

ANESTHESIOLOGY

Accuracy and Feasibility of Clinically Applied Frailty Instruments before Surgery

A Systematic Review and Meta-analysis

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ANESTHESIOLOGY 2020; 133:78–95

EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Preoperative frailty has been associated with adverse postoperative outcomes
- It remains unclear which frailty scale is the best predictor of adverse postoperative outcomes

What This Article Tells Us That Is New

- This meta-analysis of 45 articles identified that specific frailty scales may be better predictors for some adverse outcomes when compared to others
- The Clinical Frailty Scale was most strongly associated with mortality and discharge not to home
- The Edmonton Frail Scale was a better predictor of complications
- The Frailty phenotype was most strongly associated with postoperative delirium

Frailty is a state of increased vulnerability to adverse health outcomes that results from accumulation of age- and disease-related deficits.^{1,2} Since 2009, there has been a rapid accumulation of evidence demonstrating that the presence of frailty before surgery is associated with a more

ABSTRACT

Background: A barrier to routine preoperative frailty assessment is the large number of frailty instruments described. Previous systematic reviews estimate the association of frailty with outcomes, but none have evaluated outcomes at the individual instrument level or specific to clinical assessment of frailty, which must combine accuracy with feasibility to support clinical practice.

Methods: The authors conducted a preregistered systematic review (CRD42019107551) of studies prospectively applying a frailty instrument in a clinical setting before surgery. Medline, Excerpta Medica Database, Cochrane Library and the Comprehensive Index to Nursing and Allied Health Literature, and Cochrane databases were searched using a peer-reviewed strategy. All stages of the review were completed in duplicate. The primary outcome was mortality and secondary outcomes reflected routinely collected and patient-centered measures; feasibility measures were also collected. Effect estimates were pooled using random-effects models or narratively synthesized. Risk of bias was assessed.

Results: Seventy studies were included; 45 contributed to meta-analyses. Frailty was defined using 35 different instruments; five were meta-analyzed, with the Fried Phenotype having the largest number of studies. Most strongly associated with: mortality and nonfavorable discharge was the Clinical Frailty Scale (odds ratio, 4.89; 95% CI, 1.83 to 13.05 and odds ratio, 6.31; 95% CI, 4.00 to 9.94, respectively); complications was associated with the Edmonton Frail Scale (odds ratio, 2.93; 95% CI, 1.52 to 5.65); and delirium was associated with the Frailty Phenotype (odds ratio, 3.79; 95% CI, 1.75 to 8.22). The Clinical Frailty Scale had the highest reported measures of feasibility.

Conclusions: Clinicians should consider accuracy and feasibility when choosing a frailty instrument. Strong evidence in both domains support the Clinical Frailty Scale, while the Fried Phenotype may require a trade-off of accuracy with lower feasibility.

(*ANESTHESIOLOGY* 2020; 133:78–95)

than two-fold increase in the odds of dying or experiencing a complication after surgery, along with increased risk of delirium, development of new disability, and increased resource use.^{3–6}

In recognition of the important role that frailty plays in predicting adverse outcomes in older surgical patients, numerous guidelines recommend that frailty be assessed routinely before surgery. These statements come from multidisciplinary and international societies, including the American College of Surgeons (Chicago, Illinois) and American Geriatrics Society's (New York, New York) Optimal Preoperative Assessment of the Geriatric Surgical

This article is featured in "This Month in Anesthesiology," page 1A. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has a visual abstract available in the online version.

Submitted for publication October 17, 2019. Accepted for publication February 20, 2020. Published online first on March 31, 2020. From the Centre for Perioperative Medicine, University College London, London, United Kingdom (S.D.A., D.W.); the Department of Anesthesiology and Pain Medicine, (S.D.A., M.H., R.S., D.I.M.) and the School of Epidemiology and Public Health (J.S., D.I.M.), University of Ottawa, Ottawa, Canada; the Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, Ottawa, Canada (S.D.A., D.I.M.); the Department of Anesthesiology and Pain Medicine, Harborview Medical Center, University of Washington, Seattle, Washington (I.B.); and the Clinical Epidemiology Program, The Ottawa Hospital Research Institute, Ottawa, Canada (D.I.M.).

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Patient guidelines,⁷ the Association of Anesthetists' of Great Britain and Ireland's (London, United Kingdom) Perioperative Care of the Elderly Guidelines,⁸ and the Society for Perioperative Assessment and Quality Improvement's (Glenview, Illinois) Perioperative Management of Frailty guidelines.⁹ However, to date, evidence suggests that frailty assessments are not part of routine preoperative practice in most settings.¹⁰ Multiple barriers to routine preoperative frailty assessment likely exist. One clear barrier is the large number of heterogeneous frailty instruments described in the literature, reflecting a lack of consensus among experts in frailty assessment.¹¹ While multiple systematic reviews have estimated the strength of association between frailty and a variety of adverse outcomes,³⁻⁵ the common approach to analysis has been to combine all frailty instruments together to provide a single pooled estimate of association. This approach precludes the opportunity to compare different frailty instruments in terms of their ability to predict important patient- and system-level outcomes. Feasibility is likely another barrier; clinicians are unlikely to adopt an instrument that requires substantial time or resource to operationalize in practice.¹² However, reviews have not considered or synthesized data regarding the feasibility of different frailty instruments in clinical practice. Ultimately, clinicians will need to combine information about accuracy and feasibility to guide decisions about what frailty instrument to use in their clinical setting to ensure that best practices are being applied to the care of this high-risk group of older surgical patients.

To provide robust comparisons between frailty instruments, we performed a systematic review and meta-analysis of studies that prospectively assessed frailty status in preoperative clinical practice. Our objectives were to assess and compare the ability of well-studied frailty instruments to predict important post-operative outcomes, while also synthesizing available data about the feasibility of these instruments.

Materials and Methods

This systematic review and meta-analysis was conducted after best practice recommendations, including the Meta-analysis of Observational Studies in Epidemiology guidelines¹³ and the Cochrane Collaboration handbook.¹⁴⁻¹⁷ Before conducting the review, we registered a study protocol with the International Prospective Registry of Systematic Reviews (CRD42019107551). The results are reported in keeping with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.¹⁸

Data Sources and Searches

A comprehensive search strategy was developed in consultation with an information specialist, informed by previous systematic reviews related to frailty and perioperative outcomes.^{15,16,19,20} The strategy then underwent the peer

review of electronic search strategy checklist by a second independent information specialist.²¹ A copy of the search strategy is included in Supplemental Digital Content, table 1 (<http://links.lww.com/ALN/C333>). The search strategy was applied to Medline, Excerpta Medica Database, the Cochrane Library, and the Comprehensive Index to Nursing and Allied Health Literature databases, with each searched from inception to November 18, 2018. The reference lists of related systematic reviews as well as included articles were searched by hand to identify other studies that may have been missed by the initial search. No language restrictions were applied.

Study Selection

Eligible studies were included if they: (1) studied a population of surgical patients greater than or equal to 18 yr; (2) included an explicitly described frailty instrument applied prospectively in a clinical encounter before surgery; and (3) reported relevant outcomes and the association of frailty with outcomes.

Study outcomes were informed by a core outcome set for older people,²² as well as routinely reported perioperative outcomes. Mortality (in-hospital or within 30-days) was our primary outcome; complications, discharge disposition, delirium, length of stay, and measures of function or disability were secondary outcomes. Our primary focus was on effect sizes as these were the measures of predictive ability routinely reported across studies. We also collected other formal measures of predictive accuracy reported (e.g., discrimination, calibration, sensitivity, specificity, predictive values, likelihood ratios, explained variance, improvement in model fit). To address our second objective, we collected relevant feasibility outcomes as defined by Bowen *et al.* (acceptability, implementation, and practicality).²³

Studies were excluded if they: (1) included mixed populations with less than 50% of surgical patients; (2) the frailty instrument was solely applied to electronic data (e.g., electronic health records, administrative data, registries); (3) frailty status was based on comprehensive geriatric assessment only (as this approach is specific to geriatric medicine physicians and not widely available before surgery²⁴); and (4) frailty status was based on single laboratory or imaging results (e.g., sarcopenia and hypoalbuminemia, tests that represent separate, although, related conditions that are not equivalent to the multidimensional nature of frailty^{11,25}). No other restrictions were placed on frailty instrument definitions. We considered minimally invasive cardiac valve procedures as surgical, however, we did not consider coronary artery interventions (angiograms, angioplasty, stenting) as surgical procedures (as anesthesiologists are not routinely involved). Conference abstracts or sources of grey literature were not included as methodologic descriptions would be inadequate to assess study quality and risk of bias. Case studies and case series were

also excluded, as these studies lacked comparison of people with frailty to people without.

Data Extraction and Quality Assessment

Duplicate assessment of titles and abstracts was performed by independent reviewers. Studies classified as “yes” or “unsure” were advanced to full text review; agreement between both reviewers was required for exclusion. Full text review was also completed in duplicate by independent reviewers. Any uncertainties or conflicts were resolved by consensus in discussion with lead authors (S.A., D.M.). Data extraction was then performed using a form specifically designed for this study; this included quantitative and qualitative feasibility data. The form was piloted by two senior investigators before full implementation, and the first eight studies extracted by each investigator were reviewed with a senior author before proceeding with full data extraction. Data was extracted by two reviewers and independently checked for accuracy by the first author (S.A.). Study authors were contacted as required to request missing or incomplete data, or to clarify methods or findings. All stages of the review were completed using DistillerSR (Evidence Partners, Canada).²⁶

Risk of bias was analyzed using the Quality in Prognostic Studies tool.²⁷ Risk of bias was assessed independently for each study by two team members, with at least one review by a lead author. Uncertainties and disagreements were resolved by consensus in discussion with lead authors.

Data Synthesis and Analysis

Study results were pooled according to the specific type of frailty instrument used; modified versions of instruments were classified with the original version (e.g., Fatigue, Resistance, Ambulation, Illnesses, Loss of weight [FRAIL] Scale included with Frailty Phenotype group). Studies assessing physical measures of frailty, such as gait speed, handgrip strength and Short Physical Performance Battery were pooled together. Studies that reported data for more than one frailty instrument contributed data to each applicable class of frailty instrument in the meta-analyses (e.g., if a study reported on the Frailty Phenotype and Clinical Frailty Scale, the study would contribute data to both meta-analyses).

Recognizing that many studies would use differing cut-offs and categorizations of frailty instrument scores to define frailty exposure, we pre-specified that we would pool the non-frail or lowest frailty score category as the reference group, and for the comparator group with frailty: (1) the group specified with frailty for studies using a binary exposure; or (2) the group specified with moderate frailty for studies with a multi-category frailty exposure.

Data analyses were completed using Comprehensive Meta-Analysis (Biostat, USA).²⁸ We prespecified the use of random effects models using Dersimonian and Laird inverse

variance weighted meta-analyses. These models were used to generate pooled odds ratios for binary outcomes and standardized mean differences for continuous outcomes based on unadjusted effect sizes, event rates, or measures of central tendency and variance from each included study. Unadjusted data were used as clinical frailty assessment is typically employed as a risk stratification tool, as opposed to as part of a multivariable risk model (which are not routinely operationalized in preoperative clinical practice²⁹). A random effects approach was chosen to allow for expected heterogeneity across studies; epidemiologic and content knowledge would suggest that data collected from different surgical specialties and procedures would not meet the assumptions of fixed-effects meta-analysis.

Meta-analysis was performed by frailty instrument when more than two studies with appropriate outcome data were available. Where inadequate data was available to support a meta-analysis (including formal measures of predictive accuracy), results were narratively synthesized. Where medians and interquartile ranges were reported for continuous outcomes, means and standard deviations were calculated using the methods of Wan *et al.*³⁰ Heterogeneity was assessed using the I^2 statistic (although no analytic decisions were made based on measures of heterogeneity); where the I^2 statistic exceeded 75% for primary outcome analyses we assessed for sources of heterogeneity. A two-tailed, 5% significance level was used for all analyses.

