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PALLIATIVE MEDICINE (A JATOI, SECTION EDITOR)

Prevalence and Risk of Polypharmacy Among Elderly Cancer Patients Receiving Chemotherapy in Ambulatory Oncology Setting

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Abstract

Purpose of Review This was a single center, retrospective cross-sectional study looking into the incidence and types of drug-related problems (DRPs) detected among elderly cancer patients receiving at least three long-term medications concurrent with IV chemotherapy, and the types of intervention taken to address these DRPs. This paper serves to elucidate the prevalence and risk of polypharmacy in our geriatric oncology population in an ambulatory care setting, to raise awareness on this growing issue and to encourage more resource allocation to address this healthcare phenomenon.

Recent Findings DRP was detected in 77.6% of elderly cancer patients receiving at least three long-term medications concurrent with IV chemotherapy, with an average incidence of three DRPs per patient. Approximately half of DRPs were related to long-term medications. Forty percent of DRPs required interventions at the prescriber level. The use of five or more medications was shown to almost double the risk of DRP occurrence (OR 1.862, $P = 0.039$). Out of the eight predefined categories of DRPs, underprescribing was the most common (26.7%), followed by adverse drug reaction (25.0%) and drug non-adherence (16.2%).

Summary Polypharmacy leading to DRPs is a common occurrence in elderly cancer patients receiving outpatient IV chemotherapy. There should be systematic measures in place to identify patients who are at greater risk of inappropriate polypharmacy and DRPs, and hence more frequent drug therapy optimization and monitoring. The identification of DRPs is an important step to circumvent serious drug-related harm. Future healthcare interventions directed at reducing DRPs should aim to assess the clinical and economic impact of such interventions.

Keywords Geriatric oncology · Polypharmacy · Drug-related problems · Medication therapy management · Long-term medications · Elderly cancer patients · Outpatient chemotherapy · Ambulatory care

Introduction

Polypharmacy has been used to describe multiple, excessive, unnecessary, or unindicated drug consumption [1]. However, there is no consensus in the scientific community, nor standard cutoff in terms of number of medications to define polypharmacy. Although the term polypharmacy is often associated with negative connotation, appropriate polypharmacy can be beneficial for individuals with multiple medical conditions where medication use has been optimized and prescribed to the best available evidence, extending life and improving quality of life [2]. Nonetheless, polypharmacy, which is more common in older adults [3], is also associated with many negative consequences such as increased healthcare costs, adverse drug events, drug interactions, medication non-adherence, functional status decline, and numerous geriatric syndromes [4].

As an individual ages, the number of comorbidities increases, so does the incidence of cancer. According to the Singapore Cancer Registry latest report, over the period of 1976 to 2015, there was a significant rise in the crude incidence rate of cancer from one 5-year period to the next for both genders. However, the corresponding change in the age-standardized rate was

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insignificant, suggesting that the aging population partly accounts for the increase in the incidence of cancer among the Singapore resident population [5]. A review of studies involving geriatric oncology patients showed that age is a risk factor for polypharmacy among cancer patients [6]. Elderly cancer patients not only have higher prevalence of polypharmacy compared to their younger counterparts, physiologic changes associated with aging also alter the pharmacodynamic responses and drug disposition of many drugs [7], potentially enhancing adverse drug events or diminishing therapeutic effects of certain drugs. The concomitant use of chemotherapeutic agents, known for their significant acute and long-term toxicities, some of which requires additional supportive medications to manage, further increases drug burden, toxicities, and interactions. This represents increased need for specialized care for the aging Singapore population, particularly in the area of geriatric oncology.

Based on estimate from our in-house chemotherapy unit scheduling system, approximately 40% of patients receiving IV chemotherapy at our ambulatory cancer center were Singapore residents above the age of 65. Among these elderly patients, around 30% were found to have concurrent use of three or more long-term medications.

