

Revision Rev. Fam., Ciclos Vida Saúde Contexto Soc. http://seer.uftm.edu.br/revistaeletronica/index.php/refacs/index ISSN: 2318-8413 DOI: 10.18554/refacs.v10i2.5970

New lists and new technological tools on potentially inappropriate drugs for the elderly: an integrative review

Novas listas e novas ferramentas tecnológicas sobre medicamentos potencialmente inapropriados para idosos: uma revisão integrativa

Nuevas listas y nuevas herramientas tecnológicas sobre medicamentos potencialmente inapropiados para ancianos: una revisión integradora

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Received: 05/10/2021 Accepted: 20/02/2022 Published: 29/06/2022

Objective: to identify new lists and new technological tools on Potentially Inappropriate Medicines for the Elderly existing in scientific productions. Methods: an integrative review was carried out in 2020, considering the period from 2010 to 2019, in the following databases: Scientific Eletronic Library on-line, National Library of Medicine and National Institutes of Health, Latin American and Caribbean Health Sciences Literature, Spanish Bibliographic Index of Health Sciences, Cochrane Library, Network of Scientific Journals of Latin. America, the Caribbean, Spain and Portugal, Fundación Index Database – España. The languages Portuguese, English and Spanish were listed and the selected articles were categorized by thematic similarities. Results: 42 productions were considered, most of them published in English and produced in the United States of America, Canada, Spain, Germany, Belgium and Ireland. Two thematic categories were constructed: "Lists on potentially inappropriate medicines for the elderly" (with 22 publications); and, "New Technological Tools on potentially inappropriate medicines for the elderly" (with 20 publications). As main findings, the following stood out: the relevance of having lists on these drugs adapted to specific countries and/or populations; as well as the fact that new technological tools follow a trend of development and improvement, although the usability and user coverage requirements can be improved. Conclusion: this review identified that the use of potentially inappropriate medicines for the elderly represents a challenge for health care, as well as the growing initiatives to expand access to information, such as the construction of large databases and repository with simplified access. **Descriptors:** Potentially Inappropriate Medication List; Drug utilization; Inappropriate prescribing; Biomedical technology; Aged.

Objetivo: identificar novas listas e novas ferramentas tecnológicas sobre Medicamentos Potencialmente Inapropriados para Idosos existentes em produções científicas. Método: revisão integrativa realizada em 2020, considerando o período de 2010 a 2019, nas bases de dados: Scientific Eletronic Library on-line, National Library of Medicine and National Institutes of Health, Literatura Latino-Americana e do Caribe em Ciências da Saúde, Índice Bibliográfico Espanhol de Ciências de Saúde, Cochrane Library, Rede de Revistas Científicas da América Latina e Caribe, Espanha e Portugal, Base de dados da Fundacíon Index -España. Elencou-se os idiomas português, inglês e espanhol e os artigos selecionados foram categorizados por similaridades temáticas. Resultados: foram consideradas 42 produções, em sua maioria publicadas em língua inglesa e produzidas nos Estados Unidos da América, Canadá, Espanha, Alemanha, Bélgica e Irlanda. Duas categorias temáticas foram construídas: "Listas sobre medicamentos potencialmente inapropriados para idosos" (com 22 publicações); e "Novas Ferramentas Tecnológicas sobre medicamentos potencialmente inapropriados para idosos" (com 20 publicações). Como principais achados, destacou-se: a relevância de que listas sobre esses medicamentos sejam adaptadas a países e/ou populações específicas; bem como ao fato de que novas ferramentas tecnológicas seguem uma tendência de desenvolvimento e aprimoramento, embora os quesitos usabilidade e abrangência de usuários possam ser melhorados. Conclusão: esta revisão identificou que o uso de medicamentos potencialmente inapropriados para idosos representa um desafio para a assistência à saúde, bem como as crescentes iniciativas para expandir o acesso às informações, como a construção de grandes bancos de dados e repositório com acesso simplificado. Descritores: Lista de Medicamentos Potencialmente Inapropriados; Uso de medicamentos; Prescrição Inadequada; Tecnologia biomédica; Idoso.

Objetivo: identificar nuevas listas y nuevas herramientas tecnológicas sobre Medicamentos Potencialmente Inapropiados para Ancianos existentes en las producciones científicas. Método: revisión integradora realizada en el año 2020, considerando el periodo de 2010 a 2019, en las bases de datos: Scientific Electronic Library online, National Library of Medicine and National Institutes of Health, Literatura Latinoamericana y del Caribe en Ciencias de la Salud, Índice Bibliográfico Español de Ciencias de la Salud, Cochrane Library, Red de Revistas Científicas de América Latina y el Caribe, España y Portugal, Base de datos de la Fundación Index - España. Se seleccionaron los idiomas portugués, inglés y español y los artículos seleccionados se clasificaron por similitudes temáticas. Resultados: Se consideraron 42 producciones, en su mayoría publicadas en inglés y producidas en Estados Unidos de América, Canadá, España, Alemania, Bélgica e Irlanda. Se construyeron dos categorías temáticas: "Listas sobre medicamentos potencialmente inapropiados para ancianos" (con 22 publicaciones); y "Nuevas herramientas tecnológicas sobre medicamentos potencialmente inapropiados para ancianos" (con 20 publicaciones). Como principales resultados destacan: la relevancia de que las listas sobre estos medicamentos se adapten a países v/o poblaciones específicas; así como, el hecho de que las nuevas herramientas tecnológicas sigan una tendencia de desarrollo y mejora, mientras que las cuestiones de usabilidad y amplitud de usuarios pueden ser mejoradas. Conclusión: esta revisión identificó que el uso de medicamentos potencialmente inapropiados para ancianos representa un desafío para la asistencia a la salud, así como las crecientes iniciativas para expandir el acceso a informaciones, como la construcción de grandes bancos de datos y repositorios con acceso simplificado.

Descriptores: Lista de Medicamentos Potencialmente Inapropiados; Uso de medicamentos; Prescripción Inadecuada; Tecnología biomédica; Anciano.

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INTRODUCTION

he aging of populations represents a relevant epidemiological transition, showing a growing increase in the demand for health care. It is a worldwide phenomenon and, in the case of Brazil, the number of elderly people (over 60 years old) is expected to almost double in the next 35 years, as well as the number of people over 70 years old, which will triple by 2050, reaching 13.2% of the population¹. In Brazil, with the 2010 census, the projections for the population were revised: the number of elderly people should double in twenty years and the number of people over 70 years old will reach 16.2% of the population in 2050².

In this context, the elderly are considered a special therapeutic group, due to factors such as the increasing prevalence of non-communicable chronic diseases and the consequent use of medication³. Associated with this, it is important to consider that there is interference of the physiological changes of the aging process in the pharmacokinetics and pharmacodynamics, increasing the risk of toxicity caused by the drugs⁴.

Among the particularities of drug therapy for this group, potentially inappropriate medicines for the elderly (PIM) stand out, defined as those whose risk of use is greater than the clinical benefits provided, when safer and more effective alternatives are available⁵ and, due to the high potential to generate negative outcomes, such as falls and increased health costs, its prescription should be avoided⁶.

The evaluation of prescriptions containing PIM can be supported by implicit or explicit methods. The former are based on clinical judgment according to patient information (health profile, presence of health problems or relevant clinical peculiarities), and propose a more indepth pharmacotherapeutic analysis. Therefore, they require more time and depend on the professional's experience, but they provide an individualized analysis compatible with the reality of health services and the clinical variability of the geriatric population, and can be incorporated with relative ease in the therapeutic decision process, multidisciplinary clinical discussion and in pharmacotherapeutic follow-up processes. The most established implicit method is the Medication Appropriateness Index (MAI)⁷⁻⁸.

