Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Methods

The supplementary information given in this section is based on the study protocol[1].

Recruitment of family physicians

Family physicians (FPs) from the counties of Akershus and Oslo, Norway, were invited to participate in the study with patients from their lists. There were no specific eligibility criteria for the FPs. We did not have the capacity to enroll all FPs in these areas, and municipalities in Akershus within a reasonable driving distance were prioritized. The FPs received written invitations, followed by a phone call to clarify if they were interested. When possible, information about the study was also given at FP meetings within each municipality.

Patient inclusion and exclusion criteria

We assumed that our intervention would be most relevant for the oldest and most frail patients, with relatively pronounced polypharmacy, and chose the inclusion and exclusion criteria presented in eTable 1.

Screening and recruitment of patients

The majority of home-dwelling patients with medications administered by the home nursing service have their medications prepared by multi-dose packaging systems delivered by a pharmacy, and screening of these medication lists were an efficient way of finding patients for the study.

Medication lists for patients listed with participating FPs were obtained from the pharmacy and screened by the home nursing service or by FP office staff to identify patients fulfilling the inclusion criteria. The FPs then considered the eligibility of their patients based on the exclusion criteria. Patients eligible for participation were contacted by the home nursing service or the FP's office, explaining the study and asking whether the researchers might contact them. If this was accepted, the patients received a home visit from the research assistant, who gave supplementary oral and written information, and obtained an informed consent if the patient wanted to participate. To avoid selection bias, the clusters (FPs) were randomized after all patients had been included in each cluster.

Primary outcome

15D is a generic, 15-dimensional instrument concerning different aspects of health-related quality of life (HRQoL) that has been used in similar geriatric interventions[2,3]. The dimensions are mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity. Each dimension is rated on an ordinal scale with five levels, and the respondent chooses the level best describing his/her present health status. Single index scores are calculated by population-based utility weights, and range from 0 to 1 (with "0" representing "dead", and higher scores indicating better HRQoL)[4].

We hypothesize that most improvements in the total drug regimen of frail older patients, such as better pain control, better symptom control in heart failure, less parkinsonian side effects, less iatrogenic dehydration or less sedation, have the potential to improve HRQoL. In our opinion, 15D is therefore an appropriate outcome measure when the aim is to improve the total drug regimen in an individualized manner across a broad spectrum of drug classes within a heterogeneous group of patients.

The patients included in our study were old, and many were not familiar with self-administration of questionnaires of this kind. 15D was therefore administered by interview. Usually, the 15D questionnaire is filled in by the individual whom it concerns, but it can also be answered by proxy raters. If the patient had moderate or severe dementia (i.e., Clinical Dementia Rating Scale > 1), or the research assistant considered that they did not understand the questionnaire, the interview was carried out with the closest proxy. To ensure that the proxy had updated knowledge on the patient's state of health, these ratings were only used if the patient and the proxy had regular contact – at least once every second week. To account for patients that might lose their ability to respond to 15D during the follow-up period, the questionnaire was administered to the closest proxy for all patients. The same source (patient or proxy) for the 15D score was used at all assessment points for each patient.

Proxy rating of the 15D questionnaire is generally accepted as valid[5] and has been successfully used in previous studies.[6] We emphasized for the proxy raters that we expected them to score the instrument as they thought the patients themselves would have done. We cannot, however, rule out a possible bias when using proxy raters. A recent study

indicates that proxy ratings on different measures of HRQoL consistently differ from ratings given by patients.[7] However, our primary outcome is the development of HRQoL over time, and the same source for the 15D score was used at all assessment points. This can be expected to reduce the impact of a potential bias in the proxy scores.

Data collection

Background information on diagnoses and comorbidity were obtained from the FP's electronic patient records. The patients received three home visits from the research assistant; at baseline, 16 and 24 weeks (±2 weeks). These visits took place where the patient was living at that moment; in the patient's own home, a nursing facility or a rehabilitation institution. All assessments directly involving the patient were performed at these visits. Proxy information was collected through telephone calls and/or questionnaires sent by mail if the proxy was not present at the home visit.

Updated medication lists were obtained at all assessment points. The research assistant checked if medications were taken as prescribed by asking the patient and the home nursing service if there had been any discrepancies. Multi-dose packages were also inspected to see if their content matched the medication lists. Nonprescription drugs and pro re nata (PRN) drugs taken regularly were counted as "regular drugs", but PRN drugs taken only occasionally were not counted. Drugs were registered according to the Anatomical Therapeutic Chemical (ATC) classification system.

