University of Groningen

Prevalence and follow-up of potentially inappropriate medication and potentially omitted medication in older patients with cancer - The PIM POM study

van Loveren, Fianne M. A. M.; van Berlo - van de Laar, Inge R. F.; Imholz, Alex L. T.; van't Riet, Esther; Taxis, Katja; Jansman, Frank G. A.

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Prevalence and follow-up of potentially inappropriate medication and potentially omitted medication in older patients with cancer – The PIM POM study

Fianne M.A.M. van Loveren [a,1], Inge R.F. van Berlo - van de Laar [a,1,*], Alex L.T. Imholz [b], Esther van 't Riet [c], Katja Taxis [d], Frank G.A. Jansman [a,d]

[a] Department of Clinical Pharmacy, Deventer Hospital, Nico Bolkesteinlaan 75, 7416 SE Deventer, the Netherlands
[b] Department of Medical Oncology, Deventer Hospital, Nico Bolkesteinlaan 75, 7416 SE Deventer, the Netherlands
[c] Department of Research & Development, Nico Bolkesteinlaan 75, 7416 SE, Deventer Hospital, Deventer, the Netherlands
[d] PharmacoTherapy, -Epidemiology and -Economics – Groningen Research, Institute of Pharmacy, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, the Netherlands

ARTICLE INFO

ABSTRACT

Objectives: To determine the prevalence of Potentially Inappropriate Medication (PIMs) and Potentially Omitted Medication (POMs) in older patients with cancer.
Materials and Methods: In this prospective observational study (hospital) pharmacists conducted comprehensive medication reviews in older patients with cancer (aged ≥65 years) receiving parenteral chemotherapy and/or immunotherapy at the Deventer Hospital. PIMs and POMs were identified using the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP), the Screening Tool to Alert doctors to the Right Treatment (START), and pharmacists' expert opinion. Recommendations regarding PIMs and POMs were communicated to the patient's oncologist/haematologist and follow-up was measured. Associations between covariates and the prevalence of PIMs and POMs were statistically analysed.
Results: For the 150 patients included, 180 PIMs and 86 POMs were identified with a prevalence of 78%. Using pharmacists' expert opinion in addition to only STOPP/START criteria contributed to 49% of the PIMs and 23% of the POMs. A follow-up action was required in 73% of the 266 PIMs and POMs. Number of medicines and Charlson Comorbidity Index score were both associated with having at least one PIM and/or POM ($p = .031$ and $p = .016$, respectively).
Conclusion: The prevalence of PIMs and POMs and subsequent follow-up in older patients with cancer is high. A pharmacist-led comprehensive medication review is a good instrument to identify these PIMs and POMs and to optimize patients' treatment. A complete approach, including pharmacists' expert opinion, is recommended to identify all PIMs and POMs in clinical practice.

1. Introduction

Ageing, multiple morbidities, and the use of multiple medicines make older patients a high-risk group for drug-related problems (DRPs). The diagnosis of cancer further increases this risk. Cancer treatment leads to the use of more medicines, multiple involved health care providers, and a higher disease burden. Frequent hospital visits and the associated transfer of information about medication use are additional risk factors for DRPs, which can lead to compromised cancer management plans. Since this population will continue to grow, addressing the appropriateness of medication use in this population will become even more important [1–5].

Several studies show that pharmacists, in a multidisciplinary approach, can play an important role in reducing DRPs by conducting medication reviews [6–9]. Different criteria are used to identify Potentially Inappropriate Medications (PIMs) and Potentially Omitted Medications (POMs). Potentially Inappropriate Medications are defined as medicines that are used by a patient, but are either unnecessary or do not have additional value, or can be optimized in their use. Potentially Omitted Medications refer to medicines that are not used by a patient, but adding them is clinically indicated and can be beneficial for the patient. In Europe, the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and the Screening Tool to Alert doctors to the Right Treatment (START) are most recommended to identify PIMs and POMs [10]. However, using only these criteria does not lead

* Corresponding author at: Department of Clinical Pharmacy, Deventer Hospital, Nico Bolkesteinlaan 75, 7416 SE Deventer, the Netherlands.
E-mail address: i.vanberlo-vandelaar@dz.nl (I.R.F. van Berlo - van de Laar).
[1] Both authors contributed equally to this manuscript

to identification of all relevant PIMs and POMs and therefore a more comprehensive medication assessment is needed [2,11].

