# 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)<br>* Studies focusing on patients with high-impact trauma-related conditions.<br>* Studies in specific populations: e.g., those with inflammatory conditions, or receiving specific fracture treatment.<br>* Malunion & complications of prior treatments |
| **Interventions/exposures** | Different treatment options (conservative/surgical).<br>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.<br>* Socio-economic outcomes: healthcare utilisation, work absence.<br>* 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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