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Effectiveness and cost-effectiveness of proactive and multidisciplinary integrated care for older people with complex problems in general practice: an individual participant data meta-analysis

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Abstract

Purpose: to support older people with several healthcare needs in sustaining adequate functioning and independence, more proactive approaches are needed. This purpose of this study is to summarise the (cost-) effectiveness of proactive, multidisciplinary, integrated care programmes for older people in Dutch primary care.

Methods design: individual patient data (IPD) meta-analysis of eight clinically controlled trials.

Setting: primary care sector.

Interventions: combination of (i) identification of older people with complex problems by means of screening, followed by (ii) a multidisciplinary integrated care programme for those identified.

Main outcome: activities of daily living, i.e. a change on modified Katz-15 scale between baseline and 1-year follow-up.

Secondary outcomes: quality of life (visual analogue scale 0–10), psychological (mental well-being scale Short Form Health Survey (SF)-36) and social well-being (single item, SF-36), quality-adjusted life years (Euroqol-5dimensions-3level (EQ-5D-3L)), healthcare utilisation and cost-effectiveness.

Analysis: intention-to-treat analysis, two-stage IPD and subgroup analysis based on patient and intervention characteristics.

Results: included were 8,678 participants: median age of 80.5 (interquartile range 75.3; 85.7) years; 5,496 (63.3%) women. On the modified Katz-15 scale, the pooled difference in change between the intervention and control group was -0.01 (95% confidence interval -0.10 to 0.08). No significant differences were found in the other patient outcomes or subgroup analyses. Compared to usual care, the probability of the intervention group to be cost-effective was less than 5%.

Conclusion: compared to usual care at 1-year follow-up, strategies for identification of frail older people in primary care combined with a proactive integrated care intervention are probably not (cost-) effective.

Keywords: aged, primary care, integrated care, older people

Introduction

In the Netherlands, the present approach to older people in primary care is demand-driven and mainly focuses on the management of isolated diseases or health problems. Timely risk assessment and systematic, proactive provision of multidisciplinary integrated care for older people (i.e. timely provided care, triggered by identification of those at risk of functional decline) may prevent or slow down functional decline and stimulate sustainment of independent living [1]. Such an approach is also known as ‘proactive integrated care’.

There is little evidence for a positive effect of proactive integrated care on the health and daily function of older persons. Until now, outcomes have been inconclusive, i.e. some studies showed small improvements in daily functioning and a small decline in healthcare utilisation in the intervention group whereas, more often, no difference was found between intervention and control groups [2–7]. The effectiveness of the care model may vary depending on the different components of the model, such as the presence of a medical assessment or inclusion of a geriatrician in the multidisciplinary care team [6, 7].

In 2008, the National Care for the Elderly Programme (NCEP) was initiated. This was a large-scale innovation programme funded by the Dutch Ministry of Health, Welfare and Sports [8]. Eight research projects were set up across the country to evaluate proactive, multidisciplinary and integrated care for community-dwelling older people, using a similar generic structure [9–16]. Each project used a unique identification method to early identify older people at risk of functional decline. The identification was followed by multidisciplinary integrated care, coordinated by the general practitioner (GP) or the practice nurse. Although the overall aims were similar, the projects differed in their methods to identify patients at risk of functional decline and in the combination of components of multidisciplinary integrated care. The eight projects showed no

or only marginal beneficial effects on relevant outcomes, such as daily functioning, sustained independence/independent living or cost-effectiveness. However, the individual projects were too small to assess the effectiveness in specific subgroups.

To improve the statistical power, we set up an individual patient data (IPD) meta-analysis to determine the pooled effectiveness of the eight projects. The aim of the present study is to investigate the effectiveness of proactive, multidisciplinary and integrated primary care compared to usual primary care. The intervention is offered to older people at risk of functional decline. We measured the effect on patient-reported outcomes of daily functioning, quality of life (QoL) and healthcare utilisation, in pre-specified subgroups based on patient and intervention characteristics. An economic evaluation is also included.

Methods

Design

We conducted an IPD meta-analysis from a pool of eight primary care projects with proactive, multidisciplinary and integrated care for frail older people, performed within the NCEP in different regions of the Netherlands. All individual studies have been approved by their Medical Ethical Committee.

Intervention

We included projects performed within the NCEP between 2008 and 2016. The projects were conducted in primary care and evaluated proactive, multidisciplinary and integrated care comprising the following generic elements:

- An identification method (screening) for older persons with an increased risk of functional decline.
- An individual (comprehensive geriatric) assessment in the domains of somatic, functional, psychological and social health followed by a multidisciplinary integrated care

intervention with follow-up, tailored to the identified individual at risk and shaped by case management.

