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Original Study

# Pharmacist-Led Deprescribing Using STOPPFrail for Frail Older Adults in Nursing Homes

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A B S T R A C T

*Objectives:* To evaluate the impact of pharmacist-guided deprescribing using the STOPPFrail (Screening Tool of Older Persons' Prescriptions in Frail adults with a limited life expectancy) criteria in frail older nursing home residents.
*Design:* Prospective, unblinded, non-randomized, intervention study.
*Setting and Participants:* Adults aged ≥65 years with advanced frailty resident in 6 independent nursing homes in Ireland.
*Methods:* STOPPFrail-based deprescribing recommendations were developed by a pharmacist and presented to residents' general practitioners (GPs), who decided to implement or not. Measured outcomes included number of prescribed medications, medication costs, anticholinergic cognitive burden (ACB), drug burden index (DBI), modified medication appropriateness index (MMAI), quality of life (QoL), non-elective hospitalizations, emergency department visits, falls, and mortality were measured at baseline, post review, and at 6 months post review.
*Results:* Ninety-nine residents were recruited. Most (94%) were prescribed ≥1 potentially inappropriate medication (PIM). The most frequent PIMs were medications without a clearly documented indication (29.6%) and vitamin D (16.9%). Of 348 recommendations provided to GPs, 203 (58%) were accepted and 193 (55%) were implemented. Relating to baseline, post review, and at 6 months: the mean ± standard deviation (SD) number of medications was 16.0 ± 6.1, 14.6 ± 5.7 ($P < .001$), and 15.4 ± 5.5 ($P < .001$). The monthly mean ± SD medication cost per patient was €186.8 ± 123.7, €172.7 ± 119.0 ($P < .001$), and €186.4 ± 121.2 ($P = .95$). There were significant post-review decreases in the mean DBI, ACB, and MMAI of 9.7%, 9.6%, and 3.7%, respectively ($P < .001$), which remained significant at 6 months ($P < .001$). There were no significant differences in falls, emergency department visits, non-elective hospitalizations, or QoL.
*Conclusions and Implications:* STOPPFrail-guided deprescribing led by a pharmacist in nursing homes appeared to significantly reduce PIMs, medication costs (initially), and anticholinergic and sedative burdens, without adversely affecting other patient outcomes. Greater consideration should therefore be given to the wider integration of pharmacists into nursing homes to optimize the medications and health outcomes of frail older adults.


The World Health Organization predicts 1 in 6 people globally will be aged ≥60 years by 2030.[1] With populations aging worldwide, the prevalence of dementia and other chronic diseases is predicted to rise, and thus there will be greater utilization of nursing homes by older adults, who are likely to have higher levels of multimorbidity, polypharmacy, and frailty.[2] Older adults in nursing homes are more than 3

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times more likely to be prescribed potentially inappropriate medications (PIMs) than their community-dwelling counterparts.[3] Possible explanations for the higher rate of PIM prevalence in nursing home residents include higher levels of multimorbidity, more hospitalizations, and an increased number of medications compared with community-dwelling older adults.[4]

The combined effects of multimorbidity, polypharmacy, frailty, and PIM prevalence increase the risk of nursing home residents experiencing adverse drug reactions (ADRs).[5] Dilles et al found that almost two-thirds of those in a sample of older adults in nursing homes experienced ADRs.[6] In contrast, a recent study indicated that one quarter of community-dwelling older adults experienced an ADR over a 6-year period.[7] Given that one tenth of hospitalizations of older adults are associated with ADRs, this emphasizes that ADRs in older adults confer significant morbidity to patients and have significant economic implications for health care systems.[8] The prescription of PIMs to older adults has been associated with a 66% higher risk of frequent falling,[9] as well as increasing fracture risk and death.[10] Furthermore, hospitalized older adults prescribed PIMs have been shown to have 15% higher hospital costs.[10]

