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Abstract

Background: Structured medication reviews were introduced in 2020 to address polypharmacy in patients most at risk of medicines-related harm.
Aim: To evaluate the impact of SMRs on prescribing in primary care.
Design and setting: Retrospective observational cohort study of electronic health records from patients aged ≥65 years, prescribed one or more medications and fulfilling the specific eligibility criteria for a SMR, registered at practices contributing data to the Oxford Clinical Informatics Digital Hub (ORCHID), between 1st April 2020 and 30th September 2022.
Methods: The association between SMRs and prescription changes was examined by matching individuals who received an SMR to individuals who did not receive an SMR, according to age, sex and primary care practice using cumulative density sampling. Analyses were undertaken using adjusted logistic regression.
Results: Of 635,698 eligible patients, 82,285 (12.94%, 95% confidence interval [CI] 12.86%-13.02%) received at least one SMR during the study observation period. In those prescribed potentially inappropriate drug combinations prior to an SMR, between 12.5% and 40.0% were corrected up to three months later. In matched analyses, SMRs were most strongly associated with an increase in new prescriptions of ACE inhibitors (adjusted odds ratio [aOR] 1.56, 95%CI 1.35-1.81), statins (aOR 1.78, 95%CI 1.57-2.02), and antidepressants (aOR 1.45 95%CI 1.28-1.63). SMR were also most strongly associated with stopping these drug classes in those previously prescribed treatment.
Conclusions: SMRs were associated with starting new medications and stopping existing prescriptions compared to usual care. Further work is needed to understand if these changes improved patient outcomes.

Word count: 249 words

Key words: Polypharmacy, Structured Medication Review, Primary Health Care, Inappropriate Prescribing, Deprescribing, Electronic Health Records.

How this fits in

- Structured medication reviews are a National Institute for Health and Care Excellence (NICE) approved clinical intervention to address complex or problematic polypharmacy and were introduced widely in the UK NHS in 2020.
- We found that one in eight eligible patients received a structured medication review during the first two years of the programme's rollout in England.
- Structured medication reviews were associated with an increased likelihood of starting medication in those not previously prescribed treatment, and an increased likelihood of stopping medications in those with existing prescriptions.
- This analysis was limited by the data available within primary care electronic health records and so it is unclear if the observed changes in prescribing resulted in improvements in patient outcomes

Summary Sentence

In this observational study using data from electronic health records, structured medication reviews were associated with starting new medications and stopping existing prescriptions compared to usual care.

Introduction

Prescribing medicines is the most common intervention in the NHS, and most prescribing takes place in primary care.(1, 2) However, inappropriate polypharmacy (where medicines are no longer appropriate)(3) can expose the most vulnerable patients to decreased quality of life(4-6) and hospitalisation with adverse drug events.(7-9) It is estimated that £400 million is spent each year on admissions to hospital caused by harm from potentially inappropriate medication prescriptions.(10)

Over the past twenty years, initiatives have sought to reduce polypharmacy related harm in UK primary care, and the National Institute for Health and Care Excellence have recommended Structured Medication Reviews (SMR) as a clinical intervention to address complex or problematic polypharmacy.(11) Historically, medication reviews were undertaken by general practitioners, but SMRs were designed to be undertaken by clinical pharmacists embedded in primary care, reviewing medications prescribed to patients most at risk of medicines-related harm.(11, 12) This was based on evidence from studies such as the PINCER trial,(13) which showed benefits from a pharmacist-led approach to reduce hazardous prescribing in primary care. SMRs were introduced via Primary Care Networks (PCNs; groups of neighbouring GP practices in England, typically serving 30,000–50,000 people, formed to work together to deliver more proactive, integrated care) in 2020,(12) with participating GPs receiving funding receiving funding from their local PCN to employ practice based pharmacists to deliver SMRs, and further financial incentives based on the number of SMRs undertaken and the achievement of medicines optimisation within these reviews. Each year, the specification for SMRs was slightly updated, with certain populations and optimisation targets prioritised (e.g. people in nursing homes and those with severe frailty, multi-morbidity and/or polypharmacy were targeted from October 2021).

