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Development of a structured clinical pharmacology review for specialist support for management of complex polypharmacy in primary care

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Short running title: Medication reviews for complex polypharmacy

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This study did not perform interventions with or administer substances to human subjects/patients and did not have a Principal Investigator

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Abstract (249/250 words)

Polypharmacy is widespread and associated with medication-related harms, including adverse drug reactions, medication errors and poor treatment adherence. General practitioners and pharmacists cite limited time and training to perform effective medication reviews for patients with complex polypharmacy, yet no specialist referral mechanism exists. **Aims.** To develop a structured framework for specialist review of primary care patients with complex polypharmacy. **Methods**. We developed the Clinical Pharmacology Structured Review (CPSR) and Stopping By Indication Tool (SBIT). We tested these in an age-sex stratified sample of 100 people with polypharmacy aged 65-84 years from the Clinical Practice Research Datalink, an anonymised primary care database. Simulated medication reviews based on electronic records using the CPSR and SBIT were performed. We recommended medication changes or review to optimise treatment benefits, reduce risk of harm or reduce treatment burden. **Results**. Recommendations were made for all patients, for almost half (4.8±2.4) of existing medicines (9.8±3.1), most commonly stopping a drug (1.7±1.3/patient) or reviewing with patient (1.4±1.2/patient). At least one new medicine (0.7±0.9) was recommended for 51% patients. Recommendations predominantly aimed to reduce harm (44%). There was no relationship between number of recommendations made and time since last primary care medication review. We identified a core set of clinical information and investigations (polypharmacy workup) that could inform a standard screen prior to specialist review. **Conclusions**. The CPSA, SBIT and polypharmacy workup could form the basis of a specialist review for patients with complex polypharmacy. Further research is needed to test this approach in patients in general practice.

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What is already known about this subject:

- Polypharmacy is common and is associated with multiple adverse health outcomes
- Medication reviews are conducted in primary care by general practitioners and clinical pharmacists, but can be challenging in patients with complex polypharmacy
- There is no established mechanism for referral of patients with complex polypharmacy for specialist review, in contrast to other long term conditions

What this study adds:

- We have developed the Clinical Pharmacology Structured Review (CPSR), Stopping By Indication Tool (SBIT) and polypharmacy workup as a structured framework for specialist review of complex polypharmacy
- Analysis of longitudinal primary care data indicates this framework could be a useful addition to the existing medication review process
- The CPSR, SBIT and polypharmacy workup could have particular utility for primary care patients with complex polypharmacy

Keywords

clinical pharmacology, primary care, prescribing, drug utilization, quality use of medicines, medication review, frailty, long term conditions

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Introduction

Polypharmacy, the simultaneous use of multiple medicines by one person, is very common, with 21% of UK adults aged 20 and older dispensed ≥5 medicines and 6% dispensed ≥10 medicines in the previous 84 days [1]. Polypharmacy is increasingly prevalent; the number of prescriptions in England doubled from 10 to 20 per person between 1997 and 2016 [2]. Whilst polypharmacy is associated with frail older adults [1,3], it can affect people of all ages [4]. Polypharmacy is often appropriate and of benefit to patients with multiple comorbidities. However, the more medicines a person takes, the more likely they are to experience harm. For every additional prescription, the risk of an adverse drug reaction increases by 13% [5], medication error by 16% [6] and poor adherence by 14% [7]. Patients with polypharmacy are more likely to be prescribed high risk medicines [8, 9], yet changes in pharmacokinetics and pharmacodynamics in this multi-morbid population may result in reduced effectiveness of medication and increased risk of harm [10,11]. Furthermore, such patients are less likely to be prescribed prophylactic medicines [8], for example, to reduce cardiovascular risk [12,13] and the efficacy of therapy is more likely to be reduced by drug-drug interactions [14-16].