One tool created to minimize PIMs and subsequently ADRs in frail older adults is STOPPFrail (Screening Tool of Older Persons' Prescriptions in Frail adults with a limited life expectancy).[11,12] To the authors' knowledge, only 2 STOPPFrail-based interventional studies have been published thus far. The first involved a specialist registrar in geriatric medicine applying STOPPFrail to hospitalized frail older adults awaiting transfer to residential care, which significantly reduced polypharmacy and medication costs, with no significant differences found for falls, hospitalizations, quality of life (QoL), or mortality.[13] The second involved a geriatrics team in a hospital applying STOPPFrail to frail older adults' medications, which significantly reduced the number of medications, with no significant impact on unscheduled hospitalizations or mortality.[14] To date, no research has been published using STOPPFrail as part of an intervention (1) in older adults residing in nursing homes or (2) undertaken by a pharmacist. In addition, the guidelines for the review of medications of older adults in residential care facilities in Ireland do not specifically require pharmacist involvement, nor do they consider frailty as a factor in medication reviews.[15] Although general practitioners (GPs) in Ireland usually perform reviews of nursing home residents' medications every 3 months, a pharmacist may be involved (depending on the nursing home), but their involvement is not mandatory.[15] The aim of this study was therefore to demonstrate the impact that pharmacist-led application of STOPPFrail could have on reducing PIMs and clinical outcomes for frail older adults in nursing homes.

## Methods

### *Background, Setting, and Participants*

This study was a prospective unblinded non-randomized study conducted in nursing homes in Cork, Ireland. A convenience sample of nursing homes was recruited in Cork via nursing home GPs who were within the research team's professional network. Participants had their usual pharmaceutical care (medications supplied and reviewed ad hoc in an informal manner as part of the supply process to nursing homes by community pharmacists) supplemented by individualized STOPPFrail-guided deprescribing.[11] Ethics committee approval was attained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Eligible participants were those in nursing homes (aged $\geq$65 years) who met all the following STOPPFrail inclusion criteria[11]:

- End stage irreversible pathology.
- Poor 1-year survival prognosis.
- Severe functional and/or cognitive impairment.
- Symptom control is the priority as opposed to prevention of disease progression.

Patients who had capacity provided written consent to partake in the study. Where capacity was deemed not present by patients' GPs, an appropriate patient proxy provided written assent on their behalf to partake. Patients and/or their proxy were also provided with study information leaflets. A consent declaration was granted by Ireland's Health Research Consent Declaration Committee (HRCDC) to allow the use of proxy assent to recruit patients for this study. This study was reported in congruence with the template for intervention description and replication (TIDieR) checklist and guide (Supplementary Table 1).[16]

### *Data Collection*

A research pharmacist (E.H.), liaised with GPs and nursing staff in nursing homes to identify eligible patients and direct them in the consent/assent process, as outlined previously. The research pharmacist extracted the following baseline data from GPs' medical records and clinical notes (4 GPs had access to electronic medical records and 1 had access to paper-based records for nursing home residents): (1) current diagnoses; (2) long-term regular medications and pro re nata (PRN; as needed) medications; (3) QoL, and from the preceding 6 months; (4) number of falls, (5) number of emergency department visits; and (6) number of non-elective hospitalizations. These data were reassessed at a 6-month follow-up visit. QoL was measured using the EuroQol Group's EQ-5D-5 L tool.[17] Where possible, patients completed a self-reported version of the EQ-5D-5 L tool; however, if the patient was unable to, a member of nursing staff in each nursing home completed a proxy version of the EQ-5D-5L tool. The EQ-5D-5L Visual Analogue Scale (VAS) was also measured for each patient.

### *Intervention*

After baseline data collection was completed, the research pharmacist used the STOPPFrail version 2 criteria to identity PIMs for deprescribing (Supplementary Table 2).[11] Medications targeted for deprescribing were recorded in a report using Microsoft Word and emailed to patients' GPs no later than 2 weeks after the baseline data collection visit for them to review (fictional sample report shown in Appendix 3). The research pharmacist then discussed the deprescribing recommendations in a face-to-face meeting with 4 GPs and via teleconference with 1 GP no later than 2 weeks after GPs received the reports. Nursing staff were present for only 1 of the face-to-face meetings. GPs sought patients' or their next of kin's views and preferences regarding the proposed deprescribing recommendations. Patients' GPs judged whether to accept the recommendation to stop or reduce a STOPPFrail-identified PIM. GPs were asked to provide reasons for not accepting recommendations where applicable.

### *Outcomes*

The number of accepted recommendations and deprescribed STOPPFrail-defined PIMs were recorded during the face-to-face meetings with GPs and the research pharmacist. If the indication of a STOPPFrail-defined PIM was clarified or other new information was received during meetings with GPs that meant the conditions specified in STOPPFrail to deprescribe a medication were not present, then the recommendation and STOPPFrail-defined PIM were considered not clinically relevant and were therefore excluded from further analysis. The flow of this information is shown in Figure 1.

