Towards Safe Medication Use Among Geriatric Patients: A Combined Tool For Identification of Potential Drug-Related Problems

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Abstract

Background: Drug-related problems (DRP), including potentially inappropriate medications (PIMs), are a common problem in older people with multi-morbidity and polypharmacy. It is important to identify appropriate tools, preferably adjusted to specific patient groups, to deal more effectively with potential or existing DRPs. Our hypothesis is that combining PIM identification tools enables to significantly enhance the determination of DRPs. The aim of this study was to develop a combined tool for identification of DRPs in geriatric multi-morbid and polypharmacy patients, using the EU(7)-PIM and EURO-FORTA lists, with a focus on high-risk medications.

Methods: The combined PIM identification tool used the information on PIM active ingredients in both databases - the EU(7)-PIM and EURO-FORTA. PIMs were classified into four color groups based on risk profile: very significant PIMs (should be avoided in older patients) as red, significant PIMs (require dose and/or treatment duration adjustment) as yellow, non-significant PIMs/non-PIMs (low DRP risk) as green, and questionable PIMs (incomplete/missing information) as grey.

Results: The summarized list of the red PIMs contains 34 active ingredients, including one combination of two medications and one medication class. According to the Anatomical Therapeutic Chemical classification, most of the red PIMs (n=27, 79.4%) belong to the A, C and N medication groups. Only 41.2% of the red PIMs have marketing authorization in Estonia. In 2019 more frequently used red PIMs in Estonia were sodium picosulfate, propafenone, ginkgo biloba, magnesium hydroxide, and dextromethorphan. The approximate number of the yellow and green PIMs is 248, but sub-classification of this category into one or another group depends mainly on an individual patient´s clinical characteristics. The complete list of the grey PIMs will be developed in the future

Conclusions: The combined PIM tool based on the EU(7)-PIM and EURO-FORTA criteria was created to address the need for more efficient identification of DRP in geriatric multi-morbid patients. The combined PIM tool was developed with a focus on the high-risk medications for older adults and taking into consideration the availability of the PIMs in Estonia. The tool could potentially be applied as a screen to identify DRPs in different health care settings.

1 Introduction

As the world's population ages, increasing numbers of older patients are potentially vulnerable to multi-morbidity, polypharmacy, and various psychosocial problems including lack of social support, which further exacerbates physical manifestations of their disease state [1, 2].

Polypharmacy and inappropriate medication use among geriatric populations in Central and Eastern Europe requires much attention at various health care settings and should be managed also at the governmental level [3]. A 2018 cross-sectional study using the Survey of Health, Ageing, and Retirement in Europe (SHARE) database showed that the prevalence of polypharmacy in older adults ranges from 26.3–39.9% in different parts of Europe [4]. According to the same study, prevalence of use of five and more medications among older adults in Estonia was 27.5–29.9% [4].

A high risk of adverse drug reactions (ADRs), the use of potentially inappropriate medications (PIMs), non-adherence, untreated indications and complexity of prescribing medicines are reported as primary concerns in geriatric populations, and also as major antecedents to a host of other problems, such as mental impairment, confusions, physical instability and falls, malnutrition, and loss of personal independence [1, 5–9].

For the purpose of safe and effective medication prescribing in older adults, several explicit and implicit assessment tools have been created to identify potential PIMs and drug-drug interactions (DDIs), along with other types of prescribing problems [10]. Of those, the international set of Beers (or AGS, American Geriatric Society) explicit criteria is applied as a primary tool for the identification of PIMs and serves as a basis for many other corresponding evaluation sets [11, 12]. Over the last few years, the European Union EU(7)-PIM list [13] and EURO-FORTA list "Fit fOR The Aged" [14] for older patients have been published as the latest (2015 and 2018, respectively) inappropriate geriatric prescribing explicit tools accessible in Europe. Several studies have compared these two evaluation tools with other similar criteria [15–17], but there currently exists no information about the prospects of combining aspects of these two assessment methods to reach more informed decisions about safety aspects of