Two meta-regression analyses were carried out for mortality. The first evaluated whether there was evidence of effect modification by frailty instrument when all frailty instruments presenting data from more than two studies were combined. The second was an exploratory analysis to specifically determine if there was a difference in the association of the Clinical Frailty Scale *versus* the Fried Phenotype in predicting mortality (these were the two most studied instruments for this outcome).

Feasibility data were synthesized using directed content analysis.³¹ We used Bowen *et al.*'s feasibility framework to identify key coding categories.²³ Categories included aspects of acceptability (*i.e.*, satisfaction, intention to continue use, perceived appropriateness), implementation (*i.e.*, degree of successful execution, resources needed to implement, factors affecting implementation), and practicality (*i.e.*, ease of use, efficiency/speed, costs, positive/negative effects on users or targets). Coding of extracted data was performed by the first and senior authors (S.A., D.M.). Along with coding within categories, we determined whether the available data were positively, negatively, or neutrally supportive of an instrument's feasibility, as well as whether the supporting information was based on objective (*i.e.*, purposely and/or quantitatively measured) or subjective (*i.e.*, described without supporting assessment or measurement) data.

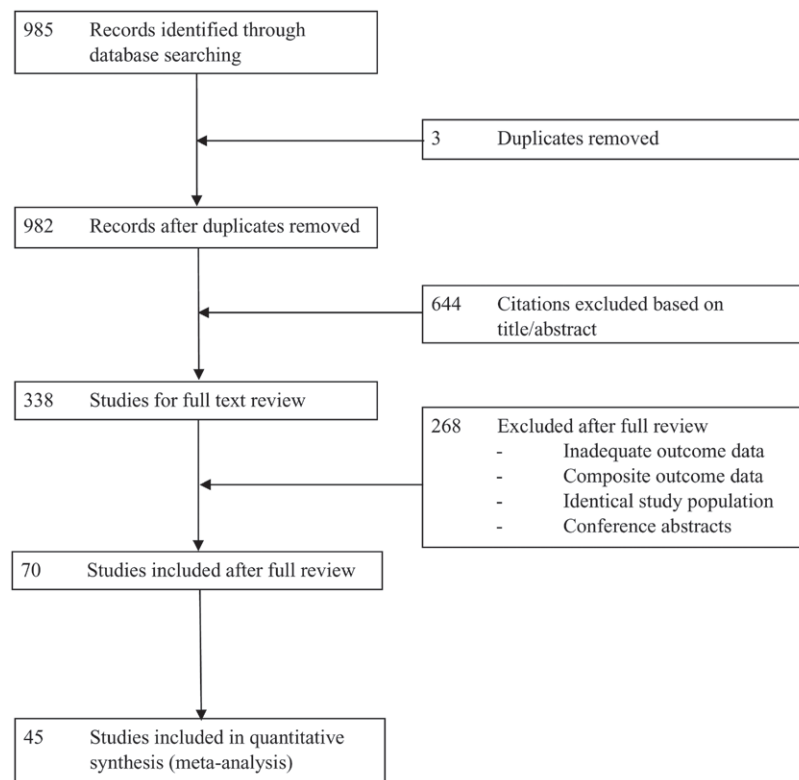


Fig. 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram documenting process of including and excluding studies.

Results

We identified 985 titles and abstracts; after removing three duplicates, we reviewed 982 (fig. 1). We assessed 338 full-text articles and included 70 studies. Together, the included studies involved 42,954 participants and were published between 2009 and 2018. Regions of origin included North America, Europe, Australia, Asia, and South America. Full details of included studies are provided in table 1.

Frailty Instruments and Classifications

Frailty was defined using 35 different instruments. The most prevalent was the Fried Phenotype or related modifications (32 studies),^{4,6,32–61} followed by the Clinical Frailty Scale (12 studies),^{6,55,56,59,62–68} a physical measure of frailty (gait speed, timed get up and go, handgrip strength, short physical performance battery; 12 studies),^{48,52,56,58,59,69–74} the Frailty Index (nine studies),^{32,64,75–81} the Edmonton Frail Scale (seven studies),^{53,67,82–86} or a measure of function or disability (Katz Instrumental Activities of Daily Living, Activities of Daily Living, Eastern Cooperative Group Performance States, self-reported mobility assessment; four studies).^{48,71,73,87} Other instruments were reported in two or fewer studies.^{40,59,69,71,73,78,88–98}

Dichotomization of a frailty instrument was the most common approach to assessing frailty (29 studies [41%]), while 23 studies (33%) categorized frailty into three levels and nine studies categorized it into four or more levels (13%). A continuous measure of frailty was used in four studies (6%). Four studies reported data for patients in the severely frail category.^{40,62,65,85}

Surgical and Patient Populations

Mixed surgical procedures were the most commonly studied populations (20 studies [29%]), followed by general and cardiac surgery (17 studies each [24%]), orthopedics (seven studies [10%]), urology (four studies [6%]) and vascular (three studies [4%]); single studies from otolaryngology, gynecology, and thoracics were also included. Average study population age ranged from 50 to 89, and the proportion of female patients ranged from 25 to 100%.

Mortality

Thirty-two studies ($n = 34,949$) reported outcome data for in-hospital or 30-day mortality (table 2).^{35,37,39,43,48–50,54,56,59,61–63,65–68,70,72,73,76,78,79,85,88,91–93,96,97,99} Seven studies reported outcomes for more than one frailty instrument.^{48,56,59,67,73,78,91}

Table 1. Summary of Included Studies

Study, Yr (Reference)	Study Design	Country of Origin	Frailty Measure	Study Size, n	Mean Age	Female (%)	Frail (%)	Surgical Procedure	Procedure Urgency
Ad <i>et al.</i> , 2016	Prospective	USA	Fried Frailty Phenotype, Gait Speed	167	74.1	25	Fried = 23; Gait = 27	Cardiac	Elective
Afilalo <i>et al.</i> , 2010	Prospective	USA, Canada	Gait Speed	131	75.8	34	46	Cardiac	Elective
Afilalo <i>et al.</i> , 2016	Prospective	USA	Gait Speed	15,171	71	30.5	37.9	Cardiac	Elective
Afilalo <i>et al.</i> , 2017	Prospective	USA, Canada, France	Fried + MMSE + Depression, Fried Frailty Phenotype, CFS, SPPB, Bern Scale, Columbia Scale, Essential Frailty Toolset	1020	82	41.3	Fried = 54; Fried = 40; CFS = 27; SPPB = 67; Bern = 46.5; Columbia = 47.6; EFT = 29.7	Cardiac	Elective
Anabali <i>et al.</i> , 2018	Prospective	Belgium	EFS	254	80	38	20.5	Cardiac	Elective
Andreou <i>et al.</i> , 2018	Prospective	Greece	Fried Frailty Phenotype	298	74.1	44	52	General	Elective
Brown <i>et al.</i> , 2016	Prospective	USA	Fried Frailty Phenotype	55	66.2	25.5	30.9	Cardiac	Elective
Chauhan <i>et al.</i> , 2016	Retrospective	USA	Frailty Score (Gait Speed + ADL + handgrip strength + serum albumin)	342	81.85	52.34	68.13	Cardiac (TAVI)	Elective
Cheung <i>et al.</i> , 2017	Prospective	Australia	EFS	100	89	58	33	Multiple	Emergency
Choi <i>et al.</i> , 2015	Retrospective	Korea	Multidimensional Frailty Score	281	74.8	100	*	Multiple	Elective
Cooper <i>et al.</i> , 2016	Prospective	USA	Fried Frailty Phenotype, Frailty Index	415	76.8	60	Fried = 89; FI = 79	Orthopaedic	Elective
Courtney-Brooks <i>et al.</i> , 2012	Prospective	USA	Fried Frailty Phenotype	37	73	100	43.2	Gynecologic	Elective
Dal Moro <i>et al.</i> , 2017	Prospective	Italy	EFS	78	78.15	14.1	21.8	Urology	*
Dasgupta <i>et al.</i> , 2009	Prospective	Canada	EFS	125	77.4	58	12.8	Multiple	Elective
Donald <i>et al.</i> , 2018	Retrospective	USA	CFS	134	69.6	29.85	29	Vascular	Elective
Dunlay <i>et al.</i> , 2014	Retrospective	USA	Cumulative Deficit Index	99	65	18	67.7	Cardiac (LVAD)	Elective
Garonzik-Wang <i>et al.</i> , 2012	Prospective	USA	Fried Frailty Phenotype	183	53	36	25	Urology	Mixed
Gleason <i>et al.</i> , 2017	Retrospective	USA	FRAIL Scale	175	82.3	74.9	83.4	Orthopaedic	Emergency
Goeteyn <i>et al.</i> , 2017	Prospective	Belgium	CFS	98	73.9	37	46.1	General	Emergency
Hall <i>et al.</i> , 2017	Prospective	USA	RAI-C	6,856	60.7	3.6	77.2	Multiple	Elective
Han <i>et al.</i> , 2018	Prospective	China	Fried Frailty Phenotype	176	69.5	53.4	8	General	Elective
Huded <i>et al.</i> , 2016	Retrospective	USA	Modified Fried Frailty Phenotype	191	82.4	49	71	Cardiac (TAVI)	Elective
Itoh <i>et al.</i> , 2018	Prospective	Japan	Gait Speed	154	67	31.8	32.5	General (Hepatic)	Elective
Jha <i>et al.</i> , 2017	Prospective	Australia	Fried Frailty Phenotype	77	50	30	32	Cardiac (LVAD)	Elective
Joseph <i>et al.</i> , 2016	Prospective	USA	CSHA FI	220	75.7	44	37.3	General	Emergency
Kapoor <i>et al.</i> , 2017	Prospective	USA	Fried Frailty Phenotype	403	72	49	18	Multiple	Elective
Katlic <i>et al.</i> , 2017	Retrospective	USA	SAGE, Fried Frailty Phenotype	1,025	80.3	64.7	SAGE = 41.5; Fried = 88.9	Multiple	Elective
Kenig <i>et al.</i> , 2018	Prospective	Poland	G8 Screening Tool	315	77	52.4	60.3	General	Emergency
Khan <i>et al.</i> , 2016	Prospective	India	Modified Fried Frailty Phenotype	25	79	68	56	Multiple	*
Kim <i>et al.</i> , 2016	Prospective	USA	Modified Fried Frailty Phenotype	197	75	51	34.5	Multiple	Elective
Kotajarvi <i>et al.</i> , 2017	Prospective	USA	Fried Frailty Phenotype	103	80.6	40.8	52	Cardiac	Elective
Kovacs <i>et al.</i> , 2017	Prospective	Romania	CFS, EFS	57	70.2	33.3	*	Cardiac	Elective
Krisjansson <i>et al.</i> , 2012	Prospective	Norway	Modified Fried Scale	176	80	57	61	General	Elective
Kua <i>et al.</i> , 2016	Prospective	Singapore	EFS, Modified Fried Frailty Phenotype	82	79.1	66	EFS = 34.1; Fried = 86.6	Orthopaedic	Emergency
Leung <i>et al.</i> , 2016	Prospective	USA	Fried Frailty Phenotype	63	72.5	54	33	Multiple	Elective
Li <i>et al.</i> , 2016	Prospective	USA	Fried Frailty Phenotype	189	62	40.2	26.5	Multiple	Elective
Li <i>et al.</i> , 2018†	Prospective	China	CSHA FI	120	65.5	73.4	71	ENT	Elective
Li <i>et al.</i> , 2018†	Prospective	Canada	CFS	308	75	45.4	41.6	General	Emergency
Lin <i>et al.</i> , 2017	Prospective	Australia	FI-CGA	246	79	62	55.7	Multiple	Mixed
Lu <i>et al.</i> , 2018	Prospective	China	High Preoperative mFI	119	82	18.5	36.1	General	Elective

