

# Polypharmacy in elderly cancer patients: Challenges and the way clinical pharmacists can contribute in resource-limited settings

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## Abstract

The aim of this study was to address the problems associated with polypharmacy in elderly cancer patients and to highlight the role of pharmacists in such cases in resource-limited settings. A narrative review of existing literature was performed to summarize the evidence regarding the impact of polypharmacy in elderly cancer patients and the pharmaceutical strategies to manage it. This review emphasizes the significance of polypharmacy, which is often ignored in real clinical practice. Polypharmacy in the elderly cancer population is mainly due to: chemotherapy with one or more neoplastic agents for cancer treatment, treatment for adverse drug reactions due to neoplastic agents, the patient's comorbid conditions, or drug interactions. The role of the clinical pharmacist in specialized oncology hospitals or oncology departments of tertiary care hospitals is well established; however, this is not the case in many developing countries. A clinical pharmacist can contribute to solving the problems associated with polypharmacy by identifying the risks associated with polypharmacy and its management in resource-limited settings. As in many developed countries, the involvement of a clinical pharmacist in cancer care for elderly patients may play a vital role in the recognition and management of polypharmacy-related problems. Further research can be conducted to support this role.

## KEYWORDS

cancer care, elderly patients, polypharmacy, resource-limited settings, role of pharmacists

## 1 | INTRODUCTION

Aging is associated with multiple—often chronic—illnesses, with an increased risk of the prescription of multiple medicines. The use of numerous medications—generally described as *polypharmacy*—can lead to unfortunate conditions and some medications are known to interact with each other.<sup>1,2</sup> Elderly patients are more likely to experience polypharmacy compared to other age groups, as they tend to suffer from more therapeutic conditions requiring pharmacotherapy. Polypharmacy in elderly individuals poses a significant risk to well-being; however, it

is difficult to avoid.<sup>3-5</sup> With this background, we aimed to summarize the existing evidence regarding the impact of polypharmacy in elderly cancer patients. We also aimed to provide some strategies for clinical pharmacists to contribute to the management of such problems.

## 2 | POLYPHARMACY

With regards to the definition of *polypharmacy*, there is contention as there is no standard meaning for the term. Be that as it may, the term

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*polypharmacy* can be characterized from multiple points of view. As indicated by Hajjar et al,<sup>6</sup> *polypharmacy* is characterized as “the use of multiple medications and/or the administration of more medications than are clinically indicated, representing unnecessary drug use.” Polypharmacy comprises of the number of medications taken by the patient, the existence of one or more wrong medications in a prescription, or an amalgamation of both, which can increase the risk for adverse drug events (ADEs), underutilization of medication, and repetition of medicine.<sup>6</sup> *Polypharmacy* can be defined as “the use of multiple drugs or more than are medically necessary, [and it] is a developing concern for senior adults.”<sup>7</sup> Because of its relationship with antagonistic medication responses and falls, the term *polypharmacy* has negative connotations with a range of adverse events among the officially powerless geriatric populace.<sup>8</sup>

Polypharmacy can be a mild to severe issue for patients of any age group, but particularly for elderly patients. For instance, due to the existence of various comorbidities in elderly cancer patients, drug therapies might be combined; furthermore, the expanded accessibility of over-the-counter, herbal, and complementary/alternative medicines (which patients often fail to declare to their specialist, doctor, or pharmacist) can contribute to polypharmacy. These populations remain at high risk for ADEs linked with polypharmacy and drug-drug interactions (DDIs). Elderly patients undergo many physiologic changes that may modify the different pharmacokinetics parameters, such as absorption, first-pass metabolism, protein binding, distribution, metabolism, and eliminations of the drugs. Molecular and cellular fluctuations may modify the pharmacodynamics of metabolism of the drug variations and may alter the effect of a drug on its target site and the narrow therapeutic windows related with chemotherapeutic agents due to the drugs that are given.<sup>9,10</sup> Together with the alterations in pharmacokinetic and pharmacodynamic variables, the risk in elderly patients is increased due to adverse drug reactions (ADRs).