medications used by older polypharmacy patients. In the recent studies, it has been found that some PIM criteria are less sensitive when used separately [18–21], and thus the authors suggested to combine two European PIM screening tools to increase the sensitivity for the identification of drug-related problems (DRPs) in geriatric patients. The EU(7)-PIM list was created as a screening tool for pharmacoepidemiologic applications with minimal clinical information about the individuals concerned. The EU(7)-PIM list is also one of the very few PIM checklists that includes suggestions for dose adjustments and therapeutic alternatives [13]. The EU(7)-PIM list, however, does not take into account an important aspect such as the aims of the treatment [13]. Thus, a prescribing appropriateness for PIMs could be additionally addressed by using the EURO-FORTA criteria strongly relying on 26 main treatment indication groups [14].

The aim of this study was to develop a combined tool for identification of DRPs in geriatric multi-morbid patients, using the existing European PIM tools: the EU(7)-PIM and EURO-FORTA lists with focus on high risk medications.

2 Materials And Methods

2.1 Tool selection

In this study, the European Union EU(7)-PIM list [13] and EURO-FORTA list "Fit fOR The Aged" [14] were selected as the basis for preparing a combined e-health tool for screening ADRs, DDIs and PIMs. The named two tools were selected, as these are designed to evaluate medicines regularly used in European countries. They require fewer patients health data compared to many other similar tools, e.g., STOPP/START criteria, to signal potential risks for medication use in patients. At the same time, the EU(7)-PIM and the EURO-FORTA tools have different approaches to the PIM identification [13, 14, 22], which thus lend well to their being combined for even greater efficiency and effectiveness (Table 1).

Table 1

Short comparison of the explicit criteria-based EU(7)-PIM[1] and EURO-FORTA[2] tools.

	The EU(7)-PIM tool	The EURO-FORTA tool
Year	2015	2018
Number of experts; number of countries involved	30; 7	46; 14
Mean Delphi consensus coefficient	0.9	0.9
Target population	older people ⩾65 years;	older people ⩾65 years; or ⩾60 years with ⩾6 medications
Number of active substances or drug classes	282 chemical substances or medication classes from 34 therapeutic groups	264 chemical substances or medication classes organized into 26 categories according to diagnosis or clinical syndrome
PIM identification	• class A: active substance (PIM) should be avoided in older adults • class B: active substance is PIM in case of certain clinical conditions/co-morbidities or active substance is only considered as PIM • combination of class A and B	• class A: indispensable medication, clear-cut benefit • class B: medication with proven or obvious efficacy in older adults, but limited extent of effect and/or safety concerns • class C: medication with questionable efficacy/safety profiles in the older adults which should be avoided or omitted; explore alternatives • class D: avoid if at all possible in older adults, omit first and use alternative substances
Specifications	• explicit • often restricted to doses or treatment duration • not related to specific illnesses or conditions (no drug–disease aspect) • has suggestions for dose adjustments and therapeutic alternatives • suitable for pharmacoepidemiological applications	• explicit • not restricted to doses or treatment duration • related to specific illnesses or conditions (drug–disease aspect) • does not suggest dose adjustments and therapeutic alternatives • suitable for pharmacoepidemiological applications

PIM – potentially inappropriate medication

[1]Renom-Guiteras A, Meyer G, Thürmann, PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol. 2015; https://doi.org/10.1007/s00228-015-1860-9

[2]Pazan F, Weiss C, Wehling M. The EURO-FORTA (Fit fOR The Aged) List: International Consensus Validation of a Clinical Tool for Improved Drug Treatment in Older People. Drugs Aging. 2018; https://doi.org/10.1007/s40266-017-0514-2

2.2 Definition of the color indicators

Based on the risk and severity of potential adverse events associated with the particular active substance or medication class use in older patients described in the EU(7)-PIM and EURO-FORTA lists, the PIMs were suggested to be classified into four general color coding groups:

1) very significant PIMs as red color PIMs: active substances or medication classes that should be avoided in geriatric patients when possible, alternative treatment must be strongly considered;

2) significant PIMs as yellow color PIMs: active substances or medication classes that require mostly dose and/or treatment duration adjustment according to the patient health status and other medical details;

3) non-significant PIMs or non-PIMs as green color PIMs: active substances or medication classes that could be used in case of adequate therapy monitoring, older patients are not at potentially high risk of DRPs;

4) questionable PIMs as grey color PIMs: active substances or medication classes with incomplete or missing information presented in the PIM criteria used; that means more sufficient data must be collected or other PIM tool should be considered (Table 2).

