Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal
Versão Final - Pós-Defesa

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Tese para obtenção do Grau de Doutor em
Medicina
(3º ciclo de estudos)

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dezembro de 2020

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Edital

As provas decorreram na Universidade da Beira Interior no dia 25 de novembro de 2020 pelas 14 horas.

O júri das provas foi constituído pela Doutora Maria da Assunção Morais e Cunha Vaz Patto, professora associada da Universidade da Beira Interior, Doutor Carlos Manuel da Silva Martins, professor auxiliar da Faculdade de Medicina da Universidade do Porto, Doutor Bruno Miguel Costa Heleno, professor auxiliar da NOVA Medical School da Universidade Nova de Lisboa, Doutora Marta Dora Feitas Ornelas, professora auxiliar da Faculdade de Ciências da Vida da Universidade da Madeira, Doutora Paula Maria Broeiro Gonçalves, professora auxiliar da Faculdade de Medicina da Universidade de Lisboa.

Acknowledgments

This journey made meet, work and learn from extraordinary people. The majority were related to scientific research, which helped me to have a critical view of science and inspired me to follow this challenge and this line of research. My sincere thanks go to:

- My PhD supervisors, Prof. Doutor Luiz Miguel Santiago and Prof. Doutor José Augusto Simões, for all the guidance and support to improve my scientific skills and to complete this journey;

- All elements of family health unit Pulsar, namely to my GP trainer, Dra. Teresa Pascoal, for all the support and time flexibility that made it possible to conciliate the GP internship and the PhD development;

- The colleagues, their patients, and Serviços Partilhados do Minstério da Saúde who collaborated in this work, for contributing with their time and understanding the purpose of this clinical research;

- My friends who supported me in this challenge, namely at leisure time, and gave the motivation to continue;

- My friends who also started their PhD with whom I shared the difficulties and challenges of conciliating the medical internship and the PhD, and we found strategy to overcome them;

- My family for all the support and motivation they gave me, especially my parents for everything they taught me and for the safe harbour they represent, and to my brother for the brainstorms and discussions about the work and for what he represents to me.

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Abstract

Drug use in older adults' patients (≥65 years) is extensive, increases substantially with age, and is associated with many adverse outcomes. Polypharmacy is commonly defined as taking 5 or more medications daily and affects between 30 and 70% of older adults. Potentially inappropriate medication (PIM) refers to medication of which the harms outweigh the benefits, and its prevalence is 20 to 65%. Several strategies have been developed to identify inappropriate prescription patterns, the most common are Beers and STOPP/START criteria. Deprescription is a systematic process to of identifying and discontinuing drugs that are not beneficial or are not aligned with the patient's care goal. Many deprescribing processes have been proposed, but none is widely used. This thesis aims to assess the knowledge of older adults about the deprescription, its effect on willingness to have regular medications deprescribed and their quality of life outcome.

To achieve these objectives, we proposed to divide the project into three phases. The first two would be cross-sectional studies carried out at the national level and the last a non-pharmacological random clinical trial in the centre region of Portugal. Of the three phases, we have completed only the first two, the last has been postponed. In the first phase, we assessed the prevalence and patterns of polypharmacy and PIM in the Portuguese older adult population. In the second phase, we evaluated the barriers and facilitators of deprescribing perceived by Portuguese polymedicated older adults and their willingness to have regular medications deprescribed and to self-medicate.

In the first study, we found that 77% of the sample had polypharmacy and 68.6% used at least one PIM. The likelihood of having polypharmacy increased with age, number of chronic health problems and number of prescribers; and the likelihood of having PIM increased with being female, number of chronic health problems, number of drugs and number of prescribers. The most common PIM were proton-pump inhibitors, nonsteroidal anti-inflammatory drugs, and benzodiazepines. In the second study, we found that 74% of the sample believed that drugs were generally beneficial. However, 19.9% indicated a high belief that drugs were harmful and 33.4% that they were generally overused. We also found that 61.8% were against the idea of deprescribing (against 24.6% who were in favour) and that 40% had a need to self-medicate. Those against being deprescribed had lower education level and a higher number of perceived morbidities than those not against being deprescribed; and the need to self-medication

was associated with higher formal education, lower feeling of overuse of medication by doctors and a lower belief that medicines are harmful.

Our results show that polypharmacy and PIM are very common occurrence in Portugal; and that most Portuguese older adults see mediation as beneficial and, therefore, are against the idea of being subject to deprescription. Self-medication is also common. These results will increase general practitioners, society and policy makers awareness for these problems and help them to better start addressing them. However, more research is needed to clarify the impact of deprescribing process in the Portuguese population health and well-being or, alternatively, to improve the process of prescription drugs, avoiding their excess.

Keywords

Polypharmacy; Potentially Inappropriate Medication; Aged; Deprescriptions; Self-Medication; Patient Acceptance of Health Care

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Resumo

O consumo de medicamentos pelos idosos (≥65 anos) é elevado, aumenta substancialmente com a idade e está associado a muitos efeitos adversos. A polifarmácia é comumente definida como a toma diária de 5 ou mais medicamentos e afeta entre 30 e 70% dos idosos. Os medicamentos potencialmente inapropriados (MPI) referem-se a medicamentos cujos malefícios são superiores aos benefícios e ocorre em 20 a 65% dos idosos. Várias estratégias foram desenvolvidas para identificar padrões de prescrição inadequada, sendo os mais comuns os critérios de Beers e STOPP/START. A desprescrição é um processo sistemático de identificação e descontinuação de medicamentos que não são benéficos ou não estão alinhados com os objetivos de saúde do paciente. Muitos processos de desprescrição foram propostos, mas nenhum é amplamente utilizado. Esta tese teve como objetivo avaliar o conhecimento dos idosos acerca da desprescrição e o seu efeito sobre a vontade de ter medicação habitual desprescrita e na qualidade de vida.

Para alcançar os objetivos propostos foi proposto a divisão do projeto em três fases, as duas primeiras seriam estudos transversais de âmbito nacional e a última um ensaio clínico randomizado não farmacológico. Das três fases apenas as duas primeiras foram realizadas, tendo sido a última adiada. Na primeira fase avaliámos a prevalência e os padrões da polifarmácia e MPI na população idosa portuguesa. Na segunda fase avaliámos as barreiras e facilitadores da desprescrição percecionados pelos idosos portugueses polimedicados e a sua vontade de ter medicação habitual desprescrita e de se automedicar.

No primeiro estudo encontrámos que 77% da amostra apresentava polifarmácia e 68,6% apresentavam pelo menos um MPI. A probabilidade de ter polifarmácia aumentou com a idade, número de doenças crónicas e número de prescritores e a de ter MPI aumentou com o ser do género feminino, com o número de problemas crónicos de saúde, o número de medicamentos prescritos e o número de prescritores. Os MPI mais comuns foram os inibidores da bomba de protões, os anti-inflamatórios não esteroides e as benzodiazepinas. No segundo estudo encontrámos que 74% da amostra acreditava que os medicamentos eram geralmente benéficos. No entanto, 19,9% indicaram uma grande crença de que os medicamentos eram prejudiciais e 33,4% de que eram usados em excesso. Também descobrimos que 61,8% eram contra a ideia de serem sujeitos a desprescrição (contra 24,6% que eram a favor) e que 40% tinham necessidade de se

automedicar. Os que eram contra a desprescrição tinham menor nível de escolaridade e maior número de doenças crónicas percecionadas do que aqueles que não eram contra a desprescrição; e a necessidade de automedicação estava associada a uma maior educação formal, uma menor crença de uso excessivo de medicamentos pelos médicos e a uma menor crença de que os medicamentos são prejudiciais.

Os nossos resultados revelam que a polifarmácia e a MPI são muito comuns em Portugal; e que a maioria dos idosos portugueses vê a mediação como benéfica e, portanto, é contra a ideia de ser sujeito a desprescrição. A automedicação também é frequente. Estes resultados aumentarão a consciencialização dos médicos de família, da sociedade e dos agentes políticos acerca destes problemas e ajudá-los-ão a começar a resolvê-los melhor. No entanto, são necessários mais estudos para esclarecer o impacto do processo de desprescrição na saúde e bem-estar da população portuguesa, ou em alternativa melhorar o processo de prescrição de medicamentos evitando o seu excesso.

Palavras-chave

Polifarmácia; Medicamento Potencialmente Inapropriado; Idoso; Desprescrição; Automedicação; Aceitação de Cuidados de Saúde pelo Paciente

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Resumo Alargado

O número de idosos (≥65 anos) tem vindo a aumentar rapidamente em todo o mundo. A prevalência das doenças aumenta exponencialmente com o avançar da idade, pelo que o consumo de medicamentos por esta faixa etária é elevado e aumenta substancialmente com a idade.

A polifarmácia é comummente definida como a toma diária de 5 ou mais medicamentos. Contudo, não existe uma definição internacional aceite havendo inúmeras propostas de definições numéricas e descritivas para a polifarmácia. A sua prevalência varia entre 30 e 70% dos idosos. A polifarmácia está comummente associada a medicação potencialmente inapropriada (MPI) que são os medicamentos cujos malefícios são superiores aos benefícios, principalmente os que não estão indicados ou para os quais não há evidência da sua eficácia, a duplicação de medicação, as interações medicamentosas, os medicamentos usados para tratar efeitos adversos de outros medicamentos e aqueles que não estão alinhados com os objetivos terapêuticos preferências e valores do paciente. Estima-se que 20 a 65% dos idosos tomem pelo menos um MPI.

Várias estratégias foram desenvolvidas para identificar padrões de prescrição inadequada. Estes são divididos em critérios implícitos (envolvem o julgamento clínico baseado em revisões da literatura médica) e/ou explícitos (baseados em listas de medicamentos a evitar criadas consensualmente). As ferramentas mais conhecidas são os critérios de Beers e STOPP/START.

O conceito de desprescrição como intervenção terapêutica é relativamente novo e consiste em identificar e descontinuar medicamentos que não são benéficos ou não estão alinhados com os objetivos de saúde do paciente. Muitos processos de desprescrição foram propostos, mas nenhum é amplamente utilizado.

Esta tese tem como objetivos gerais avaliar o conhecimento dos idosos acerca da desprescrição e o seu efeito sobre a vontade de ter medicação habitual desprescrita e na qualidade de vida.

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Para alcançar os objetivos propostos foi proposto a divisão do projeto em três fases, as duas primeiras seriam estudos transversais de âmbito nacional e a última um ensaio clínico randomizado não farmacológico, com os seguintes objetivos específicos:

- Identificar a prevalência da polifarmácia nos idosos em Portugal;
- Avaliar a proporção de MPI nos idosos em Portugal;
- Descrever os perfis sociodemográficos e clínicos dos idosos com polifarmácia em Portugal;
- Identificar as principais barreiras e facilitadores da desprescrição nos idosos portugueses;
- Avaliar a vontade dos idosos portugueses em terem medicação habitual desprescrita;
- Correlacionar a automedicação com a vontade em terem medicação habitual desprescrita;
- Avaliar o efeito na qualidade de vida após ter medicação habitual desprescrita;
- Elaborar e validar um fluxograma com o processo de desprescrição sob a perspetiva do paciente.

Das três fases apenas as duas primeiras foram realizadas, tenda última sido adiada. Foram então realizados dois estudos transversais de âmbito nacional.

Na primeira fase avaliámos a prevalência e os padrões da polifarmácia e MPI na população idosa portuguesa, com base numa amostra de 757 pacientes idosos randomizados com distribuição geográfica similar à distribuição geográfica da população idosa portuguesa. A amostra relativa às cinco administrações regionais de saúde foi-nos fornecida pelos Serviços Partilhados do Ministério da Saúde, enquanto a amostra relativa às duas regiões autónomas foi-nos fornecida por duas médicas de Medicina Geral e Familiar, uma de cada região autónoma. Obtivemos dados sociodemográficos (idade, género, área de residência), clínicos (morbilidades) e medicamentosos (medicação prescrita nos últimos 12 meses).

Na segunda fase avaliámos as barreiras e facilitadores da desprescrição percecionados pelos idosos portugueses polimedicados e a sua vontade de ter medicação habitual desprescrita e de se automedicar. Para isso obtivemos uma amostra de 386 pacientes idosos polimedicados a quem foi entregue um questionário para preenchimento. Obtivemos com o questionário dados sociodemográficos (idade, género, área de residência, nível de educação formal), auto-reporte do número de doenças crónicas e do número de medicamentos usados. No questionário também aplicámos a versão

portuguesa do "Beliefs about Medicines Questionnarie-General"; alguns pacientes aleatoriamente selecionados também responderem ao "Beliefs about Medicines Questionnaire-Specific". Por fim, o questionário também tinha uma questão de resposta aberta "O que acha de parar medicação que habitualmente toma?", uma escala visual analógica para quantificação da vontade em automedicar-se, bem como espaço para a justificação da pontuação dada.

Na fase I obtivemos uma amostra de 757 idosos com uma média de idade de 75,5 (±7,9) anos, 56,8% do género feminino e a tomar uma média de 8,2 (IC 95% 7,9 a 8,6) medicamentos por dia. Quase a totalidade (93,4%) da amostra tomava pelo menos um medicamento e 77% tomava cinco ou mais; 68,6% tomavam pelo menos um MPI e 46,1% tomavam dois ou mais MPIs. A probabilidade de ter polifarmácia aumentou com a idade [OR=1,05 (1,02-1,08)]], número de doenças crónicas [OR=1,24 (1,07-1,45)] e número de prescritores [OR=4,71 (3,42-6,48)]. Enquanto a probabilidade de ter MPI aumentou com o ser mulher [OR=1,56 (1,05-2,31)], número de doenças crónicas [OR=1,06 (1,01-1,13)], número de medicamentos [OR=1,40 (1,30-1,51)] e número de prescritores [OR=1,34 (1,09-1,65)]. Os medicamentos mais comumente envolvidos na polifarmácia foram os medicamentos cardiovasculares, metabólicos e musculosqueléticos. Já relativamente aos MPIs, os mais comumente encontrados foram os inibidores da bomba de protões, os anti-inflamatórios não esteroides e as benzodiazepinas.

Na fase II obtivemos uma amostra de 386 idosos polimedicados com uma idade média de 76,7 (±7,3) anos, 59,6% do género feminino e a tomar uma média de 7,3 (IC 95% 7,1 a 7,6) medicamentos por dia. Destes apenas 298 (77,2%) responderam à escala visual analógica e justificaram a sua resposta; 293 (75,9%) responderam à questão aberta; e 100 (25,9%) responderam à versão longa do questionário com o "Beliefs about Medicines Questionnarie-Specific". A maioria dos participantes (74%) acreditava que os medicamentos eram geralmente benéficos. No entanto, 19,9% indicaram uma grande crença de que os medicamentos eram prejudiciais e 33,4% de que eram usados em excesso. Dos que responderam à questão aberta (n=293) 61,8% eram contra a ideia de serem sujeitos a desprescrição, sendo os principais motivos a perceção de que se parassem a medicação a sua situação médica iria piorar e o valor que davam aos medicamentos; 24,6% estiveram a favor da desprescrição, sendo as principais razões "se fosse recomendado pelo médico" e "se o medicamento causasse efeitos adversos ou fosse ineficaz". Os que eram contra a ideia da desprescrição apresentavam menor nível

educacional (p=0,006) e maior número de doenças auto-relatadas (p=0,001) que os que não eram contra a ideia. Dos que responderam à escala visual analógica para quantificação da vontade em automedicar-se, 40% da amostra demonstrou ter vontade em fazê-lo, sendo as principais razões a "replicação de conselhos médicos anteriores" e a "perceção de autoconhecimento". A vontade em automedicar-se associava-se a maior educação formal, uma menor crença de uso excessivo de medicamentos pelos médicos e a uma menor crença de que os medicamentos são prejudiciais.

Os nossos resultados dos trabalhos desenvolvidos no âmbito desta tese revelam que:

- A polifarmácia e MPI são muito comuns em Portugal;
- A maioria dos idosos portugueses vê a mediação como benéfica o que pode explicar o elevado número de medicamentos consumidos por esta população, bem como o estarem contra a ideia de serem sujeitos a desprescrição;
- Existe uma importante vontade em automedicar-se.

Estes resultados aumentarão a consciencialização dos médicos de família, da sociedade e dos agentes políticos acerca destes problemas e ajudá-los-ão a começar a resolvê-los melhor.

Medidas como:

- Melhor ensino médico, quer pré quer pós-graduado, com atribuição de maior importância para estas temáticas e de como abordá-las com os pacientes;
- Organização do sistema de saúde com a necessidade de todos terem um médico coordenador (onde o médico de família se encontra em melhor posição), para que este avalie com o paciente quais são os objetivos a atingir e protegê-lo de cuidados médicos inapropriados (prevenção quaternária);
- Implementação de farmácias comunitárias com uma interação mais próxima dos médicos de família;
- Aumento da literacia em saúde;
- Consciencialização sobre a problemática da medicação potencialmente inapropriada, com vista à redução da automedicação inapropriada, principalmente os suplementos alimentares;
- Mudança de mentalidade no sentido de que a prevenção a todo o custo (com medicação e rastreio) é boa para a necessidade de se prevenir o

sobrediagnóstico, a sobre-medicalização e a medicação potencialmente inapropriada.

São, apesar de tudo, necessários mais estudos para esclarecer o impacto do processo de desprescrição na saúde e bem-estar da população portuguesa, podendo em alternativa colocar-se a questão do porquê desprescrever em vez de medicar melhor.

Palavras-chave

Polifarmácia; Medicamento Potencialmente Inapropriado; Idoso; Desprescrição; Automedicação; Aceitação de Cuidados de Saúde pelo Paciente

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List of Abbreviations

ACE	Angiotensin-converting enzime
ADR	Adverse Drug Reactions
ARB	Angiotensin II Receptor Blocker
ATC	Anatomical Therapeutic Chemical
BMQ	Beliefs about Medicines Questionnaire
CI	Confidence Interval
EQ-5D	QueroQol Five Dimensions Questionnaire
GP	General Practitioner
ICPC-2	International Classification of Primary Care, second edition
INFARMED	Instituto Nacional da Farmácia e do Medicamento
LESS-CHRON	List of Evidence-baSed deprescribing for CHRONic patients
MAI	Medication Appropriateness Index
NHANES	National Health and Nutrition Examination Survey
OR	Odds Ratio
OTC	Over-the-counter
PATD	Patients' Attitudes Towards Deprescribing
PEM	Prescrição Eletrónica de Medicamentos
PIM	Potentially Inappropriate Medication
PPI	Pump-Proton Inhibitor
RCT	Random Clinical Trial
ROC	Receiver Operating Characteristics
SPMS	Serviços Partilhados do Ministério de Saúde
SPSS	Statistical Package for the Social Sciences
START	Screening Tool to Alert doctors to Right Treatment
STOPP	Screening Tool of Older Persons' Prescriptions
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

CHAPTER ONE

General Introduction

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

General Introduction

1.1 Evolution of prescriptions

The number of the elderly is increasing rapidly in the entire world. Conventionally, "elderly" has been defined most often by a chronological age of 65 years or older because there is so far no biological age marker. Since 1950 the proportion of older people has been steadily rising, starting from just under 15% in 1950 to 28% in 2017, and it is expected to reach 38% in 2050 (1). Advances in medical practice and drug development have mainly contributed to the increased life expectancy. Since elderly individuals are living longer, more patients are getting older and with more co-morbidities, more medications and possibly no better quality of life. The number of aged patients above 79 years is currently increasing at a rate of 3.9% per year and its number is projected to triple between 2017 and 2050 (1).

The prevalence of diseases increases exponentially with advanced age. Ageing is therefore considered to be a major risk factor for many disorders in developed countries (2), with the proportion of elderly using at least one medication daily ranging from 85 to 90% (3,4). Hovstadius et al. (5) found that prevalence of dispensed drugs ≥1 in Sweden was 57.3% in the age group 0-9, 49% in the age group 10-19 and the highest prevalence (94.5%) was found in the age group 80-89. Multimorbidity, commonly defined as the co-existence of two or more chronic health conditions, is common in the older population (6) and its presence increases the complexity of therapeutic management for both health professionals and patients, and impacts negatively on health outcomes, namely decreased quality of life, self-rated health, mobility and functional ability as well as increases in hospitalisations, physiological distress, use of health care resources, mortality and costs (7–9).

The use of drugs in older patients is extensive and increases substantially with age. For example, the elderly constitute 13% of the United States population but receive 34% of all prescriptions and consume 40% of non-prescription medications (10). One recent large survey of community-dwelling subjects in the USA showed that more than 90% of individuals aged ≥65 years used at least one drug weekly, more than 40% used five or more drugs weekly and 12% used ten or more drugs weekly (11). In Portugal, there was an increase of around 75% in the number of drugs sold between 2003 and 2013 (12).

The total sale of drugs has increased successively during the last decades (5,13). The increase depends, among others, on the introduction of new medications and on new medical recommendations to treat morbidity in higher ages. Moreover, drugs are also used to prevent health-related disorders among healthy individuals (13,14). Based on weighted NHANES survey estimates (13), the median number of medications taken doubled from 2 to 4 between 1988 and 2010 and the number of the elderly taking ≥5 medications increased from 12.8% in 1988–1991

to 39.0% in 2009–2010, which was consistent across age and sex strata. The pharmacological subclasses that showed the biggest increase in use between 1988 and 2010 were statins (41.7%), antihypertensives (23.4%), proton pump inhibitors (18.0%), antidiabetic agents (10.3%) and antidepressants (10.0%). These increases were more expressive in the population aged ≥80 years (statins rose 45.6%, antihypertensives 28.6% and antidiabetic agents 10.5%).

The health burden of multimorbidity and the use and costs of drugs will continue to increase, driven by the growing number of the elderly with chronic diseases (15).

1.2 Definition of Polypharmacy and Potentially Inappropriate Medication

Polypharmacy is defined by the World Health Organisation as "the administration of many drugs at the same time or the administration of an excessive number of drugs" (16). This definition allows several accepted definitions of polypharmacy. The first part of the definition refers to the concurrent administration of medications and the word 'many' does not prejudge the excessive nature of this number. The terms "at the same time" provide a first indication regarding the temporal conditions under which polypharmacy is measured: medications that are administered simultaneously. The second part of the definition on the contrary indicates excess medication and implicitly introduces the notion of drug misuse. According to Portuguese law, "«medication» means any substance or combination of substances presented as having curative or preventive properties of diseases in humans or their symptoms or that can be used or administered to humans with a view to establishing a medical diagnosis or, exerting a pharmacological, immunological or metabolic action, to restore, correct or modify physiological functions" (17). In this case, polypharmacy refers to the administration of more drugs than clinically necessary (18), but do not consider the use of other substances, usually named as remedies (e.g. teas, alcohol, tobacco...).

Masnoon et al. (19) made a systematic review of polypharmacy definitions and found a total of 138 definitions of polypharmacy and associated terms used to define the level of polypharmacy, including minor, moderate, major, hyper, excessive, severe, appropriate, rational polypharmacy and indiscriminate prescribing, persistent, chronic and pseudopolypharmacy. There majority of all definitions (80.4%) were numerical only definitions, 10.9% were numerical definitions which incorporated a duration of therapy or healthcare setting and 8.7% were descriptive definitions.

1.2.1 Numerical only definitions of polypharmacy

Numerous thresholds have been identified in the literature regarding the number of medications above which polypharmacy is considered to exist (19–22).

The most commonly used definition for polypharmacy is ≥5 medications daily (19,23).

Certain authors even propose a more detailed segmentation of the threshold by using "5 to 7" and "8 and over" to take the increased risk into account (24). Steinman et al. (25) for example propose a threshold of 8 medications justified by the fact that below this number, the risk of under-use is greater than the risk of polypharmacy or inappropriate prescription. The reason for this is that many social factors, as the aging of the population over time and its educational level, can increases the burden of multimorbidity (26), therefore the threshold of "5 and over" can become unadjusted to the medical reality of that population in the future.

Some studies suggest using ROC curves (Receiver operating characteristics) of sensitivity and specificity so as to evaluate the threshold beyond which polypharmacy carries a serious health risk (27).

In table 1.2.1 are the associated terms used in the literature: minor is mainly defined as taking 2 to 4 medications; moderate is defined as 4 to 5 medications; major is mainly defined as ≥5 medications; hyper, excessive and severe are all defined as ≥10 medications (19,23,27).

Table 1.2.1 Various numerical only definitions of polypharmacy and associated terms in existing literature (19,23,27)

Term	Number of medications
Polypharmacy	≥2
	2 to 9
	≥3
	≥4
	≥5
	≥6
	≥7
	5 to 9
	≥9
	≥10
	≥11
Minor Polypharmacy	2 to 4
	2 to 3
	0 to 4
Moderate polypharmacy	4 to 5
Major polypharmacy	≥5
	≥6
	5 to 9
Hyperpolypharmacy	≥10
Excessive polypharmacy	≥10
Severe polypharmacy	≥10
Non-polypharmacy	<5
Oligopharmacy	≤5

1.2.2 Numerical definitions of polypharmacy incorporating a duration of therapy or healthcare setting

Unlike the previous one, these definitions incorporate a duration of therapy to their numerical definition (similar to the ones in the previous section) (19). The most common periods of time used was three-months (28–30).

Some definitions in this section also used a healthcare setting (e.g. at hospital discharge (31) or during hospital stay (32,33)) instead of a period of time.

1.2.3 Descriptive definitions of polypharmacy

These definitions use a descriptive definition instead of a numerical one (19). For example, polypharmacy can be defined as the use of "potentially inappropriate medications" (PIM) (22),

use of "medications which are not clinically indicated" (20) or "more drugs being prescribed or taken than are clinically appropriate in the context of a patient's comorbidities" (34).

Other terms used are appropriate polypharmacy, rational polypharmacy, indiscriminate prescribing or pseudopolypharmacy (patients being recorded as taking mor medications than they are actually taking (35)).

1.2.4 Appropriate and inappropriate polypharmacy

Some studies recognised the distinction between appropriate (or rational) medications and inappropriate medications (or indiscriminate prescribing) (19). These studies either defined polypharmacy using a brief description only or used a brief description and polypharmacy tools such as the Beers criteria and the Medication Appropriateness Index (MAI). An example of a polypharmacy definition which recognised the use of appropriate and inappropriate medications is "polypharmacy ranges from the use of a large number of medications, to the use of potentially inappropriate medications, medication underuse and duplication" (36). "Potentially inappropriate medications" refers to medication of which the harms outweigh the benefits, namely those that are not indicated or lack evidence of efficacy, duplication of medication, drug-drug interactions, medications used to treat adverse drug reactions of other medications and those that do not align with patients goals/preference and values (22,37). Some authors also used the term inappropriate medication prescription to classify underprescribing, misprescribing and overprescribing (38).

In a simplistic way, polypharmacy is said to be "appropriate" when the prescription of numerous medications is justified and "inappropriate" when wrongly or indiscriminately prescribed (39,40).

1.2.5 Time slots definitions of polypharmacy

There are three time slots definitions of polypharmacy found in the literature and they are simultaneous polypharmacy, cumulative polypharmacy and continuous polypharmacy (23).

Simultaneous polypharmacy corresponds to the number of drugs concurrently taken by a patient on a given day. This indicator allows the study of complex dosing regimens, the risk of drug interactions, the occurrence of polypharmacy episodes, their frequency and duration, and the identification of transitory factors that can increase the number of administered medications at a given time, such as hospitalisation or acute illnesses.

Cumulative polypharmacy is defined by the sum of different medications administered over a given period of time. The most common periods of time are three, six and twelve-month periods. The choice depends on the standard prescription renewal time. However, the longer the period of observation, the higher the prevalence of polypharmacy (5,41).

Continuous polypharmacy is similar to cumulative polypharmacy but limited to medications taken for prolonged and regular periods. It only considers medications present in two given time periods split by six months intervals. A variant of this indicator is to consider the medications for which prescription has been repeatedly renewed over the course of the year, usually with a frequency of three renewals per year (42,43).

The wide range of the prevalence of polypharmacy described in the literature can be due to the way the researcher assesses it. The prevalence of polypharmacy is higher when we use the cumulative polypharmacy, than with the continuous and simultaneous (being the lowest) polypharmacy (23).

In conclusion, the literature abounds with polypharmacy definitions, but there is no standard definition (44,45). Some studies suggest a shifting from the definitions based on the number of medications taken to notions such as the existence of drug interactions, inappropriate prescribing in relation to diagnosis, prescription of contraindicated medications and inappropriate dosages or treatment durations (22,34,46). In order to make this distinction between appropriate and inappropriate polypharmacy, the term polypharmacy needs to be clearly defined.

1.3 Prevalence and risk factors

In high-income countries, population-based surveys and cross-sectional studies have shown that polypharmacy (taking ≥5 drugs daily) affects between 30% and 70% of older adults (13,47,48). Several risk factors have been identified, such as aged ≥62 years, recent nursing home admission, number of health problems, number of prescribers, and frailty (49–52).

Recent studies have also suggested an inverted U-shaped association between age and number of drugs, with a pronounced decline in the burden of medications after the age of 85 years (53). Surprisingly little is known about incident polypharmacy, that is the development of polypharmacy over time (54–56). Patients who have no primary care physician to coordinate care or a single pharmacy to monitor current prescriptions may be particularly susceptible to these types of prescribing problems (51,52). Morin et al. (57) found an incidence rate of polypharmacy of 19.9 per 100 person-years, ranging from 16.8 per 100 person-years among people aged 65-74 years to 33.2 per 100 person-years among those aged ≥95 years (figure 1.3.1). They also found an overall incidence of excessive polypharmacy (taking ≥10 drugs daily) of 8.0 per 100 person-years.
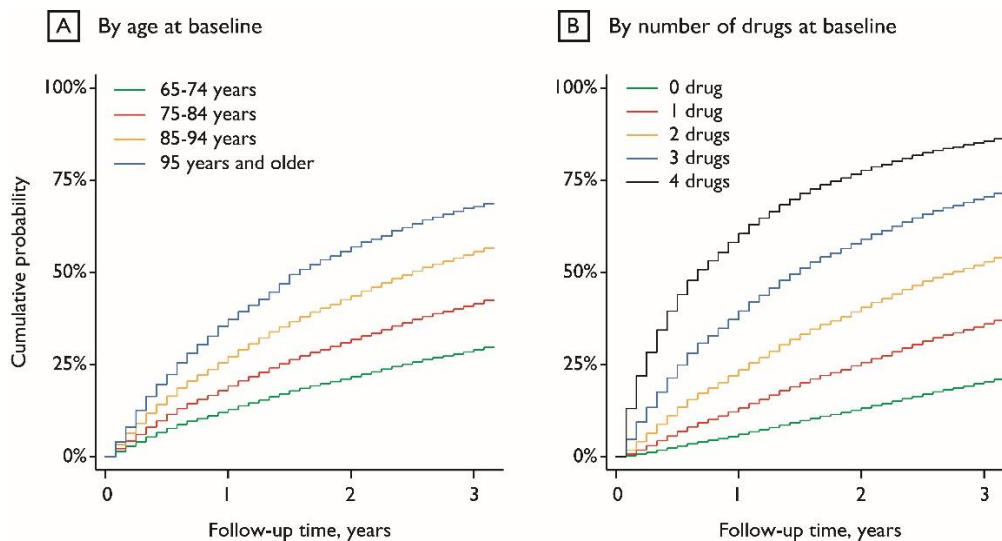
Figure 1.3.1 Cumulative incidence of polypharmacy (≥5 drugs) during follow-up. Adapted from Morin et al. (57)

The literature describes many risk factors for polypharmacy. They can be compiled in different groups: patient-related, physician-related and health care system-related (49,58,59).

The ones related with patients are:

- Increased age;
- Disability (cognitive impairment and developmental disability);
- Health status (frailty, mental health conditions, multiple chronic conditions);
- Lack of support from family or friends;
- Residing in a long-term care facility;
- Patient self-medication;
- Lacking a primary care physician;
- Access to health care (increased number of health care visits, multiple providers, type of insurance).

The ones related with physicians are:

- Medical guidelines
- Prescribing habits
- Behaviour (no proper medical review or lack of communication with patient)

The ones related with health care system are:

- Poor medical record keeping
- Poor transitions of care
- Prescribing to meet disease-specific quality metrics
- Increased use of preventive strategies
- Use of automated refill systems

Available data indicate that 20–65% of older adults are taking at least one PIM, leading to a high risk of adverse drug reactions, morbidity and mortality (37,60–62).

Whether a prescribed medication is appropriate depends on many factors such as the clinical situation, treatment goals and patient preferences. Drugs previously deemed appropriate may become inappropriate due to new diagnoses, such as a renal impairment, or change in functional ability, such as developing dysphagia or becoming immobile. So, the emphasis in our language may be wrong—all medicines are potentially inappropriate, some medicines are potentially appropriate (22,37). The burden of treatment and overall trajectory need to be considered, for example many people continue to take medications for disease prevention even in the terminal phase of chronic conditions, such as lipid lowering in the final weeks of life with advanced dementia (63). A focus on symptomatic relief is likely to be of greatest value in the context of advanced frailty.

1.4 The Burden of Polypharmacy and Potentially Inappropriate Medication

Polypharmacy is associated with many adverse outcomes. Some are patient-related, and others are health care system-related.

The ones related with patient are (64–75):

- Decrease quality of life and functional status;
- Cognitive impairment;
- Falls;
- Urinary Incontinence;
- Nutrition;
- Adverse drug reactions;
- Increased length of stay in hospital and readmission to hospital soon after discharge;
- Medication nonadherence;
- Drug-interactions;
- Mortality.

The ones related with health care system are (76–78):

- Increased burden on the health care system;
- Increased healthcare costs;
- Increased medication errors.

Sometimes it is hard to know whether this is genuinely due to the drugs or the effects of the underlying comorbidities that drove prescribing (79). However, there are some reasons that can explain why older patients are more prone to risk of adverse effects from drugs (40,75,80–82).

- First, because they take a higher number of drugs, which comes with a higher risk of harmful drug-drug interactions.
- Second, because of age-related physiological changes (e.g. decreased renal and hepatic function, decrease of cardiac output, lower lean body mass, reduced hearing, vision, cognition and mobility) that can influence the pharmacokinetic and pharmacodynamics of medication.
- Third, because the high prevalence of chronic multimorbidity in old age, which leads to an enhanced risk of drug-disease interactions.

High rates of interactions between drugs and herbal remedies or alcohol have also been reported in the elderly (83–85). From 195 elderly patients attending a memory clinic, almost one third of current users of herbal drugs were at risk of an herb–drug interaction (83). One large survey in

83,321 subjects (age range 65–106 years) demonstrated that approximately 20% of drug users reported concomitant intake of alcohol (84).

All drugs must have a periodic safety report and pharmacovigilance must be maintained throughout the life of the drug and it is the responsibility of the doctor and the person to disclose the problems deemed related to the drug. In Portugal, the Summary of Product Characteristics for all medicines has Adverse Drug Reactions section on chapter 4.8.

