

## OPEN

# Using Deprescribing Practices and the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions Criteria to Reduce Harm and Preventable Adverse Drug Events in Older Adults

Tara R. Earl, PhD, MSW, Nicole D. Katapodis, MPH,  
Stephanie R. Schneiderman, MPP, and Sarah J. Shoemaker-Hunt, PhD, PharmD

**Objectives:** Approximately 98% of older Americans are simultaneously taking 5—or more—medications to manage at least 2 chronic conditions. Polypharmacy and the use of potentially inappropriate medications (PIMs) are a concern for older adults because they pose a risk for adverse drug events (ADEs), which are associated with emergency department visits and hospitalizations and are an important patient safety priority. We sought to review the evidence of patient safety practices aimed at reducing preventable ADEs in older adults, specifically (i) deprescribing interventions to reduce polypharmacy and (ii) use of the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) to reduce PIMs.

**Methods:** We conducted a systematic review of literature published between 2008 and 2018 that studied examined the effect of these interventions to reduce preventable ADEs in older adults.

**Results:** Twenty-six studies and 1 systematic review were included (14 for deprescribing and 12 for STOPP and the systematic review). The deprescribing interventions involved decision support tools, educational interventions, and medication reviews by pharmacists and/or providers. Deprescribing studies primarily examined the effect of interventions on process outcomes and observed reductions in polypharmacy, often significantly. A few studies also examined clinical and economic outcomes. Studies of the use of the STOPP screening criteria most commonly reported changes in PIMs, as well as some economic outcomes.

**Conclusions:** Deprescribing interventions and interventions using the STOPP criteria seem effective in reducing polypharmacy and PIMs in older adults, respectively. Future research on the effectiveness of these approaches on clinical outcomes, the comparative effectiveness of different multicomponent interventions using these approaches, and how to most effectively implement them to improve uptake and evidence-based care is needed.

**Key Words:** patient safety, adverse drug events, deprescribing, STOPP criteria, older adults, patient harm

(*J Patient Saf* 2020;16: S23–S35)

From 2006 to 2016, the number of Americans 65 years and older increased from 37.2 million to 49.2 million (33% increase) and is projected to reach 98 million by 2060.<sup>1</sup> An estimated 98% of people 65 years and older deal with 2 or more chronic diseases and take

at least 5 prescription medications to treat or manage these conditions.<sup>2</sup> However, for older adults in particular, there are also associated risks. For instance, polypharmacy—taking multiple medications concurrently—and the use of potentially inappropriate medications (PIMs) can lead to adverse drug events (ADEs).<sup>3,4</sup> Broadly defined as an injury experienced by a patient that results from exposure to a medication (e.g., medication errors, adverse drug reactions, allergic reactions, or overdoses), ADEs have been associated with thousands of visits to the emergency department (ED), hospitalizations, and mortality.<sup>5</sup> However, up to half of identified ADEs are preventable,<sup>6</sup> and across all health care settings, they are one of the most common types of preventable adverse events.<sup>7</sup>

A range of interventions and approaches have been developed and studied to address preventable ADEs. This review focuses on 2 approaches in particular: (1) deprescribing to reduce polypharmacy and (2) the use of the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) criteria to reduce PIMs. Deprescribing involves reducing doses or stopping medications that are not useful or no longer needed to reduce polypharmacy, reduce harm, and improve health.<sup>8</sup> STOPP is a validated, evidence-based list of 80 criteria that are used to assess for potentially inappropriate prescribing (PIP) in older adults.<sup>9</sup>

## METHODS

For this review, we examined the question: *What is the effect of interventions for deprescribing and using the STOPP criteria on preventable ADEs for older adults?* It is important to note that deprescribing and the STOPP criteria are not themselves interventions: deprescribing is an approach, and the STOPP criteria are used in a screening tool that was part of the interventions reviewed.

First published in 2008 and revised in 2014, STOPP is often complimented with a companion tool, the Screening Tool to Alert to Right Treatment (START), to help facilitate medication reviews for multimorbid older adults. START is typically used in addition to STOPP, whereas STOPP is used both in tandem with START and as a standalone tool. In this review, the focus is on the STOPP criteria and START is referenced, as appropriate.<sup>10</sup>

## Literature Search Strategy

We searched 2 databases (CINAHL and MEDLINE) for peer-reviewed literature published from 2008 to 2018 using terms related to deprescribing and STOPP interventions, targeted at older adults and aimed at outcomes of interest (e.g., reduction of preventable ADEs, polypharmacy, or PIMs, and other relevant outcomes). See Supplemental Material for the search terms, <http://links.lww.com/JPS/A334>.

From the Abt Associates Inc, Rockville, Maryland.

Correspondence: Tara R. Earl, PhD, Abt Associates Inc, 2200 Century Parkway NE, Atlanta, GA 30345 (e-mail: Tara\_Earl@abtassoc.com).

The authors disclose no conflict of interest.

Supplemental digital contents are available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site ([www.journalpatientsafety.com](http://www.journalpatientsafety.com)).

Copyright © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

**Study Selection**

The initial search yielded 988 records across the 2 databases and an additional 9 studies identified from reference lists. After removing duplicates, 722 titles and abstracts were screened from which 194 studies were reviewed for full text (see the Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram in Fig. 1).

Studies were included if they were published in English, explicitly focused on deprescribing, polypharmacy, use of STOPP, and/or related interventions, targeted at older adults, and examined the effectiveness of these interventions on PIMs and preventable ADEs. Articles were excluded if (1) the study was out of scope, (2) the focus was on children or pediatric care, (3) not an intervention study (e.g., epidemiological studies, and commentaries), or (4) outcomes were not reported.

**RESULTS**

As shown in Table 1, 27 articles consisting of 26 studies and 1 systematic review met the inclusion criteria and evaluated interventions related to deprescribing (n = 14 studies: Table 2) or use

of the STOPP criteria to reduce PIMs (n = 12 studies, 1 systematic review; Tables 2, 3) in older adults.