Table 2. The classification of potential inappropriate medications (PIMs) according to the combined screening PIM tool based on the EU(7)-PIM[1] and EURO-FORTA[2] lists.

Description	Type of PIMs	Actions to be undertaken
EU(7)-PIM *A-class* and EURO-FORTA *D-class* (in some cases also *C-class*) active substances or medication classes	Red color Clinically very significant PIMs	Avoid in older individuals if possible, monitor patient safety, strongly consider alternative treatment
EU(7)-PIM *B- and A + B-class* and most of the EURO-FORTA *C-class* active substances or medication classes, for the majority when used in higher doses and/or for longer treatment course than recommended in geriatric patients	Yellow color Clinically significant PIMs	Monitor patient safety, collect additional patient health data, consider dose adjustment, consider alternative treatment
EU(7)-PIM *B- and A + B-class and EURO*-FORTA B-class active substances or medication classes with limited concerns on the effect or safety in geriatric patients or not considered as inappropriate when used in lower doses and/or for short treatment course in geriatric patients	Green color Clinically non-significant PIMs or non-PIMs	Monitor treatment safety, repeat medication review on regular basis, patient is more likely not at the high risk of DRPs
Any of the EU(7)-PIM and FORTA active substances or medication classes, when it is not possible to detect the color for PIM	Grey color Questionable PIMs	EU(7)-PIM and/or EURO-FORTA tools are not applicable. Collect more patient data or consider another tool
PIM – potentially inappropriate medication; DRP – drug related problem [1]Renom-Guiteras A, Meyer G, Thürmann, PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol. 2015; https://doi.org/10.1007/s00228-015-1860-9 [2]Pazan F, Weiss C, Wehling M. The EURO-FORTA (Fit fOR The Aged) List: International Consensus Validation of a Clinical Tool for Improved Drug Treatment in Older People. Drugs Aging. 2018; https://doi.org/10.1007/s40266-017-0514-2		

The content and structure of the combined PIM identification dataset based on the EU(7)-PIM and EURO-FORTA lists were defined in repeated sessions, including experts from Estonia and the Czech Republic in the period April-October 2020. These experts are also contributing to the scientific works on the EUROAGEISM H2020 ESR7 project (2017–2021) entitled "Inappropriate prescribing and availability of medication safety and medication management services in older patients in Europe and other countries".

2.3 Red PIMs

In the present study, the authors focused on the red color PIMs: active substances or medication classes as clinically very significant high-risk PIMs in older patients. According to the original PIM criteria used, both A-class EU(7)-PIM and D-class EURO-FORTA active substances or medication classes are those that should not be used in geriatric patients in general, as these can often bring potential medication-related harm to older adults. The combined PIM tool provides means for the identification of the red PIMs and looks more closely at the possible medication-related risks for aged adults.

The red PIMs were developed as follows:

- all A-class active substances or medication groups were extracted from the EU(7)-PIM list with additional information about reasoning of PIM classification and special considerations of use;
- the EURO-FORTA tool was screened for the same active substances or medication groups, and the EURO-FORTA class (A-, B-, C- or D-class) was specified for each PIM;
- in case of missing data, the EURO-FORTA class of the active substance or medication group was marked as "-";
- local (Estonia) and international (EMA, European Medicines Agency) Summaries of Product Characteristics (SmPCs) were used to collect additional information on the use of PIMs in geriatric patients (e.g., dosage and treatment duration adjustment in older adults);
- the red PIMs were checked for the availability and actual use in Estonia by addressing the official register of medications and the registered PIM volume sales (number on packages) for the period of one year (October 2019 to September 2020) in community and hospital pharmacies [23];
- the defined daily doses (DDD) were used to evaluate the incidence of red PIMs in the population in Estonia in 2019 [24].

