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# Multimorbidity : a concept for family medicine within Europe

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Préparée à Brest

# La multimorbidité : un concept pour la médecine générale en Europe

**Thèse soutenue le 19 mai 2016**

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# Multimorbidity a concept for Family Medicine within Europe

MULTIMORBIDITEIT EEN CONCEPT VOOR DE  
HUISARTSGENEESKUNDE IN EUROPA

Proefschrift voorgelegd tot het behalen van de graad van doctor in de Medische  
Wetenschappen aan de Universiteit Antwerpen (België) en  
aan de universiteit Brest (Frankrijk)  
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Stories written stories told

Words described to be hold

Ideas transformed onto a page

A fantasy released from there cage

Belief in a plan from beginning to end

Where once myth became legend

A theory was born into tragedy

Autobiographies and memoirs became history

Was the hypotheses of record enough to quell

Maybe the conceived cliffhanger will become a sequel

Where the interpretation of adventure lives after the start

While the book of knowledge remains forever in the heart

Kevin Clark

# **Chapter 1**

## **Introduction**

## 1.1 Introduction

In primary care multimorbid patients are often encountered[1]. They are described as patient with multiple chronic illnesses. For example a patient with a diabetes mellitus, an arteriopathy, a COPD and a cataract should be considered as multimorbid. Family physicians deal on an everyday basis with those patients. They try, in addition, to understand the relation between the patients' health status, the psychological and social impacts of that status and the desire and will of their patient. Multimorbidity was first described in the 1970s'[2] and was an addition to the concept of comorbidity with the intention to describe and summarize all illnesses in individuals. Comorbidity was not a clarified concept at that time and lead to many interpretations of its concept and of its related constructs as multimorbidity, morbidity burden and patient's medical and social complexity [3]. Some authors focused on the links between the concept of multimorbidity and global health, equity and primary care [4]. Others focused on the quality of care needed to manage multimorbidity [5]. These authors were especially interested in the possibility of taking up the challenge of how to provide accessible and integrated care for the ageing population. That challenge was of interest with the increasing survival from acute manifestations of illnesses, the increase of the burden of non-communicable diseases [6] [7] and the increase of the cost of care with the availability of technologic interventions. Nevertheless the concept stayed unclear especially for research and practical purposes.

This thesis will explore the concept of Multimorbidity in Family Practice. The word concept is issued from Latin *conceptum* 'fully contain', which is from *concipere*, from *com-* 'together' + *capere* 'take'). A Concept gives a general overview about the reality of an object, a situation or a phenomenon. Here the focus would be on the overview on how family physicians understand the phenomenon of multimorbidity in their patients.

To disentangle those two concepts of multimorbidity and comorbidity, some authors proposed to determine them as the co-occurrence of chronic conditions [8][9]. Comorbidity was focused on one main condition under study and its relation with multiple other conditions when multimorbidity was focused on all conditions at the same time. The introduction of the



word condition was an intention to clarify the concept and to emphasize the threats linked to multimorbidity.

Multimorbidity is considered “the rule rather than the exception in primary care” and as a threat for research [10]. Indeed most of medical research is still focused on a single chronic condition to avoid selection or confusion bias. Nevertheless while doing this the complexity of most patients is never taken into account in research [10]. Single guideline advice therefore does not fit many multimorbid patients, as they may not offer prioritizing between solutions and conditions. An older man with gout and chronic heart failure, for which he takes diuretics, may be so fed up with the pain in his toes that he decides to stop the diuretics. Which guideline is he to follow? An important amount of scales and indexes were created to explore comorbidity and/or multimorbidity in research like (between others) the Charlson index[11], the cumulative illness rating scale (CIRS) [12] and the cumulative illness rating scale geriatric [13]. Even if those indexes had face-validity for researchers, they were mostly based on diseases lists and could lead to skip complexity even if like the CIRS some of them try to assess the burden of diseases. Their results showed some differences and led to various interpretations: some showed no effect [14] and others did [15].

The World Health Organisation (WHO) in 2008 tried to clarify the concept and defined Multimorbidity as people being affected by two or more chronic health conditions [16]. The intention of the WHO was to look at all conditions in one individual that could impact on that individual’s global health status and to override comorbidity as a part of multimorbidity. The WHO highlighted the need for research and practice to take into account complexity and that multimorbidity was an efficient concept to understand and then manage complexity. However, the word “condition” was still broad but not that specific enough for research or practical purposes (for instance, whether a treated disease was a ‘condition’ in this sense). “Conditions” has led to numerous interpretations and gave great diversities for the inclusion of patients in research[10][17][18].

Multimorbidity is thus not a stabilized concept and many questions stay in the balance. A lack of knowledge and of conceptualization of what is the concept of Multimorbidity warrants further research. The aim of this thesis was to explore the concept of Multimorbidity in depth and to define its links with family medicine and complexity.

In this Chapter the focus is put on the remaining questions in the concept of multimorbidity (part 1.1). Secondly the links between the concept of Multimorbidity and family medicine are highlighted (part 1.2). Thirdly, the way family physicians manage multimorbid patients is explored (part 1.3). Fourthly, the causes for the participation of the European General Practitioner Research Network (EGPRN) are clarified (part 1.4). Fifthly the constitution, the purpose, the added value and the difficulties attended with a multinational team are explained (part 1.5). Sixthly, the data and the problems on which the research question were based are summarized (part 1.6). Finally the objectives of the thesis are described (part 1.7).

## **1.2 Multimorbidity and family medicine**

Despite varying and somewhat imprecise interpretations, Multimorbidity is a very interesting and challenging concept particularly for family medicine (FM) and long-term care due to the increasing prevalence of chronic illness in an aging population across developed countries, its related polypharmacy and the compression of morbidity [1][19]. This is also true for developing countries with the emergences of care for HIV/AIDS, diabetes, psychiatric and chronic illnesses [20] [21] [22]. Multimorbidity can also be detected in younger adult populations especially when assessing diseases with a range of demographic, social, risk and protective factors[23]. As FM is the port of call for all patients in most countries, the interaction between FM and multimorbidity management is of major interest.

Multimorbidity seemed linked with many subjects of debate in FM:

Cost of care has been linked with multimorbidity and is a major aim for health care system and FM [24].

Health related quality of life has been brought into the balance and is also of interest for FM [25][15].

Depression has been highlighted as a cause or a consequence of multimorbidity in several studies[26] [27].

Frailty has also been linked with Multimorbidity in several surveys[28][29] even if a consensus about the definition of frailty is not yet issued [30] it seems of interest for FM [31].

Complexity is described as the interactions between health status, psychological status and social status as the coherent explanation of the interactions between the parts of Engel's bio-psycho-social model [32]. Complexity is the rule rather than the exception in FM and is almost never an issue in research [33]. Complexity is a major pitfall for most recommendations in FM and lead family physicians to a misuse of recommendations aimed on a single disease [34].

A special interest for FM was the link with some core competencies of FM as defined for instance by the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) [35] were described. Management of health teams or enhanced multidisciplinary work to detect and protect multimorbid patients was emphasized [36][37] and is a part of the core competencies of FPs. Multimorbidity seemed closely related to a global or comprehensive view of the patient, which is a core competency of FM. Multimorbidity is a global 'functional' view (useful for Long-Term Care) versus a 'disease' centered point of view (useful for acute care) [38]. Multimorbidity needs a patient centered approach for its management [39][40], and that approach is also a core competency of FM. In addition Multimorbidity seems to lead to many practice challenges like collaborative care and goal oriented care [10] [41].

