

Factors associated with potentially inappropriate prescriptions and barriers to medicines optimisation among older adults in primary care settings: a systematic review

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ABSTRACT

Objective To identify factors that likely contribute to potentially inappropriate prescriptions (PIPs) among older adults in primary care settings, as well as barriers to medicines optimisation and recommended potential solutions.

Design Systematic review.

Eligibility criteria Quantitative studies that analysed the factors associated with PIPs among older adults (≥65 years) in primary care settings, and qualitative studies that explored perceived barriers and potential solutions to medicines optimisation for this population.

Information sources PubMed, EMBASE, Scopus, CINAHL, PsycINFO, Web of Science, CNKI and Wanfang.

Results Of the 13 167 studies identified, 50 were included (14 qualitative, 34 cross-sectional and 2 cohort). Nearly all quantitative studies examined patient-related non-clinical factors (eg, age) and clinical factors (eg, number of medications) and nine studies examined prescriber-related factors (eg, physician age). A greater number of medications were identified as positively associated with PIPs in 25 quantitative studies, and a higher number of comorbidities, physical comorbidities and psychiatric comorbidities were identified as patient-related clinical risk factors for PIPs. However, other factors showed inconsistent associations with the PIPs. Barriers to medicines optimisation emerged within four analytical themes: prescriber related (eg, inadequate knowledge, concerns of adverse consequences, clinical inertia, lack of communication), patient related (eg, limited understanding, patient non-adherence, drug dependency), environment related (eg, lack of integrated care, insufficient investment, time constraints) and technology related (eg, complexity of implementation and inapplicable guidance). Recommended potential solutions were based on each theme of the barriers identified accordingly (eg, prescriber-related factors: incorporating training courses into continuing medical education).

Conclusions Older adults with more drugs prescribed and comorbidities may have a greater risk of receiving PIPs in the primary care setting, but it remains unclear whether other factors are related. Barriers to medicines optimisation among primary care older adults comprise

Key points

Question

► What factors are associated with potentially inappropriate prescriptions among primary care older adults, and what are the barriers and potential solutions to optimise their medication use?

Finding

► Most studies identified that patients with a higher number of medications or comorbidities and specific physical or psychiatric comorbidities were more likely to receive potentially inappropriate prescriptions. Barriers and potential solutions to medicines optimise included the levels of prescribers, patients, the environment and technology.

Meaning

► More attention should be paid to medication safety in primary care older adults with more prescribed drugs and comorbidities. Barriers to medicines optimisation for this population comprised multiple and interactional factors, which awaits targeted interventions, policies and future studies to address these difficulties in clinical practice.

multiple factors, and evidence-based and targeted interventions are needed to address these difficulties.

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INTRODUCTION

The ageing population is a challenge to healthcare systems in China and internationally.¹ Older adults are vulnerable to non-communicable diseases and multimorbidity.² More than half of the Chinese people aged 70 and over suffer from coexisting diseases, resulting in concomitant multiple medication use, potentially inappropriate prescriptions (PIPs) and increased medication burden,

which has widely concerned policymakers and health professionals.³⁻⁵

Potentially inappropriate prescribing refers to the prescribing of medications not recommended in older adults due to significantly higher risks than benefits where more effective and safer alternatives are available.⁶ A systematic review showed that approximately 20% of prescriptions to community-dwelling older adults were considered potentially inappropriate.⁷ PIPs are independently associated with adverse drug events (ADEs), which can cause emergency department visits, hospital admissions, lower quality of life and increased health expenditure.⁸ Most ADEs resulting from PIPs are potentially avoidable, but often underestimated in clinical practice.⁷ Researchers generally used criteria based (such as Beers criteria) and judgement based (such as Medication Appropriateness Index (MAI)) screening methods to detect PIPs through databases or surveys.⁷

Primary care practitioners (PCPs) play a critical role in the appropriate prescription of medications and medicines optimisation among older adults in the community.⁹ Our previous review suggested wide variations between 1.4% and 37.9% of low-quality outpatient prescriptions in China's community health centres.¹⁰ Several quantitative systematic reviews have focused on factors associated with PIPs among older adults,^{9 11-14} and qualitative systematic reviews have synthesised barriers and enablers to minimise potentially inappropriate medications (PIMs).¹⁵⁻¹⁷ However, some reviews included studies conducted in tertiary healthcare settings or nursing homes, in which the population characteristics may vary from primary care settings. Several new studies have emerged since these systematic reviews were published, which may expand on prior findings. Moreover, none have mixed quantitative and qualitative findings, and practical recommendations for quality improvement have rarely been reviewed.

To our knowledge, factors associated with PIPs among primary care older adults and barriers to optimising their medication use have not yet been comprehensively reviewed. Such a review is needed to allow the integration of research theory and practice before preparing the design of interventions. We conducted this systematic review to comprehensively identify the factors associated with PIPs among older adults in primary care settings. This review also synthesised the perceived implementation barriers to medicines optimisation from the stakeholders and their recommended potential solutions.

METHODS

Search strategy and data sources

Before the review was carried out, a protocol was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 statement.^{18 19} A preliminary search was conducted to ensure the novelty of our systematic review. Eight literature databases (PubMed, EMBASE, Scopus, CINAHL, PsycINFO, Web of Science, CNKI and Wanfang) were systematically searched for

available original research through 31 December 2020 (date of the last search: 25 February 2021). Search terms were adapted from relevant systematic reviews,^{11 15} and were discussed within our team but not peer-reviewed by information specialists or librarians. The full search strategy is presented in online supplemental table S1.

Searches were limited to human studies reported in the Chinese or English language for relevance. Additional articles were retrieved with a manual search through Web of Science based on the reference lists and related citations of relevant reviews, editorials, commentaries, letters and original research included in the review.

Eligibility criteria

The systematic review identified quantitative (cross-sectional and cohort) studies that analysed the factors associated with PIPs among primary care older adults, and qualitative studies that explored PCPs' and older adults' perceived barriers to medicines optimisation and their recommended potential solutions.