Medicines optimisation is the process of ensuring that medicine use is safe and effective and that patients get the best possible outcomes from their medicines [17]. Medication reviews in primary care, predominantly carried out by general practitioners and clinical pharmacists, are used to optimise the impact of medicines, minimise the number of medication-related problems and reduce waste [18]. Medication reviews for the most complex patients with polypharmacy present a number of challenges. Patients with multimorbidity are typically excluded from randomised controlled trials [19,20] and so guidelines for the treatment of

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single diseases may have limited applicability to these patients [21-23]. Understandably, GPs cite a lack of time to optimise medicines and a reluctance to alter the status quo in such patients [24] and clinical pharmacists have less confidence with prescribing for complex multimorbidity [25]. Deprescribing, the process of ensuring the safe and effective withdrawal of inappropriate medicines [26] is widely recommended for inappropriate polypharmacy, but evidence-based guidelines to support this are limited [27-29]. It can therefore be difficult for clinicians to decide whether continuing or stopping a medicine would be in the best interest of their patient. In addition, the fragmented multi-speciality configuration of modern healthcare and a lack of time and resources are substantial barriers to effective deprescribing [30-32].

There is currently no established mechanism of onward referral and advice to support the care of primary care patients with complex polypharmacy in the UK. A dedicated service, provided by medicines specialists such as clinical pharmacologists (doctors with particular expertise in the use of medicines), senior pharmacists, experienced GPs or geriatricians, could be a useful addition to support complex patients. The aim of our study was to develop a structured framework for specialist review of primary care patients with complex polypharmacy.

Methods

Approvals

This study is based on data from the Clinical Practice Research Datalink (CPRD) [33] obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data

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are provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this report are those of the authors alone. The protocol number (18_023) was approved by the Independent Scientific Advisory Committee evaluation of joint protocols of research involving CPRD data in March 2018.

Clinical Pharmacology Structured Review

The Clinical Pharmacology Structured Review (CPSR), was developed as a body systems based approach for performing complex medication reviews (Supplementary table 1 shows an example review for one patient). Diagnoses are sorted by body system (e.g. cardiovascular, respiratory) as defined by British National Formulary (BNF) chapters [34]. Clinical measurements and test results required to assess disease control are aligned with diagnoses. Medicines are sorted by system/BNF chapter rather than diagnosis, due to overlapping indications and multiple medicines for individual diagnoses. This structured alignment of body systems and medication allows better recognition of over- and under-treatment than the customary chronological diagnosis and alphabetical medication listings.

Participants

The CPSR was developed using data from patients on the Clinical Practice Research Datalink (CPRD), an anonymised primary care database, which comprises 11.3 million historical records from patients in 674 practices in the UK as of 2015 [35]. Twenty-five of these practices, which were still contributing data throughout 2016, were selected at random. From each, one male and one female patient aged 65-74 and one male and one female patient aged 75-84 were randomly selected, all of whom had repeat prescriptions for 10 or more unique medication classes in 2016 and were still registered at the end of the year.

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Medicines were grouped according to the third level (paragraph) of the British National Formulary hierarchical classification of medication as per our previous research [36]. Medication classes from BNF chapters 1-13 were included [34]. Non-medication entries (e.g. medical devices) or other chapters (e.g. vaccines, anaesthesia and emergency treatment for poisoning) were excluded.

Patient information available to the researchers included historical diagnoses and every prescription issued while registered at their current practice, including the date of prescription, medicine name, strength and number (e.g. of tablets) supplied. Pathology results, symptoms, administrative data and some basic examination records were also available, including pulse rate, blood pressure and body mass index. Information up to and including 31st December 2016 was included as this was the date set for the simulated review (see protocol).

Protocol

Clinical Pharmacology Structured Review

Demographic data, including anonymised patient identification (ID) number, sex, year of birth and frailty, were collected for each patient, including the date of the last primary care medication review where applicable. Frailty was assessed using the electronic frailty index (eFI) [37], a validated measure of frailty created by using an equally weighted sum of 36 routinely recorded deficits, such as heart failure, osteoporosis, and memory and cognitive problems. The eFI calculates a frailty score by dividing the number of deficits present by the total possible.

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0-4 deficits = score 0 to 0.12 represents patients without frailty;

5-8 deficits = score >0.12 to 0.24 represents patients with mild frailty;

9-12 deficits = score >0.24 to 0.36 represents patients with moderate frailty; and

13+ deficits = score >0.36 represents patients with severe frailty.

Simulated medication reviews, using the CPSR were conducted as if they were occurring on 31st December 2016, using all clinical data available up to that date. Medicines reviewed were those prescribed as repeat prescriptions between October to December 2016, i.e. within three months preceding the review. Each patient was discussed by a team of clinical pharmacologists comprising a consultant and three trainee doctors, with additional input from primary care and pharmacy for some cases. Each prescription was discussed and reviewed in context of the patient's clinical and investigation information and the best available evidence. Evidence was used in order of hierarchy, with National Institute for Health and Care Excellence (NICE) guidelines; other national or international guidelines; meta-analyses and systematic reviews; and single randomised control trials in decreasing order of importance.

