Frailty Predicts Mortality in All Emergency Surgical Admissions regardless of Age. An observational study

Abstract words: 225

Manuscript words: 2289

Keywords: frailty, mortality, emergency surgical admissions, all ages, older people.

Keypoints:

- This cohort included patients of all ages.
- The Clinical Frailty Scale (CFS) predicts worse outcomes in emergency general surgical patients.
- There is a linear increase in poor outcome with the Clinical Frailty Scale in general surgical patients.

Abstract

Background: Frail patients in any age group are more likely to die than those that are not frail. We aimed to evaluate the impact of frailty on clinical mortality, readmission rate and length of stay for emergency surgical patients of all ages.

Methods: A multi-centre prospective cohort study was conducted on adult admissions to acute surgical units. Every patient presenting as a surgical emergency to secondary care, regardless of whether they ultimately underwent a surgical procedure was included. The study was carried out during 2015 and 2016.

Frailty was defined using the 7 point Clinical Frailty Scale. The primary outcome was mortality at Day 90. Secondary outcomes included: Mortality at day 30, length of stay and readmission within a day 30 period..

Results: The cohort included 2,279 patients (median age 54 years [IQR 36-72]; 56% female). Frailty was documented in patients of all ages: 1% in the under 40's to 45% of those aged 80+. We found that each incremental step of worsening frailty was associated with an 80% increase in mortality at Day 90 (OR 1.80, 95% CI: 1.61-2.01) supporting a linear dose-response relationship. In addition, the most frail patients were increasingly likely to stay in hospital longer, be readmitted within 30 days, and die within 30 days.

Conclusions: Worsening frailty at any age is associated with significantly poorer patient outcomes, including mortality in unselected acute surgical admissions. Assessment of frailty should be integrated into emergency surgical practice to allow prognostication and implementation of strategies to improve outcomes.

Introduction

The concept of frailty is well established. Many clinicians diagnose it and know that it may negatively impact on a patient's clinical condition. However, it is often diagnosed in a subjective "end of the bed" test rather than by using specific diagnostic criteria, despite being recognised as a factor influencing outcomes in geriatric research for many years (1–4). Frailty is a state in which a vulnerable individual, has a diminished physiological capacity to respond to external stress such as infection or trauma (5). The deleterious effects include death, falls, disability, prolonged hospital stays and institutionalisation (2,5–7). (7–14).

There are many instruments used to measure frailty, with variation in their composition (15). Some use scoring systems based on multiple domains (16–18), whilst others use a single functional measurement as a proxy for frailty, such as grip strength or the timed up and go test (19,20). The Clinical Frailty Scale (CFS) (18), is a quick, simple and validated tool. Previous work in emergency general surgery (8) has shown that when used as a binary measure (frail or not frail) this scale predicts mortality an, length of stay. This seven point scale ranges from 1 (very fit) to 7 (severely frail) and uses clinical descriptors, with all information needed available from brief observation or review of the clinical notes. In a community setting a frailty assessment may be used as a preventative tool to monitor general health, or in a surgical setting to help explain to patients, their families and carers potential additional risks of clinical management procedures (21). Development of tese tools, and frailty research generally, have historically focused on older populations, but the recent publication finding the existence of frailty and its' negative impact on outcomes in younger adults (aged over 40 years) admitted as a surgical emergency (22) suggests that frailty is not a diagnosis exclusive to older adults. The exact prevalence of frailty is currently unknown, recent studies have reported this between 8% and as high as 37%, but any estimate is a combination of heterogeneous subgroups and shows variation depending on the tool used to detect frailty (23). In older, predominantly elective surgical populations frailty is associated with adverse outcomes (8,13,14). In all specialities, not just surgery, these associations have been assessed using frailty as predominantly a binary exposure variable (frail or not) or occasionally tertiary exposure variable (not frail, pre-frail and frail). While useful they are of limited value in relating the full range of frailty seen in clinical practice to outcome.

