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# Translation and adaptation of the STOPP-START screening tool to Portuguese for detecting inappropriate prescriptions in older people: a protocol

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# Title

Translation and adaptation of the STOPP-START screening tool to Portuguese for detecting inappropriate prescriptions in older people: a protocol

# Running title

Portuguese version of the STOPP-START screening tool

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## Abstract

*Introduction*: Rational prescribing for older adults is a challenge since they usually exhibit polimorbidity and polimedication. One available and reliable tool to tackle this issue consists of the Screening Tool of Older People's Prescriptions (STOPP) and the Screening Tool to Alert to Right Treatment (START), which has been associated with improvement of clinical outcomes. Our goal is to translate, culturally adapt, and validate the STOPP-START screening tool to be used by Portuguese general practitioners/family physicians.

*Methods and analysis:*
The study will consist of four phases: Phase I - translation and cultural adaptation of the STOPP-START screening tool to Portuguese; Phase II - data collection of patient data; Phase III - Intrarater reliability study; and Phase IV - Interrater agreement study.

*Ethics and Dissemination*: This study was approved by the Ethics Committee of the Central Health Region of Portugal (where the study will take place). Every participant will sign a written consent form. We intend to publish the full article in a related peer-reviewed journal, conference presentations, reports, and in a PhD thesis.


**Keywords:** Geriatric medicine; Quality in health care ; General Medicine

**Strengths and limitations of this study**

- This study will allow the development of the first Portuguese version of the STOPP-START criteria.
- This is the first study in a Portuguese primary care setting that aims to develop a useful tool for the appropriate prescription of older patients.
- The main limitation of the study is that it is focused in Portugal and it may not apply to other countries that have Portuguese as the main language.

## Introduction

In Organisation for Economic Co-operation and Development (OECD) countries, the number of older adults is increasing (1) as well as their life expectancies (2, 3).

Caring for older adults is a challenge for healthcare systems (4), as older adults are more likely to have more than one chronic disease (5, 6). For example, multi-morbidity in the elderly can be higher than 90% in Portugal (5). Therefore, adults of ages ≥ 65 years are more likely to be prescribed with multiple drugs (7-9), which may include potentially inappropriate medications (10-12).

Potentially Inappropriate Medications (PIM) can be described as the use of medications that potentially have more risks than benefits even though safer pharmacologic and nonpharmacologic alternatives are available (10). Potentially Inappropriate Prescription (PIP) is a different concept than PIM, and includes the over, under, and misprescribing of medications (e.g., inappropriate dose or duration) (13).

There are various tools to help physicians identify PIM, such as the Beers Criteria (14) and PRISCUS (15). The combination of the Screening Tool of Older People's Prescriptions (STOPP) and the Screening Tool to Alert to Right Treatment (START)" (17) is another widely used tool. One of the advantages of this tool is that it not only takes PIM into account, but also the indications to start an appropriate medication (START).

When compared to other tools, some studies have shown that the STOPP-START tool has identified a significantly higher proportion of patients requiring hospitalisation as a result of PIM-related adverse events (16), has reduced the highest number of medications,, and has identified more potential major clinical issues (17). The criteria for STOPP-START have been associated with improvement in prescribing quality and clinical outcomes (18). These criteria have been adapted for other languages, such as French (19).

We aim to make the first translation, cultural adaptation, and validation (20) of the English STOPP-START tool for Portuguese family doctors.

## Methods and Analysis

### *Study design*

The study consists of four phases. The first phase (Phase I) is the translation and cultural adaptation to the Portuguese language, followed by data collection (Phase II). After that, we will implement Phase III, which consists of an intrarater reliability study, and Phase IV, which consists of an interrater agreement study.

### *Phase I: Translation and cultural adaptation to Portuguese language*

The translation of the STOPP-START screening tool will follow the Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes Measures (20). We have already obtained permission from STOPP-START´s author to translate and validate the tool for Portuguese. We will recruit a key in-country consultant who is a native Portugues and fluent English speaker and will be the main contact to perform and help with the translation. This consultant also has a background in health and research and experience in translating documents. We will obtain two independent translations of the STOPP-START. One will be done by the key in-country consultant, and the other will be performed by a forward translator who is also a native Portuguese and fluent English speaker. The two translations will be reconciled by the research team in order to obtain a final consensus translation that will be back-translated.

The back-translation (from Portuguese to English) will be done by a professional translator who is a native speaker of English and fluent speaker of Portuguese. This translator will have no prior knowledge of the original Portuguese version. Afterwards, the back-translation will be compared with the original by the research team to identify any relevant differences.

In the final step, the reconciled Portuguese STOPP-START version will be distributed to a group of 15 general practitioners to verify if there are any interpretations issues. After that, the research team will analyse the results from the application of the STOPP-START tool to prepare the final version.

### *Phase II: Data collection*

#### Design

This will be a cross-sectional, analytical study.

**Setting**

The study will be conducted in a primary care centre in the Centre Region of Portugal.

**Sample size**

In order to calculate the sample size for the study of intrarater agreement (n = 293), a calculation was performed in R that took into account the following parameters: estimated kappa value: 0.75 [21]; error margin: 0.1; the prevalence of each item of the STOPP criteria: 0.25; the number of observers: 3; significance level: 5%. The sample size calculation for the interrater reliability study (n = 183) was performed using the same software and took into account the same parameters. As such, the intrarater reliability study will be carried out with a sample of 300 users and the interrater agreement study will include data from randomly selected 200 users.

**Study procedures**

**Recruitment of patients**

Patients will be randomly selected (independent random sampling using computer-generated random digits) from a list of patients ≥65 years from a primary care center. They will be invited by telephone to participate in the study. After that, the investigator or a previously trained research associate will interview the patients in the general practitioner office. Recruitment will continue until 300 patients are enrolled. We will exclude participants that are unable or unwilling to participate and/or that are living in care homes.

At baseline, general practitioners will collect sociodemographic patient data such as age, gender, educational level, labour status, and marital status. Clinical data collection will include identification of total number of chronic medications, any prescribed drugs, dosage, pharmaceutical dosage form/route of administration, the reason for taking medication, allergies, drug-related conditions/history of adverse drug reactions, and current or past

conditions/diseases. Current or past conditions/diseases from which data will be collected will include diseases such as heart failure and heart block as determined by New York Heart Association Classification, supraventricular tachyarrhythmia, hypertension, liver failure, nephrotic syndrome or renal failure, history of gout, urinary incontinence, angina, history of peptic ulcer disease, bleeding diathesis, recent non-trivial spontaneous bleeding, stroke, acute coronary syndrome, coronary stent(s) inserted, carotid arterial stenosis, atrial fibrillation, coronary, cerebrovascular or peripheral arterial disease, deep venous thrombosis, thrombophilia, dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism or prior history of urinary retention, depression, parkinsonism or Lewy Body Disease, delirium, dementia, psychosis, benign essential tremor, estimated glomerular filtration rate, erosive peptic oesophagitis, constipation, chronic obstructive pulmonary disease, narrow angle glaucoma or bladder outflow obstruction, asthma, acute or chronic respiratory failure, osteoarthritis, rheumatoid arthritis, upper gastrointestinal disease, chronic cognitive impairment with symptomatic orthostatic hypotension or micturition syncope, type 2 diabetes mellitus, hypoglycaemic episodes, history of breast cancer or venous thromboembolism, primary or secondary hypogonadism, history of coronary, cerebral or peripheral vascular disease, documented chronic hypoxaemia, Parkinson's disease, depression, Alzheimer's dementia, restless legs syndrome, iron deficiency, gastro-oesophageal reflux disease, osteoporosis and/or previous fragility fracture, bone mineral density T-scores, and symptomatic atrophic vaginitis.

The investigator will also collect the following information: presence or absence of ankle oedema, bone mineral density T-scores, influenza and pneumococcal vaccine status, heart rate (bpm), and systolic blood and diastolic blood pressure (mmHg).

**Data source**

We will collect data using electronic health record consultations and clinical patient interviews.

**Database**

The information collected will not include indentity of patients. Each patient will be numbered from 1 to 300 to protect their identity.

To evaluate data obtained throughout the study, a data safety monitoring board will be set up that will be composed of two external investigators with board expertise in this clinical field and academic and scientific activities.

Following the Portuguese Clinical Research Law, all data recorded during the study will be stored for five years in a safe and proper place in the primary investigator`s health centre after the closure of the investigation. After this period, all data containing participant codes will be destroyed.

