Cost-Effectiveness of a Proactive Primary Care Program for Frail Older People: A Cluster-Randomized Controlled Trial

Bleijenberg, N.; Drubbel, I.; Neslo, R.E.; Schuurmans, M.J.; Dam, V.H. ten; Numans, M.E.; ... ; Wit, N.J. de

JAMDA 18 (2017) 1029–1036

JAMDA

journal homepage: www.jamda.com

Original Study

Cost-Effectiveness of a Proactive Primary Care Program for Frail Older People: A Cluster-Randomized Controlled Trial

Nienke Bleijenberg RN, PhD [a,*], Irene Drubbel MD, PhD [a], Rabin EJ. Neslo PhD [b], Marieke J. Schuurmans RN, PhD [c], Valerie H. ten Dam MD, PhD [a], Mattijs E. Numans MD, PhD [d], G. Ardine de Wit PhD [b,d], Niek J. de Wit MD, PhD [a]

[a] *Department of General Practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands*
[b] *Department Health Technology Assessment, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands*
[c] *Department of Nursing Science, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands*
[d] *Department of General Practice, Leiden University Medical Center (LUMC), Leiden, The Netherlands*

Keywords:
Cost-effectiveness analysis
general practice
frailty
older people
cluster-randomized controlled trial

A B S T R A C T

Background: A proactive integrated approach has shown to preserve daily functioning among older people in the community. The aim is to determine the cost-effectiveness of a proactive integrated primary care program.
Methods: Economic evaluation embedded in a single-blind, 3-armed, cluster-randomized controlled trial with 12 months' follow-up in 39 general practices in the Netherlands. General practices were randomized to one of 3 trial arms: (1) an electronic frailty screening instrument using routine medical record data followed by standard general practitioner (GP) care; (2) this screening instrument followed by a nurse-led care program; or (3) usual care. Health resource utilization data were collected using electronic medical records and questionnaires. Associated costs were calculated. A cost-effectiveness analysis from a societal perspective was undertaken. The incremental cost per quality-adjusted life-year was calculated comparing proactive screening arm with usual care, and screening plus nurse-led care arm with usual care, as well as the screening arm with screening plus nurse-led care arm.
Results: Out of 7638 potential participants, 3092 (40.5%) older adults participated. Whereas effect differences were minor, the total costs per patient were lower in both intervention groups compared with usual care. The probability of cost-effectiveness at €20,000 per QALY threshold was 87% and 91% for screening plus GP care versus usual care and for screening plus nurse-led care compared to usual care, respectively. For screening plus nurse-led care vs screening plus standard GP care, the probability was 55%.
Conclusion: A proactive screening intervention has a high probability of being cost-effective compared to usual care. The combined intervention showed less value for money.

Worldwide, the number of people aged 60 years and older will rise from 600 million in 2000 to approximately 2 billion in 2050.[1] A substantial number of these older people will experience frailty, that is, an increased risk of adverse health outcomes.[2] Frail older people often have multiple chronic diseases and limitations in their activities of daily living.[3,4] With their resulting complex care needs, the elderly population places a large burden on health care resources.[5] In the United States, total health care expenditures for people aged 65 were $368 billion in 2008, which was almost one-third of the total health care budget.[6] For people with 5 or more chronic diseases, health care spending is often 14 times higher than for people without any chronic disease.[7]

Nienke Bleijenberg and Irene Drubbel contributed equally to the study.
The authors declare no conflicts of interest.
The Utrecht Proactive Frailty Intervention Trial (U-PROFIT) was supported by a grant from the Netherlands Organization for Health Research and Development (reference 311040201) as part of the National Care for the Elderly Programme. The sponsors approved the study design but were not involved in the data collection, analysis, and interpretation or in writing of the report. The authors had full access to all data as well as the final responsibility for the submission of the manuscript.
* Address correspondence to Nienke Bleijenberg, RN, PhD, University Medical Center, Heidelberglaan 100, 3508 GA Utrecht, The Netherlands.
E-mail address: n.bleijenberg@umcutrecht.nl (N. Bleijenberg).

http://dx.doi.org/10.1016/j.jamda.2017.06.023

In the Netherlands, €33 billion (37%) of the total 2011 health care budget of €89 billion was spent on care for people aged 65 years and older.[8] Because health care costs for older people place a major burden on society, the efficient delivery of care is important to ensure that as many positive health effects as possible are realized for the money invested.

Most care needs of older people are addressed in primary care. As gatekeepers to the health care system, general practitioners (GPs) resolve more than 90% of the health problems in the overall population.[9] Based on the integrated, patient-centered approach and the long-lasting relationship with their patients, GPs have a key role in the provision and coordination of care for frail older patients.[10] However, at present, the care for older people in general practice is reactive and fragmented, and the care needs of frail older people are not adequately met.[11,12] A paradigm shift is needed from reactive care, in which GPs respond to emerging health problems of the high-needs, high-cost individual a more proactive, population-based care provision.[13,14]

The current evidence for the cost-effectiveness of proactive primary care for older people is scarce and difficult to compare across studies.[15,16] We designed and implemented a strategy for proactive primary health care for older people consisting of the systematic identification of frail older people, and a subsequent nurse-led, proactive, and personalized care program.[17] The strategy demonstrated a small but significant effect in delaying functional decline in the elderly population at 1-year follow-up.[18] The aim of the present study was to evaluate the cost-effectiveness of the Utrecht Proactive Frailty Intervention Trial (U-PROFIT) strategy and its separate intervention components.

Method

The U-PROFIT Trial

Design clinical trial

The economic evaluation was performed using data collected alongside the U-PROFIT trial, which has been described elsewhere in detail.[19] In brief, we conducted a single-blind, 3-armed, cluster-randomized controlled trial in 39 general practices in the Utrecht region of the Netherlands. These general practices provide primary health care to approximately 44,000 patients aged 60 years and older. In this trial, we evaluated the effectiveness of the frailty screening instrument followed by standard GP care, and that of the screening followed by a nurse-led proactive care program on the level of daily functioning among frail, community-dwelling older people compared with the usual primary care. The U-PROFIT trial was approved by the Institutional Review Board of the University Medical Center Utrecht (protocol ID 10-149/O).

Interventions

Arm 1. The frailty screening intervention consists of a software application that identifies patients at risk for frailty by screening routine electronic medical record (EMR) data from general practices. Patients aged 60 years and older were considered potentially frail and included in a quarterly report when they met at least 1 of the following criteria: a frailty index $\geq$0.20,[20,21] polypharmacy of $\geq$5 medications in chronic use, or a consultation gap (at least 3 years without general practice consultation except for the annual influenza vaccination).[22] In the screening plus standard GP care arm, GPs were asked to use the reports proactively, following current professional guidelines. For example, GPs were able to call patients if they felt it was necessary because of the consultation gap or comorbidities. In these practices, there was no trained registered nurse to deliver the additional steps of the proactive care program.

