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Drug-related problems in elderly general practice patients receiving pharmaceutical care

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Abstract

Objective To describe the types of drug-related problems identified by pharmacists providing pharmaceutical care to elderly patients in the primary care or general medicine setting, and the impact of their recommendations on drug-related outcomes.

Methods Searches of the MEDLINE, EMBASE, CINAHL, HealthSTAR, and International Pharmaceutical Abstracts electronic databases from 1990 to 2002 were conducted and a manual search of references from retrieved articles and references on file was performed. Large (n > 100) randomised, controlled studies comparing the provision of pharmaceutical care to usual care in seniors in primary care or general medicine settings were included. Two reviewers evaluated articles based on inclusion criteria and extracted data from the intervention arm of each study, resolving discrepancies by consensus. Nine original articles were included for analysis.

Key findings The mean number of drug-related problems (DRPs) identified per patient was 3.2 and the mean number of recommendations made per patient was 3.3. The most common DRP identified was not taking/receiving a prescribed drug appropriately (35.2%, range 4.7–49.3%). The most common recommendations made involved patient education (37.2%, range 4.6–48.2%). Implementation rates were generally high for all types of recommendations, with the highest being for provision of patient education (81.6%). The small number of studies available examining measures of drug utilisation and costs, health services utilisation, and patient outcomes produced inconsistent results, making it difficult to draw conclusions.

Conclusions Substantial numbers and a wide range of DRPs were identified by pharmacists who provided pharmaceutical care to seniors in the primary care and general medicine setting. Pharmacists' drug-therapy recommendations were well accepted; however, further study is needed to determine the impact of these recommendations on health-related outcomes.

Introduction

Although the elderly represent 12–14% of the population, they consume over one-third of prescription drugs.[1,2] Given their complex medical problems and use of multiple long-term medications, older adults are at high risk for experiencing drug-related problems (DRPs) in hospital and ambulatory settings.[3–5]. In the elderly, 10% to 31% of hospital admissions are associated with DRPs, such as inappropriate prescribing, adverse drug reactions, and non-adherence.[6–8] The costs of preventable drug-induced illnesses in this population are substantial, with estimates of (Canadian)$10.9 billion annually in Canada and (US)$177.4 billion in the United States.[9,10]

To address the growing challenges associated with improving medication use, pharmacists are assuming an integral role in collaborative medication management.[11,12] A number of studies have shown that pharmacists' interventions can improve patient outcomes in various practice settings.[13–23] Particularly in general medicine and primary care settings, pharmacists are well-positioned to assess and optimise drug therapy across multiple medical conditions and provide other patient care services including education, drug monitoring, health promotion, and continuity of care.[24]

The high rates of DRP identification among seniors with chronic medical conditions is well documented.[18,24–26] It is widely assumed that use of multiple medications is associated with increased risks to patients,[2,3] thus the pharmacist's role has been directed at reducing the number of medications in order to reduce the potential for

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adverse effects and to minimise costs. Pharmaceutical care requires a comprehensive patient assessment which focuses not only on the drug product but the net benefit patients are deriving from their medications. Thus, the process of identifying and resolving DRPs can be quite complex and involve a multitude of factors beyond simply reducing the number of medication units. Indeed in some cases the number of medication units may rise. In a study of pharmacist consultants in family physicians' offices, despite the polypharmacy use in the elderly study population, the most common DRP identified by the pharmacists was requiring drug therapy for an untreated indication.[24]

Systematic reviews of rigorous research on pharmaceutical care in the elderly, particularly in the primary care or general medicine setting, are lacking.[27,28] A recent systematic overview by Roughead et al evaluated the impact of pharmacist professional services in the community setting; however, this review was not conducted specifically in seniors and focused on quantifying the effects of pharmaceutical care on patient outcomes rather than describing the nature of the DRPs identified.[29] Studies that have assessed the types of DRPs identified and the recommendations made by pharmacists have generally been small pilot studies that were mainly descriptive in nature and subject to biases in DRP identification.[30–32] The types of DRPs identified and types of recommendations made by pharmacists providing pharmaceutical care in the elderly in larger, more rigorous studies need to be examined systematically. This will help determine the most important DRPs affecting seniors, and help pharmacists to better address the pharmaceutical care needs of this complex population. A better understanding of the types of drug therapy recommendations made by pharmacists is important from a health policy perspective, to determine how pharmacists are influencing drug utilisation and associated costs, and from a health systems perspective to better define the role of pharmacists working in the primary care and general medicine settings.

The objective of this systematic overview was to describe the types of DRPs identified and the outcomes of drug-related recommendations made by pharmacists who provide pharmaceutical care to elderly patients in the primary care or general medicine setting.

