BMJ open

Multimorbidity in primary care: MM-PT study protocol

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004113
Article Type:	Protocol
Date Submitted by the Author:	24-Sep-2013
Complete List of Authors:	Prazeres, Filipe; Faculdade de Ciências da Saúde, Universidade da Beira Interior, ; Centro de Saúde de Aveiro, Santiago, Luiz; Faculdade de Ciências da Saúde, Universidade da Beira Interior, ; USF Topázio,
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Epidemiology
Keywords:	PRIMARY CARE, EPIDEMIOLOGY, PUBLIC HEALTH

Multimorbidity in primary care: MM-PT study protocol

Filipe Prazeres MD MSc Ph.D. Candidate[a b], Luiz Santiago MD Ph.D.[a c]

a. Faculdade de Ciências da Saúde, Universidade da Beira Interior, 6200-506 Covilhã, Portugal

b. Centro de Saúde de Aveiro, 3810-000 Aveiro, Portugal

c. USF Topázio, 3020-171 Coimbra, Portugal

Address for correspondence:

Dr. Filipe Prazeres

Ph.D. Candidate

Faculdade de Ciências da Saúde

Universidade da Beira Interior

6200-506 Covilhã, Portugal

E-mail: filipeprazeresmd@gmail.com

Telephone: +351234891197

Word count - excluding title page, abstract, references, figures and tables: 2075

KEYWORDS: multimorbidity, primary care, quality of life, family support, unmet health needs

ABSTRACT

Introduction: Multimorbidity is defined as the concurrent occurrence of more than one chronic disease in one person without assigning an index disease. This condition influences patients' health and health-care services, increases the economic toll on their families and society, consequently a better understanding of multimorbidity is needed, especially in an aging country, such as Portugal. The purpose of this study is to contribute to the knowledge of the epidemiology of multimorbidity in Portugal, namely its prevalence, health and social implications.

Methods and analysis: Nation-wide three phases study. First phase, nation-wide, to access prevalence and patterns of multimorbidity. The second phase of the study will describe health-related quality of life, perceived family support and unmet health needs of patients with multimorbidity. The last phase is planned to characterize the knowledge, awareness and practices related to the management of multimorbid patients by family physicians, before and after the results of the study are known.

Ethics and dissemination: The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals in the next three years.

STRENGTHS AND LIMITATIONS OF THIS STUDY: This study will contribute to the knowledge of the epidemiology of multimorbidity in Portugal, namely its prevalence, health and social implications. It will promote a better planning of health care policies, increasing coordination and integration of care for the multimorbid patient, improving quality of life and lowering its economic burden. Such knowledge will be crucial for teaching medical students and to the continuing professional development for healthcare professionals.

INTRODUCTION

Family physicians manage the acute as well as the chronic conditions of their individual patients,[1] these are often multiple.[2] Therefore, multimorbidity is the rule in primary care settings.[3]

Multimorbidity is defined as the concurrent occurrence of more than one chronic disease within one person without assigning an index disease.[4 5]

Chronic diseases constitute a significant cause of mortality and morbidity worldwide,[6] but it is the importance of the health tapestry that needs to be understood, as the "whole is lots more than the sum of its parts".[7] For instance, disease-specific recommendations for physicians lead to considerable treatment burden in managing multimorbid patients,[8] which in turn raises medication adherence complications [9] and ultimately makes it an ineffective [10] and expensive care.[11] Multimorbidity is also associated with lower life expectancy,[12] higher hospital admissions[13] and longer hospital stays.[14] Quality of life,[15] physical functioning,[16] and psychological health[17] are also negatively affected by multimorbidity.

Despite the knowledge that prevalence estimates of multimorbidity increase with age,[3] it varies widely, and in some studies by as much as 61%.[18] The estimated differences may have several reasons, including sampling bias, period of data collection and its source, and also the definition and count of chronic diseases.[18]

The observed increase in the prevalence of chronic conditions[19] and their influence on patient's health and health-care services augments the global interest in multimorbidity and the need of a better understanding of this phenomenon, from multiple perspectives, which is the aim of this study. It will be responsible for the first perception of multimorbidity in the adult population attending general practice in Portugal (MM-PT).

This work intends to contribute to the knowledge of the epidemiology of multimorbidity, regarding its prevalence and morbidity.

Terminology:

For the purpose of defining multimorbidity we will use the list of chronic conditions[20] compiled by the Family Medicine Research Centre (FMRC), University of Sydney, available online at http://sydney.edu.au/medicine/fmrc/classifications/DefiningChronicConditions.pdf

STUDY OBJECTIVES

The primary objective is to ascertain the prevalence of multimorbidity, quality of life, family support, and unmet health needs of adult multimorbid patients attending primary care.

Specific objectives are to:

- Describe the sociodemographic and clinical profiles;
- Characterize multimorbid patient's unmet health needs;
- Evaluate the health related quality of life impact of multimorbidity;
- Assess family support;
- Analyse the relationship between multimorbidity, health related quality of life and family support.
- Describe the knowledge, awareness and practices related to the management of multimorbid patients, before and after the results of the study are known.

METHODS AND ANALYSIS

Study design

The study consists of 3 parts:

1. Cross-sectional, analytical study of the prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal.

2. Cross-sectional, analytical study of health-related quality of life, perceived family support and unmet health needs of patients with multimorbidity.

3. Descriptive, longitudinal study of family physicians' knowledge, awareness and practices related to the management of multimorbid patients.

Part I - Prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal

Design:

Cross-sectional, analytical study.

Setting:

Primary care centers in mainland Portugal, spread across the five administrative regions of health, will be randomly selected to obtain accurate morbidity data.

Study sample:

Since the prevalence of multimorbidity varies greatly across research literature and there is no available estimate for Portugal, a 2 step selection approach, based on the work of Fortin et al.[3], will be followed. Firstly, family physicians will be contacted and the ones that volunteer will recruit their own patients.

According to national data (Administração Central do Sistema de Saúde, IP; reported to 31/12/2012) there are 5541 full-service family physicians in the National Health Service. Using Epidat 4.0 (Organización Panamericana de la Salud, Washington D.C., USA) we determined that a sample of 147 family physicians is the minimum required, with an absolute precision of 8% and 95% CI. Since the expected response rate is of 30%, then to have 147 subjects completing the study, 147 / 0.3 = 490 family physicians will be needed (188 North Region, 86 Center Region, 172 Lisbon-Tejo Valley Region, 24 Alentejo Region and 21 Algarve Region, concerning

Portugal demographics). The required number of physicians will be selected using a random number generator (Independent Random Sampling),[21] from an alphabetically ordered list of physicians prearranged per groups of health centers (ACEs).

Predictably starting October 2013, and in three days on three consecutive weeks (Tuesday on week one; Wednesday on week two; and Thursday on week three) all adult (≥ 18 years old) patients that attend a primary care consultation will be included in the study. Participants will be excluded if they present incapacity to attend the interview; are diagnosed with dementia and/or present inability to understand informed consent.

Data collection:

Each patient's morbidities, classified using the International Classification of Primary Care v. 2 (ICPC-2) codes or the International Classification of Diseases - 10th version (ICD-10), will be counted and documented by family physicians, using their knowledge of the patient, the patient's self-report, and the electronic and/or paper based medical records.

Patients' social and demographic characteristics (gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status) will also be collected. A size estimate of each doctors' list of patients will also be known.

Data will be registered using MS Excel 2007 (Microsoft, Redmond, Washington, USA) spreadsheets. Information will be treated in strict confidentiality to protect the privacy of patients.

A consecutive number starting at 01 will be assigned to each participant with no other figure identifying the case.

Analysis:

Descriptive analysis will be limited to summaries of the data. Both the classic definition of multimorbidity (≥2 diseases) and ≥3 diseases will be considered. The prevalence of multimorbidity will be reported by gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status.

An exploratory factor analysis will be applied to define the associations between diseases.

Part II - Health-related quality of life, perceived family support and unmet health needs of multimorbid patients

Design:

Cross-sectional, analytical study.

Setting:

Randomly selected primary care centers in the center region of Portugal.

Study sample:

Patients will be recruited by family physicians working in primary care centers in the center region of Portugal. Purposive sampling will be used to select adult (≥18 years old) patients with multimorbidity that have at least one of four morbidities: hypertension, diabetes, asthma, and/or osteoarthrosis. Sample size will be estimated using the prevalence obtained in the Part I of the study.

Predictably starting January 2014, the investigator or a previously trained research associate will interview the patients at their convenience, either at their home or in the doctor's office. Participants will be excluded if they present incapacity to attend the interview, are diagnosed with dementia and/or present inability to understand informed consent.

Data collection:

Each patient's morbidities, social and demographic characteristics will be registered using the same methodology stated in Part I.

Health related quality of life will be evaluated using the Portuguese version of SF-12 questionnaire [22], derived from the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36).

Family APGAR (Adaptation, Partnership, Growth, Affection and Resolve) questionnaire will be used to measure multimorbid patient satisfaction with each of the five basic components of family function [23].

Based on the literature,[24-28] a patients' unmet health needs questionnaire was drafted. The unmet need for the following services will be evaluated: medical, surgical and dental care, prescription medications, mental health care or counseling, and eyeglasses or other technical aid. These will be evaluated by a set of general questions "During the past 12 months, was there a time when you wanted medical care but couldn't get it at that time?". If an unmet health need is stated, available reasons to explain it are: Couldn't you get off work? Were you too sick? Didn't you have a way to get there? Did you have responsibilities to take care of someone? Were you afraid to leave home because of personal safety? Did you have other more important things to take care of? Did you have to spend your money for food, clothing, housing, etc.? A pre-test will be undertaken prior to the patients enrolment phase. A validation process of the questionnaire will be performed to guarantee that patients understand the questions that will be written or orally asked.

Analysis:

Descriptive and inferential analysis will be performed. Parametric and nonparametric statistical testes will be used for dependent (HRQL and perceived family support) and independent variables (sociodemographic and clinical profiles).

Part III – Family physicians' knowledge, awareness and practices related to the management of multimorbid patients.

Design:

Descriptive, longitudinal study.

Setting:

Selected primary care centers in the districts of Coimbra and Aveiro.

Study sample and data collection:

Family physicians working in primary care centers in the districts of Coimbra and Aveiro will be recruited by chain-referral sampling.

Prior to the start of Part I of the study an online questionnaire will be used to evaluate knowledge, awareness and practices related to the management of multimorbid patients by the physicians, followed by a second evaluation after proper elucidation through a flyer that will include the results of Parts I and II of the study. This questionnaire will be validated.

Analysis:

Descriptive analysis will be limited to summaries of the data.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals in the next three years.

AUTHORS' CONTRIBUTIONS

FP and LS led the design of the study. FP led the writing of the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. Europe W. The European definition of general practice / family medicine. http://www.woncaeurope.org/sites/default/files/documents/Definition%203rd%20ed%202

011%20with%20revised%20wonca%20tree.pdf. Published 2002. Accessed Sptember 24, 2013.

2. Flocke SA, Frank SH, Wenger DA. Addressing multiple problems in the family practice office visit. J Fam Pract 2001;**50**(3):211-6.

3. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. Ann Fam Med 2005;**3**(3):223-8 doi: 10.1370/afm.272.

4. van den Akker M, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity. Eur J Gen Pract 1996;**2**(2):65-70 doi: 10.3109/13814789609162146.

5. van den Akker M, Buntinx F, Roos S, Knottnerus JA. Problems in determining occurrence rates of multimorbidity. J Clin Epidemiol 2001;**54**(7):675-79 doi: 10.1016/s0895-4356(00)00358-9.

6. Busse R, Bluemel M, Scheller-Kreinsen D, Zentner A. Tackling Chronic Disease in Europe. Strategies, Interventions and Challenges. http://pns.dgs.pt/files/2010/05/Doen%C3%A7as-cr%C3%B3nicas_EU_Maio_2010-2.pdf. Published 2010. Accessed Sptember 24, 2013.

7. Starfield B. Threads and yarns: weaving the tapestry of comorbidity. Ann Fam Med 2006;**4**(2):101-3 doi: 10.1370/afm.524.

8. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing 2013;**42**(1):62-9 doi: 10.1093/ageing/afs100.

9. Townsend A, Hunt K, Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. BMJ 2003;**327**(7419):837-40 doi: 10.1136/bmj.327.7419.837.

10. Fortin M, Soubhi H, Hudon C, Bayliss EA, van den Akker M. Multimorbidity's many challenges. BMJ 2007;**334**(7602):1016-7 doi: 10.1136/bmj.39201.463819.2C.

11. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;**162**:2269-76 doi: 10.1001/archinte.162.20.2269.

12. Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;**54**(7):661-74.

13. Freund T, Kunz CU, Ose D, Szecsenyi J, Peters-Klimm F. Patterns of multimorbidity in primary care patients at high risk of future hospitalization. Popul Health Manag 2012;**15**(2):119-24 doi: 10.1089/pop.2011.0026.

14. Rochon PA, Katz JN, Morrow LA, et al. Comorbid illness is associated with survival and length of hospital stay in patients with chronic disability. A prospective comparison of three comorbidity indices. Med Care 1996;**34**(11):1093-101.

15. Fortin M, Bravo G, Hudon C, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Qual Life Res 2006;**15**(1):83-91 doi: 10.1007/s11136-005-8661-z.

16. Kadam UT, Croft PR, North Staffordshire GPCG. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;**24**(5):412-9 doi: 10.1093/fampra/cmm049.

17. Fortin M, Bravo G, Hudon C, Lapointe L, Dubois MF, Almirall J. Psychological distress and multimorbidity in primary care. Ann Fam Med 2006;**4**(5):417-22 doi: 10.1370/afm.528.

18. Stewart M, Fortin M, Britt HC, Harrison CM, Maddocks HL. Comparisons of multi-morbidity in family practice--issues and biases. Fam Pract 2013;**30**(4):473-80 doi: 10.1093/fampra/cmt012.

19. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract 2008;**14 Suppl 1**:28-32 doi: 10.1080/13814780802436093.

20. O'Halloran J, Miller GC, Britt H. Defining chronic conditions for primary care with ICPC-2. Fam Pract 2004;**21**(4):381-6 doi: 10.1093/fampra/cmh407.

21. Fox N, Hunn A, Mathers N. *Sampling and sample size calculation*: The NIHR RDS for the East Midlands / Yorkshire & the Humber, 2007.

22. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med care 1996;**34**(3):220-33.

23. Smilkstein G. The family APGAR: a proposal for a family function test and its use by physicians. J Fam Pract 1978;**6**(6):1231–9.

24. Baggett TP, O'Connell JJ, Singer DE, Rigotti NA. The unmet health care needs of homeless adults: a national study. Am J Public Health 2010;**100**(7):1326-33 doi: 10.2105/AJPH.2009.180109.

25. Shi L, Stevens GD. Vulnerability and unmet health care needs. The influence of multiple risk factors. J Gen Intern Med 2005;**20**(2):148-54 doi: 10.1111/j.1525-1497.2005.40136.x.

26. Diamant AL, Hays RD, Morales LS, et al. Delays and unmet need for health care among adult primary care patients in a restructured urban public health system. Am J Public Health 2004;94(5):783-9.

27. Newacheck PW, Hughes DC, Hung YY, Wong S, Stoddard JJ. The unmet health needs of America's children. Pediatrics 2000;**105**(4 Pt 2):989-97.

28. Ayanian JZ, Weissman JS, Schneider EC, Ginsburg JA, Zaslavsky AM. Unmet health needs of uninsured adults in the United States. JAMA 2000;**284**(16):2061-9.

Multimorbidity in primary care in Portugal (MM-PT): a cross-sectional three phase observational study protocol

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004113.R1
Article Type:	Protocol
Date Submitted by the Author:	14-Dec-2013
Complete List of Authors:	Prazeres, Filipe; Faculdade de Ciências da Saúde, Universidade da Beira Interior, ; Centro de Saúde de Aveiro, Santiago, Luiz; Faculdade de Ciências da Saúde, Universidade da Beira Interior, ; USF Topázio,
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Epidemiology
Keywords:	PRIMARY CARE, EPIDEMIOLOGY, PUBLIC HEALTH

Multimorbidity in primary care in Portugal (MM-PT): a cross-sectional three phase observational study protocol

Filipe Prazeres MD MSc Ph.D. Candidate[a b], Luiz Santiago MD Ph.D.[a c]

a. Faculdade de Ciências da Saúde, Universidade da Beira Interior, 6200-506 Covilhã, Portugal

b. Centro de Saúde de Aveiro, 3810-000 Aveiro, Portugal

c. USF Topázio, 3020-171 Coimbra, Portugal

Address for correspondence:

Dr. Filipe Prazeres

Ph.D. Candidate

Faculdade de Ciências da Saúde

Universidade da Beira Interior

6200-506 Covilhã, Portugal

E-mail: filipeprazeresmd@gmail.com

Telephone: +351234891197

Word count - excluding title page, abstract, references, figures and tables: 2730

KEYWORDS: multimorbidity, primary care, quality of life, family support, unmet health needs

ABSTRACT

Introduction: Multimorbidity is defined as the co-occurrence of more than one chronic disease in one person without assigning an index disease. This rapidly increasing phenomenon markedly influences patients' overall health, has major implications for effective provision of healthcare services and has a significant economic toll on individuals and society at large. Since Portugal is a country with a growing ageing population, a better understanding of the role of multimorbidity should be assessed. The aim of this study is to further the knowledge of the epidemiological factors associated with multimorbidity in Portugal, chiefly its prevalence and the health and social implications.

Methods and analysis: This study protocol describes a primary care nationwide three phase study. The first phase is drawn to access prevalence and patterns of multimorbidity. In the second phase, individual parameters are assessed, such as patients' health related quality of life, perceived family support and unmet health needs of multimorbid patients. The third and last phase of this study aims to characterise general practitioners' knowledge, awareness and practices related to multimorbidity management.

Ethics and dissemination: The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This study will contribute to a better knowledge of the epidemiological factors associated with multimorbidity in Portugal, namely its prevalence, health and social implications.
- Study findings will help ameliorate health care policies in order to improve patient quality of life and lower multimorbidity economic burden.
- These data will also be crucial for future medical teaching and continuing medical education.

- Limitations of the study need to be stated: in phase 2, four chronic conditions have been selected based on their importance; this will exclude those patients with multimorbidity with all except the selected conditions. In phase 3, chain-referral sampling may lead to a community bias but at the same time this sampling method will improve general practitioners' enrolment.

INTRODUCTION

Multimorbidity is defined as the co-occurrence of more than one chronic disease within one person without assigning an index disease.[1 2] It is known that prevalence of multimorbidity increases with age,[3] reaching over 90%.[4] Nevertheless, variations in prevalence of more than 60% have been reported between studies. These estimated differences may be due to sampling bias, period collection and data source and also due to the broad definition of chronic diseases.[5] Multimorbidity has been previously described by Martin Fortin as the rule and not the exception in primary care settings,[3] where general practitioners (GPs) manage not only the acute but mostly the chronic conditions of their patients,[6] which are often multiple.[7]

Taking only into account disease-specific recommendations can lead to a considerable treatment burden for multimorbid patients.[8] This in turn raises several other issues such as low compliance,[9] treatment ineffectiveness[10] and high treatment costs.[11]

Multimorbidity is also associated with lower life expectancy,[12] higher hospital admissions[13] and longer hospital stays.[14] Quality of life,[15] physical functioning,[16] and psychological health[17] are also negatively affected by multimorbidity.

Chronic diseases represent a significant cause of mortality and morbidity worldwide [18] and their increasing prevalence[19] has a significant impact on patients' health and healthcare services.

Multimorbidity is therefore an area which is rapidly becoming of great importance in primary care settings, with a pressing need for a better understanding of this phenomenon from multiple perspectives. This work aims to further the knowledge of the epidemiology of multimorbidity,

regarding its prevalence and morbidity. Importantly, this will be the first study raising awareness of multimorbid conditions in adult population attending general practice in Portugal.

Terminology:

For the purpose of defining multimorbidity we will use the list of chronic conditions[20] compiled by the Family Medicine Research Centre (FMRC), University of Sydney, available online at http://sydney.edu.au/medicine/fmrc/classifications/DefiningChronicConditions.pdf. This list represents 147 ICPC-2 (International Classification of Primary Care) rubrics.

STUDY OBJECTIVES

The primary objective of this protocol is to determine the prevalence of multimorbidity, quality of life, family support, and unmet health needs of adult multimorbid patients attending primary care in Portugal.

Specific objectives are to:

- Describe the sociodemographic and clinical profiles of multimorbid patients in Portugal;
- Characterise Portuguese multimorbid patient's unmet health needs;
- Evaluate the impact of multimorbidity on patients' health related quality of life;
- Assess family support to multimorbid patients in Portugal;
- Analyse the relationship between multimorbidity, patients' health related quality of life and family support;
- Describe Portuguese GPs' knowledge, awareness and practices related to the management of multimorbidity.

METHODS AND ANALYSIS

Study design

The study consists of 3 phases:

1. Cross-sectional, analytical study of the prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal.

2. Cross-sectional, analytical study of patients' health-related quality of life, self-perceived family support and unmet health needs of adult multimorbid patients attending primary care in Portugal.

3. Cross-sectional, descriptive before-after study of Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Phase I - Prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in mainland Portugal will be randomly selected from the five Portuguese Healthcare Administrative Regions in order to obtain a national geographical representative sample.

Sample size:

Since the prevalence of multimorbidity varies greatly across research literature and there is no available estimate for Portugal, a prevalence of 50% was assumed in order to maximize the sample size. For the study to be able to estimate a 95% confidence interval for the prevalence of multimorbidity with a maximum precision error of 2.5%, a total of 1500 patients should be recruited (Epidat 4.0 - Organización Panamericana de la Salud, Washington D.C., USA).

Study procedures:

This phase of the study is expected to start in October 2014.

A two-step selection approach, based on the work of Fortin et al.[3], will be followed. Firstly, GPs will be contacted and those who accept to participate will recruit their own patients. Assuming that a GP will be able to include at least 10 patients in a 3-week period, a total of 150

GPs has to be enrolled in the study. Considering a 30% invitation response rate, then a total of 500 GPs should be invited to participate in the study: 182 in North (36%), 117 in Centre (23%), 139 in Lisbon-Tejo Valley (28%), 38 in Alentejo (8%) and 22 in Algarve (4%) in accordance with the distribution of the Portuguese adult population (18+ years old) across the five mainland Portuguese Health Administrative Regions.

The GPs to be invited will be randomly selected from an alphabetically ordered list prearranged per Health Administrative Regions, using a random number generator (Independent Random Sampling),[21].

Enrolled GPs will be instructed to invite all adult (≥ 18 years old) patients attending to the primary care consultation to participate in the study during three days on three consecutive weeks (Tuesday on week one; Wednesday on week two; and Thursday on week three). Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

GPs will be responsible for collecting all data about each patient during their consultations and through the completion of a paper questionnaire developed specifically for this study. Patient's morbidities will be captured by GPs, using their knowledge of patient history, patient's self-report and electronic and/or paper patient medical records. Morbidities will be collected using the International Classification of Primary Care v.2 (ICPC-2) codes or the International Classification of Diseases - 10th version (ICD-10), which are currently being used in Portuguese Primary Care Centres.

The personal information section of the Portuguese version of the EASY-Care questionnaire [22] will be used to collect patients' social and demographic characteristics namely gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status through the question "In general how do your family finances work out at the end of the month?".

Data will be electronically stored in a database specifically designed for this study using MS Access 2010. Data will be encrypted and password protected. Information will be treated in strict confidentiality to protect the privacy of patients.

Paper copies of all informed consents will be retained in a locked file, separate from any study data.

