Effectiveness of a Proactive Primary Care Program on Preserving Daily Functioning of Older People: A Cluster Randomized Controlled Trial

Nienke Bleijenberg, RN, PhD, Irene Drubbel, MD, PhD,* Marieke J. Schuurmans, RN, PhD,‡ Hester ten Dam, MD, PhD,* Nicolaas P.A. Zuithoff, PhD,† Mattijs E. Numans, MD, PhD,§ and Niek J. de Wit, MD, PhD**

OBJECTIVES: To determine the effectiveness of a proactive primary care program on the daily functioning of older people in primary care.

DESIGN: Single-blind, three-arm, cluster-randomized controlled trial with 1-year follow-up.

SETTING: Primary care setting, 39 general practices in the Netherlands.

PARTICIPANTS: Community-dwelling people aged 60 and older (N = 3,092).

INTERVENTIONS: A frailty screening intervention using routine electronic medical record data to identify older people at risk of adverse events followed by usual care from a general practitioner; after the screening intervention, a nurse-led care program consisting of a comprehensive geriatric assessment, evidence-based care planning, care coordination, and follow-up; usual care.

MEASUREMENTS: Primary outcome was daily functioning measured using the Katz-15 (6 activities of daily living (ADLs), 8 instrumental activities of daily living (IADLs), one mobility item (range 0–15)); higher scores indicate greater dependence. Secondary outcomes included quality of life, primary care consultations, hospital admissions, emergency department visits, nursing home admissions, and mortality.

RESULTS: The participants in both intervention arms had less decline in daily functioning than those in the usual care arm at 12 months (mean Katz-15 score: screening arm, 1.87, 95% confidence interval (CI) = 1.77–1.97; screening and nurse-led care arm, 1.88, 95% CI = 1.80–1.96; control group, 2.03, 95% CI = 1.92–2.13; $P = .03$). No differences in quality of life were observed.

CONCLUSION: Participants in both intervention groups had less decline than those in the control group at 1-year follow-up. Despite the statistically significant effect, the clinical relevance is uncertain at this point because of the small differences. Greater customizing of the intervention combined with prolonged follow-up may lead to more-robust results. **J Am Geriatr Soc 2016.**

Key words: primary care; daily functioning; randomized controlled trial; older people; nurse-led care program

Providing optimal care for the increasing number of older people with complex care needs is a major challenge in primary care.[1,2] The average primary care consultation rate for Dutch citizens increases from 4.3 to 6.2 per year between the ages of 60 and 75 to 10 or more per year after the age of 75.[3] The current approach in primary care is reactive and fragmented and does not meet the needs of older people as they experience a lack of overview and coordination when multiple care providers are involved.[4] These deficits result in unnecessary losses of daily functioning, suboptimal quality of life, and high healthcare expenditures.[5] A transition toward more-proactive primary care that focuses on maintaining independence and prevention of functional decline in older adults has been proposed,[6] but the critical components of a more-proactive primary care system remain unknown.

The literature regarding the prevention of functional decline in older adults suggests a stepwise identification of people who are at risk of adverse events followed by the provision of longitudinal personalized care.[7] The operationalization of these components in daily practice is debated, and their effectiveness in isolation and in combination remains to be determined.[8] Several comprehensive care

From the *Department of General Practice; †Department of Biostatistics; ‡Department of Rehabilitation, Nursing Science and Sports Medicine, University Medical Center Utrecht; and §Department of Public Health and Primary Care, LUMC Leiden, the Netherlands.

Address correspondence to Nienke Bleijenberg, Heidelberglaan 100. Str. 6131, room 6.105. 3508 GA, Utrecht, the Netherlands. E-mail: N.Bleijenberg@umcutrecht.nl

DOI: 10.1111/jgs.14325

© 2016, Copyright the Authors
Journal compilation © 2016, The American Geriatrics Society
0002-8614/16/$15.00

programs aimed at preventing declines in community-dwelling older people in primary care have reached inconclusive results.[9–11] A multidisciplinary approach involving individual assessments and customized care is consistently reported to be an important element of such interventions.[12]

Based on previous evidence and theoretical and practical considerations, a proactive personalized primary care strategy for frail older people was designed and evaluated.[13] This strategy consists of a frailty screening intervention based on routine primary care data followed by a personalized nurse-led care program consisting of a comprehensive geriatric assessment of individuals considered to be frail, evidence-based care planning, and care coordination. This strategy was evaluated in the Utrecht PROactive Frailty Intervention Trial (U-PROFIT), with the aim of determining its effectiveness in preserving daily functioning of frail older adults in primary care. It was hypothesized that the two interventions (screening and personalized care program) would be synergistic and that the combined intervention of screening followed by nurse-led care would result in better outcomes than screening alone.

METHODS

Study Design

This was a single-blind, three-arm, cluster-randomized controlled trial with 1-year follow-up. Because the intervention was aimed at the general practice level, a cluster-randomized design was used to prevent contamination between the comparison groups. The study protocol has been described in detail.[13] Written informed consent was obtained from all participants. The institutional review board of the University Medical Center Utrecht approved the U-PROFIT trial (protocol ID 10–149/O), which is registered as NTR2288.

Setting and Participants

Of the 44 invited general practices in the Utrecht region of the Netherlands, 39 agreed to participate. Together, these practices provide primary health care for 44,000 individuals aged 60 and older. An age threshold of 60 was selected because of the large numbers of elderly adults of non-Dutch origin in these practices in whom frailty has been reported to start at an earlier age.[14] From October 2010 to March 2011, potentially frail individuals aged 60 and older were identified by screening their electronic medical records (EMRs) using predefined screening criteria (see Intervention 1 below). Individuals who were terminally ill, defined as estimated life expectancy of 3 months or less, and those in assisted-living facilities or nursing homes were excluded.

