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ORIGINAL ARTICLE

The effect of providing prescribing recommendations on appropriate prescribing: A cluster-randomized controlled trial in older adults in a preoperative setting

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Aims: The Systematic Tool to Reduce Inappropriate Prescribing is a method to assess patient's medication and has been incorporated into a clinical decision support system: STRIP Assistant. Our aim was to evaluate the effect of recommendations generated using STRIP Assistant on appropriate prescribing and mortality in a preoperative setting.

Methods: This cluster-randomized controlled trial was carried out at the preoperative geriatric outpatient clinic. Residents who performed a comprehensive geriatric assessment were randomized to the control group and intervention group in a 1:1 ratio. Visiting patients aged 70 years or older on 5 or more medications were included. Intervention: prescribing recommendations were generated by a physician using STRIP Assistant and given to the resident. Control group residents performed a medication review according to usual care.

Primary outcome: number of medication changes made because of potential prescribing omissions (PPOs), potentially inappropriate medications (PIMs), and suboptimal dosages according to the prescribing recommendations. Secondary outcome: 3-month postoperative mortality.

Results: 65 intervention and 59 control patients were included, attended by 34 residents. Significantly more medication changes because of PPOs and PIMs were made in the intervention group than in the control group (PPOs 26.2% *vs* 3.4%, odds ratio 0.04 [95% confidence interval 0.003–0.46] $P < .05$; PIMS 46.2% *vs* 15.3% odds ratio 0.14 [95% confidence interval 0.07–0.57] $P < .005$). There were no differences in dose adjustments or in postoperative mortality.

The authors confirm that the PI for this paper is Marijke Nynke Boersma and that she had direct clinical responsibility for patients.
The data that support the findings of this study are available from the corresponding author upon reasonable request.
Nederlands trial register NTR 5750

Conclusion: Prescribing recommendations generated with the help of STRIP Assistant improved appropriate prescribing in a preoperative geriatric outpatient clinic but did not affect postoperative mortality.

KEYWORDS

prescribing, clinical pharmacology, clinical trials, elderly, geriatrics, geriatric medicine, geriatrics, drug safety, clinical pharmacology

1 | INTRODUCTION

Inappropriate prescribing is common among older people and may have serious consequences, such as inefficacy, adverse drug events, falls, (re)hospitalization or death.[1-5] The screening tool of older person's prescriptions/screening tool to alert doctors to right treatment (STOPP/START) criteria provide a structured format to evaluate patients' medications for the presence of potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs).[6] Prior research has shown that the use of the STOPP/START criteria improves appropriate prescribing, measured with the Medication Appropriate Index and Assessment of Underutilization Index in a hospital setting.[7] Furthermore, 51.7% of the PIMs that caused a serious adverse drug event were detected when the STOPP/START criteria were used.[2] Lastly, the use of the STOPP/START criteria significantly reduced the number of PIMs and PPOs and the number of falls in a geriatric chronic care facility.[8]

Explicit screening tools such as STOPP/START are included in the Systematic Tool to Reduce Inappropriate Prescribing (STRIP). STRIP consists of 5 steps to optimize an individual patient's medication and has proven to be effective in reducing inappropriate prescribing when used by final-year medical students[9] and in detecting drug-related problems (mainly PIMs) in patients with an intellectual disability.[10] STRIP is currently considered best practice in the Netherlands.[11,12]

A web-based application was developed to help physicians carry out a medication review using the STRIP method: the STRIP Assistant. STRIP Assistant helps users to formulate medication recommendations based on STOPP/START criteria version 1 and G-standaard.[6,12-14] G-standaard is a database comprising all medications registered in the Netherlands, and includes guidelines on established clinical interactions, duplicate medications, contraindications, dosage, and frequency of administration recommendations. The G-standaard forms the basis of pharmacovigilance in the Netherlands.[13] Studies have revealed that the use of STRIP Assistant by general practitioners and pharmacists increases appropriate medication decisions (58–76%), decreases inappropriate decisions (42–24%) and increases the percentage of solved drug-related problems in test cases from general practice.[14,15] As little is known about the effect of STRIP Assistant-generated prescribing recommendations in a hospital setting, we evaluated whether prescribing recommendations made with the use of the STRIP Assistant improved prescribing in a preoperative geriatric outpatient population. The primary outcome was the number of resident-implemented medication changes made because of PIMs, PPOs, and suboptimal dosages; a secondary outcome was 3-month postoperative mortality.

What is already known about this subject

- The use of screening tool of older person's prescriptions/screening tool to alert doctors to right treatment (STOPP/START) criteria to review patient medication lists results in more appropriate prescribing and fewer adverse events; however, implementation is time-consuming.
- The Systematic Tool to Reduce Inappropriate Prescribing (STRIP) Assistant is a clinical decision support system with integrated STOPP/START criteria and other guidelines to allow for a structural and efficient assessment of an individual patient's medication.
- The use of STRIP Assistant by general practitioners and pharmacists in test cases and in patients in general practice increases appropriate decision-making regarding polypharmacy optimization.