The Dutch multidisciplinary guideline 'polypharmacy in the elderly' recommends comprehensive medication reviews in patients aged ≥65 years with polypharmacy and having at least one predefined risk factor [12]. Oncology is not mentioned as a specific risk factor in this guideline and no Dutch study was found investigating PIMs and POMs and the impact of pharmacist-led comprehensive medication reviews in this population. In general, studies on the prevalence of PIMs and POMs in older patients with cancer have various limitations and methods and results differ highly [3–5,13–17].

Therefore, this study aims to determine the prevalence of PIMs and POMs in older patients with cancer by conducting pharmacist-led comprehensive medication reviews. Secondary objectives are to examine subtypes of PIMs and POMs, to determine follow-up of PIMs and POMs, and to assess risk factors for PIMs and POMs.

2. Materials and Methods

In this prospective observational study, pharmacist-led comprehensive medication reviews were conducted in a multidisciplinary team with older patients with cancer between May 2018 and January 2019 at the Deventer Hospital (a middle-sized teaching hospital in The Netherlands). Patients aged ≥65 years, treated for cancer by a medical oncologist/haematologist, and receiving parenteral chemotherapy and/or immunotherapy at the day care unit were enrolled in this study. Patients at the start of therapy as well as patients who already started therapy were included.

Patients were asked to bring all their medication or a medication overview to the day care unit. While receiving chemotherapy or immunotherapy, a pharmacist or pharmacist in training interviewed the patient. The actual medication use, including non-prescription medicines, was verified with the patient (medication reconciliation) and problems with usage of medication were addressed using a questionnaire. Based on this information and the patient's medical records, PIMs and POMs were identified by the pharmacist using the revised STOPP/START criteria (2015) [18] and pharmacists' expert opinion. Expert opinion consisted of interpretation of medication surveillance signals, practical recommendations, and guideline adherence. Reviewing medication surveillance signals generated from the pharmacy information system is standard practice in Dutch hospital pharmacies. The pharmacists' expert opinion was part of the typical work and knowledge of a hospital pharmacist responsible for medication reconciliation and medication review. No specific framework, process, or list was used for the pharmacists' expert opinion. All identified PIMs and POMs and their corresponding recommendations were double-checked and if necessary complemented by a hospital pharmacist before communicating them to the patient's oncologist/haematologist. If there were discrepancies between the pharmacist and hospital pharmacist, the PIMs and POMs and their corresponding recommendations were based on consensus between the two. For each PIM/POM the oncologist/haematologist decided if a follow-up action was required. Two follow-up actions were possible: the recommendation was implemented by the oncologist/haematologist or the PIM/POM with corresponding recommendation was sent to the patient's general practitioner.

The prevalence of PIMs and POMs (percentage of patients with at least one PIM and/or POM) was determined for PIMs and POMs combined as well as separately. PIMs and POMs were further classified by the Anatomical Therapeutic Chemical (ATC) classification, by the classification used in the STOPP/START criteria, and by the classification used in the Systematic Tool to Reduce Inappropriate Prescribing (STRIP) method [12,18,19].