Statistical Analysis:

A descriptive analysis will be performed to all study variables namely number of valid observations, mean, standard deviation, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. Prevalence of multimorbidity (considering two definitions: ≥2 diseases or ≥3 diseases) will be calculated together with corresponding 95% confidence interval (CI). Moreover, the prevalence of multimorbidity will be estimated by subgroups namely by gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status. Univariate analysis will be done to study associations between those characteristics and multimorbidity using Chi-square test (qualitative characteristics) or t-test/Mann-Whitney (quantitative characteristics). Multiple logistic regression will be carried over considering presence of multimorbidity as the dependent variable and patients' characteristics as the

independent variables in order to calculate odds ratios and corresponding 95% CIs. Total number of morbidities by patient will be also summarized together with 95% CI and multiple regression may be performed to analyse its association with patients characteristics. All analyses will be performed for both above mentioned definitions of multimorbidity. All tests will be two-sided using a significance level of 0.05. Statistical analysis will be done using SPSS version 18.0 or higher.

Phase II - Patients' health-related quality of life, perceived family support and unmet health needs of adult multimorbid patients attending primary care in Portugal.

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in the Centre region of Portugal will be randomly selected within each Care Centres Grouping (ACES and ULS) in order to obtain a regional geographical representative sample.

Sample size:

A total of 500 patients should be included in phase II in order to obtain 95% CIs for proportions with a maximum precision error of 4.5% and 95% CIs for SF-12 mean scores with a precision error of 4.5 (assuming a standard deviation of 50).

Study procedures:

Phase II of the study is expected to start in January 2014.

A two-step approach will be considered as in phase I. Assuming that each GP will enrol 10 patients and that 30% of the invited GPs will accept to participate, then about 170 GPs within the randomly selected Care Centres should be invited to participate in this phase of the study.

Primary Care Centers will be randomly selected (Independent Random Sampling)[21] and all GPs within those centers will be invited to participate (until 170 GPs are recruited).

By purposive sampling, enrolled GPs will select adult (≥18 years old) patients with multimorbidity and with at least one of four morbidities: hypertension, diabetes, asthma, and/or osteoarthritis. These morbidities were selected based on the Portuguese Directorate-General of Health (DGS – Direção-Geral da Saúde) efforts to implement specific national recommendations for the diagnosis, treatment and control of these conditions, which have high prevalence and are associated with low quality of life.[23-26]

The investigator or a previously trained research associate (GP/GP trainee) will interview the patients at their convenience, either in the GPs office or at their home. Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

All data will be collected using a paper questionnaire. Patients' morbidities, social and demographic characteristics will be registered using the same methodology as described in Phase I. Health related quality of life will be evaluated using the Portuguese Short Form-12 Health Status Questionnaire (SF-12),[27] derived from the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36),[28] through interview to the patients. The Portuguese Family APGAR (Adaptation, Partnership, Growth, Affection and Resolve) Questionnaire [29 30] that evaluates family function in five dimensions [31] will be used to measure multimorbid patients' perceived family support.

Based on the literature, [32-36] a patients' unmet health needs questionnaire was drafted. The unmet need for the following services will be evaluated: medical, surgical and dental care,

prescription medications, mental health care or counselling, and eyeglasses or other technical aid. These will be evaluated by a set of general questions, such as "During the past 12 months, was there a time when you wanted/needed medical care but couldn't get it at that time?". If an unmet health need is stated, available reasons to explain it are: Couldn't you get off work? Were you too sick? Didn't you have a way to get there? Did you have responsibilities to take care of someone? Were you afraid to leave home because of personal safety? Did you have other more important things to take care of? Did you have to spend your money for food, clothing, housing, etc.? The validation process of the questionnaire will be performed using forward-translations and back-translations, accordingly to World Health Organization guidelines.[37] A pre-test with 50 subjects will be undertaken prior to the patients enrolment phase.

Statistical Analysis:

Descriptive statistics will be computed for all variables together with 95% CIs whenever relevant and applicable. Associations between qualitative independent variables will be tested using Chi-square test. Comparisons between two or more independent groups regarding a quantitative variable are to be conducted using ANOVA or Kruskal-Wallis non-parametric test, if normality assumption is not met. ANCOVA may also be used to adjust for potential confounding factors. Associations between quantitative independent variables will be analysed using Pearson's or Spearman's correlation coefficient depending upon normality assumption. All tests will be two-sided considering a significance level of 0.05.

Phase III – Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Design:

Before-after, cross-sectional, descriptive study.

Since there is a lack of research on multimorbidity in Portugal, we believe that this concept is not usually taken into account in daily practice. We also have confidence in that the dissemination of the results of Parts I and II of the study will have the capability of raising awareness and change behaviour towards multimorbid patients. To test these hypotheses a before-after study was designed.

Setting:

Selected Primary Care Centres in two districts of the Centre region of Portugal (Coimbra and Aveiro).

Sample size:

Since this is a descriptive study, no formal calculations were performed to estimate the sample size. Notwithstanding, we are willing to include at least 10% of the population of GPs in these two districts corresponding to a sample size of approximately 60 GPs.

Study procedures:

GPs working in Primary Care Centres in the districts of Coimbra and Aveiro will be recruited by chain-referral sampling.

Data collection:

Prior to the start of Phase I of the study an online questionnaire with open text format questions will be used to evaluate GPs knowledge (definition of multimorbidity), awareness (relevance of multimorbidity in daily practice) and practices (management of multimorbidity). This will be followed by a second application of the same questionnaire after the distribution of a flyer with the results of Phases I and II of the study.

This questionnaire will have a semantic validation by 2 distinct groups. The first is composed of experts in multimorbidity and the second by possible respondents, in our case, GPs.

Statistical Analysis:

Before-after collected answers will be listed and analysed by the study investigator. If possible, answers will be converted into qualitative variables by the study investigator in order to evaluate knowledge, awareness and practices. This process will be also performed by an independent expert and results will be crosschecked. Discrepancies will be further discussed until a consensus is achieved. Results obtained will be summarized using descriptive statistics as previously described.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

AUTHORS' CONTRIBUTIONS

FP and LS led the design of the study. FP led the writing of the manuscript. All authors read and approved the final manuscript draft.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. van den Akker M, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity. Eur J Gen Pract 1996;**2**(2):65-70 doi: 10.3109/13814789609162146.

2. van den Akker M, Buntinx F, Roos S, et al. Problems in determining occurrence rates of multimorbidity. J Clin Epidemiol 2001;**54**(7):675-79 doi: 10.1016/s0895-4356(00)00358-9.

3. Fortin M, Bravo G, Hudon C, et al. Prevalence of multimorbidity among adults seen in family practice. Ann Fam Med 2005;**3**(3):223-8 doi: 10.1370/afm.272.

4. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med 2012;**10**(2):142-51 doi: 10.1370/afm.1337.

5. Stewart M, Fortin M, Britt HC, et al. Comparisons of multi-morbidity in family practice--issues and biases. Fam Pract 2013;**30**(4):473-80 doi: 10.1093/fampra/cmt012.

6. Europe W. The European definition of general practice / family medicine. http://www.woncaeurope.org/sites/default/files/documents/Definition%203rd%20ed%202011%20with%20revised%20wonca%20tree.pdf. Published 2002. Accessed September 24, 2013.

7. Flocke SA, Frank SH, Wenger DA. Addressing multiple problems in the family practice office visit. J Fam Pract 2001;**50**(3):211-6.

8. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing 2013;**42**(1):62-9 doi: 10.1093/ageing/afs100.

9. Townsend A, Hunt K, Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. BMJ 2003;**327**(7419):837-40 doi: 10.1136/bmj.327.7419.837.

10. Fortin M, Soubhi H, Hudon C, B et al. Multimorbidity's many challenges. BMJ 2007;**334**(7602):1016-7 doi: 10.1136/bmj.39201.463819.2C.

11. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;**162**(20):2269-76 doi: 10.1001/archinte.162.20.2269.

12. Gijsen R, Hoeymans N, Schellevis FG, et al. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;**54**(7):661-74.

13. Freund T, Kunz CU, Ose D, et al. Patterns of multimorbidity in primary care patients at high risk of future hospitalization. Popul Health Manag 2012;**15**(2):119-24 doi: 10.1089/pop.2011.0026.

14. Rochon PA, Katz JN, Morrow LA, et al. Comorbid illness is associated with survival and length of hospital stay in patients with chronic disability. A prospective comparison of three comorbidity indices. Med Care 1996;**34**(11):1093-101.

15. Fortin M, Bravo G, Hudon C, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Qual Life Res 2006;**15**(1):83-91 doi: 10.1007/s11136-005-8661-z.

16. Kadam UT, Croft PR, North Staffordshire GPCG. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;**24**(5):412-9 doi: 10.1093/fampra/cmm049.

17. Fortin M, Bravo G, Hudon C, et al. Psychological distress and multimorbidity in primary care. Ann Fam Med 2006;**4**(5):417-22 doi: 10.1370/afm.528.

18. Busse R, Bluemel M, Scheller-Kreinsen D, Zentner A. Tackling Chronic Disease in Europe. Strategies, Interventions and Challenges. http://pns.dgs.pt/files/2010/05/Doen%C3%A7as-cr%C3%B3nicas_EU_Maio_2010-2.pdf. Published 2010. Accessed September 24, 2013.

19. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract 2008;**14 Suppl 1**:28-32 doi: 10.1080/13814780802436093.

20. O'Halloran J, Miller GC, Britt H. Defining chronic conditions for primary care with ICPC-2. Fam Pract 2004;**21**(4):381-6 doi: 10.1093/fampra/cmh407.

21. Fox N, Hunn A, Mathers N. *Sampling and sample size calculation*: The NIHR RDS for the East Midlands / Yorkshire & the Humber, 2007.

22. Sousa L, Figueiredo D. (In)dependência na população idosa: um estudo exploratório na população portuguesa. Psychol 2003;**33**:109-22.

23. DGS. *Diagnóstico, Tratamento e Controlo da Hipertensão Arterial*. Lisboa: DGS, 2004.

24. DGS. *National Programme for the Prevention and Control of Diabetes*. Lisbon: DGS, 2008.

25. DGS. *National Programme for Asthma Control*. Lisbon: DGS, 2005.

26. DGS. *National Programme against Rheumatic Diseases*. Lisbon: DGS, 2005.

27. Pais-Ribeiro J. *O importante é a saúde: estudo de adaptação de um instrumento para avaliar o estado de saúde*. Lisboa: Fundação Merck Sharp & Dohme, 2005.

28. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;**34**(3):220-33.

29. Imperatori E. Ficha familiar dos centros de saúde: vantagens e dificuldades. Rev Port Sau Pub 1985;**3**(3):51-6.

30. Agostinho M, Rebelo L. Família: do conceito aos meios de avaliação. Rev Port Clin Geral 1988;**32**:6-17.

31. Smilkstein G. The family APGAR: a proposal for a family function test and its use by physicians. J Fam Pract 1978;**6**(6):1231–9.

32. Baggett TP, O'Connell JJ, Singer DE, et al. The unmet health care needs of homeless adults: a national study. Am J Public Health 2010;**100**(7):1326-33 doi: 10.2105/AJPH.2009.180109.

33. Shi L, Stevens GD. Vulnerability and unmet health care needs. The influence of multiple risk factors. J Gen Intern Med 2005;**20**(2):148-54 doi: 10.1111/j.1525-1497.2005.40136.x.

34. Diamant AL, Hays RD, Morales LS, et al. Delays and unmet need for health care among adult primary care patients in a restructured urban public health system. Am J Public Health 2004;**94**(5):783-9.

35. Newacheck PW, Hughes DC, Hung YY, et al. The unmet health needs of America's children. Pediatrics 2000;**105**(4 Pt 2):989-97.

36. Ayanian JZ, Weissman JS, Schneider EC, et al. Unmet health needs of uninsured adults in the United States. JAMA 2000;**284**(16):2061-9.

37. WHO. Process of translation and adaptation of instruments. http://www.who.int/substance_abuse/research_tools/translation/en/. Published 2013. Accessed September 24, 2013.