See eTable 2 for study assessment procedures and timetable and eTable 3 for details on data collection for secondary outcomes.

Intervention

Our intervention consisted of three main parts: clinical geriatric assessment of the patient combined with a thorough review of their medications; a targeted meeting between the geriatrician and the FP; and clinical follow-up.

Geriatric assessment and medication review

As soon as possible after randomization, the patients were seen by a physician trained in geriatric medicine. In advance, the geriatrician obtained necessary information on the patient's medical history and actual medication from hospital records, the FP's electronic patient record, the home nursing service and other relevant sources. The geriatrician carried out a medical history from the patient (if necessary supplemented by a close relative) and a physical examination, both with focus on conditions most relevant for the patient's total medication use. Relevant blood analyses and other supplementary tests were ordered if not already available. The geriatric work-up was aimed at evaluating whether current medications were indicated, whether the relevant conditions were satisfactorily compensated, whether the dosages were appropriate, whether the patient had symptoms of adverse drug reactions, and whether drug-drug interactions or drug-disease interactions were present or likely to occur. A drug interaction database[8] , lists of anticholinergic drugs[9,10], the STOPP/START criteria[11] and the NORGEP criteria[12] were also used. See eFigure 1 and 2 for more details on the assessments carried out by the geriatrician.

Meeting between the geriatrician and FP

The main purpose of this meeting was to combine the competence and knowledge of the geriatrician with that of the FP. The geriatrician summarized the findings from the geriatric assessment and medication review, and the two physicians discussed the patient's drug list systematically. The geriatrician could suggest changes in the drug regimen, but the FP retained the medical responsibility for the patient, and was in charge of all ordinations and medication changes.

Clinical follow-up

Depending on medication changes that had been done, the two physicians arranged the necessary follow-up within the project period. The follow-up could consist of a clinical evaluation, further drug adjustments, blood tests etc., and could be carried out by the FP, the geriatrician or through telephone contact with the patient, the relative or the home nursing service, depending on the circumstances.

Control group

The control group received usual care from their FPs during the study period. The FPs in the control group were offered our assistance in performing medication reviews after the study period was completed.

eAppendix 2. Statistical Analysis

Information given in this section is based on the Statistical Analysis Plan dated 31th January 2018, published online before any unblinding of the researchers.

Power calculation

The maximum number of patients feasible to assess during the time limits of the trial was thought to be approximately 200. As each FP could participate with 1-5 patients, the number of clusters was therefore expected to be 20-100 in each group.

It was difficult to make valid assumptions on the correlation between patients within each cluster. In order to estimate the power, we chose to estimate power in a worst case (perfect correlation) and best case (no correlation) scenario. The true correlation was expected to be much closer to the latter, as the potential for intervention varies between individual patients. Based on previous studies using 15D, the standard deviation of change over time was expected to be between 0.07 and 0.08[2,3,13]. The minimum important change (MIC) for the change in 15D score is assumed to be ± 0.015[14]. A change of more than 0.035 in the negative direction is assumed to represent "much worse HRQoL" and a change of more than 0.035 in the positive direction "much better HRQoL". Based on previous studies, in addition to a pilot study, we believed that our intervention was extensive enough to potentially lead to a difference between groups of at least 0.035.

As can be seen from eTable 4, the power to detect a difference of 0.035 would then be in the range 59 to 94 %, and most probably > 80 %, provided that 100 patients were included in each treatment group.

Protocol violations

Wrongly included patients

13 patients using < 7 regular medications were included. The researchers could not check the number of medications before consent to participation was given, and in some cases it turned out that the FP or home nursing service had counted incorrectly. In other cases, medications had been discontinued in the period from inclusion to baseline. We believe that the potential for clinical improvements in the intervention group is better the more medications the patients use. We have therefore chosen to include these patients in the analysis, as it is likely that this will underestimate the effect of the intervention rather than overestimate it.

Patients not handled according to randomization

Two patients in the intervention group were not handled according to randomization. One withdrew consent before intervention, and one was hospitalized with severe acute illness and could not be approached. The patient that withdrew consent was included in the analysis and handled with multiple imputation as described in 2.3. The hospitalized patient completed the follow up-visits, and these measurements were used.