Randomization

All participating general practices were identified before randomization. The general practices were stratified according to practice size (small, <1,000; average, 1,000–3,000; large, >3,000 patients). Within each stratum, practices were randomized using a computer-generated random allocation sequence with the aim of an allocation ratio at the individual level of 1:1:1 (Figure 1). Eligible individuals were identified after randomization. A modified informed consent procedure was used (individuals were not aware of the intervention arm that they were allocated to but were fully informed at the end of the study).[15] The general practices were instructed not to inform participants about the aims of the study. The investigators were not blinded for logistical reasons.

Interventions

Intervention 1: Frailty Screening Followed by Routine Care from a General Practitioner

The frailty screening intervention aimed to identify older adults at risk of adverse events using readily available routine care EMR data.[16] Individuals aged 60 and older were considered at risk if they were at risk for frailty, were exposed to polypharmacy, or had not had a visit with their general practitioner (GP) for 3 years or more (consultation gap). A combination of the three criteria was used to exclude older adults who did not have any health deficits. To measure risk of frailty, a frailty index (FI) was constructed based the cumulative deficit model[17,18] using routine care data regarding 50 potential health deficits. Each of these deficits was defined as the presence of one or more International Classification of Primary Care coded symptoms or diseases in the participant's EMR. (The list is provided in the study protocol.) A FI score was defined according to the frailty deficit approach.[17,18] A score between 0 and 1 represents the number of deficits present divided by the total number of deficits, and a score of 0.20 or greater indicates potential frailty. This FI was externally validated and shown to be associated with risk of adverse health outcomes.[16] Polypharmacy was defined as the chronic use of five or more different pharmacotherapeutics according to Anatomic Therapeutic Chemical coding.[19] Polypharmacy was chosen as a separate criterion because of the high quality of medication registration in the primary care records and the strong association with greater risk of adverse health outcomes.[20] A "consultation gap" (≥3 years without a general practice consultation (with the exception of annual influenza vaccination)) was included to detect possible care avoiders.[21] Older adults who do not consult their GP would otherwise not be identified through the screening instrument because they have no data registered in the EMR. Quarterly reports including older adults at risk were generated for each of the participating practices but were sent only to the practices in the intervention groups (Appendix 1). The GPs in intervention group 1 were advised to act upon these reports according to the current standards and guidelines.

Intervention 2: Frailty Screening Followed by Personalized Nurse-Led Care

In the second intervention group, the personalized nurse-led care program followed application of the screening instrument. Twenty-one registered practice nurses delivered this care and were extensively trained during a 6-week training program (48 hours total). An expert panel of older adults, nurses, and GPs participated in the development of this program. Details regarding the development and content are described elsewhere.[22] Briefly, the intervention started with a frailty assessment using the

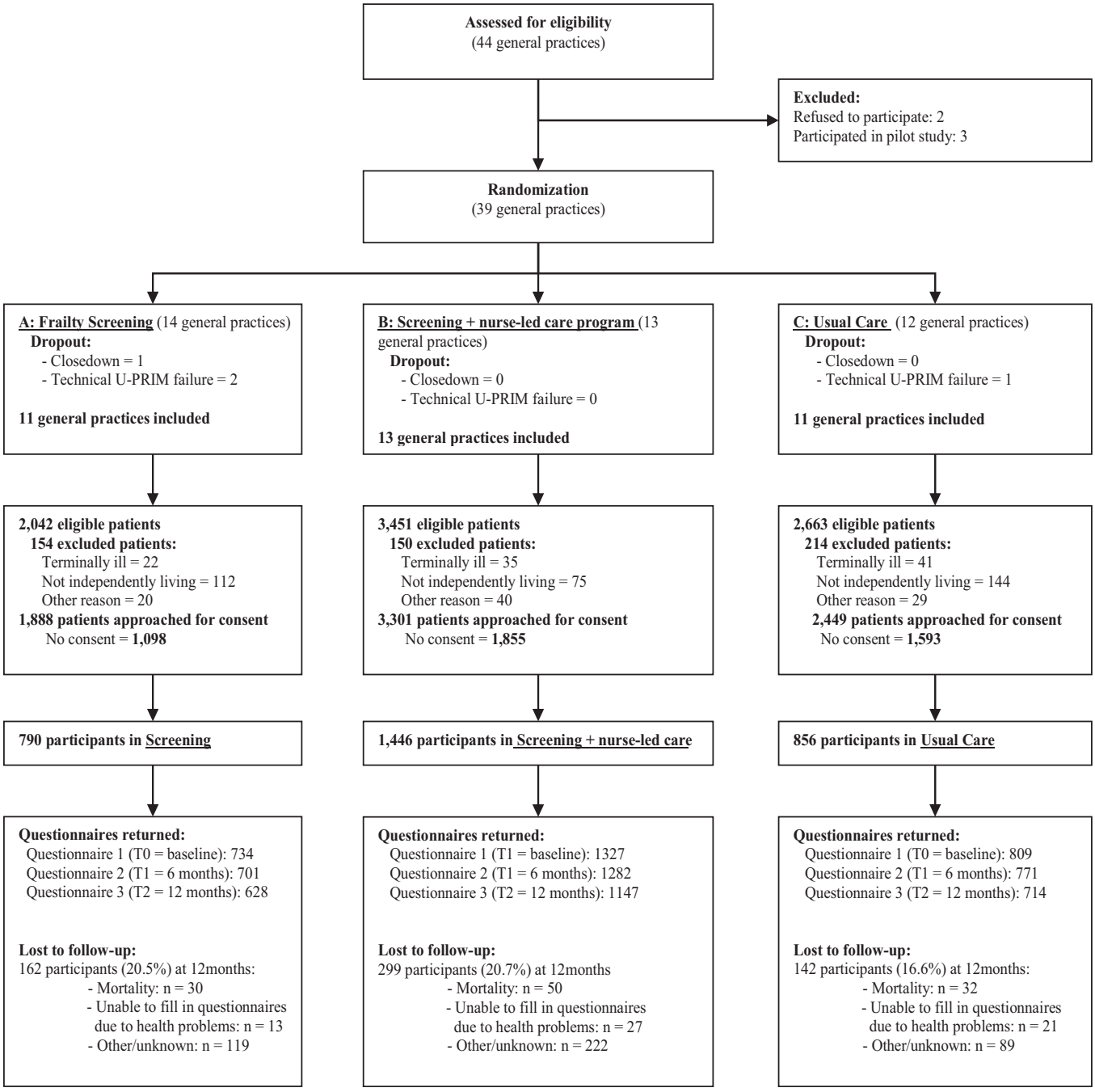

Figure 1. Flowchart of general practices and participants assigned to the intervention and control groups.