This study aimed to evaluate the prevalence of frailty its associated risk of mortality, readmission rate and length of hospital stay in all adults, regardless of age, admitted as a surgical emergency. To evaluate the impact of frailty across the full range of the frailty spectrum the 7 point Clinical Frailty Scale was used and the outcome measures assessed for each incremental point increase.

Methods

Prospective patient data were collated from six U.K. acute surgical units during two timeframes: May to July 2015 and June to August 2016. Data collection was performed in accordance with the STROBE Statement and associated checklist (24). Inclusion criteria: patients aged over 18 years old admitted with a general surgical complaint, including those undergoing surgery and those managed conservatively. Patients were excluded if they had a urological, gynaecological or vascular diagnosis.

Individual patient consent was not required as the study was deemed a service evaluation. As such it registered and approved with each institutional audit department, according to local guidelines. Anonymised data from each site was collected using a secure and anonymous data collection tool, stored in accordance with local guidelines, using standard commercially available spreadsheet software.

Baseline demographic data were recorded In order to adjust for potential comorbidity, additional markers of poor health and adverse outcome following surgical intervention were also recorded; these were the number of regular medications (<=5, >5); haemoglobin (≤12.9g/L, >12.9g/L) and albumin (≤35g/L, >35g/L).

Whether a patient underwent surgery was also recorded. Within 24 hours of admission and prior to any surgery, participants were assessed for frailty, recorded using CFS (Supplementary Figure 1). Each local team screened all new surgical admissions with the data gathered from patient electronic records, or case notes. Outcome data were collected from the hospital electronic clinical records. Data recorders were trained in the use of the CFS, by the local site lead, through face to face teaching sessions. Clinical outcomes of mortality (at 30 and 90-days), re-admission rates (at 30-days) and length of hospital stay were recorded.

Public and Patient Involvement

This work was conducted by the Older Persons Surgical Outcomes Collaborative (opsoc.eu). Public and patient involvement is integral to all of the projects developed. Our team compromises of patient representation, provided by Involving People Wales.

Statistical analysis

The study analysis was carried out using an *a priori* statistical analysis plan (available on request).

Descriptive continuous data was reported with a mean and standard deviation (or with a median and interquartile range [IQR] for data exhibiting skew); and dichotomous data with a percentage and numerator and denominator.

The primary outcome was mortality at Day 90, with secondary outcomes of: mortality at day 30; length of stay and readmission within 30 days of discharge from hospital. Baseline demographic and clinical data were summarised for each surgical unit.

Dichotomous outcomes were analysed using a multi-level logistic regression. Surgical units were fitted as hierarchical levels, to account for the clustered data. Length of stay was analysed with a negative binomial distribution to allow for modelling a varying variance structure. Our primary analysis evaluated the crude effect of frailty on clinical outcomes, fitting frailty as a categorical predictor. The secondary analyses fitted the effect of frailty after adjustment for: age group (<65, 65-79, ≥80); sex; and albumin. Odds ratios (ORs) and 95% confidence intervals (95% CI) were reported. In an additional analysis, the effect of frailty was fitted as a continuous predictor of Day 90 mortality. All statistical analysis was performed using Stata 13.0.