Timing of follow-up visits

Follow-up visits were 16 and 24 weeks (± 2 weeks) after baseline. However, if the date of the follow-up visit was exceeded by some days, these patients were still included in the analysis, and their measurements were used unchanged.

Missing data

Missing responses on 15D

To derive the 15D score, there must be a response to each question (dimension). If a maximum of three responses were missing, we used the imputation algorithm provided from the developers of the instrument (www.15d-instrument.net).

Lost to follow-up

Patients who died before follow-up were registered with the score "0" (worst possible HRQoL) on 15D. If patients were lost to follow-up for other reasons than death, they were included in the primary analysis, and missing values were handled with multiple imputation using the mi procedure in Stata with M=5 imputations.

The following variables were included in the imputation procedure:

- Age
- Sex

- Cumulative Illness Rating Scale (CIRS)[15]
- Clinical Dementia Rating Scale Sum of Boxes (CDR-SOB)[16,17]
- Use of home nursing service at baseline (minutes/week)

Sensitivity analyses

We performed an analysis by linear mixed model, with FP as a random factor, time point (baseline, 16 and 24 weeks), treatment and the interaction between time and treatment as fixed factors, and cluster size as a covariate.

In addition, missing values for the primary endpoint were analyzed in different ways in order to explore their potential influence on the results:

Sensitivity analysis 1
Patients not handled according to randomization and patients that were missing (all reasons) were excluded (per-protocol analysis).

Sensitivity analysis 2
Patients missing for other reasons than death were excluded, but deceased patients were kept with the value "0" on 15D.

Sensitivity analysis 3
Patients missing for other reasons than death were handled as "last observation carried forward" (LOCF), but deceased patients were kept with the value "0" on 15D.

Variables for adjustments

Variables with believed prognostic influence upon the outcome were included in the analysis, one by one in addition to the randomization group and cluster size. If their introduction to the model changed the effect estimate for the randomization variable with 10% or more, they were introduced in a final model including all variables with an effect of this size.

The following variables were subject to such analyses:
- Age
- Sex
- Cumulative Illness Rating Scale (CIRS)
- Clinical Dementia Rating Scale Sum of Boxes (CDR-SOB)
- Use of home nursing service at baseline (minutes/week)

Secondary outcomes

We compared the intervention group with the control group with respect to all secondary outcomes. Patients lost to follow-up were not imputed for, and results on secondary outcomes are based on patients still participating in the study. Originally, we planned to give deceased patients the "worst possible value" when reporting secondary outcomes. For some outcomes, however, this approach yielded illogical results. For the Relative Stress Scale (RSS)[18], for example, giving a deceased patient the worst possible score would mean that the nearest relative suffered a greater burden of care after the patient's death. Because of more deaths in the control group than in the intervention group, our decision of excluding these patients will underestimate the effect of the intervention rather than overestimate it.

All estimates for secondary outcomes were adjusted for age, sex, dementia severity and use of home nursing service at baseline. CIRS did not affect the estimates and was not included.

eAppendix 3. Results

The trial was stopped before reaching the planned 200 patients because of time constraints.

Primary outcome

The primary outcome, 15D at week 16, has been analyzed in various ways. All analyses conclude with a statistically significant positive effect of the intervention, with estimated between-group differences ranging from 0.030 to 0.055 (eTable 5).

Deceased patients with the value "0" represented outliers, but the distributional challenges were reduced by square-root transformations. As a general tendency, analyses on transformed data reported lower p values than non-transformed data (data not shown). The per-protocol analysis indicates that the positive result is not due to a higher number of deceased patients in the control group (eTable 5).

13 of the 15D questionnaires were filled in by proxy raters in the intervention group, 6 in the control group.

Secondary outcomes

For Trail Making Test A, we imputed values (because of cognitive difficulties) for seven patients at week 16 and for 13 patients at week 24. Trail Making Test B proved a difficult task, with 78 patients being imputed at week 16 and 79 patients at week 24. This makes the results difficult to interpret, as only about 40 patients were able to complete the test.

For Five Digits Test (FDT) 1, three patients were imputed at week 16 and five patients at week 24. For FDT2, four patients were imputed at week 16 and 16 patients at week 24. For FDT3, 16 patients were imputed at week 16 and 14 patients at week 24. For FDT4, 57 patients were imputed at week 16 and 61 patients at week 24.

