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ORIGINAL ARTICLE

Evaluating the impact of general practice pharmacist-led person-centred medicines reviews on medicines appropriateness and patient-reported outcome measures

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Abstract

Aim: The aim of this study was to investigate the impact of pharmacist-led person-centred medicines reviews in general practices on medicines appropriateness, polypharmacy indicators (high-risk prescribing markers), and patient-reported outcome measures (PROMs).

Methods: Four pharmacists conducted person-centred medicines reviews in ten general practices between January 2021 and December 2022 for patients with hyperpolypharmacy (prescribed ≥10 regular medicines) and/or at high risk of medicines-related harm. Prescribing recommendations were provided to the general practitioner and followed up with patients and/or healthcare professionals. In this single arm study, pre and post intervention: (1) polypharmacy indicators were documented, and for a sample of patients, the (2) Person-Centred Medication Appropriateness Index (PC-MAI) scores and (3) PROMs were gathered.

Results: Of the 1471 included patients, the mean age was 76 years, 88.4% had hyperpolypharmacy, whilst the mean number of medicines was 13.8 pre and 12.3 post review. Of the 1056 polypharmacy indicator occurrences identified, 70.7% were resolved post review. Of the 194 patients with pre-review and post-review PC-MAI scores, 99% had a reduction; the mean reduction was 17.3 (95% confidence interval [CI] 15.8–18.8, $P < .0001$) per patient and 1.2 (95% CI 1.0–1.3, $P < .0001$) per medicine. PROMs were collected for 179 patients; 87.7% reported the review helped their medicines understanding, 63.1% their experience of side effects, 36.9% their ability to take medicines correctly, and 30.5% the impact of medicines on their daily activities.

Conclusions: General practice pharmacist-led person-centred medicines reviews for patients with hyperpolypharmacy and/or at high risk of medicines-related harm delivered substantial improvements in medicines appropriateness and patient-reported outcomes, thus providing evidence to support their wider implementation.

KEYWORDS
general practice, medication review, patient-reported outcome measures, pharmacist, polypharmacy

1 | INTRODUCTION

There is a rising prevalence of multimorbidity worldwide,[1] with each additional chronic condition typically necessitating more medicines use.[2] Polypharmacy, most commonly defined as the concurrent use of ≥5 regular medicines,[3] is therefore often both necessary and beneficial to manage these conditions. A recent publication has found polypharmacy to be prevalent in more than half of older people in four of the six European countries studied.[4] In Ireland, the most recent figures show the prevalence of hyperpolypharmacy (i.e. concurrent use of ≥10 regular medicines) as 8.3% in those aged 45–64 years and 21.9% of people ≥65 years in 2012,[5] which has likely risen further since.[6] Polypharmacy is deemed "appropriate" if all medicines are prescribed according to best evidence for patients' conditions and personal preferences.[7] However, polypharmacy is associated with a treatment burden that can adversely affect patients' quality of life (QoL) and lead to poor adherence.[8–10] Polypharmacy is also a risk factor for potentially inappropriate prescribing (PIP), including underprescribing of appropriate medicines.[11] PIP in turn is associated with increased healthcare utilisation, functional decline and reduced QoL.[12,13] Therefore, it is vital that patients with polypharmacy have their medicines reviewed and optimised regularly.

A systematic review of qualitative studies on patients' experience of polypharmacy concluded that patients' perspectives and preferences should be elicited when addressing polypharmacy.[10] Shared decision making (SDM) is a joint process where a healthcare professional works together with a person to reach a decision about their care.[14] It aims to aid people's understanding of the benefits, harms, and possible outcomes of different options, and, when implemented correctly, empowers them to make informed treatment decisions. Using a pre-review questionnaire can help patients articulate their care goals and medicines-taking experience[15,16] and understand the rationale for medicines review, thereby enhancing the value they derive from it.[17] Questionnaires offer a means to evaluate both medicines burden and the effectiveness of medicines reviews on patient outcomes and/or experience.[18] Comprehensive medicines reviews should deliver improvements in both medicines appropriateness and patient-reported outcome measures (PROMs).

Performing comprehensive medicines reviews with patients, and considering their perspectives, takes time and requires access to detailed clinical information – neither of which community pharmacists typically have in many jurisdictions to perform reviews on a larger scale.[19] The role of general practice-based pharmacists in medicines optimisation is well established in some countries.[20–24] In Ireland, like many countries, integration of pharmacists into general practices is practically non-existent, despite evidence that they improve prescribing appropriateness and deliver substantial economic benefits.[25–27] The Irish evidence thus far has come from small-scale, short-term studies.[25,26] The "**i**mplementing **S**timulating **I**nnovation in the **M**anagement of **P**olypharmacy and **A**dherence **Th**rough the **Y**ears" (iSIMPATHY) project, funded by the European Union, afforded the opportunity to integrate pharmacists into Irish general practices as part of routine care delivery, rather than specifically as part of research.[28] Trained iSIMPATHY pharmacists supported patients in making informed decisions to optimise medicines by applying the "7 steps to appropriate polypharmacy approach",[7] establishing patients' priorities and discussing the risks and benefits of their medicines.

While most studies of pharmacist-led medicines reviews focus on measures of medicines appropriateness,[25,26] there is limited information regarding patient-reported outcomes from such pharmacist interventions in general practice settings.[17] With this evidence gap in mind, the present study aimed to assess the impact of comprehensive person-centred medicines reviews in general practice settings on high-risk prescribing, medicines appropriateness, and patient-reported outcomes.

What is already known about this subject

- Hyperpolypharmacy (the use of ≥10 regular medicines) has become increasingly prevalent worldwide, and is associated with adverse effects on patients' quality of life.
- While many studies on pharmacist-led medicines reviews focus on measures of medicines appropriateness, there is a paucity of evidence regarding patient-reported outcomes from such pharmacist interventions.

What this study adds

- Pharmacists providing comprehensive person-centred medicines reviews in general practice settings for patients with hyperpolypharmacy resulted in significant improvements in medicines appropriateness, patient-reported side effects, adherence and understanding about medicines.
- Implementing such reviews more widely in primary care should be considered to minimise the medicines-related harm associated with inappropriate hyperpolypharmacy.

2 | METHODS

2.1 | Study approval, conduct, and reporting

Advice was sought from the Health Service Executive Dublin North East Research Ethics Committee. As the work met service evaluation

criteria under national guidance,[29] ethics committee approval was not required, but the project complied fully with information governance and data protection requirements, including patient consent for data collection, processing and analysis. This study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[30]

2.2 | Study setting and participants

This study reports on medicines reviews delivered as part of the iSIMPATHY project, which aimed to improve the health and well-being of people at higher risk of medicines-related harm through medicines reviews in Scotland, Northern Ireland, and Ireland. Findings of the full iSIMPATHY project across the three jurisdictions, with reviews delivered in general practice and hospital settings (inpatient and outpatient), are reported separately.[28] This study is a substudy focusing on evaluating clinical outcome measures and PROMs for patients reviewed in general practice settings in Ireland, as reviews did not take place in hospital settings in Ireland.

The present study is a single arm pre-post study comprising a secondary analysis of all medicines reviews performed in ten general practices in Ireland (near the border with Northern Ireland) from January 2021 to December 2022 inclusive, where patients consented to data processing and met the following inclusion criteria:

1. Prescribed ≥10 regular medicines.
2. At greater risk of medicines-related harm, as defined by the presence of ≥1 polypharmacy indicator.[31]
3. Adults of any age approaching the end of their life due to any cause.
4. Aged ≥50 years and living in a residential care setting.

Of all practices that expressed interest in participation in Ireland, ten were selected to ensure a population of approximately 20 000 patients for each project pharmacist. At study initiation, these pharmacists had 7, 13, 15, and 20 years' post-registration experience (mean 13.8) across community ($n = 2$), both community and primary care ($n = 1$), and both hospital and community ($n = 1$) settings.

2.3 | Medicines review delivery

Eligible patients were (i) identified by iSIMPATHY pharmacists via general practice software (screening for inclusion criteria) or (ii) referred to the pharmacist by the general practitioner (GP) or another healthcare professional.

Eligible patients were offered a medicines review; initially, only reviews via telephone were offered due to COVID-19 restrictions. When restrictions eased, face-to-face reviews were also offered. Pharmacists asked for patients' consent to collect their data to evaluate the service. Patients who did not consent still received a medicines review, with only their unique project identifier and gender recorded.

Pharmacists conducted structured person-centred medicines reviews with each patient (and/or their nominated caregiver) using the "7 steps to appropriate polypharmacy" approach.[7] After the review, pharmacists liaised with, and/or referred to, the GP and/or other healthcare professionals to facilitate intervention implementation.

Some interventions were actioned immediately, whereas others were more complex. Follow-up occurred within 12 weeks of the review; the majority of follow-up occurred within 2–6 weeks depending on time pressures and the complexity or timeline of interventions. This follow-up included assessing whether interventions had been actioned, monitoring of patients or laboratory values, pharmacist–patient discussions, and measuring post-review outcomes. For all patients who consented to data collection, the following core dataset was recorded: demographics, inclusion criteria (all applicable), number of comorbidities, number of current regular prescription medicines pre-review and post-review, number of interventions made, and time taken for review (including follow-up).

2.4 | Outcome measures

The impact of medicines reviews was evaluated using three measures: (1) polypharmacy indicators, (2) the Person-Centred Medication Appropriateness Index (PC-MAI),[28] and (3) a set of PROMs.

1. **Polypharmacy indicators:** Sixty-nine "case-finding indicators", which represent markers of potential high-risk prescribing, were applied.[31] Many of these can be used as clinical outcomes

TABLE 1 Comparison of MAI and PC-MAI.

MAI question (rating)	PC-MAI question (rating)
Is there an indication for the drug? (3)	Is there an indication for the drug? (3)
Is the medication effective for the condition? (3)	Is the medication effective for the individual? (3)
Is the dosage correct? (2)	Is the dosage correct? (2)
Are the directions correct? (2)	-
Are the directions practical? (2)	Are the directions practical? (2)
Are there clinically significant drug–drug interactions? (2)	Are there clinically significant drug–drug interactions? (2)
Are there clinically significant drug–disease/condition interactions? (1)	Are there clinically significant drug–disease/condition interactions? (1)
Is there unnecessary duplication with other drug(s)? (1)	Is there unnecessary duplication with other drug(s)? (1)
Is the duration of therapy acceptable? (1)	Is the duration of therapy acceptable? (1)
Is this drug the least expensive alternative compared to others of equal utility? (1)	-
Maximum total MAI score per medicine = 18	**Maximum total PC-MAI score per medicine = 15**

indicators, whereby a decreased prevalence likely indicates improved prescribing appropriateness.[7] Pre-review indicators that were no longer identifiable at follow-up were deemed "resolved".