Arm 2. In the second arm, the frailty screening was followed by the nurse-led care intervention. Twenty-one registered practice nurses were trained to deliver this proactive intervention. After the frailty screening based on EMR data, patients at risk received a self-report questionnaire to measure the level of frailty using the Groningen Frailty Indicator.[23] Next, patients who were identified as frail on the Groningen Frailty Indicator received a home-based Comprehensive Geriatric Assessment, followed by evidence-based care planning, care coordination and follow-up.[17] Care coordination and the intensity of follow-up was based on patients care needs. Evidence-based care plans were developed for 11 geriatric syndromes such as falls, urinary incontinence, mobility, and nutrition.

Arm 3. The frailty screening was also performed in the control group practices, but the report was not visible for the GPs. GPs in the control group were asked to continue their usual care, based on Dutch general practice guidelines. Most practices provided reactive care to emerging health problems. Patients need a referral from the GP to get access to secondary care or to see a medical specialist. In some control group practices, nurses provided reactive and ad hoc care to older people.

Participants

Within the participating general practices, we approached 7638 eligible patients, that is, patients aged 60 years and older who met at least 1 of the frailty selection criteria based on the EMR record data as described above. In total, 3092 patients (40.5%) provided written informed consent. 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. Flowchart of the participants is provided in Appendix A. Nonresponders were phoned and, if needed, home visits were conducted for those who experienced difficulty reading or filling in the questionnaire.

Design Cost-Effectiveness Study

For the current study, we performed an incremental cost-effectiveness analysis from a societal perspective. We compared the 2 interventions for proactive care for frail older people as evaluated in the U-PROFIT trial, that is, frailty screening followed by standard GP care and frailty screening followed by nurse-led care, with usual care as the control condition and among each other. We evaluated the costs and effects at 12 months, which is the full follow-up period of the U-PROFIT trial. Because of this time frame, discounting of costs and effects was not necessary.

Data Collection and Resource Valuation

Costs

Intervention costs. The costs of the frailty screening followed by standard GP care and the frailty screening followed by nurse-led care intervention were calculated using a bottom-up approach (Appendix B). In brief, we collected information on the time required for the interventions by the GPs and registered nurses and the related costs based on their hourly wage costs. Information on costs of electronic frailty screening start-up and maintenance, the nurse-led care educational program for the registered nurses in primary care, and an evidence-based toolkit developed and used by the nurses was collected alongside the development and implementation of both interventions. Next, we calculated the number of potentially frail older people per general practice based on the frailty screening, assuming a standard Dutch practice size of 2350 patients.[24] In a standard general practice, on average, 552 patients (23.5%) are 60 years and older.[25] Within this older population, 110 patients (20%) would be selected as potentially frail in frailty screening based on routine primary care data.[19] With these data, we converted the calculated intervention costs to "costs per potentially frail older patient per year."

Health care utilization costs and informal care costs. At 12 months, we extracted EMR data on daytime GP consultations and emergency department visits. With questionnaires at 12 months, we collected data on the number of out-of-hours GP consultations (ie, consultations with GPs during nights or weekend days and can be either in-surgery or at-home consultations), hospital admissions, permanent and temporary nursing home admissions and residences in assisted living facilities, home care, and day care.[19] With questionnaires at baseline, 6 months, and 12 months directed at the patients' informal caregivers, we gathered data on how many hours per week patients received informal care. We used the Dutch Manual for costing research in health care to value the health care resources and provision of informal care in terms of their unit costs (Table 1).[26] We indexed prices to the level of 2012.[27]

Effect measures. In the questionnaires at baseline, 6 months, and 12 months, we collected data on the patients' health status using the 3-level EuroQoL EQ-5D instrument.[28] We applied the Dutch EQ-5D tariff to calculate mean utility values for the different health states derived from the EQ-5D responses.[29]

Statistical Analysis

We performed all analyses based on an intention-to-treat principle. Using 5 factors (age, sex, marital status, frailty index, and self-rated health) to predict the missing values, we employed multiple imputations to account for missing data in the health care utilization measures and the EQ-5D.[30–32] Next, we calculated the total costs for each patient by multiplying the health care resources used by the respective unit costs. In addition, we calculated the QALYs for each patient using an area under the curve approach with linear interpolation of the EQ-5D utility values among the baseline, 6-month, and 12-month data.[33] To avoid bias in the QALY calculation, we corrected for imbalances in the baseline EQ-5D utility values using a regression-based approach.[34] Using the mean total costs and effects for each intervention arm, we calculated the incremental cost-effectiveness ratios for arm 1 and arm 2 compared with usual care (arm 3) and for arm 2 compared with arm 1.

This base case analysis was performed from a societal perspective, that is, including all assessed costs in the imputed data set and the adjusted QALYs. To estimate the uncertainty around the incremental cost-effectiveness ratios, we used bootstrapping with 1000 iterations. With these bootstrapped cost-effect pairs, we constructed cost-effectiveness planes and cost-effectiveness acceptability curves alongside a spectrum of different amounts society would be willing to pay for 1 QALY. As is common for this type of intervention in the Netherlands, we adopted a willingness to pay (WTP) of €20,000 per QALY. To examine the robustness of our results, we planned a number of sensitivity analyses: first, a sensitivity analysis from the health care perspective, that is, excluding the costs related to the provision of informal care; second, a sensitivity analysis on complete cases only; and third, a sensitivity analysis using QALYs unadjusted for baseline EQ-5D imbalances.

Results

Characteristics of the Study Population

The inclusion process and baseline characteristics of our study population have been described in detail elsewhere.[18] In brief, out of 3092 patients, 790 patients received the frailty screening intervention followed by standard GP care (arm 1), 1446 patients participated in the

Table 1
Costs of Resource Use and Utilization in the Frailty Screening, Frailty Screening + Nurse-Led Care, and Control Arm

Type of Utilization	Costs		Mean Utilization (SD)		
	Unit	Unit Cost (€)	Frailty Screening + GP Care (n = 790)	Frailty + Nurse-Led Care (n = 1446)	Control Arm (n = 856)
Interventions					
Frailty screening start-up and maintenance expenses	Per patient/year	7.10	1	1	N/A
Frailty screening usage in proactive care (direct patient consultations were valued under "health care utilization")	Per patient/year	20.90	1	1	N/A
Nurse-led care education, toolkit, website	Per patient/year	1.65	N/A	1	N/A
Nurse-led care program usage in proactive care (direct patient consultations excluded)	Per patient/year	101.30	N/A	1	N/A
Health care utilization					
GP consultations (consultations per year)	Per consultation	30.95*	7.44 (5.48)	9.62 (6.94)	9.81 (8.38)
GP consultation by telephone (consultations per year)	Per consultation	14.90*	3.18 (4.14)	4.83 (5.52)	3.53 (4.71)
Out-of-hours GP consultations (consultations per year)	Per consultation	98.30†	1.02 (1.87)	1.14 (2.21)	1.18 (2.18)
Home care (hours per week)	Per hour	37.20*	1.40 (4.36)	1.40 (2.70)	1.54 (5.15)
Nursing home (days per year)	Per day	252.75*	2.11 (20.15)	1.13 (8.88)	3.06 (16.59)
Assisted living facility (days per year)	Per day	95.60*	1.57 (12.55)	1.34 (10.04)	1.26 (10.19)
Day care (days per week)	Per day	47.80*	0.05 (0.40)	0.05 (0.40)	0.03 (0.36)
Emergency department visits (visits/year)	Per visit	160.35*	0.16 (0.46)	0.15 (0.47)	0.17 (0.50)
Hospital admission (days in hospital/year)	Per day	485.30*	2.06 (5.92)	2.14 (6.66)	2.38 (5.59)
Informal care					
Care provided by informal caregiver (hours per week)	Per hour	13.30*	2.45 (9.92)	2.73 (11.50)	2.86 (11.70)
Frailty Index score, median (IQR)			0.06 (0.02-0.10)	0.08 (0.04-0.10)	0.08 (0.06-0.12)
Number of medications during last year, median (IQR)			6 (5-8)	7 (5-8)	6 (5-8)
Consultation gap in days, median (IQR)			29 (13-64)	35 (21-64)	23 (10-50)