All these outcomes suffered from many missing patients, with the main reason being poor vision.

eFigure 1. Patient Assessments Carried Out by the Geriatrician

PATIENT ASSESSMENTS

Medical history

Go through medical history obtained from family physician. Is the information accurate? Any indistinctness?

Systematic screening for current problems

Cognition: Known/suspected dementia? (IQCODE, CDR, relatives, impression of patient)? NPS?
Depression/anxiety: Screening by ICD-10 criteria.
Nutrition: Weight loss, reduced appetite, nausea, dyspepsia? BMI, MNA-SF.
Pain: Previous/current problem? Is the cause identified? In need of better analgesia?
Breathing: Dyspnea?
Hydration: Signs of dehydration? Overhydration/edema?
Natural functions: Urinary incontinence? Voiding problems? Diarrhea/constipation?
Mobility: Gait problems? Dizziness? Walking aids? History of falling?
Sleep: Any problems related to sleep?

Sort out current main problem(s) concerning the patient's health.

Medications

Are all drugs used as prescribed? Any problems with administration? Has the patient any suspicions regarding side effects? Is the patient aware of the indication for different drugs? If symptomatic medications – what is the current situation regarding the target symptom? If unclear indication, explore the patient's willingness to reconsider dosages or to discontinue the drug in order to assess effectiveness. For prophylactic medications, identify thoughts on the balance between current drug use and reducing future risks.

Clinical examination

Clinical examination with emphasis on relevant conditions and current symptoms.

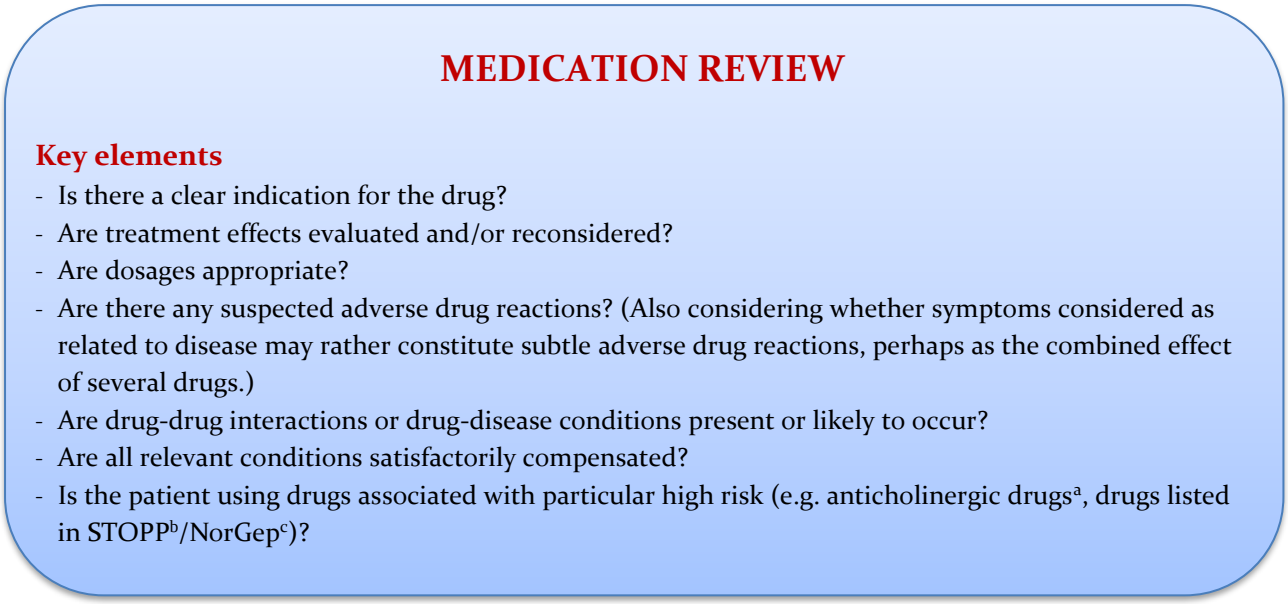
Supplementary tests

Blood pressure (including orthostatic)
Pulse rate, respiratory rate
ECG
Relevant blood analyses
Serum concentration of relevant drugs
Pharmacogenetic tests:

- CYP2C19, CYP2C9, CYP2D6 (all patients)
- CYP3A5 and SLCO1B1 if using statins
- SLC6A4 if using SSRI's
- VKORC1 if using warfarin

