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The prevalence of frailty and its association with clinical outcomes in general surgery: a systematic review and meta-analysis

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Abstract

Objectives: to investigate the prevalence and impact of frailty for general surgical patients.
Research design and methods: we conducted a systematic review and meta-analysis. Studies published between 1 January 1980 and 31 August 2017 were searched from seven databases. Incidence of clinical outcomes (mortality at Days 30 and 90; readmission at Day 30, surgical complications and length of stay) were estimated by frailty subgroup (not-frail, pre-frail and frail).
Results: 2,281 participants from nine observational studies were included, 49.3% (1013/2055) were males. Mean age ranged from 61 to 77 years old. Eight studies provided outcome data and were quality assessed and of fair or good quality, and one study only provided an estimate of prevalence and was not quality assessed. The prevalence estimate ranged between 31.3 and 45.8% for pre-frailty, and 10.4 and 37.0% for frailty. After pooling, Day 30 mortality was 8% (95% CI: 4–12%; I^2 = 0%) for frail compared to 1% for non-frail patients (95% CI: 0–2%; I^2 = 75%). Due to heterogeneity the Day 90 mortality was not pooled. Readmission rates were lower in the non-frail groups but were not pooled. Complications for the frail patients were 24%, (95% CI: 20–31%; I^2 = 92%), pre-frail subgroup 9% (95% CI: 5–14%; I^2 = 82%) and non-frail 5% (95% CI: 3–7%; I^2 = 70%). The mean length of stay in frail people was 9.6 days (95% CI: 6.2–12.9) and 6.4 days (4.9–7.9) non-frail.

Conclusions: frailty is associated with adverse post-operative outcomes in general surgery.

Keywords: *frailty, general surgery, meta-analysis, older people, systematic review*

Background

Frailty is a condition characterised by loss of biological reserves, failure of homoeostatic mechanisms and vulnerability to adverse outcomes following stressor events such as surgery. Delivery of surgical care becomes more challenging in this context [1]. Faced with an ageing population whose rate of general surgical intervention is increasing rapidly, awareness of frailty is becoming more widespread in surgical and critical care settings [2]. Similarly, the importance of the identification and management of the frail patient is increasingly being recognized. For example, the 'National Confidential Enquiry into Patient Outcome and Death, An Age Old Problem', highlighted substandard care for older surgical patients and recommended daily geriatrician clinical input for these patients [3].

In medical settings it has been shown that frailty is present in 20–50% of the middle and older aged population, depending on the exact disease and the method of frailty measurement used [4]. This review further demonstrated that mortality was higher across all specialties when frailty was present but that wide variation existed [4]. For example, one large study showed that frail people aged over 75 years admitted to hospital had an odds ratio of 1.6 for death regardless of diagnosis [5]. This is much higher than a Swedish community study which demonstrated an increased hazard ratio for all cause mortality of 1.07 for older frail people [6].

Although a modest but increasing number of studies have recently assessed a number of different frailty tools in both emergency and elective general surgery against a range of outcomes, no systematic reviews have yet attempted to give an overview of the impact of frailty for people undergoing general surgery. Hence, the aim of this review was to assess frailty prevalence and its association with clinical outcomes (death, readmission to hospital, complications and length of hospital stay) within general surgery.

Methods

This systematic review was reported within the PRISMA framework. The review was registered and the protocol is available on Research Registry (review registry129, http://www.researchregistry.com)

Search strategy

The search strategy was developed by an expert research support librarian at the University of Leeds, in full collaboration with the review team. We searched seven electronic databases (Medline, CINAHL, The Cochrane Library, AMED, PSYCINFO, EMBASE and Web of Science) for manuscripts published from 1 January 1980 to 31st August 2017. All identified and relevant studies' references were manually reviewed to identify any potential studies that met the inclusion criteria. The included studies underwent a forward citation search to identify any future studies which may have referenced them. The search terms were based on MeSH terms (Medical Subject Headings) and other controlled vocabulary. Search terms relating to surgery, frailty and risk factors were used. The search strategy is outlined in Supplementary file 1, available at *Age and Ageing* online.