2. **PC-MAI:** The Medication Appropriateness Index (MAI) was adapted for iSIMPATHY with the tool developer to create the "Person-Centred MAI" (PC-MAI), which was used for the first time in the iSIMPATHY project.[28] The MAI involves applying 10 criteria with a score of up to 18 for each medicine; the PC-MAI excludes two criteria, with a total score of up to 15 for each medicine (Table 1). For the effectiveness criterion, the PC-MAI reviews the medicine's effectiveness for the individual patient, rather than for the condition in a patient population (i.e., as per the MAI). For both tools, higher scores indicate less appropriate prescribing. Training on PC-MAI use was provided to iSIMPATHY pharmacists, with case examples and quality assurance processes, as described elsewhere.[28] Pharmacists were instructed to calculate PC-MAI for a minimum of 10% of patients. Patients were selected by pharmacists via convenience sampling (i.e., without randomisation).
3. **PROMs:** PROM questionnaires (Appendix 1), developed by the Scottish Government in partnership with Glasgow University and Digital Health and Innovation in consultation with patients and healthcare professionals,[32] were used to assess and monitor for improvements in the medicines burden and patient experience. The original questionnaire included the usual activities and anxiety/depression domains of the EQ-5D-3L instrument[33] and was amended during the project to incorporate the remaining domains. Appendix 1 shows the questions asked by pharmacists of patients and/or carers (i) before the medicines review, and (ii) at follow-up. PROMs were collected when possible, given time pressures, via convenience sampling.

2.5 | Data analysis

Descriptive statistics were generated for age, number of comorbidities, and number of medicines for all included patients, and those with complete PC-MAI, PROMs, and EQ-5D-3L data. Two-tailed student's *t*-tests were performed to check for differences between the subgroups of patients with PC-MAI data, full pre-review and post-review PROMs, EQ-5D-3L, and the overall patient group.

The prevalence and resolution rate for polypharmacy indicators overall, and per individual indicator, were calculated. Pre-review and post-review PC-MAI data were calculated and summarised at the patient level and medicine class level, the latter based on the Anatomical Therapeutic Chemical (ATC) classification system. The Wilcoxon signed rank test was used to compare the matched pre-review and post-review PC-MAI per patient, with the Mann–Whitney U-test used for the PC-MAI per medicine.

Among patients with both pre-review and post-review PROMs data, a frequency analysis was conducted for patients' responses to the Appendix 1 questions. McNemar's test was performed to assess for differences in patient responses pre and post review.

Responses to the validated EQ-5D-3L questionnaire[33] were analysed to determine the patient's pre-review and post-review health state. The distribution of responses pre and post review and percentages reporting a change in the dimension over time were calculated. Index values were calculated for patients with a full set of responses across dimensions. As no Irish value set exists for the EQ-5D-3L, a value set derived among a representative sample of Irish residents for health states using EQ-5D-5L was used,[34] in combination with the cross-walk approach for applying EQ-5D-5L value sets to EQ-5D-3L responses, as recommended by EuroQol.[33] Statistical significance was set at $P < .05$.

3 | RESULTS

Of the 2217 iSIMPATHY patients reviewed in Ireland between January 2021 and December 2022, 1906 (86%) consented to data collection, with 1471 meeting this study's inclusion criteria. The mean age was 76 years (standard deviation [SD]: 9.5; range: 35–101), 55% were female and 45% male, with a mean of 6.2 (SD: 2.3) comorbidities and 13.8 (SD: 4.7) pre-review medicines recorded. Pre review, 1301 (88.4%) were prescribed ≥10 medicines; the remaining 170 were prescribed <10 medicines but met one or more other inclusion criteria. Post review, 1128 (76.7%) were prescribed ≥10 medicines, with a mean of 12.3 (SD 4.3) medicines. Table 2 shows that the baseline demographics of patient subgroups with full pre-review and post-review PC-MAI, PROMs, and EQ-5D-3L were not different to the overall group ($P > .05$).

The total mean pharmacist time ($n = 1471$ reviews) was 157.2 min (SD 45.6), whilst mean GP time was 16.6 min (SD 7.4). The

TABLE 2 Key baseline demographics of patients included in full dataset *vs.* patient samples with PC-MAI, PROMs, or EQ-5D-3L data collected.

	Number of patients	Mean age (SD)	Mean number of co-morbidities (SD)	Mean number of medicines pre review (SD)
Full dataset	1471	76.0 (9.5)	6.2 (2.3)	13.8 (4.8)
PC-MAI	194	76 (9.1)	6.1 (2.5)	14.0 (4.4)
PROMs	179	77.0 (9.2)	6.4 (2.6)	14.0 (5.7)
EQ-5D-3L	37	73.2 (11.0)	5.8 (2.5)	13.8 (6.8)

Abbreviations: PC-MAI: Person-Centred Medication Appropriateness Index; PROM: patient-reported outcome measure; SD: standard deviation.

TABLE 3 Polypharmacy indicators identified ($n = 1471$; 100% of reviews).

Polypharmacy indicator (PI) by category	PI prevalence *n* (% of 1471)	PI resolved *n* (% resolved)	Patients with ≥1 PI occurrence n (%)
Total	**1056**[a]	**747 (70.7%)**	**693 (47.1%)**
Bleeding	**312**[a]	**240 (76.9%)**	**276 (18.8%)**
Patient on an oral anticoagulant is prescribed an antiplatelet	122 (8.3%)	75 (61.5%)	
Patient on an antiplatelet drug is prescribed an NSAID	80 (5.4%)	73 (91.3%)	
Patient on an oral anticoagulant is prescribed an NSAID	35 (2.4%)	32 (91.4%)	
Patient aged ≥65 years on aspirin is prescribed clopidogrel without gastroprotection	24 (1.6%)	23 (95.8%)	
Patient aged ≥75 years is prescribed an NSAID without gastroprotection	18 (1.2%)	15 (83.3%)	
Patient on an oral corticosteroid is prescribed an NSAID	11 (0.8%)	11 (100%)	
Patient with eGFR <30 mL/min/1.73m^2 is prescribed a factor Xa inhibitor	9 (0.6%)	0 (0%)	
Patient an oral anticoagulant has uncontrolled severe hypertension	5 (0.3%)	3 (60.0%)	
Patient with a history of peptic ulcer is prescribed an NSAID	4 (0.3%)	4 (100%)	
Patient with a history of peptic ulcer is prescribed an antiplatelet without gastroprotection	3 (0.2%)	3 (100%)	
Patient with eGFR <30 mL/min/1.73m^2 is prescribed a direct thrombin inhibitor	1 (0.0%)	1 (100%)	
Falls	**241**[a]	**82 (34.0%)**	**237 (16.1%)**
Patient without dementia aged ≥75 years is prescribed two or more drugs with significant sedating or anticholinergic effects	122 (8.3%)	39 (32.0%)	
Patient without dementia aged ≥65 years is prescribed three or more drugs with significant sedating or anticholinergic effects	62 (4.2%)	20 (32.3%)	
Patient with dementia is prescribed two or more drugs with significant sedating or anticholinergic effects	42 (2.9%)	18 (42.9%)	
Patient aged ≥75 years is prescribed a steroid long term without co-prescription of a bone protecting agent	15 (1.0%)	5 (33.3%)	
Renal	**139**[a]	**126 (90.6%)**	**91 (6.2%)**
Patient with eGFR <60 mL/min/1.73m^2 and on an ACEI or ARB is prescribed an NSAID	49 (3.3%)	43 (87.8%)	
Patient on an ACEI/ARB and a diuretic is prescribed an NSAID	46 (3.1%)	42 (91.3%)	
Patient with eGFR <60 mL/min/1.73m^2 and on a diuretic is prescribed an NSAID	32 (2.2%)	30 (93.8%)	
Patient with eGFR <30 mL/min/1.73m^2 is prescribed an NSAID	12 (0.8%)	11 (91.7%)	
Cardiac	**120**[a]	**98 (81.7%)**	**104 (7.1%)**
Patient is prescribed a beta blocker and has a pulse of <60 beats per minute	65 (4.4%)	55 (84.6%)	
Patient with heart failure is prescribed an NSAID	20 (1.4%)	19 (95.0%)	
Patient with heart failure is prescribed verapamil or diltiazem	9 (0.6%)	4 (44.4%)	
Patient on a beta blocker is prescribed verapamil or diltiazem	6 (0.4%)	3 (50.0%)	
Patient is prescribed an acetylcholinesterase inhibitor and has a pulse of <60 beats per minute	5 (0.3%)	5 (100%)	
Patient is prescribed digoxin and has a pulse of <60 beats per minute	5 (0.3%)	4 (80.%)	
Patient on a nitrate or nicorandil is prescribed a phosphodiesterase type 5 inhibitor	4 (0.3%)	4 (100%)	
Patient with eGFR <60 mL/min/1.73m^2 is prescribed digoxin at a dose >125 μg/day	4 (0.3%)	2 (50.0%)	
Patient with heart failure is prescribed a glitazone	2 (0.1%)	2 (100%)	
Electrolyte abnormalities	**86**[a]	**78 (90.7%)**	**72 (4.9%)**
Patient on an ACEI or ARB, aliskiren, potassium sparing diuretic or supplement has hyperkalaemia (potassium >5.5 mmol/L)	22 (1.5%)	21 (95.5%)	
Patient prescribed a thiazide diuretic has hyponatraemia (i.e., serum sodium <130 mmol/L)	15 (1.0%)	15 (100%)	
Patient is prescribed a combination of ACEI and ARB	15 (1.0%)	14 (93.3%)	
Patient with eGFR <30 mL/min/1.73m^2 is prescribed trimethoprim	6 (0.4%)	6 (100%)	
Loop diuretic prescribed to a patient with hyponatraemia (i.e., serum sodium <130 mmol/L)	6 (0.4%)	4 (66.7%)	
Patient with eGFR <30 mL/min/1.73m^2 is prescribed spironolactone or eplerenone	6 (0.4%)	3 (50.0%)	
Patient on an SSRI has hyponatraemia (sodium <130 mmol/L)	5 (0.3%)	5 (100%)	