**Deprescribing Interventions**

Within the deprescribing literature, 5 of the studies were randomized controlled trials (RCTs), 4 were feasibility studies, 2 were intervention studies, 1 was a cost study, 1 was a pilot study, and 1 was a hybrid implementation-effectiveness design. Most of the studies sample sizes were small, ranging from 40 to 490 participants. Studies evaluated a range of interventions, from protocols and clinical decision support tools to patient education and medication reviews. Most of the deprescribing interventions were delivered by pharmacists in a consultative role or in collaboration with providers, or conducted by providers themselves. Although the focus of this review was on older adults, only 3 interventions involved geriatricians. Most of the deprescribing interventions were in long-term care facilities, community pharmacies, inpatient hospital geriatric units, hospital outpatient departments, and hospitals during discharge. The studies varied widely in the outcomes examined, with the majority evaluating the effect of the interventions on process outcomes. Findings from the studies are presented

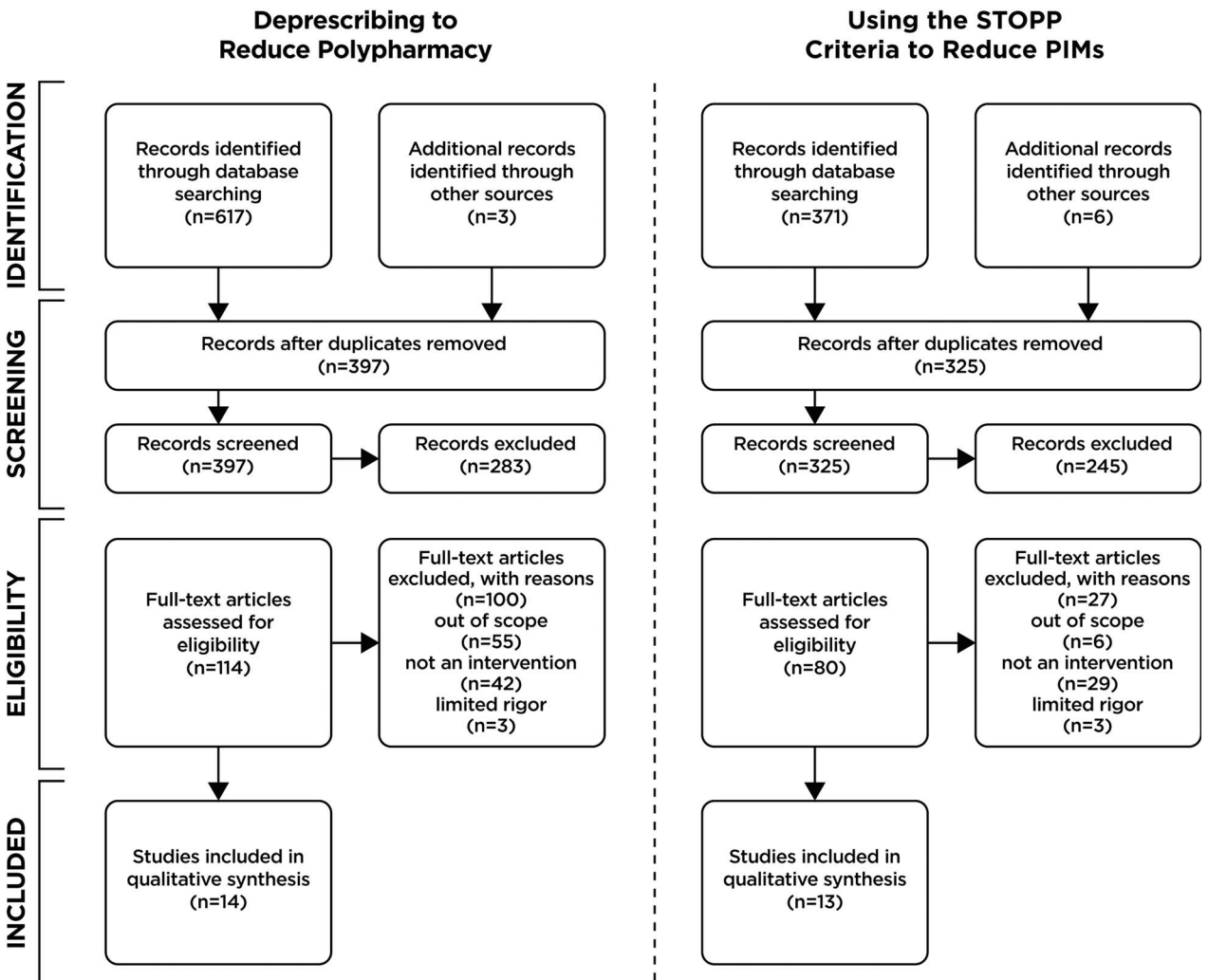


FIGURE 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram of selected literature.

**TABLE 1. Reducing ADEs in Older Adults, Deprescribing to Reduce Polypharmacy: Single Studies**

| Author, Year                             | Description of PSP  | Study Design; Sample Size; Patient Population   | Setting   | Outcomes: Benefits  |
|--|---|---|---|---|
| Ailabouni et al, 2019 <sup>11</sup>      | Pharmacist medication review with physician consult   | Design: feasibility study<br>Sample: n = 46<br>Patient population: adults 65 y and older living in residential care facilities and prescribed at least one anticholinergic or sedative medication   | Residential care facilities in New Zealand                        | Primary outcomes:<br>pharmacist-led intervention model led to implementation of 72% of deprescribing recommendations and a significant reduction in adverse drug reactions.<br>No change in cognition scores or reported quality of life.<br>Reduction in drug burden index scores, numbers of falls, and adverse drug reactions 6 mo after intervention.           |
| Ocampo et al, 2015 <sup>12</sup>         | Pharmacist medication review with an 18-mo follow-up  | Design: effectiveness-implementation hybrid design<br>Sample: n = 132<br>Patient population: community pharmacy patients, prescribed at least one medication, were offered the service when they sought advice, when a drug administration aid was required, or when the provision of service was requested during the 18-mo follow-up period | Community pharmacy in Spain                                       | Primary outcomes:<br>pharmacist-conducted medication review decreased the number of medications prescribed from 6.1 to 3.3, decreased observed hospitalizations, and decreased ED visits.<br>Intervention led to a reduction in the number of medicines used, reduction in hospitalizations, reduction in ED visits, and improvement in physical and mental health. |
| Chan et al, 2014 <sup>13</sup>           | Use of medication safety review clinics, including a team of research assistants, pharmacist, and geriatric clinician for solving drug-related problems       | Design: intervention study<br>Sample: n = 139<br>Patient population: outpatients 65 y or older who had been prescribed 8 or more chronic medications (28 d or longer) or had visited more than 3 physicians at 2 participating hospitals  | University hospital in Taiwan                                     | Implementation of medication safety review clinics led to a reduction in chronic medication prescribed and led to the improvement of good health status from 22% to 38% in 24 wk.<br>Intervention led to a reduction in chronic medication and improvement of good health status rating.  |
| Garfinkel and Mangin, 2010 <sup>14</sup> | Good-Palliative-Geriatric Practice algorithm was used to recommend drug discontinuations.   | Design: feasibility trial<br>Sample: 70 intervention adults referred by family physician or family for CGAs   | Day center for senior citizens and/or home care in Israel         | Primary outcome:<br>algorithm led to discontinuation recommendations for 58% of drugs.<br>Protocol indicated that discontinuation was recommended for 311 medications in 64 patients.   |
| Kojima et al, 2012 <sup>15</sup>         | Physician-led intervention using the Beers Criteria and the Epocrates online drug-drug interaction program to reduce polypharmacy in long-term care residents | Design: quality improvement cost study<br>Sample: n = 70<br>Patient population: patients 65 y or older with polypharmacy  | Skilled nursing facility and intermediate care facility in Hawaii | Primary outcome: physician-led, tool-assisted medication review led to a decrease in monthly medication costs by \$22 per resident and a decrease in nursing medication administration costs. Intervention led to a decrease in monthly medication costs and nursing medication administration costs.   |

