Quick and simple FRAIL scale predicts incident ADL and IADL disabilities: A systematic review and meta-analysis

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ABSTRACT

Objectives: To quantitatively examine frailty defined by FRAIL scale as a predictor of incident disability risks by conducting a systematic review and meta-analysis.

Design: Systematic review and meta-analysis.

Setting: A systematic review was conducted using four electronic databases (Embase, MEDLINE, CINAHL, and PsychINFO) in April 2018 for prospective cohort studies of middle-aged or older people examining associations between frailty and incident disability. Reference lists of the included studies were hand-searched for additional studies. Authors of potentially eligible studies were contacted for additional data if necessary. Methodological quality was assessed by the Newcastle-Ottawa scale.

Participants: Community-dwelling middle-aged and older people.

Measurements: Incident risks of activities of daily living (ADL) or instrumental activities of daily living (IADL) disability according the FRAIL scale-defined frailty.

Results: Seven studies provided odds ratios of incident disability risks according to frailty and were included in meta-analysis. A random-effects meta-analysis showed that frailty and prefrailty were significant predictors of ADL (pooled OR=9.82, 95%CI=4.71-20.46, p<0.001 for frailty (FRAIL scale=3-5) and pooled OR=2.08, 95%CI=1.77-2.45, p<0.001 for prefrailty (FRAIL scale=1-2) compared with robustness (FRAIL scale=0); pooled OR=4.44, 95%CI=3.26-6.04, p<0.001 for frailty compared with non-frailty (FRAIL scale=0-2)) and IADL (pooled OR=2.50, 95%CI=1.67-3.73, p<0.001 for frailty and pooled OR=1.74, 95%CI=1.10-2.77, p=0.02 for prefrailty compared with robustness). There was no evidence of publication bias.

Conclusions/Implications: The current study demonstrated frailty status defined by the FRAIL scale was a significant predictor of disability among community-dwelling middle-aged and older individuals. In light of feasibility of the FRAIL scale, especially in a clinical setting, it may be a promising tool to facilitate the translation of frailty research into clinical practice.

INTRODUCTION

Frailty has been gaining scientific attention and an exponential amount of research has been conducted over the last two decades,[1-3] especially since 2001 when the frailty phenotype was published by Fried and colleagues from the Cardiovascular Health Study.[4] Although the Fried phenotype is still the most commonly used criteria, there have also been numerous other tools proposed to measure frailty.[5] Irrespective of how frailty is defined, frailty has been shown to be consistently associated with negative health outcomes, including falls,[6,7] fractures,[8,9] disabilities,[10] hospitalization,[11] institutionalization,[12-14] dementia,[15] poor quality of life,[16,17] and premature death.[18-20] To date no consensus has been reached regarding a gold standard tool to assess frailty.

The FRAIL scale is a relatively new tool that was advocated by the International Association of Nutrition and Aging Task Force based on a systematic review of the literature as well as input from a panel of geriatric experts.[21] In their view, a frailty tool should be quick, inexpensive, reliable, and easy to use in clinical settings because the identification of frail older people at risk is the important initial step, leading to appropriate preventive and/or treatment interventions and ultimately to high quality care for this vulnerable population.[21] The FRAIL scale is a simple tool consisting of five yes or no questions: Fatigue, Resistance (inability to climb stairs), Ambulation (inability to walk a certain distance), Illnesses, and Loss of weight, and does not require special equipment for handgrip or such calculations as required for the frailty phenotype (population-based lowest 20% of grip strength or gait speed) or the Frailty Index (summing and dividing the number of present and absent deficits, is typically greater than 30).[22] This simple frailty tool can be administered by not only physicians but also other healthcare professionals, and can be completed by phone, mail, or email.

Frailty defined by the phenotype or other tools has been well validated and recognized as a risk factor of various adverse health outcomes. Although the evidence regarding frailty based on the FRAIL scale is still rather limited compared with other tools, an increasing amount of related research has been published in the literature, and a recent meta-analysis demonstrated that frailty defined by the FRAIL scale is a significant predictor of mortality in community-dwelling middle-aged and older populations.[18] To further strengthen validation of the FRAIL scale as a frailty tool, this paper will systematically review the literature and conduct a meta-analysis on frailty based on the FRAIL scale and disability incidence among community-dwelling middle-aged and older individuals.