To determine the association of covariates with the prevalence of PIMs and POMs, the following information was collected for each patient: age, gender, number of different medicines, polypharmacy, use of a medication roll (medication pre-packaged per intake moment), cancer type, curative intent, and the Charlson Comorbidity Index (CCI) score. The number of different medicines included all medication used at home at the time of the interview, as well as the chemotherapy and/or immunotherapy, and accompanying supportive care agents. Polypharmacy was defined as concurrent use of five or more medicines for chronic use with a different ATC classification on ATC3-level, excluding medicines for dermal use (definition by the Dutch guideline 'polypharmacy in the elderly' [12]). Use of a medication roll was included as a measure for "self-management". The patient's oncologist/haematologist indicated whether the cancer treatment was intended to be curative or not. Finally, the CCI score, determined by the classic scoring index by Charlson et al. [20], was included as a measure for vulnerability and was based on the patient's medical records.

Differences in these covariates for patients with and without PIMs/POMs were assessed using descriptive statistics (independent-samples t-test, Mann-Whitney U Test, Pearson's χ^2 test, or Fisher's exact test). For factors significantly associated with the prevalence of PIMs and POMs (p-value <.05), univariate logistic regression followed by multivariate logistic regression was used to assess odds ratios (ORs) and 95% confidence intervals (CIs).

This study was assessed and approved by the Medical Ethics Committee of Isala Hospital as a non-interventional study. All patients signed a written consent form prior to participating in this study.

3. Results

For this study, 159 patients were approached to participate of which four patients refused participation and five patients had their appointment rescheduled until after the research period. The patients' characteristics of the 150 patients included in this study are depicted in Table 1. In total, these patients used 1656 medicines, with a mean of eleven medicines per patient (range 3–21). One hundred and forty-four patients (96%) used five or more medicines and 99 patients (66%) used ten or more medicines. When excluding the chemotherapy and/or immunotherapy regimen and accompanying supportive care agents at the day care unit, the mean number of medicines per patient was seven with 77% and 23% of the patients using five or more and ten or more medicines, respectively.

A total of 180 PIMs and 86 POMs were identified. These 266 PIMs and POMs give a mean of 1.8 per patient (range 0–8). PIMs and POMs

Table 1
Patient characteristics.

	$n = 150$
Age, years (median (IQR) [range])	72 (8) [65–90]
Gender (n (%))	
Male	88 (59)
Female	62 (41)
Number of medicines (mean (SD) [range])	11.0 (3.8) [3–21]
Number of medicines without chemotherapy, immunotherapy and supportive care agents (mean (SD) [range])	7.2 (3.6) [0–17]
Polypharmacy[a] (n (%))	
Yes	91 (61)
No	59 (39)
Medication roll (n (%))	
Yes	18 (12)
No	132 (88)
Cancer type (n (%))	
Solid tumours	102 (68)
Haematologic malignancies	48 (32)
Curative intent (n (%))	
Yes	34 (23)
No	116 (77)
CCI score (median (IQR) [range])	4 (1) [3–9]

Abbreviations: CCI, Charlson Comorbidity Index; IQR, interquartile range; SD, standard deviation.

[a] Chronic use of ≥5 different medicines, excl. Dermal use.

were prevalent in 117 (78%) of the patients. The prevalence of PIMs and POMs separately was 65% and 46%, respectively (Fig. 1).

Based on the ATC classification, the most common groups of medication for the 180 PIMs were proton pump inhibitors (PPIs) (19%), antihypertensive drugs (11%), benzodiazepine agonists (9%), analgesics (8%), alpha-adrenoreceptor antagonists (6%), and antidepressants (6%). Four PIMs (2%) concerned antineoplastic agents. The most common groups of medication for the 86 POMs were statins (40%), antihypertensive drugs (19%), and vitamin D (15%). Table 2 specifies the criteria used for identification of the PIMs and POMs.

For 195 (73%) of the 266 identified PIMs and POMs a follow-up action was required according to the oncologist/haematologist. PIMs required more frequently a follow-up action than POMs, 76% vs 67% respectively. For 39% of the PIMs and POMs requiring a follow-up action, this action was realized by the oncologist/haematologist. The distribution of follow-up actions is summarized in Fig. 2.