What this study adds

- In a preoperative geriatric outpatient clinic, the use of STRIP Assistant resulted in more appropriate prescribing.
- Clinical evaluation including a patient interview is indispensable to integrate patient input and patient data with clinical decision support system-assistance for optimizing the use of multiple medications.
- Future prescribing physicians should start using a clinical decision support system when reviewing patient medication lists in order to investigate the effect on patient related outcomes.
- Clinical decision support systems such as STRIP Assistant promote appropriate prescribing when prescribing recommendations are used in combination with a clinical evaluation.

2 | METHODS

2.1 | Design, setting and participants

This cluster-randomized, controlled trial investigated the effect of written prescribing recommendations generated by a research physician using STRIP Assistant on medication changes made by residents during a preoperative comprehensive geriatric assessment. A cluster randomized design was chosen in order to avoid bias due to residents learning from the recommendations. All residents working at the geriatric outpatient clinic of the University Medical Centre Utrecht during the inclusion period were included except for 3 residents who participated as research physicians in this study. A random number generator randomly assigned the residents to the intervention group (even numbers) and the control group (odd numbers) in a 1:1 ratio.

Owing to the nature of the intervention, residents and the research physicians generating the prescribing recommendations could not be blinded; however, patients, supervisors of the residents and the nurses, who gathered information about comorbidity, cognitive function and functional status, were blinded for the intervention. Residents from the intervention group were asked not to discuss the prescribing recommendations they received with colleagues, to prevent contamination of the control group.

Cluster size was determined by the number of patients eligible for inclusion treated by one resident. The work schedule of the residents was not modified by or for this study. In the University Medical Centre Utrecht, patients aged 70 years or older scheduled for elective surgery are invited for a comprehensive geriatric assessment at the preoperative geriatric outpatient clinic. Participation is voluntarily. During this visit, patients are informed that their data could be used for research projects, unless they object.

Patients scheduled for the preoperative screening at the geriatric outpatient clinic of the University Medical Centre Utrecht between October 2014 and July 2016 were assessed for eligibility. Inclusion criteria were polypharmacy defined as the use of 5 or more different medications, including topical, inhaled and acute medications, and the availability of a Structured History taking of Medication use (SHiM) taken by a pharmacy assistant before the patient came to the geriatric outpatient clinic.[16]

Exclusion criterion was the inability to provide prescribing recommendation due to practical issues such as patient no-show, surgery cancellation etc.

2.2 | Usual care

A pharmacy assistant took the SHiM as part of usual care, prior to the comprehensive geriatric assessment. Findings were recorded in the patient's electronic medical record. The standard comprehensive geriatric assessment, performed by a resident and supported by a nurse, provided information about smoking habits and alcohol use, the Charlson comorbidity index, 15-point Katz Index of Independence in Activities of Daily Living (Katz-ADL), and mini-mental state examination (MMSE). The resident also reviewed the patients' medication. Any medication changes made by the resident (direct changes as well as recommendations to the surgeon or general practitioner regarding the medication regimen) were registered in the medical record.

2.3 | Intervention

The intervention consisted of written prescribing recommendations prepared by an independent, clinically experienced research physician using the STRIP Assistant. The input data consisted of medication use (as reported by the SHiM use), age, sex, medical history, current medical problems, blood pressure, pulse and estimated glomerular filtration rate. Prescribing recommendations were based on PPOs, PIMs and suboptimal dosages identified by STRIP Assistant and the research physician. The recommendations were given to the resident before the comprehensive geriatric assessment. Whether these recommendations were implemented either direct changes to medication regimen or recommendations forwarded to the surgeon or general practitioner was at the resident's discretion.

2.4 | Outcome measures

The primary outcomes were the number of implemented medication changes per patient made by a resident during the comprehensive geriatric assessment, corresponding with the PPOs and PIMs, and suboptimal dosages identified by the research physician using the STRIP Assistant. To compare intervention and control groups, prescribing recommendations were retrospectively generated using STRIP Assistant for the control group. In the control group, a recommendation was considered implemented when the resident identified the same PPO or PIM as recommended by the STRIP Assistant. A dose adjustment for suboptimal dosage was considered implemented when a resident adjusted the dose in the same direction (a decrease or increase) as recommended by the research physician. Secondary outcomes were prescribing appropriateness according to STOPP/START criteria version 2, 3-month and 1-year postoperative mortality rates and 3-month changes in MMSE, Katz-ADL and Fried criteria.