The included quantitative studies met the following criteria: (1) participants were adults aged 65 years and older; (2) participants were recruited from primary care settings (eg, community hospitals, clinics, community pharmacies or home) and (3) data that were used to analyse the factors associated with PIPs were collected through surveys or databases. The included qualitative studies met the following criteria: (1) primary care adults aged 65 years and older, and/or PCPs who prescribed or cared for older adults in the community were involved as participants and (2) participants reported their perceptions of barriers to medicines optimisation among older adults in primary care settings, and/or recommended potential solutions.

Qualitative studies were excluded if they (1) were not published in English or Chinese, (2) were not original research, (3) focused on participants with specific groups of pathologies or medications, or (4) included the patients discharged from the hospital. Besides the former three criteria, quantitative studies were excluded if they (1) did not use a validated screening method to detect PIPs or (2) used improper or incorrect statistical analysis methods.

Study selection

All search results were imported and organised in EndNote V.20 (Clarivate Analytics; <https://endnote.com/product-details>, accessed 26 February 2021). Duplicate citations were thereafter removed. Three reviewers (ZX, XL and YL) independently screened the titles and abstracts of the identified articles to create a form using Microsoft Excel 2019 (Microsoft; <https://www.microsoft.com/zh-cn/microsoft-365>, accessed 14 January 2021) that contained information on potentially relevant articles. Two reviewers (ZX and XL) examined full-text publications, discussed them, and reached a consensus for eligibility. When the uncertainty of the inclusion of identified

articles remained, a third reviewer (YL) was consulted to resolve the discrepancies.

Assessment of the quality of studies

The quality of the included full-text articles was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Tool (<https://jbi.global/critical-appraisal-tools>, accessed 19 February 2021). The JBI tool assists reviewers in evaluating the relevance, trustworthiness and results of research evidence ensuring that methodology, analysis and interpretations complement one another. Composed of 13 study-specific checklists for appraisal, the JBI tool has eight domains for analytic cross-sectional studies,²⁰ 11 domains for longitudinal studies²⁰ and 10 domains for qualitative studies.²¹

Two reviewers (ZX and YZ) independently applied the JBI checklists to rate the methodological quality of the included studies and determine the risk of bias in the design, conduct and analysis. The total score of the included study was calculated by summing each item's score. The disagreement in ratings was resolved through discussion and consultation with a third reviewer (YL). Studies were assessed as low-quality if the number of domains coded as no exceeded one, coded as unclear exceeded two or one domain was coded as no plus any others coded as unclear.

Data extraction process

Two reviewers (ZX and XL) independently completed the data extraction process using a standardised, pre-piloted spreadsheet designed based on the key features of the articles. The extracted information included general study characteristics (first author's name and year of publication), study design (location, study settings, study period, instrument for assessing PIPs, research and analysis methods) and study population details (sample size, participants' age range in quantitative studies and participants' identities in qualitative studies), the main findings of PIP rate and associated factors in quantitative studies, and barriers and recommendations in qualitative studies. All the results of the selected qualitative studies were entered verbatim into MAXQDA 2020 (VERBI; <https://www.maxqda.com/new-maxqda-2020#>, accessed 20 February 2021) for qualitative synthesis. Unclear or missing data in the selected articles were requested from the study authors via email. Discrepancies in the extracted data were resolved by discussion and consensus between the two reviewers and adjudicated by a third reviewer (YL) if an agreement could not be reached.

Data synthesis and analysis

Data from quantitative studies (overall PIP rate and associated factors) were synthesised using conventional content synthesis methods.²² To ensure that the synthesis reflected the original reference findings, the definition of associated factors in each study was examined. Meta-analysis was considered inappropriate due to sample heterogeneity, measurement and analysis methods.

Thematic synthesis was conducted for qualitative studies in line with the methods proposed by Thomas and Harden.²³ The process of deriving the themes was inductive. Following rereading and understanding the results section of selected studies, an initial coding manual was first established by one reviewer (ZX) through line-by-line coding to identify similar concepts across studies and subthemes regarding PCPs' and older adults' perceived barriers to medicines optimisation and recommended potential solutions. Two reviewers (ZX and XL) independently coded selected qualitative studies using this coding manual until no further subthemes emerged. Any discordance between the two reviewers was discussed and adjudicated by a third reviewer (YL) when a disagreement remained. The coding manual was refined accordingly after consensus and was subsequently discussed with all authors who provided expertise in primary care and prescribing behaviour to develop and finalise the analytical construct.

Since our review focused on different subquestions of PIPs among older adults in primary care settings (factors, barriers and recommendations) that neither refute nor confirm each other but rather complement each other, the convergent segregated approach was undertaken to integrate both quantitative and qualitative synthesised findings.²⁴

Patient and public involvement

The main findings of our review were reviewed and commented on by four patients, three primary care physicians and one community pharmacist selected from two community health centres in Hangzhou and Shenzhen. Two of the study authors (YL and YY) have served as PCPs in community health centres involved with community-dwelling older adults' healthcare and medication management. Both the authors participated in determining the research agenda, developing protocols, interpreting and reporting the results.

RESULTS

Description of study characteristics

The electronic database searches identified 13 167 references for screening, and 44 studies were eligible for the review process. Eighty-six additional studies were identified via manual searches, and six were included after screening. The PRISMA flow chart ([figure 1](#)) included a total of 50 studies and reasons for studies excluded from the review process. The most common reason for exclusion was that some studies were not conducted in primary care settings (n=43), followed by exposure not to PIPs (n=35) and associated factors of PIPs not correctly analysed (n=28).

