Association between frailty and clinical outcomes in surgical patients admitted to intensive care units: a systematic review and meta-analysis

Rachel Chan1,5,* Ryo Ueno2,6, Afsana Afroz3, Baki Billah3, Ravindranath Tiruvoipati1,4,7 and Ashwin Subramaniam1,4,7

1Department of Intensive Care, Frankston Hospital, Peninsula Health, Frankston, VIC, Australia, 2Department of Intensive Care, Eastern Health, Box Hill, VIC, Australia, 3Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia, 4Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, VIC, Australia, 5Department of Anaesthesia and Pain Management, The Canberra Hospital, ACT, Australia, 6Australian and New Zealand Intensive Care Research Centre, School of Public Health and Preventive Medicine, Monash University, VIC, Australia and 7Monash University Peninsula Clinical School, VIC, Australia

*Corresponding author. E-mails: dr.rachel.chan@gmail.com, ryo.ueno@monash.edu, Travindranath@hotmail.com, ashwin.subramaniam@monash.edu

Abstract

Background: Preoperative frailty may be a strong predictor of adverse postoperative outcomes. We investigated the association between frailty and clinical outcomes in surgical patients admitted to the ICU.

Methods: PubMed, Embase, and Ovid MEDLINE were searched for relevant articles. We included full-text original English articles that used any frailty measure, reporting results of surgical adult patients (>18 yr old) admitted to ICUs with mortality as the main outcome. Data on mortality, duration of mechanical ventilation, ICU and hospital length of stay, and discharge destination were extracted. The quality of included studies and risk of bias were assessed using the Newcastle Ottawa Scale. Data were synthesised according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.

Results: Thirteen observational studies met inclusion criteria. In total, 58,757 patients were included; 22,793 (39.4%) were frail. Frailty was associated with an increased risk of short-term (risk ratio [RR]=2.66; 95% confidence interval [CI]: 1.99–3.56) and long-term mortality (RR=2.66; 95% CI: 1.32–5.37). Frail patients had longer ICU length of stay (mean difference [MD]=1.5 days; 95% CI: 0.8–2.2) and hospital length of stay (MD=3.9 days; 95% CI: 1.4–6.5). Duration of mechanical ventilation was longer in frail patients (MD=22 h; 95% CI: 1.7–42.3) and they were more likely to be discharged to a healthcare facility (RR=2.34; 95% CI: 1.36–4.01).

Conclusion: Patients with frailty requiring postoperative ICU admission for elective and non-elective surgeries had increased risk of mortality, lengthier admissions, and increased likelihood of non-home discharge. Preoperative frailty assessments and risk stratification are essential in patient and clinician planning, and critical care resource utilisation.

Clinical trial registration: PROSPERO CRD42020210121.

Keywords: frailty; ICU; long-term mortality; meta-analysis; short-term mortality; surgical outcomes; systematic review
Frailty and critically ill surgical patients

Editor’s key points

- Frailty in critical illness is associated with poor outcomes. There is inadequate information regarding outcomes in surgical patients with frailty admitted to ICUs.
- Based on this systematic review and meta-analysis, regardless of frailty measurement tool or type of surgery, surgical patients with frailty admitted to the ICU had a greater risk of mortality, longer ICU and hospital stays, and were more likely to be discharged to healthcare facilities.
- These findings suggest that preoperative frailty assessments could assist in risk stratifying patients with frailty, particularly in the elective surgery setting.

The ageing of society and improved life expectancies has resulted in increasing numbers of older people undergoing surgery worldwide. However, there has been debate on the benefits of critical care admission after elective surgery with a large prospective data analysis from 27 countries failing to identify a survival benefit and a retrospective study concluding that the use of the ICU for older surgical patients did not improve mortality. Nevertheless, indirect or unplanned ICU admissions postoperatively were associated with increased mortality compared with planned admissions. Older patients present with unique physiologic, pharmacologic, psychological, and social challenges that increase complexities of both elective and emergency surgeries. They are more likely to have pre-existing medical comorbidities, increasing their risk of cardiovascular and cerebrovascular complications. Some older people may be more susceptible to poorer outcomes, beyond the risk explained by their age or comorbidities. This increased vulnerability is defined as frailty, which reflects a loss of physiological reserve as a result of stressors, posing major challenges and complexity in caring for the older critically ill population. The multidimensional frailty syndrome has a prevalence of >40% in ICU patients aged >80 yr. Frailty in critical illness predisposes to poor outcomes and more than doubles the risk of mortality and functional dependence.

There are two accepted paradigms of frailty: phenotypic construct, and deficit accumulation model. The phenotype construct is based on a cluster of signs and symptoms such as self-reported exhaustion, slowed performance (by walking speed), weakness (by grip strength), unintentional weight loss (4.5 kg in the past year), and low physical activity. The deficit accumulation model, however, is quantified based on the number rather than the nature of health problems, along with biochemical and physiological impairments. An overlap exists between the two constructs, their sum contributing to a risk state. These constructs of frailty are usually captured within the gold standard Comprehensive Geriatric Assessment (CGA), and are usually based on functional performance as a marker of the overall reserve.

The frailty status impacting postoperative outcomes is increasingly described in hospital-based and population-based studies. Moreover, frailty particularly assessed preoperatively, is an independent predictor of morbidity and mortality. Given that frailty was found to be associated with postoperative mortality across all levels of operative stress, further understanding of the impact of frailty on surgical ICU patients can help to better risk-stratify patients and improve the perioperative utilisation of the ICU.

To date, we have not found any reviews specifically looking at the spectrum of tools utilised in surgical ICU patients and associated clinical outcomes (mortality, discharge destination, hospital LOS). This systematic review was conducted to investigate whether frailty measured in adult surgical patients before or during admission to the ICU was predictive of adverse outcomes.

Methods

The study was conducted in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement. A checklist has been included in Appendix A (PRISMA 2009 checklist). The protocol was registered on PROSPERO (CRD42020210121).