Multimorbidity in primary care in Portugal (MM-PT): a cross-sectional three phase observational study protocol

Filipe Prazeres MD MSc Ph.D. Candidate[a b], Luiz Santiago MD Ph.D.[a c]

a. Faculdade de Ciências da Saúde, Universidade da Beira Interior, 6200-506 Covilhã, Portugal

b. Centro de Saúde de Aveiro, 3810-000 Aveiro, Portugal

c. USF Topázio, 3020-171 Coimbra, Portugal

Address for correspondence:

Dr. Filipe Prazeres

Ph.D. Candidate

Faculdade de Ciências da Saúde

Universidade da Beira Interior

6200-506 Covilhã, Portugal

E-mail: filipeprazeresmd@gmail.com

Telephone: +351234891197

Word count - excluding title page, abstract, references, figures and tables: 2730

KEYWORDS: multimorbidity, primary care, quality of life, family support, unmet health needs

ABSTRACT

Introduction: Multimorbidity is defined as the co-occurrence of more than one chronic disease in one person without assigning an index disease. This rapidly increasing phenomenon markedly influences patients' overall health, has major implications for effective provision of healthcare services and has a significant economic toll on individuals and society at large. Since Portugal is a country with a growing ageing population, a better understanding of the role of multimorbidity should be assessed. The aim of this study is to further the knowledge of the epidemiological factors associated with multimorbidity in Portugal, chiefly its prevalence and the health and social implications.

Methods and analysis: This study protocol describes a primary care nationwide three phase study. The first phase is drawn to access prevalence and patterns of multimorbidity. In the second phase, individual parameters are assessed, such as patients' health related quality of life, perceived family support and unmet health needs of multimorbid patients. The third and last phase of this study aims to characterise general practitioners' knowledge, awareness and practices related to multimorbidity management.

Ethics and dissemination: The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This study will contribute to a better knowledge of the epidemiological factors associated with multimorbidity in Portugal, namely its prevalence, health and social implications.
- Study findings will help ameliorate health care policies in order to improve patient quality of life and lower multimorbidity economic burden.
- These data will also be crucial for future medical teaching and continuing medical education.

- Limitations of the study need to be stated: in phase 2, four chronic conditions have been selected based on their importance; this will exclude those patients with multimorbidity with all except the selected conditions. In phase 3, chain-referral sampling may lead to a community bias but at the same time this sampling method will improve general practitioners' enrolment.

INTRODUCTION

Multimorbidity is defined as the co-occurrence of more than one chronic disease within one person without assigning an index disease.[1 2] It is known that prevalence of multimorbidity increases with age,[3] reaching over 90%.[4] Nevertheless, variations in prevalence of more than 60% have been reported between studies. These estimated differences may be due to sampling bias, period collection and data source and also due to the broad definition of chronic diseases.[5] Multimorbidity has been previously described by Martin Fortin as the rule and not the exception in primary care settings,[3] where general practitioners (GPs) manage not only the acute but mostly the chronic conditions of their patients,[6] which are often multiple.[7]

Taking only into account disease-specific recommendations can lead to a considerable treatment burden for multimorbid patients.[8] This in turn raises several other issues such as low compliance,[9] treatment ineffectiveness[10] and high treatment costs.[11]

Multimorbidity is also associated with lower life expectancy,[12] higher hospital admissions[13] and longer hospital stays.[14] Quality of life,[15] physical functioning,[16] and psychological health[17] are also negatively affected by multimorbidity.

Chronic diseases represent a significant cause of mortality and morbidity worldwide [18] and their increasing prevalence[19] has a significant impact on patients' health and healthcare services.

Multimorbidity is therefore an area which is rapidly becoming of great importance in primary care settings, with a pressing need for a better understanding of this phenomenon from multiple perspectives. This work aims to further the knowledge of the epidemiology of multimorbidity,

regarding its prevalence and morbidity. Importantly, this will be the first study raising awareness of multimorbid conditions in adult population attending general practice in Portugal.

Terminology:

For the purpose of defining multimorbidity we will use the list of chronic conditions[20] compiled by the Family Medicine Research Centre (FMRC), University of Sydney, available online at http://sydney.edu.au/medicine/fmrc/classifications/DefiningChronicConditions.pdf. This list represents 147 ICPC-2 (International Classification of Primary Care) rubrics.

STUDY OBJECTIVES

The primary objective of this protocol is to determine the prevalence of multimorbidity, quality of life, family support, and unmet health needs of adult multimorbid patients attending primary care in Portugal.

Specific objectives are to:

- Describe the sociodemographic and clinical profiles of multimorbid patients in Portugal;
- Characterise Portuguese multimorbid patient's unmet health needs;
- Evaluate the impact of multimorbidity on patients' health related quality of life;
- Assess family support to multimorbid patients in Portugal;
- Analyse the relationship between multimorbidity, patients' health related quality of life and family support;
- Describe Portuguese GPs' knowledge, awareness and practices related to the management of multimorbidity.

METHODS AND ANALYSIS

Study design

The study consists of 3 phases:

1. Cross-sectional, analytical study of the prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal.

2. Cross-sectional, analytical study of patients' health-related quality of life, self-perceived family support and unmet health needs of adult multimorbid patients attending primary care in Portugal.

3. Cross-sectional, descriptive before-after study of Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Phase I - Prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in mainland Portugal will be randomly selected from the five Portuguese Healthcare Administrative Regions in order to obtain a national geographical representative sample.

Sample size:

Since the prevalence of multimorbidity varies greatly across research literature and there is no available estimate for Portugal, a prevalence of 50% was assumed in order to maximize the sample size. For the study to be able to estimate a 95% confidence interval for the prevalence of multimorbidity with a maximum precision error of 2.5%, a total of 1500 patients should be recruited (Epidat 4.0 - Organización Panamericana de la Salud, Washington D.C., USA).

Study procedures:

This phase of the study is expected to start in October 2014.

A two-step selection approach, based on the work of Fortin et al.[3], will be followed. Firstly, GPs will be contacted and those who accept to participate will recruit their own patients. Assuming that a GP will be able to include at least 10 patients in a 3-week period, a total of 150

GPs has to be enrolled in the study. Considering a 30% invitation response rate, then a total of 500 GPs should be invited to participate in the study: 182 in North (36%), 117 in Centre (23%), 139 in Lisbon-Tejo Valley (28%), 38 in Alentejo (8%) and 22 in Algarve (4%) in accordance with the distribution of the Portuguese adult population (18+ years old) across the five mainland Portuguese Health Administrative Regions.

The GPs to be invited will be randomly selected from an alphabetically ordered list prearranged per Health Administrative Regions, using a random number generator (Independent Random Sampling),[21].

Enrolled GPs will be instructed to invite all adult (≥ 18 years old) patients attending to the primary care consultation to participate in the study during three days on three consecutive weeks (Tuesday on week one; Wednesday on week two; and Thursday on week three). Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

GPs will be responsible for collecting all data about each patient during their consultations and through the completion of a paper questionnaire developed specifically for this study. Patient's morbidities will be captured by GPs, using their knowledge of patient history, patient's self-report and electronic and/or paper patient medical records. Morbidities will be collected using the International Classification of Primary Care v.2 (ICPC-2) codes or the International Classification of Diseases - 10th version (ICD-10), which are currently being used in Portuguese Primary Care Centres.

The personal information section of the Portuguese version of the EASY-Care questionnaire [22] will be used to collect patients' social and demographic characteristics namely gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status through the question "In general how do your family finances work out at the end of the month?".

Data will be electronically stored in a database specifically designed for this study using MS Access 2010. Data will be encrypted and password protected. Information will be treated in strict confidentiality to protect the privacy of patients.

Paper copies of all informed consents will be retained in a locked file, separate from any study data.

Statistical Analysis:

A descriptive analysis will be performed to all study variables namely number of valid observations, mean, standard deviation, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. Prevalence of multimorbidity (considering two definitions: ≥2 diseases or ≥3 diseases) will be calculated together with corresponding 95% confidence interval (CI). Moreover, the prevalence of multimorbidity will be estimated by subgroups namely by gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status. Univariate analysis will be done to study associations between those characteristics and multimorbidity using Chi-square test (qualitative characteristics) or t-test/Mann-Whitney (quantitative characteristics). Multiple logistic regression will be carried over considering presence of multimorbidity as the dependent variable and patients' characteristics as the

independent variables in order to calculate odds ratios and corresponding 95% CIs. Total number of morbidities by patient will be also summarized together with 95% CI and multiple regression may be performed to analyse its association with patients characteristics. All analyses will be performed for both above mentioned definitions of multimorbidity. All tests will be two-sided using a significance level of 0.05. Statistical analysis will be done using SPSS version 18.0 or higher.

Phase II - Patients' health-related quality of life, perceived family support and unmet health needs of adult multimorbid patients attending primary care in Portugal.

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in the Centre region of Portugal will be randomly selected within each Care Centres Grouping (ACES and ULS) in order to obtain a regional geographical representative sample.

Sample size:

A total of 500 patients should be included in phase II in order to obtain 95% CIs for proportions with a maximum precision error of 4.5% and 95% CIs for SF-12 mean scores with a precision error of 4.5 (assuming a standard deviation of 50).

Study procedures:

Phase II of the study is expected to start in January 2014.

A two-step approach will be considered as in phase I. Assuming that each GP will enrol 10 patients and that 30% of the invited GPs will accept to participate, then about 170 GPs within the randomly selected Care Centres should be invited to participate in this phase of the study.

Primary Care Centers will be randomly selected (Independent Random Sampling)[21] and all GPs within those centers will be invited to participate (until 170 GPs are recruited).

By purposive sampling, enrolled GPs will select adult (≥18 years old) patients with multimorbidity and with at least one of four morbidities: hypertension, diabetes, asthma, and/or osteoarthritis. These morbidities were selected based on the Portuguese Directorate-General of Health (DGS – Direção-Geral da Saúde) efforts to implement specific national recommendations for the diagnosis, treatment and control of these conditions, which have high prevalence and are associated with low quality of life.[23-26]

The investigator or a previously trained research associate (GP/GP trainee) will interview the patients at their convenience, either in the GPs office or at their home. Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

All data will be collected using a paper questionnaire. Patients' morbidities, social and demographic characteristics will be registered using the same methodology as described in Phase I. Health related quality of life will be evaluated using the Portuguese Short Form-12 Health Status Questionnaire (SF-12),[27] derived from the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36),[28] through interview to the patients. The Portuguese Family APGAR (Adaptation, Partnership, Growth, Affection and Resolve) Questionnaire [29 30] that evaluates family function in five dimensions [31] will be used to measure multimorbid patients' perceived family support.

Based on the literature, [32-36] a patients' unmet health needs questionnaire was drafted. The unmet need for the following services will be evaluated: medical, surgical and dental care,

prescription medications, mental health care or counselling, and eyeglasses or other technical aid. These will be evaluated by a set of general questions, such as "During the past 12 months, was there a time when you wanted/needed medical care but couldn't get it at that time?". If an unmet health need is stated, available reasons to explain it are: Couldn't you get off work? Were you too sick? Didn't you have a way to get there? Did you have responsibilities to take care of someone? Were you afraid to leave home because of personal safety? Did you have other more important things to take care of? Did you have to spend your money for food, clothing, housing, etc.? The validation process of the questionnaire will be performed using forward-translations and back-translations, accordingly to World Health Organization guidelines.[37] A pre-test with 50 subjects will be undertaken prior to the patients enrolment phase.

Statistical Analysis:

Descriptive statistics will be computed for all variables together with 95% CIs whenever relevant and applicable. Associations between qualitative independent variables will be tested using Chi-square test. Comparisons between two or more independent groups regarding a quantitative variable are to be conducted using ANOVA or Kruskal-Wallis non-parametric test, if normality assumption is not met. ANCOVA may also be used to adjust for potential confounding factors. Associations between quantitative independent variables will be analysed using Pearson's or Spearman's correlation coefficient depending upon normality assumption. All tests will be two-sided considering a significance level of 0.05.

Phase III – Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Design:

Before-after, cross-sectional, descriptive study.

Since there is a lack of research on multimorbidity in Portugal, we believe that this concept is not usually taken into account in daily practice. We also have confidence in that the dissemination of the results of Parts I and II of the study will have the capability of raising awareness and change behaviour towards multimorbid patients. To test these hypotheses a before-after study was designed.

Setting:

Selected Primary Care Centres in two districts of the Centre region of Portugal (Coimbra and Aveiro).

Sample size:

Since this is a descriptive study, no formal calculations were performed to estimate the sample size. Notwithstanding, we are willing to include at least 10% of the population of GPs in these two districts corresponding to a sample size of approximately 60 GPs.