Groningen Frailty Indicator (GFI) questionnaire[23,24] and the Intermed Self-Assessment, which is an instrument that assesses the biopsychosocial care needs of older adults.[25,26] Individuals identified as frail according to the GFI (score ≥4) underwent a Comprehensive Geriatric Assessment at home, follow-up visits, and care coordination based on their needs. To assist and guide the nurses in proving customized care, evidence-based care plans were developed for common geriatric conditions, such as falls, urinary incontinence, and nutrition problems (all available on request). All components were pretested for feasibility and acceptability.[27] The registered nurses and GPs participated in a 3-hour workshop before initiation of the study.

Control Arm

In the control arm, GPs were instructed to provide care as usual, which was defined as the continuation of daily care practice without the implementation of either intervention.

Data Collection and Measurements

Primary Outcomes

Participant and practice data were collected at baseline and at 6 and 12 months of follow-up. The primary outcome was daily functioning as assessed according to the modified Katz-15 index of activities of daily living (ADLs)

and instrumental activities of daily living (IADLs) (range 0–15); higher scores indicate greater ADL and IADL dependence.[28,29] The Katz-6 index[30] was included in the original protocol, but it has a considerable floor effect at low disability levels, so it was replaced with the Katz-15. For reasons of transparency, results of both outcomes are provided.

Secondary Outcomes

Secondary outcomes were self-reported health-related quality of life (QoL) measured according to the RAND-36 (range 0–100),[31] the EuroQol-5D (EQ-5D),[32] perceived QoL score (range 0–10), satisfaction with primary care (range 0–10), number of hospital admissions (not included in the original protocol, post hoc analysis), admission to a nursing home or assisted-living facility, and general practice out-of-hours consultations during follow-up. Informal caregiver burden was specified in the study protocol as a secondary outcome but will be addressed in a separate article.

Information on the following secondary outcomes was collected from the EMR of participating practices: number of emergency department (ED) visits, number of general practice consultations (by telephone, in the office, home visits) during office hours, and mortality. Data quality checks were performed for the questionnaires and the EMR data, with the aim of identifying missing data and irrational values.

Statistical Analysis

All outcomes were assessed at the individual level, and an intention-to-treat analysis was performed to detect differences between the intervention groups and the control group. The primary and secondary outcomes after 6 and 12 months of follow-up were analyzed using generalized linear mixed models. Random intercepts were included in all models to account for the cluster randomization. An unstructured residual (generalized estimation equation type) covariance matrix was included to correct for the associations between the 6- and 12-month outcomes.[33,34] Linear mixed models for continuous outcomes were applied to the Katz-15, RAND-36, EQ-5D, satisfaction with care, and perceived QoL. Because all outcomes had skewed distributions, the effects were estimated using robust standard errors.[35] Group means with 95% confidence intervals (CIs) were estimated. Nursing home admissions, hospital admissions, general practice consultations within office hours, general practice after-hours consultations, and ED visits were analyzed as counts and rates with 95% CIs. Mortality was analyzed using logistic mixed models with adjusted probabilities and 95% CIs. The analyses were performed in three steps. The first model was a crude model with treatment and time of measurement was estimated. In the second model, baseline values were adjusted for. In the third model, baseline values and confounders including age, sex, socioeconomic status (SES), educational level, indication for inclusion (FI score, polypharmacy, consultation gap) and stratification factor (practice size) were adjusted for. SES was determined using Netherlands Institute for Social Research status scores, which are based on the socioeconomic status of postal areas. Education was measured at the individual level, based on self-report. Low education was defined as primary school or less, average education was defined as secondary school, and high education was defined as more than secondary school. Because the effects of treatment on outcome may be delayed, the interaction between the interventions and the time of measurement was tested. The interactions between the outcome measurements and predefined parameters (age, sex, SES, educational level) were tested. When these interactions were statistically significant after corrections for confounders and indication, subgroup analyses were performed. $P < .05$ was considered statistically significant. Multiple testing was corrected for using the Holm method.[36] Statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC) and SPSS version 20.0 (IBM, Chicago, IL).

Before initiation of the study, no valid estimations of the variances of Katz-15 results within and between general practices were available for the elderly population, and a power analysis for a cluster-randomized trial was therefore not possible. It was initially assumed that, with the inclusion of a sample of 5,000 frail older adults, statistically significant differences in the primary outcome would be observable between the three groups.

RESULTS

The 39 participating general practices were randomized into one of three groups. Four practices withdrew shortly after randomization because of technical EMR problems (Figure 1). In the remaining 35 practices, the screening intervention identified 8,156 individuals based on routine care data as being potentially at risk of adverse health events. Five hundred eighteen individuals were excluded, resulting in 7,638 eligible individuals, 3,092 of whom (40.5%) participated (Table 1). Participant characteristics did not differ between the three groups with the exceptions of education level and SES. The mean age of the participants was 74.2 ± 8.4, 55.2% were female, 28.4% were living alone, and 35.3% had a low level of education. Of the 1,327 participants in the screening followed by nurse-led care group, 835 (62.9%) were identified as frail according to the GFI questionnaire.

