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Reducing the anticholinergic and sedative load in older patients on polypharmacy by pharmacist-led medication review: a randomised controlled trial

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ABSTRACT

Objective To evaluate if a pharmacist-led medication review is effective at reducing the anticholinergic/sedative load, as measured by the Drug Burden Index (DBI).

Design Randomised controlled single blind trial.

Setting 15 community pharmacies in the Northern Netherlands.

Participants 157 community-dwelling patients aged ≥65 years who used ≥5 medicines for ≥3 months, including at least one psycholeptic/psychoanaleptic medication and who had a DBI≥1.

Intervention A medication review by the community pharmacist in collaboration with the patient's general practitioner and patient.

Primary and secondary outcomes measures The primary outcome was the proportion of patients whose DBI decreased by at least 0.5. Secondary outcomes were the presence of anticholinergic/sedative side effects, cognitive function, activities of daily living, quality of life, hospital admission and mortality. Data were collected at baseline and 3 months follow-up.

Results Mean participant age was 75.7 (SD, 6.9) years in the intervention arm and 76.6 (SD, 6.7) years in the control arm, the majority were female (respectively 69.3% and 72.0%). Logistic regression analysis showed no difference in the proportion of patients with a≥0.5 decrease in DBI between intervention arm (17.3%) and control arm (15.9%), (OR 1.04, CI 0.47 to 2.64, p=0.927). Intervention patients scored higher on the Digit Symbol Substitution Test, measure of cognitive function (OR 2.02, CI 1.11 to 3.67, p=0.021) and reported fewer sedative side effects (OR 0.61, CI 0.40 to 0.94, p=0.024) at follow-up. No significant difference was found for other secondary outcomes.

Conclusions Pharmacist-led medication review as currently performed in the Netherlands was not effective in reducing the anticholinergic/sedative load, measured with the DBI, within the time frame of 3 months. Preventive strategies, signalling a rising load and taking action before chronic use of anticholinergic/sedative medication is established may be more successful.

Trial registration number NCT02317666.

Strengths and limitations of this study

► A successfully completed randomised controlled trial, which was the first to focus on changing anticholinergic and sedative load by medication review.
► Appropriately powered to detect a clinically relevant medium difference.
► Showing the effect of 'real world' practiced medication review, rather than the theoretical approach described in guidelines.
► Three-month follow-up might have been too short to detect full effects of medication review, for example, due to stepwise reduction of medication, however very few dosage changes were seen.

BACKGROUND

Older people suffer from many medical conditions and use more medication than any other age group. Multiple medication use in combination with age-related physiological changes increase the risk of medication related harm including adverse drug events, drug-drug-interactions and drug-disease-interactions.[1] Medications with anticholinergic and/or sedative properties are of particular concern in older people, because they worsen cognitive impairment and physical functioning, increase the risk of falls and negatively impact activities of daily living, hospitalisation and mortality.[2 3] Despite the risks, these medications are commonly prescribed to older individuals.[4 5] Different measures have been developed to quantify the anticholinergic load in patients.[6] The Drug Burden Index (DBI) determines an individual's exposure to anticholinergic and sedative medication taking into account the dose.[7 8] A high DBI has been associated with impairments in both physical and cognitive functions among older individuals.[9 10] Hence, decreasing exposure to anticholinergic and

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sedative medication, as measured by the DBI, may have important health benefits in older people.

Two small Australian studies suggest that medication review could be a promising strategy in reducing the DBI in community dwelling older people.[11] [12] Medication review is 'a structured critical examination of a person's medicines with the objective of reaching an agreement with the person about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste'.[13] While meta-analyses of studies in different settings show a lack of effectiveness on outcomes such as mortality or hospital (re-)admissions,[14–16] these studies included different types of medication review. Well-structured medication review with good cooperation between pharmacist and general practitioner (GP) and involvement of the patient was most likely to be successful.[17] [18] Furthermore fee-for-pharmacist-led medication review seemed to have positive health benefits on the patient.[19] The most effective method for medication review remains unknown. Focusing on specific subgroups such as older people with multiple comorbidities and polypharmacy[20] or patients suffering from pain[21] may be one strategy to optimise medication review associated benefits. To date, there is no consensus on the effectiveness of medication review as a strategy to reduce anticholinergic and sedative load as measured by the DBI. Therefore, the primary aim of this study was to evaluate if a medication review is an effective strategy to reduce anticholinergic and sedative load as measured by the DBI. Secondarily, we evaluated the effect of a medication review on patient outcomes including cognitive function, risk of falls, activities of daily living and quality of life.