***Phase III: Intrarater reliability study***

In this phase, an independent researcher/family doctor (named investigator "A") will apply the Portuguese version of the STOPP-START criteria, based on the information collected in during Phase II, to all patients' records.

To ensure intrarater reliability, the same doctor will reapply the criteria one week later (21).

***Phase IV interrater agreement study***

Three independent investigators/family doctors (named investigators "B", "C" and "D") will independently apply the Portuguese version of the STOPP-START to the data of 200 randomly assigned participants (22).

**Statistical analysis**

Microsoft Excel 2016® software will be used for data collection. Data analyses will be made with SPSS Statistics 25.0® and the software R.

Categorical variables will be described by absolute and relative frequencies.

Continuous variables will be described by mean and standard deviation if normally distributed or by median and interquartile range if not normally distributed. Normality will be assessed by observation of histograms and implementation of the Kolmogorov-Smirnov test.

Intrarater reliability will be measured using Kappa statistics and interrater agreement will be assessed using agreement proportions and specific agreement proportions (21).

A p-value less or equal than 0.05 will be considered statistically significant.

***Patient and public involvement***

No patient or member of the public will be involved in the design of this protocol or the establishment of intervention and the outcome measures.

## Discussion

Appropriate prescriptions for older patients is a quality standard for healthcare. General practitioners are the main prescribers and they struggle to identify PIM as well as potential prescribing omissions. The STOPP-START tool is an easy way to manage the care of older patients. Further, it is easier to use daily when adapted for the language of the prescriber.

This study is innovative as it is the first development of a Portuguese version of the STOPP-START criteria. Our research will be not merely a translation but also an adaptation done by independent general practitioners that will potentially increase the use this version in the primary care setting.

Our research has some limitations such as the fact that even though it will be Portuguese language adaption of the STOPP-START criteria, it is also culturally adapted toward the country of Portugal and may not apply to other countries that have Portuguese as their main language. Furthermore, this adapted version of STOPP-START is exclusively focused towards primary healthcare centres.

## Ethics and Dissemination

Every participant will sign a written consent form (online supplementary appendix I). Identity of all participants will be protected throughout the study. The documents used to collect the data of the participants will contain only an identification code of each participant using a number from 1 to 300.

This protocol was approved on 30 July 2020 by the Ethics Committee of the Central Health Region of Portugal with the reference number 034-2020.

We intend to publish the full article in a related peer-reviewed journal, and results will also be disseminated in conference presentations, reports, and in a PhD thesis.

## Author Statement

All authors completed the ICMJE uniform disclosure at http://www.icmje.org/coi_disclosure.pdf

There are no other relationships or activities that could appear to have influenced the submitted work.

**Contributors** LM conceived of the original idea. LM, AT, and MM-S designed the protocol. LM, LFM, IV, AT, MM-S, and CM reviewed the protocol.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information

## References


1. OECD. Elderly population (indicator). doi: 10.1787/8d805ea1-en (Accessed on 04 August 2020) [Available from: https://data.oecd.org/pop/elderly-population.htm#indicator-chart.
2. World Health Organization. Ageing and health. (Accessed on 04 August 2020) [Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health.
3. World Health Organization. World Report On Ageing And Health. Geneva. (Accessed on 04 August 2020) [Available from: https://apps.who.int/iris/bitstream/10665/186463/1/9789240694811_eng.pdf.
4. World Health Organization. 2019. The global strategy and action plan on ageing and health (Accessed on 04 August 2020) [Available from: https://www.who.int/ageing/global-strategy/en/
5. Prazeres F, Santiago L. Prevalence of multimorbidity in the adult population attending primary care in Portugal: a cross-sectional study. BMJ open. 2015;5(9):e009287.
6. Formiga F, Ferrer A, Sanz H, Marengoni A, Alburquerque J, Pujol R. Patterns of comorbidity and multimorbidity in the oldest old: The Octabaix study. European journal of internal medicine. 2013;24(1):40-4.
7. Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2015;187:E130-7.
8. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. Journal of Clinical Epidemiology. 2012;65(9):989-95.
9. Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. Eur J Clin Pharmacol. 2014;70(5):575-81.

10. Motter FR, Fritzen JS, Hilmer SN, Paniz ÉV, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. European Journal of Clinical Pharmacology. 2018;74(6):679-700.

11. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: A systematic review of the literature. Ageing research reviews. 2011;10:430-9.

12. Weng MC, Tsai CF, Sheu KL, Lee YT, Lee HC, Tzeng SL, et al. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM : monthly journal of the Association of Physicians. 2013;106:1009-15.

13. Tommelein E, Mehuys E, Petrovic M, Somers A, Colin P, Boussery K. Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. Eur J Clin Pharmacol. 2015;71(12):1415-27.

14. Panel BtAGSBCUE. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Journal of the American Geriatrics Society. 2019;67(4):674-94.

15. Holt S, Schmiedl S, Thürmann PA. Potentially Inappropriate Medications in the Elderly: The PRISCUS List. Deutsches Arzteblatt international. 2010;107(31-32):543-51.

16. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age and ageing. 2008;37(6):673-9.

17. Boland B, Guignard B, Dalleur O, Lang PO. Application of STOPP/START and Beers criteria: Compared analysis on identification and relevance of potentially inappropriate prescriptions. European Geriatric Medicine. 2016;7(5):416-23.

18. Hill-Taylor B, Walsh KA, Stewart S, Hayden J, Byrne S, Sketris IS. Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies. Journal of clinical pharmacy and therapeutics. 2016;41(2):158-69.

19. Lang P-O, Hasso Y, Belmin J, Payot I, Baeyens J-P, Vogt-Ferrier N, et al. STOPP-START: adaptation of a French language screening tool for detecting inappropriate

prescriptions in older people. Canadian journal of public health = Revue canadienne de sante publique. 2009;100(6):426-31.

20. Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2005;8(2):94-104.

21. Streiner DL NG. Health Measurement Scales: A Practical Guide to their Development and Use. 3rd ed. Oxford, England: Oxford University Press; 2003

2003.

22. MM S. Measures of Interobserver Agreement. Boca Raton, Fla: Chapman & Hall/CRC; 2004.

# CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO

# PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

**Título do estudo**: critérios STOPP/START (versão 2) operacionalizados para Portugal
Enquadramento: Estudo observacional, em unidades de saúde em Portugal continental. Feito no âmbito de tese de doutoramento da Faculdade de Medicina da Universidade do Porto de Luís Monteiro, orientado pela Prof. Doutor Carlos Martins, Prof.ª Andreia Teixeira e Prof.ª Matilde Monteiro-Soares.

**Explicação do estudo**: Estudo observacional longitudinal efetuado após consulta médica, com aplicação dos critérios STOPP/START traduzidos previamente para português.

Estudo feito com pessoas com idade igual ou superior a 65 anos que recorrem a consulta, que aceitem participar no estudo e saibam ler. Serão recolhidas as variáveis: sexo, idade, formação (número de anos de escolaridade), índice socioeconómico, antecedentes pessoais, patologias atuais e no passado, inquirindo os utentes e verificando o registado nos processos clínicos.

**Condições e financiamento:** Não há pagamentos a investigadores ou participantes, nem compensação de despesas de deslocação. O estudo foi aprovado pela comissão de ética da ARS Centro. A participação no estudo é voluntária e caso não queira participar ou queira abandonar a qualquer altura, não será prejudicado.

**Confidencialidade e anonimato**: cada investigador terá uma base de identificação dos seus utentes, identificação esta codificada nos dados em Excel que serão enviados ao investigador principal. A identificação dos participantes nunca terá de ser tornada pública.

**O investigador:**

**Assinatura:** Data:

Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pela/s pessoa/s que acima assina/m. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas.

**Nome do utente:**

**Assinatura:** Data:

Este documento composto de 1 página, é feito em duplicado, uma via para o investigador e outra para o utente.

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*Methods and analysis:* The study will be conducted in four phases: Phase I - translation of the STOPP-START screening tool to Portuguese; Phase II - data collection of patient data; Phase III - intrarater reliability and agreement study; and Phase IV - interrater reliability and agreement study.

*Ethics and Dissemination*: This study was approved by the Ethics Committee of the Central Health Region of Portugal (where the study will take place). Every participant will sign a written consent form. We intend to publish the full article in a related peer-reviewed journal, conference presentations, reports, and in a PhD thesis.


