Original Research

Development of a medication review tool for residents in Korean long-term care facilities

Kwanghee Jun[iD], Soojin Lee, Ah young Lee, Young-Mi Ah and Ju-Yeun Lee[iD]

Abstract

Introduction: Residents in long-term care facilities (LTCFs) are likely to suffer from drug-related problems, such as inappropriate polypharmacy and potential prescribing omissions due to multimorbidity and high-level frailty. Medication reviews are thus necessary to identify and resolve drug-related problems in LTCF residents. In this study, we aimed to develop a medication review tool for older adults in LTCFs in Korea.

Methods: We did a systematic review to identify previously developed explicit criteria and devised preliminary potentially inappropriate medications (PIMs) list for the LTCF elderly from previous tools. Each item on this list was categorized into 23 underlying diseases/conditions, and the interventions necessary for each PIM were included. A two-round modified Delphi survey was performed sequentially for consensus evaluation of clinical appropriateness and feasibility of the list items by 12 experts (seven physicians in different specialties and five pharmacists specialized in geriatrics) and seven pharmacists, respectively.

Results: We identified 22 existing tools and devised a preliminary PIM list including 100 items. Ninety-one items were derived from the two-round Delphi survey for clinical appropriateness. In the feasibility test, 77 items were integrated into the final medication review tool for the LTCF elderly. The final list was composed of items relating to PIMs in general (18), potential drug interactions (14), PIMs under specific diseases/conditions (26), a need for dose adjustment (2), and potential omissions (17).

Conclusions: We developed a disease-category-based explicit medication review tool for detecting PIM use for LTCF residents. This tool may be helpful in implementing medication review practices to assist pharmacists or physicians for the elderly in LTCFs. Further research is required to validate the effectiveness of our tool in clinical practice.

Keywords: drug-related problem, long-term care facilities, medication review tool , potentially inappropriate medication, potential omission

Introduction

The aging of the population is increasing worldwide. Diseases that require assistance with activities of daily living, such as dementia and cognitive impairment, are also increasing in the elderly.[1,2] In addition, as the life expectancy of those over 65 has increased by more than 10 years compared with 40 years ago, the demand for elderly care, such as long-term care (LTC) services is rising.[3]

Institution-based care is an effective elderly care option for reducing the burden on family members for care and actively providing skilled care and approaches for symptom relief in elderly patients with increasing frailty, vulnerability, cognitive decline, and comorbidities.[4] LTC facilities (LTCFs) are currently the general solution, and institution-based care accounted for nearly two-thirds of total LTC costs and one-third of LTC users across the Organisation for Economic Co-operation and Development (OECD) countries in 2008.[5]

The LTC population differs from community-dwelling older adults: They are more likely to experience physiological dysfunction and complex

Correspondence to:
Ju-Yeun Lee
Professor, College of
Pharmacy and Research
Institute of Pharmaceutical
Sciences, Seoul National
University, 1, Gwanak-ro,
Gwanak-gu, Seoul 08826,
Republic of Korea.
jypharm@snu.ac.kr

Kwanghee Jun
Soojin Lee
Ah young Lee
College of Pharmacy,
Seoul National University,
Seoul, Republic of Korea

Young-Mi Ah
College of Pharmacy,
Yeungnam University,
Gyeongsan, Republic of
Korea

and chronic multimorbidity with high-level frailty, leading to a higher risk of adverse drug reactions, hospitalization, or readmission.[6] Inappropriate polypharmacy, potentially inappropriate medications (PIMs), and potential prescribing omissions (PPOs), associated with negative health consequences, such as hospital admission and readmission, are frequent among those requiring complex medication regimens.[7] The prevalence of polypharmacy in nursing homes (NHs) is high, with up to 91% and 65% of residents taking 5 or more and 10 or more different medications, respectively.[8] In the meta-analysis of studies conducted after 2005, prevalence of PIM use in LTCF recipients was estimated 50%.[9] The unplanned hospitalization rate has been reported to be five times higher in NH patients using ten or more PIMs compared with none, indicating the possibility of severe drug-related harm.[10] However, only a few studies investigated the PIM use in the Korean LTCF setting, a retrospective study showed that 41.4–58.2% of LTCF residents had received PIMs according to the 2012 Beers criteria or composite lists.[11,12]

Over the years, several tools have been developed to optimize medication therapy, such that the risk of PIMs outweighing its benefits can be prevented. Among such tools, the Beers criteria developed for the US NH patients in 1991 is the first and most well-known; this is a list of PIMs to be avoided or adjusted by the elderly in most circumstances or under certain diseases or conditions, and the American Geriatrics Society (AGS) has produced criteria updates for the general population since 2011.[13] The Screening Tool of Older Person's Prescriptions/Screening Tools to Alert Doctors to Right Treatment Medication (STOPP/START) criteria established in 2008 is commonly used in Europe.[14] In addition, numerous regional tools have been developed for general practice based on these tools, such as PRISCUS,[15] EU(7)-PIM,[16] FORTA (Fit fOR The Aged),[17] and STOPP-Japan criteria.[18]

