

Postal screening can identify frailty and predict poor outcomes in older adults: longitudinal data from INTER-FRAIL study

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Abstract

Objective: identification of older individuals at risk for health-related adverse outcomes (HRAO) is necessary for population-based preventive interventions. Aim of this study was to improve a previously validated postal screening questionnaire for frailty in non-disabled older subjects and to test its prognostic validity in a vast sample of older community-dwellers.

Methods: individuals aged 70+ underwent a mass postal screening. Physical frailty phenotype (PFP) was assessed in the unselected subsample of the first responders. After a 1-year follow-up, HRAO were recorded in the whole sample, including survival, access to Emergency Department, hospitalisation and Long-Term Care admission.

Results: the questionnaire was mailed to 17,273 subjects, whose response rate was 55%. Among the first 1,037 responders without overt disability, the revised questionnaire was 75% sensitive and 69% specific for PFP (ROC 0.772). Non-disabled subjects who screened positive had a higher risk of HRAO in comparison with those who screened negative and similar to non-responders. Risk of adverse outcome was highest among disabled subjects.

Conclusions: a simple questionnaire delivered by mail has good accuracy in detecting PFP in non-disabled older subjects and is able to predict HRAO.

Keywords: *older people, frailty, postal screening, prognosis*

Introduction

Due to the ever-growing number of older subjects in modern societies, early identification of subjects at risk of health-related adverse events has become of paramount interest and has led to different approaches to identify ‘frailty’, defined as a multifactorial condition with decreased functional reserve and diminished resistance to stressors, causing vulnerability to adverse outcomes and increased risk of death [1]. Frailty has been conceptualised as an antecedent of disability, and frail non-disabled subjects might be candidate for secondary prevention to reduce the risk of disability onset [2]. The recent

review on ageing of the World Health Organization is focused on the promotion of healthy ageing and identifies a phase of ‘declining functional capacity’, overlapping with frailty, which should be addressed with capacity-enhancing interventions to prevent the onset of ‘significant loss of capacity’ [3]. In this perspective, screening programs of frail older adults might be useful to identify ideal candidates for interventions aiming at the prevention of health-related adverse outcomes that have been proved to be useful in reducing the burden of functional decline in this high-risk population [4]. This might also result in reduced healthcare expenditures and would be particularly important in the current era of resource constraints, which are

Table 1. Questionnaire items independently associated with Fried Frailty Phenotype and relative weight in Frailty Postal Score

Item	<i>b</i> ± SE	<i>P</i>	Weighted score ^a
Is your sight good enough to read newspaper headings, even with glasses? [No]	0.507 ± 0.219	0.021	1.5
Do you easily get exhausted in daily chores? [Yes]	1.047 ± 0.189	<0.001	3
Do you have problems with your memory? [Yes]	0.383 ± 0.149	0.01	1
Did you have any falls in last 6 months? [Yes]	0.574 ± 0.165	0.001	1.5
Do you have difficulty walking 400 m on a flat surface? [Yes]	1.301 ± 0.158	<0.001	3.5
Do you take 5+ drugs on a regular basis (daily or almost daily)? [Yes]	0.359 ± 0.156	0.021	1

Results of the logistic regression analysis (backward deletion). Items excluded from the model: 'Do you live alone? Have you been admitted to hospital or ER in the last 6 months? Have you lost 3+ kg of weight unintentionally in prior year? Can you easily rely on somebody's help in case of need?'

^aCalculated as *b*/minimum *b* and rounded to 0.5.

posing serious threats to traditional healthcare approaches [5]. One of the most adopted paradigms for frailty identification is physical frailty phenotype (PFP) proposed and initially validated by Linda Fried in the Cardiovascular Health Study [6]. This model has the advantage of defining frailty as an easily detectable clinical syndrome resulting in increased risk of adverse events including disability onset [7]. Yet to identify the target condition, a clinical assessment of individuals is needed, which, although simple, poses a significant burden in a population-based screening perspective.