### 3 | POLYPHARMACY IN ELDERLY CANCER PATIENTS

Among elderly cancer patients, polypharmacy has a noteworthy consequence and its incidence is increasing. Nevertheless, its predominance and impacts in disease patients are not well defined, particularly in end-of-life scenes.<sup>11</sup> Globally, numerous elderly cancer patients, many with comorbidities, are being treated with at least one or more drugs in oncology hospitals or clinics. In the management of most cancers, chemotherapy in combination with other treatments is more common than single chemotherapy agents. The inception of chemotherapy with at least one cytotoxic or targeted agent as well as drugs for the management of growth manifestations or the harmful impacts identified with treatment can result in polypharmacy.<sup>12</sup>

Prescribing the drug or chemotherapeutic agents is one of the foremost challenges in treating elderly cancer patients; furthermore, it is not simple. Cancer patients are at great risk of

medication-connected events as they are usually prescribed an extensive number of medicines, both for the disease itself and for supportive care.<sup>13</sup>

The treatment of cancer involves multiple medications and includes the unfavorable impacts/reactions of the cytotoxic treatments.<sup>14</sup> Usage of multiple medicines is an important factor for treating the health conditions of elderly people; however, complications can arise from antineoplastic therapy, which might influence the consequences of cancer treatment.<sup>1</sup>

The practice of many medicines can prompt additional drugs to the medication regimen, as different medications are prescribed to respond to the problems of former medicines, which is especially valid in the case of cytotoxic chemotherapy for the management of malignancy. There are numerous ADRs, ranging from mild nausea to myelosuppression, because of anticancer agents, which may prompt polypharmacy.<sup>14</sup>

#### 3.1 | Prevalence of polypharmacy in elderly cancer patients

The reported prevalence of polypharmacy in the elderly population varies substantially, ranging from 10% to 96%.<sup>15</sup> Due to changes in the pharmacokinetic profile associated with aging, elderly patients have varied pharmacodynamic responses to medications. The comorbid condition due to aging leads to a higher prevalence of polypharmacy in the elderly population than that in younger patients.<sup>16</sup> Therefore this group is more likely to suffer from ADEs or decreased therapeutic/beneficial effects of the medications. Elderly cancer patients are often exposed to chemotherapy and radiotherapy and these chemotherapeutic agents may lead to acute or long-term toxicity, which might require other supportive medications. This might result in drug interactions and increased drug burden.<sup>17</sup> Balducci et al<sup>1</sup> examined numerous studies in elderly cancer patients that showed age as a risk factor for polypharmacy, which may interrupt the consequence of the cancer treatment. Similarly, Jørgensen et al<sup>18</sup> reported that 35% of elderly patients diagnosed with breast, lung, colon, rectal, prostate, or ovarian cancer were each taking more than five drugs between 1996 and 2006. They found that the prevalence of polypharmacy increased with age (39% of 80-90-year-old patients and 41% of 90-91-year-old patients). Polypharmacy was more common among older cancer patients compared to younger cancer patients and those in the same age group without cancer. Surprisingly, it was also found that an increase in several prescribed drugs was initiated before 6 months of manifestations of malignant growth, demonstrating the increase in trend of prescription drugs during such period.

A study conducted in ambulatory cancer patients in Canada suggested that in newly diagnosed cancer patients aged 60 years and above, polypharmacy was assessed as taking an average of five medications at the time of diagnosis.<sup>13</sup> A Scottish study assessed community-dispensed prescription and adverse event data from 1995 to 2010 and revealed that the number of dispensed medications was a significant forecaster for potentially serious DDIs.<sup>19</sup> Nobili et al<sup>20</sup> also supported previous findings and concluded that the elderly

population constitutes the largest group of people highly susceptible to developing DDIs.