Abbreviations: IQCODE=Informant Questionnaire on Cognitive Decline in the Elderly. CDR=Clinical Dementia Rating Scale. NPS=Neuropsychiatric symptoms. BMI=Body Mass Index. MNA-SF=Mini Nutritional Assessment Short Form. ECG=Electrocardiogram.

eFigure 2. Key Elements of the Medication Review Carried Out by the Geriatrician



[a] Duran CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. Eur J Clin Pharmacol 2013;69:1485-96.
[b] O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing 2015;44:213-8.
[c] Rognstad S, Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J. The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study. Scand J Prim Health Care 2009;27:153-9.

eTable 1. Patient Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Listed with one of the participating FPs	Expected to become permanently institutionalized within six months
Home-dwelling	Life expectancy judged to be six months or less
Medications administered by the home nursing service	Moderate/severe dementia (i.e., CDR score > 1) and contact with the closest proxy less than once every second week
Age 70 years or more	Not speaking or understanding Norwegian
Use of at least seven different systemic medications taken regularly (preparations for inhalation, vitamin supplements and laxatives are included, but not topical drugs like eye drops and ointments)	The FP does not want the particular patient to participate (in case of important reasons not covered by the other exclusion criteria)
Signed informed consent given by the patient or his/her closest proxy	

Abbreviations: FP=Family physician. CDR=Clinical Dementia Rating Scale.

eTable 2. Study Assessment Procedures and Timetable

Assessments	Baseline	16 weeks	24 weeks
Assessments directly involving the patient			
Demographics, diagnoses, CIRS, MNA-SF	x		
15D	x	x	x
SPPB	x	x	x
Gait speed	x	x	x
Grip strength	x	x	x
Digit Span	x	x	x
Trail making test A + B	x	x	x
Five Digits Test	x	x	x
Falls		x	x
Orthostatic blood pressure	x	x	x
Weight	x	x	x
Assessments of drug use			
Current drug use and changes in pharmacotherapy	x	x	x
MAI	x	x	x
AOU	x	x	x
Assessments based on observation and/or proxy information			
FIM	x	x	x
CDR	x		
Assessments based on information from a close relative			
15D	x	x	x
RSS	x	x	x
IQCODE	x		
Administrative data			
Hospital admissions		x	x
Number of days in own home		x	x
Admission to permanent institutional care		x	x
Use of home nursing service (hours per week)	x	x	x
Mortality		x	x

Abbreviations: CIRS=Cumulative Illness Rating Scale. MNA-SF=Mini Nutritional Assessment Short Form. SPPB=Short Physical Performance Battery. MAI=Medication Appropriateness Index. AOU=Assessment of Underutilization. FIM=Functional Independence Measure. CDR=Clinical Dementia Rating Scale. RSS= Relative Stress Scale. IQCODE=Informant Questionnaire on Cognitive Decline in the Elderly.

eTable 3. Details on Secondary Outcomes

Outcome measure	Description
Medication Appropriateness Index (MAI)[19]	Assessed by a clinical pharmacist experienced in geriatric pharmacotherapy. The clinical pharmacist was not involved in the intervention, and was blinded for group allocation. Assessments were based on anonymized patient summaries, including information from the FP's electronic patient record on important events during the follow-up period. Each drug in use was given a score from 0 to 18, then scores of all drugs were summated to obtain the patient's total MAI score, with higher scores representing less appropriate drug use.
Assessment of Underutilization (AOU)[20]	Assessed by a clinical pharmacist, as described for the MAI. The AOU assess the number of omissions of drugs that should have been prescribed.
Short Physical Performance Battery (SPPB)[21]	Assessed by the research assistant. Scores range from 0 to 12, with higher scores representing better physical function.
Gait speed[22]	Assessed by the research assistant, using a 4 meter long track, starting from a still, standing position.
Grip strength	Assessed by the research assistant. We carried out three measurements for each arm, using a Kern MAP 80K1 dynamometer. The highest value was used in the analyses.
Functional Independence Measure (FIM)[23]	Assessed by the research assistant. Scores range from 18 to 126, with higher scores indicating more independence.
Relative Stress Scale (RSS)[18]	Assessed by the research assistant, by interview of the closest relative. Scores range from 0 to 60, with higher scores representing a higher burden of care.
Digit span forwards[24]	Assessed by the research assistant. Reported as the maximum digit span completed by the patient.
Digit span backwards[24]	Assessed by the research assistant. Reported as the maximum digit span completed by the patient.
Trail Making Test A[25]	Assessed by the research assistant. Reported as the time (in seconds) spent on completing the test. For patients cognitively incapable of completing Trail Making Test A, a value of 500 s was imputed (worse than the slowest patient completing the test).
Trail Making Test B[25]	Assessed by the research assistant. Reported as the time (in seconds) spent on completing the test. For patients cognitively incapable of completing Trail Making Test B, a value of 550 s was imputed (worse than the slowest patient completing the test).
Five Digits Test (FDT)[26]	Assessed by the research assistant. FDT consists of four conditions; reading, counting, inhibiting and shifting. For all conditions, the time (in seconds) spent on completing the test and the number of uncorrected mistakes were registered. Because of the large amount of secondary outcomes, we chose to focus on *time* when reporting results on FDT. Patients who failed to complete FDT because of cognitive difficulties were imputed with a value worse than the slowest patient completing the test.
Five Digits Test 1 (reading)	For patients cognitively incapable of completing the test, a value of 300 s was imputed.
Five Digits Test 2 (counting)	For patients cognitively incapable of completing the test, a value of 400 s was imputed.
Five Digits Test 3 (inhibiting)	For patients cognitively incapable of completing the test, a value of 300 s was imputed.
Five Digits Test 4 (shifting)	For patients cognitively incapable of completing the test, a value of 350 s was imputed.