**Keywords:** Geriatric medicine; Quality in health care; General Medicine

**Strengths and limitations of this study**

- This study will develop the first Portuguese version of the STOPP-START criteria.
- This is the first study in a Portuguese primary care setting that aims to develop a useful tool for the appropriate prescription of older patients.
- The main limitation of the study is that it is focused in Portugal and it may not apply to other countries where Portuguese is not the main language.

## Introduction

In Organisation for Economic Co-operation and Development (OECD) countries, the number of older adults is increasing [1] as well as their life expectancies [2, 3].
Caring for older adults is a challenge for healthcare systems [4] because older adults are more likely to have more than one chronic disease [5, 6]. For example, multi-morbidity in the elderly can be higher than 90% in Portugal [5]. Therefore, adults aged ≥ 65 years are more likely to be prescribed with multiple drugs [7-9] and, may be more susceptible to inappropriate medication use [10-12].

Potentially inappropriate medications (PIM) can be described as the use of medications that potentially have more risks than benefits even though safer pharmacologic and nonpharmacologic alternatives are available [10]. Potentially inappropriate prescription (PIP) is a different concept than PIM, and includes the over-, under-, and mis-prescriptions of medications (e.g., inappropriate dose or duration) [13].

There are various tools to help physicians identify PIM such as the Beers Criteria [14] and the Potentially Inappropriate Medications in the Elderly list (PRISCUS list) [15]. The combination of the Screening Tool of Older People's Prescriptions (STOPP) and the Screening Tool to Alert to Right Treatment (START) [16, 17] is another widely used tool. One of the advantages of this tool is that it not only considers PIM, but also the indications to start an appropriate medication (START).

Versus other tools, some studies have shown that the STOPP-START tool can identify a significantly higher proportion of patients requiring hospitalisation as a result of PIM-related adverse events [16], can reduce the highest number of medications, and can identify more potential major clinical issues [18]. The criteria for STOPP-START has been associated with improvement in prescribing quality and clinical outcomes [19]. These criteria have been adapted for other languages, such as French [20]. In this adaptation 50 data sets of patients hospitalized in an academic geriatrics department were analysed independently by one geriatrician and one general practitioner. They considered 87 STOPP-START criteria of the original version. The data sets involved 418 prescribed medications. The proportions of positive and negative interraters agreements were 99% and 95%, respectively, for STOPP and 99% and 88% for START; Cohen's κ-coefficients were 0.95 for STOPP and 0.92 for START. The results indicated an excellent interrater agreement.

Interrater reliability of STOPP and START criteria was also tested between multiple physicians practicing independently in Europe [21]. After translation of the criteria into their local language doctors in Belgium, Czech Republic, Italy, Spain, and Switzerland applied the criteria to twenty datasets selected from 200 patients aged ≥ 65 years of a university teaching hospital in Ireland. The median kappa coefficient between raters was 0.93 (0.90–0.96) for STOPP criteria and 0.85 (0.82–0.91) for START criteria. The results demonstrated good interrater reliability of STOPP-STARTcriteria. Therefore, the authors concluded that STOPP and START criteria are generalisable across different European countries and languages [21].

Reliability and agreement are different concepts but have been used without distinction in many studies [22]. Reliability can be defined as the ratio of variability between scores of the same subjects (by different raters or at different moments) to the total variability of all scores in the sample. Agreement is connected to the question about whether observations are similar or the degree to which they differ.

We aim to make the first translation and validation [23] of the English STOPP-START tool for Portuguese family doctors. In the validation study, we deal with two aspects of reliability and agreement concepts: interrater reliability and agreement (different raters using the translated STOPP-START tool assess the same patients), and intrarater reliability and agreement (the same rater using the translated STOPP-START tool assess the same subjects at two different moments).

## Methods and Analysis

### *Study design*

This study will be conducted in four phases as illustrated in Figure 1 (timeline available in online supplementary appendix I). The first phase (Phase I) is the translation to the Portuguese language followed by data collection (Phase II).
Phase III consists of an intrarater reliability and agreement study, and Phase IV is an interrater reliability and agreement study. We made a pre-registration on "Open registries Network" (DOI 10.17605/OSF.IO/SK2RJ).

### *Phase I: Translation to Portuguese*

The translation of the STOPP-START screening tool will follow the Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes Measures [20]. We have already obtained permission from STOPP-START´s authors to translate and validate the tool for Portuguese. We will recruit a key in-country consultant who is a native Portuguese and fluent English speaker and will be the main contact to perform and help with the translation. This consultant also will have a background in health research and experience in translating English documents. We will obtain two independent translations of the STOPP-START. One will be done by the key in-country consultant, and the other will be performed by a forward translator who is also a native Portuguese and fluent English speaker.

The two translations will be reconciled by the research team to obtain a final consensus translation that will be back-translated.
The back-translation (from Portuguese to English) will be done by a professional translator who is a native speaker of English and fluent speaker of Portuguese. This translator will have no prior knowledge of the original English version. Afterwards, the back-translation will be compared with the original to identify any relevant differences.

In the final step, the reconciled Portuguese STOPP-START version will be distributed to a group of 15 general practitioners to verify if there are any interpretations issues. The research team will analyse the results from the application of the STOPP-START tool to prepare the final version.

### *Phase II: Data collection*

**Design**
This will be a cross-sectional, analytical study.

**Setting**
The study will be conducted in a primary care centre in the Centre Region of Portugal.

The health unit is located in Aveiro. Five family doctors follow a total of 8165 patients. 1625 patients aged ≥ 65 years.

**Sample size**
To calculate the sample size for the validation study, we used the function CIBinary of the kappaSize package of R® software [24]. For the intrarater study, we obtained a sample size

of 334 subjects considering the following parameters: estimated kappa value: 0.68 [25]; error margin: 0.1; prevalence of each item of the START criteria: 0.25; number of moments: 2; and significance level: 5%. In the interrater study, we obtained a sample size of 205 subjects considering the following parameters: estimated kappa value: 0.68 [25]; error margin: 0.1; prevalence of each item of the START criteria: 0.25; number of raters: 3; and significance level: 5%. The 205 patients for interrater assessment will be randomly selected from the 334 subjects used for the intrarater evaluation.

## Study procedures

### Recruitment of patients

Patients will be randomly selected (independent random sampling using computer-generated random digits) from a list of patients aged ≥ 65 years from a primary care centre. They will be invited by telephone to participate in the study. The investigator or a previously trained research associate will then interview the patients in the general practitioner office. Recruitment will continue until 334 patients are enrolled.

Exclusion criteria include incapacity or unwillingness to provide written informed consent, diagnostic of psychotic disorder, institutionalization, and the presence of terminal illness.
At inclusion, the main investigator will collect sociodemographic patient data such as age, gender, educational level, labour status, and marital status. Clinical data collection will include identification of total number of medications for chronic diseases, any prescribed drugs, dosage, pharmaceutical dosage form and route of administration, the reason for taking medication, allergies, drug-related conditions and history of adverse drug reactions, and current or past conditions/diseases. A detailed list of current or past conditions/diseases that will be included are given in the online supplementary appendix II.
The investigator will also collect the following information: presence or absence of ankle oedema, bone mineral density T-scores, history of influenza and pneumococcal vaccination, heart rate (bpm), and systolic blood and diastolic blood pressure (mmHg).
The data is summarized in Table 1.

*Table 1-Patients Data (Phase II).*

| Patients Data | |
|---|---|
| Sociodemographic data | age<br>gender<br>educational level<br>labour status<br>marital status |
| Clinical Data | number of medications for chronic diseases, prescribed drugs<br>pharmaceutical dosage form and route of administration,<br>reason for taking medication<br>allergies<br>drug-related conditions<br>history of adverse drug reactions<br>current or past conditions/diseases*<br>presence or absence of ankle oedema<br>bone mineral density T-scores<br>history of influenza and pneumococcal vaccination<br>heart rate (bpm)<br>systolic blood and diastolic blood pressure (mmHg).<br>estimated glomerular filtration rate<br>serum K+ mmol/l<br>serum Na+ mmol/ |

* available at online supplementary appendix II

**Data source**

We will collect data using electronic health record consultations and clinical patient interviews.

**Database**

The information collected will not include information that might identify the patients. Each patient will be numbered from 1 to 334 to protect their identity.

To evaluate data obtained throughout the study, a data safety monitoring board will be set up that will be composed of two external investigators with board expertise in this clinical field and academic and scientific activities.