Eligibility criteria

The studies were considered eligible if frailty was measured before or at admission to ICU and if it reported on patient outcomes including mortality. We included studies, between January 2000 and September 2020, of adult (≥18 yr of age) surgical patients admitted to the ICU who reported a main outcome of mortality. We assessed all the relevant studies and their citation lists to identify articles for inclusion. Studies involving burns and trauma patients requiring surgery during their admission to the ICU were also considered. Studies reporting short-term (<30 days or in-hospital) and long-term mortality (>6 months) were included. Secondary outcomes of interest included ICU and hospital length of stay (LOS), length of time on mechanical ventilation, and discharge destination. Studies were excluded if they were not original research (e.g. review articles, conference abstracts, letters, and commentaries); any non-human studies, if they were unpublished or non-peer-reviewed; not in English language or without an available full text and interventional studies. We also excluded any case reports and series (<10 patients) to avoid publication bias.

Search strategy and information sources

Two reviewers (RC and RU) searched PubMed, Embase, and Ovid MEDLINE with agreed medical subject headings (MeSH) terms. These search terms and strategies, including limits used, have been included in Supplementary Table S1. Any tool to measure frailty was considered, and frailty was defined as per each study’s definition as being frail and non-frail. References from selected articles were also examined for further relevant articles. Duplicates were removed. The reference lists of eligible studies were reviewed to identify studies not returned by the search. The search was finalised on September 18, 2020.

Study selection and data extraction

Two reviewers (RC and RU) independently performed the data extraction of included articles. Rayyan QC (Rayyan Systems Inc, Cambridge, MA, USA) software was used to shortlist articles of relevance and filter the reasons for rejected studies. Data were collected independently by two reviewers (RC and RU) using a prespecified data extraction form; any conflicts were resolved by consensus or by a third reviewer (AS). Corresponding authors were contacted for additional information, where data were incomplete. Data collection covered...
study characteristics (study design, study duration, name and country of study centre), patient characteristics (sample size, number of male/female patients, age, comorbidities), tool of frailty used, ICU characteristics, the total number of patients in each study; frail and non-frail; ICU, in-hospital, short-term and long-term mortality, length of time on mechanical ventilation, ICU and hospital LOS and discharge disposition were independently extracted, tabulated, and verified between the two reviewers (RC and RU).

Quality assessment and risk of bias in individual studies
The Newcastle-Ottawa Scale (NOS)34 is a quality assessment tool used to evaluate non-randomised studies based on an eight-item score, divided into three domains. These domains assess selection, comparability, and ascertainment of the outcome of interest. The NOS was used by three authors (RC, RU, and AS) to independently evaluate the quality of included studies and assess for risk of bias. The possibility of publication bias was assessed using Egger’s test and funnel plots. To account for the heterogeneity, two sensitivity analyses were performed for the primary outcome: to compare the outcomes between (1) prospective and retrospective studies; and (2) studies that reported on <100 patients vs those with >100 patients.

Study outcomes
The primary outcome was pooled differences in short-term (in-hospital or <3 months) and long-term (≥6 months) mortality amongst frail and non-frail patients. The secondary outcomes included duration of mechanical ventilation, ICU and hospital LOS, and discharge destination to healthcare facilities (defined as a residential aged care facility, admission to rehabilitation unit, or both).

Subgroup analysis
Planned subgroup analyses were conducted to compare the outcomes between cardiac and noncardiac patients.

Post hoc analysis
We performed post-hoc analysis to compare outcomes of those who were admitted to the ICU after elective and non-elective/emergency (trauma) surgery. Another post hoc analysis was also performed comparing outcomes of frailty measured by frailty scores which were predominantly phenotypic construct and deficit accumulation model.

Summary measures and synthesis of results
Data analysis was conducted using Stata SE version 16 (StataCorp, College Station, TX, USA). Mean and standard deviation (SD) were used for numerical data and proportion was used for categorical data. The mean values were calculated from published median and range data utilising the method and calculator by Hozo and colleagues.36 A two-tailed P-value <0.05 was considered significant. Equality of two proportions was evaluated using the Z-test. The Mantel-Haenszel method was used in dichotomous results and inverse variance was used where continuous variables were reported. Results were presented in forest plots. The pooled prevalence, log-transformed risk ratio (RR), and mean difference (MD) were calculated across studies using the random-effects models of restricted maximum-likelihood method and reported with 95% confidence interval (95% CI) for continuous and dichotomous variables, respectively. We calculated the RR using the =EXP (value) function in MS Excel. For simplicity, only the calculated RR is presented throughout. In the presence of heterogeneity (as expected and observed), random-effect models have superior properties and are more conservative than fixed-effect models.36 A random-effects model was used to calculate a pooled RR with 95% CI. Heterogeneity across the studies was evaluated using the Cochran Q test and quantified using the I² statistic. Heterogeneity among studies was categorised as high ($I^2=76–100$%), moderate ($I^2=26–75$%), and low ($I^2=0–25$%).37 Symmetry of the funnel plots was used to examine for publication bias.

Results
A total of 1395 articles were identified. After excluding unrelated articles, duplicates, and those not fitting the eligibility criteria, 54 articles were selected for full-text review (Fig. 1). Where outcomes of interest were incompletely reported, attempts were made to contact authors for further information without success. Thirteen studies were chosen for final analysis.38–50 The characteristics of the included studies are summarised in Supplementary Table S2.

Summary of included studies
Nine studies were prospective,38,39,41,43–46 and four were retrospective.40,42,49,50 Retrospective studies utilised data from surgery databases. With prospective studies, frailty assessment was conducted before surgery except for one study,46 where frailty was assessed during ICU admission once the patient was able to comply with instructions. Seven studies38–40,43–45,50 included cardiac surgery patients, two included transplant patients,41,49 two included trauma patients,42,48 and two were based in general surgical ICUs46,47 that admitted trauma, transplant, and a variety of surgical population patients (abdominal, thoracic, vascular, gynaecological). Eight studies included elective surgical populations,38,39,41,43–45,49,50 two of them included non-elective/emergency (trauma) patients,42,48 and the other three included both elective and non-elective populations.40,46,47

Of the 58757 patients included, 22793 were classified as frail (39.4%; range 5.9–58.7%). Overall, 35% of the population was female. The pooled mean [SD] age is 65.5 [8.9] yr. Frailty had been determined using nine different assessment methods: Cardiovascular Health Study frailty index,38 5 m gait speed test,50 Clinical Frailty Scale,46 Edmonton Frail Scale,39,47 Katz Index of Independence in activities of daily living,40 modified Fried’s Frailty Phenotype,43,44 modified Frailty Index,47 manual muscles testing,46,47 and Frailty Index.47,49 The characteristics of the frailty measures utilised are summarised in Table 1.