Eligibility criteria and study identification

The review process is summarised in a PRISMA flow diagram (Figure 1).

Randomized controlled trials, cohort studies and case–control study designs were eligible for inclusion. Only studies using a validated method of frailty identification were included [7]. Studies that used large scale database analysis assessing frailty and surgery were excluded [8]. Studies based solely in intensive care were excluded since these populations are atypical and could introduce additional confounders. No language restrictions were applied

Two reviewers (J.H. and S.L.) searched the literature and assessed the studies for eligibility independently. Disagreements were resolved through discussion with a third reviewer (B.C.).

Data extraction and quality assessment

Demographic information, frailty tool, frailty prevalence and outcomes data were extracted from the included studies independently by two reviewers (J.H. and S.L.) disagreements were resolved through discussion with a third reviewer (B.C.).

Study authors were contacted to clarify or provide additional data where it was missing or unclear.

For the studies included the quality assessment was conducted by two reviewers independently (J.H. and S.L.) and arbitrated by a third (B.C.) using the Newcastle–Ottawa Scale (NOS) [9, 10], which assesses the risk of bias of observational studies. Each domain examined was determined as good, fair or poor. Studies were deemed to be of good quality where they scored good for all domains, fair if they scored fair in one or more domain and likewise poor if they scored poor in any one domain.

Data analysis

Frailty prevalence was estimated using studies that had categorised frailty using standard specific cut-offs for validated frailty tools [11–15]. For consistency, prevalence was not calculated using studies where participants were defined as being frail using a non-standard cut-off.

