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Original article

Impact of Specialized Clinics on Medications Deprescribing in Older Adults: A Pilot Study in Ambulatory Care Clinics in a Teaching Hospital

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ARTICLE INFO

1. Background

Excluding older adults from clinical trials is a well-documented problem (Zulman et al., 2011, Watts 2012, Skolnick and Alexander 2015). Very older age (>80 years), life expectancy, functional and cognitive impairment, and comorbidities are among the commonly cited exclusion criteria in >45% of clinical trials (Zulman et al., 2011). This makes the safety and efficacy of many medications uncertain in this population (Gurwitz 2014). Polypharmacy is another well-known problem among older adults. It is a global burden due to the associated increase in the risk of drug interactions, adverse drug events, hospitalization, and mortality (Potter et al., 2016, Suzuki et al., 2018). The scientific community differs on the exact definition. Yet, polypharmacy can be measured quantitatively by the number of medications or qualitatively by the clinical indications and effects of a given drug regimen regardless of the number of drugs (Taghy et al., 2020). Polypharmacy leads to several drug-related problems such as the increased risks of side effects (19.8%), drug interactions (11.5%), suicidal drug ingestion (10.3%), drug abuse (7.1%), drug allergy (4%), superinfection (3.2%), and non-compliance (44.3%); almost all are deemed preventable (Alghamdy et al., 2015). The prescribing cascade further complicates polypharmacy, and it occurs when a clinician prescribes a drug to treat an adverse effect caused by another medication (Krishnaswami; et al., 2019). Older adults most commonly suffer from the prescribing cascade for reasons such as multimorbidities, polypharmacy, and multiple prescribers (Trenaman et al., 2021).

Deprescribing is one of the remedies to polypharmacy. It is defined as the process of withdrawing inappropriate medications under the supervision of a health care professional to improve health outcomes (Reeve et al., 2015). Deprescribing encompasses several good prescribing practices that include not only discontin-

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uation of unnecessary medications, but also decreasing medication doses and frequencies or switching inappropriate medications to more safe alternatives. Ideally, deprescribing incorporates measures that aid in identifying those elderly patients susceptible to inappropriate medications as a preemptive step to avoid potentially problematic drugs at the time of prescribing (Woodward 2003, Reeve et al., 2015, Scott et al., 2015, Brandt 2016, Reeve et al., 2017). Measures such as Beer's Criteria and Screening Tool of Older Person's Potentially Inappropriate Prescription (STOPP) are well-known tools developed to guide clinicians to address the complex problem of polypharmacy and potentially inappropriate medications (O'Mahony et al., 2015, Fick et al., 2019). However, in busy clinical practice, emergent situations such as adverse drug events, if the patient presents to emergency care, or at the end of life and as part of palliative care prompt clinicians to deprescribe offensive medications (Krishnaswami et al., 2019). Challenges to deprescribing are multifactorial, and it involves clinicians, patients, and the health system (Ailabouni et al., 2021, Abou et al., 2022).

At the patient level, enablers of willingness to deprescribe are highly related to the degree of trust between patients and their healthcare providers. For example, a study conducted among elderly patients in the primary care setting in Switzerland showed that most patients are comfortable with deprescribing if their physician supports the decision (Rozsnyai et al., 2020). Several randomized controlled trials also demonstrated that deprescribing interventions, particularly those attentive to patients' values and preferences and employing shared decision-making, are feasible, safe and generally effective at reducing inappropriate medications (Martin et al., 2018, Aharaz et al., 2021, Cateau et al., 2021, Gedde et al., 2021, Wong et al., 2021, McCarthy et al., 2022, McDonald et al., 2022, Nguyen-Soenen et al., 2022). On the other hand, at the prescriber level, knowledge and competency about deprescribing, availability of deprescribing guidelines, and the pharmacist's role are reported among the enablers to aid deprescribing (Tangiisuran et al., 2021).

In Saudi Arabia, elderly adults represent approximately 3.2% of the general population. The life expectancy is 75 years and is projected to increase to 80 years by 2030 (Khoja et al., 2018). Similar to the rest of the world, polypharmacy is a challenging problem for this population. Two observational studies showed a high prevalence of polypharmacy (defined as concurrent intake of ≥5 medications daily) (46% and 89%) among elderly patients aged 61 and above in Saudi Arabia (Salih et al., 2013, Balkhi et al., 2021). Moreover, among all adult visits to the emergency department from August 2016 to July 2017 at King Abdulaziz University Hospital in Jeddah, Saudi Arabia, elderly patients contributed to one-fifth of those visits (Abualenain et al., 2017). Additionally, the Saudi market's top 10 commonly used drugs are antibiotics and analgesics, specifically Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), followed by proton pump inhibitors (PPIs), diabetes medications, anti-hyperlipidemic agents, and erectile dysfunction treatments (AlKhamees et al., 2018). Many of these medications are identified as potentially harmful by many screening tools that guide deprescribing (O'Mahony et al., 2015, Fick et al., 2019, Reeve 2020). Furthermore, Al-Omar *et al.* found that the total direct costs associated with inappropriate prescribing was 518314 Saudi Riyals (US$138217) (Al-Omar et al., 2013).