Quality of studies and risk of bias within studies
All 13 studies received scores of ≥7 when evaluated with the six studies38,39,44,48–50 received an average of the maximum score of 9 (Supplementary Table S3).

Primary outcome: mortality (Fig. 2a and b; Supplementary Figs S1–S3)

Short-term mortality
Eleven studies38–42,44–48,50 reported in-hospital mortality, short-term mortality, or both (in hospital <30 days) and pooled
unadjusted data from a total of 57,517 patients, 22,707 of whom were frail (39.5%), and revealed an increased risk of short-term mortality in frail compared with non-frail patients (RR = 2.66; 95% CI: 1.99–3.56) (Fig. 2a). Despite the moderate heterogeneity ($I^2 = 69.1$%), Egger’s regression test ruled out publication bias ($P = 0.09$) (Supplementary Fig. S1a). Although sensitivity analyses demonstrated higher mortality in patients with frailty, there was no difference amongst frail patients if the studies were prospective38,39,41,44–48 or retrospective24,40,42 (RR = 3.53 [95% CI: 2.14–5.64] vs RR = 2.39 [95% CI: 1.67–3.39]; $P = 0.21$) or if the sample number was $>100$41,44,46 or $<100$24,38–40,42,45,48 patients (RR = 2.23 [95% CI: 0.87–5.70] vs RR = 2.75 [95% CI: 1.97–3.78]; $P = 0.68$) (Supplementary Fig. S2).

Long-term mortality (>6 months)

Four studies43,44,48,49 reported on longer-term mortality in 252 non-frail patients and 148 frail patients. Studies reported different lengths of time for longer-term mortality (314 days,12 months,34 and 3 yr49). Longer-term mortality was higher in frail patients RR = 2.66 (95% CI: 1.32–5.37) (Fig. 2b). There was moderate heterogeneity ($I^2 = 66$%), but there was no publication bias (Egger’s test $P = 0.45$) (Supplementary Fig. S1b). Although sensitivity analyses demonstrated higher mortality in patients with frailty, there was no difference amongst frail patients if the studies were prospective43,44,48 or retrospective49 (RR = 2.48 [95% CI: 0.98–6.29] vs RR = 3.97 [95% CI: 1.38–11.36]; $P = 0.52$). There was an increased risk of long-term mortality demonstrated when the sample size had $>100$48,49 patients (RR = 4.90 [95% CI: 2.66–9.03] vs RR = 1.67 [95% CI: 0.70–3.94]; $P = 0.05$) (Supplementary Fig. S3).

Secondary outcomes (Fig. 3a–d; Supplementary Fig. S4)

Length of time on mechanical ventilation

Five studies43,44,46,48,49 reported on length of time on mechanical ventilation in 182 frail and 305 non-frail patients. Frail
<table>
<thead>
<tr>
<th>Frailty measure/tool</th>
<th>Description</th>
<th>Characteristics</th>
<th>Definition of frailty</th>
<th>No. of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHS (Cardiovascular Health Study) frailty index</td>
<td>Five components: 1. weight loss 2. exhaustion 3. low physical activity 4. slow walk time 5. weak grip strength</td>
<td>Frailty dichotomous (yes/no) - Weight loss: self-reported &gt;10 pounds in the preceding year - Self-reported exhaustion - Physical activity calculated as expenditure per week on the Minnesota Leisure Time activity questionnaire - 5 m walk test average of 3 times Weak grip strength assessed with Jamar hand-held dynamometer</td>
<td>Considered frail if meets ≥3 components</td>
<td>1</td>
</tr>
<tr>
<td>5 m Gait speed test</td>
<td>Standardised walk test - Patients to walk at a comfortable pace until a few meters past the 5-m mark - The timer started at 0 m mark and stopped with the first footfall after the 5 m line. Test repeated 3 times, allowing time for recuperation</td>
<td>Frail if &lt;0.83 m s⁻¹</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Edmonton Frail Scale</td>
<td>Multidimensional frailty assessment tool. - Cognition, general health, functional independence, social support, medication use, nutrition, mood, continence, short up and go walk test</td>
<td>Score: range 0–17 (0–2 points/item based on severity) Frail if ≥8 0–5: not frail 6–7: vulnerable 8–17: frail (8–9: mildly; 10–11: moderately 12–17: severely)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Clinical frailty scale</td>
<td>Multidimensional frailty assessment tool</td>
<td>It is a 9-point tool that uses visual and written analogues</td>
<td>Score range 1–9 Frail if &gt;4 1–3: non-frail 4: vulnerable 5–9: frail (5: mildly, 6: moderately, 7: severely, 8: very severely, and 9: terminally ill)</td>
<td>1</td>
</tr>
<tr>
<td>Modified Frailty Index (mFI)</td>
<td>Calculated using 11 variables (9 comorbidities and 2 functional status measures) from the Canadian Study of Health and Ageing (CSHA)</td>
<td>- History of hypertension requiring medication - History of peripheral vascular disease or pain at rest - History of cerebrovascular accident with neurological deficit - History of myocardial infarction - History of prior percutaneous coronary intervention or prior coronary artery bypass grafting or angina - History of congestive cardiac failure - History of either transient ischaemic attack or cerebrovascular accident without neurological deficit - History of diabetes mellitus mFI score ranges from 0.0 to 1.0</td>
<td>0: non-frail 0–0.27: pre-frail ≥0.27: frail</td>
<td>1</td>
</tr>
</tbody>
</table>