IQR, interquartile range; N/A, not applicable.
Values reflect the imputed data of the study sample. Values are means (SD) unless stated otherwise. All costs are indexed to 2012.
*According to the Dutch manual for costing studies (Hakkaart-van Roijen, 2011).
†According to the Dutch Healthcare Authority (www.nza.nl). See "Details Resource Valuation" for detailed information on the composition of the unit costs of the interventions, health care utilization, and informal care provision.

Table 2
Mean Total Costs and Effects of the Frailty Screening, Frailty Screening + Nurse-Led Care, and Usual Care at the 12-Month Follow-up

Variable	Mean Total Effects or Costs (SD)		
	Frailty Screening + GP Care	Frailty + Nurse-Led Care	Usual Care
Costs (€)			
Costs directly related to interventions, mean (SD)	28 (0)	131 (0)	0 (0)
Health care utilization costs, mean (SD)	4928 (11,427)	4806 (7512)	5621 (12,289)
Informal caregiver costs, mean (SD)	1695 (6861)	1888 (7950)	1980 (8092)
Total costs, mean (SD)	6651 (14,686)	6825 (11,452)	7601 (15,717)
Effects			
EQ-5D utility value (complete cases)			
Baseline, mean (SD)	0.742 (0.237)	0.725 (0.244)	0.747 (0.226)
6 months, mean (SD)	0.727 (0.254)	0.712 (0.262)	0.735 (0.256)
12 months, mean (SD)	0.707 (0.291)	0.702 (0.275)	0.721 (0.269)
EQ-5D utility value (imputed data)			
Baseline, mean (SD)	0.741 (0.231)	0.724 (0.236)	0.746 (0.221)
6 months, mean (SD)	0.726 (0.246)	0.711 (0.252)	0.731 (0.248)
12 months, mean (SD)	0.703 (0.271)	0.699 (0.258)	0.714 (0.257)
QALYs			
Imputed and unadjusted, mean (SD)	0.722 (0.225)	0.710 (0.224)	0.728 (0.223)
Imputed and adjusted, mean (SD)	0.698 (0.217)	0.709 (0.222)	0.703 (0.208)

frailty screening followed by nurse-led care intervention (arm 2), and 856 patients received care as usual (arm 3). The mean age of the study population was 73.5 years (±8.2 SD), and 55.3% was female. In total, 427 patients (13.8%) had an informal caregiver who was willing to participate in the trial by answering the questionnaires targeted at informal care provision. In arm 1, arm 2, and arm 3, 162 (20.5%), 299 (20.7%) and 142 (16.6%) patients, respectively, did not complete the 12-month follow-up.

In total, 10.4% of the EQ-5D data was missing, with 2508 patients (81.1%) having complete EQ-5D data available. For the health care utilization measures, 16.8% of the data from self-reports was missing, with 2063 patients (66.7%) having complete data available. When considering the total of 427 informal caregivers, data related to the hours of provided care were missing for 14.6% of the provided informal care, with 278 informal caregivers (65.1%) having complete data available.

Health Care Utilization, Costs, and Effects

Patients in the frailty screening followed by standard GP care arm had fewer GP consultations than patients in the other 2 arms, whereas patients in the frailty screening plus nurse-led care arm had the highest rate of GP consultations by telephone (Table 1). Furthermore, patients in the frailty screening plus nurse-led care arm spent notably fewer days in a nursing home than patients in the other 2 arms. There was also a trend toward fewer days in the hospital for both intervention arms (Table 1). Over a 12-month period, patients in both the frailty screening plus standard GP care and frailty screening plus nurse-led care arm had lower health care utilization costs (€693 and €815, respectively), compared to patients in the usual care group (costs) (Table 2). When considering costs related to the hours of informal care provided, patients in the frailty screening and frailty screening plus nurse-led care arm had less costs (€285 and €92, respectively) than patients of the usual care arm.

With intervention costs of €28 for the frailty screening followed by standard GP care and €131 for the frailty screening plus nurse-led care included, the mean total costs in the intervention groups were lower than that in the usual care group (mean costs per patient in euros ± SD) per group: frailty screening plus standard GP care arm: 6651 (14,686); frailty screening plus nurse-led care arm: 6825 (11,452); usual care: 7601 (15,717).

With regard to health effects, differences between groups were significant but small, and of questionable clinical relevance. Without adjustment for EQ-5D imbalances at baseline, patients in the frailty screening plus nurse-led care arm had the lowest QALYs. After correction for the different baseline EQ-5D scores between groups, patients in the frailty screening plus nurse-led care arm had slightly higher QALYs over the 1-year period than the patients in the frailty screening plus standard GP care arm and usual care arm (Table 2).

Table 3
Results of the Cost-Effectiveness Analyses: Frailty Screening Followed by GP Care Arm Compared With Usual Care

Analysis	Δ Cost, € (95% CI)	Δ Effect (95% CI)	Distribution Cost-Effectiveness Plane (Quadrant)				
			Northeast*	Southeast†	Southwest‡	Northwest§	Probability (%) of Cost-Effectiveness at WTP of €20,000
Base case analysis							
Societal perspective, adjusted QALYs	−951 (−2545 to 477)	−0.0047 (−0.0266 to 0.0162)	0.01	0.31	0.60	0.07	87%
Sensitivity analyses							
Health care perspective	−655 (−1761 to 455)	−0.0047 (−0.0253 to 0.0166)	0.03	0.28	0.59	0.10	80%
Unadjusted QALYs	−951 (−2482 to 435)	−0.0062 (−0.0276 to 0.0159)	0.01	0.28	0.62	0.09	84%
Complete cases (adjusted QALY)	−2251 (−6185 to 1870)	0.0025 (−0.0219 to 0.0244)	0.06	0.52	0.34	0.08	86%

Δ cost is the mean difference in the costs of 1000 bootstrapped samples. Δ effect is the mean difference in the effect of 1000 bootstrapped samples.
*Frailty screening is more effective and more costly than usual care.
†Frailty screening more effective and less costly than usual care (dominant).
‡Frailty screening is less effective and less costly than usual care.
§Frailty screening is less effective and more costly than usual care (inferior).