A final recommendation (Table 1) and purpose of the recommendation were recorded. Purposes were defined as follows:

- treatment appropriate - no change is required
- optimise benefit - to improve disease or symptom control
- reduce harm - to reduce actual or potential harms of treatment

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- reduce treatment burden - where a change is unlikely to optimise benefit or reduce harm, but where stopping or reducing treatment will reduce the burden on the patient or healthcare system

Polypharmacy workup

Clinical measurements and investigation results were used to assess disease control and the appropriateness of prescriptions during medication review. The necessity of each test was considered on an individual patient basis. A test result was deemed essential where a recommendation could not be made without it and useful if it was helpful but not essential to the recommendation.

Stopping By Indication Tool

Given that there is limited evidence to support deprescribing in patients with polypharmacy and complex co-morbidities, the Stopping By Indication Tool (SBIT) was developed to guide decision making. The initial prescriptions of all patients were categorised by treatment goal into four main groups: symptom control; prevention/prognosis; disease control; and prescribing cascade, using information available regarding each patient's prescriptions and diagnoses. The treatment goal categories were defined as follows:

- Symptom control – medicine controls symptoms through mechanisms not specific to the disease process and does not affect prognosis (e.g. opioids for pain)
- Prevention/prognosis – medicine reduces the risk of onset or progression of a disease or event or prolongs survival (e.g. antihypertensives to reduce the risk of stroke)

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- Disease control – medicine targets disease process to control symptoms but does not affect prognosis (e.g. furosemide for heart failure, tamsulosin for benign prostatic hypertrophy)
- Prescribing cascade – medicine prescribed to mitigate the actual or potential harm of another medicine (e.g. proton pump inhibitors as gastroprotection for antiplatelet therapy)

Where medicines had more than one indication, the most important indication was allocated on a case-by-case basis, based on the aspect of treatment that seemed most important for the patient's care.

Supplementary table 2 shows the decision aid used for the SBIT to categorise repeat prescriptions in our dataset. This decision aid was developed using an iterative process and contains diagnoses present in the dataset.

Analysis

Continuous data were described using mean ± standard deviation (SD) where normally distributed, and median [interquartile range] where not normally distributed. Pearson correlations were used for continuous data and Spearman rank correlations for ordinal data. Mann-Whitney *U* tests were used to compare independent non-parametric variables and chi-squared tests were used to compare categorical variables. Statistical analysis was performed in SPSS (version 25).

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Results

One hundred patients were selected, age 74±6 years, 50% female. Patients had 7.5±2.8 long term conditions and, on average, were moderately frail, with an electronic frailty index (eFI) score of 0.28±0.1. In total, 982 existing repeat prescriptions were reviewed, with 9.8±3.1 (range 3-21) per patient. A substantial majority (956; 97%) of prescriptions were from the top 100 most commonly prescribed drug classes in the UK [38]. A primary care medication review was documented in the last six months for 33% and in the last year for 70% of patients. Time since last medication review was 231 [107-411] days. There were no significant differences between patients who did or did not have a medication review in the last 6 or 12 months in terms of age, eFI score or number of initial prescriptions (Table 2).

Clinical Pharmacology Structured Review

In all patients, the CPSR identified at least one potential change in medication or need for review with further information; in total, leading to 5.5±2.7 (range 1-15) recommendations per patient (Table 3). We identified recommendations for almost half (4.8±2.4) of existing medicines (9.8±3.1) and recommended starting at least one new medicine for 51% patients, with an average of 0.7±0.9 new medicines per patient.

The most common recommendations were to stop medicines (1.7±1.3 per patient) and review a medicine with the patient (1.4±1.2 per patient). In terms of the purpose of the recommendations, 2.5±1.9 (44%) aimed to reduce harm, 1.6 ±1.6 (28%) aimed to optimise benefit and 1.6±1.4 (28%) aimed to reduce treatment burden.

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Relationship between patient and medication factors and recommendations

There was no significant correlation between the number of recommendations made and patient factors (age (r=-0.06, *P*=0.53) or electronic frailty index (eFI) score (r=0.10, *P*=0.31)).

