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Pharmacist-Led Medication Assessment and Deprescribing Intervention for Older Adults with Cancer and Polypharmacy: a Pilot Study

Andrew Whitman, Pharm.D¹, Kathlene DeGregory, Pharm.D., BCOP¹, Amy Morris, Pharm.D.¹, Supriya Mohile, MD², and Erika Ramsdale, MD²

¹Department of Pharmacy, University of Virginia Health System, Charlottesville, VA

²Division of Hematology/Oncology, University of Rochester Medical Center, Rochester, NY

Abstract

Purpose—The aims of this study were to compare the application of three geriatric medication screening tools to the Beers Criteria alone for potentially inappropriate medication quantification and to determine feasibility of a pharmacist-led polypharmacy assessment in a geriatric oncology clinic.

Methods—Adult patients with cancer aged 65 and older underwent a Comprehensive Geriatric Assessment. A polypharmacy assessment was completed by a pharmacist and included a review of all drug therapies. Potentially inappropriate medications were screened using the Beers Criteria, Screening Tool to Alert doctors to Right Treatment / Screening Tool of Older Persons' Prescriptions, and the Medication Appropriateness Index. Deprescribing occurred after discussion with the pharmacist, geriatric oncologist, patient, and caregiver.

Results—Data were collected for 26 patients. The mean number of medications was 12. The Beers Criteria alone identified 38 potentially inappropriate medications compared to 119 potentially inappropriate medications with the three tool assessment; a mean of 5 potentially inappropriate medications were identified per patient. After the application of the three tool assessment, 73% of potentially inappropriate medications identified were deprescribed, resulting in a mean of 3 medications deprescribed per patient. Approximately two-thirds of patients reported a reduction in symptoms after the deprescribing intervention. Healthcare expenditures of \$4,282.27 per patient were potentially avoided as a result of deprescribing.

Conclusions—Our three tool assessment identified three times more potentially inappropriate medications than the Beers Criteria alone. Pharmacist-led deprescribing interventions are feasible and may lead to improved patient outcomes and cost savings. This three tool assessment process should be incorporated into interdisciplinary assessments of older patients with cancer and validated in future studies.

Corresponding author: Andrew Whitman, Amw6az@virginia.edu, 703-463-7260, ORCID - 0000-0002-1646-0699.

Conflict of Interest:

The authors have no financial relationships or other potential conflicts of interest to disclose. The authors have full control of all primary data and agree to allow the journal to review these data if requested.

Keywords

polypharmacy; potentially inappropriate medications; geriatric oncology; deprescribing

Introduction

Medication overuse in the general geriatric population is a growing problem. Recent data suggest that the prevalence of older adults using five or more medications is approximately 36%, up from 30% five years ago. [1]. Older patients often have multiple comorbidities, and are more susceptible to adverse effects of medications [2]. Prescribing cascades occur when medications are initiated to treat adverse effects of other existing medications, and as a result, older patients tend to accrue pill burden over time. This issue is of particular concern for older patients with cancer; this population has complex care issues related to toxicities of anti-cancer agents, comorbidities, frailty, and altered pharmacokinetics and pharmacodynamics [3].

Polypharmacy (PP) and potentially inappropriate medication (PIM) use have been described extensively in the literature, and a number of geriatric-specific medication screening tools are available to assist providers in quantifying PP and PIM use. A recent review compares and contrasts existing medication screening tools in the context of geriatric oncology. The Beers Criteria, Screening Tool to Alert doctors to Right Treatment (START)/ Screening Tool of Older Persons' Prescriptions (STOPP), Medication Appropriateness Index (MAI), and Healthcare Effectiveness Data and Information Set-Drugs to Avoid in the Elderly (HEDIS-DAE) have been applied to older adults with cancer [4].

Deprescribing is the systematic process of reducing or discontinuing medications aimed at minimizing PP and improving patient outcomes [5]. Deprescribing should take into account the patients' remaining life expectancy, goals of care, medication time-to-benefit, and the purpose of the medication (curative vs palliative for the intended indication) [6]. Guidelines for the management of chronic conditions lack specific recommendations for patients with life-limiting illnesses; continued therapy often provides minimal benefit and may result in significant adverse effects [7]. Recent studies have evaluated the risks and benefits of medication discontinuation for drugs such as statins, antihypertensives, bisphosphonates, and oral hypoglycemics in patients who have limited a life expectancy [8]. Cessation of these medications does not appear to worsen underlying conditions nor increase mortality, but more importantly, discontinuing chronic medications may increase patients' quality of life, improve symptoms, decrease pill burden, and decrease out-of-pocket costs [3, 9–13]. For example, a study evaluating discontinuation of statin medications in patients with a life expectancy of one month to one year found a statistically significant improvement in patient quality of life without an increased risk of mortality [9]. Despite these findings, there is a lack of high quality evidence regarding deprescribing in older patients with cancer, which limits the ability to develop an evidence-based, standardized deprescribing process [3]. Currently, no prospective studies exist that evaluate the process of deprescribing in the geriatric oncology population.