Methods

Study identification

The literature search included a search of the MEDLINE, EMBASE, CINAHL, HealthSTAR, and International Pharmaceutical Abstracts (IPA) electronic databases from 1990 to 2002. These dates were chosen to capture articles that were published following the seminal articles on pharmaceutical care by Hepler and Strand.[33–36] The following search terms for pharmaceutical care were used: pharmaceutical care; pharmacist consultation, assessment, recommendations or interventions; pharmacy care plan; pharmacotherapeutic plan; or therapeutic plan. These were combined with search terms for DRPs, which included: drug- or medication-related problems and drug- or medication-related needs. Search terms were entered either as keywords or text words. The search was restricted by age to subjects 65 years or older, and by publication type to randomised clinical trials. Reference lists of retrieved articles, articles on file, and relevant review articles were manually examined for further applicable studies.

Study selection

A study was included if it was published in the English language, was a randomised controlled trial (RCT) that compared the provision of pharmaceutical care to usual care within the primary care or general medicine setting, included more than 100 patients, who had a mean age of 65 years or older, and reported the numbers and types of DRPs identified and recommendations made by pharmacists as well as objective measurements of health services utilisation, costs, or clinical outcomes. We included studies if there was a clear intent to evaluate the provision of pharmaceutical care, to ensure that a systematic process was being used to identify and resolve DRPs. Less comprehensive types of clinical pharmacy services (e.g. drug-utilisation review, pharmacokinetic monitoring) were thus excluded. A study was excluded if it was an unpublished conference proceeding or poster presentation, or if it involved pharmacy students or residents as the sole providers of pharmaceutical care. The citations (titles and abstracts) obtained were independently reviewed by the two pharmacist authors (EL, LD), using the inclusion and exclusion criteria outlined above. Discrepancies were resolved by consensus. Articles potentially meeting the inclusion criteria were obtained and screened.

Data extraction

Data from the intervention group of each study were extracted. The two authors independently assessed the quality of each study and extracted data using a standardised form adapted from Kennie et al and the Cochrane collaboration (Appendix 1).[37,38] When required, an attempt to obtain additional data was made by contacting the original authors of the studies. Specific aspects of the studies that were assessed included the target patient population, pharmacists' training to provide pharmaceutical care, type of intervention, rates of DRP identification and resolution, and outcomes of pharmacists' interventions. The main outcomes of interest were health services utilisation (e.g. hospitalisations, number of prescription medications), costs of health services (e.g. costs of medications), and patient outcomes (e.g. health status, quality of life). Discrepancies in data extraction were mediated by arbitration between the two authors.

Assessment of study quality

Only RCTs were included as these were considered more likely to use a systematic approach for enrolling patients

and to use standardised data collection methods to identify DRPs. We included only large RCTs (n > 100) to minimise variation in the types of DRPs identified and to provide a more representative distribution of DRPs.

The quality of the included studies was assessed based on completeness of follow-up, blinded outcome assessment by a third party and adequate control of co-interventions during the study period. We also assessed how rigorously the following steps of the pharmaceutical care process were applied: (i) development of a pharmacist–patient therapeutic relationship; (ii) patient assessment to identify DRPs; (iii) implementation of a therapeutic plan (involves one or more recommendations to either the patient, physician or other care provider for a change in drug therapy to prevent or resolve a DRP); (iv) follow-up and monitoring for DRP resolution; and (v) documentation of pharmacists' assessments and recommendations.[33,39]

Analysis

DRPs were classified into one of eight categories using an adapted Hepler and Strand DRP classification scheme (Appendix 2).[40] The Hepler and Strand system was chosen as the standard because it takes into account both the processes and outcomes of pharmaceutical care. Each of the Hepler and Strand DRP categories was divided into subcategories based on the cause of DRP (e.g. therapeutic duplication and excessive duration of treatment fall under 'receiving a drug for no valid indication'). For studies that used a classification system other than Hepler and Strand, DRPs were adapted to the Hepler and Strand system independently and in duplicate by two reviewers, and disagreements were resolved by consensus.

Technical and administrative DRPs were defined as DRPs that were not associated with specific pharmacotherapy or that would be expected to have negligible impact on patient outcomes. These DRPs were excluded by us from four of the studies in the review because our intention was to focus only on DRPs that could be directly linked to patient outcomes. In Grymonpre et al, a total of 374 (39.2%) of DRPs were excluded because these dealt with technical issues (e.g. need for primary prevention strategy, improper storage of medications, patient has sensory/physical/cognitive limitations, inadequate knowledge, outdated label, multiple physicians or pharmacists, poor communication with healthcare professionals).[41] In Schmidt et al, 25 technical DRPs (3.1%) which were categorised as requiring follow-up of therapy (checking serum digoxin levels, measuring blood pressure) were excluded.[42] In Zermansky et al, 177 (29%) technical DRPs were excluded, including cases where drugs were still listed on the patient's repeat record but no longer taken, switching between generic and brand formulations, changing instructions to match what the patient actually takes, insufficient quantity on repeat prescription.[43,44] In Ellis et al, taking a non-formulary drug was excluded for technical reasons in 64 cases (2.1%).[45]