(Continued next page)

TABLE 1. (Continued)

| Author, Year                       | Description of PSP   | Study Design; Sample Size; Patient Population   | Setting  | Outcomes; Benefits  |
|------------------------------------|--|---|--|---|
| Lenander et al, 2014 <sup>16</sup> | Pharmacist-led structured medication review involving a patient questionnaire and pharmacist consultation in primary care setting  | Design: RCT<br>Sample: 209 total patients; 107 intervention group; 102 control group<br>Patient population: Patients 65 y or older with 5 or more prescribed medications  | Primary care center in Sweden                      | Primary outcome: drug-related problems and number of drugs<br>Secondary outcome: health care utilization and self-rated health during 12-mo follow-up.<br>Pharmacist-led medication review led to a decrease in the number of drug-related problems from 1.63 to 1.31 at follow-up and a decrease in the number of drugs prescribed.<br>No significant difference in health care utilization, but a significant change in self-rated health |
| McKean et al, 2016 <sup>17</sup>   | Physician-led education intervention supported by listing clinical and medication data linked with clinical decision support tool  | Design: prospective pilot study<br>Sample: n = 50<br>Patient population: general medicine patients 65 y or older receiving 8 or more medications  | Tertiary teaching hospital in Australia            | Primary outcome: physician-led education intervention led to a decrease in the number of medications prescribed at discharge from 10 to 7.<br>Intervention led to decrease in the number of medications per patient.  |
| Martin et al, 2018 <sup>18</sup>   | Consumer based, pharmacist-led educational intervention using an educational deprescribing brochure in parallel to sending the physicians an evidence-based pharmaceutical opinion   | Design: cluster RCT<br>Sample: 489 patients: 219 intervention group; 218 control group<br>Patient population: patients 65 y or older, prescribed at least 1 of 4 prescribed peer criteria medications (sedative-hypnotics, first-generation antihistamines, glyburide, or nonsteroidal anti-inflammatory drugs) | Community pharmacies in Canada                     | Primary outcome: pharmacist-led education intervention led to a reduction in the number of inappropriate medications prescribed by 43% in the intervention group.<br>Intervention led to a decrease in number of inappropriate medications filled.  |
| Petersen et al, 2018 <sup>19</sup> | Use of a deprescribing intervention (Shed-Meds) to identify deprescribing targets and priorities, decide on appropriate deprescribing through patient interview, synthesize and communicate deprescribing recommendations to providers | Design: single-site feasibility study<br>Sample: 40 total patients; 20 intervention group; 20 control group<br>Patient population: Medicare beneficiaries 65 y or older receiving 5 or more prescribed medications and admitted to hospital with intended discharge to a skilled nursing facility               | Tertiary care hospital in Tennessee                | Primary outcome: deprescribing protocol led to a reduction in medications at discharge from 11.6 to 9.1.<br>Intervention decreased the mean number of medications prescribed at discharge and reduced medication burden in older adults.  |
| Pope et al, 2011 <sup>20</sup>     | Intervention included medical assessment by a geriatrician and medication review by a multidisciplinary expert panel   | Design: prospective RCT<br>Sample: 225 permanent patients; 110 intervention group; 115 control group<br>Patient population: permanent patients on continuing care wards   | 2 residential continuing care hospitals in Ireland | Primary outcome: geriatric specialist medication review led to a reduction in the number of medications from 11.65 to 11.09 in the intervention group.<br>Intervention did not lead to a significant difference in mortality or acute hospitalization outcomes.<br>Intervention led to a decrease in the total amount of medications in the intervention group.   |

|                                      |  |  |   |  |
|--------------------------------------|--|--|---|--|
| Tamura et al, 2011 <sup>21</sup>     | Geriatric fellow and faculty medication review using the Beers Criteria and Epocrates online drug interaction program  | Design: intervention study<br>Sample: n = 74<br>Patient population: residents with 9 or more medications   | Kuakini Geriatric Care, long-term care facility in Hawaii | Primary outcome: geriatrician-led medication review led to a decrease in the number of prescribed regular medications. Intervention led to a decrease in the number of regular prescribed medications, as-needed medications, and high-risk medications per patient. |
| Tannenbaum et al, 2014 <sup>22</sup> | Direct-to-consumer education intervention using an 8-page booklet based on self-efficacy and a self-assessment of benzodiazepine use in community pharmacies | Design: cluster RCT<br>Sample: 303 total patients: 148 intervention; 155 control group<br>Patient population: community pharmacy patients 65 y or older with a minimum of 5 active prescriptions, one being an active benzodiazepine prescription, dispensed for at least 3 consecutive mo | Community pharmacies in Canada                            | Primary outcome: direct-to-consumer pharmacist-led intervention led to a significant decrease in benzodiazepine use in the intervention group. Intervention did not lead to a change in clinical outcomes between groups.  |
| Wouters et al, 2017 <sup>23</sup>    | Multidisciplinary Multistep Medication Review  | Design: pragmatic cluster RCT<br>Sample: total 426; 233 intervention group; 193 control group<br>Patient population: nursing home residents  | Nursing home wards for long-term care in the Netherlands  | Intervention led to a significant decrease in benzodiazepine use in the intervention group. Intervention did not lead to a change in clinical outcomes between groups. Intervention led to a decrease in the number of inappropriate medications.                    |
| Vegge and Dyb, 2008 <sup>24</sup>    | Use of a clinical pharmacist for medication review   | Design: feasibility study<br>Sample: n = 205<br>Patient population: geriatric unit patients ages 59–95 y   | Geriatric unit in hospital in Norway                      | Intervention led to a decrease in the number of inappropriate medications.   |

TABLE 2. Reducing ADEs in Older Adults, Using the STOPP Criteria to Reduce PIMs: Single Studies