The data extracted from the included studies were summarised in online supplemental table S2 and S3. Of the 50 studies included, 34 were cross-sectional studies,^{25–58} 2 were cohort studies^{59 60} and 14 were qualitative studies.^{61–74} Most studies were conducted in a single

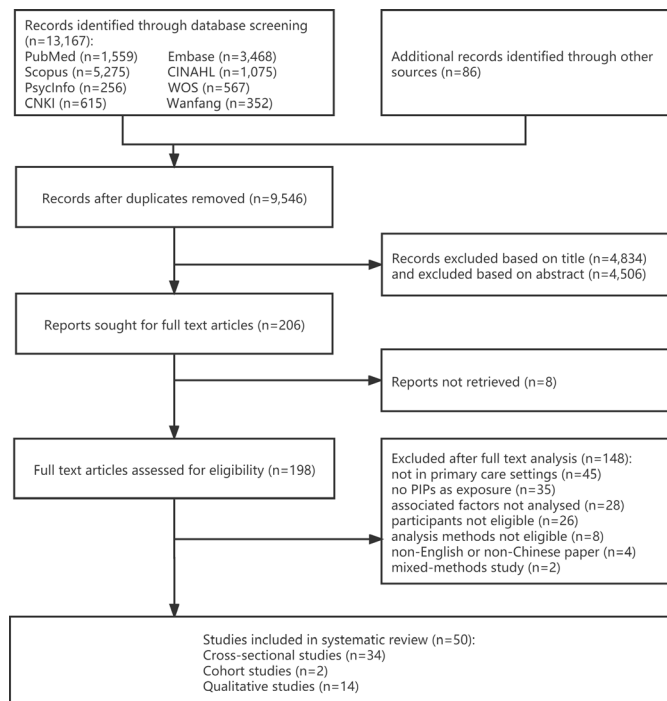


Figure 1 PRISMA flow diagram of systematic review.

country, except 1 international study involving participants in 11 European countries. In quantitative studies, the majority (84%) involved older adults aged over 65 years, and only six (16%) involved adults aged over 70 years (range of sample size: 89–1 595 054). The Beers criteria were the most commonly used screening methods to detect PIPs (53%), followed by STOPP (45%) and START (26%). In qualitative studies, six studies (43%) involved general practitioners or primary care physicians as participants, with one (7%) involving community pharmacists, and seven (50%) using a mixed sample (range of sample size: 15–152). Nine (64%) studies used semi-structured interviews to collect data, with four (29%) using focus group interviews and one (7%) using mixed methods.

Quality appraisal results

The methodological quality of the included studies varied (details of quality appraisal results were presented in online supplemental table S4). None were excluded from the quality appraisal process because all studies were of sufficient methodological quality. In quantitative studies, 14 of the included cross-sectional studies (41%) and 2 cohort studies (100%) were assessed as high quality. All cross-sectional studies reviewed met the quality criteria of detailed participants, setting, valid exposure measurement and appropriate statistical analysis. The common problems affecting study quality were failure to (1) establish how the measurement of outcomes was conducted (68%), (2) clearly define exclusion criteria (53%), (3) use standard criteria for measurement of the condition (50%) and (4) deal with confounding factors (41%). Three studies (9%) did not identify any confounding factors. Four items were considered not applicable to

the two cohort studies included in the quality appraisal process. One cohort study reviewed met all the remaining quality criteria in the appraisal, whereas the other study failed to deal with confounding factors.

Six of the included qualitative studies (43%) were assessed as high quality. None of the included qualitative studies met all the quality appraisal criteria. All studies failed to state the philosophical or theoretical premises on which the study was based. Study quality was also affected by failure to locate the researcher culturally or theoretically (36%) and failure to acknowledge and address the influence of the researcher on the research (93%). All qualitative studies reviewed met the remaining seven quality criteria.

Factors associated with PIPs

Patient-related factors

Non-clinical factors

All but one study evaluated patient-related non-clinical factors (table 1). Age and sex were the two most common demographic factors evaluated, but the results varied in these studies. Fourteen studies showed a significant positive association between advanced age and PIPs,^{25 28 31 37 39 40 43 45 46 48 50 51 55 56} whereas 5 showed a significant negative association,^{27 34 35 38 53 57} and 11 did not show a significant association.^{26 29 30 33 41 42 44 47 49 52 54} Female older adults were more likely to have PIPs than male in 11 studies.^{29 31 33 37 41 42 47 48 52 56 57} However, 4 studies showed an opposite result,^{34 35 38 53} and 15 studies showed no significant association between sex and PIPs.^{26–28 30 39 40 43–46 49–51 54 55} Moreover, one study showed mixed results that the association was relevant to specific items of the STOPP criteria.²⁵

Race,^{37 53 57} region,^{29 36 41 44 50 56} socioeconomic status^{27 29 31 33 52} and living alone^{27 29 47 49 51 53} were inconsistently associated with PIPs among primary care older adults. Nine of 10 studies showed no significant association between education and PIPs,^{29 33 42 45 47 48 51 52 55} and all 6 studies reported that marital status was not an associated factor of PIPs.^{33 48 51–53 57}

Clinical factors

The medication count was examined in most studies, and the results were consistent. Twenty-five of the 28 studies found that older adults on a greater number of medications were more likely to receive PIPs.^{26–29 31–35 37–41 44 46–50 52–56} Four studies identified specific types of medications as associated factors PIPs, such as medications for the central nervous system, digestive system, locomotive system, musculoskeletal system and metabolism.^{27 33 41 52}

The number and types of comorbidities may also affect the PIPs. Patients with more comorbidities were more likely to receive PIPs in nine studies.^{26 41 44–46 50 51 55 57} Fourteen of the 16 studies^{29–31 33 39–41 43 46 48 49 53 54 57} and 8 of the 9 studies^{27 30 33 46 48 53 54 57} showed some types of physical comorbidities (eg, diabetes, osteoporosis and rheumatoid arthritis) and psychiatric comorbidities (eg, depression and anxiety) were related to PIPs, respectively.

