Postprint of a Meta-Analysis on the Prevalence of Potentially Inappropriate Medication Use in Elderly Cancer Patients

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Abstract

Background: Multimorbidity and polypharmacy are prevalent among elderly cancer patients, predisposing them to potentially inappropriate medication (PIM) and consequently exerting adverse effects on patient prognosis. Objective: To systematically evaluate the incidence rate of PIM in elderly cancer patients. Methods: Computerized searches were conducted in CNKI, VIP, CBM, Wanfang Data, PubMed, Embase, Web of Science, and Cochrane Library databases for relevant studies on the current status of PIM incidence in elderly cancer patients from inception to September 2024. Two investigators independently screened the retrieved literature, extracted data, and assessed the risk of bias, with meta-analysis performed using Stata 17.0 software. Results: A total of 36 articles were ultimately included, encompassing 54 groups of PIM incidence rates and comprising 95,290 patients. Meta-analysis results demonstrated that the incidence rate of PIM in elderly cancer patients was 44.5% (95%CI=39.2%~49.8%). Subgroup analyses revealed that the incidence rates in elderly cancer patients aged 60-70 years and >70 years were 44.4% and 46.1%, respectively; the incidence rates in elderly male and female cancer patients were 40.9% and 42.5%, respectively; the incidence rates in patients with $ $5 and >5 comorbidities were 34.4% and 47.1%, respectively; the incidence rates in patients taking $ $5 and <5 medications were 39.9% and 30.4%, respectively; the incidence rates in patients with lung cancer, gastrointestinal cancer, hematologic malignancies, breast cancer, and prostate cancer were 45.6%, 39.4%, 42.0%, 39.4%, and 42.6%, respectively; the incidence rates in elderly cancer patients in Asia, Europe, North America, and South America were 50.2%, 45.8%, 35.7%, and 51.4%, respectively; the incidence rates in samples from hospitals, databases, Dana-Farber Cancer Institute, and cancer centers were 47.6%, 43.0%, 34.6%, and 34.5%, respectively; the incidence rates screened by Beers criteria, DAE, STOPP/START criteria, EU(7)-PIM list, and Chinese PIM criteria (2017 edition) were 46.6%, 16.5%, 44.6%, 60.0%, and

39.3%, respectively; the incidence rates in studies published before and after 2020 were 36.1% and 52.5%, respectively. Conclusion: The incidence rate of PIM is notably high in elderly cancer patients, at 44.5%. Emphasis should be placed on the prevention, screening, and intervention of potential medication inappropriateness in this population to establish a solid foundation for the health of elderly individuals with cancer.

Full Text

Prevalence of Potentially Inappropriate Medication in Older Adults with Cancer: A Meta-Analysis

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Abstract

Background The increasing phenomena of multimorbidity and polypharmacy in older adults with cancer predisposes them to potentially inappropriate medication (PIM), which adversely affects patient prognosis.

Objective To systematically evaluate the prevalence of PIM in older adults with cancer.

Methods We searched the Cochrane Library, Web of Science, Embase, PubMed, CNKI, VIP, Wanfang Data, and CBM databases to collect studies related to the prevalence of PIM in older adults with cancer from inception to September 2024. Two researchers independently screened the literature, extracted data, and assessed risk of bias. Stata 17.0 software was used to perform meta-analysis.