The number of repeat prescriptions was positively correlated with the number of recommendations made (r=0.55, *P*<0.001), but there was no significant correlation between the number of repeat prescriptions and the proportion of medicines receiving recommendations (r=-0.02, *P*=0.84).

There was no significant correlation between the time since the last primary care medication review and the number of recommendations made (r=-0.07, *P*=0.49). There were no significant differences in the number of recommendations between patients who did or did not have a medication review in the last 6 months (review 6 [4-8] recommendations; no review 5 [3-6] recommendations, *P*=0.322) or 12 months (review 5 [4-7] recommendations; no review, 5 [3-6], *P*=0.90).

Polypharmacy workup

Figure 1 shows measurements and investigations required for assessment of diagnosis and/or disease control that were considered either essential or useful in decision making at medication review. Some measurements, such as renal function, blood pressure and blood lipids were required for most patients (≥90%), whereas others, such as erythrocyte sedimentation rate (ESR), were needed less often. Serum magnesium was deemed useful mostly in the case of proton pump inhibitor use, due to risk of hypomagnesaemia.

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Stopping By Indication Tool (SBIT)

Supplementary table 3 shows medication classes reviewed for the 100 patients, categorised by their indication. For example, a proton pump inhibitor prescribed for a patient with dyspepsia was categorised as being for symptom control; in the presence of peptic ulcer disease or previous gastrointestinal (GI) bleeding, it was categorised as being for disease control, and where co-administered with drugs with gastrointestinal adverse effects (such as non-steroidal anti-inflammatories), where there was no GI diagnosis, it was categorised as being part of a prescribing cascade. Out of 982 repeat prescriptions reviewed for 100 patients, 420 (43%) of prescriptions were for disease control, 230 (23%) for symptom control, 296 (30%) for prevention/prognosis and 36 (4%) for prescribing cascade. Table 4 compares recommendations by indication. Recommendations to stop medication or reduce dose were made for 50% (18/36) of prescribing cascade medicines, 30% (68/230) of medicines for symptom control, 20% (83/420) of medicines for disease control and 16% (46/296) of medicines for prevention/prognosis. Medicines for prevention/prognosis were most likely to have no change recommended.

Discussion

Main study findings

We have developed a framework comprising the Clinical Pharmacology Structured Review (CPSR), polypharmacy workup and Stopping By Indication Tool (SBIT) for specialist review of complex polypharmacy. Using this structured approach to perform medication reviews, we

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identified many potential medication changes, irrespective of recent medication review in primary care. This indicates that a specialist assessment could add value for primary care patients with complex polypharmacy. Detailed analysis of recommendations identified clinical data that was commonly required to support decision making, and could be used to inform a standard polypharmacy workup for instigation prior to structured medication review. Recommendations to stop medicines or reduce doses were more common for medicines used for symptom control and those prescribed to mitigate against the effects of other medicines (prescribing cascade), than for medicines used for prevention/prognosis or disease control. The SBIT could potentially support deprescribing in primary care, where evidence based guidelines are lacking.

Study strengths and weaknesses

The CPSR, polypharmacy workup and SBIT were developed by clinical pharmacologists in collaboration with academic primary care colleagues (who are practising general practitioners), population health specialists and epidemiologists. It describes an approach that could be taken for the review of patients with complex polypharmacy in a specialist service. It was developed using primary care medical records of real UK patients from CPRD, a database representative of UK patients in terms of age, sex and ethnicity [35,39]. It is therefore likely to be applicable to patients across the UK. Medical records were longitudinal, allowing for a comprehensive assessment of patients' overall health and treatment. This meant that medication reviews could take into account previous therapeutic strategies and make recommendations that were more likely to be suitable for the patient.

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A patient-centred approach is important in medicines optimisation [40] and a key limitation of this project is the lack of patient involvement. Whilst medication reviews in primary care are also often undertaken without the patient present [41], there is limited evidence that participation of patients increases the identification of medication related problems [42]. Issues may have come to light if we had been able to speak to patients in our study, which could have altered our prescribing decision making. Additional benefits of medication reviews, including improving patients' knowledge, satisfaction and adherence to therapy, are also important factors to address. By not speaking to the prescribing general practitioners for the selected patients it is also difficult to estimate the proportion of our recommendations that would be acted upon in primary care. Despite receiving recommendations to change medicines, additional barriers of feasibility (e.g. a lack of time and resources, patient characteristics and preferences) and inertia (e.g. if stopping a medicine is considered futile) [30] may limit the number of recommendations implemented.