2.4 Yellow, green and grey PIMs

The process of identifying the yellow and green color PIMs according to the combined PIM tool depends directly on individual patient characteristics and many factors concerning the patient´s health status and other clinical issues. For most of the yellow and green PIMs (e.g., PPIs, NSAIDs), the clinical relevance of a particular PIM may change depending on the duration of treatment and dosing, treatment indication and possible drug-drug interactions and therapeutic duplications. Described factors make it virtually impossible to specify the color of the PIM (yellow or green) in general at the moment; however, these PIMs should be considered when the treatment rationality at an individual patient level is assessed in geriatric patients. By this, yellow and green color PIMs are expected to be all those PIMs mentioned in the EU(7)-PIM and EURO-FORTA lists that are not treated as red or grey color PIMs according to the present study methodology. The active ingredients or medication classes are categorized as yellow not only because of the active substance itself (like most of the red color PIMs), but mostly due to the long-term treatment course and high doses what are inappropriate for geriatric patients. In contrast, green color PIMs could be mostly appropriate for geriatric patients when used in lower doses and/or for a shorter period of time as is stated in the EU(7)-PIM and EURO-FORTA criteria. Still, there could be always some exceptional cases in clinical practice when the green color PIM can become inappropriate or classified as yellow color PIM. Thus, more attention should be paid to the yellow and green color PIM identification in the future, and information for software evaluation of these PIMs could potentially be more detailed.

Grey color PIMs are those with missing data that are not possible to classify as either red-yellow-green color PIMs. For these PIMs, there is frequently a need to use additional data sources (e.g., any other PIM list). In the present study, grey color PIMs are the active substances or drug classes that are treated as PIMs in one list (e.g., the EU(7)-PIM), but not in other lists (e.g., the EURO-FORTA), or when the information on both lists is inconsistent (e.g, A-class according to the EU(7)-PIM and A/B-class according to EURO-FORTA). The authors agreed to use "red* color" concept, where "*" means the EURO-FORTA criteria do not give any additional information about the use of PIM, but the EU(7)-PIM criteria and SmPCs consider these medications as high-risk medications in older adults.

3 Results

3.1 Red and red* PIMs

According to the combined PIM tool based on the EU(7)-PIM and EURO-FORTA criteria, the total list of the red and red* color PIMs contained 34 active substances, including one combination of two medications and one medication class (Appendix 1). The study methodology suggests that all 34 (100%) PIMs originally belong to the EU(7)-PIM criteria, and only 12 (35.3%) of them refer to the EURO-FORTA criteria (Table 3). In general, there were 12 (35.3%) red and 22 (64.7%) red* color PIMs in the combined tool. Most of the red and red* PIMs belonged to the A (alimentary tract and metabolism, n = 10, 29.4%), C (cardiovascular system, n = 10, 29.4%) and N (nervous system, n = 7, 20.6%) medication groups according to the ATC (Anatomical Therapeutic Chemical)

classification. Other red and red* PIMs (n = 7, 20.6%) presented in the combined tool belong to the M (musculo-skeletal system), R (respiratory system), and J (antiinfectives for systemic use) ATC groups (Table 3). For fewer than half (n = 14, 41.2%) of the red and red* PIMs, the researchers found SmPC information concerning the rational and safe use of the drug therapy in geriatric patients (Table 3, Appendix 1).

The number of authorized and marketed red and red* PIMs in Estonia in 2020 was 41.2% (n = 14) from the total number of the corresponding PIMs in the combined tool. This type of PIMs was mostly available on prescription (Rx, n = 8), but also as Over-the-Counter (OTC, n = 5) medications and one PIM was used in Estonia only as dietary supplement (Table 3, Appendix 1). The list of the red and red* color PIMs that are not authorized in Estonia, but still used by application of specialized physician, hospitals or research institutions, consists of four active substances, which corresponds to 11.8% of the total number of the red and red* PIMs using the combined tool. It was found that 16 (47%) of the red and red* PIMs are not authorized and not marketed in Estonia (Table 3, Appendix 1).