The projects operationalized these two elements in different ways (Supplementary data, Additional files 1 and 2, available in *Age and Ageing* online). The intervention groups were compared with a group receiving ‘usual care’.

Included projects

The included projects were as follows: the frail older Adults: Care in Transition study (ACT) [9], the CareWell-primary care program [10], the Embrace-study [11], the Function In Transition study (FIT) [12], the Integrated Systematic Care for Older PEople study (ISCOPE) [13], the Prevention of Care study (PoC) [14], the Utrecht primary care PROactive Frailty Intervention Trial (U-PROFIT) [15] and the Walcheren Integrated Care Model study (WICM) [16] (Supplementary data, Additional file 1, available in *Age and Ageing* online). Of the U-PROFIT study we used only one of the two intervention arms, i.e. the arm with the frailty selection and evidence-based nurse-led care planning. All the individual projects used a controlled design, a randomised (cluster (FIT, ISCOPE, PoC, U-PROFIT), individually (Embrace), or stepped wedge (ACT)), or quasi-experimental design (Carewell, WICM).

Description of usual care

In the Netherlands, most of the care for older people living at home is provided by the GP [17]. The GP acts as a gate-keeper to secondary care. In many general practices, (registered) practice nurses provide care to older persons or to people with chronic diseases. Although practices interact with other primary care professionals, such as community nurses, physiotherapists and occupational therapists [17], full integration of information and services remains a challenge due to lack of an infrastructure supporting proactive integrated care (such as multidisciplinary consultation), leaving the care fragmented.

Information sources and data collection

Within the NCEP, all projects reported on an identical set of patient characteristics and outcome measures, with identical coding. These data were collected in a national database: The Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS; <http://topics-mds.eu/>) [18]. Patient outcomes in all projects were collected with the patient-reported TOPICS-MDS questionnaire. Additional data regarding scores on the identification method, mortality and nursing home admission were collected from the individual researchers. We collected information regarding study methods and the details of the intervention from the researchers and the original publications of the projects. Supplementary data, Additional files 1 and 2, available in *Age and Ageing* online describe the designs, identification methods and interventions after screening of the eight projects.

For each study, to evaluate the risk of bias, we assessed randomisation procedures, sequence generation, allocation concealment, blinding of participants, personnel and outcome assessor (Cochrane Collaboration’s tool for assessing risk of bias in randomised trials).

Outcome measures

All projects included a measurement at baseline and at 1-year follow-up (possibly with additional measurement at 3, 6, 18 or 24 months).

Primary outcome: daily functioning—measured at 1-year follow-up in activities of daily living (ADL) measured with the modified Katz scale [15-item scale measuring Basic ADL (6 items) and Instrumental ADL (8 items) and 1 mobility item] [19]. Higher scores indicate worse daily functioning.

Secondary outcome: QoL was rated as a number from 0 to 10. Also included were items on psychological (subscale mental health SF-36, scores ranging from 0 to 100) and social functioning (item 10, SF-36, scores ranging from 1 to 5).

Patient involvement

To ensure equitable distribution of TOPICS-MDS data, an independent Societal Board reviews the societal merits of all incoming data requests (research question, outcome measures, the design of the study and the process of dissemination of the results). Members of the Societal Board were nominated by the National Care for the Elderly network and the Board. Members consist of community representatives, science representatives and health policy representatives. The members of the board have reviewed the request for this study.

Statistical analyses

We used a two-stage IPD meta-analysis [20]. First, we summarised the results of the individual projects for outcomes as registered in the TOPICS-MDS. For repeatedly measured continuous variables, differences between the groups per project were estimated with linear mixed models (LMM), correcting for age, sex, baseline scores (for each outcome its own baseline score) and clustering of patients by general practice, using random effects. For the categorical variable social functioning, odds ratio per project was estimated using generalised estimated equations (GEE) correcting for age, sex, baseline scores and clustering of patients by general practice.

All analyses followed the intention-to-treat principle. Missing data were accounted for by the statistical techniques used (LMM and GEE) [21].

Dropout caused by death was explored with logistic regression (GEE was used for the ACT study to allow for the duration of the intervention in the stepped-wedge design). After exploring mortality, participants who died during follow-up were excluded from the outcome analyses.

Second, we combined all outcomes across projects using a stratified-by-trial, two-stage, random effect model, weighting with the individual standard errors. A forest plot was created showing the outcomes for the individual projects,

the pooled outcomes and the calculated measures of heterogeneity. A P -value of ≤ 0.05 was regarded as statistically significant. Analyses were performed using SPSS version 20 and STATA 12.1.