Besides the aforementioned studies, there is other evidence that supports the higher prevalence of polypharmacy in the elderly population. For example, a retrospective cross-sectional study conducted by Goh et al<sup>17</sup> evaluated the types and incidence of drug-related problems among elderly cancer patients and showed the non-adherence, underprescribing, and ADEs. Drug-related problems were identified in 77.6% of elderly cancer patients (approximately one incidence of three drug-related problems per patient). Polypharmacy leading to drug-related problems is prevalent in elderly cancer patients receiving outpatient intravenous chemotherapy.<sup>17</sup> Prithviraj et al<sup>21</sup> conducted a cross-sectional study showing a high prevalence of polypharmacy and inappropriate medication in newly diagnosed elderly cancer patients. Another prospective and observational study—by Flood et al<sup>22</sup> showed that polypharmacy was common in elderly cancer patients during hospitalization in an oncology-acute care unit for the elderly.

Thus, elderly cancer patients have a higher risk of polypharmacy than patients of the same age without cancer.

### 3.2 | Polypharmacy and association with outcomes in geriatric oncology

Polypharmacy is associated with a major problem: the risk of hospitalization and death among elderly patients with or without cancer.<sup>23-27</sup> The review study conducted in 2016 associated multiple risks factors for adverse outcomes in geriatric oncology as a result of polypharmacy.<sup>15</sup> In an oncology setting, polypharmacy with inappropriate medications may contribute to: the patient's worsened condition, frailty syndrome, poor physical function, poor survival, and a higher number of comorbidities.<sup>28-30</sup> Some studies have aimed to associate polypharmacy and its outcomes in geriatric oncology; for example, in 2014, Kim et al<sup>31</sup> considered a group of patients aged 65 years and over who underwent a comprehensive geriatric assessment (CGA) before palliative first-line chemotherapy (various cancer sites were involved). Out of 98 patients, 40% of patients met the criteria for polypharmacy. The result was observed to have no connection with early termination of palliative chemotherapy.

The current evidence advocates that with an increase in the number of medications used in geriatric cancer patients, there is a high risk of chemotherapy-induced toxicity and adverse physiological functions. Some of the prominent ADRs associated with chemotherapies are defective blood counts, immunosuppression, nausea, vomiting, hair loss, renal toxicity, and hepatotoxicity. Lastly, the intervention and screening of polypharmacy in regular clinical practice may require precise studies to scrutinize the impact of polypharmacy and its outcomes in geriatric cancer patients.<sup>15</sup>

### 3.3 | Interventions for polypharmacy in geriatric assessment studies

To some extent, polypharmacy has been aligned with evaluation studies in geriatric oncology settings. However, there is no

assessment of polypharmacy as a factor to predispose adverse reactions; furthermore, interventions for polypharmacy are uncertain. There is an urgent need for consistent interventions to manage polypharmacy in geriatric oncology practice.<sup>15</sup>

In a prospective study of elderly cancer patients aged 70 years or more, geriatricians proposed a change in prescribed medications (mostly in switching chemotherapy to supportive care) in more than 20% of patients based on CGA results; however, the proposed medication intervention and its benefits were not reported.<sup>32</sup>

In contrast, a prospective cohort study conducted by Kalsi et al<sup>33</sup> showed an association between geriatrician-led CGA interventions and improved chemotherapy tolerance in geriatric patients aged 70 or more during chemotherapy. The intervention was applied to unnecessary medications, such as adjustment of antihypertensive medications in over- or undertreated patients wherein 19% of undertreated patients benefited.

Aparicio et al<sup>34</sup> conducted a pilot study to assess the viability of mini geriatric assessment (MGA) done by a gastroenterologist, which showed the adaptation of non-oncological therapy and social care due to MGA in 72% and 38% of patients, respectively. Yet, there was no difference in strategy, which suggested that MGA could help gastroenterologists for adaptation of treatment of cancer.

An intervention study was done by Sokol et al<sup>10</sup> in which oncologists were required to change their prescriptions based on possible drug interactions; however, the physicians did not edit prescriptions unrelated to potential drug interactions. The study concluded that physicians should consider possible outcomes in association with polypharmacy and chronic use data. Incentives should be provided to physicians for optimization of safe and effective oncologic therapeutics.

A 2012 interventional study by Horgan et al<sup>35</sup> assessing CGA provides recommendations on modification of medication for geriatric oncology patients aged above 70 years. This intervention led to the identification of previously unidentified medical problems in 70% of patients.