The frequency with which each Hepler and Strand DRP category was identified in patients who received the pharmaceutical care intervention was calculated. Data were analysed separately for studies that reported DRP frequencies at the patient level (percentage of patients with each type of DRP). Pharmacists' recommendations were categorised a priori and linked to one or more of the Hepler and Strand DRPs (Appendix 2). Although 'providing patient education' was linked primarily with 'patient not taking drug appropriately' it was recognised that this recommendation could be made for any type of DRP. Recommendations were made to physicians, patients, or both. In studies where only the resolution rates for each type of DRP were reported, we inferred that DRP resolution was attributed to implementation of pharmacists' drug therapy recommendations. The frequency with which each type of recommendation was implemented and the implementation rate for each type of recommendation was calculated for intervention patients. Changes in outcome measures were compared between patients who received the pharmaceutical care intervention and control patients. Due to the unavailability of the required numerical values (e.g. SDs), it was not possible to quantitatively combine the outcome data. Results were presented separately for each study, in a table with baseline values and the absolute change from baseline to endpoint for control and intervention groups. Cost data were annualised and converted to US dollars to allow for comparison across studies. Where quantitative outcome data were not available, data were summarised qualitatively.

Results

The electronic database search retrieved a total of 82 citations (accounting for duplications among the various databases). Six citations were retrieved by a manual search of references and from existing files, some of which were duplicates of articles found in the database search. Many articles were not research studies, but represented a cross-sectional description of experiences with the provision or implementation of pharmaceutical care. Other articles did not actually intend to evaluate pharmaceutical care, but evaluated the impact of pharmacy services such as pharmacist interventions in the absence of comprehensive patient assessments, drug utilisation review, or patient self-medication programmes. A total of 63 studies were excluded for the reasons listed above (32 after title review, 31 after abstract review). The reviewers identified a total of 20 citations as potentially meeting inclusion criteria.[14,19,41–43,45–59] Inclusion and exclusion criteria were applied to the full articles, which resulted in exclusion of four articles[19,49,54,59] leaving a total of 16 articles. The agreement rate between reviewers for study selection was 92.7% (76/82) after title review, 92.2% (47/50) after abstract review, and 75% (15/20) after full article review.

More complete information on DRP identification and resolution was obtained to supplement one of the identified studies after contacting the authors of the original publication.[44] Seven of the remaining 16 articles were not analysed based on the inability to extract data that could be compared with other studies.[14,46–48,52,56,57] One article used a risk-assessment score instead of measuring the

types of DRPs identified and thus did not provide suitable information for extraction.[14] Other articles did not provide sufficient information about the types of DRPs identified or the types of recommendations made.[46–48,56,57] A study by Kimberlin et al presented only aggregate results for the types of DRPs identified in the intervention and control groups, and thus it was not possible to analyse the effect of pharmaceutical care in the intervention group.[52] Attempts to contact the authors of these original studies yielded no further information. This systematic overview summarises the DRP, recommendation, and outcomes data for the remaining nine studies.[41–45,50,51,53,55,58] Characteristics of the included studies are presented in Table 1.

Results were available for 2602 patients who received a pharmaceutical care intervention. From the eight studies that summarised demographic information, patients had a mean age of 66.8 to 83.5 years, with the proportion of women ranging from 1.9 to 79.3%.[41–45,50,51,53,58] Based on available data from the individual studies, patients had an average of 7.6 chronic medical conditions and were taking an average of 6.8 medications.[41,50,51,53,58] Six studies were based in the community (community pharmacies or outpatient general medicine clinics),[41,43–45,50,51,53] two studies were conducted in hospital (general medicine ward),[55,58] and one study was conducted in a nursing home.[42] The duration of the studies ranged from one to twelve months.

Table 1 Characteristics of included studies

Reference	Setting	Number of subjects (number in intervention group)	Mean age in years (±SD)	Women (%)	Description of study population
Grymonpre et al (2001)[41]	Community-based interdisciplinary health clinic	135 (69)	76.9 (8.4)	79.3	Mean number of medications: 5.9
Ellis et al (2000)[45]	9 Veterans Affairs Medical Centers	(523)	66.8 (10.2)	4.0	'High risk' for DRPs based on predetermined criteria (5 or more prescription drugs, 12 or more doses/day, 4 or more drug changes in past year, 3 or more concurrent diseases, etc)
Schmidt et al (1998)[42]	15 Swedish nursing homes	1854 (626)	83.0 (N/A[a])	70	42% with dementia, 76% on one or more psychotropic drug
Zermansky et al (2001, 2002)[43,44]	4 general medical practices	1188 (608)	74.0 (6.6)	56	Median number of medications: 4.0
Hanlon et al (1996)[50]	General medicine clinic at Veterans Affairs Medical Center	208 (105)	69.7 (3.5)	1.9	Mean number of medications: 7.6; mean number of medical conditions: 9.2
Lipton et al (1992)[55]	Community hospital	236 (123)	N/A[a]	N/A[a]	≥3 chronic medications
Krska et al (2001)[53]	General medical practices in Scotland	332 (168)	74.8 (6.2)	56.5	Mean number of medications: 7.3; mean number of chronic medical conditions: 3.9
Kassam et al (2001)[51]	5 community pharmacies in Alberta	(159)	74 (6.0)	64	Mean number of prescription medicines: 8.7; OTC: 3.4; mean number of medical conditions: 10
Owens et al (1990)[58]	Geriatric assessment unit (GAU) in university-affiliated, acute-care hospital	436 (221)	83.5 (75–100)[b]	71	Mean number of medications: 4.5; mean number of medical conditions: 7.2; admitted to GAU as acutely ill; 29% admitted from nursing home

[a]Not applicable (values not reported in the study).
[b]Age range reported in this study.