We conducted subgroup analyses based on factors influencing disability prevalence (age <75 , 75 – 85 and ≥ 85 years, use of home care, living situation (residential care facility, or home)) or factors influencing healthcare consumption (education: only primary school vs. more than primary school; urbanised vs. non-urbanised living). Additionally, we analysed the modified Katz-15 score in strata above and below the median baseline modified Katz-15 score per study, the subscale mental health SF-36 based in strata above and below the median baseline subscale mental health SF-36 score per study and strata based on the level of frailty as assessed with the Frailty Index (FI) based on 45 items of the questionnaire, as developed for the NCEP (<0.25 vs. ≥ 0.25) [22]. In addition, subgroup analyses based on characteristics of the intervention protocol (one visit vs. more than one visit during intervention; core team with GP and practice nurse vs. larger team) were also performed.

Sensitivity analyses were performed by study characteristics (randomised design vs. quasi-experimental design; informed consent request by health professional vs. researcher; outcome measurement by mail vs. interview).

Economic evaluation

One-year quality-adjusted life years (QALYs) were estimated as the area under the curve of utility measurements obtained using the Dutch tariff for the EQ-5D-3L [23]. We estimated one-year costs from a healthcare perspective and reported in euros (as at 2016). Estimates for the intervention costs and regular GP visits per patient were obtained from the separate studies. Other healthcare utilisation were estimated from the TOPICS-MDS and were valued using reference prices designed to standardise Dutch economic evaluations [24]. In the economic evaluation, participants who died during follow-up remained included in the analyses, with costs and QALYs after death set at zero. Differences in costs were related to differences in QALYs using cost-effectiveness acceptability curves [25]. Depending on the willingness to pay (WTP) per QALY, cost-effectiveness acceptability curves show the probability that one policy is cost-effective compared to the other. Acceptability curves were obtained as the one-sided P -value for the treatment effect on the net benefit ($NB = WTP \times QALYs - Costs$).

Results

Study characteristics

A total of 8,678 participants at risk of functional decline were included in the projects; of these, 5,496 (63.3%) were women and the median age across all projects was 80.5 (interquartile range (IQR) 75.3; 85.7) years. Of all participants: 53% lived in an urbanised area and the proportion living in a residential care facility ranged from 0% to 17.8%.

Characteristics of the participants are shown per study in Table 1.

An assessment of the allocation, prevention of contamination, and concealment and blinding procedures is shown in Supplementary data, Additional files 3 and 4, available in *Age and Ageing* online.

Primary outcome

The pooled mean change on the modified Katz-15 score over 1 year was 0.33 (0.06; 0.60) in the intervention group and 0.37 (95% CI: 0.13–0.61) in the control group, with a pooled adjusted mean difference in change between intervention and control group from baseline to 1-year follow-up of -0.01 (95% CI: -0.10 to 0.08) (Table 2, Fig. 1).

Secondary outcomes

The pooled mean change in QoL at 1-year follow-up was -0.08 (95% CI: -0.15 to 0.00) in the intervention group and -0.12 (95% CI: -0.18 to -0.06) in the control group, with no significant difference in change in QoL between the intervention and control group between baseline and 1-year follow-up (mean difference in change: -0.01 (95% CI: -0.10 to 0.08)) (Table 2). There were no significant effects of the interventions on the other secondary outcomes (Supplementary data, Table S2; Additional file, forest plots, available in *Age and Ageing* online).

Subgroup analyses

There was no significant difference in effect in the pre-planned subgroups (Supplementary data, Additional file Table S3, Additional file forest plots, available in *Age and Ageing* online).

Economic evaluation

Mean costs of the intervention in the different projects were € 526 per person (range € 132–€ 1,624). Pooled total healthcare costs were higher by € 936 per person (95% CI: € 295–€ 1,577). There was no significant difference in QALYs between the intervention and control group (95% CI: -0.018 to 0.011).

As estimated QALYs and costs were both in favour of usual care, so was the cost-effectiveness. Depending on the WTP per QALY, the probability that proactive integrated care is cost-effective compared with usual care ranged from 0% at low WTP (i.e. when only costs count) to 5% at a WTP € 80,000 per QALY (i.e. the unofficial upper bound in the Netherlands for cost-effectiveness) (Fig 2).

Discussion

Summary of the findings

Until now, the results of studies on proactive integrated care have been mainly inconclusive [2–7]. Positive effects were either absent or relatively small so that doubt remains on the clinical relevance. In the present study, compared

Table I. Characteristics of the participants.