In an ongoing effort to improve pharmaceutical care and mitigate some of the risk associated with polypharmacy in older cancer patients, a team of pharmacists in our center routinely provides medication therapy management (MTM) service targeted at patients of any cancer and stage, receiving IV chemotherapy at our Ambulatory Treatment Unit (ATU), aged 65 years or above, taking at least three long-term medications, and provided verbal consent for this service. The aims of MTM service were to identify and address actual and potential drug-related problems (DRPs) to prevent related morbidity and mortality, reduce emergency visits or hospital admissions and healthcare cost associated with preventable drug events, empower patients to be proactive in their own chronic disease management, and integrate MTM into the broader healthcare system. Hence, the objectives of MTM service included medication reconciliation and review, identify and close drug knowledge gaps through patient education, monitor safety and efficacy of medications that patients were on, and communicate with prescribing physicians on problems related to patients' drug use.

Therefore, this study investigated the prevalence and risk of polypharmacy in geriatric oncology population in an ambulatory care setting.

Methods

Study Design and Patients

This was a retrospective cross-sectional study on cancer patients who had received MTM service at our center from the period of 1 Jan 2016 to 22 Aug 2017. The inclusion criteria were age 65 and above, active use of three or more long-term medications, undergoing IV chemotherapy at our ATU, and verbally consented for MTM service. We defined long-term medications as prescription drug therapy administered on a regular basis which was required for the management of chronic medical conditions other than cancer. Hence, by our definition, long-term medications excluded over-the-counter supplements, chemotherapeutic agents, or supportive medicines for the management of acute toxicities associated with chemotherapy. However, these medications if used, were taken into account for potential drug-drug interaction analysis.

Data Collection

An electronic database, a secondary data source used in the provision of MTM service, was used to generate reports on patient demographics, medical conditions, medication use history, the types of DRPs detected and drugs involved, and actions taken to address these DRPs.

Classification of DRPs and Interventions

A DRP is an event or circumstance involving drug treatment that actually or potentially interferes with the achievement of an optimal outcome of medical care [8]. We adopted the DRP classification by The American Society of Hospital Pharmacists (ASHP), originally developed by Hepler and Strand.

The original eight DRP categories were (1) Indication without drug/more medication required; (2) Drug without indication/discontinuation of medication required; (3) Wrong drug/inappropriate drug; (4) Overdosage/therapeutic duplication; (5) Subtherapeutic dosage; (6) Failure to receive drug/non-adherence; (7) Adverse drug reaction; and (8) Potential drug-drug interaction (PDDI) [9]. A ninth category, (9) Others, was added as some issues that could not be classified into one of the eight DRPs were deemed by MTM pharmacists to be problems associated with drug use which were of significant importance (Table 1).

The Lexi-Interact™ Online database was used to identify PDDIs. There were five risk ratings for each PDDI, namely A (no known interaction), B (no action needed), C (monitor therapy), D (consider therapy modification), and X (avoid combination). Only PDDIs with a minimum risk rating C which were clinically significant were captured in our database. This article will also further elaborate on selected PDDIs involving both a long-term medication and a chemotherapeutic agent or its supportive medication in the following section.

For each DRP, the intervention documented was classified into two broad categories: (i) intervention at the prescriber level and (ii) intervention at the patient level. Intervention at the prescriber level included prescribing, information

Table 1 Classification of drug-related problems (DRPs)

1 – Indication without drug/more medication required
2 – Drug without indication/discontinuation of medication required
3 – Wrong drug/inappropriate drug
4 – Overdosage/therapeutic duplication
5 – Subtherapeutic dosage
6 – Failure to receive drug/non-adherence
7 – Adverse drug reaction
8 – Potential drug-drug interaction (PDDI)
9 – Others

Adopted from The American Society of Hospital Pharmacists (ASHP)

exchange, discussion, or any action involving a physician. Whereas, intervention at the patient level included pharmacological and non-pharmacological advice to patient or caregiver, increased frequency of patient self-monitoring and reporting of drug efficacy and adverse events.

Statistical Analysis

Descriptive statistics was used to present patients' demographics, medical conditions, numbers of medications, the types of DRPs detected, and actions taken to address these DRPs. Categorical variables were expressed as absolute and relative frequencies and quantitative variables as mean and standard deviation or median and range.

All statistical analysis was performed with Statistical Package for Social Sciences (SPSS Version 18.0. IBM Corp. Armonk, NY). The univariate and multivariate binary logistic regression analyses were employed to investigate the potential predictors of DRPs. A P value of ≤ 0.05 was considered statistically significant.