Clinical trials focused on chronic diseases have shown that structured medication reviews can improve cardiovascular risk management. However, these studies vary widely in intervention types and measured outcomes.(14) Furthermore, there is limited evidence that medication reviews reduce adverse drug events.(15, 16) Evaluation studies of pharmacist-led medication reviews undertaken in routine clinical practice have shown mixed results in terms of prescribing and patient-centred care.(17-19) One possible reason for this is that historically, primary care practices have prioritised being time-efficient rather than being comprehensive, so that most medication reviews were carried out with little or no patient involvement, and medicines were rarely stopped or reduced.(20) In an early qualitative evaluation undertaken during the first year following the introduction of SMRs, it was suggested that the implementation of the service had been sub-optimal, failing to match the aspiration for patients that was presented in the original policy.(21)

To date, quantitative evaluations of the service have been limited to descriptive analyses of who received an SMR during the COVID-19 pandemic.(22) The impact of the SMR programme on prescribing in primary care remains unknown. The present study therefore, aimed to evaluate the impact of SMRs on prescribing in primary care by determining the proportion of eligible patients that received an SMR in the first two years and whether SMRs were associated with changes in prescribing and primary care contacts during this period.

Methods

Detailed extended methods are provided in the supplementary appendix.

Setting

This was a retrospective observational cohort study design, using routine data from primary care electronic health records (EHRs) from GP practices in England collected via the Oxford Clinical Informatics Digital Hub (ORCHID).(23, 24) This database contains all coded data regarding medical history, prescriptions and test results from over 1,800 general practices using across England. ORCHID includes data from multiple clinical software systems including EMIS (Optum, formerly EMIS Health), SystmOne (TPP, The Phoenix Partnership) and Vision (Cegedim, formerly INPS). The database represents over a quarter of English general practices and 30% of the English population, and has been shown to be representative of patients in England in terms of age, sex, ethnicity, socioeconomic status and geographical spread.(23) The study received ethical approval from South Central – Hampshire A Research Ethics Committee (ref: 22/SC/0373).

Population

Eligible patients were aged 65 years or over, prescribed one or more repeat medications and who fulfilled at least one of the eligibility criteria for a structured medication review, as defined in the PCN contract for SMRs.(25) Individuals entered the cohort on the 1st January 2020 and SMRs that occurred between 1st April 2020 and 30th September 2022 were included. Data from the three months prior to the SMR observation period (January-March 2020) were used to define treatment prescriptions. Medication changes (new prescriptions and stoppages of existing prescriptions) up to three months after an SMR were included up until 31st December 2022.

Outcomes

The primary outcome of this study was the proportion of eligible patients receiving an SMR during the SMR observation period. Secondary outcomes included changes in medication prescriptions (new prescriptions and stoppages of existing prescriptions) following an SMR. Further analyses focussed on changes in medications identified in the PCN contract as being potentially inappropriate (see table S1 for details). Finally, changes in any primary care contacts between healthcare professionals and patients before and after an SMR were examined. For this analysis, healthcare professionals were defined as general practitioners (GP), pharmacists, Health Care Assistants (HCA) or nurses.

Exposures

The exposure of interest was an SMR during the observation period 1st April 2020 to 30th September 2022, defined using the Systematized Nomenclature of Medicine (SNOMED) clinical term 1239511000000100.

Covariates

All analyses examining the association between SMRs and outcomes were adjusted for covariates defined according to data available at any timepoint prior to the observation period (i.e., before April 2020) and included body mass index (BMI) ethnicity, indices of multiple deprivation, smoking status, care home residence, baseline cholesterol, electronic frailty index score(26) and number of multiple long-term conditions. The latter were defined based on the list of 37 conditions included in the Cambridge Multimorbidity Score.(27, 28) Age (defined at the time of the index date) and sex were not included in the modelling as these were used as matching variables for the cohort.

