



## Appendix 3

1 (12)

Clinical Frailty Scale in prediction of mortality, disability and quality of life for patients in need of intensive care (2020)

# Appendix 3 Table of Included studies

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
<p><b>De Geer et al 2020</b> Sweden</p> <p>Design: Prospective study with comparison of two prediction models. 2017–2018</p> <p>Setting: Mixed, tertiary general ICU in a university hospital</p>	<p>Adults &gt;18y admitted to ICU</p> <p><b>n=872 patients</b> Age: median 64y (IQR 46–73) 59% male</p> <p><b>ICU diagnosis:</b> Sepsis, septic shock (22%) respiratory insufficiency (13%)</p> <p><b>Selection of data reported:</b> Source of transfer to ICU Treatment and events in the ICU Severity of illness: SAPS3</p> <p><b>Exclusions:</b> Patients could be included only once, in cases of multiple ICU admissions only primary admission was included</p>	<p>CFS, 9pt scale CFS <math>\geq 5</math> defined as frail</p> <p><b>Frailty assessment:</b> Premorbid frailty was defined as the level of frailty before the acute illness and hospital admission</p>	<p>Death within 30 days of ICU admission</p> <p>Survival for up to 180 days after ICU admission</p> <p>Estimate a discrimination and calibration of a model including frailty and SAPS3</p> <p>Survival analysis, unadjusted, and adjusted by: severity of illness, comorbidities, limitations of treatment, age and sex</p>	<p>375/872 (43%) frail patients</p> <p><b>Mortality non frail/frail (%):</b> ICU: 21 (4%)/67 (17%) 30 days 41 (8%)/113 (32%) 90 days 50 (10%)/138 (41%) 180 days 53 (11%)/150 (46%)</p> <p>Area under the curve (AUC): 0.74 (95% CI, 0.69 to 0.79); CFS 5 corresponded to: sensitivity of 76%, specificity of 66%, defining CFS <math>\geq 5</math> as the cut-off point.</p> <p>After adjustment, frailty remained a strong predictor of death within 30 days: HR 2.12 (95% CI, 1.44 to 3.14). ROC AUC of CFS did not differ significantly from that of SAPS3, whereas combining the two resulted in an improved discriminatory ability. The correlation of CFS to SAPS3 corresponded to an r of 0.4.</p>	<p><b>Aim:</b> To study the impact of frailty on mortality in unselected ICU patients, and to compare its discriminatory ability to an established model for outcome prediction in intensive care.</p> <p><b>Conclusion:</b> Premorbid frailty is a predictor of death in ICU patients. A strengthened predictive ability of severity of illness scores in clinical use (SAPS3) when combined with an assessment of a patient's degree of frailty. When adjusted for severity of illness and comorbidities, limitations of treatment, age and sex, the risk of death remained increased in frail patients.</p>	<p>Low risk of bias</p> <p><b>Limitations:</b> Does not report how missing data was handled in the analysis</p>
<p><b>Guidet et al 2020</b> France</p> <p>Design:</p>	<p>Consecutive patients &gt;80y, acutely admitted to ICU</p> <p><b>n=3920 patients</b> Age: mean 84y (IQR 81–87) 53.3% males</p>	<p>CFS, 9pt scale CFS <math>\geq 5</math> defined as frail</p> <p><b>Frailty assessment:</b> Frailty level present before hospital</p>	<p>Survival in the ICU</p> <p>Death within 30 days of ICU admission</p>	<p>1568/3903 (40%) frail patients</p> <p><b>Mortality at 30 days (n,%):</b> <b>CFS 1-3:</b> 509 (34%) <b>CFS 4:</b> 287(19%) <b>CFS 5-9:</b> 704 (47%)</p>	<p><b>Aim:</b> Prevalence of frailty, cognition decline and activity of daily life in addition to the presence of comorbidity and</p>	<p>Low risk of bias</p> <p><b>Limitations:</b> Only includes persons over 80</p>