The primary aim of this study was to compare the sequential application of three geriatric medication screening tools (Beers Criteria, STOPP, and MAI) to the Beers Criteria alone for PIM quantification (Fig 1). This study also evaluated the feasibility of a pharmacist-led deprescribing intervention in a geriatric oncology clinic. Initial outcomes of the intervention, such as number of medications deprescribed, cost savings, and pharmacist intervention time, are reported.

Materials and Methods

Interdisciplinary Evaluation

Adult patients with cancer aged 65 and older were assessed in the Geriatric Oncology Clinic at the University of Virginia Health System Cancer Center. These patients underwent a Comprehensive Geriatric Assessment (CGA), an interdisciplinary evaluation of an older adults' functioning across multiple domains, by a geriatric oncologist, nurse, physical therapist, and pharmacist. Data were collected prospectively from August 1, 2015 to April 30, 2016. The study protocol was approved by the Institutional Review Board.

Patients were referred by their primary oncologist for evaluation; reason for referral was documented for each patient (Table 1). The CGA consisted of an evaluation of PP, general health status (Vulnerable Elders Survey 13 [VES13]), cognition (Montreal Cognitive Assessment [MoCA]), activities of daily living (ADLs)/instrumental activities of daily living (IADLs), falls, objective functional status (Short Physical Performance Battery [SPPB]), grip strength, and physical therapy evaluation, mood (Geriatric Depression Scale [GDS]), nutrition (Mini-Nutritional Assessment [MNA]), and social impairments [14].

Polypharmacy Assessment

The PP assessment was completed by a pharmacist and included a comprehensive review of all drug therapies (prescription, over-the-counter [OTC], and complementary and alternative medicines [CAM]). A comprehensive medication list was generated through review of the electronic health record (EHR), calling outside pharmacies, patient report, and caregiver feedback. Drug-drug interactions (Table 2), drug-nutrient interactions, interactions with cancer therapies, medication allergies, patient reported symptoms and side effects, medication underuse, and barriers to deprescribing were assessed. The pharmacist asked questions regarding the patients' medication-related goals of care to help direct deprescribing recommendations (i.e., minimize pill burden, optimize quality of life, chronic disease state management). Each aspect of the PP assessment was documented in a pharmacist note in the EHR; see Box 1 for an example of a pharmacist note.

Box 1

Example of Pharmacist Deprescribing Note

89 year old female who is being seen by pharmacy for assessment of polypharmacy and potentially inappropriate medications (PIMs).

Cancer type: pancreatic (unresectable, metastatic to liver)

ECOG: 1

Current symptoms: Decreased appetite; muscle aches; dizziness

	Condition	Drug given for condition	Potential problems	Notes
1	Primary cardiac prevention	Aspirin 81 mg PO daily	GI bleeding; lack of benefit >80 years old per Beers Criteria	
2	HTN	Atenolol 50 mg PO daily	Fatigue; hypotension; orthostasis	BP = 144/64 mmHg
3	HTN	Hydrochlorothiazide 50 mg PO daily	Dehydration; orthostasis; ineffective	
4	Hyperlipidemia	Atorvastatin 40 mg PO daily	Time-to-benefit; myalgias; myopathy; fatigue	
5	Constipation	Docusate 50 mg PO BID	Ineffective therapy	Not taking
6	Hypothyroidism	Levothyroxine 50 mcg PO daily	Drug interactions; proper administration	
7	DM	Metformin 500 mg PO BID	Diarrhea; GI upset	
8	Sleep/appetite	Mirtazapine 15 mg PO HS	Sedation; falls; CNS depression	Nausea
9	Pain	Oxycodone 5 mg PO q4h PRN pain	Constipation; respiratory depression; CNS depression; falls	Not taking
10	Hypokalemia	Potassium chloride 20 meq PO BID	Pill burden; diarrhea; hyperkalemia	
11	B12 deficiency	Vitamin B12 1000 mcg PO daily		

*Bold denotes newly added medication

OTHER MEDS (OTC, herbal, vitamins, etc.): n/a

Total number of medications = 11

Rx: 8 Herbal: 0 OTC: 3 Misc: 0

Medication allergies: NKDA

Drug interactions (Up-to-date; Micromedex): There are 3 moderately significant drug interactions. Use of oxycodone with hydrochlorothiazide increases risk of orthostasis; a pharmacodynamic interaction is present between oxycodone and mirtazapine - concomitant use increases the risk of CNS depression; finally, hydrochlorothiazide is known to increase glucose levels and may impair the antidiabetic effect of metformin.