Results

Patient Baseline Characteristics

A total of 389 patients who have received MTM service between 1 Jan 2016 and 22 Aug 2017 met the inclusion criteria for analysis. There were 227 (58.4%) male and the mean age was 71.1 years (SD = 4.7). More than 90% patients had ECOG performance status of 0–1 and more than half had metastatic cancer disease at baseline. The cancer types in decreasing order of prevalence were colorectal (21.9%), lung (21.1%), breast (11.8%), genitourinary (8.5%), lymphoma (7.7%), gynecological (6.7%), stomach (5.9%), pancreas (5.7%), head and neck (4.6%), and others (7.5%). The prevalence of comorbidities in decreasing order was hypertension (89.7%), hyperlipidemia (81.5%), diabetes mellitus (53.2%), ischemic heart disease (24.9%), benign prostate hyperplasia (10.3%), chronic renal impairment (8.2%), atrial fibrillation (7.7%), osteoarthritis (7.7%), psychiatric disorders (6.2%), and cerebrovascular disease (5.4%). The median number of medications consumed was 7 (range 3–19) (Table 2).

Drug-Related Problems

A total of 1011 DRPs were detected in 302 (77.6%) MTM patients. Of all the DRPs, 504 (49.9%) were related to long-term medications, 319 (31.6%) were related to chemotherapeutic agents and the associated supportive medications, and 217 (21.5%) were related to symptomatic medications used to treat common acute conditions which may or may not be cancer-related. Examples of common acute conditions were cough, rhinitis, dry eyes, xerostomia, gastrointestinal disturbances, etc. Table 3 showed the prevalence of each DRP category.

Out of these DRPs, 404 (40.0%) required intervention at the prescriber level and 603 (59.6%) required intervention at the patient level. Table 4 detailed the incidence of each DRP category, medication types involved in each DRP, and level of intervention for each DRP.

Indication Without Drug/More Medication Required

Out of these 270 cases, 80 (29.6%) cases were related to long-term medications, 34 (12.6%) cases were related to chemotherapeutic agents and the associated supportive medications, while the majority of 156 (57.8%) cases were due to inadequate symptomatic medications for treating common acute conditions. Two hundred sixteen (80.0%) cases required intervention at the prescriber level and 52 (19.3%) cases required intervention at the patient level.

Drug Without Indication/Discontinuation of Medication Required

Out of these 55 cases, 52 (94.5%) cases were related to long-term medications. Twenty-six (47.3%) cases required intervention at the prescriber level and 29 (52.7%) cases required intervention at the patient level.

Wrong Drug/Inappropriate Drug

Out of these 27 cases, 10 (37.0%) cases were related to long-term medications, 5 (18.5%) cases were related to chemotherapeutic agents and the associated supportive medications, and 13 (48.1%) cases were related to inappropriate symptomatic medications for treating common acute conditions. Sixteen (59.3%) cases required intervention at the prescriber level and 11 (40.7%) cases required intervention at the patient level.

Table 2 Patient baseline characteristics ($N = 389$)

Characteristics	Number of patients (percentage)
Male gender	227 (58.4)
Age, mean (SD)	71.1 (4.7)
ECOG	
0	158 (40.6)
1	203 (52.2)
2	22 (5.7)
3	5 (1.3)
4	1 (0.3)
Cancer type	
Colorectal	85 (21.9)
Lung	82 (21.1)
Breast	46 (11.8)
Genitourinary	33 (8.5)
Lymphoma	30 (7.7)
Gynecological	26 (6.7)
Stomach	23 (5.9)
Pancreas	22 (5.7)
Head and neck	18 (4.6)
Others	29 (7.5)
Metastatic disease	211 (54.2)
Comorbidities	
Hypertension	349 (89.7)
Hyperlipidemia	317 (81.5)
Diabetes mellitus	207 (53.2)
Ischemic heart disease	97 (24.9)
Benign prostate hyperplasia	40 (10.3)
Chronic renal impairment	32 (8.2)
Atrial fibrillation	30 (7.7)
Osteoarthritis	30 (7.7)
Psychiatric disorders	24 (6.2)
Cerebrovascular disease	21 (5.4)
Number of medications, median (range)	7 (3–19)