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
<p>Prospective cohort study, VIP 2-study, May 2018–May 2019</p> <p>Setting: 242 ICUs from 22 countries, coordinated via European Society of Intensive Care Medicine (10 Swedish ICU, 140 patients)</p>	<p><b>ICU diagnosis:</b> Respiratory failure 944 (24.1%) Circulatory failure 541 (13.8%) Combined respiratory/circulatory failure 449 (11.5%) Sepsis 539 (13.8%)</p> <p><b>Selection of data reported:</b> Demographic data Reason for admission Severity of illness: (SOFA - Sequential Organ Failure assessment) ICU procedures Limitation of care Length of stay</p> <p><b>Exclusions:</b> Non acute admission</p>	<p>admission and not affected by the acute illness. Information was given by patients or proxy, or by patient records</p> <p>Cognitive impairment (IQCODE <math>\geq 3.5</math> defining cognitive decline)</p> <p>Disability measured by Katz activities of daily living, Katz ADL <math>\leq 4</math> defining disability</p>	<p>Potential predictive factors for 30-day survival.</p>	<p>Overall survival at 30 days: 61.2% (59.7–62.7)</p> <p><b>Predictors of 30 day mortality:</b> (HR, 95% CI): Age (increase in risk of death per 1 year increase): HR 1.02 (1–1.03); ICU admission diagnosis, SOFA (increase in risk of death per one-point increase): HR 1.15 (1.14–1.17); CFS (increase in risk of death per one point increase): HR 1.1 (1.05–1.15). The model including all geriatric parameters did not perform better than the model with CFS only.</p> <p><b>Inter-rater reliability</b> CFS was measured by two raters in 1924 patients. Weighted kappa: 0.85 (95% CI, 0.84 to 0.87)</p>	<p>polypharmacy and to assess their influence on 30-day survival.</p> <p><b>Conclusion:</b> Frailty assessment using the CFS is able to predict short-term mortality in elderly patients admitted to ICU.</p>	
<p><b>Flatten et al 2017</b></p> <p>Norway</p> <p>Design:</p>	<p>Consecutive very old (<math>\geq 80y</math>) patients admitted to the ICU</p> <p><b>n=5021 patients</b> Age: median 84y (IQR 81–86) 52.1% male</p>	<p>CFS, 9pt scale CFS <math>\geq 5</math> defined as frail</p> <p><b>Frailty assessment:</b> Frailty level before the acute illness and</p>	<p>ICU survival 30-day survival</p> <p>Multivariate analysis, adjusted by:</p>	<p>2156/5021 (43%) frail patients</p> <p><b>Survival:</b> non frail CFS 1-3/ pre frail CFS 4/ frail CFS 5-9 (%):</p>	<p><b>Aim:</b> To study the impact of frailty compared with other variables with regards to short-term</p>	<p>Low risk of bias</p> <p><b>Limitations:</b> only includes persons over 80</p>

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
<p>A transnational prospective cohort study, VIP 1-study, 2016–2017</p> <p>Setting: 311 ICUs from 21 European countries, coordinated by European Society of Intensive Care Medicine. (26 Swedish ICU, 398 patients)</p>	<p><b>ICU diagnosis:</b> Respiratory and/or circulatory failure most frequent causes</p> <p><b>Selection of data reported:</b> Severity of illness SOFA score, ICU procedures [invasive ventilation 50.7%, NIV 23%, no ICU procedures 23.8%] limitations of care, length of stay (LOS)</p> <p><b>Exclusion criteria:</b> None</p>	<p>hospital admission. The Clinical Frailty Scale (CFS) was used and information necessary to perform the assessment by the ICU staff was given by patients or proxy.</p>	<p>age, gender, SOFA score, type of ICU admission.</p>	<p>ICU survival: 1558 (82.3%)/ 775 (79.7%)/ 1578 (73.2%) 30 day survival: 1431 (75.6%)/ 686 (70.6%)/ 1278 (59.3%)</p> <p>Frailty was independently related to 30-day survival (HR 1.54; 95% CI, 1.38 to 1.73) for frail versus non-frail.</p>	<p>outcome in the very old ICU population.</p> <p><b>Conclusions:</b> Among very old patients (≥80 years) admitted to the ICU, the consecutive classes in Clinical Frailty Scale were inversely associated with short-term survival.</p>	
<p><b>Shears et al 2018</b></p> <p>Canada</p> <p>Design: Prospective</p> <p>Setting: 2 ICUs in Hamilton, Canada.</p>	<p>Patients ≥18 y admitted to ICU</p> <p><b>n=150 patients</b> Age: mean 63.8y (SD 15.3) Female 60 (40.0%)</p> <p><b>ICU admitting diagnosis:</b> Respiratory 48 (32%) Sepsis 22 (14.7%)</p> <p><b>Selection of data reported:</b> Demographic data Admission classification</p>	<p>CFS, 9pt scale CFS ≥5 defined as frail</p> <p><b>Frailty assessment:</b> At enrolment, study personnel attempted to determine pre-existing frailty at a timepoint 1-week prior to hospital admission for enrolled patients using the CFS.</p>	<p>Mortality in ICU and in hospital</p> <p>Mean differences were calculated to assess the Research Coordinator intra-rater reliability and inter-rater reliability of</p>	<p>Patients non-frail (CFS 1–4)/frail (CFS 5–9): 80/70</p> <p>CFS were similar between RC, OT, and GR chart reviews (p &gt;0.05 for all comparisons).</p> <p>There was no difference between RC chart review and RC final score, or between RC patient interview and RC final score.</p>	<p><b>Aim:</b> To describe pre-ICU frailty in critically ill patients using the Clinical Frailty Scale (CFS).</p> <p><b>Conclusions:</b> CFS scores can be generated using medical chart review and can be reliably completed by</p>	<p>Moderate risk of bias</p> <p><b>Limitations:</b> Less than 100 events (deaths)</p>