Under use (START): calcium/ vitamin D

Medications Assessment (Number of PIMs)

Beers: 1 STOPP: 1 MAI: 3

Time (mins) - Med Review	Time (mins) - Patient Encounter	Number of PIMs	Number of Updates Changes*
12	17	5	6

*Description of medication changes:

1. Discontinued aspirin
2. Discontinued hydrochlorothiazide
3. Discontinued atorvastatin
4. Discontinued potassium chloride
5. Removed docusate from the med list
6. Removed oxycodone from the med list

Pharmacist Recommendations

1. Primary prevention/PVD - the use of aspirin for primary prevention of cardiac disease in patients >80 years old lacks significant evidence (Beers Criteria). There is an increased risk of bleeding, particularly gastrointestinal. Recommend to discontinue.
2. Hypertension – the patient’s blood pressure is currently at goal (< 150/90 mmHg per JNC 8). Hydrochlorothiazide may be ineffective in elderly patients; there is a potential risk of dehydration and hypotension accompanied by the drug interaction with the patient’s metformin. Recommend to discontinue hydrochlorothiazide and to continue to monitor blood pressures.
3. Hyperlipidemia - statin medications have little utility in elderly cancer patients for primary prevention due to lack of time-to-benefit and the risk of myalgias, myopathies, and fatigue. The patient is also reporting muscle aches that could be caused by this medication. Recommend to discontinue atorvastatin without tapering.
4. Potassium supplementation - recommend to discontinue potassium chloride tablets due to normal/slightly elevated potassium levels as well as pill burden.

ECOG – Eastern Cooperative Oncology Group; PO – orally; GI – gastrointestinal; HTN – hypertension; BP – blood pressure; DM – Diabetes Mellitus; HS – at bedtime; CNS – central nervous system; q – every; PRN – as needed; BID – twice daily; OTC – over-the-counter; NKDA – no known drug allergies; Rx – prescription; STOPP; MAI; PVD – peripheral vascular disease

The choice of geriatric medication screening tools was based on existing literature and specific factors of each tool. The Beers Criteria and STOPP Criteria are both effective in capturing PIM data in patients with cancer [14]. The MAI is a well validated implicit screening tool that has been the backbone of numerous models regarding PP and deprescribing [6]. The tools were applied sequentially: Beers Criteria first, then the STOPP Criteria, followed by the MAI. This order proved to be efficient because it screened for broad information first (i.e., Beers Criteria), followed by a more specific systems based review (i.e., STOPP), and ending with clinical assessment of the remaining medications (i.e., the MAI). Medications flagged as inappropriate by one tool were not reassessed using the other two tools (e.g., if the Beers Criteria flagged diphenhydramine as a PIM, neither

STOPP nor the MAI were applied to that medication subsequently). See **Online Resource 1** for a detailed review of the three tool assessment.

Deprescribing

Real time deprescribing occurred after discussion among the geriatric oncologist, pharmacist, patient, and caregivers. The detailed medication assessment and deprescribing process is outlined in Fig 1. Each medication identified as being potentially inappropriate was considered for deprescribing. Patient reported symptoms and side effects, potential adverse effects, time-to-benefit of medications, and estimated patient life expectancy were considered in the deprescribing process. Evidence-based rationales were provided to the patient and patients' caregivers regarding deprescribing recommendations. Specific instructions on how to discontinue medications were provided to the patient. Medications requiring tapering were accompanied by a tapering schedule, a list of possible withdrawal side effects, and a detailed description of if and when to restart medications (**Online Resource 2**). Deprescribing recommendations and pharmacist notes were sent electronically to patients' other care providers (primary care providers and specialists). Patients were followed up with by phone or at subsequent visits regarding medication changes; any new information potentially correlated to recent deprescribing was documented as a patient reported outcome. Any barriers to deprescribing were assessed during the direct patient encounter and documented in patient notes.

Endpoints

The primary outcome of the study was the incidence of PIMs identified by the Beers Criteria alone compared with the three tool assessment described in Fig 1. Secondary measures include mean number of medications, mean number of medications deprescribed, potential cost avoidance, pharmacist intervention time, and patient-reported barriers to deprescribing. Potential health care savings were assessed through application of University Health System Consortium (UHC) outcomes cost data. Specifically, the authors assigned cost values to minor adverse event prevention (\$220.00), major adverse event prevention (\$2200), medication teaching (\$208.00), and detailed medication history (\$642.00). These values are based on estimated cost savings as a result of pharmacy clinical service interventions established by UHC [16].