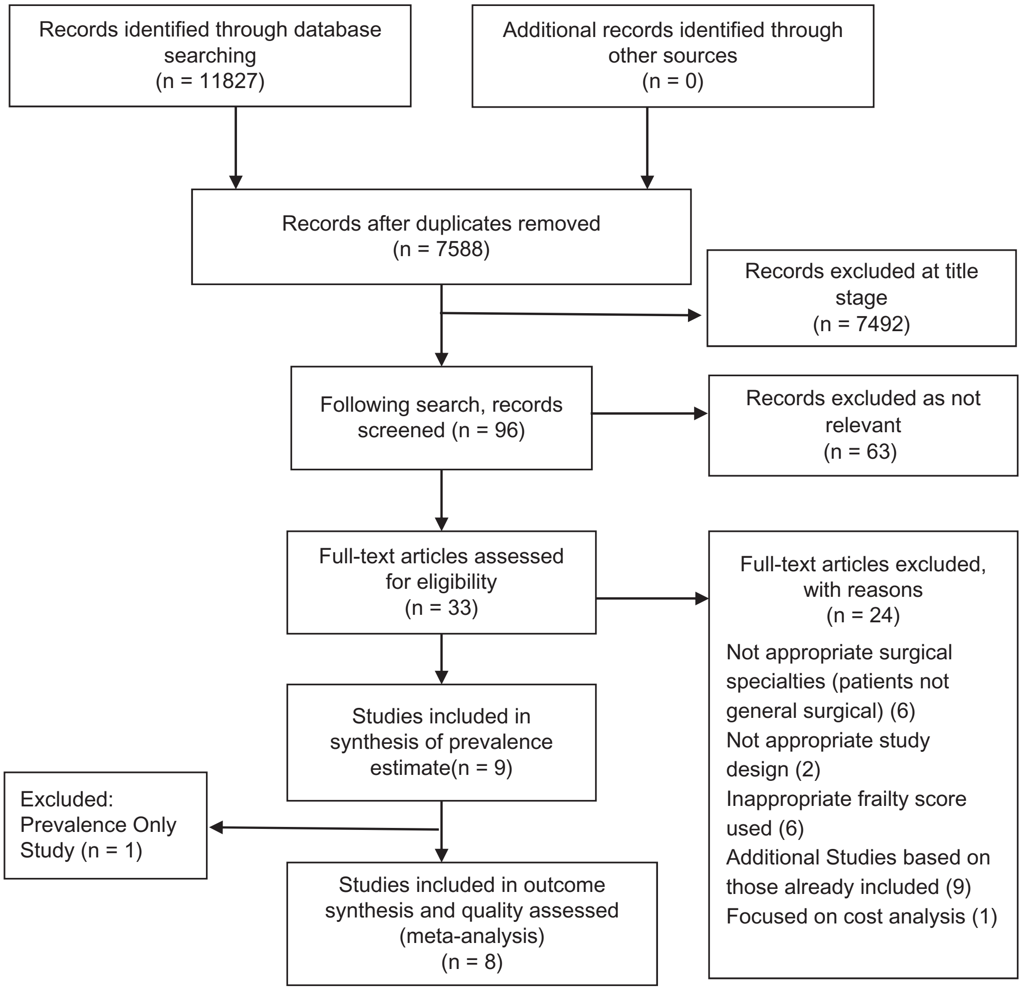

Figure 1. PRISMA flowchart of included studies.

Data were extracted for the following primary outcomes: short-term mortality (30 days), and medium-term (90–180 days months) mortality. Further data were extracted for the following secondary outcomes: 30-day readmission to hospital, complications and length of hospital stay. All outcomes captured dichotomous data except for the length of stay, and the treatment effects were measured by the proportion of patients experiencing the outcome. Continuous data for the length of stay were skewed, so were transformed and summary statistics were calculated on the transformed scale. Frailty subgroups were used to explore the association between frailty and outcomes. If study design and population did not exhibit clinical heterogeneity, data were pooled in a random effects meta-analysis. All meta-analyses were conducted using Stata version 13.0.

Assessment of subgroups and statistical heterogeneity

Heterogeneity was assessed using the I^2 statistic, and pooling that exhibited an I^2 over 85% was explored using subgroup analyses. All meta-analyses were presented as an estimated proportion, associated 95% confidence interval (95% CI), *P*-values and I^2 summary data. Frailty was a pre-specified subgroup to explore the association between frailty and outcomes. Patients were categorised as non-frail, pre-frail or frail. The following pre-specified subgroups were used to explain heterogeneity: quality assessment (high quality, versus unclear and low quality studies); age of patients (65–70, 70–80, 80+); type of surgery (elective, emergency or combined).

Results

Identified studies and quality assessment

After removal of duplicates, 7,588 records were identified, and led to 33 full texts being reviewed, where 24 were excluded. Nine were included in this analysis and are shown in the PRISMA flowchart (Figure 1) [16–24]. One study only considered frailty prevalence [16], and was excluded and not assessed for quality. This study was not considered in the meta-analysis or the quality assessment (Supplementary Table S1, available at *Age and Ageing* online). Five studies were determined as good quality [17, 18, 20, 23, 24], three were categorised as fair quality [19, 21, 25] and none were categorised as poor quality. The average NOS score was 8.3. For further details of the results of the quality assessment tool, see