In 2019 according to the DDD the top 5 red and red* PIMs in Estonia were sodium picosulfate (DDD = 4.3637), propafenone (DDD = 3.5699), ginkgo biloba (DDD = 2.3355), magnesium hydroxide (D = 1.187), and dextromethorphan (DDD = 0.6223) (Table 3, Appendix 1).

Table 3
Red and Red* color PIMs with and without marketing authorization in Estonia (n = 34, 100%).

	All red and red* color PIMs % (n)	Red and red* PIMs with marketing authorization in Estonia % (n)	Red and red* PIMs not authorized in Estonia but still marketed (ET, RT) % (n)	Red and red* PIMs not authorized and not marketed in Estonia % (n)
Originally belong to the EU(7)-PIM criteria[1]	100 (34)	41.2 (14)	11.8 (4)	47.0 (16)
Originally belong to the EURO-FORTA criteria[2]	35.3 (12)	14.7 (5)	8.8 (3)	11.8 (4)
Only red PIMs	35.3 (12)	14.7 (5)	8.8 (3)	11.8 (4)
Only red* PIMs	64.7 (22)	26.5 (9)	2.9 (1)	35.2 (12)
A (alimentary tract and metabolism) ATC group	29.4 (10)	17.7 (6)	0	11.8 (4)
C (cardiovascular system) ATC group	29.4 (10)	5.9 (2)	8.8 (3)	14.7 (5)
J (antiinfectives for systemic use) ATC group	2.9 (1)	2.9 (1)	0	0
M (musculo-skeletal system) ATC group	8.8 (3)	2.9 (1)	0	5.9 (2)
N (nervous system) ATC group	20.6 (7)	8.8 (3)	2.9 (1)	8.8 (3)
R (respiratory system) ATC group	8.8 (3)	2.9 (1)	0	5.9 (2)
Geriatric information in SmPC was found	41.2 (14)	29.4 (10)	11.8 (4)	Not applicable

Top 5 red and red* color PIMs based on the defined daily doses (DDD) marker, 2019 in Estonia: sodium picosulfate (DDD = 4.3637), propafenone (DDD = 3.5699), ginkgo biloba (DDD = 2.3355), magnesium hydroxide (D = 1.187), and dextromethorphan (DDD = 0.6223)

% and n calculated from all red and red* PIMs

ATC - Anatomical Therapeutic Chemical (classification)

DDD - defined daily doses

ET (Erialaorganisatsiooni Taotlusega ravimid, est) and RT (Ravimiameti Taotlusega ravimid, est): used by application of specialized physician, hospitals or research institutions

PIM – potentially inappropriate medication

SmPC - Summaries of Product Characteristics

[1]Renom-Guiteras A, Meyer G, Thürmann, PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol. 2015; https://doi.org/10.1007/s00228-015-1860-9

[2]Pazan F, Weiss C, Wehling M. The EURO-FORTA (Fit fOR The Aged) List: International Consensus Validation of a Clinical Tool for Improved Drug Treatment in Older People. Drugs Aging. 2018; https://doi.org/10.1007/s40266-017-0514-2

3.2 Yellow, green and grey PIMs

As the identification of the yellow and green PIMs depends directly on an individual patient clinical characteristics, it is not possible to present the complete list of the yellow/green color PIM in general at the moment. Preliminary data demonstrate about 248 possible yellow + greed PIMs as such, and it needs closer evaluation in the future. The complete list of the grey PIMs also requires further delineation.