Statistical analysis

Descriptive analyses were used to determine the proportion of patients potentially eligible to receive an SMR during the study observational period. In those who received an SMR and had continuous follow-up (i.e., those who survived and remained within ORCHID-registered practices so that medication prescription could be measured), changes in medication prescription (stopped or started) within 3 months (91 days) of an SMR were examined according to individual drug class. Furthermore, potentially inappropriate medication prescriptions were examined by identifying individuals with specific conditions or concurrent drug prescriptions which would put them at risk of adverse drug events, as detailed in the PCN contract for SMRs (see table S1 for details).(29) The proportion of these potential medication errors that were corrected within 3 months of an SMR was estimated using descriptive statistics.

To examine the associations between SMRs and prescription changes and primary care contacts, a cohort of patients who received an SMR were matched to controls who did not receive an SMR using cumulative density sampling. Individuals were matched 1:1 according to baseline age (5-year groups), sex and primary care practice. Each control was given an index date which was the date their matched case received an SMR. Analyses of the association between SMRs and outcomes were undertaken using logistic regression models, which were adjusted for baseline covariates (listed above), with missing data for index of multiple deprivation dealt with using multiple imputation (10 imputations). All analyses were undertaken using Stata version 18.0 (StataCorp, College Station, Texas, USA).

Results

A total of 635,698 patients, from 783 practices across England were identified as being eligible for an SMR. Of these, 82,285 patients (12.94%, 95% confidence interval [CI] 12.86% to 13.02%) received at least one SMR during the study observational period. More patients received an SMR in the second year of the observation period than the first year (figure S1). Patients who received an SMR were on average aged 77 years, 59.6% female, with 3.3% Asian ethnicity and 1.6% black ethnicity. Compared to those who did not receive an SMR, there were higher proportions of residents in nursing homes, moderate to severe frailty, hyper-polypharmacy (≥10 prescriptions), and complex multiple long-term conditions (≥4 conditions present) in patients who did receive one (tables 1, S2 and S3). There were no observed differences in the proportion of patients receiving an SMR on the basis of age, sex, ethnicity or social deprivation (table 1).

The majority of patients had no changes in their treatment following a SMR (table 2). In those already prescribed treatment, the medications most commonly stopped were NSAIDs (29.6% stopped), benzodiazepines (22.3% stopped), laxatives (19.9% stopped) and Z-drugs (16.1% stopped) and opioids (15.5% stopped). In patients not previously taking a given drug therapy, PPIs (11.3% started), statins (7.7% started), opioids (7.6% started) and laxatives (6.4%) were most likely to be started, although the proportion starting treatment was smaller (compared to the proportion stopping) (table 2). With regard to potentially inappropriate prescriptions, between 12.5% and 40.0% were corrected, although the overall numbers of inappropriate prescriptions were small (table 3). Medication combinations that increase the risk of a gastrointestinal bleeds were most commonly corrected (between 31.2 and 40.0% of combinations corrected), whereas drugs that could exacerbate asthma (12.5% corrected) or lead to respiratory depression (14.5% corrected) were least commonly corrected.

In 71,939 patients who received an SMR, matched to 71,939 patients who did not (table S4), medication reviews were associated with a significant increase in starting new medications and stopping existing prescriptions across nearly all drug classes of interest. This included increased prescribing of antihypertensives, cardiovascular, inhaled, pain, psychotropic, and other medications in patients receiving an SMR (figure 1). Furthermore, those already prescribed antihypertensives, cardiovascular, psychotropic,

laxatives and PPIs were more likely to have them stopped if they received an SMR (figure 2). There was no evidence of an association between SMRs and stopping inhaled or pain medications, with the exception of NSAIDs (figure 2).