Results

Data were collected for 26 patients who were referred to the Geriatric Oncology Clinic and underwent a CGA between August 1, 2015 and April 30, 2016. All patients were evaluated by the pharmacist. Patients' baseline characteristics are described in Table 1. The most common reason for referral by the primary oncologist was to determine choice and appropriateness of systemic cancer therapy. Other reasons for CGA referral included pre-operative clearance, initial decision for surgery, goals of care assessment, and impaired cognition. The 26 patients in this study were taking a total of 312 medications, of which 197 were prescription and 113 were OTC or CAM therapies. The mean number of medications per patient was 12 (range, 5 to 22). Ninety-four clinically relevant (category D or X) drug interactions were identified, with a mean of 4 interactions per patient (range, 0 to 11),

including interactions with anti-cancer therapies. Ten out of 26 patients (38%) were undergoing active treatment during the CGA and, upon review, there were 9 relevant drug-drug interactions with anticancer therapies identified; category C, D and X interactions were reviewed for anti-cancer therapies (Table 2). The Beers Criteria alone identified 38 PIMs as compared to 119 PIMs with the three tool assessment; a mean of 5 PIMs were identified per patient. See Fig 2 for breakdown of PIMs captured by each tool. The 2012 Beers Criteria identified PIMs in 84% of patients versus 100% of patients with the three tool assessment. After the application of the three tool assessment, 73% (87 of 119) of PIMs identified were deprescribed in real time by the pharmacist and geriatric oncologist, resulting in a mean of 3 medications (range, 0–12) deprescribed per patient. The most common medication classes deprescribed in this study are displayed in Table 3; potential adverse events prevented by stopping these medications are also included.

Eighteen patients (69%) in this study were available for follow up either by phone or during subsequent clinic appointments, with mean time to follow up of 14 days. All patients had at least one medication deprescribed during their CGA, and 16 of these patients had previously reported symptoms or side effects likely attributable to PP and PIMs. After follow up, all 16 patients reported a reduction in symptoms and side effects. For example, one patient reported severe lower extremity muscle aches, fatigue, dizziness, and low blood pressure during their initial CGA; orthostatic hypotension was confirmed. Using the three tool assessment and deprescribing process, atorvastatin, metoprolol, and omeprazole were discontinued. At follow up, the patient reported no muscle aches, a decrease in fatigue, and no occurrences of dizziness.

Out of the 87 medications discontinued initially, two medications (<3%) were restarted. In one case, a 77 year old male patient with cholangiocarcinoma developed a gastrointestinal (GI) bleed as a result of a large stomach ulcer. Esomeprazole was discontinued in this patient several weeks prior to this bleed during the initial geriatric oncology assessment. After cessation of this drug, the patient underwent GI surgery, putting him at risk of ulcer development. Esomeprazole was restarted at 40 mg twice daily. In another case, a 72 year old male patient with kappa light chain multiple myeloma discontinued clorazepate due to recurrent falls after his visit with the geriatric oncology team. The patient had taken clorazepate for 15 years; therefore, a 6 week clorazepate tapering schedule was developed. Several weeks after his visit he developed acute agitation and delirium during his admission for an autologous stem cell transplant. Due to concern for clorazepate withdrawal, this medication was restarted at his previous dose. During his admission a plan was put into place to taper his clorazepate over 6 months.

Based on UHC outcomes cost data, healthcare expenditures of \$111,390.00, or \$4,282.27 per person, were potentially avoided as a result of PIM assessment and deprescribing. An average of 5 minutes (range 3 to 12 minutes) was spent pre-reviewing the patient's medication regimen and applying the three tool assessment. An additional 15 minutes (range 10 to 45 minutes) was spent directly discussing deprescribing interventions with the patient, caregivers, and the geriatric oncologist. Entering pharmacist notes and patient follow up encounters took an average of 10 minutes (range 5 to 20 minutes). Therefore, the total pharmacist intervention time was approximately 30 minutes for each patient; several patients

took significantly longer depending on regimen complexity (range 18 to 77 minutes). Estimating a clinical pharmacist's average hourly rate of \$50.00 per hour, the potential net cost prevention is \$110,470.00 for 26 geriatric oncology patients.

Lastly, barriers to stopping medications were evaluated for each patient in this study. Fifty-two percent of patients reported no barriers related to stopping medications and felt comfortable with the process. Of patient reported barriers to deprescribing, the most common concern was fear of return of symptoms or worsening of underlying condition being treated (60%). Other barriers included the patient's need to check with their primary care provider before deprescribing, feeling of physical dependence, and patient and caregiver confusion about medications.

Discussion

This study demonstrates that the application of a three tool assessment identified more PIMs than the Beers Criteria alone, and resulted in deprescribing the majority of the medications identified as inappropriate. This is the first prospective study to demonstrate the process of identification of PIMs with subsequent real time deprescribing in older cancer patients. Geriatric oncologists and pharmacists trained in geriatrics and oncology have a unique opportunity to collaborate in the clinic setting. The processes of PIM identification and deprescribing can be time-intensive for physicians. Pharmacists, if incorporated into the clinic setting, have the ability to play an important role and alleviate physician workload. Pharmacist-led deprescribing interventions are feasible and could potentially lead to improved patient outcomes as well as cost savings.

