

## Long-Term Care medicines formularies: any reasons for pharmacists' concern?

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This study aimed to characterize and compare medicines formularies (MFs) used in Long-Term Care (LTC) facilities in Portugal, and to identify the prevalence of Potentially Inappropriate Medicines (PIMs). A systematic contact with LTC facilities was undertaken in December 2021. MFs were systematized according to the Anatomical Therapeutic Chemical classification system (ATC), followed by descriptive content analysis. A structured comparison between MFs developed by public organizations and private LTC facilities was performed. After duplicate removal and exclusion of medicines not for systemic use, two explicit criteria - the *Algorithm of medication review in frail older people* and the *EU(7)-PIM list* - were employed for PIMs identification. Five MFs were obtained and assessed. The three MFs developed by private institutions covered 23% of the national LTC facilities and approximately 34% of the national total of beds. Heterogeneity was particularly high for the *Alimentary tract and metabolism*, *Blood and blood-forming organs*, *Musculoskeletal system*, and *Respiratory system* ATC groups. A PIM prevalence of 29,4% was identified. Medicines distribution between the MFs suggests the need to develop national guidelines towards harmonizing medicines usage in LTC. The prevalence of PIMs found highlights the importance of a particular optimized use of this health technology in aged sub-populations.

**Keywords:** Medicines formularies. Long-Term Care. Aged. Pharmacists. Pharmacy & Therapeutics Committee.

### INTRODUCTION

Medicines are a crucial technology in healthcare systems and one of the most frequently used in Long-Term Care (Fenstermacher, 2010). Long-Term Care (LTC) comprises a range of healthcare, personal care, and other supportive services targeted to patients whose capacity for self-care is limited. In Portugal, the National Network of Long-Term Integrated Care (NNLTC) represents the country's response to the growing demand for this level of care (Ministério da Saúde and Ministério do Trabalho Solidariedade e Segurança Social, 2006; World Health Organization, 2000). Services performed by the NNLTC are delivered at patient homes and

community-based services or institutional settings, with pharmacists assisting the latter framed by hospital pharmacy regulations. Supervision and monitoring of the NNLTC are under public control (Ministério da Saúde and Ministério do Trabalho Solidariedade e Segurança Social, 2006). Nonetheless, LTC teams work autonomously regarding medicines use, leading to the heterogeneity of practices. Patients assisted by the NNLTC are mainly elderly (83% are 65 years old or over), with high prevalences of multimorbidity and polypharmacy, aligned with the international LTC patients' profile (Ministério da Saúde and ACSS, 2020; Wang *et al.*, 2018). The elderly living in LTC facilities (LTCFs) are more susceptible to experiencing Adverse Drug Events (ADEs) than non-institutionalized elderly individuals (Kapoor *et al.*, 2020). Potentially Inappropriate Prescribing (PIP) encompasses i) misprescribing, i.e., the prescription of a medication that could potentially lead to a significant risk of ADEs, due to

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erroneous posology or route of administration or due to increased risk of drug-drug or drug-disease interaction; ii) underprescribing or Potential Prescribing Omission (PPO), i.e., the omission of a medication that is clinically indicated for disease treatment or prevention; and iii) overprescribing, i.e., the prescription of medications for which no clear clinical indication exists (O'Connor, Gallagher, O'Mahony, 2012; Rankin *et al.*, 2018). Within the concept of misprescribing, Potentially Inappropriate Medications (PIMs) represent a set of medications with greater risk than benefit to a patient, consequently increasing the risk of ADEs and associated with poor health outcomes especially in aged populations. In addition, polypharmacy is a preponderant determinant for the higher prevalence of PIMs (Mekonnen *et al.*, 2021). Thus, the identification of PIMs in aged sub-populations of LTC systems represents an important field of action to improve the quality of prescribing.

Over the last decades, a plethora of tools and interventions have been published in scientific literature addressing medicines optimization through improving prescribing practices (Onder *et al.*, 2013). Tools assessing the appropriateness of prescribing can be classified as explicit (i.e., criteria-based) or implicit (i.e., judgment-based) (Kaufmann *et al.*, 2014). Implicit criteria require clinical expertise and data about the patient (e.g., previously unsuccessful treatment, preferences), whilst explicit criteria tools are medication-targeted and/or disease-targeted, making them more suitable for assisting medicines related decisions, including medicines formularies (MFs) development and optimization (Drenth-van Maanen *et al.*, 2018; Kaufmann *et al.*, 2014).