PIMs and POMs with a follow-up action realized by the oncologist/ haematologist predominantly concerned PPIs (PIMs), anti-infectives (PIMs), antineoplastic agents (PIMs), musculoskeletal medication (PIMs/POMs), and vitamin D (POMs). Potentially Inappropriate Medications and Potentially Omitted Medicationss that were sent most frequently to the general practitioner were alpha-adrenoreceptor antagonists (PIMs), respiratory medication (PIMs), antihypertensive drugs (PIMs/POMs), and statins (POMs). PIMs identified with STOPP criterion A3 'double medication' or expert opinion 'contraindication or interaction' were always considered as requiring a follow-up action. Follow-up was also high for expert opinion 'incorrect dosage' and 'problem with usage' with a follow-up action required for 87% and 86% of the PIMs, respectively. Follow-up was the lowest for START criterion B5 'statins for patients with high cardiovascular risk' with no follow-up action required for 43% of the POMs.

The number of medicines and the CCI score were associated with having at least one PIM and/or POM (Table 3). The other covariates were not statistically significant associated with the prevalence of PIMs and POMs. For an increase of one medicine, the odds of having at least one PIM and/or POM increased with 1.125. For an increase of one point in the CCI score, the odds of having at least one PIM and/or POM increased with 1.501. In multivariate logistic regression analysis both associations were no longer statistically significant. The Pearson correlation coefficient between the variables number of medicines and CCI score was 0.4.

Table 2
Criteria used for identification of PIMs and POMs.

Criteria	Classification	n (%)
PIMs		186 (100)[a]
STOPP criteria	Total	95 (51)
	A1. No evidence-based indication	42 (23)
	A2. Usage longer than recommended	25 (13)
	A3. Double medication	8 (4)
	D5. Benzodiazepine ≥4 weeks	12 (6)
	Other	8 (4)
Expert opinion	Total	91 (49)
	Medicine not effective	24 (13)
	Over treatment	15 (8)
	(Potential) side effect	9 (5)
	Contraindication or interaction	2 (1)
	Incorrect dosage	15 (8)
	Problem with usage	26 (14)
POMs		86 (100)
START criteria	Total	66 (77)
	B4. Antihypertensives, high BP	7 (8)
	B5. Statins, high cardiovascular risk	30 (35)
	H2. Bisph/vitD/calc, chronic prednisone use	10 (12)
	H3. VitD/calc, osteoporosis	6 (7)
	H5. VitD/calc, home bound / fall incidents	4 (5)
	J2. ACE-inhibitor, DM with kidney damage	5 (6)
	Other	4 (5)
Expert opinion	Total	20 (23)
	Under treatment	20 (23)

Abbreviations: ACE, angiotensin converting enzyme; bisph, bisphosphonate; BP, blood pressure; calc, calcium; DM, diabetes mellitus; PIM, potentially inappropriate medication; POM, potentially omitted medication; START, screening tool to alert doctors to the right treatment; STOPP, screening tool of older persons' potentially inappropriate prescriptions; vitD, vitamin D.

[a] The total number of criteria used for identification of PIMs (186) exceeds the total number of PIMs (180) because 6 PIMs were identified using two criteria.

4. Discussion

A high prevalence of PIMs and POMs (78%) was found in older patients with cancer by conducting pharmacist-led comprehensive medication reviews using both STOPP/START criteria and pharmacists' expert opinion.