Table 1 Patient-related factors of PIPs in included quantitative studies

Study	Non-clinical factors										Clinical factors						
	Age	Sex	Race	Education	Socioeconomic status	Region	Marital status	Living alone	No of drugs	No of drugs	Type of drugs	No of comorbidities	Physical comorbidities	Psychiatric comorbidities	Health status	Unhealthy behaviours	Use of care delivery
Bradley (2012) ²⁵	↑	▲															
Vacharavongvan (2019) ²⁶	□	□						↑	↑		↑						
Fialová (2005) ²⁷	↓	□			▲			▲	↑	▲	□		▲		□		□
Castillo-Páramo (2014) ²⁸	↑	□						↑	↑						▲		
Núñez-Montenegro (2019) ²⁹	□	F		□	□	□	□	□	↑			▲			□		□
Wang (2019) ³⁰	□	□								□		▲		▲			
Ble (2015) ³¹	↑	F			□			↑	↑		↓	▲					
Moriarty (2015) ³²								↑	↑								
Lopez-Rodriguez (2020) ³³	□	F		□	□		□	□	↑	▲	□	▲		▲			
Cahir (2014) ³⁴	↓	M						↑	↑								
Bradley (2014) ³⁵	↓	M						↑	↑		↓	□					
Lund (2012) ³⁶																	▲
Buck (2009) ³⁷	↑	F	□					↑	↑								▲
Cahir (2010) ³⁸	↓	M						↑	↑								
Vezmar Kovacevic (2014) ³⁹	↑	□						↑	↑	□	□	▲		□			
Lin (2011) ⁴⁰	↑	□						↑	↑			▲					
Simões (2019) ⁴¹	□	F				□		↑	↑	▲	↑	▲					
Howard (2004) ⁴²	□	F		□				□	□		□						□
Zeenny (2017) ⁴³	↑	□						↑	↑			▲					▲
Awad (2019) ⁴⁴	□	□						↑	↑		↑						

Continued

Table 1 Continued

Study	Non-clinical factors							Clinical factors									
	Age	Sex	Race	Education	Socioeconomic status	Region	Marital status	Living alone	No of drugs	No of drugs	Type of drugs	No of comorbidities	Physical comorbidities	Psychiatric comorbidities	Health status	Unhealthy behaviours	Use of care delivery
Gorup (2017) ⁴⁵	↑	♀	□	□				□	□	↑	↑	↑					□
Mand (2014) ⁴⁶	↑	♀						↑	↑	↑	▲	▲		▲			
Tommelein (2016) ⁴⁷	□	F	□	□			□	□	□	↑	□	▲		▲	□	□	□
Sakr (2018) ⁴⁸	↑	F	□	□			□	□	□	↑	▲	▲		▲	□		
Hamano (2014) ⁴⁹	□	□					□	□	□	↑	▲	▲					□
Zhang (2020) ⁵⁰	↑	□				□		□	□	↑	□	□					▲
Liu (2020) ⁵¹	↑	□	□	□			□	□	□	□	□	□					▲
Rogero-Blanco (2020) ⁵²	□	F	□	□	▲		□	□	□	↑	▲						
Bala (2019) ⁵³	↓	M	▲				□	▲	□	↑	▲	▲		▲	□	□	▲
Alhmod (2015) ⁵⁴	□	□						□	□	↑	▲	▲		▲			□
Sayin (2020) ⁵⁵	↑	□	□	□				□	□	□	□	□					□
Amos (2015) ⁵⁹	↑	F				▲		□	□	□	□	□					
Pugh (2011) ⁶⁰	↓	F	▲				□	□	□	□	▲	▲		▲	▲	▲	▲

↑: Significant positive association; ↓: Significant negative association; □: Not significant; ▲: Significant. Blank cells: the variable was not examined. F, female; M, male; PIPs, potentially inappropriate prescriptions.

Two studies showed that self-rated poorer health status was associated with a higher number of PIPs,^{47 53} yet this association was not found in another two studies.^{27 42}

Several studies found that more primary care visits,^{37 50} prescribed partly by secondary or tertiary care physicians,⁵¹ a history of hospitalisation in the last 90 days,⁵³ and receiving geriatric care⁶⁰ were associated with an increased risk of PIPs. Five studies examining unhealthy behaviours demonstrated that smoking was not a significant predictor,^{43 47 48 51 53} with only one suggesting that alcohol consumption may be a protective factor for PIPs.⁴³

Prescriber-related factors

Nine studies evaluated prescriber-related factors; however, no factor was identified as being associated with PIPs in over half of the studies (table 2). Prescribers' sex and year of experience were inconsistently related to PIPs,^{33 38 42 56–59} and the race was not related to PIPs.⁵⁶ Reportedly, physicians who prescribed six or more PIM types were more likely to have a board certification in internal medicine and family practice.⁵⁶ However, in another study, the physicians' family medicine certification status was not significantly associated with PIPs.⁴² Older prescribers were found to have an increased risk of PIPs in two of the four studies.^{56 59} One study showed that patients who had prescribers working as postgraduate medical trainers had lower MAI scores.³³

Patients who had two or fewer prescribers were associated with a decreased likelihood of PIPs in one study.⁴¹ Two studies found that solo practice physicians were more likely to prescribe PIMs to their older patients.^{57 59} Prescribers caring for a small number or proportion of older adults were more likely to prescribe PIMs in two studies,^{58 59} whereas one study identified caring for older adults as a risk factor.⁵⁷

Barriers to implementation of medicines optimisation

All studies described barriers to implementing medicines optimisation among older adults in primary care settings (box 1). Four themes of barrier factors were coded from the perspectives of the prescriber, patient, environment and technology. A selection of quotations from participants and interpretations of findings offered by the authors was presented in online supplemental table S5.

Prescriber-related factors

The theme prescriber-related factors described prescribers' deficiencies in knowledge and capabilities of medicines optimisation. Inadequate knowledge related to prescribers being uninformed or misinterpreting some terms of medicines optimisation and their misinterpretation or unawareness of drug-related risks. Concerns about adverse consequences emphasised the uncertainty of the benefits and harms of medicines optimisation. Clinical inertia referred to prescribers' reluctance to change PIMs prescribed by other health professionals. Lack of communication indicated that prescribers seldom initiate

discussions with patients about drug safety and medicines optimisation.

Inadequate knowledge—Prescribers from 10 studies displayed their inadequate knowledge of medicines optimisation.^{61–64 66 67 70–73} Some prescribers were unfamiliar with specific terms of medicines optimisation (eg, deprescribing) or misinterpreted the meaning of terms (eg, equating 'inappropriate' with 'carelessness').^{62 63} Others were unaware of the drug-related risks and care problem in their clinical practice,^{63–65 70 72 73} which was commonplace in older patients with long duration of PIPs use that appeared to work with few adverse effects.