Values were reported as frequency (percentage) unless otherwise stated

Table 3 Number of patients with DRP in each DRP category, in descending order

DRP category	Number of patients with DRP, *n* (%)
1 – Indication without drug/more medication required	151 (38.8)
7 – Adverse drug reaction	126 (32.4)
6 – Failure to receive drug/non-adherence	116 (29.8)
8 – Potential drug-drug interaction (PDDI)	88 (22.6)
4 – Overdosage/therapeutic duplication	50 (12.9)
2 – Drug without indication/discontinuation of medication required	42 (10.8)
5 – Subtherapeutic dosage	29 (7.5)
9 – Others	27 (6.9)
3 – Wrong drug/inappropriate drug	24 (6.2)
Total	302 (77.6)

Table 4 Incidence, medication types involved, and level of intervention for each DRP

DRP category	Incidence of DRP, *N* (%)	Types of medication involved			Level of intervention	
		Long-term medications, *N*	Chemo agents/supportive medications, *N*	Other symptomatic medications, *N*	Prescriber level, *N*	Patient level, *N*
1	270 (26.7)	80	34	156	216	52
7	253 (25.0)	26	215	5	43	210
6	164 (16.2)	128	14	22	44	120
8	121 (12.0)	112	45	1	14	106
4	58 (5.7)	47	3	8	22	36
2	55 (5.4)	52	0	3	26	29
5	34 (3.4)	27	2	5	15	19
9	29 (2.9)	22	1	4	8	20
3	27 (2.7)	10	5	13	16	11
Total	1011 (100)	504 (49.9%)	319 (31.6%)	217 (21.5%)	404 (40.0%)	603 (59.6%)

1, indication without drug; *2*, drug without indication; *3*, inappropriate drug; *4*, overdosage; *5*, underdosage; *6*, non-adherence; *7*, adverse drug reaction; *8*, potential drug-drug interaction; *9*, others

Overdosage/Therapeutic Duplication

Out of these 58 cases, 47 (81.0%) were related to long-term medications and 8 (14.5%) were related to excessive symptomatic medications for treating common acute conditions. Twenty-two (37.9%) cases required intervention at the prescriber level and 36 (62.1%) cases required intervention at the patient level.

Subtherapeutic Dosage

Out of these 34 cases, 27 (79.4%) were related to long-term medications and 5 (14.7%) were related to underdosing symptomatic medications for treating common acute conditions. Fifteen (44.1%) cases required intervention at the prescriber level and 19 (55.9%) cases required intervention at the patient level.

Failure to Receive Drug/Non-adherence

Out of these 164 cases, 128 (78.0%) were related to long-term medications and 22 (13.4%) were related to symptomatic medications for treating common acute conditions. Forty-four (26.8%) cases required intervention at the prescriber level and 120 (73.2%) cases required intervention at the patient level.

Adverse Drug Reaction

Out of these 253 cases, 26 (10.3%) cases were related to long-term medications and 215 (85.0%) cases were related to chemotherapeutic agents and the associated supportive medications. Forty-three (17.0%) cases required intervention at the prescriber level and 210 (83.0%) cases required intervention at the patient level.

Potential Drug-Drug Interaction

Out of these 121 cases, 112 (92.6%) were related to long-term medications and 45 (37.2%) were related to chemotherapeutic agents and the associated supportive medications. Of note, 39 (32.2%) of these PDDIs involved at least one long-term medication and at least one chemotherapeutic agent or the associated supportive medication. Fourteen (11.6%) cases required intervention at the prescriber level and 106 (87.6%) cases required intervention at the patient level.

Others

Twenty-nine (2.9%) DRP cases could not be classified into one of the eight DRP categories above but were deemed by MTM pharmacists to be problems associated with drug use which were of significant importance. Twenty-two (75.9%) of these cases were related to long-term medications and four (13.8%) were related to symptomatic medications for treating common acute conditions. Eight (27.6%) cases required intervention at the prescriber level and 20 (69.0%) cases required intervention at the patient level. Two main problems identified were inadequate chronic disease monitoring (e.g., HbA1c) and need for patient education on medication use.