Several studies have evaluated the incidence of PP and PIMs in older cancer patients. Definitions have varied, making it difficult to come to consensus about the best way to evaluate these parameters. A study by Turner *et al* evaluating PP in older cancer patients found that taking 5.5 or 3.5 medications increased patient falls and exhaustion, respectively. They also found that taking greater than 6.5 medications correlated with reduced performance status and frailty. This study did not evaluate PIMs or specific medication classes [17]. Studies involving a clinical intervention for PP/PIMs are sparse. Riechelmann *et al* looked at unnecessary or duplicative medications in terminally ill cancer patients. They found that after palliative care consultation and a thorough medication assessment, that PIM use decreased by 2% [18]. This study only included terminally ill cancer patients and included patients of any age. No description of deprescribing methods were discussed but the authors noted that statins were the most commonly prescribed PIM.

Lindsay *et al* developed a specialized palliative deprescribing guideline that is intended to be used as a tool to highlight potential targets for deprescribing. The guideline consists of six broad medication classes that are considered inappropriate for cancer patients with a prognosis of six months or less. Each medication class is accompanied by 'considerations for limited benefit' and an additional 'explanation' section. Sixty-one patients had a median of 10 medications per patient. There were 132 PIMs identified with 70% of patients having at least one PIM. The most common medication classes identified as suitable targets for deprescribing were antihypertensives, dyslipidemic agents, peptic ulcer prophylaxis, and

CAM [19]. This study demonstrated a high rate of PIM use in palliative cancer patients and was effective in flagging medications that were appropriate for deprescribing. A study by Gil Deza *et al* assessed medication use in adults with advanced solid tumors. Medications were classified as green (adequate [must be maintained]), yellow (questionable [could be maintained or removed]) or red (avoidable [must be removed]). Based on their PIM review, a total of 10% of medications were immediately suspended, and up to 30% of medications were candidates for deprescribing [20]. Nevertheless, there still remains limited data discussing interventions for PP/PIMs and the effects on patient outcomes, particularly for older patients with cancer with a life expectancy greater than 6 months.

The geriatric medication screening tools utilized in this study create an effective synergy when applied concomitantly, detecting many more PIMs than the Beers Criteria alone. The incidence of PIM use in the geriatric oncology population has been reported between 29% and 96% in previous studies compared to an incidence of 100% in this study. Of note, the American Geriatrics Society supports the use of the Beers Criteria, STOPP Criteria, and MAI, validating use of these specific tools [21]. These tools, along with the MAI, should be applied sequentially to be most effective. The MAI is more time-intensive, but takes into account medication indication, effectiveness of the medication, dosage, directions for use, drug-drug interactions, drug-disease interactions, medication duplication, duration of therapy, and medication expense. Specifically, this tool enables the provider to evaluate the overall value of each medication as it relates to patient and family goals, medication time-to-benefit, target of therapy, and patient life expectancy. Determining if the benefit of a medication outweighs the potential risk is the cornerstone of the deprescribing process [6].

Older patients with cancer are often managed by a plethora of providers, many managing specific chronic diseases and resulting in fragmentation of care that may potentiate PP/PIMs. Decisions regarding deprescribing should be shared with all parties involved in the care of the patient. Importantly, patients should be given open access to provider notes regarding deprescribing and other medication changes (Box 1). If possible, evidence-based medicine should be cited and providers should be encouraged to frame deprescribing decisions based on supporting data. Deprescribing chronic medications can cause stress and anxiety for patients and their family members, especially when the physician discontinuing medications is not the original prescriber. It is important to disseminate deprescribing recommendations to patients' other providers and to consult on difficult matters related to medication discontinuation. In this study, one of the most common hesitations to deprescribing occurred during discussions on stopping cardiovascular medications. Barriers to deprescribing in the general geriatric population have been described, but data regarding deprescribing in older adults with cancer and other complex comorbidities are limited [22].

Programs promoting deprescribing and minimizing health care overuse have proven effective. The Choosing Wisely Initiative (<http://www.choosingwisely.org/>) is an organization aimed at providing evidence-based recommendations, minimizing duplicative therapies, and maximizing the use of truly necessary tests, procedures, and medications. For example, a specific recommendation advises against prescribing lipid-lowering medications in patients with limited life expectancy. Other recommendations include adhering to evidence-based blood pressure goals in patients 60 years and older, avoiding nonsteroidal

anti-inflammatory drugs (NSAIDs) in patients with hypertension, heart failure, or chronic kidney disease, and minimizing long term patient exposure to acid suppressive therapies in the setting of gastroesophageal reflux disease [23]. More evidence is necessary to guide future “choosing wisely” initiatives that address the value versus burden of PP/PIMs for older patients with cancer.