Continued
<table>
<thead>
<tr>
<th>Frailty measure/ tool</th>
<th>Description</th>
<th>Characteristics</th>
<th>Definition of frailty</th>
<th>No. of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fried’s frailty phenotype</td>
<td>5 functional domains: - exhaustion - slowness - weakness - physical inactivity - loss of appetite</td>
<td>- History of impaired sensorium - History of impaired functional status. Each positive comorbidity is equivalent to one point - Self-reported exhaustion in response to 2 questions - Weak grip - Mobility—slow walking speed (&gt;6 s to complete 5 m) - Appetite—self-reported reduction in the last 3 months - Reduced physical activity &lt;1–3 times/month or hardly ever</td>
<td>Frail if score is ≥3</td>
<td>3</td>
</tr>
<tr>
<td>Manual muscle testing</td>
<td>Medical Research Council (MRC) scale using a scoring system on muscle strength testing 12 muscle groups</td>
<td>Muscle groups tested: - shoulder abductor - elbow flexor - wrist extensor - hip flexor - knee extensor - ankle dorsiflexor</td>
<td>MRC scale &lt;48=positive for ICU-acquired weakness Scoring system: 0–5 0=no muscle contraction 1=trace contraction 2=movement with gravity eliminated 3=movement against gravity 4=movement against gravity and manual resistance 5=normal strength</td>
<td>1</td>
</tr>
<tr>
<td>Handgrip dynamometry</td>
<td>Handgrip strength test using Jamar dynamometer</td>
<td>High grip strength: - &gt;11 kg for men - &gt;7 kg for women Low grip strength: - &lt;11 kg for men - &lt;7 kg for women</td>
<td>Frail if grip strength &lt;11 kg for men and &lt;7 kg for women</td>
<td>1</td>
</tr>
<tr>
<td>Frailty Index</td>
<td>The proportion of deficits present in an individual out of the total number of age-related health variables considered</td>
<td>Total of 40 possible deficits</td>
<td>The submaximal limit is ~0.67 Typically, &gt;0.25 is frail &lt;0.25 not frail</td>
<td>2</td>
</tr>
<tr>
<td>Katz index of independence of activities of daily living (ADL)</td>
<td>Tool to assess the functional status of performing 6 activities of daily living independently</td>
<td>- Bathing, dressing, toileting, transferring, continence, feeding</td>
<td>Frail if any loss of independence in activities of daily living ≥1</td>
<td>1</td>
</tr>
</tbody>
</table>
patients required a significantly longer time duration of mechanical ventilation, compared with the non-frail patients MD=22.0 h (95% CI: 1.7–42.3 h; P=0.03). Despite the high heterogeneity (I²=92%), there was no publication bias (Egger’s test P=0.13) (Supplementary Fig. S4c).

**ICU LOS**

Eight studies\(^{38,41,43-49}\) reported on ICU LOS in 292 frail and 751 non-frail patients. Frail patients demonstrated significantly longer ICU LOS, compared with non-frail patients (MD=1.5 days; 95% CI: 0.8–2.2 days; P<0.001).

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail Died</th>
<th>Frail Survived</th>
<th>Non-frail Died</th>
<th>Non-frail Survived</th>
<th>Logarithm of RR with 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee 2012</td>
<td>5</td>
<td>39</td>
<td>2</td>
<td>49</td>
<td>1.06 (0.53–2.65)</td>
<td>2.98</td>
</tr>
<tr>
<td>Buth 2014</td>
<td>52</td>
<td>324</td>
<td>238</td>
<td>5723</td>
<td>1.24 (0.96–1.52)</td>
<td>21.37</td>
</tr>
<tr>
<td>Mueller 2016</td>
<td>5</td>
<td>34</td>
<td>0</td>
<td>63</td>
<td>2.87 (0.00–5.74)</td>
<td>0.99</td>
</tr>
<tr>
<td>Ad. 2016</td>
<td>7</td>
<td>37</td>
<td>3</td>
<td>28</td>
<td>1.18 (1.57–3.93)</td>
<td>1.08</td>
</tr>
<tr>
<td>Affilalo, 2016</td>
<td>154</td>
<td>4 434</td>
<td>160</td>
<td>10 423</td>
<td>0.80 (0.58–1.02)</td>
<td>23.20</td>
</tr>
<tr>
<td>Joseph 2017</td>
<td>7</td>
<td>37</td>
<td>3</td>
<td>28</td>
<td>0.50 (0.77–1.77)</td>
<td>4.38</td>
</tr>
<tr>
<td>Hamidi 2019</td>
<td>3 154</td>
<td>14 273</td>
<td>1 690</td>
<td>15 737</td>
<td>0.62 (0.57–0.68)</td>
<td>26.43</td>
</tr>
<tr>
<td>Amabili 2019</td>
<td>8</td>
<td>44</td>
<td>9</td>
<td>193</td>
<td>1.24 (0.34–2.14)</td>
<td>7.50</td>
</tr>
<tr>
<td>DeMaria 2019</td>
<td>1</td>
<td>14</td>
<td>0</td>
<td>35</td>
<td>1.91 (1.24–5.06)</td>
<td>0.83</td>
</tr>
<tr>
<td>Kiss 2020</td>
<td>5</td>
<td>56</td>
<td>8</td>
<td>244</td>
<td>0.95 (0.13–2.03)</td>
<td>5.70</td>
</tr>
<tr>
<td>Tipping 2020 (In hospMortality data)</td>
<td>8</td>
<td>14</td>
<td>4</td>
<td>74</td>
<td>1.96 (0.86–3.06)</td>
<td>5.53</td>
</tr>
</tbody>
</table>

**Random-effects REML model**

**Fig 2.** Primary outcome: short-term (in-hospital and <30-day mortality) and long-term (>6 months) mortality. CI, confidence interval; REML, restricted maximum likelihood; RR, risk ratio.

There was high heterogeneity (I²=96.8%), with associated publication bias (Egger’s test P=0.039) (Supplementary Fig. S4a).