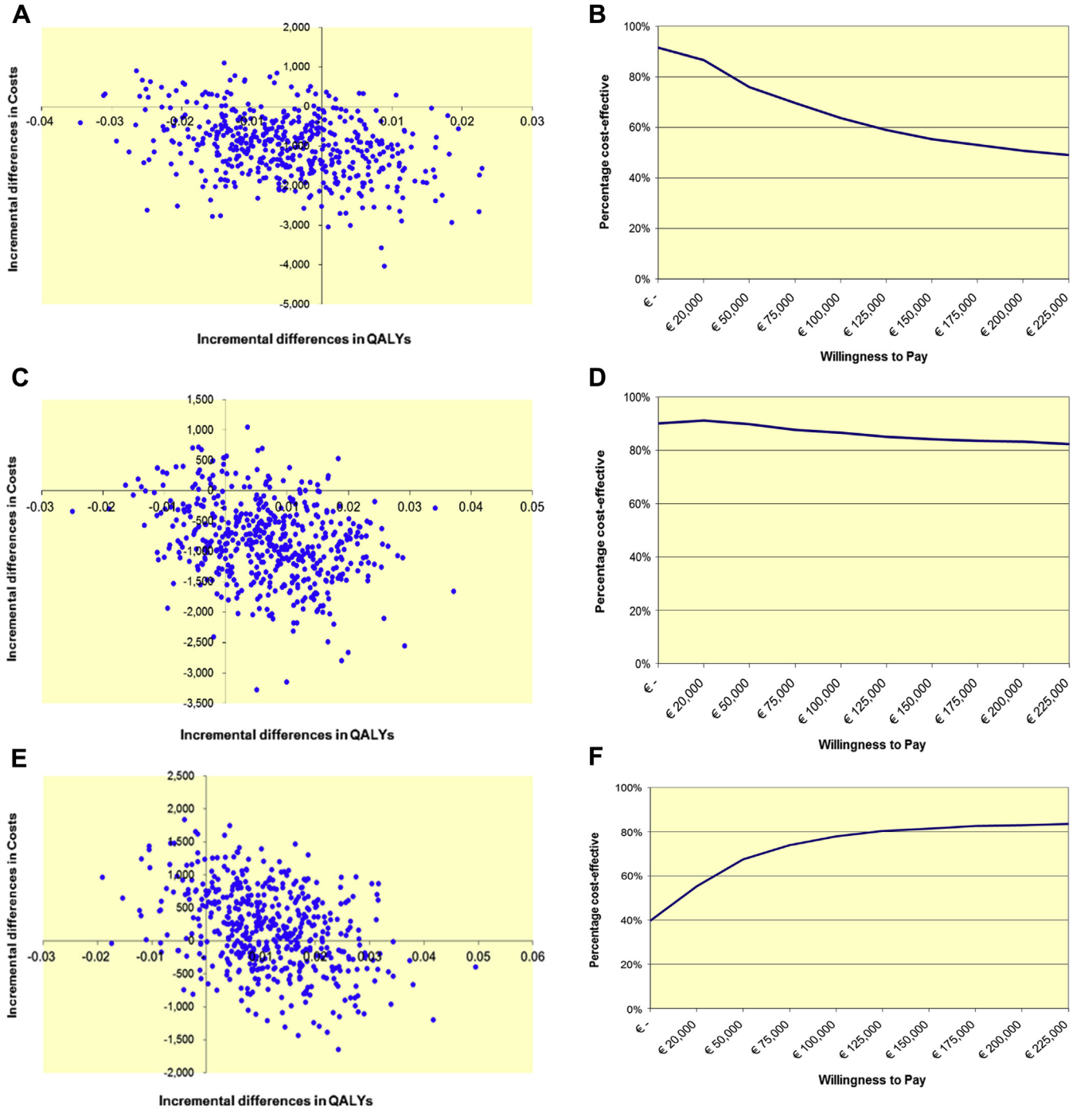


Fig. 1. Cost-effectiveness planes and cost-effectiveness acceptability curves (CEACs) for frailty screening followed by standard GP care vs usual care (A and B); frailty screening + nurse-led care vs usual care (C and D); and frailty screening + nurse-led care vs frailty screening plus standard GP care (E and F).

Cost-Effectiveness Analyses

After bootstrapping, the frailty screening intervention followed by standard GP care resulted in a cost saving of €951 [95% confidence interval (CI) −2545 to 477] and a QALY loss of 0.0047 (95% CI −0.0266 to 0.0162) compared to usual care (Table 3). Among all the bootstrapped data pairs, 60% were situated in the southwest quadrant of the cost-effectiveness plane, indicating both lower effectiveness and lower costs, whereas 31% pointed at dominance (ie, better health outcomes at lower cost). The cost-effectiveness acceptability curve demonstrated that at a WTP of €20,000, the probability of cost-effectiveness of the frailty screening intervention followed by standard GP care was 87% (Figure 1).

When the frailty screening plus nurse-led care intervention was compared to usual care, cost savings of €776 (95% CI −2025 to 350) and a QALY gain of 0.0063 (−0.0112 to 0.0243) were generated, resulting in dominance of the frailty screening plus nurse-led care intervention over usual care (Table 4). Evaluating the cost-effectiveness plane, 71% of the bootstrapped data pairs showed higher effectiveness and lower costs, that is, superiority compared with the usual care group. The probability of cost-effectiveness at a WTP of €20,000 was 91% (Figure 1).

Table 4
Results of the Cost-Effectiveness Analyses: Frailty Screening + Nurse-Led Care Arm Compared With the Usual Care Arm

Analysis	Δ Cost, € (95% CI)	Δ Effect (95% CI)	Distribution Cost-Effectiveness Plane (Quadrant)				
			Northeast*	Southeast†	Southwest‡	Northwest§	Probability (%) of Cost-Effectiveness at WTP of €20,000
Base case analysis							
Societal perspective, adjusted QALYs	−776 (−2025 to 350)	0.0063 (−0.0112 to 0.0243)	0.05	0.71	0.20	0.05	91%
Sensitivity analyses							
Health care perspective	−664 (−1671 to 211)	0.0063 (−0.0121 to 0.02614)	0.03	0.72	0.20	0.04	93%
Unadjusted QALYs	−776 (−2112 to 366)	−0.0188 (−0.0358 to 0.0009)	0.00	0.03	0.88	0.09	73%
Complete cases (adjusted QALY)	−2806 (−6335 to 196)	−0.009 (−0.0202 to 0.0203)	0.03	0.88	0.16	0.03	96%

Δ cost is the mean difference in the costs of 1000 bootstrapped samples. Δ effect is the mean difference in the effect of 1000 bootstrapped samples.
*Frailty screening + nurse-led care more effective and more costly than usual care.
†Frailty screening + nurse-led care more effective and less costly than usual care (dominant).
‡Frailty screening + nurse-led care less effective and less costly than usual care.
§Frailty screening + nurse-led careless effective and more costly than usual care (inferior).

Incremental analysis showed that addition of the nurse-led care program to the frailty screening resulted in extra costs of €175 (95% CI −1000 to 1342) and a QALY gain of 0.011 (95% CI −0.007 to 0.0312). In the cost-effectiveness plane, 51% of bootstrapped data pairs showed higher costs and higher effectiveness, whereas 37% of the data pairs showed or indicated dominance. At a WTP of €20,000, the frailty screening plus nurse-led care intervention had a probability of 55% to be cost-effective compared to the frailty screening followed by standard GP care (Table 5), which points at the fact that combined frailty screening followed by the nurse-led care intervention is less cost-effective than the frailty screening followed by standard GP care.