METHODS

Study design, setting and participants

We conducted a randomised controlled, single blind trial in 15 community pharmacies from December 2014 until October 2015 in the Northern Netherlands. Pharmacies were recruited via the regional association of pharmacists and participation was voluntary. One pharmacist per pharmacy was involved in the study. In Dutch community pharmacy practice, all registered pharmacists are allowed to perform medication reviews. Furthermore, pharmacists collaborate with GPs in their area. This includes local regular meetings of pharmacists and GPs in pharmacotherapy counselling groups.[22] In the Netherlands, each individual is registered with a single pharmacy.[23] Pharmacies hold a complete electronic medication history for each patient registered with them. When undertaking a medication review, it is routine practice of pharmacists to obtain an extensive summary of the electronic patients' medical records, including latest recorded episodes and lab-values, from the GP.[24] At the time of the study, all Dutch community pharmacists were required to perform medication reviews in cooperation with the GP for high-risk patients according to the guidelines.[25] Patients who

were aged ≥65 years, living independently, using ≥5 medications for ≥3 months, including at least one psycholeptic or psychoanaleptic medication (Anatomic Therapeutic Classification (ATC) code N05 or N06)[26] and with a DBI≥1 were identified by the pharmacist and invited to participate in the study. Exclusion criteria were limited life expectancy (<3 months), non-Dutch language speaker or advanced dementia. Patients who had received a medication review within the past 9 months before the study period and patients who needed a medication review urgently were also excluded. Exclusion criteria were identified by the pharmacist with whom the patient was registered. The study protocol has been published elsewhere.[27]

Randomisation, allocation and blinding

Eligible patients were approached by the pharmacist and asked to provide written informed consent. In each pharmacy, patients willing to participate were then matched in pairs by gender, age, DBI and number of medications. One patient of each pair was randomly assigned to the intervention condition. All participants gave written consent prior to the intervention allocation. The randomisation process was conducted by the principal investigator, who was not involved in recruitment or data collection. The researchers who enrolled the patients and collected the data were kept blind to the allocation. Pharmacists and patients could not be kept blind, but were explicitly asked not to reveal study allocation for individual patients to the researchers who collected the data. Therefore, this was a single blind study.

Intervention

The intervention was a medication review conducted by the community pharmacist in close collaboration with the patients' GP and, if needed, other medical specialists. In the Netherlands, medication review consisted of five steps.[25] Step one was a face-to-face consultation between the pharmacist and patient to discuss medication use. Second, the pharmacist undertook a pharmacotherapeutic medication review, identified potential pharmacotherapeutic problems taking into account the patient's medical records, including latest recorded episodes and lab-values. Accordingly, the pharmacist drafted written recommendations for medication optimisation to discuss with the patients' GP. Third, a multidisciplinary meeting between pharmacist and GP was held. At this meeting, the potential medication problems of the patient were discussed and draft of a pharmacotherapeutic action plan was decided. Fourth is a discussion of the draft pharmacotherapeutic action plan between patient and pharmacist and/or GP. The patients' expectations and wishes were key elements in the decision-making process and were included in the final action plan. Fifth, a follow-up of the final pharmacotherapeutic action plan was undertaken. Further detail of the medication review process and the Dutch guideline underpinning the study can be found in our previously published study protocol.[27]

The pharmacists participating in the study all undertook regular medication reviews as part of their practice and as such were familiar with the guideline. Nonetheless, we provided the guidelines to the pharmacists with the request to focus on anticholinergic and sedative medications. No additional educational material on anticholinergic and sedative medication was provided. In order to get a reflection of 'real world' practice, we let the pharmacists perform the medication reviews according to their routine practice, but we did check whether all five steps were conducted. The medication review took place within days after the baseline measurement for the intervention patients. In the control arm, patients received the medication review after the study period.