| Author, Year                       | Description of PSP   | Study Design; Sample Size; Patient Population   | Setting                              | Outcomes: Benefits  |
|------------------------------------|--|---|--------------------------------------|---|
| Campins et al, 2017 <sup>27</sup>  | Clinical pharmacist-led review based on algorithm and STOPP/START criteria   | Design: RCT. Sample: 251 control group; 252 intervention group<br>Patient population: community-dwelling older adults, 70 y and older, receiving 6 or more drugs and resident in municipalities of Martaro and Argentona, Spain   | Primary Health Care Centers in Spain | Primary outcomes: approximately 26.5% of prescriptions were rated as potentially inappropriate and 21.5% were changed (9.1% discontinuation, 6.9% dose adjustment, 3.2% substitution, and 2.2% new prescription). The mean number of prescriptions per patient was significantly lower in the intervention group at 3- and 6-mo follow-up.<br>Primary outcome: drug cessation or dosage decrease implemented in targeted PIMs. Secondary outcome: length of stay, in-hospital death, ED visits, and readmissions within 30 d of discharge.<br>1. Clinical relevance of the computer alert system alerts: 50% in the control group and 30% in the intervention group<br>2. Significant drug cessation and dosage decreases in intervention compared with control group at 48 h after alert: (30% and hospital discharge (20.8%). Average time (means) to analyze a patient file and complete the interventions was approximately 44.25 min in the intervention group.<br>3. No significant decrease in readmissions or inpatient death rates for intervention versus control group |
| Cossette et al, 2017 <sup>26</sup> | Use of a computer alert system-based pharmacist-physician intervention model to compare change in the use of PIMs with usual clinical care. A panel of experts used STOPP criteria to develop the model. | Design: RCT with block randomization. Patients were randomly assigned to control and intervention groups with a 1:1 ratio using block sizes of 2, 4, and 6, and stratification by hospital site.<br>Sample: 139 intervention (126 analyzed); 133 control group (128 analyzed).<br>Patient population: older adults, 65 y and older. With at least one geriatric-explicit criterion for PIMs | University hospital in Canada        |   |

|                                       |   |   |   |  |
|---------------------------------------|---|---|---|--|
| De Bock et al, 2018 <sup>29</sup>     | Medication review process that used STOPP to assess appropriateness of medication             | Design: RCT<br>Sample: 52 patients who were taking a median of 10 medications at the time of the study.<br>Patient population: older adults, 70 y or older, with an unplanned admission to the geriatric ward; took at least 5 drugs chronically; not hospitalized in the preceding 3 mo; and no documented cognitive impairments | University Hospital in Belgium (235 beds)   | Primary outcome: reduction in number of drug discrepancies and PIPs.<br>Secondary outcome: positive reports of satisfaction with services and opinions on interprofessional communication.<br>Medication reconciliation was time consuming and did not involve an integrated electronic patient file to record diagnoses, lab results, and medications<br>1. Time needed to review and make recommendations was considered reasonable<br>2. Successes for medication review: full access to patient file; relatively fast screening; identification of significant amount of PIMs; improvement in prescribing appropriateness; 20% of recommendations accepted<br>3. Barriers for medication review: scattered information; inefficient communication; lack of continuity of care. There were no service level agreements in place before intervention implementation. |
| Frankenthal et al, 2017 <sup>36</sup> | Review by study pharmacist using STOPP/START criteria at beginning of study and 6 mo later    | Design: retrospective cohort study<br>Sample: 160 intervention; 146 control group<br>Patient population: older adults, 65 y and older   | Chronic care geriatric facility in Israel   | Primary outcome: the prevalence of PIPs was significantly lower in the intervention group (33.3%) than in the control group (48.4%) at 24-mo follow-up ( $P = 0.02$ ).<br>Between baseline and 24 mo, there was a significant reduction in costs of medications in the intervention group (113 Israeli shekels [\$29] per patient per month, $P < 0.001$ ) but not in the control group.   |
| Gibert et al, 2018 <sup>28</sup>      | STOPP used during primary care general practitioner consultations on PIMs                     | Design: intervention study<br>Sample: 170 patients<br>Patient population: older adults, 75 y and older  | Primary care in Isere County, France  | Primary outcome: the number of PIMs decreased by 37.6% (n = 170 versus 106) with the application of STOPP criteria by general practitioners. This intervention reduced PIMs for 44.9% of patients (n = 44, $P < 0.001$ ).  |
| Hannou et al, 2017 <sup>31</sup>      | Clinical pharmacist medication reviews to reduce potentially inappropriate drug prescriptions | Design: prospective interventional study<br>Sample: 102 intervention; no control group<br>Patient population: older adults, 65 y and older, being admitted to an acute psychiatric geriatric facility   | Geriatric psychiatry admission unit of a university hospital in Switzerland (16 beds) | Primary outcome: global pharmacist intervention acceptance rate was 68% (78% for standard pharmacist recommendations [recs], and 47% for STOPP/START recs). Of 186 STOPP recs, 82 were accepted (44%).   |

(Continued next page)

TABLE 2. (Continued)

| Author, Year                          | Description of PSP  | Study Design; Sample Size; Patient Population   | Setting   | Outcomes: Benefits  |
|---------------------------------------|---|---|---|---|
| Ilic et al, 2015 <sup>32</sup>        | Using START/STOPP criteria to assess the appropriateness of prescribing before and 6 mo after the intervention implementation | Design: preobservation and postobservation trial that included a 3-mo prephase, a 1-mo intervention phase, a 6-mo postintervention phase, and a 3-mo period of repeated recording and analysis of prescribing practices.<br>Sample: 104 nursing home residents and 27 nursing home physicians; no control group.<br>Patient population: older adults, 65 y and older, who resided in the nursing home. Average age was 83 y | 20 nursing home facilities in Serbia                      | Primary outcome: 70 PIPs prescribed preintervention and 20 PIPs 6 mo after intervention (median, 3.5 [range 1–20] preintervention; median, 1.5 [range, 0–6] postintervention). The decrease in PIPs was significant ( $z = 2.823$ ; $P < 0.005$ ).  |
| Kiel and Phillips, 2017 <sup>30</sup> | Clinical pharmacist comprehensive medication reviews using START/STOPP criteria   | Design: prospective cohort with post hoc analysis<br>Sample: 26 intervention and 26 control group participants<br>Patient population: older adults, 65 y and older, taking at least 5 prescription medications  | Primary care clinic in Michigan                           | Primary outcome: difference in number of medication-related problems, as defined by the START and STOPP criteria. The acceptance rate for recommendations on STOPP/START med problems was 35% (n = 17).   |
| Kimura et al, 2017 <sup>38</sup>      | Clinical pharmacist medication reviews using STOPP-2 criteria to reduce PIMs  | Design: prospective observational study<br>Sample: 822 in the intervention group; no control group<br>Patient population: older adults, 65 y and older, who were newly admitted into inpatient care and prescribed more than one prescription medication  | University hospital in Japan                              | Primary outcomes: number of PIMs was 651; of these, it was recommended to doctors that 310 (47.6%) be changed, and 292 (44.9%) were discontinued/changed after the pharmacist's assessment. Acceptance rate of pharmacists' recommendations was 94.2%. The mean time for pharmacist's assessment was 6.2 ± 3.1 min per patient.   |
| O'Connor et al, 2016 <sup>35</sup>    | Using START/STOPP criteria to help attending physicians identify PIMs   | Design: single-blinded, clustered RCT<br>Sample: 732 in the intervention group; no control group<br>Patient population: consecutively admitted adults 65 y and older  | Tertiary referral hospital in Ireland                     | Primary outcome: when STOPP/START was applied, 451 recommendations were made on 233 participants (64.7%). Of these, 292 were STOPP recommendations; attending doctors accepted and implemented 237 STOPP recs (81.2%). Application of STOPP/START criteria resulted in significant reductions in adverse drug reaction incidence and medication costs in acutely ill older adults but did not affect median length of stay. |
| Tamura et al, 2011 <sup>21</sup>      | Geriatric fellow and faculty medication review using the Beers Criteria and Epocrates online drug interaction program         | Design: intervention study<br>Sample: n = 74<br>Patient population: residents with 9 or more medications  | Kuakini Geriatric Care, long-term care facility in Hawaii | Primary outcome: geriatrician-led medication review led to a decrease in the number of prescribed regular medications. Intervention led to a decrease in the number of regular prescribed medications, as-needed medications, and high-risk medications per patient.  |