1.5 Where to focus our search of Polypharmacy and Potentially Inappropriate Medication

We should search the presence of inappropriate polypharmacy and potentially inappropriate medications in all patients, every time we prescribed. However, we should focus this search namely in the frail elderly because they have a higher number of comorbidities (despite their age) (86) and they also have a reduced ability to withstand illness without loss of function (87). Besides that, people recruited for randomised controlled trials are typically younger and with fewer comorbidities than the elderly present in the practice. Therefore, must of the time is only indirect evidence for older people (extrapolated from younger people). But due to the number of comorbidities and age-related physiological changes they are at higher risk of adverse drug reactions (ADR). This is described in the literature as the drug-ageing paradox (where medications gave smaller beneficial effects and a greater risk of ADR (79).

Duerden et al., in their report for the King's Fund (40), outline a pragmatic approach to identifying patients with polypharmacy and identifying 'at risk' patients using a combination of patient characteristics and the number of drugs prescribed. This approach is based on prior research showing an association between adverse health outcomes and polypharmacy, and that this association is more marked in patients with major illnesses. They recommend focusing on patients who are on 10 or more drugs; or patients receiving 5-9 drugs who have other risk factors such as a major comorbidity (e.g. diabetes or rheumatoid arthritis), have suffered previous adverse drug reaction, or are from a vulnerable group (e.g. people living in care homes or with a learning disability). Another UK study from 2004 (88) reported that the three commonest drugs linked to adverse drug reactions that resulted in hospital admission were non-steroidal anti-inflammatory agents, diuretics, and warfarin.

Studies such as this can guide clinicians as to which patients to focus on so they can identify those who may be at highest risk from the complications associated with polypharmacy. Therefore, one method of facilitating guidance on managing patients with polypharmacy would be through the development and application of "risk prediction tools" for quantifying the risk of adverse drug reactions. A systematic review published in 2014 (89) evaluated the quality of validated risk-prediction tools for adverse drug reactions in people over 65 years of age. However, all the risk prediction tools had limitations and hence their performance was generally modest. In addition to their relatively weak performance, these tools were all developed using data for hospital inpatients and we do not therefore know how well they would perform for patients in ambulatory or primary care settings.

1.6 Screening tools

Various strategies have been developed to identify inappropriate prescription patterns. Methods can be based on implicit criteria, involving clinical judgment grounded in reviews of the medical literature (e.g. Medication Appropriateness Index); explicit criteria, based on consensually generated lists of drugs to be avoided (e.g. Beers and STOPP/START criteria); or a mixed approach (explicit/implicit) (40,52,79,90–93).

1.6.1 Explicit criteria

The most known explicit criteria are the Beers Criteria, last updated in 2019 (94), and Screening Tool of Older Persons' Prescriptions/ Screening Tool to Alert doctors to Right Treatment (STOPP/START), last updated in 2014 (95).

The Beers Criteria were first developed in 1991 as a tool to determine potentially inappropriate prescribing of medications for elderly patients. The criteria are based on expert consensus and extensive literature review.

STOPP/STARTT comprises two screening tools that were developed by a consensus panel of 18 experts. The STOPP is a list that evaluates existing medication regimens, according to 65 criteria organized by physiologic system, and with additional focus on analgesics, duplicate drug classes, and drugs that increase fall risk. On the other hand, the START is a comprehensive tool used to determine appropriateness of initial prescribing of medications, according to 22 criteria organized by physiologic system (cardiovascular, central nervous system, gastrointestinal, musculoskeletal, respiratory, urogenital, and endocrine). These screening tools were developed by a consensus panel of 18 experts.

Other explicit criteria are modifications and adaptations from the different versions of the Beers Criteria over the time (90).

More recently (2017) was develop the LESS-CHRON criteria (List of Evidence-baSed depreScribing for CHRONic patients) (96) that is a comprehensive and standardized methodology to identify clinical situations for deprescribing drugs in chronic patients with multimorbidity.

1.6.2 Implicit criteria

The most known implicit criteria are the Medication Appropriateness Index (97) and the Garfinkel algorithm (98).

The MAI was developed in 1992 and measures appropriate prescribing based on a 3-point rating scale of a 10-item list. For each criterion (indication, effectiveness, dosage, directions, drug-drug interactions, drug-disease interactions, medication duplication, and cost), the evaluator rates whether the medication is appropriate, marginally appropriate, or inappropriate.

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

The Garfinkel algorithm was developed in 2010 and is used to re-evaluate each medication for each patient, enabling the doctors to decide whether to continue with the same dose, reduce it, or discontinue the drug completely.

1.7 Deprescribing of Polypharmacy and Potentially Inappropriate Medication

Although stopping medicines has been around since shortly after their first discovery, the concept of deprescribing as a specific therapeutic intervention is relatively new. Many definitions of deprescribing have been proposed (99), however it has been usually defined as "the process of withdrawal of an inappropriate medication, supervised by a healthcare professional with the goal of managing polypharmacy and improving outcomes" (100,101).

This definition may be too narrow as deprescribing does not necessarily involve polypharmacy, only inappropriate medication. Therefore, stopping the only drug someone is taking if inappropriate can also be valid. In addition, dose reduction, switching to a safer drug or a lower-frequency formulation can all be viewed as deprescribing (79). There is some complexity in judging which medicines are inappropriate for a given person and what constitutes an improved outcome. Therefore, Scott el al. (102) define deprescribing as the systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient's care goals, current level of functioning, life expectancy, values, and preferences.

Deprescribing should be viewed as part of the good prescribing continuum, which spans therapy initiation, dose titration, changing or adding drugs, and switching or ceasing drug therapies. It can also be argued that deprescribing need not even improve outcomes. If the same results can be achieved when taking fewer medications, then this is also a positive, for example by lessening treatment burden and financial cost (51,79,102,103).

Deprescribing is not therapeutic nihilism, denying effective treatment to eligible patients, but instead a positive, patient-centred intervention that recognises that the risks and benefits of medications need to be balanced and requires shared decision making, informed patient consent, and close monitoring of effects (the same good prescribing principles that should be used when drug therapy is initiated) (79,102).

Besides the potential benefits of deprescribing (e.g. reduction of PIM, treatment burden and financial cost) there are also potential harms of deprescribing. These includes adverse drug withdrawal reactions, pharmacokinetic and pharmacodynamic changes and return of a medical condition (104).

1.8 Deprescribing processes

Several deprescribing processes have been proposed in the literature.

The most common deprescribing process described in the literature is a 5-stepped process that involve review of all medications, identification of inappropriate medications (with consideration of harms and benefits of medication use in the individual and in the setting of life expectancy and care goals), prioritisation of medications for withdrawal, withdrawal of medications (often with tapering) and monitoring, support and documentation (102,104−107).

Other deprescribing processes have been proposed, namely:

Deprescription in 4 steps

Jansen et al. (103) defined the following steps:

1. Creating awareness that options exists;
2. Discussing the options and their benefits and harms;
3. Exploring patient preferences for the different options;
4. Making the decision.

Endsley et al. (51) defined the following steps:

1. Review all current medications (beginning with a "brown bag" review);
2. Identify any inappropriate, unnecessary, or harmful medications (is it potentially inappropriate? Lacking an indication? Failing to provide an additional benefit? Lacking efficacy? Causing an adverse reaction? Complex in its regimen?);
3. Plan deprescribing with the patient (consider discontinuing one medication at a time or tapering medications);
4. Regularly review medications.

Deprescription in 10 steps (108):

1. Ascertain all drugs;
2. Identify patients at high risk of or experiencing ADRs;
3. Estimate life expectancy;
4. Define care goals in reference to life expectancy, level of functional incapacity, quality of life, and patient/caregivers priorities;
5. Define and confirm existent indications for ongoing treatment with reference to defined care goals;
6. Determine time until benefit for preventive disease-specific medications;
7. Determine disease-specific benefit-harm threshold that may support treatment discontinuation;

8. Review the relative utility of individual drugs;
9. Identify drugs may be discontinued or have their dosing modified;
10. Implement and monitor revised therapeutic plan with ongoing reappraisal of drug utility and patient adherence.

After analysing the information from different deprescribing processes we found that there were many common aspects (as mentioned above) and others specific to each other.

Ideally, the deprescribing process should be applied to all patients, namely in the Portuguese primary care context. Its feasibility and outcomes must be studied. Therefore, we decide to compile the information from different 5-stepped deprescribing process and introduce a step 0: doctor active search and prioritization of patients that are at higher risk of or already experiencing ADR. This step 0 is an important aspect if we want to have person-centered medicine as the core of deprescribing.
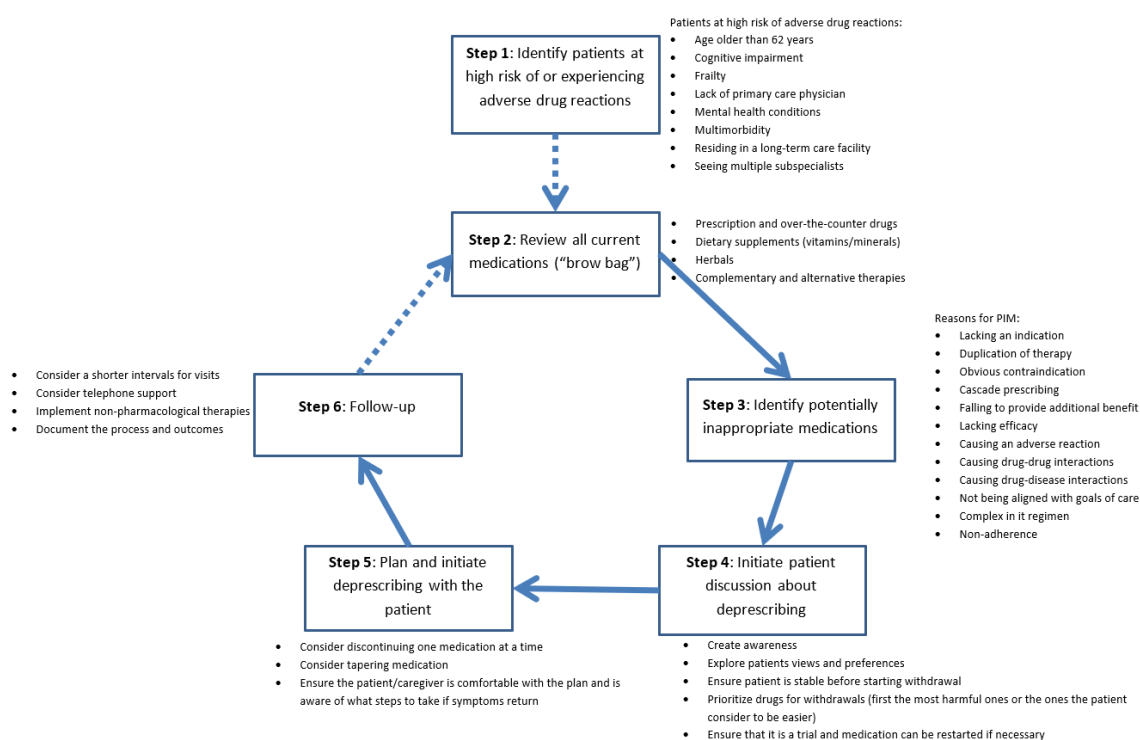

Figure 1.8.1 Proposed deprescribing process (102,104–107)

1.9 Evidence to support the effectiveness of deprescribing

The timing of deprescribing may be reactive to a significant event such as an ADR, hospitalisation or care home admission. It may be in response to a functional change, significant new diagnosis or when a patient is having difficulty managing their healthcare burden (109). It may tie in with an advance care planning process or it may be proactive at a time of stability to try to prevent future problems (110). Over time the clinical picture slowly evolves—people develop frailty, accumulate new diagnoses and medications. Re-prescribing long-term prescriptions can occur automatically without thought. It may be difficult to identify the point where the balance shifts from efficacious to potentially hazardous or burdensome. It is important during clinical encounters to raise awareness of deprescribing as an option and having shared decision-making because studies suggest that many older people would choose this if offered (61,111). Being particularly important in people with frailty or limited life expectancy who have less capacity to benefit from pharmacological interventions (40).

Several meta-analyses and systematic reviews of deprescribing trials have been conducted (112–118). There is a wide variation in the size, duration, methodology and population among the included studies making comparison difficult. There are mixed findings. Interventions are generally well tolerated with little evidence of harm, but some medications had to be restarted. The size of reduction was typically only modest (0.2–2.0 drugs/person).The evidence for a beneficial effect on mortality is weak, although one meta-analysis found a significant reduction when patient-specific outcomes were considered (as opposed to educational programmes alone), relative risk 0.62 (95% confidence interval 0.43–0.88) (115). There are only limited data to evaluate other outcomes. The risk of bias is high in many of the included studies. Those of shorter duration may be misleading by failing to detect medications later restarted. There seems to be a better chance of success if the study included an educational component and pharmacist–physician collaboration (118).

Three professional organizations in the American Board of Internal Medicine Foundation's Choosing Wisely campaign (American Geriatrics Society, American Society of Health-System Pharmacists, and American Psychiatric Association) specifically mention polypharmacy and the need to review medications regularly, question the utility of adding new medications, and deprescribe when appropriate (119). Such recommendations can persuade physicians to consider deprescribing and can reassure patients that deprescribing medications is evidence based and beneficial.

As mentioned above, the evidence base for deprescribing is only just emerging, but this must be offset by the lack of evidence for the benefit of continuing medications in frail older people. It will take time to accumulate enough high-quality studies. The potential benefits of any deprescribing intervention are inversely proportional to the quality of baseline prescribing (79).

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CHAPTER TWO
Aims and Research Methods

Aims and Research Methods

2.1 Deprescribing in primary care in Portugal (DePil17-20): a three-phase observational and experimental study protocol

Abstract

Introduction: Polypharmacy is commonly defined as the simultaneous taking of five or more drugs. Deprescribing is the process of tapering or stopping medications with the aim of improving patient outcomes and optimising current therapy, and there are several tools aiming at identifying such problem, especially in the elderly. The direct involvement of patients and their caregivers in the choice and administration of drugs has long been known to be very important, but it isn't usually applied. The aim of this study is to assess the knowledge of older adults about deprescription, the effect on willingness to have regular medications deprescribed and its quality of life outcome.

Methods and Analysis: This study protocol comprises three phases. The first two phases will be nationwide and aim to evaluate the prevalence and patterns of polypharmacy and assess the barriers and facilitators of deprescribing perceived by older adults, as well as their willingness to have regular medications deprescribed and to self-medicate. The third and last phase will be a non-pharmacological randomised clinical study to measure older patients' acceptance to have regular medications deprescribed and related quality of life.

Ethics and dissemination: The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has been approved by the Ethics Committee of University of Beira Interior and Portuguese National Data Protection Commission. Study results will be published in peer-reviewed journals and presented at national and international conferences. In short, no action will be taken without written consent from patients and doctors.

Introduction

Polypharmacy is commonly defined as the simultaneous taking of five or more drugs (1), but it can also be defined as using medication that is not indicated, not effective or therapeutic duplication (2). It is present in 30-70% of older adults (3) and it's a significant predictor of the risk of falls (4), inappropriate prescriptions, reduced patient's adherence, drug interactions, hospital admissions (5,6) and mortality (7). It is estimated that at least 75% of this adverse event is potentially preventable (8).

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

Potentially Inappropriate Medications (PIM) are those for which the harms outweigh the benefits, namely those that are not indicated or lack evidence of efficacy and those that do not align with patients goals/preference and values (9). So it is necessary to distinguish between appropriate and inappropriate medications (10), because as people get older the benefit/risk ratio of medications changes, meaning that medications that were once appropriately prescribed may have become inappropriate (11). An Australian study reported that 60% patients had at least one PIM, leading to a high risk of adverse drug reactions, morbidity and mortality (12). There are a lot of guidelines about when to start medication that is safe and effective, but there is a lack of similar guidelines for ceasing inappropriate medication (13).

Deprescribing is the process of tapering or stopping medications with the aim of improving patient outcomes and optimising current therapy (14) However, it is not free of risks, namely withdrawal syndromes, rebound effects, pharmacokinetic/pharmacodynamic changes in the remaining drugs and recurrence of the symptoms (3,15). So the decision to deprescribe results from a careful weighting between the therapeutic objectives and the risk/benefit ratio.

Many deprescribing processes have been proposed in the literature (15,16). One of the most widely used is a simple 5-step protocol consisting of a comprehensive medication history, identifying PIMs (attending to the harms and benefits of medication, as well as to the life expectancy and care goals), determining whether medication can be ceased and prioritization (taking into account the patient's preferences), planning and initiating medication withdrawal (one at a time and often with tapering) and close monitoring and documenting the improvement in health and quality of life and the reduction of adverse effects (17).

Almost a dozen medication screening tools exist in order to aid identifying PIMs in older adults and improve their care. The most widely used are Beers criteria and the STOPP/START criteria (Screening Tool of Older Person's Prescriptions and Screening Tool to Alert Doctors to Right Treatment). Both the Beers criteria and the STOPP component of the STOPP/START criteria are lists of medications that should be avoided in older adults because of its adverse effects and drug-drug and drug-disease interactions. On the other hand, the START component of the STOPP/START criteria consists of a list of medications that should be considered to initiate in the presence of certain conditions. Another useful tool is the Medication Appropriateness Index that consist of issues to be taken into account before prescribing a medication (18).

Many studies have recognized that the implementation of a deprescribing process is feasible in practice and acceptable to participants (19,20) and, hypothetically, may result in favourable patient health and quality of life outcomes (21), further studies are needed to confirm it. There are already a few number of strategies that appear to be effective and promising (22), however assessing the effectiveness of these interventions is difficult because different studies have different study designs, settings and types of interventions. Many of these studies have short follow-up periods (2 months to 1 year), so it may not provide on the long-term impact of the

interventions, and/or lack of clinical outcome measurements (23). One outcome measurement rarely used was the effect on health-related quality of life.

Patients are uncertain about their willingness to have a medication deprescribed because they are confused by conflicting advice on benefit and harm from different health care professionals (15). The majority of patients want to be involved in the decision making process (17,24) and this has long been known to be very important, but shared decision making is not routine (25). It is assumed that older people generally consider they take a lot of medications and complain about it, but they are reluctant to cease specific medications in practice (26,27). So, it's important to understand this incongruity between not liking to take multiple medications and reluctance to accept the proposal to stop them. In particular for Portuguese context, there are no studies on these matters so making it necessary to understand such ambivalence which can help solving many problems arising from polypharmacy, as adverse drug reactions (28).

There are only some studies about the prevalence of polypharmacy in some region of Portugal, none nationwide. Also, there are no studies about the Portuguese older adults' attitudes and beliefs regarding medication and very few around the world. Finally, most of the studies focus on the effect of deprescribing in clinical outcomes as falls, consultations rates, hospitalizations and/or mortality. Very few focuses on the effect on quality of life and older adults' willingness. In order to study the phenomenon, as well to create rationales, this work is necessary.

Terminology

For the purpose of defining polypharmacy, we will use the list of active ingredients of drugs and consider three definitions: ≥5 drugs vs. ≥ the median number of drugs vs. presence of at least one PIM. The rationale for such resides in the scarcity of studies on the number of medications simultaneously taken. In fact, due to multimorbidity, many elderly patients are taking more and more drugs (29). So, we want to compare the international accepted definition (≥5 drugs) with this new approach to see if there are differences.

Study objectives

The primary objective is to assess the knowledge of older adults about deprescription, the effect on willingness to have regular medications deprescribed and their quality of life outcome.

Specific objectives are:

- To identify the prevalence of polypharmacy in older adults in Portugal;
- To evaluate the proportion of PIMs in older adults in Portugal;
- To describe the sociodemographic and clinical profiles of older adults with polypharmacy in Portugal;
- To identify the main Barriers to and the Facilitators of Deprescribing in Portuguese older adults;

- To evaluate the Portuguese older adults Willingness to have regular medications deprescribed;
- To correlate the Self-medication with the Willingness to have regular medications deprescribed;
- To evaluate the effect in Quality of Life after having regular medications deprescribed;
- To elaborate and validate a flowchart with the Deprescribing process, in the patient's perspective.

Methods and analysis

Study design

This is a three-phase study:

1. Cross-sectional, analytical study of the prevalence and patterns of polypharmacy, namely sociodemographic and clinical profiles (age, gender, area of residence and years of study) and about medication (number of drugs and their active component), in older adults attending Primary Care in Portugal.
2. Cross-sectional, triangulation study of older adults' perception of Barriers to and Facilitators of Deprescribing, Willingness to have regular medications deprescribed and Willingness to Self-medicate.
3. Non-pharmacological randomised clinical study of older patients' acceptance to have regular medications deprescribed and related Quality of Life.

Phase I

Objectives: To assert the prevalence of polypharmacy in older adults attending primary care in Portugal and describe their sociodemographic and clinical profiles.

Design: Cross-sectional, analytical study.

Setting: Primary Care Centres in Portugal will be randomly selected from the five main-land Portuguese Healthcare Administrative Regions and two Autonomous Regions (Madeira and Azores), in order to obtain a national geographical representative sample.

Sample size: Since the prevalence of polypharmacy in older adults is unknown, we will use as base of population all older adults in Portugal. For the study, we will use a 95% confidence interval (CI) and a maximum precision error of 5%. According to Pordata (www.pordata.pt), the population of Portugal is around 10.33 million of which 2.18 million are over the age of 65. Since the literature suggests that the range of polypharmacy is 30-70% and we think that it is over 50%, we estimate that we would need at least 742 patients.

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Study procedures: This phase of the study starts in March 2018. We will ask the information department of the ministry of health for the data of patients (electronically stored) of 757 randomized patients: 245 in North of Portugal, 190 in Centre of Portugal, 211 in Lisbon-Tejo Valley, 65 in Alentejo, 33 in Algarve, 6 in Azores and 7 in Madeira in accordance with the distribution of Portuguese old adult population (≥65 years) in Portugal according with Pordata.

Data collection: The collection of the data will occur in March 2018. Data will be given electronically stored in a database specifically designed for this study. Data will be encrypted, and password protected. Information will be treated in strict confidentiality to protect the privacy of patients. The investigators will have no access to the data of the patient, except the one provided by the information department of the ministry of health.

Statistical analysis: A descriptive analysis will be performed to all study variables, namely the number of valid observations, mean±SD, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. Prevalence of polypharmacy (considering the three definitions) will be calculated together with corresponding 95% CI. Moreover, the prevalence of polypharmacy will be estimated by subgroups, namely age, gender, residence area and formal education. Univariate analysis will be conducted to study the associations between those characteristics and polypharmacy using $\chi2$ test (qualitative characteristics) or t test/Mann-Whitney (quantitative characteristics). Multiple logistic regressions will be carried out considering the presence of polypharmacy as the dependent variable and patients' characteristics as the independent variables in order to calculate odds ratio (ORs) and corresponding 95% CI. Total number of drugs taken by patient and their pharmacological classes will also be summarised together with 95% CI, and multiple regressions may be performed to analyse its association with patients' characteristics. All tests will be two-sided using a significance level of 0.05. Statistical analysis will be conducted using SPSS V.23.0 or higher.

Phase II

Objectives: To determine older peoples' attitudes and beliefs regarding medication use and their willingness to have regular medications deprescribed.

Design: Cross-sectional, analytical study.

Setting: It will be the same of the phase I.

Sample size: Since the prevalence of polypharmacy in older adults is unknown, we will consider that it is around 60% of the older adults' population. So we need at least of 385 patients with polypharmacy, to obtain a sample with a 95% CI and a maximum precision error of 5%.

Study procedures: This phase of the study is expected to start in October 2018. General Practitioners (GPs) sampling is made according to existing files of previous projects adherent

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GPs, in other epidemiological studies. After the selection of GPs, those who agree to participate will recruit their own patients, after their consent. Assuming that a GP will be able to include at least 6 patients, a total of 65 GPs will be enrolled in the study: 21 in North of Portugal, 16 in Centre of Portugal, 18 in Lisbon-Tejo Valley, 5 in Alentejo, 3 in Algarve, 1 in Azores and 1 in Madeira in accordance with the distribution of Portuguese old adult population (≥65 years) in Portugal according with Pordata (www.pordata.pt). Enrolled GPs will be instructed to give the questionnaire and the informed consent to all older adults (≥65 years) patients, with polypharmacy, attending a primary care consultation during the period of study: we will randomize 6 consultation's days for data collection. GPs will collect all necessary data about the patients that sign the informed consent and fill all questions of the questionnaire. After that, we will randomize the pool of data according gender and region, in order to obtain an sample in accordance to Portuguese distribution of old adult population (≥65 years). GPs and patients willing to participate in the study must give written informed consent and present ability to comply with the study requirements. Exclusion criteria will be: Being acutely unwell in the last three weeks, and refusal to participate.

Data collection: The collection of the data will occur in October 2018. GPs will be responsible for collecting all data about patients' sociodemographic characteristics, as well as morbidity and medication, during their consultations. Moreover, the perception of medication will be evaluated using Portuguese general Beliefs about Medicines Questionnaire (BMQ), the willingness to have regular medications deprescribed will be assessed with one open-question ("What do you think about withdrawing medication?"), to evaluate the qualitative knowledge about the patient's acceptance, and the need to self-medicate with over-the-counter medication will be evaluated with a visual analogue scale (0 to 10) about the need to self-medicate and its justification. For those not knowing how to write or read, they can choose someone they know (e.g. a family member or a friend) to write the answer. In case of less than 50% of answers of the open questions, two patient groups will be invited to make a focus group asserting reasons for accepting deprescribing. Data will be given electronically stored in a database specifically designed for this study using MS Excel 2010. Data will be encrypted, and password protected. Information will be treated in strict confidentiality to protect the privacy of patients. The investigators will have no access to the data of the patient. The only person to know who is being studied is the GP. Before the collection of data, there will be online reunions with the GPs participating in the study. We have been authorized to use BMQ by the authors.

Statistical analysis: A descriptive analysis will be performed to all study variables, namely the number of valid observations, mean±SD, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. We will categorize the willingness to have regular medications deprescribed in 2 groups (high and low). The perception of medication, willingness to have regular medications deprescribed and need to self-medicate will be estimated by subgroups, namely age, gender, residence area and formal education. Univariate analysis will be conducted to study the associations between those characteristics

and the perception of medication, willingness to have regular medications deprescribed and need to self-medicate using χ2 test (qualitative characteristics) or t test/Mann-Whitney (quantitative characteristics). Multiple logistic regressions will be carried out considering the perception of medication, willingness to have regular medications deprescribed and need to self-medicate as the dependent variable and patients' characteristics as the independent variables in order to calculate odds ratio (ORs) and corresponding 95% CI. All tests will be two-sided, considering a significance level of 0.05.

Null hypothesis: The people with more willingness to have their regular medications deprescribed believe that medications are harmful and overused by doctors; The need to self-medicate is present in people with less fear of medication and less overuse belief; People with polypharmacy see no or little harm in the medication and don't think they have polypharmacy.

Phase III
Registered in ClincalTrials.gov with ID: NCT03283735

Objectives: To measure older patients' acceptance to have regular medications deprescribed and related quality of life.

Design: Non-pharmacological cluster randomised clinical study, intended to last for six months.

Outcomes: Primary outcome will be the quality of life; secondary outcome will be the willingness to have regular medications deprescribed.

Setting: Primary Care Centres in Portugal will be randomly selected from six Health Centres of Centre of Portugal (Aveiro, Castelo Branco, Coimbra, Guarda, Leiria and Viseu).

Sample size: Since the prevalence of polypharmacy in older adults in Centre of Portugal is unknown, we will consider that it is around 60% of the older adults' population in this region (around 520 thousand). So, we need at least 380 patients with polypharmacy, to obtain a sample with a 95% CI and a maximum precision error of 5%. However, assuming a dropout's rate of around 25%, we will increase the sample in 25% of the initial one, so we will need at least 474 patients with polypharmacy. Then we will create two groups with a minimum of 237 patients each (one will be the intervention group and the other the control).

Study procedures: This phase of the study is expected to start in September 2019 and will last for 6 months. Again, GPs sampling will be made according to existing files and those who agree to participate will recruit their own patients, after their consent. Patients from previous phase can be enrolled. Assuming that a GP will be able to include at least 10 patients, a total of 48 GPs has to be enrolled in the study. Enrolled GPs will be instructed to invite all older adult (≥65 years) patients with polypharmacy, attending to the primary care consultation to participate in the study during until obtaining the sample size and being randomized according to the table for

study entry. The geographical areas of work, the Districts, will be randomized for entry into exposed and unexposed groups, in order to minimize the contamination of the intervention that could happen if we use randomization at patient level. The purpose is to have doctors performing only one task in each district. To make both groups as homogenous as possible, we will group similar districts in order for them to be in different branch of the study. Patients willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. The patients' recruitment procedure will be the same as the one described for the phase II. Exclusion criteria: Being acutely unwell in the last three weeks, and refusal to participate. Two groups will be created with a minimum of 237 patients each, one of which will be composed from patients from the region of Aveiro, Coimbra and Guarda and the other from patients from the region of Castelo Branco, Leiria and Viseu. In the intervention group we will give empowerment tools and talks with their GPs about how to issue the problem of polypharmacy and the control group will receive the usual care. The information given in this group will result from the knowledge obtained in phase II as small leaflets and other informational materials to be made according to the best practice, to be given and remembered at scheduled times to the intervention group. To summarize, this information will be used to educate GPs how to approach the issue of deprescribing and material provided to participants, during a consult, so they can learn more about it.

Data collection: The collection of the data will occur in the beginning (baseline) and end of phase III (at 6 months), in order to analyse changes from baseline. GPs will be responsible for collecting all data. Patient's socio-demographic and clinical characteristics and medication will be registered using the same methodology as described in phase II. Perception of medication will be evaluated using Portuguese general Beliefs about Medicines Questionnaire (BMQ), the willingness to have regular medications deprescribed will be assessed with one open-question (the same as phase II), and the quality of life we will assessed with EuroQol Five Dimensions Questionnaire (EQ-5D), a validated tool for Portugal. The aim is to observe the impact of deprescription on Health-Related Quality of Life, even if, to our knowledge no study has used EQ-5D in this specific domain in Portugal. For those not knowing how to write or read, they can choose someone they know (e.g. a family member or a friend) to write the answer. We have been authorized to use BMQ and EQ-5D by the authors.

Statistical analysis: It will be similar to the phase II. Comparisons between baseline and the 6 months groups regarding a quantitative variable are to be conducted using t test or Sign/Wilcoxon non-parametric test, if normality assumption is not met.

Null hypothesis: The intervention will result in statistical higher quality of life so creating a tool for active patient deprescription.

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CHAPTER THREE
Results

Results

3.1 Prevalence of Polypharmacy in the Older Adult Population within Primary Care in Portugal: A Nationwide Cross-Sectional Study

Abstract

Background: Polypharmacy is commonly defined as the simultaneous use of five or more medications; however, there exists a lack of consensus regarding the most appropriate definition. It is a significant predictor of morbidity and mortality. The aim of this study was to determine the prevalence of polypharmacy in the population of older adults attending primary care in Portugal and to identify associated sociodemographic and clinical factors.

Methods: We conducted a cross-sectional, analytical study in primary care centres from the five Portuguese healthcare administrative regions and the two autonomous regions. We used a random sample of 757 older adult patients provided by the information department of the ministry of health (SPMS) and family doctors from the autonomous regions. Data collection occurred March 2018. The variables utilised were sociodemographic characteristics, clinical profile and medication. For each patient, polypharmacy was measured either by the concurrent use of ≥5 drugs or by the median number of drugs at the time of data collection. Logistic regression analyses were performed to determine associations between polypharmacy and other variables.

Results: Polypharmacy (≥5 drugs) was present in 77% of the sample. A cut-off of over the median number of drugs was present in 55%. The likelihood of having polypharmacy increased significantly with age [OR=1.05 (1.02-1.08)], number of chronic health problems [OR=1.24 (1.07-1.45)] and number of prescribers [OR=4.71 (3.42-6.48)]. Cardiovascular, metabolic and musculoskeletal medications were the most commonly involved in polypharmacy.

Conclusions: Polypharmacy was a very common occurrence in Portugal. Future primary healthcare policies should address polypharmacy.

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Background

Polypharmacy is commonly defined as the simultaneous use of five or more drugs (1). But other definitions has been proposed: some authors propose a more detailed breakdown of the cut-off ("5 to 7" and "8 and over") allowing for the identification of those with an increased risk (2); Steinman et al. (3) proposes a threshold of 8 medications justified by the fact that below this number, the risk of under-use is greater than the risk of polypharmacy or inappropriate prescription; and others consider polypharmacy as the use of inappropriate, ineffective or duplicate medication (4).

Polypharmacy is estimated to affect 30-70% of older adults (5), and it has been associated with an increased risk of falls (6), inappropriate prescriptions, reduced patient adherence, drug interactions, hospital admissions (7) and mortality (8). It is estimated that at least 75% of these adverse events are potentially preventable (9). In some cases, an adverse drug reaction can be misinterpreted as a new medical condition and a new drug is prescribed, placing the patient at a higher risk of developing additional adverse drug reactions, this problem is known as the "prescribing cascade"(10).

According to Charlesworth et al. (11) the increased number of prescription medications seen in older adults in the USA between 1988 and 2010 was driven, in part, by higher use of cardioprotective medications (statins, anti-hypertensives, and antidiabetics). Still the use of antidepressants, as well as the use of medication from other classes and subclasses (proton-pump inhibitors, thyroid hormones, bisphosphonate, among others) also increased.

In Portugal there are a few studies about the prevalence of polypharmacy in some of its regions, none on a national scale. A 2016 study in a primary care health centre in the north of Portugal identified a prevalence of polypharmacy of 59.2%; more frequent in women (62%) than in men (54.8%) (12). In Portuguese' public health system the patients can only go to secondary care through referral from primary care, but once in both levels of care both doctors can prescribe and renew all patient's medication. The medications prescription occurs through the mandatory nationwide electronic prescription platform (PEM).

The aim of this study was to identify the nationwide prevalence of polypharmacy in older adults in Portugal and its sociodemographic and clinical profiles. Although, polypharmacy can be linked to drug-drug interactions (both pharmacokinetics or pharmacodynamics) and to adverse drug reactions, these results were presented in a previous paper (13). Moreover, given the lack of consensus for the definition of polypharmacy and since multimorbidity and the use of multiple medications is common in the older adults (14) we also intended to use a new definition of polypharmacy (equal to or greater than the median number of drugs, taken by the population) and compare it to the most commonly used.

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Methods

Study design

Cross-sectional study whose details, definitions and methods were previously published (15).