Following the Portuguese Clinical Research Law, all data recorded during the study will be stored for five years in a safe and proper place in the primary investigator`s health centre

after the closure of the investigation. All data containing participant codes will be destroyed after this period.

***Phase III: Intrarater reliability and agreement study***

An independent researcher/family doctor (named investigator "A") will apply the Portuguese version of the STOPP-START criteria to all the patients using the information collected in Phase II.
Investigator "A" is an independent researcher with more than 10 years of experience of clinical practice.
To ensure intrarater reliability and agreement, the same doctor will re-evaluate these patients' records applying the same criteria two weeks later to avoid recall bias [26, 27].

***Phase IV: Interrater reliability and agreement study***

Three independent investigators/family doctors (named investigators "B", "C" and "D") will independently apply the Portuguese version of the STOPP-START using the data, collected in phase II, of 205 randomly selected participants [28]. These three physicians are based in different health units and they will only have contact with the corresponding author that will give them the comprised data. Investigators "B", "C" and "D" will independently assess the STOPP and START criteria in each of the 205 datasets and will be invited to give written comments if necessary. Interrater agreement will be assessed by comparing the results of the three raters.

**Statistical analysis**

Data will be stored with Microsoft Excel® software. Data analyses will be made with SPSS Statistics 27.0® and the software R.
Categorical variables will be described by absolute and relative frequencies.
Continuous variables will be described by mean and standard deviation if normally distributed or by median and interquartile range if not normally distributed. Normality will be assessed by observation of histograms and implementation of the Kolmogorov-Smirnov test.

Intrarater/interrater reliability will be measured using Cohen's κ-coefficient and the respective 95% confidence interval [22]. The Cohen's κ-coefficient will be interpreted as poor ($\kappa \leq 0.2$), fair ($0.21 \leq \kappa \leq 0.40$), moderate ($0.51 \leq \kappa \leq 0.6$), substantial ($0.61 \leq \kappa \leq 0.8$) and good ($0.81 \leq \kappa \leq 1.00$) [29]. Intrarater/interrater agreement will be assessed using agreement proportions and specific (positive and negative) agreement proportions and the respectives 95% confidence interval [22].
A p-value less or equal than 0.05 will be considered statistically significant.

***Patient and public involvement***

No patient or member of the public will be involved in the design of this protocol or the establishment of intervention and the outcome measures.

## Discussion

Appropriate prescriptions for older patients are a quality standard for healthcare. General practitioners are the main prescribers and they struggle to identify PIM as well as potential prescribing omissions. The STOPP-START tool is an easy way to manage the care of older patients. It is easier for daily use when adapted for the language of the prescriber.

This study is innovative because it is the first development of a Portuguese version of the STOPP-START criteria. Our research will not be merely a translation but also an adaptation done by independent general practitioners that will potentially increase the use of this version in the primary care setting.

Our research has some limitations such as the fact that even though it will be Portuguese language adaption of the STOPP-START criteria. It is also focused on Portugal and may not apply to other countries where Portuguese is used. This adapted version of STOPP-START is exclusively focused towards primary healthcare centres.

## Ethics and Dissemination

Every participant will sign a written consent form (online supplementary appendix III). The identity of all participants will be protected throughout the study. The documents used to collect the data of the participants will contain only an identification code of each participant using a number from 1 to 334.
This protocol was approved on 30 July 2020 by the Ethics Committee of the Central Health Region of Portugal with the reference number 034-2020.
We intend to publish the full article in a related peer-reviewed journal, and results will also be disseminated in conference presentations, reports, and in a PhD thesis.

## Author Statement

All authors completed the ICMJE uniform disclosure at http://www.icmje.org/coi_disclosure.pdf

There are no other relationships or activities that could appear to have influenced the submitted work.

**Contributors:** LM conceived of the original idea. LM, AT, and MM-S designed the protocol. LM, LFM, IV, AT, MM-S, and CM reviewed the protocol.

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**Competing interests:** None declared.

**Patient and public involvement:** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

**Patient consent for publication:** Not required.

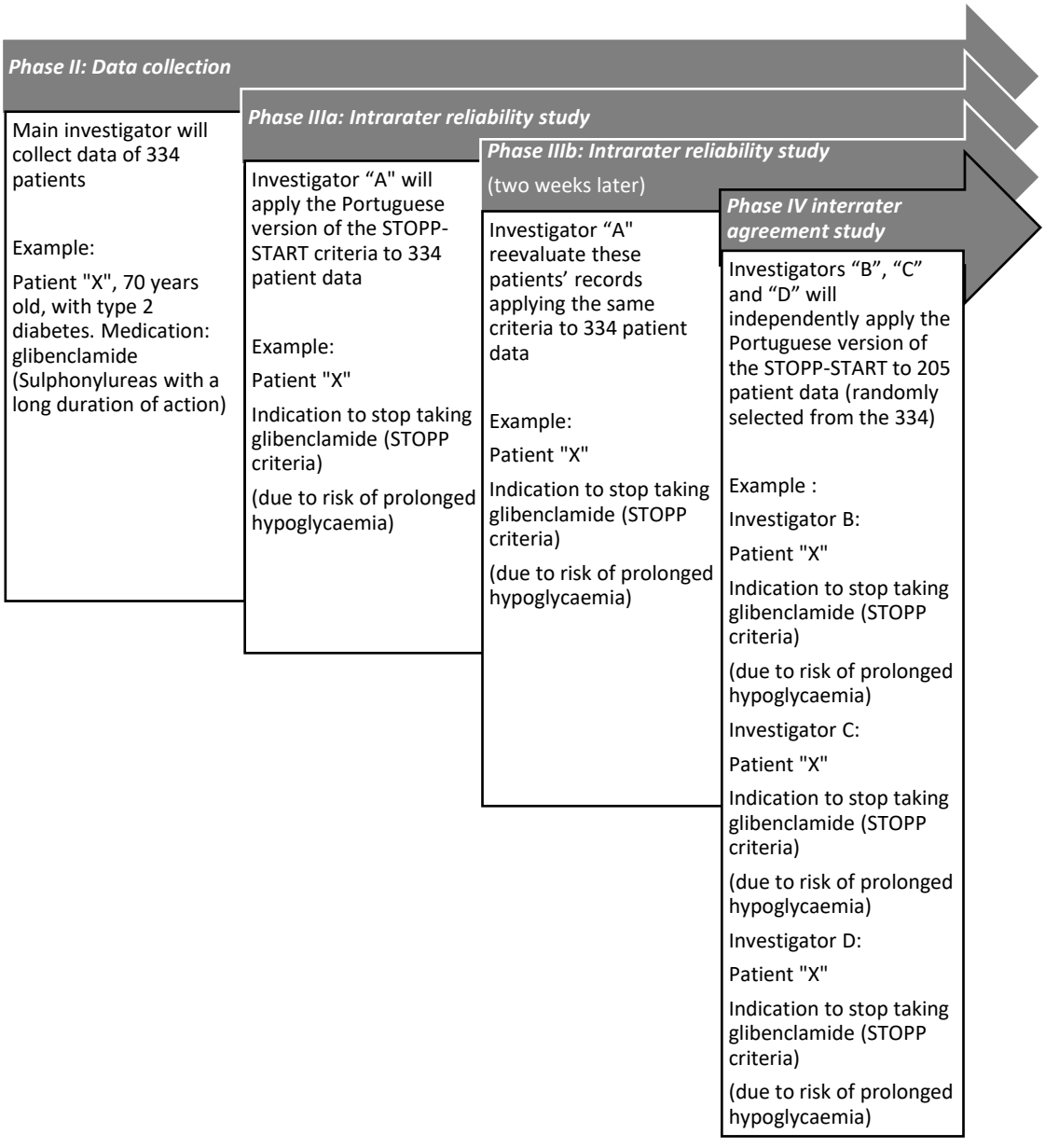
**Provenance and peer review:** Not commissioned; externally peer reviewed.