In 2009, the Italian Center for Prevention and Disease Control (Centro per la Prevenzione e il Controllo delle Malattie) funded a project, whose aims were to develop a simple, low-cost strategy for intercepting frailty (INTER-FRAIL), based on postal screening, and to suggest interventions to prevent or slow down the progression from frailty to overt disability. The rationale and methods of the INTER-FRAIL study, and the initial validation of the postal questionnaire as a screening tool for PFP, based on the model of the Sherbrook Postal Questionnaire [8], have been published recently [9]. Yet not all the 10 items included in the original version of the questionnaire actually showed the expected association with the studied outcome [9]. Therefore in the present study, we aimed at both reducing the number of items and weighting them, to make self-administration easier and to improve concurrent validity towards PFP in older subjects without overt disability. Moreover, we assessed the ability of the revised tool to predict adverse health-related outcomes, including death, access to Emergency Department (ED), hospitalisation and admission to a Long-Term Care (LTC) program, in a vast sample of community-dwelling older subjects.

Methods

Study population

The INTER-FRAIL study is a prospective cohort study of all community-dwellers aged 70–84 living in the Fiorentina Sud-Est and the Valdichiana Senese health districts of Tuscany, whose population in the target age range is of ~20,000 individuals. Between March 2011 and December 2012, all the potentially eligible residents were identified from the census registry, with the only exclusion of known beneficiaries of LTC services for disabled individuals.

The postal questionnaire

All subjects were mailed a questionnaire screening for PFP via their Local Health Authority (LHA), as previously described [9]. Participants who did not return the questionnaire after a second shipping were considered as non-responders. The tool included 11 yes/no questions designed for self-administration. The first question (Are you usually able to dress and undress yourself, without help from others?) was previously found to be 81% sensitive and 94% specific in detecting disability in activities of daily living (ADL) [9], defined as being dependent in 2+ Katz's ADL [10]. The remaining 10 questions were used to screen for frailty (Table 1). Missing answers in returned questionnaires were treated as 'no'.

Frailty assessment (concurrent validity)

A first group of responders underwent in-home comprehensive geriatric assessment (CGA), regardless of the questionnaire result, including the assessment of independence in ADL, of lower extremity performance with Short Physical Performance Battery (SPPB) [11] and of depressive symptoms with 15-item Geriatric Depression Scale [12]. In agreement with standard criteria [6], the presence of PFP was clinically diagnosed by the presence of 3+ of the following five components: (i) unintentional weight loss of 5+ kg in prior year (single-item question); (ii) poor muscle strength, inferred from a score <3 upon 4 at the repeated chair standing test of the SPPB (time >13.7 s); (iii) reduced walking speed, defined by a score <4 upon 4 at the 4-m walk test of the SPPB (time >4.8 s); (iv) exhaustion in common chores, identified by an answer of 'No' to the GDS item 'Do you feel full of energy?'; (v) and <30 min/day of physical activity of moderate intensity (single item question).

Outcome assessment (predictive validity)

Death, first access to ED, first hospitalisation and admission to LTC programs (home care, day care or nursing home) over the first year after questionnaire shipping were recorded by consulting Local Health Authority (LHA) administrative databases.

A synopsis of the study is reported in Supplementary data, Appendix 1, available in *Age and Ageing* online.

Ethics and economic support

Subjects gave written consent to study participation while returning the questionnaire. LHA transmitted to the researchers anonymised unique identifiers of all participants, to trace their health-related outcome. The study was approved by the institutional review board of Florence Health District (0103787/10.11.2010). Data were processed according to Italian regulation on privacy.

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Statistical analysis

To simplify the original questionnaire, a logistic regression model with backward deletion of redundant variables was performed, assessing independent association of each item with PFP among non-disabled subjects. Items selected in the final model were rescaled dividing each regression coefficient by the lowest one and rounding the score obtained to the nearest 0.5. A summary score was then computed for the revised questionnaire by addition of the six weighted subscores to obtain the Frailty Postal Score (FPS). Sensitivity, specificity and receiver operating characteristic (ROC) area under the curve (AUC) of the FPS were evaluated against the presence of PFP, to identify possible cut-offs. Estimates of the sample size required were preliminary performed (Supplementary data, Appendix 2, available in *Age and Ageing* online).