Explicit methods are based on more rigidly established criteria, usually developed through reviews, expert opinions, and consensus techniques. They focus on the drug and do not take into account the clinical suitability of each patient. As they are based on less flexible criteria, they are good instruments to carry out more punctual and simpler geriatric prescription reviews. The Beers Criterion is considered one of the most important explicit methods, listing classes and specificities of drugs and in categories, such as those potentially inappropriate⁷⁻⁸.

Considering that the use of PIM has a high prevalence in several countries, ranging from 25.5% to 98.2%⁹⁻¹⁰, knowing the updates of lists on PIM, as well as new technological tools applied to them, becomes of great importance. value to the field of practices. Thus, this study aims to identify new lists and new technological tools on Potentially Inappropriate Medicines for the Elderly existing in scientific productions.

METHODS

This is an integrative review, defined as the method that brings together the synthesis of knowledge from the relevant scientific production on a given topic, offering quick and synthesized access to the scientific results of greatest relevance to the area studied¹¹.

The guiding question listed was: What is the state of the art, in scientific productions, between 2010 and 2019, about new lists and new technological tools on Potentially Inappropriate Medicines for the Elderly?

The search was carried out in 2020 and the databases considered were: SciELO (Scientific Electronic Library on-line); PubMed/Medline (National Library of Medicine and National Institutes of Health), LILACS (Latin American and Caribbean Health Sciences Literature); IBECS (Spanish Bibliographic Index of Health Sciences); Cochrane; Redalyc (Network of Scientific Journals of Latin. America, the Caribbean, Spain and Portugal); and Cuiden (Fundación Index database – España).

The primary search in the databases consisted of the following strategy: ("Potentially Inappropriate Medication List" [All Fields] OR "*Lista de Medicamentos Potencialmente Inapropriados*] OR "*Lista de Medicamentos Potencialmente Inapropiados*" AND "aged" [All Fields]] OR "elderly" [All Fields] OR "elder people" [All Fields] OR "*anciano*" [All Fields] OR "*idoso*" [All Fields]).

However, for two databases it was necessary to reformulate the search strategy; in the case of PubMed it consisted of: 'Potentially Inappropriate Medication List aged'; and for SciELO: 'Potentially Inappropriate Medication List'.

For the composition of the corpus, the articles obeyed the following criteria:

• Inclusion criteria: complete research articles, in Portuguese, English and Spanish, published in scientific journals from 2010 to 2019. Regarding the theme, articles dealing with: Lists/Updates of Lists on PIM were included; Consensus; Derived Lists about PIM; Construction Studies and/or Validation of New Technological Tools applied to the theme.

• Exclusion criteria: observational, case-control and cohort studies; editorials; reviews; reports of experiences and theoretical reflections; dissertations; theses and monographs; abstracts published in annals of events, repeated articles, and those that had no direct relationship with the topic.

The analysis of the articles was based on Evidence-Based Practice (EBP), which is defined as an approach that associates the best scientific evidence with clinical experience and patient choice¹². The EBP is important to support professional practice, as it describes that its implementation is essential to achieve effectiveness, reliability and safety in health practices¹³.

All publications were initially filtered by reading title and abstract, thus identifying the articles that apparently addressed the topic and answered the research question. In a second phase, the articles considered were read in full and categorized by thematic similarities.

The articles were presented in tables that focus on the <u>reference</u> (identification of the title, author and year), *language and country, objective, proposal of the study* (which summarizes in a critical rereading the direction of the article - method; without the intention of copying the statements of the authors). authors of the production, therefore critical re-reading; also seeking to interpret the contributions, novelties, results and defended aspects) and, level of scientific evidence. The latter followed the classification proposed by Melnyk and Fineout-Overholt¹⁴: Level I – evidence from a systematic review or meta-analysis of relevant randomized controlled trials (RCTs) or from clinical guidelines based on systematic reviews of controlled RCTs; Level II – evidence obtained from at least one well-designed controlled RCT; Level III – evidence from well-designed clinical trials without randomization; Level IV – evidence from well-designed cohort and case-control studies; Level V – evidence from a systematic review of descriptive and qualitative studies; Level VI – evidence from a single descriptive or qualitative study; Level VII – evidence from the opinion of authorities and/or the report of expert committees.

From the categories obtained, the articles were discussed in the light of the analytical process, with emphasis on Nóbrega and Karnikowski¹⁵, directing the discussion to the state of the art, the main specific lines of research and gaps, dialoguing with the critical analysis of scientific evidence and the main contributions.

The journals involved in the publications were identified, including their scope of circulation (national/international). The countries and languages were presented in their abbreviated forms, aiming at the best configuration of the data. The countries presented the following correspondences: Germany (DEU); Argentina (ARG); Australia (AUS); Austria (AUT); Belgium (BEL); Brazil (BRA); Canada (CAN); Korea (KOR); Spain (ESP); United States of

America (USA); Ireland (IRL); Italy (ITA); Japan (JPN); Norway (NOR); Netherlands (NLD); United Kingdom (GBR); Sweden (SWE); Switzerland (CHE); Taiwan (TWN). The publication languages were represented by the abbreviations: English (en) and Spanish (sp).

RESULTS

A total of 554 references were identified and 42 of them were included for analysis. The detail is presented in the flow diagram (Figure 1).

Figure 1: Flow diagram of articles filtered, evaluated for eligibility, included and excluded. Uberaba, MG, 2021.



In the first filter step, 46 articles were excluded for being duplicates, and another 442 articles for not meeting the study typology eligibility criteria. In the second stage of the filter, 23 articles were excluded for deviating from the theme, and one for incompleteness of methodological information and results.

The 42 productions analyzed were published in 25 journals of international circulation, the most frequent being the Journal of the American Geriatrics Society, in which there were six articles, followed by the European Journal of Clinical Pharmacology, with four articles, and three articles each in the journals Geriatrics & Gerontology International and BMC Geriatrics.

The main language used by the publications was English, observed in 39 of the publications, which does not necessarily imply that all of them are from English-speaking countries, but only that the adoption of English as the main language of dissemination has been required by journals from different countries. Spanish appears as the language of the other three remaining articles, with no articles written only in Portuguese.

Most of the articles identified came from studies carried out in the United States of America (8 articles – 1 of them in partnership with Italy); Canada and Spain (five articles each); Germany, Belgium and Ireland (three articles each); Norway, Switzerland and Taiwan (two articles each); Argentina, Australia, Austria, Brazil, Korea, Japan, Netherlands, United Kingdom and Sweden (one article each).

By production similarities, two categories were constructed, namely: "*Lists on potentially inappropriate medicines for the elderly*" and "*New Technological Tools on potentially inappropriate medicines for the elderly*", being Categories 1 and 2, respectively.

Category 1. Lists on potentially inappropriate medicines for the elderly

This category with 22 studies brings new lists on PIM, including translations and adaptations of pre-existing lists for specific localities and contexts.

Of the 22 publications analyzed in this category, most of them (14) presented level of scientific evidence I, due to the basis on systematic reviews; the other eight studies mentioned reviews, followed by expert consensus (Delphi Method), but did not indicate the performance or basis of systematic reviews.

Some of these new lists, in addition to expert reviews and opinions, were also guided by pre-existing PIM criteria, namely: Beers^{18,23,30-32,35-36}, Screening Tool to Alert doctors to the Right Treatment (START)^{21,23,25-26,32,34}, Screening Tool of Older Person's Prescriptions (STOPP)^{18,21,23,25-26,28,32,34-35}, The Norwegian General Practice (NORGEP)^{23,31-32,35}, lista Laroche criteria^{23,32,35}, PRISCUS^{23,32}, Winit-Watjana criteria^{32,35}, Korean and Austrian Criterai²³, McLeod criteria^{32,35}, The European Union (EU)(7)-PIM list¹⁸, Rancourt criteria³⁵, Basger Criteria³².