Results

There were 2,279 patients included in the study [median age 54 years (IQR 36-72); 56% female (1276/2279)]. No patients were excluded. Recruitment varied in number per surgical site, but demographic and baseline clinical status of patients were similar across sites as were outcomes (Supplementary Tables 1 and 2 respectively). On admission, 12.7% (289/2279) of the cohort were frail (CFS >=5). Frailty was present across the entire age range; 1% (8/646) under 40's; 5% (32/668) 40-59 years; 9% (30/331) 60-69 years; 25% (82/328) 70-79 years and 45% (137/306) ≥80 years old (Supplementary Table 3). For follow-up data, seven patients (0.3%) had missing data. The analyses were based on a complete case analysis. A total of 128 patients were dead at Day 90 (6%) (Table 1). For secondary outcomes, the median length of hospital stay was 4 days (IQR 2-7); 404 patients were re-admitted (19%) and 79 (4%) had died at 30 days post-admissin (Supplemental Table 2). Within the frail group (CFS >=5), 19% (54/286) experienced mortality at 90-days compared to 3.6% (72/1985) of non-frail (Supplementary Table 4). Similar results were found from 30-day mortality. Re-admission occurred in 23% (64/284) of frail patients versus 17% (340/1974) of non-frail patients. The length of stay was 3 (IQR 2-5) days in those who were not frail compared to 5 (IQR 3-11), 7.5 (IQR 4-18) and 5 (IQR 3-7) days for patients who were mildly frail (CFS=5), moderately frail (and CFS=6) severely frail (CSF=7).Primary outcome: The odds of mortality at Day 90 was higher for those patients with an increased level of frailty. Patients with a CFS of very well (CFS=2) had a crude odds ratio (OR) of 2.25 (95% CI 1.08-4.68) compared to patients with a CFS of very fit (CFS=1). The OR of mortality increased to 8.54 (95% CI 4.12-17.73), 19.5 (95% CI 9.16-41.88) and 58.2 (95% CI 22.6-149.9) for patients with a CFS of: mildly frail (CFS=5); moderately frail (CFS=6); and severely frail (CFS=7) respectively (Table 2). An incremental single unit increase in frailty was found to increase odds of Day 90 mortality by 80% (95% CI 1.61-2.01; Figure 1). Secondary outcomes: Increased frailty was linked to increased mortality at Day 30 (Supplementary Table 5). The mean length of stay was found as 4.6 days for patients with a CFS of very fit (CFS=1). The increase mean length of stay increased for patients with worsening frailty. The mean length of stay increased by 2.60 (95CI% 2.25-3.02), 2.89 (95% CI 2.37-3.53), 2.30 (95% CI 1.64-3.30) times for patients with CFS of mildly to severely frail (CFS=5-7) (Supplementary Table 6). Increased frailty was associated with an increased re-admission rate, the ORs were 1.96 (95% CI 1.28-2.98), 2.56 (95% CI 1.49-4.37), and 0.90 (0.26-3.06) for a CFS of mildly to severely frail (Supplementary Table 7).

Secondary analyses, after adjustment by age group, sex and albumin the effect of frailty was lower, but remained clinically important (Table 2, Supplementary Tables 5-7). The adjusted odds ratio (aOR) of mortality at Day 90 was 2.62 (95% CI 1.14-6.03), 5.39 (95% CI 2.28-12.76), and 24.6 (95% CI 8.42-71.88) for frailty score 5 to 7. Similar results were reported from the other secondary outcomes (Supplementary Tables 5-7).

Discussion

This is the first study to assess frailty in adults of all ages admitted as a surgical emergency, finding that frailty exists in all age groups and is not exclusive to the older adult population. In addition, the presence of frailty predicts mortality in these patients regardless of age and for each incremental point of frailty, the OR for 90 day mortality increased by 80%. After adjusting for key confounding effects, including patient age, gender and comorbidity, frailty was still associated with poorer clinical outcomes. Given the fact that our study was conducted in the real world setting using data from consecutive surgical admissions, our findings highlight the need for routine integration of frailty scores in clinical practice and interventions to modify frailty and improve outcomes.

In other studies, mortality rates for frail people have varied widely (OR ranging from 1.1 to 31.84), with results being difficult to compare due to the heterogeneity in study designs, and the type of frailty assessment used (8,14,25–28). In acute general surgery, two studies have previously reported an association between frailty and 90 day mortality (8,14), however, these studies focussed on older patients only. Other studies have linked length of stay to frailty however these are predominantly from elective surgical populations who are likely to have been pre-operatively assessed as fit enough to undergo planned surgery (10,12,13,29–31). For example Robinson *et al* found that in both elective colorectal, and a mixed cohort of cardiothoracic and colorectal patients increasing frailty was associated with readmission to hospital and an increased length of hospital stay (13,32).