Patients receiving a structured medication review had an average of 4 (IQR 2-7) primary care contacts with clinical personnel in the three months prior to their review, and 5 (IQR 3-8) contacts in the three months after. In contrast, those not receiving an SMR had an average of 3 (IQR 1-5) contacts before and after the index date, meaning that SMRs were associated with a significant increase in primary care contacts of 0.14 (95% CI 0.13 to 0.16; equivalent to 14 extra patient contacts for every 100 individuals receiving an SMR). Results were similar in analyses using different definitions to describe primary care contacts, including those where contacts with a code for an SMR were excluded (table S5).

Discussion

Summary

In this analysis, one in eight eligible patients received an SMR in the first two years of the SMR service rollout in England. This reflected a time of significant change for the UK National Health Service as initial implementation coincided with the first winter of the COVID-19 pandemic alongside major changes in staffing including a large increase in the numbers of pharmacists employed in primary care.(30) SMRs that were undertaken appeared appropriately targeted toward patients with greater frailty and multiple long-term conditions, without any clear demographic or socioeconomic bias.

As might be expected, many people continued with their prescribed medication following an SMR, but modest net changes in prescribing masked a significant increase in starting new medications and stopping existing prescriptions across nearly all drug classes of interest. In particular, SMRs were associated with an increased likelihood of stopping preventative medications, NSAIDs, and some psychotropic medications such as antidepressants, benzodiazepines and gabapentin. However, other psychotropic medications, such as pregabalin and z-drugs, and pain medications such as opioids were less likely to be stopped following an SMR, reflecting clinical caution or patient resistance to discontinuing medications that are prescribed for persistent symptoms despite limited evidence for long-term benefit.

Strengths and limitations

This was a large nationwide observational study including SMRs undertaken across England covering the first two years of the service. The completion and coding of SMRs was incentivised through the Investment and Impact Fund during the period of this study meaning that our estimates of SMR completion from the electronic health records are likely to be accurate. The large sample size available meant that medication prescription changes before and after an SMR could be examined across a range of drug classes. Almost all medication prescriptions are electronic and automatically coded in English primary care health records and therefore these data accurately reflect prescribing practice. However, the present analyses were unable to take into account changes in dosing, likely to be an important aspect of an SMR, which tend to be recorded in free text fields which were not available for this study.

Analyses of inappropriate medication indicators included prescriptions of certain drug combinations, in the presence of medical conditions that would make prescription inappropriate. Many of these scenarios required information about whether an individual had recently attended hospital with an acute event (e.g. a fall or gastrointestinal bleed). However, since linked hospital data were not available, and information about acute events occurring in secondary care is not well coded in GP records,(31, 32) this aspect of the analysis should be interpreted with caution.

The before and after study design defined medications changes in the three months before and three months after an SMR. This was chosen as representing the longest time period that repeat prescriptions of medications for long term conditions are likely to be prescribed.(33) However, medication prescribing patterns are rarely uniform and therefore defining the exposures using shorter or longer time frames may have resulted in slightly different findings.

Comparison with existing literature

Few studies have sought to determine the impact of structured medication reviews on prescribing practices in primary care. One previous study using data from routine electronic health record data from the OpenSafely database observed a lower percentage of patients (3.6%) receiving SMRs,(22) however, that study had a broader focus on all types of medication review, and the denominator population was not limited to patients eligible for an SMR.

Approximately one third of inappropriate medication combinations associated with gastrointestinal bleeding (NSAIDs, anticoagulants, aspirin and antiplatelets but not PPIs) were corrected following an SMR in the present study. Similar findings were observed in a recent study examining the scale-up and rollout of the PINCER intervention, a pharmacist-led approach to reduce hazardous prescribing in primary care.(13) Across 343 general practices implementing the intervention in routine clinical care, decreases in inappropriate prescribing were observed for all indicators, including a 24% reduction in medication combinations associated with gastrointestinal bleeding.(34)

Evidence from randomised controlled trials suggests that medication reviews result in changes in prescribing and some surrogate clinical endpoints such as blood pressure and cholesterol,(14) however, there is no evidence that they reduce mortality, hospital admissions, healthcare use, number of patients falling, or improve physical and cognitive functioning and quality of life.(15, 16, 35) The present analysis shows that these effects on prescribing could be realised in routine clinical practice as well, however, the effect on clinical and cost-effectiveness outcomes remains unknown.