Study procedures:

GPs working in Primary Care Centres in the districts of Coimbra and Aveiro will be recruited by chain-referral sampling.

Data collection:

Prior to the start of Phase I of the study an online questionnaire with open text format questions will be used to evaluate GPs knowledge (definition of multimorbidity), awareness (relevance of multimorbidity in daily practice) and practices (management of multimorbidity). This will be followed by a second application of the same questionnaire after the distribution of a flyer with the results of Phases I and II of the study.

This questionnaire will have a semantic validation by 2 distinct groups. The first is composed of experts in multimorbidity and the second by possible respondents, in our case, GPs.

Statistical Analysis:

Before-after collected answers will be listed and analysed by the study investigator. If possible, answers will be converted into qualitative variables by the study investigator in order to evaluate knowledge, awareness and practices. This process will be also performed by an independent expert and results will be crosschecked. Discrepancies will be further discussed until a consensus is achieved. Results obtained will be summarized using descriptive statistics as previously described.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

AUTHORS' CONTRIBUTIONS

FP and LS led the design of the study. FP led the writing of the manuscript. All authors read and approved the final manuscript draft.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. van den Akker M, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity. Eur J Gen Pract 1996;**2**(2):65-70 doi: 10.3109/13814789609162146.
2. van den Akker M, Buntinx F, Roos S, Knottnerus JA. Problems in determining occurrence rates of multimorbidity. J Clin Epidemiol 2001;**54**(7):675-79 doi: 10.1016/s0895-4356(00)00358-9.
3. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. Ann Fam Med 2005;**3**(3):223-8 doi: 10.1370/afm.272.
4. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med 2012;**10**(2):142-51 doi: 10.1370/afm.1337.
5. Stewart M, Fortin M, Britt HC, Harrison CM, Maddocks HL. Comparisons of multi-morbidity in family practice--issues and biases. Fam Pract 2013;**30**(4):473-80 doi: 10.1093/fampra/cmt012.
6. Europe W. The European definition of general practice / family medicine. http://www.woncaeurope.org/sites/default/files/documents/Definition%203rd%20ed%202011%20with%20revised%20wonca%20tree.pdf. Published 2002. Accessed September 24, 2013.
7. Flocke SA, Frank SH, Wenger DA. Addressing multiple problems in the family practice office visit. J Fam Pract 2001;**50**(3):211-6.

8. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing 2013;**42**(1):62-9 doi: 10.1093/ageing/afs100.

9. Townsend A, Hunt K, Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. BMJ 2003;**327**(7419):837-40 doi: 10.1136/bmj.327.7419.837.

10. Fortin M, Soubhi H, Hudon C, Bayliss EA, van den Akker M. Multimorbidity's many challenges. BMJ 2007;**334**(7602):1016-7 doi: 10.1136/bmj.39201.463819.2C.

11. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;**162**(20):2269-76 doi: 10.1001/archinte.162.20.2269.

12. Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;**54**(7):661-74.

13. Freund T, Kunz CU, Ose D, Szecsenyi J, Peters-Klimm F. Patterns of multimorbidity in primary care patients at high risk of future hospitalization. Popul Health Manag 2012;**15**(2):119-24 doi: 10.1089/pop.2011.0026.

14. Rochon PA, Katz JN, Morrow LA, et al. Comorbid illness is associated with survival and length of hospital stay in patients with chronic disability. A prospective comparison of three comorbidity indices. Med Care 1996;**34**(11):1093-101.

15. Fortin M, Bravo G, Hudon C, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Qual Life Res 2006;**15**(1):83-91 doi: 10.1007/s11136-005-8661-z.

16. Kadam UT, Croft PR, North Staffordshire GPCG. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;**24**(5):412-9 doi: 10.1093/fampra/cmm049.

17. Fortin M, Bravo G, Hudon C, Lapointe L, Dubois MF, Almirall J. Psychological distress and multimorbidity in primary care. Ann Fam Med 2006;**4**(5):417-22 doi: 10.1370/afm.528.

18. Busse R, Bluemel M, Scheller-Kreinsen D, Zentner A. Tackling Chronic Disease in Europe. Strategies, Interventions and Challenges. http://pns.dgs.pt/files/2010/05/Doen%C3%A7as-cr%C3%B3nicas_EU_Maio_2010-2.pdf. Published 2010. Accessed September 24, 2013.

19. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract 2008;**14 Suppl 1**:28-32 doi: 10.1080/13814780802436093.

20. O'Halloran J, Miller GC, Britt H. Defining chronic conditions for primary care with ICPC-2. Fam Pract 2004;**21**(4):381-6 doi: 10.1093/fampra/cmh407.

21. Fox N, Hunn A, Mathers N. *Sampling and sample size calculation*: The NIHR RDS for the East Midlands / Yorkshire & the Humber, 2007.

22. Sousa L, Figueiredo D. (In)dependência na população idosa: um estudo exploratório na população portuguesa. Psychol 2003;**33**:109-22.

23. DGS. *Diagnóstico, Tratamento e Controlo da Hipertensão Arterial*. Lisboa: DGS, 2004.

24. DGS. *National Programme for the Prevention and Control of Diabetes*. Lisbon: DGS, 2008.

25. DGS. *National Programme for Asthma Control*. Lisbon: DGS, 2005.

26. DGS. *National Programme against Rheumatic Diseases*. Lisbon: DGS, 2005.

27. Pais-Ribeiro J. *O importante é a saúde: estudo de adaptação de um instrumento para avaliar o estado de saúde*. Lisboa: Fundação Merck Sharp & Dohme, 2005.

28. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;**34**(3):220-33.

29. Imperatori E. Ficha familiar dos centros de saúde: vantagens e dificuldades. Rev Port Sau Pub 1985;**3**(3):51-6.

30. Agostinho M, Rebelo L. Família: do conceito aos meios de avaliação. Rev Port Clin Geral 1988;**32**:6-17.

31. Smilkstein G. The family APGAR: a proposal for a family function test and its use by physicians. J Fam Pract 1978;**6**(6):1231–9.

32. Baggett TP, O'Connell JJ, Singer DE, Rigotti NA. The unmet health care needs of homeless adults: a national study. Am J Public Health 2010;**100**(7):1326-33 doi: 10.2105/AJPH.2009.180109.

33. Shi L, Stevens GD. Vulnerability and unmet health care needs. The influence of multiple risk factors. J Gen Intern Med 2005;**20**(2):148-54 doi: 10.1111/j.1525-1497.2005.40136.x.

34. Diamant AL, Hays RD, Morales LS, et al. Delays and unmet need for health care among adult primary care patients in a restructured urban public health system. Am J Public Health 2004;**94**(5):783-9.

35. Newacheck PW, Hughes DC, Hung YY, Wong S, Stoddard JJ. The unmet health needs of America's children. Pediatrics 2000;**105**(4 Pt 2):989-97.

36. Ayanian JZ, Weissman JS, Schneider EC, Ginsburg JA, Zaslavsky AM. Unmet health needs of uninsured adults in the United States. JAMA 2000;**284**(16):2061-9.

37. WHO. Process of translation and adaptation of instruments. http://www.who.int/substance_abuse/research_tools/translation/en/. Published 2013. Accessed September 24, 2013.

Multimorbidity in primary care in Portugal (MM-PT): a cross-sectional three phase observational study protocol

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004113.R2
Article Type:	Protocol
Date Submitted by the Author:	21-Jan-2014
Complete List of Authors:	Prazeres, Filipe; Faculdade de Ciências da Saúde, Universidade da Beira Interior, ; Centro de Saúde de Aveiro, Santiago, Luiz; Faculdade de Ciências da Saúde, Universidade da Beira Interior, ; USF Topázio,
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Epidemiology
Keywords:	PRIMARY CARE, EPIDEMIOLOGY, PUBLIC HEALTH

Multimorbidity in primary care in Portugal (MM-PT): a cross-sectional three phase observational study protocol

Filipe Prazeres MD MSc Ph.D. Candidate[a b], Luiz Santiago MD Ph.D.[a c]

a. Faculdade de Ciências da Saúde, Universidade da Beira Interior, 6200-506 Covilhã, Portugal

b. Centro de Saúde de Aveiro, 3810-000 Aveiro, Portugal

c. USF Topázio, 3020-171 Coimbra, Portugal

Address for correspondence:

Dr. Filipe Prazeres

Ph.D. Candidate

Faculdade de Ciências da Saúde

Universidade da Beira Interior

6200-506 Covilhã, Portugal

E-mail: filipeprazeresmd@gmail.com

Telephone: +351234891197

Word count - excluding title page, abstract, references, figures and tables: 2777

KEYWORDS: multimorbidity, primary care, quality of life, family support, unmet health needs

ABSTRACT

Introduction: Multimorbidity is defined as the co-occurrence of more than one chronic disease in one person without assigning an index disease. This rapidly increasing phenomenon markedly influences patients' overall health, has major implications for effective provision of healthcare services and has a significant economic toll on individuals and society at large. Since Portugal is a country with a growing ageing population, a better understanding of the role of multimorbidity should be assessed. The aim of this study is to further the knowledge of the epidemiological factors associated with multimorbidity in Portugal, chiefly its prevalence and the health and social implications.

Methods and analysis: This study protocol describes a primary care nationwide three phase study. The first phase is drawn to access prevalence and patterns of multimorbidity. In the second phase, individual parameters are assessed, such as patients' health related quality of life, perceived family support and unmet health needs of multimorbid patients. The third and last phase of this study aims to characterise general practitioners' knowledge, awareness and practices related to multimorbidity management.

Ethics and dissemination: The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This study will contribute to a better knowledge of the epidemiological factors associated with multimorbidity in Portugal, namely its prevalence, health and social implications.
- Study findings will help ameliorate health care policies in order to improve patient quality of life and lower multimorbidity economic burden.
- These data will also be crucial for future medical teaching and continuing medical education.

- Limitations of the study need to be stated: in phase 2, four chronic conditions have been selected based on their importance; this will exclude those patients with multimorbidity with all except the selected conditions. In phase 3, chain-referral sampling may lead to a community bias but at the same time this sampling method will improve general practitioners' enrolment.

INTRODUCTION

Multimorbidity is defined as the co-occurrence of more than one chronic disease within one person without assigning an index disease.[1 2] It is known that prevalence of multimorbidity increases with age,[3] reaching over 90%.[4] Nevertheless, variations in prevalence of more than 60% have been reported between studies. These estimated differences may be due to sampling bias, period collection and data source and also due to the broad definition of chronic diseases.[5] Multimorbidity has been previously described by Martin Fortin as the rule and not the exception in primary care settings,[3] where general practitioners (GPs) manage not only the acute but mostly the chronic conditions of their patients,[6] which are often multiple.[7]

Taking only into account disease-specific recommendations can lead to a considerable treatment burden for multimorbid patients.[8] This in turn raises several other issues such as low compliance,[9] treatment ineffectiveness[10] and high treatment costs.[11]

Multimorbidity is also associated with lower life expectancy,[12] higher hospital admissions[13] and longer hospital stays.[14] Quality of life,[15] physical functioning,[16] and psychological health[17] are also negatively affected by multimorbidity.

Chronic diseases represent a significant cause of mortality and morbidity worldwide[18] and their increasing prevalence[19] has a significant impact on patients' health and use of healthcare services.

Multimorbidity is therefore a subject which is rapidly becoming of great importance in primary care settings, with a pressing need for a better understanding of this phenomenon from multiple perspectives. This work aims to further the knowledge of the epidemiology of multimorbidity,

regarding its prevalence and morbidity. Importantly, this will be the first study raising awareness of multimorbid conditions in adult population attending general practice in Portugal.

Terminology:

For the purpose of defining multimorbidity we will use the list of chronic conditions[20] compiled by the Family Medicine Research Centre (FMRC), University of Sydney, available online at http://sydney.edu.au/medicine/fmrc/classifications/DefiningChronicConditions.pdf. This list represents 147 ICPC-2 (International Classification of Primary Care) rubrics.