Most studies on deprescribing in Saudi Arabia have investigated the knowledge, attitudes, and willingness toward deprescribing among patients and healthcare providers. However, there is a gap in knowledge about deprescribing practices, implementation, and related outcomes in the general healthcare practice in Saudi Arabia. Therefore, this study investigated specialized clinics' impact on deprescribing potentially inappropriate medications (PIMs) in elderly patients visiting King Saud University Medical City (KSUMC). The primary objective was to determine whether deprescribing would reduce the total number of PIMs at 12 months.

Secondary objectives included investigating the effects of deprescribing on unplanned healthcare utilization and mortality.

2. Methodology

2.1. Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki standards and was approved by the institutional review board at KSUMC, **E-19-3951.** Informed consent was obtained from participants in the intervention group. The recruitment period in this study was extended from October 2019 to March 2021 due to the COVID-19 pandemic circumstances.

2.2. Study design and setting

We conducted a non-randomized interventional controlled study targeting all elderly patients following up in the ambulatory care clinics at KSUMC, Riyadh, Saudi Arabia.

2.3. Study population

Patients were eligible if they were aged ≥65 years, followed with the ambulatory care clinics, had at least one of five targeted PIMs, had clinically stable diseases and were on the same medication regimens for the past six months. Patients were excluded if diagnosed with a severe mental illness or dementia, significant cognitive impairment (score < 24 on the Mini-Mental State Examination), an unstable chronic disease or advanced illness, or clinically unstable per the enrolling clinician's assessment.

2.4. Intervention

We targeted six specialized clinics; two clinics run by geriatricians and four by clinical pharmacists. The geriatricians and clinical pharmacists agreed on the deprescribing of five classes of medications commonly encountered in the primary care setting. These included low-dose aspirin (LD-ASA) for primary prevention, NSAIDs, PPIs, tricyclic antidepressants (TCAs), and antihyperglycemics (insulin, sulfonylurea). The team adapted the deprescribing process described by Potter et al. (Potter et al., 2016). Using published guidance documents on deprescribing of each targeted PIM, a summary pathway was shared with all six healthcare providers (HCPs) to guide the decision-making process and conversation with patients (Farrell et al., 2017a; 2017b). Patients were consecutively recruited.

Each patient in the intervention group received a comprehensive medication review. The HCPs then engaged the patients in decision-making discussions after fully educating them about the PIM and the deprescribing process. Four deprescribing strategies were used "stop PIM", "Taper PIM", "Stop PIM and use alternative", and "use PIM on-demand". The strategy selection is based on the guidance document of each PIM, clinician judgment, and patient preference. The deprescribing intervention was considered successful if the patient and healthcare provider agreed to deprescribe during the index clinic encounter. The IRB judged that it would be unethical to withhold the deprescribing intervention from a control group. Therefore, after applying the same inclusion and exclusion criteria, control patients were randomly sampled from a list of elderly patients visiting primary care clinics other than the six clinics targeted for the intervention arm and during the same study period. Control participants received only usual care. Data on participants sociodemographic (age, gender, height and weight), clinical (comorbidities, healthcare visits in the previous three months), number of medications, deprescribing intervention (PIM involved,

strategy of deprescribing, patient and HCP agreement), pharmacy refills, dates and reasons for healthcare visits to the emergency department or hospitalization and date and cause of death were collected at baseline and 3, 6, 9, and 12 months after recruitment. We planned to conduct a weekly phone call for the intervention arm in the first four weeks post-deprescribing visit to assess the presence of withdrawal side effects.

2.5. Study outcomes

The primary outcome was the difference in the number of PIMs at 12 months between both groups. We considered deprescribing to be successful and sustained if the PIM was absent from the medication refills (after considering the day's supply from the previous quarter) over the 12 months. Secondary outcomes included the rate of unplanned healthcare utilization, emergency room visits or hospitalization, and mortality at 12 months between the intervention and the usual care groups.