Results A total of 36 studies with 54 prevalence estimates were included, comprising 95,290 patients. Meta-analysis indicated that the prevalence of PIM in older adults with cancer was 44.5% (95%CI=39.2%~49.8%). Subgroup analysis showed that the prevalence of PIM in patients aged 60-70 and >70 years was 44.4% and 46.1%, respectively; in elderly male and female patients was 40.9% and 42.5%, respectively; in patients with $ $5 and >5 diseases was 34.4% and 47.1%, respectively; in patients with $ $5 and <5 medications was 39.9% and 30.4%, respectively; in patients with lung cancer, gastrointestinal cancer, hematologic malignancies, breast cancer, and prostate cancer was 45.6%, 39.4%, 42.0%, 39.4%, and 42.6%, respectively; in patients from Asia, Europe, North America, and South America was 50.2%, 45.8%, 35.7%, and 51.4%, respectively; in patients from hospitals, databases, Dana-Farber Cancer Institute, and cancer centers was 47.6%, 43.0%, 34.6%, and 34.5%, respectively; when screened by the Beers criteria, DAE, STOPP/START criteria, EU(7)-PIM list, and the 2017 Chinese criteria was 46.6%, 16.5%, 44.6%, 60.0%, and 39.3%, respectively; and

in studies published in 2020 and before and after 2020 was 36.1% and 52.5%, respectively.

Conclusion The prevalence of PIM is relatively high in older adults with cancer, at 44.5%. The prevention, screening, and intervention of potentially inappropriate medication among relevant populations should be emphasized to lay a solid foundation for the health of older adults with cancer.

Keywords Potentially inappropriate medication; Cancer; Aged; Prevalence; Meta-analysis

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Introduction

Global cancer statistics show that in 2020, there were 19.29 million new cancer cases worldwide, and this number is projected to reach 28.4 million by 2040, with 64% of patients aged 60 years and older, and elderly cancer deaths accounting for 71% of all cancer-related deaths [1]. Older adults with cancer often have critical conditions, multimorbidity, and polypharmacy. Due to changes in pharmacokinetics and pharmacodynamics, their medication risks increase significantly, making them more susceptible to drug-drug interactions and adverse drug reactions, leading to poor health outcomes [2]. The aging body has poorer drug tolerance, making older cancer patients more prone to drug-related problems such as adverse drug reactions [3]. Potentially inappropriate medication (PIM) refers to medications whose effectiveness has not been established and/or whose risk of adverse events exceeds the expected clinical benefit, and for which safer alternatives are lacking [4]. Researchers worldwide have investigated PIM in older cancer patients, but results vary significantly due to differences in assessment tools and other factors. This study aims to systematically review the prevalence of PIM in older cancer patients to provide scientific evidence for developing intervention strategies, with the goal of delaying or even preventing PIM and ultimately improving patients' quality of life.

Methods

1.1 Inclusion and Exclusion Criteria **1.1.1 Inclusion Criteria:** (1) Study design: cross-sectional studies, cohort studies, case-control studies, or other studies providing relevant data; (2) Participants: cancer patients aged 60 years and older; (3) Outcome measure: PIM prevalence.

1.1.2 Exclusion Criteria: (1) Duplicate publications; (2) Reviews, case reports, conference abstracts; (3) Studies with incomplete data; (4) Low-quality studies.

1.2 Search Strategy We searched CNKI, VIP, Wanfang Data, CBM, PubMed, Embase, Web of Science, and Cochrane Library for studies on PIM prevalence in older cancer patients from inception to September 2024. This

study used a combination of subject headings and free terms for comprehensive searching, supplemented by manual searches. Chinese search terms included: potentially inappropriate medication, inappropriate medication, elderly, older adults, cancer, tumor, etc. English search terms included: Inappropriate Prescribing, Potentially Inappropriate Medications, Aged, Elderly, Neoplasms, Tumor, Cancer, etc. The PROSPERO registration number for this study is CRD42024525587.

1.3 Data Extraction Two researchers independently screened literature, extracted data, and cross-checked results. Disagreements were resolved through consultation with a third researcher. Literature screening began with reading titles, followed by abstracts and full texts if inclusion criteria were met. Extracted data included: first author, publication year, country, study design, population, region, sample size, PIM assessment tool, sample source, and PIM prevalence.