**Data availability statement:** All data relevant to the study are included in the article or uploaded as supplementary information

## References

1. OECD. Elderly population (indicator). doi: 10.1787/8d805ea1-en (Accessed on 12 May 2019) [Available from: https://data.oecd.org/pop/elderly-population.htm#indicator-chart.
2. Organization WH 2019. [Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health.
3. Organization WH. World report on ageing and health. 2015.
4. Organization WH. The Global strategy and action plan on ageing and health. 2019.
5. Prazeres F, Santiago L. Prevalence of multimorbidity in the adult population attending primary care in Portugal: a cross-sectional study. BMJ open. 2015;5(9):e009287.
6. Formiga F, Ferrer A, Sanz H, Marengoni A, Alburquerque J, Pujol R. Patterns of comorbidity and multimorbidity in the oldest old: The Octabaix study. European journal of internal medicine. 2013;24(1):40-4.
7. Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2015;187(4):E130-e7.
8. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol. 2012;65(9):989-95.
9. Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. Eur J Clin Pharmacol. 2014;70(5):575-81.
10. Motter FR, Fritzen JS, Hilmer SN, Paniz ÉV, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. European Journal of Clinical Pharmacology. 2018;74(6):679-700.
11. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: A systematic review of the literature. Ageing research reviews. 2011;10:430-9.
12. Weng MC, Tsai CF, Sheu KL, Lee YT, Lee HC, Tzeng SL, et al. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM : monthly journal of the Association of Physicians. 2013;106:1009-15.
13. Tommelein E, Mehuys E, Petrovic M, Somers A, Colin P, Boussery K. Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. Eur J Clin Pharmacol. 2015;71(12):1415-27.
14. Panel BtAGSBCUE. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Journal of the American Geriatrics Society. 2019;67(4):674-94.
15. Holt S, Schmiedl S, Thürmann PA. Potentially Inappropriate Medications in the Elderly: The PRISCUS List. Deutsches Arzteblatt international. 2010;107(31-32):543-51.

16. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age and ageing. 2008;37(6):673-9.
17. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age and ageing. 2014;44(2):213-8.
18. Boland B, Guignard B, Dalleur O, Lang PO. Application of STOPP/START and Beers criteria: Compared analysis on identification and relevance of potentially inappropriate prescriptions. European Geriatric Medicine. 2016;7(5):416-23.
19. Hill-Taylor B, Walsh KA, Stewart S, Hayden J, Byrne S, Sketris IS. Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies. Journal of clinical pharmacy and therapeutics. 2016;41(2):158-69.
20. Lang P-O, Hasso Y, Belmin J, Payot I, Baeyens J-P, Vogt-Ferrier N, et al. STOPP-START: adaptation of a French language screening tool for detecting inappropriate prescriptions in older people. Canadian journal of public health = Revue canadienne de sante publique. 2009;100(6):426-31.
21. Gallagher P, Baeyens JP, Topinkova E, Madlova P, Cherubini A, Gasperini B, et al. Inter-rater reliability of STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. Age and ageing. 2009;38(5):603-6.
22. Kottner J, Audigé L, Brorson S, Donner A, Gajewski BJ, Hróbjartsson A, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. J Clin Epidemiol. 2011;64(1):96-106.
23. Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation. Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research. 2005;8(2):94-104.
24. Michael A Rotondi (2013). kappaSize: Sample Size Estimation Functions for Studies of Interobserver Agreement. R package version 1.1 https://CRAN.R-project.org/package=kappaSize
25. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. International journal of clinical pharmacology and therapeutics. 2008;46(2):72-83.
26. Streiner DL NG. Health Measurement Scales: A Practical Guide to their Development and Use. 3rd ed. Oxford, England: Oxford University Press; 2003 2003.
27. Beemster TT, van Velzen JM, van Bennekom CAM, Reneman MF, Frings-Dresen MHW. Test–Retest Reliability, Agreement and Responsiveness of Productivity Loss (iPCQ-VR) and Healthcare Utilization (TiCP-VR) Questionnaires for Sick Workers with Chronic Musculoskeletal Pain. Journal of Occupational Rehabilitation. 2019;29(1):91-103.
28. Shoukri MM. Measures of interobserver agreement. 2004.
29. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-74.



# Appendix I Timeline

| | 2021 | | | | 2022 | | | | 2023 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Tasks/Trimester** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** |
| **Phase I**<br>Translation to the Portuguese language | | | | | | | | | | | | |
| **Phase II**<br>Data collection | | | | | | | | | | | | |
| **Phase III**<br>Intrarater reliability and agreement study | | | | | | | | | | | | |
| **Phase IV**<br>Interrater reliability and agreement study | | | | | | | | | | | | |

Appendix II - list of diseases that will be collected by the main investigator in phase II for each patient.

| Current or past conditions/diseases |
|---|
| Heart failure and heart block as determined by New York Heart Association Classification |
| Supraventricular tachyarrhythmia |
| Hypertension |
| Liver failure |
| Nephrotic syndrome or renal failure |
| History of gout |
| Urinary incontinence |
| Angina |
| History of peptic ulcer disease |
| Bleeding diathesis |
| Recent non-trivial spontaneous bleeding |
| Stroke |
| Acute coronary syndrome |
| Coronary stent(s) inserted |
| Carotid arterial stenosis |
| Atrial fibrillation |
| Coronary, cerebrovascular or peripheral arterial disease |
| Deep venous thrombosis |
| Thrombophilia |
| Dementia |
| Narrow angle glaucoma |
| Cardiac conduction abnormalities |
| Prostatism or prior history of urinary retention |
| Depression |
| Parkinsonism or Lewy Body Disease |
| Delirium |
| Psychosis |
| Benign essential tremor |
| Erosive peptic oesophagitis |
| Constipation |
| Chronic obstructive pulmonary disease |
| Bladder outflow obstruction |
| Asthma |
| Acute or chronic respiratory failure |
| Osteoarthritis |
| Rheumatoid arthritis |
| Upper gastrointestinal disease |
| Chronic cognitive impairment with symptomatic orthostatic hypotension or micturition syncope |
| Type 2 diabetes mellitus |
| Hypoglycaemic episodes |
| History of breast cancer |
| Venous thromboembolism |
| Primary or secondary hypogonadism |
| Documented chronic hypoxaemia |
| Parkinson's disease |
| Alzheimer's dementia |
| Restless legs syndrome |
| Iron deficiency |
| Gastro-oesophageal reflux disease |
| Osteoporosis and/or previous fragility fracture |
| Symptomatic atrophic vaginitis |

# CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO

# PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

**Título do estudo**: critérios STOPP/START (versão 2) operacionalizados para Portugal
Enquadramento: Estudo observacional, em unidades de saúde em Portugal continental. Feito no âmbito de tese de doutoramento da Faculdade de Medicina da Universidade do Porto de Luís Monteiro, orientado pela Prof. Doutor Carlos Martins, Prof.ª Andreia Teixeira e Prof.ª Matilde Monteiro-Soares.

**Explicação do estudo**: Estudo observacional longitudinal efetuado após consulta médica, com aplicação dos critérios STOPP/START traduzidos previamente para português.

Estudo feito com pessoas com idade igual ou superior a 65 anos que recorrem a consulta, que aceitem participar no estudo e saibam ler. Serão recolhidas as variáveis: sexo, idade, formação (número de anos de escolaridade), índice socioeconómico, antecedentes pessoais, patologias atuais e no passado, inquirindo os utentes e verificando o registado nos processos clínicos.

**Condições e financiamento:** Não há pagamentos a investigadores ou participantes, nem compensação de despesas de deslocação. O estudo foi aprovado pela comissão de ética da ARS Centro. A participação no estudo é voluntária e caso não queira participar ou queira abandonar a qualquer altura, não será prejudicado.

**Confidencialidade e anonimato**: cada investigador terá uma base de identificação dos seus utentes, identificação esta codificada nos dados em Excel que serão enviados ao investigador principal. A identificação dos participantes nunca terá de ser tornada pública.

**O investigador:**

**Assinatura:** Data:

Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pela/s pessoa/s que acima assina/m. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas.

**Nome do utente:**

**Assinatura:** Data:

Este documento composto de 1 página, é feito em duplicado, uma via para o investigador e outra para o utente.

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# Translation and adaptation of the STOPP-START screening tool to Portuguese for detecting inappropriate prescriptions in older people: a protocol

| | |
|---|---|
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| Primary Subject Heading: | General practice / Family practice |
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| Keywords: | GERIATRIC MEDICINE, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, GENERAL MEDICINE (see Internal Medicine) |
| | |

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# Title

Translation and adaptation of the STOPP-START screening tool to Portuguese for detecting inappropriate prescriptions in older people: a protocol

# Running title

Portuguese version of the STOPP-START screening tool

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## Abstract

*Introduction*: Rational prescribing for older adults is a challenge because they usually exhibit multi-morbidity and multi-medication. One available and reliable tool to tackle this issue consists of the Screening Tool of Older People's Prescriptions (STOPP) and the Screening Tool to Alert to Right Treatment (START), which has been associated with improvements in clinical outcomes. Our goal here is to translate and validate the STOPP-START screening tool for use with Portuguese general practitioners/family physicians.