(Continued)

Table 1. (Continued)

Study, Yr (Reference)	Study Design	Country of Origin	Frailty Measure	Study Size, n	Mean Age	Female (%)	Frail (%)	Surgical Procedure	Procedure Urgency
Lybryn <i>et al.</i> , 2017	Prospective	Canada	Modified Fried Frailty Phenotype, SPPB, CFS	188	71	29.3	Fried = 49.5; SPPB = 51.6; CFS = 31.9	Cardiac	Mixed
Madbouly <i>et al.</i> , 2017	Retrospective	Saudi Arabia	CSHA mFI	54	64.9	*	*	Urology	Elective
Makary <i>et al.</i> , 2010	Prospective	USA	Fried Frailty Phenotype	594	74	60.3	41	Multiple	Elective
Makhani <i>et al.</i> , 2017	Prospective	USA	Fried Frailty Phenotype	330	58	45.8	20	Multiple	Elective
Marshall <i>et al.</i> , 2016	Prospective	Australia	Fried + bloodwork + falls + ADL	123	77.1	31	13.7	Cardiac	Mixed
McGuckin <i>et al.</i> , 2018	Prospective	UK	CFS	164	77.1	63	50.6	Multiple	Emergency
McIsaac <i>et al.</i> , 2018	Prospective	Canada	CFS, Modified Fried Frailty Phenotype	702	73	49	CFS = 42.3; Fried = 36.6	Multiple	Elective
Orouji Jorak <i>et al.</i> , 2016	Prospective	USA	EGSFI	260	74.8	48	49	General	Emergency
Partridge <i>et al.</i> , 2015	Prospective	UK	EGSFI	125	76.3	31.2	52	Vascular	Mixed
Pelavski <i>et al.</i> , 2017	Prospective	Spain	Gait Speed, Fried Frailty Phenotype, Katz Index	127	87	55.1	Gait = 59.1; Fried = 74; Katz = 34.9	Multiple	Elective
Pol <i>et al.</i> , 2011	Prospective	Netherlands	GFI	142	68	30	35.2	Vascular	Elective
Reichert <i>et al.</i> , 2018	Retrospective	Finland, France, Italy, Germany, Sweden, UK	CFS	6,156	68.6	17.4	60.8	Cardiac	Mixed
Revenig <i>et al.</i> , 2013	Prospective	USA	Hopkins Frailty Score	189	62	40.2	26.5	Multiple	Elective
Revenig <i>et al.</i> , 2014	Prospective	USA	Fried Frailty Phenotype	80	60	42.5	16.2	Multiple	Elective
Revenig <i>et al.</i> , 2015	Prospective	USA	Fried Frailty Phenotype	351	63	39	27	Multiple	Elective
Robinson <i>et al.</i> , 2013	Prospective	USA	Multidimensional Frailty Score	201	74	2	47.8	Multiple	Elective
Rodrigues <i>et al.</i> , 2017	Prospective	Brazil	CFS	221	71.3	34.4	65.2	Cardiac	Elective
Sarcaoğlu <i>et al.</i> , 2018	Prospective	Turkey	CSHA mFI	392	79	62	27.6	Orthopaedic	Emergency
Sato <i>et al.</i> , 2016	Prospective	Japan	Hand Grip Strength, TUG, Fall Risk Assessment, CES-D Fatigue Scale	215	67	18.6	*	Urology	Elective
Saxton <i>et al.</i> , 2011	Retrospective	USA	SF-36, CSHA FI	226	61	53	*	General	Elective
Sikder <i>et al.</i> , 2018	Prospective	Canada	Fried Frailty Phenotype	144	78	54.9	77.8	General	Elective
Singer <i>et al.</i> , 2018	Prospective	USA	SPPB, Fried Frailty Phenotype	386	59	44	SPPB = 20; Fried = 33	Thoracic-Lung Transplant	Elective
Sundermann <i>et al.</i> , 2014	Prospective	Switzerland	CAF, FORECAST	450	79	50	CAF = 49; FORECAST = 63	Cardiac	Elective
Tan <i>et al.</i> , 2012	Prospective	Singapore, Japan	Fried Frailty Phenotype	83	81.2	*	27.7	General	Elective
Tanaka <i>et al.</i> , 2018	Prospective	Japan	KCL	217	75	31	29	General	Elective
Tagels <i>et al.</i> , 2014	Retrospective	Netherlands	GFI	127	72.2	41.1	9	General	*
Ugolini <i>et al.</i> , 2015	Prospective	Italy	TUG, ADL, IADL, ECOG PS, GFI, VES-13	46	80.52	47.8	Timed get up and go = 23.9; ADL = 23.9; IADL = 39.1; ECOG = 21.7; GFI = 52.2; VES-13 = 43.5	General	Elective
Van der Windt <i>et al.</i> , 2018	Prospective	USA	RAI	162	61.5	51	*	General	Elective
Vasu <i>et al.</i> , 2018	Prospective	India	CSHA mFI	60	*	43.3	50	Orthopaedic	Elective
Wang <i>et al.</i> , 2018	Prospective	Canada	FRAIL Scale, CFS	87	72	65.5	FRAIL = 84.9; CFS = 53.9	Orthopaedic	Elective

*Information not available; †Li S, Nie Y, Zhan J, *et al.* The analysis of correlation between frailty index and postoperative complications of aged patients with nodular goiter. *Aging Med.* 2018;1(1):18-22. doi:10.1002/agm2.12016; ‡Li Y, Pederson JL, Churchill TA, *et al.* Impact of frailty on outcomes after discharge in older surgical patients: A prospective cohort study. *Cmaj.* 2018;190(E184-E190). doi:10.1503/cmaj.161403.

ADL, Activities of Daily Living; CAF, Comprehensive Assessment of Frailty; CES-D, Center for Epidemiologic Studies Depression Scale; CFS, Clinical Frailty Scale; CSHA FI, Canadian Study of Health and Aging Frailty Index; ECOG PS, Eastern Cooperative Group Performance Status; EGSFI, Emergency General Surgery Specific Frailty Index; EFS, Edmonton Frail Scale; FRAIL, Fatigue, Resistance, Ambulation, Illness, Loss of weight; FI-CGA, Frailty Index based on Comprehensive Geriatric Assessment; FORECAST, Frailty predicts death One year after Elective Cardiac Surgery Test; G8, Geriatric 8; GFI, Groningen Frailty Indicator; IADL, Instrumental Activities of Daily Living; KCL, Khon Check-Lst; mFI, Modified Frailty Index; MMSE, Mini Mental State Examination; RAI, Risk Analysis Index; RAI-C, Clinical Risk Analysis Index; SAGE-Snai Abbreviated Geriatric Evaluation; SF-36, Short Form Health Survey; SPPB, Short Physical Performance Battery; TUG, Timed Get Up and Go; VES-13, Vulnerable Elders Survey.

Table 2. Summary of Primary Outcome: Mortality

Study, Year (Reference)	Frailty Measure Category	Specific Frailty Measurement	Outcome Window	% Frail	Crude HR/OR	95% CI
Afilalo <i>et al.</i> , 2017	CFS	CFS	90 days	27	3.26	2.27–4.69
Donald <i>et al.</i> , 2018	CFS	CFS	30 days	28.8	51.54	2.89–918.61
Goeteyn <i>et al.</i> , 2017	CFS	CFS	30 days	46.1	2.73†	0.56–13.23
Rodrigues <i>et al.</i> , 2017	CFS	CFS	In-hospital	65.2	3.25	1.29–8.17
McGuckin <i>et al.</i> , 2018	CFS	CFS	30 days	50.6	18.35	1.04–323.45
Reichart <i>et al.</i> , 2018	CFS	CFS	30 days	60.8	Low vs. none = 5.47 Moderate vs. none = 16.05	3.07–9.77 7.60–33.89
Revenig <i>et al.</i> , 2015	Frailty Phenotype	Fried Criteria	30 days	27.3	14.27	1.65–123.81
Tan <i>et al.</i> , 2012	Frailty Phenotype	Fried Criteria	30 days	27.7	2.57	0.05–133.55
Revenig <i>et al.</i> , 2013	Frailty Phenotype	Fried Criteria	90 days	26.5	19.34	0.98–380.85
Lytwyn <i>et al.</i> , 2017	Frailty Phenotype	Modified Fried Criteria	In-hospital	49.5	3.14	0.32–30.70
Afilalo <i>et al.</i> , 2017	Frailty Phenotype	Fried Criteria	90 days	40.2	2.24	1.57–3.20
Brown <i>et al.</i> , 2016	Frailty Phenotype	Fried Criteria	90 days	30.9	0.42	0.02–9.16
Gleason <i>et al.</i> , 2017	Frailty Phenotype	FRAIL Scale	30 days	83.4	Low vs. none = 1.22 Moderate vs. none = 3.82	0.05–30.83 0.20–73.23
Pelavski <i>et al.</i> , 2017	Frailty Phenotype	Fried Criteria	30 days	59.1	Low vs. none = 6.09 Moderate vs. none = 15.04	0.37–113.58 0.79–284.97
Kristjansson <i>et al.</i> , 2012	Frailty Phenotype	Modified Fried Criteria	30 days	60.2	Low vs. none = 2.05† mod vs. none = 3.35†	0.94–4.46 1.17–9.59
Huded <i>et al.</i> , 2016	Frailty Phenotype	Modified Fried Criteria	30 days	71	Low vs. none = 2.51 Moderate vs. none = 1.81	0.25–24.78 0.16–20.47
Pelavski <i>et al.</i> , 2017	Physical Measure	Gait Speed	30 days	59.1	2.99	0.61–14.67
Afilalo <i>et al.</i> , 2017	Physical Measure	SBBP	90 days	67.4	3.97	2.37–6.62
Afilalo <i>et al.</i> , 2010	Physical Measure	Gait Speed	In-hospital	46	7.78	0.91–14.67
Afilalo <i>et al.</i> , 2016	Physical Measure	Gait Speed	30 days	37.9	Low vs. none = 1.77 Moderate vs. none = 3.16	1.34–2.34 2.31–4.22
Joseph <i>et al.</i> , 2016	Frailty Index	CSHA FI	In-hospital	37.3	27.52	1.55–488.46
Saxton <i>et al.</i> , 2011	Frailty Index	CSHA FI	30 days	*	0.55	0.07–4.12
Pelavski <i>et al.</i> , 2017	Physical Function	Katz Index	30 days	23.2	Low vs. none = 2.89 Moderate vs. none = 3.55	0.68–12.36 0.58–21.69
Afilalo <i>et al.</i> , 2017	Other	Bern Scale	90 days	46.5	3.74	2.53–5.54
Afilalo <i>et al.</i> , 2017	Other	Columbia Scale	90 days	47.6	4.35	2.90–6.54
Afilalo <i>et al.</i> , 2017	Other	Essential Frailty Toolset	90 days	29.7	4.91	3.40–7.09
Afilalo <i>et al.</i> , 2017	Other	Fried + MMSE + depression	90 days	54	3.52	2.33–5.33
Kenig <i>et al.</i> , 2018	Other	G8 Screening Tool	30 days	60.3	12.37	5.18–29.56
Lu <i>et al.</i> , 2018	Other	High Preoperative mFI	90 days	36.1	1.02	0.47–2.20
Marshall <i>et al.</i> , 2016	Other	Fried + bloodwork + falls + ADL	In-hospital	13.8	2.15	0.21–21.92
Saxton <i>et al.</i> , 2011	Other	SF-36, general health	30 days	*	1.96	0.65–5.88
Tanaka <i>et al.</i> , 2018	Other	KCL	30 days	29	7.42	0.29–184.52
Tegels <i>et al.</i> , 2014	Other	GFI	In-hospital	*	5.60	1.63–19.26
Sundermann <i>et al.</i> , 2014	Other	CAF	30 days	49	Low = 3.93 Moderate = 4.00	1.53–10.11 0.95–16.89
Sundermann <i>et al.</i> , 2014	Other	FORECAST	30 days	63	Low = 3.05 Mod = 9.00	0.93–10.10 2.98–27.23
Chauhan <i>et al.</i> , 2016	Other	Frailty Score (gait speed + ADL + handgrip strength + serum albumin)	90 days	68.13	Low = 3.07 Moderate = 5.67 Severe = 7.93	0.62–15.10 1.14–28.14 1.38–45.57

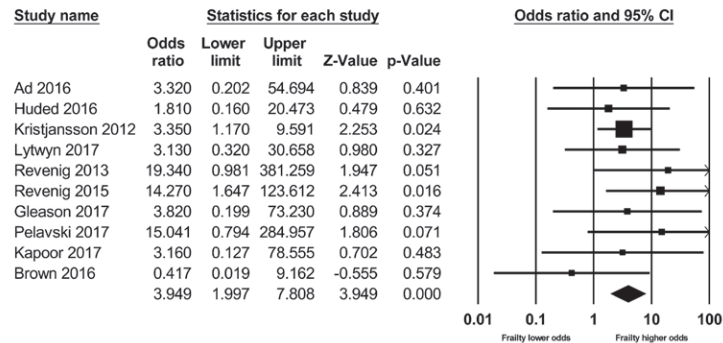
*Information not available; †indicates heart rate. All other effect measures are odds ratio.