TABLE 3 (Continued)

Polypharmacy indicator (PI) by category	PI prevalence *n* (% of 1471)	PI resolved *n* (% resolved)	Patients with ≥1 PI occurrence n (%)
Patient with eGFR <30 mL/min/1.73m^2 is prescribed amiloride or triamterene	3 (0.2%)	3 (100%)	
Patient prescribed a loop diuretic has hypokalaemia (i.e., serum potassium <3.0 mmol/L)	3 (0.2%)	3 (100%)	
Patient prescribed a thiazide diuretic has hypokalaemia (i.e., serum potassium <3.0 mmol/L)	2 (0.1%)	2 (100%)	
Patient on an ACEI or ARB is prescribed a potassium supplement	2 (0.1%)	1 (50.0%)	
Patient on a thiazide diuretic has hypercalcaemia (i.e., corrected serum calcium >2.65 mmol/L)	1 (0.1%)	1 (100%)	
Cardiovascular disease events	**43**[a]	**21 (48.8%)**	**43 (2.9%)**
Patient with AF and CHA_2DS_2-VASc score ≥3 is not prescribed an oral anticoagulant	31 (2.1%)	17 (54.8%)	
Patients aged ≥65 years with dementia is prescribed an antipsychotic	12 (0.8%)	4 (33.3%)	
Low blood pressure	**40**[a]	**36 (90.0%)**	**39 (2.7%)**
Patient with dementia is on two or more blood pressure-lowering drugs and blood pressure is <130/75 mmHg	21 (1.4%)	18 (85.7%)	
Patient without heart failure is on blood pressure-lowering treatment and blood pressure is <110/65 mmHg	19 (1.3%)	18 (94.7%)	
Other	**41**[a]	**36 (87.8%)**	**36 (2.4%)**
Patient aged ≥65 years is prescribed metoclopramide on repeat	18 (1.2%)	15 (83.3%)	
Patient with eGFR <30 mL/min/1.73m^2 is prescribed metformin	9 (0.6%)	9 (100%)	
Patient on lithium is prescribed an NSAID	4 (0.3%)	4 (100%)	
Patient is prescribed an opioid at an average daily dose equivalent to >180 mg morphine/day in previous 6 months	3 (0.2%)	2 (66.7%)	
Patient on methotrexate is not prescribed folic acid	3 (0.2%)	3 (100%)	
Patient on methotrexate is on two different strengths of methotrexate tablets	2 (0.1%)	2 (100%)	
Patient with asthma requiring treatment is prescribed a non-selective beta-blocker (oral or topical)	2 (0.1%)	1 (50.0%)	
Hypoglycaemia	**34**[a]	**30 (88.2%)**	**34 (2.3%)**
Patient aged ≥75 years without dementia is on intensive hypoglycaemic therapy and HbA1c is <53 mmol/mol (7.0%)	14 (1.0%)	11 (78.6%)	
Patient aged ≥65 years without dementia is on intensive hypoglycaemic therapy and HbA1c is <48 mmol/mol (<6.5%)	14 (1.0%)	13 (92.9%)	
Patient with dementia is on intensive hypoglycaemic therapy and glycaemic control is <53 mmol/mol (7.0%)	4 (0.3%)	4 (100%)	
Patient is prescribed insulin without being prescribed glucose test strips	2 (0.1%)	2 (100%)	

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin-II receptor blocker; eGFR: estimated glomerular filtration rate; HbA1c: glycosylated haemoglobin type A1c; NSAID: non-steroidal anti-inflammatory drug, SSRI: selective serotonin reuptake inhibitor.
[a]A percentage figure is not provided as it is not a percentage of 1,471 patients, as patients may have had more than 1 polypharmacy indicator in that particular category.

pharmacist time comprised a mean of 61.6 min (SD 16.2) for review preparation, 36.5 min (SD 11.0) to conduct the person-centred review, and 59.1 min (SD 29.7) for follow-up.

3.1 | Polypharmacy indicators

Of the 69 polypharmacy indicators, 55 (79.7%) were identified. Overall, 1056 indicator occurrences were identified (Table 3), representing a mean of 0.72/patient, with ≥1 indicator identified in 47.1% of patients (693/1471). The most common occurrences were bleeding-related ($n = 312$, 29.5%), falls-related ($n = 241$, 22.8%), and renal-related ($n = 139$, 13.2%). The overall resolution rate was 70.7%; it was highest for electrolyte abnormality (90.7%) and renal categories (90.6%) and lowest for the falls-risk category (34%). Fourteen indicators were not identified and are listed in Appendix 2.

3.2 | PC-MAI

The pre-review and post-review PC-MAI was calculated for 194 patients (13.2% of patients). The mean pre-review PC-MAI per

patient was 27.1 (SD 14.8; range 4–99) and post-review PC-MAI was 9.8 (SD 9.9; range 0–68). The mean PC-MAI reduction was 17.3 (SD 10.7, range 0–54, 95% CI 15.8–18.8), a statistically significant change ($P < .0001$). A post-review reduction was achieved for 99% of patients ($n = 192$).

The maximum pre-review PC-MAI and post-review PC-MAI attributed to a single medicine was 13 and 11 respectively. The PC-MAI was calculated for 2624 pre-review medicines (mean: 2.0/medicine, SD 2.7) and 2287 post-review medicines (mean: 0.8/medicine, SD 1.7), corresponding to a mean reduction of 1.2/medicine (95% CI 1.0–1.3), $P < .0001$. Table 4 shows the 25 medicines classes (ATC level 3 coded) with the highest total pre-review PC-MAI scores. The full list of PC-MAI-scored medicines classes are tabulated in Appendix 3.

3.3 | Patient-reported outcome measures

Pre-review and post-review PROMs were collected from 179 patients. Figure 1 shows patients' reported improvements in understanding, experience of side effects, impact of medicines on daily activities, and adherence. All were significantly different post review ($P < .05$) except one adherence measure ("*Did you ever take more medicines than prescribed or for a different purpose than prescribed?*"; $P = .13$).

Figure 2 shows the reductions in patient-reported side effects from before the review to after, all of which were significantly lower post review ($P < .05$) except for headache ($P = .07$).

When asked more specifically about the medicines review's impact, patients agreed to varying degrees that it helped with medicines understanding (87.7%; $n = 157/179$), side effects (63.1%; $n = 113/179$), adherence (36.9%; $n = 65/176$), and medicines' impact on daily activities (30.5%; $n = 51/167$). Most reported improvement in ≥1 domain (93.9%), with 29.6% reporting improvement in one, 23.5% in two, 25.7% in three, and 15.1% in all four domains.

Patients showed improvements in all EQ-5D-3L dimensions, with fewer reporting "*some*" or "*major*" problems post review (Table 5). Among those reporting some or major problems pre review, the highest proportions of improvement were with problems performing usual activities and anxiety/depression (33.3% and 22.9%, respectively).

TABLE 4 Top 25 medicine classes (ATC level 3) ordered by total associated pre-review PC-MAI scores ($n = 194$; 13.2% of reviews).

		Total PC-MAI score			Number of medicines			Mean PC-MAI score		
Medicine class	ATC level 3	Pre	Post	Pre minus post	Pre	Post	Pre minus post	Pre	Post	Pre minus post
Drugs for peptic ulcer and gastro-oesophageal reflux disease	A02B	312	101	211	162	155	7	1.93	0.65	1.27
Antithrombotic agents	B01A	307	65	242	172	143	29	1.78	0.45	1.33
Non-steroidal anti-inflammatories[a]	M01A	291	55	236	49	15	34	5.94	3.67	2.27
Antidepressants	N06A	287	143	144	85	74	11	3.38	1.93	1.44
Blood glucose lowering drugs, excluding insulins	A10B	242	58	184	128	115	13	1.89	0.50	1.39
Hypnotics and sedatives	N05C	223	177	46	42	38	4	5.31	4.66	0.65
Opioids	N02A	204	115	89	53	46	7	3.85	2.5	1.35
Urologicals	G04B	174	52	122	46	26	20	3.78	2	1.78
Paracetamol[a]	N02B	172	92	80	120	120	0	1.43	0.77	0.67
Lipid modifying agents	C10A	167	63	104	160	158	2	1.04	0.4	0.65
Vitamin B12 and folic acid	B03B	159	35	124	42	21	21	3.79	1.67	2.12
Beta blocking agents	C07A	141	54	87	107	96	11	1.32	0.56	0.76
High-ceiling Diuretics	C03C	135	44	91	50	37	13	2.7	1.19	1.51
Inhalant adrenergics	R03A	124	51	73	111	116	-5	1.12	0.44	0.68
Antipsychotics	N05A	119	43	76	19	12	7	6.26	3.58	2.68
Drugs for constipation	A06A	106	26	80	63	56	7	1.68	0.46	1.22
Systemic antihistamines	R06A	102	34	68	21	17	4	4.86	2	2.86
Inhaled drugs for obstructive airway diseases	R03B	99	31	68	58	52	6	1.71	0.6	1.11
Thiazides	C03A	84	6	78	20	7	13	4.2	0.86	3.34
Iron preparations	B03A	83	10	73	30	18	12	2.77	0.56	2.21
Drugs used in benign prostatic hypertrophy	G04C	80	22	58	41	34	7	1.95	0.65	1.3
Dihydropyridine calcium channel blockers[a]	C08C	79	32	47	76	72	4	1.04	0.44	0.6
Vitamin D and analogues[a]	A11C	71	5	66	87	86	1	0.82	0.06	0.76
ACE Inhibitors, plain	C09A	71	26	45	69	65	4	1.03	0.4	0.63
Anxiolytics	N05B	71	52	19	15	13	2	4.73	4	0.73

[a]More specific title provided where all identified medicines relate to a more specific group of medicines or a single medicine.