Efforts to optimize medication use among NH residents have been undertaken in many countries. Most NH interventions utilize the aforementioned general explicit criteria targeting the geriatric population, while some have developed their own specific guidelines. Only a few explicit lists, such as the Norwegian General Practice – Nursing Home criteria (NORGEP-NH),[19] STOPP/START criteria for the US NH (STOPP/START-US NH),[20] and the Rancourt criteria,[6]

have focused on the NH population. As risk–benefit consideration of pharmacotherapy in patients receiving hospice care or end-of-life care can be different, the specialized guideline for this population has been developed, Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail).[21]

Although the clinical benefits of medication reviews, such as reducing hospitalization and mortality, have not been consistently proven,[22] medication management and multidisciplinary approaches have turned out to be effective strategies for lowering drug-related iatrogenic risks, inappropriate medication use, and drug expenditure for the elderly recipients.[23,24] Nonetheless, medication management programs for residents in LTCFs have not been implemented in Korea. The principal purpose of the LTCF was to provide ongoing assistance in daily activities rather than medical care; electronic medical records are not compulsory, contracted physicians visit LTCF according to a set schedule (usually twice a month), examine the patients, order nursing care, prescribe medications, and refer residents to the hospital, if necessary.[25] Prescriptions for LTCF residents are issued by physicians from external medical institutions as well as contracted physicians. So, the risk of unintentional drug–drug interaction, one of PIMs, could be high. However, there are no regulatory requirements regarding medication management in Korea, unlike in other countries, and no specific medication review tools or strategies for LTCF residents have been developed. Although several NH-specific guidelines have been developed in other countries, they are difficult to apply directly to Korean LTCF residents because of differences in the country's circumstances, healthcare practices, prescribing patterns, or approved drugs which are significant factors for the development of guidelines.[26] In addition, medication review tools should be updated regularly to confirm conclusions based on up-to-date evidence.

In Korea, hospice and palliative care services were covered by the national health insurance from hospitals in 2015 to LTCF and home in 2019;[27] patients at the end-of-life stage still go to (LTC) hospitals for suitable hospice and palliative care services. Thus, the average stay of residents in the LTCF in Korea is 2.3 years, and the stay proportion longer than the 1-year LTCF is 81.4%.[28] Furthermore, NH as a site of death in the elderly is only 11% in Korea,[29] compared with

18% worldwide and 25% in the United States.[30,31] Nevertheless, people in LTCF residents have different characteristics, such as limited activities of daily living and more severe comorbidities than community-dwelling elders, so that, medication review tools containing detailed consideration points for LTCF residents need to be developed. In addition, it could be appropriate to develop deprescribing guidelines, such as STOPPFrail for all healthcare settings rather than targeting LTCF residents, considering the characteristics of hospice and palliative care services in Korea.

Therefore, we aimed to develop a specific clinical tool to assist medication review pharmacists in optimizing therapy for LTCF residents, not in end-of-life care.

Methods
This study was conducted between September 2020 and December 2021 and comprised the following three stages.

Stage 1: systematic literature review and derivation of the preliminary list
To identify previously developed explicit tools, systematic reviews according to the methodological manuals of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were searched in PubMed, Embase, and Cochrane Library databases between 1991 and 2020, since the Beers criteria had been developed in 1991. We included studies involving adults above 65 years of age and explicit tools validated by expert consensus and scientific evidence, such as guidelines or recommendations for assessing medication therapy appropriateness. In addition, we excluded articles that met any of the following criteria: criteria based on little evidence, implicit criteria, tools restricted to a specific disease or medication class, country- or region-specific criteria as a revision of an existing tool, and involvement of only inpatients or community-dwelling elderly or patients with limited life expectancy.

Twenty-two articles were identified based on a thorough systematic literature review (Figure 1, Supplementary Table 1). Among them, the preliminary PIMs list was created based on seven main tools: specifically designed or applicable for NH patients, such as the NORGEP-NH, STOPP/START-US NH, and GheOP³S-tool;[32] tools most widely referenced by other developed tools, such as the Beers criteria and STOPP/START criteria; recently developed tool, such as the Turkish inappropriate medication use in the elderly (TIME) criteria[33] designed in 2020; and established for the Korean elderly in 2018.[34]

The preliminary PIMs list was classified as PIM in general (General-PIM), potentially inappropriate drugs due to drug interactions (DDI-PIM), PIM under specific diseases or conditions (Ds-PIM), potentially inappropriate drugs needed for monitoring and dose adjustment (Dose-PIM), and potential medication omissions (Omission). Among the items from the seven main tools, items in the type of 'General-PIM', 'Ds-PIM', and 'Dose-PIM' were involved as items included by more than five tools in 22 based tools. Also, the items to be considered in the Korean clinical context due to misuse or overuse, such as tramadol, were included in the preliminary list, even if included by less than five tools. Items in the type of 'Omission' and 'DDI-PIM' were considered in our list, even if they were not in the seven main tools. After, we excluded medications that are not labeled or marketed in Korea. All items were categorized into underlying diseases/conditions based on major indications and contraindications related to PIMs. Each item was elaborated on to describe the possible adverse effects, alternatives, and recommended interventions. The preliminary PIMs list consisted of 100 items classified into the five types of PIM.