2.6. Statistical analyses

The sample size was calculated to detect a mean change of ±1.34 in the number of PIMs (α = 0.05 and 1-β = 0.8, SD 3), and 79 patients in each arm were needed. In this study, we aimed to pilot the deprescribing process, so we planned to recruit 40 patients in each arm. Based on this, 80 patients (40 patients in each arm) were recruited. Data were collected, coded and entered in the Statistical Package for Social Sciences (SPSS) version 27. Data were cleaned using cross-tabulation. Depending on the normality of distribution, continuous variables were reported as mean, standard deviation or median, interquartile range. Categorical variables were reported as numbers and percentages. Differences between usual care and intervention concerning continuous variables were explored using the independent sample t-test or non-parametric Mann-Whitney test. Differences between groups of categorical variables were analyzed using Chi-square or Fisher's exact test whenever appropriate. A p-value of <0.05 for differences between intervention and usual care was considered significant. Binary logistic regression was performed and an odds ratio with 95% confidence intervals was calculated for intervention with usual care as the reference group. In addition, the reported odds were adjusted for confounding variables significantly different between groups at baseline (age, hypertension and dyslipidemia).

3. Results

A total of 80 patients were enrolled and included in the final analysis. The mean (SD) age was 70 ± 7, and the majority of patients were female (69%) and had a body mass index of 32 ± 8 kg/m^2. Participants in the intervention group (n = 40) had a significantly younger age with a mean (SD) of 68 ± 7 years, p value = 0.019. The prevalence of hypertension (52%, p = 0.031) and dyslipidemia (52%, p = 0.026) was significantly higher in the usual care group. Other baseline characteristics such as laboratory values, comorbidities, and the number of medications per patient were comparable between the usual care and intervention groups. Sociodemographic data and comorbidities with bivariate analysis of the difference are summarized in Table 1.

Across both groups, at baseline, 113 PIMs were identified (usual care = 56, intervention = 57), and there was no statistical difference between the two groups in the baseline number of PIMs (p = 0.8027). Overall, LD-ASA was the most common PIM (44%) present, followed by PPIs (36%), antihyperglycemics (9%), NSAIDs (7%), while TCA was the least common PIM encountered (4%). At 12 months, there were 50 PIMs in both groups (usual care = 37,

intervention = 13). Compared to baseline, there was a significant decrease in the number of PIMs in each group at 12 months. This is translated into 77% reduction in PIM in the intervention group and 34% in usual care. Fig. 1 shows the number of PIMs in both groups at baseline and over the 12-month observation period. Additionally, the intervention group had significantly lower PIMs than the usual care group at all four-time points over the 12-month follow-up time (mean difference = 0.6000, 95% CI: 0.3187 to 0.8813 (p=<0.0001).

Deprescribing in the intervention group at the first encounter was successful in 86% of cases. The most frequent strategy for deprescribing was "stop PIM" (71%), followed by "use PIM on-demand" (14%), while "taper PIM" was the least deprescribing strategy used (4%). LD-ASA was the PIM mostly deprescribed using the "stop PIM" deprescribing strategy (91%). All deprescribing of NSAIDs used the "stop PIM" strategy, and it was 100% successful in all 7 cases. TCAs were deprescribed using "taper PIM" and were successful in 50% of the cases. PPIs were successfully deprescribed mostly using the "use drug on-demand" strategy (54%). Finally, the "stop PIM and use alternative" strategy mainly was used with antihyperglycemic drugs and was used in 71% of the cases. In eight patients, deprescribing was unsuccessful, with half of the cases involving a PPI. Table 2 summarizes the results of deprescribing in the intervention group, and the strategies used for each PIM class. There was a high acceptance from patients (50-100%) and physicians (77-100%) on deprescribing PIMs as presented in Fig. 2.

For the primary outcome, at all-time points of measurement, there was a significantly lower number of PIMs in the intervention group compared to usual care (Table 3). The secondary outcome of unplanned healthcare utilization was lower in the intervention (n=4) compared to usual care (n=10) but this difference was not not statistically significant (p = 0.1057). One participant died during follow-up in the usual care group.

Sustained deprescribing in the intervention group was measured by the absence of PIM from the subsequent refills (Table 4). LD-ASA remained deprescribed in the intervention group at three of the four measurement points (p=<0.001). PPIs were significantly absent at the 12-months refill only (p = 0.028). For the remaining three classes of PIMs, antihyperglycemics remained deprescribed only at 3-month of follow-up. In contrast, NSAIDs and TCAs appeared on the refill history at the four measurement points. Due to logistic reasons, weekly follow up calls in the first month following deprescribing were not performed.

Further analysis using healthcare utilization as a primary outcome variable was explored using binary logistic regression between the usual care and intervention groups. The resulting odds ratio was adjusted to significantly different factors at baseline (age, hypertension and dyslipidemia). There were fewer odds of being hospitalized in the intervention groups at 3, 9, and 12 months (OR = 0.231, 0.487, and 0.352, respectively), but this was not statistically significant. The odds did not significantly change when adjusting for age and comorbidities. Furthermore, the intervention group had fewer odds of having LD-ASA and PPIs on their medication list at significantly different follow-up periods based on bivariate analysis. The adjusted odds of having LD-ASA in the intervention was AOR = 0.126 (95% CI 0.032–0.496), at 6 months AOR = 0.235 (95% CI 0.064–0.856), and at 12 months AOR = 0.120 (95% CI 0.030–0.481) (Table 5).