Corcoran et al<sup>36</sup> suggested reducing the risks associated with polypharmacy by: educating patients and physicians, drug monitoring, and intervention. Additionally, investigations into the pharmacokinetic parameters of chemotherapeutic agents provide information on: possible drug interactions and adverse outcomes, how to decide on toxicity levels, and how to prevent the pharmacological responses of drug interactions.

Finally, an intervention study involving a multidisciplinary team, including clinical pharmacists, enrolled high-risk geriatric patients with polypharmacy and showed an effective reduction of unnecessary medications resulting in improved patient health outcomes.<sup>7</sup>

## 4 | RISKS AND PROBLEMS ASSOCIATED WITH POLYPHARMACY

There are various unfavorable results related to polypharmacy, which is regrettable as it is often unavoidable. These include ADRs,

drug interactions, prolonged hospitalization or increased hospital stay, and an increase in the cost of health care.

#### 4.1 | Adverse drug reactions

The burden of polypharmacy increases the greater cost of health care. It is also connected to elevated risk of ADEs in elderly patients due to: the greater possibility of DDIs, medication adherence, the vulnerability of the elderly populace to side-effects of medications, and physical changes identified with aging that trigger difficulties in taking medicines as proposed.<sup>37,38</sup> Runciman et al<sup>39</sup> affirmed that ADEs are accountable for more than 30% of unexpected hospital admissions in people aged 75 years and above in Australian health care settings.

#### 4.2 | Drug interactions

The frequency of drug interactions in elderly patients is not well documented. Senior patients are at greatest risk of having drug-related interactions and various kinds of drug interactions can happen, including drug-drug, drug-disease, drug-food, drug-alcohol, drug-herbal-products, and drug-nutritional-status interaction. The variables, including age-related physiologic alterations in pharmacokinetics and pharmacodynamics, infirmity, inter-individual variability, decreased homeostatic mechanisms of the human body, and psychosocial concerns (which are almost universal among patients who have progressive life-threatening diseases), should be considered when drug interactions are evaluated.<sup>40</sup> One of the most important challenges in elderly patients with cancer is a drug interaction that is inescapable.<sup>41</sup>

Polypharmacy and drug interactions have been recognized as the most hazardous factors for ADR, which is one of the most common outcomes.<sup>42</sup> This may be the reason for multiple visits to the emergency department.<sup>43</sup> The threat of polypharmacy plus DDI is greater in elderly individuals, who regularly experience the ill effects of a variety of therapeutic conditions and are thus prescribed multiple medications, several of which are connected with each other to deliver undesirable impacts. Ruitter et al<sup>44</sup> found that ADRs and DDIs increased the risk of hospitalization by fourfold in patients aged 75 or more, compared to those aged 55 to 74 years. Alkan et al<sup>45</sup> found that out of 445 elderly cancer patients, nearly one-third were exposed to potentially inappropriate medications and drug interactions that were very severe. In this study, the investigators found that polypharmacy (with more than five drugs), inpatient status, and diagnosis of lung cancer were connected with severe drug interactions. This study, which was carried out in Turkey, suggests that clinicians should be more restrained when prescribing and preparing drugs for elderly patients. Girre et al<sup>41</sup> conducted a study in France among 105 patients and found that almost half of the interactions were moderate.

#### 4.3 | Increased health care cost

Another possible issue that accompanies polypharmacy is increased health care cost, which may be direct or indirect. An association

among polypharmacy, DDIs, ADRs, and repeated hospital admission has been demonstrated by researchers.<sup>46-48</sup> ADEs increase health care costs by increasing hospital admissions, or as a result of unpredicted drug interaction,<sup>14,49</sup> along with increased visits to the emergency department and clinics.<sup>50</sup>

Polypharmacy is associated with increased cost,<sup>1</sup> increasing medical expenses for the patient and the health care institution. Increased health care costs include the price of unsuitable or identical medications, additional medicines for treating newly induced symptoms, laboratory costs, and supplementary patient monitoring that may be obligatory.<sup>12</sup>