Patient Factors and DRP Occurrence

A logistic regression was performed to ascertain the effects of age, gender, ECOG performance status, metastatic stage disease, number of comorbidities, and number of medications on

the likelihood that patients have a DRP. The logistic regression model met the assumption of linearity and did not have serious collinearity problem. The univariate analyses found that the use of ≥ 5 medications was significantly associated with the presence of one or more DRP (OR 1.791, $P = 0.046$). In the multivariate analysis employed to minimize confounding factors, the use of ≥ 5 medications was shown to almost double the risk of one or more DRP (OR 1.862, $P = 0.039$). Age, gender, ECOG performance status, metastatic stage disease, and comorbidities were not found to influence the occurrence of DRP (Table 5).

Our results were consistent with our previous report that the use of five or more chronic medications was significantly associated with the presence one or more DRPs (OR 3.166, $P = 0.006$) [10].

Discussion

Our data showed that underprescribing (DRP1) was more prevalent than overprescribing (DRP2) in the elderly cancer patients with polypharmacy receiving IV chemotherapy (DRP incidence rate 26.7 vs 5.4%), especially when it comes to medications for symptomatic management of common acute conditions. One of the reasons identified was the short consultation time patients had with oncologists, where priority was on cancer disease management—hence these common acute conditions became secondary and sometimes neglected. It could also represent a common medical dilemma faced by physicians when it comes to initiating medications for this group of patients. Factors that had been identified to contribute to underprescribing include polypharmacy, comorbidity, ageism, lack of or scanty evidence concerning the benefit and risk of drugs in elderly, fear of adverse drug events, and economic constraints [11]. Some patients expected their oncologists to take over the management of their chronic conditions while they were under the oncologists' care, while most oncologists expected their patients to return to their regular care providers. A mismatch in care expectation between patients and oncologists also indirectly contributed to underprescribing.

On the other hand, overprescribing was mostly related to long-term medications, in particular antihypertensive agents, which contributed to more than half of the documented DRP2. These incidences were usually detected when patients reported frequent postural giddiness or there were more than one documented low blood pressure reading.

Most DRPs due to drug overdosing and underdosing (DRP4 and DRP5) were related to long-term medications—of which more than a third (26 out of 74) were antihypertensive agents and slightly less than a third (23 out of 74) were hypoglycemic agents.

Close to a third of MTM patients were found to be non-adherent to prescription drug therapy (DRP6), especially to medications for the management of chronic conditions. The extent of non-adherence reported in the literature varies widely, ranging from as low as 10% to as high as 92% [12]. WHO reported that adherence among patients with chronic diseases averages only 50% in developed countries [13]. It is widely recognized that medication non-adherence is an important public health consideration, affecting health outcomes and overall healthcare costs. Causes of non-adherence may be related to the patient, provider, and external factors [14]. For example, patients may not believe the treatment is necessary, complex treatment plans may increase the risk of non-adherence, or there may be insufficient communication between patient and provider [15]. From our experience, patients' reasons for non-adherence could be intentional or unintentional, and reasons include high pill burden, forgetfulness, discontinuity during transition of care settings, miscommunication between physician and patient, and poor health literacy. There were also many instances where patients neglected their long-term medications or chronic conditions' review with their primary care providers during the time they receive chemotherapy for various reasons, including but not limited to reduced appetite hence perceived less need for antihypertensive, hypoglycemic, or antilipemic agents; inconvenience with keeping to various

Table 5 Univariate and multivariate analyses of association between patient factors and presence of one or more DRP (vs none)

Patient factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age > 70 years	0.679 (0.421–1.096)	0.113	0.679 (0.418–1.105)	0.119
Male gender	1.113 (0.688–1.802)	0.663	1.184 (0.720–1.947)	0.506
ECOG ≥ 1	1.176 (0.726–1.905)	0.510	1.234 (0.753–2.021)	0.404
Metastatic disease	0.897 (0.555–1.451)	0.659	0.805 (0.489–1.325)	0.393
> 3 comorbidities	0.967 (0.597–1.568)	0.893	0.905 (0.550–1.490)	0.695
≥ 5 medications	1.791 (1.009–3.178)	*0.046**	1.862 (1.032–3.361)	*0.039**

DRP, drug-related problem; *OR*, odds ratio; *CI*, confidence interval

*Statistically significant *P* value (values in italics)

providers' appointments in view of chemotherapy schedule; and reduced priority for chronic condition management due to cancer disease.