Concerns of adverse consequences—Most prescribers expressed their concerns about the adverse consequences of reducing or changing medicines.^{61 64 65 67 69 70 73 74} Prescribers feared that deprescribing PIMs may contribute to unexpected clinical efficacy and even worse outcomes, such as withdrawal syndrome, relapse or death.^{61 64 65 67 69 70 74} One study demonstrated that the fears also encompassed outcomes regarding reputational damage and deteriorated relationships with patients.⁷⁰

Clinical inertia—Eight studies described a tendency that prescribers in primary care settings maintained PIPs initiated by other health professionals.^{61–63 65 70 72–74} Prescribers lacked motivation or felt it difficult to reconsider the appropriateness of existing prescriptions, particularly for long-term prescriptions or discharge medications.^{61–63 65 70 72–74} Prescribers from one study thought reducing medicines initiated by others was against professional etiquette.⁷⁰ Furthermore, prescribers' ageism against PIP discontinuation was reported as a cause of clinical inertia in one study.⁶³

Lack of communication—Six studies showed a lack of patient education and communication concerning PIP use and medicines optimisation for a variety of reasons.^{62 63 65 68 71 73} Poor communication contributed to mutual misunderstandings and patient non-adherence, which impeded the medicines optimisation implementation.^{62 65 68 71} Patients in one study reported that they obtained PIPs via telephone, instead of regular personal contact with prescribers.⁶³

Patient-related factors

The theme of patient-related factors described the reasons for patient resistance to medicines optimisation. Limited understanding emphasised patients underestimating the potential risks of ADEs and their reluctance to learn. Drug dependency referred to drug addiction and patients demanding drugs for perceived therapeutic effects. Patient non-adherence described patients' unwillingness to change medication regimens because of misunderstandings or fear of worse outcomes.

Limited understandings—Nine studies identified the limited understanding of PIPs as patient-related barriers to medicines optimisation.^{62–64 66 68 69 71 73} Patients often lack understanding of their medications and health risks, particularly those with low education and advanced age.^{62 63 68 69 71 73} They may accept ADEs, attribute

Table 2 Prescriber-related factors of PIPs in included quantitative studies

Study	Sex	Age	Race	Position	Practice status	Year of experience	Certification	No of prescriber	No of older patients	Proportion of older patients
Nuñez-Montenegro (2019) ²⁹								α		
Lopez-Rodriguez (2020) ³³	F	α		▲		↑				
Cahir (2014) ³⁸	M									
Simões (2019) ⁴¹								↑		
Howard (2004) ⁴²	α					α	α			
Imai (2007) ⁵⁶	α	↑	α		α	↓	▲			
Brekke (2008) ⁵⁷	α	α			▲	↑		↑		
Ie (2017) ⁵⁸	α	α				α				↓
Amos (2015) ⁵⁹	M	↑			▲			↓		▲

↑: Significant positive association; ↓: Significant negative association; α: Not significant; ▲: Significant. Blank cells: the variable was not examined. F: female; M, male; PIPs, potentially inappropriate prescriptions.

Box 1 Barriers to medicines optimisation for primary care older adults

Prescriber-related factors

Inadequate knowledge

- ▶ Limited knowledge of medicines optimisation.^{61–64 66 67 70–73}
- ▶ Misunderstanding of potentially inappropriate prescriptions (PIPs).^{62 63}
- ▶ Unawareness of adverse consequences.^{63–65 70 72 73}

Concerns of adverse consequences

- ▶ Fear of contributing to a worse outcome.^{61 64 65 67 69 70 73 74}
- ▶ Fear of reputational damage and moral blame.⁷⁰
- ▶ Concern about deteriorated relationships with patients.⁷⁰

Clinical inertia

- ▶ Lack of motivation to reconsider long-term medications.^{61 65}
- ▶ Prescriber's ageism against PIPs discontinuation.⁶³
- ▶ Reluctance to change medications prescribed by others.^{63 70 72–74}

Lack of communication

- ▶ Lack of communication with patients.^{62 65 68 71 73}
- ▶ Inadequate personal contact with patients.⁶³

Patient-related factors

Limited understandings

- ▶ Lack of knowledge of PIPs.^{62 63 68 69 71 73}
- ▶ Inhibited or not interested to know more information.^{63 64 71}
- ▶ Misunderstanding of medicines optimisation.^{61 66 68 70 71}

Drug dependency

- ▶ Drug addiction.^{61 63 64}
- ▶ Ineffectiveness of alternatives.⁶³
- ▶ Preferences for drugs due to perceived therapeutic effects.^{63–65 68 73 74}
- ▶ Demands of receiving PIPs.^{63 65 69 74}
- ▶ Distress to be relieved.^{65 71}

Patient non-adherence

- ▶ Little willingness to change lifestyle.⁶¹
- ▶ Delay of implementing medication changes.⁶¹
- ▶ Under-reporting medication use or adverse drug events.^{62 64 68}
- ▶ Tolerance to side effects.^{63 68}
- ▶ Patient's ageism against PIPs discontinuation.⁶³

Environment-related factors

Lack of integrated care

- ▶ Inadequate information exchanged among prescribers.^{61 62 64 65 68–71 73}
- ▶ Underdeveloped interprofessional relationships and collaboration.^{61 64–67 70 71 73}
- ▶ Difficulty to reach a consensus among prescribers.^{61 62 66 68}
- ▶ Limitations of disease-specific care.^{65 74}

Insufficient investment

- ▶ Incomplete infrastructure.⁶¹
- ▶ Defects of the electronic health record system.^{64 66}
- ▶ Unsatisfactory financial remuneration.⁷¹

Time constraints

- ▶ Time constraints in clinic consultations.^{61 64–67 70 73}
- ▶ Non-clinical tasks.⁶⁹

Technology-related factors

Complexity of implementation

- ▶ Challenges of polypharmacy and multimorbidity.^{62 66–68 72 73}
- ▶ Complex trade-offs between benefits and harms.^{67 68 72}
- ▶ Non-pharmaceutical alternatives not used.^{63 70}
- ▶ Time and resource-intensive processes.^{66 67 70}