Of the total number of publications^{16-17,19-20,22,24,27,29,33},37 did not mention pre-existing criteria.

Chart 1. Articles considered on PIM Lists from 2010 to 2019. Uberaba, 2021.

References	Languag	Type of Study	Objective	Proposal	Level of
	e				Evidence
01 - American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Griebling TL et al. – 2019 ¹⁶	en/USA	Validation by Delphi Method	Update the Beers Criteria and classify the evidence on drug- related problems (DRP) and adverse events in the elderly.	Update by a Panel of 13 Experts, incorporating new evidence to the 2015 version. Clinical guideline based on systematic reviews, generating the addition of 46 new criteria, including individual and specific. The authors reinforce the importance of non-pharmacological approaches, with emphasis on patients with dementia and delirium.	Ι
02 - Spanish list of potentially inappropriate drugs in the elderly (ES-PIA project). Harmand MGC et al. – 2019 ¹⁷	sp/ESP	Validation by Delphi Methodi	Develop and validate a Spanish PIM list.	Elaboration of the Spanish PIM list, by 25 specialists from different areas of geriatrics and gerontology, with questionnaires in two rounds. Of the 160 items initially proposed, 138 made up the final version, all with a strong level of agreement. It represents an important advance as it is adapted to the Spanish pharmacopoeia and prescribing habits.	VII
03 - Pain and Inflammation Management in Older Adults: A Brazilian Consensus of Potentially Inappropriate Medication and Their Alternative Therapies. Motter FR et al. – 201 ¹⁸	en/BRA	Validation by Delphi Method	Develop and validate a list of PIM and alternative therapies for the treatment of pain and inflammation in the elderly adapted to the Brazilian context.	Adaptation of three international lists to the Brazilian context, by a Panel of 9 Specialists in geriatric pharmacotherapy, with validation of 144 PIM at the end of the Consensus. It represents the update of the 1 st List on Brazilian PIM, published in 2016. For two drugs, phenylbutazone and tizanidine, there was no consensus among experts even after the second round of the Delphi method.	VII
04 - Development of an Anticholinergic Burden Scale specific for Korean older adults.Jun K et al. – 2019 ¹⁹	en/KOR	Validation by Delphi Method	Develop the Korean anticholinergi c load scale.	Clinical guideline based on a systematic review for the development of an anticholinergic scale, applied to drugs available in Korea. From 10 pre-existing tools, 655 drugs were initially analyzed, generating a final version with 56 drugs classified as strong, 23 moderate and 59 weak. Drugs with	Ι

				anticholinergic action are associated with negative health	
				outcomes, requiring more careful medical prescriptions.	
05 - Potentially Inappropriate	en/NOR	Validation by	Develop the	Elaboration of the NorGeP, explicit criteria composed of 36	
Prescribing to Older Patients:	-	Delphi Method	Norwegian	PIM, and subsequent 1-year educational intervention involving	
Criteria, Prevalence and an		and large	criterion	454 general practitioners. The use of this criterion showed a	
Intervention to Reduce It: The		randomized	(NorGeP) on	prevalence rate of 24.7 MPI per 100 patients ≥70 years per	VII
Prescription Peer Academic		cluster	PIM and apply	year. Older physicians were the ones who most generated PIM	
Detailing (Rx-PAD) Study - A		educational	it in an	prescriptions in the pre-study period, and were the ones who	
Cluster-Randomized,		intervention	educational	best accepted the educational intervention. Highlight for drugs	
Educational Intervention in			intervention	with anticholinergic and antipsychotic action, and interactions	
Norwegian General Practice.				resulting from combinations with warfarin and those with	
Rognstad S et al. – 2018 ²⁰				Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).	
06 - Uso potencialmente	sp/ESP	Translation/A	Present an	The list adapted to Spanish through Consensus by 17 experts,	
inapropiado de fármacos en		daptation by	adapted and	called STOPP-Pal, was developed for decision-making on	
cuidados paliativos: versión en		Delphi Method	translated	medications in elderly people undergoing palliative care,	VII
castellano de los criterios			version of the	further clarifying the semantic confusion between frailty and	
STOPP-Frail (STOPP-Pal).			STOPP-Frail	palliative care. There was final consensus for 27 criteria. This	
Delgado-Silveira E, et al. –			list into	translated list can contribute to improving the quality of care	
2018 ²¹			Spanish	provided to palliative care patients in different health systems	
				in Spain and Latin America.	
07 - Adequate, questionable,	en/SWE	Systematic	Identify drugs	Clinical guideline based on a systematic review for the	
and inadequate drug		Review and	and drug	characterization of drugs and drug classes, by forty experts	
prescribing for older adults at		Validation by	classes that	from ten different countries, at three levels of adequacy	
the end of life: a European		Delphi Method	are most often	(adequate, questionable and inadequate). Among the	Ι
expert consensus. Morin L, et			appropriate,	questionable drugs, an important proportion of them is	
al. – 2018 ²²			questionable,	represented by anticoagulants. Forty-nine drug classes were	
			or	submitted to consensus, with the final inclusion of 75% of the	
			inappropriate	items presented. The work reinforces the importance of studies	
			for late-life	such as RCTs for high-quality evidence, but states that the	
			seniors.	present criteria can support important clinical decisions.	
08 - Ingredientes	en/ARG	Validation by	Develop/Adap	Clinical guideline based on a systematic review for the	
Farmacéuticos Activos		Delphi Method	t a list on PIM	elaboration/adaptation of foreign lists to the Argentine	
Potencialmente Inapropiados			(Potentially	context, by a Panel of 10 Experts, generating the 1st Latin	Ι
en Adultos Mayores: Lista			Inappropriate	American List on PIM, with validation of 128 PIM at the end of	
IFAsPIAM: Panel de Consenso			Active	the Consensus. Medications for the Nervous System	
Argentino. Marzi MM, et al. –			Pharmaceutica	represented the largest proportion of PIM (47%), followed by	
2018 ²³			l Ingredients in	the Cardiovascular and Musculoskeletal groups. The IFAsPIAM	

			Adults Major -	List can contribute to the rational use of medicines in the	
			IFAsPIAM List)	elderly, constituting a valuable tool in Argentine public health.	
			adapted to the		
			local		
			Argentine		
			context.		
09 - Development and Application of the GheOP ³ S- Tool Addendum on Potentially Inappropriate Prescribing (PIP) of Renally Excreted Active Drugs (READs) in Older Adults with Polypharmacy. Wazzan AAA, et al. – 2018 ²⁴	en/BEL	Validation by Delphi Method / Retrospective cross- sectional study	Expand the Ghent Older People's Prescription community Pharmacy Screening (GheOP3 S-) tool with the first addendum for PIM screening of frequently used renally excreted active drugs (DAER) and perform a cross-sectional analysis using the addendum and history of medication of a group of elderly people with polypharmacy.	Construction/Application of the GheOP3S clinical tool, through a Panel of Experts, with 61 substances included as DAER and considered inappropriate for use in elderly people with renal failure. This tool can contribute to the reduction of inappropriate prescriptions for this group of patients, with emphasis on cases of polypharmacy (concurrent use of \geq 5 medications). For glomerular filtration rate \leq 60 mL/min, the following DAERs were considered PIM: perindopril, spironolactone, metformin, allopurinol, digoxin, indapamide, hydrochlorothiazide and potassium-sparing agents and others.	VII
10 - STOPPFrail (Screening	en/IRL	Validation by	Validate the	Elaboration of the STOPPFrail list, a list of explicit criteria for	
Tool of Older Persons	,	Delphi Method	Screening Tool	the use of PIM in frail older adults with limited life expectancy	
Prescriptions in Frail adults		- F	of Older	(LLE), by means of a Consensus by 17 experts. Initial proposal	VII
with limited life expectancy):			Persons	of 30 criteria; final version with 27 criteria. This list can help	
consensus validation Lavan			Prescriptions	physicians prescribe medication to patients with LLE	
AH, et al. – 2017 ²⁵			in Frail adults	r J r	