All subjects were then categorised into four groups as: non-responders (NR, subjects who did not return the questionnaire), responders disabled (RD, according to the disability screening item), responders positive (RP) and responders negative (RN) according to FPS cut-off. Longitudinal comparison were performed with a Cox regression model adjusted for age and gender for survival and with Competing Risk Regression Models for first access to ED, first hospitalisation and admission to LTC, taking into account the competing risk of death. A first set of comparisons was performed between responders and NR. A second set of comparison was performed across the previously defined groups (RN, RP, RD and NR).

Analyses were performed using the STATA 8.0 statistical package. Data were summarised as mean [95% CI] for continuous variables. A *P* value of <0.05 was considered statistically significant.

Results

A total of 17,273 questionnaires were mailed, and 9,515 were returned (55% response rate). In comparison to responder subjects, NR were significantly older (mean age 79.9 [79.8, 80.0] versus 79.2 [79.2, 79.3]) and more often female (58 versus 56%, *P* < 0.001). Follow-up time was 1 year after questionnaire delivery.

Concurrent validity

To assess the concurrent validity of the questionnaire, all the first 1,139 responders underwent CGA, regardless of the score achieved. Of them, 102 were disabled in 2+ ADL items at the CGA and were excluded from subsequent analysis, leaving a sample of 1,037 subjects without overt disability, with 380 (37%) showing the PFP. In this sub-sample, among single questionnaire items, poor sight, self-report of exhaustion, memory problems, fall in the previous 6 months, difficulty walking for 400 m and taking 5+ drugs were independently associated with PFP, while not living alone, hospitalisation in prior year, unintentional weight loss in prior year and person(s) available to provide help did not show a significant association in the final model, and were excluded. Each of the included items was assigned a relative weight (Table 1). The FPS, resulting from the sum of single items, ranged from 0 to 11.5, with higher score indicating higher likelihood to show the PFP and an area under the ROC curve of 0.772. The best cut-off score to achieve a good sensitivity with a satisfactory sensitivity was 6.5, obtaining a 75% sensitivity with a 69% specificity (Supplementary data, Appendix 3, available in *Age and Ageing* online).

Predictive validity

In the subsequent analysis, we assessed the prognostic validity of the combined information regarding disability and frailty according to the questionnaire results. RD were defined according to ADL disability screening question [9] and were 1,148. According to the identified cut-off, non-disabled responder subjects (*n* = 8,367) with a FPS ≥ 6.5 were identified as RP (*n* = 2,384), while the remaining as RN (*n* = 5,983). In Cox regression analysis, using RN as reference group, hazard ratio for mortality was 2.7 for RP, 4.5 for NR and 6.7 for RD (Table 2). Adjacent-group comparisons were all highly significant (*P* < 0.001) (Figure 1a). In Competing Risk Regression Model, access to ED was lowest among RN and highest among RD; RP risk was intermediate between RN and RD and NR risk was intermediate between RN and RP (*P* < 0.001 for all comparisons) (Table 2, Figure 1b). In the same model, hospitalisation and admission to LTC risks were lowest among RN, highest among RD, and intermediate and overlapping among RP and NR (*P* < 0.001 for all comparisons except RP versus NR, *P* > 0.05) (Table 2, Figure 1c and d).

Discussion

In the present study, a simple postal questionnaire was able to reliably intercept PFP among non-disabled older subjects. Moreover, the combined information regarding frailty and disability status yielded by the questionnaire was able to predict the incidence of health-related adverse events, including death, ED access, hospitalisation and LTC admission, in a large sample of community-dwelling older adults.

Table 2. Hazard ratio [95% CI] for single health-related adverse outcomes as resulting from adjacent group comparison of questionnaire response

	Hazard ratio [95% CI]			
	Mortality	ED access	Hospitalisation	LTC admission
Responders negative (<i>n</i> = 5,983)	Ref	Ref	Ref	Ref
Responders positive (<i>n</i> = 2,384)	2.711 [1.938–3.791]	1.676 [1.531–1.835]	1.916 [1.647–2.229]	3.927 [2.609–5.911]
Non-responders (<i>n</i> = 7,758)	4.473 [3.449–5.801]	1.435 [1.339–1.539]	1.894 [1.686–2.127]	3.276 [2.296–4.676]
Responders disabled (<i>n</i> = 1,148)	6.743 [4.923–9.235]	2.169 [1.945–2.417]	3.360 [2.869–3.936]	10.014 [6.726–14.908]

Survival probability was computed with a Cox regression model adjusted for age and gender. Risk of first access to ED, first hospitalisation and admission to LTC was calculated with Competing Risk Regression Models, taking into account the competing risk of death.