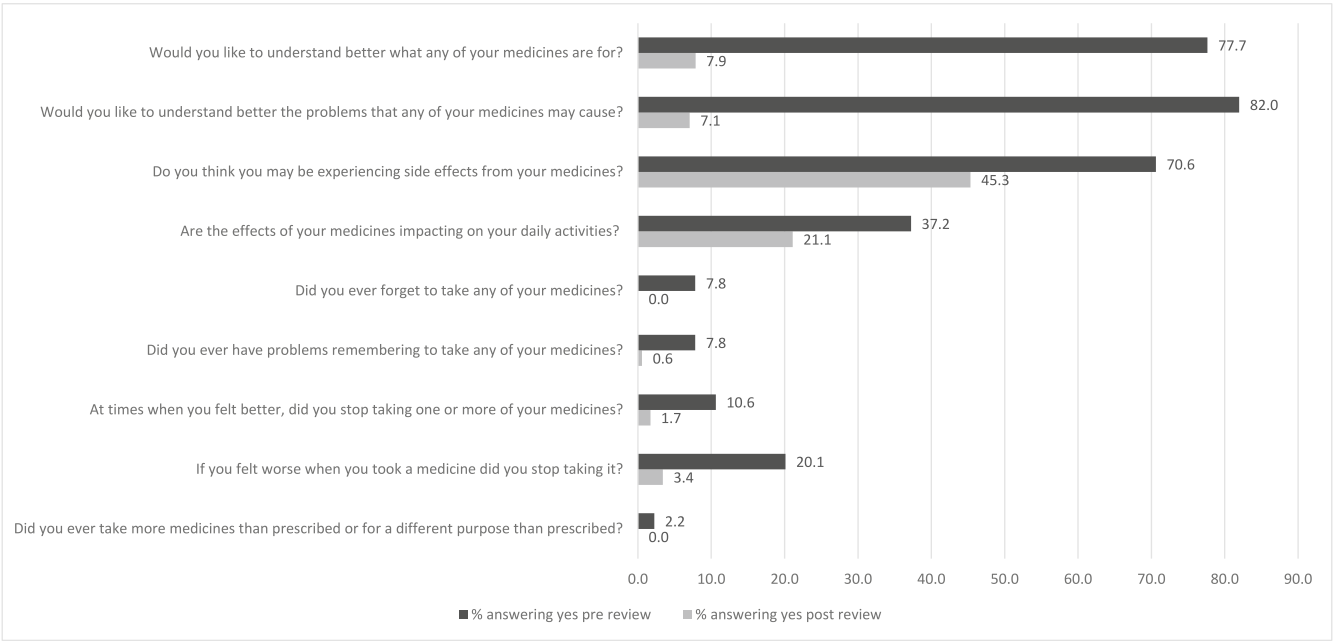

FIGURE 1 Patient-reported medicines understanding, side effects experience, medicines impact on daily activities and adherence pre and post review.

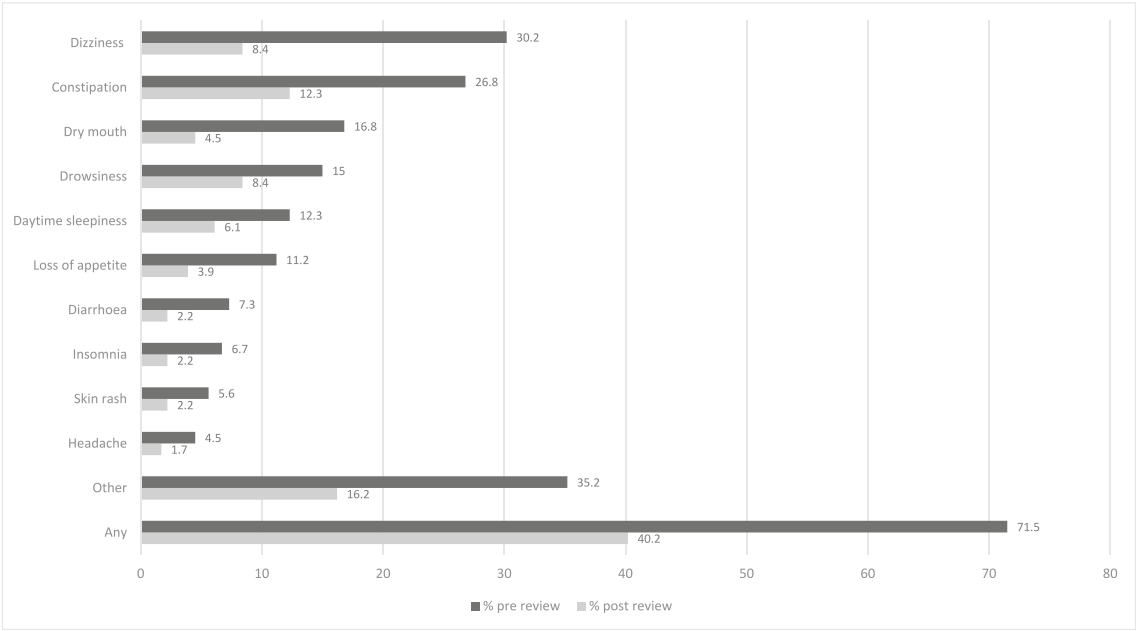

FIGURE 2 Patients indicating any side effect(s) they were experiencing pre and post review.

The mean EQ-5D-3L index value for the 37 patients with a complete set at both time points was 0.871 (SD 0.123) pre review and 0.885 (SD 0.115) post review (mean difference 0.014; $P = .14$).

4 | DISCUSSION

This study has shown that general practice pharmacist-provided person-centred medicines reviews can significantly improve medicines appropriateness in patients with hyperpolypharmacy and/or at high risk of medicines-related harm. Polypharmacy indicators were identified in nearly half of patients (47.1%), with the majority resolved within the follow-up period (70.7%). The mean baseline PC-MAI score per patient was 27.0 ($n = 194$), reflecting high levels of inappropriate polypharmacy. The mean PC-MAI reduction of 17.3 per patient, a 64.4% reduction, demonstrated that reviews achieved considerable improvements in medicines appropriateness. Most patients (93.9%) reported improvement in ≥1 PROM domain, and

TABLE 5 EQ-5D-3L dimensions analysis for patients with pre-review and post-review responses.

	Mobility		Self-care		Usual activities		Pain/ discomfort		Anxiety/ depression	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
No problems (Level 1)	22	23	29	30	58	70	22	24	55	63
Some problems (Level 2)	16	15	10	9	28	23	13	17	32	26
Major problems (Level 3)	1	1	1	1	8	1	6	0	3	1
Total responses	**39**	**39**	**40**	**40**	**94**	**94**	**41**	**41**	**90**	**90**
Reporting some/major problems	17	16	11	10	36	24	19	17	35	27
Change in the number reporting some/major problems (*n*, %)		−1 (−5.9%)		−1 (−9.1%)		−12 (−33.3%)		−2 (−10.5%)		−8 (−22.9%)
Health status change										
Worse	–	2 (5.1%)	–	0 (0%)	–	0 (0%)	–	0 (0%)	–	3 (3.3%)
Better	–	3 (7.7%)	–	1 (2.5%)	–	16 (17%)	–	7 (17.1%)	–	9 (10%)
Same	–	34 (87.2%)	–	39 (97.5%)	–	78 (83%)	v	34 (82.9%)	–	78 (86.7%)

15.1% in all four domains. The greatest PROM improvements were for patients' understanding (87.7%) and experience of side effects (63.1%).

It is challenging to compare this study to others. A recent systematic review assessing the effectiveness of pharmacist integration into general practices showed great inter-study variety: patients' mean number of baseline medicines varied from 6 to 14 and pharmacist integration duration ranged from 3 to 24 months.[21] Furthermore, another systematic review demonstrated substantial heterogeneity between the populations, outcome measures, and interventions to address inappropriate polypharmacy.[35] Whilst the present study was planned as a service evaluation from the outset, it would be prudent for future similar studies to consider using core outcome sets to aid consistency in outcome measures and better inter-study comparison.[21]

This study examined the impact of general practice pharmacists providing comprehensive medicines reviews incorporating SDM to those with hyperpolypharmacy and/or at high risk of medicines-related harm. SDM has been proposed as an important component in addressing inappropriate polypharmacy.[10] The relationships GPs have established with their patients, alongside access to their full medical and social history, supports the SDM necessary to facilitate such reviews.[36–38] However, GP-reported deprescribing barriers include insufficient training and time, a reluctance to discontinue medicines that specialists initiated, and difficulties communicating with hospital specialists.[26,39–42] The average GP consultation time in Ireland has been found to be 13.7 min,[43] and shorter consultation times are associated with more prescriptions.[44] Introducing iSIMPATHY pharmacists into general practice overcame many of these barriers, adding capacity to allow comprehensive medicines reviews and follow-up. The total mean pharmacist time ($n = 1471$ reviews) for review preparation, conduct and follow-up was 157.2 min. This included a mean time of 36.5 min to conduct the person-centred review, which is similar to the minimum required time of 30 min for appointments for structured medication review in England.[45] There may be potential to reduce the mean time to prepare for reviews (61.6 min in this study) if information access is improved with future eHealth developments. The mean follow-up time of 59.1 min reflects the complexity of interventions and the complexity of communication and follow-up with the GP.

In Northern Ireland and Scotland, iSIMPATHY pharmacists worked as independent prescribers in hospital and mixed settings – where the mean pharmacist times per review were 46.9 min (95% CI 43.8–50.1) and 94.8 min (95% CI 90.3–99.2), respectively.[28] The mean pharmacist time per review for the full iSIMPATHY cohort in Ireland was 127.7 min (95% CI 124.9–130.5); it may be the case that having pharmacists as independent prescribers in Ireland could help reduce the total time per review. Nevertheless, although time-consuming, the economic analysis of these reviews demonstrated substantial net cost savings in this high-risk patient cohort.[27] A systematic review found that medicines optimisation interventions – largely involving a pharmacist, doctor, and patient – may provide benefits that outweigh their implementation costs.[46] A qualitative study found that UK general practices tended to prioritise efficient medicines reviews over thorough medicines reviews, meaning that patients were rarely involved and medicines were rarely stopped or reduced.[47] Therefore, whilst investing greater time in reviews adds to the intervention cost, this may be needed to achieve positive outcomes for patients (e.g. having inappropriate medicines discontinued).