The American Society of Health-Systems Pharmacists defines a drug or medicine formulary as “*a continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis, prophylaxis, or treatment of disease and promotion of health*” (Tyler *et al.*, 2008). Medicines formularies play an important role in healthcare systems. The ‘Model List of Essential Medicines’ was first published in 1977 by the World Health Organization and is updated every two years, highlighting the importance of medicines in healthcare systems (World Health Organization, 2022).

Medicines formularies for LTC settings will be under assessment in the present study. Medicines formularies can generically be classified as ‘open’ or ‘closed,’ and the main difference between the two types relies on the process of selection. ‘Open formularies’ chiefly rely on prescribing orders; in contrast, ‘closed formularies’ are based on a previous assessment of medicines or medical devices according to clinical and economic criteria. Closed formularies are usually developed by Pharmacy and Therapeutics Committees, especially common in hospital settings (Parrish, 2018; Puigventós Latorre *et al.*, 2011; Sofat, 2020).

Medicines formularies can positively impact clinical and economic outcomes by selecting the safest, most efficacious, and cost-effective medicines (Schiff, Cremers, Ferner, 2012). Given the importance of medicines optimization for the elderly living in LTC settings, this study aimed to characterize and compare MFs regarding the medicines selected and their suitability for aged individuals by identifying PIMs.

## MATERIAL AND METHODS

The overall study design followed a statistical descriptive analysis approach, using medicines formularies in use or recommended for Long-Term Care Facilities of the Portuguese National Network of Long-Term Care.

### Sampling

Medicines formularies from public institutions were retrieved from institutional websites. Contacts with LTCFs were carried out during December 2021. Direct contact with an 83-facilities LTC chain was undertaken, considering that this LTC chain’s formulary was employed in 22% of the national LTCF and approximately 32% of the total national beds. The remaining 288 LTCFs were systematically contacted via email and telephone.

A sample of five MFs was obtained. Two formularies were developed by public entities - National Coordination (MF1) and a Regional Health Authority (MF2 - responsible for regional supervision and coordination of the NNLTC). The remaining three formularies (MF3,

MF4, MF5) were developed by LTCFs' healthcare teams, covering the three types of inpatient facilities, i.e., Convalescence, Middle Term and Rehabilitation and Long-Term and Maintenance.

MF1 was released in 2011 by the National Coordination and was targeted to the entire NNLTC - i.e., 371 LTCFs and 9.289 beds (inpatient settings). MF2 was released in 2016 by a Regional Health Authority; there were 19 facilities and 532 beds (inpatient settings) under the influence of MF2. MF3 was obtained from a 120-beds LTCF. MF4 was obtained from an LTCFs chain comprising 83 LTCFs and approximately 3000 beds. MF5 was obtained from a 59-beds LTCF. Excluding MFs 1 and 2, the remaining three MFs covered 23% (85/371) of the national total of LTCFs and approximately 34% (3179/9289) of the national total of beds.

#### Data extraction.

All medicines included in each MF were extracted to MS Excel file and coded according to the Anatomical Therapeutical Chemical (ATC) Classification system (World Health Organization, 2022). Duplicates were removed from this data set. To identify potentially inappropriate medications for elderly patients, the *Algorithm of medication review in frail older people* ("Poudel's criteria") (Poudel *et al.*, 2016) and the *EU(7)-PIM list* explicit criteria (Renom-Guiteras, Meyer,

Thürmann, 2015; Rodrigues *et al.*, 2020) were employed. These two criteria were selected based on previous study findings published elsewhere (Gonçalves *et al.*, 2021b).

#### Data comparisons

Initially, medicines formularies developed by LTCFs (MF3, MF4, MF5) were compared to a unified characterization of the national and regional formularies ('MF1 + MF2'), considering all medicines. Next, medicines not for systemic use (e.g., *D - Dermatologics*; *S - Sensory organs*) were excluded, knowing that the explicit criteria employed only refer to systemic use, followed by simple descriptive data analysis.