In a Swedish study, Hovstadius et al<sup>51</sup> describe increases in prescription medication spending of 6.2% and 7.3% for patients taking five or more and 10 or more medications, respectively. Shrestha et al<sup>14</sup> also discuss the financial burden of patients due to ADRs and chemotherapy where more ADRs were seen in patients aged more than 60 years. In a retrospective cohort study, Akazawa et al<sup>52</sup> showed an association among polypharmacy, increased risk of taking possibly unsuitable medicines, and increased hospital admissions, leading to increments in medical costs of approximately 30%.<sup>52</sup>

### 5 | MANAGEMENT OF POLYPHARMACY BY CLINICAL PHARMACISTS IN ELDERLY CANCER PATIENTS

Polypharmacy is a problem that requires a rational and organized method. Incorporating clinical pharmacy services into the multidisciplinary oncology team can play a crucial role in the identification of risks accompanying polypharmacy and management of polypharmacy.<sup>53</sup> There are various strategies for managing polypharmacy in elderly cancer patients, which can also be applicable to other chronic diseases.

#### 5.1 | Taking an appropriate medication history

Evaluating the relevance of a patient's present drug therapy and guidance to forthcoming treatment selections can be obtained from an appropriate medication history. This can be obtained by close teamwork among health professionals (i.e., patients, doctors, nurses, and clinical pharmacists), in cooperation with patients. Existing procedures intended for documenting drug histories have been identified as insufficient, needing improvement, and in some cases actually hazardous.<sup>54</sup> Health professionals should consolidate their medical records and keep them up to date. A thorough medication history includes an interview with questions about: the currently prescribed drugs; doses; routes of administration; frequencies; treatment duration; other medications (e.g., over-the-counter, herbal remedies, complementary/alternative medicines); assessment of drug containers or lists, or both; and communication with community pharmacies or specific doctors. Additionally, other information on the history from previous medical reports can be obtained, such as earlier prescriptions, previous drug interactions, the aforementioned ADRs, and previous hypersensitivity reactions.<sup>55</sup> One of the

most important responsibilities of clinical pharmacists is to obtain accurate medication histories with the above-described methods to confirm that the patient's present and forthcoming therapy is harmless and effective.

## 5.2 | Medication reconciliation and medication review

According to St Peter,<sup>56</sup> individual procedures are required to avoid and resolve medication-related complications and subsequently to reduce polypharmacy. These include parameters such as medication reconciliation, medication review, and ongoing patient-centered medication therapy management.<sup>56</sup> A multidisciplinary approach involving clinical pharmacists in the medical oncology group can effectively manage polypharmacy in elderly cancer patients.

Medication reconciliation and medication review are both imperative tools for pharmaceutical care. The two terms are different and require definition. *Medication reconciliation* is the straightforward management of drugs,<sup>57</sup> that is, the method of building a list of correct medications.<sup>58</sup> Medication reconciliation is preliminary to medication review.

A critical involvement for addressing polypharmacy is a systematic and detailed medication review to evaluate whether the patient has obtained therapeutic advantage from their medication, whether there are continuing medical needs, and whether risks and side-effects are balanced by probable pros.<sup>59</sup> The patient's medication regimen should be assessed for safety and correctness from the perspective of the specific patient's multiple morbid illnesses, health literacy, and issues of sociodemographics. Advanced clinical drug therapy expertise is necessary for medication review and it is well recognized that pharmacists own these clinical skill sets.<sup>60</sup>

Medication reconciliation and medication review will potentially involve the prescription and deprescription of drugs. Similar decent practices and standards ought to be connected when medical treatment is started and when it is discontinued.<sup>61</sup> In the global scenario of the health care system, deprescribing is an impartially innovative theory, which is the way toward decreasing or halting medications, aimed at minimizing multiple uses of drugs and improving health outcomes for patients.

## 5.3 | Multidisciplinary approach

In most cases, polypharmacy can be managed with a multidisciplinary approach. The study by Holland conducted at an Irish teaching hospital demonstrates how interdisciplinary teamwork between the clinical pharmacist and doctor can develop the comprehensiveness and accurateness of discharge medicines through the establishment of a discharge medication reconciliation service, which is commanded by the pharmacist.<sup>57</sup> Shrestha et al<sup>53</sup> also stated that the clinical pharmacist can act as a bridge between the medical oncologist and the patient in an oncology setting by providing clinical pharmacy services. These services, such as discharge medication reconciliation, can be best provided by the clinical pharmacist.