**Hospital LOS**

Nine studies\(^{38,41,43-49}\) reported on hospital LOS in 336 frail and 782 non-frail patients. Despite two studies having shorter LOS in frail patients,\(^{35,48}\) the overall MD demonstrated significantly longer hospital LOS for frail patients of 3.9 days (95% CI: 1.4–6.5 days; P<0.001). Despite the high heterogeneity (I²=99.3%), there was no publication bias (Egger’s test P=0.13).
### Figure 3: Secondary outcomes

#### ICU length of stay

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail N</th>
<th>Mean</th>
<th>SD</th>
<th>Non-frail N</th>
<th>Mean</th>
<th>SD</th>
<th>Mean difference 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee 2012</td>
<td>44</td>
<td>6</td>
<td>7.25</td>
<td>51</td>
<td>4</td>
<td>6.5</td>
<td>2.00 (0.77–4.77)</td>
<td>4.58</td>
</tr>
<tr>
<td>Mueller 2016</td>
<td>39</td>
<td>6.2</td>
<td>6.2</td>
<td>63</td>
<td>3.6</td>
<td>2.3</td>
<td>2.50 (0.81–4.19)</td>
<td>8.41</td>
</tr>
<tr>
<td>Wilson 2016</td>
<td>46</td>
<td>7.5</td>
<td>3.1</td>
<td>56</td>
<td>6</td>
<td>1.3</td>
<td>1.50 (0.61–2.39)</td>
<td>13.10</td>
</tr>
<tr>
<td>Ad, 2016</td>
<td>39</td>
<td>2.2</td>
<td>8</td>
<td>127</td>
<td>1.2</td>
<td>.2</td>
<td>1.00 (0.85–1.15)</td>
<td>16.59</td>
</tr>
<tr>
<td>Jha 2017 (Heart Transplant cohort)</td>
<td>18</td>
<td>9.3</td>
<td>3.3</td>
<td>59</td>
<td>6</td>
<td>1.8</td>
<td>3.30 (2.12–4.48)</td>
<td>11.30</td>
</tr>
<tr>
<td>DeMaria 2019</td>
<td>15</td>
<td>5</td>
<td>2.2</td>
<td>35</td>
<td>3</td>
<td>.5</td>
<td>2.00 (1.24–2.76)</td>
<td>13.92</td>
</tr>
<tr>
<td>Kiss 2020</td>
<td>61</td>
<td>2</td>
<td>.75</td>
<td>252</td>
<td>1</td>
<td>.17</td>
<td>1.00 (0.90–1.10)</td>
<td>16.67</td>
</tr>
<tr>
<td>Tipping 2020</td>
<td>30</td>
<td>5.2</td>
<td>1.3</td>
<td>108</td>
<td>5</td>
<td>1.2</td>
<td>0.20 (0.29–0.89)</td>
<td>19.42</td>
</tr>
</tbody>
</table>

**Overall**

<table>
<thead>
<tr>
<th>Mean difference 95% CI</th>
<th>Weight (%)</th>
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<tbody>
<tr>
<td>3.93 (1.31–4.68)</td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** $\tau^2 = 0.75, \hat{\rho} = 96.76\%, H^2 = 30.90$

**Test of $\theta = 0$:** $Q(7) = 36.02, P = 0.00$

**Test of $I^2$:** $z = 4.27, P = 0.00$

#### Hospital length of stay

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail N</th>
<th>Mean</th>
<th>SD</th>
<th>Non-frail N</th>
<th>Mean</th>
<th>SD</th>
<th>Mean difference 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee 2012</td>
<td>44</td>
<td>15</td>
<td>16</td>
<td>51</td>
<td>10</td>
<td>13</td>
<td>5.00 (0.83–10.83)</td>
<td>7.47</td>
</tr>
<tr>
<td>Mueller 2016</td>
<td>39</td>
<td>14.6</td>
<td>11.7</td>
<td>63</td>
<td>8.4</td>
<td>5</td>
<td>6.20 (2.92–9.48)</td>
<td>10.27</td>
</tr>
<tr>
<td>Wilson 2016</td>
<td>46</td>
<td>14</td>
<td>2.8</td>
<td>56</td>
<td>10.5</td>
<td>2.2</td>
<td>3.50 (2.53–4.47)</td>
<td>12.21</td>
</tr>
<tr>
<td>Ad, 2016</td>
<td>39</td>
<td>8</td>
<td>1.5</td>
<td>127</td>
<td>5</td>
<td>.7</td>
<td>3.00 (2.66–3.34)</td>
<td>12.40</td>
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<tr>
<td>Jha 2017 (Heart Transplant cohort)</td>
<td>18</td>
<td>31.2</td>
<td>9.7</td>
<td>59</td>
<td>25</td>
<td>6</td>
<td>6.20 (2.50–9.90)</td>
<td>9.81</td>
</tr>
<tr>
<td>Joseph 2017</td>
<td>44</td>
<td>29</td>
<td>6.4</td>
<td>31</td>
<td>20</td>
<td>4.1</td>
<td>9.00 (6.44–11.56)</td>
<td>11.02</td>
</tr>
<tr>
<td>DeMaria 2019</td>
<td>15</td>
<td>15</td>
<td></td>
<td>2</td>
<td>35</td>
<td>1.5</td>
<td>7.00 (6.00–8.00)</td>
<td>12.19</td>
</tr>
<tr>
<td>Kiss 2020</td>
<td>61</td>
<td>8</td>
<td>.6</td>
<td>252</td>
<td>8</td>
<td>.3</td>
<td>0.00 (0.11–0.11)</td>
<td>12.43</td>
</tr>
<tr>
<td>Tipping 2020</td>
<td>30</td>
<td>14.8</td>
<td>3.1</td>
<td>108</td>
<td>17.5</td>
<td>2.3</td>
<td>–2.70 (–3.70–1.70)</td>
<td>12.19</td>
</tr>
</tbody>
</table>

**Overall**

<table>
<thead>
<tr>
<th>Mean difference 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.93 (1.41–4.64)</td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** $\tau^2 = 13.35, \hat{\rho} = 99.29\%, H^2 = 141.52$