2.5 | Standardization of intervention

To check the accuracy and consistency of the prescribing recommendations generated by the research physician using STRIP Assistant, the recommendations for the first 39 patients (both intervention and controls) were compared with consensus recommendations from an expert panel consisting of a geriatrician–clinical pharmacologist and a clinical pharmacist–clinical pharmacologist. This resulted in 11 instructions to standardize the application of STOPP/START criteria and dose adjustments in order to improve the consistency of the intervention (Table 1). These instructions were applied to all patients included after the first 61 patients (64.4% of control group and 35.4% of

TABLE 1 Consensus-bases instructions to standardize the prescribing recommendations

STOPP/START criteria	Confusion leading to discrepancies	Instructions how to use STOPP/START criteria and guidelines panel
PPO:		
1.START, A6/7	ACE inhibitor and β-blocker in all patients with coronary disease or only in patients who experienced cardiac ischaemia?	Beta-blocker in patients with a history of coronary bypass or coronary stent (myocardial infarction not prerequisite) and ACE inhibitor (only) in patients with history of acute myocardial infarction.
2.	The number of available blood pressure measurements was often limited. Should advice be given on the basis of fewer than 3 measurements?	Antihypertensive medication in patients in whom the target blood pressure was not achieved, regardless of the number of blood pressure measurements.
3.START, E5	Do all older patients need to use vitamin D supplement?	Vitamin D supplement in patients with known osteoporosis or other musculoskeletal disease (e.g. rheumatoid arthritis, intermittent claudication) and insufficient sunlight exposure.
4.START, E3	Do all older patients need to use calcium supplement?	Calcium supplement in patients with osteoporosis in combination with low dairy intake.
PIM:		
5.STOPP, A1	Antidepressant use without a documented depression or anxiety disorder in medical history. Possibly the available medical history is not complete.	Antidepressant without documented depression in medical history.
6.STOPP, A1	Analgesic use without documentation of pain or disease that causes pain. Possibly the available medical history is not complete.	Analgesic without documentation of pain or disease that causes pain (e.g. osteoporosis, rheumatoid disease, (metastatic) cancer, surgery within 2 weeks) in medical history.
Dose adjustment:		
7.	Should the maximum dose for acetaminophen be 3 times daily or 4 times daily?	Acetaminophen >1 g 3 times daily adjust to a maximum 1 g 3 times daily in patients with chronic use.
8. START A5	Which dose should be advised for statins?	Simvastatin adjusted to 40 mg once daily, atorvastatin adjusted to dose 20 or 40 mg once daily.
9. STOPP, F2	Which dose should be advised for proton-pump inhibitors?	Proton-pump inhibitor pantoprazole or omeprazole as prophylaxis adjusted to 20 mg once daily.
Change in medication:		
10. START A7	Should the following medication be changed?	Change drug when the patient is not using the first-choice drug according to guidelines, for example:
10A.		Metoprolol instead of propranolol in a patient with a history of myocardial infarction.
10B.		Metoprolol instead of sotalol or digoxin in a patient with a history of permanent atrial fibrillation.
10C.		Thiazide diuretic instead of diltiazem in a patient with a history of hypertension.
Other considerations:		
11.	Is angiotensin inhibitor an alternative when there is an indication for an ACE inhibitor?	Angiotensin inhibitor is considered equivalent to ACE inhibitor.

ACE = angiotensin-converting-enzyme; PIM = potentially inappropriate medication; PPO = potential prescribing omission; START = screening tool to alert doctors to right treatment; STOPP = screening tool of older person's prescriptions.

intervention group). The effect of these instructions on the primary outcome was investigated.

2.6 | Statistical analysis

Differences between intervention and control groups regarding patient characteristics, numbers of PPOs and PIMs at baseline identified with STOPP/START criteria version 2, resident characteristics, and clinical data were analysed using descriptive statistics. Normally distributed data are presented as means with standard deviations and analysed using *t*-tests. Non-parametric data are reported as median and interquartile range (IQR) and analysed using the Pearson χ^2 test, Mann–Whitney *U* test and Fisher exact test.

As a result of the clustered design, generalized estimating equation regression models were used for the primary outcome to adjust

for the numbers of recommended medication changes because of PPOs and PIMs.

Generalized estimating equation regression models were also used to investigate the appropriateness of prescribing according to STOPP/START criteria adjusted for baseline PPOs and PIMs, the effect of the intervention on mortality adjusted for age, sex, and Charlson comorbidity index at screening, and to investigate the effect of the standardization instructions by comparing the control group and the intervention group before and after application of instructions.

To measure any effect of learning or contamination of the control group, the effect of the duration of the residents' participation in the study (in months) on the number of resident-implemented PPO and PIM changes was measured using generalized estimating equation regression models.

Statistical significance levels were set at $P < .05$ (2 tailed). Statistical analyses were performed using IBM SPSS Statistics version 21 (IBM SPSS, Chicago, IL, USA).