As a conclusion: multimorbidity is a very challenging concept for FM. The concept of multimorbidity seems not restricted to the biomedical disease paradigm and could be linked to the biopsychosocial model and to complexity. A lack of knowledge is persistent for the use of the concept of multimorbidity in FM.

### **1.3 Multimorbidity and family physicians**

Family physicians are the first port of call in most European countries for all patients. Patients with multimorbidity are detected and managed by their family physicians (FPs). Nevertheless very few recommendations are implemented by the national health system to help FPs for that peculiar management. FPs manage on a daily basis:

- Multiple drug interactions[42][43],
- Conflict between diseases[44][45],
- Social effect[46],
- Caregivers protection[47],

Patient's quality of life[48],  
Inappropriate patient's coping strategies[49][50],  
Patient's beliefs and expectations[51],  
Family support[52],  
Lack of social network[53][54],  
Lack of health systems[55]...

Those factors are hardly found in recommendations. They are common factors for FPs and are explaining the little usefulness of recommendations in daily practice for multimorbid patients.

FPs intend to be more in line with their patient's expectations due to their longitudinal relationship with patients and their involvement with many conditions and problems and they could perhaps add some factors to the concept of multimorbidity to further define it and help our understanding. They also have a multi problem approach [56] that could better integrate screening, identification, care and management of Multimorbidity. They integrate in everyday practice contextual data [57] and integrate social dimensions [33][40]. This could be of importance as academic authors were unable to establish an encompassing definition of the concept of multimorbidity that is also relevant to practice.

#### **1.4 European General Practice Research Network implication in multimorbidity conceptualization**

The European General Practice Research Network (EGPRN) is a 40 years old network. It was created to enhance research capacities in FM throughout Europe. EGPRN include nations from all over Europe and the mediterranean (Algeria, Israel, Morocco, Tunisia and Turkey). Nowadays EGPRN create research courses and European collaborative studies. EGPRN gives funding for collaborative studies and achieves two meetings a year to create connections between European researchers in FM. The EGPRN was interested with the concept of Multimorbidity. As it was described upper, Multimorbidity is a challenging concept for FM. The EGPRN is committed to concepts that could advance research in primary care throughout Europe. The EGPRN has created a research agenda specifically designed for methodological and instrumental research. This agenda includes the development of primary care

epidemiology, focusing on patient-centered health [58]. In October 2010 in Dubrovnik (Croatia) an EGPRN meeting was aimed at Multimorbidity [59] showing the interest for the concept of multimorbidity for this network.

The EGPRN is also concerned with patient's complexity as a pitfall for national health services and the implementation of recommendations in FM. The links between complexity and multimorbidity were emphasized during Dubrovnik's meeting. A clear definition of the concept of multimorbidity (ie one which is both understandable and usable for further collaborative research) is an important objective for a research network of this type. It will help researchers in FM to investigate the complexity of patients' conditions and their overall impact on patients' health.

To translate the relevant concept of multimorbidity into a workable definition could be an additional tool for FPs enabling them to identify frail patients. This is of importance for FM and actually quite complicated to do with the use of several existing indexes to screen the patients [60]. Complicated screenings were known to be a threat for "real life practice" and a usable concept or multimorbidity could be of help for such screenings especially if it could be linked with the international classification of primary care (ICPC) [61]. This work of defining chronic conditions for primary care with ICPC was going on and needed further implementations. A special notice should be done as ICPC had a specific committee of the Wonca that issued the coding [62] and that the EGPRN is the research network of Wonca Europe.

Such a Network had the capacity to undertake research throughout Europe. Its participation to the research process was of importance as relevance of the concept could be assessed by in practice FPs throughout Europe with its help.

As a conclusion for this part the participation of the EGPRN to the research process about the concept of multimorbidity and its usefulness for FM research was highlighted.

### **1.5 Constitution, purpose, added value and difficulties attended with a multinational team**

The constitution of a multinational research team, started in Zurich (Switzerland) during the EGPRN meeting in October 2010. It was composed of researchers from Belgium (University of Antwerp), France (University of Brest), Germany (University of Hannover and Gottingen), Greece (Association of Greek GPs- ELEGEIA), Italy (Association of Italian GPs), Poland (University of Torun), Spain (University of Barcelona and University of Vigo) and The Netherlands (VUmc Amsterdam). In October 2011 during the EGPRN meeting in Krakow (Poland) researchers from Bosnia (University of Sarajevo) and Croatia (University of Zagreb) joined the team. They were followed during the EGPRN meeting in Spring 2012 in Ljubljana (Slovenia) by researchers from Bulgaria (University of Plovdiv).

The purpose of the research team was to better understand the concept of multimorbidity for FM throughout Europe. An initial review, presented in the spring 2011 EGPRN meeting in Nice (France) [63], identified more than one hundred different definitions used by academic researchers. The research group decided to follow the whole process of this thesis in order to clarify the concept of Multimorbidity for FM.

The added value of such a large group was:

- Its linguistic abilities for literature review
- Its linguistic abilities for translations
- The resources of the different universities and association of FPs
- The former research network that were already in use in all countries
- The former Practice network that was already in use in all countries.

The difficulties attended with such a large group were:

- Comprehension difficulties according to the use of English language
- Comprehension difficulties according to mixed culture (linguistic, health system, political systems...)
- Lack of motivation within the participants

To overcome those difficulties and to enhance the richness of this multinational group we needed to:

- Have the agreement of all teams for each step of research to ensure their participation
- Write relevant research protocols at each step of research (Annex A)

Send those protocols to all participants and check their comprehension  
Help all teams for translation's purposes  
Undertake physical meetings to ensure collection and validation of data  
Help all teams for publication  
Assume publication rank for each team (Annex B)

As a conclusion for part 1.4 a motivated multinational research group was recruited to ensure the data collection, the analysis and the follow up of the thesis.

### **1.6 summarization of the lack of knowledge and research question**

There is a great lack of data about what multimorbidity conceptually is and what usefulness practical operationalisations could have.

For some authors, multimorbidity is a related construct to comorbidity. For others comorbidity is an underitem of Multimorbidity. For the WHO multimorbidity is “people being affected by two or more chronic health conditions”. The WHO highlighted the need for research and practice to take into account complexity and that multimorbidity was an efficient concept to understand and then manage complexity. However the word “condition” was broad but not that manifest for research or practical purpose. “Conditions” has lead to numerous interpretations and gave great diversities for the inclusion of patients in research.

Multimorbidity is a very challenging concept for older patients in their home situations across Europe and therefore for FM. A lack of knowledge is persistent for the usefulness of the concept of multimorbidity in FM. Some authors linked Multimorbidity with cost of care, health related quality of life, depression, frailty, patient's complexity... The links with complexity could be of high interest for the implementation of usable recommendations in practice.

The EGPRN was concerned with the concept of Multimorbidity and constituted a research group to help this thesis production. The management of that research group was a challenge of this thesis.