Explicit criteria can be used to identify medicines considered "potentially" inappropriate in certain circumstances, but clinical judgement and individualised patient circumstances should also be considered.[48] The MAI and PC-MAI are implicit tools, which are less objective and more time-consuming to apply, and do not detect potential prescribing omissions.[49] Using an implicit and an explicit tool when performing a comprehensive medicines review is recommended as best practice.[50] Three outcome measures were used in this study: an explicit measure (polypharmacy indicators), an implicit measure (PC-MAI), and a measure of patients' experiences (PROMs) – all of which are discussed in the following sections.

4.1 | Polypharmacy indicators

Polypharmacy indicators are associated with an increased likelihood of a serious adverse outcome due to medicines-related harm,[28] and 70.7% of those identified were resolved by these medicines reviews. Bleeding risk indicators were the most prevalent, 76.9% of which were resolved. This is important because 33% of hospital admissions related to adverse drug reactions (ADRs) in Ireland are caused by bleeding.[51] Resolution rates of ≥77% were achieved for all indicator categories other than those relating to cardiovascular disease events (49%) and falls (34%). Falls-risk indicators were the second most prevalent, and falls are another common cause of ADR-related hospital admission.[52] The need for specialist referral and/or tapering of falls risk increasing medicines may have meant that whilst risk was reduced, indicator resolution was not achieved at follow-up.

Explicit criteria developers have acknowledged that some criteria are of greater clinical significance than others.[52] Polypharmacy indicators were developed as high-risk case finding indicators. Resolving all polypharmacy indicators is not appropriate due to clinical and patient factors. Some indicators less suitable for use as outcome measures may have had lower resolution rates; for example, "*Patient with eGFR <30 ml/min/1.73m^2 is prescribed a factor Xa inhibitor*" had a 0% resolution rate. Factor Xa inhibitors are cautioned but not contraindicated at this level of renal function; therefore, this indicator can be appropriately addressed by closer patient monitoring, but without indicator resolution. Focusing on fewer high-risk criteria has been proposed as an efficient way to reduce medicines-related harm.[12]

4.2 | PC-MAI

The MAI has been found to predict ADR risk[53] and is negatively correlated with QoL, as measured by the EQ-5D index.[54,55] The PC-MAI yields lower maximum scores than the MAI due to fewer criteria, yet a mean baseline PC-MAI score of 27 was found in this study, which is higher than the mean baseline MAIs reported in the literature.[56] In the OPTICA study, for example, the median total MAI score was 12 at baseline for older adults with multimorbidity and polypharmacy in primary care (median number of long-term medications: 7).[57] One reason for the high PC-MAI score in this study may be because 88.4% of our included patients had hyperpolypharmacy, and the number of medicines has been shown to be the greatest contributor to higher MAI scores.[58,59] Additionally, patient involvement in medicines reviews may yield higher MAI scores, as it is more comprehensive than reviewing medical records alone in establishing inappropriateness.[60] The mean baseline PC-MAI for the overall iSIMPATHY cohort in Ireland was 25.4 (SD 15.2), which was more than double compared to patients in Scotland (12.5; SD 11.3) and Northern Ireland (12.4; SD 9.5).[28] Addressing this higher level of inappropriateness may have contributed to reviews in Ireland taking longer than in Scotland and Northern Ireland.[28] This may indicate the need for general practice pharmacists in countries where they do not yet exist, as they yield positive impacts in optimising medicines,[24] and these would be welcomed by both GPs and pharmacists.[61–63]

Almost all patients had a PC-MAI score reduction post review (99%), with the mean decrease of 17.3 being higher than generally reported.[56] MAI reduction has been found to be proportionate to the baseline MAI and number of medicines.[58,59] Greater reductions are achieved through more intensive healthcare professional collaboration,[64] and more sustained interventions lead to incremental MAI improvements over time.[59] A similar mean MAI reduction of 17 was attributed to adding a pharmacist to a hospital geriatric team; that intervention also involved direct patient interaction and patients in the intervention group had a high baseline summated MAI (mean 24.1; SD 17.0), which may explain why it achieved a similar reduction.[65] Whilst QoL has been shown to be significantly lower in patients with MAI scores above 36,[54] a clinically relevant threshold change in MAI score has yet to be established for patient-relevant outcomes.[58] Therefore, this represents a gap for future research.

Due to their prescription frequency, antithrombotics and drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD) were associated with high total pre-review PC-MAI scores (Table 4). Other medicines classes were found to have a much higher level of inappropriateness per individual prescription (i.e. higher mean PC-MAI scores), including non-steroidal anti-inflammatory drugs (NSAIDs), hypnotics and sedatives, antipsychotics, antihistamines, and anxiolytics. Medicines reviews resulted in large decreases in total PC-MAI scores for NSAIDs, but discontinuation of hypnotics, sedatives, and anxiolytics proved more challenging. Although SDM has been successfully used to achieve benzodiazepine withdrawal,[66] slow tapering is usually necessary, and discontinuation may not have been achieved at follow-up. In patients with PC-MAI scores calculated, NSAIDs were discontinued in almost 70% prescribed them, while 80% prescribed a medication for peptic ulcer and GORD remained on at least one; however, the PC-MAI score for these latter medicines was still decreased by 1.27 per prescription. This demonstrates that PC-MAI score reductions can be achieved by dose decreases or switches to more appropriate agents within some drug classes, and not solely by discontinuation.

4.3 | PROMs

This study's reviews yielded patient-reported benefits across all PROM domains, with the highest improvements in medicines understanding (87.7%) and experience of side effects (63.1%) post review.

In a similar intervention study with similar medicines changes, 91% of patients strongly agreed that the pharmacist-provided information was beneficial.[21]

The standardised EQ-5D-3L responses showed greatest resolution of problems engaging in usual activities and with anxiety/depression. No change was identified in overall QoL based on index score change. Utility of QoL measures in detecting meaningful change in studies of medicines reviews and deprescribing has been questioned.[67] Previous research has found a decline in QoL scores from baseline to follow-up in control groups with no change in intervention groups,[21,68] so maintaining health-related QoL may be a positive outcome.

4.4 | Strengths and limitations

Given the large dataset including 1471 patient reviews by four pharmacists working across 10 general practices, our findings are likely generalisable to similar settings; this is further supported by a single-practice study using the "7 steps" approach reporting a similarly positive impact.[69]

Some polypharmacy indicators were utilised as "case-finding" criteria (i.e., they were searched for in practice software to identify patients), meaning their reported prevalence may not reflect their true prevalence in a typical sample of community-dwelling patients who would meet other eligibility criteria. This non-systematic searching also means that some indicators present may not have been identified.

The PROMs questionnaire did not use independently validated measures for medicines understanding, ADRs, activities of daily living, or adherence; however, ideal measures of these patient-reported parameters have not yet been established.[32] Questionnaire changes during the project resulted in a larger number of patients being asked about their ability to engage in their usual activities and levels of anxiety/depression than the remaining three EQ-5D-3L domains. The small sample size with a full index score limits the power and generalisability of the EQ-5D-3L analysis.

Standardised guidance and training on PC-MAI calculation were provided alongside quality assurance (including inter-rater reliability evaluation and peer review).[28] Acceptable inter-rater reliability for PC-MAI scores was reached among iSIMPATHY pharmacists (Gwet's agreement coefficient 0.78),[28] and good MAI inter-rater reliability is well established.[58,64,70]

PC-MAI score calculation and PROMs collection (primarily by telephoning patients) by the reviewing pharmacist may have introduced a patient selection and social desirability bias; therefore, PROM improvements may have been different with independent data collectors. Data entry support was available at an earlier project stage, facilitating a larger proportion of PC-MAI and PROMs data collection then. While patients exhibiting signs of inappropriate polypharmacy may have been prioritised initially, baseline demographics of patients with PC-MAI and PROMs data were similar to the study population when compared. It is unclear if the extent of these PC-MAI and PROM improvements would be achievable in all patients meeting inclusion criteria and further research to establish the best ways of prioritising patients for review may be beneficial.

Follow-up and data collection was completed within 2–6 weeks usually, but up to 12 weeks post review. Other studies have found that 12%, 15.9% and 17.3% of discontinued medications had been restarted at 3, 6, and 12 months post intervention, respectively.[71] Due to the lack of longer-term follow-up (and inconsistent follow-up periods between patients), this means we cannot quantify whether agreed changes were reversed or further actioning of recommendations took place following the data collection point.

5 | CONCLUSION

This study has demonstrated that the introduction of pharmacists to multiple general practices to deliver comprehensive person-centred medicines reviews incorporating SDM for patients with hyperpolypharmacy and/or at high risk of medicines-related harm was effective in improving medicines appropriateness, reducing patient-reported side effects and decreasing the potential for medicines-related harm. Patients reported improved understanding, adherence, and ability to engage in daily activities alongside significantly improved medicines appropriateness. Given the substantial benefits to patients, such comprehensive person-centred medicines reviews should be considered for implementation in general practice settings more widely.

AUTHOR CONTRIBUTIONS

Conceptualisation: CKinahan, CKirke, LOH, KM, LS, COM, EC, SB, KD. Methodology: CKinahan, CKirke, LOH, FM, KM, LS, EC, SB, KD. Formal analysis: CKinahan, CKirke, LOH, FM, KM, COM, KD. Investigation: CKinahan, CKirke, LOH, EC. Data Curation: CKinahan, CKirke, LOH, KM, COM, EC, KD. Writing—original draft: CKinahan, CKirke, LOH, FM, KM, LS, EC, KD. Writing—review and editing: CKinahan, CKirke, LOH, FM, KM, LS, EC, SB, KD. Visualisation: CKinahan, CKirke, LOH, FM, KM, LS, EC, KD. Supervision: CKirke, KM, LS, SB, KD. Project administration: CKinahan, CKirke, KD. Funding acquisition: CKirke, FM, KM, LS, SB, KD.

The iSIMPATHY project Lead in Ireland was Ciara Kirke, whilst the primary author was the lead researcher on this study.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest that are pertinent to this study.

DATA AVAILABILITY STATEMENT

The data associated with this study will not be made publicly available.