Sensitivity Analyses

In the comparison of frailty screening followed by standard GP care with usual care, sensitivity analyses revealed no major results that were notably different from the base case analysis (Table 3). When comparing the frailty screening plus nurse-led care intervention with usual care in the sensitivity analysis with unadjusted QALYs, the bootstrapped data pairs shifted on the cost-effectiveness plane from dominance in the base case analysis to the majority being situated in the southwest quadrant, indicating higher costs and lower benefits (Table 4). However, the probability of being cost-effective stayed relatively high at 73%. The probability of cost-effectiveness of the frailty screening plus nurse-led care intervention compared to the frailty screening intervention followed by standard GP care decreased to 30% in the sensitivity analysis with unadjusted QALYs, whereas in the analyses from a health care perspective, the probability of cost-effectiveness increased to 69% (Table 5).

Discussion

In this cost-effectiveness analysis, we demonstrated that the frailty screening intervention based on routine care data followed by standard GP care is cost-effective compared with usual primary care. However, in the comparisons of both intervention groups with the usual care group, the differences were relatively minor and of doubtful clinical relevance. The magnitude of the incremental cost-effectiveness ratio was mainly determined by the size of the cost savings. As a stand-alone intervention, the frailty screening intervention followed by standard GP care provides more value for money than the combined frailty screening plus nurse-led care intervention at 1-year follow-up.

Comparison Literature

To optimize the care for frail older persons in the community and reduce health care costs among this population, several complex multicomponent interventions have been evaluated in the last decade showing inconclusive results.[35,36] Cost-effectiveness analysis of these programs are rarely performed. A good comparison of our results with those published previously is challenging because of many reasons such as different intervention components, follow-up, perspective, and implementation practice. When comparing our results to other community-based interventions aimed to prevent disability, the results in terms of cost-effectiveness are inconclusive. Fairhall et al evaluated the (cost)-effectiveness of a multifactorial interdisciplinary intervention to reduce frailty in 216 frail older adults aged 70 and older in Australia. Their results pointed at better value for money

Table 5
Results of the Cost-Effectiveness Analyses: Frailty Screening + Nurse-Led Care Arm Compared With Frailty Screening Followed by Standard GP Care Arm

Analysis	Δ Cost (€) (95% CI)	Δ Effect (95% CI)	Distribution Cost-Effectiveness Plane (Quadrant)				
			Northeast*	Southeast†	Southwest‡	Northwest§	Probability (%) of Cost-Effectiveness at WTP of €20,000
Base case analysis							
Societal perspective, adjusted QALYs	175 (−1000 to 1342)	0.011 (−0.007 to 0.0312)	0.51	0.37	0.02	0.09	55%
Sensitivity analyses							
Health care perspective	−19 (−883 to 790)	0.011 (−0.007 to 0.0302)	0.42	0.46	0.05	0.07	69%
Unadjusted QALYs	175 (−1047 to 1354)	−0.0126 (−0.0327 to 0.0065)	0.05	0.07	0.33	0.56	30%
Complete cases (adjusted QALY)	−456 (−4033 to 2872)	0.0064 (−0.0134 to 0.0256)	0.29	0.42	0.13	0.16	58%

Δ cost is the mean difference in the costs of 1000 bootstrapped samples. Δ effect is the mean difference in the effect of 1000 bootstrapped samples.
*Frailty screening + nurse-led care more effective and more costly than frailty screening followed by standard GP care.
†Frailty screening + nurse-led care more effective and less costly than frailty screening followed by standard GP care (dominant).
‡Frailty screening + nurse-led care less effective and less costly than frailty screening followed by standard GP care.
§Frailty screening + nurse-led care less effective and more costly than frailty screening only (inferior).

compared with usual care, especially among the very frail. The probability of both cost-savings and effectiveness was high.[37] In contrast, a similar intervention was developed in Dutch elderly (N=346) aged 70 and older and showed that the intervention led to an increase in health care utilization, especially in primary care and related costs without additional benefits. The authors provide several explanations for the findings such as the relatively high standard of primary care in the Netherlands as a result of the gatekeeping function of the primary care physician and preventive care programs for chronically ill people.[36] Although overall, patients in the intervention group had less health care costs than patients in the usual care group, we observed an increased use of primary care in our study as well.

Strengths and Limitations

Our study has some limitations. First, we partly used self-reported data, which increases the risk of underreporting service use because of recall bias.[38,39] This risk may be aggravated by using questionnaires with a 12-month recall period in a vulnerable population of older people. However, because we applied a modified informed consent procedure in the U-PROFIT trial, patients were unaware of their group assignment. Therefore, we assume that the risk of underreporting is equal among the groups and unlikely to have influenced the incremental cost-effectiveness ratios. Second, to fully assess the effect of these complex interventions on health care utilization and QALYs, a longer follow-up period would have been preferable, as proactive care may pay out more profoundly in the longer run. However, for logistical reasons, such a follow-up was not feasible, and there were not enough data available in the literature to consider a modeling approach. Third, the EMR did not distinguish between actions performed by the GP and those by registered nurses. However, we resolved this issue by using previously published estimates of the time investments of GPs and nurses for the proactive primary care of older people (Appendix B). Finally, we did not take into account other effect measures. We considered a cost-effectiveness analysis using the Katz-15 index, the questionnaire on the activities of daily living, which was the primary outcome measure in the U-PROFIT trial, as an outcome parameter. However, in the absence of a threshold value for the WTP for 1 unit of improvement in activities of daily living, drawing conclusions with relevance for both policymakers and clinical practitioners would have been difficult.

The current study is unique because it was embedded in a robustly designed, large cluster-randomized controlled trial evaluating the effectiveness of proactive, personalized primary care on the level of daily functioning of frail older people. As the U-PROFIT trial was a pragmatic trial embedded within routine primary care, it closely reflected daily clinical practice, ensuring that the results of this cost-effectiveness analysis have high practical relevance. The results are highly generalizable because of the participation of a large number of diverse general practices from both rural and urban areas. We used the societal perspective, employed a multiple imputation strategy to account for missing data, corrected for baseline imbalances in the EQ-5D, used an accurate bottom-up approach to calculate the intervention costs, and performed various sensitivity analyses to evaluate the robustness of our results.

Implications for Practice

Improving care for older patients with complex care needs and multimorbidity is a high priority worldwide. Developing evidence-based integrated care programs for people at high risk that are (cost) effective is therefore crucial. Our results indicate that both interventions have a high probability of being cost-effective compared with usual primary care because of the cost-saving aspect. However, because no significant health benefits were observed, the clinical interpretation and long-term impact are unclear. Our hypothesis was that the combined intervention, that is, the frailty screening followed by the nurse-led care intervention, would result in additional benefits in terms of health and cost savings. However, adding the nurse-led care intervention to the frailty screening had a low probability to be cost-effective. Moreover, post hoc analyses showed that the intervention effect was not different for participants enrolled on each specific inclusion criteria (eg, polypharmacy, frailty index, and consultation gap). This study showed that the frailty screening intervention followed by standard GP care had the best value for money. The relatively inexpensive frailty intervention resulted in increased awareness among GPs and nurses about the presence of potentially frail older people in their patient population.[40] Adequate data registration is a prerequisite because the frailty screening is based on computerized extraction from routine care data.