Outcomes

The primary outcome was defined as the difference in proportion of patients having a decrease of DBI≥0.5 at 3-month follow-up. We chose a 3-month follow-up because this was a reasonable time frame to detect medication changes by the medication review. A longer follow-up would have increased the chance of medication changes due to other reasons, such as changes in disease status. Our hypothesis was that the proportion with a 0.5 decrease in DBI would be higher in the intervention arm compared with the control arm. We chose 0.5, as this equals the cessation of one drug, which we considered a clinically relevant decrease. The DBI was calculated using the following formula[8]:

$$DBI = \sum \frac{D}{D + \delta}$$

D=daily dose and δ=minimum recommended daily dose were derived for the study from Dutch standard reference sources.[28 29] Except for sensory and dermatological preparations, all chronic medications (ie, those used for ≥3 months) with anticholinergic properties (dry mouth, constipation and urine retention) and sedative properties based on Dutch standard reference sources[28–30] were included in the calculation. Medication data were derived from electronic pharmacy dispensing data and were verified with the patient.

We included the following secondary outcomes: anticholinergic side effects, measured by the Udvalg for Kliniske Undersogelser side effect rating scale,[31] sedative side effects, derived from a patient-reported adverse drug event questionnaire[32] and risk of falls, determined by the Up&Go test.[33] Cognitive function was measured using validated tests for memory and executive function, namely the Seven Minute Screen (7 MS),[34] the Trailmaking Test A & B[35] and Digit Symbol Substitution Test (DSST).[36] The latter has also previously been used to examine the validity of the DBI.[8] Activities of daily living were derived using the validated Groningen Activity Restriction Scale (GARS)[37 38] and quality of life was measured by the Euroqol-5 Dimension-3 Level questionnaire, including visual analogue scale.[39] All tools were administered in Dutch and data were collected in a standardised manner, using data collection sheets, by researchers who were trained by a psychologist. Data collection took place at baseline and 3-month follow-up for both allocations. Patients with the inability to walk were excluded from the Up&Go test and the GARS questionnaire. At follow-up, the number of fall incidents, hospital admission and mortality were assessed based on patient/relative reporting.

Sample size calculation

To the best of our knowledge, only one randomised pilot study has been conducted assessing the DBI.[12] We therefore could not calculate the sample size 'a priori'. However, we estimated a sample size based on a power of 80% at a significance of 0.05 and an intraclass correlation coefficient up to 0.2 to detect a medium effect size on the primary outcome.[40] We chose a medium effect size as we considered a small effect size to be not clinically relevant and a power to detect a medium effect size also to be capable of detecting a large effect size. For this calculation, around 160 participants (80 in control arm and 80 in intervention arm) were needed. We expected a non-response rate of 60% and therefore aimed to invite 400 patients to participate in the study.

Statistical analysis

We performed two analyses. In the first analysis, we included all patients with a baseline measurement. In the second analysis, we included all patients who were not lost to follow-up and who received the intervention as allocated. Descriptive statistics were calculated for both allocation arms at baseline. For the analysis of the primary outcome, we initially considered a generalised linear mixed effects model to adjust for dependence of observations (ie, clustering of patients within pharmacies). However, as the intraclass correlation was not significant and no significant clustering was observed, extension of the model with random effects at the level of pharmacies was not necessary. Therefore, only fixed effects were considered and standard fixed effects logistic regression model applied. Most secondary outcomes were examined with standard regression models. Variables with a skewed distribution were transformed before analysis. For dichotomous variables, we reported percentages and numbers of patients in the best scoring group, for skewed variables we report the median and IQR and for normally distributed data, we report the mean and SD. Further detail on the analysis of secondary outcome tests and questionnaires data can be found in online supplementary appendix table 1. Reported falls, hospitalisation and mortality were only assessed from patients with a follow-up measurement. These variables were dichotomised, reported as number and percentages of patients and analysed using Fisher's exact test. A sensitivity analysis was conducted on outliers (online supplementary appendix table 2) and all analyses were adjusted for gender, age and number of medication at baseline. Secondary outcomes were also adjusted for baseline scores. Analyses were done in SPSS 24 and MLwiN 2.36, and statistical tests were two-sided and conducted at the 5% significance level.

Missing data

Few data were missing for the primary outcome. Of the two patients, who were lost to follow-up, the baseline observation for medication use was carried forward to follow-up. For eight patients, medication use could not be verified with the patient, as they could not be reached by telephone despite several attempts. For these patients, the medication data from the pharmacy dispensing system were used. For secondary outcomes, 5.3% of data were missing in the complete dataset, mostly at follow-up (4.8%). In the intervention arm, 7.0% of data were missing (6.1% at follow-up) across 18 patients, whereas in the control arm 3.7% were missing (3.4% at follow-up) across 12 patients. In total, 30 patients had missing data, of whom two were lost to follow-up. Eight patients were not able to complete one or more cognitive tests (0.5% of all data). Eleven patients could not be tested at follow-up within the study period, six patients due to sickness, four patients due to practical reasons (despite numerous attempts, we were unsuccessful to arrange an appointment for the follow-up measurement) and one patient had died 2 days before the follow-up appointment. A few data were missing for other reasons across nine patients, for example patients forgetting their glasses, due to time constraints or other reasons.