This study's outcomes were chosen based on 3 published core outcome sets for studies aiming to optimize older adults'

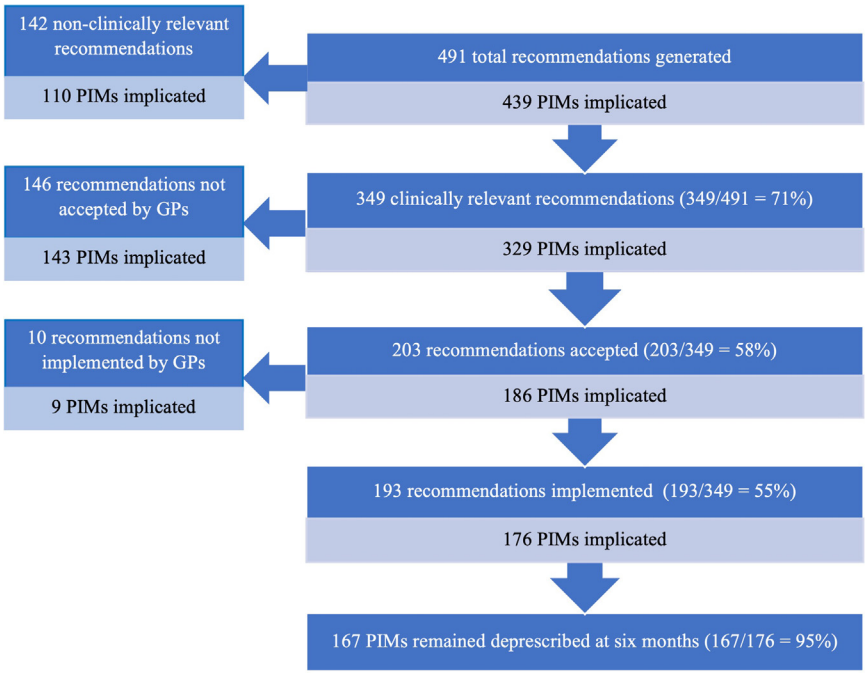


**Fig. 1.** Flowchart of the number of STOPPFrail recommendations and subsequent GP acceptance and implementation.

pharmacotherapy.[18-20] The following outcomes were determined pre and post medication review (immediately after the face-to-face meeting with GPs ± nursing staff) as well as at the 6-month post-medication review follow-up visit.

- Total number of medications (pre review, post review, and 6-month follow-up).
- Mean modified medication appropriateness index (MMAI) (pre review, post review, and 6-month follow-up).[21,22]
- Drug Burden Index (DBI) (pre review, post review, and 6-month follow-up).[23]
- Anticholinergic Cognitive Burden (ACB) (pre review, post review, and 6-month follow-up).[24]
- Number of falls in preceding 6 months (pre review and 6-month follow-up).
- EQ-5D-5L summary score (pre review and 6-month).
- EQ-5D-5L VAS (pre review and 6-month follow-up).
- Number of non-elective hospital admissions in preceding 6 months (pre review and 6-month follow-up).
- Number of emergency department visits in preceding 6 months (pre review and 6-month follow-up).
- Death (at 6-month follow-up only).

### *Statistical Analysis*

Standard descriptive statistics were used, that is, mean and standard deviation (SD) for parametric data and median and interquartile range (IQR) for non-parametric data in addition to (1) $\chi^2$ or Fisher's exact tests to compare categorical variable differences pre review, post review, and at follow-up; (2) the paired samples *t* test for normally distributed continuous variables; and (3) the Wilcoxon Signed-Rank test for non-parametric variables. Variables were checked for normal distribution by visually inspecting plotted histograms and the Kolmogorov-Smirnov normality test. Differences were considered statistically significant where $P < .05$. IBM SPSS version 28 was used to perform descriptive and inferential statistics. All participants' data were used in the calculation of outcome measures, given final valid, verifiable medication lists were available to the research team for those patients who died before the 6-month follow-up.[13]

## Results

### *Baseline Characteristics*

Between August 2021 and April 2023, 99 participants were recruited from 6 independent nursing homes across Cork, Ireland, with their baseline characteristics shown in Table 1.

