Rehabilitation required	667 (crude analysis); 570 (adjusted analysis)	2 years	Univariable and multivariable logistic regression	Frequencies (%s) Crude and adjusted OR (95% CI)	Age, previous residence, fracture site, treatment	Males: 30.8% of 91 Females: 38.2% of 576 Crude OR: 1.39 (0.86, 2.24) Adjusted OR: 1.59 (0.91, 2.77)
Marchewka 2019	Male vs female	Risk of mortality	n=256 men and 1052 women	1 year	Kaplan-Meier estimator and log-rank tests with univariate and multivariate Cox proportional hazards model	Hazard ratios (HR)	Age	Multivariate Cox regression: males were almost twice more likely to die than females (HR: 1.92, 95% CI: 1.34-2.77; p<0.001) at any point of the study
Modarresi 2019	Sex	Recovery based on Patient-Rated Wrist Evaluation (PRWE) scale	n=318	3, 6 and 12 months	Latent growth curve analysis (LGCA) was used to identify the recovery trajectories. Comparisons of proportion between the emergent classes were then conducted using chi-square and Kruskal-Wallis tests	%	n/a	The LGCA revealed three distinct trajectories (rapid-recovery: (69%), slow-recovery: (23%), and nonrecovery: (8%) as the best fit to the data. The proportion of females were significantly lower in the non-recovery (64%) compared to the slow (85%) and the rapid-recovery classes (81%).

Morin, 2011/2012	Male/female wrist fracture Vs male/female non-wrist fracture	Institutinalization, mortality	13,585 (2575 males; 11010 females)	1 year	Institutinalization: Multivariable Cox regression Mortality: Poisson regression	Institutinalization: %s; HR (95% CI) Mortality: RR (95%CI)	Institutinalization: Age, comorbidity Mortality: Age	Institutionalisation Males: HR 2.06 (1.48, 2.87) Females: HR 1.44 (1.35, 1.67) Males: proportion institutionalized range 1.73% to 12.67% Females: proportion institutionalized range 0.88% to 12.73% Mortality Males: 1.5 (1.2, 1.9) Females: 0.8 (0.7, 1.0) Males: mortality rate: range from 4.1% to 9.0% Females: mortality rate: range from 1.8% to 5.7% NB: HRs and RRs are given in relation to controls (non-wrist group)
Owen, 1982	Gender-specific results given	Hip fracture	394 (males 44, females 350)	Unclear	Descriptive statistics	Frequencies (%)	Unadjusted	Males: 7 out of 44 Females: 47 out of 350
Oyen, 2014	Male/female wrist fracture Vs male/female non-wrist fracture	Mortality	799 (118 males 681 females)	1 year	SMRs based on mortality risk of the standard Norwegian population	Mortality rates, SMR	Unadjusted	Males: mortality rate 5.9% Females: mortality rate 2.9% Males: SMR 1.8 (0.5, 2.7) Females: SMR 0.9 (0.5, 1.3). NB: SMRs are given in relation to general population
Rozental, 2002	Male (reference female)	Mortality	325	7 years (max)	Multivariable logistic regression Multivariable Cox regression	HR (95% CI)	Age, comorbidity, Charlson comorbidity index	OR Males: 2.65 (1.31, 5.36) HR Males: 1.83 (1.07, 3.14)
Shauver, 2015	Female (reference male)	Mortality	81568	5 years	Unclear	HR (95% CI)	Age	HR females: 0.77 (0.75, 0.79)
Shortt, 2005	Male (reference female)	Mortality	7486	Median 46 months (IQR 16-82)	Multivariable Cox regression	HR (95% CI)	Age, mobility	HR 1.413 (1.139, 1.753)
torchia	male vs female (male ref)	opioid use	34385	1 year	Multivariable model	OR, p value	age, sex, race, Charlson co-morbidity index, month post-fracture, and treatment type (surgical vs. non-surgical)	female 1.21 , p<0.01 No CI given
van leerdem	male vs female	PRWE EQ5D EQVAS	272	3 yrs 10 months	PRWE and EQ-5D scores were compared between patient groups (sex, treatment, dominant hand fractured, AO classification) using t Students' t-test or 1-way ANOVA. Multiple linear regression analysis to identify which patient and fracture charac teristics (age, sex, fracture type, dominance of the fractured hand, treatment) were associated with the PRWE score.	p value for difference in mean outcome	unadjusted	8(13) VS 12(20) P 0.2 Poorer outcomes for women compared to men, for QoL 0.92 (0.16) VS 0.87(0.21) P 0.09 83(14) VS 79(16) P 0.09

Vergara, 2016	Female (reference male)	BADL performance IADL performance	680	6 months	Univariable and multivariable logistic regression	Adjusted OR (95% CI)	Age, cardiovascular disease, baseline HRQoL, previous falls	BADL: 0.91 (0.46, 1.78) IADL: 0.37 (0.20, 0.69)
Yeoh, 2016	Female (reference male)	DASH Score (0-100)	228	1 year	Multivariable linear regression	Beta (95% CI)	Age, surgery, Katz Comorbidity Index score, complication, depression at baseline	3.1 (-0.57, 6.8)
ziebart	female vs male	pain - PRWE	1508	2 yrs	Mixed-Effects Hierarchical Model including Interaction Terms	unstandardised beta coeffiecient (95% CI)	other variables included in model	Unstandardized B coefficient (SE): 5.5 (1.9), Z statistic: 2.84, p value: 0.005, 95%CI 1.7-9.3. overall women greater pain, but when stratfified for age, men higher pain 51-65