Missing data in cognitive tests due to inability of the patient to complete the task were replaced with the worst score for that specific group. Missing data of patients who could not be tested at follow-up within the study period or who had missing data for other reasons were replaced by multiple imputation (five times) in SPSS 24. In this paper, we report on the imputed dataset. Sensitivity analysis showed no difference between the dataset with and without missing data.

Patient and public involvement

Patients and or public were not involved in the design or conduct of the study. After the study period, all participants received a thank you letter including a brief summary of the overall results.

RESULTS

Participant flow

Overall, 498 patients were approached for participation, 164 patients provided informed consent (32.9% response rate) and 157 patients completed at least the baseline measurement and were included in the first analysis (figure 1). The dropout rate was 4.3%.
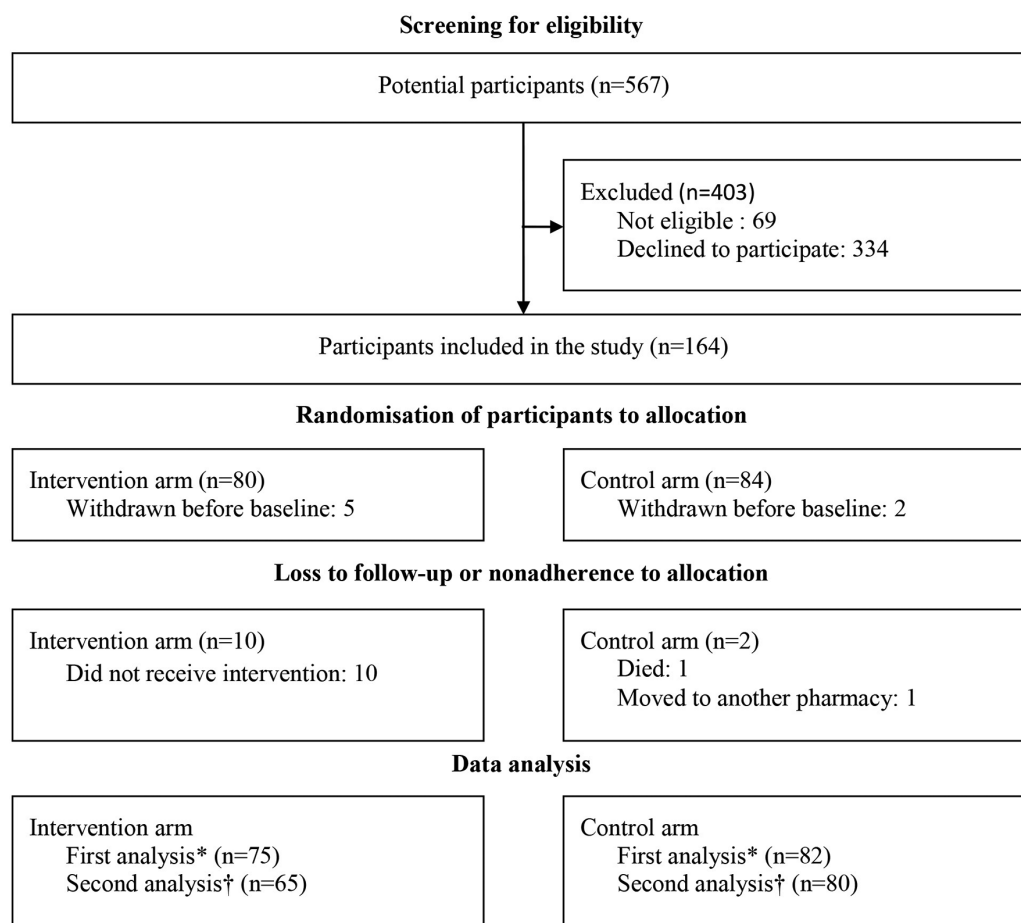
Screening for eligibility

Potential participants (n=567)

Excluded (n=403)
    Not eligible : 69
    Declined to participate: 334

Participants included in the study (n=164)