### *STOPPFrail Deprescribing Recommendations*

At least one STOPPFrail-defined PIM was initially identified for 97 (98%) of the participants at baseline, of which 95 (94%) had a clinically relevant STOPPFrail-defined PIM that resulted in the generation of ≥1 recommendation to stop/dose reduce medications. The frequency, type, and subsequent implementation rate of recommendations made is shown in Table 2 and Table 3. Clinically relevant recommendations were generated from 19 of the 25 STOPPFrail criteria (76%). Clarify indication was the most prevalent type of clinically relevant STOPPFrail-defined PIM, followed by vitamin D. The classes of medications implicated most often by the clarify indication STOPPFrail criterion are shown in Supplementary Table 3.

Figure 1 shows the following:

(1) the total number of recommendations (n = 49) and PIMs (n = 439), and those that were clinically relevant (n = 349 recommendations and n = 329 PIMs)
(2) the number of clinically relevant recommendations accepted and implemented (n = 203 and n = 193) and the associated number of PIMs implicated (n = 186 and n = 176)
(3) the number of clinically relevant PIMs that remained deprescribed at 6 months (n = 167/176; 95%).

The 10 recommendations shown as not implemented in Figure 1 were from a single GP, where the recommendations were delivered remotely via teleconference. The other 4 GPs received the

**Table 1**
Baseline Characteristics of Study Participants (n = 99)

| | |
|---|---|
| Female n (%) | 76.7 (76) |
| Mean age (SD) | 86.24 (6.9) |
| Mean number of comorbidities (SD) | 14.9 (5.3) |
| Mean age-adjusted CCI[53] (SD) | 7.04 (2.1) |
| Mean number of regular medications (SD) | 10.9 (4.1) |
| Mean number of PRN medications (SD) | 5.4 (3.8) |
| Number of patients with hyperpolypharmacy (prescribed ≥10 regular medications) (%) | 59 (59.6) |
| Diagnoses (ICD-11 code), n (%) | |
| Dementia (6D80) | 64 (64.6) |
| Hypertension (BA00) | 53 (53.5) |
| Hypercholesterolemia (5C80) | 39 (39.4) |
| Stroke (8B20) | 36 (36.4) |
| Anxiety disorder (6B00) | 33 (33.3) |
| Atrial fibrillation (BC81.3) | 30 (30.3) |
| Depression (6A71) | 29 (29.3) |
| Osteoarthritis (FA0Z) | 26 (26.3) |
| Chronic kidney disease (GB61) | 22 (22.2) |
| Osteoporosis/osteopenia (FB83.1) | 22 (22.2) |
| Non-vertebral fracture (ND32) | 19 (19.2) |
| Diabetes (5A11) | 19 (19.2) |
| Hypothyroidism (5A00) | 19 (19.2) |
| Heart failure (BD10) | 18 (18.2) |
| GORD (DA22) | 16 (16.2) |
| Ischemic heart disease (BA52) | 14 (14.1) |
| COPD (CA22) | 10 (10.1) |
| Asthma (CA23) | 7 (7.10) |
| Myocardial infarction (BA41) | 7 (7.10) |

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; GORD, gastro-esophageal reflux disease; ICD, International Classification of Diseases.

recommendations in a face-to-face meeting and 100% of their accepted recommendations were implemented. The pharmacist required a mean (±SD) of 35 (±9) minutes to perform a review per patient and GPs required a mean (±SD) of 3.6 (±1.2) minutes to review recommendations generated per patient.

The 142 non-clinically relevant recommendations that implicate 110 PIMs are shown in Supplementary Table 4 with reasons for their lack of clinical relevance. Notably, most of these recommendations were due to medications without a clearly documented indication, which subsequently had their indication clarified on discussion with the GP (77.4%; 110 of 142). In total, 329 of 1589 (20.7%) medications at baseline were considered clinically relevant PIMs. The implementation of 193 clinically relevant recommendations by GPs resulted in 176 clinically relevant PIMs being discontinued (151 of 176, 85.8%) or dose reduced (25 of 176, 14.2%). Of the 349 clinically relevant recommendations, 300 pertained to regular medications (86%), of which 162 (54%) were implemented. The remaining 49 pertained to PRN medications (14%), of which 31 (63.3%) were implemented. Reasons for non-acceptance of clinically relevant recommendations are shown in Supplementary Table 5. At follow-up, only 9 PIMs had been restarted (5.1%), which are listed in Supplementary Table 6 with reasons for restarting.