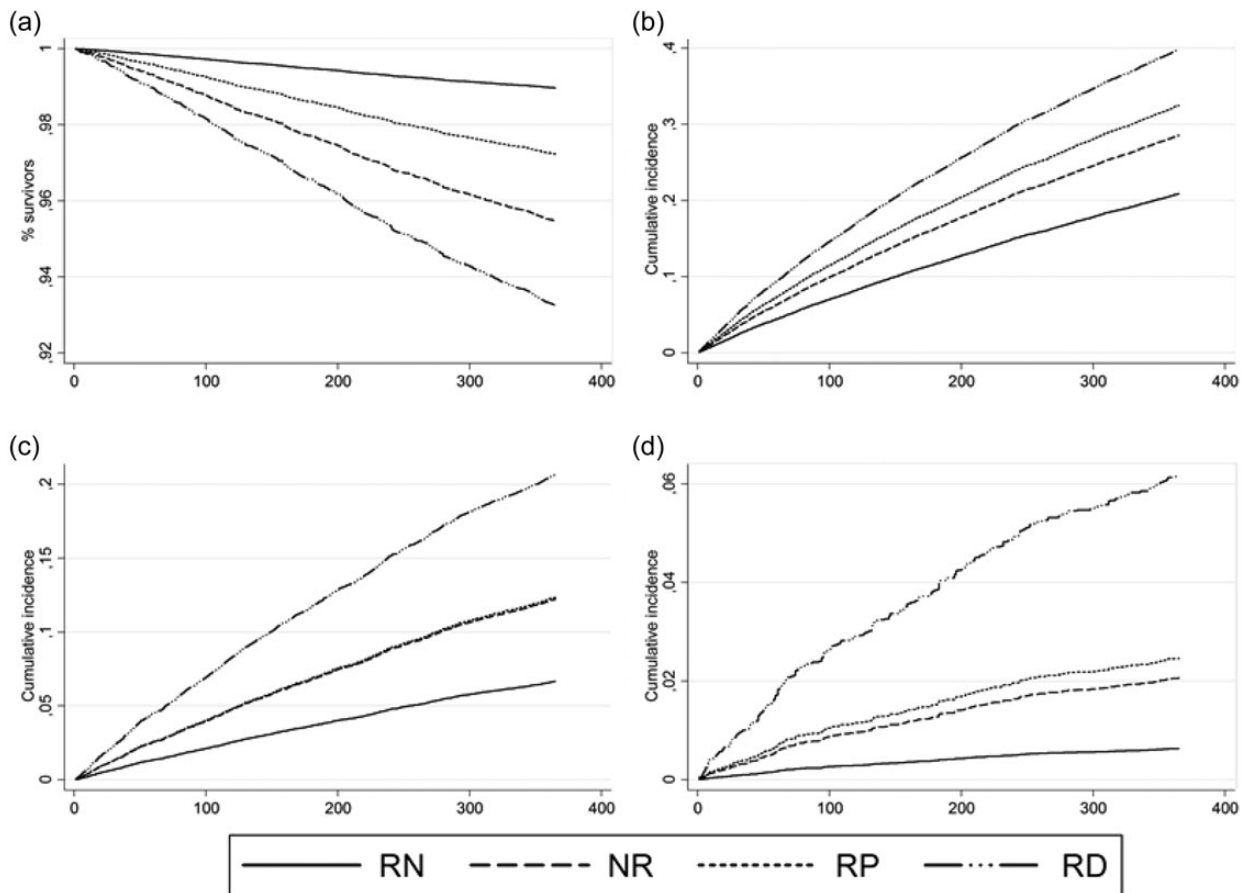


Figure 1. Adverse health-related outcomes by postal questionnaire status: results of multivariate analysis for survival (a), Emergency Department access (b), hospitalisation (c) and Long-Term Care admission (d) by postal questionnaire status.