	ACT <i>n</i> = 1,147 Groups 1: 456; 2: 227; 3: 238; 4: 226	Carewell <i>n</i> = 536 I: 287; C: 249	Embrace <i>n</i> = 602 I: 309; C: 293	FIT <i>n</i> = 2,283 I: 1,209; C: 1,074	ISCOPE <i>n</i> = 1,104 I: 866; C: 238	PoC <i>n</i> = 346 I: 193; C: 153	U-PROFIT <i>n</i> = 2,214 I: 1,384; C: 830	WICM <i>n</i> = 446 I: 221; C: 225
Age in years (median, IQR)	81.1 (74.9; 86.4)	82.2 (77.2; 86.6)	80.8(77.8; 85.2)	82.7 (77.0; 87.1)	83.2 (79.7; 87.7)	77.3 (73.6; 81.3)	74.0 (67.2; 80.7)	81.7 (78.9; 86.1)
Female, <i>n</i> (%)	763 (66.5)	352 (65.7)	397 (65.9)	1460 (64.0)	812 (73.6)	199 (57.5)	1225 (55.3)	288 (64.4)
Only primary education, <i>n</i> (%)	263 (22.9)	169 (31.5)	234 (38.9)	536 (23.5)	272 (24.6)	115 (33.2)	401 (18.1)	206 (46.1)
Marital status								
Married/living together	431 (37.6)	208 (38.8)	285 (47.4)	1052 (46.1)	312 (28.2)	164 (47.4)	1231 (55.6)	182 (40.7)
Widowed	508 (44.3)	257 (47.9)	284 (47.2)	972 (42.6)	662 (60.0)	147 (42.5)	548 (24.8)	241 (53.9)
Not married/divorced	207 (18.0)	71 (13.2)	31 (5.2)	244 (10.7)	130 (11.7)	35 (10.2)	239 (15.3)	21 (4.7)
Living situation								
Alone	628 (54.8)	318 (59.3)	225 (37.4)	997 (43.7)	641 (58.1)	152 (43.9)	856 (38.7)	203 (45.4)
With others	439 (38.3)	218 (40.7)	248 (41.2)	979 (42.9)	292 (26.4)	161 (46.5)	1221 (55.1)	168 (37.6)
Residential care	80 (7.0)	†	78 (17.8)	292 (12.8)	171 (15.5)	22 (6.4)	a	76 (17.0)
Mortality 12 months, <i>n</i> (%)	84 (2.7)	52 (9.7)	8 (1.3)	89 (3.9)	73 (6.6)	25 (7.2) ^b	32 (1.4)	26 (5.8)
Immigrant (i.e. participant not born in the Netherlands), <i>n</i> (%)	112 (9.8)	38 (7.1)	15 (2.5)	93 (4.1)	94 (8.5)	21 (6.1)	140 (6.3)	20 (4.5)
Living in urbanised area, <i>n</i> (%)	841 (73.4)	–	1 (0.2)	1080 (47.3)	680 (61.6)	0 (0.0)	1392 (62.9)	294 (65.8)
Daily functioning at baseline (modified Katz-15 score, range 0–15 ^c) (median, IQR)	3 (2; 6)	5 (3; 7)	3 (1; 5)	2 (1; 5)	4 (2; 7)	2 (1; 4)	1 (0; 2)	3 (1; 6)
Mental health (subscale RAND- 36, range 0–100 ^d) (median, IQR)	72 (56; 84)	76 (60; 86)	68 (56; 80)	72 (60; 84)	68 (56; 80)	60 (48; 72)	72 (56; 84)	72 (60; 84)
Impediment to social activity most or all of the time, <i>n</i> (%)	361 (31.5)	106 (19.8)	121 (20.1)	408 (17.9)	245 (22.2)	86 (24.9)	373 (16.8)	121 (27.1)
Health-related QoL (EQ-5D, range 0–1) (median, IQR)	0.69 (0.35; 0.81)	0.69 (0.33; 0.81)	0.69 (0.65; 0.78)	0.78 (0.68; 0.84)	0.68 (0.31; 0.81)	0.72 (0.57; 0.81)	0.81 (0.68; 0.84)	0.72 (0.43; 0.81)
QoL (0–10)	7 (6; 8)	7 (6; 8)	7 (6; 7)	7 (7; 8)	6 (6; 8)	7 (6; 8)	7 (7; 8)	7 (6; 7)
≥2 chronic diseases	1108 (96.9)	298 (55.6) ^e	492 (81.7)	1846 (80.9)	1020 (92.4)	319 (92.2)	1527 (69.0)	405 (90.6)
FI (range 0–1) (median, IQR)	0.29 (0.21; 0.38)	0.25 (0.18; 0.33)	0.25 (0.18; 0.33)	0.24 (0.15; 0.34)	0.30 (0.22; 0.39)	0.28 (0.20; 0.37)	0.18 (0.11; 0.27)	0.28 (0.19; 0.36)

^aExcluded.^bMortality at 24 months.^cHigher score indicates decreased function.^dHigher score indicates better mental health.^eCollected through the electronic patient records of the GP not recorded.