Primary Outcome

After 6 months, the mean Katz-15 scores of participants in the three groups did not differ (screening group, 1.69, 95% CI = 1.61–1.77; screening and nurse-led care group, 1.70, 95% CI = 1.60–1.79; control group, 1.74, 95% CI = 1.67–1.82). After 12 months, participants in both of the intervention groups had less decline in daily functioning than those in the control group (mean Katz scores: screening group, 1.87, 95% CI = 1.77–1.97; screening and nurse-led care group, 1.88, 95% CI = 1.80–1.96; control group, 2.03, 95% CI = 1.92–2.13, $P = .03$ time*treatment; Table 2). The intraclass correlation coefficient (ICC) for the Katz-15 corrected for time was 0.031 (95% CI = 0.01–0.05). The more highly educated participants in the screening and nurse-led care group had statistically

Table 1. Practice and Participant Baseline Characteristics

Baseline Characteristic	Screening[a]	Screening Plus Nurse-Led Care[a]	Usual Care[c]	*P*-Value
Practice				
Cluster size, median (IQR)	37 (22–92)	62 (33–129)	71 (42–121)	
Cluster size (number of patients), n				
Small (<1,000)	5	7	5	
Average (1,000–3,000)	2	3	3	
Large (>3,000)	4	3	3	
Full-time equivalent general practitioners per practice, mean ± SD	1.9 ± 1.1	2.7 ± 1.7	2.9 ± 1.3	
Participant				
Age, mean ± SD	73.5 ± 8.2	74 ± 8.2	74.6 ± 8.8	.22
Female, n (%)	406 (55.3)	772 (58.2)	453 (56.0)	.39
Living independently alone, n (%)	226 (31.7)	379 (29.3)	229 (29.1)	.56
Living with another person, n (%)	411 (56.4)	766 (58.2)	465 (58.0)	.93
Have children, n (%)	595 (85.0)	1,079 (85.5)	627 (81.5)	.05
Native Dutch, n (%)	669 (91.8)	1,223 (93.1)	757 (94.3)	.16
Education, n (%)[d]				
Low	288 (39.5)	529 (40.2)	210 (26.2)	<.001
Moderate	335 (46.0)	589 (44.8)	364 (45.4)	
High	106 (14.5)	198 (14.3)	228 (28.4)	
Socioeconomic status score, n (%)[e]				
Low	403 (55)	535 (40.4)	139 (17.2)	<.001
Moderate	224 (30.6)	536 (42)	295 (36.5)	
High	106 (14.5)	234 (17.7)	374 (46.3)	
Katz-15 score, mean ± SD (range 0–15)	1.60 ± 2.29	1.73 ± 2.22	1.74 ± 2.36	.40
EuroQol-5D questionnaire, Dutch version score, mean ± SD (range –0.59–1.00)	0.75 ± 0.23	0.73 ± 0.24	0.75 ± 0.22	.09
Self-reported quality of life, mean ± SD (range 0–10)	7.2 ± 1.3	7.1 ± 1.3	7.2 ± 1.3	.21
RAND-36, mean ± SD (range 0–100)				
Physical	58.9 ± 29.6	56.8 ± 29.4	59.8 ± 30.0	.06
Mental	68.5 ± 19.5	69.2 ± 19.1	71.6 ± 17.9	.002
Social	43.8 ± 10.8	42.8 ± 11.5	43.5 ± 10.2	.09
Vitality	55.7 ± 20.6	55.6 ± 20.2	57.5 ± 19.3	.09
Frailty Index score, median (IQR) (range 0–1)	0.06 (0.02–0.10)	0.08 (0.04–0.10)	0.08 (0.06–0.12)	<.001
Number of chronically used medication during last year, median (IQR)	6 (5–8)	7 (5–8)	6 (5–8)	<.001
Consultation gap, days, median (IQR)	29 (13–64)	35 (21–64)	23 (10–50)	<.001

IQR = interquartile range; SD = standard deviation.

Percentages represent valid percentages. *P*-values for continuous outcomes were calculated using analysis of variance. *P*-values for categorical variables were calculated using Kruskal–Wallis test. *P*-values for dichotomous outcomes were calculated using the chi-square test.

[a]N = 11 practices, n = 790 participants.

[b]N = 13 practices, n = 1,446 participants.

[c]N = 11 practices, n = 856 participants.

[d]Low = primary school or less, moderate = secondary school, high = more than secondary school.

[e]Based on ZIP code.

significant better preservation of daily functioning than all participants in the screening and control groups (Table 2).

Secondary Outcomes

No statistically significant differences were observed between the three groups with respect to quality of life and satisfaction with care at 6- or 12-month follow-up (Table 3). These participants consulted their general practice more frequently than participants in the other groups (by telephone, $P = .001$; in-practice consultations and home-visits, $P = .01$; Table 4). No statistically significant differences in number of hospital admissions, number of ED visits, or mortality were observed. Multivariate analysis of nursing home admissions (n = 32) and admissions to an assisted-living facility (n = 62) was not possible because of the small number of events. Whether polypharmacy and level of frailty index were modifying factors of the intervention was tested, but the associations were not statistically significant, which indicated that the effect did not differ between participants with different frailty levels ($P = .29$).

DISCUSSION

In this large-scale cluster-randomized trial, a frailty screening instrument to identify older adults at risk of adverse events based on routine primary care data and the subsequent application of personalized nurse-led care did not demonstrate a clear and convincing effect on daily

Table 2. Estimated Katz-6 and Katz-15 Scores at 6 and 12 Months

	6-Month Follow-Up			12-Month Follow-Up			
	Screening	Screening Plus Nurse-Led Care	Usual Care	Screening	Screening Plus Nurse-Led Care	Usual Care	
Outcome	Mean (95% Confidence Interval)						*P*-Value
Katz-6 (range 0–6)	0.49 (0.46–0.53)	0.54 (0.50–0.59)	0.54 (0.50–0.59)	0.55 (0.50–0.61)	0.58 (0.53–0.62)	0.67 (0.61–0.73)	.02[a]
Katz-15[c] (range 0–15)	1.69 (1.61–1.78)	1.70 (1.59–1.80)	1.75 (1.67–1.82)	1.87 (1.76–1.97)	1.88 (1.80–1.96)	2.03 (1.93–2.13)	.03[a]
Katz-15	2.25 (2.11–2.39)	2.22 (2.11–2·.3)	2.47 (2.29–2.65)	2.50 (2.31–2.69)	2.46 (2.34–2.58)	2.71 (2.51–2.91)	.003
Education—low							.03[b]
Education–moderate	1.54 (1.44–1.63)	1.65 (1.51–1.79)	1.60 (1.47–1.73)	1.68 (1·.4–1.81)	1.82 (1.70–1.93)	1.78 (1.63–1.93	.20[b]
Education–high	1.14 (0.98–1.31)	0.91 (0.78–1.05)	0.88 (0.79–0.98)	1.26 (1.04–1.47)	1.01 (0.83–1.18)	1.40 (1.19–1.61)	<.001[a]