### *Outcomes*

Measured outcomes are displayed in Table 4, which show differences between baseline, post-review, and at the 6-month follow-up visit. Table 4 shows that there were significant improvements in most of the outcomes post-review and at 6-month follow-up, except for mean monthly medication costs, which were €186.8 per patient pre review and €186.4 at 6-month follow-up ($P = .95$). No significant differences were found for the rates of falls, non-elective hospitalizations, emergency department visits, and QoL between baseline and 6-month follow-up ($P > .05$). Table 4 also shows that the number of PRN medications increased at 6-month follow-up compared with post review; this was an increase from 495 to 584 medications, whereas the number of regular medications decreased by 10 from 960 to 950 medications. Most (n = 78 of 89; 88%) of newly prescribed PRN medications were potentially to manage distressing end-of-life symptoms: (1) oral and subcutaneous morphine (n = 20); (2) subcutaneous midazolam (n = 19); (3) oral benzodiazepines and benzodiazepines derivatives (n = 18); (4) subcutaneous hyoscine butylbromide (n = 16); and (5) oral, subcutaneous, and transdermal hyoscine hydrobromide (n = 5).

**Table 2**
Frequency Summary of STOPPFrail Recommendations and STOPPFrail-Defined PIMs and Subsequent Acceptance

| | |
|---|---|
| Mean number of initial STOPPFrail Recommendations generated (SD) | 5.0 (3.0) |
| Mean number of clinically relevant STOPPFrail recommendations generated (SD) | 3.5 (2.5) |
| Median number of STOPPFrail-defined PIMs (IQR) | 4.0 (2.0–6.0) |
| Median number of clinically relevant STOPPFrail-defined PIMs (IQR) | 3.0 (2.0–5.0) |
| Median number of STOPPFrail recommendations accepted (IQR) | 2.0 (1.0–3.0) |
| Median number of STOPPFrail-defined PIMs reduced/stopped (IQR) | 1.0 (1.0–3.0) |

## Discussion

This study shows for the first time the potential impact of a pharmacist-led deprescribing intervention using STOPPFrail for frail older adults in nursing homes. The intervention significantly reduced the number of regularly prescribed medications, with 1 in 10 medications discontinued post review and the reduction remained significant at 6 months. Although the number of PRN medications was significantly higher than baseline at 6 months, this was expected and appropriate given the role of PRN medications to manage distressing end-of-life symptoms.[25] The decrease in the number of prescribed medications post review resulted in a significant 7.5% reduction in monthly medications costs; although not maintained at 6 months, this is also likely because of medication initiation for managing end-of-life symptoms. No significant differences were found for health-related outcomes, including unplanned hospital admissions, emergency department visits, falls, and QoL. Furthermore, no deaths were related to deprescribed medications, thus emphasizing the safety of pharmacist-led deprescribing and perhaps the unnecessary nature of the deprescribed medications from the outset. Therefore, this reaffirms previous research findings that deprescribing interventions to reduce PIMs in older adults can be conducted without compromising patient safety or well-being.[26]

There was a significant 3.6% post-review decrease in the MMAI, 9.7% decrease in the DBI, and 9.6% decrease in ACB, with changes for all remaining significant at 6 months. It was interesting to see that anticholinergic burden remained significantly lower at 6 months despite the initiation of medications with anticholinergic activity to manage end-of-life symptoms (eg, hyoscine hydrobromide, morphine, and benzodiazepines).[27] Anticholinergic and sedative burdens have been associated with an increase in falls, mortality, hip fractures, frailty, and reduced QoL.[28-31] The reduction of potentially unnecessary anticholinergic burden to preserve QoL in older adults is important, given the side-effect profile of anticholinergic medications.[32] However, because of this study's 6-month follow-up, the full benefits of reduced anticholinergic/sedative burden may not have been realized because studies that have determined the risk associated with anticholinergic/sedative burden typically involve a