The cost-effectiveness and clinical effectiveness beyond 12 months are unknown. Because the implementation of complex interventions in daily clinical practice always takes time, we hypothesize that the cost savings and effects will at least consolidate or even increase after 12 months of follow-up. However, further studies are necessary to evaluate this hypothesis.[41] Much work needs to be done to determine the effective components, and effort is needed to develop strategies that are beneficial for those at high risk and in urgent need of targeted treatment.

Acknowledgments

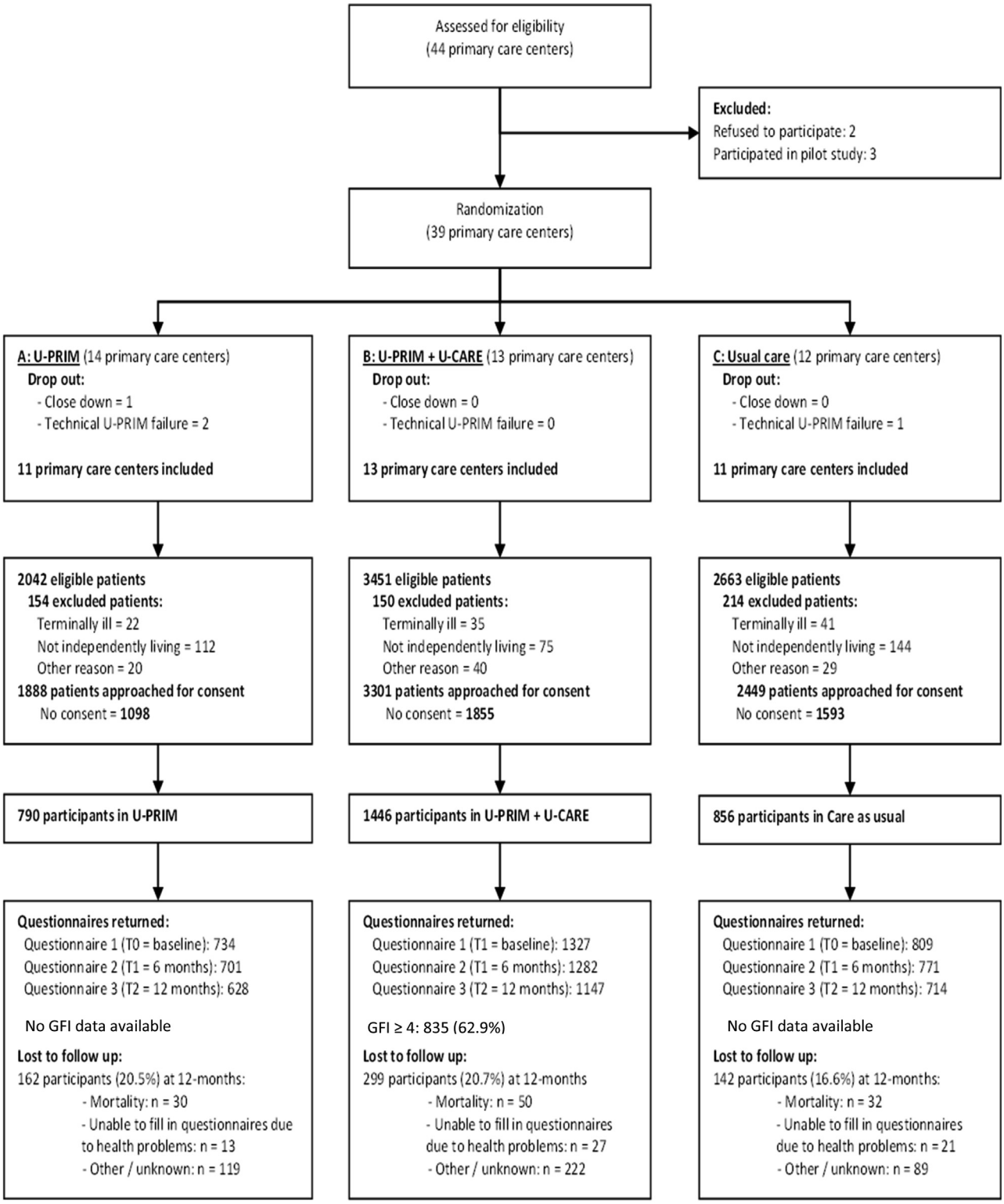
We gratefully acknowledge all patients, general practitioners, and nurses who participated in this study.

References

1. World Health Organization. 10 facts on ageing and the life course. Geneva: WHO; 2011.
2. Rodriguez-Manas L, Feart C, Mann G, et al. Searching for an operational definition of frailty: A Delphi method based consensus statement: The Frailty Operative Definition—consensus conference project. J Gerontol A Biol Sci Med Sci 2013;68:62–67.
3. Theou O, Rockwood MR, Mitnitski A, Rockwood K. Disability and co-morbidity in relation to frailty: How much do they overlap? Arch Gerontol Geriatr 2012;55:e1–e8.
4. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: A systematic review of the literature. Ageing Res Rev 2011;10:430–439.
5. Chatterji S, Byles J, Cutler D, et al. Health, functioning, and disability in older adults—Present status and future implications. Lancet 2015;385:563–575.
6. Soni A. The five most costly conditions, 1996 and 2006: Estimates for the US civilian noninstitutionalized population. Statistical Brief 248. July 2009.
7. Agency for Healthcare Research and Quality. AHRQ Quality Indicators, 2002.
8. Poos MJJC PN. Wat zijn de zorgkosten? In: Volksgezondheid toekomst verkenning, nationaal kompas volksgezondheid. Bilthoven: RIVM. 2013. Available at: http://www.nationaalkompas.nl&gt. Nationaal Kompas Volksgezondheid, Zorg.
9. Cardol M, Dijk LV, De Jong J, et al. Tweede nationale studie naar ziekten en verrichtingen in de huisartspraktijk: Huisartsenzorg: Wat doet de poortwachter?; 2004.
10. Lacas A, Rockwood K. Frailty in primary care: A review of its conceptualization and implications for practice. BMC Med 2012;10:4.
11. Bower P, Macdonald W, Harkness E, et al. Multimorbidity, service organization and clinical decision making in primary care: A qualitative study. Fam Pract 2011;28:579–587.
12. Bodenheimer T. The future of primary care: Transforming practice. N Engl J Med 2008;359:2089.
13. Margolius D, Bodenheimer T. Transforming primary care: From past practice to the practice of the future. Health Aff (Millwood) 2010;29:779–784.
14. Blumenthal D, Chernof B, Fulmer T, et al. Caring for high-need, high-cost patients—An urgent priority. N Engl J Med 2016;375:909–911.
15. Smith SM, Soubhi H, Fortin M, et al. Managing patients with multimorbidity: Systematic review of interventions in primary care and community settings. BMJ 2012;345:e5205.
16. Tappenden P, Campbell F, Rawdin A, et al. The clinical effectiveness and cost-effectiveness of home-based, nurse-led health promotion for older people: A systematic review. Health Technol Assess 2012;16:1–72.
17. 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 Sch 2013;45:230–237.
18. Bleijenberg N, Drubbel I, Schuurmans MJ, et al. The effectiveness of a proactive patient-centered primary care programme on daily functioning of frail older