Stage 2: two-round modified expert Delphi survey for clinical appropriateness
The list of criteria was elaborated on through expert consensus using a two-round modified Delphi method. First, 12 expert panels (7 physicians and 5 pharmacists specialized in geriatrics) were convened, including geriatric specialists, internal medicine specialists, family medicine specialists, geriatric pharmacists, and clinical pharmacy specialists.

In the first round, the expert panel members were asked to review the appropriateness of each item and insert additional comments in a preliminary list. They rated the appropriateness of each item using a 9-point Likert-type scale (9 = very strongly agree, 1 = very strongly disagree) by applying RAND/UCLA appropriateness method.[35] 'Consensus' among panelists was defined as a median
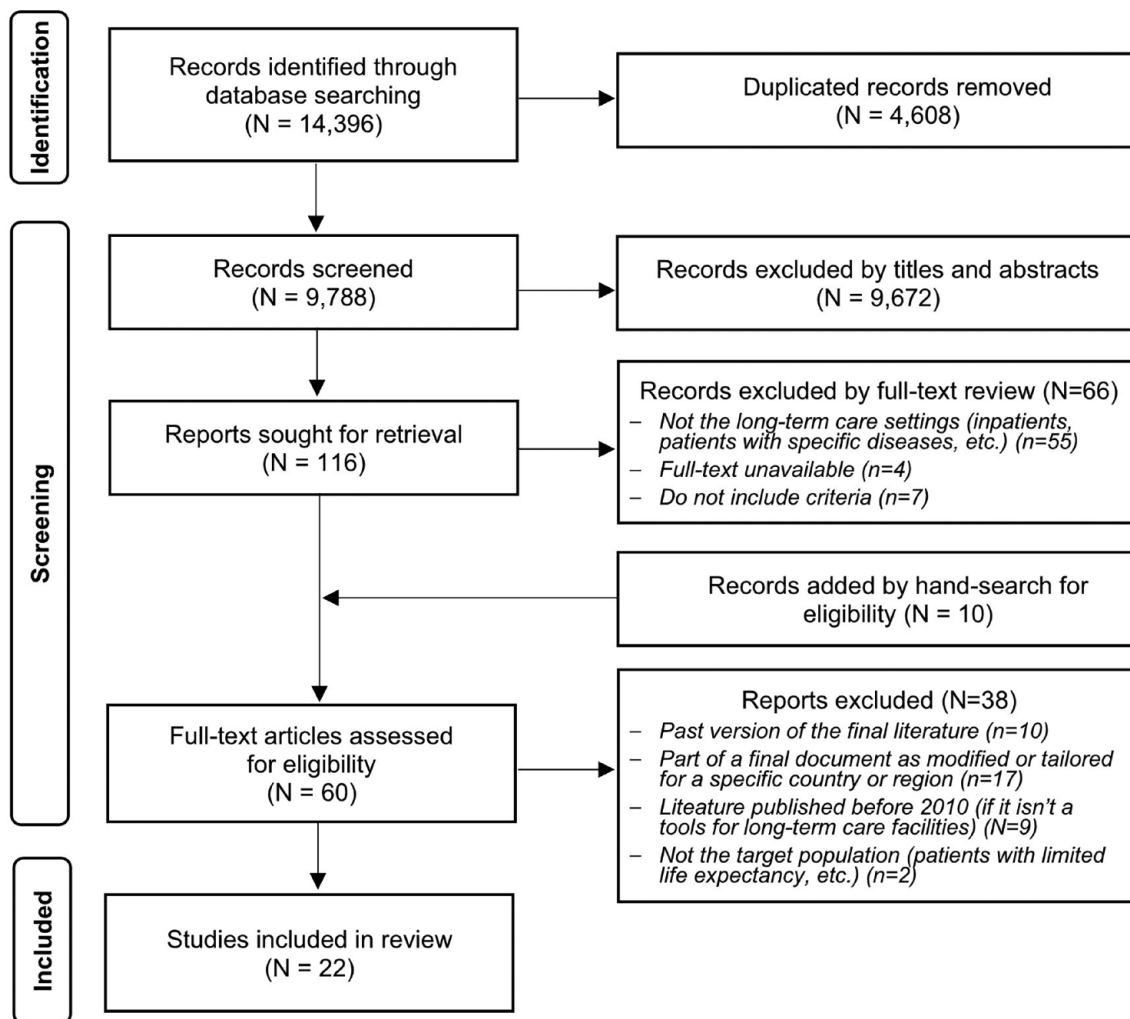
Figure 1. Flowchart of the systematic literature search.

score higher than seven without 'disagreement' (≥4 panelists rating 1–6 points, or more than one panelist rating 1–3 points) or not 'uncertain'(median of 4–6 or any median with 'disagreement').[36] In the second round, expert panels were given lists of modifications, including a summary of the first round as well as information, such as the proportion of those who responded 'appropriate' (7–9 points), 'inappropriate' (1–3 points), the median score, and previous responses. Similar to the first round, experts were also requested to score and comment on items that did not reach a 'consensus'.