			with limited	This list avoided generating a generalized statement about	
			life expectancy	controversial treatments, as in the case of antihypertensives,	
			list	thus focusing on drugs not usually used as 1st line.	
			(STOPPRail)		
11 - Screening Tool of Older	en/USA	Validation by	Develop a set	Clinical guideline based on a systematic review for the	
Person's		Delphi Method	of measurable	adaptation of the START-STOPP criteria to the USA, by a panel	
Prescriptions/Screening Tools		•	prescribing	of 17 experts. Of the 114 criteria reviewed, 53 were considered	
to Alert Doctors to Right			indicators,	compatible with the nursing homes in the USA, 48 of them	
Treatment Medication Criteria			adapted from	considered valid and 24 of great clinical relevance. In the end,	Ι
Modified for U.S. Nursing			the START-	22 measures of medicines were obtained related to PIM and 2	
Home Setting. Khodyakov D, et			STOPP criteria	related to underused medicines. One of the highlights of this	
al. – 2017 ²⁶			and underused	modified list is the inclusion of criteria on important clinical	
			drugs for the	care for initiating annual influenza vaccinations and	
			USA, with a	pneumococcal vaccination at least once if you are 65 years of	
			focus on	age or older. These are the first explicit criteria for assessing	
			nursing	prescribing quality in US nursing homes.	
			homes.		
12 - [Criteria for defining	en/ESP	Validation by	Develop	Construction and Validation of an index (Yq) to analyze the	
consensus achievement in		Delphi Method	criteria to	agreement of pairs of evaluators on MPI. Pilot study with 12	
Delphi studies that assess		_	define the	drugs evaluated by Likert scale. According to the study, three	
potentially inappropriate			reach of	criteria guarantee the achievement of a consensus: a) Number	VII
medications in the elderly].			consensus in	of evaluators $\geq 60\%$ of the panel members, b) Yq ≥ 0.800 ; c)	
Marzi MM et al. – 2016 ²⁷			Delphi studies	frequency of statistical mode \geq 60%. The index considers the	
			carried out to	real distances between the Likert scale categories and the	
			assess PIM in	developed criteria constitute a simple tool for the analysis of	
			the elderly.	the Delphi questionnaires in the evaluation of the use of PIM in	
				the elderly.	
13 - Intervention to Improve	en/AUS	Intervention	Test the	Efficacy and safety assessment of a 5-point checklist applied by	
Appropriate Prescribing and		Study	effectiveness	ward physicians of internal medicine, comparing the	
Reduce Polypharmacy in			of an easy	proportion of PIM prescription (based on START/STOPP	
Elderly Patients Admitted to			checklist to	criteria) and polypharmacy before and after application of the	
an Internal Medicine Unit.			support	checklist in 450 patients . Reduced risk of PIM prescription by	VII
Urfer M, et al. – 2016 ²⁸			clinicians'	22% and actual reduction of observed polypharmacy less than	
			therapeutic	20%. The reduction of deaths in the first 30 days after hospital	
			reasoning to	discharge was one of the confirmed effects of this checklist, due	
			reduce	to the significant reduction in the risk of PIM prescriptions at	
			inappropriate	hospital discharge.	
			prescribing		

			and		
			polypharmacy		
14 - Screening Tool for Older	en/JPN	Validation by	Update and	Clinical guideline based on systematic review for the	
Persons' Appropriate		Delphi Method	Revise the	update/revision of Japan's "Guidelines for medical treatment	
Prescriptions for Japanese:			Japanese	and its safety in the elderly 2005", including a Section on PIM,	Ι
Report of the Japan Geriatrics			Guidelines	adapted to the Japanese context. Among the drugs to be	
Society Working Group on			(2005	carefully prescribed, the classes 'antipsychotics', 'muscarinic	
"Guidelines for medical			version), and	receptor antagonists' and NSAIDs deserve to be highlighted	
treatment and its safety in the			add a	due to the high proportion of items mentioned. This list differs	
elderly". Kojima T, et al. –			comprehensiv	from other explicit criteria (eg, Beers and STOPP) in that it is	
2016 ²⁹			e list on PIM	based on a systematic review.	
15 - 2015 updated AGS Beers	en/USA	Validation by	Update the	Updated by an Expert Panel, incorporating new evidence into	
Criteria offer guide for safer		Delphi Method	Beers Criteria	the 2012 version. Review of over 6,700 clinical trials and	
medication use among older			(2015) and	research studies. Organization of recommendations into an	Ι
adults. Counsell SR– 2015 ³⁰			classify the	expanded set of five lists, in addition to non-drug	
			evidence on	recommendations for nursing care. Inclusion of two additional	
			DRP and	lists: one specific to "drug-drug" interactions, and the other a	
			adverse events	summary of drugs that should be avoided or administered	
			in the elderly	differently in people with kidney failure.	
16 - The Norwegian General	en/NOR	Validation by	Develop a set	Development of the Norwegian General Practice - Nursing	
PracticeNursing Home		Delphi Method	of explicit	Home (NORGEP-NH) list (based on the NORGEP List), a list of	VII
criteria (NORGEP-NH) for			criteria for the	34 explicit criteria for PIM use in Norwegian nursing homes, by	
potentially inappropriate			use of PIM in	a Panel of 49 Experts. The NORGEP-NH list can serve as a tool	
medication use: A web-based			nursing	in the prescribing process and drug list review and can also be	
Delphi study. Nyborg G, et al. –			homes.	used for quality assessment and research purposes. Emphasis	
2015 ³¹				is given to the recommendation that the term 'deprescription'	
				be adopted internationally, and to the risk of drug	
				combinations with NSAIDs and the combination of	
				bisphosphonates and statins, by elderly people with EVL.	
17 - The development of the	en/GBR	Validation by	Develop a	Instrument called 'PRescribing Optimally in Middle-aged	
PROMPT (PRescribing		Delphi Method	specific	People's Treatments' (PROMPT) and developed by a panel of	
Optimally in Middle-aged			prescription	17 experts in internet-based consensus. Comprised of 22	VII
People's Treatments) criteria.			instrument for	recommendations, the PROMPT addresses drugs commonly	
Cooper AJ et al. – 2014 ³²			the middle-	used in the UK and Ireland, and aims to explore PIM burden and	
			aged	associated factors, identifying prescribing patterns and	
			population,	predictors for potentially inappropriate drug use in this age	
			containing	group (45-59 years).). It represents the first criteria for this	
			criteria	age group and needs future tests to assess its effectiveness. A	