1.4 Quality Assessment We used the Agency for Healthcare Research and Quality (AHRQ) recommended criteria for cross-sectional studies [5]. The AHRQ scale includes 11 items, with 1 point for "yes" and 0 points for "no" or "unclear." Scores of 8-11 indicate high quality, 4-7 moderate quality, and 0-3 low quality. The Newcastle-Ottawa Scale (NOS) was used for case-control and cohort studies [6], with scores of 7-9 indicating high quality, 5-6 moderate quality, and 0-4 low quality.

1.5 Statistical Analysis We performed meta-analysis using Stata 17.0 software, with PIM prevalence in older cancer patients as the effect measure and 95% confidence intervals (CI) calculated. Heterogeneity among studies was assessed using Cochrane' s Q test and I^2 statistic, where values of 25%, 50%, and 75% indicate low, moderate, and high heterogeneity, respectively. If $I^2 \geq 50\%$ and $P \leq 0.10$, indicating substantial heterogeneity, a random-effects model was used; otherwise, a fixed-effects model was applied. For clinical heterogeneity, subgroup analysis and sensitivity analysis were conducted to explore sources. When $ $10 studies were included, Begg' s and Egger' s tests were used to assess publication bias, with $P > 0.05$ indicating low publication bias.

Results

2.1 Literature Search Results A total of 4,814 relevant articles were identified (1,527 Chinese and 3,287 English). After screening, 36 studies [7-42] were included. The literature screening process is shown in Figure 1 [Figure 1: see original paper].

2.2 Basic Characteristics of Included Studies The included studies were published between 2014-2024, covering 16 countries and 95,290 participants. Basic characteristics and quality assessments are shown in Table 1 .

2.3 Meta-Analysis Results **2.3.1 PIM Prevalence:** Heterogeneity testing showed high heterogeneity among the 36 studies (I^2=99.7%, P<0.001), so a random-effects model was used. Meta-analysis showed the prevalence of PIM in older cancer patients was 44.5% (95%CI=39.2%~49.8%), as shown in Figure 2 [Figure 2: see original paper].

2.3.2 Subgroup Analysis: Subgroup analyses were conducted by age, sex, number of diseases, number of medications, cancer type, continent, sample source, assessment tool, and publication year. Results showed: (1) By age: 44.4% in patients aged 60-70 and 46.1% in those >70; (2) By sex: 40.9% in males and 42.5% in females; (3) By disease count: 34.4% with $ $5 diseases and 47.1% with >5 diseases; (4) By medication count: 39.9% with $ $5 medications and 30.4% with <5 medications; (5) By cancer type: highest in lung cancer (45.6%), followed by gastrointestinal cancer (39.4%), hematologic malignancies (42.0%), breast cancer (39.4%), and prostate cancer (42.6%); (6) By continent: highest in South America (51.4%), followed by Asia (50.2%), Europe (45.8%), North America (35.7%), and Oceania (26.5%); (7) By sample source: 47.6% from hospitals, 43.0% from databases, 34.6% from Dana-Farber Cancer Institute, and 34.5% from cancer centers; (8) By assessment tool: 46.6% by Beers criteria, 16.5% by DAE, 44.6% by STOPP/START criteria, 60.0% by EU(7)-PIM list, and 39.3% by 2017 Chinese criteria; (9) By publication year: 36.1% in studies published in 2020 and before, and 52.5% after 2020. See Table 2 for details.

2.4 Sensitivity Analysis Sensitivity analysis was performed by sequentially excluding each study. The pooled PIM prevalence ranged from 39.0% to 50.0%, with no significant change, indicating stable results.

2.5 Publication Bias Funnel plot analysis showed relatively symmetric distribution of studies (Figure 3 [Figure 3: see original paper]). Egger's test yielded t=0.51, P=0.615, indicating no significant publication bias.