Implications for Research and/or practice

The present study found evidence that structured medication reviews are associated with significant increases in starting new medications and stopping existing prescriptions, in vulnerable patients with frailty, multiple long-term conditions and polypharmacy. There was evidence that some inappropriate medication combinations, such as those related to an increased risk of gastrointestinal bleeding were corrected following an SMR, although the majority were still prescribed in the three months after an SMR. Addressing such inappropriate prescriptions could have significant consequences for the healthcare system, where recent analyses suggest that inappropriate prescribing of NSAIDs alone (without proton-pump inhibitors) could cost the NHS £2.46 billion per year, with a loss of nearly 2,000 quality adjusted life years.(36)

SMRs were associated with a small increase in primary care contacts, defined as face-to-face or telephone/ video appointments with GPs, pharmacists, HCAs or nurses. Whether this is to be expected is unclear, however, the PCN contract specification for SMRs(29) does outline expectations for follow-up of SMRs, which could explain the observed increase in primary care contacts.

Despite first being rolled out during the COVID-19 pandemic, 1 in 8 eligible patients received an SMR, with evidence of targeting patients with greater frailty, more polypharmacy and larger numbers of long-term

conditions, with no evidence of demographic or socioeconomic bias. This suggests that SMRs were targeted as intended, at those most likely to be at risk of inappropriate polypharmacy and adverse drug events.(37)

Although this study showed that SMRs were associated with changes in prescribing and deprescribing following an SMR, the effect on clinically relevant patient outcomes remains unknown. Future studies should utilise linked data from both primary and secondary care to examine the association between SMRs and clinical outcomes such as hospitalisation due to adverse drug events. Such analyses will require careful adjustment for confounding by indication and classification of outcomes which may be captured with varying accuracy. Furthermore, it remains unclear whether the investment in practice-based pharmacists to deliver SMRs is a cost-effective approach, and health economic modelling of this service would provide valuable information for policy makers in the future.

This study found that 1 in 8 eligible patients received a structured medication review within the first two years of the service rollout. SMRs were associated with a significant increase in starting new medications and stopping existing prescriptions across nearly all drug classes of interest. However, further work is needed to understand whether these changes in prescribing improved patient outcomes in the longer-term.

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Competing interests declaration
All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdfwww.icmje.org/coi_disclosure.pdf and declare no conflicts of interest.

Ethics approval
The study protocol was approved by South Central – Hampshire A Research Ethics Committee (ref 22/SC/0373).

Data sharing
Requests for data sharing should be made directly to the Primary Care Hosted Research Datasets Independent Scientific Committee (PrimDISC), based at the University of Oxford. Code lists used to define variables included in the dataset are available at https://github.com/ndpchs-cprd/PD-0002-2022-OSCAR.

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Tables and figures

Table 1. Baseline characteristics of those receiving and not receiving a structured medication review