METHOD

Search strategy and selection criteria

The systematic review was conducted along with a protocol developed in accordance with the PRISMA statements[23] and registered at PROSPERO (registration number CRD42018094603). Four electronic databases (Embase, MEDLINE, CINAHL, and PsychINFO) were searched in April 2018 for prospective cohort studies of middle-aged or older people who were free of disability at baseline examining incident activities of daily living (ADL) or instrumental activities of daily living (IADL) disability according to frailty defined by the FRAIL scale. Publication years ranged from 2008, when the FRAIL scale was initially described,[21,22] to April 2018. Comprehensive search terms included both Medical Subjective Headings and text words related to the FRAIL scale and mortality was used (available at PROSPERO). Reference lists of

the included studies were hand-searched for additional studies. Authors of potentially eligible studies were contacted for additional data if necessary. Adequate methodological quality was defined as meeting more than five of the nine items of the Newcastle-Ottawa scale.[24]

Statistical analysis

If two or more studies provided the same effect measures of incident disability according to frailty defined by $\geq$ 3 components of the FRAIL scale, a meta-analysis was attempted. When multiple studies used the same cohort, only the study with the largest sample size was included in the meta-analysis. A random-effects meta-analysis with the generic inverse variance method was performed due to the anticipated high heterogeneity. Heterogeneity was assessed using the chi square test and I^2 statistic. Publication bias was assessed by visual inspection of funnel plots. Subgroup and sensitivity analyses were considered if possible. All analyses were performed using Review Manager 5 (Cochrane Collaboration, Denmark).

RESULTS

Selection process

Figure 1 shows a PRISMA flow diagram of the systematic search of the literature. A total of 141 citations were identified by four electronic databases. After removing 57 duplicates, 76 by title and abstract screening, and one by full-text evaluation, seven studies remained for methodological quality assessment. All seven studies were considered to have adequate study quality (Newcastle-Ottawa scale score range=5-7, mean=6.1) and therefore were included in this review.

Study characteristics

Table 1 summarizes characteristics and findings of the included studies. All seven studies[25-31] provided the data on ADL disability risks and three[27-29] of them also provided the data on IADL. The studies were from various countries, including Australia, China, the UK, US, and Mexico. The sample size ranged from 779 to 8933. The shortest and longest follow-up periods were 2 and 15 years, respectively. All studies controlled at least for age and gender (age if one gender only cohort) except for one study,[30] for which an unadjusted OR was calculated. Most studies defined disability based on Katz ADL and Lawton IADL[27-29,31] while some used different definitions.[25,26,30]

ADL disability risk

In five studies,[25-28,30] frailty status was categorized into three groups: robust, prefrail, and frail defined by 0, 1-2, and 3-5 of FRAIL scale, respectively. Incident ADL disability risks for frailty and prefrailty were significantly higher than robustness in a dose-response manner (frailty: 4 studies, pooled OR=9.82, 95%CI=4.71-20.46, p<0.001; prefrailty: 5 studies, pooled OR=1.97, 95%CI=1.60-2.45, p<0.001). Four studies provided data based on two frailty groups: non-frail and frail defined by 0-2 and 3-5 of FRAIL scale, respectively.[25,26,29,31] Frailty was associated with a significantly higher incident ADL disability risk compared with non-frailty (3 studies, pooled OR=4.90, 95%CI=3.33-7.21, p<0.001). (**Figure 2A**)

IADL disability risk

Three studies examined risks of developing IADL disability.[27-29] Frailty and prefrailty were associated with significantly higher risk of incident IADL disability compared with robustness

(frailty: 2 studies, pooled OR=2.50, 95%CI=1.67-3.73, prefrailty: 2 studies, pooled OR=1.74, 95%CI=1.10-2.77, p=0.02). Incident IADL disability risk based on two frailty group (non-frail and frail) was provided by one study (OR=4.90, 95%CI=3.67-6.54, p<0.001).[29] (**Figure 2B**)

Sensitivity or subgroup analyses were not pursued because of the small number of studies included. There was no evidence of publication bias in the funnels plots.