Discussion

Understanding PIM prevalence in older cancer patients is crucial for safe medication management. This study analyzed data from 36 studies across 16 countries, including cohort and cross-sectional studies, with a total sample of 95,290 patients and moderate-to-high quality evidence. The PIM prevalence of 44.5% in older cancer patients is higher than the 36.7% reported in a meta-analysis of 17 countries [43]. Lung cancer patients had the highest PIM prevalence (45.6%), possibly due to poorer resistance to aggressive factors, increased disease burden, and poorer physical condition [54]. When caring for older patients with multimorbidity, greater attention should be paid to their health status. Multidisciplinary teamwork, enhanced medication review, and improved education and training for healthcare providers and older cancer patients can promote safe and rational medication use.

Regarding sample sources, older cancer patients in hospitals had higher PIM prevalence, likely due to more complex diseases, more complications, and greater medication variety [55]. However, PIM prevalence remains high across different settings. Healthcare providers need to improve appropriate medication measures and management based on specific PIM situations to reduce adverse drug reactions. Clinical pharmacists should minimize unnecessary polypharmacy and strictly evaluate combination therapy risks to prevent PIM.

Different assessment tools yielded varying PIM prevalence rates. The Beers criteria, the earliest tool developed for PIM, is also the most widely used in older cancer patients [44]. The 2019 version incorporates the latest evidence-based medicine, deleting and updating items from previous versions, making it the most sensitive [43]. The STOPP/START criteria focus on inappropriate medication use in older cancer patients under disease conditions, where STOPP assesses existing medications and START determines appropriateness of initial prescriptions [45]. In addition to these tools, many countries have developed their own criteria for assessing PIM in older adults. Different standards have different specificities, so combining multiple assessment tools can comprehensively evaluate PIM in older cancer patients from various perspectives to improve medication safety.

Subgroup analysis showed South America had the highest PIM prevalence, higher than Asia, Oceania, Europe, and North America. South America has the highest multimorbidity rate [46], and as multimorbidity increases in older cancer patients, PIM risk also increases [47]. Future research should investigate PIM with larger sample sizes and greater regional diversity to improve result reliability.

By publication year, PIM prevalence reported after 2020 (52.5%) was higher than that reported in 2020 and before (36.1%). The global proportion of older adults is rising, and this population is susceptible to various diseases, especially chronic conditions [48], leading to increased PIM during medical visits.

Subgroup analysis also revealed higher PIM prevalence in female patients >70 years. A US systematic review found higher PIM rates in older women than men [49]. Studies show older women are more vulnerable to drug-related harm due to pharmacodynamic and pharmacokinetic changes [50]. Advanced age is an important independent risk factor for PIM [51]. As physiological functions decline significantly in older patients, drug efficacy decreases and metabolism slows, increasing medication risk and PIM occurrence [52]. Special attention should be paid to medication assessment and intervention in older female cancer patients.

PIM prevalence was higher in older cancer patients taking $ $5 medications and with >5 diseases. With aging, the likelihood of multiple diseases increases significantly, symptoms become more severe, and different medication types are often needed to control conditions [53], thereby increasing PIM risk. Patients with multiple diseases require more attention to their health status.

This study has several limitations: (1) All included studies were cross-sectional or cohort studies, making sample selection and measurement bias unavoidable; (2) Assessment tools for PIM in older cancer patients are not standardized, and differences between tools may affect prevalence accuracy; (3) Included studies differed in basic characteristics, survey regions, and timing, which may affect result stability.

In conclusion, PIM prevalence is high in older cancer patients, with variations across regions and assessment tools. Higher rates were found in females, patients >70 years, those with >5 diseases, those taking $ $5 medications, lung cancer patients, and those from hospitals. Future large-sample, high-quality longitudinal studies are needed to verify these findings.

References

[1] MILLER K D, NOGUEIRA L, DEVASIA T, et al. Cancer treatment and survivorship statistics, 2022[J]. CA Cancer J Clin, 2022, 72(5): 409-436. DOI:10.3322/caac.21731.