4 Discussion

To the authors' best knowledge this is the first study that focuses on the possibility of using EU(7)-PIM and EURO-FORTA criteria jointly to create a combined PIM tool that could be applied in integrated e-health systems identifying potentially inappropriate prescribing for geriatric patients in Estonia. For similar purposes it can be used also in other countries, which may benefit from applied methodology into combination of these two EU international tools. In this study, the combined PIM list was created using active substances or medication classes defined as PIMs according to the EU(7)-PIM and EURO-FORTA lists and applying a red-yellow-green-grey color system of categorization of medication risks (according to the risk of active ingredient on the ageing organism, risk of dosing or length of treatment), with a special emphasis on those high-risk PIMs licensed in Estonia.

The present study showed that the actual use of some red and red* color PIMs in Estonia differ from the concept provided by the EU(7)-PIM and EURO-FORTA lists. Thus, (1) two PIMs are used only with other pharmaceuticals in combined medicinal products (dextromethorphan, magnesium hydroxide), (2) aloe is not registered as a medication; it is a food supplement with no clear indication and relevant patient information provided by the manufacturer, (3) ginkgo folium, magnesium hydroxide and senna glucosides are licensed as OTC medications, but also marketed as food supplements where data about dosing and indication remains unclear, (4) niacin (nicotinic acid) is available only in an injection pharmaceutical dosage form, and (5) viscous paraffin is used exceptionally as an external product in Estonia, and the information provided by the EU(7)-PIM list is not relevant (Appendix 1). The study results suggest a need to further explore the problem of combined medicinal products and other discrepancies mentioned above before the combined PIM tool becomes a widely available instrument for clinical use, and this suggestion is corroborated by the implications discussed in other studies [12, 16, 25].

Future research in needed to better identify discrepancies between the yellow and green color PIMs that may differ depending on the specific country and local drug prescribing traditions and guidelines, as well as based on clinical characteristics of the patient. At the same time, although the list of the red and red* color PIMs was accepted unanimously by all authors of the present study, the red* PIMs are those that need closer inspection and consideration by experts in the field. It is conceivable that for these PIMs, there should be even more detailed explanation on how or whether to use them in older adults, because only one of the lists (the EU(7)-PIM list) classifies them as red.

Since the present study showed that only for 41.2% (n = 14) of the red and red* color PIMs was information found concerning the rational and safe use in older adults (e.g., dosage and treatment duration adjustment or any other recommendations for the geriatric patients) from the SmPCs, the additional information concerning this aspect must be collected, including appropriate medication safety studies.

The idea to combine the two most well-known European PIM criteria independent of specific clinical conditions, was supported by the fact that there are several existing PIM tools, whereas every single tool has both strengths and limitations and that there exist differences between them. Other tools are more country-specific (e.g., the German PRISCUS list) [19] or need more clinical information about the patient for their application (e.g., STOPP/START criteria) [22]. By using international EU sets of PIM criteria, it is possible to reach better results in PIM identification, as tools have different approaches to identification of PIMs. The EU(7)-PIM tool shows in general very high sensitivity in PIM recognition according to the previous research [13, 17], but the tool lacks important consideration of treatment indications for many PIMs. It was crucial to address this aspect by applying EURO-FORTA list that was related to the patients´ specific illnesses or conditions (drug−disease aspect) [14]. Previous experience by other authors demonstrated that it is not enough to use only one PIM criteria in the study design, because it may give inconclusive results [26, 27]. From this perspective, the current idea was to use a combination of both PIM criteria, both identifying PIMs disregarding detailed clinical information about the patients, that provides more beneficial and valuable insights into the number

and conditions of inappropriateness of identified PIMs. Authors of the current study believe that this concept is beneficial for current improvement of e-health Estonian software programs in the future and helps to better determine prescribing problems in multi-morbid geriatric patients with polypharmacy, as current software packages have been focused on only multimorbid patients, or polypharmacy, but did not screen geriatric risks of medications. A similar approach was taken in Finland in 2010, when the Meds75 + e-database was developed based on the Beers, STOPP/START, and EU(7)-PIM criteria [28]. At the moment, it contains recommendation for nearly 500 substances or their combination and classifies them similarly into four categories: A (green), B (grey), C (yellow) and D (red). The Meds75 + database aims to support clinical decision-making processes in primary health care for the patients who are over 75 years of age. It is maintained by the Finnish Medicines Agency [28].