			relevant to this	limitation of the study was the non-inclusion of drugs suitable	
			age group	for use under specialized care.	
18 - The St Vincent's	en/IRL	Validation by	Develop a list	Development of the PIMHF by an expert panel of 35	
potentially inappropriate		Delphi Method	of PIM for	cardiologists, two general practitioners; four specialized	
medicines study: development		_	Heart Failure	nurses; and six specialist pharmacists. The final version counts	VII
of a disease-specific consensus			(HF), the	11 MPI; the medication profile of 350 patients was analyzed,	
list and its evaluation in			PIMHF list; to	and one or more Consensus PIMs were prescribed to 14.6% of	
ambulatory heart failure care.			evaluate the	these patients. The PIMHF list provides the first HF-specific	
Bermingham M, et al. – 2014 ³³			relationship	drug review tool and reinforces the importance of specific MPI	
			between the	lists for certain clinical conditions. Of the drugs on this new list,	
			prescription of	the most prescribed to the elderly in the study were: non-	
			these PIMHF	dihydropyridine calcium channel blockers (n = 15, 26.3%),	
			items and the	followed by oral corticosteroids and metformin in patients	
			clinical	with renal dysfunction.	
			outcome in an		
			outpatient HF		
			population		
19 - Mejorando la prescripción	sp/ESP	Revision/Tran	Translate a list	Translation of the START-STOPP List (2014 version) into	
de medicamentos en las		slation by	about PIM into	Spanish, through a panel of experts with geriatricians and	
personas mayores: una nueva		Delphi Method	Spanish	specialized pharmacists. The translated version maintains the	
edición de los criterios STOPP-				87 STOPP and 34 START recommendations of the English	VII
START [Improving drug				version, and represents an advance in the quality of detection	
prescribing in the elderly: a				of PIM use by Hispanic-speaking professionals. The authors	
new edition of STOPP/START				also reinforce that they can avoid frequent omissions (START)	
criteria]. Silveira ED et al. –				due to the lack of prescription drugs for cardiovascular	
2014 ³⁴				diseases, diabetes and vitamin D calcium supplements.	
20 - Using published criteria to	en/TWN	Validation by	Describe a	Elaboration of a list of explicit criteria on PIM based on at least	
develop a list of potentially		Delphi Method	process for	three pre-existing criteria, through a Consensus by 21 experts,	
inappropriate medications for			developing	applied to the Taiwanese context. The final version has 24 PIM	VII
elderly patients in Taiwan.			explicit	to be avoided by any elderly person (explicit criteria), in	
Chang CB, et al. – 2012 ³⁵			country-	addition to 12 comorbidities associated with 6 PIM classes.	
			specific PIM	Long-acting benzodiazepines and drugs with anticholinergic	
			criteria	action received clear definitions. More prospective studies are	
				needed to validate its use in clinical and research settings.	
21 - Using explicit criteria to	en/USA-	Validation by	Establish	Update of the 2002 Beers Criteria with adaptation to the Italian	
evaluate the quality of	ITA	Delphi	explicit	prescription standard, through a Consensus with nine experts,	
prescribing in elderly Italian		Method/	criteria for	with subsequent application in the elderly at a Local Health	VII
			prescribing	Unit in Parma, Italy, through a retrospective cohort study. The	

outpatients: a cohort study.		Retrospective	PIM and assess	final version had 23 MPI, allocated into three categories, and	
Maio V, et al. – 2012 ³⁶		cohort study.	the prevalence	the cohort study involved 91,741 elderly people aged ≥ 65	
			and factors	years, and at least one prescribed medication. 25.8% of the	
			associated	elderly analyzed were prescribed at least one PIM, based on	
			with PIM,	these adapted criteria. As an example of the consensus results,	
			according to	fluoxetine, due to its long half-life and its active metabolites,	
			the criteria	was considered PIM, with its use limited to cases of failure of	
			developed.	other therapeutic agents. The study corroborates that PIM use	
				among outpatient elderly people is a substantial problem in	
				this Italian locality.	
22 - Potentially inappropriate	en/AUT	Validation by	Develop the	Elaboration of the Austrian list on PIM, by a Panel of 8 Experts	
medication in geriatric		Delphi Method	Austrian	in geriatric medicine, composed of 73 PIM, in addition to	VII
patients: the Austrian			criterion on	suggestions of therapeutic alternatives, and pharmacokinetic	
consensus panel list. Mann E et			PIM	and pharmacological information of the listed drugs. This list	
al. – 2011 ³⁷				can be a useful tool for clinicians to improve the quality of	
				prescribing for the elderly, and its validity needs to be proven	
				in validation studies.	

Category 2. New Technological Tools on potentially inappropriate medicines for the elderly

This category with 20 articles presents new technological tools on PIM, including studies aimed at the development/application/presentation of technological tools applied to the identification and support of decision-making on PIM.

Of the 20 publications analyzed, most of them (10) presented level of scientific evidence VI, as the data generated, despite the initial interventionist approach, are characterized as descriptive. Evidence levels II and VII had four publications each; level II was assigned because it was data obtained from at least one RCT and the attribution of level VII was justified by the fact that the publications presented methodological studies based on expert opinions.

Two studies were classified as level VI^{43,54} because they were qualitative research, initiated by the construction of a technological tool, but with an outcome focused on the perceptions and attitudes of the interviewees.

Most of these publications (18) mentioned that their tools were based on pre-existing IPM criteria. The use of criteria in the construction of these technological tools has the following distribution: Beers (5)^{39,44,50,53-5}4; Beers and STOPP (4)^{40,47,49,57}; Beers, STOPP-START and EU(7)-PIM(1)⁴⁶; Beers, ACOVE, BEDNURS (1)⁵⁶; STOP (1)⁴⁵; START-STOPP (3)^{38,41,48}; EU(7)-PIM(2)^{43,55}; EU(7)PIM, FORTA, PRISCUS (1)⁴². Two studies⁵¹⁻⁵² did not mention pre-existing PIM criteria.

The tools described in this review, which have an intervention rather than a consultation nature, are based on two main lines of action: generation of Computerized Alerts (CA) or provision of reports to support clinical decisions. Most of the tools listed (9)^{39-40,45,49,51,53-54,56-57} work in this first line, generating CA and, therefore, evidencing the presence of PIM in therapies for the elderly. The second line is used by eight studies^{38,41,43-44,47,50,52,55}, generating reports with the presence of PIM or the recommendation to include certain drugs in the therapy, and allowing a comprehensive review of the case.

Three publications do not fit into the generation of CA or reports, namely: building a database⁴², building a repository⁴⁶ and testing the applicability of an PIM algorithm to a database⁴⁸.

In some cases, these technological tools are addressed to specific groups or professionals, such as: physicians $(3)^{38,41,43}$; assistant physicians in nursing homes $(1)^{56}$; physicians and patients $(3)^{42,47,54}$; medical residents in training $(3)^{52-54}$; doctors and pharmacists $(4)^{40,49,53,57}$. Of the 20 publications, six are not directed by the authors to any specific group^{39,45-46,48,50-51}.

Three publications^{41,44,55} present the tools and projections for when they are applied, but do not represent studies applying them and, therefore, do not address the results achieved.

Chart 2. Articles considered on New Technological Tools on MPI from 2010 to 2019. Uberaba, 2021.

References	Language	Type of	Objective	Proposal	Level of
	/Country	Study			Evidence
01 - 'Optimising	en/CHE	Clustered ECR	Test whether the	Systematized review of multimorbid and polypharmacy therapy for	
Pharmaco			use of a systematic	elderly patients supported by the 'Systematic Tool to Reduce	II
Therapy In the			software-assisted	Inappropriate Prescribing'-Assistant' (STRIPA) software and	
multimorbid			drug review	underutilization assessment, involving 40 primary care units. This type	
elderly in primary			intervention leads	of software-based review has been shown to improve decision making	
CAre' (OPTICA) to			to more	about appropriate therapy in multimorbid patients.	
improve			appropriate drug		
medication			use than a sham		
appropriateness:			usual care		
study protocol of			intervention		
a cluster					
randomised					
controlled trial.					
Jungo KT, et al. –					
2019 ³⁸					
02 - Utilization of	en/CAN	Retrospective	To assess the	Study in two outpatient clinics for an observation period of 30 months.	VI
computerized		methodologic	frequency of	The performance of CA was 17.2% in both clinics, not showing clinical	
clinical decision		al/observatio	clinical interaction	significance in the detection of PIM (Beers). The authors point to the	
support for		nal study	of medical record	phenomenon of 'alert fatigue' as the cause of the lack of clinical impact	
potentially			computerized	of these tools. The potential for low-cost impact points to the relevance	
inappropriate			alerts (CA) and	of further studies	
medications.			associated		
Alagiakrishnan K,			prescribing		
et al. – 2019 ³⁹			behaviors in		
			outpatient settings.		
03 - A pharmacist-	en/CAN	Intervention	To assess the	Knowledge translation strategy, implemented by a family health team	VI
physician		Study	applicability of an	including a medical-pharmaceutical intervention model based on CA.	
intervention			interdisciplinary	One or more alerts were clinically significant for 42% of patients. This	
model using a			pharmacist-	intervention proved to be efficient in reducing the use of high-risk drugs	
computerized			physician	in hospitalized elderly patients.	
alert system to			intervention model		
reduce high-risk			to reduce the use of		
medication use in			high-risk drugs and		
primary care.			the clinical		
			relevance of CA.		