[2] WANG Lingfei, DAI Haibin. Analysis of potentially inappropriate medication and related influencing factors in elderly outpatients[J]. Chinese Journal of Modern Applied Pharmacy, 2019, 36(7): 864-869. DOI:10.13748/j.cnki.issn1007-7693.2019.07.019.

[3] KORC-GRODZICKI B, BOPARAI M K, LICHTMAN S M. Prescribing for older patients with cancer[J]. Clin Adv Hematol Oncol, 2014, 12(5): 309-318.

[4] BEERS M H, OUSLANDER J G, ROLLINGHER I, et al. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine[J]. Arch Intern Med, 1991, 151(9): 1825-1832.

[5] ZENG Xiantao, LIU Hui, CHEN Xi, et al. Meta-analysis series IV: quality assessment tools for observational studies[J]. Chinese Journal of Evidence-Based Cardiovascular Medicine, 2012, 4(4): 297-299. DOI:10.3969/j.1674-4055.2012.04.004.

[6] STANG A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses[J]. Eur J Epidemiol, 2010, 25(9): 603-605. DOI:10.1007/s10654-010-9491-z.

[7] ALKAN A, YAŞAR A, KARCı E, et al. Severe drug interactions and potentially inappropriate medication usage in elderly cancer patients[J]. Support Care Cancer, 2017, 25(1): 229-236. DOI:10.1007/s00520-016-3409-6.

[8] BANDIDWATTANAWONG C, RATTANASERIKULCHAI P, JETSADAVANIT N. Polypharmacy and potentially-inappropriate medications are prevalent in the elderly cancer patients receiving systemic cancer therapy and they co-relate with adverse outcomes[J]. BMC Geriatr, 2023, 23(1): 775. DOI:10.1186/s12877-023-04471-3.

[9] HAM L, GEIJTEMAN E C T, AARTS M J, et al. Use of potentially inappropriate medication in older patients with lung cancer at the end of life[J]. J Geriatr Oncol, 2022, 13(1): 53-59. DOI:10.1016/j.jgo.2021.07.009.

[10] HONG S, LEE J H, CHUN E K, et al. Polypharmacy, inappropriate medication use, and drug interactions in older Korean patients with cancer receiving first-line palliative chemotherapy[J]. Oncologist, 2020, 25(3): e502-e511. DOI:10.1634/theoncologist.2019-0085.

[11] HSHIEH T T, DUMONTIER C, JAUNG T, et al. Association of polypharmacy and potentially inappropriate medications with frailty among older adults with blood cancers[J]. J Natl Compr Canc Netw, 2022, 20(8): 915-923.e5. DOI:10.6004/jnccn.2022.7033.

[12] KARUTURI M S, HOLMES H M, LEI X D, et al. Potentially inappropriate medication use in older patients with breast and colorectal cancer[J]. Cancer, 2018, 124(14): 3000-3007. DOI:10.1002/cncr.31403.

[13] KARUTURI M S, HOLMES H M, LEI X D, et al. Potentially inappropriate medications defined by STOPP criteria in older patients with breast and colorectal cancer[J]. J Geriatr Oncol, 2019, 10(5): 705-708. DOI:10.1016/j.jgo.2019.01.024.

[14] KREČAK I, PIVAC L, LUCIJANIĆ M, et al. Polypharmacy, drug interactions in patients with chronic myeloproliferative neoplasms[J]. Biomedicines, 2023, 11(5): 1301. DOI:10.3390/biomedicines11051301.

[15] KUMAR S, CASTELINO R, RAO A, et al. Performance of potentially inappropriate medications assessment tools in older Indian patients with cancer[J]. Cancer Med, 2024, 13(1): e6797. DOI:10.1002/cam4.6797.

[16] LEGER D Y, MOREAU S, SIGNOL N, et al. Polypharmacy, potentially inappropriate medications and drug-drug interactions in geriatric patients with hematologic malignancy: Observational single-center study of 122 patients[J]. J Geriatr Oncol, 2018, 9(1): 60-67. DOI:10.1016/j.jgo.2017.07.015.