The study was conducted in agreement with the principles of the Declaration of Helsinki and received ethical approval from the Institutional Ethics Committee of the University of Beira Interior and Portuguese Healthcare Administrative Regions. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Participants

Since there were 2.18 million older adults (≥65 years) in Portugal and the literature suggests that the range of polypharmacy is between 30 and 70%, we assumed the rate to be over 50% because of epidemiological concern for better evidence and larger sampling. We estimated a sample of a minimum 742 patients for a 95% CI and a maximum precision error of 5%. In agreement with the geographical distribution of the population of Portuguese aged 65 and older across the five mainland healthcare administrative regions and two autonomous regions (Madeira and Azores), noted in PORDATA (16), a random sample of 757 patients was provided by the information department of the ministry of health, SPMS (Serviços Partilhados do Ministério da Saúde), and invited family doctors from autonomous regions, due to lack of digital databases within these last regions.

Data collection procedures

Data collection occurred in March 2018 (data extracted on March 30th). In brief, the SPMS provided us with an electronic file with the variables of the study from the randomly selected (by patient's national health number) sample of the five healthcare administrative regions. This electronic file contained anonymised information stored in the patient's electronic medical records. Since SPMS doesn't have access to electronic medical records from patients in the two autonomous regions, we invited two medical doctors, one from each autonomous region, to provide us with the needed information. The patients selected met the inclusion criteria and also had had an appointment in six pre-randomized days of the month. We studied the prescribed medications using the mandatory nationwide, PEM (17). There is an unknown number of over-the-counter medications consumed by the Portuguese population and as they can be bought without prescription, there is no way to access this information. SPMS couldn't provide us with information regarding level of education, since in most cases it was missing from medical records.

Outcome variable

For each patient, polypharmacy was measured either by the simultaneous taking of ≥5 drugs or by the median number of drugs at the time of data collection. The rationale for such a study resides in the lack of consensus regarding definition of polypharmacy (18), also because of

multimorbidity older patients are consuming an increasing number of medications (19). There is a study (2) that proposes a threshold of 8 medications, this is justified by the fact that below this number, there is a big risk of under-use. Prescribed medication (from April 2017 to March 2018) was encoded following the Portuguese pharmacotherapeutic classification using the most discriminative level possible. The Portuguese pharmacotherapeutic classification has similarities with the ATC (Anatomical Therapeutic Chemical) classification and was adapted by INFARMED (National Authority of Medicines and Health Problems) (20). We defined chronic medication as medication prescribed for more than three months.

Independent variables

Sociodemographic characteristics such as age, gender (male/female), area of residence (in terms of health administrative region) and clinical profile (chronic health problems according to International Classification of Primary Care, second edition – ICPC-2).

Statistical analysis

In addition to the descriptive analysis, we also performed χ2 test for nominal qualitative characteristics. Lastly, we performed a logistic regression with all the statistically significant variables. All tests were two-sided using a significance level of 0.05. Statistical analysis was conducted using SPSS V.24.0.

Results

Characteristics of participants

The sample consisted of 757 people sample, mean age was of 75.5±7.9 years (75.1±7.9 years for men and 75.8±7.8 years for women) and median number of drugs was 8. Table 3.1.1 shows the characteristics of the sample.

Table 3.1.1 – Characteristics of the sample

Characteristics	% (n)
Gender	
Women	56.8 (430)
Men	43.2 (327)
Health administrative region	
North	32.2 (244)
Centre	25.1 (190)
Lisbon-Tejo Valley	27.7 (210)
Alentejo	8.7 (66)
Algarve	4.5 (34)
Madeira	0.9 (7)
Azores	0.8 (6)
Age	
<75 years	51.5 (390)
≥75 years	48.2 (365)
Number of chronic health problems	
0-2	17.3 (131)
3-4	19.3 (146)
5-6	17.6 (133)
7-8	16.8 (127)
9-10	11.9 (90)
≥11	17.2 (130)
Chronic health problems (ICPC2) (*)	
A	11.2 (85)
B	7.5 (57)
D	36.5 (276)
F	20.5 (155)
H	11.5 (87)
K	77.5 (587)
L	51.8 (392)
N	15.7 (119)
P	34.3 (260)
R	23.4 (177)
S	19.3 (146)
T	68.6 (519)
U	21.5 (163)
X	9.5 (72)
Y	15.2 (115)
Z	3.6 (27)
Number of drugs	
0-4	23.1 (175)
5-9	39.0 (295)
≥10	37.9 (287)
Pharmacological classes (INFARMED)	
2	74.5 (564)
3	81.8 (619)
4	36.9 (279)
5	21.1 (160)
6	50.6 (383)
7	16.5 (125)
8	42.5 (322)
9	53.9 (408)
10	20.3 (154)
16	1.6 (12)
Number of prescribers	
≤2	63.9 (484)
>2	36.1 (273)

(*) Note: A - General and unspecified; B - Blood, blood forming organs, lymphatics, spleen; D - Digestive; F - Eye; H - Ear; K - Circulatory; L - Musculoskeletal; N - Neurological; P - Psychological; R - Respiratory; S - Skin; T - Endocrine, metabolic and nutritional; U - Urology; X - Female genital system and breast; Y - Male genital system; Z - Social problems; 2 - Central nervous system; 3 - Cardiovascular system; 4 - Blood; 5 - Respiratory system; 6 - Digestive system; 7 - Genitourinary system; 8 - Hormones and medications used to treat endocrine diseases; 9 - Locomotive system; 10 - Antiallergic medication; 16 - Antineoplastic and immunomodulatory drugs

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Prevalence of polypharmacy

More than 9 out of 10 older patients (93.4%) were at least 1 medication, with an overall average of 8.2 (95% CI 7.9 to 8.6), 7.5 (95% CI 7 to 8) in men and 8.8 (95% CI 8.3 to 9.3) in women.

Polypharmacy, use of 5 or more drugs simultaneously, was of 77% (95% CI 74 to 80%). With a cut-off of equal to or more than the median number of drugs (equal to 8), an important percentage of polypharmacy 55% (95% CI 51 to 58%) remained present.

According to table 3.1.2 there was a significant relationship between health administrative region, age, number of chronic health problems and number of prescribers and both definitions for polypharmacy (≥5 drugs and ≥median number of drugs). Gender was only significant in our new definition of polypharmacy.

After adjustments, table 3.1.3 shows that the likelihood of having polypharmacy (as ≥5 drugs) increased significantly with age [OR=1.05 (1.02-1.08)], number of chronic health problems [OR=1.24 (1.07-1.45)] and number of prescribers [OR=4.71 (3.42-6.48)].

The likelihood of having polypharmacy with our new definition (as ≥ median of drugs taken by the sample) increased significantly in females [OR=1.86 (1.24-2.80)], with number of chronic health problems [OR=1.11 (1.02-1.20)] and number of prescribers [OR=2.32 (1.97-2.73)].

Pharmacological subclasses and patterns of polypharmacy

Table 3.1.3 shows the odds ratio measured impact of having each specific chronic health problems (according to ICPC2). For patients suffering from chronic health problems related to cardiovascular system there were 3.8 times and 2.4 times greater probability of having a polypharmacy (as ≥5 drugs and ≥median number of drugs taken, respectively) when comparing to those not suffering from health problems related to that specific system.

Table 3.1.4 shows the most used pharmacological subclasses in this random sample. Three pharmacological subclasses were present in more than half of the sample: ACE inhibitor/ARBs (56.8%), statins (52%) and analgesics and antipyretics (50.6%).

Comparation between both definitions of polypharmacy in detecting potentially inappropriate medication

The common definition (≥5 drugs taken) had a sensibility of 91.3%, specificity of 54.2%, positive predictive value of 81.3% and negative predictive value of 74.1%.

Our definition (≥ median number of drugs taken) had a sensibility of 72.6%, specificity of 84.0%, positive predictive value of 90.8% and negative predictive value of 58.5%.

The mean number of PIM in older adults with polypharmacy according to the common definition was 2.19 (CI 95% 2.03 to 2.34) compared to 0.34 (CI 95% 0.24 to 0.44) in those without polypharmacy. According to our definition (≥ median number of drugs taken) we found

a prevalence of 2.64 PIMs (CI 95% 2.46-2.83) in those with polypharmacy compared to 0.69 PIMs (CI 95% 0.58 to 0.80).

Table 3.1.2 – Prevalence of polypharmacy according to characteristics

Characteristics	Older adults without polypharmacy % (n)	Percentage of older adults with polypharmacy (95% CI)				Mean number of drugs (95% CI) [median]
		≥5 drugs	p-value (χ² test)	≥8 drugs	p-value (χ² test)	
Gender			0.059		<0.001	
Women	20.5 (88)	79.5 (342)		60.5 (260)		8.78 (8.30-9.25) [8]
Men	26.3 (86)	73.7 (342)		47.4 (155)		7.47 (6.98-7.96) [7]
Health administrative region			0.022		0.017	
North	26.6 (65)	73.4 (179)		49.6 (121)		7.77 (7.18-8.36) [7]
Centre	17.9 (34)	82.1 (156)		58.9 (112)		8.62 (7.96-9.28) [8]
Lisbon-Tejo Valley	20.,0 (42)	80.0 (168)		59.5 (125)		8.69 (8.02-9.36) [8]
Alentejo	27.3 (18)	72.7 (48)		53.0 (35)		7.48 (6.33-8.64) [8]
Algarve	41.2 (14)	58.8 (20)		41.2 (14)		6.29 (4.49-8.10) [6]
Madeira	14.3 (1)	85.7 (6)		28.6 (2)		9.43 (5.13-13.73) [6]
Azores	0 (0)	100 (6)		100 (6)		14.17 (9.50-18.83) [13]
Age			<0.001		0.001	
<75 years	28.2 (110)	71.8 (280)		49,2 (192)		7.73 (7.25-8.22) [7]
≥75 years	17.4 (64)	82.6 (303)		60,8 (223)		8.72 (8.24-9.21) [9]
Number of chronic health problems			<0.001		<0.001	
0-2	48.1 (63)	51.9 (68)		35.9 (47)		5.44 (4.67-6.21) [5]
3-4	35.6 (52)	64.4 (94)		41.1 (60)		6.97 (6.17-7.78) [6]
5-6	23.3 (31)	76.7 (102)		48.1 (64)		7.80 (7.06-8.55) [7]
7-8	12.6 (16)	87.4 (111)		63.8 (81)		9.22 (8.50-9.94) [9]
9-10	7.8 (7)	92.2 (83)		64.4 (58)		9.21 (8.36-10.06) [9]
≥11	3.8 (5)	96.2 (125)		80.8 (105)		11.15 (10.34-11.95) [10]
Chronic health problems (ICPC2)						
A	10.6 (9)	89.4 (76)	0.004	62.4 (53)	0.139	9.40 (8.42-10.38) [9]
B	15.8 (9)	84.2 (48)	0.179	66.7 (38)	0.062	9.25 (7.98-10.52) [9]
D	13.0 (36)	87.0 (240)	<0.001	60.1 (166)	0.026	8.93 (8.38-9.49) [8,5]
F	17.4 (27)	82.6 (128)	0.065	63.9 (99)	0.011	9.25 (8.43-10.08) [9]
H	12.6 (11)	87.4 (76)	0.015	63.2 (55)	0.094	9.70 (8.58-10.82) [9]
K	16.9 (99)	83.1 (488)	<0.001	61.2 (359)	<0.001	8.98 (8.60-9.37) [9]
L	17.6 (69)	82.4 (323)	<0.001	62.0 (243)	<0.001	8.95 (8.49-9.42) [8]
N	16.0 (19)	84.0 (100)	0.047	67.2 (80)	0.003	10.06 (9.13-10.99) [10]
P	16.5 (43)	83.5 (217)	0.002	60.4 (157)	0.026	9.01 (8.43-9.59) [8]
R	10.7 (19)	89.3 (158)	<0.001	67.2 (119)	<0.001	9.72 (9.03-10.41) [9]
S	19.2 (28)	80.8 (118)	0.224	56.2 (82)	0.717	8.66 (7.87-9.44) [8]
T	17.3 (90)	82.7 (429)	<0.001	60.5 (314)	<0.001	8.97 (8.56-9.38) [9]
U	16.0 (26)	84.0 (137)	0.016	65.0 (106)	0.003	9.09 (8.35-9.83) [9]
X*	10.9 (7)	89.1 (57)	0.041	67.2 (43)	0.233	9.72 (8.45-10.99) [10]
Y**	19.1 (22)	80.9 (93)	0.030	58.3 (67)	0.004	8.63 (7.78-9.47) [8]
Z	18.5 (5)	81.5 (22)	0.574	63.0 (17)	0.387	9.44 (7.65-11.24) [10]

Table 3.1.2 Cont.

Pharmacological classes (INFARMED)						
2	9.2 (52)	90.8 (512)	<0.001	68.8 (388)	<0.001	9.77 (9.42-10.12) [9]
3	11.8 (73)	88.2 (546)	<0.001	63.8 (395)	<0.001	9.35 (9.01-9.69) [9]
4	2.5 (7)	97.5 (272)	<0.001	83.5 (233)	<0.001	11.27 (10.78-11.75) [11]
5	7.5 (12)	92.5 (148)	<0.001	78.1 (125)	<0.001	11.14 (10.42-11.85) [11]
6	5.7 (22)	94.3 (361)	<0.001	78.1 (299)	<0.001	10.81 (10.37-11.24) [10]
7	13.6 (17)	86.4 (108)	0.006	63.2 (79)	0.039	9.49 (8.68-10.30) [9]
8	8.4 (27)	91.6 (295)	<0.001	74.2 (239)	<0.001	10.64 (10.14-11.14) [10]
9	8.6 (35)	91.4 (373)	<0.001	74.3 (303)	<0.001	10.11 (9.69-10.53) [10]
10	5.2 (8)	94.8 (146)	<0.001	79.9 (123)	<0.001	11.07 (10.39-11.76) [11]
16	0 (0)	100 (12)	0.056	91.7 (11)	0.010	13.58 (9.80-17.37) [13.5]
Number of prescribers			<0.001		<0.001	
≤2	34.5 (167)	65.5 (317)		39.5 (191)		6.48 (6.10-6.86) [6]
>2	2.6 (7)	97.4 (266)		82.1 (224)		11.29 (10.78-11.80) [11]

* considering only women   ** considering only men
A - General and unspecified; B - Blood, blood forming organs, lymphatics, spleen; D - Digestive; F - Eye; H - Ear; K - Circulatory; L - Musculoskeletal; N - Neurological; P - Psychological; R - Respiratory; S - Skin; T - Endocrine, metabolic and nutritional; U - Urology; X - Female genital system and breast; Y - Male genital system; Z - Social problems; 2 - Central nervous system; 3 - Cardiovascular system; 4 - Blood; 5 - Respiratory system; 6 - Digestive system; 7 - Genitourinary system; 8 - Hormones and medications used to treat endocrine diseases; 9 - Locomotive system; 10 - Antiallergic medication; 16 - Antineoplastic and immunomodulatory drugs

Table 3.1.3 – Logistic regression model for polypharmacy

Characteristics	Polypharmacy					
	≥5 drugs			≥8 drugs		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender						
Women	---	---	---	1.86	1.24-2.80	0.003
Men	---	---	---	base	---	---
Age	1.05	1.02- 1.08	0.002	1.02	1.00-1.04	0.109
Number of chronic health problems	1.24	1.07-1.45	0.005	1.11	1.02-1.20	0.016
A	1.17	0.47-3.00	0.735	---	---	---
D	1.55	0.88-2.75	0.131	0.77	0.51-1.16	0.204
F	---	---	---	0.91	0.56-1.47	0.696
H	1.20	0.49-2.91	0.688	---	---	---
K	2.43	1.37-4.30	0.002	2.53	1.56-4.11	<0.001
L	0.66	0.39-1.13	0.130	0.99	0.67-1.48	0.974
N	0.62	0.31-1.27	0.195	1.13	0.68-1.87	0.644
P	0.98	0.55-1.75	0.953	0.96	0.64-1.46	0.851
R	1.19	0.61-2.33	0.619	1.06	0.68-1.67	0.788
T	1.49	0.86-2.61	0.159	1.32	0.87-2.01	0.192
U	0.67	0.35-1.26	0.214	1.03	0.64-1.65	0.909
X	1.24	0.45-3.38	0.678	---	---	---
Y	0-77	0.39-1.53	0.451	1.33	0.75-2.33	0.329
Number of prescribers	4.71	3.42-6.48	<0.001	2.32	1.97-2.73	<0.001

OR - Odds ratio; A - General and unspecified; D - Digestive; F - Eye; H - Ear; K - Circulatory; L - Musculoskeletal; N - Neurological; P - Psychological; R - Respiratory; T - Endocrine, metabolic and nutritional; U - Urology; X - Female genital system and breast; Y - Male genital system

Table 3.1.4 – 15 most used pharmacological subclasses and common chronic health problems

INFARMED pharmacotherapeutic classification	% (n)	ICPC-2 chronic health problems	% (n)
3.4.2 ACE inhibitor/ARBs	56.8 (430)	K86 Hypertension uncomplicated	54.7 (414)
3.7.1 Statins	52.0 (394)	T93 Lipid disorder	48.1 (364)
2.10 Analgesics and antipyretics	50.6 (383)	T90 Diabetes non-insulin dependent	24.0 (182)
6.2.2.3 PPIs	38.2 (289)	L86 Back syndrome with radiating pain	17.7 (134)
3.4.1.1 Thiazide	37.5 (284)	L90 Osteoarthrosis of knee	16.2 (123)
2.9.1.3 Benzodiazepines	33.6 (254)	T82 Obesity	14.8 (112)
3.4.3 Calcium channel blockers	26.7 (202)	K87 Hypertension complicated	14.1 (107)
2.9.3 Antidepressants	24.7 (187)	P76 Depressive disorder	13.2 (100)
4.3.1.3 Antiplatelet agents	23.6 (179)	Y85 Benign prostatic hypertrophy	12.9 (98)
9.1.3 NSAIDs - Propionic acid derivatives	22.3 (169)	T83 Overweight	12.2 (92)
3.4.4.2 Beta blockers	21.9 (166)	L91 Osteoarthrosis other	10.8 (82)
8.4.2.1 Biguanide	21.4 (162)	K95 Varicose veins of leg	10.0 (76)
8.2 Corticosteroids	18.1 (137)	F92 Cataract	9.4 (71)
10.1.2 H1 non-sedative antihistamines	17.7 (134)	P74 Anxiety disorder / anxiety state	9.4 (71)
2.12 Narcotic analgesics	15.3 (116)	L87 Bursitis / tendinitis / synovitis NOS	8.6 (65)

Discussion

As described in the project protocol (15), the objectives for phase I of the project were to identify the prevalence and its characteristics of polypharmacy and PIMs in the elderly Portuguese population. The results related to the PIMs have already been published (13), but they are not necessarily related to the polypharmacy.

Strengths of the study

This was the first study to report the prevalence and patterns of polypharmacy in older adults attending primary care consultations on a national scale in Portugal.

We performed a cross-sectional study, which is the most frequent design to assess prevalence and its characteristics.

We used the most discriminative chemical subgroup of the Portuguese pharmacotherapeutic classification, to assess polypharmacy; this can minimize the bias of medical changes.

We assessed the number of medications taken by older adults using doctor's prescription records to minimise memory bias.

Since the data was mainly obtained by SPMS from national records (which allowed for a more representative sample of the population) and by sampling according to the patient's national health number in most health regions, we avoided an over-representation of frequent users of primary care services (normally the ones with higher number of morbidities and medication).

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Statement of overall findings

The study results show a high prevalence of polypharmacy in the Portuguese older population (77%), exceeding the reported prevalence of other studies (30-70%) (5). One of the explanations can be the period of time we used in this study (12-months), which can increase polypharmacy (21), making this high prevalence misrepresentative of reality, since medication could have been ceased. We used a more prolonged period of time because we conceived it would allow differentiation between chronic and acute medication, done by evaluating the number of times each medication was prescribed in order to obtain a more accurate value (22). Further research is needed to better assess which methodology is more suitable, a 12-month or a 6-month period.

Another explanation can be that we assessed the prescribed drugs and not the ones that were dispensed or consumed by the patient (therapeutic adhesion). This can be misrepresentative of reality, patients could have stopped taking their medication (due to adverse effects, financial problems...) and not have informed their doctor. On the other hand, we didn't consider over-the-counter medications and the medications prescribed without the use of the electronic program PEM (e.g. manually), which may have a residual effect.

It is likely that differences in the rate of polypharmacy can be found at the prescriber level (14). This variation could be explained by practitioners single handily treating diseases and illnesses and the lack of guidelines regarding polypharmacy or its prescription (23). However, efforts to address polypharmacy within evidence-based deprescribing guidelines are being pursued (24).

In line with previous reports (11,25,26), we found a significant association between increased age and prevalence of polypharmacy. This could be due to the increase in the prevalence of age-related chronic diseases, which are accompanied by an increase in medications and possibly also because of prescribing for social problems (27). However, in our new definition ($\geq$ median number of drugs taken) there wasn't a significant association between increased age and prevalence of polypharmacy. This could be due to the increase of the threshold of polypharmacy that can be preventing labelling polypharmacy to older adults just because of the increase of comorbidities and drugs that can be necessary to them, commonly referred as appropriate polypharmacy as suggested by Steinman et al. (3).

There was no difference in risk of polypharmacy between genders with the common definition of polypharmacy. Our findings met the ones of other studies (11,28). However, there are studies that found an increased risk of polypharmacy in men (26) and women (14,25). A higher prevalence of polypharmacy was also present in our study when we considered polypharmacy as a value equal to or greater than the median number of drugs ($\geq$8) taken by the population. One of the explanations can be that women tend to live more than men, therefore having more chronic health problems and needing more drugs. However, more studies are needed to assess if there is a difference in risk of polypharmacy between genders.

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As expected, the number of chronic health problems affects the number of medications taken by the patient and this association has been well described in the literature (11,14,25,28). However, in our study there were some chronic health problems with a stronger impact on the risk of polypharmacy, for example group classification D (digestive problems) for polypharmacy as ≥5 drugs and K (cardiovascular) for our definition (≥ the median number of drugs taken).

More prescribers per patient were associated with higher risk of polypharmacy, namely for the common definition (≥5). One of the explanations is that having multiple prescribers may unknowingly duplicate or induce contraindicated medication regimens due to lack of information available, which increases the risk of serious adverse drug events (29). On the other hand, more complex patients (with multimorbidity) need to be assisted by more doctors and take more drugs. To our knowledge, this is one of the first studies to assess the impact of having multiple prescribers on polypharmacy.

In agreement with previous reports (14,26), cardiovascular, metabolic and musculoskeletal medications were the most common in our study sample. These are in line with the most common chronic health problems described in Portugal, (19) which are cardiovascular (such lipid disorder and hypertension), metabolic (such diabetes and obesity) and musculoskeletal (such back syndrome pain, osteoarthritis and osteoarthrosis) problems (30). Highlighting the importance of prescribing the best drug option for the patient.

Our proposed definition had a better specificity in detecting PIM than the common definition, which means a much lower number of false positive "result". This occurred at the cost of diminished sensibility. However, we found a similar mean number of PIMs in both groups (with polypharmacy and without) according to both definitions. These results are in line with those of Steinman et al. (3), which raise the question of whether we should raise the threshold to avoid the risk of under-use as there does not seem to be a greater risk of inappropriate prescription. For us the advantage of our definition compared to others that propose a higher threshold is that it is not a rigid definition and can be adapted to a specific population morbidity burden, since different populations have different needs. Therefore, it would be like standardizing the risk of inappropriate prescription according to the population´s morbidity burden to help us compare the impact of different health systems and policies on this problem.

Limitations of the study

There are some limitations in this study.

Firstly, we used a 12-months period to assess the chronic prescribed medication, which can increase the prevalence of polypharmacy, since medication could have been ceased or not purchased (non-compliance). Therefore, the number of medications per older adult may be overestimated.

Secondly, since the SPMS couldn't provide us with data from both autonomous regions (Madeira and Azores), representing 1.7% of the sample, data were collected by local GPs, making the sample and data processes in these two regions different from the rest. Nevertheless, randomisation was performed for these data.

Thirdly, we intended to evaluate the effects of level of education on polypharmacy. Such was not possible due to lack of information in the patients' electronic records.

Fourthly, the sample size was chosen to achieve a sufficiently precise overall proportion estimate of polypharmacy in the Portuguese older adults' population, but not to find differences among different population strata.

Fifthly, we could not find any study using an approach like ours (polypharmacy as ≥ median number of drugs taken by the population) and had great difficulty making comparisons between different studies.

Sixthly, we could not have data on over-the-counter medications, so the prevalence of polypharmacy can be underestimated.

Finally, this was a cross-sectional study and so no causal relationship could be proven, and we could not study the health consequences of polypharmacy, namely drug-drug interactions and adverse drug reactions. Therefore, longitudinal studies are needed to understand if these factors are responsible for the prevalence of polypharmacy. However, we intended to study prevalence and raise questions and not determine causality, so other studies are required to study causality, frequency and outcomes.

Conclusion

This study found a high prevalence of polypharmacy in the studied sample; the most important factors were number of chronic health problems and number of prescribers in both used definitions and age in the most common definition and being female in our new definition.

Polypharmacy should consider medical constraints, pathological needs and patients' feelings and fears, implying future studies on the accurateness of prescription and the need of deprescription.

We think that our new definition of polypharmacy is of relevance for practitioners since it will identify patients with higher risks. However, further studies are needed to increase its reliability and usefulness.

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3.2 Prevalence of Potentially Inappropriate Medication in the Older Adult Population within Primary Care in Portugal: A Nationwide Cross-Sectional Study

Abstract

Background: In potentially inappropriate medications harm potentially outweighs benefits. Even appropriately prescribed medications may become inappropriate. They can lead to a high risk of adverse drug reactions, morbidity and mortality. The aim of this study was to determine the prevalence of potentially inappropriate medication in the older adult population attending primary care in Portugal and to identify associated sociodemographic and clinical factors.

Methods: We conducted a cross-sectional, analytical study in primary care centres from the five Portuguese healthcare administrative regions and the two autonomous regions. We used a random sample of 757 older patients provided by the information department of the ministry of health (SPMS) and family doctors from the autonomous regions. Data collection occurred March 2018 and we studied sociodemographic characteristics, clinical profile and medication. We used 2015 Beers Criteria to assess potentially inappropriate medications. Logistic regression analyses were performed to determine associations between potentially inappropriate medications' prescriptions and other variables.

Results: Potentially inappropriate medication was present in 68.6% and 46.1% of the sample had two or more. The likelihood of having potentially inappropriate medication increased significantly with being female [OR=1.56 (1.05 to 2.31)], number of chronic health problems [OR=1.06 (1.01 to 1.13)], number of pharmacological subclasses [OR=1.40 (1.30 to 1.51)] and number of prescribers [OR=1.34 (1.09 to 1.65)]. Proton-pump inhibitors, Nonsteroidal anti-inflammatory drugs and Benzodiazepines were the most commonly found ones.

Conclusion: Potentially inappropriate medication in older adults was found to be a common occurrence in Portugal. It is important that doctors are aware of this problem, namely in the primary care setting due to the longitudinal care.

Keywords: potentially inappropriate medication, aged, polypharmacy, multimorbidity

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

Background

Potentially Inappropriate Medications (PIM) are those in which harm potentially outweighs the benefits, namely those that are not indicated or lack evidence of efficacy and those that do not align with patients goals/preferences and values (1). The importance of this increases as people get older because of decreased hepatic and renal functional that changes the benefit/risk ratio of medications, so even when appropriately prescribed medications can become inappropriate (2,3). An Australian study reported that 60 of 100 hospitalized patients had at least one PIM, leading to a high risk of adverse drug reactions, morbidity and mortality (4). There is international consensus about when to start many medications that are safe and effective, but there are no guidelines regarding cessation of inappropriate medications (5).

Many medication screening tools were developed to aid identification of PIMs in older adults and improve their care (6–8). The medication screening tools can be divided in explicit checklists (lists of medications to be avoided in older adults) and implicit checklists (issues to be taken into account before prescribing a medication) (9). The most widely used are Beers criteria (10) and the STOPP/START criteria (STOPP-screening tool of older persons potentially inappropriate prescriptions/ START-screening tool to alert doctors to right treatment) (11). The Medication Appropriateness Index is an example of an implicit checklist (9).

Older patients, particularly those aged 65 and over, are more frequently diagnosed with more pathologies, multimorbidity, and conditions prone to involve more prescription drugs (12,13).

In Portugal there are only studies about the prevalence of PIM in some of its regions, none conducted nationwide (14,15). The most recent study in a primary care health centre in north of Portugal identified a 37.0% prevalence of PIM, more frequent in women (40.7%) than in men (30.9%) (14).

The aim of this study was to identify the nationwide prevalence of PIM in older adults, identified in primary care setting, in Portugal and its sociodemographic and clinical profiles.

Material and methods

Study design

Cross-sectional study-details, definitions and methods were previously published (16).

The study was conducted in agreement with the principles of the Declaration of Helsinki (17) and received ethical approval from University of Beira Interior and Portuguese healthcare administrative regions Institutional Ethics Committees. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (18).

Sampling

Since there were 2.18 million older adults (≥65 years) in Portugal and the national literature suggested that the range of PIM is around 40% and the international literature around 60%, we assumed the rate to be over 50% because of epidemiological concern for better evidence and larger sampling. We estimated a sample of a minimum 742 patients for a 95% CI and a maximum precision error of 5%. In agreement with the geographical distribution of the Portuguese population aged 65 and older across the five mainland healthcare administrative regions and the two autonomous regions (Madeira and Azores), noted in PORDATA (19), a random sample of 757 patients was provided by the information department of the ministry of health, Serviços Partilhados do Ministério da Saúde (SPMS), and invited family doctors from autonomous regions, due to lack of digital databases within these last regions.

Data collection procedures

Data collection occurred in March 2018 (data extracted on March 30th). In brief, the SPMS provided us with an electronic file with the variables of the study from the randomly selected (by patient's national health number) sample of the five healthcare administrative regions. This electronic file contained anonymised information stored in the patient's electronic medical records. Since SPMS doesn't have access to electronic medical records from patients in the two autonomous regions, we invited two medical doctors, one from each autonomous region, to provide us with the needed information. We studied the prescribed medications using the mandatory nationwide, electronic prescription platform (PEM) (20). There is an unknown number of over-the-counter medications consumed by the Portuguese population and as they can be bought without prescription, there is no way to access this information. SPMS couldn't provide us with information regarding level of education, since in most cases it was missing from medical records.

Outcome variable

For each patient, PIM was measured as the presence of one or more drugs, that are inappropriate for older patients, according only to table 2 of 2015 Beers Criteria (10).

Independent variables

Sociodemographic characteristics such as age, gender (male/female), area of residence (in terms of health administrative region), clinical profile (chronic health problems according to International Classification of Primary Care, second edition – ICPC-2) and prescribed medication (from April 2017 to March 2018 and was encoded following the Portuguese pharmacotherapeutic classification using the more discriminate level possible). The Portuguese pharmacotherapeutic classification has similarities with the ATC (Anatomical Therapeutic Chemical) classification and was adapted by INFARMED (National Authority of Medicines and Health Products) (21).

Statistical analysis

In addition to the descriptive analysis, χ2 tests were performed for nominal qualitative characteristics. Lastly, we performed a logistic regression with all the statistically significant variables in previous χ2 tests. All tests were two-sided using a significance level of 0.05. Statistical analysis was conducted using SPSS V.24.0.

Results

Characteristics of participants

The sample consisted of 757 individuals; the mean age was of 75.5±7.9 years (75.1±7.9 years for men and 75.8±7.8 years for women). Table 3.2.1 shows the characteristics of the sample.

Table 3.2.1 Characteristics of the sample

Characteristic	Total % (n)
Gender	
Women	56.8 (430)
Men	43.2 (327)
Health administrative region	
North	32.2 (244)
Centre	25.1 (190)
Lisbon-Tejo Valley	27.7 (210)
Alentejo	8.7 (66)
Algarve	4.5 (34)
Madeira	0.9 (7)
Azores	0.8 (6)
Age	
<75 years	51.5 (390)
≥75 years	48.2 (365)
Number of chronic health problems	
0-2	17.3 (131)
3-4	19.3 (146)
5-6	17.6 (133)
7-8	16.8 (127)
9-10	11.9 (90)
≥11	17.2 (130)
Chronic health problems (ICPC2)	
A	11.2 (85)
B	7.5 (57)
D	36.5 (276)
F	20.5 (155)
H	11.5 (87)
K	77.5 (587)
L	51.8 (392)
N	15.7 (119)
P	34.3 (260)
R	23.4 (177)
S	19.3 (146)
T	68.6 (519)
U	21.5 (163)
X	9.5 (72)
Y	15.2 (115)
Z	3.6 (27)
Number of pharmacological subclasses	
0-4 drugs	23.1 (175)
5-9 drugs	39.0 (295)
≥10 drugs	37.9 (287)
Pharmacological classes (INFARMED)	
2	74.5 (64)
3	81.8 (619)
4	36.9 (279)
5	21.1 (160)
6	50.6 (383)
7	16.5 (125)
8	42.5 (322)
9	53.9 (408)
10	20.3 (154)
16	1.6 (12)
Number of prescribers	
≤2	63.9 (484)
>2	36.1 (273)

A - General and unspecified; B - Blood, blood forming organs, lymphatics, spleen; D - Digestive; F - Eye; H - Ear; K - Circulatory; L - Musculoskeletal; N - Neurological; P - Psychological; R - Respiratory; S - Skin; T - Endocrine, metabolic and nutritional; U - Urology; X - Female genital system and breast; Y - Male genital system; Z - Social problems; 2 - Central nervous system; 3 - Cardiovascular system; 4 - Blood; 5 - Respiratory system; 6 - Digestive system; 7 - Genitourinary system; 8 - Hormones and medications used to treat endocrine diseases; 9 - Locomotive system; 10 - Antiallergic medication; 16 - Antineoplastic and immunomodulatory drugs

Prevalence of Potentially Inappropriate Medication

More than 9 out of 10 older patients of the sample (93.4%) had at least 1 medication prescribed, with an overall average of 8.2 (95% CI 7.9 to 8.6), 7.5 (95% CI 7 to 8) in men and 8.8 (95% CI 8.3 to 9.3) in women.

Potentially inappropriate medication was present in 68.6% (95% CI 65 to 72%) of the sample and 2 or more PIMs were present in 46.1% (95% CI 42.5 to 49.7%), with an overall average of 1.76 (95% CI 1.63 to 1.89), 1.35 (95% CI 1.18 to 1.52) in men and 2.07 (95% CI 1.88 to 2.26) in women.

According to table 3.2.2, there was no significant relationship between PIM and health administrative region. There was a significant relationship between PIM and number of chronic health problems, number of medications taken, number of prescribers and with many of the ICPC-2 classes and pharmacological subclasses.