**Table 3**
Frequency of the Categories of Clinically Relevant* STOPPFrail Recommendations and Subsequent Implementation Rate (n = 349 Total Recommendations)

| STOPPFrail Criterion | Frequency, n (%) | Implementation Rate Within Each STOPPFrail Criterion, n (%) |
|---|---|---|
| Any drug without a clear clinical indication | 103 (29.5) | 76 (73.8) |
| Vitamin D | 59 (16.9) | 31 (52.5) |
| Neuroleptic antipsychotics in dementia | 31 (8.9) | 6 (19.3) |
| Proton pump inhibitors: full therapeutic dose ≥8 weeks | 25 (7.2) | 16 (64.0) |
| Memantine in moderate to severe dementia | 25 (7.2) | 5 (20.0) |
| Oral nutritional supplements, unless malnutrition | 17 (4.9) | 9 (52.9) |
| Calcium supplements | 13 (3.7) | 7 (53.8) |
| Folic acid | 13 (3.7) | 8 (61.5) |
| Antihypertensives | 10 (2.9) | 7 (70.0) |
| Any drug for symptoms that have now resolved | 10 (2.9) | 5 (50.0) |
| Regular long-term oral corticosteroids ≥2 months | 8 (2.3) | 0 (0) |
| Lipid-lowering agents | 6 (1.7) | 4 (66.7) |
| Multivitamins | 6 (1.7) | 4 (66.7) |
| Anticholinergics/mirabegron | 6 (1.7) | 5 (83.3) |
| Antidiabetic agents | 5 (1.4) | 3 (60.0) |
| Any drug with persistent failure to take/tolerate | 5 (1.4) | 4 (80.0) |
| Antiresorptive agents | 5 (1.4) | 2 (40.0) |
| Antiplatelets for primary cardiovascular prevention | 1 (0.3) | 0 (0) |
| Regular long-term oral non-steroidal anti-inflammatory drugs ≥2 months | 1 (0.3) | 1 (100) |

*Clinically relevant: Recommendations that were deemed to be definite STOPPFrail-defined PIMs on discussion with patients' GPs (eg, a PIM that appeared to not have a clear clinical indication on initial review by the pharmacist, but whose indication was then clarified when the pharmacist met with the GP to discuss the recommendations).

minimum of 12 months' observation.[29,31,33] In addition, although significant, the relatively modest change in the ACB and DBI scores may not have been sufficient to realize a clinically significant effect. Boustani et al denote medications with a score of 2 more as having a clinically significant effect and this may present a target for magnitude of change required to elicit a clinically significant impact.[24]

**Table 4**
Comparison of Outcomes Pre and Post Review and at 6-Month Follow-Up

| Outcome | Baseline | Post-review | Mean or Median† Difference Between Baseline and Post Review (95% CI, *P*) | Six-month Follow-up | Mean or Median† Difference Between Baseline and Follow-Up (95% CI, *P*) | % Change From Baseline to Follow-Up |
|---|---|---|---|---|---|---|
| Mean total number of medications (SD) | 16.0 (6.1) | 14.6 (5.7) | −1.5* (1.1 to 1.8, $P < .001$) | 15.4 (5.5) | −0.6* (0.4 to 1.2, $P = .031$) | −3.8 |
| Mean number of regular medications (SD) | 10.9 (4.1) | 9.7 (3.7) | −1.2* (0.9 to 1.5, $P < .001$) | 9.6 (3.4) | −1.3* (0.8 to 1.7, $P < .001$) | −9.2 |
| Mean number of PRN medications (SD) | 5.4 (3.8) | 5.0 (3.6) | −0.4* (0.1 to 0.6, $P < .001$) | 5.9 (4.1) | +0.5* (0.1 to 0.8, $P = .01$) | +9.3 |
| Mean monthly medication cost in euro per patient (SD) [Sum total for all patients] | 186.8 (123.7) [18,479] | 172.7 (119.0) [17,092] | −14.1* (9.4 to 18.8, $P < .001$) | 186.4 (121.2) [18,454] | −0.4 (−10.6 to 11.3, $P = .95$) | −0.2 |
| Mean MMAI (SD) | 2.19 (0.73) | 2.11 (0.74) | −0.08* (0.03 to 0.13, $P < .001$) | 2.08 (0.71) | −0.10* (0.0 to 0.16, $P < .001$) | −4.6 |
| Median DBI (IQR) | 1.03 (0.5-2.0) | 0.93 (0.5-1.8) | −0.10*,† ($P < .001$) | 0.93 (0.5 -1.8) | −0.10*,† ($P < .001$) | −9.7 |
| Mean ACB (SD) | 4.27 (2.45) | 3.86 (2.54) | −0.41* (0.26 to 0.57, $P < .001$) | 3.94 (2.70) | −0.34* (−0.03 to 0.6, $P = .032$) | −8.0 |
| Number of patients with a fall (number of events) | 21 (36) | N/A | N/A | 17 (31) | N/A | −13.9 |
| Mean number of non-elective hospitalizations in the preceding 6 months per patient (SD) | 0.08 (0.27) | N/A | N/A | 0.07 (0.29) | −0.01 (−0.06 to 0.08, $P = .78$) | −12.5 |
| Number of patients who had at least 1 non-elective hospitalization) in the preceding 6 months | 8 (8) | N/A | N/A | 6 (7) | N/A | −12.5 |
| Mean number of emergency department visits in the preceding 6 months per patient (SD) | 0.01 (0.10) | N/A | N/A | 0.04 (0.24) | +0.03 (−0.08 to 0.02, $P = .26$) | +300.0 |
| Number of patients with at least 1 emergency department visit in the preceding 6 months | 1 (1) | N/A | N/A | 3 (4) | N/A | +300.0 |
| Mean EQ-5D-5L Summary score (SD) | 0.183 (0.286) | N/A | N/A | 0.159 (0.312) | −0.024 (0.01 to 0.06, $P = .18$) | −13.1 |
| Mean EQ-5D-5L VAS score (SD) | 60.3 (22.8) | N/A | N/A | 61.8 (19.9) | 1.53 (−5.59 to 2.52, $P = .45$) | 2.5 |
| Number of deaths | N/A | N/A | N/A | 29 | N/A | N/A |