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REFERENCES

1. Chowdhury SR, Chandra Das D, Sunna TC, Beyene J, Hossain A. Global and regional prevalence of multimorbidity in the adult population in community settings: a systematic review and meta-analysis. *EClinicalMedicine*. 2023;57:101860. doi:10.1016/j.eclinm.2023.101860
2. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract*. 2011;28(5):516-523. doi:10.1093/fampra/cmr013
3. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17(1):230. doi:10.1186/s12877-017-0621-2
4. Bennie M, Santa-Ana-Tellez Y, Galistiani GF, et al. The prevalence of polypharmacy in older Europeans: a multi-national database study of general practitioner prescribing. *Br J Clin Pharmacol*. 2024;90(9):2124-2136. doi:10.1111/bcp.16113
5. Moriarty F, Hardy C, Bennett K, Smith SM, Fahey T. Trends and interaction of polypharmacy and potentially inappropriate prescribing in primary care over 15 years in Ireland: a repeated cross-sectional study. *BMJ Open*. 2015;5(9):e008656. doi:10.1136/bmjopen-2015-008656
6. Wang X, Liu K, Shirai K, et al. Prevalence and trends of polypharmacy in U.S. adults, 1999-2018. *Glob Health Res Policy*. 2023;8(1):25. doi:10.1186/s41256-023-00311-4
7. Scottish Government Polypharmacy Model of Care Group. *Polypharmacy guidance, realistic prescribing*. 3rd ed. Scottish Government; 2018.
8. Krska J, Morecroft CW, Poole H, Rowe PH. Issues potentially affecting quality of life arising from long-term medicines use: a qualitative study. *Int J Clin Pharmacol*. 2013;35(6):1161-1169. doi:10.1007/s11096-013-9841-5
9. Sav A, King MA, Whitty JA, et al. Burden of treatment for chronic illness: a concept analysis and review of the literature. *Health Expect*. 2015;18(3):312-324. doi:10.1111/hex.12046
10. Eriksen CU, Kyriakidis S, Christensen LD, et al. Medication-related experiences of patients with polypharmacy: a systematic review of qualitative studies. *BMJ Open*. 2020;10(9):e036158. doi:10.1136/bmjopen-2019-036158
11. Xu Z, Liang X, Zhu Y, et al. Factors associated with potentially inappropriate prescriptions and barriers to medicines optimisation among older adults in primary care settings: a systematic review. *Fam Med Commun Health*. 2021;9(4):e001325. doi:10.1136/fmch-2021-001325
12. Moriarty F, Bennett K, Cahir C, Kenny RA, Fahey T. Potentially inappropriate prescribing according to STOPP and START and adverse outcomes in community-dwelling older people: a prospective cohort study. *Br J Clin Pharmacol*. 2016;82(3):849-857. doi:10.1111/bcp.12995
13. Pérez T, Moriarty F, Wallace E, McDowell R, Redmond P, Fahey T. Prevalence of potentially inappropriate prescribing in older people in primary care and its association with hospital admission: longitudinal study. *BMJ*. 2018;363:k4524. doi:10.1136/bmj.k4524
14. National Institute for Health and Care Excellence (NICE). Shared Decision Making, 2021. Accessed June 22, 2024. https://www.nice.org.uk/guidance/ng197
15. Eton DT, Elraiyah TA, Yost KJ, et al. A systematic review of patient-reported measures of burden of treatment in three chronic diseases. *Patient Relat Outcome Meas*. 2013;4:7-20. doi:10.2147/PROM.S44694
16. Katusiime B, Corlett S, Reeve J, Krska J. Measuring medicine-related experiences from the patient perspective: a systematic review. *Patient Relat Outcome Meas*. 2016;7:157-171. doi:10.2147/PROM.S102198
17. McCahon D, Duncan P, Payne R, Horwood J. Patient perceptions and experiences of medication review: qualitative study in general practice. *BMC Prim Care*. 2022;23(1):293. doi:10.1186/s12875-022-01903-8
18. Beuscart JB, Knol W, Cullinan S, et al. International core outcome set for clinical trials of medication review in multi-morbid older patients with polypharmacy. *BMC Med*. 2018;16(1):21. doi:10.1186/s12916-018-1007-9
19. Stewart D, Whittlesea C, Dhital R, Newbould L, McCambridge J. Community pharmacist led medication reviews in the UK: a scoping review of the medicines use review and the new medicine service literatures. *Res Social Adm Pharm*. 2020;16(2):111-122. doi:10.1016/j.sapharm.2019.04.010
20. Tan ECK, Stewart K, Elliott RA, George J. Pharmacist services provided in general practice clinics: a systematic review and meta-analysis. *Res Social Adm Pharm*. 2014;10(4):608-622. doi:10.1016/j.sapharm.2013.08.006
21. Croke A, Cardwell K, Clyne B, Moriarty F, McCullagh L, Smith SM. The effectiveness and cost of integrating pharmacists within general practice to optimize prescribing and health outcomes in primary care patients with polypharmacy: a systematic review. *BMC Prim Care*. 2023;24(1):41. doi:10.1186/s12875-022-01952-z
22. Hasan Ibrahim AS, Barry HE, Hughes CM. A systematic review of general practice-based pharmacists' services to optimize medicines management in older people with multimorbidity and polypharmacy. *Fam Pract*. 2021;38(4):509-523. doi:10.1093/fampra/cmaa146
23. Joseph RM, Knaggs RD, Coupland CAC, et al. Frequency and impact of medication reviews for people aged 65 years or above in UK primary care: an observational study using electronic health records. *BMC Geriatr*. 2023;23(1):435. doi:10.1186/s12877-023-04143-2
24. Syafhan NF, Al Azzam S, Williams SD, et al. General practitioner practice-based pharmacist input to medicines optimisation in the UK: pragmatic, multicenter, randomised, controlled trial. *J Pharm Policy Pract*. 2021;14(1):4. doi:10.1186/s40545-020-00279-3
25. Clyne B, Smith SM, Hughes CM, et al. Effectiveness of a multifaceted intervention for potentially inappropriate prescribing in older patients in primary care: a cluster-randomized controlled trial (OPTI-SCRIPT study). *Ann Fam Med*. 2015;13(6):545-553. doi:10.1370/afm.1838

26. Cardwell K, Smith SM, Clyne B, et al. Evaluation of the general practice pharmacist (GPP) intervention to optimise prescribing in Irish primary care: a non-randomised pilot study. *BMJ Open*. 2020;10(6):e035087. doi:10.1136/bmjopen-2019-035087
27. O'Mahony C, Dalton K, O'Hagan L, et al. Economic cost-benefit analysis of person-centred medicines reviews by general practice pharmacists. *Int J Clin Pharm*. 2024;46(4):957-965. doi:10.1007/s11096-024-01732-y
28. Mair A, Kirke C, Scott M, et al. iSIMPATHY evaluation report, Edinburgh, iSIMPATHY consortium; 2023.
29. Health Service Executive. HSE National Framework for Governance, Management and Support of Health Research. Accessed June 22, 2024. https://hseresearch.ie/wp-content/uploads/2021/09/HSE-Framework-for-the-Governance-Web-Optimised.pdf
30. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg*. 2014;12(12):1495-1499. doi:10.1016/j.ijsu.2014.07.013
31. Scottish Government. *Polypharmacy indicators* 2017. Accessed June 22, 2024. https://www.therapeutics.scot.nhs.uk/wp-content/uploads/2017/10/Polypharmacy-Indicators.pdf
32. Kotronoulas G, Cooper M, Johnston B. Core patient-reported outcomes (PROs) and PRO measures (PROMs) for polypharmacy medicines reviews: a sequential mixed-methods study. *Patient Prefer Adherence*. 2019;13:2071-2087. doi:10.2147/PPA.S236122
33. EuroQol Research Foundation. EQ-5D-3L User Guide, 2018. Available from: https://euroqol.org/publications/user-guides
34. Hobbins A, Barry L, Kelleher D, et al. Utility values for health states in Ireland: a value set for the EQ-5D-5L. *Pharmacoeconomics*. 2018;36(11):1345-1353. doi:10.1007/s40273-018-0690-x
35. Cole JA, Gonçalves-Bradley DC, Alqahtani M, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev*. 2023;10(10):CD008165. doi:10.1002/14651858.CD008165.pub5
36. Jansen J, Naganathan V, Carter SM, et al. Too much medicine in older people? Deprescribing through shared decision making. *BMJ*. 2016;353:i2893. doi:10.1136/bmj.i2893
37. Weir K, Nickel B, Naganathan V, et al. Decision-making preferences and deprescribing: perspectives of older adults and companions about their medicines. *J Gerontol B Psychol Sci Soc Sci*. 2018;73(7):e98-e107. doi:10.1093/geronb/gbx138
38. Reeve E, Low LF, Hilmer SN. Beliefs and attitudes of older adults and carers about deprescribing of medications: a qualitative focus group study. *Br J Gen Pract*. 2016;66(649):e552-e560. doi:10.3399/bjgp16X685669
39. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. *BMJ Open*. 2014;4(12):e006544. doi:10.1136/bmjopen-2014-006544
40. Cullinan S, Fleming A, O'Mahony D, et al. Doctors' perspectives on the barriers to appropriate prescribing in older hospitalized patients: a qualitative study. *Br J Clin Pharmacol*. 2015;79(5):860-869. doi:10.1111/bcp.12555
41. Gillespie RJ, Harrison L, Mullan J. Deprescribing medications for older adults in the primary care context: a mixed studies review. *Health Sci Rep*. 2018;1(7):e45. doi:10.1002/hsr2.45
42. Palagyi A, Keay L, Harper J, Potter J, Lindley RI. Barricades and brickwalls—a qualitative study exploring perceptions of medication use and deprescribing in long-term care. *BMC Geriatr*. 2016;16:15. doi:10.1186/s12877-016-0181-x
43. Collins C, Homeniuk R. How many general practice consultations occur in Ireland annually? Cross-sectional data from a survey of general practices. *BMC Fam Pract*. 2021;22(1):40. doi:10.1186/s12875-021-01377-0
44. Wilson A, Childs S. The relationship between consultation length, process and outcomes in general practice: a systematic review. *Br J Gen Pract*. 2002;52(485):1012-1020.
45. NHS England. Network Contract Directed Enhanced Service: Structured medication reviews and medicines optimisation: guidance. 2021. Accessed November 16, 2024. https://www.england.nhs.uk/wp-content/uploads/2021/03/B0431-network-contract-des-smr-and-mo-guidance-21-22.pdf
46. Laberge M, Sirois C, Lunghi C, et al. Economic evaluations of interventions to optimize medication use in older adults with polypharmacy and multimorbidity: a systematic review. *Clin Interv Aging*. 2021;16:767-779. doi:10.2147/CIA.S304074
47. Duncan P, Cabral C, McCahon D, Guthrie B, Ridd MJ. Efficiency versus thoroughness in medication review: a qualitative interview study in UK primary care. *Br J Gen Pract*. 2019;69(680):e190-e198. doi:10.3399/bjgp19X701321
48. Steinman MA, Fick DM. Using wisely: a reminder on the proper use of the American Geriatrics Society Beers Criteria®. *J Am Geriatr Soc*. 2019;67(4):644-646. doi:10.1111/jgs.15766
49. Muth C, Harder S, Uhlmann L, et al. Pilot study to test the feasibility of a trial design and complex intervention on PRIoritising MUltimedication in Multimorbidity in general practices (PRIMUMpilot). *BMJ Open*. 2016;6(7):e011613. doi:10.1136/bmjopen-2016-011613
50. Lopez-Rodriguez JA, Rogero-Blanco E, Aza-Pascual-Salcedo M, et al. Potentially inappropriate prescriptions according to explicit and implicit criteria in patients with multimorbidity and polypharmacy. MULTIPAP: A cross-sectional study. *PLoS ONE*. 2020;15(8):e0237186. doi:10.1371/journal.pone.0237186
51. Cahir C, Curran C, Walsh C, et al. Adverse drug reactions in an ageing PopulaTion (ADAPT) study: prevalence and risk factors associated with adverse drug reaction-related hospital admissions in older patients. *Front Pharmacol*. 2022;13:1029067. doi:10.3389/fphar.2022.1029067
52. Thevelin S, Mounaouar LE, Marien S, Boland B, Henrard S, Dalleur O. Potentially inappropriate prescribing and related hospital admissions in geriatric patients: a comparative analysis between the STOPP and START criteria versions 1 and 2. *Drugs Aging*. 2019;36(5):453-459. doi:10.1007/s40266-018-00635-8
53. Lund BC, Carnahan RM, Egge JA, Chrischilles EA, Kaboli PJ. Inappropriate prescribing predicts adverse drug events in older adults. *Ann Pharmacother*. 2010;44(6):957-963. doi:10.1345/aph.1m657
54. Olsson IN, Runnamo R, Engfeldt P. Medication quality and quality of life in the elderly, a cohort study. *Health Qual Life Outcomes*. 2011;9(1):95. doi:10.1186/1477-7525-9-95
55. Müller BS, Uhlmann L, Ihle P, et al. Development and internal validation of prognostic models to predict negative health outcomes in older patients with multimorbidity and polypharmacy in general practice. *BMJ Open*. 2020;10(10):e039747. doi:10.1136/bmjopen-2020-039747
56. Hanlon JT, Schmader KE. The medication appropriateness index at 20: where it started, where it has been, and where it may be going. *Drugs Aging*. 2013;30(11):893-900. doi:10.1007/s40266-013-0118-4
57. Jungo KT, Ansorg AK, Floriani C, et al. Optimising prescribing in older adults with multimorbidity and polypharmacy in primary care (OPTICA): cluster randomised clinical trial. *BMJ*. 2023;381:e074054. doi:10.1136/bmj-2022-074054
58. Krisch L, Mahlknecht A, Bauer U, et al. The challenge to define a relevant change in medication appropriateness index score in older adults—an approach. *Br J Clin Pharmacol*. 2020;86(2):398-399. doi:10.1111/bcp.14167
59. Rose O, Mennemann H, John C, et al. Priority setting and influential factors on acceptance of pharmaceutical recommendations in collaborative medication reviews in an ambulatory care setting—analysis of a cluster randomized controlled trial (WestGem-study). *PLoS ONE*. 2016;11(6):e0156304. doi:10.1371/journal.pone.0156304