2.7 | Sample size

The study size was calculated by assuming that the number of PIM changes made by the resident would be 0.5 per patient in the intervention group and 0.2 per patient in the control group. This was based on a detection rate, using STOPP criteria, of 0.86 in a study involving hospitalized older adults[17] and 0.36 in a study involving primary care patients older than 70 years.[18] Standard levels for type I and II errors ($\alpha = 0.05$, $\beta = 0.8$) were used. The calculated number of patients was multiplied by 1.15 because of the cluster randomized design, with an expected mean cluster size of 4 patients and $\rho = 0.05$ (1 + (cluster size − 1)ρ), resulting in a required number of 50 patients per study arm.

2.8 | Ethics

The Research Ethics Committee of University Medical Centre Utrecht confirmed that the Medical Research involving Human Subjects Act was not applicable to this study, and a waiver was granted.

3 | RESULTS

All 34 randomized residents (i.e. the clusters) participated in the study, 19 were assigned to the intervention group and 15 to the control group; the median number of patients per cluster was 3 (IQR 1–4; Figure 1). The trial was ended after the calculated sample size was reached for both groups. No data are available for the patients who rejected the invitation for the preoperative comprehensive geriatric assessment. None of the included patients objected to participation in research. After randomization of 170 eligible patients, 45 patients had to be excluded, mainly because of patient no-show (Figure 1). The data of 124 included patients could be analysed for the primary outcome.