The Canadian Deprescribing Network (<http://deprescribing.org/>) has released deprescribing guidelines to help aid patients and providers in reducing PIMs. Currently, the site has published guidance documents on deprescribing proton pump inhibitors, benzodiazepines, anti-hyperglycemics, and antipsychotics. Each published document provides an evidence based algorithm that is driven by indication, symptoms, and duration of therapy. Tapering instructions as well as pharmacological and non-pharmacologic alternatives are also discussed. Older patients with cancer may benefit from use of resources related to medication overuse and deprescribing [24–27]. Further research is warranted to determine applicability of these guidelines in the geriatric oncology population.

Use of this three tool assessment in this population, with subsequent deprescribing, may be complemented by recommendations from organizations such as Choosing Wisely and the Canadian Deprescribing Network. The three tool assessment described here has demonstrated an efficient way to identify the maximum number of PIMs but is still lacking specific recommendations for deprescribing individual medication classes. While this study demonstrates subjective reports of improved quality of life and a decrease in symptoms, future research should incorporate specific, quantifiable metrics. The majority of patients targeted for deprescribing in this study wished to minimize the number of medications they were taking, indicating that additional efforts are needed to empower patients to initiate conversations about deprescribing with their providers. In alignment with deprescribing based on patient goals and medication time-to-benefit, metrics linking the seriousness of chronic disease states and decisions about deprescribing need to be established.

One limitation of this study is the use of the 2012 Beers Criteria; the updated 2015 criteria incorporate additional information on PPI use, drug interactions, and renal dosing in the elderly. This pilot feasibility study had a small sample size, limiting conclusions that could be drawn. Patients referred to the geriatric oncology clinic for evaluation may have been sicker than other older cancer patients not referred, thus displaying a higher rate of PP and PIM use. Established patient reported outcome metrics and screening tools were not utilized for patient follow up in this study. Finally, the best method for determining in what order to deprescribe medications is not well defined (one-at-a-time approach versus all-at-once approach). There are advantages and disadvantages to each but the authors in this study chose the all-at-once approach to ensure optimal deprescribing. The one-at-a-time approach may be more effective in the primary care setting where follow up is more consistent. The data from this pilot study is being used to develop larger, cluster-randomized trials of deprescribing interventions for older patients with cancer.

Conclusion

This study adds to the body of literature examining the assessment and management of PP, PIMs, and deprescribing in older cancer patients. Our medication assessment process uses the Beers Criteria, STOPP, and MAI in a sequential manner and identified three times more PIMs than the 2012 Beers Criteria alone. This three tool assessment process should be incorporated into interdisciplinary assessments of older patients with cancer and validated in future studies. Projects such as the Choosing Wisely Initiative and the Canadian Deprescribing Network are important supplements to this process. Deprescribing should be seen as an individualized assessment of medications that is driven by patient and caregiver goals as well as evidence based medicine.