[17] KIM S, PARK S, YOO S H, et al. Potentially inappropriate medication use based on two deprescribing criteria and related factors in patients with terminal cancer: a cross-sectional study[J]. J Geriatr Oncol, 2023, 14(3): 101472. DOI:10.1016/j.jgo.2023.101472.

[18] MAGGIORE R J, DALE W, GROSS C P, et al. Polypharmacy and potentially inappropriate medication use in older adults with cancer undergoing chemotherapy: effect on chemotherapy-related toxicity and hospitalization during treatment[J]. J Am Geriatr Soc, 2014, 62(8): 1505-1512. DOI:10.1111/jgs.12942.

[19] MACHADO T R L, DE PÁDUA C A M, DE MIRANDA DRUMMOND P L, et al. Factors associated with potentially inappropriate medications in elderly with multiple myeloma[J]. J Oncol Pharm Pract, 2024, 30(5): 873-879. DOI:10.1177/10781552231190009.

[20] MOHAMED M R, RAMSDALE E, LOH K P, et al. Association of polypharmacy and potentially inappropriate medications with physical functional impairments in older adults with cancer[J]. J Natl Compr Canc Netw, 2021, 19(3): 267-274. DOI:10.6004/jnccn.2020.7628.

[21] NIGHTINGALE G, HAJJAR E, SWARTZ K, et al. 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]. J Clin Oncol, 2015, 33(13): 1453-1459. DOI:10.1200/JCO.2014.58.7550.

[22] NORONHA V, RAMASWAMY A, GATTANI S C, et al. Polypharmacy and potentially inappropriate medication use in older Indian patients with cancer[J]. Cancer Res Stat Treat, 2021, 4(1): 67-73. DOI:10.4103/crst.crst_{{{50}}_{{21}}}.

[23] OZKAN M, KARAHAN I, YALCIN S, et al. Effects of potentially inappropriate medications in older patients with gastrointestinal system cancer[J]. Medeni Med J, 2023, 38(4): 284-290. DOI:10.4274/MMJ.galenos.2023.03063.

[24] PAKSOY C, ÖZKAN Ö, USTAALIOĞLU B B, et al. Evaluation of potentially inappropriate medication utilization in elderly patients with cancer at outpatient oncology unit[J]. J Oncol Pharm Pract, 2019, 25(6): 1321-1327. DOI:10.1177/1078155218788698.

[25] PARK J W, ROH J L, LEE S W, et al. Effect of polypharmacy and potentially inappropriate medications on treatment and posttreatment courses in elderly patients with head and neck cancer[J]. J Cancer Res Clin Oncol, 2016, 142(5): 1031-1040. DOI:10.1007/s00432-015-2108-x.

[26] RAMSDALE E, MOHAMED M, YU V, et al. Polypharmacy, potentially inappropriate medications, and drug-drug interactions in vulnerable older adults with advanced cancer initiating cancer treatment[J]. Oncologist, 2022, 27(7): e580-e588. DOI:10.1093/oncolo/oyac053.

[27] REIS C M, DOS SANTOS A G, DE JESUS SOUZA P, et al. Factors associated with the use of potentially inappropriate medications by older adults with cancer[J]. J Geriatr Oncol, 2017, 8(4): 303-307. DOI:10.1016/j.jgo.2017.05.003.

[28] SAARELAINEN L K, TURNER J P, SHAKIB S, et al. Potentially inappropriate medication use in older people with cancer: prevalence and correlates[J]. J Geriatr Oncol, 2014, 5(4): 439-446. DOI:10.1016/j.jgo.2014.07.001.

[29] TIAN F Y, ZHAO M N, CHEN Z Y, et al. Prescription of potentially inappropriate medication use in older cancer outpatients with multimorbidity: concordance among the Chinese, AGS/Beers, and STOPP criteria[J]. Front Pharmacol, 2022, 13: 857811. DOI:10.3389/fphar.2022.857811.