ADL, Activities of Daily Living; CAF, Comprehensive Assessment of frailty; CFS, Clinical Frailty Scale; CSHA FI, Canadian Study of Health and Aging Frailty Index; FORECAST, Frailty predicts death One year after Elective CArdiac Surgery Test; GFI, Groningen Frailty Indicator; G8, Geriatric 8; HR, hazard ratio; KCL, Kihon Check-List; mFI, Modified Frailty Index; MMSE, Mini-Mental State Examination; OR, odds ratio; SF-36, Short Form Health Survey; SPPB, Short Physical Performance Battery.

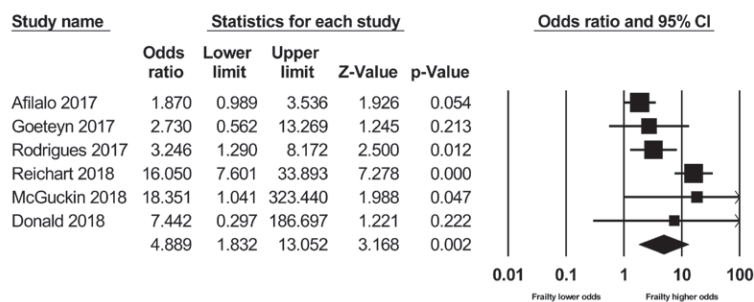
The Fried Phenotype was examined in the largest number of studies (10, $n = 2,022$).^{35,37,39,43,48–50,56,61,70} Across studies, frailty based on the Fried Phenotype was associated with mortality (odds ratio, 3.95; 95% CI, 2.00 to 7.81; $P < 0.0001$; $I^2 = 0$; fig. 2A). The next most studied instrument was the Clinical Frailty Scale (six studies; $n = 7,793$),^{59,62,63,65,66,68} which was also associated with

mortality (odds ratio, 4.89; 95% CI, 1.83 to 13.05; $P = 0.002$; $I^2 = 75.3$; fig. 2B), with the largest effect size of any instrument. Heterogeneity appeared to be attributable to the three studies of the Clinical Frailty Scale in cardiac surgery^{59,66,68} (I^2 in cardiac studies, 89%; noncardiac, 0%; pooled odds ratio cardiac, 4.59; 95% CI, 1.19 to 17.69; pooled odds ratio noncardiac, 4.64; 95% CI, 1.30 to 16.60). Physical measures of

A Association of Frailty Phenotype with Mortality



B Association of Clinical Frailty Scale with Mortality



C Association of Physical Frailty with Mortality

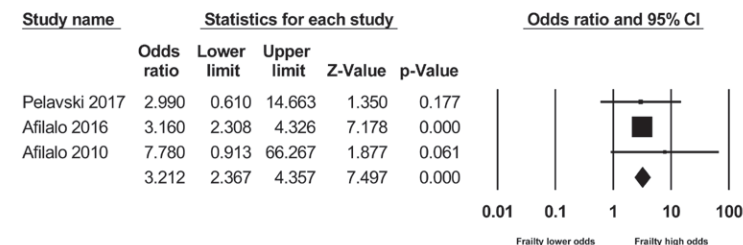


Fig. 2. Forest plots of pooled unadjusted strengths of association between frailty instruments and mortality (for frailty instruments reported in more than two independent studies). (A) Frailty Phenotype; (B) Clinical Frailty Scale; (C) Physical measures of frailty.

frailty (gait speed, short physical performance battery) were evaluated in three studies, but involved the largest total number of patients ($n = 15,429$)^{48,59,70,72} and reported the smallest pooled effect size (odds ratio, 3.21; 95% CI, 2.37 to 4.36; $P < 0.0001$; $I^2 = 0$; fig. 2C).

There were insufficient data for meta-analysis of other frailty instruments; however, all but one study⁷⁸ that investigated the relationship between a frailty instrument and mortality found a directionally consistent association where mortality was more common in people with frailty. These results are reported in table 2.

The meta-regression for mortality across frailty instruments demonstrated no evidence of a significant effect modification by instrument ($P = 0.545$). There was no evidence that the Clinical Frailty Scale had a stronger association with mortality than the Fried Phenotype (meta-regression odds ratio, 1.16; 95% CI, 0.35 to 3.82; $P = 0.807$).

Five studies reported other measures of predictive accuracy for mortality (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/C333>). As individual predictors, the G8 Screening tool, Edmonton Frail Scale, and

Risk Analysis Index were weakly to moderately discriminative (area under the receiver operating characteristic curve [AUC] approximated 0.7 for each instrument).^{96,97} When added to the Society of Thoracic Surgery (Chicago, Illinois) and EuroScore II cardiac surgery risk models, frailty instruments demonstrated improvements in model discrimination.^{59,68}

Complications

Fifty studies reported outcome data for postoperative complications (total $n = 31,408$; Supplemental Digital Content, table 3, <http://links.lww.com/ALN/C333>).^{30–34,36–39,41–43,45–48,51,53–56,58,60,63,64,66,69,71,73–76,80–82,84,86,88,89,91,94–101} Eight studies reported postoperative complication data for more than one frailty instrument.^{32,40,48,53,56,58,67,78} Thirty-eight effect sizes were included in a meta-analysis. The definition of a postoperative complication varied between studies. Some studies used the Clavien-Dindo Classification of Surgical Complications¹⁰⁴ or the National Surgical Quality Improvement Program definition.¹⁰⁵ Others included complications that were relevant to the surgical procedure (e.g., sternal wound infection or delayed graft function for kidney transplant).

Again, the Fried Phenotype was the most studied instrument (22 studies; $n = 4,250$)^{30–34,36–43,45,47,48,51,53,54,56,58,85} and was associated with complications (odds ratio, 2.47; 95% CI, 2.00 to 3.04; $P < 0.0001$; $I^2 = 9.4$; Supplemental Digital Content, fig. 1A, <http://links.lww.com/ALN/C333>). The Edmonton Frail Scale (five studies; $n = 510$)^{53,82–84,86} and Frailty Index (five studies; $n = 1,072$)^{64,76–78,106} were the next most studied, with both the Edmonton Frail Scale (odds ratio, 2.92; 95% CI, 1.52 to 3.46; $P = 0.001$; $I^2 = 54.0$; Supplemental Digital Content, fig. 1B, <http://links.lww.com/ALN/C333>) and Frailty Index (odds ratio, 2.29; 95% CI, 1.52 to 3.46; $P < 0.0001$; $I^2 = 61.1$; Supplemental Digital Content, fig. 1C, <http://links.lww.com/ALN/C333>) significantly predicting complications. Three studies evaluated the Clinical Frailty Scale's association with complications ($n = 519$)^{62,63,66} and found a directional, but nonsignificant, association with complications (odds ratio, 1.68; 95% CI, 0.95 to 2.95; $P = 0.073$; $I^2 = 73.2$; Supplemental Digital Content, fig. 1D, <http://links.lww.com/ALN/C333>). Physical measures of frailty, namely gait speed, were also evaluated in five studies and ($n = 15,750$)^{62,63,66} and were associated with complications (odds ratio, 1.98; 95% CI, 1.47 to 2.68; $P < 0.0001$; $I^2 = 35.8$; Supplemental Digital Content, fig. 1E, <http://links.lww.com/ALN/C333>). All studies evaluating other frailty instruments and complications also found that people with frailty had higher odds of complications.

Eighteen studies reported other measures of predictive accuracy for complication outcomes (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/C333>). Six studies provided data on the Fried Phenotype, which had weak to moderate discrimination (AUC, 0.60

to 0.76);^{36,39,40,46,49} three studies of the Edmonton Frail Scale demonstrated weak discrimination (AUC, 0.65 to 0.69).^{53,67,84} The Frailty Index demonstrated moderate to strong discrimination (AUC, 0.71 to 0.82).^{88,98,107} All frailty instruments tested improved discrimination and/or explained variance when added to existing multivariable models.

Discharge Disposition

Twenty-five studies reported discharge disposition data (Supplemental Digital Content, table 4, <http://links.lww.com/ALN/C333>), defined as new admission to nursing home, transitional care, or rehabilitation facility (total $n = 6,558$);^{6,32,33,35,37,39,40,46,48,55,57,58,62,63,70,76,77,83–85,92,94,95,101,102} six studies reported outcome data for more than one instrument.^{6,32,40,48,55,58}

Eleven studies included the Fried Phenotype^{4,6,32,33,35,37,39,46,48,53,55,57–59} ($n = 3,202$; odds ratio, 5.18; 95% CI, 3.34 to 8.03; $P < 0.0001$; $I^2 = 56.4$; Supplemental Digital Content, fig. 2A, <http://links.lww.com/ALN/C333>), five studies included the Clinical Frailty Scale^{6,55,62,63,101} ($n = 1,186$; odds ratio, 6.31; 95% CI, 4.01 to 9.36; $P < 0.0001$; $I^2 = 0$; Supplemental Digital Content, fig. 2B, <http://links.lww.com/ALN/C333>), four studies included the Frailty Index^{32,76,77,90} ($n = 1,141$; odds ratio, 2.29; 95% CI, 1.52 to 3.46, $P = 0.006$, $I^2 = 78.9$; Supplemental Digital Content, fig. 2C, <http://links.lww.com/ALN/C333>), and three studies included physical measures of frailty^{48,58,72} ($n = 15,429$; odds ratio, 3.94; 95% CI, 2.49 to 6.24; $P < 0.001$; $I^2 = 0$; Supplemental Digital Content, fig. 2D, <http://links.lww.com/ALN/C333>). Again, all other studies also found increased odds of nonfavorable discharge in people with frailty.

Five studies provided other measures of predictive performance for adverse discharge outcomes (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/C333>).^{6,40,46,87,94} The Fried Phenotype demonstrated moderate to strong discrimination (AUC, 0.78, 0.83) and increased discrimination when added to the American Society of Anesthesiologists, Lee, and Eagle scores. The Clinical Frailty Scale was more sensitive (80 vs. 67%), but less specific (61 vs. 66%) than the Fried Phenotype when identifying older people who were not discharged home after surgery.