4. Discussion

4.1. Success and sustainability of deprescribing

This study demonstrated that deprescribing is safe and feasible. Deprescribing using a standardized process, guidance tools for the

Table 1
Participant demographics at baseline.

	Usual Care N = 40	Intervention N = 40	Total N = 80	*p*-value
Age, years, mean (Standard deviation, SD)	72 ± 6	68 ± 7	70 ± 7	**0.019***
Gender, *n* (%) Male	15 (60.0)	10 (40.0)	25 (31.3)	0.335
Female	25 (45.5)	30 (54.5)	55 (68.8)	
Body mass index, kg/cm^2, mean (SD)	32 ± 7	33 ± 8	32 ± 8	0.304
Systolic blood pressure, mmHg, mean (SD)	137 ± 16	137 ± 18	137 ± 17	0.889
Diastolic blood pressure, mmHg, mean (SD)	72 ± 9	71 ± 13	71 ± 11	0.894
Serum creatinine, mg/dl, mean (SD)	75 ± 26	80 ± 32	78 ± 29	0.382
Estimated Glomerular filtration rate£, ml/min/1.73 m^2, mean (SD)	88 ± 25	81 ± 27	85 ± 26	0.280
HgA1c, %, mean (SD)	7.7 ± 1.7	9.7 ± 9.0	8.7 ± 6.5	0.191
Low density lipoprotein, mg/dl, mean (SD)	2.37 ± 0.52	2.54 ± 0.79	2.45 ± 0.67	0.269
High density lipoprotein, mg/dl, mean (SD)	1.33 ± 0.28	5.97 ± 28.39	3.68 ± 20.21	0.331
Cholesterol, mg/dl, mean (SD)	4.37 ± 0.73	4.41 ± 0.78	4.39 ± 0.75	0.817
Triglycerides, mg/dl, mean (SD)	1.56 ± 0.71	1.43 ± 0.56	1.50 ± 0.64	0.390
No. of Comorbidities, median (IQR)	4 (4–5)	4 (4–5)	4 (4–5)	0.426
No. of medication, median (IQR)	7 (6–8)	8 (8–10)	8 (8–9)	0.858
Hypertension⊥	38 (52.1)	35 (47.9)	73 (93.6)	**0.031***
Diabetes Meletus⊥	29 (47.5)	32 (52.5)	61 (76.3)	0.600
Dyslipidaemia⊥	31 (51.7)	29 (48.3)	60 (90.9)	**0.026***
Number of PIMs⊥	**56**	**57**	**113**	1.000
Average PIMs per patient, mean (SD)	1.4 ± 0.6	1.4 ± 0.5	1.4 ± 1	0.891
Class of PIMs⊥:				
LD-ASA	27 (54.0)	23 (46.0)	50 (62.5)	0.356
NSAID	1 (12.5)	7 (87.5)	8 (10.0)	**0.025***
PPI	24 (58.5)	17 (41.5)	41 (51.2)	0.117
TCA	2 (50.0)	2 (50.0)	4 (5%)	1.000
Antihyperglycemics	2 (20.0)	8 (80.0)	10 (12.5)	**0.043***

*Significant according to a significance level of < 0.05 using Chi-square or Fisher exact test, independent sample *t*-test and non-parametric Mann-Whitney test. £using a modification of diet in renal disease equation. ⊥ Data presented as N(%). IQR: interquartile range, SD: standard deviation. PIMs: Potentially Inappropriate Medications, LD-ASA: low dose aspirin, NSAID: non-steroidal anti-inflammatory drug, PPI: proton pump inhibitor, TCA: tricyclic antidepressants.
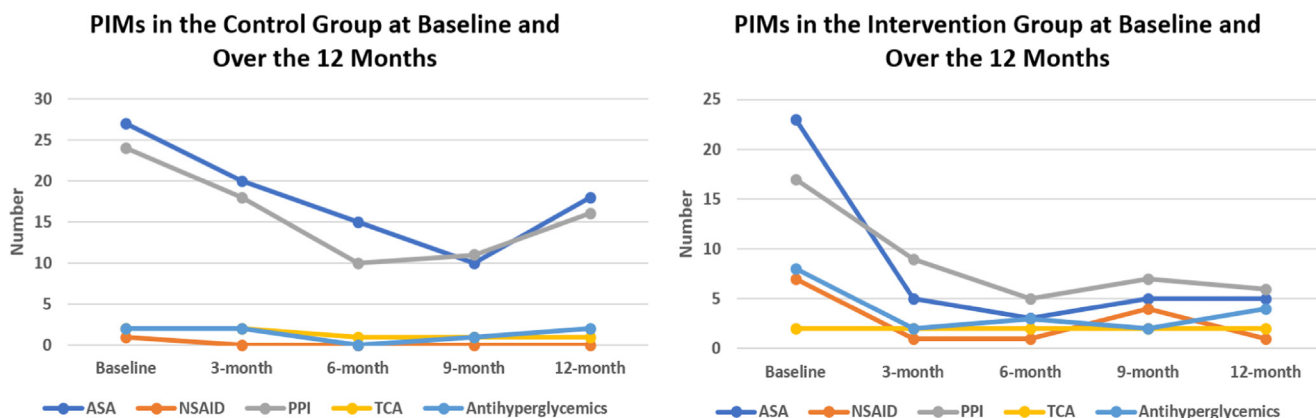