Table 1. Included studies, all are observational

Author	Year	Country	Population details	No. patients	Age[c]	Sex (%) (M:F)	Frailty measure	Quality assessment
Chen C.	2015	Taiwan	Elective abdominal surgery (upper abdominal = 147, lower abdominal 232), expected LOS > 6 days and able to communicate	379	>65 years, 74.5 ± 5.9 SD	216 (57.0) 163 (43.0)	5-Point phenotype model	NA
Hewitt J.	2014	UK	Emergency general surgery admissions (upper and lower abdominal surgery), older patients. Not all patients underwent surgery	325	>65 years, 77.3 (65–101)	140 (43.1) 185 (56.9)	CHSA 7-point scale (deficit derived)	Good
Joseph B.	2014	USA	Emergency General Surgery (all underwent surgery), older patients	220	>65 years, 75.5 ± 7.7 SD	123 (55.9) 97 (44.1)	DAI 50 variables, >0.25 = frail	Good
Kenig J.	2015 (2)	Poland	Emergency abdominal surgery, tertiary referral centre, operated within 24 h	184	>65 years, 76.9 ± 5.8 (65–100)	86 (46.7) 98 (53.3)	VES-13 (≥3), TRST (≥1), G8 (≤14), GFI (≥4), Rockwood (≥2), Balducci (1)	Fair
Makary M.	2010	USA	Elective surgery recruited from a pre-assessment centre, older patients	594	>65 years, 71.3 (65–94)	236 (39.7) 358 (60.3)	5-Point phenotype model	Good
Reisinger K.	2015	Netherlands	Emergency and elective colorectal cancer surgery, non-academic centre	154[a]	>70 years	Not stated	Groningen frailty indicator (≥5)	Fair
Robinson T.	2013	USA	Elective Colorectal Surgery, all surgery performed after at least 72 h after presentation to hospital	201	>65 years, 74 ± 6 SD	Not stated	7 Domain based scoring system	Fair
Saxton A.	2011	USA	Elective General Surgery, older patients	226	No age cut off. 61 ± 13 SD	106 (46.9) 120 (53.1)	CHSA 70-point deficit model, >0.12 taken as frail	Good
Tegels J.	2014	Netherlands	Elective gastric adenocarcinoma cancer surgery, in a community teaching hospital	127[b]	No age cut off. 69.8 (73–88)	106 (58.9) 74 (41.1)	Groningen frailty indicator (≥3)	Good

[a]Only patients aged over 70 were assessed for frailty.
[b]Patients with complete frailty data.
[c]Range unless stated as standard deviation (SD).

Supplementary Tables S1A and B, available at *Age and Ageing* online.

Characteristics of the included studies

From the nine studies 2,281 patients were included, 49.3% were male (1,013/2,055) and six studies only recruited older patients (over 65 year olds).The mean age ranged from 61 to 77 years old (Table 1).

Frailty prevalence

The nine included studies used a range of frailty assessment tools, of which seven were deemed suitable for inclusion in the prevalence estimation. One study [23] oversampled complex cases, as such it was not a representative sample to be included in the prevalence data. The other excluded study used a range of frailty scales and was not suitable for inclusion [19]. Of the included studies, two used the phenotype model [16, 20], two the Groningen Frailty Indicator [21, 24], two the deficit based model [17, 18] and one a 7-point assessment of frailty traits [25]. The prevalence of pre-frail ranged between 31.3 and 45.8%, frailty prevalence ranged between 10.4 and 37.0%. The included studies and the prevalence estimated are shown in Supplementary Table S2, available at *Age and Ageing* online.

Short-term mortality (Day 30) and medium-term mortality (Days 90–180)

Three studies reported mortality at Day 30 [17, 18, 21], this included 9% (17/192) patients who were determined as frail, and 3% (12/479) who were non-frail. After pooling, the proportion who were frail was 8% (95% CI: 4–12%; I^2 = 0%), which compared to 1% of non-frail patients (95% CI: 0–2%; I^2 = 75%, Figure 2).

Two studies reported mortality in the medium term [17, 24], 23% (24/105) died who were frail, compared to 11% (34/300) who were not frail (Figure 3). Pooling was not possible due to severe heterogeneity, and caution is needed in the interpretation of the two subgroups (Figure 3).