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
McMaster University	APACHE II score Duration of ICU ICU procedures mechanical ventilation (80.7%), non-invasive ventilation (19.3%)  <b>Exclusion criteria:</b> projected stay in ICU for ≤24 h.	The ICU Research Coordinator generated 3 CFS scores using: 1) chart review, 2) family interview, 3) patient interview.  An overall impression was captured in a final score (when available).	chart reviews made by the research coordinator, Occupational Therapist, and Geriatrics Resident.  Analysis of the relationship between CFS scores and mortality.	Scores following the RC family interview and the RC final score were significantly different (-0.24, 95% CI, -0.38, -0.09).  <b>Mortality non frail/frail:</b> ICU mortality: 20/17 Hospital mortality: 26/21  Each 1-point increase in the final CFS scored by the RC was weakly associated with ICU mortality: OR 1.18 (95% CI 0.84–1.66), and hospital mortality: OR 1.19 (95% CI 0.89, -1.59)	ICU clinicians and research staff.	
<b>Bagshaw et al 2014</b>  Canada  Design: Prospective multicentre cohort study  Setting: 6 ICUs in the province of Alberta, Canada	Adults ≥50 admitted to ICU  <b>n=421 participants</b> Age: mean 67y ± 10 61% male  <b>Selection of data reported:</b> Demographic data ADL Comorbidity score (Elixhauser) Source of transfer to ICU Postoperative ICU admission Limitation of medical therapy Cardiac arrest APACHE score	CFS, 9pt scale CFS ≥5 defined as frail  <b>Frailty assessment:</b> Trained research coordinators masked to the study hypotheses determined the Clinical Frailty Scale scores by interviewing participants or surrogates and reviewing	In hospital mortality ICU mortality mortality at 6 and 12 months  Health-related quality of life at 6 and 12 months  Length of stay  Discharge disposition	138/ 21 (33%) frail patients  <b>Mortality</b> (frail ; not frail (%): In ICU: 16 (12%) ; 27 (9%) In hospital: 44 (32%) ; 45 (16%) 12 months: 66 (48%); 71 (25%) In-hospital mortality was higher among frail patients than among nonfrail patients adjusted odds ratio: aOR 1.81 (95% CI, 1.09 to 3.01) and remained higher at 1 year adjusted hazard ratio: aHR 1.82 (95% CI, 1.28 to 2.60).	<b>Aim:</b> We determined the prevalence, correlates and outcomes associated with frailty among adults admitted to intensive care.  <b>Conclusions:</b> Frailty was common among critically ill adults aged 50 years or more and identified a vulnerable population at increased risk of adverse	<b>Moderate risk of bias:</b> Mortality  <b>High risk of bias:</b> Quality of Life  <b>Limitations:</b> Less than 100 events (deaths). Results missing regarding EQ5D assessments. Only data from