Randomisation of participants to allocation

Intervention arm (n=80)
    Withdrawn before baseline: 5

Control arm (n=84)
    Withdrawn before baseline: 2

Loss to follow-up or nonadherence to allocation

Intervention arm (n=10)
    Did not receive intervention: 10

Control arm (n=2)
    Died: 1
    Moved to another pharmacy: 1

Data analysis

Intervention arm
    First analysis* (n=75)
    Second analysis† (n=65)

Control arm
    First analysis* (n=82)
    Second analysis† (n=80)

Figure 1 Participant flow. *All patients who had a baseline measurement. †All patients who were not lost to follow-up and received the intervention as allocated.

Table 1 Demographic characteristics at baseline

	Intervention (n=75)	Control (n=82)
Age (years) mean (SD)	75.7 (6.9)	76.6 (6.7)
Sex (female) (n (%))	52 (69.3)	59 (72.0)
Number of medicines (mean (SD)	8.4 (2.4)	9.3 (3.2)
DBI (mean (SD)	3.1 (1.0)	3.2 (1.0)
Marital status (n (%))		
Partner	33 (44.0)	44 (53.6)
Widow/widower/Divorced/single	34 (45.3)	32 (39.0)
Unknown	8 (10.6)	6 (7.3)
Level of education (n (%))		
No/low/middle	58 (77.3)	64 (78.0)
High	9 (12.0)	13 (15.8)
Unknown	8 (10.6)	5 (6.0)
Medication use at baseline (top 5 (n (%)))		
ATC nervous system	75 (100)	82 (100)
ATC cardiovascular	70 (93.3)	74 (90.2)
ATC alimentary tract	64 (85.3)	71 (86.6)
ATC blood/blood forming organs	49 (65.3)	46 (56.1)
ATC respiratory tract	20 (26.7)	38 (46.3)

ATC, Anatomic Therapeutic Classification; DBI, Drug Burden Index.

Participant characteristics

The average participant age was 75.7 (SD, 6.9) years in the intervention arm and 76.6 (SD, 6.7) years in the control arm, and the majority were female (respectively 69.3% and 72.0%). Participants in the control arm used slightly more medicines at baseline (9.3 (SD, 3.2) to 8.4 (SD, 2.4)), and more control patients were living with a partner (53.6%–44%)%) (table 1).

Primary outcome

In the first analysis, which included all patients with a baseline measurement, the proportion of patients with a decrease of DBI≥0.5 did not differ between patients in intervention arm and control arm (17.3% to 15.9%, OR 1.04, CI 0.47 to 2.64, p=0.927). Similar results were obtained in the second analysis, which included all patients who were not lost to follow-up and who received the intervention as allocated (table 2). Descriptive analysis showed medication changes (starting, stopping, dosage change) of DBI medications on ATC code level

1 in 53.8% of patients from intervention arm and in 45.0% of patients from control arm. For cardiovascular DBI medications, dose increases and dose decreases of different medications occurred in 10.8% patients from intervention arm compared with 1.3% of patients from control arm (online supplementary appendix table 3).

Secondary outcome

Secondary outcome tests and questionnaires were analysed including all patients who were not lost to follow-up and who received the intervention as allocated (table 3). A difference was seen in the DSST and reporting of sedative side effects between allocation arms. Patients in the intervention arm scored higher at follow-up on average (3 (SD, 1) to 1 (SD, 0) point (s), OR 2.02, CI 1.11 to 3.67, p=0.021) and reported less sedative side effects at follow-up compared with the control arm (−1 (IQR, −2) to 1 (IQR, 0) point(s), OR 0.61, CI 0.40 to 0.94, p=0.024). For all other secondary outcomes, no difference was found between intervention and control arm.

Table 2 Proportion of patients having a decrease in DBI≥0.5 by analysis type

	Proportion with decrease of DBI≥0.5 (%, n)			
Analysis type	Intervention	Control	OR (95% CI)*	P values
First analysis (n=157)	17.3 (13)	15.9 (13)	1.04 (0.47 to 2.64)	0.927
Second analysis (n=145)	18.5 (12)	16.3 (13)	1.09 (0.45 to 2.63)	0.857

First analysis: all patients with a baseline measurement.
Second analysis: all patients who were not lost to follow-up and who received the intervention as allocated.
*Binary logistic regression, adjusted for age, gender, number of medication at baseline.
DBI, Drug Burden Index.