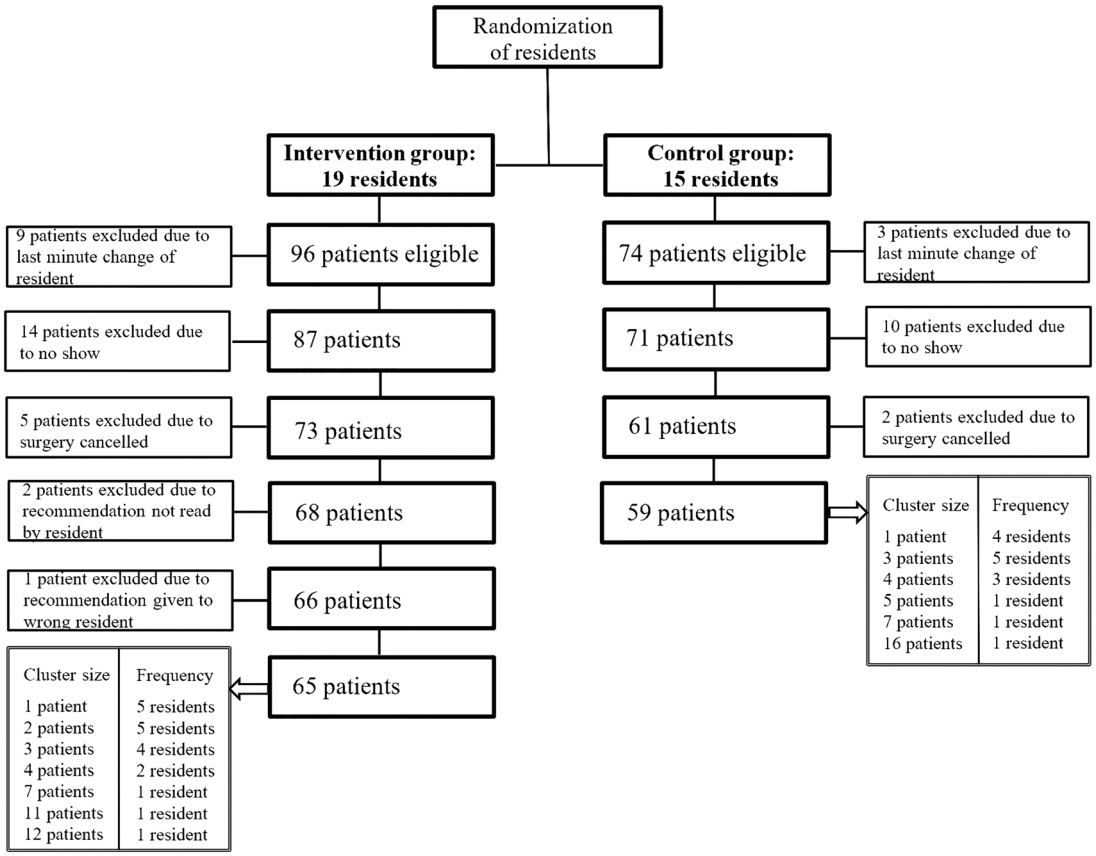

FIGURE 1 Participant flow and cluster size

TABLE 2 Baseline characteristics

Characteristics		Intervention group (*n* = 65)	Control group (*n* = 59)	*P* value
Sex, *n* (%), male		34 (53.8)	30 (5.8)	.94 [d]
Age (years) [a]		77.8 ± 5.7	79.0 ± 6.0	.29 [f]
Renal function [b c]		69.0 (52.0–84.0)	69.5 (52.0–85.0)	.92 [f]
Smoking, *n* (%), yes		10 (16.1)	6 (1.2)	.43 [e]
Alcohol consumption, *n* (%) >1 unit/day		10 (16.1)	8 (13.5)	.72 [d]
Total number of medications used per patient [b]		9 (6–12)	9 (7–12)	.86 [g]
Number of PPOs per patient [b]		1 (0–2)	1 (0–2)	.08[g]
Number of PIMs per patient [b]		3 (1–5)	2 (.5–3.5)	.87[g]
Specialty operation, *n* (%)				.13 [d]
General surgery		3 (4.6)	9 (15.3)	
Cardiology		12 (18.5)	13 (22.0)	
Oncological surgery		23 (35.4)	14 (23.7)	
Orthopedic surgery		15 (23.0)	13 (22.0)	
Urology		5 (7.7)	1 (1.7)	
Vascular surgery		7 (1.8)	7 (11.7)	
Other		0 (0)	2 (3.4)	
CCI[b]		3 (0–9)	3 (0–10)	.74 [g]
MMSE <24, *n* (%)		5 (8.2)	4 (6.8)	.81 [d]
Katz-ADL ≥ 7, *n* (%)		9 (14.1)	3(5.5)	.06 [e]
Specialty and year of residency of the resident who treated the patient, *n* (%)				<.001 [d]
Geriatric medicine	2nd	0	1 (1.7)	
	3rd	9 (13.6)	3 (5.1)	
	4th	4 (6.1)	4 (6.8)	
	5th	17 (26.2)	13 (22.0)	
	6th	0	17 (27.1)	
Internal medicine	1st	0	1 (1.7)	
General practice medicine	2nd	10 (16.7)	10 (16.9)	
Elderly care medicine	2nd	25 (38.5)	10 (16.9)	

PPOs = potential prescribing omissions based on screening tool of older person's prescriptions/screening tool to alert doctors to right treatment (STOPP/START) criteria version 2; PIMs = potentially inappropriate medications based on STOPP/START criteria version 2; CCI = Charlson comorbidity index; Katz-ADL = 15 point Katz Index of Independence in Activities of Daily Living; MMSE = mini-mental state examination. Missing n: renal function 7, smoking 5, alcohol consumption 5, CCI 4, MMSE 6, 15 Katz-ADL index 5.

[a]mean ± standard deviation.

[b]median (interquartile range).

[c]renal function measured as eGFR in ml/min/1,73m^2.

[d]*P* value based on χ^2-test.

[e]*P* value based on Fisher exact test (2-sided).

[f]*P* value based on independent Student *t* test.

[g]*P* value based on Mann–Whitney *U* test.

Patients in the intervention (*n* = 65) and control (*n* = 59) groups did not differ regarding age (mean 77.8 ± 5.7, *vs* 79, ± 6.0 respectively), sex, smoking, alcohol consumption, renal function, number of medications (median; IQR; 9; 6–12 and 9; 7–12 respectively), prescribing appropriateness, surgical specialty, comorbidity, cognitive function or functional status at baseline (Table 2). Residents in the control group were generally more experienced and were more often specializing in geriatrics, whereas the residents in the intervention group were more often specializing in nursing home medicine (Table 2).

The primary outcome was the number of resident-implemented medication changes made because of PIMs, PPOs and suboptimal dosages.

More recommended PPO and PIM changes were implemented in the intervention group than in the control group (PPOs 26.2% *vs* 3.4%, *P* < .001; PIMs 46.2% *vs* 15.3%, *P* < .001; Table 3). When the

TABLE 3 Number of resident-implemented medication changes because of potential prescribing omission (PPO), potentially inappropriate medication (PIM) and suboptimal dosages made per patient by the resident in accordance with prescribing recommendations. Mortality in the intervention group *vs* control group

	Intervention group (n = 65)	Control group (n = 59)	P value
Number of PPO changes per patient (%)	48 (73.8)	57 (96.6)	<.001[a] <.05[b]
0	11 (16.9)	2 (3.4)	
1	6 (9.2)	0	
2			
Number of PIM changes per patient (%)	35 (53.8)	50 (84.7)	<.001[a] <.005[b]
0	14 (21.5)	8 (13.6)	
1	8 (12.3)	0	
2	8 (12.3)	1 (1.7)	
≥ 3			
Number of suboptimal dosage changes per patient (%)			
0	62 (95.4)	59 (100)	.096[a]
1	3 (4.6)	0	
Mortality, n (%)	8 (13.1)	7 (12.1)	.859[c]

[a]P value based on Mann–Whitney U.

[b]P value based on generalized estimating equation analysis of association between intervention and number of patients with 0 or ≥ 1 PPOs/PIMs. Adjusted for the number of recommended PPO/PIM medication changes.