#### RESULTS

The sum of the five MFs resulted in a total of 1560 medicines. After duplicate removal, 595 different medicines were listed, of which 97 medicines were common to the five MFs (see supplemental material 1). To assess their distribution, national and regional recommendations ('MF1 + MF2') were compared to MFs autonomously developed by LTFCs (MF3, MF4, MF5). Higher rates of heterogeneity were found for the *Alimentary tract and metabolism*, *Blood and blood-forming organs*, and *Musculoskeletal and Respiratory system* ATC groups. Results are described next (Table I).

**TABLE I** - Medicines formularies comparison

ATC group	No. of medicines 'MF1 + MF2'	MF3		MF4		MF5	
		No. of medicines in common with MF1+MF2 (%)	No. of medicines different from 'MF1+MF2'	No. of medicines in common with MF1+MF2 (%)	No. of medicines different from 'MF1+MF2'	No. of medicines in common with MF1+MF2 (%)	No. of medicines different from 'MF1+MF2'
A	52	21 (68%)	10	46 (58%)	33	32 (67%)	16
B	22	12 (75%)	4	21 (57%)	16	10 (53%)	9
C	54	21 (91%)	2	48 (72%)	19	38 (81%)	9
D	9	4 (67%)	2	8 (20%)	33	6 (19%)	26
G	8	4 (80%)	1	7 (47%)	8	7 (88%)	1

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H	10	6 (100%)	0	10 (100%)	0	8 (100%)	0
J	29	14 (100%)	0	27 (82%)	6	18 (90%)	2
L	2	0 (0,0)	0	0 (0,0)	2	2 (100)	0
M	16	7 (78%)	2	16 (67%)	8	10 (63%)	6
N	61	47 (92%)	4	58 (53%)	52	45 (85%)	8
P	2	1 (100%)	0	1 (33%)	2	0 (0,0)	1
R	25	7 (58%)	5	22 (58%)	16	10 (59%)	7
S	13	2 (100%)	0	10 (21%)	37	7 (32%)	15
V	1	0 (0,0%)	1	0 (0,0%)	6	0 (0,0%)	8
Total	304	146 (82%)	31	274 (54%)	238	193 (64%)	108

After employing the exclusion criterion (i.e., medicines not for systemic use), 156 medicines were excluded (156/595, 26.2%). The final list of 439 medicines was mainly distributed to the following ATC groups: *Nervous system* (113/439, 25.7%); *Alimentary tract and metabolism* (88/439, 20.0%); *Cardiovascular system* (71/439, 16.2%); *Blood and blood-forming organs* (40/439, 9.1%); *Antiinfective for systemic use* (36/439, 8.2%); *Respiratory system* (35/439, 8.0%) and

*Musculoskeletal system* (22/439, 5.0%). From applying the explicit criteria to the sample of 439 medicines, 129 (29.4%) Potentially Inappropriate Medications (PIMs) were identified. Forty medicines (40/129, 31.0%) were common to the “Poudel’s criteria” and the *EU(7)-PIM List*, with three medicines being exclusively identified from the “Poudel’s criteria” and 86 medicines (86/129, 66,7%) from the *EU(7)-PIM List*. The 129 PIMs are described next (Table II).

**TABLE II** - Potentially Inappropriate Medications

ATC group	ATC subgroup	Medicine	ATC code
A - Alimentary tract and metabolism (25/129; 19.4%)	Drugs for acid related disorders	Calcium carbonate and magnesium carbonate	A02AD
		Dihydroxialumini sodium carbonate	A02AB04
		Dihydroxialumini sodium carbonate and dimethicone	A02AB10
		Esomeprazole	A02BC05
		Aluminium phosphate	A02AB03
		Aluminium hydroxide	A02AB01
		Magnesium hydroxide	A02AA04
		Omeprazole	A02BC01
		Pantoprazole	A02BC02
		Ranitidine	A02BA02
	Drugs for functional gastrointestinal disorders	Otilonium bromide	A03AB06
		Pinaverium	A03AX04
		Domperidone	A03FA03
		Mebeverine	A03AA04
		Metoclopramide	A03FA01
	Drugs for constipation	Bisacodyl	A06AB02
		Liquid paraffin	A06AA01
		Sodium picosulfate	A06AB08
		Senna glycosides	A06AB06
	Antidiarrheals, intestinal anti-inflammatory/antiinfective agents	Loperamide	A07DA03
		Racecadotril	A07XA04
	Drugs used in diabetes	Acarbose	A10BF01
		Glibenclamide	A10BB01
		Glimepiride	A10BB12
		Sitagliptin	A10BH01