Table 3 Secondary outcome tests and questionnaires at follow-up

Outcome	Intervention (n=65)		Control (n=80)		Treatment difference at FU (95% CI)
	BL score	Δ with FU	BL score	Δ with FU	
Trailmaking Test A, median (IQR)	59.0 (36.9)	−8.4 (−4.8)	61.0 (27.8)	−6.0 (1.6)	−0.01 (−0.11 to 0.09)*
Trailmaking Test B, median (IQR)	149.0 (103.0)	−3.9 (24.1)	152.0 (103.0)	1.0 (19.0)	−0.01 (−0.14 to 0.11)*
DSST, mean (SD)	36.4 (12.2)	2.6 (1.2)	36.4 (13.2)	1.0 (−0.3)	0.70 (0.11 to 1.30)*†
7 MS enhanced cued recall, % (n) best scoring	85 (55)	0 (0)	84 (71)	5 (4)	0.54 (0.15 to 1.90)‡
7 MS Benton temporal orientation, % (n) best scoring	95 (62)	−3 (−2)	99 (79)	−4 (−3)	1.38 (0.28 to 6.88)‡
7 MS clock drawing, % (n) best scoring	80 (52)	−8 (−5)	86 (69)	−6 (−5)	0.67 (0.28 to 1.62)‡
7 MS category fluency, mean (SD)	16.1 (5.5)	0.1 (−0.6)	15.9 (5.0)	0.4 (−0.3)	−0.18 (−1.55 to 1.20)*
GARS, % (n) best scoring	72 (46)	2 (−1)	69 (54)	0 (0)	1.73 (0.62 to 4.84) ‡§
Sedative side effects, median (IQR)	3.0 (5.0)	−1.0 (−2.0)	2.0 (4.0)	1 (0)	0.61 (0.40 to 0.94)¶†
UKU, median (IQR)	17.0 (22.0)	−3.0 (1.0)	18.0 (27.0)	−1.6 (−2.4)	0.97 (0.67 to 1.39)¶
EQ-5D-3L, % (n) best scoring	74 (48)	9 (6)	76 (61)	4 (3)	1.43 (0.51 to 4.03)‡
VAS, mean (SD)	6.6 (1.6)	−0.2 (0.0)	6.8 (1.4)	−0.1 (0.1)	−0.09 (−0.50 to 0.32)*
Up&Go, % (n) best scoring	66 (42)	0 (0)	64 (50)	4 (3)	1.37 (0.60 to 3.14)‡§

*Linear regression analysis (reporting unstandardised b).
†Statistically significant difference (p<0.05).
‡Logistic regression analysis (reporting OR).
§Deviation of number of patients: n=64 for intervention, n=78 for control, three patients were excluded from this test/questionnaire.
¶Negative binomial regression analysis (reporting incident rate ratio) used, all adjusted for age, gender, number of medication at baseline.
BL, baseline; FU, follow up, DSST, Digit Symbol Substitution Test; EQ-5D-3L, Euroqol-5 Dimension-3 Level; GARS, Groningen Activities Restriction Scale; UKU, Udvalg for Kliniske Undersogelser (measuring anticholinergic side effects); VAS, visual analogue scale (part of EQ-5D-3L); 7 MS, seven minute screen.

Reported falls and hospitalisation could be assessed from 136 patients who were included in the second analysis. No significant difference was found in reported falls between control arm and intervention arm, respectively, with 15 patients (19.5%) vs 18 patients (30.5%) (p=0.100). There was also no difference found between control arm and intervention arm in hospitalisation, with 9 (11.7%) vs 3 (5.1%) patients reporting unplanned hospital admission (p=0.149). Of all patients who were included in the study, two died, one (1.2%) in control arm and one (1.3%) in intervention arm (p=0.732).

DISCUSSION

In our study, pharmacist-led medication review did not reduce the anticholinergic and/or sedative medication load in older people within the first 3 months following review. In addition, medication review did not improve cognitive function, apart from the DSST. We also found that medication review had no effect on anticholinergic side effects, quality of life, activities of daily living, risk of falls, hospitalisation and mortality. However, intervention patients reported fewer sedative side effects.