[c]P value based on generalized estimating equation analysis of association between intervention and 3-month postoperative mortality (death of all causes). Adjusted for age, sex and Charlson comorbidity index at screening. Missing n = 5.

number of implemented PPO and PIM changes was adjusted for the number of recommended PPO and PIM changes, this difference remained significant (PPOs odds ratio (OR) 0.04, [95% confidence interval (CI) 0.003–0.46] P < .05; PIMs OR 0.14 [95% CI 0.07–0.57] P < .005). The number of dose changes made because of suboptimal dosages was very low and did not differ significantly between the 2 groups (4.6% *vs* 0.0%, p = .1). Changes in dosing frequency were recommended twice in the control group.

In addition to the medication changes because of PPOs, PIMs, and suboptimal dosages, made in accordance with the prescribing recommendations of the research physician with the STRIP Assistant, the residents also identified additional PPO, PIM and suboptimal dosage changes that were not included in the prescribing recommendations (Figure 2). These numbers did not significantly differ between the groups (PPOs 9.3% *vs* 8.5%, P = 0.843; PIMs 7.7% *vs* 3.4%, P = .308; suboptimal dosages 4.6% *vs* 6.8%, P = .603). When combining these additional PPO, PIM and suboptimal dosage changes with the implemented prescribing recommendations, the difference between the total number of PPO and PIM changes made by the residents in the 2 groups remained significant (PPOs 35.4% *vs* 10.2%, p < .05; PIMs 47.7% *vs* 16.9%, p < .01; dose adjustment changes 9.2% *vs* 6.8%, p = .618; Figure 2).

The appropriateness of prescribing measured by the numbers of PPOs and PIMs identified by STOPP/START criteria version 2 before and after the intervention, increased significantly in the intervention group for the number of PIMs (OR 0.14 [95% CI 0.08–0.25] p < .001). The number of PIM changes made in the control group and the number of PPO changes made in intervention group and control group did not differ before and after the intervention or medication review (Table 4).

Three-month postoperative mortality did not significantly differ between intervention and control groups; 8 patients in the intervention group (13.1%) and 7 in the control group (12.1%) died (OR 1.01 [95% CI 0.40–3.05], p = 0.859; Table 3). Owing to missing data, the difference in MMSE (62.9% missing), Katz-ADL (28.2% missing), Fried criteria (24.2% missing) between baseline and 3 months postoperatively, and 1 year postoperative mortality (47.9% missing) could not be analysed. Standardization instructions for the application of STOPP/START criteria and guidelines were introduced after 61 patients had been included and were based on a sample of 39 patients from both groups. Comparison of periods before and after the introduction of these instructions showed no significant difference in resident-implemented PPO and PIM changes before and after the introduction within the intervention group. Moreover, the difference in resident-implemented recommended PPO and PIM changes between intervention and control groups remained significant when the control group of the complete period was compared with both the intervention group before and intervention group after introduction of standardization instructions (PPOs respectively OR 0.03 [95% CI 0.002–0.66] P < .05 and OR 0.04 [95% CI 0.004–0.45] P < .01; PIMs respectively OR 0.17 [95% CI 0.06–0.47] P < .005 and OR 0.20 [95% CI 0.06–0.74] P < .05).

The duration of the residents' participation in the study did not affect the number of resident-implemented PPO and PIM changes.

The most frequently recommended and implemented recommendations regarding PPOs involved vitamin D, angiotensin-converting-enzyme inhibitors and statins. The most frequently recommended and implemented recommendations regarding PIMs involved proton pump inhibitors, benzodiazepines, analgesics and antiplatelet drugs.

4 | DISCUSSION

Individualized prescribing recommendations generated by a research physician using STRIP Assistant increased appropriate prescribing in patients attending a preoperative geriatric outpatient clinic.

The number of resident-implemented recommended medication changes because of PPOs and PIMs was significantly higher in the intervention group than in the control group. The appropriateness of prescribing improved by the intervention, based on the decrease in PIMs identified with STOPP/START version 2. No statistically significant effect on 3-month postoperative mortality was found.