Cossette B, et al. – 2019 ⁴⁰					
04 - The effect of SENATOR (Software ENgine for the Assessment and optimisation of drug and non- drug Therapy in Older peRsons) on incident adverse drug reactions (ADRs) in an older hospital cohort - Trial Protocol. Lavan AH, et al. – 2019 ⁴¹	en/IRL	RCT (multinationa l, pragmatic, parallel-arm, prospective, open, blind endpoint)	To evaluate the effect of the Software ENgine for the Assessment and optimization of drug and non-drug Therapy in Older persons (SENATOR) in adverse drug reactions (ADRs) in elderly, multimorbid and hospitalized patients	Software evaluation that produces reports that optimize prescriptions for elderly patients, highlighting drug-drug and drug-disease interactions and providing non-pharmacological recommendations aimed at reducing the risk of incident delirium. This is the first clinical trial to examine the effectiveness of a software intervention on ADR incidents and associated health care costs during hospitalization in older adults with multimorbidity and polypharmacy. This publication presents the study's projections, but does not disclose results yet.	II
$\begin{array}{c c} 05 & - \mbox{ Data-Driven} \\ Assessment & of \\ Potentially \\ Inappropriate \\ Medication in the \\ Elderly. \\ Friedrichs M, et al. \\ - 2018^{42} \end{array}$	en/DEU	Methodologic al Study	Develop database on PIM (PIMBase)	Development tool that integrates well-known PIM lists and unifies their rating scales. The benefits of this combination of lists are supported by pharmacovigilance data. PIMBase allows identification of PIM and is based on the address: https://pimbase.kalis-amts.de.	VII
06 - Reduction of inappropriate medication in older populations by electronic decision support (the PRIMA-eDS study): a qualitative study of practical implementation	en/DEU	Validation/Qu alitative Study	Explore the use of the 'Polypharmacy in chronic diseases- Reduction of Inappropriate M edication and Adverse drug events in older populations' (PRIMA) tool for	Conducting interviews with 21 physicians using the PRIMA-eDS tool. This tool seeks to reduce the use of PIM in elderly patients with polypharmacy. After entering prescription-relevant patient data into an electronic case report form, the physician receives a comprehensive medication review with recommendations on missing indications, laboratory tests needed, evidence base of current medication, dose adjustments for dysfunction impairment, potentially harmful drug interactions, contraindications, and possible adverse drug events. The present qualitative validation concludes that the use of this tool in the future is unfeasible due to the delay in entering patient data in the form.	VI

in primary care. Rieckert A, et al. – 2018 ⁴³			evidence-based electronic decision support (eDS), analyzing attitudes and perceptions physicians, to optimize the tool and prepare it for future implementation.		
07 - A Cloud Based Potentially Inappropriate Medication Management System Using Patient Owned Personal Health Records. Lee HÁ, et al. – 2018 ⁴⁴	en/TWN	Methodologic al Study	Design a cloud- based personal health management platform ("My Health Bank").	Development of a platform that allows the analysis and storage of information in two databases, one for the health insurance medication table and the other for the PIM. The authors believe that this tool will increase medication safety and improve the self-reliance management of the elderly. This publication presents the study's projections, but does not disclose results yet.	VI
08 - Polimedication: applicability of a computer tool to reduce polypharmacy in nursing homes. García-Caballero TM, et al. – 2018 ⁴⁵	en/ESP	Methodologic al Study / Observational Retrospective	Assess the effect of therapeutic alerts on PIM detection	Processing of medical prescriptions from 115 institutionalized elderly people in a nursing home to assess the generation of therapeutic alerts about PIM in order to minimize analysis time. Of the total number of alerts (average: 10.04 alerts/patient), 12.12% were considered relevant, with a time spent of 6.26min/patient and savings of €32.77 per resident/year on medications. The use of this tool provided significant savings in pharmaceutical expenses, in addition to reducing medication review time.	VI
09 - European repository of explicit criteria of potentially inappropriate medications in old age. Ivanova I, et al. – 2018 ⁴⁶	en/BEL	Methodologic al Study	Build a European repository of explicit PIM criteria suitable for electronic assessment	Construction of a repository contemplating the description of the PIM, drug information, clinical information and the level of evidence. It was possible to insert most of the original criteria from three selected PIM lists in the repository. The authors hope that in the future, developers of new PIM lists will take semantic interoperability into account and consider the suitability of the criteria for electronic use.	VI

10 - Effect of the Tool to Reduce Inappropriate Medications on Medication Communication and Deprescribing. Fried TR, et al. – 2017 ⁴⁷	en/USA	RCT	To examine the effects of the Tool to Reduce Inappropriate Medication (TRIM) in reducing PIM use and shared decision making.	Evaluation of a web tool that connects an electronic medical record to a clinical decision support system, with an emphasis on communication and medication prescription. These automated algorithms identify discrepancies in medication reconciliation, PIM, and potentially inappropriate regimens. The authors point out that the association of this tool with electronic medical records improved shared decision-making and reduced medication reconciliation errors, but did not change the prescription.	ΙΙ
11 - Application of the STOPP/START criteria to a medical record database. Nauta KJ, et al. – 2017 ⁴⁸	en/NLD	Intervention Study	Test computer algorithms to apply PIM criteria to a medical records database.	Application of computer algorithms based on the STOPP/START criteria and defined by the Anatomical-Therapeutic-Chemical codes, to a Dutch primary care database, with patients aged ≥ 65 years using ≥ 5 chronic drugs and coded diagnoses International Classification Codes for Primary Care (ICPC). In total, 65% of the criteria could be converted into a computer algorithm. The inapplicability of the other criteria resulted from the lack of information on the severity of a condition and the insufficient coverage of ICPC codes.	VI
12 - Reduction in targeted potentially inappropriate medication use in elderly inpatients: a pragmatic randomized controlled trial. Cossette B, et al. – 2017 ⁴⁹	en/CAN	RCT	To assess change in MPI use with an AC- based pharmacist- physician intervention model compared to usual clinical care.	Single-site RCT through CA based on two PIM criteria. The primary endpoint was cessation of PIM or dose reduction. A significantly higher number (absolute difference of 30% 48h after use of alerts) of interruption and reduction of PIM dosage was observed in the intervention group.	Π
13 - Quality of Provider Practices for Older Adults in the Emergency Department (EQUiPPED).	en/USA	Intervention Study	Assess the effectiveness and sustainability of the Enhancing Quality of Provider Practices for Older Adults in the Emergency	Educational intervention (didactic lectures) and clinical decision support (with PIM criteria) based on informatics, with drug order sets embedded in electronic medical records, dose adjustments for renal failure, PIM prescribing guidance and links to content synthesized geriatric. The proportion of PIM use dropped from 11.9% to 5.1% (pre and post intervention). The authors classified the intervention as sustainable and stated that a multicomponent program has an influence	VII