Table 3.2.2 Prevalence of PIM according to characteristics

Characteristic	No PIM % (n)	PIM % (n)	p-value (χ2 test)	Mean number of PIMs (95% CI) [median]
Gender			<0.001	
Women	32.3 (139)	67.7 (291)		2.07 (1.88 to 2.26) [2]
Men	47.7 (156)	52.3 (171)		1.35 (1.18 to 1.52) [1]
Health administrative region			0.201	
North	32.0 (78)	68.0 (166)		1.66 (1.44 to 1.89) [1]
Centre	31.1 (59)	68.9 (131)		1.85 (1.59 to 2.12) [1]
Lisbon-Tejo Valley	28.9 (58)	71.1 (152)		2.00 (1.75 to 2.26) [2]
Alentejo	37.9 (25)	62.1 (41)		1.38 (0.95 to 1.81) [1]
Algarve	44.1 (15)	55.9 (19)		1.32 (0.53 to 2.11) [1]
Madeira	42.9 (3)	57.1 (4)		0.57 (0.08 to 1.07) [1]
Azores	0 (0)	100 (6)		2.33 (1.25 to 3.42) [2]
Age			0.048	
<75 years	34.6 (135)	65.4 (255)		1.70 (1.52 to 1.88) [1]
≥75 years	27.9 (102)	72.1 (263)		1.83 (1.64 to 2.03) [1]
Number of chronic health problems			<0.001	
0-2	54.2 (71)	45.8 (60)		1.14 (0.85 to 1.42) [0]
3-4	43.8 (64)	56.2 (82)		1.40 (1.10 to 1.70) [1]
5-6	30.1 (40)	69.9 (93)		1.65 (1.33 to 1.96) [1]
7-8	18.9 (24)	81.1 (103)		2.08 (1.76 to 2.40) [2]
9-10	25.6 (23)	74.4 (67)		1.83 (1.47 to 2.20) [2]
≥11	12.3 (16)	87.7 (114)		2.55 (2.22 to 2.89) [2]
Chronic health problems (ICPC2)				
A	22.4 (19)	77.6 (66)	0.063	2.07 (1.66 to 2.49) [2]
B	24.6 (14)	75.4 (43)	0.299	1.91 (1.40 to 2.43) [1]
D	21.0 (58)	79.0 (218)	<0,001	2.14 (1.90 to 2.38) [2]
F	27.1 (42)	72.9 (113)	0.208	2.06 (1.74 to 2.37) [2]
H	21.8 (19)	78.2 (68)	0.049	2.21 (1.80 to 2.61) [2]
K	29.1 (171)	70.9 (416)	0.012	1.82 (1.67 to 1.97) [1]
L	23.2 (91)	76.8 (301)	<0.001	2.06 (1.86 to 2.25) [2]
N	21.8 (26)	78.2 (93)	0.018	2.29 (1.93 to 2.65) [2]
P	22.7 (59)	77.3 (201)	<0.001	2.21 (1.97 to 2.46) [2]
R	19.8 (35)	80.2 (142)	<0.001	2.19 (1.91 to 2.47) [2]
S	27.4 (40)	72.6 (106)	0.275	1.72 (1.45 to 1.99) [1]
T	27.9 (145)	72.1 (374)	0.002	1.83 (1.67 to 1.99) [1]
U	23.3 (38)	76.7 (125)	0.013	1.94 (1.67 to 2.20) [2]
X	18.1 (13)	81.9 (59)	0.011	2.22 (1.79 to 2.66) [2]
Y	28.7 (33)	71.3 (82)	0.515	1.67 (1.34 to 2.00) [1]
Z	14.8 (4)	85.2 (23)	0.089	2.30 (1.58 to 3.01) [2]
Number of pharmacological subclasses			<0.001	
0-4 drugs	73.7 (129)	26.3 (46)		0.35 (0.25 to 0.45) [0]
5-9 drugs	29.2 (86)	70.8 (209)		1.42 (1.27 to 1.58) [1]
≥10 drugs	8.0 (23)	92.0 (264)		2.97 (2.73 to 3.21) [3]
Pharmacological classes (INFARMED)				
2	17.9 (101)	82.1 (463)	<0.001	2.21 (2.05 to 2.36) [2]
3	26.0 (161)	74.0 (458)	<0.001	1.94 (1.79 to 2.09) [2]
4	19.7 (55)	80.3 (224)	<0.001	2.14 (1.91 to 2.37) [2]
5	18.1 (29)	81.9 (131)	<0.001	2.43 (2.12 to 2.73) [2]
6	8.6 (33)	91.4 (350)	<0.001	2.78 (2.58 to 2.98) [2]
7	28.0 (35)	72.0 (90)	0.400	1.89 (1.55 to 2.22) [1]
8	22.4 (72)	77.6 (250)	<0.001	2.02 (1.80 to 2.23) [2]
9	10.3 (42)	89.7 (366)	<0.001	2.51 (2.33 to 2.70) [2]
10	14.3 (22)	85.7 (132)	<0.001	2.51 (2.22 to 2.81) [2]
16	8.3 (1)	91.7 (11)	0.117	2.83 (1.28 to 4.39) [2]
Number of prescribers			<0.001	
≤2	42.8 (207)	57.2 (277)		1.24 (1.10 to 1.38) [1]
>2	11.4 (31)	88.6 (242)		2.69 (2.46 to 2.92) [2]

A - General and unspecified; B - Blood, blood forming organs, lymphatics, spleen; D - Digestive; F - Eye; H - Ear; K - Circulatory; L - Musculoskeletal; N - Neurological; P - Psychological; R - Respiratory; S - Skin; T - Endocrine, metabolic and nutritional; U - Urology; X - Female genital system and breast; Y - Male genital system; Z - Social problems; 2 - Central nervous system; 3 - Cardiovascular system; 4 - Blood; 5 - Respiratory system; 6 - Digestive system; 7 - Genitourinary system; 8 - Hormones and medications used to treat endocrine diseases; 9 - Locomotive system; 10 - Antiallergic medication; 16 - Antineoplastic and immunomodulatory drugs

After adjustment, table 3.2.3 shows that the likelihood of having PIM increased significantly in females [OR=1.56 (1.05-2.31)], with number of chronic health problems [OR=1.06 (1.01-1.13)], number of pharmacological subclasses [OR=1.40 (1.30-1.51)] and number of prescribers [OR=1.34 (1.09-1.65)]. No differences in the odds of PIM were associated with age [OR=0.99 (0.97-1.05)].

Table 3.2.3 Adjusted analysis for factors associated with PIM use

Characteristics	PIM		
	OR	95% CI	p-value
Gender			
Women	1,56	1.05- 2.31	0.026
Men	base	-	-
Age	0.99	0.97-1.05	0.512
Number of chronic health problems	1.06	1.01-1.13	0.028
A	0.88	0.52-1.48	0.632
D	1.41	1.11-1.78	0.004
H	0.94	0.56-1.58	0.814
K	1.23	1.04-1.45	0.014
L	1.27	1.10-1.48	0.001
N	1.16	0.79-1.70	0.455
P	1.29	0.99-1.66	0.052
R	1.49	1.09-2.04	0.014
T	1.17	0.99-1.38	0.056
U	1.19	0.88-1.60	0.253
X	1.29	0.73-2.27	0.375
Number of pharmacological subclasses	1.40	1.30-1.51	<0.001
2	2.35	1.95-2.84	<0.001
3	1.08	0.94-1.24	0.301
4	0.94	0.65-1.36	0.749
5	1.09	0.74-1.60	0.662
6	4.86	3.18-7.42	<0.001
8	1.07	0.85-1.36	0.552
9	5.25	3.53-7.81	<0.001
10	1.55	0.81-2.97	0.185
Number of prescribers	1.34	1.09-1.65	0.005

OR - Odds ratio; A - General and unspecified; D - Digestive; H - Ear; K - Circulatory; L - Musculoskeletal; N - Neurological; P - Psychological; R - Respiratory; T - Endocrine, metabolic and nutritional; U - Urology; X - Female genital system and breast; 2 - Central nervous system; 3 - Cardiovascular system; 4 - Blood; 5 - Respiratory system; 6 - Digestive system; 8 - Hormones and medications used to treat endocrine diseases; 9 - Locomotive system; 10 - Antiallergic medication

Chronic health problems / pharmacological subclasses and patterns of PIM

Table 3.2.3 shows the odds ratio measured impact of having each specific chronic health problems (according to ICPC2). For patients suffering from chronic health problems related to digestive, circulatory, musculoskeletal and respiratory systems there is 1.4 times, 1.2 times, 1.3 times and 1.5 times, respectively, greater probability of having a PIM when comparing to those not suffering from health problems related to that specific system. Older adults taking medication from central nervous system, digestive system and locomotive system groups (according to Portuguese pharmacotherapeutic classification) are 2.4 times, 4.9 times and 5.3 times, respectively, more likely to have PIM than those not taking any drug from that system

group. The most common pharmacological subclasses causing PIM were Proton-pump inhibitors (present in 45.6% of the sample), Nonsteroidal anti-inflammatory drugs (in 34.5%) and Benzodiazepines (in 27.3%).

Discussion

Strengths of the study

This is the first study to report the prevalence and patterns of PIM in older adults attending primary care consultations nationwide in Portugal. It is a cross-sectional study with a randomised sample, which is the most frequent design to assess prevalence and its characteristics. We used the most discriminative chemical subgroup of the Portuguese pharmacotherapeutic classification, to assess polypharmacy; this can minimize the bias of medical changes. We also used active components according to 2015 Beers Criteria (10) for assessing PIM, since for some pharmacological classes some active pharmaceutical ingredients are potentially inappropriate while others are safe.

Since the data was obtained from SPMS on a nationwide scale, we could obtain a size representative sample of the population, avoiding over-representation of the more frequent users of primary care services, which could happen if the data were collected from GP records of most frequent prescriptions.

Statement of overall findings

The study results show a high prevalence of PIMs in the Portuguese older population (68.6%), exceeding the reported prevalence of other studies (11.5-62.5%) (22). One of the explanations can be the period of time we used in this study (12-months), which can increase polypharmacy (23) and affect the number of PIM, making this high prevalence misrepresentative of reality, since medication could have been ceased or not purchased. Given the lack of consensus of classification for PIM (6), we used the list of drugs in table 2 of 2015 Beers Criteria. We used Beers Criteria because it is the most commonly used tool to identify PIM in the literature with regular updates.

We found no difference in risk of PIM with increasing age. Our findings don´t match those from other studies; most of them found an increased risk of PIM in younger and older ages (22,24). Since there are mixed results, more studies are needed to assess this relation. One hypothesis for this discrepancy is that there is a higher awareness of this problem in overall patients with ≥65 years due to increased susceptibility to adverse drug events, age-related drug-drug and drug-disease interactions, making it possible to think that there is no difference in pharmacological care in people equal and older than 65 in Portugal as age increases (25).

In line with previous reports (22), we found an increased risk of PIM in women. We can hypothesise that women tend to live longer and be more prone to have complaints, either physical or psychological. More studies are necessary to study this issue.

As expected, the number of medications affects the number of PIMs, since with an increased number of drugs there is an increased probability of adverse drug reactions and drug-drug interactions. This association is described in the literature (22,24,26).

We found a difference in risk of PIM with the number of comorbidities, showing the impact that multimorbidity also affects the health of older adult population through the increased risk of PIM (12). Our results again do not match those from other studies. Differences in the pharmacological and health problems data collection could explain such discrepancies (24,26). However an increase number of comorbidities can lead to and can be the cause of an increase number of prescribed drugs, increasing the risk of PIM (12). From the four ICPC-2 classes with high impact on the risk of PIM according to our finding (digestive, cardiovascular, musculoskeletal and respiratory problems), only the musculoskeletal problems are described in the literature (26).

In line with previous reports (27), more prescribers were associated with higher risk for PIM. One hypothesis is that prescribers may not be aware of all the medication the patient is taking nor of the changes made by other prescribers to the list of medication; this increases the risk of duplicated drugs, adverse drug reactions, drug-drug interactions and drug-disease interactions. On the other hand, more complex patients (with multiple comorbidities) need to be assisted by more doctors and take more drugs, increasing the risk of PIM. This is of extreme importance, since 17% of our older adults had 4 or more prescribers within the last year. It is also important for previously prescribed medication to be listed for everyone on the national electronic drugs prescription system (PEM).

According to previous reports (24,26), PPIs, NSAID and benzodiazepines are among the most common PIM in the older adult population in primary health care in Portugal. Therefore, there is a need to quantify the resulting harms for individuals, families and society, and to make its economic and financial impact known to medical and lay communities, in order to help deprescribing to become easier for doctors and better accepted by patients.

Limitations of the study
There are some limitations of this study.

Firstly, we used a 12-month period to assess the chronic prescribed medication, which can increase the prevalence of polypharmacy and PIM, since medication could have been ceased or not purchased. Therefore, the number of medications, as well as the number of PIMs, per older adult may be overestimated.

Secondly, since the SPMS couldn't give us data from both autonomous regions (Madeira and Azores), representing 1.7% of the sample, data was collected by local GPs, making the sample and collection data processes in these two regions different from the rest. Nevertheless, randomisation was performed.

Thirdly, there was the intention of evaluating the effect of level of education on polypharmacy. Such was not possible due to lack of information in patient's electronic records.

Fourthly, we only used the table 2 of 2015 Beers Criteria for assessing PIM, therefore PIM due to drug-disease and drug-drug were not assess due to the complexity of this analysis and our 12-month period assessment of prescribed medication. Also, the Beers criteria was updated in April 2019, where some drugs were eliminated from and others added to the previous list (2015 Beers Criteria), but since at the time of study (2018) the most recent list was 2015 Beers criteria we kept them.

Fifthly, the sample size was chosen to achieve a sufficiently precise overall proportion estimate of PIMs in the Portuguese older adults' population, but not to find differences among different population strata.

Finally, this is a cross-sectional study and so no causal relationship could be proven. However, we only intended to raise questions and not determine causality, so other studies are required to study causality, frequency and outcomes.

Conclusion

This study found a high prevalence of PIM in the studied sample; the most important factors were being female, number of chronic health problems, number of pharmacological classes and number of prescribers.

It is important that doctors are aware of this problem, namely in the primary care setting due to the longitudinal profile of care in general practice.

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3.3 Elderly patients facing the idea of being deprescribed: a mixed method study in Portuguese primary health care

Abstract

Background: Deprescribing is the process of tapering or stopping medications with the aim of improving patient outcomes and optimising current therapy. While some studies tried to identify which patients will respond positively to deprescribing interventions, none found any association between age, gender, education level, general health status, previous attempt of deprescribing the number of medicines or duration of use and deprescribing process and its success. The aim of this study is to determine Portuguese elderly patients' attitudes and beliefs regarding medication use and their willingness to have regular medications deprescribed.

Methods: We conducted a cross-sectional, analytical study in primary care centres from the five Portuguese healthcare administrative regions and the two autonomous regions. We used a random sample of 386 polymedicated older adult patients that answered the questionnaire between October 2018 and February 2019. For the quantitative analysis we used sociodemographic characteristics, clinical profile and medication. For the qualitative analysis was adopted an open-question. We adopted a convergent mixed methods design.

Results: Most participants (74%) believed that medicines were generally beneficial. However, 19.9% indicated a high belief that medicines were harmful and 33.4% that they were generally overused. Most participants were against the idea of deprescribing (61.8%), with 24.6% being in favour. Those against being deprescribed had lower education level (p=0.006) and a higher number of perceived morbidities (p=0.001) than those not against being deprescribed.

Conclusion: Most patients had a strong belief in medication benefits and were against the idea of deprescribing. It is important that doctors are aware of this reality, namely in the primary care setting, in order to address the patients' fears and beliefs and make the deprescribing possible whenever it benefits the patient.

Keywords: Deprescriptions; Aged; Patient Acceptance of Health Care

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

Background

The prevalence of potentially inappropriate medications (PIMs) is considered to be high in Portuguese elderly patients (≥65 years) in the primary care setting (1).

Deprescribing is the process of tapering or stopping medications with the aim of improving patient outcomes and optimising current therapy (2). While some studies were made in the search of identifying which patients will respond positively to deprescribing interventions, none found any association between age, gender, education level, general health status, previous attempt of deprescribing the number of medicines or its length of use and a deprescribing process and its success (3–5). One of the barriers to deprescribing in the primary care setting is the lack of time in the consultation (6,7). Therefore, creating an accurate profile of patients who are willing to be deprescribed is critical to improve clinical efficiency.

The Beliefs about Medicines Questionnaire (8) is composed of two sections: the General section (BMQ-General), which assesses more general beliefs about medicines and includes the overall perception of Harm (General-Harm subscale) and Overuse (General-Overuse subscale) of medication; and the Specific section (BMQ-Specific), which assesses beliefs about particular medication and explores the needs (Specific-Necessity subscale) and concerns (Specific-Concern subscale) perceived about the medication. This questionnaire is validated for Portuguese population (9).

The aim of this study is to determine Portuguese elderly patients' attitudes and beliefs regarding medication use and their willingness to have regular medications deprescribed. The only previous study about the elderly patients' beliefs regarding medication use was the cross-cultural adaptation of Beliefs about Medicines Questionnaire into Portuguese (9).

Material and methods

Study design

Cross-sectional study-details, definitions and methods were previously published (10). We adopted a convergent mixed methods design (11). Secondary analysis of available quantitative and qualitative data were conducted separately as described below, and the findings were triangulated during the interpretation stage (11,12).

The study was performed in agreement with the principles of the Declaration of Helsinki (13) and received ethical approval from University of Beira Interior and Portuguese healthcare administrative five regions Institutional Ethics Committees. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (14).

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

Setting

The study was carried in randomly selected primary care health centres in Portugal that accepted to participate form the five mainland Portuguese healthcare administrative regions and two autonomous regions (Madeira and Azores).

Sampling

Since the prevalence of polypharmacy in elderly population in Portugal is 77% (15), we estimated a sample of a minimum 385 patients with polypharmacy for a 95% CI and a maximum precision error of 5%.

Assuming that a General Practitioner (GP) would be able to include at least 6 patients, a total of 65 GPs was invited to recruit. The GPs were randomly selected from existing files of previous projects adherent GPs, in other epidemiological studies, for higher adherence rate. The adherence rate was 47.7% (n=31), but since each GPs on average recruited 13 patients and we obtained 403 elderly patients (386 respected the inclusion criteria) we stopped recruiting GPs for the study.

Data Collection Procedures

The invitation of GPs and of patients' recruitment occurred between October 2018 and February 2019. GPs were individually instructed to give the questionnaire and the informed consent to all elderly patients with polypharmacy, equal or more than five drugs per day, attending a primary care consultation during six randomised consultations days selected for the month after their acceptance to collaborate. GPs were responsible for explaining the study, answering questions, delivering the questionnaire and the informed consent and collecting them. Exclusion criteria were being acutely unwell in the previous three weeks and refusal to participate.

Quantitative data collection and analysis

A questionnaire to collect sociodemographic information such as age, gender (male/female), area of residence (the health administrative region), perceived number of chronic health problem and auto-referred number of daily medications, was used in the study. We used Beliefs about Medicines Questionnaire-General (BMQ-General). Some researchers were randomly selected to deliver to their participants an extended version of the questionnaire with also BMQ-Specific questionnaire, in order to obtain a more detailed information about patients' beliefs about specific medications they were on, since it comprises two scales assessing personal beliefs about the necessity of prescribed medication for controlling illness and concerns about the potential adverse consequences of medications.

Participants' questionnaires were excluded if any item of BMQ was missing.

Outcome variables:

We calculated mean and median scores for both BMQ parts.

For the BMQ-Specific we created four attitudinal groups towards medication, as used in previous studies (16,17).

- Sceptical (low necessity, high concerns);
- Indifferent (low necessity, low concerns);
- Ambivalent (high necessity, high concerns);
- Accepting (high necessity, low concerns).

Statistical analysis was conducted using SPSS V.24.0 and we used a significance level of 0.05.

Qualitative data collection and analysis

An open-question ("What do you think about stopping some of the medications you are on?") was made on the questionnaire all participants received. Two individual investigators coded the participants' answers summarising the content. The common codes features were grouped together. According to the will to be deprescribed we created four main categories (against, in favour, indecisive and indifferent) and subcategories emerged from the answers. According to the centre for decision of deprescribing, three main categories (the person himself, the doctor and other) were constructed (18,19).

Results

Characteristics of participants

Of the 386 participants, 59.7% were female, mean age of 76.7 (95% CI 76.0 to 77.4) years and the mean number of drugs per person was 7.3 (95% CI 7.1 to 7.6) (Table 3.3.1).

Of the 100 participants that answered to extended version of the questionnaire, 59% were female, mean age of 80.1 (95% CI 78.5 to 81.7) years and the mean number of drugs per person was 8.1 (95% CI 7.5 to 8.7).

Table 3.3.1 Characteristics of the sample

Characteristic	Total % (n)	BMQ-Specific responders % (n)	Open-question responders % (n)
Gender			
Women	59.6 (230)	59.0 (59)	57.1 (177)
Men	40.4 (156)	41.0 (41)	42.9 (133)
Age			
65 to 74 years	43.5 (168)	28.0 (28)	43.5 (135)
≥75 years	56.5 (218)	72.0 (72)	56.5 (175)
Education			
Low level (<6 years)	75.1 (290)	84.0 (84)	76.1 (236)
Medium level (6 to 9 years)	13.2 (51)	10.0 (10)	13.5 (42)
High level (>9 years)	10.9 (42)	6.0 (6)	9.4 (29)
Unknown	0.8 (3)	0.0 (0)	1.0 (3)
Perceived number of chronic health problems			
0 to 2	16.8 (65)	55.0 (55)	21.3 (66)
3 to 4	38.1 (147)	19.0 (19)	32.9 (102)
5 to 6	27.5 (106)	8.0 (8)	25.8 (80)
7 to 8	7.5 (29)	1.0 (1)	8.7 (27)
9 to 10	2.8 (11)	0.0 (0)	3.5 (11)
≥11	0.8 (3)	0.0 (0)	1.0 (3)
NA	6.5 (25)	17.0 (17)	6.8 (21)
Number of medications			
5 to 9 drugs	79.5 (307)	68.0 (68)	76.8 (238)
≥10 drugs	21.5 (79)	32.0 (32)	23.2 (72)

Most participants (74%) believed that medicines were generally beneficial. However, 19.9% indicated a high belief that medicines were harmful and 33.4% that they were generally overused (Table 3.3.2).

Analysing the group of 100 participants that answered the extended version, we found similar results for the belief that medicines were harmful (14%) and that they were generally overused (45%).

According to the belief in the need for medication (BMQ-Specific Necessity), 97% agreed for maintaining health (score greater than the scale mid-point), but 45% were concerned about potential adverse consequences of medications (score greater than the scale mid-point). Most of them (74%) indicated strong beliefs that the benefits of their medication outweighed the risks (the difference between the need and concern scores was positive). When participants were categorised by belief group, the majority was found to be accepting (46%) and ambivalent (44%) (Figure 3.3.1).

Table 3.3.2 Patients' beliefs about medicines

BMQ subscale	Mean (95% CI)	p-value	% (n) above the scale mid-pont
General overuse[a]	11.4 (11.1-11.6)		33.4 (129)[g]
Women	11.2 (10.8-11.6)	0.217[e]	31.7 (73)
Men	11.5 (11.1-12.0)		35.9 (56)
65 to 75 years	11.1 (10.7-11.5)	0.306[e]	31.5 (53)
≥75 years	11.5 (11.1-11.9)		34.9 (76)
General harm[a]	10.3 (10.0-10.6)		19.9 (77)[g]
Women	10.3 (9.9-10.8)	0.672[e]	22.2 (51)
Men	10.1 (9.6-10.5)		16.7 (26)
65 to 75 years	10.5 (10.0-10.9)	0.225[e]	23.2 (39)
≥75 years	10.1 (9.6-10.5)		17.4 (38)
Necessity[b]	21.3 (20.1-22.5)		97.0 (97)[h]
Women	21.6 (20.9-22.3)	0.116[e]	96.6 (57)
Men	20.8 (20.0-21.5)		97.6 (40)
65 to 75 years	21.6 (20.6-22.6)	0.423[e]	96.4 (27)
≥75 years	21.1 (20.5-21.7)		97.2 (70)
Concern[c]	17.5 (16.7-18.3)		45.0 (45)[h]
Women	17.3 (16.2-18.5)	0.580[e]	45.8 (27)
Men	17.7 (16.7-18.8)		43.9 (18)
65 to 75 years	17.5 (15.5-19.5)	0.984[e]	42.9 (12)
≥75 years	17.5 (16.7-18.3)		45.8 (33)
Necessity-concern differential[d]	3.8 (2.9-4.7)		74.0 (74)[h]
Women	4.3 (3.0-5.6)	0.171[f]	76.3 (45)
Men	3.0 (1.9-4.2)		70.7 (29)
65 to 75 years	4.1 (2.0-6.2)	0.631[f]	75.0 (21)
≥75 years	3.6 (2.7-4.6		73.6 (53)

[a]Scale from 4 to 20 where high scores indicate higher agreement.
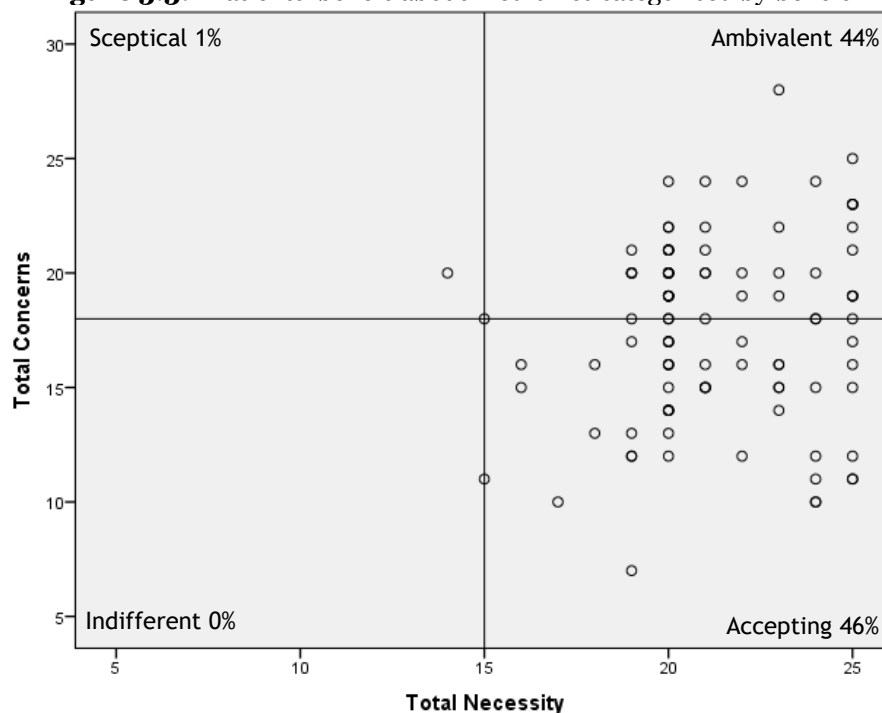[b]Scale from 5 to 25 where high scores indicate higher agreement.
[c]Scale from 6 to 30 where high scores indicate higher agreement.
[d]Scale from -20 to 20 where positive scores indicate patient perceives benefits outweigh risks.
[e]U Mann-Whitney test=386. [f]T-student test.
[g]N=386. [h]N=100.

Figure 3.3.1 Patients' beliefs about medicines categorised by beliefs

Note: n=100

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Participants' views on deprescribing

In order to obtain the participants' views on deprescribing we asked the open-question "What do you think about stopping some of the medications you are on?". From the 386 participants, only 75.9% (n=293) answered this question. From its analysis we found that 61.8% (n=181) of the patients inquired were against the idea of deprescribing.

– *"I don't think it's possible to stop medicines, I have to take them all." [P327, 89 years]*

In favour of the idea were 24.6% (n=72) of the responders; 7.2% (n=21) were indifferent;

– *"I agree, medicines are bad." [P402, 66 years]*
– *"It's the doctor who knows." [P21, 71 years]*
– *"I don't think it's good or bad." [P319, 80 years]*

and 6.5% (n=19) were indecisive.

– *"I would like it, but I think they are what support my health." [P105, 74 years]*
– *"Yes, but I'm afraid." [P131, 78 years]*
– *"It's hard to answer because I don't know what the effect will be on the clinical level." [P380, 76 years]*

From the 181 participants that were against deprescription we could subcategorise 55.2% (n=100) of the answers. Almost half of them (41%) were against because of the perception that it would worse their medical situation;

– *"I can't stop because otherwise I will die" [P36, 76 years]*
– *"There are medications that if I quit my system soon changes, for example cholesterol and tension. If I do not take the inhaler, asthma appears." [P182, 77 years]*

31% were against because of the value they put in the medicines;

– *"I must not stop because they are good for my health" [P35, 66 years]*

Others, 18%, because they felt well as they were;

– *"I think not. If I feel well, there is no need to take away medications." [P339, 83 years]*

6% said that they should take it because if it was prescribed by the doctor;

– *"In my opinion I trust the doctor and I think he prescribes within my needs as a patient." [P150, 72 years]*

and 4% were against because they had already tried stop some medication and it did not go well.

– *"I thought so, but I came to the conclusion that I am addicted to medicines." [P15, 82 years]*
– *"If you stop 2/3 days you will not notice a difference. If it is more days problems arise." [P70, 75 years]*

From the 72 participants that were in favour we could subcategorise 83.3% (n=60) of the answers. The most common reason was because of the will to reduce the medication list (35%). Some patients said:

– *"I would like them to be reduced. I think it was possible." [P295, 83 years]*
– *"The less the better." [P333, 93 years]*

33.3% would agree to stop medication if the doctor told them to;

– *"I do not do it. Only with doctor's indication." [P34, 72 years]*
– *"If the doctor indicates I have no problem stopping the medication. On my own initiative I exclude the possibility of stopping the medication." [P93, 83 years]*
– *"I liked it! But I'm scared! But if the doctor proposed, I would accept it." [P104, 88 years]*

20% if there were side effect or if the medication was ineffective;

– *"I agree perfectly. I think I need to take it off now, because, for example, I sleep a lot now." [P318, 69 years]*
– *"I agree if the medication is not doing well." [P390, 66 years]*
– *"Yes, I would like to reduce the number of medicines I take as they cause unwanted effects." [P400, 68 years]*

and 11.7% were in favour of deprescribing because they had already tried, and it went well.

– *"I do it from time to time when I feel better." [P395, 86 years]*
– *"Sometimes I forget some because I feel good." [P398, 83 years]*

From 190 answers we could deduct were the decision centre about the idea of deprescribing was. In 60.5% the ideas and feelings about medicines and deprescription centre were in the patient.

– *"There are medicines to stop, others not." [P58, 79 years]*
– *"I don't want to stop any medication because I need them all." [P301, 86 years]*
– *"When I am better, I try to reduce, but sometimes I have to go back to what I have prescribed." [P312, 62 years]*

In 39.0% of the answers, patients put the centre of decision in the doctor and 0.5% in a third person.

– *"Error. I would not do it without talk with the physician." [P40, 76 years]*
– *"This opinion I think belongs to the doctor." [P386, 73 years]*
– *"Yes, I think I take too many medications, but it depends on the doctor" [P401, 91 years]*
– *"I was told that I couldn't." [P24, 79 years]*

Will to be deprescribed

We compared the characteristics of the group against the idea of being deprescribed with those of the group not against being deprescribed (in favour, indifferent and indecisive).

We found no significant differences according to age, gender and number of medications. However, we found that those against being deprescribed had lower education level (p=0.006, mean difference of -1.11 years [-1.87 to -0.34]) and had a higher number of perceived morbidities (p=0.001, mean difference of +0.97 [0.41 to 1.52]) than those not against being deprescribed.

Table 3.3.3 shows the differences in responses between both groups according to BMQ (General and Specific). We found statistically significant differences in statement:

- Number 2 "People who take medicines should stop their treatment for a while every now and again" of BMQ general (p<0.001), those against mostly disagreeing with the statement and those not against agreeing with the sentence;
- Statement number 4 "Natural remedies are safer than medicines" of BMQ general (p=0.047), where those against mostly disagreeing with the statement and those not against neither agreeing or disagreeing;
- For BMQ general overuse (p<0.001) those against mostly disagreeing that there was an overuse of medicines and those not against perceiving an overuse of medicines;
- For BMQ general harm (p=0.003) most of the participants in both groups answered that the medication was beneficial but in a lesser degree.

There were no statically significant differences between both groups according to the needs and concerns about medication. However, we found that those against the idea of being deprescribed perceived that the benefits of medication outweigh the risks in a higher degree than those not against the idea (p=0.027, mean difference = 1.97 [0.22 to 3.72]).