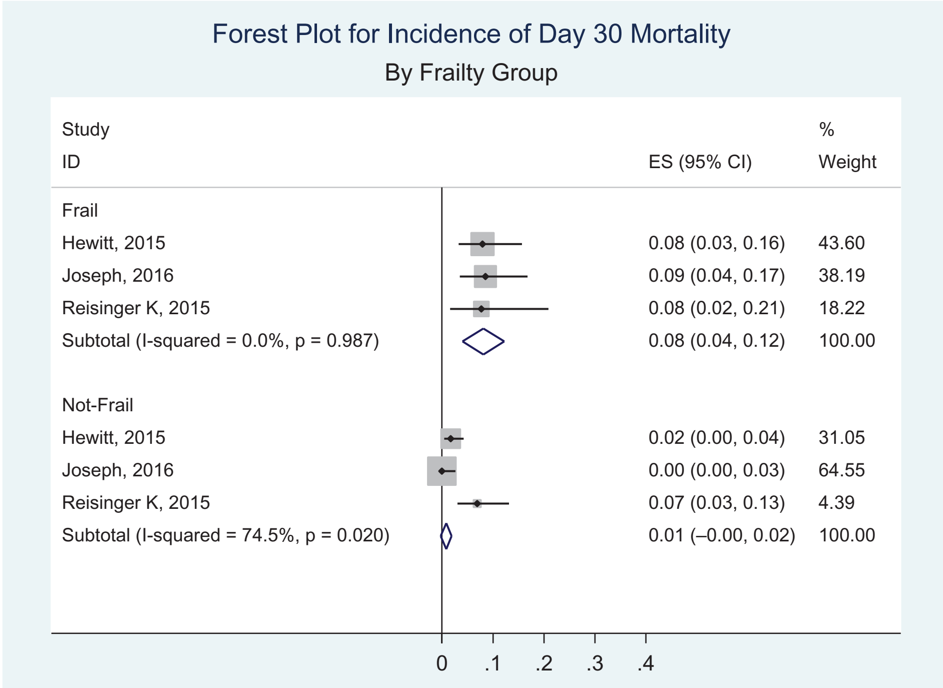

Figure 2. Mortality at Day 30.

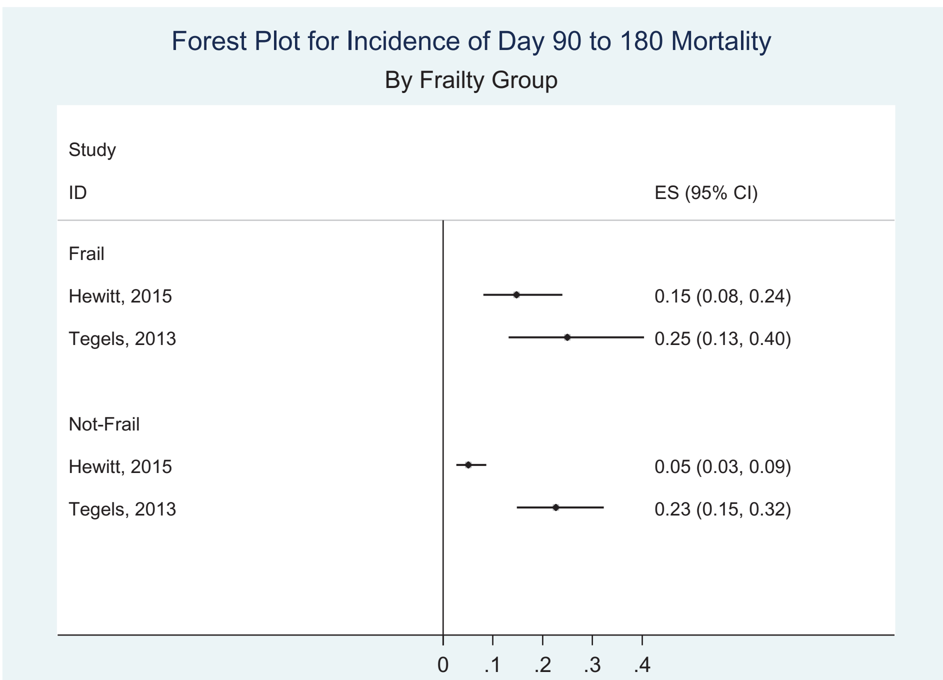

Figure 3. Mortality at Days 90–180.

Readmission at Day 30

Two studies reported the proportion of patients with a readmission [17, 25]. One study found the proportion who were re-admitted was 14% in both the frail and the non-frail groups [17] and the second 29% in the frail group, compared to 7% in the non-frail group [25].