Stage 3: a feasibility study
A feasibility study was conducted by five pharmacists who had participated in the pilot project on polypharmacy management in NH, one pharmacist running NH by herself, and one pharmacist mainly dispensing the prescriptions for NH residents. Similar to stage 2, the two-round modified Delphi method was used to assess the applicability and relevance of the list items in the pharmacy practice for the LTCF elderly. However, for this stage, 'consensus' was specified as a median score higher than seven, without 'disagreement' of at least two participants rating in each extreme region (i.e. 1–3 and 7–9 ratings). The final tool was reviewed by the expert panel from stage 2.

Results
The preliminary PIMs list was structurally designed and extracted through multiple iterations of assessment and selection of items. Each
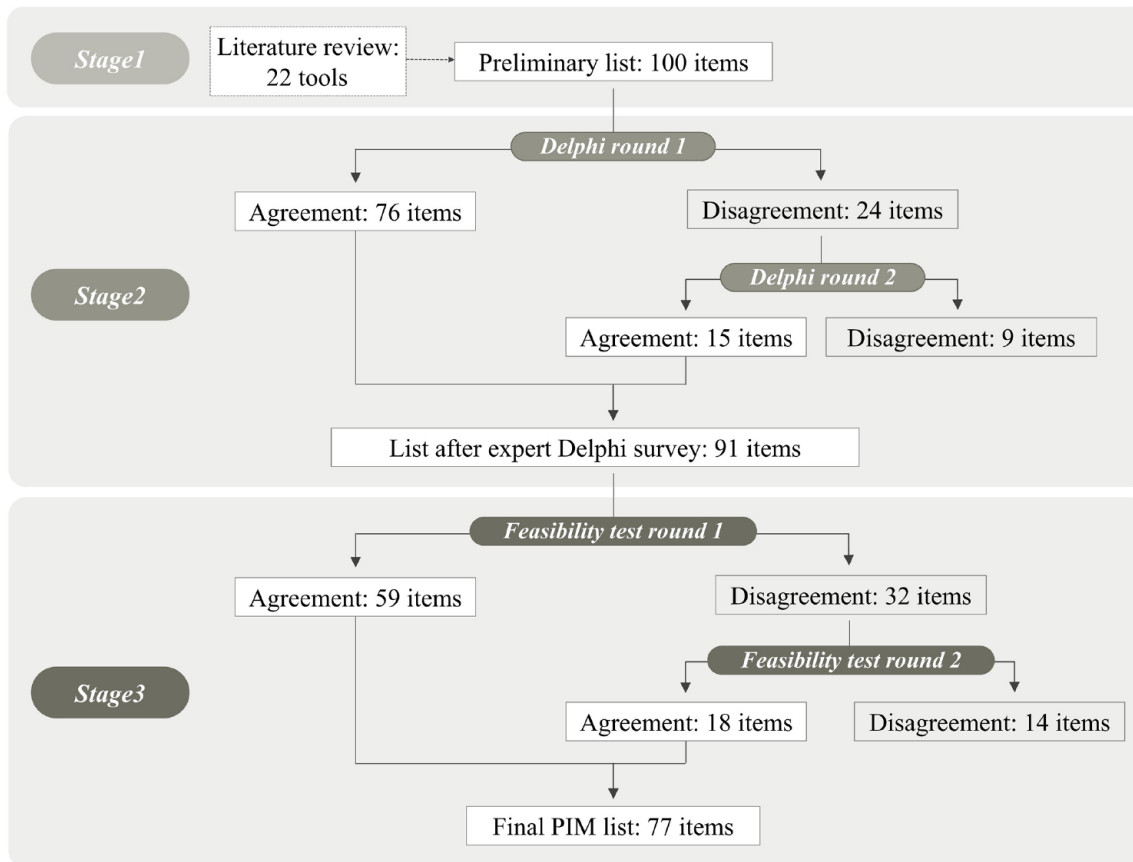
Figure 2. Process of deriving the medication review tool for the LTCF elderly.

of the 100 items was separated into 20 General-PIMs, 21 DDI-PIMs, 29 Ds-PIMs, 3 Dose-PIMs, and 27 Omission items. Furthermore, all items were categorized into 23 underlying diseases/conditions. The interventions necessary for each PIM were included.