**TABLE II** - Potentially Inappropriate Medications

ATC group	ATC subgroup	Medicine	ATC code	
B - Blood and blood-forming organs (10/129; 7.8%)	Antithrombotic agents	Acenocoumarol	B01AA07	
		Apixaban	B01AF02	
		Dabigatran etexilate	B01AE07	
		Dipyridamole	B01AC07	
		Rivaroxaban	B01AF01	
		Ticlopidine	B01AC05	
		Warfarin	B01AA03	
	Antianemic preparations	Ferrous gluconate	B03AA03	
		Ferrous succinate	B03AA06	
		Ferrous sulfate	B03AA07	
C - Cardiovascular system (17/129; 13.2%)	Cardiac therapy	Amiodarone	C01BD01	
		Digoxin	C01AA05	
		Ivabradine	C01EB17	
		Propafenone	C01BC03	
		Trimetazidine	C01EB15	
	Antihypertensives	Clonidine	C02AC01	
		Doxazosin	C02CA04	
		Methyldopa	C02AB01	
		Rilmenidine	C02AC06	
	Diuretics	Spirolactone	C03DA01	
	Peripheral vasodilators	Naftidrofuryl	C04AX21	
		Pentoxifylline	C04AD03	
	Beta blocking agents	Propranolol	C07AA05	
		Sotalol	C07AA07	
	Calcium channel blockers	Diltiazem	C08DB01	
		Nifedipine	C08CA05	
		Verapamil	C08DA01	
	G - Genito urinary system and sex hormones (3/129; 2.3%)	Urologicals	Trospium	G04BD09
			Flavoxate	G04BD02
			Oxybutynin	G04BD04
J - Antiinfectives for systemic use (2/129; 1.6%)	Antibacterials for systemic use	Nitrofurantoin	J01XE01	
		Ofloxacin	J01MA01	

**TABLE II** - Potentially Inappropriate Medications

ATC group	ATC subgroup	Medicine	ATC code
M - Musculoskeletal system (14/129; 10.9%)	Anti-inflammatory and antirheumatic products	Aceclofenac	M01AB16
		Mefenamic acid	M01AG01
		Celecoxib	M01AH01
		Diclofenac	M01AB05
		Ibuprofen	M01AE01
		Meloxicam	M01AC06
		Naproxen	M01AE02
		Nimesulide	M01AX17
		Piroxicam	M01AC01
	Musculoskeletal system: muscle relaxants	Baclofen	M03BX01
		Cyclobenzaprine	M03BX08
		Tizanidine	M03BX02
	Antigout preparations	Colchicine	M04AC01
	Drugs for the treatment of bone diseases	Strontium ranelate	M05BX03
N - Nervous system (54/129; 41.9%)	Analgesics	Acetylsalicylic acid	N02BA01
		Tramadol	N02AX02
		Zolmitriptan	N02CC03
	Antiepileptics	Carbamazepine	N03AF01
		Clonazepam	N03AE01
		Phenytoin	N03AB02
		Phenobarbital	N03AA02
		Topiramate	N03AX11
	Anti-parkinson drugs	Amantadine	N04BB01
		Biperiden	N04AA02
		Bromocriptine	N04BC01
		Dihydroergocryptine mesylate	N04BC03
		Piribedil	N04BC08
		Pramipexole	N04BC05
		Ropinirole	N04BC04
		Rotigotine	N04BC09
		Selegiline	N04BD01
Trihexyphenidyl		N04AA01	