This study demonstrated that for each incremental shift to a higher level of frailty there was an associated worsening of outcomes, a concept that is readily understood and explainable to patients and carers. Previously frailty has been evaluated in terms of frail or not, and occasionally with an intermediate category of pre-frail in between. By demonstrating that frailty is associated with worsening outcome across an incremental range of the condition and changes for each step-wise increase the opportunities for frailty research and potential interventions are substantially broadened. These results clearly demonstrate the potential impact and likely benefit on clinical outcomes through population level frailty prevention strategies or interventions. Furthermore, the CFS has the benefit of being an extremely simple, quick and easy to perform frailty measure.

Strengths and Limitations of the study

There are several strengths to this study: consecutive emergency patients recruited under general surgeons in multiple UK acute hospitals resulted in inclusion of differing populations and minimising of any influence of local population or admission practices; patient characteristics and outcome data demonstrated that the patients were similar across all of the sites and finally, less than 0.5% of outcome data were missing.

However, the authors acknowledge limitations, primarily that the population assessed was based in the UK which could limit generalisability beyond similar Western populations and settings. Most notably the surgical population used in this study considered any patient admitted under a surgical team, regardless of whether they undergo surgery or not. Another potential limitation is that although the data collectors were trained to use the CFS tool, no validation took place meaning that intra-rater bias cannot be excluded. However, the prevalence of individual frailty scores were consistent across sites, which does potentially mitigate against this.

The implications for future clinical practice:

The management of the frail, emergency surgical patient is challenging, regardless of age. Patients are living longer and are becoming increasingly co-morbid (33). The idea that frailty contributes to an increased risk of mortality is not new in older patients but these data show that this can now be applied to all surgical admissions irrespective of age.

Surgeons are faced with challenging decision-making processes and it is not standard practice to 'turn down' a frail patient for emergency surgery based on their clinical condition. In the UK, recent recommendations from the National Emergency Laparotomy Audit NELA framework are that higher risk surgical patients are managed in intensive care (34). Unfortunately, however, resources for intensive care post operatively are costly, not limitless and not appropriate for all patients. This has led to an increased focus on futility of surgical intervention and what the likelihood is of returning the patient to reasonable quality of life. This simple frailty assessment should be included in that rigorous assessment process alongside American Society of Anaesthesiologists (ASA) grade and P-Possum score.

Public health awareness and education is required to manage frail patients in the community, and the CFS could be used to identify those at risk by clinicals in primary care. By the time a frail patient presents as a surgical emergency, it is too late to alter the potential risk of death. Whilst Interventions to try to improve frailty can be started in the community if those at risk are identified and offered the opportunity to reduce their risk. Part of any frailty intervention should include clear information on the risk of death associated with the frail state and the decision making process that may occur if they were to develop an acute surgical problem. The CFS could easily be used by emergency physicians before assessment by surgical teams has begun to begin to inform health care choices in relation to surgical intervention.

Much work has been done to improve outcomes in all patients undergoing elective major surgery, regardless of age. For example, the enhanced recovery programme after surgery (ERAS) consists of a multi-modal approach that includes: pre-operative counselling; shorter-fasting times; early mobility and avoidance of drains. This pathway is now standard peri-operative practice across the UK, leading to optimisation of patient outcomes (35,36). However, these programs are typically focused on older age groups, in future a more targeted approach to improve post-operative outcomes may be facilitated by using the CFS. In high resource settings, use of electronic frailty index has been shown to be associated with mortality in older adults (37) and thus such electronic based tools may also provide useful information in surgical patients, but the prognostic value in surgical setting in all ages needs to be tested perhaps using the same approach.

Conclusions

This study has shown that frailty can exist in all ages of the adult emergency general surgical population. There is an approximately linear relationship between increasing CFS at admission and increased odds of Day 90 mortality. The CFS should be integrated into primary care for education and management. Frailty can be used emergency surgical practice to allow prognostication and implementation of strategies to improve outcomes in this vulnerable population.