Delirium

Twelve studies reported outcome data for postoperative delirium (total $n = 2,537$; Supplemental Digital Content, table 5, <http://links.lww.com/ALN/C333>).^{35,40,41,44,53,56,61,69,82,84,89,92} and four of these reported outcome data for more than one frailty instrument.^{40,53,56,69} Eight effect measures were meta-analyzed, six for the Fried Phenotype ($n = 594$)^{35,41,44,56,61} and three ($n = 307$)^{53,82,83} for the Edmonton Frail Scale. Both the Fried Phenotype (odds ratio, 3.79; 95% CI, 1.75 to 8.22; $P = 0.001$; $I^2 = 27.6$; Supplemental Digital

Content, fig. 3A, <http://links.lww.com/ALN/C333>) and Edmonton Frail Scale (odds ratio, 2.11; 95% CI, 1.06 to 4.21; $P = 0.034$; $I^2 = 0$; Supplemental Digital Content, fig. 4B, <http://links.lww.com/ALN/C333>) were associated with delirium. Three studies provided other measures of predictive accuracy (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/C333>).^{40,69,89} The Fried Phenotype, Groningen Frailty Indicator, and Sinai Abbreviated Geriatric Evaluation were all moderately discriminative (AUC, 0.74, 0.77, and 0.70, respectively) when predicting delirium.

Other Outcomes

Adequate data were available for meta-analysis of length of stay for the Frailty Index, Clinical Frailty Scale, and Fried Phenotype, which were all associated with increased length of stay (standardized mean difference, 0.83, 0.54, and 0.38, respectively; Supplemental Digital Content, fig. 4A to 4C, and table 6, <http://links.lww.com/ALN/C333>). Ten studies reported postoperative functional outcomes (five Fried Phenotype, three Edmonton Frail Scale, and two Clinical Frailty Scale) with heterogeneity in outcome definitions and analyses precluding pooling. Frailty was typically associated with worse functional outcomes (Supplemental Digital Content, table 7, <http://links.lww.com/ALN/C333>).

Feasibility

Thirty-two studies reported aspects of feasibility.^{6,39,46,55,56,60,63–65,67,68,70,76–78,82–84,86,92,93} Findings are summarized in table 3 (full details in Supplemental Digital Content, table 8, <http://links.lww.com/ALN/C333>); only 19 of 50 available data points were based on objective data, compared to 31 of 50 that were subjectively supported. Overall, the Clinical Frailty Scale, Edmonton Frail Scale, Frailty Index, and Fried Phenotype had the largest amounts of available data. All available data positively supported the Clinical Frailty Scale, while the Edmonton Frail Scale and

Frailty Index also had predominantly positive feasibility ratings, compared to the Fried Phenotype, where the majority of data did not support feasibility. Only one study directly compared objectively-measured feasibility ratings between frailty instruments, reporting that the Clinical Frailty Scale was easier to use ($P < 0.0001$), had fewer logistical and environmental barriers ($P < 0.0001$), and was faster to administer ($P < 0.0001$) than the Fried Phenotype.⁶ Time was the most frequent feasibility measure reported,^{4,6,46,56,60,64,67,77,78,82,84,86,92} ranging from 44 s for the Clinical Frailty Scale to 5 to 20 min for the Fried Phenotype. The need for additional equipment was identified as a significant barrier to the use of Fried Phenotype³⁹, and in some versions of the Frailty Index,⁷⁷ while physical measurements were identified as barriers for assessment of emergency surgery patients.^{39,55,56,76,83} Missing assessment data was noted for the Frailty Index and Fried Phenotype,^{6,77} while difficulty with patient interpretation of questions was reported for the Edmonton Frail Scale.⁶⁷

Risk of Bias

Risk of bias results according to the Quality in Prognostic Studies tool are reported in Supplemental Digital Content, table 9 (<http://links.lww.com/ALN/C333>). There was 96% between-rater agreement across all items and no disagreements were greater than ± 1 level. The main contributor to high risk of bias were issues of confounding (typically because of combining surgical procedures or urgency categories) and unclear risk of bias was most commonly present due to a lack of reporting of study attrition.

Discussion

In this systematic review and meta-analysis of 70 studies that reported the association of frailty, prospectively assessed in preoperative clinical settings, with postoperative outcomes, we found that the Clinical Frailty Scale had largest effect size when predicting postoperative mortality (our primary outcome), with a greater than 4.5-fold increase in the odds

Table 3. Summary of Measures Positively or Negatively Supporting Feasibility of Different Frailty Instruments

Category	FP		CFS		FI		EFS		GFI		RAI-C		Gait Speed		SPPB	
	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-
Acceptability (satisfaction, intention to continue use, perceived appropriateness)			1													
Implementation (degree of successful execution, resources needed to implement, factors affecting implementation)	1	1	1		2	1	1	1	1		1				1	
Practicality (ease of use, efficiency/speed, costs, positive/negative effects on users or targets)	1	2	8		3		5		1				3		1	

Numbers represent count of data points pertaining to feasibility of a given frailty instrument in reported studies.

+, positively supports feasibility; -, negatively supports feasibility; CFS, Clinical Frailty Scale; EFS, Edmonton Frail Scale; FI, Frailty Index; FP, Frailty Phenotype; GFI, Groningen Frailty Indicator; RAI-C, Risk Analysis Index-Clinical; SPPB, Short Physical Performance Battery.

of death. Our findings also provide novel pooled effect estimates for mortality, complications, nonfavorable discharge, delirium, and impaired postoperative function, as well as measures of predictive accuracy, specific to five unique frailty instruments, which can directly inform preoperative frailty assessment. Our review has further identified that future studies should address not only effect sizes, but also considerations of feasibility and predictive accuracy, which were rarely reported. Available evidence currently supports the feasibility of the Clinical Frailty Scale over other frailty instruments for preoperative use.

Routine preoperative assessment of frailty in older adults has been recommended by best practice guidelines since 2012, when a joint guideline from the American College of Surgeons and American Geriatrics Society included frailty assessment as a key component of the optimal assessment of the older surgical patient. Similar recommendations have subsequently emerged from international and multidisciplinary organizations.^{9,108} However, low rates of guideline uptake may be related to a lack of evidence comparing different frailty instruments in perioperative medicine,¹² including systematic reviews that have examined the relationship between preoperative frailty and postoperative outcomes by pooling all frailty exposures into a single effect.^{4,16,17,19,20,109,110} In contrast, our study was designed to allow comparison between instruments by separately pooling data from adequately studied frailty tools (*i.e.*, more than two studies of a given instrument) and summarizing measures of predictive accuracy and feasibility. This allows readers to directly assess the strength of association and accuracy for each instrument across outcomes of key importance, while also informing decisions about actual use of different frailty instruments in routine clinical practice.

Based on our results, it appears that frailty measured using the Clinical Frailty Scale has the strongest association with postoperative mortality, although the significance of this difference compared to other instruments is uncertain. Therefore, from a strength of association perspective the Fried Phenotype could also receive strong consideration from clinicians. The Fried Phenotype had the largest amount of available data, was strongly associated with mortality, and demonstrated low heterogeneity between studies. However, time requirements and other logistical considerations suggest that the Fried Phenotype is less feasible than the Clinical Frailty Scale. Minimal data comparing the predictive accuracy of frailty instruments for mortality were available, although available data did not clearly identify a single instrument as highly discriminative, leaving this as an area for future research.

While we specified mortality as our study's primary outcome, it is well recognized that outcomes beyond mortality are of key importance to older people and the healthcare system. When identifying older individuals at high risk of complications, which may occur in a majority of older people with frailty,⁵ both the Edmonton Frail Scale and the

Fried Phenotype were associated with an approximately 2.9-fold increase in the odds of experiencing a complication, however, the Fried Phenotype had more available data and a lower degree of heterogeneity. The Frailty Index or Fried Phenotype appear to have the strongest discrimination when predicting complications. Older people strongly value maintenance of independence and prioritize getting home.^{22,111} Therefore, discussing risk of nonhome discharge is highly relevant before surgery where the strongest evidence supports the Clinical Frailty Scale, as it had the largest association with nonhome discharge and lower heterogeneity compared to the Fried Phenotype and Frailty Index. Delirium is also a priority outcome for older surgical patients; however, it was the least well-studied of our outcomes eligible for pooling. Here, the Fried Phenotype was more strongly associated than the Edmonton Frail Scale (odds ratio, 4.1 *vs.* 2.1). As highlighted by recent publications, however, new findings could still alter our conclusions.¹¹² Therefore, frailty instrument selection decisions could be aided through accumulation of additional data for the Clinical Frailty Scale in terms of complications and for all instruments in terms of delirium and length of stay prediction. Overall, when considering strength of association and predictive accuracy in choosing a frailty instrument, clinicians and institutions may need to identify the outcomes (and related processes) that are of highest priority to them.

Future research evaluating the predictive accuracy of frailty instruments should also consider patient-centered and -reported outcomes. Despite identifying 70 studies of preoperative clinical frailty assessment, only 10 reported relevant function, quality of life or disability outcomes. Such data are key considerations for older people with frailty considering surgery and will be needed to support evidence-based interventions, such as shared decision making, that might help older people with frailty ensure that their medical decisions are congruent with their values and preferences.

Ultimately, adequate predictive accuracy is a foundational consideration when choosing a risk stratification tool. However, given the lack of undisputable evidence to support the accuracy of one instrument over another and a lack of consensus on frailty definitions in general,¹¹ feasibility should be strongly considered. Many measures of feasibility exist, but in the preoperative setting we would suggest that acceptability, practicality and integration may be most relevant.²³ Based on limited, but consistent data, the Clinical Frailty Scale appears to be the most feasible instrument among those routinely studied. In the area of practicality (*e.g.*, need for resources and time) the Clinical Frailty Scale appears to be meaningfully faster than the Fried Phenotype and requires no extra tools or physical measurements of subdomain scoring. Currently, researchers can contribute by formally comparing objective measures of feasibility between leading instruments while implementation programs could scientifically

evaluate the implementation process to inform future efforts. Comparisons of clinically applied instruments with instruments that can be applied *via* electronic data are also warranted, as electronic frailty indices could be a feasible manner to assess for frailty in certain settings and jurisdictions.^{113,114}

Strengths and Limitations

This study should be appraised in terms of its strengths and limitations. Protocol preregistration and adherence to best-practice recommendations for systematic reviews supports a robust and low risk of bias review. Furthermore, application of a broad, peer-reviewed search strategy to medical and allied health databases ensured that the available literature was thoroughly included. We also considered a variety of outcomes known to be important to patients, clinicians, and the healthcare system, while considering feasibility to ensure that our findings can directly inform clinical practice. However, a lack of formal assessment of feasibility in many studies decreases the certainty of our findings. Furthermore, only the Fried Phenotype had at least five studies in each meta-analysis, which suggests that further studies for other frailty instruments could lead to changes for some estimates. Our decision to focus on unadjusted effect measures likely reflected typical use of frailty instruments in clinical practice and maximized available data; however, lack of confounder adjustment further limits the robustness of causal inference using observational data. Other measures of predictive performance (*e.g.*, discrimination and calibration, among others) were inadequately reported to synthesize, hence, our analysis is largely based on strength of association, not formal prediction metrics.¹¹⁵ Reliability is also an important consideration when evaluating risk assessment tools, but was not considered in our review and was rarely reported in included studies; poor reliability can lead to attenuation of effect sizes¹¹⁶ and may be of particular importance for instruments that require subjective evaluation. Inadequate data were available to test the impact of potential effect modifiers, such as surgery type, on our pooled measures of association; lack of head to head comparisons precluded techniques such as network meta-analysis. Clinicians may also consider the underlying framework supporting different frailty instruments (*e.g.*, physical manifestations of cellular dysfunction with the Fried Phenotype *vs.* accumulating multidimensional deficits with the Frailty Index¹¹⁷) when choosing a tool; we did not directly assess these underlying conceptual frameworks. Finally, we excluded comprehensive geriatric assessment (as this is a technique limited to geriatricians), however, this technique is considered as a gold standard approach to frailty assessment in some settings.