*Methods and analysis:* The study will be conducted in four phases: Phase I - translation of the STOPP-START screening tool to Portuguese; Phase II - data collection of patient data; Phase III - intrarater reliability and agreement study; and Phase IV - interrater reliability and agreement study.

*Ethics and Dissemination*: This study was approved by the Ethics Committee of the Central Health Region of Portugal (where the study will take place). Every participant will sign a written consent form. We intend to publish the full article in a related peer-reviewed journal, conference presentations, reports, and in a PhD thesis.


**Keywords:** Geriatric medicine; Quality in health care; General Medicine

**Strengths and limitations of this study**

- This study will develop the first Portuguese version of the STOPP-START criteria.
- This is the first study in a Portuguese primary care setting that aims to develop a useful tool for the appropriate prescription of older patients.
- The main limitation of the study is that it is focused in Portugal and it may not apply to other countries where Portuguese is not the main language.

## Introduction

In Organisation for Economic Co-operation and Development (OECD) countries, the number of older adults is increasing [1] as well as their life expectancies [2, 3].
Caring for older adults is a challenge for healthcare systems [4] because older adults are more likely to have more than one chronic disease [5, 6]. For example, multi-morbidity in the elderly can be higher than 90% in Portugal [5]. Therefore, adults aged ≥ 65 years are more likely to be prescribed with multiple drugs [7-9] and, may be more susceptible to inappropriate medication use [10-12].

Potentially inappropriate medications (PIM) can be described as the use of medications that potentially have more risks than benefits even though safer pharmacologic and nonpharmacologic alternatives are available [10]. Potentially inappropriate prescription (PIP) is a different concept than PIM, and includes the over-, under-, and mis-prescriptions of medications (e.g., inappropriate dose or duration) [13].

There are various tools to help physicians identify PIM such as the Beers Criteria [14] and the Potentially Inappropriate Medications in the Elderly list (PRISCUS list) [15]. The combination of the Screening Tool of Older People's Prescriptions (STOPP) and the Screening Tool to Alert to Right Treatment (START) [16, 17] is another widely used tool. One of the advantages of this tool is that it not only considers PIM, but also the indications to start an appropriate medication (START).

Versus other tools, some studies have shown that the STOPP-START tool can identify a significantly higher proportion of patients requiring hospitalisation as a result of PIM-related adverse events [16], can reduce the highest number of medications, and can identify more potential major clinical issues [18]. The criteria for STOPP-START has been associated with improvement in prescribing quality and clinical outcomes [19]. These criteria have been adapted for other languages, such as French [20]. In this adaptation 50 data sets of patients hospitalized in an academic geriatrics department were analysed independently by one geriatrician and one general practitioner. They considered 87 STOPP-START criteria of the original version. The data sets involved 418 prescribed medications. The proportions of positive and negative interraters agreements were 99% and 95%, respectively, for STOPP and 99% and 88% for START; Cohen's κ-coefficients were 0.95 for STOPP and 0.92 for START. The results indicated an excellent interrater agreement.

Interrater reliability of STOPP and START criteria was also tested between multiple physicians practicing independently in Europe [21]. After translation of the criteria into their local language doctors in Belgium, Czech Republic, Italy, Spain, and Switzerland applied the criteria to twenty datasets selected from 200 patients aged ≥ 65 years of a university teaching hospital in Ireland. The median kappa coefficient between raters was 0.93 (0.90–0.96) for STOPP criteria and 0.85 (0.82–0.91) for START criteria. The results demonstrated good interrater reliability of STOPP-STARTcriteria. Therefore, the authors concluded that STOPP and START criteria are generalisable across different European countries and languages [21].

Reliability and agreement are different concepts but have been used without distinction in many studies [22]. Reliability can be defined as the ratio of variability between scores of the same subjects (by different raters or at different moments) to the total variability of all scores in the sample. Agreement is connected to the question about whether observations are similar or the degree to which they differ.

We aim to make the first translation and validation [23] of the English STOPP-START tool for Portuguese family doctors. In the validation study, we deal with two aspects of reliability and agreement concepts: interrater reliability and agreement (different raters using the translated STOPP-START tool assess the same patients), and intrarater reliability and agreement (the same rater using the translated STOPP-START tool assess the same subjects at two different moments).

## Methods and Analysis

### *Study design*

This study will be conducted in four phases as illustrated in Figure 1 (timeline available in online supplementary appendix I). The first phase (Phase I) is the translation to the Portuguese language followed by data collection (Phase II).
Phase III consists of an intrarater reliability and agreement study, and Phase IV is an interrater reliability and agreement study. We made a pre-registration on "Open registries Network" (DOI 10.17605/OSF.IO/SK2RJ).

### *Phase I: Translation to Portuguese*

The translation of the STOPP-START screening tool will follow the Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes Measures [20]. We have already obtained permission from STOPP-START´s authors to translate and validate the tool for Portuguese. We will recruit a key in-country consultant who is a native Portuguese and fluent English speaker and will be the main contact to perform and help with the translation. This consultant also will have a background in health research and experience in translating English documents. We will obtain two independent translations of the STOPP-START. One will be done by the key in-country consultant, and the other will be performed by a forward translator who is also a native Portuguese and fluent English speaker.

The two translations will be reconciled by the research team to obtain a final consensus translation that will be back-translated.
The back-translation (from Portuguese to English) will be done by a professional translator who is a native speaker of English and fluent speaker of Portuguese. This translator will have no prior knowledge of the original English version. Afterwards, the back-translation will be compared with the original to identify any relevant differences.

In the final step, the reconciled Portuguese STOPP-START version will be distributed to a group of 15 general practitioners to verify if there are any interpretations issues. The research team will analyse the results from the application of the STOPP-START tool to prepare the final version.

### *Phase II: Data collection*

**Design**
This will be a cross-sectional, analytical study.

**Setting**
The study will be conducted in a primary care centre in the Centre Region of Portugal.

The health unit is located in Aveiro. Five family doctors follow a total of 8165 patients. 1625 patients aged ≥ 65 years.

**Sample size**
To calculate the sample size for the validation study, we used the function CIBinary of the kappaSize package of R® software [24]. For the intrarater study, we obtained a sample size

of 334 subjects considering the following parameters: estimated kappa value: 0.68 [25]; error margin: 0.1; prevalence of each item of the START criteria: 0.25; number of moments: 2; and significance level: 5%. In the interrater study, we obtained a sample size of 205 subjects considering the following parameters: estimated kappa value: 0.68 [25]; error margin: 0.1; prevalence of each item of the START criteria: 0.25; number of raters: 3; and significance level: 5%. The 205 patients for interrater assessment will be randomly selected from the 334 subjects used for the intrarater evaluation.

## Study procedures

### Recruitment of patients

Patients will be randomly selected (independent random sampling using computer-generated random digits) from a list of patients aged ≥ 65 years from a primary care centre. They will be invited by telephone to participate in the study. The investigator or a previously trained research associate will then interview the patients in the general practitioner office. Recruitment will continue until 334 patients are enrolled.

Exclusion criteria include incapacity or unwillingness to provide written informed consent, diagnostic of psychotic disorder, institutionalization, and the presence of terminal illness.
At inclusion, the main investigator will collect sociodemographic patient data such as age, gender, educational level, labour status, and marital status. Clinical data collection will include identification of total number of medications for chronic diseases, any prescribed drugs, dosage, pharmaceutical dosage form and route of administration, the reason for taking medication, allergies, drug-related conditions and history of adverse drug reactions, and current or past conditions/diseases. A detailed list of current or past conditions/diseases that will be included are given in the online supplementary appendix II.
The investigator will also collect the following information: presence or absence of ankle oedema, bone mineral density T-scores, history of influenza and pneumococcal vaccination, heart rate (bpm), and systolic blood and diastolic blood pressure (mmHg).
The data is summarized in Table 1.