The research question of this thesis was:

How can we better formulate the concept of Multimorbidity, translate and validate it (conceptualization) for academic researchers and for European family physicians? What research could be issued from that reformulated concept?

### **1.7 Objectives of the thesis**

Regarding the research question of this thesis, it was decided to follow precise objectives for the thesis to fulfill our aims. Five steps were followed using various designs:

- To publish the research protocol. The hypothesis was that it would be of help to manage the international research team.
- To define the concept of multimorbidity in academic literature. The hypothesis was that academic researchers should have used inclusion criteria that could describe multimorbidity.
- To translate the defined concept of multimorbidity in the languages of the international team. The hypothesis was that cultural and linguistic differences could be of importance and lead to misunderstanding in the defined concept of multimorbidity.
- To assess if European FPs recognized the defined concept of multimorbidity throughout Europe and to check if they would add factors to this concept. The hypothesis was that FPs are more in line with patients than other specialists and academic researchers and that they could give an added value to the concept.
- To establish a research agenda about the concept of Multimorbidity in FM. The hypothesis was that researchers in the field of Multimorbidity could assess if the concept of multimorbidity was useful for research in FM.



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If you can make one heap of all your winnings  
And risk it on one turn of pitch-and-toss,  
And lose, and start again at your beginnings  
And never breathe a word about your loss;  
If you can force your heart and nerve and sinew  
To serve your turn long after they are gone,  
And so hold on when there is nothing in you  
Except the Will which says to them: 'Hold on!'

Rudyard Kipling

# Chapter 2

## Methods

In this chapter, a brief overview will be given of the methodologies used in this thesis to answer the research questions

2.1 Research protocol

2.2 Systematic literature review

2.3 Forward Backward translations using a Delphi Consensus method

2.4 Qualitative surveys

2.5 Nominal group consensus survey

## Overview

Each step of the thesis used a specific research method. The first phase was an informal group consensus on the research protocol. Second a systematic literature review looking at criteria for including multimorbid patients in published surveys was performed in order to propose a comprehensive definition of the concept of multimorbidity. The third phase translated this definition into the teams' languages using a forward backward translation method with a Delphi consensus procedure. The aim was to take into account all cultural and linguistic differences that could lead to misunderstandings between the members of the international team. The fourth phase was to use the translated definition of the concept of multimorbidity into each country with the aim to find the added value of FPs to that definition using it as the basis of a critical theory method. The fifth phase was to establish a research agenda on the concept of multimorbidity using a nominal group consensus procedure.

### 2.1 Research protocol

The first goal of the thesis was to have an agreement of all participants on the research protocol. It was important to have a strong motivation of all participants. The threat on the thesis was to begin with an unmotivated team and to lose participants after participants during the research process. All members of the team were academic researchers in FM or FPs organisation researchers.

The strengths of the group members were:

- Their high motivation for research in FM,

- Their need of publications for their university or organization,

- Their membership in the same network (EGPRN),

- Their faith in the fact that the research process was not linked to any commercial firm,

- The fact that they already participated in research

- The follow up of the research group by an academic department of FM

The weaknesses for the group were:



The lack of financial support,

The limited time that every participants could offer to the research process

Those strengths and weaknesses were described in some former publications [1] and were carefully taken into account during the meetings for the group consensus. The only way to achieve that peculiar consensus was to obtain unanimity for the research process and the publication plan.

## 2.2 Systematic Literature review

This systematic literature review was an overview of all criteria describing multimorbidity in scientific publications. Its aim was to describe and summarize this literature[2]. After this first stage of collection it was important to ensure the quality and to classify those criteria. And finally to analyze them in order to produce a comprehensive definition of the concept of multimorbidity.

The systematic literature review was undertaken with a multilingual team representing 8 different nationalities (Belgian, French, German, Greek, Italian, Dutch, Polish and Spanish). The collective linguistic ability of the team enabled the inclusion and interpretation of articles in various languages. The entire process was undertaken by groups of four different researchers, drawn from at least two different national teams. The review protocol strictly followed the preferred reporting items for systematic reviews and meta analyses (PRISMA) statement [3]. The PRISMA statement includes the rationale of the study, the objectives, the eligibility criteria, the studies' characteristics, the sources' information, the selection of process, the data extraction, the methods to assess bias and a discussion on strengths and limitations. Because of the comprehensiveness and completeness of the subject, adaptation of the method was managed and is described below[4][5].

As multimorbidity first came to prominence in the early 1990s, the team included articles published between 01/01/1990 and 12/31/2010. The databases searched were Pubmed, Embase and Cochrane, those being the most frequently used medical databases. For the purpose of initial identification, the only keyword searched for was multimorbidity.

The complete list of the selected documents was divided into 8 sets. Each set of documents was analyzed for identification and screening by four separate researchers. Those researchers were working 'blind,' and were drawn from at least two national groups. They searched for the appearance of the term 'multimorbidity' within the abstract.

In selecting for eligibility, another group of four researchers, also working 'blind,' read each screened abstract and searched for explicit multimorbidity criteria.

A further group of four researchers (working 'blind') subsequently made the selection for inclusion by reading each article to look for explicit multimorbidity criteria stated within the article. Excluded articles were those that were concerned with animals; those that were not scientific (i.e. having no formal or informal IMRAD format) or those judged to be of poor quality. Quality appraisal was evaluated with two pro-forma, one for qualitative research and one for quantitative research. The pro-forma focused on the accuracy of the research question, the quality of the methodology, the coherence between results and discussion and whether the discussions were scientifically well reasoned.

Quality assessment grids were extracted from the journal exercer® and approved by the study's scientific committee. A total score of 28 points was allocated. Articles scoring below

14 were excluded. Differences of opinions were dealt with by discussion or by referral to the study's scientific committee.

For analysis entire articles were scanned for multimorbidity criteria data. Those articles were divided into eight sets. Each set of articles was analyzed by a group of four independent researchers, all English speaking or speakers of the language used in the article (at least 2 native speakers in each group). The analysis method was based on a phenomenological perspective[6][7], using a grounded theory framework with an open coding followed by an axial coding and finally a selective coding [8][9][10]. All criteria, all scales used and all definitions of multimorbidity were extracted from the articles with the open coding. The axial coding determined themes and sub-themes. Then five independent researchers from four national groups (French, German, Greek and Italian) undertook the selective coding. They successfully classified the extracted criteria, according to theme, and arrived at a definition using a thematic classification [11][12].

The final definition underwent one last qualitative appraisal, with the help of native English speaking researchers (three members of the Irish College of General Practitioners, one member of the Malta College of Family Doctors, two translators from the Brest Department of General Practice). The purpose of this final check was to ensure that every keyword in the definition was clear and that the phrasing of the definition was expressed in academic English.

### 2.3 Forward Backward translations using a Delphi Consensus method

The aim of those translations was to maintain homogeneity throughout European languages. This was an important issue to achieve. In medicine most translations are poorly managed. In most cases they do not incorporate any cultural background with the lack of consensus procedure with experts of the field leading to a change into the docimological qualities of the translated tools[13]. In addition for most translated tools the lack of forward backward translation method led to changes in meaning[14]. Maintaining homogeneity between translations needed a cautious and step by step method [15][16][17].