Table 3.3.3 Comparation of BMQ according to the will to be deprescribed

BMQ	Will to be deprescribed	Strongly disagree % (n)	Disagree % (n)	Uncertain % (n)	Agree % (n)	Strongly agree % (n)	p-value (χ^2)
G1	Against	18.2 (33)	55.2 (100)	12.7 (23)	9.4 (17)	4.5 (8)	0.177
	Not against	2.7 (3)	12.5 (14)	17.0 (19)	58.9 (66)	8.9 (10)	
G2	Against	22.0 (40)	37.7 (68)	15.4 (28)	19.9 (36)	5.0 (9)	**<0.001**
	Not against	6.3 (7)	29.5 (33)	14.3 (16)	40.1 (45)	9.8 (11)	
G3	Against	11.6 (21)	27.0 (49)	14.4 (26)	36.5 (66)	10.5 (19)	0.308
	Not against	4.4 (5)	28.6 (32)	13.4 (15)	42.9 (48)	10.7 (12)	
G4	Against	15.5 (28)	30.4 (55)	27.0 (49)	19.9 (36)	7.2 (13)	**0.047**
	Not against	5.3 (6)	30.4 (34)	25.0 (28)	30.4 (34)	8.9 (10)	
G5	Against	32.0 (58)	53.1 (96)	6.6 (12)	6.1 (11)	2.2 (4)	0.145
	Not against	24.1 (27)	52.7 (59)	14.3 (16)	8.0 (9)	0.9 (1)	
G6	Against	31.5 (57)	47.5 (86)	10.5 (19)	5.0 (9)	5.5 (10)	0.206
	Not against	26.8 (30)	47.3 (53)	11.6 (13)	11.6 (13)	2.7 (3)	
G7	Against	8.3 (15)	18.2 (33)	25.4 (46)	36.5 (66)	11.6 (21)	0.058
	Not against	2.7 (3)	25.0 (28)	16.1 (18)	40.1 (45)	16.1 (18)	
G8	Against	7.7 (14)	38.2 (69)	26.5 (48)	21.0 (38)	6.6 (12)	0.056
	Not against	1.8 (2)	29.6 (33)	37.5 (42)	22.3 (25)	8.9 (10)	
Overuse (G1, G4, G7, G8)	Against	-	59.7 (108)	14.3 (26)	26.0 (47)	-	**<0.001**
	Not against	-	40.2 (45)	10.7 (12)	49.1 (55)	-	
Harm (G2, G3, G5, G6)	Against	-	72.9 (132)	17.2 (31)	9.9 (18)	-	**0.003**
	Not against	-	64.3 (72)	12.5 (14)	23.2 (26)	-	
N1	Against	-	0 (0)	4.4 (2)	95.6 (43)	-	0.641
	Not against	-	1.8 (1)	5.5 (3)	92.7 (51)	-	
N2	Against	-	2.2 (1)	2.2 (1)	95.6 (43)	-	0.238
	Not against	-	5.5 (3)	9.1 (5)	85.4 (47)	-	
N3	Against	-	0 (0)	2.2 (1)	97.8 (44)	-	0.144
	Not against	-	3.6 (2)	9.1 (5)	87.3 (48)	-	
N4	Against	-	0 (0)	4.4 (2)	95.6 (43)	-	0.174
	Not against	-	5.5 (3)	9.1 (5)	85.4 (47)	-	
N5	Against	-	0 (0)	6.7 (37)	93.3 (42)	-	0.425
	Not against	-	3.6 (2)	5.5 (3)	90.9 (50)	-	
Total Necessity	Against	-	0 (0)	0 (0)	100 (45)	-	0.354
	Not against	-	1.8 (1)	3.6 (2)	94.6 (52)	-	
C1	Against	-	33.3 (15)	4.4 (2)	62.3 (28)	-	0.487
	Not against	-	32.7 (18)	10.9 (6)	56.4 (31)	-	
C2	Against	-	46.7 (21)	4.4 (2)	48.9 (22)	-	0.308
	Not against	-	34.5 (19)	10.9 (6)	54.6 (30)	-	
C3	Against	-	28.9 (13)	6.7 (3)	64.4 (29)	-	0.824
	Not against	-	34.5 (19)	5.5 (3)	60.0 (33)	-	
C4	Against	-	84.4 (38)	6.7 (3)	8.9 (4)	-	0.409
	Not against	-	76.3 (42)	5.5 (3)	18.2 (10)	-	
C5	Against	-	44.4 (20)	4.5 (2)	51.1 (23)	-	0.284
	Not against	-	34.6 (19)	12.7 (7)	52.7 (29)	-	
C6	Against	-	80.0 (36)	6.7 (3)	13.3 (6)	-	0.807
	Not against	-	74.5 (41)	9.1 (5)	16.4 (9)	-	
Total Concerns	Against	-	51.1 (23)	4.4 (2)	44.5 (20)	-	0.666
	Not against	-	43.6 (24)	10.9 (6)	45.5 (25)	-	

G1 – "Doctors use too many medicines."; G2 – "People who take medicines should stop their treatment for a while every now and again."; G3 – "Most medicines are addictive."; G4 – "Natural remedies are safer than medicines."; G5 – "Medicines do more harm than good."; G6 – "All medicines are poisons."; G7 – "Doctors place too much trust on medicines."; G8 – "If doctors had more time with patients they would prescribe fewer medicines."; N1 – "My health, at present, depends on these medicines."; N2 – "My life would be impossible without these medicines."; N3 – "Without these medicines I would be very ill."; N4 – "My health in the future will depend on these medicines."; N5 – "These medicines protect me from becoming worse."; C1 – "Having to take medicines worries me."; C2 – "I sometimes worry about long-term effects of these medicines."; C3 – "These medicines are a mystery to me."; C4 – "These medicines disrupt my life."; C5 – "I sometimes worry about becoming too dependent on these medicines."; C6 – "These medicines give me unpleasant side effects."

Discussion

Strengths and limitations

Combining qualitative and quantitative data allows a richer analysis for the comprehension of the questions in study.

Participants had to deliver their questionnaire to their doctor, which may have influenced some responses due to fear of doctor evaluation, even though the questionnaires were returned in a closed envelope.

Not all participants answered the BMQ-Specific, so the strength is smaller.

The presented themes emerged from open-answers, which does not give so much information about the patient's perspective as it would give if it was an interview.

We found a limited number of studies comparing elderly patients according to their desire to be deprescribed with the sociodemographic characteristics. Some studies selected mainly older adults already willing to be deprescribed and compared those who successfully did it to those who didn't succeed. Other studies only reported qualitative results or compared the desire to be deprescribed only scales, namely BMQ and PATD questionnaires.

Comparing with existing literature

This study results reveal that there was a strong belief in medication benefits. For 19.9% a high belief that medicines were harmful and for 33.4% medicines were overused. Our findings concerning the general harm and overuse of the medication were higher than those reported in other studies, namely comparing with a study in Ireland (17) that found that only 3% patients believed that the medication was harmful and just over 5% that it was overused. In relation to the BMQ-Specific, we found that 97% viewed the medication as necessary and 45% were concerned about potential adverse consequences, these results being in line with those in Ireland (12). When participants were categorised by belief group, we found a lower number of participants accepting the medication comparing with Clyne et al (46% vs. 63.4%) but a higher number of participants ambivalent (44% vs. 32.6%).

Overall, literature rates of 85-90% of older adults are willing to stop one or more medications (5,20), but according to Turner et al. (5) from 86% willing to stop only 41% successfully discontinued their prescription at 6-month post-intervention.

We found no difference in the will of being deprescribed according to age. Our findings matched those in the literature (3–5) that reveal no association between age and the success of being deprescribed.

However, some studies found that the older adults notice differences between stopping preventive medications and being symptom's relieved. They perceived clear efficacy for many

medicines, namely the ones prescribed for symptomatic relief since they notice the symptoms again when they reduce or stop medicines, recognising that the benefits of prophylactic or specific treatment medicines are not so net and are prone to stop them (21–23).

We found no difference in the will of being deprescribed according to gender. Our findings are in line with the previous studies (3–5) that found no association between gender and the success of being deprescribed.

We found that the will of being deprescribed increased with the level of education in accordance to the literature (3–5) showing an association between education level and the success of being deprescribed. One possible explanation is that people with a higher educational level are more knowledgeable and able to make a critical assessment of drugs, knowing that they have benefits and risks and that, at some point, their risks may outweigh their benefits. However, most of the participants in both groups didn't have more than 6 years of education, so we can't extrapolate to the other education levels.

We found difference in the will of being deprescribed according to the number of perceived morbidities. Our findings do not match those from previous studies (3–5) that did not find any association between self-reported health and the success of being deprescribed. One possible explanation is that, as the person does not feel so sick, he does not see the need to take some of the medication, making him more willing to stop it.

We found no difference in the will of being deprescribed according to the number of regular medications in line with those of the literature (3–5).

We found difference in the will of being deprescribed according to BMQ General Overuse, namely in the statement number 4 "Natural remedies are safer than medicines". This is reflected in some answers to the open-question "What do you think about stopping some of the medication you are on?" namely in those that want to be deprescribed. This could be due to general dislike of taking medications, including the feeling that medications are "unnatural", wanting to be more in control of their life and to the desire to be "normal" for patients taking psychiatric medication so reducing the stigma associated with medication use (24). We can use these facilitators to help in the deprescription process of potentially inappropriate medication (those whose risks outweigh benefits, those with no clear indication or those that aren't effective). A study found that patient's belief in the importance of medications correlated poorly with their GPs' belief in its importance, highlighting the need for continual dialogue between doctors and patients (25). Therefore, we need to be careful so that patients do not replace scientifically studied drugs for other untested substances, whose effects and interaction may still be unknown.

We found difference in the will of being deprescribed according to BMQ General Harm, namely with the statement number 2 "People who take medicines should stop their treatment for a

while every now and again". Comparing with the answers to the open-question "What do you think about stopping some of the medication you are on?", we found that 20% of the patients willing to be deprescribed in case there were side effects or if the medication was ineffective and 11.7% because they had already successfully tried. This can make some patients stop or think about stopping some of their medications for a period of time when they feel better. As mentioned before, patient's belief in the importance of medications correlates poorly with their GPs' belief (25) and sometimes it is difficult for them to perceive the efficacy of medications, namely the ones prescribed for prophylactic or specific treatable conditions (21–23).

According to Reeve et al. (24) one of the enablers of deprescribing is the fear of addiction, namely in those affecting the nervous system. However, we did not find differences between the group against the idea of deprescribing and the group that wasn't against in the statement number 3 "Most medicines are addictive" of BMQ general.

According to where patients place the decision centre about being deprescribed, we deduct from the answers that 60.5% prefer to be the centre of decision and 39.0% prefer to place it in their doctors. This does not match with other studies where most participants reported that they would like to withdraw one or more of their drugs if their doctor told them that they could do so (6,26,27). A Danish survey (26) found that 85% of the participants would be willing to stop one or more of their regular medications if their doctor said it was possible. They also found that half of the participants preferred being deprescribed for one or more of their drugs if followed by a healthcare professional in consultation, and the other half of the participants would have liked phone or email follow-up. Another study (28) found that several patients did not know which medications they took and what their indications were because they didn't give it any importance, as they had complete trust in the responsible healthcare professionals. Still some studies have found that, in addition to the high interest in stopping medications, a significant number refuses to undergo deprescribing when it was proposed (29–31). This shows that if the patients don't have health literacy, they cannot give an opinion on their health, they feel powerless, assume a passive attitude, and become dependent on their doctor's judgement. Thus, when their GP refills the prescription, they see it as a sign that they need to continue taking it (24), as expressed by some of the participants as the reason for rejecting the idea of being deprescribed. The interpersonal trust (between patient and clinician) is a key element of the doctor-patient relationship, one particularly valued by older patients (17,21,24,32,33). So, doctor's knowledge about medicines is a key subject in deprescribing, as it is in the prescribing process.

However, further studies are needed to better understand the reason why older adults place the decision centre in them and what are the reasons for that (e.g. Lack of information? Fear? Results not consistent with what they expect?). In order to increase the success of the deprescription.

Conclusion

This study found a strong belief in medication benefits. It was also observed that the majority (61.8%) of the patients inquired were against the idea of deprescribing.

Belief group categorizing shows that most of the participants thought to be either accepting medication or ambivalent. We also found that most participants were against the idea of deprescribing, being the most common reasons: the perception that it would worse their medical situation; and the value they put in the medicines. The factors that appear to be related to being against the idea of deprescribing are lower education level and a worse perception of their health.

In this study, we note that there is a group of patients who believe that the decision to stop taking medication should be up to them. Such finding requires thinking about the importance of a relationship of trust and openness for dialogue with the doctor and the need for time in the consultation for knowledge and information to the patient.

It is important that doctors are aware of the specificity of the contexts and of its consultants, namely in the primary care setting, in order to address the patients' fears and beliefs. Only this way, we can be getting the patient collaboration and give them the better evidence-base care.

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3.4 Self-medication prevalence in the Portuguese polymedicated older adult population and its deprescribing willingness: an observational study

Abstract

Background: Self-medication is characterized by autonomous administration of medicines, without a prescription. Its prevalence ranges from 20 and 60%. The most involved medications are analgesics, antipyretics, cough and cold preparations and vitamins. Older people are most vulnerable to drug-drug and drug-disease interactions arising from it. The aim of this study was to determine the reported prevalence of self-medication in Portuguese polymedicated older adult population and its relationship with the willingness to have some regular medications deprescribed.

Methods: Cross-sectional, analytical study in a random population of primary health care centres from the five Portuguese healthcare administrative regions and the two autonomous regions. A sample of 386 polymedicated older adult patients answered a questionnaire between October 2018 and February 2019. For quantitative analysis sociodemographic characteristics, clinical and medication profile and visual analogue scale about the will to self-medicate was used. For qualitative analysis an open-question a visual analogic scale and their answer justification were used. Convergent mixed methods design was used.

Results: A response rate of 77.2% to the visual analogue scale and its justification was obtained. For 40% of the participants the will to self-medicate was indicated, the main reasons being the replication of previous medical advices and perception of self-knowledge. The will to self-medicate was associated with a higher formal education and a lower agreement with Beliefs about Medicines Questionnaire General Harm and its statements numbers 1, 5 and 6. No association between the will to self-medicate and the willingness to have regular medications deprescribed was found.

Conclusion: Self-medication was common in Portuguese older population. Doctors must be aware of this problem, namely in the primary care setting due to longitudinal care.

Keywords: Self Medication, Aged, Polypharmacy; Patient Acceptance of Health Care

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

Background

Over-the-counter (OTC) drugs, health food/supplements and remedies are used for self-medication aiming to disease prevention and health promotion (1).

Self-medication is the selection and use of medicines by individuals to treat self-recognised illness or symptoms without prior medical consultation regarding indication, dosage and duration of treatment (2). OTCs, prescription medicines and remedies can be used for such end. Generally, such task is suggested by a relative, a friend or professionals with no license to prescribe, stimulated by sociocultural and behavioural factors, like empiric experiences from past occasions (3–5). There are several benefits linked to appropriate self-medication (e.g. increased patient access to medication and relief; active patient role in own health care; reduced health expenditure for the treatment of minor health conditions), with health authorities approved non-prescribed drugs. This behaviour can cause inappropriate use of drugs, increased risk of adverse events, drug-drug interactions and worsening of comorbidities (6).

The prevalence of self-medication in the literature ranges from 4% to 87%, most of the studies reporting a prevalence between 20 and 60% and a mean of 38%. This wide range of prevalence can be explained by use of different criteria to measure self-medication (7). One study in Portugal found a prevalence of 21% in rural areas (8) and another one a prevalence of 19% for antibiotics (9).

The most used OTCs or non-prescribed drugs are analgesics, antipyretics, cough and cold preparations and vitamins (3,7,10). Antibiotics (9,11,12) and benzodiazepines (13) are also referred in the literature. Older people are most vulnerable to drug-drug and drug-disease interactions from such consumption of OTCs and drugs without prescription (14).

The objective of this study was to determine the reported self-medication prevalence in Portuguese polymedicated older adult population and its relationship with the willingness to have regular medications deprescribed.

Material and methods

Study design

We adopted a convergent mixed methods design (15). Secondary analysis of available quantitative and qualitative data were conducted separately as described below, and the findings were triangulated during the interpretation stage (15,16).

Context and study setting

Data were obtained from a cross-sectional study, whose details, definitions and methods were previously published (17). The study was carried out in randomly selected primary health care

centres in Portugal form the five mainland Portuguese healthcare administrative regions and two autonomous regions (Madeira and Azores) that accepted to participate.

Data Collection Procedures

The invitation of GPs and patients' recruitment occurred between October 2018 and February 2019. GPs were individually instructed to hand over the questionnaire and the informed consent to all elderly patients with polypharmacy, equal or more than five drugs per day, attending their primary care consultation during six randomised consultation days selected for the month after their acceptance to collaborate. GPs were responsible for study explanation, answering questions or doubts, delivering the questionnaire and the informed consent and collecting them. Exclusion criteria were patients being acutely unwell in the previous three weeks and refusal to participate.

Quantitative data collection and analysis

We used a questionnaire to collect sociodemographic information such as age, gender (male/female), area of residence (the health administrative region), perceived number of chronic health problems and auto-referred number of daily medications. We also used Beliefs about Medicines Questionnaire-General (BMQ-General), which assesses general beliefs about medicines and includes de General-Harm and the General-Overuse subscales.

Outcome variables:

The will to self-medicate with OTC or prescribed medications was evaluated with a visual analogic scale (0 to 10). A justification for it was then asked.

Qualitative data collection and analysis

We used an open-question ("What do you think about stopping some of the medications you are on?") on the questionnaire. A justification for the response to the visual analogue scale question was so asked. Two individual investigators coded the participants' answers summarising its content. The common codes features were grouped together. According to the will to be deprescribed we created four main categories (against, in favour, indecisive and indifferent) (as mentioned in chapter 3.3).

Statistical analysis

In addition to the descriptive analysis, we also performed χ2 test for nominal qualitative characteristics and T-student or Mann-Whitney U test for quantitative characteristics comparisons, depending if the variable had or not a normal distribution. All tests were two-sided using a significance level of 0.05. Statistical analysis was conducted using SPSS V.24.0.

Results

Characteristics of participants

Of the 386 participants, 59.7% were female, mean age was of 76.7 (95% CI 76.0 to 77.4) years and the mean number of drugs per person was of 7.3 (95% CI 7.1 to 7.6) (Table 3.4.1). From these, 77.2% (n=298) answered the visual analogue scale (0 to 10) about their will to self-medicate with OTC medication and justified their response.

Table 3.4.1 Characteristics of the sample

Characteristic	Total % (n)	Visual analogue scale responders
Gender		
Women	59.6 (230)	59.4 (177)
Men	40.4 (156)	40.6 (121)
Age		
65 to 74 years	43.5 (135)	48.7 (145)
≥75 years	56.5 (175)	51.3 (153)
Education		
Low level (<6 years)	75.1 (290)	72.5 (216)
Medium level (6 to 9 years)	13.2 (51)	14.1 (42)
High level (>9 years)	10.9 (42)	12.4 (37)
Unknown	0.8 (3)	1 (3)
Perceived number of chronic health problems		
0 to 2	16.8 (65)	5.4 (16)
3 to 4	38.1 (147)	46.6 (139)
5 to 6	27.5 (106)	31.5 (94)
7 to 8	7.5 (29)	9.1 (27)
9 to 10	2.8 (11)	3.7 (11)
≥11	0.8 (3)	1 (3)
NA	6.5 (25)	2.7 (8)
Number of medications		
5 to 9 drugs	79.5 (307)	70.5 (210)
≥10 drugs	21.5 (79)	29.5 (88)

Participants' views on the will to self-medicate

In order to obtain the participants' views on the will to self-medicate we asked the participants to justify their response on the visual analogue scale. All 298 participants that answered the visual analogue scale also justified their answer.

From the analysis of the responses to the visual analogue scale, 39.6% of the participants had the will to self-medicate. By analysing the justification for their response, we found that the main reason was the replication of previous medical advices (70%), followed by the perception of self-knowledge (22%).

- *"If it's just a headache, I take a paracetamol because I already know. But if it's something else, I don't take anything, my doctor must prescribe it to me, because I don't know, he knows, he studies." [P3, 77 years]*
- *"I never self-medicated except taking cough and cold preparations or over-the-counter antipyretics or painkillers" [P9, 66 years]*

- *"In mild situations of fever or pain I take medication not prescribed by the doctor." [P63, 65 years]*
- *"In the flu uses home medicines. Uses a lot of traditional medicine." [P70, 75 years]*
- *"I don't know enough to self-medicate, unless it's a simple headache or cold." [P145, 69 years]*
- *"There are some drugs that, because*I *they are known and tried, are not dangerous." [P168, 73 years]*
- *"It is my opinion. I only trust drugs prescribed by a doctor. I refer to pills for diseases like high blood pressure or cholesterol. But if I have a headache, I feel confident about taking an aspirin or over-the-counter drugs at the pharmacy." [P175, 67 years]*

Around 58% did not feel the will to self-medicate and it was mainly due to lack of knowledge (35%), trust in the doctor (33%) and perception of risk (25%).

- *"I trust my doctor." [P98, 78 years]*
- "Because as layman I have no medical knowledge to self-medicate.*" [P178, 74 years]*
- "Because patients should take only what is prescribed by doctors.*" [P384, 81 years]*
- *"I already take too many medications and they can be bad." [P400, 68 years]*
- *"When I need, I go to the doctor." [P403, 78 years]*

Will to self-medicate

We compared the characteristics of both groups.

There was no statistically significant relationship between the will to self-medicate and gender (p-value=0.22), as well as with the age, perceived number of chronic health problems and number of medications.

However, we found a statistically significant relationship between the will to self-medicate and formal education, BMQ General Harm and BMQ statements (table 3.4.2):

Table 3.4.2 Quantitative characteristics according to the will to self-medicate

Characteristic	Mean (95% CI)		
	No will to self-medicate	Will to self-medicate	p-value
Age	75.4 (74.4 to 76.4)	75.2 (74.0 to 76.5)	0,662
Formal Education (number of years)	4.9 (4.4 to 5.4)	5.8 (5.1 to 6.5)	0,034
BMQ			
1- "Doctors use too many medicines."[a]	3.7 (3.5 to 3.9)	3.4 (3.2 to 3.6)	0.044
2- "People who take medicines should stop their treatment for a while every now and again."[a]	3.5 (3.3 to 3.6)	3.2 (3.0 to 3.4)	0.065
3- "Most medicines are addictiv [a]	2.8 (2.7 to 3.0)	2.9 (2.7 to 3.1)	0.889
4- "Natural remedies are safer than medicines."[a]	3.4 (3.2 to 3.5)	3.2 (3.1 to 3.4)	0.341
5- "Medicines do more harm than good."[a]	3.8 (3.6 to 3.9)	3.5 (3.3 to 3.6)	0.007
6- "All medicines are poisons."[a]	3.8 (3.6 to 4.0)	3.4 (3.2 to 3.7)	0.015
7- "Doctors place too much trust on medicines."[a]	2.7 (2.6 to 2.9)	2.8 (2.6 to 2.9)	0.885
8- "If doctors had more time with patients they would prescribe fewer medicines."[a]	3.1 (3.0 to 3.3)	2.9 (2.7 to 3.1)	0.093
BMQ General Overuse[b]	13.0 (12.5 to 13.4)	12.4 (11.9 to 12.9)	0,077
BMQ General Harm[b]	13.9 (13.3 to 14.4)	13.0 (12.5 to 13.5)	0,018
Perceived number of chronic health problems	4.9 (4.6 to 5.2)	4.5 (4.2 to 4.8)	0,076
Number of medications	6.8 (6.4 to 7.2)	6.7 (6.2 to 7.2)	0,825

[a]Scale from 1 to 5 where high scores indicate higher agreement
[b]Scale from 4 to 20 where high scores indicate higher agreement
BMQ General Overuse – BMQ1 + BMQ4 + BMQ7 + BMQ8
BMQ General Harm – BMQ2 + BMQ3 + BMQ5 + BMQ6

Correlation between the will to self-medicate and the willingness to have regular medications deprescribed

We found no association between the will to self-medicate and the willingness to have regular medications deprescribed (p=0.072, X^2).

Discussion

Strengths and limitations

Combining qualitative and quantitative data allows a richer analysis for the comprehension of the questions in study.

Participants had to deliver their questionnaire to their doctor, which may have influenced some responses due to fear of doctor evaluation, even though the questionnaires were returned in a closed un-marked envelope.

The presented themes emerged from open-answers, so this is a one side study presenting information the patient's perspective. A pre-specified questionnaire or an interview would probably give different answers. Still, we intended to know patients' perspectives.

We found no other studies comparing the BMQ questionnaire with the will to self-medicate.

Comparing with existing literature

The study results reveal that 39.6% of the participants were willing to self-medicate, mainly because of replication of previous medical advices and the perception of self-knowledge (the empiric experiences). Our study prevalence is in line with the prevalence reported in most studies (20 to 60%, with a mean prevalence of 38%) (7).

We found no difference in the will to self-medicate according to age. Our findings matched most of those of the literature (3,7,18–20). However, some studies found an increased risk of self-medication in the younger (4,7,8,21).

We found no difference in the will to self-medicate according to gender. Our results are in line with most of the previous studies (3,4,7,20,21) that also found no association. However, some studies found an increased risk of self-medication in women (1,19,22,23) or in men (21).

We found that the will to self-medicate increased with the increase of the level of education. There are divergent results in the literature, but most of the studies are in line with our findings (4,7,8,22,23). Others show an increase risk in lower levels of education (3,10) or no association (19,20). One possible explanation is that people with a higher educational level have higher perception of self-knowledge, possibly better anticipating the benefits and risks of medication. Other studies (24) found that a common reason for self-medication was "being able to manage one's own pathology". However, the result is not entirely statistically significant since there is an overlap of the 95% CI.

We found no difference in the will to self-medicate according to the number of perceived morbidities. Our findings match those from most of the studies (3,4,7,18). However, some studies found an increased risk of self-medication in patients with poorer perceived health (19,21), while others found an increase risk in those with good perceived health (22).

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We found no difference in the will to self-medicate according to the number of regular medications taken. There are divergent results in the literature, with some showing a positive association (10) and others a negative association (23). One explanation for these findings can be that our sample was only of polymedicated older adults.

We could not compare the will to self-medicate between those with and without polypharmacy.

One of the main reasons our study perceived for self-medication was the replication of previous medical advices. This is in line with other studies (11,12,20,24) stating that having an old prescription for the same symptoms, previous good experience with the drug, or considering symptoms as minor were common reasons for self-medication.

We did not find difference in the will to self-medicate according to BMQ General Overuse. However, we did find difference with the statements number 1 "Doctors use too many medicines". For this statement those willing to self-medicate did not consider that "doctors use too many medicines" as much as those not willing to self-medicate. One possible explanation is that they are open to take more medication if needed, therefore, when they feel ill, they self-medicate. We could find similar results in the literature (11,12,20,24), for "symptoms started at odd hours", "a subjective feeling of being able to manage one's own pathology", "to alleviate symptomatic distress" as common reasons for self-medication. However, the result is not entirely statistically significant since there is an overlap of the 95% CI.

We found difference in the will to self-medicate according to BMQ General Harm, namely with statements number 5 "Medicines do more harm than good"; and number 6 "All medicines are poisons". Those willing to self-medicate perceived lesser harm in medication use than those not willing to self-medicate. Since they do not anticipate much harm from taking medication, they are more prone to use them even without medical prescription outweighing the benefits. The literature (11,12,20,24) also reveals that many patients self-medicate because they had a previously good experience with the drug, its convenience (since they did not have to set a medical appointment) and feel that patients are able to manage their own problems. However, our results are not entirely statistically significant since there is an overlap of the 95% CI.

The results found are unique in Portugal and should lead to the search for ways to reduce the economic burden of consultations due to adverse drug reactions. This must imply that doctors have full knowledge of the medications that elderly people are taking, and they practice a Person-Centered Medicine, where they clearly define the goals and roles of each person in the consultation, in order to reduce this problem.

Finally, the medical education about pharmacology should be improved, beginning in pre-graduate, so that doctors are more prepared to manage the problems of polypharmacy, potentially inappropriate medications, and self-medication, in association with soft skills as communication and empathy.

Conclusion

This study found that 39.6% of patients were willing to self-medicate, the main reasons for such being the replication of previous medical advices and the perception of self-knowledge.

The most important factors related to the willingness to self-medicate were high level of education and a lower perception on medicines' harms. However, further studies are needed to better understand the relation of self-medication with BMQ questionnaire as a useful tool to screen patients at higher risk of self-medication in order to a proactive doctor's role in health education, preventing possible adverse drug reactions.

It is important that doctors are aware of this problem, namely in the primary care setting due to the longitudinal profile of care in general practice.

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CHAPTER FOUR

General Discussion

General Discussion

This thesis intended to study, from multiple perspectives within the primary care setting in Portugal, polypharmacy, potentially inappropriate medications and deprescription and to explore its relevance (1). Ultimately it aimed at raising the awareness/interest of Portuguese GPs as of the Portuguese population for these topics.

This research project was supposed to be divided into three phases, but with more time than expected to perform phase three (non-pharmacological randomised clinical trial) we decided to postpone phase three (explanation below) (1).

Phase I, a cross-sectional study, consisting of 757 patients aged older than 65, attending primary care consultations across the five Portuguese Healthcare Administrative Regions and the two Autonomous Regions, found that 77% of the sample was on five or more drugs daily (2) and that 68.6% of had one or more potentially inappropriate medications (3).

These findings support previous research suggestions that polypharmacy and PIMs are common so being a reason for concern in the older adult population in primary care setting (4–6). The high percentage of primary care older adult patients with polypharmacy and PIM makes it evident that dealing with this is the virtually everyday work of Portuguese GP. So there is the need to raise the awareness/interest of GPs and of the general population to the concept of deprescribing.

In the studied sample, the determinants of polypharmacy were age, number of chronic health problems and number of prescribers (2), the determinants of PIM being female, the number of chronic health problems, the number of pharmacological subclasses and the number of prescribers (3).

So, the common determinants to polypharmacy and PIM were number of chronic health problems and number of prescribers.

Many of these determinants are known in the literature. However, we found difference in the risk of PIM with the number of comorbidities that other studies did not find. This could be due to differences in the pharmacological and health problems data collection, but we suggest that an increase in the number of comorbidities can lead to and be the cause of an increased number of prescribed drugs, increasing the risk of PIM (7). We also found four ICPC-2 classes with high impact on the risk of PIM (digestive, cardiovascular, musculoskeletal and respiratory problems), but only the musculoskeletal problems were so far described in the literature (8). Why then so many prescriptions leading to the need to deprescription? What reasons for it?

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This ambience presents a great challenge to Portuguese GPs due to the ageing of population, with increased multimorbidity, and consequently the need of more specialist in the follow-up of the patients, not attending to the whole picture but rather to its own ground. This is where GP have their more exquisite field (9,10). Personalised health care to these patients enhancing patient-physician communication, attending to patients' fears and beliefs, empowering them in deciding about their own health care including deprescription is essential. For this, GPs must be well-versed on these subjects and have a good patient-physician relationship in order to have a good open environment to discuss these topics with the patient (11,12).

Cardiovascular, metabolic and musculoskeletal medications were the ones most involved in polypharmacy; for the PIM, the most common were proton-pump inhibitors, nonsteroidal anti-inflammatory drugs and benzodiazepines, which are in line with the literature (8,13–15). Therefore, the indication, efficiency and presence of adverse drug reaction from these drugs should be systematically assessed by GPs when dealing with older adult patients (16,17), in order to prescribe the best treatment option. To address the problematic of PIM the Choosing Wisely movement created deprescribing algorithms for drugs that are inappropriate in older adults (18).

Finally, for phase I it was intended to test a possible new definition of polypharmacy: Number of taken drugs equal or higher than the median number of drugs taken by the population, so that it could be more flexible and adjusted to a population specific morbidity burden. This way patients at higher risk would be kept in good treatment. Our proposed definition showed a better specificity in detecting PIM than the common definition which means a much lower number of false positive results. Such occurred at the cost of diminished sensibility, but we think it is important to prevent labelling all the patients taking five or more medications as polymedicated and, instead, to focus on searching if polypharmacy is appropriate or inappropriate to the clinical context of the patient and prevent underuse of appropriate medication.

Phase II, a cross-sectional study, consisting of 385 polymedicated patients aged 65 and older attending primary care consultations across the five Portuguese Healthcare Administrative Regions and the two Autonomous Regions, found that there was a strong belief in medication benefits, but 33.4% of the sample perceived medicines were overused and 19.9% that they were harmful. These percentages are higher than those reported by other studies, namely a study in Ireland (19) that found percentage of 5% and 3%, respectively. We also found that participants attitudes towards medication were mainly of acceptance or ambivalence (46% and 44%, respectively), which make Portuguese older adults more ambivalent when compared with Irish study (63.4% and 32.6%, respectively). The reasons are now to be studied.

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In our sample, the willingness to be deprescribed was associated with a higher educational level, lower number of perceived morbidities, higher feeling of medication overuse and their harm. Of our results only the association with the number of perceived morbidities had not yet been described in the literature, still, it makes sense that a person who does not feel sick, sees no need to take some of the medication, willing to stop it.

Regarding the decision centre for being deprescribed, it was found that the majority of patients (60.5%) believed that the decision to stop taking medication should be up to them, and only 39% put the decision centre on their doctors. This is possibly explaining why despite high interest in stopping medications, many patients refuse to undergo deprescribing when the proposition comes from their doctors (20–22). Therefore, it is important, namely in primary care setting, that doctors be aware of the specificity and of the contexts of their patients, promote health literacy, are empowered in the context of finding common grounds in health. Still for such doctors need time in the consultation (23).

Phase II also aimed at studying the prevalence of self-medication and its correlation with the willingness to have regular medications deprescribed. We found that 40% of the sample was willing to self-medicate, mainly due to the replication of previous medical advices and due to the perception of self-knowledge. These findings are in line with the literature with a reported a prevalence ranging between 20 to 60% (24) and describing similar reasons for it (25–28). The willingness to self-medicate was associated with higher educational level, lower feeling of overuse of medication by doctors or that medications were harmful, which is consistent with the literature. However, there are studies that also found association with poorer perceived health (29,30). We found no correlation between the will to self-medicate and the willingness to have regular medications deprescribed.

Phase III will be a non-pharmacological random clinical trial (RCT) with 380 polymedicated patients aged 65 and older attending primary care consultations from six Health Centres of Centre of Portugal (Aveiro, Castelo Branco, Coimbra, Guarda, Leiria and Viseu). With this RCT we want to measure the impact of our intervention (empowerment tools and GPs education about how to address the issue of polypharmacy and patients' beliefs and fears) in the older adult patients' acceptance to have regular medications deprescribed and in related quality of life. In the end of this phase, we shall compile the results and the information used in the intervention group to create a tool for active patient deprescription.

However, we decided to postpone the RCT for a postdoc study because of several reasons:

Firstly, the need to better explore the findings from phase II in order to better address the beliefs and fears of patients and to better empower them during the phase III protocol. We have already two other studies in process to better understand this topic. Both are being made in

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University of Beira Interior by two medical students as their master's degree thesis. In one of them we made 17 individual interviews to patients with different socioeconomic context, literacy levels and clinical burdens. In the other a focus groups and debate the topics of polypharmacy and deprescription will be performed.

Secondly, the logistic needs and help to build the RCT and put it in practice have not yet been met.

Thirdly, we think we will need to do a pilot RCT first to see if it feasible or not due to doctor's constrains.

Fourthly, the financial restrain since the study is unfunded until now.

Finally, the 6-months period could be too short and a 12-months one being necessary.

What can we take from these results?

Polypharmacy is hard to deal with and challenges the health system. That comes from population aging and the increase of drugs burden. The reasons for such are still to be understood. In fact, why to deprescribe instead of making rational prescriptions?

Therefore, we need to start addressing these problems in many levels:

- Medical education/training
  - We need to start exposing undergraduate medical students to polymedicated patients and their problems, in order for them to understand the impact of medication not only on diseases, but also on the socioeconomic context of the patients, increasing their empathic, communication and patient-centred skills;
  - We also need to expose and teach medical specialists and residents on these topics, in order to swift from a prescribing mentality to an appropriate prescribing mentality, with the patient's goals at the centre of decision.

- Health system organization
  - We need to reinforce the idea that everyone should have a coordinating doctor (the GPs being at the best position), evaluating with the patient the goals to achieve and with him reviewing all medical care given in an appropriate way including quaternary prevention. However, for a doctor to do this consultation´s time constrains must be solved in order to understand what the patients' and the medical perspectives, beliefs and fears are, as well to empower them. Therefore, the list of patients for each GP should be reduced. It is probable that the present COVID19 pandemic will change our beliefs about Medicine;

- ○ We should test the implementation of community pharmacies with a closer interaction with GPs for a better interchanging information about the patients (as present in other countries).