eTable 3. Details on secondary outcomes (continued)

Outcome measure	Description
Orthostatic blood pressure	Assessed by the research assistant, using a validated, automated blood pressure monitor (UA-767 Plus 30, A&D Medical, San Jose, CA, USA). Supine blood pressure and pulse rate were measured twice, after a minimum of five minutes of rest, and the mean value was used for the analyses. The patient then stood up, and measurements were repeated after one minute.
Falls	Falls were registered in calendars handed out to patients or caregivers (in case of dementia), and the number of falls were assessed by the research assistant at each follow-up visit.
Use of home nursing service	Assessed by the research assistant. Information on the current use of home nursing service was given by the home nursing service at each follow-up visit.
Hospital admissions	The research assistant asked the patients, their closest proxy and the home nursing service about admissions to hospital, nursing home or other institutions. The FP's electronic patient record for the follow-up period was also checked for notes on hospital admissions etc. In case of hospital admissions, the discharge summary was obtained.

eTable 4. Estimation of Power in Different Scenarios, Provided a Total of 200 Participants

Δ	SD	r	Power %
0.035	0.08	1	59
0.035	0.08	0	87
0.035	0.07	1	71
0.035	0.07	0	94

Δ = Difference in change in 15D HRQoL single index score
SD = Standard deviation of change over time in 15D score
r = Correlation between patients within each cluster

eTable 5. Estimated Effect of Intervention by Various Analyses of Primary Outcome at Week 16

Analysis	Estimated effect of intervention (95% CI)	P value
Primary analysis, unadjusted[a]	0.045 (0.004 to 0.086)	0.033
Primary analysis, adjusted[b]	0.055 (0.014 to 0.096)	0.010
Linear mixed model, unadjusted[c]	0.048 (0.006 to 0.090)	0.025
Linear mixed model, adjusted[d]	0.048 (0.006 to 0.090)	0.026
Sensitivity analysis 1, unadjusted[e]	0.030 (0.008 to 0.052)	0.009
Sensitivity analysis 1, adjusted[f]	0.036 (0.015 to 0.057)	0.001
Sensitivity analysis 2, unadjusted[g]	0.045 (0.003 to 0.086)	0.036
Sensitivity analysis 2, adjusted[h]	0.055 (0.013 to 0.096)	0.010
Sensitivity analysis 3, unadjusted[i]	0.042 (0.002 to 0.083)	0.040
Sensitivity analysis 3, adjusted[j]	0.053 (0.012 to 0.094)	0.012

[a] Deceased patients were given the value “0” on 15D, and patients missing for other reasons were handled with multiple imputation. Analyzed by analysis of covariance, adjusted for baseline values and stratum. Robust estimation of standard errors with FP as the cluster was applied. N=174.

[b] Deceased patients were given the value “0” on 15D, and patients missing for other reasons were handled with multiple imputation. Analyzed by analysis of covariance, adjusted for baseline values, stratum and CDR-SOB score. Robust estimation of standard errors with FP as the cluster was applied. N=174.