For all participating countries (Bosnia, Bulgaria, Croatia, France, Germany, Greece, Italy, Poland, Spain) the forward and backward translation of the original English definition has been assessed using a Delphi consensus procedure [18].

#### *Ethics Statement*

The study was approved by the ethic committee of the University de Bretagne Occidentale. The participants provided their written informed consent to participate in the study. The ethic committee approved the consent procedure.

#### *Research team*

First, a research team (including several medical researchers and official translators for each country) was asked to translate the definition from English into their native language. For Spain and Catalonia, a double-language team was used as Catalan is a regional language of Spain.

### *Participant selection*

The next stage was to send the English multimorbidity definition and its native translation by email to a group of at least 10 and, if possible, 30 national expert FPs. Those changes in the sample size were due to the limited number of such experts in small countries and the need to have a larger purposive sample, if possible, allowing a less tentative interpretation of results. [19]. These expert FPs had to be known as English-speaking and to be involved in research or teaching activities. Each participant was contacted separately using emails to avoid contamination, according to the methodology for Delphi procedure [20].

### *Data collection*

From May 2012 to December 2012 all experts were then asked to assess the equivalence of the translations on a scale from 1 (absolutely no agreement) to 9 (full agreement) and had to write down their remarks and opinions for each ranked below 7. Consensus was defined as at least 70 % of the participants rating the consensual definition at 7 or above. This process, called a Delphi round, had to go on until a consensus was achieved. Between each round all discordances had to be taken into account. All suggestions and remarks made by the experts were incorporated into the translation with the objective of defining a new version for the next round. Once the consensual definition in the native language had been established, two other translators did a backward translation from the native language into English.

### *Data Analysis*

Those English consensual back translations had to be examined in order to ensure their semantic and conceptual homogeneity by the study's scientific committee (4 professors of Family Medicine, one associate professor in public health and one associate professor in

Family Medicine drawn from Belgium, France and The Netherlands). Changes could be instigated at that point, depending on the advice of the scientific committee.

To ensure cultural homogeneity, they were then analysed by the research group by employing a cultural check [13][21]. It was an iterative procedure including a physical meeting in May 2013 during the EGPRN meeting in Kusadasi (Turkey) and exchanges by e-mail before and after the meeting to prepare data and validate the results. The group was composed of all team leaders and an English linguist from the university of Torun (Poland). The cultural check needed to take into account that some language conventions (affirmative or passive voice, for example) could express the same meaning within two languages. It had to be very cautious about:

- The control of the study quality within the complete follow-up to the research process which was confirmed by the national team's leaders and the scientific committee of the study
- The decision to look carefully at changes in meaning and especially at concepts within the translations using tables to help comparison between translations
- The control of the quality of each final translation as the expression of all the concepts in the original language, using tables to record discordances and each participant's comment.
- The synthesis of all the translations in order to compare them. Their presentation to the research group used tables for all translations, all changes and all comments.

Depending on the result of the cultural check, some changes in the definition's phrasing were undertaken to ensure homogeneity within the definitions. Then all final translations and their backward translations had to be sent for agreement to the study's scientific committee.

The final aim was to achieve homogeneous translations of the definition of the concept of multimorbidity into the languages of all teams to be able to use those translations as the heart of a critical theory method.

## 2.4 Qualitative surveys

As the research was looking at what FPs could think about the developed concept of multimorbidity a critical theory paradigm appears to be the best possible research perspective [22]. Data collection techniques were using interviews and focus groups. Interviews were used in order to find a more intimate perspective [23] and to complete the group effect perspective of focus groups [24][25]. The guide used for both data collection techniques were even going intimately inside the FPs' thoughts asking them how they were "feeling" multimorbid patients. The objective was to go deeply into their consultation skills in order to have the broadest possible point of view from FPs.

The study was a set of 13 qualitative surveys involving 7 European countries (Bulgaria, Croatia, France, Germany, Greece, Italy and Poland). France as the pilot team performed 6 surveys, Germany 2 and the other countries 1. The samples in each country and in each study were built to achieve maximal variation on age, gender, experience, practice type and practice setting for practicing FPs.

The data analysis technique was based on grounded theory with an open coding followed by an axial coding and a selective coding [10]. For each study a pair of national researchers analyzed the data blind with a merging of results at the end of the open coding and another at the end of the axial coding. When all countries completed the axial coding they had to translate one to three verbatim for each axial codes to explicit them.

Those translations were used to achieve the international codebook during the EGPRN

meeting in Malta (October 2013). The international codebook was designed while comparing the qualitative axial codes obtained with the criteria of the definition of the concept of multimorbidity. If some axial codes would not be comparable to the criteria of the concept of multimorbidity they would define the added value of FPs to it.

Then each national team applied the international coding book to all coding process with two pairs of two researchers (one pair from the pilot team and one pair from the national team) working blind. This was undertaken to ensure the completeness and the consistency of the coding process. The quality of the whole data was checked with a manual check of the coherence between the native verbatim and the open coding. A selective coding was consecutively proposed by the pilot team to all national teams. That selective coding was finally validated with a physical meeting during the EGPRN meeting in Barcelona (May 2014).

A final step was undertaken to ensure the internationalization of coding. An axial code founded by at least 5 countries on 7 would be considered as international to achieve a 70 % consensus as in a Delphi consensus procedure[20]. An axial code founded by 4 or less countries would be considered as national specific.

The final aim of those studies was to ensure that FPs recognize the developed definition of the concept of multimorbidity in their practice. It was also to check if they would add some themes or criteria to that concept.

## 2.5 Nominal group consensus survey

The aim of this step was to establish a research agenda about the concept of multimorbidity in family medicine. A nominal group technique was chosen to fulfil that aim[26].

Nominal group technique was a consensus technique that is easy to undertake with a group meeting or by mail [27]. It is a well known technique that was already used by members of



the research group[28]. With an international group it needed an adaptation to be completed and an email system was used as it was already developed in several studies [29][30][31].

An international panel of experts in the field of multimorbidity was convened. The group was selected from three organizations: the EGPRN, the Threads and Yarns network members, and some professors in Multimorbidity coming from Dutch and English Universities. The group was made of clinicians, researchers, methodologists and epidemiologists. Some individuals could be involved in two different groups, while a number were not.

Firstly they were asked to read the publications about the concept of Multimorbidity issued from this thesis (protocol, systematic review and qualitative surveys). Second they were asked to send a maximum of five propositions of research themes issued from that definition with a commentary for each. Third all propositions were sorted out with their commentaries and classified to sort out duplicates. Duplicates commentaries were summarized and send back to designers to verify the congruence with their initial wills. If needed corrections to the commentaries were achieved. Fourthly all propositions with their commentaries were sent back to all participants for analysis and ranking. Open discussions by mail were possible if needed between members to have clarifications on the submitted propositions. Then all participants were asked to rank the proposition regarding their first their interest for family medicine research and their feasibility.

The research agenda for further research about the developed concept of multimorbidity of this thesis was then achieved.