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
	SOFA score  <b>Exclusions:</b> ICU stay or survival was less than 24 hours, or previously enrolled in the study	each participant's medical record. Patients were considered to be frail if they had a score greater than 4 immediately before the index hospital admission.	Major adverse events  The models were adjusted for potential confounding factors, which were included based on their clinical importance, evidence from the literature or their significance at $p < 0.20$ in the univariable analysis.	Adjusted hazard ratios for death within 12 months after admission to ICU, stratified by CFS (>4 indicating frailty). Unadjusted HR (95% CI): CFS 1–3: 1.00 reference CFS 4: HR 2.01 (1.25–3.24) CFS 5: HR 2.88 (1.65–5.02) CGS 6–8: HR 3.76 (2.33–6.07)  <b>Function and QoL</b> Compared with nonfrail survivors, frail survivors were more likely to become functionally dependent (71% v. 52%; OR 2.25, 95% CI, 1.03 to 4.89), had significantly lower quality of life.	events, morbidity and mortality. Our findings suggest that routine assessment of frailty could provide more accurate prognostication and identify a vulnerable population that might benefit from follow-up and intervention.	SF12 and EuroQol visual analogue scale presented.
<b>Langlais et al 2018</b>  France  Design: Prospective observational study, 2015–2016  Setting: ICU of a	Adults $\geq 65$ y hospitalized $\geq 24$ h in the ICU  <b>n=189 patients</b> Age: mean 74y (SD 6) 62% male  <b>Selection of data reported:</b> Reasons for ICU admission Source of infection, Life expectancy (McCabe) Disability (Katz ADL), Comorbidity (Charlson score),	CFS, 9pt scale. CFS $\geq 5$ defined as frail  <b>SOFA score:</b> Sequential organ failure assessment score, calculated based on the worst variables observed during the first 24 h of hospitalization  <b>Frailty assessment:</b>	In hospital mortality  ROC curves: Receiver operating characteristic curves were used to determine the likelihood ratios for the abilities of the CFS score,	27% (51/189) frail patients  <b>Mortality:</b> Mortality overall: 51/189 Hospital mortality: 19/51 (37%) frail patients 32/138 (22%) nonfrail  The probability of remaining alive according to frailty status was significantly higher in patients who had a CFS $\geq 5$ .	<b>Aim:</b> To determine whether the addition of the frailty status assessed by the CFS score to the SOFA score (SOFA+CFS) improves the performance of the SOFA score alone, in predicting the hospital mortality of elderly critically ill patients.	Moderate risk of bias  <b>Limitations:</b> Less than 100 events (deaths), information not clear regarding analysis of missing data.

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
university hospital, Rennes	SAPS II, SOFA. Glasgow coma score  <b>ICU diagnosis:</b> Pulmonary infection (25%) Shock (50%)  <b>Exclusions:</b> Patients who could not be interviewed or who had no proxy(ies) or family member available.	Frailty was determined during the first 24h of ICU hospitalization by ICU physicians based on clinical examination, patient medical record and interview of patient or proxy(ies).	SOFA score and SOFA+CFS to predict hospital mortality.	<b>Predictions:</b> SOFA-CFS score did not improve the performance of the SOFA score alone in predicting hospital mortality: AUC CFS+SOFA: 0.66 (95% CI, 0.58 to 0.74) AUC SOFA: 0.63 (95% CI, 0.55 to 0.72) AUC CFS: 0.62 (95% CI, 0.53 to 0.71)  In multivariable analysis, age (OR 1.09 (95% CI, 1.03 to 1.16), McCabe score, Glasgow coma score at admission, and SOFA score were risk factors for hospital mortality.	<b>Conclusions:</b> The performance of the SOFA score in predicting hospital mortality was low, although it was an independent risk factor for mortality. The combination of frailty status with the SOFA score did not improve the performance of the SOFA score alone.	
<b>Hope et al 2019</b>  USA  Design: Prospective observational cohort, 2016–2017	Adults ≥50y admitted to ICUs  <b>n=302 patients</b> Age: mean 67–69y (SD 10) 48-54% male)  <b>Selection of data reported:</b> Demographics Frailty markers SOFA score APACHE	CFS, 9pt scale CSF ≥5 defined as frail  <b>Frailty assessments:</b> Prehospital frailty assessed by study physicians within 3d of ICU admission  <b>Organ failure assessments:</b>	Posthospital disability  Information regarding frailty and in hospital mortality presented	61.7% (50/81) frail of deceased patients 45.7% (101/221) frail of patients that survived  <b>Mortality:</b> Hospital mortality: 81/302 (27%) overall 50/81 (61.7%) frail patients 6 month mortality: 116/302 (38%) overall	<b>Aim:</b> To describe the association between prehospital frailty, acute organ dysfunction, and posthospital disability outcome in older adults admitted to the intensive care unit.  <b>Conclusion:</b>	Moderate risk of bias  <b>Limitations:</b> Less than 100 events (deaths)