[c] Linear mixed model with FP as a random factor, time point (baseline and 16 weeks), treatment and the interaction between time and treatment as fixed factors, and cluster size as a covariate. N=174.

[d] Linear mixed model with FP as a random factor, time point (baseline and 16 weeks), treatment and the interaction between time and treatment as fixed factors, and cluster size, age, sex, CDR-SOB and use of home nursing service as covariates. N=174.

[e] Patients not handled according to randomization and patients that were missing (all reasons) were excluded (per protocol analysis). Analyzed by analysis of covariance, adjusted for baseline values and stratum. Robust estimation of standard errors with FP as the cluster was applied. N=162.

[f] Patients not handled according to randomization and patients that were missing (all reasons) were excluded (per protocol analysis). Analyzed by analysis of covariance, adjusted for baseline values, stratum and CDR-SOB score. Robust estimation of standard errors with FP as the cluster was applied. N=162.

[g] Patients missing for other reasons than death were excluded, but deceased patients were kept with the value “0” on 15D. Analyzed by analysis of covariance, adjusted for baseline values and stratum. Robust estimation of standard errors with FP as the cluster was applied. N=169.

[h] Patients missing for other reasons than death were excluded, but deceased patients were kept with the value “0” on 15D. Analyzed by analysis of covariance, adjusted for baseline values, stratum and CDR-SOB score. Robust estimation of standard errors with FP as the cluster was applied. N=169.

[i] Patients missing for other reasons than death were handled as “last observation carried forward” (LOCF), but deceased patients were kept with the value “0” on 15D. Analyzed by analysis of covariance, adjusted for baseline values and stratum. Robust estimation of standard errors with FP as the cluster was applied. N=174.

[j] Patients missing for other reasons than death were handled as “last observation carried forward” (LOCF), but deceased patients were kept with the value “0” on 15D. Analyzed by analysis of covariance, adjusted for baseline values, stratum and CDR-SOB score. Robust estimation of standard errors with FP as the cluster was applied. N=174.

eTable 6. Secondary Outcomes

Outcome	Time	Estimated effect of intervention (95% CI)	Comment
		OR	
Assessment of Underutilization	Week 16	0.24 (0.09 to 0.61)[a]	OR for having ≥ 1 medication omission
	Week 24	0.33 (0.15 to 0.71)[a]	OR for having ≥ 1 medication omission
Falls	Entire study period	0.75 (0.35 to 1.60)[a]	OR for experiencing ≥ 1 fall
Hospital admissions	Entire study period	2.03 (0.98 to 4.24)[a]	OR for being admitted to hospital at least once
Admission to permanent institutional care	Entire study period	0.49 (0.09 to 2.72)[a]	
Mortality	Week 24	0.36 (0.08 to 1.58)[a]	
		Mean difference	
Weight, kg	Week 16	0.23 (-0.97 to 1.42)[b]	
	Week 24	0.37 (-0.72 to 1.47)[b]	
Use of home nursing service, min/week	Week 16	-2.6 (-37.4 to 32.1)[b]	
	Week 24	-2.2 (-31.7 to 27.3)[b]	
Time spent in own home, days	Entire study period	1.9 (-3.7 to 7.6)[c]	

Abbreviations: CI=Confidence interval. OR=Odds ratio.

[a] Analyzed by logistic regression, adjusted for cluster size, age, sex, severity of dementia and use of home nursing service at baseline, and using a clustered sandwich estimator to estimate standard errors. The control group constitutes the reference.

[b] Analyzed by linear mixed model, adjusted for cluster size, age, sex, severity of dementia and use of home nursing service at baseline, applying an unstructured covariance matrix, and using a clustered sandwich estimator to estimate standard errors.

[c] Analyzed by multiple linear regression, adjusted for cluster size, age, sex, severity of dementia and use of home nursing service at baseline, and using a clustered sandwich estimator to estimate standard errors.