*Table 1-Patients Data (Phase II).*

| Patients Data | |
|---|---|
| Sociodemographic data | age<br>gender<br>educational level<br>labour status<br>marital status |
| Clinical Data | number of medications for chronic diseases, prescribed drugs<br>pharmaceutical dosage form and route of administration,<br>reason for taking medication<br>allergies<br>drug-related conditions<br>history of adverse drug reactions<br>current or past conditions/diseases*<br>presence or absence of ankle oedema<br>bone mineral density T-scores<br>history of influenza and pneumococcal vaccination<br>heart rate (bpm)<br>systolic blood and diastolic blood pressure (mmHg).<br>estimated glomerular filtration rate<br>serum K+ mmol/l<br>serum Na+ mmol/ |

* available at online supplementary appendix II

**Data source**

We will collect data using electronic health record consultations and clinical patient interviews.

**Database**

The information collected will not include information that might identify the patients. Each patient will be numbered from 1 to 334 to protect their identity.

To evaluate data obtained throughout the study, a data safety monitoring board will be set up that will be composed of two external investigators with board expertise in this clinical field and academic and scientific activities.

Following the Portuguese Clinical Research Law, all data recorded during the study will be stored for five years in a safe and proper place in the primary investigator`s health centre

after the closure of the investigation. All data containing participant codes will be destroyed after this period.

***Phase III: Intrarater reliability and agreement study***

An independent researcher/family doctor (named investigator "A") will apply the Portuguese version of the STOPP-START criteria to all the patients using the information collected in Phase II.
Investigator "A" is an independent researcher with more than 10 years of experience of clinical practice.
To ensure intrarater reliability and agreement, the same doctor will re-evaluate these patients' records applying the same criteria two weeks later to avoid recall bias [26, 27].

***Phase IV: Interrater reliability and agreement study***

Three independent investigators/family doctors (named investigators "B", "C" and "D") will independently apply the Portuguese version of the STOPP-START using the data, collected in phase II, of 205 randomly selected participants [28]. These three physicians are based in different health units and they will only have contact with the corresponding author that will give them the comprised data. Investigators "B", "C" and "D" will independently assess the STOPP and START criteria in each of the 205 datasets and will be invited to give written comments if necessary. Interrater agreement will be assessed by comparing the results of the three raters.

**Statistical analysis**

Data will be stored with Microsoft Excel® software. Data analyses will be made with SPSS Statistics 27.0® and the software R.
Categorical variables will be described by absolute and relative frequencies.
Continuous variables will be described by mean and standard deviation if normally distributed or by median and interquartile range if not normally distributed. Normality will be assessed by observation of histograms and implementation of the Kolmogorov-Smirnov test.

Intrarater/interrater reliability will be measured using Cohen's κ-coefficient and the respective 95% confidence interval [22]. The Cohen's κ-coefficient will be interpreted as poor ($\kappa \leq 0.2$), fair ($0.21 \leq \kappa \leq 0.40$), moderate ($0.51 \leq \kappa \leq 0.6$), substantial ($0.61 \leq \kappa \leq 0.8$) and good ($0.81 \leq \kappa \leq 1.00$) [29]. Intrarater/interrater agreement will be assessed using agreement proportions and specific (positive and negative) agreement proportions and the respectives 95% confidence interval [22].
A p-value less or equal than 0.05 will be considered statistically significant.

***Patient and public involvement***

No patient or member of the public will be involved in the design of this protocol or the establishment of intervention and the outcome measures.

## Discussion

Appropriate prescriptions for older patients are a quality standard for healthcare. General practitioners are the main prescribers and they struggle to identify PIM as well as potential prescribing omissions. The STOPP-START tool is an easy way to manage the care of older patients. It is easier for daily use when adapted for the language of the prescriber.

This study is innovative because it is the first development of a Portuguese version of the STOPP-START criteria. Our research will not be merely a translation but also an adaptation done by independent general practitioners that will potentially increase the use of this version in the primary care setting.

Our research has some limitations such as the fact that even though it will be Portuguese language adaption of the STOPP-START criteria. It is also focused on Portugal and may not apply to other countries where Portuguese is used. This adapted version of STOPP-START is exclusively focused towards primary healthcare centres.

## Ethics and Dissemination

Every participant will sign a written consent form (online supplementary appendix III). The identity of all participants will be protected throughout the study. The documents used to collect the data of the participants will contain only an identification code of each participant using a number from 1 to 334.
This protocol was approved on 30 July 2020 by the Ethics Committee of the Central Health Region of Portugal with the reference number 034-2020.
We intend to publish the full article in a related peer-reviewed journal, and results will also be disseminated in conference presentations, reports, and in a PhD thesis.

## Author Statement

All authors completed the ICMJE uniform disclosure at http://www.icmje.org/coi_disclosure.pdf

There are no other relationships or activities that could appear to have influenced the submitted work.

**Contributors:** LM conceived of the original idea. LM, AT, and MM-S designed the protocol. LM, LFM, IV, AT, MM-S, and CM reviewed the protocol.

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**Competing interests:** None declared.

**Patient and public involvement:** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

**Patient consent for publication:** Not required.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

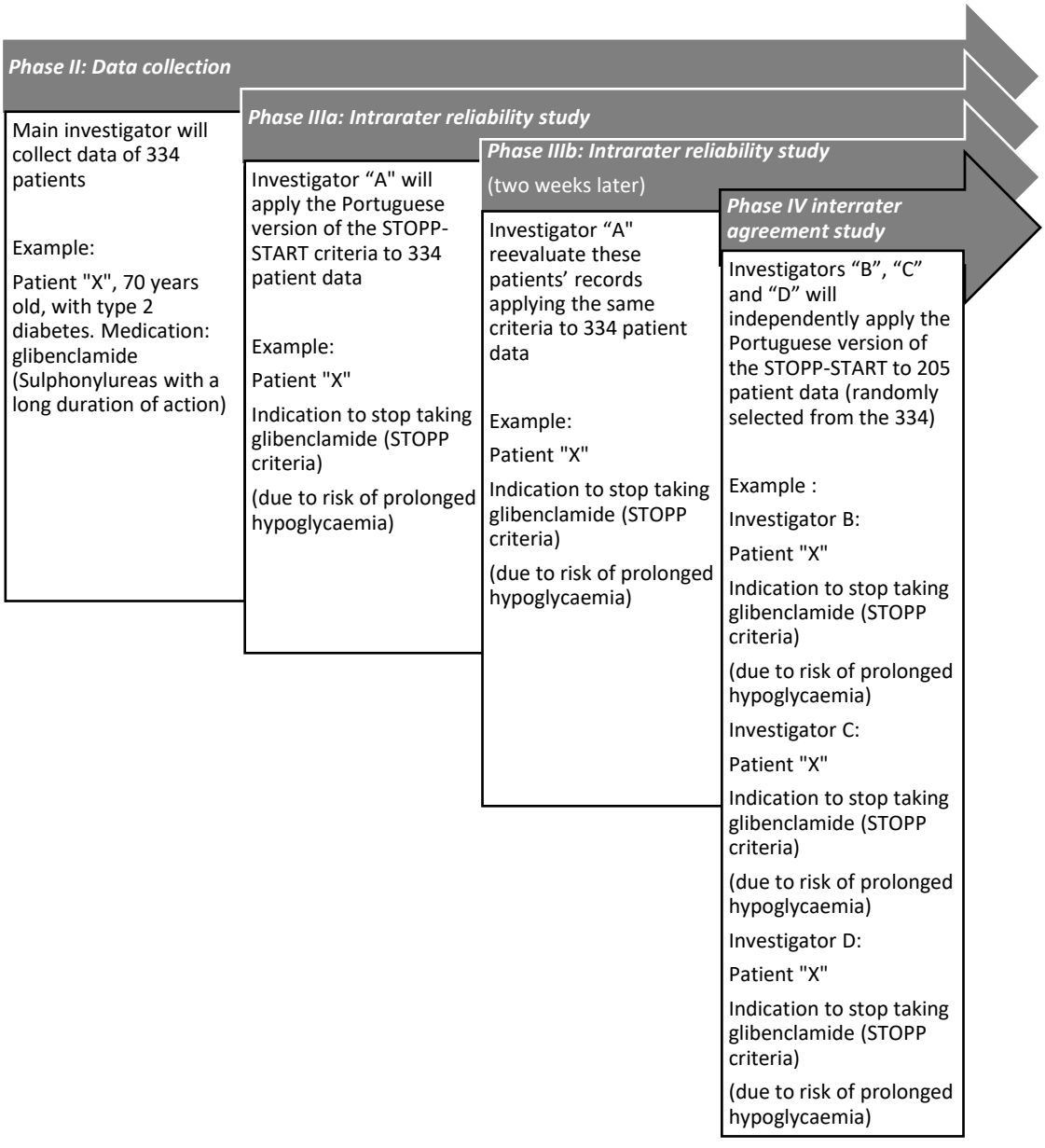
**Data availability statement:** All data relevant to the study are included in the article or uploaded as supplementary information