Inapplicable guidance

- ▶ Recommendations inapplicable to individuals.^{61 62 64–70 72 74}

Continued

Box 1 Continued

- ▶ Discrepancy between guideline recommendations.^{61 73}
- ▶ Lack of recommendations informed by high-quality evidences.^{67 68 70 72 73}

 All studies cited in the box are high-quality apart from references.^{66–73}

drug-related syndrome to part of their ageing, and did not understand the purpose of medicines optimisation.^{61 66 68 70 71} Patients from three studies were inhibited or not interested in knowing more information about their medications.^{63 64 71}

Drug dependency—Eight studies reported patient preference for their PIMs.^{61 63–65 68 69 73 74} Some patients that chronically used certain drugs (eg, hypnotics) were influenced by drug addiction.^{61 63 64} The ineffectiveness of alternatives was cited as one barrier to stopping medications.⁶³ Other patients were described as demanding drug treatment and resisting to medicines optimisation for other reasons, such as positive drug side effects and loyalty to former physicians' prescription orders.^{63 65 69 74}

Patient non-adherence—Five studies described situations in which patients failed to adhere to medicines optimisation.^{61–64 68} Patients may feel embarrassed to discuss their ADEs with prescribers and under-reported medication discontinuation.^{62 68} Some patients adopted a passive approach to their medication management. For example, they 'postponed implementing medication changes', or had 'wish to take fewer drugs but little willingness to change their lifestyle'.⁶¹ Some patients even asked someone else for medications if the former prescriber declined their request for PIPs.⁶⁴ Two studies reported that patients continued medications as long as they could endure the side effects of their medications.^{63 68} One study showed patient's ageism against PIPs discontinuation was a cause of non-adherence among older adults.⁶³

Environment-related factors

The theme of environment-related factors described the challenges of the working environment in primary care settings. Lack of integrated care referred to the fragmentation of care and inadequate collaboration between PCPs and other health professionals. Insufficient investment related to unsatisfactory incentives and underdeveloped infrastructure to support medicines optimisation. Time constraints described PCPs' busy work and limited time for clinic consultations.

Lack of integrated care—Twelve of 14 studies identified the barrier of lack of integrated care for primary care older patients.^{61 62 64–71 73 74} Respondents emphasised inadequate timely information exchange between health professionals,^{61 62 64 65 68–71 73} and acknowledged underdeveloped interprofessional relationships and collaboration.^{61 64–67 70 71} Four studies reported that PCPs found it difficult to reach a consensus with the specialists,^{61 62 66 68} and respondents in two studies criticised the limitations

of disease-specific care lacking comprehensive consideration, which played a role in PIPs.^{65 74}

Insufficient investment—Respondents from four studies described insufficient support for infrastructure.^{61 64 66 71} No internet access,⁶¹ and the poor EHR system was described as obstacles to following the instant guidance of appropriate prescribing.^{64 66} One study reported pharmacists' complaints about financial difficulties and unsatisfactory financial remuneration for home medication reviews.⁷¹

Time constraints—Eight studies reported that PCPs' lack of time leads to suboptimal medicines optimisation.^{61 64–67 69 70 73} The causes of this barrier included many patients who possibly had varied clinical priorities except medication management,^{61 64–67 69 70 73} and working time and energy occupied by non-clinical tasks (eg, administrative work).⁶⁹

Technology-related factors

Theme technology-related factors described the complexity of implementing medicines optimisation and the limitations of guidance. The complexity of implementation emphasised the technical difficulties faced by prescribers in medicines optimisation for primary care for older adults. Inapplicable guidance related to the limited feasibility, applicability and reliability of guideline recommendations.

Complexity of implementation—Technical difficulties in medicines optimisation for primary care older adults were reported in eight studies.^{62 63 66–68 70 72 73} Medicines optimisation was a time-and resource-intensive process,^{66 67 70} and patients with polypharmacy, multimorbidity and non-adherence further contributed to the complexity of implementation.^{62 66–68 72 73} Many respondents emphasised the pivotal challenge of weighing up benefits and harms of medicines optimisation for individuals.^{67 68 72} Little access to other services, such as non-pharmaceutical alternatives, was also considered a challenge in implementing medicines optimisation.^{63 70}

Inapplicable guidance—Eleven of 14 studies discussed that current guideline recommendations were considered not feasible or applicable to the individuals—further disabling prescribers implementing medicines optimisation.^{61 62 64 65 67–70 72–74} First, prescribers thought that the recommendations were reasonable but inapplicable to individuals of different age groups or with complex comorbidities.^{61 62 64 65 67 69 72 74} Second, the guidance did not provide quantification of the risk and non-pharmaceutical options.^{65 68 70 72} Third, there were discrepancies between recommendations of medicines optimisation and general guidelines.^{61 73} Fourth, many recommendations were not based on high-quality evidence.^{67 68 70 72 73}

Recommended potential solutions

Twelve of the 14 studies provided recommendations and potential solutions to address barriers to implementing medicines optimisation among older adults in primary care settings (box 2). These recommendations were

Box 2 Recommended potential solutions of implementing medicines optimisation

Prescriber-related factors

- ▶ Starting with easier options.⁶⁷
- ▶ Adopting a gradual approach with close patient follow-up.⁶
- ▶ Waiting for favourable circumstances.⁷²
- ▶ Finding an alternative path to avoid worse outcomes.⁶⁷
- ▶ Repeated positive experience.^{67 68}
- ▶ Training for medication review and optimisation.^{66 69 70 74}
- ▶ Incorporating training courses into continuing medical education.⁶⁹
- ▶ Being more reflective in decision-making about prescriptions.⁷⁴
- ▶ Risk stratification and clinical monitoring.^{65 72}

Patient-related factors

- ▶ Earning patient trust.⁶⁴
- ▶ Continuous therapeutic relationship.⁶⁷
- ▶ Patient counselling and education.^{63 65 73}
- ▶ Communication skills.⁶⁴
- ▶ Electronic communication.⁶⁶
- ▶ Shared decision making.⁶⁴
- ▶ Activating patients to make them more involved.⁷⁰
- ▶ Public health campaign and advertising.⁶⁹
- ▶ Involving caregivers to assist medication management.⁶⁶