DISCUSSION

The current study found seven studies examining ADL and/or IADL disability risks according to frailty defined by the FRAIL scale among community-dwelling middle-aged and older people. The meta-analyses showed frailty and prefrailty defined by the FRAIL scale were associated with significantly higher risks of developing ADL and IADL disability.

A previous systematic review and meta-analysis including 20 original studies, most of which used the frailty phenotype criteria from the Cardiovascular Health Study, showed that frailty is associated with more than twice higher risks of incident ADL and IADL disability than that of robustness (ADL: 8 studies, pooled OR=2.85, 95%CI=2.18-3.71, p<0.00001, IADL: 3 studies, pooled OR=2.69, 95%CI=1.12-6.43, p=0.03).[10] Although the ADL disability risks according to the FRAIL scale seem to be higher (pooled OR=4.44 compared with non-frailty, pooled OR=9.82 compared with robustness), whether there is a significant difference is not certain due to the wide 95%CI resulting from the small number of studies using the FRAIL scale.

Although frailty research has increasingly been conducted, relatively limited evidence supports implementation into clinical practice.[32,33] The first step is identification of the target: frail or prefrail older individuals who require interventions to prevent further progression and adverse outcomes due to frailty.[33] The frailty phenotype and the Frailty Index are the two most popular approaches to measure frailty.[2,5] However, these two instruments may not necessarily be designed for use in busy clinical practice due to the dearth of time, space, and equipment. For example, the frailty phenotype requires measurement of gait speed and grip strength and in general 30 or more deficits need to be collected to calculate the Frailty Index. Meanwhile, feasibility of the FRAIL scale is noteworthy. The five criteria included are brief, simple, and quick, as well as cost-effective as it does not require any special equipment or training. The FRAIL scale can be easily incorporated into comprehensive geriatric assessment in a busy clinical setting to identify frail older individuals.

There are some limitations in this study. This study identified and used only seven studies for meta-analysis. Due to the small number of studies, it was not possible to conduct additional analyses to explore causes of high heterogeneity. Although it would have been ideal for two researchers to conduct the systematic review independently to reduce errors and missing studies, only one researcher (G.K) was available.

Strengths of this study include the robust and reproducible methodology according to the PRISMA statements. The literature search of four electronic databases was extensive and comprehensive using a combination of the Medical Subjective Headings and text terms. Furthermore, methodological quality and publication bias were also assessed. Additional data were requested and, although not all but some, were provided by authors of the original studies

and used for the meta-analyses. Most of the odds ratios included in the meta-analyses were adjusted for important covariates, such as age, gender, and socioeconomic factors.

Conclusion

This systematic review and meta-analysis identified currently available evidence of the FRAIL scale and disabilities among community-dwelling middle-aged and older individuals and demonstrated that the FRAIL scale is a plausible and effective tool to measure frailty with regards to incident disability risks. In light of its feasibility, especially in a clinical setting, the FRAIL scale may be a promising tool to facilitate the translation of frailty research into clinical practice.

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Figure 1. PRISMA flow diagram.