Table 2. Outcomes of the meta-analyses.

Outcome measures	Usual care group ^a	Proactive integrated care group ^a	Adjusted mean difference between intervention and usual care (95% CI) ^b
Patient outcomes (mean change over 12 months)			
Modified Katz-15 score (0–15)	0.37 (0.13; 0.61)	0.33 (0.06; 0.60)	−0.01 (−0.10; 0.08) ^c
QoL (0–10)	−0.12 (−0.18; −0.06)	−0.08 (−0.15; 0.00)	−0.05 (−0.11; 0.00) ^d
Subscale RAND-36 mental well-being (0–100)	−0.36 (−1.95; 1.23)	−0.90 (−2.73; 0.93)	0.02 (−0.92; 0.97) ^d
Mortality (<i>n</i> , OR, 95%CI)	175	130	1.18 (0.91; 1.54)
Impediment to social activity (<i>n</i> , OR, 95%CI)	736	694	1.02 (0.90; 1.17)
Health economic outcomes (during 12 months)			
QALYs	0.645	0.636	−0.004 (−0.018; 0.011)
Number of regular GP visits	10.83	11.55	0.55 (−0.22; 1.33)
Number of out-of-hours GP visits	0.45	0.46	−0.02 (−0.06; 0.02)
Number of days in hospital	2.09	2.25	0.11 (−0.17; 0.40)
Number of days in nursing home	1.06	1.58	0.29 (−0.21; 0.79)
Number of days in care home	4.19	2.30	0.14 (−0.29; 0.57)
Number of days in day treatment	0.69	1.11	0.24 (−0.16; 0.63)
Number of days in day care	5.40	5.56	0.48 (−0.20; 1.16)
Number of hours of home care per week	1.81	2.04	0.14 (−0.02; 0.30)
Intervention costs	€ 0	€ 526	€ 526 (€ 431; € 622)
Non-intervention healthcare costs	€ 6963	€ 7697	€ 422 (€ −41; € 884)
Total healthcare costs	€ 6963	€ 8224	€ 936 (€ 295; € 1577)

^aWithout correction for covariates.

^bCorrected for age, sex, GP clustering and time of measurement.

^cNegative score in favour of intervention group.

^dNegative score in favour of control group.

with usual care, implementation of proactive identification of older persons at risk of functional decline combined with multidisciplinary integrated care showed no beneficial effect on daily functioning or QoL at 1-year follow-up. Subgroup analyses based on age, education, use of home care, residential care, baseline functioning and frailty, and on intervention characteristics (team composition, number of visits during the intervention) showed similar results. Moreover, proactive, multidisciplinary and integrated care increased healthcare costs and is unlikely to be cost-effective compared with usual care over a 1-year period.

Strengths and limitations

In this study, all projects collected data using the same measurement instruments (TOPICS-MDS) [8, 18]. This implies that there was no loss of information or lower efficiency in outcome measurement. Embedding of all the projects within the same healthcare system may have reduced the risk of system-related differences.

Some limitations need to be discussed. In some projects, selective non-response may have occurred. Response rates were lower among older and frailer persons, or eligible older people did not participate, possibly related to the informed consent procedure. This may have resulted in a selection towards older people with a relatively low level of frailty. However, subgroup analysis based on functioning at baseline or level of frailty in the IPD showed no differential effects on ADL function.

Since all projects made use of individually tailored goals, this implies that improvements over time were focused on the individual. However, projects were unable to take personal goals into account when assessing the generic outcome measures. Furthermore, the relation between health problems at old age and function is relatively diffuse, possibly leading to a poor effect on functioning of ADL. It is possible that different outcome measures, e.g. goal attainment scaling, patient-generated indexes [26, 27] might be better suited to assess the effectiveness of these interventions.

An issue with the modified Katz-15 is a possible ceiling effect [28]. The average baseline score on this outcome was 3 or less (on a scale from 0 to 15) in six of the included projects (ACT, Embrace, FIT, PoC, U-PROFIT, WICM), which did not leave much room for improvement.

In most of the projects, the follow-up was only 1 year, which may have been too short a period for an effect on individual health outcomes. Since many complex interventions and screening programmes take several years to reach optimal benefit, a longer follow-up may have resulted in more positive effects. However, although some of the projects in our meta-analysis had a slightly longer follow-up (24 months), they still failed to show any effect (ACT, FIT, PoC).

The intensity of the intervention may be related to effectiveness, with more intense interventions likely to be more effective. Although we performed stratified analyses based on the number of protocolized home visits and on team composition as a proxy for the intensity of the intervention, this did not yield better results.