**TABLE II** - Potentially Inappropriate Medications

ATC group	ATC subgroup	Medicine	ATC code
N - Nervous system (54/129; 41.9%)	Psycholeptics	Alprazolam	N05BA12
		Aripiprazole	N05AX12
		Bromazepam	N05BA08
		Brotizolam	N05CD09
		Cyamemazine	N05AA06
		Clobazam	N05BA09
		Potassium clorazepate	N05BA05
		Chlorpromazine	N05AA01
		Cloxazolam	N05BA22
		Clozapine	N05AH02
		Diazepam	N05BA01
		Estazolam	N05CD04
		Fluphenazine	N05AB02
		Flurazepam	N05CD01
		Haloperidol	N05AD01
		Hydroxyzine	N05BB01
		Levomepromazine	N05AA02
		Lithium	N05AN01
		Ethyl loflazepate	N05BA18
		Lorazepam	N05BA06
		Midazolam	N05CD08
		Olanzapine	N05AH03
		Oxazepam	N05BA04
		Risperidone	N05AX08
		Ziprasidone	N05AE04
		Zolpidem	N05CF02
		Amitriptyline	N06AA09
		Bupropion	N06AX12
		Clomipramine	N06AA04
		Dosulepin	N06AA16
Fluoxetine	N06AB03		
Fluvoxamine	N06AB08		
Methylphenidate	N06BA04		

**TABLE II** - Potentially Inappropriate Medications

ATC group	ATC subgroup	Medicine	ATC code
N - Nervous system (54/129; 41.9%)	Psychoanaleptics	Nortriptyline	N06AA10
		Paroxetine	N06AB05
		Venlafaxine	N06AX16
R - Respiratory system (4/129; 3.1%)	Drugs for obstructive airway diseases	Theophylline	R03DA04
	Cough and cold preparations	Codeine	R05DA04
		Dimetindene	R06AB03
	Antihistamines for systemic use	Ebastine	R06AX22

## DISCUSSION

Despite not only targeted at aged people, the most frequent patients assisted at the National Network of Long-Term Care are the elderly, and “management of therapeutical regimen” is a common reason for admission (Ministério da Saúde and ACSS 2021). Additionally, *i*) the under-representation of geriatric populations in clinical trials during medicines development (van Marum, 2020); *ii*) the age-related pharmacokinetics and pharmacodynamics changes (McLean, Le Couteur, 2004); *iii*) as well as the extensively reported increase of multimorbidity, polypharmacy and pharmacotherapy complexity with aging (Nobili, Garattini, Mannucci, 2011; Nunes *et al.*, 2016), explain the highest rates of Adverse Drug Events among the elderly. Thus, this research can improve prescribing quality in this population by addressing the identification of PIMs in geriatric sub-populations from real-world data (i.e., medicines formularies).

The reasoning for the selection of the explicit criteria employed was based on evidence adapted to the reality of the national network, that is, the “Poudel’s criteria” and the *EU(7)-PIM List* were selected from a consensus-based study developed in the context of the NNLTC, and which also included hospital pharmacists as participants (Gonçalves *et al.*, 2021b); the latter criteria were developed in Europe and recently adapted to the national context (Rodrigues *et al.*, 2020). Employing “Poudel’s criteria” identified 43 PIMs, while the *EU(7)-PIM list* identified 126 PIMs, with only 3 PIMs uniquely identified by “Poudel’s criteria”

(fluphenazine, methyldopa, and warfarin). This fact may indicate that, in future research, the *EU(7)-PIM List* can be used as the only assessment tool. Furthermore, given the commonly identified constraints in LTC pharmacy practice - e.g., lack of time and/or human resources (Gonçalves *et al.*, 2021b) the *EU(7)-PIM list* seems better positioned to be used as the only assessment tool given the difficulties in using multiple tools in daily practice. The list of 129 PIMs summarised in Table II comprehends medicines whose classification as a PIM varies. Some PIMs classifications are dose-dependent (e.g., iron doses > 325mg), duration-dependent (e.g., proton pump inhibitors > 8 weeks), or due to lack of proven efficacy (e.g., acarbose); thus, the prevalence of PIMs identified in our sample (29.4%) should be analyzed carefully within the patient-centered approach of medicine usage. Moreover, clinical reasoning may justify the use of some medicines classified as PIMs for specific clinical cases, such as, when medicines of first choice have proven to be ineffective, when the alternative is not available or in off-label use, a common practice in LTC and palliative care (Hagemann, Bausewein, Remi, 2019; Jackson, Jansen, Mangoni, 2012). The list of PIMs identified should flag medicines that might negatively impact patients’ safety. Indeed, both the “Poudel’s criteria” and the *EU(7)-PIM list* include reasons for considering medication as potentially inappropriate, with the *EU(7)-PIM list* also presenting clinical recommendations and alternatives medication and/or/therapies. For these reasons, our findings can be valuable to clinical practice not only because they allow identifying PIMs, but also because the prescribing-assessment tools

employed can support and facilitate daily clinical-decision making within interprofessional work.