patients: A cluster randomised controlled trial. J Am Geriatr Soc 2016;64:1779–1788.
19. 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 Geriatri 2012;12:16.
20. 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;68:301–308.
21. Garcia-Gonzalez JJ, Garcia-Pena C, Franco-Marina F, Gutierrez-Robledo LM. A frailty index to predict the mortality risk in a population of senior Mexican adults. BMC Geriatr 2009;9:47.
22. Franzini L, Dyer CB. Healthcare costs and utilization of vulnerable elderly people reported to adult protective services for self-neglect. J Am Geriatr Soc 2008;56:667–676.
23. Peters LL, Boter H, Buskens E, Slaets JP. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. J Am Med Dir Assoc 2012;13:546–551.
24. Jurling B, Koster L, Batterink M, et al. Praktijkkosten—en inkomensonderzoek huisartsenzorg. 2012. Google Scholar.
25. CBS. CBS gezondheid en zorg in cijfers; 2013.
26. Tan SS, Bouwmans-Frijters CA, Hakkaart-van Roijen L. Handleiding voor kostenonderzoek: Methoden en referentieprijzen voor economische evaluaties in de gezondheidszorg. Tijdschrift voor gezondheidswetenschappen 2012;90:367–372.
27. Statline. Dutch population, percentage older people. Available at: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=70660NED&D1=19,26-27,73,79&D2=(l-11)-l&VW=T. Updated 2010. Accessed May 16, 2011.
28. EuroQol Group. EuroQol—A new facility for the measurement of health-related quality of life. Health Policy 1990;16:199–208.
29. Lamers LM, McDonnell J, Stalmeier PF, et al. The Dutch tariff: Results and arguments for an effective design for national EQ-5D valuation studies. Health Econ 2006;15:1121–1132.
30. Manca A, Palmer S. Handling missing data in patient-level cost-effectiveness analysis alongside randomised clinical trials. Appl Health Econ Health Policy 2005;4:65–75.
31. Schafer JL. Multiple imputation: A primer. Stat Methods Med Res 1999;8:3–15.
32. Rubin DB. Inference and missing data. Biometrika 1976;63:581–592.
33. Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. BMJ 1990;300:230–235.
34. Manca A, Hawkins N, Sculpher MJ. Estimating mean QALYs in trial-based cost-effectiveness analysis: The importance of controlling for baseline utility. Health Econ 2005;14:487–496.
35. Blom J, den Elzen W, van Houwelingen AH, et al. Effectiveness and cost-effectiveness of a proactive, goal-oriented, integrated care model in general practice for older people. A cluster randomised controlled trial: Integrated systematic care for older people—the ISCOPE study. Age Ageing 2016;45:30–41.
36. Metzelthin SF, van Rossum E, Hendriks MR, et al. Reducing disability in community-dwelling frail older people: Cost-effectiveness study alongside a cluster randomised controlled trial. Age Ageing 2015;44:390–396.
37. Fairhall N, Sherrington C, Kurrle SE, et al. Economic evaluation of a multifactorial, interdisciplinary intervention versus usual care to reduce frailty in frail older people. J Am Med Dir Assoc 2015;16:41–48.
38. Bhandari A, Wagner T. Self-reported utilization of health care services: Improving measurement and accuracy. Med Care Res Rev 2006;63:217–235.
39. Richards SH, Coast J, Peters TJ. Patient-reported use of health service resources compared with information from health providers. Health Social Care Commun 2003;11:510–518.
40. 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.
41. McNellis RJ, Genevro JL, Meyers DS. Lessons learned from the study of primary care transformation. Ann Fam Med 2013;11:S1–S5.

Appendix A



Appendix A. Flowchart Participants

Appendix B. Determination of the Unit Costs of the Interventions, Health Care Utilization, and Informal Care Provision

General Approach Used Throughout the Unit Cost Calculations

First, in general, we defined the number of potentially frail older people per general practice, assuming a standard Dutch practice size of *2350 patients*.[1] On average, 552 patients (23.5%) in a standard practice are 60 years and older.[2] Within this older population, *110 patients (20%)* were selected as potentially frail in the Frailty Screening report.[3] With these data, we converted all calculated intervention costs to the unit "costs per potentially frail older patient per year." Second, in all calculations, we applied a VAT tariff of 21%. Third, for surcharges related to items such as social obligations and vacation bonuses on wages defined within collective labor agreements, we apply *39%* for practice nurses, and *35%* for general practitioners.[4] Fourth, for the below-mentioned calculation of the costs directly related to the interventions, we have only taken into account the actions of the GPs and practice nurses, not involving direct patient contact as this latter category is already covered in the administration of health care utilization. Fifth, all costs mentioned in this appendix have been indexed to 2012.[5]

Unit Costs of the Frailty Screening Followed by Standard GP Care and Frailty Screening Followed by Nurse-Led Care Intervention

Frailty screening followed by standard GP care start-up and maintenance expenses

Scenarios given by different software development companies (Proigia, http://www.proigia.nl; and Insider, http://www.insider.nl):

	First Scenario	Second Scenario	Mean of 2 Scenarios
One-time installation charges written off over 3 years, per year	€181.50	€82.50	€132
Maintenance expenses per patient per year*	€0.04	€0.40	€0.22

*Per patient in overall practice population.

Adoption of the mean of the 2 scenarios:

(132 + 0.22 × 2350) × 1.21 = €785.29 per standard general practice, including VAT.

785.29/110 = €7.10 per potentially frail older patient per year for the frailty screening installation charges and maintenance expenses.

Frailty Screening Usage in Proactive Care

Assumption of a time investment of 1 hour per week for evaluating the total frailty screening report and preparing proactive care according to current professional guidelines (personal communication of time estimation by Prof Numans, professor of general practice). The assumption is that half of this time will be invested by the GP and the remaining half by the practice nurse.

Wage costs, practice nurse[6]:

Salary scale 50, step 4 = €18.54/h.

Hourly honorarium: 18.54 × 1.39 = €25.77/h.

Wage costs, GP[7,8]:

Honorarium derived from tax data: €45.18/h.

Honorarium derived from collective labor agreement, step 4: €47.73/h.

Mean honorarium, GP: €46.46/h.

Hourly honorarium: 46.46 × 1.35 = €62.72/h.

Taking the mean of the hourly wages of practice nurses and GPs:

(25.77 + 62.77)/2 = €44.27/weekly hour of frailty screening usage in proactive care for all patients in the report.

44.27 × 52 = €2302.04/y of the frailty screening usage in proactive care for all patients in the report.

2302.04/110 = €20.90 per potentially frail older patient per year for frailty screening usage in proactive care.

Total frailty screening intervention costs: 7.10 + 20.90 = €28 per potentially frail older patient. This calculation was performed with the exception of direct patient contacts, as these are taken into account within the registered health care utilization.

Nurse-Led Care Intervention: Education, Toolkit, and Website

Education

Based on the workload and number of potentially frail older patients per standard practice, 0.33 full-time equivalents (FTEs) of practice nurse per general practice was estimated to be needed for adequate provision of the nurse-led care program.

Costs of delivery of the educational program

Invoice for 48 hours of education of 21 practice nurses at the school of advanced education: €5851.