Characteristics	Received an SMR	Did not receive an SMR
Total cohort population (%)	82,285 (12.9%)	553,413 (87.1%)
Age at index date (median yrs (p25, p75))	77 (72 to 84)	76 (71 to 83)
Sex (% Female)	48,997 (59.6%)	316,779 (57.2%)
Asian ethnicity	2,745 (3.3%)	15,952 (2.9%)
Black ethnicity	1,326 (1.6%)	6,906 (1.2%)
Mixed ethnicity	281 (0.3%)	1,887 (0.3%)
Other ethnicity	337 (0.4%)	2,170 (0.4%)
White ethnicity	73,027 (88.8%)	478,213 (86.4%)
Unknown ethnicity	4,569 (5.5%)	48,295 (8.7%)
BMI (Mean (SD))	28.5 (6.2)	28.0 (6.0)
Smoking status		
Active Smoker	8,443 (10.3%)	59,412 (10.7%)
Ex-smoker	34,224 (41.6%)	229,455 (41.5%)
Non-smoker	38,082 (46.3%)	254,902 (46.1%)
Missing	1,536 (1.9%)	9,644 (1.7%)
IMD quintile 1 (most deprived)	12,580 (15.3%)	76,084 (13.7%)
IMD quintile 2	14,675 (17.8%)	92,435 (16.7%)
IMD quintile 3	16,606 (20.2%)	108,167 (19.6%)
IMD quintile 4	16,278 (19.8%)	117,894 (21.3%)
IMD quintile 5 (least deprived)	15,579 (18.9%)	118,462 (21.4%)
Missing	6,567 (8.0%)	40,371 (7.3%)
Living in a rural area	18,590 (22.6%)	125,805 (22.7%)
Living in an urban area	59,331 (72.1%)	401,094 (72.5%)
Missing	4,364 (5.3%)	26,514 (4.8%)
Systolic blood pressure (mmHg, mean (SD))	132.7 (17.0)	133.3 (17.1)
Missing (n patients (%))	41,478 (50.4%)	332,018 (60.0%)
Diastolic blood pressure (mmHg, mean (SD))	74.2 (10.0)	74.5 (10.1)
Missing (n patients (%))	44,039 (53.5%)	346,540 (62.6%)
Total cholesterol (mM, mean (SD))	4.49 (1.18)	4.61 (1.29)
Missing (n patients (%))	2,204 (2.7%)	16,807 (3.0%)
HDL cholesterol (mM, mean (SD))	1.45 (0.45)	1.48 (0.63)
Missing (n patients (%))	2,970 (3.6%)	22,734 (4.1%)
Residing in a care home	8,209 (10.0%)	25,884 (4.7%)
Frailty		
Fit	5,991 (7.3%)	79,774 (14.4%)
Mild	24,450 (29.7%)	202,346 (36.6%)
Moderate	27,770 (33.8%)	160,602 (29.0%)
Severe	24,074 (29.3%)	110,691 (20.0%)
eFI Score		
<= 0.36 (Not severe)	64,122 (77.9%)	471,827 (85.3%)
> 0.36 (Severe)	18,163 (22.1%)	81,586 (14.7%)
Polypharmacy		
0-4	3,297 (4.0%)	50,664 (9.1%)
5-9	21,475 (26.1%)	187,579 (33.9%)
>= 10	57,513 (69.9%)	315,170 (57.0%)
Number of MLTC		
0-1	2,803 (3.4%)	34,411 (6.2%)
2-3	15,364 (18.7%)	142,428 (25.7%)
4 or more	64,118 (77.9%)	376,574 (68.1%)

SMR=structured medication review; SD=standard deviation; BMI=body mass index; IMD=index of multiple deprivation; MLTC=multiple long-term conditions; eFI=electronic frailty index

Table 2. Changes in medication prescription following a structure medication review (n=82,285)