Environment-related factors

- ▶ Financial remuneration and professional acknowledgement.^{69 70}
- ▶ Mutual multidisciplinary involvement and cooperation.^{66 69 73}
- ▶ Timely communication with health professionals.^{67 69 70 73}
- ▶ Open channels of interdisciplinary communication.^{69 70 73}
- ▶ Increasing workflow efficiency through teamwork.⁶⁶
- ▶ Scheduling special timing for medicines optimisation.^{64 69 70}

Technology-related factors

- ▶ Electronic surveillance of medications.⁶⁶
- ▶ Centralised storage of accessible information in the electronic health record (EHR) system.⁷⁰
- ▶ Using a chat in the EHR system among healthcare providers.⁷³
- ▶ Providing accessible decision support.^{67 70 73}
- ▶ Developing guidelines for the management of common comorbidities.^{68 70}
- ▶ Feasible and concrete guidance.^{66 68}
- ▶ Reliable information sources.⁶⁷

All studies cited in the box are high-quality apart from references.^{66–70 72 73}

categorised into four themes based on the identified barrier factors. A selection of quotations from participants and interpretations of findings offered by the authors were presented in online supplemental table S6.

Training about medication review and optimisation was the most consistent recommendation for prescriber-related barrier factors.^{66 69 70 74} One respondent suggested incorporating a training course into continuing medical education to make pharmacists more inclined to participate.⁶⁹ Two studies reported that repeated positive experiences could reinforce PCPs' motivation to implement medicines optimisation.^{67 68} Respondents emphasised the principle of being reflective in decision making about prescriptions,⁷⁴ and regular clinical monitoring of potential side effects.^{65 72} Several implementation techniques

were suggested, such as starting medicines optimisation with easier options, waiting for favourable circumstances to obtain patient engagement, adopting a gradual approach with close patient follow-up and finding alternative paths to avoid worse outcomes.^{67 72}

Eight studies reported recommendations for improved patient–physician interactions to patient-related barriers.^{63–67 69 70 73} A continuous therapeutic patient–physician relationship was considered critical for medicines optimisation implementation,⁶⁷ with relevant practical recommendations, including shared decision making,⁶⁴ electronic communication⁶⁶ and communication skills.⁶⁴ Patient counselling and education to improve patients' awareness of PIPs was recommended in three studies.^{63 65 73} One study suggested that campaigns from health authorities to patients could be carried out to raise their awareness of PIPs.⁶⁹ Another study described that caregivers or family members were helpful in assisting with medication optimisation for complex patients.⁶⁶

Recommendations for environment-related barriers were described in seven studies, and the majority focused on improving cross-disciplinary collaboration.^{64 66–70 73} Primary care physicians needed staff support from pharmacists or nurses to implement medicines optimisation in primary care settings.^{66 69 73} Direct phone calls were recommended as a feasible strategy for timely information exchange between prescribers and other health professionals.^{67 70} Four studies reported solutions to address the barriers to time constraints, such as scheduling a special appointment^{64 69 70} and teamwork.⁶⁶ Additionally, respondents in two studies suggested that financial remuneration and professional acknowledgement were necessary for medicines optimisation.^{69 70}

Five studies reported EHR optimisation and advanced technical aids as two main solutions to address technology-related barriers.^{66–68 70 73} EHR optimisation involved adding functions of alerting drug errors and interactions, centralised storage of accessible information and online chat to achieve timely communication between prescribers and other health professionals.^{66 70 73} Respondents reported their urgent need for guidance that was concrete, evidence based and applicable to older patients with common multimorbidities.^{68 70} The ease of access to guidance was emphasised in three studies,^{67 70 73} and one respondent took an iPad app as an example of an accessible tool to optimise medications in clinical practice.⁷⁰

DISCUSSION

In this systematic review, we comprehensively identified 16 patient-related factors (eight non-clinical and eight clinical, respectively) and ten prescriber-related factors of PIPs among primary care older adults. Also, we synthesised four analytical themes of stakeholders' perceived barrier factors to medicines optimisation and their corresponding recommendations and potential solutions. The results of qualitative studies showed that barriers to medicines optimisation involved factors related to prescribers,

patients, environment and technology. The recommended potential solutions were based on each theme of the barriers identified accordingly. The main findings of our study were reviewed and commented on by stakeholders in different areas to strengthen their practicality. Our study expands on previous systematic reviews by mixing quantitative and qualitative findings, which allowed for greater scope and insights into the factors associated with PIPs and barriers and recommendations to medicines optimisation.

A recent systematic review of 22 papers by Nothelle *et al*¹⁴ explored patient, clinician and environmental factors associated with PIM use in community-dwelling older adults in the USA. Their review identified four patient-related associated factors: a higher number of prescribed (reported by 14 studies), female sex (reported by 10 of 16 studies), psychiatric comorbidity (reported by 6 of 8 studies) and geographical region (reported by 7 of 8 studies), which partly coincided with our findings. However, only three studies examining clinician factors were included in their systematic review, and few were statistically significant.¹² In two systematic reviews, the number of medications, sex and age were the factors most often associated with PIMs among community-dwelling elderly, and both reviews showed a mixed association between PIMs and sex or age.^{13 14} Although this result was in line with our findings, the proportion of studies included in our review reporting the positive association was smaller. Similar patient-related factors have been shown in systematic reviews exploring PIPs across different healthcare settings.^{15 16}

Despite many factors that previous reviews and our study had identified, it is vital to note that a greater number of medications were the most consistent risk factors for PIPs in all settings. Alarming, the number of medications has been increasing over the years. Qato *et al*⁷⁵ reported that 31% of older adults in the USA were taking five or more prescription medications in 2005–2006, rising to 36% in 5 years. These two proportions further increased to 53% and 67% if over-the-counter medications and dietary supplements were included.⁷⁵ Moriarty *et al* conducted a repeated cross-sectional study and found that the prevalence of polypharmacy among the elderly (≥65 years) in Ireland increased from 17.8% in 1997 to 60.4% in 2012.³² Therefore, measures to curb the growth trend of medication use, particularly those unnecessary, ineffective and harmful prescribing, should be the priority in reducing medication-related harms.