Another limitation of this analysis was the lack of secondary care data. Most repeat prescriptions initiated in secondary care are continued in primary care by general practitioners, either directly or under shared care agreements, and these would be picked up by CPRD. However, rarer, secondary care only prescribing (e.g. biologics, chemotherapy etc.) are not recorded routinely in primary care and would be missing or incomplete in CPRD. Indications for some medicines were also not always clear, possibly because secondary care diagnoses were not always documented in CPRD. In real patient consultations, incomplete medical records would negatively impact the utility of the CPSR. In such cases it might only be possible to make recommendations on a limited number of medicines and plan to repeat the process once more information had been gathered.

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However, this would also be the case in any other medical consultation. When conducting real medication reviews using the CPSR, the clinician would need access to primary care records, which would include clinic letters and discharge summaries containing the majority of salient secondary care data. Further information could also be obtained from the patient.

Analysis of the relationship between previous medication review and recommendations made as a result of the CPSR and SBIT framework were limited by a lack of information of the type of medication reviews documented in our data. There are many different types of medication review, differing in terms of the purpose (holistic or focussed on a specific condition or medication), the level of access to patient records, the healthcare professional undertaking the review and whether or not the patient was present for the review [43]. These potential confounding factors may have influenced our findings, because the type of review may have impacted on the appropriateness of medication and thus the number of recommendations made during this study.

Comparison with other studies

There are a number of existing tools for medication review, and these can be broadly categorised as explicit or implicit. Explicit tools, such as the STOPP/START criteria [44] and Beers criteria [45] provide specific, algorithm-based guidance about medication. Explicit tools do not rely on users to have a detailed knowledge of medicines and thus are useful even for relatively inexperienced healthcare professionals. Explicit tools benefit from being widely used and generalisable to the majority of patients. However, this rules-based approach means such tools are less adaptable to individual patients' preferences, lifestyles and patterns of comorbidities.

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Implicit tools, such as the Medication Appropriateness Index [46] provide a framework whereby clinical judgements of the appropriateness of medication can be made. They require healthcare professionals to have the knowledge, experience and time to make judgements, but allow for a more flexible and thus patient-centred approach. Implicit tools, whilst time consuming, offer the potential for specialist review for complex patients. A recent study of an implicit tool for deprescribing multiple medicines ('poly-de-prescribing') demonstrated significant improvement, or less deterioration, in general satisfaction, functional, mental and cognitive status, sleep quality, appetite and sphincter control in patients with extensive polypharmacy where poly-de-prescribing was achieved [47]. Whilst this was not a randomised controlled trial, it indicates the potential for implicit tools to benefit a subset of patients with extensive polypharmacy.

The CPSR and SBIT framework is an implicit tool to support specialist review of patients with complex polypharmacy. By taking a body systems focussed approach to medication review, it allows recommendations to be made to optimise medicines for patients that can supplement and support the primary care medication review process. Increases in multimorbidity and frailty, complexity of medication regimens, patient expectations and pressure in the healthcare system make the medication review process ever more complex. Specialist input could support primary care networks in managing the most complex patients.

Components of the CPSR and SBIT could be used more widely to support medication reviews. To our knowledge, this is the first time that the clinical measurements required to support polypharmacy review have been described. We found, for example, that renal function was essential or useful for 99% of reviews, but was not available in 10% of cases.

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The majority of these measurements are routinely made in primary care but absence of these data could impact decision making. Consistent availability of results would ensure that healthcare professionals have sufficient information to make informed recommendations regarding medicines optimisation. These investigations could be used to develop a 'polypharmacy workup' to be initiated prior to referral to increase the efficiency of the medication review process for the most complex patients.

Deprescribing can be particularly difficult, with barriers including lack of evidence-based guidelines. The SBIT can be used to support discussions around deprescribing by classifying medicines by their general clinical purpose and considering the consequences of stopping (Table 5). For example, where a medicine is prescribed for symptom control, the risk of stopping that medicine is a return or worsening of symptoms. Therefore a treatment holiday, or changing the administration from 'regular' to 'as required' may be an acceptable first step for many patients. For example, in a meta-analysis of studies where the dosing regimen for proton pump inhibitors was changed from 'regular' to 'as required', 84% of patients reported adequate symptom relief, compared to 91% of those with no change in treatment, indicating that the majority of patients tolerated the change and could step down treatment [48]. The SBIT can facilitate discussion between the clinician and patient about the potential consequences of reducing or stopping the medicine in order to make a personalised deprescribing plan.