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# Chapter 3

**A research group from the European General Practice Research Network (EGPRN) explores the concept of Multimorbidity for further research into Long Term Care.**

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The concept of multimorbidity was first published in 1976 [1] in Germany and remained almost entirely restricted to German publications for 14 years. Between 1976 and 1990 only

72 articles had multimorbidity in their text of which 66 were written in German. In 1990 the concept began its internationalization through research [2]. It was an addition to the concept of comorbidity. Comorbidity was defined as any disease or risk factors that could interact with one main disease with the effect of making it worse [3][4][5]. Multimorbidity has been defined by the World Health Organisation (WHO) as people being affected by two or more chronic conditions [6]. The intention of WHO was to look at all conditions in one individual that could impact on that individual's global health status. However the word "condition" was not sufficiently clear for practical purposes (for instance, whether hypertension which is medicated may be considered a 'condition' in this sense) and could lead to numerous interpretations.

Multimorbidity is a very interesting and challenging concept for Family Medicine and for Long Term Care given the increasing prevalence of chronic illness in an ageing population across Europe and all developed countries. It is closely related to a global or comprehensive vision of the patient, which is a core competency of Family Medicine as defined, for instance, by the World Organization of National Colleges, Academies and Academic Associations of Family Physicians (WONCA) [7]. Multimorbidity is a global *functional* patient centered view that could help modeling and restructuring health care with a view to provide greater support for the patient: a new health care challenge. [8]. It is also a very interesting concept when applied to patients as it gives an overview of all the factors that could lead to frailty [9][10]. Frailty is a new concept formulated to help physicians to identify decompensating patients especially in Long Term Care. Its link with multimorbidity has already been discussed [11].

The European General Practice Research Network (EGPRN) is committed to concepts that could advance research in primary care throughout Europe. It has defined a research agenda

especially designed for methodological and instrumental research with development of primary care epidemiology respect to patient oriented health[12]. A clear definition of the concept of multimorbidity (*ie* understandable and usable for further collaborative epidemiologic research) is an important aim for such a network. It will help researchers in Family medicine investigate the complexity of patients' conditions and their overall impact on patient health. This definition of multimorbidity could be an additional tool for practicing Family Physicians (FPs) working to identify frail patients with the intention of preventing decompensation.

A research team including 8 European national research groups all active within EGPRN has created a research community in order to clarify the multimorbidity concept for family medicine throughout Europe. Their first hypothesis was that academic researchers should have defined what constituted a multimorbid patient within their research using clear inclusion criteria, and that a review of the scientific literature could then lead the way to a clearer definition. Their second hypothesis was that FPs could use a concept of multimorbidity that differs from those of other specialists. They are justified in doing so because they appear to be more in line with the patient's expectations about chronic illnesses like depression [13]. Qualitative research throughout Europe could then lead to the identification of new concepts of multimorbidity. Their third hypothesis was that current databases in family medicine were not designed to record multimorbidity and that a new ICPC code or code combination [14] should be established for the implementation of multimorbidity in databases. These databases could then lead to quantitative research into multimorbidity and especially its links with frailty. Quality assessment in family medicine with regards to Long Term Care will be one final task for the research team now that the link between quality assessment in family medicine and multimorbidity is being highlighted [15].

A step-by-step methodology was and will be used by the EGPRN research team:

The constitution of a multinational research team, which emerged from the EGPRN, started in Zurich (Switzerland) during the EGPRN meeting in October 2010. It was composed of researchers from Belgium (University of Antwerp), France (University of Brest), Germany (University of Hannover and Gottingen), Greece (Association of Greek GPs- ELEGEIA), Italy (Association of Italian GPs), Poland (University of Torun), Spain (University of Barcelona and Vigo) and The Netherlands (Free University of Amsterdam). In October 2011 during the EGPRN meeting in Krakow (Poland) researchers from Bosnia (University of Sarajevo) and Croatia (University of Zagreb) joined the team. They were followed during the EGPRN meeting in Spring 2012 in Ljubljana (Slovenia) by researchers from Bulgaria (University of Plovdiv).

To achieve the research goals the European team will undertake the following tasks in succession:

A systematic review of relevant literature according to the PRISMA Guidelines for systematic review [16]. The research question will be: “what are the definitions of and criteria for multimorbidity found in scientific medical literature?» The outcome of the first part of the research will be the emergence of an exhaustive definition of multimorbidity drawn from scientific literature.

A translation of that exhaustive definition into all the languages represented within the team, with a forward backward translation using a Delphi procedure [17].

A Qualitative research throughout Europe, using semi structured interviews and focus groups, to find the added value by FPs in the concept of multimorbidity. Analysis of



the data will be undertaken in two ways: a grounded theory analysis and a deductive analysis from the translated definition of Multimorbidity.

Then an ICPC code will be put forward to the ICPC committee of the WONCA for further implementation into databases.

These implementations will then be used for further epidemiological collaborative research throughout Europe. Which, in turn, will guide the international research team in the design of further studies to investigate the links between multimorbidity and frailty. At this stage the research team will test the usefulness of multimorbidity as a quality assessment tool in medical decision making for frail patients. Multimorbidity will then be able to help European researchers and medical teams modeling and restructuring health care centered on the patients who use it.

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# Chapter 4

**The European General Practice Research Network presents a comprehensive definition of Multimorbidity in Family Medicine and Long-Term Care, following a systematic review of relevant literature.**

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**Abstract:**

Background: Multimorbidity is a new concept encompassing all the medical conditions of an individual patient. The concept links into the European definition of Family Medicine and its core competencies. However, the definition of multimorbidity and its subsequent operationalization are still unclear. The European General Practice Research Network (EGPRN) wanted to produce a comprehensive definition of multimorbidity.

Method: Systematic review of literature involving eight EGPRN national teams. The databases searched were Pubmed, Embase and Cochrane (1990-2010). Only articles containing descriptions of multimorbidity criteria were selected for inclusion. The multi-national team undertook a methodic data extraction, according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.

Results: The team identified 416 documents, selected 68 abstracts, included 54 articles and found 132 definitions with 1631 different criteria. These criteria were aggregated into 11 themes which led to the following definition: Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor. Any bio-psychosocial factor, any risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of multimorbidity). Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.

Conclusion: This study has produced a comprehensive definition of multimorbidity. The resulting improvements in the management of multimorbidity, and its usefulness in Long-Term Care and in Family Medicine, will have to be assessed in future studies.

## **Introduction:**

The concept of multimorbidity was first published in 1976 [1] in Germany and remained almost entirely restricted to German publications for 14 years. Between 1976 and 1990 only 72 articles used the term multimorbidity in their text, of which 66 were written in German. In 1990 the concept became internationally recognized through research [2].

The concept of multimorbidity was an addition to the concept of comorbidity. Comorbidity was defined as any disease or risk factors that could interact with one main disease with the effect of making it worse [3][4][5]. Multimorbidity has been defined by the World Health Organisation (WHO) as people being affected by two or more chronic health conditions [6]. The intention of the WHO was to look at all conditions in one individual that could impact on that individual's global health status. However the word 'condition' is not sufficiently clear for practical purposes (for instance, whether a treated disease is a 'condition' in this sense), and could lead to numerous interpretations.

Multimorbidity is a very interesting and challenging concept particularly for Family Medicine and Long-Term Care, given the increasing prevalence of chronic illness in an aging population across Europe and all developed countries. It is closely related to a global or comprehensive view of the patient, which is a core competency of Family Medicine, as defined for instance by the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) [7]. It is a global 'functional' view (useful for Long-Term Care) versus a 'disease' centered point of

view (useful for acute care) [8]. It is also a very interesting concept, when applied to patients, as it gives a global overview of all the factors that could lead to frailty [9][10]. Frailty is a new concept, formulated to help physicians identify decompensating patients. Its link with multimorbidity has already been discussed [11].