60. Riordan DO, Walsh KA, Galvin R, Sinnott C, Kearney PM, Byrne S. The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: a systematic review. *SAGE Open Med*. 2016;4:2050312116652568. doi:10.1177/2050312116652568
61. Hurley E, Walsh E, Foley T, Heinrich CH, Byrne S, Dalton K. General practitioners' perceptions of pharmacists working in general practice: a qualitative interview study. *Fam Pract*. 2023;40(2):377-386. doi:10.1093/fampra/cmac115
62. Hurley E, Foley T, Walsh E, Byrne S, Dalton K. GPs' perceptions of pharmacists working in general practices: a mixed methods survey study. *Eur J Gen Pract*. 2023;29(1):2273841. doi:10.1080/13814788.2023.2273841
63. Morcos P, Dalton K. Exploring pharmacists' perceptions of integrating pharmacists into the general practice setting. *Explor Res Clin Soc Pharm*. 2021;2:100027. doi:10.1016/j.rcsop.2021.100027
64. Romskaug R, Skovlund E, Straand J, et al. Effect of clinical geriatric assessments and collaborative medication reviews by geriatrician and family physician for improving health-related quality of life in home-dwelling older patients receiving polypharmacy: a cluster randomized clinical trial. *JAMA Intern Med*. 2020;180(2):181-189. doi:10.1001/jamainternmed.2019.5096
65. Spinewine A, Swine C, Dhillon S, et al. Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. *J Am Geriatr Soc*. 2007;55(5):658-665. doi:10.1111/j.1532-5415.2007.01132.x
66. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. *JAMA Intern Med*. 2014;174(6):890-898. doi:10.1001/jamainternmed.2014.949
67. Thompson W, Lundby C, Bleik A, et al. Measuring quality of life in deprescribing trials: a scoping review. *Drugs Aging*. 2024;41(5):379-397. doi:10.1007/s40266-024-01113-0
68. Blum MR, Sallevelt BTGM, Spinewine A, et al. Optimizing therapy to prevent avoidable hospital admissions in multimorbid older adults (OPERAM): cluster randomised controlled trial. *BMJ*. 2021;374:n1585. doi:10.1136/bmj.n1585
69. Ciardha Ó, Blake AM, Creane D, Callaghan MÓ, Darker C. Can a practice pharmacist improve prescribing safety and reduce costs in polypharmacy patients? A pilot study of an intervention in an Irish general practice setting. *BMJ Open*. 2022;12(5):e050261. doi:10.1136/bmjopen-2021-050261
70. Spinewine A, Schmader KE, Barber N, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet*. 2007;370(9582):173-184. doi:10.1016/S0140-6736(07)61091-5
71. Campins L, Serra-Prat M, Palomera E, Bolibar I, Martínez MÀ, Gallo P. Reduction of pharmaceutical expenditure by a drug appropriateness intervention in polymedicated elderly subjects in Catalonia (Spain). *Gac Sanit*. 2019;33(2):106-111. doi:10.1016/j.gaceta.2017.09.002

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APPENDIX 1: Patient reported outcome measures assessed

1. EQ-5D-3L questions asked pre and post review

Under each heading below, please tick the ONE box below that best describes your health TODAY.

Usual activities

- I have no problems with performing my usual activities.
- I have some problems with performing my usual activities.
- I am unable to perform my usual activities.

Anxiety/depression

- I am not anxious or depressed.
- I am moderately anxious or depressed.
- I am extremely anxious or depressed.

Mobility*

- I have no problems in walking about.
- I have some problems in walking about.
- I am confined to bed

Self-care*

- I have no problems with self-care.
- I have some problems washing or dressing myself
- I am unable to wash or dress myself.

Pain/discomfort*

- I have no pain or discomfort.
- I have moderate pain or discomfort.
- I have extreme pain or discomfort.

*Added during the project.

2. Questions asked pre and post review

- Would you like to understand better what any of your medicines are for?
- Would you like to understand better the problems that any of your medicines may cause?
- Do you think you may be experiencing side effects from your medicines?
- Are the effects of your medicines impacting on your daily activities?
- Did you ever forget to take any of your medicines?
- Did you ever have problems remembering to take any of your medicines?
- At times when you felt better, did you stop taking one or more of your medicines?
- If you felt worse when you took a medicine did you stop taking it?
- Did you ever take more medicines than prescribed or for a different purpose than prescribed?

3. Questions asked post review only

- Overall, did your medicines review help your understanding of your medicines?
- Overall, did your medicines review help with side effects you are experiencing from your medicines?
- Overall, did your medicines review help with the impact of medicines on your daily activities?
- Overall, did your medicines review help you to take your medicines correctly?

APPENDIX 2: Polypharmacy indicators not identified in the study

Cardiac

- Patient with heart failure but without atrial fibrillation and on digoxin is prescribed digoxin of strength >125 μg/day.
- Patient on verapamil is prescribed digoxin at a dose >125 μg/day.

Electrolyte abnormalities

- Patient on an ACE inhibitor or angiotensin II receptor blocker is prescribed a combination of potassium sparing diuretic and aliskiren.
- Patient with eGFR <30 mL/min/1.73m^2 is prescribed aliskiren.
- Patient with eGFR <30 mL/min/1.73m^2 is prescribed a potassium supplement.
- Patient prescribed digoxin has hypokalaemia.

Cardiovascular disease events

- Female patient with a history of venous thromboembolism is prescribed an oestrogen

Other

- Patient with eGFR <30 mL/min/1.73m^2 is prescribed colchicine.
- Patient on methotrexate is co-prescribed trimethoprim on repeat.
- Patient is prescribed gabapentin or pregabalin at an average daily dose of >4800 mg. gabapentin per day over the previous 6 months.
- Patient prescribed levodopa is prescribed metoclopramide or prochlorperazine on repeat.
- Female patient with a history of breast cancer is prescribed an oestrogen.
- Female patient with intact uterus is prescribed an oestrogen without progestogen.
- Patient on lithium has recently been started on a thiazide diuretic.