Implications for future practice and research

The CPSR will need to be validated in clinical practice to establish its value in medicines optimisation before its widespread use can be recommended. It will be of particular

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importance to assess its use in both face-to-face patient consultations and in team meetings where multidisciplinary healthcare professionals discuss patient care.

The 2019 NHS long term plan [49] sets out a strategy to develop primary care networks of local GP practices and to integrate primary and specialist care, through new integrated care systems. This strategy, along with the commitment of over £100 million to support an extra 1,500 clinical pharmacists by 2020 [50], will mean that clinical pharmacists will play a greater role in patient care, for example through pharmacist-led medication reviews. This may represent an ideal opportunity to test the CPSR in practice, on those patients with the most complex polypharmacy, where initial attempts at medicines optimisation have not been successful. A multi-professional specialist service [51] of clinical pharmacologists (doctors with particular expertise in the use of medicines), senior pharmacists, experienced GPs or geriatricians could use the CPSR to perform medication reviews and support GPs and clinical pharmacists in primary care.

Conclusions

We have developed the Clinical Pharmacology Structured Review, Stopping By Indication Tool and polypharmacy workup in order to provide a framework for specialist medication reviews for patients with complex polypharmacy. These tools could be incorporated into an integrated specialist service to support the care of patients with complex polypharmacy where existing medicines optimisation has not been successful. Validation of these tools in consultations with patients will identify whether this approach will be useful for clinical practice.

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Author contribution statement

Emma Baker had the original idea for the study and all authors contributed to the study design. Emma Baker, Chris Threapleton and James Kimpton performed the simulated medication reviews. Emma Baker and Iain Carey led the data analysis and all authors contributed to the interpretation of the data. Chris Threapleton wrote the first draft of the manuscript. All authors contributed to the revision of the manuscript related to its intellectual content. All authors approved the final version submitted for publication.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Table 1. Categories of recommendations for medicines changes following review using the Clinical Pharmacology Structured Review

Recommendation categories
Drug changes:
a) Stop medicine b) Start medicine c) Reduce dose d) Increase dose
Review with further information:
a) Review indication Where there is no documented indication, but stopping is potentially harmful b) Review with patient Where further information from the patient, such as symptom control, is required c) Review with results Where prescription review is dependent on monitoring or investigation results d) Review with specialist Where further information or advice is required from a specialist, or medication changes should be made by a specialist only a) Planning future treatment Where no changes are recommended at present, but an important consideration needs to be made in the future
No change

Table 2. Demographics of patients who did or did not have a medication review in the previous 6 or 12 months

	Last medication review					
	<6 months n=33	**≥6 months** n=67	***P***	**<12 months** n=70	**≥12 months** n=30	***P***
Age (years)	74±5.6	74±5.7	0.95	75±5.6	73±5.6	0.12
Gender n(%) male	18 (55%)	32 (48%)	0.52	34 (49%)	16 (53%)	0.66
eFI score	0.28 [0.21-0.35]	0.25 [0.22-0.33]	0.20	0.28 [0.21-0.33]	0.25 [0.22-0.33]	0.83
Number of initial medicines	10.0±3.4	9.7±2.9	0.73	9.9±3.0	9.5±3.3	0.54

eFI, electronic frailty index

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Table 3. Recommendations made per patient following the Clinical Pharmacology Structured Review

Recommendations	Number of changes per patient (mean±SD)	Patients receiving at least one recommendation (%)
Existing medicines reviewed:	**9.8±3.0**	**100%**
• Medication changes	2.4±1.4	93%
• Review with further information	2.4±1.9	88%
• No change	5.0±2.5	100%
New medicines to start	0.7±0.9	51%
Total recommendations (change, review or start)	**5.5±2.7**	**100%**
Summary of recommendations to change existing medicines:		
• Stop medicine	1.7±1.3	80%
• Reduce dose	0.5±0.7	34%
• Increase dose	0.2±0.5	20%
Summary of recommendations to review existing medicines:		
• Review indication	0.3±0.8	18%
• Review with patient	1.4±1.2	72%
• Review with results	0.2±0.5	20%
• Review with specialist	0.4±0.9	23%
• Planning future treatment	0.1±0.2	5%
Reasons for existing and new medication recommendations:		
• Optimise benefit	1.6±1.6	77%
• Reduce harm	2.5±1.9	85%
• Reduce treatment burden	1.6±1.4	77%