The prevalence of PIMs in the current study is higher than in most previous studies. This might be due to a more thorough and complete
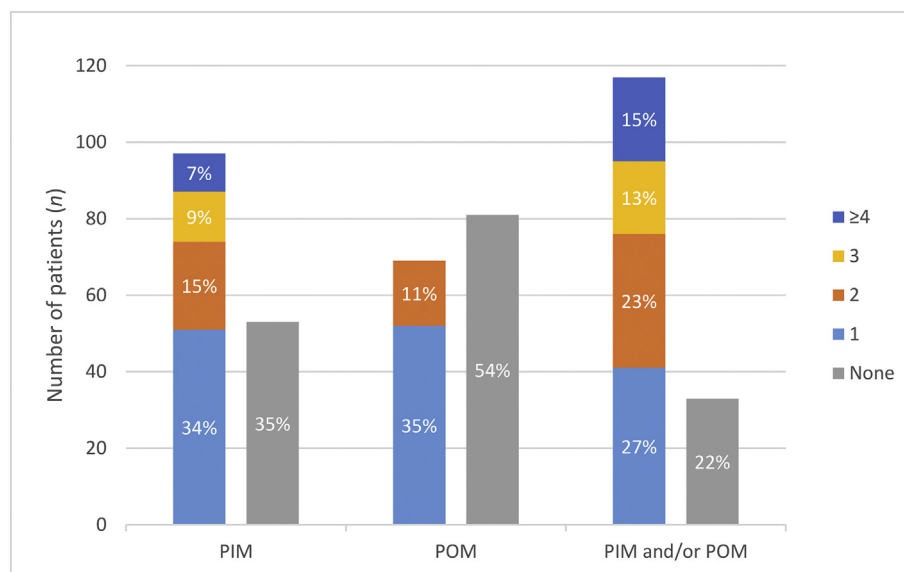

Fig. 1. – Prevalence of PIMs and POMs. The number of patients with no, 1, 2, 3, or ≥ 4 PIMs (separately), POMs (separately), and PIMs and/or POMs (combined). Percentages are calculated as part of the total (n = 150) per category. Abbreviations: PIM, Potentially Inappropriate Medication; POM, Potentially Omitted Medication.
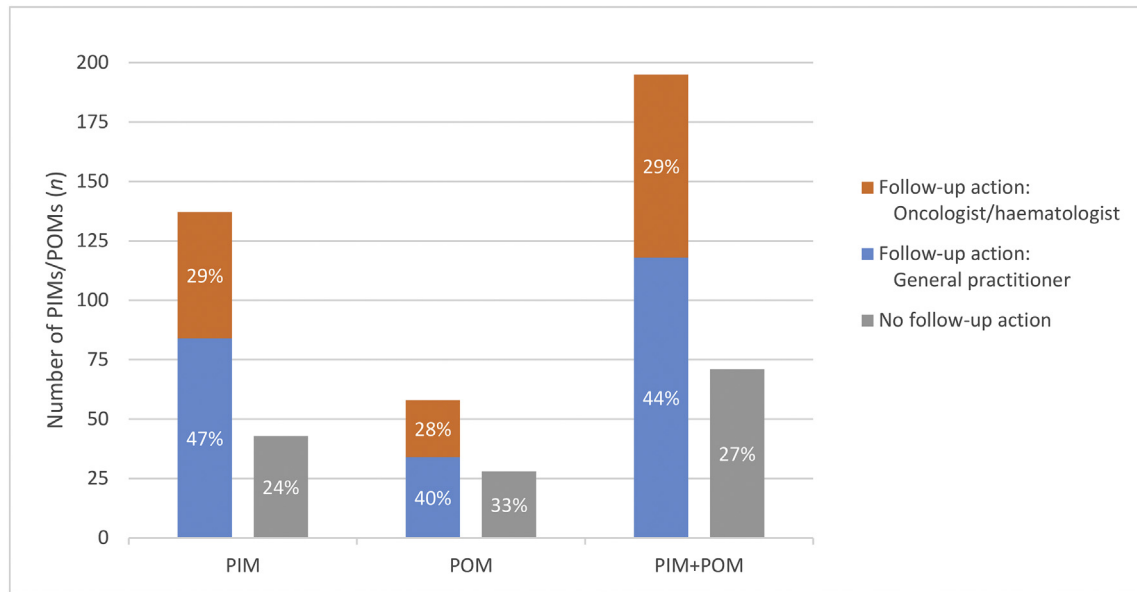
Fig. 2. – Follow-up actions of PIMs and POMs. Follow-up actions of 180 PIMs (separately), 86 POMs (separately), and 266 PIMs and POMs (combined). Percentages are calculated as part of the total per category. Abbreviations: PIM, Potentially ilappropriate Medication; POM, Potentially Omitted Medication.