APPENDIX 3: All medicine classes (ATC level 3 coded) ordered by total associated pre-review PC-MAI scores ($n = 194$; 13.2% of reviews)

Medicine	ATC level 3	Total PC-MAI score			Number of medicines			Mean PC-MAI score		
		Pre	Post	Pre minus post	Pre	Post	Pre minus post	Pre	Post	Pre minus post
Drugs for peptic ulcer and gastro-oesophageal reflux disease	A02B	312	101	211	162	155	7	1.93	0.65	1.27
Antithrombotic agents	B01A	307	65	242	172	143	29	1.78	0.45	1.33
Non-steroidal anti-inflammatory and anti-rheumatic products	M01A	291	55	236	49	15	34	5.94	3.67	2.27
Antidepressants	N06A	287	143	144	85	74	11	3.38	1.93	1.44
Blood glucose lowering drugs (excluding insulins)	A10B	242	58	184	128	115	13	1.89	0.50	1.39
Hypnotics and sedatives	N05C	223	177	46	42	38	4	5.31	4.66	0.65
Opioids	N02A	204	115	89	53	46	7	3.85	2.5	1.35
Urologicals	G04B	174	52	122	46	26	20	3.78	2	1.78
Paracetamol	N02B	172	92	80	120	120	0	1.43	0.77	0.67
Lipid modifying agents	C10A	167	63	104	160	158	2	1.04	0.4	0.65
Vitamin B12 and folic acid	B03B	159	35	124	42	21	21	3.79	1.67	2.12
Beta blocking agents	C07A	141	54	87	107	96	11	1.32	0.56	0.76
High-ceiling diuretics	C03C	135	44	91	50	37	13	2.7	1.19	1.51
Inhalant adrenergics	R03A	124	51	73	111	116	-5	1.12	0.44	0.68
Antipsychotics	N05A	119	43	76	19	12	7	6.26	3.58	2.68
Drugs for constipation	A06A	106	26	80	63	56	7	1.68	0.46	1.22
Systemic antihistamines	R06A	102	34	68	21	17	4	4.86	2	2.86
Inhaled drugs for obstructive airway diseases	R03B	99	31	68	58	52	6	1.71	0.6	1.11
Thiazide diuretics	C03A	84	6	78	20	7	13	4.2	0.86	3.34
Iron preparations	B03A	83	10	73	30	18	12	2.77	0.56	2.21
Drugs used in benign prostatic hypertrophy	G04C	80	22	58	41	34	7	1.95	0.65	1.3
Dihydropyridine calcium channel blockers*	C08C	79	32	47	76	72	4	1.04	0.44	0.6
Vitamin D and analogues*	A11C	71	5	66	87	86	1	0.82	0.06	0.76
ACE Inhibitors (plain)	C09A	71	26	45	69	65	4	1.03	0.4	0.63
Anxiolytics	N05B	71	52	19	15	13	2	4.73	4	0.73
Angiotensin II antagonists (plain)	C09C	63	34	29	51	50	1	1.24	0.68	0.56
Sulfonamide low-ceiling diuretics*	C03B	55	8	47	17	10	7	3.24	0.8	2.44
Corticosteroids (plain)	D07A	54	34	20	26	22	4	2.08	1.55	0.53
Calcium (including combinations with vitamin D)	A12A	48	20	28	51	51	0	0.94	0.39	0.55
Dopaminergic agents	N04B	48	35	13	22	21	1	2.18	1.67	0.52
Anti-dementia drugs	N06D	48	23	25	17	15	2	2.82	1.53	1.29
Ranolazine*	C01E	47	19	28	11	8	3	4.27	2.38	1.9
Propulsives	A03F	45	6	39	7	2	5	6.43	3	3.43
Vasodilators used in cardiac diseases	C01D	41	18	23	27	26	1	1.52	0.69	0.83
Sulfonamides and trimethoprim	J01E	40	0	40	5	0	5	8	N/A	N/A
Doxazosin*	C02C	36	19	17	15	12	3	2.4	1.58	0.82
Antimalarials	P01B	36	14	22	13	10	3	2.77	1.4	1.37
All other non-therapeutic products	V07A	35	9	26	43	35	8	0.81	0.26	0.56
Anti-gout preparations	M04A	34	8	26	18	16	2	1.89	0.5	1.39

Medicine	ATC level 3	Total PC-MAI score			Number of medicines			Mean PC-MAI score		
		Pre	Post	Pre minus post	Pre	Post	Pre minus post	Pre	Post	Pre minus post
Potassium-sparing agents	C03D	33	12	21	12	10	2	2.75	1.2	1.55
Muscle relaxants (centrally acting agents)	M03B	32	6	26	5	2	3	6.4	3	3.4
Other systemic drugs for obstructive airway diseases	R03D	32	12	20	10	7	3	3.2	1.71	1.49
Sumatriptan*	N02C	28	6	22	3	1	2	9.33	6	3.33
Anti-vertigo preparations	N07C	28	7	21	14	12	2	2	0.58	1.42
Topical corticosteroids in combinations with antibiotics	D07C	27	4	23	4	1	3	6.75	4	2.75
Drugs affecting bone structure and mineralisation	M05B	26	11	15	29	29	0	0.9	0.38	0.52
Decongestants and other nasal preparations for topical use	R01A	26	26	0	25	26	-1	1.04	1	0.04
Artificial tears and other indifferent preparations*	S01X	26	15	11	44	43	1	0.59	0.35	0.24
Other vitamin combination products	A11J	24	19	5	8	7	1	3	2.71	0.29
Class I and III antiarrhythmics	C01B	22	10	12	12	9	3	1.83	1.11	0.72
Angiotensin II receptor blockers in combinations	C09D	22	22	0	8	7	1	2.75	3.14	−0.39
Corticosteroids for systemic use	H02A	22	10	12	10	9	1	2.2	1.11	1.09
Ondansetron*	A04A	20	9	11	2	1	1	10	9	1
Thiamine*	A11D	19	5	14	6	5	1	3.17	1	2.17
Midodrine*	C01C	18	3	15	6	5	1	3	0.6	2.4
Thyroid Preparations	H03A	18	6	12	36	38	−2	0.5	0.16	0.34
Topical products for joint and muscular pain	M02A	18	3	15	34	31	3	0.53	0.1	0.43
Hyoscine butylbromide*	A03B	17	4	13	5	3	2	3.4	1.33	2.07
Selective calcium channel blockers with direct cardiac effects	C08D	16	10	6	6	5	1	2.67	2	0.67
Azithromycin*	J01F	16	11	5	6	5	1	2.67	2.2	0.47
Oral nutritional supplements*	V06D	16	1	15	6	4	2	2.67	0.25	2.42
Drugs for functional gastrointestinal disorders	A03A	14	2	12	8	5	3	1.75	0.4	1.35
Insulins and analogues	A10A	14	5	9	18	17	1	0.78	0.29	0.48
Drugs used in addictive disorders	N07B	14	0	14	4	1	3	3.5	0	3.5
Carbocisteine*	R05C	13	9	4	9	8	1	1.44	1.13	0.32
Loperamide*	A07D	11	11	0	4	4	0	2.75	2.75	0
Intestinal anti-inflammatory agents	A07E	11	0	11	2	0	2	5.5	N/A	N/A
Aliskiren*	C09X	10	0	10	1	0	1	10	N/A	N/A
Potassium	A12B	9	0	9	1	0	1	9	N/A	N/A
Monoclonal antibodies	L01F	9	0	9	1	0	1	9	N/A	N/A
Chemotherapeutics for topical use	D06B	8	0	8	3	2	1	2.67	0	2.67
Multivitamin combinations	A11A	7	3	4	3	2	1	2.33	1.5	0.83
Agents for treatment of haemorrhoids and anal fissures for topical use	C05A	7	1	6	2	1	1	3.5	1	2.5
Tetracycline antibiotics	J01A	7	0	7	2	1	1	3.5	0	3.5
Nitrofurantoin*	J01X	7	6	1	1	1	0	7	6	1
Orlistat*	A08A	6	0	6	1	0	1	6	N/A	N/A
Cardiac glycosides	C01A	5	2	3	11	11	0	0.45	0.18	0.27
Naftidrofuryl*	C04A	4	0	4	3	3	0	1.33	0	1.33

(Continues)

Medicine	ATC level 3	Total PC-MAI score			Number of medicines			Mean PC-MAI score		
		Pre	Post	Pre minus post	Pre	Post	Pre minus post	Pre	Post	Pre minus post
Antifungals for topical use	D01A	4	1	3	9	8	1	0.44	0.13	0.32
Antipsoriatics for topical use	D05A	4	4	0	2	2	0	2	2	0
Raloxifene*	G03X	4	0	4	1	0	1	4	N/A	N/A
Cefalexin*	J01D	4	0	4	1	0	1	4	N/A	N/A
Methotrexate*	L01B	4	0	4	4	2	2	1	0	1
Local anaesthetics	N01B	4	0	4	2	2	0	2	0	2
Anti-epileptics	N03A	4	2	2	4	4	0	1	0.5	0.5
Ophthalmological anti-inflammatory agents and anti-infectives in combination	S01C	4	0	4	1	0	1	4	N/A	N/A
Anti-glaucoma preparations and miotics	S01E	4	0	4	28	27	1	0.14	0	0.14
Furosemide/amiloride combinations*	C03E	3	3	0	1	1	0	3	3	0
Immunosuppressants	L04A	3	3	0	3	4	−1	1	0.75	0.25
Ursodeoxycholic acid*	A05A	2	0	2	1	1	0	2	0	2
Intestinal anti-infectives	A07A	2	0	2	1	1	0	2	0	2
Emollients and protectives	D02A	1	0	1	13	14	−1	0.08	0	0.08
Carbimazole*	H03B	1	1	0	3	3	0	0.33	0.33	0
Teriparatide*	H05A	1	1	0	1	1	0	1	1	0
Antacids	A02A	0	0	0	3	2	1	0	0	0
Pancrelipase*	A09A	0	0	0	1	1	0	0	0	0
Ascorbic acid*	A11G	0	0	0	1	0	1	0	N/A	N/A
Magnesium*	A12C	0	0	0	3	3	0	0	0	0
Darbepoetin*	B03X	0	0	0	4	4	0	0	0	0
Mupirocin (topical)*	D06A	0	0	0	1	0	1	0	N/A	N/A
Retinol (topical)*	D10A	0	0	0	2	2	0	0	0	0
Testosterone*	G03B	0	0	0	1	1	0	0	0	0
Oestrogens	G03C	0	0	0	5	5	0	0	0	0
Progestogens and oestrogens in combination	G03F	0	0	0	1	1	0	0	0	0
Calcitonin preparations	H05B	0	0	0	4	4	0	0	0	0
Pyridostigmine*	N07A	0	0	0	1	1	0	0	0	0
Drugs for treatment of hyperkalaemia and hyperphosphataemia*	V03A	0	0	0	5	5	0	0	0	0

Abbreviation: N/A: Not applicable. *More specific title provided where all identified medicines relate to a more specific group of medicines or a single medicine.