Conclusions

Clinicians should consider accuracy and feasibility when choosing a frailty instrument. Strong evidence in both domains support the Clinical Frailty Scale, which had the largest pooled effect size for predicting mortality and non-home discharge after surgery and appears to be the fastest and most practical instrument that has been widely studied. Strong associations with complications and delirium, and a largest amount of available data, also support the Fried Phenotype, but its use appears to require a trade-off between high accuracy with lower feasibility.

Acknowledgments

The authors wish to acknowledge Ms. Sascha Davis, Learning Services, The Ottawa Hospital, for her expertise in designing and executing the systematic review search strategy.

Research Support

Dr. McIsaac receives salary support from The Ottawa Hospital Department of Anesthesiology and Pain Medicine (Ottawa, Ontario, Canada) and is supported by the Canadian Anesthesiologists' Society (Toronto, Ontario, Canada) Career Scientist Award, but reports no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 yr and no other relationships or activities that could appear to have influenced the submitted work. The authors acknowledge The Ottawa Hospital Department of Anesthesiology and Pain Medicine for supporting use of Distiller SR software.

Competing Interests

The authors declare no competing interests.

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References

1. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A: A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; 173:489–95
2. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group: Frailty in older adults:

- evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56:M146–56
3. Lin HS, Watts JN, Peel NM, Hubbard RE: Frailty and post-operative outcomes in older surgical patients: A systematic review. *BMC Geriatr* 2016; 16:157
 4. Kim DH, Kim CA, Placide S, Lipsitz LA, Marcantonio ER: Preoperative Frailty Assessment and outcomes at 6 months or later in older adults undergoing cardiac surgical procedures: A systematic review. *Ann Intern Med* 2016; 165:650–60
 5. Watt J, Tricco AC, Talbot-Hamon C, Pham B, Rios P, Grudniewicz A, Wong C, Sinclair D, Straus SE: Identifying older adults at risk of harm following elective surgery: A systematic review and meta-analysis. *BMC Med* 2018; 16:2
 6. McIsaac DI, Taljaard M, Bryson GL, Beaulé PE, Gagné S, Hamilton G, Hladkiewicz E, Huang A, Joannise JA, Lavallée LT, MacDonald D, Moloo H, Thavorn K, Walraven C van, Yang H, Forster AJ: Frailty as a predictor of death or new disability after surgery: A prospective cohort study. *Ann Surg* 2020; 271:283–9
 7. Chow WB, Rosenthal RA, Merkow RP, Ko CY, Esnaola NF; American College of Surgeons National Surgical Quality Improvement Program; American Geriatrics Society: Optimal preoperative assessment of the geriatric surgical patient: A best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg* 2012; 215:453–66
 8. Association of Anaesthetists of Great Britain and Ireland: Peri-operative care of the elderly. *Anaes* 2014; 69 s1:81–98
 9. Alvarez-Nebreda ML, Bentov N, Urman RD, Setia S, Huang JC, Pfeifer K, Bennett K, Ong TD, Richman D, Gollapudi D, Alec Rooke G, Javedan H: Recommendations for preoperative management of frailty from the Society for Perioperative Assessment and Quality Improvement (SPAQI). *J Clin Anesth* 2018; 47:33–42
 10. Eamer G, Gibson JA, Gillis C, Hsu AT, Krawczyk M, MacDonald E, Whitlock R, Khadaroo RG: Surgical frailty assessment: A missed opportunity. *BMC Anesthesiol* 2017; 17:99
 11. Rodríguez-Mañas L, Féart C, Mann G, Viña J, Chatterji S, Chodzko-Zajko W, Gonzalez-Colaço Harmand M, Bergman H, Carcaillon L, Nicholson C, Scuteri A, Sinclair A, Pelaez M, Cammen T Van Der, Beland F, Bickenbach J, Delamarche P, Ferrucci L, Fried LP, Gutiérrez-Robledo LM, Rockwood K, Rodríguez Artalejo F, Serviddio G, Vega E: Searching for an operational definition of frailty: A delphi method based consensus statement. The frailty operative definition-consensus conference project. *Journals Gerontol - Ser A Biol Sci Med Sci* 2013; 68:62–7
 12. Tang VL, Covinsky K: Frailty and surgical decision making. *Ann Intern Med* 2016; 165:669–70
 13. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB: Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283:2008–12
 14. Higgins J, Green S: *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* [updated March 2011]. Cochrane Collab 2011
 15. Shen Y, Hao Q, Zhou J, Dong B: The impact of frailty and sarcopenia on postoperative outcomes in older patients undergoing gastrectomy surgery: A systematic review and meta-analysis. *BMC Geriatr* 2017; 17:188
 16. Lin H-S, Watts JN, Peel NM, Hubbard RE, Griebbling TL: Re: frailty and post-operative outcomes in older surgical patients: A systematic review. *BMC* 2016; 16
 17. Wang J, Zou Y, Zhao J, Schneider DB, Yang Y, Ma Y, Huang B, Yuan D: The impact of frailty on outcomes of elderly patients after major vascular surgery: A systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2018 doi:10.1016/j.ejvs.2018.07.012
 18. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement 2009; 151:264–9
 19. Oakland K, Nadler R, Cresswell L, Jackson D, Coughlin PA: Systematic review and meta-analysis of the association between frailty and outcome in surgical patients. *Ann R Coll Surg Engl* 2016; 1–6 doi:10.1308/rcsann.2016.0048
 20. Watt J, Tricco AC, Talbot-Hamon C, Pham B, Rios P, Grudniewicz A, Wong C, Sinclair D, Straus SE: Identifying older adults at risk of delirium following elective surgery: A systematic review and meta-analysis. *J Gen Intern Med* 2018; 33:500–9
 21. Sampson M, McGowan J, Lefebvre C, Moher D, Grimshaw JM: PRESS: Peer Review of Electronic Search Strategies. 2008 doi:10.1111/1540-4560.00063
 22. Akpan A, Roberts C, Bandeen-Roche K, Batty B, Bausewein C, Bell D, Bramley D, Bynum J, Cameron ID, Chen LK, Ekdahl A, Fertig A, Gentry T, Harkes M, Haslehurst D, Hope J, Hurtado DR, Lyndon H, Lynn J, Martin M, Isden R, Raso FM, Shaibu S, Shand J, Sherrington C, Sinha S, Turner G, De Vries N, Yi GJ, Young J, Banerjee J: Standard set of health outcome measures for older persons. *BMC Geriatr* 2018; 18:36
 23. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, Bakken S, Kaplan CP, Squiers L, Fabrizio C, Fernandez M: How we design feasibility studies. *Am J Prev Med* 2009; 36:452–7
 24. McIsaac DI, Huang A, Wong CA, Wijeyesundera DN, Bryson GL, van Walraven C: Effect of preoperative geriatric evaluation on outcomes after elective surgery:

- A population-based study. *J Am Geriatr Soc* 2017; 65:2665–72
25. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G: Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004; 59:255–63
 26. Distiller SR. Systematic Review and Literature Review Software by Evidence Partners. Available at: <https://www.evidencepartners.com/>. Accessed March 12, 2020.
 27. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C: Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013; 158:280–6
 28. Comprehensive Meta-Analysis Software (CMA). Available at: meta-analysis.com. Accessed March 12, 2020.
 29. Harris EP, MacDonald DB, Boland L, Boet S, Lalu MM, McIsaac DI: Personalized perioperative medicine: A scoping review of personalized assessment and communication of risk before surgery. *Can J Anaesth* 2019; 66:1026–37
 30. Wan X, Wang W, Liu J, Tong T: Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014; 14:135
 31. Hsieh HF, Shannon SE: Three approaches to qualitative content analysis. *Qual Health Res* 2005; 15:1277–88
 32. Cooper Z, Rogers SO Jr, Ngo L, Guess J, Schmitt E, Jones RN, Ayres DK, Walston JD, Gill TM, Gleason LJ, Inouye SK, Marcantonio ER: Comparison of frailty measures as predictors of outcomes after orthopedic surgery. *J Am Geriatr Soc* 2016; 64:2464–71
 33. Courtney-Brooks M, Tellawi AR, Scalici J, Duska LR, Jazaeri AA, Modesitt SC, Cantrell LA: Frailty: An outcome predictor for elderly gynecologic oncology patients. *Gynecol Oncol* 2012; 126:20–4
 34. Garonzik-Wang JM, Govindan P, Grinnan JW, Liu M, Ali HM, Chakraborty A, Jain V, Ros RL, James NT, Kucirka LM, Hall EC, Berger JC, Montgomery RA, Desai NM, Dagher NN, Sonnenday CJ, Englesbe MJ, Makary MA, Walston JD, Segev DL: Frailty and delayed graft function in kidney transplant recipients. *Arch Surg* 2012; 147:190–3
 35. Gleason LJ, Benton EA, Alvarez-Nebreda ML, Weaver MJ, Harris MB, Javedan H: FRAIL Questionnaire screening tool and short-term outcomes in geriatric fracture patients. *J Am Med Dir Assoc* 2017; 18:1082–6
 36. Han B, Wang Y, Chen X: Predictive value of frailty on postoperative complications in elderly patients with major abdominal surgery. *Biomed Res* 2018; 29:1308–15
 37. Huded CP, Huded JM, Friedman JL, Benck LR, Lindquist LA, Holly TA, Sweis RN, Ricciardi MJ, Malaisrie SC, Davidson CJ, Flaherty JD: Frailty status and outcomes after transcatheter aortic valve implantation. *Am J Cardiol* 2016; 117:1966–71
 38. Jha SR, Hannu MK, Newton PJ, Wilhelm K, Hayward CS, Jabbour A, Kotlyar E, Keogh A, Dhital K, Granger E, Connellan M, Jansz P, Spratt PM, Montgomery E, Smith A, Harkess M, Tunicliff P, Davidson PM, Macdonald PS: Reversibility of frailty after bridge-to-transplant ventricular assist device implantation or heart transplantation. *Transplant Direct* 2017; 3:e167
 39. Kapoor A, Matheos T, Walz M, McDonough C, Maheswaran A, Ruppell E, Mohamud D, Shaffer N, Zhou Y, Kaur S, Heard S, Crawford S, Cabral H, White DK, Santry H, Jette A, Fielding R, Silliman RA, Gurwitz J: Self-reported function more informative than frailty phenotype in predicting adverse postoperative course in older adults. *J Am Geriatr Soc* 2017; 65:2522–8
 40. Katlic MR, Coleman J, Khan K, Wozniak SE, Abraham JH: Sinai Abbreviated Geriatric Evaluation: Development and validation of a practical test. *Ann Surg* 2019; 269:177–83
 41. Khan SA, Chua HW, Hirubalan P, Karthekeyan RB, Kothandan H: Association between frailty, cerebral oxygenation and adverse post-operative outcomes in elderly patients undergoing non-cardiac surgery: An observational pilot study. *Indian J Anaesth* 2016; 60:102–7
 42. Kotajarvi BR, Schafer MJ, Atkinson EJ, Traynor MM, Bruce CJ, Greason KL, Suri RM, Miller JD, LeBrasseur NK: The impact of frailty on patient-centered outcomes following Aortic valve replacement. *J Gerontol A Biol Sci Med Sci* 2017; 72:917–21
 43. Kristjansson SR, Ronning B, Hurria A, Skovlund E, Jordhoy MS, Nesbakken A, Wyller TB: A comparison of two pre-operative frailty measures in older surgical cancer patients. *J Geriatr Oncol* 2012; 3:1–7
 44. Leung JM, Tsai TL, Sands LP: Brief report: Preoperative frailty in older surgical patients is associated with early postoperative delirium. *Anesth Analg* 2011; 112:1199–201
 45. Li JL, Henderson MA, Revenig LM, Sweeney JE, Kooby DA, Maithel SK, Master VA, Ogan K: Frailty and one-year mortality in major intra-abdominal operations. *J Surg Res* 2016; 203:507–512.e1
 46. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, Takenaga R, Devgan L, Holzmüller CG, Tian J, Fried LP: Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg* 2010; 210:901–8
 47. Makhani SS, Kim FY, Liu Y, Ye Z, Li JL, Revenig LM, Vaughan CP, Johnson TM 2nd, García PS, Ogan K, Master VA: Cognitive impairment and overall survival in frail surgical patients. *J Am Coll Surg* 2017; 225:590–600.e1
 48. Pelavski AD, De Miguel M, Alcaraz Garcia-Tejedor G, Villarino L, Lacasta A, Señas L, Rochera MI: Mortality