[30] UMIT E G, BAYSAL M, BAS V, et al. Polypharmacy and potentially inappropriate medication use in older patients with multiple myeloma, related

to fall risk and autonomous neuropathy[J]. J Oncol Pharm Pract, 2020, 26(1): 43-50. DOI:10.1177/1078155219835303.

[31] VAN LOVEREN F M A M, VAN BERLO-VAN DE LAAR I R F, IMHOLZ A L T, et al. Prevalence and follow-up of potentially inappropriate medication and potentially omitted medication in older patients with cancer - The PIM POM study[J]. J Geriatr Oncol, 2021, 12(1): 80-84. DOI:10.1016/j.jgo.2020.06.014.

[32] TAKAHASHI M, MATSUI M, INOUE R, et al. Potentially inappropriate medication discontinued or changed based on pharmacists' recommendations in older end-stage cancer patients receiving palliative care: a cross-sectional study[J]. Ann Palliat Med, 2021, 10(11): 11301-11307. DOI:10.21037/apm-21-3226.

[33] FENG X, HIGA G M, SAFARUDIN F, et al. Potentially inappropriate medication use and associated healthcare utilization and costs among older adults with colorectal, breast, and prostate cancers[J]. J Geriatr Oncol, 2019, 10(5): 698-704. DOI:10.1016/j.jgo.2019.01.012.

[34] FENG X, HIGA G M, SAFARUDIN F, et al. Prevalence and factors associated with potentially inappropriate medication use in older medicare beneficiaries with cancer[J]. Res Social Adm Pharm, 2020, 16(10): 1459-1471. DOI:10.1016/j.sapharm.2019.12.018.

[35] DELIENS C, DELIENS G, FILLEUL O, et al. Drugs prescribed for patients hospitalized in a geriatric oncology unit: Potentially inappropriate medications and impact of a clinical pharmacist[J]. J Geriatr Oncol, 2016, 7(6): 463-470. DOI:10.1016/j.jgo.2016.05.001.

[36] JØRGENSEN T L, HERRSTEDT J, ACADEMY OF GERIATRIC CANCER RESEARCH (AGECARE). The influence of polypharmacy, potentially inappropriate medications, and drug interactions on treatment completion and prognosis in older patients with ovarian cancer[J]. J Geriatr Oncol, 2020, 11(4): 593-602. DOI:10.1016/j.jgo.2019.12.005.

[37] LAVAN A H, O' MAHONY D, O' MAHONY D, et al. Potentially inappropriate medication (PIM) use and severe drug interactions (SDIs) in older adults with cancer[J]. J Geriatr Oncol, 2021, 12(6): 872-880. DOI:10.1016/j.jgo.2021.02.021.

[38] SAMUELSSON K S, EGENVALL M, KLARIN I, et al. Inappropriate drug use in elderly patients is associated with prolonged hospital stay and increased postoperative mortality after colorectal cancer surgery: a population-based study[J]. Colorectal Dis, 2016, 18(2): 155-162. DOI:10.1111/codi.13077.

[39] WANG Junping, HUANG Lingling, ZHU Wenjing, et al. Analysis of potentially inappropriate medication and influencing factors in elderly cancer patients[J]. China Pharmacy, 2023, 34(6): 740-745. DOI:10.6039/j.issn.1001-0408.2023.06.19.

[40] HE Bishan, ZHAN Luankun. Analysis of rational drug use in elderly cancer outpatients[J]. China Prescription Drug, 2020, 18(10): 6-8. DOI:10.3969/j.issn.1671-945X.2020.10.004.

[41] JIANG Xuehua, HU Yingke. Analysis and early warning model construction of potentially inappropriate medication in elderly cancer inpatients[J]. Clinical Medication Journal, 2023, 21(8): 76-81. DOI:10.3969/j.issn.1672-3384.2023.08.014.