Assessment of study quality

In four studies,[41,50,55,58], the identification and resolution of DRPs were independently adjudicated by a third party. All but one study defined DRPs a priori.[43] Three studies did not report withdrawal rates, thus it was not possible to assess completeness of follow-up.[42,55,58] The remaining six studies had adequate follow-up and relatively low drop-out rates (4.8–18.2%). None of the studies reported the methods used to randomise patients to the different treatment groups. In Kassam et al,[51] randomisation was done at the level of the pharmacy; therefore, selection bias could have been introduced by pharmacists in the intervention groups if they enrolled patients whom they thought would be good candidates for pharmaceutical care.

Studies were assessed according to how closely pharmacists followed the steps of the pharmaceutical care process to identify and resolve DRPs. In two studies, DRPs were identified by an independent party or panel based on data collected by the study pharmacists, not by the study pharmacists themselves.[55,58] In two studies, it was unclear if the pharmacist developed an ongoing therapeutic relationship with the patients,[42,58] and in two studies it was unclear whether the pharmacist monitored patients for resolution of DRPs.[50,55]

Types of DRPs identified

Three studies classified DRPs using standard Hepler and Strand definitions.[41,45,51] The other six studies used different definitions to classify DRPs, which meant that their definitions had to be adapted to better fit the Hepler and Strand classification.[42,43,50,53,55,58] The Medication Appropriateness Index (MAI) dimensions used in Hanlon et al.[50] and the Pharmaceutical Care Issues (PCIs) used in Krska et al,[53] were converted to DRPs to fit the Hepler and Strand classification. From the seven studies that used number of DRPs as the unit of analysis,[41–45,50,51,53] 7135/7894 (90.4%) of DRPs fitting the Hepler and Strand classification scheme were included (Table 2). The mean number of DRPs identified per patient was 3.2. In the two studies that used the patient as the unit of analysis,[55,58] 216/344 (62.8%) patients were found to have at least one Hepler and Strand DRP (Table 3). Not taking/receiving a prescribed drug appropriately was the most common DRP identified (35.2%, range 4.7–49.3%), followed by requiring drug therapy but not receiving it (16.6%, range 6.9–54.5%), and not taking/receiving the appropriate drug therapy (14.5%, range 3.6–42.6%). The least common DRP identified was a drug interaction (1.9%, range 0–9.2%) (Table 2).

Types of recommendations made and implemented

From the five studies that reported the types of recommendations made by pharmacists,[41,43–45,51,55] 4916/5171 (95%) recommendations were included in our analysis. Recommendations were excluded if they dealt with administrative issues or issues that did not relate directly to patient care (e.g. recommendation for generic drug substitution). Pharmacists made an average of 3.3 recommendations per patient. The most common recommendations made were provision of patient education (37.2%, range 4.6–48.2%), followed by taking preventative measures (23.8%, range 19.2–27.0%), and changes in dose, timing, or method of drug administration (18.8%, range 9.0–58.0%).

From the five studies that reported information on implemented recommendations (n = 3409),[41–45,53] the most common types of recommendations implemented were: providing patient education (42.6%, range 8.0–55%) and any change in medication dose, schedule or formulation (29.4%, range 8.0–33%). In three studies,[41,43–45] results were reported for both the number of recommendations made by pharmacists and the number of recommendations implemented by physicians and/or patients (Table 4). Based on these results, the implementation rate was 2556/3879 (65.9%) across all categories of recommendations, with the highest implementation rates seen for providing patient education (81.6%) and initiating preventive action (78.6%).