*Paired *t* test or Wilcoxon signed-rank test $P < .05$.
†Median difference has been used rather than the mean difference.

Furthermore, for outcomes like QoL, which are influenced by a multitude of factors, changes in anticholinergic and sedative burdens alone may not have been sufficient to result in significant change.[34]

Because of incomplete documentation of medical histories, 77.4% of non-clinically relevant recommendations were for "clarify indication" STOPPFrail-defined. However, those "clarify indication" STOPPFrail-defined PIMs that were clinically relevant were the most frequent type of STOPPFrail recommendation (29.5%). This is similar to other studies that have examined the prevalence of STOPPFrail-defined PIMs. Although some studies have found that proton pump inhibitors were the most prevalent PIM (accounting for 18% to 40.8% of PIMs),[35,36] Chae et al and Heinrich et al both reported that "clarify indication" STOPPFrail-defined PIMs were the most prevalent type and accounted for 26.6% and 57.8% of PIMs, respectively.[37,38] This finding concerning documentation of indications is reinforced by a systematic review that examined data quality in electronic primary care records and found significant variability in diagnoses recording.[39] The use of paper-based medical records in some of this study's nursing homes may have further exacerbated the suboptimal documentation of diagnoses. Studies have shown that fully electronic health records are more complete and accurate than paper-based records.[40,41] Improved documentation of diagnoses through shared electronic medical records between GP practices and nursing homes could reduce the number of non-clinically relevant STOPPFrail recommendations made. As computerized decision support can be effective in reducing PIMs in older adults,[42] it may be worthwhile to integrate STOPPFrail into such software — ensuring accurate diagnoses information and meticulous design to minimize irrelevant recommendations.[43]

The discrepancy between the acceptance and implementation of 10 recommendations was the result of recommendations being delivered remotely via teleconference to the first GP. As a result, it may be prudent going forward to ensure, where possible, the delivery of recommendations in person to maximize implementation rates, as previous research has also suggested that face-to-face in-person recommendations are usually implemented at a higher rate than those provided remotely.[44,45] Furthermore, GPs unfamiliar with pharmacists working in general practice have also expressed a preference for pharmacists to be present on site.[46]