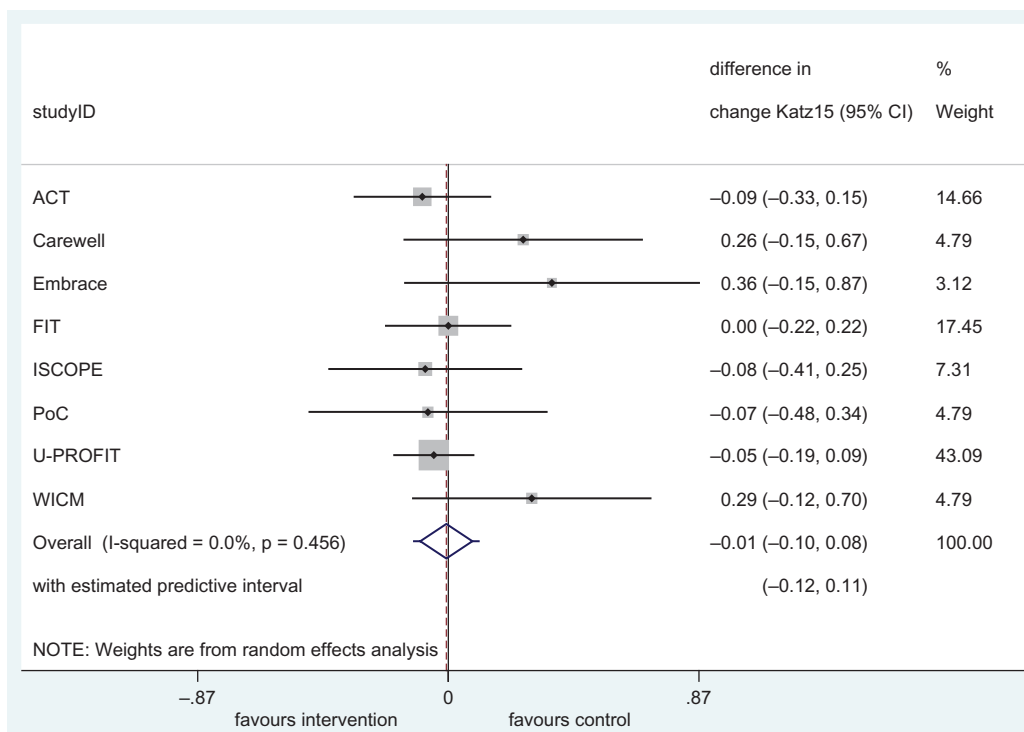


Figure 1 Forest plot of pooled effect on the difference in change of the modified Katz-15 score over a 1-year follow-up period, between usual care and intervention.

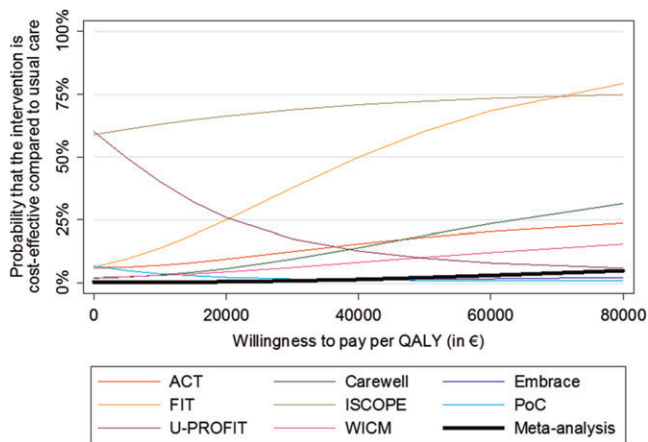


Figure 2 Cost-effectiveness acceptability curves, i.e. the probability that proactive integrated care is cost-effective compared to usual care, depending on the WTP per QALY.

Apart from limitations related to the design of the projects, there may have been more generic reasons that explain the absence of effect. The Dutch healthcare system already incorporates many of the components required for a high-quality healthcare delivery for older people with multiple health problems, possibly making it difficult to realise further improvements. Important aspects, e.g. a strong primary care sector with easy access, free of costs for patients, alignment with secondary care and multidisciplinary collaboration with communication with social/specialist care, are already available.

The identification methods used may not have been sufficiently aligned to the subsequent multidisciplinary integrated care intervention, i.e. they may not have identified the optimal target group for these specific interventions. Previous studies have failed to clarify whether to target the more or the less frail older persons; i.e. some show an effect on mortality or hospitalisation mainly by screening in the general population, others also in the frail population [5].

Unsolicited interventions have more often proven to be less successful, indicating a non-alignment between participants' preferences and the proposed interventions [29–31]. Conversely, solicited interventions focusing on frail older people with an incident geriatric problem appear more successful in improving functional abilities and well-being [25].