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
Setting: Two tertiary care hospitals, Bronx, New York, Albert Einstein College of Medicine	Comorbidity (Charlson score) ADL (Katz ADL) Cognitive impairment (IQCODE)  <b>ICU diagnosis:</b> respiratory failure (28–43%) sepsis (16–20%)  <b>Exclusions:</b> Patients admitted to ICU directly after an elective procedure, Patients not expected to be in ICU >24h; Patients in hospital ≥30 days prior to ICU transfer or in ICU >72h Patients who did not speak English or Spanish	SOFA, using the most abnormal value within first 24h of ICU admission  <b>Disability assessments:</b> By research coordinators from interviews with patients or surrogates. Posthospital ADL obtained through discharge or telephone interviews with patients, surrogates, nurses, or physical therapists or, where appropriate, through chart review.		<b>Frailty associations:</b> Prehospital frailty was associated with posthospital disability (adjusted incident rate ratio [aIRR] per unit increase in CFS: aIRR 1.38 (95% CI, 1.15 to 1.67). Total day 1 SOFA score was weakly associated with posthospital discharge: aIRR 1.05 (95% CI, 1.00 to 1.10); Day 1 SOFA neurologic score was strongly associated with posthospital discharge: aIRR 1.42 (95% CI, 1.24 to 1.62) per unit increase in SOFA neurologic score. Effects were independent of prehospital frailty and other premorbid factors.	Both prehospital frailty and early acute brain dysfunction are important factors associated with increasing posthospital disability in older adults who survive critical illness.	
<b>Brummel et al 2017</b>  USA  Design: Prospective multicenter cohort study, 2007–2010	Patients ≥18 y treated for respiratory failure or shock from the medical and/or surgical ICUs  <b>n=1040 patients</b> Age: median 62y (IQR 53–72) 60% male  <b>ICU diagnosis:</b> acute respiratory failure (17%)	CFS, 7pt scale CFS≥5 defined as frail  <b>Frailty assessment:</b> Pre-existing frailty at enrollment, assessed by study personnel, trained by a geriatrician with expertise in frailty	Mortality  ADL (Katz ADL) Cognition (Repeatable Battery for Assessment of Neuro-psychological Status)	307/1040 (30%) frail patients  Half of patients with CFS ≥5 were younger than 65y.  <b>Mortality:</b> Overall mortality: 329/1040 (32%) at 3mo 409/1040 (39%) at 12mo	<b>Aim:</b> To describe the prevalence and severity of frailty in adults age 18 years of age and older and to determine the independent association between preexisting frailty (i.e., frailty present before critical illness)	Moderate risk of bias  <b>Limitations:</b> Several exclusion criteria applied. Some details missing in regard to description of analysis