5851/21 = €279 educational costs per practice nurse.

279/3 = €93 educational costs per general practice.

93/110 = €0.85 per potentially frail older patient per year for the education itself.

Costs of Time Investment of Practice Nurse in Educational Program

Time investment practice nurse = 48 hours.

Hourly honorarium practice nurse = €25.77.

48 × €25.77 = €1236.96 per practice nurse.

1236.96/3 = €412.32 per general practice.

Deprivation of Time Investment Costs Over a Period of 5 Years, Assuming a Necessity to Follow Education Every 5 Years

0.20 × 412.32 = €82.46 per general practice per year.

82.46/110 = €0.75 per potentially frail older patient per year for the time investment of registered practice nurses in the education of the nurse-led care program.

0.85 + 0.75 = €1.60 per potentially frail older patient per year.

Toolkit

Actual expenses (Invoice printing office) for 500 toolkits: €2448.60.

2448.60/500 = €4.90 per toolkit.

One practice nurse needs 1 toolkit, and 1 general practice needs 0.33 FTE registered practice nurses:

4.90/3 = €1.63 per general practice.

1.63/110 = €0.01 per potentially frail older patient per year for the toolkit.

Website (this website is used by the practice nurse to register patient questionnaire data)

First estimation website developer: €0.04/potentially frail older patient per year.

Total costs for nurse-led care intervention, toolkit, and website = 1.60 + 0.01 + 0.04 = €1.65 per potentially frail older patient per year.

Nurse-Led Care Program Usage in Proactive Care

The time investments mentioned below are based on estimations of the time investments of GPs and practice nurses for the provision of

proactive care for older people, which have been published by a cooperation of insurance companies.[9]

Time investment per year of GPs per potentially frail older patient: 57 minutes. These 57 minutes include consultations of the GP with the practice nurse, multidisciplinary consultations, and the preparation of proactive care actions. Actions involving direct patient contact are excluded because they are already taken into account in the health care utilization costs.

Time investment per year of practice nurses per potentially frail older patient: 97 minutes. These 97 minutes include consultations of the practice nurse with the GP, the construction of tailored, personalized care plans, multidisciplinary consultations, and administrative tasks. Again, actions involving direct patient contact are excluded because they are already accounted for in the health care utilization costs.

Costs of nurse-led care program usage in the proactive care by the GP:

Time investment: 57 minutes.

Hourly honorarium: €62.72 (see 2.2).

(57 × 62.72)/60 = €59.58 per potentially frail older patient per year.

Costs of nurse-led care program usage in the proactive care by the practice nurse:

Time investment: 97 minutes.

Hourly honorarium: €25.77.

(97 × 25.77)/60 = €41.66 per potentially frail older patient per year.

59.58 + 41.66 = €101.24 for the time investment of GPs and practice nurses for nurse-led care program per potentially frail older patient per year.

Total intervention costs for the frailty screening + nurse-led care strategy: €28 + €1.65 + €101.24 = €131 per potentially frail older patient. This calculation excludes the costs related to direct patient contacts, as these are included in the health care utilization costs.

Unit Costs of Health Care Utilization

As defined in Table 1 of the main manuscript, all unit costs were defined according to the Dutch manual for cost studies and indexed to 2012. For a number of health care utilization types, some additional specifications were made, which are specified in this section.

GP consultations during office hours

This type of health care utilization refers to consultations with the patients' own GPs during office hours, either in surgery or at home.

Unit cost of in-surgery GP consultation: €29.73.

Unit cost of GP consultation at home: €45.66.

The mean ratio of in-surgery consultations to consultations at home is 12 to 1.[10]

This calculation results in the following summary measure:

[(12 × 29.73) + 45.66]/13 = €30.95 per GP consultation.

Out-of-Hours GP consultations

This type of health care utilization refers to consultations with GPs during nights or weekend days and can be either in-surgery or at-home consultations.

The unit cost of this type of health care utilization was not provided in the Dutch manual for costing studies, and has therefore been taken from another source.[11]

Unit cost of out-of-hours, in-surgery GP consultation: €90.75.

Unit cost of out-of-hours, at-home GP consultation: €136.13.

The mean ratio of out-of-hours, in-surgery consultations to at-home consultations is 5 to 1.[12]

This calculation results in the following summary measure:

[(5 × 90.75) + 136.13]/6 = €98.30 per out-of-hours GP consultation.

References

1. Jurling B, Koster L, Batterink M, et al. Praktijkkosten- en inkomensonderzoek huisartsenzorg [in dutch, Research on expenditures and revenues in primary care]. 2012.
2. Statistics Netherlands. Population demographics: Sex, age, marital status, and region. Available at: http://statline.cbs.nl/StatWeb/publication/default.aspx?DM=SLNL&PA=70233NED&D1=0&D2=116-125&D3=0-4&D4=l&HDR=T&STB=G1%2cG2%2cG3&VW=T. Accessed July 11, 2013.
3. Bleijenberg N, Drubbel I, Schuurmans MJ, et al. Development and effectiveness of a patient-centered care program on physical functioning of frail older persons. .
4. Hakkaart-van Roijen L, Tan SS, Bouwmans CAM. Handleiding voor kostenonderzoek. methoden en standaard kostprijzen voor economische evaluaties in de gezondheidszorg. Rotterdam: Institute for Medical Technology Assessment, by order of the Dutch College of Health Insurances; 2010.
5. Statistics Netherlands. Consumer price indices 1996-2012. Available at: http://statline.cbs.nl/StatWeb/publication/?DM=SLNL&PA=71311NED&D1=0&D2=0&D3=12,25,38,51,64,77,90,103,116,129,142,155,168,181,194,219,232&VW=T. Updated 2013. Accessed July 11, 2013.
6. Collective labour agreement 2010-2012 for care in nursing homes and assisted living facilities; home care; maternity care; and childhood care. Available at: http://www.abvakabofnv.nl/mijn-sector/alle-caos/vvt/. Accessed September 30, 2013.
7. Collective labour agreement 2009-2011 for health care centers. Available at: http://www.fbz.nu/cao_gezondheidscentra.htm. Accessed September 30, 2013.
8. The income of self-employed general practitioners. Available at: http://www.vphuisartsen.nl/Nieuws/Het-echte-inkomen-van-de-huisarts.html. Accessed September 30, 2013.
9. Individual general practitioners' agreement. Care for frail older people, appendix 4: Estimates of time investments of general practitioners and practice nurses for the care for frail older people. Available at: http://www.unive.nl/zorgaanbieders/huisartsen/contracten. Accessed September 30, 2013.
10. The mean ratio of in surgery consultations to consultations at home. Available at: http://www.vektis.nl/index.php/nieuws/onderzoeken/61-uitgedrukt-in-cijfers-huisartsconsulten. Accessed September 30, 2013.
11. Unit costs for out-of-hours general practitioner consultations in surgery and at home. Available at: http://www.huisartsenpost-degeldersevallei.nl/wat-zijn-de-tarieven.
12. Mean ratio of out-of-hours general practitioner in surgery consultations versus home visits. Available at: http://www.henw.org/archief/volledig/id4403-patintcontacten-op-de-huisartsenpost.html. Accessed September 30, 2013.