As expected, the majority of adverse drug reactions (DRP7) were secondary to chemotherapeutic agents due to their narrow therapeutic index and toxic nature. Recently, a prediction model and scoring algorithm for chemotherapy toxicity that consisted of 11 prechemotherapy variables—5 geriatric assessment questions, 2 laboratory values, cancer type, planned treatment (dose and number of chemotherapy agents), and age—has been developed and externally validated in an elderly cancer patient cohort in the USA [16•]. A validation study using such tool in our local population may prove beneficial in helping to identify patients who are at risk of more chemotherapy toxicities, so that pre-emptive measures can be taken to ameliorate these undesirable consequences.

A Scottish population registry covering 310,000 residents revealed that the number of medications dispensed was the single most important predictor of potentially serious drug-drug interactions [17•], reflecting similar trend in their Swedish and Italian counterparts [18, 19]. PDDIs do not always translate to actual harm, and hence may be a risk worth taking for the benefits. A common example would be the co-prescription of amlodipine and simvastatin. Therefore, risk communication to patients is important to allow patients to identify early problematic symptoms, potentially averting clinically serious consequences. Of note, approximately one third (39 cases) of PDDIs (DRP8) identified during MTM service involved at least one long-term medication and at least one chemotherapeutic agent or the associated supportive medication. The most commonly implicated chemotherapeutic agents and supportive medications were fluorouracil derivatives (23 cases), and two antiemetic classes: dopamine antagonists (8 cases) and first-generation 5-HT3 antagonists (8 cases). The most common long-term medications that have the potential to interact with fluorouracil derivatives were sulfonylureas (15 cases) and losartan (5 cases) due to CYP enzyme inhibition; with anti-dopamine antiemetic, were psychiatric medications (6 cases) due to mechanism of action on a common pathway; and with first-generation 5-HT3 antagonists (namely ondansetron and granisetron), were antiarrhythmics and antidepressants (3 cases each) due to potential QTc prolongation.

Our team previously reported that MTM service significantly improved patient satisfaction [20]. Besides proactively identifying and addressing actual or potential DRPs through medication review, a recent systematic review suggested that improved communication, delineation, and coordination of responsibilities between community care providers and oncologists may help to improve patient and physician satisfaction and cancer care coordination [21].

Challenges and Limitations

The retrospective nature and the use of secondary data source were the main limitations of this study. Incomplete or erroneous data entry could have affected certain indicator measurements. The lack of independent checks for the classification of DRPs could result in reporting bias, especially for DRPs that may fit into more than one DRP categories. For example, a patient on antihypertensive regimen experiencing symptomatic hypotension can be classified as DRP2, DRP4, and DRP7 (discontinuation of drug required, overdosage, and adverse drug reaction respectively).

Even though the identification of DRPs was an important step to circumvent serious drug-related harm, our study objective was not designed to show that MTM service improved clinically important outcome indicators such as reducing morbidity and healthcare costs. Future healthcare interventions directed at reducing DRPs should ideally also measure the clinical and economic impact of such interventions, although such indicators are inherently complex and challenging to measure.

Summary and Conclusions

DRP was detected in 77.6% elderly cancer patients receiving three or more long-term medications concurrent with IV chemotherapy, with an average incidence of three DRPs per patient. The most common DRPs were underprescribing, adverse drug reaction, and non-adherence—which also represent the top three categories requiring intervention at the prescriber level. By reporting these DRPs, our study provides clinicians with greater awareness on some of the common healthcare challenges pertaining to medication use in elderly cancer patients with polypharmacy, thus promoting greater collaboration among healthcare professionals and patients to address the problems early.

Polypharmacy leading to DRPs is a common occurrence in elderly cancer patients receiving outpatient IV chemotherapy. There should be systematic measures in place to identify patients who are at greater risk of inappropriate polypharmacy and DRPs, and hence more frequent drug therapy optimization and monitoring. Clinicians should regularly review the adequacy and appropriateness of medications used in patients, and personalize drug therapy by taking into account changing care goals, thereby improving pharmaceutical care outcome. The identification of DRPs is an important step to circumvent serious drug-related harm. Future healthcare interventions directed at reducing DRPs should aim to assess the clinical and economic impact of such interventions.