Strengths and limitations of the study

This randomised controlled trial was the first to focus on changing anticholinergic and sedative medication load by medication review. The trial was completed successfully,

allocation arms were comparable and we achieved a medium response rate. We also believe our study was appropriately powered to detect a clinically relevant medium difference between intervention and control arm. Yet there are some methodological limitations that should be considered when interpreting our findings. First, our study design might have introduced a risk of contamination between intervention arm and control arm, as pharmacists and GPs could have been triggered to optimise medication use also for patients in the control arm during the study period. We know from the pharmacists that no structured medication reviews were performed for control patients during the study period. Therefore, we believe that changes we observed in control patients were due to usual care. Cluster randomisation may have prevented the chance of contamination, but this method has other disadvantages.[41] Second, although we did check whether all steps of the medication review were conducted, it was outside the scope of our study to investigate to what extent pharmacists adhered to methods recommended by the guideline on performing the medication review. Informal conversations with pharmacists suggested that although the guidelines recommend a face-to-face meeting between the pharmacist and GP, some pharmacists contacted the GP by phone, fax or email due to lack of time. This might have had an effect on the implementation of medication suggestions.[18] Furthermore, while as part of the

established collaboration between pharmacists and GPs in Dutch primary care, Dutch pharmacists routinely request an extensive summary of the electronic patient's medical records from the GP to perform a medication review, it is possible that some pharmacists did not do this. We performed a pragmatic trial and therefore our results reflect 'real-world' practice of how medication reviews were carried out in Dutch healthcare practice at the time of the study. Third, we followed patients for 3 months after the intervention. Possibly, more time may have been necessary to determine the effect of the intervention. We were not able to collect data about timing of the medication review steps, so in some cases there may have been delay in performing all steps. But in Dutch primary care, pharmacists and GP's have an established close collaboration and therefore we believe that long delays were unlikely. Another argument for a longer follow-up could be that changes in medication use may require more time, for example withdrawing of medication by stepwise reduction of dosing. However, there did not seem to be a difference in dosage changes between intervention arm and control arm. Finally, one-third of all eligible patients were willing to participate in the study. Given the frailty of this population and the time consuming nature of participation, we think this is a very reasonable response rate. Nevertheless, our results may not be generalisable to the total population.

Comparison with other studies

The medication changes in both arms were comparable. Small changes in different therapeutic medication groups suggest fluctuations of medication use over time as prescribing is a dynamic—rather than a static process. We do not know the pattern of fluctuations in anticholinergic and sedative medication prescribing; this should be explored in longitudinal studies powered to detect changes at medication level. Our results are in line with a number of meta-analyses, which also reported a lack of effect of medication reviews on a variety of patient outcomes.[14–16] Our results are in contrast to a number of studies, which found medication reviews to be effective in specific subgroups of patients with multiple comorbidities, polypharmacy and pain.[20 21] The medication reviews in these studies, however, were not specifically focusing on medication with anticholinergic and/or sedative properties as we did. Two small Australian studies suggest that the DBI can be lowered, but these studies were based on pharmacist recommendations and did not investigate actual implementation of these by the GP.[11 12] Although some lowering of the DBI was seen, the latter study did find that GPs had difficulties in changing medications, for example with those medications initiated by specialists. A recent study also showed that while it was possible to optimise use for a number of medication classes, psychotropic medications were among the most difficult to adjust.[42] So, despite guidance how to reduce anticholinergic and sedative medication,[43–45] as highlighted by our findings, there seem to be important barriers preventing reduction in clinical practice.

Conclusion and implications

Using the DBI, a highly vulnerable population group in need of medication optimisation can be identified. Pharmacist-led medication review as currently performed in the Netherlands did not appear effective in reducing the DBI. While our study was powered to detect a difference in medication use, it should be acknowledged that other patient outcomes, like geriatric syndromes (eg, risk of falls) and adverse events (eg, drug-related hospital admission) are very important for the evaluation of medication review in older patients. Further studies should ensure sufficient sample sizes to study these outcomes.[46 47] Despite some practical issues with the DBI, such as the lack of an international consensus-based list of anticholinergic/sedative medication including minimum doses,[10] we suggest to use the DBI as a tool to identify harmful medication users. This deprescribing approach may be suitable for other patient groups and in other settings such as nursing homes or GP practice with colocated pharmacist.[4 48–50] Enlarging the multidisciplinary team should also be considered, for example psychiatrists advising GPs on lowering or ceasing medication and psychologists assisting patients during withdrawal. Furthermore, signalling a rising load and taking action before chronic use of medication with anticholinergic and/or sedative properties is established may be the preferred approach.

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