Medication prescription	Total on prescription prior to an SMR	Prescription stopped after SMR	Total not on prescription prior to an SMR	Prescription started after SMR
Antihypertensives				
ACE inhibitors	23,282	1,188 (5.1%)	59,003	1,111 (1.9%)
Alpha blockers	5,108	379 (7.4%)	77,177	472 (0.6%)
Angiotensin II receptor blockers	14,376	619 (4.3%)	67,909	733 (1.1%)
Beta blockers	28,403	973 (3.4%)	53,882	1,325 (2.5%)
Calcium channel blockers	25,304	1,545 (6.1%)	56,981	1,747 (3.1%)
Thiazide & Thiazide-like diuretics	7,407	774 (10.4%)	74,878	584 (0.8%)
Other Cardiovascular medications				
Statins	47,896	1,752 (3.7%)	34,389	2,662 (7.7%)
Aspirin	16,958	1,438 (8.5%)	65,327	1,094 (1.7%)
Other Antiplatelets	10,918	890 (8.2%)	71,367	780 (1.1%)
DOAC	16,822	600 (3.6%)	65,463	1,467 (2.2%)
Vitamin K antagonists	3,284	338 (10.3%)	82,142	143 (0.2%)
Inhaled medication				
Inhaled beta agonist	15,279	1,226 (8.0%)	67,006	1,436 (2.1%)
Inhaled corticosteroids	14,188	1,491 (10.5%)	68,097	1,648 (2.4%)
Pain medications				
NSAIDS	13,102	3,882 (29.6%)	69,183	3,934 (5.7%)
Opioids	27,364	4,230 (15.5%)	54,921	4,197 (7.6%)
Other medications				
Antidepressants	27,675	1,828 (6.6%)	54,610	1,923 (3.5%)
Benzodiazepines	5,073	1,130 (22.3%)	77,212	1,324 (1.7%)
Donepezil	2,639	95 (3.6%)	79,646	159 (0.2%)
Gabapentin	5,856	598 (10.2%)	76,429	519 (0.7%)
Pregabalin	4,335	380 (8.8%)	77,950	458 (0.6%)
Z-drugs	3,946	637 (16.1%)	78,339	681 (0.9%)
Laxatives	17,205	3,427 (19.9%)	65,080	4,194 (6.4%)
PPI	46,337	2,414 (5.2%)	35,948	4,075 (11.3%)

SMR=Structured medication review; ACE=Angiotensin converting enzyme; DOAC=Direct oral anticoagulant; NSAIDS= Non-steroidal anti-inflammatory drugs; PPI=Proton pump inhibitors

Table 3. Changes in potentially inappropriate medication prescriptions following a structured medication review

Indicator	Condition	Drug or drug combination	Total with inappropriate medication combinations	Not corrected following SMR (n(%))	Corrected following SMR (n(%))
GIB01	GI bleed	NSAID, but not PPI	101	65 (64.4%)	36 (35.6%)
GIB02	GI bleed	NSAID & anticoagulant	190	114 (60.0%)	76 (40.0%)
GIB03	GI bleed	NSAID & anticoagulant, but not PPI	35	27 (77.1%)	8 (40.0%)
GIB04	GI bleed	Aspirin & Antiplatelet, but not PPI	93	64 (68.8%)	29 (31.2%)
GIBCI	GI bleed	Unique patients from GIB01 to GIB04	324	201 (62.0%)	123 (34.0%)
PAIN01	Respiratory depression/confusion	Opioid & Benzo/Gabapentin/ Pregabalin/Z-drug	72	57 (79.2%)	15 (20.8%)
PAIN02	Constipation	Opioid, but not laxative	1,001	766 (76.5%)	235 (23.5%)
PAIN03	Respiratory depression/confusion	Opioid	202	172 (85.1%)	30 (14.9%)
FRAC01a	Fall	Z-drug	1,218	1002 (82.3%)	216 (17.7%)
FRAC01b	Fracture	Z-drug	276	226 (81.9%)	50 (18.1%)
FRAC02a	Fall	Benzo	1,741	1295 (74.4%)	446 (25.6%)
FRAC02b	Fracture	Benzo	456	331 (72.6%)	125 (27.4%)
FRAC03a	Fall	Benzo/Z-drug	191	119 (62.3%)	72 (37.7%)
FRAC03b	Fracture	Benzo/Z-drug	687	480 (69.9%)	207 (30.1%)
RESP01	Asthma	LABA, but not inhaled corticosteroid	112	98 (87.5%)	14 (12.5%)

GI=gastro-intestinal bleed; NSAID=non-steroidal anti-inflammatory drug; PPI=proton pump inhibitor; SMR=Structured medication review; DOAC=direct oral anticoagulant; LABA=inhaled Long Acting Beta-agonist