Figure 2 shows how the medication review tool for the LTCF elderly was derived. In stage 2, 12 experts reached a consensus on 76 items in the first round. In the second round, an additional 15 items were classified as PIMs. Thus, 91 items were judged by the expert panels as potentially inappropriate for the LTCF elderly.

In stage 3 (the feasibility study), seven pharmacists evaluated 91 items in the first round and reached a consensus on 59 items. After the second round, the pharmacists agreed on 18 items. Thus, 77 clinically appropriate items were included in the final prescription review tool for

the LTCF elderly in Korea (Table 1). Removed items from the preliminary list during the Delphi survey were provided as supplementary information. (Supplementary Table 2)

Discussion

We developed an explicit medication review tool to support medication reviews in LTCFs in order to enhance the safety and quality of medication use by detecting and reducing inappropriate medication use. This tool covers five types of drug therapy problems and consists of 77 items with 23 disease bases, and was designed for implementation in daily practice with limited time and clinical information for a medication review.

Our tool encompasses 23 major underlying conditions or diseases based on the approved indications or contraindications associated with the medications for convenience in clinical practice.

Table 1. Final results of the Delphi survey for the medication review tool for LTCF residents.

Type		Criteria	Stage 2 median	Stage 3 median
A. General				
1	Omission	Seasonal influenza vaccination annually	9.0	8.0
2	Omission	At least one pneumococcal vaccination after 65 years of age	9.0	8.0
3	Omission	Recommend oral nutritional supplements for malnourished patients with chewing disorders[a]	8.5	7.0
4	General-PIM	First-generation antihistamines[a]	9.0	8.0
5	General-PIM	First-generation antihistamines for relieving symptoms of nausea, vomiting, and dizziness[a]	9.0	7.0
6	DDI-PIM	Two or more strong anticholinergic drugs (including over-the-counter drugs)	9.0	8.0
7	Dose-PIM	Oral iron supplement doses greater than 200 mg/day with elemental iron (>600 mg with ferrous sulfate)[b]	9.0	7.0
B. Hypertension				
8	Ds-PIM	Continued use of NSAIDs (including over-the-counter drugs) in patients using three or more antihypertensive drugs	9.0	7.0
9	Ds-PIM	Alpha-blockers as first-line treatment for hypertension in patients without BPH[b]	9.0	8.0
C. Ischemic heart disease (angina, acute coronary syndrome, myocardial infarction), stroke, TIA				
10	Omission	Recommend PPI when a patient using antiplatelet drugs (especially a patient using two types of antiplatelet drugs) and NSAIDs (including over-the-counter drugs) for more than 1 week together without an appropriate gastroprotective agent (PPI is the first choice. weak evidence for H2RA)	9.0	7.0
11	General-PIM	Short-acting nifedipine[a,b]	9.0	7.0
12	Omission	Check the use of antiplatelet agents for secondary prevention of ischemic lesions in patients with past myocardial infarction, coronary stenting, coronary artery bypass surgery, cerebrovascular stent, past stroke, transient ischemic attack, and peripheral arterial vascular disease (except if anticoagulants are being used)	9.0	7.0
13	Omission	Check the statin treatment for secondary prevention of cardiovascular disease in patients with a past history of myocardial infarction, coronary stenting, coronary artery bypass surgery, cerebrovascular stent, past stroke, transient ischemic attack, and peripheral arterial disease.[a] Exceptions applied for fragile, old patients and patients over 85 years old.	9.0	7.0
D. Heart failure				
14	Ds-PIM	Continued use of NSAIDs (including over-the-counter drugs) in patients with heart failure	9.0	7.0

(Continued)

Table 1. (Continued)