A systematic review identified the Alimentary tract and metabolism, the Cardiovascular system, and the Nervous system ATC groups as those more frequently associated with Drug-Related Problems or involved in medication management interventions by pharmacists in LTC settings (Gonçalves *et al.*, 2021a). Alongside the Musculoskeletal system ATC group, the medicines included in these four ATC groups comprised the most PIMs identified in our study. This evidence can help develop tailored strategies for improved medicine usage in the NNLTC inpatient settings for prescribers, pharmacists, other healthcare professionals, and policy-makers. Additionally, this work allowed us to map the most common medicines used in Long-Term Care. Formularies provide “improved patient care at decreased cost through improved selection and rational medicine use” (Management Sciences for Health and World Health Organization, 2007). Medicines formularies and Pharmacy & Therapeutic (P&T) committees seem to positively impact cost containment and influence prescribing (Godman *et al.*, 2011; Larsen *et al.*, 2014; de Vries *et al.*, 2008). The national recommendations for the usage of medicines in the NNLTC are dated from 2011. This work may represent a starting point toward developing national policies to enhance medicine usage in the NNLTC, such as creating a national P&T committee for LTC and an updated national MF to address the heterogeneity identified. Through a P&T committee or similar structure, supplemented with solid guideline development methods, consensual alternatives to PIMs could be reached, increasing the clinical practice applicability of our findings. Hospital pharmacists have a broad experience in P&T committees participation, and the similarities between LTC and hospital settings are high - for instance, hospital pharmacy recommendations extensively frame Long-Term Care pharmacy practice. Therefore, hospital pharmacists can play an essential role in assisting and developing a national P&T committee and an updated national formulary.

Despite belonging to the same nationwide network, LTCFs from where formularies were sampled can assist patients with different profiles (e.g., physical rehabilitation

specialized LTCFs vs. cognitive diseases specialized LTCFs). Nonetheless, the heterogeneity of the studied sample - e.g., the minimum and maximum number of medicines per formulary varies between 512 to 177, respectively; and the similarity between national recommendations and LTCF's formularies ranges from 82% to 54% - suggests the need for a national harmonization in medicines usage adjusted to this level of care. For particular ATC groups - *Alimentary tract and metabolism* and *Respiratory system* - similarities range between 58% to 68%, maximum. On the other hand, excluding sex hormones and insulins groups, the similarity between formularies is 100% for the systemic hormonal preparations. For other relevant groups - *Nervous systems, Blood and blood-forming organs*, and *Cardiovascular system* - heterogeneity is also worth mentioning, not only compared to national and regional recommendations but also among LTCF's formularies.

Medicines for *Antiinfectives for systemic use* - a frequent group of medicines used in LTC contexts (Jump *et al.*, 2018) - similarities are around 100% between formularies, which can be explained by the extensive awareness campaigns and interventions on antibiotics management and consequent alignment of prescribing patterns by physicians.

According to the World Health Organization, *p(ersonal)-drugs* “are the drugs you have chosen to prescribe regularly, and with which you have become familiar” (de Vries *et al.*, 1994). Baker *et al.* (2011) stated that the “identification of ‘commonly-prescribed drugs’ to support prescribing training has proved controversial”. Therefore, further interventions aiming to improve prescribing practices at LTC levels through the set of medicines used daily should be delivered, taking prescribers' preferences and behaviors into account. Evidence gathered here could work as a starting point to reach a national consensus on the most suitable medicines to use in LTC patients, raise awareness of medicines used in older patients, and assist in pharmacotherapy training.

Further research should increase formularies sample enrollment and investigate relationships between the presence of pharmacists, the profile of patients assisted, formularies heterogeneity, and suitability to elderly sub-populations of the National Network of Long-Term Care.

Although the sample encompasses a substantial proportion of LTCFs and beds, an increase in MFs enrolment would better control for potential biases or confounders, considering the low rate response (out of 288 LTCFs contacted, 2 replied). Furthermore, only Portuguese lists were considered, hindering the generalization of our findings to other countries (i.e., medication market differences, different prescription profile, population).

Hospital pharmacists' experience and expertise would be of utmost importance to pursue these objectives.