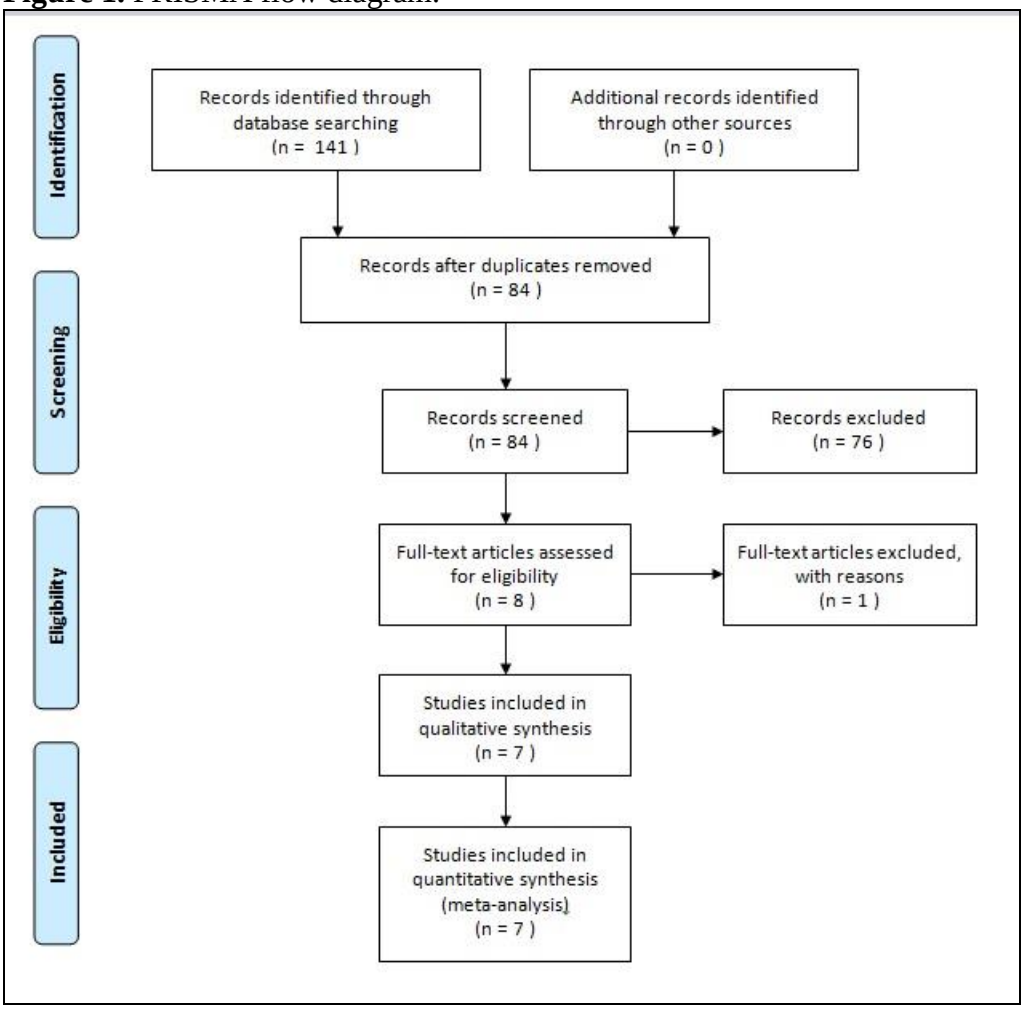
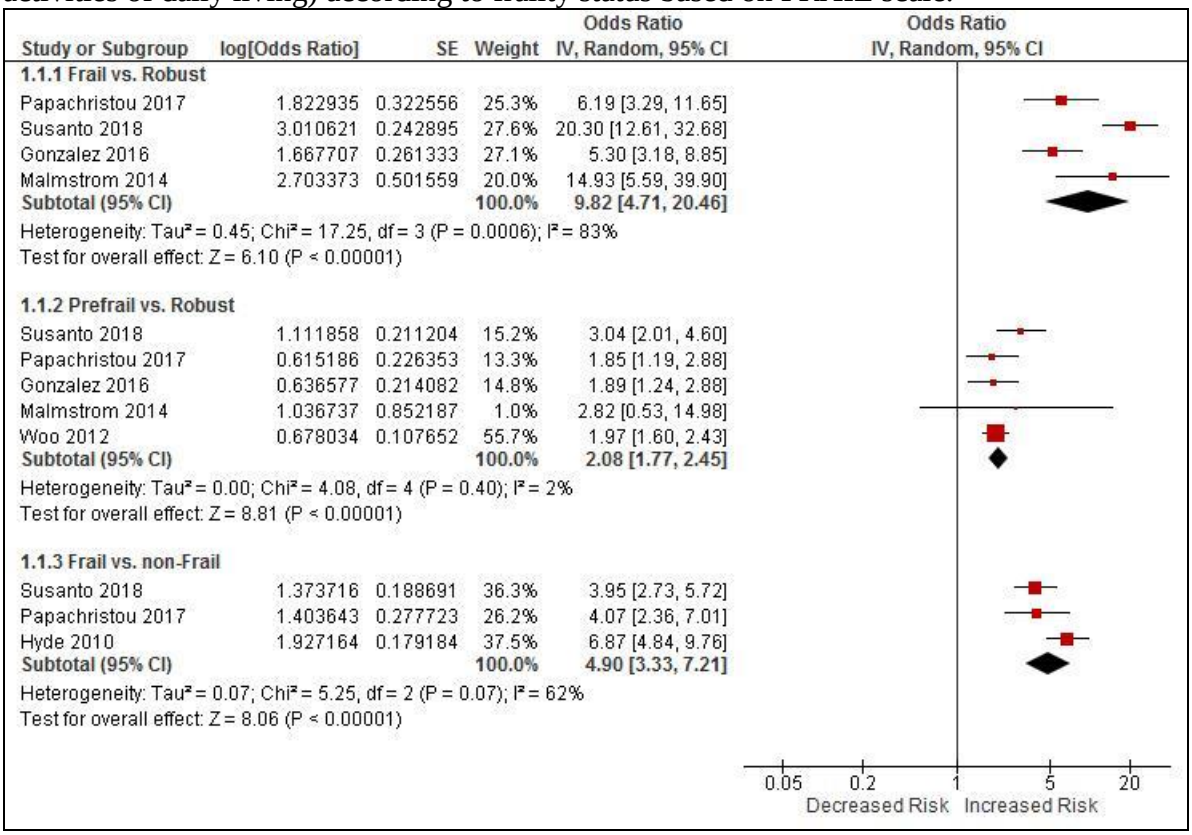