References

1. Qato DM, Wilder J, Schumm LP, et al. Changes in prescription and over-the-counter medication and dietary supplement use among older adults in the United States, 2005 vs 2011. *JAMA Intern Med.* 2016; 176(4):473–82. [PubMed: 26998708]
2. Lees J, Chan A. Polypharmacy in elderly patient with cancer: clinical implications and management. *Lancet Oncol.* 2011; 12(13):1249–57. [PubMed: 21741307]
3. Todd A, Husband A, Andrew I, Pearson SA, et al. Inappropriate prescribing of preventative medication in patients with life-limiting illness: a systematic review. *BMJ Support Palliat Care.* 2016; Epub ahead of print. doi: 10.1136/bmjspcare-2015-000941
4. Whitman AM, DeGregory KA, Morris AL, Ramsdale EE. A comprehensive look at polypharmacy and medication screening tools for the older cancer patient. *Oncologist.* 2016; 21(6):723–30. [PubMed: 27151653]
5. Scott IA, Hilmer SN, Reeve E, Potter K, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med.* 2015; 175(5):827–34. [PubMed: 25798731]
6. Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. *Arch Intern Med.* 2006; 166(6):605–609. [PubMed: 16567597]
7. Maddison AR, Fisher J, Johnston G. Preventive medication use among persons with limited life expectancy. *Prog Palliat Care.* 2011; 19(1):15–21. [PubMed: 21731193]
8. Garfinkel D, Ilhan B, Bahat G. Routine deprescribing of chronic medications to combat polypharmacy. *Ther Adv Drug Saf.* 2015; 6(6):212–33. [PubMed: 26668713]
9. Kutner JS, Blatchford PJ, Taylor DH, Ritchie CS, et al. Safety and benefit of discontinuing statin therapy in the setting of advanced life-limiting illness: a randomized clinical trial. *JAMA Intern Med.* 2015; 175(5):691–700. [PubMed: 25798575]
10. Holmes HM, Todd A. Evidence-based deprescribing of statins in patient with advanced illness. *JAMA Intern Med.* 2015; 175(5):701–2. [PubMed: 25799203]
11. Todd A, Holmes H, Pearson S, Hughes C, et al. ‘I don’t think I’d be frightened if the statins went’: a phenomenological qualitative study exploring medicines use in palliative care patients, carers and health care professionals. *BMC Palliat Care.* 2016; 15:13. [PubMed: 26822776]
12. Rossello X, Pocock SJ, Julian DG. Long-term use of cardiovascular drugs: challenges for research and for patient care. *J Am Coll Cardiol.* 2015; 66(11):1273–85. [PubMed: 26361160]
13. Bayliss EA, Bronsert MR, Reifler LM, Ellis JL, et al. Statin prescribing patterns in a cohort of cancer patients with poor prognosis. *J Palliat Med.* 2013; 16(4):412–18. [PubMed: 23305190]
14. Burhenn PG, McCarthy AL, Begue A, et al. Geriatric assessment in daily oncology practice for nurses and allied health care professionals: opinion paper of the Nursing and Allied Health Interest Group of the International Society of Geriatric Oncology (SIOG). *J Geriatr Oncol.* 2016; 7(5): 315–325. [PubMed: 26961585]
15. Nightingale G, Hajjar E, Swartz K, Andrel-Sendecki J, Chapman A. Evaluation of a pharmacist-led medication assessment used to identify prevalence of and associations with polypharmacy and

- potentially inappropriate medication use among ambulatory senior adults with cancer. *J Clin Oncol*. 2015; 33(13):1453–1459. [PubMed: 25800766]
16. Rough SS, McDaniel M, Rinehart J. Effective use of workload and productivity monitoring tools in health-system pharmacy, part 1. *Am J Health Syst Pharm*. 2010; 67(4):300–311. [PubMed: 20133536]
17. Turner JP, Jansen KM, Shakib S, Singhal N, Prowse R, Bell JS. Polypharmacy cut-points in older people with cancer: how many medications are too many? *Support Care Cancer*. 2015; 24(4): 1831–1840. [PubMed: 26449548]
18. Riechelmann RP, Krzyzanowska MK, Zimmermann C. Futile medication use in terminally ill cancer patients. *Support Care Cancer*. 2009; 17(6):745–748. [PubMed: 19030900]
19. Lindsay J, Dooley M, Martin J, Fay M, Kearney A, et al. The development and evaluation of an oncological palliative care deprescribing guideline: the ‘OncPal deprescribing guideline’. *Support Care Cancer*. 2015; 23(1):71–78. [PubMed: 24975044]
20. Gil Deza E, Morgenfeld ED, Rivarola EGJ, Muino M, et al. Patient safety: A progressive deprescribing model in patients with advanced solid tumors assisted at Instituto Oncologico Henry Moore (IOHM). *J Clin Oncol*. 2017; 35(15):6594.
21. Network National Comprehensive Cancer. NCCN Clinical Practice Guidelines in Oncology: Older Adult Oncology. 2015. [cited; 2016 December 28. Available from: http://www.nccn.org/professional/physician_gls/pdf/senior.pdf
22. Reeve E, To J, Hendrix I, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of deprescribing: a systematic review. *Drugs Aging*. 2013; 30(10):793–807. [PubMed: 23912674]
23. AMDA—the Society for Post-acute and Long-term Care Medicine. [Accessed June 1, 2016] Five things physicians and patients should question. Choosing Wisely website. 2013. <http://www.choosingwisely.org/doctor-patient-lists/amda/>
24. Pottie K, Thompson W, Davies S, Grenier J, Sadowski C, Welch V. , et al. Evidence-based clinical practice guideline for deprescribing benzodiazepine receptor agonists. 2016. <http://www.open-pharmacy-research.ca/wordpress/wp-content/uploads/deprescribing-algorithm-benzodiazepines.pdf>
25. Farrell B, Black CD, Thompson W, McCarthy L, Rojas-Fernandez C, Lochnan H. , et al. Evidence-based clinical practice guideline for deprescribing antihyperglycemics. 2016. http://deprescribing.org/wp-content/uploads/2015/11/deprescribing_algorithms2016_AHG_vf-cc-Sept-2016-InDesign.pdf
26. Farrell B, Pottie K, Thompson W, Boghossian T, Pizzola L, Rashid J, Rojas-Fernandez C, Walsh K, Welch V, Moayyedi P. Evidence-based clinical practice guideline for deprescribing proton pump inhibitors. 2015. <http://www.open-pharmacy-research.ca/wordpress/wp-content/uploads/ppi-deprescribing-algorithm-cc.pdf>
27. Bjerre LM, Ferrell B, Hogel M, Graham L, Lemay G, McCarthy L. , et al. Deprescribing antipsychotics for behavioral and psychological symptoms of dementia (BPSD) and insomnia: an evidence-based clinical practice guideline. 2015. <http://www.open-pharmacy-research.ca/wordpress/wp-content/uploads/antipsychotic-deprescribing-algorithm.pdf>
28. Chu MP, Hecht JR, Slamon D, et al. Association of proton pump inhibitors and capecitabine efficacy in advanced gastroesophageal cancer: secondary analysis of the TRIO-013/LOGiC randomized clinical trial. *JAMA Oncol*. 2017; 3(6):767–773. [PubMed: 27737436]