Table 3
Associations between covariates and prevalence of PIMs and POMs.

Covariate	Descriptive statistics			Logistic regression	
	No PIMs/POMs	Any PIMs/POMs[a]	p-value	Univariate analysis OR (95% CI)	Multivariate analysis OR (95% CI)
Total (n (%))	33 (100)	117 (100)			
Age, years (median (IQR))	71 (7)	73 (9)	0.059[b]		
Gender, male (n (%))	21 (64)	67 (57)	0.512[c]		
Number of medicines (mean (SD))	9.8 (4.0)	11.4 (3.7)	0.031[d]	1.125 (1.009–1.253)	1.084 (0.963–1.221)
Polypharmacy, yes (n (%))	16 (48)	75 (64)	0.105[c]		
Medication roll, yes (n (%))	2 (6)	16 (14)	0.364[e]		
Cancer type, solid tumours (n (%))	19 (58)	83 (71)	0.146[c]		
Curative intent, yes (n (%))	10 (30)	24 (21)	0.235[c]		
CCI score (median (IQR))	4 (2)	4 (1)	0.016[b]	1.501 (1.043–2.160)	1.360 (0.922–2.006)

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; IQR, interquartile range; OR, odds ratio; PIM, potentially inappropriate medication; POM, potentially omitted medication; SD, standard deviation.

[a] This group consists of all patients who have at least one PIM and/or POM.
[b] Mann-Whitney U Test
[c] Pearson's χ^2 test
[d] independent-samples t-test
[e] Fisher's exact test.

approach for the comprehensive medication reviews. Most studies based their PIMs on the medical records rather than having an interview involving the patient. Furthermore, the current study used pharmacists' expert opinion in addition to the standardized STOPP/START criteria.

Studies that did not include a patient interview and only used standardized criteria (Beers or STOPP) found a prevalence of PIMs ranging from 16% to 57% [5,13–16]. Fourteen percent of the PIMs in the current study regarded problems with usage, most of which were identified based on the interview with the patient. These PIMs were missed in these previous studies. In addition, the medication reconciliation with the patient attributes to a more complete overview of the actual medication use and therefore to potentially more PIMs. Reis et al. [17], Nightingale et al. [3], and Deliens et al. [4] found a prevalence of 48%, 51%, and 52%, respectively, when interviewing the patient or conducting a full comprehensive medication review. However, not all PIMs and POMs can be identified with a set of standardized criteria and therefore the knowledge and expertise of a pharmacist is necessary to attribute to these criteria. This is well shown in this study where half of the PIMs and a quarter of the POMs were identified by pharmacists' expert opinion.

To fully optimize patients' treatment, inappropriate medication should be addressed as well as omitted medication. Only two studies were found in which POMs were identified in older patients with cancer, with a prevalence of 34% and 98% [4,5]. The high prevalence found by Paksoy et al. [5] is largely attributed to omitted vaccinations, which is not applicable to the Dutch situation. In the Netherlands, older patients are annually offered an influenza vaccination and a pneumococcal vaccine is not included in the Dutch START criteria [18].

The high prevalence of PIMs on PPIs and benzodiazepine agonists and POMs on statins, antihypertensive drugs, and vitamin D are in line with several other studies in patients with cancer as well as patients without cancer [4,6,16,17,21,22]. Only four PIMs concerned antineoplastic drugs. Because most PIMs involved regular medication, the problems identified in the oncology population may not be much different from other populations of older polypharmacy patients and therefore STOPP/START criteria seem well applicable. Associations with the prevalence of PIMs and POMs were found for the number of medicines and the CCI score, in line with previous studies [3,5,13]. However, in this study these variables were not very strongly associated and borderline

F.M.A.M. van Loveren et al. / Journal of Geriatric Oncology 12 (2021) 80–84

significant. The significant associations were no longer present in the multivariate logistic regression analysis possibly due to a lack of power and the mild correlation (Pearson correlation coefficient 0.4) between CCI score and number of medicines. Because of the time investment needed, implementation in daily practice can be challenging. This study indicates that a specific focus on patients with more medicines and/or a higher CCI score could be considered. However, ORs were small, associations were not statistically significant in multivariate logistic regression analysis, and this study was not designed to determine which (sub)group of patients would benefit most from pharmacist-led comprehensive medication reviews. Future research could provide more insight on this subject.