1	**Very fit**
	Robust, active, energetic, well-motivated and fit; these people commonly exercise regularly and are in the most fit group for their age
2	**Well**
	Without active disease but less well than those in category 1
3	**Well, with treated comorbid disease**
	Disease symptoms are well controlled compared with those in category 4
4	**Apparently vulnerable**
	Although not frankly dependent, these people commonly complain of being “slowed up” or have disease symptoms
5	**Mildly frail**
	With limited dependence on others for instrumental activities of daily living
6	**Moderately frail**
	Help is needed with both instrumental and non-instrumental activities of daily living
7	**Severely frail**
	Completely dependent on others for activities of daily living, or terminally ill

Supplementary Figure 1 – The Canadian Study of Health and Ageing (CSHA) Clinical Frailty Scale (18)

References

1. Rodriguez-Mañas L, Fried LP. Frailty in the clinical scenario. Lancet. 2015;385(9968):e7–9.
2. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752–62.
3. Fried LP, Tangen CM, Walston J, Newman a B, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol Ser A, Biol Sci Med Sci. 2001 Mar;56(3):M146-56.
4. Bandeen-Roche K, Xue Q-L, Ferrucci L, Walston J, Guralnik JM, Chaves P, et al. Phenotype of frailty: Characterization in the Women's Health and Aging Studies. journals Gerontol Ser A, Biol Sci Med Sci. 2006;61(3):262–6.
5. Morley J, Vellas B, van Kan GA, Ankar S, Bauer J, et al. Frailty Consensus: A Call to Action. J Am Med Dir Assoc. 2013;14(6):392–7.
6. Hubbard RE, Story D a. Patient frailty: The elephant in the operating room. Anaesthesia. 2014;69(Suppl. 1):26–34.
7. Partridge JSL, Harari D, Dhesi JK. Frailty in the older surgical patient: a review. Age Ageing. 2012 Mar;41(2):142–7.
8. Hewitt J, Moug SJ, Middleton M, Chakrabarti M, Stechman MJ, McCarthy K. Prevalence of frailty and its association with mortality in general surgery. Am J Surg. 2015;209(2):254–9.
9. Rockwood K, Hubbard R. Frailty and the geriatrician. Age Ageing. 2004;33(5):429–30.
10. Lee DH, Buth KJ, Martin B-J, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010 Mar 2;121(8):973–8.
11. 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(1):78–83.
12. Makary M a, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg. 2010 Jun;210(6):901–8.
13. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. Am J Surg. 2013;206(4):544–50.
14. Farhat JS, Velanovich V, Falvo AJ, Horst HM, Swartz A, Patton JH, et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. J Trauma Acute Care Surg. 2012;72(6):1526–31.
15. de Vries NM, Staal JB, van Ravensberg CD, Hobbelen JSM, Olde Rikkert MGM, Nijhuis-van der Sanden MWG. Outcome instruments to measure frailty: A systematic review. Ageing Res Rev. 2011;10(1):104–14.
16. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing. 2006 Sep;35(5):526–9.
17. Ravaglia G, Forti P, Lucicesare A, Pisacane N, Rietti E, Patterson C. Development of an easy prognostic score for frailty outcomes in the aged. Age Ageing. 2008;37(2):161–6.
18. Rockwood K, Song X, Macknight C, Bergman H, Hogan DB, Mcdowell I, et al. A global clinical measure of fitness and frailty in elderly people. Can Med Assoc J. 2005;173(5):489–95.
19. Syddall H, Cooper C, Martin F, Briggs R, Sayer AA. Is grip strength a useful single marker of frailty? Age Ageing. 2003;32(6):650–6.
20. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991 Feb;39(2):142–8.
21. Neuman MD, Allen S, Schwarze ML, Uy J. Using Time-limited Trials to Improve Surgical Care for Frail Older

Adults. Ann Surg. 2015;261(4):639–41.

22. Smart R, Carter B, McGovern J, Luckman S, Connelly A, Hewitt J, et al. Frailty exists in younger adults admitted as surgical emergency leading to adverse outcomes. J Frailty Aging. 2017;In print.

23. Hewitt J, Long S, Carter B, Bach, Mccarthy K, Clegg A. The Prevalence of Frailty and its association with poorer clinical outcomes in General Surgery: A Systematic Review and Meta-Analysis. Age Ageing.