The high number of PIMs detected by the research physician using STRIP Assistant in this study (average of 2.59 per patient) as compared to earlier studies (average of 0.47–1.81) might be explained by the

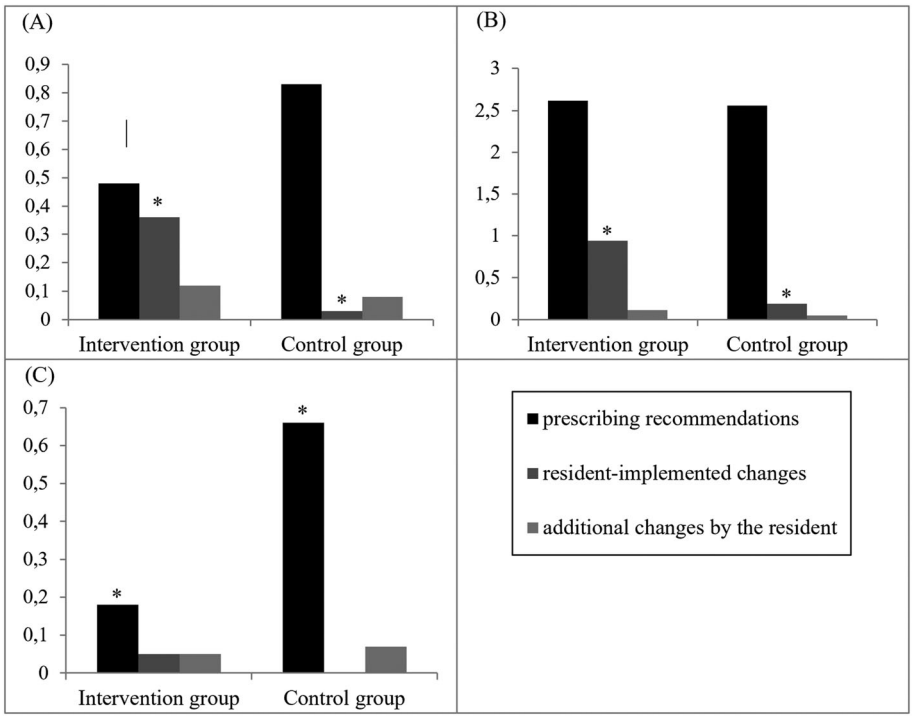

FIGURE 2 Average number of prescribing recommendations per patient, average number of medication changes in accordance with prescribing recommendations, and average number of additional changes by the resident per patient, because of potential prescribing omissions (PPOs); (A), potentially inappropriate medications (PIMs); (B), and suboptimal dosages (C) in the control and intervention groups. *P < .001. P values calculated using Mann–Whitney U

higher number of medications used by patients in our study (mean 9.5 *vs* 6–9.5).[2,17-20] Furthermore, the incorporation of guidelines in the STRIP Assistant might lead to a higher detection rate when compared with STOPP/START criteria alone. In contrast, the lack of relevant clinical information could have resulted in the identification of unjustified PIMs by the research physician. The lack of relevant clinical information might also explain the discrepancy between recommended and implemented changes regarding PPOs, PIMs and suboptimal dosages. Dalleur *et al.*[17] found that the average number of PIMs identified per patient after a comprehensive geriatric assessment was 0.86, whereas the number of implemented changes made after discharge was 0.26. This illustrates that even recommended changes based on a comprehensive geriatric assessment are not fully implemented.

The most frequently recommended and implemented changes regarding PIMs involved proton pump inhibitors, benzodiazepines, analgesics and antiplatelet drugs, as reported earlier.[2,17-20] These PIMs are clinically relevant because antiplatelet drugs and medications that act on the central nervous system are major causes of medication-related hospital admissions.[1] The most frequently recommended and implemented changes regarding PPOs in our study involved vitamin D, angiotensin-converting-enzyme inhibitors and statins, and are comparable with the main PPOs found by Dalleur *et al.* (vitamin D, statins).[20]

The fact that we did not find a significant difference in mortality is probably because of the small sample size and the short follow-up period. However, a Cochrane meta-analysis including 3218 patients did not reveal a significant effect of medication review on 1-year mortality rates in hospitalized patients.[21]

There is no gold standard to determine the best medication regimen for individual patients.[21] In our study, the individualized prescribing recommendations were considered most appropriate since the STRIP Assistant combines the explicit STOPP/START criteria with other prescribing guidelines, clinical parameters and judgement of an experienced physician. Therefore, the prescribing recommendations provided by the research physician and subsequently implemented by the residents were considered appropriate. Residents within the control group could be expected to make different medication changes or dose adjustments as they did not receive the prescribing recommendations. However, we detected a trend towards more changes additional to the prescribing recommendations in the intervention group than in the control group.

In contrast to the decrease in PIMs, the number of PPOs according to the STOPP/START criteria version 2 did not significantly decrease by the intervention or usual care. However, there was a trend towards less PPOs after the intervention and usual care compared to baseline. This lack of significance could be due to the fact that the study was not powered for this outcome.