Type		Criteria	Stage 2 median	Stage 3 median
15	DDI-PIM	Combination of diuretics (especially loop diuretics) and NSAIDs (including over-the-counter drugs)	9.0	7.0
16	DDI-PIM	Combination of ACEI and ARB	9.0	7.0
E. Atrial fibrillation, deep vein thrombosis				
17	DDI-PIM	Combination of oral anticoagulants with antiplatelet drugs. Not applied when the same doctor prescribes those drugs at the same time, and the patient recognizes it.	9.0	7.0
18	DDI-PIM	Combination of warfarin and sulfamethoxazole/ trimethoprim[a]	9.0	7.0
19	DDI-PIM	Combination of warfarin with macrolide antibacterial agents (except azithromycin) or quinolones[a] (ciprofloxacin/ ofloxacin, etc.)	9.0	7.0
20	Omission	Check the use of oral anticoagulants in chronic atrial fibrillation[a]	9.0	7.0
F. Edema				
21	Ds-PIM	Continuous use of loop diuretics for simple edema in patients without heart failure, liver cirrhosis, chronic renal failure, or nephrotic syndrome[b]	8.5	7.0
G. Type 2 diabetes				
22	General-PIM	Long-acting sulfonylurea	9.0	8.0
23	Ds-PIM	A diabetic patient who has been on oral steroids for more than 1 week and does not have blood glucose monitoring	8.5	8.0
24	Ds-PIM	Nonselective beta-blockers (exception, sotalol) in diabetic patients[a,b]	8.0	7.0
25	Ds-PIM	Metformin in patients with end-stage renal failure or dialysis[a]	9.0	7.0
H. Chronic renal failure, dialysis, end-stage renal disease				
26	Ds-PIM	NSAIDs in patients with renal failure	9.0	8.0
27	Ds-PIM	Bisphosphonate use in patients with chronic renal failure confirmed as CrCl < 30 mL/min in renal function tests[b]	8.0	7.0
28	Omission	Check the use of vitamin D (Vit. D) in patients with severe renal impairment (CrCl < 30 mL/min)[a,b]	8.0	7.0
I. Menopause syndrome				
29	General-PIM	Hormone replacement therapy with estrogen	9.0	8.0
J. Musculoskeletal system: Arthrosis, degenerative arthritis, rheumatoid arthritis				
30	General-PIM	Oral NSAIDs (including over-the-counter) use in high-risk patients (high-risk patient group: patients over 75 years of age, patients taking oral steroids, anticoagulants, and antithrombotic drugs)	9.0	8.0

(Continued)

Table 1. (Continued)

Type		Criteria	Stage 2 median	Stage 3 median
31	DDI-PIM	Combination of anticoagulants and NSAIDs (including over-the-counter drugs)	9.0	8.0
32	DDI-PIM	Combination of NSAIDs/Coxib and an ACE inhibitor/ARB[a]	8.0	7.0
33	DDI-PIM	Combination of oral NSAIDs (including over-the-counter drugs) and oral steroids	9.0	8.0
34	Ds-PIM	COX2-selective inhibitors in patients with cardiovascular disease	9.0	8.0
35	Omission	Check if folic acid was prescribed for patients prescribed methotrexate for rheumatoid arthritis	8.5	8.0
36	DDI-PIM	Combination of benzodiazepines and opioid analgesics	9.0	7.0
37	General-PIM	Anticholinergic muscle relaxant	9.0	8.0
K. Osteoporosis				
38	Omission	Check if the patient is taking Vit. D and calcium supplements in cases where a patient stays indoors only, or experiences a fall, or is at high risk of osteoporosis, or patients taking oral steroids for more than 1 month. If not, recommend its use (recommended intake amount: calcium 800–1000 mg, Vit. D 800 IU/day)	9.0	8.0
39	Omission	Recommendation of calcium/Vit D supplementation and, if necessary, bisphosphonate in patients using oral steroids (prednisolone 7.5 mg/day or more) for more than 3 months[a]	8.0	7.0
40	Omission	Check whether osteoporosis treatment is prescribed in patients diagnosed with osteoporosis (bone density T score < 2.5) or in patients with past fragility fractures (osteoporotic fractures)	9.0	7.0
41	Omission	Check if calcium/Vit. D supplementation is prescribed in patients treated with bisphosphonate and denosumab[a]	9.0	7.0
42	Ds-PIM	Oral bisphosphonates in patients with the active esophageal disease, dysphagia, and coma	9.0	8.0
43	DDI-PIM	Check how to take and when to take bisphosphonate to prevent inhibition of absorption and esophageal ulcer[b]	8.5	9.0
L. Pain				
44	Omission	Check short-acting opioid analgesics for sudden pain control in patients taking long-acting opioid analgesics to relieve cancer pain, and so on	8.0	7.0
45	Omission	Check whether prophylactic laxatives are prescribed for patients taking regular opioid analgesics (except naloxone combination drugs)	9.0	8.0
46	Dose-PIM	When starting tramadol, start with a low dose and check whether the dose is gradually increased	9.0	8.0

(Continued)

Table 1. (Continued)