STUDY OBJECTIVES

The primary objective of the study described in the protocol is to determine the prevalence of multimorbidity, quality of life, family support, and unmet health needs of adult patients with multimorbidity attending primary care in Portugal.

Specific objectives are to:

- Describe the sociodemographic and clinical profiles of patients with multimorbidity in Portugal;

- Characterise the unmet health needs of Portuguese patients with multimorbidity;

- Evaluate the impact of multimorbidity on patients' health related quality of life;

- Assess family support to patients with multimorbidity in Portugal;

- Analyse the relationship between multimorbidity, patients' health related quality of life and family support;

- Describe Portuguese GPs' knowledge, awareness and practices related to the management of multimorbidity.

METHODS AND ANALYSIS

Study design

The study consists of 3 phases:

1. Cross-sectional, analytical study of the prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal.

2. Cross-sectional, analytical study of patients' health-related quality of life, self-perceived family support and unmet health needs of adult patients with multimorbidity attending primary care in Portugal.

3. Descriptive before-after study of Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Phase I - Prevalence of multimorbidity in the adult population attending primary care in Portugal

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in mainland Portugal will be randomly selected from the five Portuguese Healthcare Administrative Regions in order to obtain a national geographical representative sample.

Sample size:

Since the prevalence of multimorbidity varies greatly across research literature and there is no available estimate for Portugal, a prevalence of 50% was assumed in order to maximize the sample size. For the study to be able to estimate a 95% confidence interval for the prevalence of multimorbidity with a maximum precision error of 2.5%, a total of 1500 patients should be recruited (Epidat 4.0 - Organización Panamericana de la Salud, Washington D.C., USA).

Study procedures:

This phase of the study is expected to start in October 2013.

A two-step selection approach, based on the work of Fortin et al.[3], will be followed. Firstly, GPs will be contacted and those who accept to participate will recruit their own patients.

Assuming that a GP will be able to include at least 10 patients in a 3-week period, a total of 150 GPs has to be enrolled in the study. Considering a 30% invitation response rate, then a total of 500 GPs should be invited to participate in the study: 182 in North (36%), 117 in Centre (23%), 139 in Lisbon-Tejo Valley (28%), 38 in Alentejo (8%) and 22 in Algarve (4%) in accordance with the distribution of the Portuguese adult population (18+ years old) across the five mainland Portuguese Healthcare Administrative Regions.

The GPs to be invited will be randomly selected from an alphabetically ordered list prearranged per Healthcare Administrative Regions, using a random number generator (Independent Random Sampling)[21].

Enrolled GPs will be instructed to invite all adult (≥ 18 years old) patients attending to the primary care consultation to participate in the study during three days on three consecutive weeks (Tuesday on week one; Wednesday on week two; and Thursday on week three). Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

GPs will be responsible for collecting all data about each patient during their consultations and through the completion of a paper questionnaire developed specifically for this study. Patient's morbidities will be captured by GPs, using their knowledge of patient history, patient's self-report and electronic and/or paper patient medical records. Morbidities will be collected using the International Classification of Primary Care v.2 (ICPC-2) codes or the International

Classification of Diseases - 10th version (ICD-10), which are currently being used in Portuguese Primary Care Centres.

The personal information section of the Portuguese version of the EASY-Care questionnaire [22] will be used to collect patients' social and demographic characteristics namely gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status through the question "In general how do your family finances work out at the end of the month?".

Data will be electronically stored in a database specifically designed for this study using MS Access 2010. Data will be encrypted and password protected. Information will be treated in strict confidentiality to protect the privacy of patients.

Paper copies of all informed consents will be retained in a locked file, separate from any study data.

Statistical Analysis:

A descriptive analysis will be performed to all study variables namely number of valid observations, mean, standard deviation, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. Prevalence of multimorbidity (considering two definitions: ≥2 diseases or ≥3 diseases) will be calculated together with corresponding 95% confidence interval (CI). Moreover, the prevalence of multimorbidity will be estimated by subgroups namely by gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status. Univariate analysis will be done to study associations between those characteristics and multimorbidity using Chi-square test (qualitative characteristics) or t-test/Mann-Whitney

(quantitative characteristics). Multiple logistic regression will be carried over considering presence of multimorbidity as the dependent variable and patients' characteristics as the independent variables in order to calculate odds ratios and corresponding 95% CIs. Total number of morbidities by patient will be also summarized together with 95% CI and multiple regression may be performed to analyse its association with patients characteristics. All analyses will be performed for both above mentioned definitions of multimorbidity. All tests will be two-sided using a significance level of 0.05. Statistical analysis will be done using SPSS version 18.0 or higher.

Phase II - Patients' health-related quality of life, perceived family support and unmet health needs of adult patients with multimorbidity attending primary care in Portugal.

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in the Centre region of Portugal will be randomly selected within each Care Centres Grouping (ACES and ULS) in order to obtain a regional geographical representative sample.

Sample size:

A total of 500 patients should be included in phase II in order to obtain 95% CIs for proportions with a maximum precision error of 4.5% and 95% CIs for SF-12 mean scores with a precision error of 4.5 (assuming a standard deviation of 50).

Study procedures:

Phase II of the study is expected to start in January 2014.

A two-step approach will be considered as in phase I. Assuming that each GP will enrol 10 patients and that 30% of the invited GPs will accept to participate, then about 170 GPs within the randomly selected Care Centres should be invited to participate in this phase of the study.

Primary Care Centers will be randomly selected (Independent Random Sampling)[21] and all GPs within those centers will be invited to participate (until 170 GPs are recruited).

By purposive sampling, enrolled GPs will select adult (≥18 years old) patients with multimorbidity and with at least one of four morbidities: hypertension, diabetes, asthma, and/or osteoarthritis. These morbidities were selected based on the Portuguese Directorate-General of Health (DGS – Direção-Geral da Saúde) efforts to implement specific national recommendations for the diagnosis, treatment and control of these conditions, which have high prevalence and are associated with low quality of life.[23-26]

The investigator or a previously trained research associate (GP/GP trainee) will interview the patients at their convenience, either in the GPs office or at their home. Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

All data will be collected using a paper questionnaire. Patients' morbidities, social and demographic characteristics will be registered using the same methodology as described in Phase I. Health related quality of life will be evaluated using the Portuguese Short Form-12 Health Status Questionnaire (SF-12),[27] derived from the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36),[28] through interview of the patients. The Portuguese Family APGAR (Adaptation, Partnership, Growth, Affection and Resolve) Questionnaire [29 30] that evaluates family function in five dimensions [31] will be used to measure the perceived family support of patients with multimorbidity.

Based on the literature,[32-36] a patients' unmet health needs questionnaire was drafted. The unmet need for the following services will be evaluated: medical, surgical and dental care,

prescription medications, mental health care or counselling, and eyeglasses or other technical aid. These will be evaluated by a set of general questions, such as "During the past 12 months, was there a time when you wanted/needed medical care but couldn't get it at that time?". If an unmet health need is stated, available reasons to explain it are: Couldn't you get off work? Were you too sick? Didn't you have a way to get there? Did you have responsibilities to take care of someone? Were you afraid to leave home because of personal safety? Did you have other more important things to take care of? Did you have to spend your money for food, clothing, housing, etc.? These questions will be translated to Portuguese by the study investigator and the translation will be subsequently reviewed by an independent GP expert. Any disagreements will be discussed between both in order to achieve a consensus. Furthermore, a pre-test will be undertaken and the translated questions will be applied to 50 subjects prior to patients enrolment phase in order to verify subjects' comprehensibility of those.

Statistical Analysis:

Descriptive statistics will be computed for all variables together with 95% CIs whenever relevant and applicable. Associations between qualitative independent variables will be tested using Chi-square test. Comparisons between two or more independent groups regarding a quantitative variable are to be conducted using ANOVA or Kruskal-Wallis non-parametric test, if normality assumption is not met. ANCOVA may also be used to adjust for potential confounding factors. Associations between quantitative independent variables will be analysed using Pearson's or Spearman's correlation coefficient depending upon normality assumption. All tests will be two-sided considering a significance level of 0.05.

Phase III – Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Design:

Before-after, descriptive study.

Since there is a lack of research on multimorbidity in Portugal, we believe that this concept is not usually taken into account in daily practice. We also have confidence in that the dissemination of the results of Parts I and II of the study will have the capability of raising awareness and change behaviour towards patients with multimorbidity. To test these hypotheses a before-after study was designed.

Setting:

Selected Primary Care Centres in two districts of the Centre region of Portugal (Coimbra and Aveiro).

Sample size:

Since this is a descriptive study, no formal calculations were performed to estimate the sample size. Notwithstanding, we are willing to include at least 10% of the population of GPs in these two districts corresponding to a sample size of approximately 60 GPs.

Study procedures:

GPs working in Primary Care Centres in the districts of Coimbra and Aveiro will be recruited by chain-referral sampling.

Data collection:

Prior to the start of Phase I of the study an online questionnaire with open text format questions will be used to evaluate GPs knowledge (definition of multimorbidity), awareness (relevance of multimorbidity in daily practice) and practices (management of multimorbidity). This will be followed by a second application of the same questionnaire after the distribution of a flyer with the results of Phases I and II of the study.

This questionnaire will have a semantic validation by 2 distinct groups. The first is composed of experts in multimorbidity and the second by possible respondents, in our case, GPs.

Statistical Analysis:

Before-after collected answers will be listed and analysed by the study investigator. If possible, answers will be converted into qualitative variables by the study investigator in order to evaluate knowledge, awareness and practices. This process will be also performed by an independent expert and results will be crosschecked. Discrepancies will be further discussed until a consensus is achieved. Results obtained will be summarized using descriptive statistics as previously described.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

AUTHORS' CONTRIBUTIONS

FP and LS led the design of the study. FP led the writing of the manuscript. All authors read and approved the final manuscript draft.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. van den Akker M, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity. Eur J Gen Pract 1996;**2**(2):65-70 doi: 10.3109/13814789609162146.

2. van den Akker M, Buntinx F, Roos S, et al. Problems in determining occurrence rates of multimorbidity. J Clin Epidemiol 2001;**54**(7):675-79 doi: 10.1016/s0895-4356(00)00358-9.

3. Fortin M, Bravo G, Hudon C, et al. Prevalence of multimorbidity among adults seen in family practice. Ann Fam Med 2005;**3**(3):223-8 doi: 10.1370/afm.272.

4. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med 2012;**10**(2):142-51 doi: 10.1370/afm.1337.

5. Stewart M, Fortin M, Britt HC, et al. Comparisons of multi-morbidity in family practice--issues and biases. Fam Pract 2013;**30**(4):473-80 doi: 10.1093/fampra/cmt012.

6. Europe W. The European definition of general practice / family medicine. http://www.woncaeurope.org/sites/default/files/documents/Definition%203rd%20ed%202011%20with%20revised%20wonca%20tree.pdf. Published 2002. Accessed September 24, 2013.

7. Flocke SA, Frank SH, Wenger DA. Addressing multiple problems in the family practice office visit. J Fam Pract 2001;**50**(3):211-6.

8. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing 2013;**42**(1):62-9 doi: 10.1093/ageing/afs100.

9. Townsend A, Hunt K, Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. BMJ 2003;**327**(7419):837-40 doi: 10.1136/bmj.327.7419.837.

10. Fortin M, Soubhi H, Hudon C, et al. Multimorbidity's many challenges. BMJ 2007;**334**(7602):1016-7 doi: 10.1136/bmj.39201.463819.2C.

11. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;**162**(20):2269-76 doi: 10.1001/archinte.162.20.2269.

12. Gijsen R, Hoeymans N, Schellevis FG, et al. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;**54**(7):661-74.

13. Freund T, Kunz CU, Ose D, et al. Patterns of multimorbidity in primary care patients at high risk of future hospitalization. Popul Health Manag 2012;**15**(2):119-24 doi: 10.1089/pop.2011.0026.

14. Rochon PA, Katz JN, Morrow LA, et al. Comorbid illness is associated with survival and length of hospital stay in patients with chronic disability. A prospective comparison of three comorbidity indices. Med Care 1996;**34**(11):1093-101.

15. Fortin M, Bravo G, Hudon C, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Qual Life Res 2006;**15**(1):83-91 doi: 10.1007/s11136-005-8661-z.