The European General Practice Research Network (EGPRN) is committed to concepts that could advance research in primary care throughout Europe. The EGPRN has created a research agenda specifically designed for methodological and instrumental research, which includes the development of primary care epidemiology, focusing on patient-centered health [12]. A clear definition of the concept of multimorbidity (ie one which is both understandable and usable for further collaborative research) is an important objective for a research network of this type. It will help researchers in Family Medicine to investigate the complexity of patients' conditions and their overall impact on patients' health. This definition of multimorbidity could be an additional tool for Family Physicians (FPs), enabling them to identify frail patients and prevent decompensation. However the word 'conditions,' according to the WHO's multimorbidity definition, needs clarification in order to be of use in practice and research.

A research team, including 8 national groups, all active within the EGPRN, has created a research community for the purpose of clarifying the concept of multimorbidity for Family Medicine and Long-Term Care throughout Europe [13]. The team assumed that academic researchers had already formulated clear inclusion criteria for the multimorbid patient within their research. Therefore a review of relevant scientific literature could pave the way to one



comprehensive definition. An initial review, presented in an EGPRN meeting in spring 2011 [14], identified more than one hundred different definitions used by academic researchers. Such a large number of definitions added more confusion than clarification to the discussion and led the group to the research question for this study: what are the criteria for multimorbidity found in scientific medical literature and what definition could be produced with these criteria?

**Method:**

The method adopted was a systematic literature review with a multilingual team representing 8 different nationalities (Belgian, French, German, Greek, Italian, Dutch, Polish and Spanish). The collective linguistic ability of the team enabled the inclusion and interpretation of articles in various languages. The entire process was undertaken by groups of four different researchers, drawn from at least two different national teams. The review protocol, following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [15], is available on demand.

As multimorbidity first came to prominence in the early 1990s, the team included articles published between 01/01/1990 and 12/31/2010. The databases searched were Pubmed, Embase and Cochrane, those being the most frequently used medical databases. For the purpose of initial identification, the only keyword searched for was multimorbidity. The complete list of the selected documents was divided into 8 sets. Each set of documents was analyzed for identification and screening by four separate researchers. Those researchers were working ‘blind,’ and were drawn from at least two national groups. They searched for the appearance of the term ‘multimorbidity’ within the abstract. In selecting for eligibility, another group of four researchers, also working ‘blind,’ read each screened abstract and searched for explicit multimorbidity criteria. A further group of four researchers (working ‘blind’) subsequently selected for inclusion by reading each article to look for explicit multimorbidity criteria stated within the article. Excluded articles were those which were concerned with animals; those which were not scientific (i.e. having no formal or informal Introduction, Method, Results And Discussion (IMRAD) format) or those judged to be of poor quality. Quality appraisal was evaluated with two proforma, one for qualitative research and one for quantitative research. The proforma focused on the accuracy of the research

question, the quality of the methodology, the coherence between results and discussion and whether the discussion were scientifically well reasoned. Quality assessment grids were extracted from the journal *exercer*® and approved by the study's scientific committee. A total score of 28 points was allocated. Articles scoring below 14 were excluded. Differences of opinions were dealt with by discussion or by referral to the study's scientific committee.

For analysis entire articles were scanned for multimorbidity criteria data. Those articles were divided into eight sets. Each set of articles was analyzed by a group of four independent researchers, all English speaking or speakers of the language used in the article (at least 2 native speakers in each group). The analysis method was based on a phenomenological perspective, using a grounded theory framework with an open coding followed by an axial coding and finally a selective coding. All criteria, all scales employed and all definitions of multimorbidity were extracted from the articles with the open coding. The axial coding determined themes and sub-themes. Then the selective coding was undertaken by five independent researchers from four national groups (French, German, Greek and Italian). They successfully classified the extracted criteria, according to theme, and arrived at a definition using a thematic classification.

The final definition was subjected to one last qualitative appraisal, with the help of native English speaking researchers (three members of the Irish College of General Practitioners, one member of the Malta College of Family Doctors, two translators from the Brest Department of General Practice). The purpose of this final check was to ensure that every keyword in the definition was clear and that the phrasing of the definition was expressed in academic English.

## Results

Identification, screening, eligibility and inclusion processes are shown in figure 1.

Figure 1

### Identification

365 in Pubmed® (35 specific, 330 duplicates)  
381 in Embase® (51 specific, 330 duplicates)  
Only duplicates in Cochrane  
No additional sources

### Screening

Number of records screened  
(After duplicates removal):  
416

Number of records  
excluded: 348

### Eligibility

Number of full text articles  
assessed for eligibility:  
68

Number of Full text  
articles excluded:  
14  
(Reasons below)

### Inclusion

Articles included in  
qualitative  
synthesis: 54

Eligible articles are shown in table 1 with their study type.

**Table 1:** Eligible articles with type of included and excluded studies.

<b>Study type (n=68)</b>	<b>Included</b>	<b>Excluded</b>
<b>Editorial</b>	0	5
<b>Peer review</b>	0	1
<b>Review</b>	4	0
<b>Cross sectional</b>	28	4
<b>Cohort</b>	16	0
<b>Case control</b>	3	3
<b>Qualitative</b>	3	0
<b>Not found</b>	0	1
<b>Total</b>	54	14

One article was not found, despite the help of three different university libraries. Of the thirteen other excluded articles, four were editorials with no exclusion/inclusion criteria, seven were using multimorbidity without a clear description, and two were excluded on the basis of poor quality (i.e. the average score awarded by the four researchers was below 14 out of 28).