Effect of pharmaceutical care on outcomes

DRP resolution rates were reported in four studies.[41,45,51,53] The proportion of DRPs resolved in intervention patients ranged from 28.0% to 78.8%, with the highest mean resolution rate for the DRP of not taking/receiving a prescribed drug appropriately (80.5%) and the lowest mean resolution rate for drug interactions (49.2%). A total of six studies reported data on outcome measures.[41,43,44,50,51,53,58] No significant differences in the mean number of medications prescribed per patient were seen between intervention and control patients in three studies,[41,50,58] while one study found that intervention patients had a significantly smaller increase in mean number of prescription medications compared to control ($P = 0.01$) (Table 5).[43,44] No significant changes in mean prescription drug costs per patient were seen between intervention and control patients in two studies,[41,53] whereas one study found a significantly smaller increase in mean prescription drug costs per patient in the intervention group compared to the control group ($P = 0.0001$) (Table 5).[43,44] In a study by Hanlon et al, health-related quality of life scores (SF-36) in three domains (social functioning, energy, and general health perception) were improved in the intervention group but the change was not significantly different from control,[50] while in the study by Krska et al, none of the SF-36 domains showed any significant changes in either the intervention or control group at follow-up.[53] Two studies showed an initial increase in the number of scheduled primary care visits for drug-related or therapy monitoring purposes in intervention patients,[43,44,53] but the cumulative number of visits at 12 months was no different between intervention and control patients in one study.[43,44] Two studies found that there were fewer emergency and elective hospital admissions in intervention compared to control patients; however, event rates were too low to make any statistical comparisons.[43,44,53] In one study, pharmacists' recommendations were judged to have improved outcomes

Table 2 Numbers (%) of DRPs identified according to DRP category

Study	No indication	Requires drug therapy	Inappropriate drug	Too little drug	Too much drug	Inappropriate dose[c]	Not taking drug appropriately	Adverse drug reaction	Drug interaction	Total DRPs	Mean DRPs per patient
Kassam et al (2001)[51] (n = 159)	34 (6.1)	302 (54.5)	56 (10.1)	28 (5.1)	28 (5.1)	N/A[a]	50 (9.0)	45 (8.1)	11 (2.0)	554	3.5
Hanlon et al (1996)[50] (n = 105)	246 (22.4)	N/A[a]	285 (26.0)	N/A[a]	N/A[a]	139 (12.7)	426 (38.9)	N/A	0	1096	10.4
Krska et al (2001)[53] (n = 168)	157 (16.4)	66 (6.9)	158 (16.5)	N/A[a]	N/A[a]	69 (7.2)	209 (21.8)	300 (31.3)	Unknown[b] (< 2.8)	959	5.7
Grymonpre et al (2001)[41] (n = 69)	65 (11.2)	65 (11.2)	67 (11.6)	72 (12.4)	32 (5.5)	N/A[a]	27 (4.7)	197 (34.1)	53 (9.2)	578	8.4
Ellis et al (2000)[45] (n = 523)	150 (5.2)	487 (16.8)	106 (3.6)	346 (11.9)	112 (3.8)	N/A[a]	1432 (49.3)	225 (7.7)	48 (1.6)	2906	5.6
Zermansky et al (2001, 2002)[43,44] (n = 608)	95 (38.3)	17 (6.9)	23 (9.3)	N/A[a]	N/A[a]	N/A[a]	86 (34.7)	22 (8.9)	5 (2.0)	248	0.4
Schmidt et al (1998)[42] (n = 626)	276 (34.8)	65 (8.2)	338 (42.6)	N/A[a]	N/A[a]	89 (11.2)	N/A	10 (1.3)	16 (2.0)	794	1.3
Combined results for all studies	1023 (14.3)	1002 (16.6)	1033 (14.5)	446 (11.0)	172 (4.3)	297 (4.2)	2230 (35.2)	799 (13.2)	133 (1.9)	7135	3.2

[a]Not applicable (was not a recognised DRP category in the study).
[b]Original article included potential drug–drug interactions as one of the 'other' types of DRPs but the exact number of drug–drug interactions was not provided.
[c]'Inappropriate dose' used in place of 'too much drug' and 'too little drug' (unable to distinguish between these two categories based on available data).

Table 3 Number (%) of patients with DRPs in each category[a]

Study	No indication	Inappropriate drug	Inappropriate dose[b]	Not taking drug appropriately	Adverse drug reaction	Drug interaction	Total number of patients in intervention group	Number (%) of patients with at least one DRP in any category
Lipton et al. (1992)[55] (n = 123)	22 (18.0)	63 (51.0)	53 (43.0)	60 (49.0)	5 (4.0)	55 (45.0)	123	103 (83.7)
Owens et al. (1990)[58] (n = 221)	73 (64.6)	40 (35.4)	N/A[c]	N/A[c]	N/A[c]	N/A[c]	221	113 (51.1)
Combined results for all studies	95 (25.6)	103 (27.8)	53 (14.3)	60 (16.2)	5 (1.3)	55 (14.8)	344	216 (62.8)

[a]Requires drug therapy not listed as a DRP category in these studies.
[b]'Inappropriate dose' used in place of 'too much drug' and 'too little drug' (unable to distinguish between these two categories based on available data).
[c]Not applicable (was not a recognised DRP category in the study).