16. Kadam UT, Croft PR, North Staffordshire GPCG. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;**24**(5):412-9 doi: 10.1093/fampra/cmm049.

17. Fortin M, Bravo G, Hudon C, et al. Psychological distress and multimorbidity in primary care. Ann Fam Med 2006;**4**(5):417-22 doi: 10.1370/afm.528.

18. Busse R, Bluemel M, Scheller-Kreinsen D, et al. Tackling Chronic Disease in Europe. Strategies, Interventions and Challenges. http://pns.dgs.pt/files/2010/05/Doen%C3%A7as-cr%C3%B3nicas_EU_Maio_2010-2.pdf. Published 2010. Accessed September 24, 2013.

19. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract 2008;**14 Suppl 1**:28-32 doi: 10.1080/13814780802436093.

20. O'Halloran J, Miller GC, Britt H. Defining chronic conditions for primary care with ICPC-2. Fam Pract 2004;**21**(4):381-6 doi: 10.1093/fampra/cmh407.

21. Fox N, Hunn A, Mathers N. *Sampling and sample size calculation*: The NIHR RDS for the East Midlands / Yorkshire & the Humber, 2007.

22. Sousa L, Figueiredo D. (In)dependência na população idosa: um estudo exploratório na população portuguesa. Psychol 2003;**33**:109-22.

23. DGS. *Diagnóstico, Tratamento e Controlo da Hipertensão Arterial*. Lisboa: DGS, 2004.

24. DGS. *National Programme for the Prevention and Control of Diabetes*. Lisbon: DGS, 2008.

25. DGS. *National Programme for Asthma Control*. Lisbon: DGS, 2005.

26. DGS. *National Programme against Rheumatic Diseases*. Lisbon: DGS, 2005.

27. Pais-Ribeiro J. *O importante é a saúde: estudo de adaptação de um instrumento para avaliar o estado de saúde*. Lisboa: Fundação Merck Sharp & Dohme, 2005.

28. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;**34**(3):220-33.

29. Imperatori E. Ficha familiar dos centros de saúde: vantagens e dificuldades. Rev Port Sau Pub 1985;**3**(3):51-6.

30. Agostinho M, Rebelo L. Família: do conceito aos meios de avaliação. Rev Port Clin Geral 1988;**32**:6-17.

31. Smilkstein G. The family APGAR: a proposal for a family function test and its use by physicians. J Fam Pract 1978;**6**(6):1231–9.

32. Baggett TP, O'Connell JJ, Singer DE, et al. The unmet health care needs of homeless adults: a national study. Am J Public Health 2010;**100**(7):1326-33 doi: 10.2105/AJPH.2009.180109.

33. Shi L, Stevens GD. Vulnerability and unmet health care needs. The influence of multiple risk factors. J Gen Intern Med 2005;**20**(2):148-54 doi: 10.1111/j.1525-1497.2005.40136.x.

34. Diamant AL, Hays RD, Morales LS, et al. Delays and unmet need for health care among adult primary care patients in a restructured urban public health system. Am J Public Health 2004;**94**(5):783-9.

35. Newacheck PW, Hughes DC, Hung YY, et al. The unmet health needs of America's children. Pediatrics 2000;**105**(4 Pt 2):989-97.

36. Ayanian JZ, Weissman JS, Schneider EC, et al. Unmet health needs of uninsured adults in the United States. JAMA 2000;**284**(16):2061-9.

Multimorbidity in primary care in Portugal (MM-PT): a cross-sectional three phase observational study protocol

Filipe Prazeres MD MSc Ph.D. Candidate[a b], Luiz Santiago MD Ph.D.[a c]

a. Faculdade de Ciências da Saúde, Universidade da Beira Interior, 6200-506 Covilhã, Portugal

b. Centro de Saúde de Aveiro, 3810-000 Aveiro, Portugal

c. USF Topázio, 3020-171 Coimbra, Portugal

Address for correspondence:

Dr. Filipe Prazeres

Ph.D. Candidate

Faculdade de Ciências da Saúde

Universidade da Beira Interior

6200-506 Covilhã, Portugal

E-mail: filipeprazeresmd@gmail.com

Telephone: +351234891197

Word count - excluding title page, abstract, references, figures and tables: 2777

KEYWORDS: multimorbidity, primary care, quality of life, family support, unmet health needs

ABSTRACT

Introduction: Multimorbidity is defined as the co-occurrence of more than one chronic disease in one person without assigning an index disease. This rapidly increasing phenomenon markedly influences patients' overall health, has major implications for effective provision of healthcare services and has a significant economic toll on individuals and society at large. Since Portugal is a country with a growing ageing population, a better understanding of the role of multimorbidity should be assessed. The aim of this study is to further the knowledge of the epidemiological factors associated with multimorbidity in Portugal, chiefly its prevalence and the health and social implications.

Methods and analysis: This study protocol describes a primary care nationwide three phase study. The first phase is drawn to access prevalence and patterns of multimorbidity. In the second phase, individual parameters are assessed, such as patients' health related quality of life, perceived family support and unmet health needs of multimorbid patients. The third and last phase of this study aims to characterise general practitioners' knowledge, awareness and practices related to multimorbidity management.

Ethics and dissemination: The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- This study will contribute to a better knowledge of the epidemiological factors associated with multimorbidity in Portugal, namely its prevalence, health and social implications.
- Study findings will help ameliorate health care policies in order to improve patient quality of life and lower multimorbidity economic burden.
- These data will also be crucial for future medical teaching and continuing medical education.

- Limitations of the study need to be stated: in phase 2, four chronic conditions have been selected based on their importance; this will exclude those patients with multimorbidity with all except the selected conditions. In phase 3, chain-referral sampling may lead to a community bias but at the same time this sampling method will improve general practitioners' enrolment.

INTRODUCTION

Multimorbidity is defined as the co-occurrence of more than one chronic disease within one person without assigning an index disease.[1 2] It is known that prevalence of multimorbidity increases with age,[3] reaching over 90%.[4] Nevertheless, variations in prevalence of more than 60% have been reported between studies. These estimated differences may be due to sampling bias, period collection and data source and also due to the broad definition of chronic diseases.[5] Multimorbidity has been previously described by Martin Fortin as the rule and not the exception in primary care settings,[3] where general practitioners (GPs) manage not only the acute but mostly the chronic conditions of their patients,[6] which are often multiple.[7]

Taking only into account disease-specific recommendations can lead to a considerable treatment burden for multimorbid patients.[8] This in turn raises several other issues such as low compliance,[9] treatment ineffectiveness[10] and high treatment costs.[11]

Multimorbidity is also associated with lower life expectancy,[12] higher hospital admissions[13] and longer hospital stays.[14] Quality of life,[15] physical functioning,[16] and psychological health[17] are also negatively affected by multimorbidity.

Chronic diseases represent a significant cause of mortality and morbidity worldwide[18] and their increasing prevalence[19] has a significant impact on patients' health and use of healthcare services.

Multimorbidity is therefore a subject which is rapidly becoming of great importance in primary care settings, with a pressing need for a better understanding of this phenomenon from multiple perspectives. This work aims to further the knowledge of the epidemiology of multimorbidity,

regarding its prevalence and morbidity. Importantly, this will be the first study raising awareness of multimorbid conditions in adult population attending general practice in Portugal.

Terminology:

For the purpose of defining multimorbidity we will use the list of chronic conditions[20] compiled by the Family Medicine Research Centre (FMRC), University of Sydney, available online at http://sydney.edu.au/medicine/fmrc/classifications/DefiningChronicConditions.pdf. This list represents 147 ICPC-2 (International Classification of Primary Care) rubrics.

STUDY OBJECTIVES

The primary objective of the study described in the protocol is to determine the prevalence of multimorbidity, quality of life, family support, and unmet health needs of adult patients with multimorbidity attending primary care in Portugal.

Specific objectives are to:

- Describe the sociodemographic and clinical profiles of patients with multimorbidity in Portugal;

- Characterise the unmet health needs of Portuguese patients with multimorbidity;

- Evaluate the impact of multimorbidity on patients' health related quality of life;

- Assess family support to patients with multimorbidity in Portugal;

- Analyse the relationship between multimorbidity, patients' health related quality of life and family support;

- Describe Portuguese GPs' knowledge, awareness and practices related to the management of multimorbidity.

METHODS AND ANALYSIS

Study design

The study consists of 3 phases:

1. Cross-sectional, analytical study of the prevalence and patterns of multimorbidity in the adult population attending primary care in Portugal.

2. Cross-sectional, analytical study of patients' health-related quality of life, self-perceived family support and unmet health needs of adult patients with multimorbidity attending primary care in Portugal.

3. Descriptive before-after study of Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Phase I - Prevalence of multimorbidity in the adult population attending primary care in Portugal

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in mainland Portugal will be randomly selected from the five Portuguese Healthcare Administrative Regions in order to obtain a national geographical representative sample.

Sample size:

Since the prevalence of multimorbidity varies greatly across research literature and there is no available estimate for Portugal, a prevalence of 50% was assumed in order to maximize the sample size. For the study to be able to estimate a 95% confidence interval for the prevalence of multimorbidity with a maximum precision error of 2.5%, a total of 1500 patients should be recruited (Epidat 4.0 - Organización Panamericana de la Salud, Washington D.C., USA).

Study procedures:

This phase of the study is expected to start in October 2013.

A two-step selection approach, based on the work of Fortin et al.[3], will be followed. Firstly, GPs will be contacted and those who accept to participate will recruit their own patients.

Assuming that a GP will be able to include at least 10 patients in a 3-week period, a total of 150 GPs has to be enrolled in the study. Considering a 30% invitation response rate, then a total of 500 GPs should be invited to participate in the study: 182 in North (36%), 117 in Centre (23%), 139 in Lisbon-Tejo Valley (28%), 38 in Alentejo (8%) and 22 in Algarve (4%) in accordance with the distribution of the Portuguese adult population (18+ years old) across the five mainland Portuguese Healthcare Administrative Regions.

The GPs to be invited will be randomly selected from an alphabetically ordered list prearranged per Healthcare Administrative Regions, using a random number generator (Independent Random Sampling)[21].

Enrolled GPs will be instructed to invite all adult (≥ 18 years old) patients attending to the primary care consultation to participate in the study during three days on three consecutive weeks (Tuesday on week one; Wednesday on week two; and Thursday on week three). Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

GPs will be responsible for collecting all data about each patient during their consultations and through the completion of a paper questionnaire developed specifically for this study. Patient's morbidities will be captured by GPs, using their knowledge of patient history, patient's self-report and electronic and/or paper patient medical records. Morbidities will be collected using the International Classification of Primary Care v.2 (ICPC-2) codes or the International

Classification of Diseases - 10th version (ICD-10), which are currently being used in Portuguese Primary Care Centres.

The personal information section of the Portuguese version of the EASY-Care questionnaire [22] will be used to collect patients' social and demographic characteristics namely gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status through the question "In general how do your family finances work out at the end of the month?".

Data will be electronically stored in a database specifically designed for this study using MS Access 2010. Data will be encrypted and password protected. Information will be treated in strict confidentiality to protect the privacy of patients.

Paper copies of all informed consents will be retained in a locked file, separate from any study data.

Statistical Analysis:

A descriptive analysis will be performed to all study variables namely number of valid observations, mean, standard deviation, median and range for quantitative variables and absolute and relative frequencies for qualitative variables. Prevalence of multimorbidity (considering two definitions: ≥2 diseases or ≥3 diseases) will be calculated together with corresponding 95% confidence interval (CI). Moreover, the prevalence of multimorbidity will be estimated by subgroups namely by gender, age, residence area, current marital status, number of years of formal education, living arrangements, professional status and self-perceived economic status. Univariate analysis will be done to study associations between those characteristics and multimorbidity using Chi-square test (qualitative characteristics) or t-test/Mann-Whitney

(quantitative characteristics). Multiple logistic regression will be carried over considering presence of multimorbidity as the dependent variable and patients' characteristics as the independent variables in order to calculate odds ratios and corresponding 95% CIs. Total number of morbidities by patient will be also summarized together with 95% CI and multiple regression may be performed to analyse its association with patients characteristics. All analyses will be performed for both above mentioned definitions of multimorbidity. All tests will be two-sided using a significance level of 0.05. Statistical analysis will be done using SPSS version 18.0 or higher.