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
Setting: Five US centers. patients enrolled in the identical BRAIN-ICU (NCT00392795) and MIND-ICU (NCT00400062) studies	sepsis (32%)  <b>Selection of data reported:</b> APACHE II score at admission Mean daily SOFA score Diagnosis at admission, Mechanical ventilation Duration of ICU stay Duration of hospital stay  <b>Exclusions:</b> Organ dysfunction >72 hours, recent ICU exposure, severe cognitive impairment, substance abuse, homelessness. Patients who died or withdrew before follow-up from the disability, cognitive, and HRQoL analyses.	assessments, used patient/proxy interviews and medical records to determine preexisting frailty with the CFS.	Health-related quality of life (SF-36)  Adjustments (a priori): age, sex, education, comorbidities, baseline disability, baseline cognition, severity of illness (SOFA score), delirium, coma, sepsis, mechanical ventilation, and sedatives/ opiates.	<b>Associations:</b> Greater CFS scores were independently associated with greater mortality. Greater CFS scores were independently associated with greater odds of disability in instrumental ADL. CFS scores were not associated with disability in basic activities of daily living or with cognition. Higher CFS score at enrolment, however, was associated with lower SF-36 Physical Component Scores at 3 and 12 months. CFS score was not associated with SF-36 Mental Component Scores at either follow-up assessment.	and long-term outcomes 3 and 12 months after critical illness.  <b>Conclusions:</b> Our results suggest that pre-existing frailty, as measured by the Clinical Frailty Scale, is common in critically ill patients, regardless of age. Moreover, the risk of death, disability, and poor health-related quality of life increased along the fitness-frailty continuum, independent of many traditional risk factors, including age.	
<b>Hope et al 2019</b>  USA  Design: Observational cohort study, 2016–2017  Setting:	Adults ≥50 y admitted to medical/ surgical ICU within 30 d of emergency admission  <b>n=298 patients</b> Age: mean 67.2y (SD 10.5)  <b>Selection of data reported:</b> Prehospital disability, Primary diagnosis in ICU APACHE	CFS, 9pt scale CFS≥5 defined as frail  <b>Frailty assessment:</b> On admission, patients' surrogates quantified prehospital frailty. Researchers blinded to surrogates'	Agreement was described with kappa scores, McNemar tests, and Bland- Altman plots.  Validity was compared by using Chi-2	Researcher assessment: frail/non frail: 148/150 Surrogate assessment: frail/non frail: 111/187  <b>Hospital mortality:</b> Frail vs non frail (%): Researcher CSF assessment 49 (33.1%) vs 30 (20.0%) Surrogate assessment 35 (31,5%) vs 44 (23,5%)	<b>Aim:</b> To compare agreement and validity between surrogates' and researchers' assessments of frailty in critically ill older adults.  <b>Conclusion:</b>	Moderate Risk of bias

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
Tertiary academic medical center, Albert Einstein College of Medicine, Bronx, New York	Charlson Comorbidity score, ADL  <b>Exclusions:</b> Patients expected to be discharged from ICU within 24h, patients with no available surrogate or next of kin who knew their pre-hospitalization medical and social history.	assessments also quantified frailty.	tests and logistic regression.	Both surrogates' and researchers' frailty assessment scores ranged from 1 to 9, with moderate to substantial agreement between scores (kappa $\geq 0.40$ ). Surrogates' frailty assessment scores were significantly lower than researchers', mean difference: $-0.62$ 95% CI, $-0.77$ to $-0.48$ Surrogates were less likely than researchers to identify as frail those patients who experienced adverse hospital outcomes (death, prolonged stay, or disability newly identified at discharge).	Surrogates identified fewer patients as frail than did researchers. Factors involved in surrogates' assessments of patients' prehospital frailty status should be studied to see if the Clinical Frailty Scale can be modified to facilitate more accurate surrogate assessments.	
<b>Pugh et al 2019</b>  UK  Design: Prospective observational multicentre study  Setting:	Adults $\geq 60$ y receiving active treatment with an expectation to remain in critical care for at least 24 h.  <b>n=101 patients</b> Age: 69y (IQR 60–80) 58% male  <b>ICU diagnosis:</b> Respiratory (35%) gastrointestinal (27%),	CFS 9pt scale CFS $\geq 5$ defined as frail  <b>Frailty assessments:</b> Compare assessments of frailty by study investigators working within the critical care team and staff from medical, nursing and physiotherapy backgrounds.	Interrater reliability  Hospital mortality	Linear weighted Kappa: 0.74 (95% CI, 0.67 to 0.80) indicating a good level of agreement between assessors.  Frailty rating differed by at least one category in 47% cases. Among different staff pairings, the lowest level of agreement was found for the sub-group of patients for whom one assessor	<b>Aim:</b> To investigate the inter-rater reliability of the Clinical Frailty Scale for assessing frailty in patients admitted to critical care.  <b>Conclusion:</b> We identified a good level of agreement in frailty assessment using	<b>Moderate risk of bias:</b> interrater reliability  <b>High risk of bias:</b> mortality  <b>Limitations:</b> Not consecutive sample, some information missing