Fig. 1. Number of PIMs in the usual care and intervention groups at baseline and over the 12 months.

Table 2
Deprescribing strategies per medication class in the intervention group.

PIM⊥	Stop PIM	Taper PIM	Stop PIM and alternative	Use PIM on-demand	Unsuccessful Deprescribing
LD-ASA	21(91%)				2(9%)
NSAID	7(100%)				0%
PPI	6(35%)			7(41%)	4(24%)
TCA		1(50%)			1(50%)
Antihyperglycemics	1(13%)	1(13%)	5(63%)		1(13%)

LD-ASA: low dose aspirin, NSAID: non-steroidal anti-inflammatory drug, PPI: proton pump inhibitor, TCA: tricyclic antidepressants, PRN: use per need. ⊥data is presented as N(%).
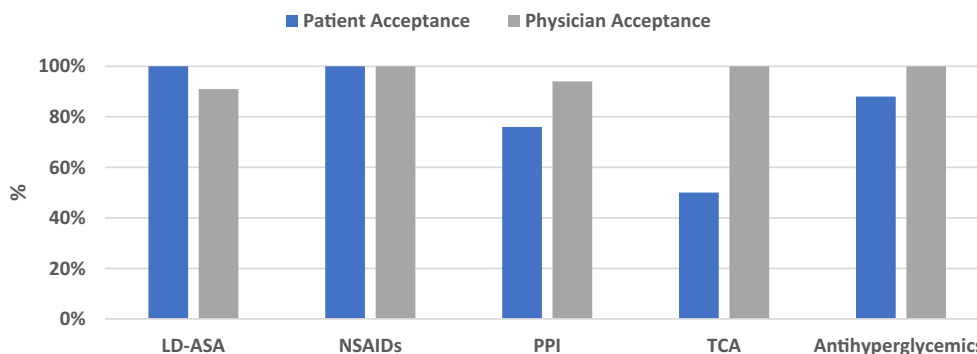
Fig. 2. Patient's and Physician's Acceptance of PIM deprescribing. *LD-ASA: low dose aspirin, NSAID: non-steroidal anti-inflammatory drug, PPI: proton pump inhibitor, TCA: tricyclic antidepressants.*

Table 3
Primary outcome and healthcare utilization (emergency or hospital admission) during the study period with the difference between usual care and intervention groups.

Months	Usual Care[£] N = 40	Intervention N = 40	*p*-value
Potentially inappropriate medication[π]			
3-month	1 (1–2)	0.5 (0–1)	**0.009***
6-month	1 (1–2)	0	**0.008***
9-month	1 (1–2)	0	**0.008***
12-month	1 (1–2)	0	**<0.001***
Hospitalization and/or emergency visit[⊥]			
3-month	4 (80.0)	1 (20.0)	0.166
6-month	1 (50.0)	1 (50.0)	1.000
9-month	2 (66.7)	1 (33.3)	1.000
12-month	3 (75.0)	1 (25.0)	0.617

[£] There was one death in the usual care group. [π]Data presented as median (interquartile range). *Significant according to a significance level of < 0.05 using Chi-square or Fisher exact test and non-parametric Mann-Whitney test. [⊥]Data presented as N(%).

clinicians, and engaging patients in the decision-making process to address their concerns are essential components for successful outcomes. The high percentage of PIMs (86%) deprescribed during the first encounter indicates the importance of such engagement steps.

In this study, the number of PIMs at all four time points of assessment remained significantly lower in the intervention group compared to the usual care group. In concordance with this, Zechmann et al. conducted a cluster-randomized study that implemented an intervention comprised of a 2-hour primary care physician training session, a validated deprescribing algorithm, and a shared decision-making aid to deprescribe PIMs in an elderly population in Swiss primary care clinics (Zechmann et al., 2020). The study found deprescribing to be significantly successful immediately after the intervention (defined as at the end of the first consultation), and 81% of the initially deprescribed medications remained deprescribed at 12-months. However, the study showed no significant differences at six and 12-months. The primary difference from our study was that Zechmann *et al.* looked at PIMs identified at baseline and those consecutively added to treat emerging

Table 4
Number of PIMs absent from subsequent refills during 12 months with bivariate analysis of differences between usual care and intervention.