Table 4. Recommendations for reviewed medicines by indication

	Symptom control		Prevention / prognosis		Disease control		Prescribing cascade		All medicines	
	Number	%	Number	%	Number	%	Number	%	Number	%
No change	106	46%	193	65%	188	45%	13	36%	500	51%
Stop or reduce dose	68	30%	46	16%	83	20%	18	50%	215	22%
Increase dose	1	0%	15	5%	7	2%	0	0%	23	2%
Review with more information	55	24%	42	14%	142	34%	5	14%	244	25%
Total	230	100%	296	100%	420	100%	36	100%	982	100%

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Table 5. Stopping By Indication Tool (SBIT) to facilitate deprescribing

Indication	Risk of stopping	Approach to deprescribing
Symptom control	Symptom flare	Change from regular to as required Treatment holiday
Disease control	Disease exacerbation	Stop if burden > benefit
Prevention/prognosis	Increased risk of disease event	Stop if burden > risk, consider time to event for patients with limited prognosis
Prescribing cascade	Adverse drug reaction	Withdraw as other treatments stop

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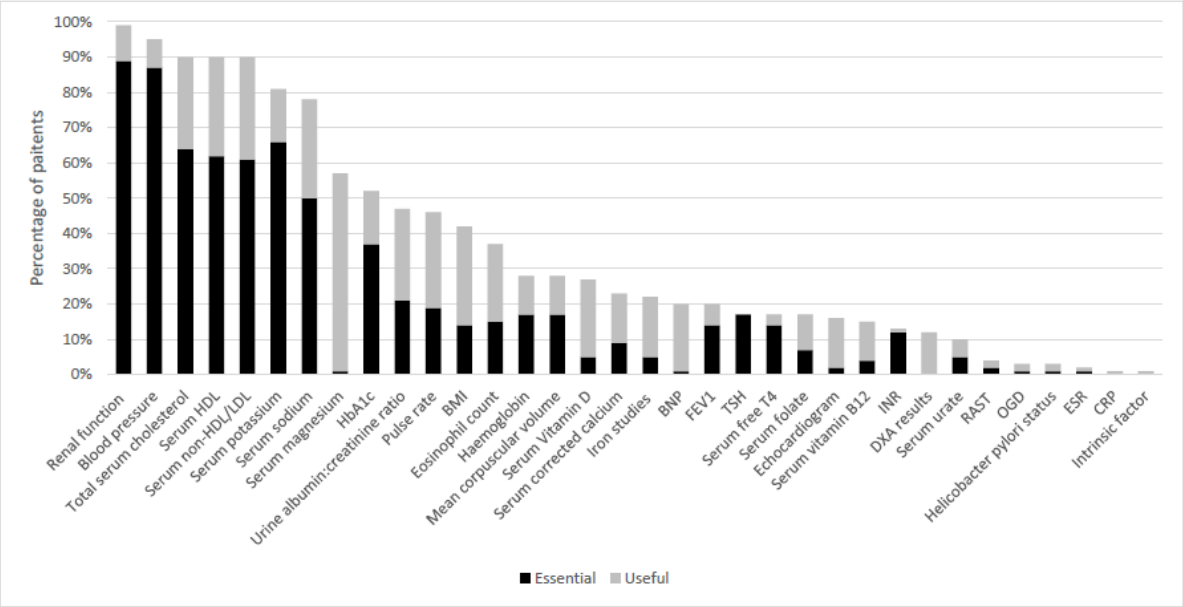

Figure 1. Clinical measurements and investigation results considered essential (black bars) and useful (grey bars) for making prescribing decisions

Abbreviations: BMI, body mass index; BNP, B-type natriuretic peptide; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; FEV-1, forced expiratory volume in 1 s; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; INR, international normalised ratio; LDL, low-density lipoprotein; OGD, oesophagogastroduodenoscopy; RAST, radioallergosorbent test; TSH, thyroid stimulating hormone

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