When compared with another STOPPFrail-led interventional medication review study by Curtin et al,[13] we had a lower recommendation implementation rate (55.3% vs 87.8%). However, our implementation rate is similar to a recent Australian study that integrated pharmacists into 7 nursing homes and showed prescribers accepted 55.5% of deprescribing recommendations.[47] There are several possible explanations for the difference between this study and the study by Curtin et al,[13] the first being the setting. The Curtin et al study was performed in an inpatient setting where access to specialist care and more intensive monitoring may provide a safer place to deprescribe medications.[13] Furthermore, recommendations were delivered by a specialist registrar in geriatric medicine, who worked clinically in that setting, whereas the recommendations in this study were delivered by a pharmacist not working routinely alongside the GPs. Previous research has shown that prescriber implementation of physician-delivered deprescribing recommendations was approximately double that of pharmacist-delivered deprescribing recommendations.[48] Third, the proportion of STOPPFrail recommendation types varied between the 2 studies. Antipsychotics, memantine, and oral corticosteroids accounted for n = 9 (4.4%), n = 4 (2%), and n = 0 (0%) recommendations given in Curtin et al,[13] compared with n = 31 (8.9%), n = 25 (7.2%), and n = 8 (2.3%) in this study. Antipsychotics, memantine, and oral corticosteroids had the lowest acceptance rates (≤40%) of all STOPPFrail recommendation types in this study, with GPs frequently citing fear of behavioral destabilization or that the medication was commenced by a specialist as barriers to deprescribing (Supplementary Table 5). This is in congruence with a recent qualitative evidence synthesis that concluded that beliefs about negative outcomes of deprescribing are an important factor when considering deprescribing medications in long-term care facilities.[49]

Our study has some limitations. First, this was a prospective non-randomized uncontrolled study, from which clear causal inferences cannot be made, so caution should be exercised in drawing definitive conclusions that the improved outcomes are the result of the intervention. In addition, the recruitment of a small convenience sample and the fact that the research team was local may have had a small influence on the acceptance of deprescribing recommendations due to social desirability bias. The intervention's impact on some of the measured outcomes was uncertain given low event numbers as a result of a small sample size (ie, falls, hospitalizations, and emergency department visits). Furthermore, because of the small sample size and measurement of several outcomes, this study was likely underpowered to detect differences in outcomes like falls, hospitalizations, emergency department visits, and QoL. In addition, the EQ-5D-5 L instrument was used to measure QoL, which is quite a brief instrument compared with other instruments.[50] However, there was already a burden on GPs and nursing staff in identifying eligible patients and consenting/assenting patients or an appropriate proxy; therefore, the EQ-5D-5L was a pragmatic choice to reduce their workload. In addition, the study's generalizability to other jurisdictions may be hindered because of differences in how medications are reviewed in nursing homes (eg, their frequency and whether pharmacist review is mandatory).

Importantly, the study has several relevant strengths. To the authors' knowledge, it is the first interventional study to apply STOPPFrail to nursing home residents and also the first to involve pharmacist-led application of STOPPFrail. The study was conducted with 5 GPs across 6 different nursing home facilities. Outcomes measured were informed by 3 published core outcome sets.[18-20] Using these in the study design facilitates future comparison and combination with other studies, and enhances the useability of the study information.[51] Furthermore, the study population consisted of a real-world representative sample of frail older adults, many of whom were multimorbid, prescribed hyperpolypharmacy (≥10 regular medications), and nearly two-thirds of study participants had a dementia diagnosis. Patients of this phenotype are typically underrepresented in research studies despite their increasing prevalence in practice and greater clinical need given the levels of disease and treatment burden they experience.[52]

## Conclusions and Implications

This study has shown that PIM prevalence is high for frail older adults in nursing homes, with nearly all participants prescribed at least 1 PIM. Incomplete documentation of medical comorbidities made reviews challenging and led to the generation of many recommendations asking for medications' indications. Nonetheless, pharmacist-led application of STOPPFrail was shown to be a potentially effective intervention in reducing 1 PIM on average per patient, significantly lowering medication costs (initially), improving medication appropriateness, as well as sedative and anticholinergic burdens, while not adversely affecting falls, hospitalizations, emergency department visits, or QoL. Enhanced awareness among the GP community of the STOPPFrail criteria and the integration of the criteria into GP and nursing home information technology systems would enhance medication rationalization in frail older adults in nursing homes. A randomized controlled trial of a longer duration of pharmacist-led application of the STOPPFrail criteria in nursing homes should be conducted to further build on the evidence generated by this study. Finally, policymakers need to consider the wider

integration of pharmacists into GP practices and nursing homes to aid in the optimization of medications of frail older adults.

## Disclosures

The authors declare no conflicts of interest.

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