- geriatric, and nongeriatric surgical risk factors among the eldest old: A prospective observational study. *Anesth Analg* 2017; 125:1329–36
49. Revenig LM, Canter DJ, Kim S, Liu Y, Sweeney JF, Sarmiento JM, Kooby DA, Maithel SK, Hill LL, Master VA, Ogan K: Report of a simplified frailty score predictive of short-term postoperative morbidity and mortality. *J Am Coll Surg* 2015; 220:904–11.e1
 50. Revenig LM, Canter DJ, Taylor MD, Tai C, Sweeney JF, Sarmiento JM, Kooby DA, Maithel SK, Master VA, Ogan K: Too frail for surgery? Initial results of a large multidisciplinary prospective study examining preoperative variables predictive of poor surgical outcomes. *J Am Coll Surg* 2013; 217:665–670.e1
 51. Revenig LM, Canter DJ, Master VA, Maithel SK, Kooby DA, Pattaras JG, Tai C, Ogan K: A prospective study examining the association between preoperative frailty and postoperative complications in patients undergoing minimally invasive surgery. *J Endourol* 2014; 28:476–80
 52. Singer JP, Diamond JM, Anderson MR, Katz PP, Covinsky K, Oyster M, Blue T, Soong A, Kalman L, Shrestha P, Arcasoy SM, Greenland JR, Shah L, Kukreja J, Blumenthal NP, Easthausen I, Golden JA, McBurnie A, Cantu E, Sonett J, Hays S, Robbins H, Raza K, Bacchetta M, Shah RJ, D'Ovidio F, Venado A, Christie JD, Lederer DJ: Frailty phenotypes and mortality after lung transplantation: A prospective cohort study. *Am J Transplant* 2018; 18:1995–2004
 53. Kua J, Ramason R, Rajamoney G, Chong MS: Which frailty measure is a good predictor of early post-operative complications in elderly hip fracture patients? *Arch Orthop Trauma Surg* 2016; 136:639–47
 54. Tan KY, Kawamura YJ, Tokomitsu A, Tang T: Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimized. *Am J Surg* 2012; 204:139–43
 55. Wang HT, Fafard J, Ahern S, Vendittoli PA, Hebert P: Frailty as a predictor of hospital length of stay after elective total joint replacements in elderly patients. *BMC Musculoskelet Disord* 2018; 19:14
 56. Lytwyn J, Stammers AN, Kehler DS, Jung P, Alexander B, Hiebert BM, Dubiel C, Kimber D, Hamm N, Clarke M, Fraser C, Pedreira B, Duhamel TA, Tangri N, Arora RC: The impact of frailty on functional survival in patients 1 year after cardiac surgery. *J Thorac Cardiovasc Surg* 2017; 154:1990–9
 57. Sikder T, Sourial N, Maimon G, Tahiri M, Teasdale D, Bergman H, Fraser SA, Demyttenaere S, Bergman S: Postoperative recovery in frail, pre-frail, and non-frail elderly patients following abdominal surgery. *World J Surg* 2019; 43:415–24
 58. Ad N, Holmes SD, Halpin L, Shuman DJ, Miller CE, Lamont D: The effects of frailty in patients undergoing elective cardiac surgery. *J Card Surg* 2016; 31:187–94
 59. Afilalo J, Lauck S, Kim DH, Lefèvre T, Piazza N, Lachapelle K, Martucci G, Lamy A, Labinaz M, Peterson MD, Arora RC, Noiseux N, Rassi A, Palacios IF, Gagnéux P, Lindman BR, Asgar AW, Kim CA, Trnkus A, Morais JA, Langlois Y, Rudski LG, Morin JF, Popma JJ, Webb JG, Perrault LP: Frailty in older Adults undergoing aortic valve replacement: The FRAILTY-AVR study. *J Am Coll Cardiol* 2017; 70:689–700
 60. Andreou A, Lasithiotakis K, Venianaki M, Xenaki S, Chlouverakis G, Petrakis I, Chalkiadakis G: A comparison of two preoperative frailty models in predicting postoperative outcomes in geriatric general surgical patients. *World J Surg* 2018; 42:3897–902
 61. Brown CH 4th, Max L, LaFlam A, Kirk L, Gross A, Arora R, Neufeld K, Hogue CW, Walston J, Pustavoitau A: The association between preoperative frailty and post-operative delirium after cardiac surgery. *Anesth Analg* 2016; 123:430–5
 62. McGuckin DG, Mufti S, Turner DJ, Bond C, Moonesinghe SR: The association of peri-operative scores, including frailty, with outcomes after unscheduled surgery. *Anaesthesia* 2018; 73:819–24
 63. Donald GW, Ghaffarian AA, Isaac F, Kraiss LW, Griffin CL, Smith BK, Sarfati MR, Beckstrom JL, Brooke BS: Preoperative frailty assessment predicts loss of independence after vascular surgery. *J Vasc Surg* 2018; 68:1382–9
 64. Li S, Nie Y, Zhan J, Wang Y, Huang W, Wang Y, He J, Liu Y: The analysis of correlation between frailty index and postoperative complications of aged patients with nodular goiter. *Aging Med (Milton)* 2018; 1:18–22
 65. Goeteyn J, Evans LA, De Cleyn S, Fauconnier S, Damen C, Hewitt J, Ceelen W: Older Persons Surgical Outcomes Collaborative: Frailty as a predictor of mortality in the elderly emergency general surgery patient. *Acta Chir Belg* 2017; 117:370–5
 66. Rodrigues MK, Marques A, Lobo DML, Umeda IIK, Oliveira MF: Pre-frailty increases the risk of adverse events in older patients undergoing cardiovascular surgery. *Arq Bras Cardiol* 2017; 109:299–306
 67. Kovacs J, Moraru L, Antal K, Cioc A, Voidazan S, Szabo A: Are frailty scales better than anesthesia or surgical scales to determine risk in cardiac surgery? *Korean J Anesthesiol* 2017; 70:157–62
 68. Reichart D, Rosato S, Nammias W, Onorati F, Dalén M, Castro L, Gherli R, Gatti G, Franzese I, Faggian G, Feo M De, Khodabandeh S, Santarpino G, Rubino AS, Maselli D, Nardella S, Salsano A, Nicolini F, Zanobini M, Saccocci M, Bounader K, Kinnunen E, Tauriainen T, Airaksinen J, Seccareccia F, Mariscalco G, Ruggieri VG, Perrotti A, Biancari F: Clinical frailty scale and outcome after coronary artery bypass grafting. *Eur J Cardio-Thoracic Surg* 2018; 0:1–8

69. Sato T, Hatakeyama S, Okamoto T, Yamamoto H, Hosogoe S, Tobisawa Y, Yoneyama T, Hashiba E, Yoneyama T, Hashimoto Y, Koie T, Hirota K, Ohya C: Slow gait speed and rapid renal function decline are risk factors for postoperative delirium after urological surgery. *PLoS One* 2016; 11:e0153961
70. Afilalo J, Eisenberg MJ, Morin JF, Bergman H, Monette J, Noiseux N, Perrault LP, Alexander KP, Langlois Y, Dendukuri N, Chamoun P, Kasparian G, Robichaud S, Gharacholou SM, Boivin JF: Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. *J Am Coll Cardiol* 2010; 56:1668–76
71. Ugolini G, Pasini F, Ghignone F, Zattoni D, Bacchi Reggiani ML, Parlanti D, Montroni I: How to select elderly colorectal cancer patients for surgery: A pilot study in an Italian academic medical center. *Cancer Biol Med* 2015; 12:302–7
72. Afilalo J, Kim S, O'Brien S, Brennan JM, Edwards FH, Mack MJ, McClurken JB, Cleveland JC Jr, Smith PK, Shahian DM, Alexander KP: Gait speed and operative mortality in older adults following cardiac surgery. *JAMA Cardiol* 2016; 1:314–21
73. Chauhan D, Haik N, Merlo A, Haik BJ, Chen C, Cohen M, Mosenthal A, Russo M: Quantitative increase in frailty is associated with diminished survival after transcatheter aortic valve replacement. *Am Heart J* 2016; 182:146–54
74. Itoh S, Yoshizumi T, Sakata K, Motomura T, Mano Y, Toshima T, Harimoto N, Harada N, Ikegami T, Soejima Y, Kusaba R, Kamishima T, Nishie A, Maehara Y: Slow gait speed is a risk factor for complications after hepatic resection. *J Gastrointest Surg* 2019; 23:1810–6
75. Madbouly K, AlHajeri D, Habous M, Binsaleh S: Association of the modified frailty index with adverse outcomes after penile prosthesis implantation. *Aging Male* 2017; 20:119–24
76. Joseph B, Zangbar B, Pandit V, Fain M, Mohler MJ, Kulvatunyou N, Jokar TO, O'Keeffe T, Friese RS, Rhee P: Emergency general surgery in the elderly: Too old or too frail? *J Am Coll Surg* 2016; 222:805–13
77. Lin H, Peel NM, Scott IA, Vardesh DL, Sivalingam P, McBride RL, Morong JJ, Nelson MJ, Hubbard RE: Perioperative assessment of older surgical patients using a frailty index-feasibility and association with adverse post-operative outcomes. *Anaesth Intensive Care* 2017; 45:676–82
78. Saxton A, Velanovich V: Preoperative frailty and quality of life as predictors of postoperative complications. *Ann Surg* 2011; 253:1223–9
79. Saricaoglu F, Aksoy SM, Yilmazlar A, Ozkan D, Copuroglu E, Unlusoy EO, Ekmekci P, Suzer MA, Argun G, Sunul H, Demirel I, Eroglu A, Alkaya FS, Yuce D, Hayran M: Predicting mortality and morbidity of geriatric femoral fractures using a modified frailty index and perioperative features: A prospective, multicentre and observational study. *Turk Geriatr Derg* 2018; 21:118–27
80. Vasu BK, Ramamurthi KP, Rajan S, George M: Geriatric patients with hip fracture: Frailty and other risk factors affecting the outcome. *Anesth Essays Res* 2018; 12:546–51
81. Dunlay SM, Park SJ, Joyce LD, Daly RC, Stulak JM, McNallan SM, Roger VL, Kushwaha SS: Frailty and outcomes after implantation of left ventricular assist device as destination therapy. *J Heart Lung Transplant* 2014; 33:359–65
82. Partridge JS, Fuller M, Harari D, Taylor PR, Martin FC, Dhesi JK: Frailty and poor functional status are common in arterial vascular surgical patients and affect postoperative outcomes. *Int J Surg* 2015; 18:57–63
83. Cheung SC, Ahmad LA, Hardy JE, Hilmer SN: A prospective cohort study of older surgical inpatients examining the prevalence and implications of frailty. *J Clin Gerontol Geriatr* 2017; 8:71–6
84. Dasgupta M, Rolfson DB, Stolee P, Borrie MJ, Speechley M: Frailty is associated with postoperative complications in older adults with medical problems. *Arch Gerontol Geriatr* 2009; 48:78–83
85. Amabili P, Wozolek A, Noirot I, Roediger L, Senard M, Donneau AF, Hubert MB, Brichant JF, Hans GA: The Edmonton Frail Scale improves the prediction of 30-day mortality in elderly patients undergoing cardiac surgery: A prospective observational study. *J Cardiothorac Vasc Anesth* 2019; 33:945–52
86. Moro FD, Morlacco A, Motterle G, Barbieri L, Zattoni F: Frailty and elderly in urology: Is there an impact on post-operative complications? *Cent European J Urol* 2017; 70:197–205
87. Kim S, Marsh AP, Rustowicz L, Roach C, Leng XI, Kritchevsky SB, Rejeski WJ, Groban L: Self-reported mobility in older patients predicts early postoperative outcomes after elective noncardiac surgery. *ANESTHESIOLOGY* 2016; 124:815–25
88. Orouji Jokar T, Ibraheem K, Rhee P, Kulvatunyou N, Haider A, Phelan HA, Fain M, Mohler MJ, Joseph B: Emergency general surgery specific frailty index: A validation study. *J Trauma Acute Care Surg* 2016; 81:254–60
89. Pol RA, van Leeuwen BL, Visser L, Izaks GJ, van den Dungen JJ, Tielliu IF, Zeebregts CJ: Standardised frailty indicator as predictor for postoperative delirium after vascular surgery: A prospective cohort study. *Eur J Vasc Endovasc Surg* 2011; 42:824–30
90. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC Jr, Moss M: Simple frailty score predicts postoperative complications across surgical specialties. *Am J Surg* 2013; 206:544–50