- Society
  - ○ Increase health literacy and awareness for the potentially inappropriate medications, reducing the rate of inappropriate self-medication and use of over-the-counter medication, namely supplements and vitamins with no clinical benefit and a huge burden on families' health and economies; Once again it is probable that the present COVID19 pandemic will change our beliefs about Medicine;
  - ○ A swift from the mentality that the prevention at any cost (with medication or screenings) is good to the need to prevent overdiagnosis and potentially inappropriate medications.

In summary, the most important strengths of this research project are:

Being – the first study to assess the prevalence and patterns of polypharmacy and PIMs in older adults attending primary care consultations on a national scale in Portugal;

Being - the first study assessing the Portuguese older adults' views on the idea of having regular medication deprescribed and one of the few studies assessing Portuguese older adults' beliefs about medication and self-medication.

The are many important limitations that impacted the research project.

Firstly, the financial and economic restrains, that delayed some phases of the study and did not make it possible to compensate the GPs collaborators for their work, which can be one of the reasons for some difficulty in recruiting collaborators, namely in phase II.

Secondly, SPMS not having access to medical data from the autonomous regions, which made that we needed to use two difference data collection methods for phase I.

Thirdly, we did not consider the over-the-counter medication for the medication burden in phase I, which can make the prevalence of polypharmacy and PIM underestimated.

Fourthly, in phase II it was not possible to have a sample with similar distribution as the Portuguese older adults' distribution across the country.

Fifthly, in phase II we used questionnaires instead of interviews due to the financial and time restrains, which could not get us so much information about the patient's perspectives as it would give if it was an interview.

Finally, the cross-sectional design does not allow to establish causal relationships, nor trends or interactions over time.

For the future, there are many potential research directions.

First, further work, as mentioned above, to better understand the patient's perspectives.

Second, the non-pharmacological RCT to measure the impact of patient's empowerment and the de-prescribing process in the older adult patients' acceptance to have regular medications de-prescribed relating it with quality of life.

Third, the differences in the beliefs about medicines between users of traditional and alternative medicines and the understanding of what are the beliefs and fears behind it.

Finally, the development of a deprescribing algorithm for the Portuguese reality.

In conclusion, these results will increase the GPs, society and policy makers awareness for these problems and help them to better start addressing them.

However, more research will be needed to fully grasp the picture of polypharmacy and PIM in Portugal. That picture must surely have a mark of the why so many pharmacologic prescriptions are made.

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CHAPTER FIVE
Appendixes

Appendixex

Appendix I – Curriculum Vitae

INFORMAÇÃO PESSOAL

Pedro Augusto Gomes Rodrigues Marques Simões

Rua Teófilo Braga nº 25 – 5º Dto, 3030-076 Coimbra (Portugal)

968384396

pedro.agrm.simoes@gmail.pt

https://www.researchgate.net/profile/Pedro_Simoes14

http://orcid.org/0000-0003-4692-2003

Nome clínico Pedro Augusto Simões

Sexo Masculino | Data de nascimento 22/04/1990 | Nacionalidade Portuguesa

POSIÇÃO

Interno de MGF / Doutorando

EXPERIÊNCIA PROFISSIONAL

2017-2021 **Interno de Medicina Geral e Familiar**

ARS Centro / ACeS Baixo Mondego / USF Pulsar, Coimbra (Portugal)

▪ Corresponsável por um ficheiro na USF Pulsar com 1.811 utentes

2016 **Interno de Ano Comum**

ULS Matosinhos, Matosinhos (Portugal)

EDUCAÇÃO E FORMAÇÃO

2016-2020 **Doutoramento (PhD) em Medicina**

Universidade da Beira Interior, Covilhã (Portugal)

2009-2015 **Mestrado Integrado em Medicina**

Universidade da Beira Interior, Covilhã (Portugal)

COMPETÊNCIAS PESSOAIS

Língua materna   Português

Outras línguas

COMPREENDER		FALAR		ESCREVER
Compreensão oral	Leitura	Interacção oral	Produção oral	
Inglês B2	B2	B2	B2	B2

Níveis: A1/A2: utilizador básico - B1/B2 utilizador independente - C1/C2: utilizador avançado
Quadro Europeu Comum de Referência para as Línguas

Competências de comunicação	Boa capacidade de comunicação adquirida através da experiência como interno de Medicina Geral e Familiar e pela apresentação de comunicações orais em Congressos Nacionais e Internacionais.

Competências de organização	Boa capacidade de organização e dinamização adquirida através da experiência como:

- Atual membro da Secção Regional do Centro da Ordem dos Médicos no órgão: Gabinete de Apoio ao Médico Residente no Estrangeiro;
- Atual membro do grupo editorial da Revista Portuguesa de Medicina Geral e Familiar;
- Atual membro do Grupo de Estudos em Diabetologia da Associação Portuguese de Medicina Geral e Familiar;
- Atual membro do Grupo de Investigação do Centro de Saúde Norton de Matos;
- Membro da Comissão Organizadora do 1º curso START MGF – Curso de 3 dias para internos do 1º ano de Medicina Geral e Familiar, realizado na Secção Regional do Centro da Ordem dos Médicos;
- Membro da Comissão Organizadora do XX Congresso Nacional de Medicina em 2017;
- Membro da Direção do Núcleo de Estudantes de Medicina da Universidade da Beira Interior (MedUBI), como Coordenador do Departamento de Comunicação e Imagem no ano letivo 2012/2013, tendo dinamizado o site do núcleo;
- Membro da Direção do MedUBI, como Coordenador do Departamento de Saúde Pública, no ano letivo 2013/2014, tendo organizado e dinamizado várias atividades de intervenção na comunidade;
- Membro da Comissão Organizadora do IV Congresso MedUBI "VIAS VERDES – Time is life!" , realizado na Faculdade de Ciências da Saúde da Universidade da Beira Interior;
- Membro da Comissão Organizadora do V Congresso MedUBI "IMUNOLOGIA: Quando a defesa é o pior ataque!", realizado na Faculdade de Ciências da Saúde da Universidade da Beira Interior.

Competências em formação	Formador no:

Formador no:

- Ciclo formativo "Desafios em MGF: Burocracias" na sessão intitulada "Como elaborar cartas de referenciação?", promovido pelo Núcleo Regional do distrito de Lisboa da USF-NA e inserido no projeto inShare, que decorreu em Lisboa em junho de 2019, com o intuito de capacitar os internos de MGF para as várias procedimentos que são da responsabilidade do médico de família;
- Curso de Doenças Respiratórias Agudas, realizado na Escola de Medicina Familiar – Primavera 2019 que decorreu em Soure em maio de 2019, com o intuito de capacitar os internos e especialistas de MGF para o diagnóstico e orientação das Doenças Respiratórias Agudas mais prevalentes e das mais graves;
- Workshop do Grupo de Estudo em Diabetologia da Associação Portuguesa de Medicina Geral e Familiar "Insulinoterapia em Pessoas com Diabetes Mellitus Tipo 2 – Uma Opção Terapêutica ao Alcance de Qualquer Médico de Família", realizado no 36º Encontro Nacional de MGF que decorreu em Braga em março de 2019, com o intuito de capacitar os internos e especialistas de MGF para a utilização da insulinoterapia;
- Mini-Curso de Diabetes Mellitus – O que nos trouxe de novo o ano de 2018 para aplicar na prática clínica em 2019?, realizado nas 34as Jornadas de Cardiologia, Hipertensão e Diabetes, promovidas pelo Instituto de Cardiologia Preventiva de Almada que decorreu em Sesimbra, com o intuito de atualizar os conhecimentos acerca da Diabetes Mellitus;
- Workshop "Ser (ou não) eticamente correto quando o médico tutor não o é", realizado no IX Congresso MedUBI que decorreu na Covilhã em janeiro de 2018, com o intuito de sensibilizar os alunos para esta problemática;
- Workshop do Grupo de Estudo de Bioética e Ética Médica da Associação Portuguesa de Medicina Geral e Familiar "Referenciar em Medicina Geral e Familiar", realizado no 21º Congresso Nacional de MGF que decorreu em Vila Real em setembro de 2017, com o intuito de sensibilizar os internos e especialistas de MGF para esta problemática;
- Workshop do Grupo de Estudo de Bioética e Ética Médica da APMGF "Os Pedidos Desapropriados pelo Paciente em Medicina Geral e Familiar", realizado no 34º Encontro Nacional de MGF que decorreu no Estoril em março de 2017, com o intuito de sensibilizar os internos e especialistas de MGF para esta problemática;
- Projeto de investigação/ação "Antes Que Te Queimes" na Covilhã entre 2011-2013, com o intuito de fornecer aos estudantes de medicina competências de intervenção na prevenção de comportamentos de risco relacionados com o excesso de álcool, consumo de substâncias ilícitas e comportamentos sexuais de risco;
- DRSR *on tour* em Santo Tirso em 2011, com o intuito de educação sexual para alunos do 3º ciclo e secundário.

Co-orientador em Teses de Mestrado de alunos da Faculdade de Medicina da Universidade de Coimbra;

Contacto com realidades de saúde diferentes à de Portugal aquando de intercâmbio:

- Brasil / Niterói / Hospital Universitário Antônio Pedro em Medicina Interna, Cirurgia Geral e Pediatria, durante 5 meses, no ano letivo 2014/2015;
- Taiwan / Taipei / Chang Gung University Hospital em Cardiologia, durante 1 mês, em 2013;
- Brasil / Recife / Hospital Universitário Oswaldo Cruz em Medicina Tropical, durante 1 mês, em 2012.

Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal

INFORMAÇÃO ADICIONAL

Publicações

- Simões PA, Santiago L, Simões JA. Prevalence of polypharmacy in the older adult population within primary care in Portugal: a nationwide cross-sectional study. Arch Med Sci. 2020. Doi: 10.5114/aoms.2020.93537.
- Simões PA, Santiago LM, Maurício K, Simões JA. Prevalence Of Potentially Inappropriate Medication In The Older Adult Population Within Primary Care In Portugal: A Nationwide Cross-Sectional Study. Patient Preference and Adherence. 2019; 13: 1569-76. doi: 10.2147/PPA.S219346
- Simões PA, Santiago LM, Simões JA. Deprescribing in primary care in Portugal (DePil17-20): a three-phase observational and experimental study protocol. *BMJ Open* 2018;**8**:e019542. doi: 10.1136/bmjopen-2017-019542

Apresentações

- Revisão sistemática intitulada "Evidence of education interventions for the elderly in reducing NSAID use: a systematic review" no 2019 European Forum on Prevention and Primary Care em novembro de 2019;
- Projeto de Investigação intitulado "Prevalência das Interações Medicamentosas com Fármacos Anti-hipertensores na População Idosa Portuguesa no 13º Congresso Português de Hipertensão e Risco Cardiovascular Global em fevereiro de 2019;
- Projeto de Investigação intitulado "Impacto das doenças cardiovasculares na multimorbilidade, polimedicação e PIM" no 34as Jornadas de Cardiologia, Hipertensão e Diabetes em janeiro de 2019;
- Projeto de Investigação intitulado "Prevalência da Polimedicação em Portugal" no 22º Congresso Nacional de MGF em setembro de 2018;
- Projeto de Investigação intitulado "Desprescrição: o olhar do próprio sobre a redução da polimedicação" no 21º Congresso Nacional de MGF em setembro de 2017;
- Revisão de Tema intitulada "*Desprescribing in the Elderly*" na 22nd *WONCA Europe Conference* em junho de 2017.

Projetos

- Revisão sistemática intitulada "Evidence of education interventions for the elderly in reducing NSAID use: a systematic review" no 2019 European Forum on Prevention and Primary Care em novembro de 2019;
- Projeto de Investigação intitulado "Prevalência das Interações Medicamentosas com Fármacos Anti-hipertensores na População Idosa Portuguesa no 13º Congresso Português de Hipertensão e Risco Cardiovascular Global em fevereiro de 2019;
- Projeto de Investigação intitulado "Impacto das doenças cardiovasculares na multimorbilidade, polimedicação e PIM" no 34as Jornadas de Cardiologia, Hipertensão e Diabetes em janeiro de 2019;
- Projeto de Investigação intitulado "Prevalência da Polimedicação em Portugal" no 22º Congresso Nacional de MGF em setembro de 2018;
- Projeto de Investigação intitulado "Desprescrição: o olhar do próprio sobre a redução da polimedicação" no 21º Congresso Nacional de MGF em setembro de 2017;
- Projeto de tese de doutoramento intitulado "Deprescribing: a self-portrait about the reduction of polypharmacy in Portugal".

Appendix II – Approvals from Ethics Committee and Local Health Administrations; Data Protection Authority

Comissão de Ética
Universidade da Beira Interior

comissaodeetica@ubi.pt
Convento de Santo António
6201-001 Covilhã | Portugal

Parecer relativo ao processo n.º CE-UBI-Pj-2017-029

Na sua reunião de 10 de outubro de 2017 a Comissão de Ética apreciou, retrospectivamente, a documentação científica submetida referente ao pedido de parecer do projeto, **"Deprescribing: a Portrait and Out-comes of the Reduction of Polypharmacy in Portugal (DePil17-20)"** do proponente **Pedro Augusto Gomes Rodrigues Marques Simões**, a que atribuiu o código n.º CE-UBI-Pj-2017-029.

Na sua análise não identificou matéria que ofenda os princípios éticos e morais sendo de parecer que o estudo em causa pode ser aprovado.

Covilhã e UBI, 25 de outubro de 2017

O Presidente da Comissão de Ética

Professor Doutor José António Martinez Souto de Oliveira
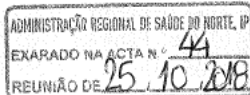Professor Catedrático

REPÚBLICA PORTUGUESA
SAÚDE

40 ANOS

SNS
SERVIÇO NACIONAL
DE SAÚDE 1979-2019

ARS NORTE
Administração Regional
de Saúde do Norte, I.P.

☐ COMUNICAÇÃO ☒ INFORMAÇÃO ☐ PARECER DATA : 04.10.2018
Nº <Processo> <Registo>

PARA ....: Conselho Diretivo da ARS Norte

DE   : Comissão de Ética para a Saúde

ASSUNTO ...:Parecer nº 135/2018

ADMINISTRAÇÃO REGIONAL DE SAÚDE DO NORTE, IP
EXARADO NA ACTA N.º 44
REUNIÃO DE 25 / 10 /2018

Levo ao conhecimento do Conselho Diretivo o Parecer nº 135/2018 sobre o Estudo "Deprescribing: a portrait anda out-comes of the reduction of polypharmacy in Portugal ", aprovado na reunião de 2: de outubro de 2018, por unanimidade.

À consideração superior

Ana Paula Capela
Ana Paula Capela
(Assessoria CES/UIC)

DELIBERADO CONCORDAR
25, 10 /2018

Dr. Pimenta Marinho
Presidente do C.D.

Rita Moreira
Vice-Presidente do CD

Paula Duarte
Vogal do CD

Dr. Ponciano Oliveira
.... Vogal C.D.

COMISSÃO DE ÉTICA PARA A SAÚDE

PARECER FINAL: Favorável	DESPACHO: *Homologado* *28·06·2018* Conselho Directivo da A.R.S. do Centro, I.P.

Dr.ª Rosa Reis Marques

ASSUNTO: Título: "Deprescribing: a Portrait and Out-comes of the Reduction of Polypharmacy in Portugal (DePil17-20) (projeto de tese de doutoramento)
Autores: Pedro Augusto R Marques Simões (PI) (UBI), Luiz Santiago (FMUC) e José Augusto Rodrigues Simões (UBI) – 12 / 2018

Dr. Luis Manuel Militão Mendes Cabral
Vogal.

Dr. Mário Ruivo
Vogal.

Objetivos: Avaliar a capacidade dos idosos para aceitarem e valorizarem a desprescrição. Também se pretende avaliar a polimedicação, caracterizar a prescrição inapropriada no idoso, identificando as principais barreiras e facilitadores, avaliar a automedicação.
O estudo será dividido em 3 fases:

Estudo transversal, analítico da prevalência e padrões da polimedicação, nomeadamente perfis sociodemográficos, clínicos e medicamentosos, nos idosos (≥65 anos) que frequentam os Cuidados de Saúde Primários (CSP) em Portugal;

Estudo transversal, em triangulação, das barreiras e facilitadores percecionados pelos pacientes, vontade em serem sujeitos a desprescrição e vontade em automedicarem-se;

Ensaio clínico não medicamentoso randomizado com duração de 6 meses sobre o impacto da capacitação dos idosos na sua vontade em serem sujeitos a desprescrição e na sua qualidade de vida.

As primeiras duas fases terão lugar em Unidades de CSP das cinco Regiões Administrativas de Saúde e das duas Regiões Autónomas, de forma a obter uma amostra representativa da geografia nacional.

A última fase terá lugar apenas em Unidades da região Centro (Aveiro, Castelo Branco, Coimbra, Guarda, Leiria e Viseu).

Nas duas primeiras fases serão convidados médicos de família (MF) através de listagens existentes de MF aderentes a projetos anteriores. Após esta seleção, os que aceitarem participar irão recrutar os seus pacientes. O tamanho da amostra nestas duas primeiras fases é no mínimo 385 idosos [para um intervalo de confiança (IC) de 95% e um erro de estimação máximo de 5%]. Assumindo que cada MF incluirá no mínimo 6 pacientes num período de 3 semanas, serão recrutados no mínimo 65 MF, com distribuição geográfica representativa da distribuição da população idosa, segundo dados do Pordata (www.pordata.pt).

Exmo. Senhor

Dr. Pedro Augusto Simões

pedro.augusto.simoes@ubi.pt

C/C:

Sua Referência	Sua Comunicação de	Nossa Referência	Data
		8634/CES/2018	17.09.2018

Assunto: Deprescribing in primary care in Portugal (DePil17-20): a three-phase observational and experimental study protocol.

A Comissão de Ética para a Saúde da ARSLVT, apreciou na sua reunião da secção de investigação do dia 14.09.2018 o projecto em epígrafe e emitiu um parecer favorável ao estudo.

Declaração de conflito de interesses: Nada a declarar

O Conselho Directivo, atento ao teor do parecer emitido, entende estarem reunidas as condições para a concretização deste estudo.

Com os melhores cumprimentos,

O Conselho Directivo

LUÍS PISCO
Presidente do Conselho Diretivo da

ENT-ARSA/2019/4599
28.03.2019

O CONSELHO DIRETIVO 9/4/2019
O Presidente: José Marques Róbalo
O Vogal: José António Martinho Lopes
A Vogal: Paula Ribeiro Marques

PARECER 04/2019/CES

28.02.2019
(Processo 33/CES/2018)

Sobre o estudo *"Desprescrição: o olhar do próprio sobre a redução da polimedicação (DePil17-20)"*

(*Deprescribing: a Portrait and Out-comes of the Reduction of Polypharmacy in Portugal (DePil17-20)*")

A – RELATÓRIO

A.1. A Comissão de Ética para a Saúde (CES) da Administração Regional de Saúde do Alentejo (ARSA) deu início ao **Processo nº 33/2018/CES** com base no pedido formulado a esta CES pelo Conselho Directivo da ARSA após envio de documentação pelos investigadores entre a 10 de Julho de 2018. Este estudo é realizado no âmbito do doutoramento em Medicina, da Faculdade de Ciências da Saúde da Universidade da Beira Interior (UBI), pelo Investigador Principal, o Dr. Pedro Augusto Simões e foi já apreciado e aprovado pela CE da UBI e pela CES da ARS Centro........................

A polimedicação é definida como a toma simultânea de cinco ou mais fármacos. A desprescrição pode ser definida como a suspensão de medicamentos potencialmente inapropriados sob supervisão médica e existem várias ferramentas que ajudam a identificar esta medicação nos idosos. O envolvimento directo dos pacientes e dos seus cuidadores na escolha e administração dos fármacos é conhecido como muito importante, mas geralmente não é aplicado. O objectivo deste estudo é identificar a prevalência da polimedicação nos idosos em Portugal e os seus padrões.................

Este estudo é um estudo observacional, transversal, em triangulação, das barreiras e facilitadores percecionados pelos pacientes em relação à polimedicação, à sua vontade em serem sujeitos a desprescrição e vontade em automedicarem-se.....................

A.2. Fazem parte do processo de avaliação os seguintes documentos:.................

1) Protocolo do estudo (Em língua inglesa e versão resumida em língua portuguesa); ....

2) Parecer do Conselho Nacional de Ética e Deontologia Médica da OM sobre estudos multicêntricos e que implicam a apreciação por várias Comissões de Ética; ....

REPÚBLICA PORTUGUESA
SAÚDE

SNS SERVIÇO NACIONAL DE SAÚDE

ARS algarve
Ministério da Saúde

15108 009715

Exmo Senhor
Dr. Pedro Miguel Simões
pedro.augusto.simoes@ubi.pt

SUA REFERÊNCIA	SUA COMUNICAÇÃO DE	NOSSA REFERÊNCIA	DATA
		Nº: CES 29/2018	12/10/2018
		PROC. Nº: #18/2018	

ASSUNTO: **Parecer da CES da ARS Algarve sobre pedido n.º 18/2018 "A portrait and out-comes of the reduction of plypharmacy in Portugal" – Requerente:** Pedro Miguel Simões

Serve o presente para informar V. Exa. que o projeto em questão mereceu parecer Positivo por parte da CES da ARS Algarve na sua reunião de 20 de setembro de 2018, e autorização do Conselho Diretivo em reunião de 10/10/2018 para a sua realização no ano 2018.

Solicita-se igualmente que, ao abrigo do disposto no n.º 23º da atual Declaração de Helsínquia, dê conhecimento à CES da ARS Algarve, I.P., de eventuais alterações ao protocolo de investigação e demais informações tidas por relevantes, bem como do relatório final com as conclusões do estudo.

Aproveitamos ainda para desejar o maior sucesso no desenvolvimento deste trabalho.

Com os melhores cumprimentos,

Josélia Gonçalves
Vogal do Conselho Diretivo
da ARS Algarve, I.P

E.N. 125 Sítio das Figuras, Lote 1, 2.º andar, 8005-145 Faro
Telf: 289889900 - Fax: 289807405
email: cd@arsalgarve.min-saude.pt - www.arsalgarve.min-saude.pt

1/1

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Autorização n.º 11328/ 2017

Pedro Augusto Gomes Rodrigues Marques Simões notificou à Comissão Nacional de Protecção de Dados (CNPD) um tratamento de dados pessoais com a finalidade de realizar um Estudo Clínico com Intervenção, denominado Deprescribing: a Portrait and Out-comes of the Reduction of Polypharmacy in Portugal (DePil17-20) , com o Protocolo n.º NCT03283735.

A investigação é multicêntrica, decorrendo, em Portugal, nos centros de investigação identificados na notificação.

O participante é identificado por um código especificamente criado para este estudo, constituído de modo a não permitir a imediata identificação do titular dos dados; designadamente, não são utilizados códigos que coincidam com os números de identificação, iniciais do nome, data de nascimento, número de telefone, ou resultem de uma composição simples desse tipo de dados. A chave da codificação só é conhecida do(s) investigador(es).

É recolhido o consentimento expresso do participante ou do seu representante legal.

A informação é recolhida diretamente do titular e indiretamente do processo clínico.

As eventuais transmissões de informação são efetuadas por referência ao código do participante, sendo, nessa medida, anónimas para o destinatário.

A CNPD já se pronunciou na Deliberação n.º 1704/2015 sobre o enquadramento legal, os fundamentos de legitimidade, os princípios aplicáveis para o correto cumprimento da Lei n.º 67/98, de 26 de outubro, alterada pela Lei n.º 103/2015, de 24 de agosto, doravante LPD, bem como sobre as condições e limites aplicáveis ao tratamento de dados efetuados para a finalidade de investigação clínica.

No caso em apreço, o tratamento objeto da notificação enquadra-se no âmbito daquela deliberação e o responsável declara expressamente que cumpre os limites e condições aplicáveis por força da LPD e da Lei n.º 21/2014, de 16 de abril, alterada pela Lei n.º 73/2015, de 27 de junho – Lei da Investigação Clínica –, explicitados na Deliberação n.º 1704/2015.

O fundamento de legitimidade é o consentimento do titular.

A informação tratada é recolhida de forma lícita, para finalidade determinada, explícita e legítima e não é excessiva – cf. alíneas a), b) e c) do n.º 1 do artigo 5.º da LPD.

Assim, nos termos das disposições conjugadas do n.º 2 do artigo 7.º, da alínea a) do n.º 1 do artigo 28.º e do artigo 30.º da LPD, bem como do n.º 3 do artigo 1.º e do n.º 9 do artigo 16.º ambos da Lei de Investigação Clínica, com as condições e limites explicitados na Deliberação da CNPD n.º 1704/2015, que aqui se dão por reproduzidos, autoriza-se o presente tratamento de dados pessoais nos seguintes termos:

Responsável – Pedro Augusto Gomes Rodrigues Marques Simões

Finalidade – Estudo Clínico com Intervenção, denominado Deprescribing: a Portrait and Out-comes of the Reduction of Polypharmacy in Portugal (DePil17-20) , com o Protocolo n.º NCT03283735

Categoria de dados pessoais tratados – Código do participante; idade/data de nascimento; género; dados da história clínica; medicação prévia concomitante; dados de qualidade de vida/efeitos psicológicos; eventos adversos

Exercício do direito de acesso – Através dos investigadores, presencialmente/ outro

Comunicações, interconexões e fluxos transfronteiriços de dados pessoais identificáveis no destinatário – Não existem

Prazo máximo de conservação dos dados – A chave que produziu o código que permite a identificação indireta do titular dos dados deve ser eliminada 5 anos após o fim do estudo.

Da LPD e da Lei de Investigação Clínica, nos termos e condições fixados na presente Autorização e desenvolvidos na Deliberação da CNPD n.º 1704/2015, resultam obrigações que o responsável tem de cumprir. Destas deve dar conhecimento a todos os que intervenham no tratamento de dados pessoais.

Lisboa, 10-10-2017

A Presidente

Filipa Calvão

Appendix III – Material used throughout the study (informed consent form and questionnaires applied to participants)

CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

Título do estudo: Desprescrição: o olhar do próprio sobre a redução da polimedicação (DePil17-20)

Enquadramento: Estudo de investigação no âmbito da obtenção do grau de doutor pela Faculdade de Ciências da Saúde da Universidade da Beira Interior, sob orientação do Professor Doutor Luiz Miguel Santiago e do Professor Doutor José Augusto Simões.

Explicação do estudo: Com o estudo pretende-se perceber as barreiras e facilitadores da desprescrição percecionados pelos pacientes, a sua vontade em serem sujeitos a desprescrição e a vontade em automedicarem-se. Para isso serão recolhidos dados do processo clínico do paciente acerca das suas caraterísticas sociodemográficas (idade, género, área de residência e número de anos de estudo) e clínicas (morbilidades) e da sua medicação (número de fármacos e o seu composto ativo) pelo seu médico de família. A perceção da medicação será avaliada usando a versão portuguesa do *Beliefs about Medicines Questionnaire* (BMQ), a vontade de ser sujeito a desprescrição será aferida com recurso a uma questão aberta acerca do que a pessoa idosa pensa de parar medicação que toma habitualmente, e a vontade em se automedicar será avaliada usando uma escala visual analógica (0 a 10) acerca da necessidade de se automedicar e a sua justificação. A recolha de dados ocorrerá em novembro de 2018 e serão recolhidos os dados de todos os pacientes idosos (≥65 anos) que recorram a consulta nos cuidados de saúde primários durante o período de estudo: 6 dias aleatorizados.

Condições e financiamento: O próprio investigador financiará o estudo e não há pagamentos a colaboradores ou participantes, sem compensação de despesas ou proveitos financeiros diretos ou indiretos resultantes do trabalho final. A participação será voluntária e não haverá prejuízo ou outros caso não queira participar ou abandonar o estudo a qualquer momento. O estudo foi submetido à Comissão de Ética da Universidade da Beira Interior, Comissão Nacional de Proteção de Dados e Comissão de Ética de todas as Administrações Regionais de Saúde.

Confidencialidade e anonimato: O investigador não terá acesso à identidade dos participantes, pois este será codificado e apenas o seu médico de família saberá a quem corresponde cada código. O investigador apenas terá acesso aos dados recolhidos pelos médicos de família e às respostas às questões.

Investigador: Pedro Augusto Gomes Rodrigues Marques Simões, médico interno da especialidade de Medicina Geral e Familiar na USF Pulsar em Coimbra, doutorando na Faculdade de Ciências da Saúde da Universidade da Beira Interior.
Endereço eletrónico: pedro.augusto.simoes@ubi.pt

Por favor, leia com atenção a seguinte informação. Se achar que algo está incorreto ou que não está claro, não hesite em solicitar mais informações. Se concorda com a proposta que lhe foi feita, queira assinar este documento.

Assinatura/s de quem pede consentimento: ... ...

Declaro ter lido e compreendido este documento. Foi-me garantida a possibilidade de, em qualquer altura, recusar participar neste estudo sem qualquer tipo de consequências. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando em que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas pelo investigador.

Nome: ... ...

Assinatura:... ... ...   Data: ...... /...... /...........

SE NÃO FOR O PRÓPRIO A ASSINAR POR INCAPACIDADE

NOME: ... ...

BI/CC N.º: ....   DATA OU VALIDADE ..... /..... /........

GRAU DE PARENTESCO OU TIPO DE REPRESENTAÇÃO: ....

ASSINATURA ... ...

ESTE DOCUMENTO É COMPOSTO DE 2 PÁGINAS E FEITO EM DUPLICADO: UMA VIA PARA O INVESTIGADOR, OUTRA PARA A PESSOA QUE CONSENTE

Sexo: Masculino ☐ Feminino ☐   Idade: _____ anos

Área de Residência (Concelho): _____

Educação Formal (em anos): ____

Morbilidades: _____
_____
_____
_____
_____
_____

Número de medicamentos que toma? ____

Quais os componentes ativos?

_____
_____
_____
_____
_____
_____

BMQ geral

Afirmações:	A sua concordância				
1 - Os médicos receitam demasiados medicamentos.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
2 - Quem toma medicamentos deveria parar o tratamento, por algum tempo, de vez em quando.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
3 - A maior parte dos medicamentos cria habituação.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
4 - Os remédios são mais seguros que os medicamentos.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
5 - Os medicamentos fazem mais mal do que bem.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
6 - Todos os medicamentos são venenos.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
7 - Os médicos confiam demasiado nos medicamentos.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)
8 - Se os médicos estivessem mais tempo com os doentes receitariam menos medicamentos.	Concordo Totalmente ☐(1)	Concordo ☐(2)	Sem opinião ☐(3)	Discordo ☐(4)	Discordo Totalmente ☐(5)

O que acha de parar medicação que habitualmente toma?

Qual a sua vontade em automedicar-se?

0
Nenhuma

10
Máxima

Justifique a sua pontuação:

Appendix IV – Published article of study protocol

Deprescribing in primary care in Portugal (DePil17-20): a three-phase observational and experimental study protocol

Pedro Augusto Simões,[1,2] Luiz Miguel Santiago,[3,4] José Augusto Simões[1,5,6]

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ABSTRACT

Introduction Polypharmacy is commonly defined as the simultaneous taking of five or more drugs. Deprescribing is the process of tapering or stopping medications with the aim of improving patient outcomes and optimising current therapy, and there are several tools aiming at identifying potentially inappropriate medications, especially in the elderly. The direct involvement of patients and their caregivers in the choice and administration of drugs has long been known to be very important, but it is not usually applied. The aim of this study is to assess the knowledge of older adults about deprescription, the effect on willingness to have regular medications deprescribed and its quality-of-life outcome.

Methods and analysis This study protocol comprises three phases. The first two phases will be nationwide and aim to evaluate the prevalence and patterns of polypharmacy and assess the barriers and facilitators of deprescribing perceived by older adults, as well as their willingness to have regular medications deprescribed and to self-medicate. The third and last phase will be a non-pharmacological randomised clinical study to measure older patients' acceptance to have regular medications deprescribed and related quality of life.

Ethics and dissemination The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has been approved by the Ethics Committee of the University of Beira Interior and Portuguese National Data Protection Commission. Study results will be published in peer-reviewed journals and presented at national and international conferences. In short, no action will be taken without written consent from patients and doctors.

Trial registration number >NCT03283735.

Strengths and limitations of this study

► Phase I and II will be nationwide and will be the first ones to take place in Portugal.
► This will be one of the first to assess the impact of deprescribing in health and quality-of-life outcomes on older adults.
► Study methodology comprehensively aims at getting the whole picture of the problem from its epidemiological study, through the understanding of what polymedicated patients feel about being on less medication load, until the perception of quality-of-life study when deprescription has been made.
► The relatively small sample will be a methodological limitation because it will not allow getting so strong conclusions as if the sample was bigger, due to medical short adherence because of the workload.
► The possible contamination of the intervention in phase III, due to parallel sources of information, taking place as a confounding variable.

It is estimated that at least 75% of this adverse event is potentially preventable.[8]

Potentially inappropriate medications (PIM) are those for which the harms outweigh the benefits, namely those that are not indicated or lack evidence of efficacy and those that do not align with patients goals/preference and values.[9] So, it is necessary to distinguish between appropriate and inappropriate medications[10] because as people get older the benefit:risk ratio of medications changes, meaning that medications that were once appropriately prescribed may have become inappropriate.[11] An Australian study reported that 60% patients had at least one PIM, leading to a high risk of adverse drug reactions, morbidity and mortality.[12] There are a lot of guidelines about when to start medication that is safe and effective, but there is a lack of similar guidelines for ceasing inappropriate medication.[13]

Deprescribing is the process of tapering or stopping medications with the aim of

INTRODUCTION

Polypharmacy is commonly defined as the simultaneous taking of five or more drugs,[1] but it can also be defined as using medication that is not indicated, not effective or is therapeutic duplication.[2] It is present in 30%–70% of older adults[3] and it is a significant predictor of the risk of falls,[4] inappropriate prescriptions, reduced patient adherence, drug interactions, hospital admissions[5 6] and mortality.[7]

improving patient outcomes and optimising current therapy.[14] However, it is not free of risks, namely withdrawal syndromes, rebound effects, pharmacokinetic/pharmacodynamic changes in the remaining drugs and recurrence of the symptoms.[3 15] So, the decision to deprescribe results from a careful weighting between the therapeutic objectives and the risk:benefit ratio.