Table 4 Number (%) of recommendations implemented within each category[a]

Study	Stop drug	Start drug	Change drug	Change in dose, timing or method of drug administration	Preventative steps (i.e. referral, monitoring)	Patient education	All recommendations
Grymonpre et al. (2001)[41] (n = 69)	15/44 (34.1)	19/56 (33.9)	75/281 (26.7)	19/80 (23.8)	N/A[b]	8/22 (36.4)	136/483 (28.2)
Ellis et al. (2000)[45] (n = 523)	61/150 (40.7)	307/487 (63.0)	249/443 (56.2)	274/458 (59.8)	N/A[b]	1179/143 (82.3)	2070/2970 (69.7)
Zermansky et al. (2001, 2002)[43,44] (n = 608)	104/118 (88.1)	12/17 (70.6)	31/43 (72.1)	74/86 (86.0)	48/82 (78.6)	80/80 (100)	349/426 (81.9)
Combined results for all studies	57.7	60.3	46.3	58.8	78.6	81.6	65.9

[a]Implementation rates calculated as a percentage of number of recommendations implemented out of number of recommendations made.
[b]Not applicable (was not a recognised drug-related recommendation in the study).

in intervention patients in 40% of cases, partially improved or resulted in no change in 18% of cases, and worsened outcomes in 1% of cases,[51] while another study found that 19% of pharmacists' recommendations had a significant beneficial effect on the intervention patients, 47% resulted in no observable change, and 8% had a negative effect on the patient.[42] Medication knowledge was assessed in two studies by how well patients knew the purpose of their medications,[41,50] while medication adherence was assessed in one study by the agreement between patient-reported medication use and prescribed use,[50] and in another study based on refill intervals from administrative data.[41] No significant differences were seen between intervention and control patients in medication knowledge or adherence in either study.[41,50]

Discussion

This review has shown that pharmacists providing pharmaceutical care to seniors in the primary care and general medicine setting identify approximately three DRPs and make over three recommendations per patient. The high number of DRPs addressed by the pharmacists in this review is consistent with what is shown in previous pharmaceutical care studies in the elderly.[18,21,23,24,60] These results are not surprising, given that patients included in these studies had multiple chronic medical conditions and were taking over six medications on average, thus placing them at high risk for DRPs.[6,57,61]

Table 5 Drug utilisation and cost outcomes in patients receiving pharmaceutical care versus usual care

Outcome	Intervention			Control			*P* value[a]
	Baseline	Follow-up	Change	Baseline	Follow-up	Change	
Mean no. of prescription medications per patient							
Owens et al (1990)[58]	4.5	6.0	1.5	4.4	6.0	1.6	>0.05
Grymonpre et al (2001)[41]	5.9	5.9	0	6.5	6.7	0.2	0.760
Zermansky et al (2001, 2002)[43,44]	4.8	5.0	0.2	4.6	5.0	0.4	0.01
Hanlon et al (1996)[50]	7.6	6.9	−0.7	8.2	7.9	−0.3	0.83
Mean prescription drug costs per patient (US$)[b]							
Krska et al (2001)[53]	895.81	885.32	−10.49	975.84	971.51	−4.33	N/A[c]
Grymonpre et al (2001)[41]	669.56	614.84	−54.72	717.44	664.24	−53.20	0.971
Zermansky et al (2001, 2002)[43,44]	667.36	754.00	86.64	643.64	794.58	150.94	0.0001

[a] *P* value for change in intervention compared with control group.
[b] Annualised costs in US dollars.
[c] Stated in Krska et al[53] that change was not significantly different (no *P* value shown).

There was variability seen in the types of DRPs identified across studies, which may be explained by differences in the types of patients or settings encountered by the pharmacists, in the duration of follow-up for DRP identification, and in how the pharmaceutical care process was applied by different pharmacists. In addition, there is also variability inherent in the different DRP classification systems used. Although a standardised classification system for DRPs has been proposed,[40] the validity and reliability of DRP classification remains unknown. Some classification systems are oriented more towards the patient's perspective and the outcomes of drug therapy, while others are oriented more towards the process of prescribing, dispensing, and drug use evaluation.[62] The classification systems used by Krska et al and Hanlon et al were developed for drug use evaluations,[25,53] which may explain the higher rates of particular DRPs identified in these two studies. For example, the higher rates of not taking a medication appropriately in Hanlon et al were due to the inclusion of practical or incorrect directions as factors that may potentially lead to inappropriate medication use. Krska et al identified an above average number of adverse drug reactions (ADRs) because their ADR category included cases where a medication was prescribed without evidence of monitoring in the ensuing 12-month period. As the results of these studies suggest, there is a clear need for a more consistent and reliable system of DRP classification. Despite the variability seen, there were notable patterns apparent in the types of DRPs identified by pharmacists across studies.

Not taking medications appropriately was the most common DRP identified in this review. The high numbers of DRPs in this category were derived from the high numbers of patients who required further education about their medications and from the high rates of medication non-adherence. Previous studies have shown that many factors place seniors at risk for medication non-adherence, including cognitive or physical impairment, social isolation, financial constraints, and complex medication regimens.[60,61,63] It is possible that some patients were non-adherent to their medications for legitimate reasons (e.g. experiencing side-effects, prescribed medications that were not necessary), in which case they would have been more appropriately classified into these other DRP categories.