The input for the research physician using the STRIP Assistant was the SHiM use, the medical history, blood pressure, heart rate and estimated glomerular filtration rate. The residents in both groups used information gathered during the comprehensive geriatric assessment. Consequently, the residents had access to more information than did the research physician who used the STRIP Assistant, such as

TABLE 4 Number of potential prescribing omissions (PPOs) and potentially inappropriate medications (PIMs) before and after intervention/usual care identified with screening tool of older person's prescriptions/screening tool to alert doctors to right treatment criteria version 2

Intervention group	Before intervention	After intervention
Numbers of patients (%) with PPOs		
0	30 (46.2)	36 (55.4)
1	19 (29.2)	17 (26.2)
2	14 (21.5)	10 (15.4)
≥ 3	2 (3.0)	2 (3.0)
Numbers of patients (%) with PIMs		
0	8 (12.3)	12 (18.5)
1	12 (18.5)	16 (24.6)
2	10 (15.4)	11 (16.9)
≥ 3	35 (53.8)	26 (40.0)
Control group	**Before usual care**	**After usual care**
Numbers of patients (%) with PPOs		
0	20 (33.9)	21 (35.6)
1	18 (30.5)	16 (27.1)
2	13 (22.0)	15 (25.4)
≥ 3	8 (13.6)	7 (11.9)
Numbers patients (%) with PIMs		
0	0 (1.7)	3 (5.1)
1	15 (25.4)	15 (25.4)
2	15 (25.4)	14 (23.7)
≥ 3	28 (47.6)	27 (45.9)

P values were based on generalized estimating equation regression model analysis of association between intervention and number of patients with 0 or ≥ 1 PPO/PIM, adjusted by the number of PPOs/PIMs at baseline. PPOs $P = .36$. PIMs $P < .001$.

complaints, expectations, previous (negative) experiences, and more physical and biochemical information. The residents in both groups identified PPOs additional to those identified by the research physician using the STRIP Assistant, possibly as a result of this extra information and the process of shared decision-making. This underlines the importance of a clinical evaluation as part of a medication review.

The discrepancy between the recommended and implemented PPO, PIM and suboptimal dose changes can also be explained by the specific choices made by residents. For example, in a hypertensive patient on a low dose of an antihypertensive, both a dose increase (dose adjustment) and starting a new antihypertensive agent (PPO) can be advised.

A potential limitation of this study is that the control group contained more experienced residents, more residents specializing in geriatrics, and fewer residents specializing in nursing home medicine. This might have caused bias, since there may be a difference in willingness to implement recommendations and a difference in capability to identify inappropriate medication between more and less-experienced residents. Another potential limitation is the variable and small cluster size (median 3), which was determined by the number of patients per resident. Since the objective of this study was to measure the effect of the prescribing recommendations in clinical practice, we decided not to interfere with the working schedule of the residents thereby accepting the variable and small cluster size.

Consensus-based instructions to standardize the prescribing recommendations were introduced during the study, which could have changed the intervention. However, the impact was negligible. When the groups were analysed for the 2 different periods (before and after standardization) the difference between the control group and the intervention group persisted without a significant difference between the intervention group before and after the standardization.

While both the research physicians and residents could have gained experience in generating prescribing recommendations, this learning effect over time was expected to be similar in the 2 groups. Although residents from the intervention group were instructed not to discuss the prescribing recommendations with colleagues, there might have been contamination of the control group due to joined care for other patients with residents from the intervention group. However, this contamination is considered to be minor since most residents worked for only 3–4 months at our centre. Furthermore, the number of resident-implemented recommended PPO and PIM changes did not increase during the participation of the residents in the study.

Lastly, the STRIP Assistant generates prescribing recommendations according to STOPP/START version 1, which is not the most recent version at the moment. However, by the time of patient inclusion, this version was the most recent.

This study showed that prescribing recommendations generated with the use of the STRIP Assistant resulted in more appropriate prescribing at a preoperative geriatric outpatient clinic. Therefore, we recommend the use of a clinical decision support system, such as STRIP Assistant, by the treating health care professional in clinical practice. Additionally, this study underlines the importance of clinical evaluation and judgement as part of a medication review.

Further research should focus on the effect of prescribing recommendations on clinical, patient-reported and economic outcomes.

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COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

M.N.B.: Developed study design. Had the main role in the acquisition, analysis and interpretation of data. Prepared the manuscript, drafted the manuscript, approved the final version to be published and gave final approval of the version to be published. C.J.A.H.: Developed the concept of the study, gathered data, revised the manuscript critically and approved the final version of the manuscript to be published, and gave final approval of the version to be published. A.C.D.-v.M.:

Gathered data, analysed and interpreted data, revised the manuscript critically, approved the final version of the manuscript to be published, and gave final approval of the version to be published. M.H.E.-V.: Developed the concept of the study design, revised the manuscript critically, approved the final version of the manuscript to be published, and gave final approval of the version to be published. I.W.: Developed concept and design of the study and played a significant role in data analysis and interpretation. Revised the manuscript critically, approved the final version of the manuscript to be published and gave final approval of the version to be published. W.K.: Developed concept and design of the study and played a significant role in de data analysis and interpretation. Revised the manuscript critically, approved the final version of the manuscript to be published, and gave final approval of the version to be published.

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