PIM		Usual care N = 40	Intervention N = 40	*p*-value
LD ASA[⊥]	Baseline	27 (54.0)	23 (46.0)	1.000
	Three months	7 (28.0)	18 (72.0)	**<0.001***
	Six months	12 (37.5)	20 (62.5)	**0.008***
	Nine months	17 (48.6)	18 (51.4)	0.488
	Twelve months	9 (33.3)	18 (66.7)	**<0.001***
NSAIDs[⊥]	Baseline	1 (12.5)	7 (87.5)	0.057
	Three months	1 (14.3)	6 (85.7)	1.000
	Six months	1 (14.3)	6 (85.7)	1.000
	Nine months	1 (25.0)	3 (75.0)	1.000
	Twelve months	1 (14.3)	6 (85.7)	1.000
PPI[⊥]	Baseline	24 (58.5)	17 (41.5)	0.117
	Three months	6 (42.9)	8 (57.1)	0.104
	Six months	14 (53.8)	12 (46.2)	0.279
	Nine months	13 (56.5)	10 (43.5)	0.601
	Twelve months	8 (42.1)	11 (57.9)	**0.028***
TCA[⊥]	Baseline	2 (50.0)	2 (50.0)	1.000
	Three months	0 (0.0)	2 (100.0)	0.333
	Six months	1 (33.3)	2 (66.7)	1.000
	Nine months	1 (33.3)	2 (66.7)	1.000
	Twelve months	1 (33.3)	2 (66.7)	1.000
Antihyperglycemics[⊥]	Baseline	2 (20.0)	8 (80.0)	**0.043***
	Three months	2 (25.0)	6 (75.0)	0.467
	Six months	2 (28.6%)	5 (71.4)	1.000
	Nine months	1 (14.3)	6 (85.7)	1.000
	Twelve months	0 (0.0)	4 (100.0)	0.444

*Significant according to a significance level of < 0.05 using Chi-square or Fisher exact test. [⊥]Data presented as N(%). **LD ASA:** low dose aspirin, **NSAID:** non-steroidal anti-inflammatory drug, **PPI:** proton pump inhibitor, **TCA:** tricyclic antidepressants.

Table 5
Unadjusted and adjusted binary logistic regression with odds ratio of PIMs in the intervention compared to usual care during 12 months.

Outcome	Unadjusted			Adjusted[**]		
	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Number of PIMs at 3-month	0.400	0.197—0.816	**0.012***	0.415	0.198—0.871	**0.020***
Number of PIMs at 6-month	0.462	0.255—0.839	**0.011***	0.492	0.277—0.873	**0.015***
Number of PIMs at 9-month	0.396	0.196—0.800	**0.010***	0.448	0.221—0.908	**0.026***
Number of PIMs at 12-month	0.204	0.s085—0.491	**<0.001***	0.228	0.094—0.553	**0.001***
LD-ASA at 3-month	0.136	0.040—0.464	**0.001***	0.126	0.032—0.496	**0.003***
LD-ASA at 6-month	0.200	0.058—0.691	**0.011***	0.235	0.064—0.856	**0.028***
LD-ASA at 12- month	0.111	0.029—0.427	**0.001***	0.120	0.030—0.481	**0.003***
PPI at 12-month	0.227	0.059—0.882	**0.032***	0.191	0.043—0.858	**0.031***

*Significant according to a significance level of < 0.05; **adjusted to age, hypertension, and dyslipidaemia.
LD-ASA: low dose aspirin, PPI: proton pump inhibitor.

diseases during the study period; therefore, this diluted the initial success. In the current study, we focused on outcomes related to the targeted PIM classes at baseline and repeated deprescribing counselling was not attempted.

Nonetheless, it is essential to recognize that the geriatric population will benefit from repeated deprescribing as part of their routine care since they are more prone to changes in health status due to multiple comorbidities, new clinical events, and hospitalization that may add additional PIMs (Lam et al., 2013, von Buedingen et al., 2018). Our study results also concurred with another small randomized controlled study conducted in a subacute medical outpatient clinic targeting physician deprescribing interventions of analgesics, cardiovascular, and gastrointestinal medications in collaboration with a pharmacist (Aharaz et al., 2021). The collaboration resulted in a significant reduction in the number of PIMs immediately and at 12-month follow up compared to the control group. Our results also underscore the benefits of engaging specialized health care professionals, including the expertise of geriatricians and clinical pharmacists, to lead and sustain deprescribing efforts in the busy primary care setting to improve patient outcomes (Lui et al., 2021, Wong et al., 2021).