Figure 2. Forest plots of disability risks (A: activities of daily living disability, B: instrumental activities of daily living) according to frailty status based on FRAIL scale.



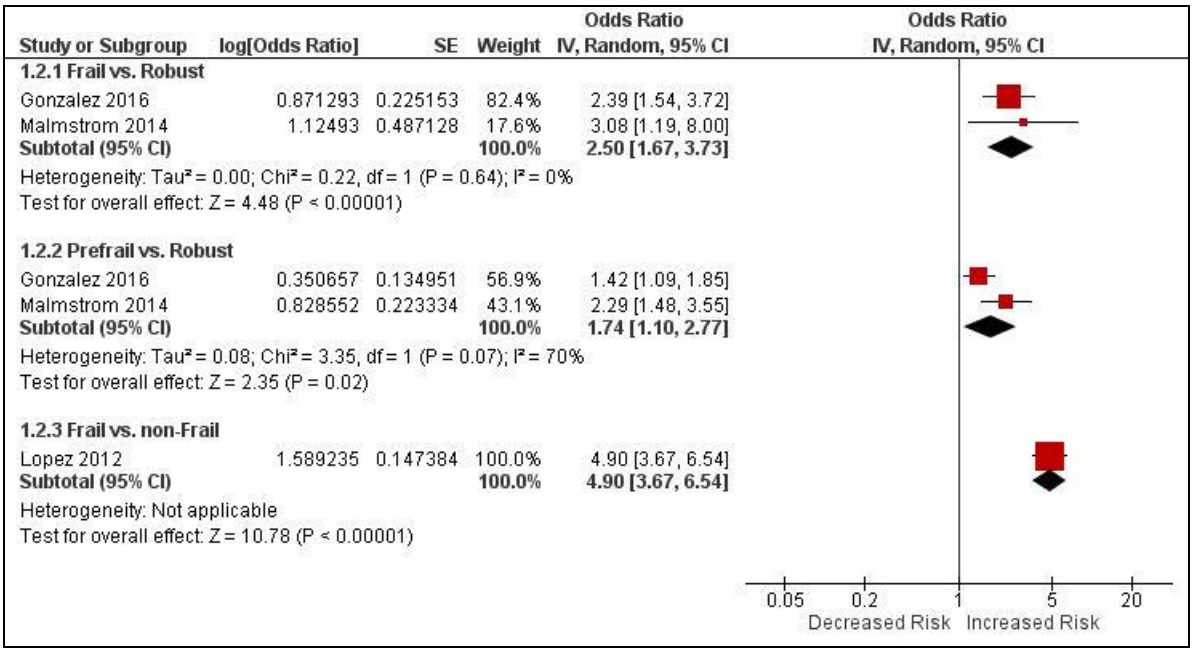


Table 1. Characteristics of the included studies examining FRAIL scale and incident disability risk among community-dwelling middle-aged and older people.