It remains difficult to demonstrate the effectiveness of complex care interventions not only for proactive care interventions for older persons but also for disease management and self-management programmes. This may be due to the intrinsic limitations of randomised controlled trials when studying complex interventions at the level of the group rather than the individual. Hence, 'real-life' evaluations in observational studies in daily clinical practice, as well as qualitative studies, may better reflect the true benefit of intervention programmes [32].

Conclusions and future perspectives

Programmes for proactive care for older people, consisting of systematic identification of older persons at risk of

functional decline and eligible for subsequent multidisciplinary integrated care, are unlikely to be (cost-) effective after 1 year. Heterogeneity of the interventions, the fact that the programmes were aimed at individuals but evaluated at the group level, the absence of adequate evaluation methods and the high levels of standard care may all have contributed to the neutral findings. The current findings indicate that (after a study period of 1 year) large-scale implementation cannot be recommended.

Despite the fact that effectiveness could not be demonstrated, programmes for proactive multidisciplinary integrated care for older people are positively evaluated by both the older persons and the professionals [33–35] and have been embedded in healthcare systems in the Netherlands. This clear appreciation, and the challenges of complex care for older individuals, warrants further research focusing on a more personalised rather than a protocolized approach.

Key points

- Proactive identification of older people at risk of functional decline in primary care is unlikely to be (cost-) effective after 1 year.
- In subgroup analyses based on patient and intervention characteristics also, there were no effects.
- Still proactive integrated care for older people in primary care is positively evaluated by older persons and professionals

Supplementary data

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

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Authors' contributions

Guarantor: Gussekloo J affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Obtained funding: Blom JW and Gussekloo J.

All authors agree to be accountable for all aspects of the work.

Conflict of interest

All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

The studies using TOPICS-MDS fall outside the scope of the Medical Research Involving Human Subjects Act (WMO), as is stated in the Ethical Approval of TOPICS-MDS by the Medical Ethical Committee of the Radboud University Medical Center Nijmegen, the Netherlands (Radboud University Medical Centre Ethical Committee review reference number: CMO: 2012/120). All individual studies have been approved by their Medical Ethical Committee.

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Data sharing

The dataset(s) supporting the conclusions of this article is available at TOPICS-MDS. To access data, send a completed TOPICS-MDS Data Request Form to topics-mds@radboudumc.nl (<http://topics-mds.eu/>).

Trial registration

Not applicable. This is a secondary analysis in existing trial data.

References

- Guiding principles for the care of older adults with multimorbidity: an approach for clinicians. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians. American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. *J Am Geriatr Soc* 2012; 60: E1–E25.
- Mayo-Wilson E, Grant S, Burton J, Parsons A, Underhill K, Montgomery P. Preventive home visits for mortality, morbidity, and institutionalization in older adults: a systematic review and meta-analysis. *PLoS One* 2014; 9: e89257.
- Huss A, Stuck AE, Rubenstein LZ, Egger M, Clough-Gorr KM. Multidimensional preventive home visit programs for community-dwelling older adults: a systematic review and meta-analysis of randomized controlled trials. *J Gerontol A Biol Sci Med Sci* 2008; 63: 298–307.
- 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: 2157–66.
- 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: 725–35.
- Ploeg J, Feightner J, Hutchison B, Patterson C, Sigouin C, Gauld M. Effectiveness of preventive primary care outreach interventions aimed at older people: meta-analysis of randomized controlled trials. *Can Fam Physician* 2005; 51: 1244–5.
- Daniels R, van Rossum E, de Witte L, Kempen GI, van den Heuvel W. Interventions to prevent disability in frail community-dwelling elderly: a systematic review. *BMC Health Serv Res* 2008; 8: 278.
- <http://www.nationaalprogrammaouderenzorg.nl/english/the-national-care-for-the-elderly-programme/>
- Hoogendijk EO, van der Horst HE, van de Ven PM *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.
- Ruikes FG, Zuidema SU, Akkermans RP, Assendelft WJ, Schers HJ, Koopmans RT. Multicomponent program to reduce functional decline in frail elderly people: a cluster controlled trial. *J Am Board Fam Med* 2016; 29: 209–17.
- Uittenbroek RJ, Kremer HP, Spoorenberg SL, Reijneveld SA, Wynia K. Integrated care for older adults improves perceived quality of care: results of a randomized controlled trial of embrace. *J Gen Intern Med* 2017; 32: 516–23.
- Suijker JJ, van Rijn M, Buurman BM, Ter Riet G, Moll van Charante EP, de Rooij SE. Effects of nurse-led multifactorial care to prevent disability in community-living older people: cluster randomized trial. *PLoS One* 2016; 11: e0158714.
- Blom JW, den Elzen WPJ, 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 randomized controlled trial: Integrated Systematic Care for older People—the ISCOPE study. *Age Ageing* 2016; 45: 30–41.
- Metzelthin SF, Van Rossum E, De Witte LP *et al*. Effectiveness of an interdisciplinary primary care approach to reduce disability in community-dwelling frail older people: a cluster randomised controlled trial. *Br Med J* 2013; 347: f5264.
- Bleijenberg N, Drubbel I, Schuurmans MJ *et al*. Effectiveness of a proactive primary care program on preserving daily functioning of older people: a cluster randomized controlled trial. *J Am Geriatr Soc* 2016; 64: 1779–88.
- Looman WM, Fabbriotti IN, de Kuyper R, Huijsman R. The effects of a pro-active integrated care intervention for frail community-dwelling older people: a quasi-experimental study with the GP-practice as single entry point. *BMC Geriatr* 2016; 16: 43.
- van Weel C, Schers H, Timmermans A. Health care in the Netherlands. *J Am Board Fam Med* 2012; 25(Suppl 1): S12–7.
- Lutomski JE, Baars MA, Schalk BW *et al*. TOPICS-MDS Consortium. The development of the Older Persons and Informal Caregivers Survey Minimum DataSet (TOPICS-MDS): a large-scale data sharing initiative. *PLoS One* 2013; 8: e81673.
- Laan W, Zuithoff NP, 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: 848–54.
- Burke DL, Ensor J, Riley RD. Meta-analysis using individual participant data: one-stage and two-stage approaches, and why they may differ. *Stat Med* 2017; 36: 855–75.
- Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *J Clin Epidemiol* 2013; 66: 1022–8.
- Lutomski JE, Baars MA, van Kempen JA *et al*. Validation of a frailty index from the older persons and informal caregivers survey minimum data set. *J Am Geriatr Soc* 2013; 61: 1625–7.