**Test of $\theta = 0$:** $Q(8) = 588.41, P = 0.00$

**Test of $I^2$:** $z = 3.05, P = 0.00$

#### Duration of mechanical ventilation

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail N</th>
<th>Mean</th>
<th>SD</th>
<th>Non-frail N</th>
<th>Mean</th>
<th>SD</th>
<th>Mean difference 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee 2012</td>
<td>39</td>
<td>42</td>
<td>168</td>
<td>49</td>
<td>12</td>
<td>78</td>
<td>30.00 (–22.98–82.98)</td>
<td>9.18</td>
</tr>
<tr>
<td>Wilson 2016</td>
<td>46</td>
<td>48</td>
<td>12</td>
<td>56</td>
<td>48</td>
<td>12</td>
<td>0.00 (–4.68–4.68)</td>
<td>24.36</td>
</tr>
<tr>
<td>Jha 2017 (Heart Transplant cohort)</td>
<td>18</td>
<td>68.75</td>
<td>28.75</td>
<td>59</td>
<td>31</td>
<td>29.5</td>
<td>37.75 (22.27–53.23)</td>
<td>21.57</td>
</tr>
<tr>
<td>Joseph 2017</td>
<td>37</td>
<td>71.6</td>
<td>39.9</td>
<td>28</td>
<td>25.6</td>
<td>8.18</td>
<td>46.00 (30.96–61.04)</td>
<td>21.72</td>
</tr>
<tr>
<td>Tipping 2020</td>
<td>30</td>
<td>88.8</td>
<td>26.4</td>
<td>108</td>
<td>84</td>
<td>25.6</td>
<td>4.80 (–5.62–15.22)</td>
<td>23.16</td>
</tr>
</tbody>
</table>

**Overall**

<table>
<thead>
<tr>
<th>Mean difference 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.00 (1.74–42.26)</td>
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</table>

**Heterogeneity:** $\tau^2 = 432.95, \hat{\rho} = 92.40\%, H^2 = 13.15$

**Test of $\theta = 0$:** $Q(4) = 50.42, P = 0.00$

**Test of $I^2$:** $z = 2.13, P = 0.03$

#### Discharge to healthcare facility

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail Logarithm of RR with 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bath 2014</td>
<td>1.41 (1.27–1.54)</td>
<td>20.35</td>
</tr>
<tr>
<td>Mueller 2016</td>
<td>0.68 (0.20–1.16)</td>
<td>17.76</td>
</tr>
<tr>
<td>Ad, 2016</td>
<td>1.36 (0.78–1.95)</td>
<td>16.64</td>
</tr>
<tr>
<td>Hannisd 2019</td>
<td>1.02 (0.99–1.05)</td>
<td>20.58</td>
</tr>
<tr>
<td>DeMaria 2019</td>
<td>0.85 (1.02–2.71)</td>
<td>6.01</td>
</tr>
<tr>
<td>Tipping 2020</td>
<td>0.23 (–0.62–0.16)</td>
<td>16.66</td>
</tr>
</tbody>
</table>

**Overall**

<table>
<thead>
<tr>
<th>Logarithm of RR with 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.85 (0.31–1.39)</td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** $\tau^2 = 0.37, \hat{\rho} = 97.46\%, H^2 = 39.38$

**Test of $\theta = 0$:** $Q(5) = 75.66, P = 0.00$

**Test of $I^2$:** $z = 3.07, P = 0.00$

**Random-effects REML model**

Calculated RR = 2.34 (1.36–4.01)

---

Fig 3: Secondary outcomes. CI, confidence interval; REML, restricted maximum likelihood; RR, risk ratio; SD, standard deviation.
Discharge to healthcare facility

Six studies reported on discharge to a healthcare facility in 17,917 frail and 23,721 non-frail patients. Frail patients were found to be more likely discharged to a healthcare facility (RR = 2.34; 95% CI: 1.36–4.01). Despite the high heterogeneity (I² = 97.5%), there was no publication bias (Egger’s test P = 0.83).

Subgroup analysis (Fig. 4)

Cardiac vs noncardiac

Seven studies reported on 22,416 cardiac surgery patients (5,192 frail and 17,224 non-frail patients) and six studies reported on 35,341 noncardiac surgical patients (17,601 frail and 17,740 non-frail patients). The pooled mean age was similar between cardiac and noncardiac surgical patients (63.8 [9.4] yr vs 64.7 [10.6] yr). Frail patients who underwent cardiac surgery were more likely to be discharged to a healthcare facility than noncardiac surgical patients (RR = 4.00 [95% CI: 3.60–4.62] vs RR = 1.72 [95% CI 0.89–3.29]; P = 0.01). There was no difference between cardiac and noncardiac surgical patients for short-term mortality, long-term mortality, ICU LOS, and hospital LOS.

Post-hoc analysis (Supplementary Figs S5 and S6)

Elective vs non-elective/emergency/trauma

Eight studies reported on 16,231 elective surgery patients (4,877 frail and 11,354 non-frail patients) and two studies reported on 35,004 non-elective/emergency/trauma surgical patients (17,499 frail and 17,505 non-frail patients). Based on one study, frail patients who underwent non-elective surgery were more likely to have a decreased hospital LOS (MD = −2.7 days; 95% CI: −3.7 to −1.7 days). The hospital LOS was significantly longer for frail patients who underwent elective surgery (MD = 4.6 days; 95% CI: 1.9–7.2 days). There was no difference in short-term mortality, long-term mortality, ICU LOS, mechanical ventilation, and discharge to healthcare facility between the frail non-elective (trauma) and elective surgical patients.

Phenotypic construct and deficit accumulation model frailty score

Ten studies used a phenotype construct to determine frailty in 22,661 patients (5,273 frail and 17,388 non-frail) and three studies used a deficit accumulation scoring system to determine frailty in 35,058 patients (17,512 frail and 17,546 non-frail). No significant differences were found in the main outcomes of interest between the phenotypic construct and deficit accumulation models of frailty scoring systems.