Over the 12 months, there was only one death in the usual care group during the study period. Unplanned healthcare utilization was lower in the intervention group, but the difference was not statistically significant. The small sample and the relatively short follow-up time of 12 months can explain these results. Systematic reviews demonstrated that deprescribing was effective in reducing inappropriate medication use. However, the evidence of the effectiveness on reducing hospital admissions and mortality has mixed results that can be attributed to short follow up (most studies durations ≤ 12 months), study rigour, setting, and the age of the population studied (Kua et al., 2021a; 2021b; Shrestha et al., 2021).

4.2. Patient and healthcare provider acceptance of deprescribing PIMs

The study showed that older adults were agreeable to clinician-initiated deprescribing recommendations in almost all patients and across all five classes of PIMs (91%-100%). Although our study did not explore factors influencing patients' perspectives and attitudes, several published studies showed that older adults are willing to stop their medications if their doctors suggest it (Galazzi et al., 2016, Reeve et al., 2018, Kua et al., 2019, Reeve et al., 2019, Kua et al., 2021a; 2021b). Moreover, within the context of Saudi arabia, Alshammari et al. found that among 114 Saudi patients with a mean age of 68.9 ± 7.4, the majority (87.7%) would agree with their prescribers if deprescribing was discussed with them (Alshammari et al., 2021). Several patient-related factors are asso-

ciated with older adults' willingness to deprescribe medications. These factors include trust in the healthcare provider (physicians or pharmacists), medication side effects, less concern about stopping the medication, the prospect of follow up monitoring, being on chronic medications and the perceived burden of polypharmacy (Sirois et al., 2017, Chock et al., 2021, Crutzen et al., 2021, Seewoodharry et al., 2022). As for healthcare professionals, their acceptance to deprescribe was supportive in this study. The use of guidance documents could be one of the reasons for such a high level of agreement (Abou et al., 2022); in addition, most of the deprescribing was performed by the HCPs involved in the study.

4.3. Deprescribing success according to PIM class

4.3.1. Low dose aspirin

The 2019 Beer's criteria added aspirin for primary prevention to its list of medications that should be used cautiously in elderly patients (>70 years) in response to accumulated evidence of increased harm with minimal or no benefit in reducing cardiovascular events (Fick et al., 2019, Krishnaswami; et al., 2019). In this study, LD-ASA was the only PIM that showed a significant difference between the intervention and usual care groups for 75% of the 12-month duration. Difficulty in deprescribing aspirin lies in the potential of a rebound effect that may lead to cardiovascular (CV) events. In a population-based cohort study, discontinuation of aspirin increased the CV event rate per year to 1 of every 146 and 1 of every 36 patients using aspirin for primary and secondary prevention, respectively (Sundström et al., 2017). However, the observational study design limits the results of the study. Although our research has a short follow up (12 months), none of the patients in this study experienced CV events following deprescribing of aspirin. Ultimately, using a shared-decision-making approach that focuses on patient goals and preferences will better guide healthcare providers to individualize interventions for each patient (Jhaveri et al., 2021).

4.3.2. Proton pump inhibitors

Proton pump inhibitors are on the Beer's Criteria list of potentially harmful medications due to the increased risk of *Clostridium difficile* infection, bone loss, and fractures associated with prolonged use (>8 weeks) (Fick et al., 2019). Deprescribing guidelines suggested abrupt discontinuation or tapering to deprescribe PPIs (Targownik et al., 2022). In this study, at baseline, >50% of deprescribing failures were associated with PPIs. Different studies demonstrated variable difficulties in deprescribing PPIs. A systematic review found that PPIs and psychotropic medications are more resistant to deprescribing than cardiovascular drugs (Dills et al., 2018).

Long-term use and the anxiety of rebound hyperacidity symptoms are reasons behind patients' reluctance to stop PPIs (Thompson et al., 2018). In the current study, there was no difference between the two groups in PPI deprescribing at 3-, 6-, and 9-months. However, at 12-months, there was a significant difference favoring the intervention. One explanation could be related to the strategy of deprescribing. Using a PPI "on-demand" rather than abrupt discontinuation or tapering may have been favored by many of the patients. In concordance with this, a "DESPIBP Project" implemented patient-centred PPI deprescribing in a cohort of hospitalized patients in a tertiary hospital in Spain utilizing deprescribing strategies that involved abrupt stop, tapering dose then stop, reducing PPI dose to the lowest effective dose, or switching to on-demand use (Calvo et al., 2021). The intervention was successful and maintained at 24 weeks in 72% of the participants, with no significant differences based on the deprescribing strategy. The investigators of the DESPIBP Project attributed the sustained deprescribing of PPIs to four primary strategic approaches: patient empowerment, trust, shared decisions with the patient, and follow up monitoring. Conversely, the study allowed patients to use PPI on-demand as a rescue step when necessary. In our research, educating the patients about the reasons for deprescribing and encouraging their involvement in the shared decision-making may have led them to prefer the on-demand strategy and hence success at 12-months.