|                                   |  |   |   |  |
|-----------------------------------|--|---|---|--|
| Price et al, 2017 <sup>37</sup>   | Using STOPP guidelines as part of an electronic medical records clinical decision support system to identify PIPs for older adults | Design: mixed-method, pragmatic, cluster RCT<br>Sample: 44,290 in the intervention group; 37,615 in the control group<br>Patient population: consecutively admitted adults 65 y and older | Primary care offices  | Primary outcome: regression analysis showed no significant difference in change of recorded PIPs in the control versus intervention group ( $P = 0.80$ ).<br>Barriers to implementation: the STOPP rules were presented in a different location from simple drug alerts; the guideline tool did not have a clear way to support users in prioritizing suggestions and alerts as recommended. |
| Unutmaz et al, 2018 <sup>34</sup> | CGA complemented by STOPP/START criteria   | Design: retrospective assessment of before and after intervention<br>Sample: 1579 patients<br>Patient population: older adults, 65 y and older  | Geriatrics outpatient clinic of tertiary hospital in Turkey | Primary outcome: mean number of drugs decreased from $5.3 \pm 3.4$ before CGA to $4.6 \pm 2.5$ ( $P < 0.05$ ).<br>After CGA, monthly saved total per capita cost of PIMs was \$12.8 and monthly increased total per capita cost of PPOs was \$5.6.   |

by clinical, process, and economic outcomes, and then by type of intervention within each of these categories of outcomes.

### Clinical Outcomes

Only 2 studies evaluated the effect of deprescribing interventions on clinical outcomes, and the outcomes varied with the specific interventions. Ocampo et al<sup>12</sup> found that a pharmacist-led medication review with an 18-month follow-up period in community pharmacies identified 408 negative uncontrolled health problems related to prescriptions and resolved 393 of these problems, resulting in a significant decrease in hospitalizations ( $P = 0.039$ ) and ED visits ( $P = 0.001$ ). Physical and mental health summary scales increased from 65.8 to 82.7 ( $P < 0.0001$ ) and 66.2 to 81.1 ( $P < 0.0001$ ), respectively, whereas the number of patients who were not adherent decreased from 68 to 1 ( $P < 0.0001$ ). Others reported that discontinuing multiple medications simultaneously was significantly associated with reductions in both the number of reported falls and frailty scores for older adults.<sup>11</sup> These researchers also examined collaborative medication reviews with general practitioners of patients 65 years and older in a residential care facility. Their study also noted a significant reduction in drug burden index scores by 0.34 ( $P < 0.001$ ), reflecting a decrease in the cumulative exposure to the medications, and the number of falls and frailty measured using the Edmonton frailty scale dropped by a mean difference of 1.35 ( $P < 0.05$ ). In addition, the number of adverse drug reactions decreased by 4.24 ( $P < 0.05$ ) after 6 months.<sup>11</sup> However, in a multidisciplinary geriatric specialist medication review panel intervention including registrars in geriatric medicine, hospital pharmacists, and geriatric nurse practitioners, no significant difference was found in mortality ( $P = 0.226$ ) or frequency of hospital transfers ( $P = 0.213$ ) between intervention and regular care groups.<sup>20</sup> Wouters et al<sup>23</sup> sought to improve prescribing in nursing home residents by implementing the Multidisciplinary Multistep Medication Review. The randomized control trial took place on nursing home wards and consisted of an evaluation of the patient’s perspective, health history, and use of medications; a meeting between the physician and pharmacist; and the execution of medication changes. In the 4 months after the baseline assessment, there was no deterioration of clinical outcomes, such as neuropsychiatric symptoms, cognitive function, or quality of life, in either group.

### Process Outcomes

Many deprescribing studies focused on process-related outcomes such as number of medications prescribed or polypharmacy, which is expected to lead to clinical improvements or a reduction in ADEs. Findings from these studies are presented by the types of interventions.

### Protocols, Algorithms, and Clinical Decision Support Systems

Among the 3 studies focusing on the use of protocols, algorithms, and clinical decision support systems to promote deprescribing, 2 studies found significant decreases in the number of medications prescribed. Petersen et al<sup>19</sup> found that a patient-centered deprescribing protocol called Shed-MEDS, implemented in 4 phases: (1) medication history and list confirmed, (2) evaluate medication for deprescribing, (3) decide with the patient, and (4) synthesize and communicate recommendations among Medicare beneficiaries prescribed 5 or more medications, significantly reduced the mean number of prescribed medications from 11.6 to 9.1 ( $P = 0.032$ ) for those with whom the protocol was used. Garfinkel and Mangin<sup>14</sup> worked with elderly patients in Israel to implement the Good Palliative-Geriatric Practice algorithm, an evidence-based

**TABLE 3.** Reducing ADEs in Older Adults, Using the STOPP Criteria to Reduce PIMs: Systematic Reviews

| Author, Year (Reference)              | Description of PSP  | Setting/s, Population/s              | Summary of Systematic Review Findings  |
|---------------------------------------|---|--------------------------------------|--|
| Hill-Taylor et al, 2013 <sup>25</sup> | Assessment of effectiveness of STOPP/START criteria on prescribing quality and clinical, humanistic, and economic outcomes in adults 65 y and older (updating a 2013 review). | Acute care admission, long-term care | Primary outcomes: all follow-up rates showed improvement in PIM rates in both the intervention and control groups. At every time point in every study, the intervention demonstrated some success, with the intervention PIM rates being lower than control rates. Three studies reported a significant and sustained drop in PPOs in the intervention group. There was also a reduction in PPOs in all control groups on follow-up. 2 studies reported cost outcomes and found cost efficiencies in medication choices in the intervention group compared with the control group. |

flowchart for medication discontinuation, which recommended discontinuing a total of 311 medications for 64 patients. McKean et al<sup>17</sup> worked with patients 65 or older taking 8 or more medications to implement an intervention consisting of a formal medication review among rounding clinicians, followed by receipt of a paper-based or computerized form listing clinical and medication data linked with a 5-step clinical decision support (CDS) tool to determine medications eligible for discontinuation. The intervention led to a 34.3% decrease in non-PRN medications, a small but non-significant decrease in PRN (as needed) medications and a significant decrease in the number of medications per patient at discharge compared with at admission (median change, 7 versus 10 medications;  $P < 0.001$ ).