The highest significance level of *P*-values is reported: [a]*P*-value for interaction of intervention with time; [b]*P*-value for intervention. Results pairwise comparison: screening vs control: $P = .06$; screening plus nurse-led care vs control, $P = .04$: screening vs screening plus nurse-led care, $P = .98$. [c]Adjusted for baseline, age, sex, socioeconomic status, education, frailty index, polypharmacy, consultation gap, and practice size.

functioning after 1 year of follow-up. Although the participants in both of the intervention groups had statistically significant less decline in daily functioning than control group participants, the differences were small, and the clinical relevance of these results is uncertain. No overall differences in the quality of life or healthcare consumption were observed, except that participants in the screening followed by the nurse-led care group consulted their general practice more often than the participants in the other two groups. This may be because the nurses detected undiscovered health problems.

The hypothesis that both of the interventions would be synergistic and that the combined intervention would result in a more-beneficial effect than screening alone did not hold.[13] The additional benefit of screening followed by nurse-led care was observed only in a subgroup of highly educated people, and the Katz-15 score nearly tripled (0.39 points), whereas the benefit of screening alone remained in the same range (0.14 points). This suggests that the effectiveness of this intervention is related to individual characteristics. Educational level is associated with health-related and psychosocial factors[37] in older adults.[38] Furthermore, it was hypothesized that educational level is related to health literacy and communication skills, which affects the quality of the patient–doctor relationship, resulting in better adherence,[39] more-customized care, and better outcomes.[40] A priori, it was hypothesized that the intervention might have a different effect on the oldest adults or the level of frailty, but no such effects were observed (results not shown).

The current study is unique in its robust design and magnitude. To the best of the authors' knowledge, this is the largest three-arm cluster-randomized trial in primary care to evaluate the effectiveness of a proactive personalized care program for older people. In the design, recruitment, and evaluation stages, the recommendations of trials aimed at preventing or delaying functional declines in older people were followed.[7] This strategy was implemented in routine primary care, and exclusion criteria were minimized to improve generalizability. To maintain a single-blind design, a modified informed consent procedure was used to reduce selection bias and dropout in the control group. An innovative frailty screening intervention based on existing EMR primary care data was developed following recommendations in the literature.[8,18] This intervention included a frailty index that predicts adverse health outcomes in older people[16] and can be implemented in daily practice, although validation in other settings and countries is needed. Experienced nurses and GPs and a panel of older persons developed the nurse-led care intervention, which was feasible and acceptable in daily practice.[22] To enhance the delivery of the intervention, the nurses participated in monthly training meetings during the trial to improve fidelity.

Some methodological aspects should be considered. First, an a priori formal power calculation was not possible, and the suggested sample size of 5,000 participants proved unattainable. Of the 7,638 eligible participants, only 41% participated. Although responders did not differ from nonresponders in most aspects, selective inclusion cannot be excluded. To reduce selective inclusion, maximal efforts were made to include frail people (i.e., the nurses and research assistants offered assistance when needed). Second, a relatively independent population was included. Approximately 60% of the participants had a baseline Katz-15 score of 0 or 1, indicating that the majority were (almost) fully independent. Consequently, these individuals had little room for improvement. Although broad selection criteria were chosen to ensure that no older people were missed, GPs indicated that older people with poor cognitive function were less likely to be included. Third, despite the frequent use of self-report ADL and IADL scales, they lack sensitivity for detecting small changes and have considerable floor effects.[41,42] Fourth, the observed effectiveness in the screening followed by nurse-led care intervention group may be an underestimation of the true effect. In this group, a two-step approach was used to identify frail elderly, as recommended previously.[7] In the first step, participants at risk for frailty were identified using a screening procedure based on EMR data. In the next step, the nurse performed a more-detailed frailty assessment in this group using the GFI questionnaire. Based on this two-step frailty assessment, 62.9% (n = 835) of the participants in this group were identified as frail

Table 3. Estimated Quality of Life and Satisfaction with Care Scores at 6 and 12 Months

Outcome	6-Month Follow-Up			12-Month Follow-Up				
	Screening	Screening Plus Nurse-Led Care	Usual Care	Screening	Screening Plus Nurse-Led Care	Usual Care	*P*-Value	Corrected *P*-Value[a]
	Mean (95% Confidence Interval)							
RAND-36 (range 0–100)								
Physical	59.5 (58.0–60.5)	59.5 (58.6–60.3)	58.4 (57.4–59.4)	57.2 (55.5–58.8)	58.3 (57.3–59.3)	56.6 (55.1–58.1)	.13[b]	.50
Social	42.5 (41.7–43.3)	43.0 (42.3–43.8)	42.6 (41.6–43.6)	42.5 (41.6–43.4)	42.7 (42.1–43.2)	42.3 (41.7–42.9)	.54[b]	>.99
Mental	70.7 (69.8–71.6)	70.2 (69.4–71.1)	69.9 (69.0–70.8)	68.9 (67.7–70.0)	69.7 (69.0–70.4)	68.3 (67.5–69.2)	.11[b]	.50
Vitality	56.7 (55.5–58.0)	56.7 (55.8–57.6)	56.6 (55.5–57.6)	56.3 (55.4–57.3)	56.0 (55.1–56.9)	55.0 (53.7–56.3)	.10[c]	.50
EuroQol-5D questionnaire, Dutch version (range −0.59–1.00)	0.75 (0.7–0.8)	0.78 (0.7–0.8)	0.8 (0.7–0.8)	0.7 (0.7–0.8)	0.7 (0.7–0.8)	0.7 (0.7–0.8)	.54[c]	>.99
Quality of life (range 0–10)	7.2 (7.1–7.3)	7.2 (7.2–7.3)	7.2 (7.1–7.2)	7.2 (7.1–7.3)	7.2 (7.1–7.3)	7.1 (7.0–7.2)	.02[b]	.14
Satisfaction with care (range 0–10)	7.9 (7.8–8.0)	8.1 (8.0–8.1)	8.02 (8.0–8.1)	7.8 (7.7–8.0)	8.0 (7.9–8.1)	7.9 (7.8–8.0)	.05[b]	.29