The DRP categories 'no indication' and 'needs drug therapy' were identified at similar frequencies, with the overall numbers in each category being driven by the results of one or two studies. For example, Kassam et al. considered that almost all of their high-risk population would benefit from influenza vaccination to prevent flu-related complications, thus contributing to the high frequency of the 'needs drug therapy' DRP in this study.[51] Despite the numerous medications taken by the elderly, 'needs drug therapy' was commonly identified as a DRP. Given the increasing evidence that the elderly are under-treated for chronic medical conditions,[61,64–68] this suggests that pharmacists can contribute to improved medication management by identifying cases where necessary medications were omitted because of undetected health problems, providing evidence to physicians of the relative risk and benefit of starting new medications, and ensuring that patients are being treated to target in accordance with evidence-based guidelines.

Drug interactions and taking too much of the correct medication were among the least common DRPs identified. Although the underlying reasons for this were not clear from the original studies, the use of computerised checks by physicians for drug interactions could have precluded the need for pharmacists to intervene. The extra caution commonly exercised by physicians when prescribing to elderly patients may have accounted for the low numbers of the 'high dose' DRP.

Pharmacists' recommendations were well accepted, with the majority of recommendations being implemented by both physicians and patients. The types of drug therapy recommendations made by pharmacists generally corresponded with the types of DRPs identified, which suggests that pharmacists were resolving DRPs in a systematic manner. Interestingly, the recommendations with the highest implementation rates did not involve any direct changes

to the patient's medication regimen (i.e. recommendation for increased monitoring, referral to physician for consult), which could suggest that patients and physicians were more receptive to making changes one step at a time.

Pharmacists' recommendations did not always lead to reductions in numbers of prescribed medications or prescription costs. These results challenge the presumption that pharmacists can only contribute to cost-effective use of medications by decreasing direct medication costs. Recommendations for increased use of appropriate drug therapy (i.e. starting a medication shown to be beneficial for prevention of health complications) may help reduce costs in other areas of healthcare if patient morbidity is reduced as a result (i.e. reduction in hospitalisations).

Further study is needed to determine the impact of pharmacists' recommendations on health-related outcomes. This review provides some limited evidence of a decrease in hospitalisations in patients receiving pharmaceutical care, but the degree to which this was attributable to a reduction in drug-related adverse events from pharmacists' recommendations was unclear. The increase in patient primary care visits was consistent with the high number of recommendations made by pharmacists for patients to seek follow-up and monitoring with their primary care providers. This appeared to be a necessary step in the pharmaceutical care process, as patients would have had to make appointments with their physicians to confirm advice given by the pharmacist or to have drug therapy recommendations implemented.

No significant differences were seen in other outcome measures including medication knowledge, medication adherence, and patient quality of life. It may have been difficult for pharmacists to demonstrate an improvement in the first two outcomes, given that patients had high baseline levels of medication knowledge and adherence, and in some studies control patients may have received more than the usual level of care. Health-related quality of life was measured using a generic measure of health reflecting patient's overall chronic disease activity and comorbidity that may have been minimally influenced by medication use, and thus not as responsive to the pharmaceutical care intervention.

We restricted our analysis to larger RCTs to minimise the effects of individual pharmacists' biases towards DRP identification and help ensure a representative distribution of DRPs. The methodological quality of the studies in this review was relatively high as all studies allocated patients to the intervention at random, most studies had defined DRPs a priori, and ensured that follow-up of patients was complete. A large number of patients from a wide range of practice sites were included in this review, thus it is likely that the types of DRPs and recommendations we identified are representative of what older patients with chronic medical conditions generally experience in the primary care or general medicine settings.

Several limitations should be considered when interpreting and applying the results of this overview. Many pharmaceutical care studies do not fully describe the pharmaceutical care process they used, making it difficult to assess the extent to which pharmaceutical care was implemented in those studies.[37] Only studies in which the pharmaceutical care process was explicitly described were included in this review, thus we may have missed studies that intended to evaluate pharmaceutical care but did not clearly describe this in their methodology. The accuracy of the DRP and recommendation data may have been influenced by over- or under-reporting between pharmacists, although we attempted to minimise this by including only studies where pharmacists used standardised, predefined protocols to collect information on their patients. There was variability in how some of the outcomes were measured and in the time interval of measurement across studies, which may have accounted for some of the differences in results, especially with drug utilisation and medication costs. Event rates and hospitalisations were reported in only two studies, and it was difficult to draw conclusions from these studies due to short duration of follow-up and low event rates. The evidence for improved clinical outcomes may have been limited by biases, as blinded, independent outcome assessments were not performed and there was incomplete follow-up on the impact of pharmacists' recommendations on the outcomes of interest. Further studies using more rigorous methods to validate the impact of pharmaceutical care on clinical outcomes are needed.

Conclusions

The results of this overview demonstrate the contribution that pharmacists can make in the primary care and general medicine settings, by identifying a large number of DRPs in high-risk seniors. There was variability in the types of DRPs across studies, but taking or receiving a medication inappropriately and requiring drug therapy were consistently found to be two of the most common DRPs identified. Pharmacists' drug therapy recommendations were well accepted by both physicians and patients, especially those prompting preventative action and involving patient education. Further study is needed to more fully document the impact of pharmacists' drug therapy recommendations on clinical outcomes and drug-related hospitalisations before it can be concluded that pharmacists have a positive effect on these outcome measures.