Surgical complications

Four studies reported the proportion of patients who suffered surgical complications [18, 20, 21, 25]. Severe clinical heterogeneity was exhibited between the studies, which was explained in part by frailty. The estimated proportion to exhibit complications from the frail subgroup of patients was 24%, (95% CI: 20–31%; I^2 = 92%, Supplementary Table S1, available at *Age and Ageing* online) pre-frail subgroup 9% (95% CI: 5–14%; I^2 = 82%); and from the not-frail subgroup 5% (95% CI: 3–7%; I^2 = 70%). Post-operative complications were assessed using a variety of tools, including the Accordion Severity Classification [25], the American College of Surgeons National Surgical Improvement Program definitions [18, 20] and those constructed directly by the study authors [21].

Length of stay

Four studies presented data on the length of stay and applied cut-offs for participants as either frail, or non-frail [17, 18, 24, 25]. The pooled mean length of stay in frail people was 9.6 days (95% CI: 6.2–12.9) and in those who were non-frail was 6.4 days (4.9–7.9), see Supplementary Figure S2, available at *Age and Ageing* online. However, substantial heterogeneity was found within both of the frailty subgroups that was not able to be explained.

Sensitivity analyses and pre-specified subgroups used to explain the heterogeneity

Due to the few numbers of included studies no sensitivity analyses were carried out. Apart from the subgroups stated explicitly stated above, none of the other pre-specified subgroup were able to explain the heterogeneity exhibited in the pooled meta-analyses.

Discussion

This study identified nine studies, of which eight were included in the analyses and were quality assessed. The studies covered a wide range of upper and lower abdominal surgical conditions, including both benign and malignant conditions, five of which were good quality and the remaining three fair quality.

We found evidence of an increase in the proportion of patients that suffered mortality and surgical complications in those that were frail, compared to those patients who were not frail. Analysis identified short-term (up to 30 days) mortality to be more frequent in those people who were frail. Post-operative complications were more frequent and length of hospital stay longer in frail individuals following their surgical illness. Both of these associations are demonstrated by a summary statistic and therefore generalising to every older surgical population must be done with caution. For example, our population contained a wide range of ages and both elective and emergency cases, factors that may have confounded the overall association with 30-day mortality and increased post-operative complications that was demonstrated.

This review is the first review to characterise frailty in a general surgery patient group. Other recent reviews, whilst also demonstrating that frailty was associated with post-operative complications examined studies from a range of surgical specialties, not solely general surgery: for example, Lin *et al.* [26] and the narrative review by Beggs *et al.* [27]. This review also differs as it considers eight studies for meta-analysis. Lin *et al.* identified three general surgical articles for review but did not perform meta-analysis [26]. Of the three studies which were considered by those authors, two [17, 19] are considered in this review and one [28] was excluded as the frailty assessment tool used was constructed by the study authors.

Strengths and weaknesses

All of the studies included were of at least moderate quality, with more than half being judged as good quality. However, even studies deemed to have been of good quality may still contain bias. This study did identify some study specific biases. These included three studies providing a poor description of their methods of data collection methods and in one [22] a very large male prevalence of the study participants, another used only a single surgeons caseload [23] and another considered only patients with gastric adenocarcinoma [24]. The degree to which these affect the overall finding is hard to determine but does need to be noted. Further, due to the non-randomized nature of the included studies the findings of this review should be viewed with caution. Since the included study designs were cross-sectional, we took a conservative approach by comparing proportions, rather than estimating the increased relative risk of those with increased frailty.

However, a strength of the evidence linking frailty to poorer outcomes is consistent, with little heterogeneity demonstrated in most outcomes. The findings also suggest a dose–response of poorer outcomes linked to the presence of frailty when compared with the pre-frail subgroup, although we acknowledge that the pre-frail group was comprised of a comparatively small number of participants. The biological plausibility and a reasonable consistency across the varying studies is indicative that frailty is linked with poorer post-surgical outcomes.