### Pharmacist-Led Medication Review Interventions

Two pharmacist-led medication review interventions across a number of settings involved deprescribing. Lenander et al.<sup>16</sup> found that a pharmacist-led medication review in a primary care setting targeting patients 65 years and older with 5 or more different medications led to a decrease in drug-related problems. Using American Geriatric Society's Beers Criteria, after 12 months, drug-related problems decreased for the intervention group from 1.73 to 1.31 ( $P < 0.05$ ). There was also a larger reduction in the number of medications prescribed in the intervention group ( $P < 0.046$ ). Veggeland and Dyb<sup>24</sup> observed the effect of adding a clinical pharmacist performing medication reviews to a geriatric care hospital team. They found that it led to changes including discontinuation of medications, dose reduction, or decision to adjust medications at a later stage of hospitalization.

### Clinician-Led Medication Reviews

We found one study of a clinician-led medication review. Tamura et al<sup>21</sup> worked with geriatric medicine fellows in a long-term care facility to implement a medication review using the updated Beers Criteria for patients (average age, 83 years) with 9 or more medications, leading to an average reduction of total medications from 16.64 to 15.53 ( $P < 0.001$ ), average number of scheduled medications from 11.3 to 10.99 ( $P < 0.001$ ), average number of PRN medications from 5.33 to 4.56 ( $P < 0.001$ ), and average number of high-risk medications from 5.33 to 4.56 ( $P < 0.001$ ), which were statistically significant but may be not be clinically significant.

### Pharmacist and Clinician Medication Reviews

Two studies combined pharmacist and clinician medication review. Chan and colleagues<sup>13</sup> examined the effectiveness of

a medications safety review clinic for geriatric outpatients 65 years or older who were prescribed 8 or more chronic medications or who had visited at least 3 different physicians at the 2 participating hospitals within 3 months. Four medication review sessions were performed by 2 research assistants, 1 clinical pharmacist, and 1 geriatrician, leading to a mean decrease in chronic medications from 9.0 to 8.6 ( $P < 0.05$ ). In addition to what was previously discussed, the RCT of the Multidisciplinary Multistep Medication Review intervention by Wouters and colleagues<sup>23</sup> found that successful discontinuation without relapse or severe withdrawal symptoms of at least one inappropriate medication was greater for nursing home residents in the intervention group compared with those who were not exposed to the intervention (i.e., the control group; 39.1% versus 29.5%; 95% confidence interval [CI], 1.02–1.75).

### Patient Educational Interventions

Educational interventions for patients have also been used to reduce polypharmacy. Tannenbaum et al<sup>22</sup> found that a direct-to-consumer educational intervention using an 8-page booklet to describe the risks of benzodiazepine use and a stepwise tapering protocol led to a 27% discontinuation of benzodiazepines among community pharmacy patients 65 years or older in the intervention group compared with 5% in the control group (95% CI, 14%–32%) at 6 months after the intervention. Martin et al<sup>18</sup> studied a consumer-based educational intervention led by pharmacists in community pharmacies providing an educational brochure to patients 65 years and older. The study resulted in 43% of the intervention group no longer filling inappropriate medications compared with 12% of the control group (95% CI, 23%–38%).

### Economic Outcomes

One study assessed the economic impact of a deprescribing intervention. Kojima et al<sup>15</sup> evaluated the effect on medication costs of a physician intervention using 2 tools: the Beers Criteria and the Epocrates online drug-drug interaction program to reduce polypharmacy among long-term care residents. Findings showed that residents undergoing the intervention had significantly lower health care costs after the intervention. Average monthly medication costs declined from \$874 to \$843 ( $P < 0.0001$ ), scheduled medication costs from \$814 to \$801 ( $P = 0.007$ ), PRN medication costs from \$60 to \$42 ( $P < 0.0001$ ), and nursing medication administration costs from \$483 to \$461 ( $P < 0.0001$ ).

## STOPP Interventions

All of the 12 studies in this review used the STOPP criteria in screening followed by steps for making, accepting, or rejecting recommendations generated. One article was a systematic review with meta-analysis and narrative summary. Among the individual studies, 5 of the studies were RCTs, 2 were intervention studies, 1 was a retrospective cohort study, 1 was a retrospective before and after design, 1 was a prospective cohort study, and 2 were observational studies. Most of the studies sample sizes were small, ranging from 52 to 1579 participants. In the studies, most of the interventions integrated STOPP criteria into medication reviews as part of a usual checkups and geriatric assessments. The STOPP interventions were delivered by pharmacists or providers during medication reviews. All 13 studies focused on patients 65 years and older, whereas one of those studies restricted inclusion to patients 75 years and older. The study settings included inpatient, long-term care settings, and primary care. The 12 single studies that evaluated the STOPP criteria examined clinical, process, and economic outcomes.

## Clinical Outcomes

One single study and the systematic review examined clinical outcomes. In the systematic review, Hill-Taylor et al<sup>25</sup> found that one study showed an association between a STOPP/START intervention and improvement in medication appropriateness, as measured by the Medication Appropriateness Index (absolute risk reduction of 35.7%) and the Assessment of Underutilization index (absolute risk reduction of 21.2%). No significant findings were noted in the relationship between STOPP/START interventions and reduction of falls or all-cause mortality. No studies within the systematic review measured quality of life outcomes.

Cossette et al<sup>26</sup> looked at readmissions and inpatient death rates but found no significant decrease between the intervention and control groups.

## Process Outcomes

Seven studies examined the use of the STOPP criteria on prescribing practices. Campins et al<sup>27</sup> reported that the STOPP tool used by pharmacists found that 27% of the intervention population's (n = 252) prescriptions were potentially inappropriate. Most of these prescriptions were then changed as follows: 43% were discontinued, 33% received a dose adjustment, 14% were substituted for more appropriate medications, and 10% received a new prescription. Similarly, Gibert et al<sup>28</sup> used STOPP in primary care consultations in France, resulting in a 38% reduction in the number of PIMs (n = 170 versus 106) across about 45% of patients (n = 44;  $P < 0.001$ ). Also, De Bock et al<sup>29</sup> used STOPP as part of a medication review and found that 20% of recommendations were accepted. Kiel and Phillips<sup>30</sup> used the STOPP/START criteria in a pharmacist-led medication review with an acceptance rate of 35%.

Cossette et al<sup>26</sup> used STOPP to develop a computer alert system as part of a pharmacist-physician intervention to reduce PIMs. The intervention group saw a significant drug cessation and dosage decrease at 48 hours after alert (30%) and hospital discharge (20.8%) compared with the control group.

Hannou et al<sup>31</sup> introduced a part-time ward-based clinical pharmacist to a psychiatric unit's multidisciplinary team and screened prescriptions for potentially inappropriate drug prescribing using the STOPP/START criteria. The intervention was measured by the acceptance rate of pharmacist interventions. The global pharmacist intervention acceptance rate was 68%, and that based on STOPP/START was 47%. When 2 STOPP criteria (the prescribing of benzodiazepines and the prescribing of neuroleptic drugs to

patients who had fallen in the last 3 months) were removed from the analysis, the acceptance rate for STOPP/START-based pharmacist interventions increased to 67%.