23. Lamers LM, McDonnell J, Stalmeier PF, Krabbe PF, Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. *Health Econ* 2006; 15: 1121–32.
24. Hakkaart-van Roijen L, Bouwmans C, Kanters T, Tan SS. *Kostenhandleiding: Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg* [in Dutch]. Zorginstituut Nederland, 2015.
25. Zethraeus N, Johannesson M, Jonsson B, Lothgren M, Tambour M. Advantages of using the net-benefit approach for analysing uncertainty in economic evaluation studies. *Pharmacoeconomics* 2003; 21: 39–48.
26. Rockwood K, Stolee P, Fox RA. Use of goal attainment scaling in measuring clinically important change in the frail elderly. *J Clin Epidemiol* 1993; 46: 1113–8.
27. Wright JG, Young NL. The patient-specific index: asking patients what they want. *J Bone Joint Surg Am* 1997; 79: 974–83.
28. 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): S297–307.
29. de Craen AJ, Gussekloo J, Blauw GJ, Willems CG, Westendorp RG. Randomised controlled trial of unsolicited occupational therapy in community-dwelling elderly people: the LOTIS trial. *PLoS Clin Trials* 2006; 1: e2.
30. van der Weele GM, de Waal MW, van den Hout WB *et al.* Effects of a stepped-care intervention programme among older subjects who screened positive for depressive symptoms in general practice: the PROMODE randomised controlled trial. *Age Ageing* 2012; 41: 482–8.
31. Gussekloo J, de Bont LE, von Faber M *et al.* Auditory rehabilitation of older people from the general population—the Leiden 85-plus study. *Br J Gen Pract* 2003; 53: 536–40.
32. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008; 337: a1655.
33. Bleijenberg N, Boeije HR, Onderwater AT, Schuurmans MJ. Frail older adults' experiences with a proactive, nurse-led primary care program: a qualitative study. *J Gerontol Nurs* 2015; 41: 20–9.
34. Muntinga ME, Van Leeuwen KM, Schellevis FG, Nijpels G, Jansen AP. From concept to content: assessing the implementation fidelity of a chronic care model for frail, older people who live at home. *BMC Health Serv Res* 2015; 15: 18.
35. Metzelthin SF, Daniëls R, van Rossum E *et al.* A nurse-led interdisciplinary primary care approach to prevent disability among community-dwelling frail older people: a large-scale process evaluation. *Int J Nurs Stud* 2013; 50: 1184–96.

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Cardiovascular risk factors and frailty in a cross-sectional study of older people: implications for prevention

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Abstract

Objective: to examine the associations of cardiovascular disease (CVD) and cardiovascular risk factors with frailty.

Design: a cross-sectional study.

Setting: the Irish Longitudinal Study on Ageing (TILDA).

Participants: frailty measures were obtained on 5,618 participants and a subset of 4,330 participants with no prior history of CVD.