## 5.4 | Patient-centered medication therapy

The service given by the clinical pharmacist is patient-centered medication therapy management, which is a developing treatment plan that concentrates on each intention associated with a patient's medication. Recently, medication therapy management has been extended as an important initiative, largely due to the need to enhance patients' medication treatment.<sup>62</sup> Most prolonged disease conditions, such as cancer, require that patients persist in treatment indefinitely, even when asymptomatic, in order to meet therapeutic objectives. For the improvement of patients' health-related results, certain pharmacist-managed medication therapy programs should be maintained.<sup>63</sup> This will also help to lower the health care cost of the patients.

This is an era of information technology and most hospitals are very much linked to this technology, which can enhance the care of patients. Online computer software for checking DDIs may diminish DDIs. According to the Beers Criteria record, elderly patients should be made aware of the possibility that the wrong medication might be administered. Regulatory authorities should focus on the distribution of appropriate medications, such as prescriptions for elderly patients, and also support safer alternatives.<sup>64</sup>

## 5.5 | Pharmacovigilance center

When it comes to the treatment of cancer patients of any age group, ADRs are being documented universally as one of the unavoidable constituents of management. ADRs are normal and expectable. Once the ADRs are identified, ADR alert stickers or notes mentioning ADRs can be placed in the patient's medical file. This will help in future and alert the concerned physicians.<sup>65</sup> Additionally, the information should be circulated to the patients and related doctors.

## 5.6 | Drug information center

The drug information center can play a vital role for elderly cancer patients in providing information on polypharmacy and ADEs. It can also help in the management of polypharmacy. The pharmacist can provide the information to elderly patients on different categories, such as general information of their diseases and medications, how the prescribed medicine works or what it does to the body, possible side-effects and interactions, and duration of the treatments. Elderly patients need information on drugs that are dispensed to them or prescribed.

## 5.7 | Educational intervention and awareness of polypharmacy

Educational intervention and awareness can shape patients' attitudes toward polypharmacy. Numerous elderly patients struggle to deal with their issues in health care. Limited health literacy exaggerates such struggles and creates a greater diversity of

adverse health activities and consequences for elderly patients. The effect of a lack of health literacy on the lives of the elderly populace requires greater consideration and understanding from community services practice.<sup>66</sup> An elderly populace with little health literacy is at increased risk of nonadherence, unintentional medication experience, and adverse events. Whittaker et al<sup>67</sup> recommend educational involvement that can build familiarity with poison inhibition means and medication safety strategies in older adults with low well-being proficiency. Numerous approaches to educational intervention and awareness among patients regarding polypharmacy can be used in elderly patients, such as audiovisual activities, presentations, and brochures in understandable or local languages. Raising physicians' awareness and ventures to support higher experts with respect to polypharmacy and the noxious effects of drug interactions may result in healthier outcomes for elderly patients.

## 6 | CONCLUSION

This review has successfully discussed the challenges associated with polypharmacy in elderly cancer patients and the ways in which pharmacists can contribute to managing such problems in low- and middle-income settings. Polypharmacy in elderly cancer patients is one of the most important and growing public health issues; it is a grave concern to those who are associated with the management of cancer, such as medical oncologists and other clinicians, as polypharmacy is also related to negative health outcomes. The clinical pharmacist has a major role to play in selecting the best interventions needed to enhance suitable polypharmacy and consequently managing problems associated with polypharmacy properly to accomplish better clinical results for patients.

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## CONFLICT OF INTEREST

The authors declare that no conflicts of interest exist with this work.

## AUTHOR CONTRIBUTIONS

Sunil Shrestha conceptualized the idea of this manuscript and wrote the initial version of the manuscript. Sudip Shrestha added the content of the manuscript and revised it substantially. Saval Khanal added his ideas and content of the initial version and helped substantially in improving the manuscript through all stages of the manuscript writing. All authors read and approved the final manuscript.

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