## REFERENCES

- Baker E, Pryce Roberts A, Wilde K, Walton H, Suri S, Rull G, et al. Development of a core drug list towards improving prescribing education and reducing errors in the UK. *Br J Clin Pharmacol*. 2011 Feb;71(2):190–8.
- Drenth-van Maanen AC, Leendertse AJ, Jansen PAF, Knol W, Keijsers CJPW, Meulendijk MC, et al., The Systematic Tool to Reduce Inappropriate Prescribing (STRIP): Combining implicit and explicit prescribing tools to improve appropriate prescribing. *J Eval Clin Pract*. 2018 Apr 1;24(2):317–22.
- Fenstemacher PA. Long-Term Care Medicine: A Pocket Guide [Internet]. 1st ed. Fenstemacher PA, Winn P, editors. Humana Press; 2010. Available from: [www.springer.com/series/7633](http://www.springer.com/series/7633)
- Godman B, Sakshaug S, Berg C, Wettermark B, Haycox A. Combination of prescribing restrictions and policies to engineer low prices to reduce reimbursement costs. *Expert Rev Pharmacoecon Outcomes Res*. 2011 Feb;11(1):121–9.
- Gonçalves JR, Ramalhinho I, Sleath BL, Lopes MJ, Cavaco AM. Probing pharmacists' interventions in Long-Term Care: a systematic review. *Eur Geriatr Med*. 2021a Aug 1;12(4):673–93.
- Gonçalves JR, Sleath BL, Lopes MJ, Cavaco AM. Prescribing-Assessment Tools for Long-Term Care Pharmacy Practice: Reaching Consensus through a Modified RAND/UCLA Appropriateness Method. *Pharmacy* [Internet]. 2021b Dec 3;9(4):194. Available from: <https://www.mdpi.com/2226-4787/9/4/194>
- Hagemann V, Bausewein C, Remi C. Drug use beyond the licence in palliative care: A systematic review and narrative synthesis. *Palliat Med*. 2019 Jun 24;33(6):650–62.
- Jackson SHD, Jansen PAF, Mangoni AA. Off-Label Prescribing in Older Patients. *Drugs Aging*. 2012 Jun;29(6):427–34.
- Jump RLP, Crnich CJ, Mody L, Bradley SF, Nicolle LE, Yoshikawa TT. Infectious Diseases in Older Adults of Long-Term Care Facilities: Update on Approach to Diagnosis and Management. *J Am Geriatr Soc*. 2018 Apr 1;66(4):789–803.
- Kapoor A, Field T, Handler S, Fisher K, Saphirak C, Crawford S, et al. Characteristics of Long-Term Care Residents That Predict Adverse Events after Hospitalization. *J Am Geriatr Soc*. 2020 Nov 1;68(11):2551–7.
- Kaufmann CP, Tremp R, Hersberger KE, Lampert ML. Inappropriate prescribing: A systematic overview of published assessment tools. *Eur J Clin Pharmacol*. 2014. p. 1–11.
- Larsen MD, Schou M, Kristiansen AS, Hallas J. The influence of hospital drug formulary policies on the prescribing patterns of proton pump inhibitors in primary care. *Eur J Clin Pharmacol*. 2014;70(7):859–65.
- Management Sciences for Health and World Health Organization. Drug and Therapeutics Committee Training Course [Internet]. 2007. Available from: [www.msh.org/rpmlplus](http://www.msh.org/rpmlplus)
- van Marum RJ. Underrepresentation of the elderly in clinical trials, time for action. *Br J Clin Pharmacol*. 2020 Oct 1;86(10):2014–6.
- McLean AJ, Le Couteur DG. Aging biology and geriatric clinical pharmacology. *Pharmacol Rev*. 2004. p. 163–84.
- Mekonnen AB, Redley B, de Courten B, Manias E. Potentially inappropriate prescribing and its associations with health-related and system-related outcomes in hospitalised older adults: A systematic review and meta-analysis. *Br J Clin Pharmacol*. 2021 Nov 1;87(11):4150–72.
- Ministério da Saúde, ACSS. Monitorização da Rede Nacional de Cuidados Continuados Integrados (RNCCI) - 2020 [Internet]. 2020. Available from: <http://www.acss.min-saude.pt/2016/07/22/documentacao/>
- Ministério da Saúde, ACSS. Relatório de monitorizacao da RNCCI - 1º semestre 2021 [Internet]. 2021. Available from: <https://www.acss.min-saude.pt/category/cuidados-de-saude/continuados/?lang=pt>
- Ministério da Saúde, Ministério do Trabalho Solidariedade e Segurança Social. Decreto-Lei 101/2006. 101/2006 Portugal: Diário da República; Jun 6, 2006.
- Nobili A, Garattini S, Mannucci PM. Multiple diseases and polypharmacy in the elderly: challenges for the internist of the third millennium. *J Comorb*. 2011;1:28–44.
- Nunes BP, Flores TR, Mielke GI, Thumé E, Facchini LA. Multimorbidity and mortality in older adults: A systematic review and meta-analysis. *Arch Gerontol Geriatr*. 2016 Nov 1;67:130–8.