Measuring follow-up further distinguishes this study from previous studies on PIMs and POMs in older patients with cancer. It was outside the scope of this study to assess actual changes in medication, additional laboratory measurements, or actions by the general practitioner, which could lead to an overestimation of the follow-up on PIMs and POMs. However, the follow-up percentage found in this study (73%) is in line with other studies that found action to be taken in 69%–82% of recommendations made by pharmacists [6,23,24]. For all STOPP/START criteria, a follow-up action was required for the majority of PIMs and POMs. Even for criteria that might seem less relevant in older patients with cancer (for example starting statins or vitamin D + calcium), more than half of the POMs required a follow-up action and were therefore considered clinically relevant by the oncologist/haematologist. This shows that the criteria, which were used, are relevant to this patient population.

Strengths of this study are the combination of a pharmacist-led comprehensive medication review and medication reconciliation with the patient, the incorporation of pharmacists' expert opinion, the identification of PIMs as well as POMs, and measuring the follow-up of recommendations. Limitations are that this is a single-institution study and only patients who received parenteral chemotherapy and/or immunotherapy were included. In addition, only the prevalence of PIMs and POMs was measured with the immediate follow-up, so long-term outcomes for patient and healthcare cannot be assessed.

In conclusion, PIMs and POMs are highly prevalent among older patients with cancer and a pharmacist-led comprehensive medication reviews is a good instrument to optimize patients' treatment. A complete approach, including pharmacists' expert opinion, is recommended to identify all PIMs and POMs.

Author Contributions

Conception and Design: FMAM van Loveren, IRF van Berlo – van de Laar, ALT Imholz, E van 't Riet, K Taxis, FGA Jansman.
Data Collection: FMAM van Loveren.
Analysis and Interpretation of Data: FMAM van Loveren, IRF van Berlo – van de Laar, E van 't Riet.
Manuscript Writing: FMAM van Loveren, IRF van Berlo – van de Laar.
Approval of Final Article: FMAM van Loveren, IRF van Berlo – van de Laar, ALT Imholz, E van 't Riet, K Taxis, FGA Jansman.

Disclosure

None.

Declaration of Competing Interest

None.

Acknowledgements

The authors thank pharmacists in training Carlijn van der Velde and Marjolein Niewenhuijse for their contribution to the comprehensive medication reviews and data collection.

References

[1] Hamaker ME, Jonker JM, De Rooij SE, Vos AG, Smorenburg CH, Van Munster BC. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. Lancet Oncol 2012; 13 e437-e44.

[2] Sharma M, Loh KP, Nightingale G, Mohile SG, Holmes HM. Polypharmacy and potentially inappropriate medication use in geriatric oncology. J Geriatr Oncol 2016;7: 346–53.

[3] 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;33:1453–9.

[4] Deliens C, Deliens G, Filleul O, Pepersack T, Awada A, Piccart M, et al. Drugs prescribed for patients hospitalized in a geriatric oncology unit: potentially inappropriate medications and impact of a clinical pharmacist. J Geriatr Oncol 2016;7:463–70.

[5] Paksoy C, Özkan Ö, Ustaalioğlu BB, Sancar M, Demirtunç R, Izzettin FV, et al. Evaluation of potentially inappropriate medication utilization in elderly patients with cancer at outpatient oncology unit. J Oncol Pharm Pract 2019;25:1321–7.