Discussion

This systematic review and meta-analysis, despite the significant heterogeneity, demonstrated that frailty status measured before or during admission to ICU was associated with adverse clinical outcomes. More specifically, being frail increased the risk of short-term (intraoperative, ICU, in-hospital, and 30-day) and longer-term (≥6 months) mortality, longer duration of mechanical ventilation, ICU, and hospital LOS. Frail patients were more likely to be discharged to a healthcare facility. The risk of discharge to a healthcare facility was significantly higher in cardiac surgery patients with frailty when compared with noncardiac counterparts, although there were no differences in short-term or long-term mortality. As a subgroup, frail patients undergoing elective surgery were also found to be at risk of long-term mortality, hospital LOS, and mechanical ventilation.

The results of this study had certain similarities and differences from the recent mixed-ICU systematic review looking at frailty outcomes. We had concurring findings on an increased risk of short- and long-term mortality and discharge disposition for frail patients. However, we found in the surgical ICU population, differences in ICU and hospital LOS, and duration of mechanical ventilation between frail and non-frail patients. The pooled prevalence of frailty (39.4%) was markedly different from the recent meta-analysis that pooled 10 observational studies and estimated a frailty prevalence of 30% among patients in ICU settings. There was a heterogeneous range in the prevalence of frailty observed, partly because of the different frailty measures used. There is good evidence that frailty measures rely heavily on pre-existing comorbidities for frailty classification, for instance, modified frailty index. However, this systematic review demonstrated that phenotype frailty measurements were utilised more in the surgical patients admitted to ICU.

The findings of a significantly increased risk of long-term mortality in frail patients concur with previous literature where frailty was independently associated with long-term mortality and that frailty-related mortality was inversely proportional to age in patients after cardiac surgery. Although our findings support the notion that frailty status could be reversed upon correction of the intrinsic or secondary cardiac conditions, as demonstrated in a few small-sample studies.

The more complex cardiac and lung transplant patients included in our review could explain the variations in long-term mortality. A recent study found that frailty within 6 months of a heart transplant was independently associated with increased mortality post-transplantation. A more recent systematic review of perioperative and critical care patients demonstrated that frailty status correlated with mortality, postoperative complications, ICU and hospital LOS, and discharge to a healthcare facility. However, as a meta-analysis was not conducted the strength or significance of the correlation was not quantified.

Given our findings, it is essential to individualise perioperative pathways for patients requiring postoperative ICU management, including a multidisciplinary shared decision-making conference to ascertain deficits, risks, and therapy goals. Recently, the importance of considering patient frailty as a factor predicting outcomes in the perioperative setting has been recognised. Frailty screening and appropriate preoperative comprehensive multidisciplinary assessment would assist in appropriate patient selection for those who must undergo surgery and pre-emptively optimise health status in frail older people to avoid poor outcomes. Furthermore, prehabilitation measures should be considered where possible in an attempt to improve the preoperative status and minimise perioperative risk. There is evidence that prehabilitation, either alone or as part of a multicomponent
### Short-term mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail Died</th>
<th>Non-frail Died</th>
<th>Logarithm of RR with 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buth 2014</td>
<td>52</td>
<td>238</td>
<td>5.723</td>
<td>1.24 (0.96–1.52)</td>
</tr>
<tr>
<td>Ad, 2016</td>
<td>1</td>
<td>126</td>
<td></td>
<td>1.18 (–1.57–3.93)</td>
</tr>
<tr>
<td>Afflalo, 2016</td>
<td>154</td>
<td>160</td>
<td>10.423</td>
<td>0.80 (0.58–1.02)</td>
</tr>
<tr>
<td>Joseph 2017</td>
<td>7</td>
<td>3</td>
<td>28</td>
<td>0.50 (–0.77–1.77)</td>
</tr>
<tr>
<td>Amabili 2019</td>
<td>8</td>
<td>9</td>
<td>193</td>
<td>1.24 (0.34–2.14)</td>
</tr>
<tr>
<td>Kiss 2020</td>
<td>5</td>
<td>8</td>
<td>244</td>
<td>0.95 (–0.13–2.03)</td>
</tr>
<tr>
<td>Tipping 2020 (In hospMortality data)</td>
<td>8</td>
<td>14</td>
<td>74</td>
<td>1.96 (0.86–3.06)</td>
</tr>
<tr>
<td>Calculated RR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: $\chi^2=0.05$, $I^2=42.39%$, $H^2=1.74$</td>
<td></td>
<td></td>
<td>0.05 (0.01–0.18)</td>
<td>1.06 (0.75–1.37)</td>
</tr>
<tr>
<td>Test of $H_0$: $Q(6)=9.93$, $P=0.13$</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noncardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee 2012</td>
<td>5</td>
<td>2</td>
<td>49</td>
<td>1.06 (–0.53–2.65)</td>
</tr>
<tr>
<td>Mueller 2016</td>
<td>5</td>
<td>6</td>
<td>63</td>
<td>2.87 (–0.00–5.74)</td>
</tr>
<tr>
<td>Hamidi 2019</td>
<td>3 154</td>
<td>1690</td>
<td>15 737</td>
<td>0.62 (0.57–0.68)</td>
</tr>
<tr>
<td>DeMaria 2019</td>
<td>1</td>
<td>14</td>
<td>35</td>
<td>1.91 (–1.24–5.06)</td>
</tr>
<tr>
<td>Heterogeneity: $\chi^2=0.14$, $I^2=18.01%$, $H^2=1.22$</td>
<td></td>
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<td>0.84 (0.20–1.49)</td>
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<tr>
<td>Test of $H_0$: $Q(3)=3.28$, $P=0.35$</td>
<td></td>
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</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: $\chi^2=0.08$, $I^2=69.05%$, $H^2=3.23$</td>
<td></td>
<td></td>
<td>0.98 (0.69–1.27)</td>
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</tr>
<tr>
<td>Test of $H_0$: $Q(10)=30.12$, $P=0.00$</td>
<td></td>
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<tr>
<td>Test of group differences: $Q_k(1)=0.37$, $P=0.54$</td>
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<td></td>
</tr>
<tr>
<td>Random-effects REML model</td>
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</tbody>
</table>