Adjusted for baseline, age, sex, socioeconomic status, education, frailty index, polypharmacy, consultation gap, and practice size. [a]Corrected *P*-value for multiple testing using Holm correction. The highest significant level of *P*-values is reported: [b]*P*-value for interaction of intervention with time; [c]*P*-value for intervention.

and received the nurse-led care, although the total intervention group was analyzed to compare these participants with participants in the other groups. Furthermore, because GPs in the control group were not blinded, they may have upgraded their usual care, resulting in diminished effectiveness of the intervention. Finally, a follow-up period of 1 year was probably too short to observe maximum benefit. Given the observed trend of increasing effect over time, treatment effects may be more pronounced after longer follow-up. Moreover, full and adequate implementation in daily practice requires time; the nurses reported a learning curve in provision of the intervention and acknowledged that it was initially difficult.[27]

No three-arm cluster-randomized trials in the literature that evaluated the effectiveness of screening and a nurse-led intervention program on daily functioning concurrently were identified and no studies that identified individuals at risk based on existing GP patient record data. Several systematic reviews and meta-analyses have been conducted comparing preventive programs aimed at preventing functional decline in frail older people in the community, but the results are inconclusive.[10,42] The results of the current trial are in line with a meta-analysis that found a small but significant change in pooled ADL outcomes favoring the intervention and a comparable, although not statistically significant, change in IADL outcomes in a general (unselected) community-dwelling population and in individuals at risk of decline.[42] Although several two-arm trials with comparable interventions aimed at preventing functional decline in community-dwelling older adults were conducted, variation in outcomes measures for ADLs and IADLs and in the selection criteria for frailty are substantial.[10,11,42–46] Moreover, the heterogeneity of the interventions and the failure of many trials to fully describe the components of the intervention make comparison difficult.[42] It has been reported that an in-home visit program conducted by nurses reduced ADL disability in older adults at low risk of decline, but not in those at high risk, after 3 years of follow-up.[11] Another study evaluated the effectiveness of an interdisciplinary primary care approach for frail older adults in a randomized trial of 270 participants aged 75 and older and found no beneficial effects on disability (measured using the Groningen Activity Restricted Scale) or healthcare use after 24 months.[44] The authors proposed possible explanations for the lack of effects; the study population may have been too frail, not all intervention components were implemented as planned, and the high level of standard health care in the Netherlands may have created a ceiling effect.[44] In the current study, a much larger sample was included, with a relatively young age threshold of 60, a lower frailty threshold, and a different outcome measure on functioning, which may explain the difference in the primary outcome. One trial was found that used the modified Katz-15 scale as a secondary outcome. The effectiveness of a geriatric care model for frail older adults in primary care evaluated in that stepped-wedge cluster-randomized trial demonstrated a small intervention effect on IADLs after 18 months of follow-up.[47] Despite the fact that ADLs and IADLs are commonly used outcome measures, different instruments are used, making small changes over time difficult to detect.[41,42] Moreover, the minimally important differences necessary to interpret the

Table 4. Rates of Healthcare Consumption and Mortality After 12 Months of Follow-Up

Healthcare Consumption and Mortality	Screening	Screening Plus Nurse-Led Care	Usual Care	*P*-Value	Corrected *P*-Value[a]
	Mean Rate (95% CI)				
Consultations in general practice and home visits[b]	7.02 (6.20–7.94)	9.34 (8.17–10.68)	7.12 (6.00–8.46)	.002	.01
Telephone consultations with general practice[b]	2.76 (2.16–3.51)	4.27 (3.71–4.91)	2.66 (2.01–3.53)	<.001	.001
General practice out-of-hours consultation[b]	0.77 (0.63–0.95)	0.96 (0.78–1.19)	0.98 (0.81–1.17)	.18	.72
Number hospital admission[b]	0.29 (0.25–0.35)	0.27 (0.24–0.31)	0.33 (0.29–0.39)	.26	.78
Emergency department visits[c]	0.12 (0.07–0.18)	0.10 (0.07–0.15)	0.14 (0.10–0.21)	.49	.98
Mortality, adjusted for age	0.002 (0–0.01)	0.003 (0–0.01)	0.004 (0.001–0.2)	.70	.98

[a]Corrected *P*-value for multiple testing using Holm correction.
[b]Adjusted for baseline, age, sex, education, socioeconomic status (SES), frailty index, polypharmacy, consultation gap, and practice size.
[c]Adjusted for age, sex, education, SES, frailty index, polypharmacy, consultation gap, and practice size.

clinical significance of these outcomes, as well as for the Katz-15, have not been identified.[42] In addition, the level of frailty was different between the studies. Although interventions at an early stage of frailty are promising in preventing further decline,[7] it is unknown which cutoff may lead to a successful intervention response.

The results indicate that the current intervention was suboptimal for individuals with low education, who are known to be at greater risk of adverse health outcomes.[38] The intervention needs to be further customized for this subgroup. Based on previous studies and the findings of the current study, it is likely that interventions implemented at an early stage of decline and targeted at risk factors for specific functional difficulties are most promising.[11] An integrated approach and strong multidisciplinary collaboration between GPs, nurses, and other healthcare professionals seem to be other important ingredients of success. A good relationship and an understanding of the individual's needs are important prerequisites for the acceptance of personalized care by older adults.[48,49]

In conclusion, a screening intervention that used routine primary care data and was followed by a personalized nurse-led care intervention did not have a clear and convincing effect on daily functioning after 1 year of follow-up. Despite the statistically significant effect, the clinical relevance is uncertain because of the small differences. Better customizing of the intervention to the individual, combined with prolonged follow-up, may lead to more-robust outcomes. Future studies are needed to identify the target population that will benefit most and to determine the optimal combination and intensity of the intervention components to match the individual needs of older people.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the participants and their caregivers, GPs, and nurses.