Type		Criteria	Stage 2 median	Stage 3 median
M. Fall history				
47	Ds-PIM	Use of opioids, benzodiazepines, antidepressants, antipsychotics, sedatives, and antiepileptics in patients with fall history	9.0	8.0
N. Asthma, chronic obstructive pulmonary disease				
48	Ds-PIM	Nonselective beta-blockers in uncontrolled asthma and chronic obstructive pulmonary disease	9.0	8.0
49	Ds-PIM	Oral steroid use instead of inhaled steroid use in patients with asthma	9.0	8.0
50	General-PIM	Oral theophylline	8.0	7.0
51	DDI-PIM	Combination of ciprofloxacin and theophylline[a]	9.0	7.0
52	Omission	Check regular use of long-acting bronchodilator inhalers in patients with chronic obstructive pulmonary disease (e.g. tiotropium, indacaterol, salmeterol, aclidinium, umeclidinium, and glycopyrronium)	9.0	8.0
O. Gastrointestinal disease				
53	General-PIM	Use of full therapeutic doses PPI for >8 weeks[a]	9.0	7.0
54	General-PIM	Anticholinergic antispasmodics [e.g. butylscopolamine, dicyclomine (dicycloverine), cimetropium, difemerin, oxapium, belladonna alkaloid]	9.0	7.0
55	General-PIM	Metoclopramide	9.0	8.0
56	Ds-PIM	Nonselective NSAIDs in peptic ulcer patients	9.0	8.0
P. Constipation				
57	Ds-PIM	Strong anticholinergic drugs in constipation patients	9.0	7.0
58	Ds-PIM	Calcium channel blockers in constipation patients[a,b]	8.0	7.0
59	Omission	Check the use of laxatives when constipation-causing drug use is inevitable in patients with persistent constipation	9.0	8.0
Q. Genitourinary disease				
60	Ds-PIM	Strong anticholinergic agents in patients with benign prostatic hyperplasia and urinary retention	9.0	8.0
61	General-PIM	Oxybutynin for the treatment of overactive bladder, such as urinary incontinence, urgency, and frequency	9.0	7.0
62	Ds-PIM	Diuretics in people with incontinence[b]	8.0	7.0
R. Insomnia				
63	General-PIM	Continued use (more than 30 days) or regular daily use of hypnotics (e.g. z-drugs, benzodiazepines)	9.0	8.0

(Continued)

Table 1. (Continued)

Type		Criteria	Stage 2 median	Stage 3 median
64	General-PIM	Over-the-counter drugs for inducing sleep (e.g. doxylamine, diphenhydramine)	9.0	7.0
65	Ds-PIM	Oral, nasal decongestants in insomnia patients (e.g. pseudoephedrine, phenylephrine)	9.0	7.0
S. Patients with cognitive decline or dementia, or delirium				
66	Ds-PIM	Strong anticholinergic drugs in patients with dementia, delirium, or cognitive decline	9.0	8.0
T. Orthostatic hypotension				
67	Ds-PIM	Acetylcholine esterase inhibitor in patients experiencing syncope and bradycardia	9.0	8.0
68	Ds-PIM	Alpha-1 blockers in patients with orthostatic hypotension	9.0	8.0
U. Parkinson's disease				
69	Ds-PIM	Antipsychotics other than clozapine and quetiapine in patients with Parkinson's disease	9.0	8.0
70	Ds-PIM	Metoclopramide and clebopride in Parkinson's disease patients[b]	9.0	8.0
V. Neuropsychiatric disorders				
71	General-PIM	Multiple prescriptions within each class of hypnotics/sedatives, including Z-drugs, antidepressants, benzodiazepines, and antipsychotics[b]	9.0	7.0
72	General-PIM	Tricyclic antidepressants	9.0	8.0
73	General-PIM	Fluoxetine as an antidepressant	8.5	7.0
74	General-PIM	Benzodiazepines	9.0	7.0
75	DDI-PIM	Combination of phenytoin and sulfamethoxazole/trimethoprim[a]	8.5	7.0
76	DDI-PIM	Combination of NSAIDs and SSRIs	8.5	7.0
W. Closed-angle glaucoma				
77	Ds-PIM	Strong anticholinergic agents in patients with closed-angle glaucoma	9.0	7.0

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; BPH, benign prostatic hyperplasia; CHA2DS2-VASc, congestive heart failure or left ventricular dysfunction hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled)–vascular disease, age 65–74, sex category; CrCl, creatinine clearance; H2RA, H2 receptor antagonist; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history, or predisposition, labile international normalized ratio, elderly, drugs/ alcohol concomitantly; IQR, interquartile range; NSAIDs, non-steroidal anti-inflammatory drugs; PCI, percutaneous coronary intervention; PPI, proton pump inhibitor; RAS, renin–angiotensin system; SNRI, serotonin and norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors.
Note 1. The type of medication review tool is classified as follows: potentially inappropriate medication in general (General-PIM), potentially inappropriate drugs due to drug interactions (DDI-PIM), potentially inappropriate medication under specific diseases or conditions (Ds-PIM), potentially inappropriate drugs needed for monitoring and dose adjustment (Dose-PIM), and potential medication omissions (Omission).
Note 2. The consensus of appropriate was defined as a median score higher than seven without 'disagreement' (≥4 panelists rating 1–6 points, or more than one panelist rating 1–3 points) or not 'uncertain'(median of 4–6 or any median with 'disagreement').
[a]Criteria reached the consensus in round two of stage 3 (feasibility study).
[b]Criteria reached the consensus in round two of stage 2 (expert Delphi survey).

PIMs tool organized using a physiological system, such as the STOPP/START criteria could be applied quickly in practice and are helpful to identify medication-related problems and omission involved in diagnoses or patient conditions.[37] Considering the advantage of a physiological classification, we reconstructed the classification system of our tool and focused on the common underlying diseases/conditions based on primary PIM-related indications and contraindications.