Many deprescribing processes have been proposed in the literature.[15 16] One of the most widely used is a simple five-step protocol consisting of a comprehensive medication history, identifying PIM (attending to the harms and benefits of medication, as well as to the life expectancy and care goals), determining whether medication can be ceased and prioritisation (taking into account the patient's preferences), planning and initiating medication withdrawal (one at a time and often with tapering) and close monitoring and documenting the improvement in health and quality of life and the reduction of adverse effects.[17]

Almost a dozen medication screening tools exist in order to aid identifying PIM in older adults and improve their care. The most widely used are Beers criteria and the Screening Tool of Older Person's Prescriptions and Screening Tool to Alert Doctors to Right Treatment (STOPP/START) criteria. Both the Beers criteria and the STOPP component of the STOPP/START criteria are lists of medications that should be avoided in older adults because of its adverse effects and drug–drug and drug–disease interactions. On the other hand, the START component of the STOPP/START criteria consists of a list of medications that should be considered to initiate in the presence of certain conditions. Another useful tool is the Medication Appropriateness Index that consist of issues to be taken into account before prescribing a medication.[18]

Many studies have recognised that the implementation of a deprescribing process is feasible in practice and acceptable to participants[19 20] and, hypothetically, may result in favourable patient health and quality-of-life outcomes[21]; further studies are needed to confirm it. There are already a few number of strategies that appear to be effective and promising,[22] however assessing the effectiveness of these interventions is difficult because different studies have different study designs, settings and types of interventions. Many of these studies have short follow-up periods (2 months to 1 year), so they may not provide information about the long-term impact of these interventions, and/or lack of clinical outcome measurements.[23] One outcome measurement rarely used was the effect on health-related quality of life.

Patients are uncertain about their willingness to have a medication deprescribed because they are confused by conflicting advice on benefit and harm from different healthcare professionals.[15] The majority of patients want to be involved in the decision-making process,[17 24] and this has long been known to be very important, but shared decision-making is not routine.[25] It is assumed that older people generally consider they take a lot of medications and complain about it, but they are reluctant to cease specific medications in practice.[26 27] So it is important to understand this incongruity between not liking to take multiple medications and reluctance to accept the proposal to stop them. In particular for Portuguese context, there are no studies on these matters, so it is necessary to understand such ambivalence, because it will help us solve many problems arising from polypharmacy, such as adverse drug reactions.[28]

There are only some studies about the prevalence of polypharmacy in some region of Portugal, none nationwide. Also, there are no studies about the Portuguese older adults' attitudes and beliefs regarding medication, and there are very few studies around the world. Finally, most of the studies focus on the effect of deprescribing in clinical outcomes such as falls, consultations rates, hospitalisations and/or mortality. Very few focus on the effect on quality of life and older adults' willingness. In order to study the phenomenon, as well as to create rationales, this work is necessary.

Terminology

For the purpose of defining polypharmacy, we will use the list of active ingredient of drugs and consider three definitions: ≥5 drugs versus ≥the median number of drugs versus presence of at least one PIM. The rationale for such resides in the scarcity of studies on the number of medications simultaneously taken. In fact, due to multimorbidity, many elderly patients are taking more and more drugs.[29] So, we want to compare the international accepted definition (≥5 drugs) with this new approach to see if there are differences.

Study objectives

The primary objective is to assess the knowledge of older adults about deprescription, the effect on willingness to have regular medications deprescribed and their quality-of-life outcome.

Specific objectives are:
▶ To identify the prevalence of polypharmacy in older adults in Portugal.
▶ To evaluate the proportion of PIM in older adults in Portugal.
▶ To describe the sociodemographic and clinical profiles of older adults with polypharmacy in Portugal.
▶ To identify the main barriers to and the facilitators of deprescribing in Portuguese older adults.
▶ To evaluate the Portuguese older adults willingness to have regular medications deprescribed.
▶ To correlate the self-medication with the willingness to have regular medications deprescribed.
▶ To evaluate the effect in quality of life after having regular medications deprescribed.
▶ To elaborate and validate a flow chart with the deprescribing process, in the patient's perspective.

METHODS AND ANALYSIS
Study design
This is a three-phase study:
1. Cross-sectional, analytical study of the prevalence and patterns of polypharmacy, namely sociodemographic and clinical profiles (age, gender, area of residence and years of study) and about medication (number of drugs and their active component), in older adults attending primary care in Portugal.
2. Cross-sectional, triangulation study of older adults' perception of barriers to and facilitators of deprescribing, willingness to have regular medications deprescribed and willingness to self-medicate.
3. Non-pharmacological randomised clinical study of older patients' acceptance to have regular medications deprescribed and related quality of life.

Phase I
Objectives
To assert the prevalence of polypharmacy in older adults attending primary care in Portugal and describe their sociodemographic and clinical profiles.

Design
Cross-sectional, analytical study.

Setting
Primary care centres in Portugal will be randomly selected from the five mainland Portuguese healthcare administrative regions and two autonomous regions (Madeira and Azores), in order to obtain a national geographical representative sample.

Sample size
Since the prevalence of polypharmacy in older adults is unknown, we will use as base of population all older adults in Portugal. For the study, we will use a 95% CI and a maximum precision error of 5%. According to Pordata (www.pordata.pt), the population of Portugal is around 10.33 million, of which 2.18 million are over the age of 65. Since the literature suggests that the range of polypharmacy is 30%–70% and we think that it is over 50%, we estimate that we would need at least 742 patients.

Study procedures
This phase of the study will start in March 2018.

We will ask the information department of the ministry of health for the data of 757 randomised patients (electronically stored): 245 in North of Portugal, 190 in Centre of Portugal, 211 in Lisbon-Tejo Valley, 65 in Alentejo, 33 in Algarve, 6 in Azores and 7 in Madeira in accordance with the distribution of Portuguese old adult population (≥65 years) in Portugal according to Pordata.

Data collection
The collection of data will occur in March 2018.

Data will be electronically stored in a database specifically designed for this study. It will be encrypted and password protected. Information will be treated in strict confidentiality to protect the privacy of the patients. The investigators will have no access to the data of the patients, except the one provided by the information department of the ministry of health.

Statistical analysis
A descriptive analysis of all study variables will be performed, namely the number of valid observations, mean±SD, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. Prevalence of polypharmacy (considering the three definitions) will be calculated together with corresponding 95% CI. Moreover, the prevalence of polypharmacy will be estimated by subgroups, namely age, gender, residence area and formal education. Univariate analysis will be conducted to study the associations between those characteristics and polypharmacy using χ^2 test (qualitative characteristics) or Student's t-test/Mann-Whitney U test (quantitative characteristics). Multiple logistic regressions will be carried out considering the presence of polypharmacy as the dependent variable and patients' characteristics as the independent variable in order to calculate the OR and corresponding 95% CI. Total number of drugs taken by the patients and their pharmacological classes will also be summarised together with 95% CI, and multiple regressions may be performed to analyse its association with patients' characteristics. All tests will be two-sided using a significance level of 0.05. Statistical analysis will be conducted using SPSS V.23.0 or higher.

Phase II
Objectives
To determine older peoples' attitudes and beliefs regarding medication use and their willingness to have regular medications deprescribed.

Design
Cross-sectional, analytical study.

Setting
It will be the same as phase I.

Sample size
Since the prevalence of polypharmacy in older adults is unknown, we will consider that it is around 60% of the older adults' population. So, we need at least 385 patients with polypharmacy, to obtain a sample with a 95% CI and a maximum precision error of 5%.

Study procedures
This phase of the study is expected to start in October 2018.

For general practitioners (GPs) sampling we used existing files of previous projects adherent GPs, in other epidemiological studies, in order to have an higher adherence rate. After the selection of GPs, those who agree to participate will recruit their own patients, after their consent. Assuming that a GP will be able to include at

3

least six patients, a total of 65 GPs will be enrolled in the study: 21 in North of Portugal, 16 in Centre of Portugal, 18 in Lisbon-Tejo Valley, 5 in Alentejo, 3 in Algarve, 1 in Azores and 1 in Madeira in accordance with the distribution of Portuguese old adult population (≥65 years) in Portugal according to Pordata (www.pordata.pt).

Enrolled GPs will be instructed to give the questionnaire and the informed consent to all older adults (≥65 years) patients, with polypharmacy, attending a primary care consultation during the period of study: we will randomise six consultation days for data collection. GPs will collect all necessary data about the patients who sign the informed consent and fill all questions of the questionnaire. After that, we will randomise the pool of data according to gender and region, in order to obtain a sample in accordance with Portuguese distribution of old adult population (≥65 years).

GPs and patients willing to participate in the study must give written informed consent and present ability to comply with the study requirements.

Exclusion criteria will be: being acutely unwell in the last 3 weeks and refusal to participate.

Data collection

The collection of data will occur in October 2018.

GPs will be responsible for collecting all data about patients' sociodemographic characteristics, as well as morbidity and medication, during their consultations. Moreover, the perception of medication will be evaluated using Portuguese general Beliefs about Medicines Questionnaire (BMQ), the willingness to have regular medications deprescribed will be assessed with one open-question ('What do you think about withdrawing medication?'), to evaluate the qualitative knowledge about the patient's acceptance, and the need to self-medicate with over-the-counter medication will be evaluated with a Visual Analogue Scale (0–10) about the need to self-medicate and its justification.

Those who do not know how to write or read can choose someone they know (eg, a family member or a friend) to write the answer.

In case of less than 50% of answers of the open questions, two patient groups will be invited to make a focus group asserting reasons for accepting deprescribing.

Data will be electronically stored in a database specifically designed for this study using MS Excel 2010. It will be encrypted and password protected. Information will be treated in strict confidentiality to protect the privacy of patients. The investigators will have no access to the data of the patients. The only person to know who is being studied will be the GP.

Before the collection of data, there will be online reunions with the GPs participating in the study.

We have been authorised to use BMQ by the authors.

Statistical analysis

A descriptive analysis of all study variables will be performed, namely the number of valid observations, mean±SD, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. We will categorise the willingness to have regular medications deprescribed in two groups (high and low). The perception of medication, willingness to have regular medications deprescribed and need to self-medicate will be estimated by subgroups, namely age, gender, residence area and formal education. Univariate analysis will be conducted to study the associations between those characteristics and the perception of medication, willingness to have regular medications deprescribed and need to self-medicate using χ^2 test (qualitative characteristics) or t-test/Mann-Whitney (quantitative characteristics). Multiple logistic regressions will be carried out considering the perception of medication, willingness to have regular medications deprescribed and need to self-medicate as the dependent variable and patients' characteristics as the independent variable in order to calculate the OR and corresponding 95% CI. All tests will be two-sided, considering a significance level of 0.05.

Null hypothesis

The people with more willingness to have their regular medications deprescribed believe that medications are harmful and overused by doctors.

The need to self-medicate is present in people with less fear of medication and less overuse belief.

People with polypharmacy see no or little harm in the medication and do not think they have polypharmacy.

Phase III

Objectives

To measure older patients' acceptance to have regular medications deprescribed and related quality of life.

Design

Non-pharmacological cluster randomised clinical study, intended to last for 6 months.

Outcomes

Primary outcome will be the quality of life.

Secondary outcome will be the willingness to have regular medications deprescribed.

Setting

Primary care centres in Portugal will be randomly selected from six health centres of Centre of Portugal (Aveiro, Castelo Branco, Coimbra, Guarda, Leiria and Viseu).

Sample size

Since the prevalence of polypharmacy in older adults in Centre of Portugal is unknown, we will consider that it is around 60% of the older adults' population in this region (around 520 000). So we need at least 380 patients with polypharmacy, to obtain a sample with a 95% CI and a maximum precision error of 5%. However, assuming a dropout rate of around 25%, we will increase the required sample by 25% in order to compensate for dropouts, so we will need at least 474 patients with

polypharmacy. Then we will create two groups with a minimum of 237 patients each (one will be the intervention group and the other the control).

Study procedures

This phase of the study is expected to start in September 2019 and will last for 6 months.

Again, GPs sampling will be made according to existing files and those who agree to participate will recruit their own patients, after their consent. Patients from previous phase can be enrolled. Assuming that a GP will be able to include at least 10 patients, a total of 48 GPs have to be enrolled in the study. Enrolled GPs will be instructed to invite all older adult (≥65 years) patients with polypharmacy, attending the primary care consultation to participate in the study until we obtain the required sample size, they will be randomised as described below. The geographical areas of work, the districts, will be randomised for entry into exposed and unexposed groups, in order to minimise the contamination of the intervention that could happen if we use randomisation at patient level. The purpose is to have doctors performing only one task in each district. To make both groups as homogenous as possible, we will group similar districts in order for them to be in different branches of the study.

Patients willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. The patients' recruitment procedure will be the same as the one described for phase II.

Exclusion criteria: being acutely unwell in the last 3 weeks and refusal to participate.

Two groups will be created with a minimum of 237 patients each, one of which will be composed of patients from the regions of Aveiro, Coimbra and Guarda and the other from patients from the regions of Castelo Branco, Leiria and Viseu. In the intervention group, we will give empowerment tools and will talk with their GPs about how to approach the problem of polypharmacy and the control group will receive the usual care. The information given in the intervention group will result from the knowledge obtained in phase II, it will be compiled in small leaflets and other informational materials to be made according to the best practice, to be given and remembered at scheduled times to this group. To summarise, this information will be used to educate GPs about how to approach the issue of deprescribing and to provide material to participants, during a consult, so that they can learn more about it.

Data collection

The collection of data will occur in the beginning (baseline) and end of phase III (at 6 months), in order to analyse changes from baseline.

GPs will be responsible for collecting all data. Patient's sociodemographic and clinical characteristics, and medication will be registered using the same methodology as described in phase II.

Perception of medication will be evaluated using Portuguese general BMQ, the willingness to have regular medications deprescribed will be assessed with one open question (the same as phase II), and the quality of life will be assessed with EuroQol Five Dimensions Questionnaire (EQ-5D), a validated tool for Portugal. The aim is to observe the impact of deprescription on health-related quality of life, even if, to our knowledge no study has used EQ-5D in this specific domain in Portugal.

Those who do not know how to write or read can choose someone they know (eg, a family member or a friend) to write the answer.

We have been authorised to use BMQ and EQ-5D by the authors.

Statistical analysis

It will be similar to phase II. Comparisons between baseline and the 6-month groups regarding a quantitative variable are to be made using t-test or Sign/Wilcoxon non-parametric test, if normality assumption is not met.

Null hypothesis

The intervention will result in higher quality of life.

Patient and public involvement

Patients and/or public were not involved.

DISCUSSION

This will be the first study to assess prevalence and patterns of polypharmacy in older adults in Portugal and one of the first to assess the impact of deprescribing in health and quality-of-life outcomes on older adults. We hope that the results will help clinicians to better understand patient's perception regarding polypharmacy and deprescribing.

However, many Portuguese GPs are not very keen to participate in studies like this because they have a heavy workload. Therefore, special attention and care are put on the size of the sample to achieve the goal of the study and in the recruitment methodology. Moreover, we will support and interact constantly with the participant GPs, in order to maintain their motivation. Because of this anticipated short adherence, we conclude that it would be impracticable to conduct phase III at the national level.

For phase III, a strategy was thought of trying to make geographical contamination as little as possible. Therefore we randomized the geographical areas instead of GPs or patients, so that GPs wouldn't discuss the intervention between themselves. As it is an area still unknown in Portugal, we will try to control external interventions about deprescription, but, of course, in a interconnected world where the news spreads via the internet, some contamination will surely happen and may be a confounding variable, but it will be a systematic one. Also, in order to make both groups as homogenous as possible, we will group similar, but apart, districts, where doctors will perform the tasks. GPs will be the focus of meetings

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and ongoing mails so that the study is completed. Since there is no access to the identification of patients, the most suitable way to conduct the study is through randomisation of patients by voluntary GPs. This will probably be a bias but, in light of the Portuguese laws, there is no other way to do it and, once again, there is no fee for task study. The fact that there is randomisation of patients, guaranteed by the size of the epidemiological representative samples, will provide a clear picture of the intended study problem.

Ethics and dissemination
The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. Study results will be published in peer-reviewed journals and presented at national and international conferences. In short, no action will be taken without written consent from patients and doctors.

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Appendix V – Published article of study phase I about polypharmacy

Prevalence of polypharmacy in the older adult population within primary care in Portugal: a nationwide cross-sectional study

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Abstract

Introduction: Polypharmacy is commonly defined as the simultaneous use of five or more medications; however, there is a lack of consensus regarding the most appropriate definition. It is a significant predictor of morbidity and mortality. The aim of this study was to determine the prevalence of polypharmacy in the population of older adults attending primary care in Portugal and to identify associated sociodemographic and clinical factors.

Material and methods: We conducted a cross-sectional, analytical study in primary care centres from the five Portuguese healthcare administrative regions and the two autonomous regions. We used a random sample of 757 older adult patients provided by the information department of the ministry of health (SPMS) and family doctors from the autonomous regions. Data collection occurred in March 2018. The variables utilised were sociodemographic characteristics, clinical profile and medication. For each patient, polypharmacy was measured either by the concurrent use of ≥ 5 drugs or by the median number of drugs at the time of data collection. Logistic regression analyses were performed to determine associations between polypharmacy and other variables.

Results: Polypharmacy (≥ 5 drugs) was present in 77% of the sample. A cut-off of over the median number of drugs was present in 55%. The likelihood of having polypharmacy increased significantly with age (OR = 1.05 (1.02–1.08)), number of chronic health problems (OR = 1.24 (1.07–1.45)) and number of prescribers (OR = 4.71 (3.42–6.48)). Cardiovascular, metabolic and musculoskeletal medications were the most commonly involved in polypharmacy.

Conclusions: Polypharmacy was a very common occurrence in Portugal. Future primary healthcare policies should address polypharmacy.

Key words: polypharmacy, aged, multimorbidity.

Introduction

Polypharmacy is commonly defined as the simultaneous use of five or more drugs [1]. But other definitions has been proposed: some authors propose a more detailed breakdown of the cut-off ("5 to 7" and

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"8 and over"), allowing for the identification of those with an increased risk [2]; Steinman *et al.* [3] proposes a threshold of 8 medications justified by the fact that below this number, the risk of under-use is greater than the risk of polypharmacy or inappropriate prescription; and others consider polypharmacy as the use of inappropriate, ineffective or duplicate medication [4].

Polypharmacy is estimated to affect 30–70% of older adults [5], and it has been associated with an increased risk of falls [6], inappropriate prescriptions, reduced patient adherence, drug interactions, hospital admissions [7] and mortality [8]. It is estimated that at least 75% of these adverse events are potentially preventable [9]. In some cases, an adverse drug reaction can be misinterpreted as a new medical condition and a new drug is prescribed, placing the patient at a higher risk of developing additional adverse drug reactions; this problem is known as the "prescribing cascade" [10].

According to Charlesworth *et al.* [11] the increased number of prescription medications seen in older adults in the USA between 1988 and 2010 was driven, in part, by higher use of cardioprotective medications (statins, anti-hypertensives, and antidiabetics). Still the use of antidepressants, as well as the use of medication from other classes and subclasses (proton-pump inhibitors, thyroid hormones, bisphosphonate, among others), also increased.

In Portugal there are a few studies about the prevalence of polypharmacy in some of its regions, none on a national scale. A 2016 study in a primary care health centre in the north of Portugal identified a prevalence of polypharmacy of 59.2%, higher in women (62%) than in men (54.8%) [12]. In the Portuguese public health system the patients can only go to secondary care through referral from primary care, but once in both levels of care both doctors can prescribe and renew all the patient's medications. The medications' prescription occurs through the mandatory nationwide electronic prescription platform (PEM).

The aim of this study was to identify the nationwide prevalence of polypharmacy in older adults in Portugal and its sociodemographic and clinical profiles. Although polypharmacy can be linked to drug-drug interactions (both pharmacokinetics and pharmacodynamics) and to adverse drug reactions, these results were presented in a previous paper [13]. Moreover, given the lack of consensus for the definition of polypharmacy and since multimorbidity and the use of multiple medications is common in older adults [14] we also intended to use a new definition of polypharmacy (equal to or greater than the median number of drugs taken by the population) and compare it to the most commonly used.

Material and methods

Study design

A cross-sectional study whose details, definitions and methods were previously published [15].

The study was conducted in agreement with the principles of the Declaration of Helsinki and received ethical approval from the Institutional Ethics Committee of the University of Beira Interior and Portuguese Healthcare Administrative Regions. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Participants

Since there were 2.18 million older adults ($\geq$ 65 years) in Portugal and the literature suggests that the range of polypharmacy is between 30% and 70%, we assumed the rate to be over 50% because of epidemiological concern for better evidence and larger sampling. We estimated a sample of a minimum 742 patients for a 95% CI and a maximum precision error of 5%. In agreement with the geographical distribution of the population of Portuguese aged 65 and older across the five mainland healthcare administrative regions and two autonomous regions (Madeira and Azores), noted in PORDATA [16], a random sample of 757 patients was provided by the information department of the ministry of health, SPMS (Serviços Partilhados do Ministério da Saúde), and invited family doctors from autonomous regions, due to lack of digital databases within these regions.

Data collection procedures

Data collection occurred in March 2018 (data extracted on March 30th). In brief, the SPMS provided us with an electronic file with the variables of the study from the randomly selected (by patient's national health number) sample of the five healthcare administrative regions. This electronic file contained anonymised information stored in the patient's electronic medical records. Since SPMS does not have access to electronic medical records from patients in the two autonomous regions, we invited two medical doctors, one from each autonomous region, to provide us with the needed information. The patients selected met the inclusion criteria and also had had an appointment in six pre-randomized days of the month. We studied the prescribed medications using the mandatory nationwide PEM [17]. There is an unknown number of over-the-counter medications consumed by the Portuguese population and as they can be bought without prescription, there is no way to access this information. SPMS could not

provide us with information regarding level of education, since in most cases it was missing from the medical records.

Outcome variable

For each patient, polypharmacy was measured either by the simultaneous taking of ≥ 5 drugs or by the median number of drugs at the time of data collection. The rationale for such a study resides in the lack of consensus regarding definition of polypharmacy [18]; also because of multimorbidity older patients are consuming an increasing number of medications [19]. There is a study [2] that proposes a threshold of 8 medications, justified by the fact that below this number, there is a big risk of under-use. Prescribed medication (from April 2017 to March 2018) was encoded following the Portuguese pharmacotherapeutic classification using the most discriminative level possible. The Portuguese pharmacotherapeutic classification has similarities with the ATC (Anatomical Therapeutic Chemical) classification and was adapted by INFARMED (National Authority of Medicines and Health Problems) [20]. We defined chronic medication as medication prescribed for more than three months.

Independent variables

These were sociodemographic characteristics such as age, gender (male/female), area of residence (in terms of health administrative region) and clinical profile (chronic health problems according to International Classification of Primary Care, second edition – ICPC-2).

Compliance with ethical standards

Ethical approval was obtained from Institutional Ethics Committee at the University of Beira Interior and Portuguese Healthcare Administrative Regions.

Statistical analysis

In addition to the descriptive analysis, we also performed the χ^2 test for nominal qualitative characteristics. Lastly, we performed a logistic regression with all the statistically significant variables. All tests were two-sided using a significance level of 0.05. Statistical analysis was conducted using SPSS V.24.0.

Results

Characteristics of participants

The sample consisted of 757 people, mean age was 75.5 ±7.9 years (75.1 ±7.9 years for men and 75.8 ±7.8 years for women) and median number of drugs was 8. Table I shows the characteristics of the sample.

Prevalence of polypharmacy

More than 9 out of 10 older patients (93.4%) were on at least 1 medication, with an overall average of 8.2 (95% CI: 7.9–8.6), 7.5 (95% CI: 7–8) in men and 8.8 (95% CI: 8.3–9.3) in women.

The rate of polypharmacy, use of 5 or more drugs simultaneously, was 77% (95% CI: 74–80%). With a cut-off of equal to or more than the median number of drugs (equal to 8), an important percentage of polypharmacy 55% (95% CI: 51–58%) remained present.

According to Table II there was a significant relationship between health administrative region, age, number of chronic health problems and number of prescribers and both definitions for polypharmacy (≥ 5 drugs and ≥ median number of drugs). Gender was only significant in our new definition of polypharmacy.

After adjustments, Table III shows that the likelihood of having polypharmacy (as ≥ 5 drugs) increased significantly with age (OR = 1.05 (1.02–1.08)), number of chronic health problems (OR = 1.24 (1.07–1.45)) and number of prescribers (OR = 4.71 (3.42–6.48)).

The likelihood of having polypharmacy with our new definition (as ≥ median of drugs taken by the sample) increased significantly in females (OR = 1.86 (1.24–2.80)), with number of chronic health problems (OR = 1.11 (1.02–1.20)) and number of prescribers (OR = 2.32 (1.97–2.73)).

Pharmacological subclasses and patterns of polypharmacy

Table III shows the odds ratio measured impact of having each specific chronic health problem (according to ICPC2). For patients suffering from chronic health problems related to the cardiovascular system there were 3.8 times and 2.4 times greater probability of having polypharmacy (as ≥ 5 drugs and ≥ median number of drugs taken, respectively) compared to those not suffering from health problems related to that specific system.

Table IV shows the most used pharmacological subclasses in this random sample. Three pharmacological subclasses were present in more than half of the sample: ACE inhibitor/ARBs (56.8%), statins (52%) and analgesics and antipyretics (50.6%).

Comparison between both definitions of polypharmacy in detecting potentially inappropriate medication

The common definition (≥ 5 drugs taken) had a sensitivity of 91.3%, specificity of 54.2%, posi-

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Table I. Characteristics of the sample

Characteristics	% (n)	Characteristics	% (n)
Gender:		L	51.8 (392)
Women	56.8 (430)	N	15.7 (119)
Men	43.2 (327)	P	34.3 (260)
Health administrative region:		R	23.4 (177)
North	32.2 (244)	S	19.3 (146)
Centre	25.1 (190)	T	68.6 (519)
Lisbon-Tejo Valley	27.7 (210)	U	21.5 (163)
Alentejo	8.7 (66)	X	9.5 (72)
Algarve	4.5 (34)	Y	15.2 (115)
Madeira	0.9 (7)	Z	3.6 (27)
Azores	0.8 (6)	Number of drugs:	
Age [years]:		0–4	23.1 (175)
< 75	51.5 (390)	5–9	39.0 (295)
≥ 75	48.2 (365)	≥ 10	37.9 (287)
Number of chronic health problems:		Pharmacological classes (INFARMED):	
0–2	17.3 (131)	2	74.5 (564)
3–4	19.3 (146)	3	81.8 (619)
5–6	17.6 (133)	4	36.9 (279)
7–8	16.8 (127)	5	21.1 (160)
9–10	11.9 (90)	6	50.6 (383)
≥ 11	17.2 (130)	7	16.5 (125)
Chronic health problems (ICPC2)*:		8	42.5 (322)
A	11.2 (85)	9	53.9 (408)
B	7.5 (57)	10	20.3 (154)
D	36.5 (276)	16	1.6 (12)
F	20.5 (155)	Number of prescribers:	
H	11.5 (87)	≤ 2	63.9 (484)
K	77.5 (587)	> 2	36.1 (273)

*A – general and unspecified, B – blood, blood forming organs, lymphatics, spleen, D – digestive, F – eye, H – ear, K – circulatory, L – musculoskeletal, N – neurological, P – psychological, R – respiratory, S – skin, T – endocrine, metabolic and nutritional, U – urology, X – female genital system and breast, Y – male genital system, Z – social problems, 2 – central nervous system, 3 – cardiovascular system, 4 – blood, 5 – respiratory system, 6 – digestive system, 7 – genitourinary system, 8 – hormones and medications used to treat endocrine diseases, 9 – locomotive system, 10 – antiallergic medication, 16 – antineoplastic and immunomodulatory drugs.

tive predictive value of 81.3% and negative predictive value of 74.1%.

Our definition (≥ median number of drugs taken) had a sensitivity of 72.6%, specificity of 84.0%, positive predictive value of 90.8% and negative predictive value of 58.5%.

The mean number of PIM in older adults with polypharmacy according to the common definition was 2.19 (95% CI: 2.03–2.34) compared to 0.34 (95% CI: 0.24–0.44) in those without polypharmacy. According to our definition (≥ median number of drugs taken) we found a prevalence of 2.64 PIMs (95% CI: 2.46–2.83) in those with polypharmacy compared to 0.69 PIMs (95% CI: 0.58–0.80).

Discussion

As described in the project protocol [15], the objectives for its phase I were to identify the prev-

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Table II. Prevalence of polypharmacy according to characteristics

Characteristics	Older adults without poly-pharmacy % (n)	Percentage of older adults with polypharmacy (95% CI)				Mean number of drugs (95% CI) [median]
		≥ 5 drugs	P-value (χ² test)	≥ 8 drugs	P-value (χ² test)	
Gender:			0.059		< 0.001	
Women	20.5 (88)	79.5 (342)		60.5 (260)		8.78 (8.30–9.25) [8]
Men	26.3 (86)	73.7 (342)		47.4 (155)		7.47 (6.98–7.96) [7]
Health administrative region:			0.022		0.017	
North	26.6 (65)	73.4 (179)		49.6 (121)		7.77 (7.18–8.36) [7]
Centre	17.9 (34)	82.1 (156)		58.9 (112)		8.62 (7.96–9.28) [8]
Lisbon-Tejo Valley	20.0 (42)	80.0 (168)		59.5 (125)		8.69 (8.02–9.36) [8]
Alentejo	27.3 (18)	72.7 (48)		53.0 (35)		7.48 (6.33–8.64) [8]
Algarve	41.2 (14)	58.8 (20)		41.2 (14)		6.29 (4.49–8.10) [6]
Madeira	14.3 (1)	85.7 (6)		28.6 (2)		9.43 (5.13–13.73) [6]
Azores	0 (0)	100 (6)		100 (6)		14.17 (9.50–18.83) [13]
Age [years]:			< 0.001		0.001	
< 75	28.2 (110)	71.8 (280)		49.2 (192)		7.73 (7.25–8.22) [7]
≥ 75	17.4 (64)	82.6 (303)		60.8 (223)		8.72 (8.24–9.21) [9]
Number of chronic health problems			< 0.001		< 0.001	
0-2	48.1 (63)	51.9 (68)		35.9 (47)		5.44 (4.67–6.21) [5]
3-4	35.6 (52)	64.4 (94)		41.1 (60)		6.97 (6.17–7.78) [6]
5-6	23.3 (31)	76.7 (102)		48.1 (64)		7.80 (7.06–8.55) [7]
7-8	12.6 (16)	87.4 (111)		63.8 (81)		9.22 (8.50–9.94) [9]
9-10	7.8 (7)	92.2 (83)		64.4 (58)		9.21 (8.36–10.06) [9]
≥ 11	3.8 (5)	96.2 (125)		80.8 (105)		11.15 (10.34–11.95) [10]
Chronic health problems (ICPC2):						
A	10.6 (9)	89.4 (76)	0.004	62.4 (53)	0.139	9.40 (8.42–10.38) [9]
B	15.8 (9)	84.2 (48)	0.179	66.7 (38)	0.062	9.25 (7.98–10.52) [9]
D	13.0 (36)	87.0 (240)	< 0.001	60.1 (166)	0.026	8.93 (8.38–9.49) [8,5]
F	17.4 (27)	82.6 (128)	0.065	63.9 (99)	0.011	9.25 (8.43–10.08) [9]
H	12.6 (11)	87.4 (76)	0.015	63.2 (55)	0.094	9.70 (8.58–10.82) [9]
K	16.9 (99)	83.1 (488)	< 0.001	61.2 (359)	< 0.001	8.98 (8.60–9.37) [9]
L	17.6 (69)	82.4 (323)	< 0.001	62.0 (243)	< 0.001	8.95 (8.49–9.42) [8]
N	16.0 (19)	84.0 (100)	0.047	67.2 (80)	0.003	10.06 (9.13–10.99) [10]
P	16.5 (43)	83.5 (217)	0.002	60.4 (157)	0.026	9.01 (8.43–9.59) [8]
R	10.7 (19)	89.3 (158)	< 0.001	67.2 (119)	< 0.001	9.72 (9.03–10.41) [9]
S	19.2 (28)	80.8 (118)	0.224	56.2 (82)	0.717	8.66 (7.87–9.44) [8]
T	17.3 (90)	82.7 (429)	< 0.001	60.5 (314)	< 0.001	8.97 (8.56–9.38) [9]
U	16.0 (26)	84.0 (137)	0.016	65.0 (106)	0.003	9.09 (8.35–9.83) [9]
X*	10.9 (7)	89.1 (57)	0.041	67.2 (43)	0.233	9.72 (8.45–10.99) [10]
Y**	19.1 (22)	80.9 (93)	0.030	58.3 (67)	0.004	8.63 (7.78–9.47) [8]
Z	18.5 (5)	81.5 (22)	0.574	63.0 (17)	0.387	9.44 (7.65–11.24) [10]
Pharmacological classes (INFARMED):						
2	9.2 (52)	90.8 (512)	< 0.001	68.8 (388)	< 0.001	9.77 (9.42–10.12) [9]
3	11.8 (73)	88.2 (546)	< 0.001	63.8 (395)	< 0.001	9.35 (9.01–9.69) [9]

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Table II. Cont.

Characteristics	Older adults without poly-pharmacy % (n)	Percentage of older adults with polypharmacy (95% CI)				Mean number of drugs (95% CI) [median]
		≥ 5 drugs	P-value (χ² test)	≥ 8 drugs	P-value (χ² test)	
4	2.5 (7)	97.5 (272)	< 0.001	83.5 (233)	< 0.001	11.27 (10.78–11.75) [11]
5	7.5 (12)	92.5 (148)	< 0.001	78.1 (125)	< 0.001	11.14 (10.42–11.85) [11]
6	5.7 (22)	94.3 (361)	< 0.001	78.1 (299)	< 0.001	10.81 (10.37–11.24) [10]
7	13.6 (17)	86.4 (108)	0.006	63.2 (79)	0.039	9.49 (8.68–10.30) [9]
8	8.4 (27)	91.6 (295)	< 0.001	74.2 (239)	< 0.001	10.64 (10.14–11.14) [10]
9	8.6 (35)	91.4 (373)	< 0.001	74.3 (303)	< 0.001	10.11 (9.69–10.53) [10]
10	5.2 (8)	94.8 (146)	< 0.001	79.9 (123)	< 0.001	11.07 (10.39–11.76) [11]
16	0 (0)	100 (12)	0.056	91.7 (11)	0.010	13.58 (9.80–17.37) [13.5]
Number of prescribers:			< 0.001		< 0.001	
≤ 2	34.5 (167)	65.5 (317)		39.5 (191)		6.48 (6.10–6.86) [6]
> 2	2.6 (7)	97.4 (266)		82.1 (224)		11.29 (10.78–11.80) [11]

*Considering only women. **considering only men. A – general and unspecified, B – blood, blood forming organs, lymphatics, spleen, D – digestive, F – eye, H – ear, K – circulatory, L – musculoskeletal, N – neurological, P – psychological, R – respiratory, S – skin, T – endocrine, metabolic and nutritional, U – urology, X – female genital system and breast, Y – male genital system, Z – social problems, 2 – central nervous system, 3 – cardiovascular system, 4 – blood, 5 – respiratory system, 6 – digestive system, 7 – genitourinary system, 8 – hormones and medications used to treat endocrine diseases, 9 – locomotive system, 10 – antiallergic medication, 16 – antineoplastic and immunomodulatory drugs.

alence and its characteristics of polypharmacy and PIMs in the elderly Portuguese population. The results related to the PIMs have already been published [13], but they are not necessarily related to the polypharmacy.