24. PLoS Medicine Editors. Observational Studies: Getting Clear about Transparency. PLoS Med. Public Library of Science; 2014 Aug 26;11(8):e1001711.

25. Adams P, Ghanem T, Stachler R, Hall F, Velanovich V, Rubinfeld I. Frailty as a predictor of morbidity and mortality in inpatient head and neck surgery. JAMA Otolaryngol Head Neck Surg. 2013;139(8):783–9.

26. Hodari A, Hammoud ZT, Borgi JF, Tsiouris A, Rubinfeld IS. Assessment of morbidity and mortality after esophagectomy using a modified frailty index. Ann Thorac Surg. 2013;96(4):1240–4.

27. Tsiouris A, Hammoud ZT, Velanovich V, Hodari A, Borgi J, Rubinfeld I. A modified frailty index to assess morbidity and mortality after lobectomy. J Surg Res. 2013;183(1):40–6.

28. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: Its application to a national database. J Surg Res. 2013;183(1):104–10.

29. Pol R a, van Leeuwen BL, Visser L, Izaks GJ, van den Dungen JJ a M, Tielliu IFJ, et al. Standardised frailty indicator as predictor for postoperative delirium after vascular surgery: a prospective cohort study. Eur J Vasc Endovasc Surg. 2011 Dec;42(6):824–30.

30. Lasithiotakis K, Petrakis J, Venianaki M, Georgiades G, Koutsomanolis D, Andreou A, et al. Frailty predicts outcome of elective laparoscopic cholecystectomy in geriatric patients. Surg Endosc Other Interv Tech. 2013;27(4):1144–50.

31. Cohen R-R, Lagoo-Deenadayalan SA, Heflin M, Sloane R, Eisen I, Thacker J, et al. Exploring Predictors of Complication in Older Surgical Patients: A Deficit Accumulation Index and the Braden Scale. J Am Geriatr Soc. 2012;60(9):1609–15.

32. Robinson TN, Wu DS, Stiegmann G V., Moss M. Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. Am J Surg. 2011;202(5):511–4.

33. Cesari M, Prince M, Thiyagarajan JA, De Carvalho IA, Bernabei R, Chan P, et al. Frailty: An Emerging Public Health Priority. J Am Med Dir Assoc. 2016 Mar;17(3):188–92.

34. NELA Project Team. Second Patient Report of the National Emergency Laparotomy Audit. London; 2016.

35. Fearon KCH, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CHC, Lassen K, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr. 2005 Jun;24(3):466–77.

36. Wood T, Aarts M-A, Okrainec A, Pearsall E, Victor JC, McKenzie M, et al. Emergency Room Visits and Readmissions Following Implementation of an Enhanced Recovery After Surgery (iERAS) Program. J Gastrointest Surg. Springer US; 2017 Sep 15;1–8.

37. Romero-Ortuno R, Wallis S, Biram R, Keevil V. Clinical frailty adds to acute illness severity in predicting mortality in hospitalized older adults: An observational study. Eur J Intern Med. 2016 Nov;35:24-34.

Table 1 – Demographic characteristics of the study participants, by Mortality at Day 90.

		Mortality at Day 90					
		Yes (n=126)		No (n=2145)		Total (n=2271)	
Patient Age (years)	Under 65	34	27%	1,419	66%	1,453	64%
	65 - 79	39	31%	475	22%	514	23%
	Over 80	53	42%	251	12%	304	13%
Gender	Female	56	44%	1,219	57%	1,275	56%