Compliance with Ethical Standards

Conflict of Interest Ivy Goh, Olive Lai, and Lita Chew declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- • Of importance

1. Mortazavi SS, Shati M, Keshtkar A, Malakouti SK, Bazargan M, Assari S. Defining polypharmacy in the elderly: a systematic review protocol. BMJ Open. 2016;6:e010989. https://doi.org/10.1136/bmjopen-2015-010989.
2. Duerden M, Avery AJ, Payne RA. Polypharmacy and medicines optimisation: making it safe and sound. London: King's Fund; 2013.
3. Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. Eur J Clin Pharmacol. 2014;70:575–81. https://doi.org/10.1007/s00228-013-1639-9.
4. Maher Jr RL, Hanlon JT, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf. 2014 Jan;13(1):57–65. https://doi.org/10.1517/14740338.2013.827660.
5. Singapore Cancer Registry, Annual registry report 2015. Released 19 June 2017.
6. Balducci L, Goetz-Parten D, Steinman MA; Polypharmacy and the management of the older cancer patient, Annals of Oncology, Volume 24, Issue suppl_7, 1 October 2013, Pages vii36–vii40, doi: https://doi.org/10.1093/annonc/mdt266.
7. Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. Br J Clin Pharmacol. 2004;57(1):6–14. https://doi.org/10.1046/j.1365-2125.2003.02007.x.
8. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm. 1990;47(3):533–43.
9. American Society of Hospital Pharmacists. ASHP statement on pharmaceutical care. Am J Hosp Pharm. 1993:1720–3.
10. Yeoh TT, Tay XY, Si P, Chew L. Drug-related problems in elderly patients with cancer receiving outpatient chemotherapy. J Geriatr Oncol. 2015;6(4):280–7. https://doi.org/10.1016/j.jgo.2015.05.001.
11. Cherubini A, Corsonello A, Lattanzio F. Underprescription of beneficial medicines in older people: causes, consequences and prevention. Drugs Aging. 2012;29(6):463–75.
12. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. Oman Med J. 2011 March;26(3):155–9.
13. Sabaté E, editor. Adherence to long-term therapies: evidence for action. Geneva, Switzerland: World Health Organization; 2003.
14. Iuga AO, McGuire MJ. Adherence and health care costs. Risk Manag Healthc Policy. 2014;7:35–44.
15. Hugtenburg JG, Timmers L, Elders PJ, Vervloet M, van Dijk L. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. Patient Prefer Adherence. 2013;7:675–82.
16. • Hurria A, Mohile S, Gajra A, Klepin H, Muss H, Chapman A, et al. Validation of a prediction tool for chemotherapy toxicity in older adults with cancer. J Clin Oncol. 2016;34(20):2366–71. **This study externally validated a chemotherapy toxicity predictive model for older adults with cancer, from eight institutions across the USA. This study fills a gap in the literature by providing evidence of external validation and developing a validated tool to assess chemotherapy toxicity risk among older adults who receive chemotherapy in everyday practice to aid in clinical decision-making.**
17. • Guthrie B, Makubate B, Hernandez-Santiago V, Dreischulte T. The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995-2010. BMC Med. 2015;13:74. **This is one of the largest population database analysis of community-dispensed prescribing data, comparing all 310,000 adult residents in the Tayside region of Scotland in 1995 and 2010. Receipt of ≥10 drugs was strongly associated with increasing age and the number of drugs dispensed was the characteristic most strongly associated with the proportion with potentially serious drug-drug interactions.**
18. Johnell K, Klarin I. The relationship between number of drugs and potential drug-drug interactions in the elderly: a study of over 600,000 elderly patients from the Swedish Prescribed Drug Register. Drug Saf. 2007;30(10):911–8.
19. Nobili A, Pasina L, Tettamanti M, Lucca U, Riva E, Marzona I, et al. Potentially severe drug interactions in elderly outpatients: results of an observational study of an administrative prescription database. J Clin Pharm Ther. 2009;34(4):377–86.
20. Yeoh TT, Si P, Chew L. The impact of medication therapy management in older oncology patients. Support Care Cancer. 2013;21(5):1287–93.
21. Dossett LA, Hudson JN, Morris AM, Lee MC, Roetzheim RG, Fetters MD, et al. The primary care provider (PCP)-cancer specialist relationship: a systematic review and mixed-methods meta-synthesis. CA Cancer J Clin. 2017;67(2):156–69. https://doi.org/10.3322/caac.21385.