4.3.3. Non-steroidal anti-inflammatory drugs

NSAIDs are associated with an increased risk of gastrointestinal bleeding in high-risk patients, especially in the elderly (>70 years) (Fick et al., 2019). There were eight patients on NSAIDs in this study and most of them were in the intervention group (n = 7). The deprescribing efforts showed no significant differences between the usual care and intervention groups at any time point. This finding contradicts the results of a study by Schapira and colleagues that reported significant successful deprescribing of NSAID (73.08%) using multimodal interventions, including email alerts sent to prescribers at least 48-hrs before every appointment with a patient using PIM (Schapira et al., 2021). An explanation of the conflicting results may be due to the deprescribing strategy used between the two studies. We used "stop PIM" approach in our study, while in Schapira study, switching to an alternative medication strategy along with using an alert system for repeated deprescribing enhanced their deprescribing success.

4.3.4. Tricyclic antidepressants

TCAs are considered a potentially harmful drug because of the high anticholinergic effects that increase elderly adults' risks of dementia and falls (Fick et al., 2019). Deprescribing of TCAs in our study was performed by tapering and then stopping the drug. Across all five classes of drugs, patient acceptance was the lowest with TCA deprescribing (50%). These results conflict with an open-label study conducted in the ambulatory setting in Argentina, where TCA was significantly lower in the intervention group (Schapira et al., 2021). Again, the email alert system and a "safe alternative" approach to deprescribing were the main differences between the two studies. Additionally, the current study included a small number of participants on TCAs and utilized deprescribing by tapering the medication without offering an alternative.

4.3.5. Antihyperglycemics

Sulfonylureas use in the elderly population increases the risk of severe and prolonged hypoglycemia and hence is listed among drugs to avoid (Fick et al., 2019). Guidance on deprescribing antihyperglycemic medications is scarce and primarily based on low-quality evidence; however, stopping or switching to safer alternatives are documented as reasonable approaches (Farrell et al., 2017a; 2017b; Mannucci and Silverii 2021). Antihyperglycemic drugs in this study were mainly deprescribed by switching to a safer option. The small number of participants on antihyperglycemic PIMs limited the proper assessment of the deprescribing impact.

4.3.6. Study strengths and limitations

To our knowledge, this is the first published interventional controlled study to implement deprescribing practices in the Saudi population. The study intervention was integrated into the everyday practice rather than creating a controlled practice environment. Nonetheless, the study has several limitations. First, the study was conducted in a single center and it was of a relatively short duration. Second, we relied on refill history to verify the presence or absence of PIMs, but patients might have access to the deprescribed PIMs from other sources. Third, we evaluated the overall effect of deprescribing without investigating the impact of each intervention component (i.e. use of deprescribing guides and processes, patient education and shared decision-making, and involvement of specialized clinicians). Nonetheless, we believe that successful deprescribing requires a multimodal approach rather than a single intervention.

Finally, although planned in the initial protocol, we did not conduct follow up phone calls to assess withdrawal symptoms or harms related to deprescribing due to logistic reasons. However, in the subset of patients who had unplanned healthcare utilization, none were determined to be associated with the deprescribed medication.

5. Conclusion

Deprescribing is a safe and effective intervention to reduce PIMs in elderly patients. However, successful deprescribing requires combined efforts to enhance healthcare providers' knowledge of evidence-based guidelines for deprescribing and empower patients in the decision-making process that values their preferences and concerns. In addition, implementing solutions into the process to identify patients for repeated deprescribing is advisable to ensure sustained outcomes. Further research on deprescribing's clinical, humanistic, and economic impact in well-powered studies is warranted.

CRediT authorship contribution statement

Ghada Bawazeer: Conceptualization, Methodology, Investigation, Data curation, Validation, Writing - review & editing, Visualization, Project administartion. **Saad Alsaad:** Conceptualization, Methodology, Investigation, Writing - review & editing. **Haya Almalag:** Investigation, Formal analysis, Writing - review & editing. **Alhanouf Alqahtani:** Conceptualization, Methodology, Investigation, Data curation, Validation, Writing - review & editing. **Noura Altulaihi:** Conceptualization, Methodology, Investigation, Data curation, Writing - review & editing. **Abdulaziz Alodhayani:** Methodology, Investigation, Writing - review & editing. **Abdulaziz Alhossan:** Methodology, Investigation, Writing - review & editing. **Ibrahim Sales:** Methodology, Investigation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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