**Table 2:** Included articles list (n=54). [11, 16–68]

Title of article	Year	Journal
Multimorbidity in old age <sup>(16)</sup>	1995	Die Medizinische Welt
Morbidity and health-related quality of life among ambulant elderly citizens <sup>(17)</sup>	1997	Aging (Milano)
Depression in the very elderly <sup>(18)</sup>	1998	Nervenarzt
Influencing factors and results of geriatric rehabilitation treatment - Einflussfaktoren Und Ergebnisse Geriatrischer Rehabilitation <sup>(19)</sup>	1998	Geriatric Forschung
The influence of multimorbidity and old age on geriatric rehabilitation <sup>(20)</sup>	1999	Geriatric Forschung
Marginal impact of psychosocial factors on multimorbidity: results of an explorative nested case-control study <sup>(21)</sup>	2000	Social Science & Medicine
Utilization of medical services and medication intake of patients over 60 in Germany-- health related, social structure related, socio-demographic and subjective factors <sup>(22)</sup>	2000	Zeitschrift für Gerontologie und Geriatric
Psychosocial patient characteristics and GP-registered chronic morbidity: a prospective study <sup>(23)</sup>	2001	Journal of Psychosomatic Research
The distribution of psychiatric and somatic III health: associations with personality and socioeconomic status <sup>(24)</sup>	2001	Psychosomatic Medicine
Multimorbidity of psychiatric disorders as an indicator of clinical severity <sup>(25)</sup>	2002	European Archives of Psychiatry and Clinical Neuroscience
Patterns and impact of comorbidity and multimorbidity among community-resident American Indian elders <sup>(26)</sup>	2003	The Gerontologist
Multimorbidity is common to family practice: is it commonly researched? <sup>(27)</sup>	2005	Canadian Family Physician
Collaborative care needs and preferences of primary care patients with multimorbidity <sup>(28)</sup>	2005	Health Expectations
Comparative assessment of three different indices of multimorbidity for studies on health-related quality of life <sup>(29)</sup>	2005	Health and Quality of Life Outcomes
Single index of multimorbidity did Not predict multiple outcomes <sup>(30)</sup>	2005	Journal of Clinical Epidemiology
Prevalence of multimorbidity among adults seen in family practice. <sup>(31)</sup>	2005	Annals of Family Medicine
In an exploratory prospective study on multimorbidity general and disease-related susceptibility could be distinguished <sup>(32)</sup>	2006	Journal of Clinical Epidemiology
Psychiatric morbidity is related to a chain of prenatal and perinatal adversities <sup>(33)</sup>	2006	Early Human Development
Overlap of clusters of psychiatric symptoms among clients of a comprehensive addiction treatment service <sup>(34)</sup>	2006	Psychology of Addictive Behaviors
Relationship between multimorbidity and health-related quality of life of patients in primary care <sup>(35)</sup>	2006	Quality of Life Research
Psychological distress and multimorbidity in primary care <sup>(36)</sup>	2006	Annals of Family Medicine
Clinical multimorbidity and physical function in older adults: a record and health status linkage study in general practice <sup>(37)</sup>	2007	Family Practice
The combined effect of visual impairment and cognitive impairment on disability in older people <sup>(38)</sup>	2007	Journal of the American Geriatrics Society

The challenges of multimorbidity from the patient perspective <sup>(39)</sup>	2007	Journal of General Internal Medicine
Subjective health and illness, coping and life satisfaction in an 80-year-old Swedish population-implications for mortality <sup>(40)</sup>	2007	International Journal of behavioral medicine
Multimorbidity is associated with better quality of care among vulnerable elders <sup>(41)</sup>	2007	Medical Care
Setting and registry characteristics affect the prevalence and nature of multimorbidity in the elderly <sup>(42)</sup>	2008	Journal of Clinical Epidemiology
Relationship between multimorbidity and physical activity: secondary analysis from the Quebec health survey <sup>(43)</sup>	2008	BioMed Central Public Health
Prevalence and patterns of multimorbidity in Australia <sup>(44)</sup>	2008	The Medical Journal of Australia
Multimorbidity and risk among patients with established cardiovascular disease: a cohort study <sup>(45)</sup>	2008	The British Journal of General Practice
Co- and multimorbidity patterns in primary care based on episodes of care: results from the German CONTENT project <sup>(46)</sup>	2008	BioMed Central Health Services Research
Weighted multimorbidity indexes predicted mortality, health service use, and health-related quality of life in older women <sup>(47)</sup>	2008	Journal of Clinical Epidemiology
Total lymphocyte count and in-hospital mortality in older persons with multimorbidity <sup>(48)</sup>	2008	Aging Clinical and Experimental Research
The impact of education on risk factors and the occurrence of multimorbidity in the EPIC-Heidelberg cohort <sup>(49)</sup>	2008	BioMed Central Public Health
Does age modify the relationship between morbidity severity and physical health in English and Dutch family practice populations? <sup>(50)</sup>	2009	Quality of Life Research
The impact of chronic multimorbidity and disability on functional decline and survival in elderly persons. A community-based, longitudinal study <sup>(51)</sup>	2009	Journal of internal medicine
Seniors' self-reported multimorbidity captured biopsychosocial factors not incorporated into two other data-based morbidity measures <sup>(52)</sup>	2009	Journal of Clinical Epidemiology
Patterns of chronic multimorbidity in the elderly population <sup>(53)</sup>	2009	Journal of the American Geriatrics Society
Multimorbidity: prevalence, effect on quality of life and daily functioning, and variation of this effect when one condition is a rheumatic disease <sup>(54)</sup>	2009	Seminars in Arthritis & Rheumatism
Multimorbidity and health-related quality of life among elderly persons <sup>(55)</sup>	2009	Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz
Analysis of multimorbidity in individual elderly nursing home residents. Development of a multimorbidity matrix <sup>(56)</sup>	2009	Archives of Gerontology and Geriatrics
Self-care and depression in patients with chronic heart failure <sup>(57)</sup>	2009	Heart and Lung: Journal of Acute and Critical Care
Defining comorbidity: Implications for understanding health and health services <sup>(58)</sup>	2009	Annals of Family Medicine
Prevalence estimates of multimorbidity: a comparative study of two sources <sup>(59)</sup>	2010	BioMed Central Health Services Research
Multimorbidity - Not just an older person's issue. Results from an Australian biomedical study <sup>(60)</sup>	2010	BioMed Central Public Health
GPs' and pharmacists' experiences of managing multimorbidity: a 'Pandora's box' <sup>(61)</sup>	2010	The British Journal of General Practice
Clustering of psychiatric and somatic illnesses in the general population: Multimorbidity and socioeconomic correlates <sup>(62)</sup>	2010	Brazilian Journal of Medical and Biological Research
Co-occurring medical, psychiatric, and alcohol-related disorders among veterans returning from Iraq and Afghanistan <sup>(63)</sup>	2010	Psychosomatics

Relationship between health-related quality of life and multimorbidity - Gesundheitsbezogene Lebensqualität bei Multimorbidität <sup>(64)</sup>	2010	Das Gesundheitswesen Bundesverband der Ärzte des Öffentlichen Gesundheitsdienstes
The Measurement of Multiple Chronic Diseases--A Systematic Review on Existing Multimorbidity Indices <sup>(65)</sup>	2010	The Journals of Gerontology. Series A, Biological sciences and medical sciences
Influence of multimorbidity on cognition in a normal aging population: a 12-year follow-up in the Maastricht Aging Study <sup>(66)</sup>	2010	International Journal of Geriatric Psychiatry
An 'endless struggle': a qualitative study of general practitioners' and practice nurses' experiences of managing multimorbidity in socio-economically deprived areas of Scotland <sup>(67)</sup>	2010	Chronic Illness
Determinants of frailty <sup>(11)</sup>	2010	Journal of the American Medical Directors Association
Multimorbidity and its relation to subjective memory complaints in a large general population of older adults <sup>(68)</sup>	2010	International Psychogeriatrics

Data extraction found 132 different definitions, as well as 241 lists, classifications, scales or indexes used to evaluate multimorbidity. These, in turn, included 1631 different criteria. Definitions ranged from very simple (ie comorbidity) to very complex (*overall impact of the different diseases in an individual, taking into account their severity and other health-related attributes or non-health-related individual attributes*). Criteria were grouped into 11 themes: chronic disease, acute disease, bio-psychosocial factors and somatic risk factors, coping strategies of the patient, burden of disease, health care consumption, disability, quality of life, frailty, social network, health outcome.