Our list items were categorized into five types of drug therapy problems because essential aspects in medication review practice include checking the drugs and indications, considering underlying diseases, reducing inappropriate medication use, identifying PPOs, considering the effectiveness of medicines or inadequate dosage, and assessing any drug–drug interactions or adverse effects.[38] Fog *et al.*[39] showed that the most frequent problems in NHs were unnecessary drugs, including inappropriate drug choice (39.8%), followed by excess- or under-dosing, a requirement to monitor the drug use, drug–drug interactions, and the need for an additional drug. As shown in research to identify PIMs for NH recipients by Tommelein *et al.*,[40] the most prevalent problems were PIMs independent of the diagnosis (85%), PPOs (61%), drug–drug interactions of specific relevance (58%), and PIMs dependent on the diagnosis (55%).

Our tool was developed through a robust consensus methodology using the Delphi method based on systematically merging literature reviews with expert consensus processes to create knowledge-based measures[41] due to the underrepresentation of the older patients with multimorbidity in clinical trials and relatively limited number of high-quality evidence in the elderly[42] This tool was developed through a comprehensive review of the most wide-ranging criteria according to a systematic literature review. The STOPP/START-US NH adapted the STOPP/START criteria for the US NH residents. The NORGEP-NH was built based on the NORGEP criteria. Other region- or patient-specific tools identified in this systematic review had been created primarily based on a revision or composition of a few specific references.[6,16,33,37,43–47] However, a complementary approach is recommended for each tool to improve the sensitivity and relevance of detecting PIMs,[48] because there is little agreement between different tools on prevalence and associations with outcomes,[49] and several limitations of each criterion.

Among the items of the NH-specific tools, oxazepam, zopiclone, and clomethiazole were excluded from the preliminary list because of unapproved medication in the Korean drug market. Also, items with relatively new knowledge and little in previously developed tools were excluded, such as the concomitant use of bisphosphonate and proton pump inhibitors.[42] Finally, more than half of our final criteria items (52 of 77) came from NH-related tools, 24 items came from the seven main tools, and one omission item was derived from other criteria.

Only a few PIM tools, such as the GheOP3S-tool, have been tested for feasibility and reproducibility. To make the tool relevant and practical for assessing medication use appropriateness in the LTCF elderly, a feasibility test was performed in this study. Items that needed laboratory values and medical histories, such as ejection fraction and a cholesterol level that is inaccessible in general NH settings and cannot be obtained from patients, were excluded during this process.

This study has some limitations. First, we did not thoroughly review all evidence from clinical trials for the LTCF elderly, although our tool was developed through the Delphi consensus method, based on a systematic literature review and up-to-date evidence. The strength of the evidence for each item was not included in most PIM criteria except for the Beers criteria. As a result, the strength of evidence for each item could not be included in this tool. Second, our tool does not cover all populations in LTCFs, and end-of-life or palliative care patients were not considered because the risk–benefit assessment of medicines in connection with these individuals could differ according to complex patient conditions. There still remains a lack of consensus on deprescribing in palliative care in Korea. Specific tools for assessing medication usage in palliative care patients need to be developed in the future. Third, the difference in medication use and healthcare system between geographical regions might limit the generalizability of our tool. However, this tool would be helpful in other countries as we derived a preliminary list referring to global literature.

Our tool was developed primarily to improve safe and effective prescriptions in Korean LTCF residents. Further research is needed to validate the effectiveness and applicability of our tool in clinical practice and to develop a medication review tool for frail elderly with limited life expectancy excluded from this study.

Conclusion

In this study, we developed a disease-category-based explicit medication review tool to detect and reduce inappropriate medication use for the LTCF elderly. The tool consists of 77 items covering 23 disease bases and five types of inappropriate medication use. The tool may be helpful in implementing medication management practices in LTCFs to assess medication appropriateness and improve the quality of medication use.

Declarations

Ethical approval and consent to participate
This study was approved by the Seoul National University Institutional Review Board (IRB No. 2107/003-005). All expert panel participants signed written informed consent prior to commencement of the Delphi Survey.

Consent for publication
None.

Author contributions
Kwanghee Jun: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing – original draft.

Soojin Lee: Data curation; Formal analysis; Investigation; Methodology; Writing – review & editing.

Ah young Lee: Investigation; Methodology; Writing – original draft.

Young-Mi Ah: Conceptualization; Methodology; Validation; Writing – review & editing.

Ju-Yeun Lee: Conceptualization; Funding acquisition; Methodology; Supervision; Validation; Writing – review & editing.

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Competing interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and materials
Data are available from the corresponding author on request.

ORCID iDs
Kwanghee Jun   iD   https://orcid.org/0000-0002-9568-2651

Ju-Yeun Lee   iD   https://orcid.org/0000-0002-2261-7330

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