	Male	70	56%	926	43%	996	44%
Albumin	Normal	24	19%	1,263	59%	1,287	57%
	Low	101	80%	811	38%	912	40%
	missing	1	1%	71	3%	72	3%
Haemoglobin	Normal	47	37%	1,342	63%	1,389	61%
	Low	78	62%	778	36%	856	38%
	missing	1	1%		0%		0%
	Normal	76	60%	1,874	87%	1,950	86%
eGFR	<60	32	25%	219	10%	251	11%
	<30	18	14%	52	2%	70	3%
CRP	Normal	2	2%	181	8%	183	8%
	>3	124	98%	1,964	92%	2,088	92%
Poly pharmacy	No	36	29%	1,342	63%	1,378	61%
	Yes	84	67%	785	37%	869	38%
	missing	6	5%	18	1%	24	1%
Multimorbidity	No	49	39%	1,261	59%	1,310	58%
	Yes	67	53%	665	31%	732	32%
	missing	10	8%	219	10%	229	10%
Clinical Frailty Scale	1 – Very Fit	12	10%	753	35%	765	34%
	2 – Very Well	19	15%	528	25%	547	24%
	3 – Well, with comorbid disease	21	17%	394	18%	415	18%
	4 – Apparently vulnerable	20	16%	238	11%	258	11%
	5 – Mildly Frail	21	17%	154	7%	175	8%
	6 – Moderately Frail	20	16%	64	3%	84	4%
	7 – Severely Frail	13	10%	14	1%	27	1%

Table 2 – Odds of Day 90 mortality in those with an increased frailty index, compared with those that are defined as very fit (Primary outcome)

Variable	Level	Unadjusted OR (95% CI)	p-value	OR (95% CI)	p-value
Clinical Frailty Scale[&]	1	- Reference -		- Reference -	
	2	2.25, (1.08, 4.68)	0.029	1.68, (0.79, 3.58)	0.175
	3	3.34, (1.62, 6.86)	0.001	1.63, (0.75, 3.55)	0.211
	4	5.26, (2.53, 10.93)	<0.001	2.09, (0.93, 4.66)	0.071
	5	8.54, (4.12, 17.73)	<0.001	2.62, (1.14, 6.03)	0.022
	6	19.5, (9.16, 41.88)	<0.001	5.39, (2.28, 12.76)	<0.001
	7	58.2, (22.6, 149.9)	<0.001	24.6, (8.42, 71.88)	<0.001
Age group	Under 65	- Reference -		- Reference -	
	65 to 80	2.26, (1.34, 3.81)	0.002	1.72, (1.01, 2.94)	0.043
	Over 80	3.88, (2.23, 6.75)	<0.001	3.28, (1.89, 5.71)	<0.001
Sex	Female	1.68, (1.15, 2.26)	0.007	1.66, (1.12, 2.47)	0.01
Albumin	Abnormal	4.85, (3.02, 7.80)	<0.001	4.55, (2.82, 7.36)	<0.001

Key:[&] 1=Very Fit;

2=Very Well;
3= Well, with comorbid disease;
4=Apparently vulnerable;
5= Mildly frail;
6=Moderately Frail;
7=Severely Frail

Figure 1 – Crude Odds ratio of mortality at Day 90, for individuals with an increased risk of frailty, using the compared to very fit participants, using the Clinical Frailty Scale (CFS).

Acknowledgments

Cardiff and Vale University Health Board: Aimee Browning, Svetlana Kulikouskaya, Rebecca Best, Andrew Forrester, Joseph Ereaut, James Moore, Dominic Hampson, Stephanie Owen, Shaanjan Islam, Nicolas Gill, Stephan Merrix, Jack Topham, Pip Killingworth, Syed Rahman and Nurulaida Mohd Darus

North Bristol NHS Trust: Emily Benson, Tom Wright, Sarah Blake, Calum Honeyman, Simon Huf, Anni Dong, Indira Garaeva, Manuk Wijeyaratne, Michael Campbell and Eng Hean Teh

Royal Alexandra Hospital: Adam Tay and Nurwasimah Haj Asnan
NHS Grampian: Matthew Greig, Vincent Quan
Central Manchester University Hospitals: Elizabeth Norr

Funding information We acknowledge the support of the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London (B. C.).

Contributions of Authors

Conception of the study (JH, KM, MS, SM, PM), Development of Protocol (JH, BC, SM, PM) Data collection (JH, KM, LP, JL, FW, HT, CM, SM, PM), Study Statistician, analysis methods (BC), reporting and interpretation of results (BC, JH, SM, PM), Drafting of manuscript (BC, JH, PM…), approval of manuscript (LP, JL, FW, HT, CM, MS)