### Long-term mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Frail Died</th>
<th>Non-frail Died</th>
<th>Logarithm of RR with 95% CI</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jha 2017</td>
<td>10</td>
<td>8</td>
<td>60</td>
<td>0.98 (0.15–1.81)</td>
</tr>
<tr>
<td>Joseph 2017</td>
<td>14</td>
<td>9</td>
<td>22</td>
<td>0.09 (–0.61–0.79)</td>
</tr>
<tr>
<td>Heterogeneity: $\chi^2=0.24$, $I^2=68.88%$, $H^2=2.56$</td>
<td></td>
<td></td>
<td>0.51 (–0.36–1.37)</td>
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<td>Test of $H_0$: $Q(1)=2.56$, $P=0.11$</td>
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</tr>
<tr>
<td>Noncardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilson 2016</td>
<td>13</td>
<td>4</td>
<td>52</td>
<td>1.38 (0.32–2.43)</td>
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<tr>
<td>Tipping 2020 (1-yr mortality data)</td>
<td>12</td>
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<td>97</td>
<td>1.69 (0.94–2.44)</td>
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<tr>
<td>Heterogeneity: $\chi^2=0.00$, $I^2=0.00%$, $H^2=1.00$</td>
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<td></td>
<td>1.59 (0.98–2.20)</td>
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</tr>
<tr>
<td>Test of $H_0$: $Q(1)=0.23$, $P=0.63$</td>
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<tr>
<td>Overall</td>
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<td></td>
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</tr>
<tr>
<td>Heterogeneity: $\chi^2=0.37$, $I^2=68.24%$, $H^2=3.15$</td>
<td></td>
<td></td>
<td>1.01 (0.28–1.73)</td>
<td></td>
</tr>
<tr>
<td>Test of $H_0$: $Q(3)=10.18$, $P=0.02$</td>
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<tr>
<td>Test of group differences: $Q_k(1)=4.00$, $P=0.05$</td>
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<tr>
<td>Random-effects REML model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Fig 4. Subgroup analysis: cardiac vs noncardiac surgical patients.
Fig 4. Continued.
structured programme,\textsuperscript{64–66} improves functional capacity and resilience to offset postoperative complications, through the demand-based prescription of preoperative exercise programs, nutrition optimisation, and psychological interventions in the elective surgical setting. Furthermore, multidisciplinary multicomponent interventions applied in the postoperative period have been shown to improve post-discharge function and caregiver burden in frail older people undergoing vascular, trauma, and cardiothoracic surgical interventions.\textsuperscript{87}

We also found that there was marked heterogeneity surrounding how frailty is measured in the surgical population requiring ICU, with phenotype construct measurements more predominantly utilised. Although the concept of a single unified measurement tool that would enhance adaptability and ease of use seems logical or tempting, this may not be pragmatic. This is because it is unclear if one tool is superior to another in a particular setting and more recent concepts advocate for prescribed, validated standardised tools for different clinical settings.\textsuperscript{65,69} Yet, the post-hoc subgroup analyses between the two types did not reveal significant differences in any of the outcomes of interest. However, the result should be interpreted with caution, as the deficit accumulation model was only included in three studies leading to relatively wider CIs.

**Limitations**

Some limitations need to be acknowledged. Firstly, many subgroup analyses and pooled results were not performed because of the small number of studies with marked heterogeneous frailty definitions and measurements used. This probably contributed to the heterogeneity in some of the meta-analyses and hence pooled results could be considered imprecise.\textsuperscript{70} However, nine of these studies included assessments with objectively measured physical function from the same domain. We have also partly addressed the heterogeneous nature of frailty measurements by performing post-hoc analyses comparing the main constructs of frailty, which revealed no significant differences in outcomes regardless of measurement. Secondly, the inclusion of only full-text articles introduced an element of publication bias. However, our search strategy incorporated very broad medical subject heading terms to capture as much relevant data on the subject as possible to answer the clinical question. Furthermore, the references from each result were scanned to maximise relevant results. Besides, the included studies scored highly in the NOS, indicating a low risk of methodological bias, and increasing the reliability of our findings. Thirdly, limitations of the NOS in terms of interrater reliability and external validation should be acknowledged.\textsuperscript{71} Fourth, observational studies would be prone to selection and confirmation bias, however, 60% of the included studies were prospective with frailty measurements conducted before surgery. Furthermore, all the studies were adjusted for confounding factors in multivariate analyses. Fifth, attempting to capture a wide surgical population would also have contributed to the heterogeneity. However, testing for subgroup differences across two separations within the surgical population, namely elective vs non-elective and cardiac vs noncardiac, did not yield many statistically significant subgroup effects, with a sufficient number of patients in each subgroup. A final limitation is that there could be a selection bias. This study has not captured the outcomes of all frail surgical patients. Only those for whom a decision has been made would best benefit from ICU intervention. However, this captures the ‘real-world’ decision-making with regards to ICU admissions and we believe this study has been large enough to capture outcomes for patients who would ordinarily have been offered (electively or emergently) ICU level management.

**Implications**

This review lends strength to the concept that frailty assessments conducted before surgery for patients who require postoperative ICU can inform patients and clinicians on the degree of morbidity and risks of conducting the surgery, particularly in the elective setting. It also assists in the planning and utilisation of critical care services. It does reinforce the need for an objective, reproducible measurement of frailty.

**Conclusions**

This systematic review demonstrated that regardless of the measurement of frailty, the relationship between frailty and poorer outcomes including increased the risk of short-term and longer-term mortality, longer ICU and hospital LOS, and increased likelihood of discharge to a healthcare facility in surgical patients, both elective and emergent, admitted to ICU. Our findings suggest that preoperative frailty assessments and risk stratification are essential in patient and clinician planning, and critical care resource utilisation.

**Authors’ contributions**

Study conception and design: RC, RU, BB, RT, AS
Selection of included studies: RC, RU, AS
Data collection: RC, RU
Data analysis: AA, BB, RC, AS
Data interpretation: AA, BB, RC, RU, AS
Writing and editing: RC, RU, RT, AS

**Declarations of interest**

The authors declare that they have no conflicts of interest.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2021.11.018.

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