Author/Year/Study	Location	Sample size	Female (%)	Age (range)	Follow-up period	Adjustment	Definition of disability	OR (95%CI)for incident disability by FRAIL scale
Susanto 2018 ALSWH	Australia	8933	100%	-	15 years	age, body mass index, education, income management, physical activity	ADL "daily tasks"	ADL: 0: ref 1: aOR=1.97 (1.36-2.85) 2: aOR=3.84 (2.49-5.91) 3: aOR=11.28 (7.02-18.14) 4-5: aOR=31.15 (14.25-68.08) ADL: 0-2: ref 3-5: aOR=6.87 (4.84-9.77)
Papachristou 2017 BRHS	UK	1615	0%	- (71-92)	3 years	age	Mobility limitation, difficulty in going up or down stairs, or walking 400 yards.	ADL: 0: ref 1-2: aOR=1.85 (1.19-2.89), p=0.01 3-5: aOR=6.19 (3.29-11.65), p<0.001 ADL: 0-2: ref 3-5: aOR=4.07 (2.36-7.01), p<0.001
González 2016 MHAS	Mexico	3270 3550	53.4%	≥60	2 years	age, gender, depressive symptoms, chronic diseases, cognition	ADL: Bathing, dressing, toileting, moving, eating, and being continent. IADL: Preparing hot food, buy food, taking medications, and managing money.	ADL: 0: ref 1-2: aOR=1.89 (1.24-2.87), p=0.003 3-5: aOR=5.30 (3.17-8.83), p<0.001 IADL: 0: ref 1-2: aOR=1.42 (1.09-1.85), p=0.01 3-5: aOR=2.39 (1.63-3.94), p<0.001
Malmstrom 2014 AAH	US	779	-	- (49-65)	9 years	age, gender	ADL: Bathing, dressing, eating, transferring bed or chair, walking across a room, getting outside, or using toilet. IADL: Preparing meals, shopping for groceries, managing money, making telephone calls, doing light housework, doing heavy housework, getting to places outside walking distance, or managing medications.	ADL: 0: ref 1-2: aOR=2.82 (1.7-48), p<0.001 3-5: aOR=14.93 (5.6-40.0), p<0.001 AUC=0.68 (0.62-0.75) IADL: 0: ref 1-2: aOR=2.29 (1.5-3.6), p<0.001 3-5: aOR=3.08 (1.2-8.1), p=0.02 AUC=0.62 (0.57-0.68)

Author/Year/Study	Location	Sample size	Female (%)	Age (range)	Follow-up period	Adjustment	Definition of disability	OR (95%CI)for incident disability by FRAIL scale
Lopez 2012 ALSWH	Australia	8646	100%	77.8 (74-82)	6 years	age, body mass index, education, living alone	ADL: Katz ADL IADL: Lawton IADL	ADL: 0: ref 1: aOR=1.86 (1.55-2.22) 2: aOR=3.41 (2.82-4.13) 3: aOR=6.84 (5.46-8.56) 4-5: aOR=6.35 (4.35-9.27) ADL: 0-2: ref 3-5: aOR=3.63 (3.05-4.32) IADL: 0: ref 1: aOR=2.59 (2.18-3.07) 2: aOR=5.71 (4.55-7.16) 3: aOR=9.17 (6.66-12.62) 4-5: aOR=23.02 (9.34-56.74) IADL: 0-2: ref 3-5: aOR=4.90 (3.67-6.54)
Woo 2012	China	3153	50.3%	≥65	4 years	-	ADL: climbing stairs, performing household activities such as moving chairs or tables and cleaning the floor using a vacuum cleaner or mop	ADL: 0: ref 1-2: cOR=1.97 (1.60-2.44), p<0.001 3-5: unable to calculate due to small number AUC=0.56 (0.53-0.59) for men AUC=0.53 (0.50-0.55) for women
Hyde 2010 HIMS	Australia	3616	0%	76.9 (70-88)	7 years	age, body mass index, medical comorbidity, smoking.	Any inability in Katz ADL or Lawton IADL	ADL: 0-2: ref 3-5: aOR=3.95 (2.73-5.72), p<0.001

AAH: African American Health
ADL: Activity of daily living
ALSWH: Australian Longitudinal Study on Women's Health
aOR: Adjusted odds ratio
BRHS: British Regional Heart Study
CI: Confidence interval
cOR: Calculated Odds ratio
HIMS: Health in Men Study
IADL: Instrumental activity of daily living
MHAS: Mexican Health and Aging Study