In the study by Ilic et al,<sup>32</sup> an educational intervention targeting both physicians and nursing home residents provided information on the START/STOPP and Beers Criteria, as well as adherence, adverse drug reactions, and drug-drug interactions. According to the STOPP criteria, 70 medications were inappropriately prescribed before the intervention and 20 medications after 6 months. The median number of inappropriately prescribed medications according to the STOPP criteria before education was 3.5 (range, 1.0–20.0), and the median number after education was 1.5 (range, 0.0–6.0;  $z = 2.823$ ;  $P < 0.005$ ).<sup>33</sup>

## Economic Outcomes

Studies of using STOPP criteria examined economic outcomes. After implementing a comprehensive geriatric assessment (CGA) that included the STOPP criteria, the findings reported by Unutmaz et al<sup>34</sup> suggested that by using the tool to assess PIMs, medication costs were reduced by approximately \$13 a month, per patient. In addition to the economic savings of not having patients pay for medications that they did not need, the tool was associated with savings of \$5.68 per month per patient to improve errors of omission like potentially prescribing omissions (PPOs) where medications that may be more appropriate are not prescribed. O'Connor et al<sup>35</sup> also reported significant reductions in medication costs. At discharge, median medication cost was significantly lower in the intervention group than in the control group ( $P < 0.001$ ). Frankenthal et al<sup>36</sup> found that when pharmacists and prescribing physicians discussed medication reviews rather than communicating in writing, the reviews were more effective. Furthermore, the authors reported that the costs of medications were significantly lower in the intervention group than in the control group ( $P < 0.001$ ) at the 24-month follow-up. Hill-Taylor et al<sup>25</sup> reviewed 3 studies on the direct costs of PIPs and PPOs that found the cost associated with PIP and PPO ranged from €188 to €318 per patient per year.

## DISCUSSION

This review contributes to the evidence of effectiveness on interventions using deprescribing and STOPP screening criteria to address preventable ADEs in older adults. The deprescribing interventions included in this review used protocols, algorithms, CDS tools, educational interventions, and most commonly medication reviews conducted either by pharmacists, providers, or a combination thereof. Deprescribing interventions, commonly part of medication reviews if not within protocols or decision tools, were often found to significantly reduce polypharmacy in the studies we reviewed. Medication reviews involving both pharmacists and clinicians effectively decreased medication use in 2 studies. The STOPP screening criteria were used within interventions to identify PIMs and make recommendations or changes accordingly. Many of the interventions using the STOPP criteria—regardless of who or how the criteria were used—decreased PIMs, often significantly. Although studies in this review observed some statistically significant differences in polypharmacy or PIMs, given these are process or intermediate outcomes, it is unclear whether these differences were always going to be clinically significant. In addition, the heterogeneity of the often multicomponent interventions in which deprescribing or STOPP criteria were used as well as the range of health care settings and professionals conducting the interventions limited the extent to which findings could be synthesized across studies. The strength of evidence was further limited by the study designs and often small

sample sizes, especially within deprescribing interventions, whereas the STOPP criteria interventions included a few studies with observations in larger sample sizes.

This review also points to several gaps and future directions for research and interventions to advance the field. Recommendations for future deprescribing interventions and studies could factor in perspectives and preferences of patients during the deprescribing process<sup>11</sup>; develop protocols that target multiple rather than specific medications and/or diseases<sup>11</sup>; and, with the expanding role of pharmacists, focus further on the involvement of community pharmacists,<sup>14</sup> especially with pharmacists expanding scopes of practice and the ability to establish collaborative practice agreements between pharmacists and providers. More rigorous, long-term studies with larger sample sizes are needed to further understand deprescribing interventions long-term effects in reducing polypharmacy and preventable ADEs.<sup>12,17,19</sup> Studies would also be improved if they examined clinical outcomes, not just process or intermediate outcomes. Comparative effectiveness study of different deprescribing interventions, whether single or multi-component would also be beneficial to the field.

Recommendations for future research related to the STOPP criteria include embedding it within CDS tools in electronic health records, as a means to improve efficiency during the screening process.<sup>37</sup> Combining use of the STOPP criteria with, or comparing it with, other screening tools such as the Beers Criteria or the Medication Appropriateness Index could improve clinical appropriateness.<sup>38</sup> Unutmaz et al<sup>34</sup> have recommended that future research examine the long-term clinical effects of using the STOPP criteria to reduce inappropriate medications and reduce ADEs.

Regardless of the type of intervention, an essential component to ensure that any evidence-based approaches or criteria effectively change prescribing practices and that key outcomes can be the implementation approaches or strategies that are used.<sup>39,40</sup> Although this review included one study that was an implementation-effectiveness design study, there is vast opportunity to expand the field's understanding of how to effectively implement these interventions.<sup>41</sup> Further systematic reviews and meta-analyses, where feasible, for other patient safety practices addressing preventable ADEs in older adults would also be valuable to the field.

## CONCLUSIONS

This review offers additional insights into the effectiveness of deprescribing interventions and interventions involving the STOPP criteria on key process outcomes, as well as some clinical and economic outcomes. It also points to opportunities for future research to understand effective interventions to reduce the harms of preventable ADEs in older adults.

## ACKNOWLEDGMENT

*This work was funded by the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services (contract numbers HHSP2332015000131 and HHSP23337002T).*