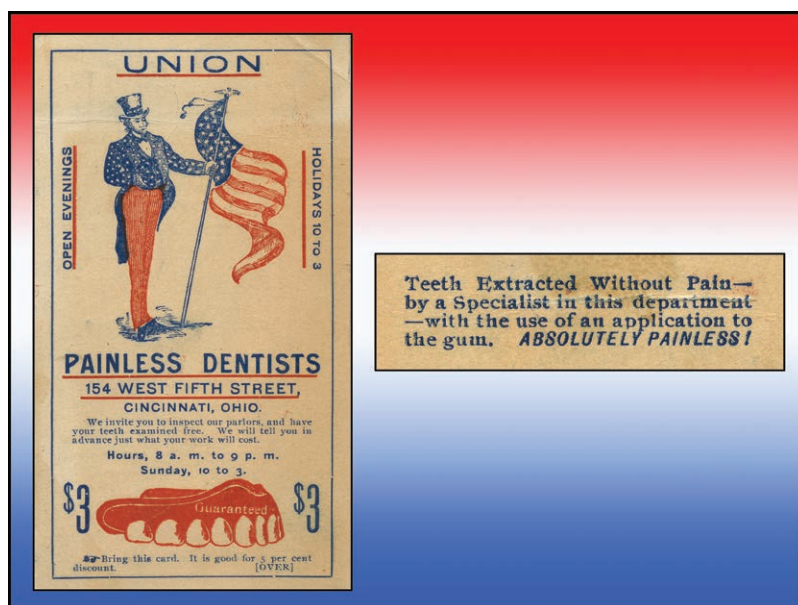
91. Sündermann SH, Dademasch A, Seifert B, Rodriguez Cetina Bieffer H, Emmert MY, Walther T, Jacobs S, Mohr FW, Falk V, Starck CT: Frailty is a predictor of short- and mid-term mortality after elective cardiac surgery independently of age. *Interact Cardiovasc Thorac Surg* 2014; 18:580–5
92. Tanaka S, Ueno M, Iida H, Kaibori M, Nomi T, Hirokawa F, Ikoma H, Nakai T, Eguchi H, Kubo S: Preoperative assessment of frailty predicts age-related events after hepatic resection: A prospective multicenter study. *J Hepatobiliary Pancreat Sci* 2018; 25:377–87
93. Tegels JJ, de Maat ME, Hulsewé KW, Hoofwijk AG, Stoot JH: Value of geriatric frailty and nutritional status assessment in predicting postoperative mortality in gastric cancer surgery. *J Gastrointest Surg* 2014; 18:439–45; discussion 445–6
94. Windt DJ van der, Bou-Samra P, Dadashzadeh ER, Chen X, Varley PR, Tsung A: Preoperative risk analysis index for frailty predicts short-term outcomes after hepatopancreatobiliary surgery. *HPB* 2018; 20:1181–8
95. Choi JY, Yoon SJ, Kim SW, Jung HW, Kim KI, Kang E, Kim SW, Han HS, Kim CH: Prediction of postoperative complications using multidimensional frailty score in older female cancer patients with American Society of Anesthesiologists Physical Status class 1 or 2. *J Am Coll Surg* 2015; 221:652–60.e2
96. Hall DE, Arya S, Schmid KK, Blaser C, Carlson MA, Bailey TL, Purviance G, Bockman T, Lynch TG, Johanning J: Development and initial validation of the risk analysis index for measuring frailty in surgical populations. *JAMA Surg* 2017; 152:175–82
97. Kenig J, Mastalerz K, Lukasiewicz K, Mitus-Kenig M, Skorus U: The Surgical Apgar Score predicts outcomes of emergency abdominal surgeries both in fit and frail older patients. *Arch Gerontol Geriatr* 2018; 76:54–9
98. Lu J, Zheng HL, Li P, Xie JW, Wang JB, Lin JX, Chen QY, Cao LL, Lin M, Tu RH, Huang CM, Zheng CH: High preoperative modified frailty index has a negative impact on short- and long-term outcomes of octogenarians with gastric cancer after laparoscopic gastrectomy. *Surg Endosc Other Interv Tech* 2018; 32:2193–200
99. Marshall L, Griffin R, Mundy J: Frailty assessment to predict short term outcomes after cardiac surgery. *Asian Cardiovasc Thorac Ann* 2016; 24:546–54
100. Botto F, Alonso-Coello P, Chan MT V, Villar JC, Xavier D, Srinathan S, Guyatt G, Cruz P, Graham M, Wang CY, Berwanger O, Pearse RM, Biccari BM, Abraham V, Malaga G, Hillis GS, Rodseth RN, Cook D, Polanczyk CA, Szczeklik W, Sessler DI, Sheth T, Ackland GL, Leuwer M, Garg AX, LeManach Y, Pettit S, Heels-Ansdell D, LuratiBuse G, Walsh M, Sapsford R, Schünemann HJ, Kurz A, Thomas S, Mrkobrada M, Thabane L, Gerstein H, Paniagua P, Nagele P, Raina P, Yusuf S, Devereaux PJ: Myocardial injury after noncardiac surgery. *ANESTHESIOLOGY* 2014; 120:564–78
101. Li Y, Pederson JL, Churchill TA, Wagg AS, Holroyd-Leduc JM, Alagiakrishnan K, Padwal RS, Khadaroo RG: Impact of frailty on outcomes after discharge in older surgical patients: A prospective cohort study. *CMAJ* 2018; 190:E184–90
102. Orouji J, Joka T, Ibraheem K, Rhee P, Kulavatunyou N, Haider A, Phelan HA, Fain M, Jane Mohler M, Joseph B: Emergency general surgery specific frailty index: A validation study AAST Continuing Medical Education Article Accreditation Statement doi:10.1097/TA.0000000000001120
103. Hall DE, Arya S, Schmid KK, Carlson MA, Lavedan P, Bailey TL, Purviance G, Bockman T, Lynch TG, Johanning JM: Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. *JAMA Surg* 2017; 152:233–40
104. Clavien PA, Strasberg SM: Severity grading of surgical complications. *Ann Surg* 2009; 250:197–8
105. National Surgical Quality Improvement Program Database. 2013. Available at: <https://www.facs.org/quality-programs/acs-nsqip/participant-use>. Accessed March 13, 2020.
106. Walker EMK, Bell M, Cook TM, Grocott MPW, Moonesinghe SR; Central SNAP-1 Organisation; National Study Groups: Patient reported outcome of adult perioperative anaesthesia in the United Kingdom: A cross-sectional observational study. *Br J Anaesth* 2016; 117:758–66
107. Joseph B, Phelan H, Hassan A, Orouji J, Joka T, O'Keeffe T, Azim A, Gries L, Kulvatunyou N, Latifi R, Rhee P: The impact of frailty on failure-to-rescue in geriatric trauma patients: A prospective study. *J Trauma Acute Care Surg* 2016; 81:1150–5
108. Beech F, Brown A, Dhese J, Foo I, Goodall J, Harrop-Griffiths W, Jameson J, Love N, Pappenheim K, White S: Peri-operative care of the elderly 2014. *Anaesthesia* 2014; 69:81–98
109. Hewitt J, Long S, Carter B, Bach S, McCarthy K, Clegg A: The prevalence of frailty and its association with clinical outcomes in general surgery: A systematic review and meta-analysis 2018; 47:pp 793–800
110. Sepehri A, Beggs T, Hassan A, Rigatto C, Shaw-Daigle C, Tangri N, Arora RC: The impact of frailty on outcomes after cardiac surgery: A systematic review. *J Thorac Cardiovasc Surg* 2014; 148:3110–7
111. Fried TR, Bradley EH, Towle VR, Allore H: Understanding the treatment preferences of seriously ill patients. *N Engl J Med* 2002; 346:1061–6
112. Sonny A, Kurz A, Skolaris LA, Boehm L, Reynolds A, Cummings KC, Makarova N, Yang D, Sessler DI: Deficit accumulation and phenotype assessments of

frailty Both poorly predict duration of hospitalization and serious complications after noncardiac surgery. *ANESTHESIOLOGY* 2020; 132:82–94

113. Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, Mohammed MA, Parry J, Marshall T: Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age Ageing* 2016; 45:353–60
114. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, Arora S, Street A, Parker S, Roberts HC, Bardsley M, Conroy S: Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: An observational study. *Lancet* 2018; 391:1775–82
115. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N, Pencina MJ, Kattan MW: Assessing the performance of prediction models: A framework for traditional and novel measures. *Epidemiology* 2010; 21:128–38
116. Muchinsky PM: The correction for attenuation. *Educ Psychol Meas* 1996; 56:63–75
117. Robinson TN, Walston JD, Brummel NE, Deiner S, Brown CH 4, Kennedy M, Hurria A: Frailty for surgeons: Review of a National Institute on Aging Conference on frailty for specialists. *J Am Coll Surg* 2015; 221:1083–92

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

Aftershocks for Quake-rattled Frueh: Dan “Wood’s Local Anaesthetic” Levels Its Namesake



Named for a Union general from Indiana, Hoosier dentist Daniel Macauley Wood (1868 to 1934) moved to Ohio as founding business manager by 1900 for Cincinnati’s Union Painless Dentists (*left*, “Uncle Sam” holds “Old Glory” on their trade card’s obverse). In 1906, Wood began training his replacement, a patriotic Spanish-American War veteran who had actually been born on Independence Day, Dr. John F. Frueh (1877 to 1920). The hapless Frueh had recently married in Cincinnati after his original wedding plans had been flattened by the Great 1906 San Francisco Earthquake. Dr. Frueh took pains to use and advertise the cocaine-laced “application to the gum” (*right*, from the trade card’s reverse) previously popularized by “Specialist” Wood. Unfortunately, Dr. Dan Wood may have self-medicated his manic behavior with his namesake anesthetic. Indeed, divorce proceedings revealed that Dr. Wood had bankrupted his household while maintaining three mistresses. So ironically, his cocaine concoction had salvaged the seismically shifted Frueh, but its aftershocks had leveled the house of Wood. (Copyright © the American Society of Anesthesiologists’ Wood Library-Museum of Anesthesiology.)

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