[6] Chau SH, Jansen AP, Van de Ven PM, Hoogland P, Elders PJ, Hugtenburg JG. Clinical medication reviews in elderly patients with polypharmacy: a cross-sectional study on drug-related problems in the Netherlands. Int J Clin Pharmacol 2016;38:46–53.

[7] Tjia J, Velten SJ, Parsons C, Valluri S, Briesacher BA. Studies to reduce unnecessary medication use in frail older adults: a systematic review. Drugs Aging 2013;30: 285–307.

[8] Patterson SM, Cadogan CA, Kerse N, Cardwell CR, Bradley MC, Ryan C, et al. Interventions to improve the appropriate use of polypharmacy for older people. Cochrane Database Syst Rev 2014:CD008165.

[9] Onder G, Van der Cammen TJ, Petrovic M, Somers A, Rajkumar C. Strategies to reduce the risk of iatrogenic illness in complex older adults. Age Ageing 2013;42: 284–91.

[10] Hill-Taylor B, Sketris I, Hayden J, Byrne S, O'Sullivan D, Christie R. Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. J Clin Pharm Ther 2013;38:360–72.

[11] Verdoorn S, Kwint HF, Faber A, Gussekloo J, Bouvy ML. Majority of drug-related problems identified during medication review are not associated with STOPP/START criteria. Eur J Clin Pharmacol 2015;71:1255–62.

[12] Dutch College of General Practitioners. Multidisciplinary guideline 'polypharmacy in the elderly' 2012 Utrecht ; 2012.

[13] Prithviraj GK, Koroukian S, Margevicius S, Berger NA, Bagai R, Owusu C. Patient characteristics associated with polypharmacy and inappropriate prescribing of medications among older adults with cancer. J Geriatr Oncol 2012;3:228–37.

[14] Feng X, Higa GM, Safarudin F, Sambamoorthi U, Tan X. Potentially inappropriate medication use and associated healthcare utilization and costs among older adults with colorectal, breast, and prostate cancers. J Geriatr Oncol 2019;10:698–704.

[15] Karuturi MS, Holmes HM, Lei X, Johnson M, Barcenas CH, Cantor SB, et al. Potentially inappropriate medications defined by STOPP criteria in older patients with breast and colorectal cancer. J Geriatr Oncol 2019;10:705–8.

[16] Saarelainen LK, Turner JP, Shakib S, Singhal N, Hogan-Doran J, Prowse R, et al. Potentially inappropriate medication use in older people with cancer: prevalence and correlates. J Geriatr Oncol 2014;5:439–46.

[17] Reis CM, Dos Santos AG, De Jesus Souza P, Reis AMM. Factors associated with the use of potentially inappropriate medications by older adults with cancer. J Geriatr Oncol 2017;8:303–7.

[18] Knol W, Verduijn MM, Lelie-Van der Zande AC, Van Marum RJ, Brouwers JR, Van der Cammen TJ, et al. Detecting inappropriate medication in older people: the revised STOPP/START criteria. Ned Tijdschr Geneeskd 2015;159:A8904.

[19] WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2019. https://www.whocc.no/atc_ddd_index; 2019. [accessed 22 March 2019].

[20] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

[21] Bo M, Gibello M, Brunetti E, Boietti E, Sappa M, Falcone Y, et al. Prevalence and predictors of inappropriate prescribing according to the screening tool of older People's prescriptions and screening tool to alert to right treatment version2 criteria in older patients discharged from geriatric and internal medicine wards: a prospective observational multicenter study. Geriatr Gerontol Int 2019;19:5–11.

[22] Dalleur O, Spinewine A, Henrard S, Losseau C, Speybroeck N, Boland B. Inappropriate prescribing and related hospital admissions in frail older persons according to the STOPP and START criteria. Drugs Aging 2012;29:829–37.

[23] Krska J, Cromarty JA, Arris F, Jamieson D, Hansford D, Duffus PR, et al. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. Age Ageing 2001;30:205–11.

[24] Gillespie U, Alassaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H, et al. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. Arch Intern Med 2009;169:894–900.