## REFERENCES

- Administration for Community Living. *2017 Profile of Older Adults*. Washington, DC: U.S. Department of Health and Human Services, Administration for Community Living; 2019. Available at: <https://acl.gov/sites/default/files/Aging%20and%20Disability%20in%20America/2017OlderAmericansProfile.pdf>. Accessed November 7, 2019.
- National Center for Health Statistics. *Health, United States, 2016: With Chartbook on Long-term Trends in Health*. Hyattsville, MD: National Center for Health Statistics (US); 2017.
- Classen DC, Jaser L, Budnitz DS. Adverse drug events among hospitalized Medicare patients: epidemiology and national estimates from a new approach to surveillance. *Jt Comm J Qual Patient Saf*. 2010;36:12–21.
- Cousins D, Rosario C, Scarpello J. Insulin, hospitals and harm: a review of patient safety incidents reported to the National Patient Safety Agency. *Clin Med (Lond)*. 2011;11:28–30.
- Agency for Healthcare Research and Quality. Patient Safety Primer: Medication Errors and Adverse Drug Events [PS Net website]. September 2019. Available at: <https://psnet.ahrq.gov/primer/medication-errors-and-adverse-drug-events>. Accessed November 7, 2019.
- Office of Disease Prevention and Health Promotion. *National Action Plan for Adverse Drug Event Prevention*. Washington, DC: U.S. Department of Health and Human Services; 2014. Available at: <https://health.gov/hcq/pdfs/ADE-Action-Plan-508c.pdf>. Accessed November 7, 2019.
- Institute of Medicine Committee on Quality of Health Care in A. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academies Press. Copyright 2001 by the National Academy of Sciences. All rights reserved, 2001.
- Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med*. 2015;175:827–834.
- Gallagher P, Ryan C, Byrne S, et al. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) consensus validation. *Int J Clin Pharmacol*. 2008;46:72–83.
- STOPP/START criteria for potentially inappropriate medications/potential prescribing omissions in older people: origin and progress. *Expert Rev Clin Pharmacol*. 2020;13:15–22.
- Ailabouni N, Mangin D, Nishtala PS. DEFEAT-polypharmacy: deprescribing anticholinergic and sedative medicines feasibility trial in residential aged care facilities. *Int J Clin Pharmacol*. 2019;41:167–178.
- Ocampo CC, Garcia-Cardenas V, Martinez-Martinez F, et al. Implementation of medication review with follow-up in a Spanish community pharmacy and its achieved outcomes. *Int J Clin Pharmacol*. 2015;37:931–940.
- Chan DC, Chen JH, Wen CJ, et al. Effectiveness of the medication safety review clinics for older adults prescribed multiple medications. *J Formos Med Assoc*. 2014;113:106–113.
- Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy. *Arch Intern Med*. 2010;170:1648–1654.
- Kojima G, Bell C, Tamura B, et al. Reducing cost by reducing polypharmacy: the polypharmacy outcomes project. *J Am Med Dir Assoc*. 2012;13:818.e11–818.e15.
- Lenander C, Elfsson B, Danielsson B, et al. Effects of a pharmacist-led structured medication review in primary care on drug-related problems and hospital admission rates: a randomized controlled trial. *Scand J Prim Health Care*. 2014;32:180–186.
- McKean M, Pillans P, Scott IA. A medication review and deprescribing method for hospitalised older patients receiving multiple medications. *Intern Med J*. 2016;46:35–42.
- Martin P, Tamblyn R, Benedetti A, et al. Effect of a pharmacist-led educational intervention on inappropriate medication prescriptions in older adults: the D-PRESCRIBE randomized clinical trial. *JAMA*. 2018;320:1889–1898.
- Petersen AW, Shah AS, Simmons SF, et al. Shed-MEDS: pilot of a patient-centered deprescribing framework reduces medications in hospitalized older adults being transferred to inpatient postacute care. *Ther Adv Drug Saf*. 2018;9:523–533.
- Pope G, Wall N, Peters CM, et al. Specialist medication review does not benefit short-term outcomes and net costs in continuing-care patients. *Age Ageing*. 2011;40:307–312.

21. Tamura BK, Bell CL, Lubimir K, et al. Physician intervention for medication reduction in a nursing home: the polypharmacy outcomes project. *J Am Med Dir Assoc.* 2011;12:326–330.
22. Tannenbaum C, Martin P, Tamblin R, et al. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. *JAMA Intern Med.* 2014;174:890–898.
23. Wouters H, Scheper J, Koning H, et al. Discontinuing inappropriate medication use in nursing home residents: a cluster randomized controlled trial. *Ann Intern Med.* 2017;167:609–617.
24. Veggeland T, Dyb S. The contribution of a clinical pharmacist to the improvement of medication at a geriatric hospital unit in Norway. *Pharm Pract (Granada).* 2008;6:20–24.
25. Hill-Taylor B, Sketris I, Hayden J, et al. Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. *J Clin Pharm Ther.* 2013;38:360–372.
26. Cossette B, Ethier JF, Joly-Mischlich T, et al. Reduction in targeted potentially inappropriate medication use in elderly inpatients: a pragmatic randomized controlled trial. *Eur J Clin Pharmacol.* 2017;73:1237–1245.
27. Campins L, Serra-Prat M, Gozalo I, et al. Randomized controlled trial of an intervention to improve drug appropriateness in community-dwelling polymedicated elderly people. *Fam Pract.* 2017;34:36–42.
28. Gibert P, Cabaret M, Moulis M, et al. Optimizing medication use in elderly people in primary care: impact of STOPP criteria on inappropriate prescriptions. *Arch Gerontol Geriatr.* 2018;75:16–19.
29. De Bock L, Tommelein E, Baekelandt H, et al. The introduction of a full medication review process in a local hospital: successes and barriers of a pilot project in the geriatric ward. *Pharmacy (Basel).* 2018;6.
30. Kiel WJ, Phillips SW. Impact of pharmacist-conducted comprehensive medication reviews for older adult patients to reduce medication related problems. *Pharmacy (Basel).* 2017;6.
31. Hannou S, Voirol P, Pannatier A, et al. Pharmacist intervention acceptance for the reduction of potentially inappropriate drug prescribing in acute psychiatry. *Int J Clin Pharmacol.* 2017;39:1228–1236.
32. American Geriatrics Society. American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2015;63:2227–2246.
33. Ilic D, Bukumiric Z, Jankovic S. Impact of educational intervention on prescribing inappropriate medication to elderly nursing homes residents. *Srp Arh Celok Lek.* 2015;143(3–4):174–179.
34. Unutmaz GD, Soysal P, Tuven B, et al. Costs of medication in older patients: before and after comprehensive geriatric assessment. *Clin Interv Aging.* 2018;13:607–613.
35. O'Connor MN, O'Sullivan D, Gallagher PF, et al. Prevention of hospital-acquired adverse drug reactions in older people using screening tool of older Persons' prescriptions and screening tool to alert to right treatment criteria: a cluster randomized controlled trial. *J Am Geriatr Soc.* 2016;64:1558–1566.
36. Frankenthal D, Israeli A, Caraco Y, et al. Long-term outcomes of medication intervention using the screening tool of older persons potentially inappropriate prescriptions screening tool to alert doctors to right treatment criteria. *J Am Geriatr Soc.* 2017;65:e33–e38.
37. Price M, Davies I, Rusk R, et al. Applying STOPP guidelines in primary care through electronic medical record decision support: randomized control trial highlighting the importance of data quality. *JMIR Med Inform.* 2017;5:e15.
38. Kimura T, Ogura F, Yamamoto K, et al. Potentially inappropriate medications in elderly Japanese patients: effects of pharmacists' assessment and intervention based on screening tool of older Persons' potentially inappropriate prescriptions criteria ver.2. *J Clin Pharm Ther.* 2017;42:209–214.
39. Perry CK, Damschroder LJ, Hemler JR, et al. Specifying and comparing implementation strategies across seven large implementation interventions: a practical application of theory. *Implement Sci.* 2019;14:32.
40. Shoemaker-Hunt S. Issue Brief: Implementation Research to Understand Effective Approaches to Opioid Management in Health Systems. AcademyHealth. 2019. Available at: <https://www.academyhealth.org/sites/default/files/issuebriefshoemakerhuntoioidimplementationresearchdec2019.pdf>. Accessed May 27, 2020.
41. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Med Care.* 2012;50:217–226.