There was heterogeneity found within the post-operative complications outcomes, but we believe that this was introduced by differing methods used to assess post-operative complications. For example, two studies [18, 20] used the American College of Surgery National Surgical Quality Improvement Program definition, one [25] the American Society Guidelines and another [21] defined their own list of post-operative complications. Future studies should consider using a standardised post-operative complication definition, as this will aid accurate comparison between frail surgical patients across studies.

The quantity of robust published data for individual outcomes was limited. None of the preselected outcome measures were reported in more than four studies and two (medium-term mortality and readmission to hospital) were only reported in two studies. Using small numbers of studies for meta-analysis requires a degree of caution when interpreting results, but throughout all of the outcomes there is a consistent and repeated effect of frailty.

A potential limitation was the absence of data from patients with special clinical situations such as intensive care admission. The decision was taken to exclude these data to avoid introducing confounding. However, it should be noted as a potential area for future dedicated systematic review in light of evidence that frailty predicts risk of institutionalisation in surgical patients who are admitted to intensive care [12].

The present review found a range of frailty assessment tools were chosen and implemented across the studies which will have introduced heterogeneity. This is to be expected as there are two broad models used for frailty assessment, the phenotype model and the accumulation of deficits model. Both models are valid and can be applied to research and clinical situations with the proviso that staff using these tools are trained in their use [29]. The search criteria in this review stated that we would only include studies that employed recognized frailty assessment methods. Eight of the included studies used either phenotype or deficit accumulation models. The only caution and deviation from the inclusion criteria was the decision to include the study by Robinson *et al.* [25]. This study did not use an established frailty assessment tool which conformed to either of the models described above. However, the primary author and the associated team have published widely in the field of surgical disease in the older person and the assessment tool they use is robust, validated and is being used by additional research groups. Therefore, following consensus, it was decided to include this study.

It is also of note that one study [24] met our inclusion criteria but did not form part of the analysis. It was not possible to extract data from those contained in the manuscript. No response was received from the study authors for a more detailed breakdown of data which may have been usable. Should future studies wish to revisit this area, perhaps to address a different outcome, these data need to be included for completeness. The findings of the study were all in keeping with the reported meta-analysis and frailty showed an association with morbidity ($P = 0.02$).

Additionally we excluded large database type assessments of frailty [8] from our analysis. The primary rationale was 2-fold. Firstly, these studies used frailty assessments derived specifically for each database according to the factors available within them and were not uniform in construction and secondly, they were of such scale that to have included them would have influenced the results to such an extent that other smaller studies would have had virtually no effect on the outcome measures generated.

Implications for research and clinical practice

All of the included studies were published since 2010, and it is likely that further studies will be suitable for combination with the data shown here to further reinforce (or repudiate) our findings. Perhaps more importantly, it is likely that additional outcome data will become available for measures such as long-term mortality, and for patient-facing measures such as quality of life after surgery and requirement for social care provision. Further research in these areas will allow more comprehensive assessment of the impact that surgical conditions and their management have on frail patients.

By establishing the impact of frailty on both morbidity and mortality, this study further highlights the importance of this clinical condition. Clinicians can use the presence of frailty to help predict worse outcomes in general surgery. Where possible frailty should be identified pre-operatively, allowing the use of targeted interventions such as Comprehensive Geriatric Assessment [30, 31] with the aim of optimising clinical condition prior to surgical management.

Conclusions

This study demonstrated that frailty is common in both elective and emergency general surgery. Despite a limited number of studies included in each of the meta-analyses frailty demonstrated a consistent association with both mortality and morbidity.

Key points

- Previous studies have used a range of frailty tools and found association with a broad range of different negative outcomes.
- This systematic review in general surgery used nine studies.
- Frailty is associated with mortality at Day 30 in both emergency and elective general surgery.
- Frailty is associated with post-operative complications and length of hospital stay.
- This review consolidates the evidence base for using frailty in the assessment of the older general surgical patient.

Supplementary data

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

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Conflicts of interest

None.

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