The European pharmaceutical industry and market have undergone significant changes resulting in the marketing authorization of a wide range of new medicines while at the same time many products have been withdrawn from the pharmaceutical market [29]. This has led to the urgent need to update the PIM lists on a regular basis by inserting newly identified PIMs or changing the content of already existing PIMs. A 2016 study on the availability and actual PIM use from the EU(7)-PIM list in the Belgian market already showed that only 157 (57.1%) of 275 active substances in the EU(7)-PIM list were available in Belgium [30]. A similar study conducted by the EU COST Action research team on the project "Heathy clinical strategies for healthy ageing" between 2017 and 2018 in several European countries showed that in Estonia, 90.8% of the PIMs from the EU(7)-PIM tool were available on prescription, but specialists' prescription limits were established for only 3 PIMs. At the same time, the freely accessible OTC PIMs from the EU(7)-PIM toolwere available in 19.9% of the cases [31].

The integration of the combined PIM tool to the e-health system in Estonia is the expected future step that should be discussed within the tool developers, including IT specialists and other experts in the future, in case the new combined dataset of this list along with the Inxbase/Riskbase existing database [32] are piloted and considered as a relevant clinical tool to identify patients´ at risk and improve safety and efficacy of drug prescribing to older adults. As the concept (color coding) of the combined tool is intentionally similar to the drug interaction and counter indication decision support software based on the Inxbase/Riskbase database used in Estonia [32], the combined PIM tool can become a part of this software, and will be focused more on the older populations' drug consumption and safe and rational medication use. In this scenario, access to the combined PIM tool may be provided in the future to health care employees from different care settings, including family doctors and specialists, nurses, pharmacists, and others. At the moment, the existing PIM tools (e.g., Beers criteria, EURO-FORTA list) are available in Estonia only as an original research papers (e.g., PDF documents), that makes them inconvenient to use in everyday practice, and this may contribute to these tools not being very commonly known or used among health care professionals in Estonia.

5 Conclusion

This study proffered a combined PIM tool based on the two European most widely known and used explicit EU(7)-PIM and EURO-FORTA criteria to address the need for more efficient identification of DRP in geriatric, multi-morbid patients. The explicit list of active ingredients was developed for categorization of PIMs described in both existing tools, but had a special focus on the medications with the highest health risks for older adults that should be generally avoided. In the future, it can be applied in Estonia as a combined screening e-tool to identify PIMs and geriatric prescribing problems in different health care settings, and also in a context of little clinical information available. For similar purposes it can also be used in other countries which may benefit from applied methodology into combination of these two internationally, widely recognized tools.

Abbreviations

ADRs: Adverse Drug Reactions

ATC-code: Anatomical Therapeutic Chemical (classification) code

AGS: American Geriatric Society

DDD: Defined Daily Doses

DDIs: Drug-Drug Interactions

DRPs: Drug-Related Problems

EMA: European Medicines Agency

EU(7)-PIM: European Union list of Potentially Inappropriate Medications for older patients

EURO-FORTA: "Fit fOR The Aged" screening tool

ET ("*Erialaorganisatsiooni Taotlusega ravimid*", *est*) and RT ("*Ravimiameti Taotlusega ravimid*", *est*): drugs used by application of specialized physician, hospitals or research institutions in Estonia

INXBASE: Drug interaction decision support e-software

IT: Information Technology

NSAIDs: NonSteroidal Anti-Inflammatory Drugs

OTC: Over-The-Counter (drugs)

PPIs: Proton-Pump Inhibitors

PIMs: Potentially Inappropriate Medications

PRISCUS (*"old and venerable" latin):* German list of potentially inappropriate medications for elderly persons

RISKBASE: Drug counter indication decision support e-software

Rx: Prescription drugs

SmPCs: Summaries of Product Characteristics

SHARE: Survey of Health, Ageing, and Retirement in Europe

START: Screening Tool to Alert to Right Treatment lists

STOPP: Screening Tool of Older People's Prescriptions

Declarations

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Consent for publication: Not applicable

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