U-PROFIT was supported by a grant from The Netherlands Organization for Health Research and Development (311040201) as part of the National Care for the Elderly Program.

Conflict of Interest: None of the authors have declared any conflict of interest.

Author Contributions: MJS, MEN, NJW: study design, obtaining funding. MEN, ID, NJW: developing the U-PRIM intervention. MJS, NB, VHD: developing the nurse-led care intervention. NB, ID, VHD, MJS, MEN, NJW: implementation of the program in clinical practice. NB, ID: data collection and cleaning. NB, NPZ, ID: clinical analyses. All authors: interpretation of findings, preparation of report, approval of final version.

Sponsor's Role: The sponsors approved the study design but were not involved in data collection, analysis and interpretation, or writing the report. There were no financial relationships with any organizations that might have an interest in or have influenced the submitted the manuscript.

REFERENCES

1. Lacas A, Rockwood K. Frailty in primary care: A review of its conceptualization and implications for practice. BMC Med 2012;10:4.
2. Boult C, Wieland GD. Comprehensive primary care for older patients with multiple chronic conditions. JAMA 2010;304:1936–1943.
3. CBS Statline. Health, lifestyle and care consumption [on-line]. Available at http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=03799&D1 = 20,28-36,106,277&D2 = 2,13-17,36-44&D3 = 0&D4 = a&VW=T Accessed May 16, 2011.
4. Schoen C, Osborn R, Squires D et al. New 2011 survey of patients with complex care needs in eleven countries finds that care is often poorly coordinated. Health Aff (Millwood) 2011;30:2437–2448.
5. Bodenheimer T. The future of primary care: Transforming practice. N Engl J Med 2008;359:2089.
6. Prevention in the Elderly. Focus on Functioning in Daily Life. The Hague: Dutch Health Council of the Netherlands, 2009.
7. Ferrucci L, Guralnik JM, Studenski S et al. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: A consensus report. J Am Geriatr Soc 2004;52:625–634.
8. Clegg A, Young J, Iliffe S et al. Frailty in elderly people. Lancet 2013;381:752–762.
9. Boult C, Reider L, Leff B et al. The effect of guided care teams on the use of health services: Results from a cluster-randomized controlled trial. Arch Intern Med 2011;171:460–466.
10. Beswick AD, Rees K, Dieppe P et al. Complex interventions to improve physical function and maintain independent living in elderly people: A systematic review and meta-analysis. Lancet 2008;371:725–735.
11. Stuck AE, Minder CE, Peter-Wüest I et al. A randomized trial of in-home visits for disability prevention in community-dwelling older people at low and high risk for nursing home admission. Arch Intern Med 2000;160:977–986.
12. Daniels R, van Rossum E, de Witte L et al. Interventions to prevent disability in frail community-dwelling elderly: A systematic review. BMC Health Serv Res 2008;8:278.
13. Bleijenberg N, Drubbel I, ten Dam VH et al. Proactive and integrated primary care for frail older people: Design and methodological challenges of the Utrecht primary care PROactive Frailty Intervention Trial (U-PROFIT). BMC Geriatr 2012;12:16.