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Appendix 1 Adapted Pharmaceutical Care Research Checklist[37,38,40]

Criteria	Check (√)
Research question(s)/study objective(s) clearly stated	☐
Criteria for pharmaceutical care process	
Pharmacist–patient relationship established to involve the patient in drug therapy decisions	☐
Outcomes established in conjunction with patient	☐
Patient assessment to identify DRPs	☐
Implementation of a therapeutic plan (involves one or more recommendations to either the patient, physician or other care provider for a change in drug therapy to prevent or resolve a DRP)	☐
Method indicated for monitoring/follow-up	☐
Pharmacist's activities/assessment documented	☐
Methodology	
Research design described in sufficient detail	☐
Clinical setting described	☐
Sampling procedure specified	☐
Randomisation procedure specified	☐
Description of sample provided	☐
Control of co-interventions	☐
Follow-up complete	☐
Dropouts specified	☐
Pharmacist training/qualifications in pharmaceutical care described	☐
Measurement/outcomes	
Source of DRP (and recommendation) criteria specified	☐
DRP criteria specified a priori	☐
DRPs identified in unbiased fashion	☐
Blinded outcome assessment of recommendation acceptance and implementation	☐
Appropriate numerical data given for DRPs (and recommendations)	☐
Relevant and interpretable data presented for outcome measures	☐
Discussion	
Limitations discussed	☐
Conclusions supported by results	☐
Implications for practice/future research discussed	☐

Appendix 2 Hepler and Strand DRP classification[40]

Hepler and Strand DRP category	Example	Pharmacist's recommendation[a]
1 Patient is taking/receiving a drug for which there is no valid indication Therapeutic duplication Excessive duration of treatment Repeat prescription no longer required 'Unpaired medications' (medications in patient's drug profile for which an indication was not found)	Patient is no longer receiving a diuretic and no longer requires potassium supplementation that was prescribed for diuretic-induced hypokalaemia	Stop drug (includes: decrease duration of drug therapy, reassess need for drug therapy)
2 The patient requires drug therapy for an indication and is not receiving/taking this therapy The patient has a diagnosed disease, which requires drug therapy, for which drug therapy is not being prescribed The patient requires additional drug therapy to synergise or potentiate primary drug therapy The patient requires preventative drug therapy (i.e. immunisations or antibiotics)	Patient is at risk of developing osteoporosis and needs preventative therapy	Start drug (includes: referral to physician to assess need for drug therapy)
3 The patient is not taking/receiving the appropriate drug or drug product The drug is known to be ineffective for the prescribed indication The drug is known to be effective for the prescribed indication, but is not effective for a particular patient for a known or unknown reason The patient is at risk because there is toxicity associated with the current drug therapy (e.g. allergies, contraindications, drug–disease interaction) An inappropriate route or formulation has been prescribed (i.e. patient cannot take/receive the drug) Choice of drug/drug product is not the most cost-effective Non-formulary drug prescribed	Patient is at risk of exacerbating congestive heart failure (CHF) secondary to taking a non-steroidal anti-inflammatory drug (NSAID)	Change drug
4 The patient is taking/receiving too little drug The dose is too low The drug is administered too infrequently	Patient is experiencing uncontrolled asthma and requires an increase in dose of inhaled corticosteroid	Change dose or timing of drug administration
5 The patient is taking/receiving too much drug The dose is too high The drug is administered too frequently	Patient is experiencing nausea secondary to supra-therapeutic levels of digoxin	Change dose or timing of drug administration
6 The patient is not taking/receiving the prescribed drugs appropriately The patient is non-adherent The patient requires education about his/her drug therapy The drug is prescribed with incorrect or impractical directions	Patient continues to have uncontrolled chronic obstructive pulmonary disease (COPD) secondary to poor inhaler technique	Patient education/ counseling[b]; Change in dose, timing or method of drug administration
7 The patient is experiencing an adverse drug reaction (not dose related) The patient is experiencing an effect known to be associated with the current drug therapy in either an idiosyncratic manner or via an extension of the pharmacological effect The patient has experienced an allergic reaction to the drug	Patient is experiencing urinary retention secondary to use of amitriptyline	Change drug Start drug (to treat the drug reaction)
8 The patient is experiencing a drug–drug, drug–food, or drug–laboratory interaction	Patient has supratherapeutic INRs (International normalised ratios) secondary to use of ciprofloxacin in combination with warfarin	Change drug Change dose, timing or method of drug administration

[a]For some DRPs, a choice of more than one recommendation could be made. Preventative steps (i.e. recommendations for tests, additional monitoring, referring patient to physician to discuss options or for consultation) could apply to any DRP category.
[b]Patient education could apply to any DRP category (e.g. for DRP no.1: educating patient about the need for a drug if s/he doesn't want to start)