Strengths of the study

This was the first study to report the prevalence and patterns of polypharmacy in older adults attending primary care consultations on a national scale in Portugal.

We performed a cross-sectional study, which is the most frequent design to assess prevalence and its characteristics.

We used the most discriminative chemical subgroup of the Portuguese pharmacotherapeutic classification, to assess polypharmacy; this can minimize the bias of medical changes.

We assessed the number of medications taken by older adults using doctor's prescription records to minimise memory bias.

Since the data were mainly obtained by SPMS from national records (which allowed for a more representative sample of the population) and by sampling according to the patient's national health number in most health regions, we avoided over-representation of frequent users of primary care services (normally the ones with a higher number of morbidities and medication).

Statement of overall findings

The study results show a high prevalence of polypharmacy in the Portuguese older population (77%), exceeding the reported prevalence of other studies (30–70%) [5]. One of the explanations can be the period of time we used in this study (12-months), which can increase polypharmacy [21], making this high prevalence misrepresentative of reality, since medication could have been ceased. We used a more prolonged period of time because we believed it would allow differentiation between chronic and acute medication, done by evaluating the number of times each medication was prescribed in order to obtain a more accurate value [22]. Further research is needed to better assess which methodology is more suitable, a 12-month or a 6-month period.

Another possible explanation is that we assessed the prescribed drugs and not the ones that were dispensed or consumed by the patient (therapeutic adhesion). This may be misrepresentative of reality; patients could have stopped taking their medication (due to adverse effects, financial problems, etc.) and not have informed their doctor. On the other hand, we did not consider over-the-counter medications and the medications prescribed without the use of the electronic program PEM (e.g. manually), which may have a residual effect.

It is likely that differences in the rate of polypharmacy can be found at the prescriber level [14]. This variation could be explained by practitioners single-handedly treating diseases and illnesses and the lack of guidelines regarding polypharmacy or its prescription [23]. However, efforts to address polypharmacy within evidence-based deprescribing guidelines are being pursued [24].

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Table III. Logistic regression model for polypharmacy

Characteristics	Polypharmacy					
	≥ 5 drugs			≥ 8 drugs		
	OR	95% CI	P-value	OR	95% CI	P-value
Gender:						
Women	–	–	–	1.86	1.24–2.80	0.003
Men	–	–	–	Base	–	–
Age	1.05	1.02–1.08	0.002	1.02	1.00–1.04	0.109
Number of chronic health problems:	1.24	1.07–1.45	0.005	1.11	1.02–1.20	0.016
A	1.17	0.47–3.00	0.735	–	–	–
D	1.55	0.88–2.75	0.131	0.77	0.51–1.16	0.204
F	–	–	–	0.91	0.56–1.47	0.696
H	1.20	0.49–2.91	0.688	–	–	–
K	2.43	1.37–4.30	0.002	2.53	1.56–4.11	< 0.001
L	0.66	0.39–1.13	0.130	0.99	0.67–1.48	0.974
N	0.62	0.31–1.27	0.195	1.13	0.68–1.87	0.644
P	0.98	0.55–1.75	0.953	0.96	0.64–1.46	0.851
R	1.19	0.61–2.33	0.619	1.06	0.68–1.67	0.788
T	1.49	0.86–2.61	0.159	1.32	0.87–2.01	0.192
U	0.67	0.35–1.26	0.214	1.03	0.64–1.65	0.909
X	1.24	0.45–3.38	0.678	–	–	–
Y	0-77	0.39–1.53	0.451	1.33	0.75–2.33	0.329
Number of prescribers	4.71	3.42–6.48	< 0.001	2.32	1.97–2.73	< 0.001

OR – odds ratio, A – general and unspecified, D – digestive, F – eye, H – ear, K – circulatory, L – musculoskeletal, N – neurological, P – psychological, R – respiratory, S – skin, T – endocrine, metabolic and nutritional, U – urology, X – female genital system and breast, Y – male genital system.

Table IV. Fifteen most used pharmacological subclasses and common chronic health problems

INFARMED pharmacotherapeutic classification		% (n)	ICPC-2 chronic health problems		% (n)
3.4.2	ACE inhibitor/ARBs	56.8 (430)	K86	Hypertension uncomplicated	54.7 (414)
3.7.1	Statins	52.0 (394)	T93	Lipid disorder	48.1 (364)
2.10	Analgesics and antipyretics	50.6 (383)	T90	Diabetes non-insulin dependent	24.0 (182)
6.2.2.3	PPIs	38.2 (289)	L86	Back syndrome with radiating pain	17.7 (134)
3.4.1.1	Thiazide	37.5 (284)	L90	Osteoarthrosis of knee	16.2 (123)
2.9.1.3	Benzodiazepines	33.6 (254)	T82	Obesity	14.8 (112)
3.4.3	Calcium channel blockers	26.7 (202)	K87	Hypertension complicated	14.1 (107)
2.9.3	Antidepressants	24.7 (187)	P76	Depressive disorder	13.2 (100)
4.3.1.3	Antiplatelet agents	23.6 (179)	Y85	Benign prostatic hypertrophy	12.9 (98)
9.1.3	NSAIDs – propionic acid derivatives	22.3 (169)	T83	Overweight	12.2 (92)
3.4.4.2	β-Blockers	21.9 (166)	L91	Osteoarthrosis other	10.8 (82)
8.4.2.1	Biguanide	21.4 (162)	K95	Varicose veins of leg	10.0 (76)
8.2	Corticosteroids	18.1 (137)	F92	Cataract	9.4 (71)
10.1.2	H1 non-sedative antihistamines	17.7 (134)	P74	Anxiety disorder/anxiety state	9.4 (71)
2.12	Narcotic analgesics	15.3 (116)	L87	Bursitis/tendinitis/synovitis NOS	8.6 (65)

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In line with previous reports [11, 25, 26], we found a significant association between increased age and prevalence of polypharmacy. This could be due to the increase in the prevalence of age-related chronic diseases, which are accompanied by an increase in medications and possibly also because of prescribing for social problems [27]. However, in our new definition ($\geq$ median number of drugs taken) there was not a significant association between increased age and prevalence of polypharmacy. This could be due to the increase of the threshold of polypharmacy that can prevent labelling older adults with polypharmacy just because of the increase of comorbidities and drugs that may be necessary for them, commonly referred to as appropriate polypharmacy, as suggested by Steinman *et al.* [3].

There was no difference in risk of polypharmacy between genders with the common definition of polypharmacy. Our findings were in line with those of other studies [11, 28]. However, there are studies that found an increased risk of polypharmacy in men [26] and women [14, 25]. A higher prevalence of polypharmacy was also present in our study when we considered polypharmacy as a value equal to or greater than the median number of drugs ($\geq$ 8) taken by the population. One explanation can be that women tend to live longer than men, hence having more chronic health problems and needing more drugs. However, more studies are needed to assess whether there is a difference in risk of polypharmacy between genders.

As expected, the number of chronic health problems affects the number of medications taken by the patient and this association has been well described in the literature [11, 14, 25, 28]. However, in our study there were some chronic health problems with a stronger impact on the risk of polypharmacy, for example group classification D (digestive problems) for polypharmacy as $\geq$ 5 drugs and K (cardiovascular) for our definition ($\geq$ the median number of drugs taken).

A higher number of prescribers per patient was associated with higher risk of polypharmacy, namely for the common definition ($\geq$ 5). One explanation is that having multiple prescribers may unknowingly duplicate or induce contraindicated medication regimens due to lack of information available, which increases the risk of serious adverse drug events [29]. On the other hand, more complex patients (with multimorbidity) need to be assisted by more doctors and take more drugs. To our knowledge, this is one of the first studies to assess the impact of having multiple prescribers on polypharmacy.

In agreement with previous reports [14, 26], cardiovascular, metabolic and musculoskeletal medications were the most common in our study sample. This is in line with the most common chronic health problems described in Portugal [19], which are cardiovascular (such as lipid disorder and hypertension), metabolic (such as diabetes and obesity) and musculoskeletal (such as back pain syndrome, osteoarthritis and osteoarthrosis) problems [30]. This highlights the importance of prescribing the best drug option for the patient.

Our proposed definition had better specificity in detecting PIM than the common definition, which means a much lower number of false positive "results". This occurred at the cost of diminished sensitivity. However, we found a similar mean number of PIMs in both groups (with polypharmacy and without) according to both definitions. These results are in line with those of Steinman *et al.* [3], which raises the question of whether we should raise the threshold to avoid the risk of under-use as there does not seem to be a greater risk of inappropriate prescription. The advantage of our definition compared to others that propose a higher threshold is that it is not a rigid definition and can be adapted to a specific population morbidity burden, since different populations have different needs. Therefore, it would be like standardizing the risk of inappropriate prescription according to the population's morbidity burden to help us compare the impact of different health systems and policies on this problem.

There are some limitations in this study.

Firstly, we used a 12-month period to assess the chronic prescribed medication, which can increase the prevalence of polypharmacy, since medication could have been ceased or not purchased (non-compliance). Therefore, the number of medications per older adult may be overestimated.

Secondly, since the SPMS could not provide us with data from both autonomous regions (Madeira and Azores), representing 1.7% of the sample, data were collected by local GPs, making the sample and data processes in these two regions different from the rest. Nevertheless, randomisation was performed for these data.

Thirdly, we intended to evaluate the effects of level of education on polypharmacy. This was not possible due to lack of information in the patients' electronic records.

Fourthly, the sample size was chosen to achieve a sufficiently precise overall proportion estimate of polypharmacy in the Portuguese older adults' population, but not to find differences among different population strata.

Fifthly, we could not find any study using an approach like ours (polypharmacy as $\geq$ median number of drugs taken by the population) and had great difficulty making comparisons between different studies.

Sixthly, we could not have data on over-the-counter medications, so the prevalence of polypharmacy may be underestimated.

Finally, this was a cross-sectional study and so no causal relationship could be proven, and we could not study the health consequences of polypharmacy, namely drug-drug interactions and adverse drug reactions. Therefore, longitudinal studies are needed to understand whether these factors are responsible for the prevalence of polypharmacy. However, we intended to study prevalence and raise questions and not determine causality, so other studies are required to study causality, frequency and outcomes.

In conclusion, this study found a high prevalence of polypharmacy in the studied sample; the most important factors were number of chronic health problems and number of prescribers in both used definitions and age in the most common definition and being female in our new definition.

Polypharmacy should consider medical constraints, pathological needs and patients' feelings and fears, implying future studies on the accurateness of prescription and the need of deprescription.

We think that our new definition of polypharmacy is of relevance for practitioners since it will identify patients with higher risks. However, further studies are needed to increase its reliability and usefulness.

Acknowledgments

Conflict of interest

The authors declare no conflict of interest.

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Appendix VI – Published article of study phase I about potentially inappropriate medication

Open Access Full Text Article

ORIGINAL RESEARCH

Prevalence Of Potentially Inappropriate Medication In The Older Adult Population Within Primary Care In Portugal: A Nationwide Cross-Sectional Study

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Background: In potentially inappropriate medications harm potentially outweighs benefits. Even appropriately prescribed medications may become inappropriate. They can lead to a high risk of adverse drug reactions, morbidity and mortality. The aim of this study was to determine the prevalence of potentially inappropriate medication in the older adult population attending primary care in Portugal and to identify associated sociodemographic and clinical factors.

Methods: We conducted a cross-sectional, analytical study in primary care centres from the five Portuguese healthcare administrative regions and the two autonomous regions. We used a random sample of 757 older patients provided by the information department of the ministry of health (SPMS) and family doctors from the autonomous regions. Data collection occurred March 2018 and we studied sociodemographic characteristics, clinical profile and medication. We used 2015 Beers Criteria to assess potentially inappropriate medications. Logistic regression analyses were performed to determine associations between potentially inappropriate medications' prescriptions and other variables.

Results: Potentially inappropriate medication was present in 68.6% and 46.1% of the sample had two or more. The likelihood of having potentially inappropriate medication increased significantly with being female (OR=1.56 [1.05 to 2.31]), number of chronic health problems (OR=1.06 [1.01 to 1.13]), number of pharmacological subclasses (OR=1.40 [1.30 to 1.51]) and number of prescribers (OR=1.34 [1.09 to 1.65]). Proton-pump inhibitors, nonsteroidal anti-inflammatory drugs and benzodiazepines were the most commonly found ones.

Conclusion: Potentially inappropriate medication in older adults was found to be a common occurrence in Portugal. It is important that doctors are aware of this problem, namely in the primary care setting due to the longitudinal care.

Keywords: potentially inappropriate medication, aged, polypharmacy, multimorbidity

Background

Potentially inappropriate medications (PIM) are those in which harm potentially outweighs the benefits, namely those that are not indicated or lack evidence of efficacy and those that do not align with patients goals/preferences and values.[1] The importance of this increases as people get older because of decreased hepatic and renal function that changes the benefit/risk ratio of medications, so even when appropriately prescribed medications can become inappropriate.[2,3] An Australian study reported that 60 of 100 hospitalized patients had at least one PIM, leading to a high risk of adverse drug reactions, morbidity and mortality.[4] There is an international consensus about when to

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start many medications that are safe and effective, but there are no guidelines regarding the cessation of inappropriate medications.[5]

Many medication screening tools were developed to aid identification of PIMs in older adults and improve their care.[6-8] The medication screening tools can be divided into explicit checklists (lists of medications to be avoided in older adults) and implicit checklists (issues to be taken into account before prescribing a medication).[9] The most widely used are Beers criteria[10] and the STOPP/START criteria (STOPP-screening tool of older persons potentially inappropriate pre-scriptions/START-screening tool to alert doctors to right treatment).[11] The Medication Appropriateness Index is an example of an implicit checklist.[9]

Older patients, particularly those aged 65 and over, are more frequently diagnosed with more pathologies, multi-morbidity, and conditions prone to involve more prescrip-tion drugs.[12,13]

In Portugal, there are only studies about the prevalence of PIM in some of its regions, none conducted nationwide.[14,15] The most recent study in a primary care health centre in north of Portugal identified a 37.0% prevalence of PIM, more frequent in women (40.7%) than in men (30.9%).[14]

The aim of this study was to identify the nationwide prevalence of PIM in older adults, identified in primary care setting, in Portugal and its sociodemographic and clinical profiles.

Materials And Methods

Study Design

Cross-sectional study-details, definitions and methods were previously published.[16]

The study was conducted in agreement with the prin-ciples of the Declaration of Helsinki[17] and received ethical approval from University of Beira Interior and Portuguese healthcare administrative regions Institutional Ethics Committees. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[18]

Sampling

Since there were 2.18 million older adults (≥65 years) in Portugal and the national literature suggested that the range of PIM is around 40% and the international litera-ture around 60%, we assumed the rate to be over 50% because of epidemiological concern for better evidence and larger sampling. We estimated a sample of a minimum

742 patients for a 95% CI and a maximum precision error of 5%. In agreement with the geographical distribution of the Portuguese population aged 65 and older across the five mainland healthcare administrative regions and the two autonomous regions (Madeira and Azores), noted in PORDATA,[19] a random sample of 757 patients was pro-vided by the information department of the ministry of health, Serviços Partilhados do Ministério da Saúde (SPMS), and invited family doctors from autonomous regions, due to lack of digital databases within these last regions.

Data Collection Procedures

Data collection occurred in March 2018 (data extracted on March 30). In brief, the SPMS provided us with an electronic file with the variables of the study from the randomly selected (by patient's national health number) sample of the five healthcare administrative regions. This electronic file contained anonymised information stored in the patient's electronic medical records. Since SPMS does not have access to electronic medical records from patients in the two auton-omous regions, we invited two medical doctors, one from each autonomous region, to provide us with the needed information. We studied the prescribed medications using the mandatory nationwide, electronic prescription platform (PEM).[20] There is an unknown number of over the counter medications consumed by the Portuguese population and as they can be bought without prescription, there is no way to access this information. SPMS could not provide us with information regarding the level of education, since in most cases it was missing from medical records.

Outcome Variable

For each patient, PIM was measured as the presence of one or more drugs, that are inappropriate for older patients, according only to Table 2 of 2015 Beers Criteria.[10]

Independent Variables

Sociodemographic characteristics such as age, gender (male/female), area of residence (in terms of health administrative region), clinical profile (chronic health problems according to International Classification of Primary Care, second edi-tion – ICPC-2) and prescribed medication (from April 2017 to March 2018 and was encoded following the Portuguese pharmacotherapeutic classification using the more discrimi-nate level possible). The Portuguese pharmacotherapeutic classification has similarities with the ATC (Anatomical Therapeutic Chemical) classification and was adapted by

INFARMED (National Authority of Medicines and Health Products).[21]

Statistical Analysis

In addition to the descriptive analysis, χ^2 tests were performed for nominal qualitative characteristics. Lastly, we performed a logistic regression with all the statistically significant variables in previous χ^2 tests. All tests were two-sided using a significance level of 0.05. Statistical analysis was conducted using SPSS V.24.0.

Results

Characteristics Of Participants

The sample consisted of 757 individuals; the mean age was of 75.5±7.9 years (75.1±7.9 years for men and 75.8±7.8 years for women). Table 1 shows the characteristics of the sample.

Prevalence Of Potentially Inappropriate Medication

More than 9 of 10 older patients of the sample (93.4%) had at least 1 medication prescribed, with an overall average of 8.2 (95% CI 7.9 to 8.6), 7.5 (95% CI 7 to 8) in men and 8.8 (95% CI 8.3 to 9.3) in women.

Potentially inappropriate medication was present in 68.6% (95% CI 65% to 72%) of the sample and 2 or more PIMs were present in 46.1% (95% CI 42.5% to 49.7%), with an overall average of 1.76 (95% CI 1.63 to 1.89), 1.35 (95% CI 1.18 to 1.52) in men and 2.07 (95% CI 1.88 to 2.26) in women.

According to Table 2, there was no significant relationship between PIM and health administrative region. There was a significant relationship between PIM and number of chronic health problems, number of medications taken, number of prescribers and with many of the ICPC-2 classes and pharmacological subclasses.

After adjustment, Table 3 shows that the likelihood of having PIM increased significantly in females [OR=1.56 (1.05–2.31)], with number of chronic health problems [OR=1.06 (1.01–1.13)], number of pharmacological subclasses [OR=1.40 (1.30–1.51)] and number of prescribers [OR=1.34 (1.09–1.65)]. No differences in the odds of PIM were associated with age [OR=0.99 (0.97–1.05)].

Chronic Health Problems/Pharmacological Subclasses And Patterns Of PIM

Table 3 shows the odds ratio measured the impact of having each specific chronic health problems (according to ICPC2).

Table I Characteristics Of The Sample

Characteristic	Total % (n)
Gender	
Women	56.8 (430)
Men	43.2 (327)
Health Administrative Region	
North	32.2 (244)
Centre	25.1 (190)
Lisbon-Tejo Valley	27.7 (210)
Alentejo	8.7 (66)
Algarve	4.5 (34)
Madeira	0.9 (7)
Azores	0.8 (6)
Age	
<75 years	51.5 (390)
≥75 years	48.2 (365)
Number of Chronic Health Problems	
0–2	17.3 (131)
3–4	19.3 (146)
5–6	17.6 (133)
7–8	16.8 (127)
9–10	11.9 (90)
≥11	17.2 (130)
Chronic Health Problems (ICPC2)	
A	11.2 (85)
B	7.5 (57)
D	36.5 (276)
F	20.5 (155)
H	11.5 (87)
K	77.5 (587)
L	51.8 (392)
N	15.7 (119)
P	34.3 (260)
R	23.4 (177)
S	19.3 (146)
T	68.6 (519)
U	21.5 (163)
X	9.5 (72)
Y	15.2 (115)
Z	3.6 (27)
Number of Pharmacological Subclasses	
0–4 drugs	23.1 (175)
5–9 drugs	39.0 (295)
≥10 drugs	37.9 (287)
Pharmacological Classes (INFARMED)	
2	74.5 (64)

(Continued)

Table 1 (Continued).

Characteristic	Total % (n)
3	81.8 (619)
4	36.9 (279)
5	21.1 (160)
6	50.6 (383)
7	16.5 (125)
8	42.5 (322)
9	53.9 (408)
10	20.3 (154)
16	1.6 (12)
Number of Prescribers	
≤2	63.9 (484)
>2	36.1 (273)

Notes: A, general and unspecified; B, blood, blood forming organs, lymphatics, spleen; D, digestive; F, eye; H, ear; K, circulatory; L, musculoskeletal; N, neurological; P, psychological; R, respiratory; S, skin; T, endocrine, metabolic and nutritional; U, urology; X, female genital system and breast; Y, male genital system; Z, social problems; 2, central nervous system; 3, cardiovascular system; 4, blood; 5, respiratory system; 6, digestive system; 7, genitourinary system; 8, hormones and medications used to treat endocrine diseases; 9, locomotive system; 10, antiallergic medication; 16, antineoplastic and immunomodulatory drugs.

For patients suffering from chronic health problems related to digestive, circulatory, musculoskeletal and respiratory systems, there are 1.4 times, 1.2 times, 1.3 times and 1.5 times, respectively, greater probability of having a PIM when comparing to those not suffering from health problems related to that specific system. Older adults taking medication from central nervous system, digestive system and locomotive system groups (according to Portuguese pharmacotherapeutic classification) are 2.4 times, 4.9 times and 5.3 times, respectively, more likely to have PIM than those not taking any drug from that system group. The most common pharmacological subclasses causing PIM were proton-pump inhibitors (present in 45.6% of the sample), nonsteroidal anti-inflammatory drugs (in 34.5%) and benzodiazepines (in 27.3%).

Discussion
Strengths Of The Study
This is the first study to report the prevalence and patterns of PIM in older adults attending primary care consultations nationwide in Portugal. It is a cross-sectional study with a randomised sample, which is the most frequent design to assess the prevalence and its characteristics. We used the most discriminative chemical subgroup of the Portuguese pharmacotherapeutic classification, to assess polypharmacy; this can minimize the bias of medical changes. We also used active components according to 2015 Beers

Criteria[10] for assessing PIM, since for some pharmacological classes some active pharmaceutical ingredients are potentially inappropriate while others are safe.

Since the data were obtained from SPMS on a nationwide scale, we could obtain a size representative sample of the population, avoiding over-representation of the more frequent users of primary care services, which could happen if the data were collected from GP records of most frequent prescriptions.

Statement Of Overall Findings
The study results show a high prevalence of PIMs in the Portuguese older population (68.6%), exceeding the reported prevalence of other studies (11.5–62.5%).[22] One of the explanations can be the period of time we used in this study (12 months), which can increase polypharmacy[23] and affect the number of PIM, making this high prevalence misrepresentative of reality, since the medication could have been ceased or not purchased. Given the lack of consensus of classification for PIM,[6] we used the list of drugs in Table 2 of 2015 Beers Criteria. We used Beers Criteria because it is the most commonly used tool to identify PIM in the literature with regular updates.

We found no difference in risk of PIM with increasing age. Our findings do not match those from other studies; most of them found an increased risk of PIM in younger and older ages.[22,24] Since there are mixed results, more studies are needed to assess this relation. One hypothesis for this discrepancy is that there is a higher awareness of this problem in overall patients with ≥65 years due to increased susceptibility to adverse drug events, age-related drug–drug and drug–disease interactions, making it possible to think that there is no difference in pharmacological care in people equal and older than 65 in Portugal as age increases.[25]

In line with previous reports,[22] we found an increased risk of PIM in women. We can hypothesise that women tend to live longer and be more prone to have complaints, either physical or psychological. More studies are necessary to study this issue.

As expected, the number of medications affects the number of PIMs, since with an increased number of drugs there is an increased probability of adverse drug reactions and drug–drug interactions. This association is described in the literature.[22,24,26]

We found a difference in risk of PIM with the number of comorbidities, showing the impact that multimorbidity also affects the health of older adult population through the increased risk of PIM.[12] Our results again do not match

Table 2 Prevalence Of PIM According To Characteristics

Characteristic	No PIM % (n)	PIM % (n)	p-Value (χ^2 Test)	Mean Number Of PIMs (95% CI) [Median]
Gender			<0.001	
Women	32.3 (139)	67.7 (291)		2.07 (1.88 to 2.26) [2]
Men	47.7 (156)	52.3 (171)		1.35 (1.18 to 1.52) [1]
Health Administrative Region			0.201	
North	32.0 (78)	68.0 (166)		1.66 (1.44 to 1.89) [1]
Centre	31.1 (59)	68.9 (131)		1.85 (1.59 to 2.12) [1]
Lisbon-Tejo Valley	28.9 (58)	71.1 (152)		2.00 (1.75 to 2.26) [2]
Alentejo	37.9 (25)	62.1 (41)		1.38 (0.95 to 1.81) [1]
Algarve	44.1 (15)	55.9 (19)		1.32 (0.53 to 2.11) [1]
Madeira	42.9 (3)	57.1 (4)		0.57 (0.08 to 1.07) [1]
Azores	0 (0)	100 (6)		2.33 (1.25 to 3.42) [2]
Age			0.048	
<75 years	34.6 (135)	65.4 (255)		1.70 (1.52 to 1.88) [1]
≥75 years	27.9 (102)	72.1 (263)		1.83 (1.64 to 2.03) [1]
Number of Chronic Health Problems			<0.001	
0–2	54.2 (71)	45.8 (60)		1.14 (0.85 to 1.42) [0]
3–4	43.8 (64)	56.2 (82)		1.40 (1.10 to 1.70) [1]
5–6	30.1 (40)	69.9 (93)		1.65 (1.33 to 1.96) [1]
7–8	18.9 (24)	81.1 (103)		2.08 (1.76 to 2.40) [2]
9–10	25.6 (23)	74.4 (67)		1.83 (1.47 to 2.20) [2]
≥11	12.3 (16)	87.7 (114)		2.55 (2.22 to 2.89) [2]
Chronic Health Problems (ICPC2)				
A	22.4 (19)	77.6 (66)	0.063	2.07 (1.66 to 2.49) [2]
B	24.6 (14)	75.4 (43)	0.299	1.91 (1.40 to 2.43) [1]
D	21.0 (58)	79.0 (218)	<0.001	2.14 (1.90 to 2.38) [2]
F	27.1 (42)	72.9 (113)	0.208	2.06 (1.74 to 2.37) [2]
H	21.8 (19)	78.2 (68)	0.049	2.21 (1.80 to 2.61) [2]
K	29.1 (171)	70.9 (416)	0.012	1.82 (1.67 to 1.97) [1]
L	23.2 (91)	76.8 (301)	<0.001	2.06 (1.86 to 2.25) [2]
N	21.8 (26)	78.2 (93)	0.018	2.29 (1.93 to 2.65) [2]
P	22.7 (59)	77.3 (201)	<0.001	2.21 (1.97 to 2.46) [2]
R	19.8 (35)	80.2 (142)	<0.001	2.19 (1.91 to 2.47) [2]
S	27.4 (40)	72.6 (106)	0.275	1.72 (1.45 to 1.99) [1]
T	27.9 (145)	72.1 (374)	0.002	1.83 (1.67 to 1.99) [1]
U	23.3 (38)	76.7 (125)	0.013	1.94 (1.67 to 2.20) [2]
X	18.1 (13)	81.9 (59)	0.011	2.22 (1.79 to 2.66) [2]
Y	28.7 (33)	71.3 (82)	0.515	1.67 (1.34 to 2.00) [1]
Z	14.8 (4)	85.2 (23)	0.089	2.30 (1.58 to 3.01) [2]
Number of Pharmacological Subclasses			<0.001	
0–4 drugs	73.7 (129)	26.3 (46)		0.35 (0.25 to 0.45) [0]
5–9 drugs	29.2 (86)	70.8 (209)		1.42 (1.27 to 1.58) [1]
≥10 drugs	8.0 (23)	92.0 (264)		2.97 (2.73 to 3.21) [3]
Pharmacological Classes (INFARMED)				
2	17.9 (101)	82.1 (463)	<0.001	2.21 (2.05 to 2.36) [2]

(Continued)

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Table 2 (Continued).

Characteristic	No PIM % (n)	PIM % (n)	p-Value (χ^2 Test)	Mean Number Of PIMs (95% CI) [Median]
3	26.0 (161)	74.0 (458)	<0.001	1.94 (1.79 to 2.09) [2]
4	19.7 (55)	80.3 (224)	<0.001	2.14 (1.91 to 2.37) [2]
5	18.1 (29)	81.9 (131)	<0.001	2.43 (2.12 to 2.73) [2]
6	8.6 (33)	91.4 (350)	<0.001	2.78 (2.58 to 2.98) [2]
7	28.0 (35)	72.0 (90)	0.400	1.89 (1.55 to 2.22) [1]
8	22.4 (72)	77.6 (250)	<0.001	2.02 (1.80 to 2.23) [2]
9	10.3 (42)	89.7 (366)	<0.001	2.51 (2.33 to 2.70) [2]
10	14.3 (22)	85.7 (132)	<0.001	2.51 (2.22 to 2.81) [2]
16	8.3 (1)	91.7 (11)	0.117	2.83 (1.28 to 4.39) [2]
Number of Prescribers			<0.001	
≤2	42.8 (207)	57.2 (277)		1.24 (1.10 to 1.38) [1]
>2	11.4 (31)	88.6 (242)		2.69 (2.46 to 2.92) [2]

Notes: A, general and unspecified; B, blood, bloodforming organs, lymphatics, spleen; D, digestive; F, eye; H, ear; K, circulatory;L, musculoskeletal; N, neurological; P, psychological; R, respiratory; S, skin;T, endocrine, metabolic and nutritional; U, urology; X, female genital systemand breast; Y, male genital system; Z, social problems; 2, central nervoussystem; 3, cardiovascular system; 4, blood; 5, respiratory system; 6, digestivesystem; 7, genitourinary system; 8, hormones and medications used to treatendocrine diseases; 9, locomotive system; 10, antiallergic medication; 16, antineoplasticand immunomodulatory drugs.

those from other studies. Differences in the pharmacological and health problems data collection could explain such discrepancies.[24,26] However, an increase number of comorbidities can lead to and can be the cause of an increase number of prescribed drugs, increasing the risk of PIM.[12] From the four ICPC-2 classes with high impact on the risk of PIM according to our finding (digestive, cardiovascular, musculoskeletal and respiratory problems), only the musculoskeletal problems are described in the literature.[26]

In line with previous reports,[27] more prescribers were associated with higher risk for PIM. One hypothesis is that prescribers may not be aware of all the medication the patient is taking nor of the changes made by other prescribers to the list of medication; this increases the risk of duplicated drugs, adverse drug reactions, drug–drug interactions and drug–disease interactions. On the other hand, more complex patients (with multiple comorbidities) need to be assisted by more doctors and take more drugs, increasing the risk of PIM. This is of extreme importance, since 17% of our older adults had 4 or more prescribers within the last year. It is also important for previously prescribed medication to be listed for everyone on the national electronic drug prescription system (PEM).

According to previous reports,[24,26] PPIs, NSAID and benzodiazepines are among the most common PIM in the older adult population in primary health care in Portugal. Therefore, there is a need to quantify the resulting harms for individuals, families and society, and to make its economic and financial impact known to medical and lay communities, in order to help deprescribing to become easier for doctors and better accepted by patients.

Limitations Of The Study

There are some limitations of this study.

Firstly, we used a 12-month period to assess the chronic-prescribed medication, which can increase the prevalence of polypharmacy and PIM, since medication could have been ceased or not purchased. Therefore, the number of medications, as well as the number of PIMs, per older adult may be overestimated.

Secondly, since the SPMS could not give us data from both autonomous regions (Madeira and Azores), representing 1.7% of the sample, data were collected by local GPs, making the sample and collection data processes in these two regions different from the rest. Nevertheless, randomisation was performed.

Thirdly, there was the intention of evaluating the effect of level of education on polypharmacy. Such was not possible due to lack of information in patient's electronic records.

Fourthly, we only used Table 2 of 2015 Beers Criteria for assessing PIM; therefore, PIM due to drug–disease and drug–drug were not assessed due to the complexity of this analysis and our 12-month period assessment of prescribed medication. Also, the Beers criteria were updated in April 2019, where some drugs were eliminated from and others added to the previous list (2015 Beers Criteria), but since at the time of study (2018), the most recent list was 2015 Beers criteria we kept them.

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Table 3 Adjusted Analysis For Factors Associated With PIM Use

Characteristics	PIM		
	OR	95% CI	p-Value
Gender			
Women	1.56	1.05 to 2.31	0.026
Men	base	–	–
Age	0.99	0.97 to 1.05	0.512
Number of Chronic Health Problems	1.06	1.01 to 1.13	0.028
A	0.88	0.52 to 1.48	0.632
D	1.41	1.11 to 1.78	0.004
H	0.94	0.56 to 1.58	0.814
K	1.23	1.04 to 1.45	0.014
L	1.27	1.10 to 1.48	0.001
N	1.16	0.79 to 1.70	0.455
P	1.29	0.99 to 1.66	0.052
R	1.49	1.09 to 2.04	0.014
T	1.17	0.99 to 1.38	0.056
U	1.19	0.88 to 1.60	0.253
X	1.29	0.73 to 2.27	0.375
Number of Pharmacological Subclasses	1.40	1.30 to 1.51	<0.001
2	2.35	1.95 to 2.84	<0.001
3	1.08	0.94 to 1.24	0.301
4	0.94	0.65 to 1.36	0.749
5	1.09	0.74 to 1.60	0.662
6	4.86	3.18 to 7.42	<0.001
8	1.07	0.85 to 1.36	0.552
9	5.25	3.53 to 7.81	<0.001
10	1.55	0.81 to 2.97	0.185
Number of prescribers	1.34	1.09 to 1.65	0.005

Notes: OR, odds ratio; A, general and unspecified; D, digestive;H, ear; K, circulatory; L, musculoskeletal; N, neurological; P, psychological;R, respiratory; T, endocrine, metabolic and nutritional; U, urology; X, female genitalsystem and breast; 2, central nervous system; 3, cardiovascular system; 4, blood;5, respiratory system; 6, digestive system; 8, hormones and medications used totreat endocrine diseases; 9, locomotive system; 10, antiallergic medication.

Fifthly, the sample size was chosen to achieve a sufficiently precise overall proportion estimate of PIMs in the Portuguese older adults' population, but not to find differences among different population strata.

Finally, this is a cross-sectional study and so no causal relationship could be proven. However, we only intended to raise questions and not determine causality, so other studies are required to study causality, frequency and outcomes.

Conclusion

This study found a high prevalence of PIM in the studied sample; the most important factors were being female, number of chronic health problems, number of pharmacological classes and number of prescribers.

It is important that doctors are aware of this problem, namely in the primary care setting due to the longitudinal profile of care in general practice.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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