[42] LI Yue, ZHAO Rui, XIE Cheng, et al. Evaluation of potentially inappropriate medication in elderly inpatients based on the 2019 Beers criteria[J]. Chinese Pharmaceutical Journal, 2020, 55(15): 1305-1309. DOI:10.11669/cpj.2020.15.014.

[43] TIAN F Y, CHEN Z Y, ZENG Y, et al. Prevalence of use of potentially inappropriate medications among older adults worldwide: a systematic review and meta-analysis[J]. JAMA Netw Open, 2023, 6(8): e2326910. DOI:10.1001/jamanetworkopen.2023.26910.

[44] MOHAMED M R, RAMSDALE E, LOH K P, et al. Associations of polypharmacy and inappropriate medications with adverse outcomes in older adults with cancer: a systematic review and meta-analysis[J]. Oncologist, 2020, 25(1): e94-e108. DOI:10.1634/theoncologist.2019-0406.

[45] O' MAHONY D. STOPP/START criteria for potentially inappropriate medications/potential prescribing omissions in older people: origin and progress[J]. Expert Rev Clin Pharmacol, 2020, 13(1): 15-22. DOI:10.1080/17512433.2020.1697676.

[46] CHOWDHURY S R, CHANDRA DAS D, SUNNA T C, et al. Global and regional prevalence of multimorbidity in the adult population in community settings: a systematic review and meta-analysis[J]. EClinicalMedicine, 2023, 57: 101860. DOI:10.1016/j.eclinm.2023.101860.

[47] TIAN F Y, YANG R N, CHEN Z Y, et al. The prevalence and factors associated with potentially inappropriate medication use in Chinese older outpatients with cancer with multimorbidity[J]. J Geriatr Oncol, 2022, 13(5): 629-634. DOI:10.1016/j.jgo.2022.02.006.

[48] LENANDER C, BONDESSON Å, VIBERG N, et al. Effects of medication reviews on use of potentially inappropriate medications in elderly patients; a cross-sectional study in Swedish primary care[J]. BMC Health Serv Res, 2018, 18(1): 616. DOI:10.1186/s12913-018-3425-y.

[49] NOTHELLE S K, SHARMA R, OAKES A, et al. Factors associated with potentially inappropriate medication use in community-dwelling older adults in the United States: a systematic review[J]. Int J Pharm Pract, 2019, 27(5): 408-423. DOI:10.1111/ijpp.12541.

[50] SOLDIN O P, MATTISON D R. Sex differences in pharmacokinetics and pharmacodynamics[J]. Clin Pharmacokinet, 2009, 48(3): 143-157.

DOI:10.2165/00003088-200948030-00001.

[51] HILL-TAYLOR B, SKETRIS I, HAYDEN J, et al. 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]. J Clin Pharm Ther, 2013, 38(5): 360-372. DOI:10.1111/jcpt.12059.

[52] CHEN Yanwen, YE Yongfeng, WANG Ani. Investigation and analysis of influencing factors of potentially inappropriate medication in elderly outpatients[J]. China Pharmaceuticals, 2020, 29(4): 27-30. DOI:10.3969/j.issn.1006-4931.2020.04.009.

[53] LAI X X, ZHU H W, HUO X P, et al. Polypharmacy in the oldest old ($ $80 years of age) patients in China: a cross-sectional study[J]. BMC Geriatr, 2018, 18(1): 64. DOI:10.1186/s12977-018-0754-y.

[54] TINETTI M E, STUDENSKI S A. Comparative effectiveness research and patients with multiple chronic conditions[J]. N Engl J Med, 2011, 364(26): 2478-2481. DOI:10.1056/NEJMp1100535.

[55] LIN Yang, WANG Fang, WANG Han, et al. Meta-analysis of frailty prevalence in elderly patients with multimorbidity[J]. Chinese General Practice, 2023, 26(25): 3185-3193.

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Note: Figure translations are in progress. See original paper for figures.