Stevens M, et al. –			Department	on the generation of safer prescriptions for elderly people who are	
201750			initiative	discharged from the emergency room.	
			(EQUIPPED) to		
			reduce MPI usage		
14 - Evaluating	en/USA	Intervention	Assess changes in	AC-based intervention to reduce PIM prescription, with 1539 pre-alert	VI
the Impact of	,	Study	PIM prescribing in	patients and 1490 post-alert patients; 1952 and 1897 PIM prescribed,	
Medication Safety		5	pre-	respectively. There was no significant difference in the rate of new pre-	
Alerts on			implementation	alert and post-alert PIMs overall, but there was a significant reduction	
Prescribing of			and post-	in the rate of the 10 most common newly prescribed PIMs, from 9.0% to	
Potentially			implementation of	8.3% (P = 0.016). The study concludes that CA use may decrease the	
Inappropriate			CA.	incidence of more frequently prescribed PIM in older adults who receive	
Medications for				care in an outpatient setting.	
Older Veterans in					
an Ambulatory					
Care Setting.					
Vanderman AJ, et					
al. – 2017 ⁵¹					
15 - PIM-Check:	en/CHE	Validation by	Develop an	Development of an electronic tool, based on literature review, semi-	VII
development of		Delphi	electronic	structured interviews and consensus by 40 physicians and 25 clinical	
an international		Method	prescription	pharmacists. The final checklist includes 160 statements; 17 medical	
prescription-			screening checklist	domains; 56 pathologies; algorithm of approximately 31,000 lines was	
screening			0	developed. PIM-Check is the first electronic prescription screening	
checklist				checklist designed to detect PIM in internal medicine.	
designed by a					
Delphi method for					
internal medicine					
patients.					
Desnoyer A, et al.					
- 2017 ⁵²					
16 - Knowledge	en/CAN	Intervention	To evaluate the	Intervention based on the distribution of educational materials,	VII
Translation	-	Study	effect of a	presentations by geriatricians, medical-pharmaceutical interventions	
Strategy to		-	knowledge	by CA and comprehensive geriatric assessments.	
Reduce the Use of			translation (kt)	A 3.5% (P<0.001) absolute decrease in patient-days with at least one	
Potentially			strategy to reduce	PIM was observed immediately after the intervention. The authors point	
Inappropriate			PIM use in	out that this strategy resulted in a decrease in the use of PIM in elderly	
Medications in			hospitalized	adults in the hospital.	
Hospitalized			elderly.		
Elderly Adults.			-		

Cossette B, et al. –					
2016 ⁵³					
17 - Physicians' use of computerized clinical decision supports to improve medication management in the elderly - the Seniors Medication Alert and Review Technology intervention. Alagiakrishnan K,	en/CAN	Intervention Study	Create an AC of physician- acceptable medications and deploy them into an outpatient Electronic Medical Record (EMR); and figure out how to deploy this tool with the least disruption to the workflow and the most attention from the clinician.	Pre-production, development and post-production optimization of an electronic medical clinical decision support tool embedded in electronic medical records (with criteria on PIM) and Cockcroft-Gault formula to estimate glomerular filtration rates (GFR). The "Seniors Medication Alert and Review Technologies" (SMART) intervention generates chart messages and order entry alerts, exposing MPI, decreased GFR, and the possible need for medication adjustments. About 36% of eligible cases triggered at least one SMART alert, with a GFR alert, with ~25% of alerts ignored and ~15% generating evidence verification. This tool has proven acceptable to specialist and primary care physicians, with no significant negative impacts on workflow.	VII
et al. – 2016 ⁵⁴					
18 - Polypharmacy in chronic diseases- Reduction of Inappropriate Medication and Adverse drug events in older populations by electronic Decision Support (PRIMA-eDS): study protocol for a randomized controlled trial. Sönnichsen A, et al 2016 ⁵⁵	en/DEU en/BEL	Methodologic al study/RCT Methodologic	Develop the PRIMA-eDS tool to help clinicians reduce inappropriate prescribing and test its effectiveness in a large-scale RCT.	Construction and effectiveness testing of the PRIMA-eDS tool that comprises an indication check and recommendations for polypharmacy and PIM reduction based on systematic reviews and guidelines on PIM, SFINX interactions database, PHARAO database on adverse effects and RENBASE database on renal dosage. The tool was built, and the RCT designed (3500 patients and 325 general practitioners involved). The main hypothesis is that reduced polypharmacy and inappropriate prescribing can reduce hospitalizations or deaths. This publication presents the study's projections, but does not disclose results yet.	II
prescribing in	CII/ DEL	al/cross-	computerized	underused medications by elderly residents in nursing homes by	V I
Belgian nursing		sectional	assessment tool to	combining three PIM criteria and a list of drug interactions. Most PIMs	

REFACS (online) Apr/June 2022; 10(2)

homes: an		observational	monitor the quality	were detected by the ACOVE criteria for underutilization with 58% of	
electronic		study	of prescribing in	patients having at least one PIM. Using the BEDNURS and Beers criteria,	
assessment of the			Belgian nursing	at least one PIM was observed in 56% and 27% of patients, respectively.	
medication chart.			homes.	The study concludes that the development of a combined assessment	
Elseviers MM, et				tool and the implementation of a computerized PIM monitoring system	
al. – 2014 ⁵⁶				is highly recommended to improve care in nursing homes.	
20 - Electronic	en/USA	Intervention	Develop and	Development and application of computerized panel on PIM. There was	VII
surveillance and		study (pilot)	evaluate an	signaling of subjects with at least one administered PIM or a high	
pharmacist			electronic tool to	calculated anticholinergic score. The panel also displayed the	
intervention for			assist clinical	cumulative administration of narcotics and benzodiazepines over 48	
vulnerable older			pharmacists in	hours. Intervention applied to elderly people (\geq 65 years) admitted to	
inpatients on			reviewing PIM in	general medicine, orthopedics and urology services for 3 weeks in 2011.	
high-risk			hospitalized older	After the intervention, 22% of patients had signs of using at least one	
medication			adults	PIM and physicians approved 78% of the recommendations subsequent	
regimens.				pharmaceuticals. This tool allowed clinical pharmacists to quickly	
Peterson JF, et al.				review the medication regimens of hospitalized older adults and	
- 2014 ⁵⁷				provide a timely point-of-care intervention when indicated.	

DISCUSSION

The use of medicines by the elderly is increasingly attracting the interest of scientific investigations, which is easy to understand – one of the main therapeutic resources today and the age group with the highest growth rate. In turn, there is irrational use, with consequent risks. This scenario shows the need for more information and more tools to be made available, in order for the elderly to benefit from their drug therapies with the highest possible level of safety.

The search for updating through a comprehensive analysis of scientific publications is shown to be one of the most acceptable and promising ways, allowing to know successful initiatives that can be reproduced, and others that are not so successful, but which, even so, become data and point out what not to do.

The classification of findings into two thematic categories allowed a clearer analysis of two important aspects on the PIM theme; the first, presenting the state of the art regarding the new lists of drugs that pose risks to the elderly, in addition to adaptations for local contexts, for subgroups or for specific clinical conditions. The second category presents scientific efforts for new tools to reach the field of practice, promoting the integration of health care for the elderly, safe drug therapy and ways to educate professionals and patients.

There were efforts by several countries to develop or adapt PIM criteria for their contexts. One of the reasons for these local initiatives is that many drugs on important international lists may be unavailable in certain countries. This scenario was observed in Brazil, where only 60% of the drugs mentioned in the Beers criterion are marketed in the country, based on the National List of Essential Medicines (2013), creating a bias in the results of several Brazilian studies⁵⁸.