In the cross-sectional analysis, we could simplify the previously validated postal questionnaire [9], reducing the number of items from 10 to 6 and obtaining a greater concurrent validity versus PFP, increasing AUC from 0.695 to 0.772, sensitivity from 71 to 75% and specificity from 58 to 69%. The improvement of specificity is consistent with the previous observation that three of the excluded items, namely ‘not living alone’ (originally included in the Sherbrook questionnaire [8]), ‘hospitalisation in prior year’ and ‘persons available to provide help’, did not show the expected association with PFP [9]. Therefore, for future studies, we advise to use

the present version of the questionnaire, which is shorter and more predictive in comparison with the original one.

Few data are available so far correlating frailty screening by self-administered questionnaires with PFP and none has an optimal diagnostic performance [13]. In a selected sample of 102 primary care older patients, PRISMA-7 questionnaire showed a good concurrent validity (AUC 0.85) and Groningen Frailty Indicator (GFI) showed a moderate concurrent validity (AUC 0.64) with PFP [14]. Of notice, PRISMA-7 is a 7-item case-finding tool designed to identify older adults with moderate to severe disabilities [15] and, like GFI [16], actually includes items evaluating ADL, differently from the present one.

Recently, the FIND questionnaire has been proposed, which was found to identify adequately PFP without mobility disability, with 95% sensitivity and 76% specificity in a pilot study of 45 older subjects [17].

Moreover, in the present study, we showed the predictive validity of the revised postal questionnaire. The poor outcome of RD subjects in the longitudinal analysis is consistent with the well-known observation that disability is associated with poor outcome in a geriatric population [18] and extends the finding to a single-item assessment of this condition by mail. The ability of the PFS to predict prognosis is consistent with the ability of Sherbrook postal questionnaire to predict significant functional decline [6], ED access and hospitalisation [19, 20], and mortality risk [20]. Similar data exist for few other frailty screening instruments, such as GFI and Tilburg Frailty Indicator [20, 21]. In those studies, however, disabled subjects were included, while in the present one PFS, coupled with the disability screening item, was shown to predict prognosis in non-disabled older subjects. The ability to detect at-risk non-disabled older individuals is crucial, as they are the most appropriate recipients of preventive interventions aimed at reducing the risk of functional decline. The design of such interventions is urgently needed, as a recent prevention study targeting frail older subjects according to GFI was not able to show any beneficial effect on disability progression [22]. This might be explained by the high level of disability of participants, which might have precluded the efficacy of the preventive intervention, in agreement with data demonstrating the preventing functional decline and mortality is possible only among subjects without severe health impairment [23].

Present data also show that NR subjects are similar to RP in regard to adverse health-related outcomes. This is consistent with the results of a disability case-finding study, which has previously shown that non-responders to a postal questionnaire paradoxically show a greater disability in comparison with responder subjects [24]. In a previous study conducted in the same area, we found that non-response to a similar frailty questionnaire was associated with older age, and this might partly explain the worse prognosis observed [25]. Of notice, in the validation of Sherbrooke Postal Questionnaire, a similar increase of functional decline risk was observed among non-responder and positive screenees, and non-response to questionnaire was included among frailty criteria in the original case-finding algorithm [8].

In view of the last observation, an important limitation of the present study is the high rate of non-response. Due to the poor prognosis observed in this probably heterogeneous population, future studies should clarify health and social characteristics of this large sample. However, for screening purposes, NR should be considered 'at risk' and be offered a comprehensive assessment. To avoid this problem, the present screening instrument might be tested for self-administration in primary care, as easy and validated instruments for frailty interception are needed in this setting [26].

We acknowledge that the operationalisation of PFP is partly different from the original study [6], main differences being the self-report of weight loss and the use of repeated chair stand as a measure of muscle strength [27], with the advantage of not needing instrumental measures.

In conclusion, the present study shows in a large population-based sample that a postal screening of non-disabled frail older subjects is feasible and that the proposed instrument has satisfactory concurrent and predictive validity. Intervention studies are needed to show that a proactive preventive approach can prevent health-related adverse events in this high-risk, yet relatively well-functioning population.

Key points

- Postal screening has satisfactory accuracy in detecting physical frailty in non-disabled older subjects.
 - A simple postal questionnaire can predict health-related adverse outcomes among older subjects.
 - Identification of frail, yet non-disabled subjects is needed to design effective prevention programs.
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Supplementary data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Conflicts of interest

None declared.

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