Figure legends

Figure 1. Association between structured medication reviews and starting medications for the first time. Models adjusted for body mass index, ethnicity, indices of multiple deprivation, smoking status, care home residence, baseline cholesterol, electronic frailty index score(26) and number of multiple long-term conditions.(27) SMR=Structured medication review; CI=Confidence interval; ACE=Angiotensin-converting enzyme; DOAC=Direct oral anticoagulant; Vit K=Vitamin K; NSAIDS= Non-steroidal anti-inflammatory drugs; PPI=Proton pump inhibitors

Figure 2. Association between structured medication reviews and stopping medications prescribed prior to the index date. Models adjusted for body mass index, ethnicity, indices of multiple deprivation, smoking status, care home residence, baseline cholesterol, electronic frailty index score(26) and number of multiple long-term conditions.(27) SMR=Structured medication review; CI=Confidence interval; ACE=Angiotensin converting enzyme; DOAC=Direct oral anticoagulant; Vit K=Vitamin K; NSAIDS= Non-steroidal anti-inflammatory drugs; PPI=Proton pump inhibitors

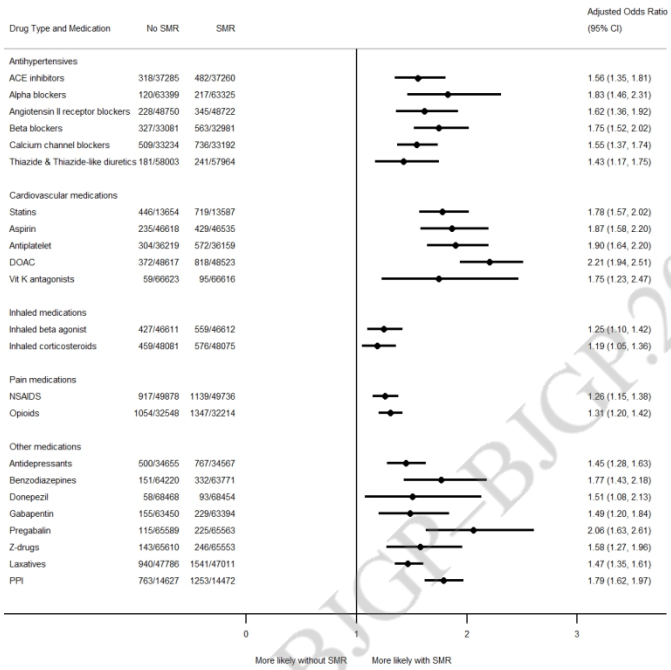

Figure 1.

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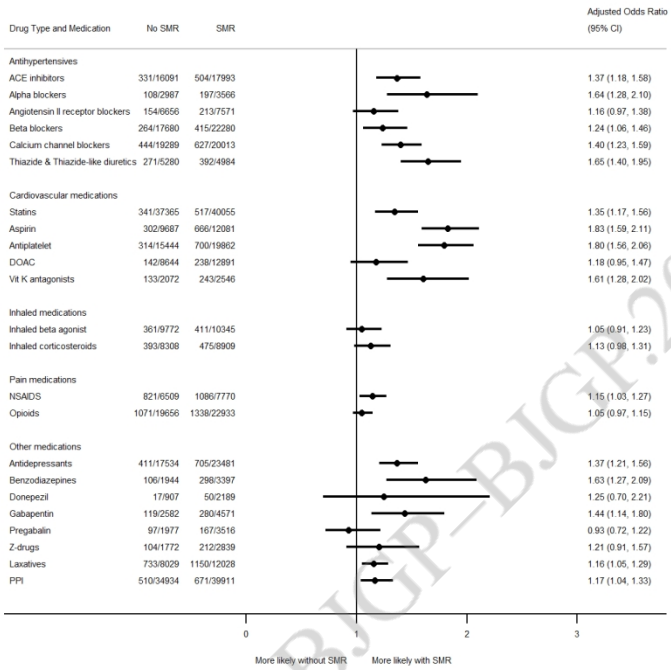

Figure 2.

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