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
6 hospitals Wales and Scotland	cardiovascular (16%) non-surgical patients (74%)  <b>Selection of data reported:</b> APACHE II GCS (Glasgow Coma Scale) Dependence Mechanical ventilation during first 24h (62%)	Total number of assessments: 202. Most assessments were performed by medical staff (47%) or staff from a nursing background, including advanced critical care practitioners (44%), with a much smaller number by physiotherapists (9%)		was from a medical and one from a nursing background.  <b>Associations:</b> Factors independently associated with higher frailty rating: female sex; higher APACHE II score, higher category of pre- hospital dependence; and the assessor having a medical background.  <b>Mortality:</b> Hospital mortality: 12/40 (30%) in frail patients 13/61 (21%) in nonfrail patients In-hospital mortality was similar between frail and non-frail patients.	the Clinical Frailty Scale, supporting its use in clinical care, but identified factors independently associated with higher ratings which could indicate personal bias.	regarding analysis and results.
<b>Gense et al 2020</b>  Netherlands  Design: Prospective cohort study, 2016–2017  Setting:	Adult ≥16y patients expected to survive the ICU, admitted for at least 12 h to the ICU Length of stay (LOS)  <b>n=1300 patients</b> Age: mean 61y (SD 14.9) 65% male  <b>ICU diagnoses:</b> Chronic diagnoses (26%)	CSF, 9pt scale, Dutch version CFS≥5 defined as frail  <b>Frailty assessment:</b> Assessed by patients or proxies before or at ICU admission (planned or unplanned admissions), at	CFS in survivors of ICU at 3 and 12 months  Length of stay (LOS)  Linear regression to explore which factors were associated with	153/1300 (11.8%) frail at baseline  <b>Frail patients:</b> 50.3% frail patients had chronic diagnosis. APACHE IV mean 55.4 (SD 18.9)  <b>Mortality</b> frail vs non frail (%): Hospital mortality:	<b>Aim:</b> Examine changes in frailty in the year after ICU admission, and its associated factors.  <b>Conclusion:</b> Frailty levels changed following ICU admission, with higher frailty levels at hospital discharge,	<b>Moderate risk of bias</b>  <b>Limitations:</b> Primary research question is related to how frailty changes after ICU stay. Some information missing regarding analysis

Study (Author, Year) Country Study design Setting	Population (Number, age, sex, Patient characteristics, Selection of data reported <sup>1</sup> )	Scale used Definition of frailty	Outcome Analyses	Results <sup>2</sup>	Aims Conclusions	Risk of bias Limitations
One university medical center, data from ongoing multicenter study (MONITOR-IC study)	planned admission (66%), after elective surgery (65%) acute surgical (11.7%) medical (23.6%)  <b>Selection of data reported:</b> APACHE IV, mechanical ventilation (70%)  <b>Exclusions:</b> Life expectancy of <48 h Deceased before informed consent, ICU LOS <12 h	hospital discharge, and three and 12months after ICU admission,	changes in frailty 12 months after ICU admission	1 (0.7%); 5 (0,4%) 1 year mortality: 24 (15.7%); 92 (8%)  Frailty levels changed among ICU survivors, with higher levels at hospital discharge and lower levels in the following months. After one year, 42% of the unplanned and 27% of the planned patients were more frail. For both groups, older age, longer hospital length of stay, and discharge location were associated with being more frail.	and lower levels at 12 months.	and results I relation to mortality

**ABBREVIATIONS:** **ADL** = Activities of daily living; **aOR** = Adjusted odds ratio; **APACHE** = Acute Physiology and Chronic Health Evaluation; **AUC** = Area Under Curve; **CFS** = Clinical frailty scale; **CI** = Confidence interval; **CVC** = Central venous catheter; **d** = Days; **h** = Hours; **HR** = Hazard ratio; **HRQoL** = Health related quality of Life; **ICU** = Intensive care unit; **IQR** = Interquartile range; **LOS** = Length of stay; **LST** = Limitation of life-sustaining therapies; **mo** = Months; **NIV** = Non-invasive ventilation; **pt** = Points; **QoL** = Quality of Life; **ROC** = Receiver operating characteristic; **RR** = Risk ratio; **RRT** = Renal replacement therapy; **SAPS** = Simplified Acute Physiology Score; **SD** = Standard deviation; **SOFA** = The sequential organ failure assessment; **y** = years.

**FOOTNOTES:** <sup>1</sup> A selection of most relevant reported data from the published study; <sup>2</sup> A selection of most relevant reported outcomes of the published study.

**ICU interventions:** (also referred as resource utilization or treatment intensity): includes: mechanical ventilation, noninvasive ventilation, intubation, reintubation, tracheostomy, vasoactive drugs, CVC (central venous catheter), arterial line, transfusion, renal replacement therapy, decision to withhold/ withdraw life sustaining treatment.