Two systematic reviews by Anderson *et al*¹⁵ and Reeve *et al*¹⁶ synthesised qualitative studies regarding prescribers' and patients' perceived barriers and enablers to minimise PIMs, respectively. Despite differences in the eligibility criteria of participants and healthcare settings, most of the results reported in both reviews were similar to ours. However, one additional barrier described in our study was that PCPs may have no Internet access or computerised decision support systems (CDSSs) owing to underdeveloped infrastructure.^{61 62 65 67} CDSSs are considered

promising solutions to improving medication safety since they can efficiently help PCPs process complex clinical information, increase PCPs' adherence to guidelines, and improve the quality of prescribing decisions.⁷⁶ Accordingly, potential solutions were recommended for streamlining the EHR system to help prescribers work efficiently and wisely, such as developing CDSS and online chat systems.^{67 71 74}

A meta-synthesis by Cullinan *et al*¹⁷ described the prescribers' viewpoints on why PIPs occurred in older patients in detail. They found that prescribers tend to satisfy patients' requests, partly because some patients became aggressive and demanded their medications. This finding was supported by a factorial experiment revealing that patient requests for a specific medication significantly increase the rate at which physicians prescribe that medication.⁷⁷ Our study synthesised several practical recommendations to cope with this problem, including patient counselling and education,^{64 66 74} shared decision making⁶⁵ and involving caregivers for assistance.⁶⁷ Furthermore, our findings also added important recommendations regarding deepening cross-disciplinary cooperation among clinical pharmacists, specialists and primary care physicians. However, PCPs' barriers to and experience in responding to older patients demanding PIPs need to be explored in future studies.

Our study analysed both quantitative and qualitative studies and identified the consistency between these findings. For instance, quantitative studies have found that patients with a higher number of comorbidities, and specific physical (eg, osteoporosis) or mental diseases (eg, Alzheimer's disease) were more likely to receive PIPs. This challenge impacts on the qualitative findings of barriers to medicines optimisation, which requires more professional knowledge of physicians, and decreases patient adherence. The challenge could be more severe when the integrated care and applicable guidance were absent. Therefore, many potential solutions have been recommended focusing on improving the ability of PCPs to manage elderly patients with comorbidities, such as shared decision-making and developing guidelines for the management of common comorbidities. In the part of quantitative synthesis, this systematic review demonstrated the associations between PIPs and factors from both patient and prescriber aspects among primary care older adults.

We also identified gaps between the quantitative and qualitative findings. Although prescribers have a greater impact on PIPs, most studies have focused on patient characteristics and clinical information. In contrast, prescriber information has not been adequately investigated, which hampers our ability to identify prescriber-related factors. Many barriers already reported by qualitative studies (eg, patients' limited understanding and drug dependency) were not included as potential risk factors in quantitative studies to date. A possible reason for this gap was the difficulties in data collection because research solely based on the data of patients' prescriptions is easier to conduct.

Future studies in this area may need to consider relevant qualitative findings and design more practice-based approaches to explore the associated factors.

The results of our thematic synthesis disclosed perceived barrier factors of the prescriber, patient, environment and technology that shape PCPs' behaviour towards minimising PIPs in routine clinical practice. Several strategies to improve medicines optimisation could be implemented. First, professional training, including screening methods to detect PIPs, drug-related risk stratification and clinical monitoring, and communication skills of medication use, could be provided to PCPs. One example is the academic detailing. Previous systematic reviews demonstrated that the academic detailing was effective at changing PCPs' prescribing behaviours and improving their capacity for medicines optimisation.^{78 79} However, there is still room for improvement in the content design, and more high-quality research is needed to examine the acceptability and feasibility of the training programmes.⁷⁸

Second, patient education on medication use should be integrated into routine clinical practice in primary care settings. A continuous and high-trust therapeutic relationship helps engage patients in self-management of medication. Therefore, PCPs need to understand the motivation of patient use of PIMs and help them make wise decisions. Public health campaigns and advertising are also conducive to patient involvement, apart from direct patient counselling.⁶⁹ For example, PCPs may give lectures or send health information via social media to the community-dwelling older adults regularly to increase their awareness of medication safety.

Third, policy initiatives and health system reforms should improve PCPs' working environment of medicines optimisation, such as financial remuneration. Essentially, open channels of information exchange among health professionals are beneficial for developing interprofessional relationships and collaboration. Staff support from pharmacists or nurses can help address difficulties in many ways. They provide reassurance on treatment decisions, contribute to decreased workload and increase patient access to PCPs.⁸⁰⁻⁸² Policies should be made to encourage PCPs to integrate the pharmacists, nurses and other health professionals on the healthcare team to improve the quality of prescribing. Finally, besides advanced electronic health record (EHR) systems and accessible decision support to reduce PIPs, PCPs need concrete and evidence-based medicines optimisation procedures. This again implies an urgent need for high-quality studies involving individualised and complex interventions.

Our study has several limitations. First, it is difficult to quantitatively evaluate the degree of association between PIPs and factors, and compare the results from the included studies because of the heterogeneity of the sample, measurement and analysis methods. Second, since studies involving participants with specific diseases or medications were excluded from our review, the study results may not be generalisable to specific groups. Third, there remained great variations in the terminology used

for medicines optimisation, increasing the difficulties in identifying relevant studies. To address this problem, we formulated comprehensive search terms that were applied to multiple databases and manually searched reference lists and related citations. Fourth, a proportion of the studies included in our review were assessed to have a high risk of bias. This may reduce the strength of the evidence presented, and conclusions drawn from these must be treated with caution. However, the research quality was acceptable overall, and all studies could help improve the comprehensiveness of the results. Finally, publications were limited to English and Chinese languages only, which contributed to the potential omission of relevant evidence.

CONCLUSIONS

Older adults with more drugs prescribed and comorbidities may have a greater risk of receiving PIPs in the primary care setting, but whether other factors were related remain unclear owing to the inconsistent or limited findings of associations. Barriers to medicines optimisation among primary care older adults comprised multiple and interactional factors regarding prescriber, patient, environment and technology. Recommended potential solutions could be used to develop targeted interventions to address difficulties in clinical practice.

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