14. Denktas S, Koopmans G, Birnie E et al. Ethnic background and differences in health care use: A national cross-sectional study of native Dutch and immigrant elderly in the Netherlands. Int J Equity Health 2009;8:35.
15. Boter H, van Delden JJM, de Haan RJ et al. Modified informed consent procedure: Consent to postponed information. BMJ 2003;327:284–285.
16. Drubbel I, de Wit NJ, Bleijenberg N et al. Prediction of adverse health outcomes in older people using a frailty index based on routine primary care data. J Gerontol A Biol Sci Med Sci 2013;68A:301–308.
17. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. ScientificWorldJournal. 2001;1:323–336.
18. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. Clin Geriatr Med 2011;27:17–26.
19. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC Classification and DDD Assignment 2011. Oslo: Norwegian Institute of Public Health, 2010.
20. Jorgensen T, Johansson S, Kennerfalk A et al. Prescription drug use, diagnoses, and healthcare utilization among the elderly. Ann Pharmacother 2001;35:1004–1009.
21. Mosqueda L, Dong X. Elder abuse and self-neglect: "I don't care anything about going to the doctor, to be honest." JAMA 2011;306:532–540.
22. Bleijenberg N, ten Dam VH, Drubbel I et al. Development of a proactive care program (U-CARE) to preserve physical functioning of frail older people in primary care. J Nurs Scholarsh 2013;45:230–237.
23. Steverink N, Slaets J, Schuurmans H et al. Measuring frailty. Development and testing of the Groningen Frailty Indicator (GFI). Gerontologist 2001;41:236–237.
24. Peters LL, Boter H, Buskens E et al. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. JAMDA 2012;13:546–551.
25. Wild B, Lechner S, Herzog W et al. Reliable integrative assessment of health care needs in elderly persons: The INTERMED for the Elderly (IM-E). J Psychosom Res 2011;70:169–178.
26. Peters LL, Boter H, Slaets JP et al. Development and measurement properties of the self-assessment version of the INTERMED for the elderly to assess case complexity. J Psychosom Res 2013;74:518–522.
27. Bleijenberg N, Ten Dam VH, Steunenberg B et al. Exploring the expectations, needs and experiences of general practitioners and nurses towards a proactive and structured care programme for frail older patients: A mixed-methods study. J Adv Nurs 2013;69:2262–2273.
28. Weinberger M, Samsa GP, Schmader K et al. Comparing proxy and patients' perceptions of patients' functional status: Results from an outpatient geriatric clinic. J Am Geriatr Soc 1992;40:585–588.
29. Laan W, Zuithoff N, Drubbel I et al. Validity and reliability of the Katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. J Nutr Health Aging 2014;18:848–854.
30. Katz S, Ford AB, Moskowitz RW et al. Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. JAMA 1963;185:914–919.
31. Vander Zee KI, Sanderman R, Heyink JW et al. Psychometric qualities of the RAND 36-item health survey 1.0: A multidimensional measure of general health status. Int J Behav Med 1996;3:104–122.
32. Krabbe PF, Stouthard ME, Essink-Bot ML et al. The effect of adding a cognitive dimension to the EuroQol multiattribute health-status classification system. J Clin Epidemiol 1999;52:293–301.
33. Zeger SL, Liang K, Albert PS. Models for longitudinal data: A generalized estimating equation approach. Biometrics 1988;44:1049–1060.
34. Zeger SL, Liang K. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986;42:121–130.
35. Twisk JW. Applied Multilevel Analysis: A Practical Guide for Medical Researchers. Cambridge, UK: Cambridge University Press, 2006.
36. Levin B. On the Holm, Simes, and Hochberg multiple test procedures. Am J Public Health 1996;86:628–629.
37. Etman A, Burdorf A, Van der Cammen TJM, et al. Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. J Epidemiol Community Health 2012;66:1116–1121.
38. Barnett K, Mercer SW, Norbury M et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. Lancet 2012;380:37–43.
39. Willems S, De Maesschalck S, Deveugele M et al. Socio-economic status of the patient and doctor–patient communication: Does it make a difference? Patient Educ Couns 2005;56:139–146.
40. Aelbrecht K, Rimondini M, Bensing J et al. Quality of doctor–patient communication through the eyes of the patient: Variation according to the patient's educational level. Adv Health Sci Educ Theory Pract 2015;20:873–884.
41. White DK, Wilson JC, Keysor JJ. Measures of adult general functional status: SF-36 physical functioning subscale (PF-10), Health Assessment Questionnaire (HAQ), Modified Health Assessment Questionnaire (MHAQ), Katz Index of Independence in Activities of Daily Living, Functional Independence Measure (FIM), and Osteoarthritis-Function-Computer Adaptive Test (OA-function-CAT). Arthritis Care Res (Hoboken) 2011;63(Suppl 11): S297–S307.
42. Lin JS, Whitlock EP, Eckstrom E et al. Challenges in synthesizing and interpreting the evidence from a systematic review of multifactorial interventions to prevent functional decline in older adults. J Am Geriatr Soc 2012;60:2157–2166.
43. Markle-Reid M, Weir R, Browne G et al. Health promotion for frail older home care clients. J Adv Nurs 2006;54:381–395.
44. Metzelthin SF, van Rossum E, de Witte LP et al. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: Cluster randomised controlled trial. BMJ 2013;347: f5264.
45. Fairhall N, Sherrington C, Kurrle SE et al. Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: Randomised controlled trial. BMC Med 2012;10:120.
46. Imhof L, Naef R, Wallhagen MI et al. Effects of an advanced practice nurse in-home health consultation program for community-dwelling persons aged 80 and older. J Am Geriatr Soc 2012;60:2223–2231.
47. Hoogendijk EO, van der Horst Henriëtte E et al. Effectiveness of a geriatric care model for frail older adults in primary care: Results from a stepped wedge cluster randomized trial. Eur J Intern Med 2016;28:43–51.
48. Bayliss EA, Edwards AE, Steiner JF et al. Processes of care desired by elderly patients with multimorbidities. Fam Pract 2008;25:287.
49. Bleijenberg N, Boeije HR, Onderwater AT et al. Frail older adults' experiences with a proactive, nurse-led primary care program: A qualitative study. J Gerontol Nurs 2015;41:20–29.
50. Suijker JJ, Buurman BM, ter Riet G et al. Comprehensive geriatric assessment, multifactorial interventions and nurse-led care coordination to prevent functional decline in community-dwelling older persons: Protocol of a cluster randomized trial. BMC Health Serv Res 2012;12:85.
51. Lingsma H, Roozenbeek B, Steyerberg E et al. IMPACT investigators. Covariate adjustment increases statistical power in randomized controlled trials. J Clin Epidemiol 2010;63:1391; author reply 1392–1393.

APPENDIX. POST HOC POWER CALCULATION

A scenario with a difference of 0.2 between the screening and control group and a difference of 0.5 between the screening and nurse-led care and control group after 12 months was hypothesized. Because the intraclass correlation coefficient (ICC) for a primary care program such as in this study is not documented, an ICC value of 0.05 was hypothesized. With a significance level of 5%, 90% power, and a cluster size of 60 participants, this would result in a sample size of 4,788. The hypothesized value of the ICC for the sample size calculation was somewhat higher than a recently reported value of 0.015[50] and the observed value of 0.03 in this study. These values were not available when this study was designed.

Given that all values used for this calculation were highly speculative, it was decided not to construct a sample size based on speculative data but instead to explain this in article and the protocol paper. Furthermore, repeated measurements and correction for the primary outcome at baseline were not included. With a response rate of 41%, more than 3,000 individuals we included. The correction for known confounders influenced the significance of the findings. In particular, the baseline measurements of the outcome reduced the sample size needed, a phenomenon well described in the methodological literature[51], although the observed effect was lower than the effect provided in the scenario when designing the trial. To illustrate the point of baseline correction further, sample size calculations were performed for the presented

outcomes after 12 months with proc power in SAS, a procedure that allows for sample size calculation with (and without) correction for known confounders (without cluster correction). In a scenario in which correction for baseline was not included, the sample size required for a significance level of .05 with a power of 0.80 would have been 12,504, but after correction for baseline Katz-15, this sample size was reduced to 170, largely because of the high correlation of 0.83 between the Katz-15 at baseline and after 12 months.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Estimated Daily Functioning, Quality of Life and Satisfaction with Care Scores at 6 and 12 Months, Crude and Adjusted Analyses

Table S2. Healthcare Consumption and Mortality After 12 Months of Follow-Up

Please note: Wiley-Blackwell is not responsible for the content, accuracy, errors, or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.