Relevance statement

Polypharmacy is a significant issue for older patients, including those with cancer. Due to the complexity of this issue and the potential negative impacts of polypharmacy in older adults, polypharmacy should be seen as a disease. Deprescribing has been touted as one way to reduce polypharmacy and improve patient outcomes. Older adults with cancer may benefit significantly from a reduction in polypharmacy, and pharmacists may be the ideal health care professional to evaluate this issue. With rising health care costs, an aging population, and an increasing number of patients with multiple co-morbidities, the optimization of medications is essential to the health of our patients.

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Fig 1. Medication Assessment and Deprescribing Process

*ADE, Adverse Drug Effects; START, Screening Tool to Alert doctors to Right Treatment; STOPP, Screening Tool of Older Persons' Prescriptions; MAI, Medication Appropriateness Index

Fig 2.
Incidence of PIMs Identified by the Beers Criteria Compared With the 3 Tool Assessment

Table 1

Baseline Characteristics

Characteristic	N=26
Age, mean years (range)	81 (65–92)
Distribution, years – n (%)	
• 65–74	9 (35)
• 75–84	7 (27)
• 85	10 (38)
Male, n (%)	14 (54)
Number of medications, mean (range)	12 (5–24)
ECOG score, mean (range)	2 (0–3)
Pharmacist time spent on intervention, mean (range)	30 (18–77)
Reason for referral to geriatric oncology clinic, n (%)	
• Decision for systemic cancer therapy	13 (50)
• Preoperative clearance	4 (15)
• Initial decision for surgery	4 (15)
• Goals of care assessment	3 (12)
• Cognitive impairment	2 (8)
Cancer type, n (%)	
• Colon	8 (31)
• Pancreatic	6 (23)
• Cholangiocarcinoma	3 (12)
• Leukemia/Myelodysplastic Syndrome	3 (12)
• Melanoma	2 (8)
• Lymphoma	2 (8)
• Multiple Myeloma	1 (4)
• Gastric	1 (4)

Table 2

Summary of Interactions with Anticancer Therapies [28]

Interacting Therapies	Number of Interactions	Risk Category	Interaction Details
Capecitabine - citalopram	2	D	Increased risk of QTc prolongation
Capecitabine - pantoprazole	2	C	High gastric pH may reduce the absorption of capecitabine. Concurrent use of these therapies resulted in poorer PFS and OR in several studies
Dasatinib – apixaban	1	C	Potential for increased bleeding risk due to dasatinib's thrombocytopenic properties
Dasatinib – aspirin	1	C	Potential for increased bleeding risk due to dasatinib's thrombocytopenic properties
Dasatinib – trazodone	1	C	Dasatinib weakly inhibits CYP3A4 possibly resulting in higher concentrations of trazodone
Bortezomib – doxazosin	1	C	Potential hypotension or orthostasis
Bortezomib – escitalopram	1	C	Increased risk of QTc prolongation

* PFS – progression free survival; OS – overall survival; CYP3A4 – cytochrome P450 3A4 hepatic enzyme

Table 3

Commonly Deprescribed Medication Classes

Medication Class	Potential Adverse Events Prevented
Vitamins/minerals (n=18)	Pill burden, ineffectiveness, drug interactions
Antihypertensives (n=11)	Fatigue, orthostatic hypotension, dizziness, falls
Statins (n=8)	Fatigue, myalgias, myopathies, lack of benefit
Benzodiazepines (n=7)	CNS depression, falls, delirium, somnolence
Aspirin/NSAIDS (n=6)	Gastrointestinal bleeding, lack of benefit
Proton pump inhibitors (n=6)	Hypocalcemia, hypomagnesemia, fractures, infections, chronic kidney disease, dementia
Omega-3 fatty acids (n=5)	Increase bleeding risk, pill burden
Electrolyte supplements (n=5)	Pill burden
Other (n=21)	Various adverse drug effects