- O'Connor MN, Gallagher P, O'Mahony D. Inappropriate Prescribing Criteria, Detection and Prevention. *Drugs Aging*. 2012;29(6):437–52.
- Onder G, van der cammen TJM, Petrovic M, Somers A, Rajkumar C. Strategies to reduce the risk of iatrogenic illness in complex older adults. *Age Ageing*. 2013. p. 284–91.
- Parrish R. What Is a Formulary, Anyway? Part 2. *Pharmacy (Basel)*. 2018 Jul 23;6(3):72.
- Poudel A, Balloková A, Hubbard RE, Gray LC, Mitchell CA, Nissen LM, et al. Algorithm of medication review in frail older people: Focus on minimizing the use of high-risk medications. *Geriatr Gerontol Int*. 2016 Sep 1;16(9):1002–13.
- Puigventós Latorre F, Santos-Ramos B, Ortega Eslava A, Durán-García ME. Variability in Activity and Results From Drug Assessments by Pharmacy and Therapeutics Committees in Spanish Hospitals. *Farmacia Hospitalaria (English Edition)*. 2011 Nov;35(6):305–14.
- Rankin A, Cadogan CA, Patterson SM, Kerse N, Cardwell CR, Bradley MC, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database of Systematic Reviews*. 2018 Sep 3;2018(9).
- 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 Jul 13;71(7):861–75.
- Rodrigues DA, Herdeiro MT, Thurmann PA, Figueiras A, Coutinho P, Roque F. Operationalisation for portugal of the EU(7)-PIM list for identification of potentially inappropriate medicines in older adults. *Acta Med Port*. 2020;33(13).
- Schiff GD, Galanter WL, Duhig J, Koronkowski MJ, Lodolce AE, Pontikes P, et al. A prescription for improving drug formulary decision making. *PLoS Med*. 2012 May;9(5).
- Sofat R, Cremers S, Ferner RE. Drug and therapeutics committees as guardians of safe and rational medicines use. *Br J Clin Pharmacol*. 2020 Jan 1;86(1):10–2.
- Tyler LS, Cole SW, May JR, Miliare M, Valentino MA, Vermeulen LC, et al. ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System. *Am J Health-Syst Pharm*. 2008 Jul 1;65(13):1272–83.
- de Vries TPGM, Daniels JMA, Mulder CW, Groot OA, Wewerinke L, Barnes KI, et al. Should medical students learn to develop a personal formulary? An international, multicentre, randomised controlled study. *Eur J Clin Pharmacol*. 2008 Jun;64(6):641–6.
- de Vries TPGM, Henning RH, Hogerzeil HV, Fresle DA, Haaijer-Ruskamp M, van Gilst RM. Guide to good prescribing - a practical manual [Internet]. Geneva; 1994. Available from: <https://apps.who.int/iris/handle/10665/59001>
- Wang KN, Bell JS, Chen EYH, Gilmartin-Thomas JFM, Ilomäki J. Medications and Prescribing Patterns as Factors Associated with Hospitalizations from Long-Term Care Facilities: A Systematic Review. *Drugs Aging*. 2018 May 1;35(5):423–57.
- World Health Organization. Towards an international consensus on policy for long-term care of the ageing [Internet]. WHO. 2000. Available from: <https://apps.who.int/iris/handle/10665/66339>
- World Health Organization. World Health Organization Model List of Essential Medicines - 22nd List [Internet]. World Health Organization. 2021. Available from: <https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02>
- World Health Organization. WHOCC - ATC/DDD Index. 2022.

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