Figure 1: Flowchart and example

## References

1. OECD. Elderly population (indicator). doi: 10.1787/8d805ea1-en (Accessed on 12 May 2019) [Available from: https://data.oecd.org/pop/elderly-population.htm#indicator-chart.
2. Organization WH 2019. [Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health.
3. Organization WH. World report on ageing and health. 2015.
4. Organization WH. The Global strategy and action plan on ageing and health. 2019.
5. Prazeres F, Santiago L. Prevalence of multimorbidity in the adult population attending primary care in Portugal: a cross-sectional study. BMJ open. 2015;5(9):e009287.
6. Formiga F, Ferrer A, Sanz H, Marengoni A, Alburquerque J, Pujol R. Patterns of comorbidity and multimorbidity in the oldest old: The Octabaix study. European journal of internal medicine. 2013;24(1):40-4.
7. Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2015;187(4):E130-e7.
8. Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol. 2012;65(9):989-95.
9. Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. Eur J Clin Pharmacol. 2014;70(5):575-81.
10. Motter FR, Fritzen JS, Hilmer SN, Paniz ÉV, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. European Journal of Clinical Pharmacology. 2018;74(6):679-700.
11. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: A systematic review of the literature. Ageing research reviews. 2011;10:430-9.
12. Weng MC, Tsai CF, Sheu KL, Lee YT, Lee HC, Tzeng SL, et al. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM : monthly journal of the Association of Physicians. 2013;106:1009-15.
13. Tommelein E, Mehuys E, Petrovic M, Somers A, Colin P, Boussery K. Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review. Eur J Clin Pharmacol. 2015;71(12):1415-27.
14. Panel BtAGSBCUE. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Journal of the American Geriatrics Society. 2019;67(4):674-94.
15. Holt S, Schmiedl S, Thürmann PA. Potentially Inappropriate Medications in the Elderly: The PRISCUS List. Deutsches Arzteblatt international. 2010;107(31-32):543-51.

16. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age and ageing. 2008;37(6):673-9.
17. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age and ageing. 2014;44(2):213-8.
18. Boland B, Guignard B, Dalleur O, Lang PO. Application of STOPP/START and Beers criteria: Compared analysis on identification and relevance of potentially inappropriate prescriptions. European Geriatric Medicine. 2016;7(5):416-23.
19. Hill-Taylor B, Walsh KA, Stewart S, Hayden J, Byrne S, Sketris IS. Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies. Journal of clinical pharmacy and therapeutics. 2016;41(2):158-69.
20. Lang P-O, Hasso Y, Belmin J, Payot I, Baeyens J-P, Vogt-Ferrier N, et al. STOPP-START: adaptation of a French language screening tool for detecting inappropriate prescriptions in older people. Canadian journal of public health = Revue canadienne de sante publique. 2009;100(6):426-31.
21. Gallagher P, Baeyens JP, Topinkova E, Madlova P, Cherubini A, Gasperini B, et al. Inter-rater reliability of STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. Age and ageing. 2009;38(5):603-6.
22. Kottner J, Audigé L, Brorson S, Donner A, Gajewski BJ, Hróbjartsson A, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. J Clin Epidemiol. 2011;64(1):96-106.
23. Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation. Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research. 2005;8(2):94-104.
24. Michael A Rotondi (2013). kappaSize: Sample Size Estimation Functions for Studies of Interobserver Agreement. R package version 1.1 https://CRAN.R-project.org/package=kappaSize
25. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. International journal of clinical pharmacology and therapeutics. 2008;46(2):72-83.
26. Streiner DL NG. Health Measurement Scales: A Practical Guide to their Development and Use. 3rd ed. Oxford, England: Oxford University Press; 2003 2003.
27. Beemster TT, van Velzen JM, van Bennekom CAM, Reneman MF, Frings-Dresen MHW. Test–Retest Reliability, Agreement and Responsiveness of Productivity Loss (iPCQ-VR) and Healthcare Utilization (TiCP-VR) Questionnaires for Sick Workers with Chronic Musculoskeletal Pain. Journal of Occupational Rehabilitation. 2019;29(1):91-103.
28. Shoukri MM. Measures of interobserver agreement. 2004.
29. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-74.



# Appendix I Timeline

| | 2021 | | | | 2022 | | | | 2023 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Tasks/Trimester** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** |
| **Phase I**<br>Translation to the Portuguese language | | | | | | | | | | | | |
| **Phase II**<br>Data collection | | | | | | | | | | | | |
| **Phase III**<br>Intrarater reliability and agreement study | | | | | | | | | | | | |
| **Phase IV**<br>Interrater reliability and agreement study | | | | | | | | | | | | |

Appendix II - list of diseases that will be collected by the main investigator in phase II for each patient.

| Current or past conditions/diseases |
|---|
| Heart failure and heart block as determined by New York Heart Association Classification |
| Supraventricular tachyarrhythmia |
| Hypertension |
| Liver failure |
| Nephrotic syndrome or renal failure |
| History of gout |
| Urinary incontinence |
| Angina |
| History of peptic ulcer disease |
| Bleeding diathesis |
| Recent non-trivial spontaneous bleeding |
| Stroke |
| Acute coronary syndrome |
| Coronary stent(s) inserted |
| Carotid arterial stenosis |
| Atrial fibrillation |
| Coronary, cerebrovascular or peripheral arterial disease |
| Deep venous thrombosis |
| Thrombophilia |
| Dementia |
| Narrow angle glaucoma |
| Cardiac conduction abnormalities |
| Prostatism or prior history of urinary retention |
| Depression |
| Parkinsonism or Lewy Body Disease |
| Delirium |
| Psychosis |
| Benign essential tremor |
| Erosive peptic oesophagitis |
| Constipation |
| Chronic obstructive pulmonary disease |
| Bladder outflow obstruction |
| Asthma |
| Acute or chronic respiratory failure |
| Osteoarthritis |
| Rheumatoid arthritis |
| Upper gastrointestinal disease |
| Chronic cognitive impairment with symptomatic orthostatic hypotension or micturition syncope |
| Type 2 diabetes mellitus |
| Hypoglycaemic episodes |
| History of breast cancer |
| Venous thromboembolism |
| Primary or secondary hypogonadism |
| Documented chronic hypoxaemia |
| Parkinson's disease |
| Alzheimer's dementia |
| Restless legs syndrome |
| Iron deficiency |
| Gastro-oesophageal reflux disease |
| Osteoporosis and/or previous fragility fracture |
| Symptomatic atrophic vaginitis |

# CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO

# PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

**Título do estudo**: critérios STOPP/START (versão 2) operacionalizados para Portugal
Enquadramento: Estudo observacional, em unidades de saúde em Portugal continental. Feito no âmbito de tese de doutoramento da Faculdade de Medicina da Universidade do Porto de Luís Monteiro, orientado pela Prof. Doutor Carlos Martins, Prof.ª Andreia Teixeira e Prof.ª Matilde Monteiro-Soares.

**Explicação do estudo**: Estudo observacional longitudinal efetuado após consulta médica, com aplicação dos critérios STOPP/START traduzidos previamente para português.

Estudo feito com pessoas com idade igual ou superior a 65 anos que recorrem a consulta, que aceitem participar no estudo e saibam ler. Serão recolhidas as variáveis: sexo, idade, formação (número de anos de escolaridade), índice socioeconómico, antecedentes pessoais, patologias atuais e no passado, inquirindo os utentes e verificando o registado nos processos clínicos.

**Condições e financiamento:** Não há pagamentos a investigadores ou participantes, nem compensação de despesas de deslocação. O estudo foi aprovado pela comissão de ética da ARS Centro. A participação no estudo é voluntária e caso não queira participar ou queira abandonar a qualquer altura, não será prejudicado.

**Confidencialidade e anonimato**: cada investigador terá uma base de identificação dos seus utentes, identificação esta codificada nos dados em Excel que serão enviados ao investigador principal. A identificação dos participantes nunca terá de ser tornada pública.

**O investigador:**

**Assinatura:** Data:

Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pela/s pessoa/s que acima assina/m. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas.

**Nome do utente:**

**Assinatura:** Data:

Este documento composto de 1 página, é feito em duplicado, uma via para o investigador e outra para o utente.