eTable 7. Drugs in Use at Baseline

ATC group	Intervention group (n=87)		Control group (n=87)	
	Prescriptions	Patients, n (%)	Prescriptions	Patients, n (%)
Alimentary tract and metabolism (ATC group A)	**184**	**75 (86)**	**184**	**77 (89)**
A02 Drugs for acid related disorders	30	28 (32)	29	29 (33)
A03 Drugs for functional gastrointestinal disorders	1	1 (1)	0	0 (0)
A06 Drugs for constipation	22	20 (23)	21	16 (18)
A07 Antidiarrheals, antiinflammatory agents	7	6 (7)	3	3 (3)
A10 Drugs used in diabetes	27	17 (20)	27	18 (21)
A11 Vitamins	69	51 (59)	76	56 (64)
A12 Mineral supplements	28	26 (30)	28	25 (29)
Blood and blood forming organs (ATC group B)	**112**	**76 (87)**	**89**	**72 (84)**
B01 Antithrombotic agents	87	70 (81)	74	68 (78)
B03 Antianemic preparations	25	23 (26)	15	13 (15)
Cardiovascular system (ATC group C)	**243**	**77 (89)**	**246**	**80 (92)**
C01 Cardiac therapy	13	13 (15)	18	17 (20)
C02 Antihypertensives	2	2 (2)	4	4 (5)
C03 Diuretics	48	41 (47)	61	56 (64)
C07 Beta blocking agents	55	55 (63)	52	52 (60)
C08 Calcium channel blockers	27	27 (31)	29	28 (32)
C09 Agents acting on the renin-angiotensin system	46	44 (51)	47	47 (54)
C10 Lipid modifying agents	52	52 (60)	35	35 (40)
Genitourinary system and reproductive hormones (ATC group G)	**31**	**23 (26)**	**17**	**14 (16)**
G03 Sex hormones and modulators of the genital system	4	4 (5)	4	4 (5)
G04 Urological drugs	27	20 (23)	13	11 (13)
Systemic hormonal preparations, excl. reproductive hormones and insulin (ATC group H)	**20**	**18 (21)**	**21**	**20 (23)**
H02 Corticosteroids for systemic use	9	9 (10)	5	5 (6)
H03 Thyroid therapy	11	11 (13)	15	15 (17)
H05 Calcium homeostasis	0	0 (0)	1	1 (1)

eTable 7. Drugs in use at baseline (continued)

ATC group	Intervention group (n=87)		Control group (n=87)	
	Prescriptions	Patients, n (%)	Prescriptions	Patients, n (%)
Antiinfectives for systemic use (ATC group J)	**9**	**9 (10)**	**12**	**12 (14)**
J01 Antibacterials for systemic use	9	9 (10)	12	12 (14)
Antineoplastic and immunomodulating agents (ATC group L)	**3**	**3 (3)**	**4**	**4 (5)**
L01 Antineoplastic agents	2	2 (2)	1	1 (1)
L02 Endocrine therapy	1	1 (1)	2	2 (2)
L04 Immunosuppressants	0	0 (0)	1	1 (1)
Musculoskeletal system (ATC group M)	**23**	**22 (25)**	**21**	**21 (24)**
M01 Antiinflammatory and antirheumatic products	2	2 (2)	2	2 (2)
M04 Antigout preparations	10	10 (12)	11	11 (13)
M05 Drugs for treatment of bone diseases	11	11 (13)	8	8 (9)
Nervous system (ATC group N)	**174**	**68 (78)**	**156**	**69 (79)**
N02A Opioids	15	13 (15)	18	16 (18)
N02B Non-opioids	33	33 (38)	28	27 (31)
N03 Antiepileptics	19	15 (17)	16	15 (17)
N04 Anti-parkinson drugs	6	3 (3)	6	3 (3)
N05A Antipsychotics	11	10 (12)	4	3 (3)
N05B Anxiolytics	9	9 (10)	11	11 (13)
N05C Hypnotics and sedatives	37	31 (36)	34	32 (37)
N06A Antidepressants	31	26 (30)	30	27 (31)
N06D Anti dementia drugs	12	11 (13)	7	6 (7)
Respiratory system (ATC group R)	**75**	**31 (36)**	**72**	**32 (37)**
R03 Drugs for obstructive airway diseases	57	22 (25)	48	18 (21)
R05C B Mucolytics	6	6 (7)	5	5 (6)
R05D A04 Codeine[a]	3	3 (3)	8	8 (9)
R06 Antihistamins for systemic use	9	9 (10)	10	10 (12)
Various (ATC group V)	**0**	**0 (0)**	**1**	**1 (1)**
V03AE Drugs for treatment of hyperkalemia and hyperphosphatemia	0	0 (0)	1	1 (1)

[a] All prescriptions of codeine classified in ATC group R are codeine used as an analgesic (in combination with paracetamol)

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