Phase II - Patients' health-related quality of life, perceived family support and unmet health needs of adult patients with multimorbidity attending primary care in Portugal.

Design:

Cross-sectional, analytical study.

Setting:

Primary Care Centres in the Centre region of Portugal will be randomly selected within each Care Centres Grouping (ACES and ULS) in order to obtain a regional geographical representative sample.

Sample size:

A total of 500 patients should be included in phase II in order to obtain 95% CIs for proportions with a maximum precision error of 4.5% and 95% CIs for SF-12 mean scores with a precision error of 4.5 (assuming a standard deviation of 50).

Study procedures:

Phase II of the study is expected to start in January 2014.

A two-step approach will be considered as in phase I. Assuming that each GP will enrol 10 patients and that 30% of the invited GPs will accept to participate, then about 170 GPs within the randomly selected Care Centres should be invited to participate in this phase of the study.

Primary Care Centers will be randomly selected (Independent Random Sampling)[21] and all GPs within those centers will be invited to participate (until 170 GPs are recruited).

By purposive sampling, enrolled GPs will select adult (≥18 years old) patients with multimorbidity and with at least one of four morbidities: hypertension, diabetes, asthma, and/or osteoarthritis. These morbidities were selected based on the Portuguese Directorate-General of Health (DGS – Direção-Geral da Saúde) efforts to implement specific national recommendations for the diagnosis, treatment and control of these conditions, which have high prevalence and are associated with low quality of life.[23-26]

The investigator or a previously trained research associate (GP/GP trainee) will interview the patients at their convenience, either in the GPs office or at their home. Subjects willing to participate in the study must give written informed consent and present willingness and ability to comply with the study requirements. Participants will be excluded if they are acutely unwell or refuse to participate.

Data collection:

All data will be collected using a paper questionnaire. Patients' morbidities, social and demographic characteristics will be registered using the same methodology as described in Phase I. Health related quality of life will be evaluated using the Portuguese Short Form-12 Health Status Questionnaire (SF-12),[27] derived from the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36),[28] through interview of the patients. The Portuguese Family APGAR (Adaptation, Partnership, Growth, Affection and Resolve) Questionnaire [29 30] that evaluates family function in five dimensions [31] will be used to measure the perceived family support of patients with multimorbidity.

Based on the literature,[32-36] a patients' unmet health needs questionnaire was drafted. The unmet need for the following services will be evaluated: medical, surgical and dental care,

prescription medications, mental health care or counselling, and eyeglasses or other technical aid. These will be evaluated by a set of general questions, such as "During the past 12 months, was there a time when you wanted/needed medical care but couldn't get it at that time?". If an unmet health need is stated, available reasons to explain it are: Couldn't you get off work? Were you too sick? Didn't you have a way to get there? Did you have responsibilities to take care of someone? Were you afraid to leave home because of personal safety? Did you have other more important things to take care of? Did you have to spend your money for food, clothing, housing, etc.? These questions will be translated to Portuguese by the study investigator and the translation will be subsequently reviewed by an independent GP expert. Any disagreements will be discussed between both in order to achieve a consensus. Furthermore, a pre-test will be undertaken and the translated questions will be applied to 50 subjects prior to patients enrolment phase in order to verify subjects' comprehensibility of those.

Statistical Analysis:

Descriptive statistics will be computed for all variables together with 95% CIs whenever relevant and applicable. Associations between qualitative independent variables will be tested using Chi-square test. Comparisons between two or more independent groups regarding a quantitative variable are to be conducted using ANOVA or Kruskal-Wallis non-parametric test, if normality assumption is not met. ANCOVA may also be used to adjust for potential confounding factors. Associations between quantitative independent variables will be analysed using Pearson's or Spearman's correlation coefficient depending upon normality assumption. All tests will be two-sided considering a significance level of 0.05.

Phase III – Portuguese GPs' knowledge, awareness and practices regarding multimorbidity and its management.

Design:

Before-after, descriptive study.

Since there is a lack of research on multimorbidity in Portugal, we believe that this concept is not usually taken into account in daily practice. We also have confidence in that the dissemination of the results of Parts I and II of the study will have the capability of raising awareness and change behaviour towards patients with multimorbidity. To test these hypotheses a before-after study was designed.

Setting:

Selected Primary Care Centres in two districts of the Centre region of Portugal (Coimbra and Aveiro).

Sample size:

Since this is a descriptive study, no formal calculations were performed to estimate the sample size. Notwithstanding, we are willing to include at least 10% of the population of GPs in these two districts corresponding to a sample size of approximately 60 GPs.

Study procedures:

GPs working in Primary Care Centres in the districts of Coimbra and Aveiro will be recruited by chain-referral sampling.

Data collection:

Prior to the start of Phase I of the study an online questionnaire with open text format questions will be used to evaluate GPs knowledge (definition of multimorbidity), awareness (relevance of multimorbidity in daily practice) and practices (management of multimorbidity). This will be followed by a second application of the same questionnaire after the distribution of a flyer with the results of Phases I and II of the study.

This questionnaire will have a semantic validation by 2 distinct groups. The first is composed of experts in multimorbidity and the second by possible respondents, in our case, GPs.

Statistical Analysis:

Before-after collected answers will be listed and analysed by the study investigator. If possible, answers will be converted into qualitative variables by the study investigator in order to evaluate knowledge, awareness and practices. This process will be also performed by an independent expert and results will be crosschecked. Discrepancies will be further discussed until a consensus is achieved. Results obtained will be summarized using descriptive statistics as previously described.

ETHICS AND DISSEMINATION

The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki. It has full approval from the Ethics Committee of the Faculty of Health Sciences, University of Beira Interior, and the Ethics Committee of the Central Health Region of Portugal. Study results will be published in peer-review journals and presented at national and international conferences.

AUTHORS' CONTRIBUTIONS

FP and LS led the design of the study. FP led the writing of the manuscript. All authors read and approved the final manuscript draft.

COMPETING INTERESTS

The authors declare that they have no competing interests.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. van den Akker M, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity. Eur J Gen Pract 1996;**2**(2):65-70 doi: 10.3109/13814789609162146.
2. van den Akker M, Buntinx F, Roos S, Knottnerus JA. Problems in determining occurrence rates of multimorbidity. J Clin Epidemiol 2001;**54**(7):675-79 doi: 10.1016/s0895-4356(00)00358-9.
3. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. Ann Fam Med 2005;**3**(3):223-8 doi: 10.1370/afm.272.
4. Fortin M, Stewart M, Poitras ME, Almirall J, Maddocks H. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med 2012;**10**(2):142-51 doi: 10.1370/afm.1337.
5. Stewart M, Fortin M, Britt HC, Harrison CM, Maddocks HL. Comparisons of multi-morbidity in family practice--issues and biases. Fam Pract 2013;**30**(4):473-80 doi: 10.1093/fampra/cmt012.
6. Europe W. The European definition of general practice / family medicine. http://www.woncaeurope.org/sites/default/files/documents/Definition%203rd%20ed%202011%20with%20revised%20wonca%20tree.pdf. Published 2002. Accessed September 24, 2013.
7. Flocke SA, Frank SH, Wenger DA. Addressing multiple problems in the family practice office visit. J Fam Pract 2001;**50**(3):211-6.

8. Hughes LD, McMurdo ME, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. Age Ageing 2013;**42**(1):62-9 doi: 10.1093/ageing/afs100.

9. Townsend A, Hunt K, Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. BMJ 2003;**327**(7419):837-40 doi: 10.1136/bmj.327.7419.837.

10. Fortin M, Soubhi H, Hudon C, Bayliss EA, van den Akker M. Multimorbidity's many challenges. BMJ 2007;**334**(7602):1016-7 doi: 10.1136/bmj.39201.463819.2C.

11. Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;**162**(20):2269-76 doi: 10.1001/archinte.162.20.2269.

12. Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;**54**(7):661-74.

13. Freund T, Kunz CU, Ose D, Szecsenyi J, Peters-Klimm F. Patterns of multimorbidity in primary care patients at high risk of future hospitalization. Popul Health Manag 2012;**15**(2):119-24 doi: 10.1089/pop.2011.0026.

14. Rochon PA, Katz JN, Morrow LA, et al. Comorbid illness is associated with survival and length of hospital stay in patients with chronic disability. A prospective comparison of three comorbidity indices. Med Care 1996;**34**(11):1093-101.

15. Fortin M, Bravo G, Hudon C, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Qual Life Res 2006;**15**(1):83-91 doi: 10.1007/s11136-005-8661-z.

16. Kadam UT, Croft PR, North Staffordshire GPCG. Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice. Fam Pract 2007;**24**(5):412-9 doi: 10.1093/fampra/cmm049.

17. Fortin M, Bravo G, Hudon C, Lapointe L, Dubois MF, Almirall J. Psychological distress and multimorbidity in primary care. Ann Fam Med 2006;**4**(5):417-22 doi: 10.1370/afm.528.

18. Busse R, Bluemel M, Scheller-Kreinsen D, Zentner A. Tackling Chronic Disease in Europe. Strategies, Interventions and Challenges. http://pns.dgs.pt/files/2010/05/Doen%C3%A7as-cr%C3%B3nicas_EU_Maio_2010-2.pdf. Published 2010. Accessed September 24, 2013.

19. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract 2008;**14 Suppl 1**:28-32 doi: 10.1080/13814780802436093.

20. O'Halloran J, Miller GC, Britt H. Defining chronic conditions for primary care with ICPC-2. Fam Pract 2004;**21**(4):381-6 doi: 10.1093/fampra/cmh407.

21. Fox N, Hunn A, Mathers N. *Sampling and sample size calculation*: The NIHR RDS for the East Midlands / Yorkshire & the Humber, 2007.

22. Sousa L, Figueiredo D. (In)dependência na população idosa: um estudo exploratório na população portuguesa. Psychol 2003;**33**:109-22.

23. DGS. *Diagnóstico, Tratamento e Controlo da Hipertensão Arterial*. Lisboa: DGS, 2004.

24. DGS. *National Programme for the Prevention and Control of Diabetes*. Lisbon: DGS, 2008.

25. DGS. *National Programme for Asthma Control*. Lisbon: DGS, 2005.

26. DGS. *National Programme against Rheumatic Diseases*. Lisbon: DGS, 2005.

27. Pais-Ribeiro J. *O importante é a saúde: estudo de adaptação de um instrumento para avaliar o estado de saúde*. Lisboa: Fundação Merck Sharp & Dohme, 2005.

28. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;**34**(3):220-33.

29. Imperatori E. Ficha familiar dos centros de saúde: vantagens e dificuldades. Rev Port Sau Pub 1985;**3**(3):51-6.

30. Agostinho M, Rebelo L. Família: do conceito aos meios de avaliação. Rev Port Clin Geral 1988;**32**:6-17.

31. Smilkstein G. The family APGAR: a proposal for a family function test and its use by physicians. J Fam Pract 1978;**6**(6):1231–9.

32. Baggett TP, O'Connell JJ, Singer DE, Rigotti NA. The unmet health care needs of homeless adults: a national study. Am J Public Health 2010;**100**(7):1326-33 doi: 10.2105/AJPH.2009.180109.

33. Shi L, Stevens GD. Vulnerability and unmet health care needs. The influence of multiple risk factors. J Gen Intern Med 2005;**20**(2):148-54 doi: 10.1111/j.1525-1497.2005.40136.x.

34. Diamant AL, Hays RD, Morales LS, et al. Delays and unmet need for health care among adult primary care patients in a restructured urban public health system. Am J Public Health 2004;**94**(5):783-9.

35. Newacheck PW, Hughes DC, Hung YY, Wong S, Stoddard JJ. The unmet health needs of America's children. Pediatrics 2000;**105**(4 Pt 2):989-97.

36. Ayanian JZ, Weissman JS, Schneider EC, Ginsburg JA, Zaslavsky AM. Unmet health needs of uninsured adults in the United States. JAMA 2000;**284**(16):2061-9.