In addition to the search for specific lists for the elderly in each country or region, the elaboration of a list for subgroups was observed. This is the case of the Norwegian list NORGEP NH31, adapted from the national list (NORGEP²⁰) on PIM, and aimed at institutionalized elderly people. This initiative was motivated after a Norwegian study pointed out the high prevalence of PIM use (31% of the analyzed population) in nursing homes⁵⁹. A similar adaptation involved the START-STOPP criteria for institutionalized North American elderly people²⁶, which explains the existence of subgroups within special age groups, such as the elderly.

In the relevance of special subgroups contained in the large group of elderly, three other subgroups should be highlighted: elderly in palliative care²¹, elderly with HF³³ and elderly with renal failure²⁴. The elaboration of lists on specific PIM such as these demonstrate the scope of

REFACS (online) Apr/June 2022; 10(2)

the theme and the need for continuous innovations so that various developments can be studied.

As for studies that showed clinical convergence, two publications^{22,25} agreed to discontinue anticoagulants in elderly people with limited life expectancy, as the risk of bleeding and the cost of treatment outweighed the potential benefits for patients, but recommended the analysis of specific cases, as the risk of stroke.

One of the publications³⁰ addresses the relevance of geriatric nursing care in patients with 'behavioral problems', avoiding the use of antipsychotics, except in cases of inefficiency of non-pharmacological measures, or risks to the patient or others. Although nursing has a fundamental role in the provision of care and in detecting the use of PIM, only one study³³, aimed at the elderly with HF, had specialized nurses in the composition of its panel of experts, which signals the need for greater appreciation of the inter and transdisciplinary work.

Regarding Category 2, in general terms, all the technological tools listed aim at some aspect related to the use or detection of PIM in the elderly, characterized as individuals aged \geq 65 years. Only one study³² addressed an age group transitioning to senescence, that of middle-aged individuals (defined as age between 45 and 64 years), indicating the existence of evidence⁶⁰ that multimorbidity is also prevalent in this group, but so far, studies related to PIM have been little considered for these individuals.

In this category, there was a case of cumulative scientific contribution related to the PRIMA-eDS tool, aimed at reducing PIM prescriptions. The first publication⁵⁵ presents the construction of this tool and designs an ECR; the second publication⁴³ is a qualitative study on the attitudes and perceptions of assistant physicians who used the tool in their clinical practices. Although the tool is considered capable of generating clinical reports and recommendations of great scope and quality, the qualitative validation this study showed that the physicians interviewed found it unfeasible to apply the tool in question in their practices, due to the delay in entering patient data in the form⁴³.

Cumulative contributions such as this one reinforce the importance of new investigative findings in the construction of knowledge and overcoming gaps and, although a tool can be discarded after the judgment of practical infeasibility, a lot of knowledge is generated by its development and tests, contributing to future successes.

The analysis of the technological tools of this review reveals another important data; although there are at least three professional groups that work directly with drug therapies in clinical practice, only two of these groups had tools aimed at the best performance of their work: physicians, including medical residents, and pharmacists, with no mention of nurses in any of the publications.

The construction of tools that signal the risks of drug therapy for the elderly also for nurses can represent a big step towards greater safety and rational use of medicines in this public. Analyzing the profile and purpose, it is evident, as in the case of the STRIPA³⁸, SENATOR⁴¹, PRIMA-eDS⁴³ and TRIM⁴⁷ tools, an important power of detection and decision support for physicians and pharmacists about PIM prescription. However, none of these tools was able to reach the role of nursing in the reception of elderly patients, aiming at the detection of PIM in the first stage of the care itinerary.

It is worth noting the insignificant participation of Latin American countries in international publications on the PIM theme, with emphasis on Brazil, with only one study found focused on Category 1. This finding is consistent with the report Science and Engineering Indicators 2020⁶¹, by the National Science Foundation (USA), and presented by Pesquisa FAPESP magazine, which shows that Brazil, despite having advanced six positions between 2000 and 2018, occupies the 11th position in the ranking of countries that produce the most international scientific publications, in a list led by China, followed by the USA and India.

This review highlights the importance of continually drawing up new lists on PIM, ensuring compatibility with specific contexts and the availability of medications in each location, in addition to showing that the technological tools applied to the safety of medication use in the elderly can be improved, with emphasis on usability and inclusion of a larger audience of users, including nurses.

Two possible knowledge gaps were also found; the first one is the lack of a list on PIM applied to obese elderly people, justified by the possibility of body deposits of certain active principles, it is worth noting that aging, analyzed separately, causes a reduction of 20 to 30% in muscle mass (sarcopenia) and bone mass (osteopenia/osteoporosis)⁶², and a 20 to 30% increase in total body fat (2 to 5%/decade, after age 40)⁶³.

The second gap refers to technological tools that allow the outpatient evaluation of signs and symptoms in elderly patients, and that establish a possible causal relationship with the use of PIM. A tool of this nature can contribute to quick assessments in medical, nursing and pharmaceutical consultations in Primary Health Care, minimizing aggravations resulting from the non-detection of PIM use.

CONCLUSION

This study identified that there is an important national and international movement focused on the elaboration and adaptation of lists on PIM applied to specific countries, populations and subgroups. New technological tools for detecting and evaluating PIM follow a trend of development and improvement, and make evident the need for these efforts to continue.

This review also identified initiatives to expand access to PIM information, such as building large databases and repository with simplified access for professionals and patients.

The sum of these initiatives builds, gradually and cumulatively, a scenario of greater safety for the elderly in their drug therapies, whether in primary health care environments or hospitals with greater technological density, in addition to adding important educational value by allowing, in many cases, the possibility of updating for future health professionals.

As limitations, there was the non-use of databases such as the Web of Science and CINAHL, the latter specific to nursing, and the non-inclusion of languages other than Portuguese, English and Spanish. In turn, the present study brings evidence and new contributions on the PIM theme, through the analysis of publications with varied methodological designs, in addition to covering works published around the world.

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Associated Publisher: Vania Del Arco Paschoal.

Conflict of Interest: the authors declare that there is no conflict of interest.

Financing: none.

CONTRIBUTIONS

Rodrigo Rodrigues Silva contributed to the design, collection and analysis of data, writing and revision. **Luan Augusto Alves Garcia** collaborated in the writing and revision. **Ana Luisa Zanardo Buso, Daiane Silva Marques** and **Fabiana Fernandes Silva de Paula** acted in the revision. **Álvaro da Silva Santos** supported the design, writing and revision.

How to cite this article (Vancouver)

Silva RR, Garcia LAA, Buso ALZ, Paula FFS, Marques DS, Santos AS. New lists and new technological tools on potentially inappropriate drugs for the elderly: an integrative review. Rev. Fam., Ciclos Vida Saúde Contexto Soc. [Internet]. 2022 [cited in *insert day, month and year of access*]; 10(2):340-69. Available from: *insert access link*. DOI: *insert DOI link*.

How to cite this article (ABNT)

SILVA, R. R.; GARCIA, L. A. A.; BUSO, A. L. Z.; PAULA, F. F. S.; MARQUES, D. S.; SANTOS, A. S. New lists and new technological tools on potentially inappropriate drugs for the elderly: an integrative review. **Rev. Fam., Ciclos Vida Saúde Contexto Soc.**, Uberaba, MG, v. 10, n. 2, p. 340-369, 2022. DOI: *insert DOI link.* Available from: *insert access link*. Access in: *insert day, month and year of access*.

How to cite this article (APA)

SILVA, R.R., GARCIA, L.A.A., BUSO, A.L.Z., PAULA, F.F.S., MARQUES, D.S., & SANTOS, A.S. (2022). New lists and new technological tools on potentially inappropriate drugs for the elderly: an integrative review. *Rev. Fam., Ciclos Vida Saúde Contexto Soc., 10*(2), 340-369. Retrieved in *insert day, month and year of access* from *insert access link*. DOI: *insert DOI link*.



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