**Table 3:** Themes and sub themes identified for Multimorbidity conditions



## Themes

## Sub themes

Chronic disease	<ul style="list-style-type: none"> <li>• Chronic condition</li> <li>• Chronic diseases</li> <li>• Psycho-somatic diseases/psychical Implications</li> <li>• Complexity characteristics of chronic disease</li> </ul>
Acute disease	<ul style="list-style-type: none"> <li>• Acute conditions</li> <li>• Acute disease</li> <li>• Reaction to severe stress and adjustment disorders</li> <li>• Complexity characteristics of acute disease</li> </ul>
Bio psycho social factors and somatic risk factors	<ul style="list-style-type: none"> <li>• Somatic risk factors</li> <li>• Psychological risk factors</li> <li>• Psycho-social risk factors</li> <li>• Lifestyle</li> <li>• Demography: age, sex...</li> <li>• Psychological distress</li> <li>• Socio-demographic characteristics</li> <li>• Aging</li> <li>• Patients beliefs /expectations</li> <li>• Physiology</li> <li>• Physiopathology</li> </ul>
Coping	<ul style="list-style-type: none"> <li>• Patients coping strategies</li> </ul>
Burden of diseases	<ul style="list-style-type: none"> <li>• Disease complication</li> </ul>

Health care  
consumption

- Disease morbidity
- Use of carers
- Treatment or medication
- Management
- Disease management
- Medical procedure
- Malpractice
- Healthcare services
- Healthcare
- Healthcare policy
- Medical history
- Family history
- Assessment
- Prevention
- Pain
- Health services / setting / treatment
- Symptoms/signs/complaints
- Cost of care
- Poly-pharmacy

Disability

- Handicap
- Functional impairments

Quality of life

- Quality of life

	<ul style="list-style-type: none"> <li>• Health status</li> <li>• Impairment</li> <li>• Morbidity implications</li> </ul>
Frailty	<ul style="list-style-type: none"> <li>• Frailty</li> </ul>
Social network	<ul style="list-style-type: none"> <li>• Social network</li> </ul>
Health outcomes	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Indicator</li> <li>• Outcome</li> <li>• Medical research epidemiology / Instruments / Level of multimorbidity</li> <li>• Classification of morbidity statistics</li> </ul>

The working group organized these themes into one definition using an interactive and iterative process. The data revealed that the definition had to be divided in three sentences. The first sentence reveals the definition of Multimorbidity. The second sentence is indicative of possible modifiers of the burden of multimorbidity for Long-Term Care workers and

patients (i.e. apart from defining multimorbidity, they could also ease or increase the multimorbidity burden). The third sentence reveals the outcomes of Multimorbidity.

Then a final qualitative assessment was undertaken, with four native English speaking FPs (involved in academic research) and two English translators to check that all key words were understandable and that the final phrasing was in academic English. The following definition is the result of the complete process:

Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.

Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of Multimorbidity).

Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.

Finally, as a quality control check, the research team operated a forward-backward system to ensure consistency. They checked whether all the definitions and all the scales listed in the included articles to describe multimorbidity, could indeed be included within that definition. This final check was positive.

**Discussion:**

This study was undertaken in order to provide a comprehensive definition of multimorbidity which would be understandable and usable for further collaborative research. The research team selected a systematic review methodology. Data extraction and analysis were based on a phenomenological perspective, using a grounded theory framework. The multilingual team successfully classified the extracted criteria and arrived at a definition using a thematic classification.

There are several important issues to note about the definition:

Some of the concepts revealed in the definition were also in the WHO definition. The concept of the co-occurrence of chronic diseases is parallel to, or interchangeable with, the WHO concept of the co-occurrence of chronic conditions.

The research team anticipated some concepts found in this study:

The burden of disease appears on the Cumulative Illness Rating Scale (CIRS) [69] in spite of the fact that it is not in the WHO definition[6]. Indeed mild asthma, with less than one attack a year, does not seem too complicated to handle whereas very aggressive genetic gout, with extensive joint destruction, is a far greater cause for concern.

The health care consumption was also predictable, as it makes sense to look at cost and patient uptake.

The health outcomes are less obvious but just as important as the conditions leading to them.

Frailty, increased disability or a reduction in quality of life are the consequences of multimorbidity. These are the factors which make FPs aware of multimorbidity in many patients.

However, some of the concepts were not anticipated by the research team:

The WHO definition was limited to two or more chronic conditions in one individual [6]. The data identified in our review used acute disease to define multimorbid patients. It seems logical to concentrate on acute disease that may lead to chronic conditions in the patient, such as when myocardial infarction leads to chronic cardiac ischemia [65]. However, purely acute disease, such as infectious diseases [50] or surgical abdominal pathologies [65] were also included by researchers themselves, or through the use of classifications such as the International Classification of Primary Care (ICPC).

Somatic risk factors were also included in the term ‘conditions’ by researchers. Somatic risk factors are not illnesses and were not anticipated by the research team. However, it is pragmatic for FPs or other Long-Term Care physicians to take them into account when considering the management of their patients.

The bio-psychosocial model [70] posits that biological, psychological (encompassing thoughts, emotions, and behaviors), and social factors, all play a significant role in human functioning in the context of disease or illness. This model is promoted as an appropriate model for Family Medicine but its importance, in this instance, was not anticipated by the team.

The social network of the patient was included as a modifier to cope with multimorbidity. It is apparent that FPs should take into account the patient’s social network (family, friends, relatives) to help the patient adapt his lifestyle to the situation.

Also included were the coping strategies of the patient. Coping strategies were differentiated from social networks and the bio-psychosocial model because the patients' coping strategies were sometimes described independently of these factors in the articles examined.

The purposes of a standardized and reproducible definition of multimorbidity are numerous. A more comprehensive definition leads to better focused research, especially for quality of care and cost of care. This is of importance in developed countries where a larger proportion of the population is elderly. This comprehensive definition is helpful for targeting resources in a far more accurate way than the WHO definition. In addition it gives more focused prognoses for individuals and improves risk management. It improves clinical decision making, in terms of risk/benefit evaluation. It could help decision-making when considering the position of an individual on the spectrum of palliative versus aggressive care.

The 21-year time span applied to the sourcing of documents could be seen as a limitation although it should be noted that multimorbidity is rarely described before that period [2]. The selection process was very broad in order to avoid losing information. The three main medical databases were screened in order to avoid any information bias. The use of the single keyword multimorbidity provided a protection against conflation with related terms such as “comorbidity, morbidity, multiple morbidity...”, as it was felt that the literature around those terms was already diverse. However the search was less comprehensive than one encompassing all synonyms of multimorbidity. There was a voluntary selection bias (looking only at medical databases) as the object was to find a pre-existing model (ie multimorbidity) in medical studies.

**Conclusion:**

This definition is intended to help researchers who are studying the inclusion/exclusion process in the detection of multimorbid patients. This definition is also intended to help FPs to identify multimorbid patients. The effect modifiers direct FPs, or other Long-Term Care Physicians, towards the tools to help these patients. It provides new opportunities, where medical management is optimal, to lower the burden of multimorbidity. This definition brings into focus the possible outcomes of multimorbidity (health outcomes, disability, quality of life, frailty) to keep physicians alert to those patients' needs. It also provides information for managers and policy-makers, equipping them to make a better evaluation of the global burden of multimorbidity in aging societies, as found in developed countries.

However it is still not known whether this could be useful for Family Medicine and Long-Term Care. In the next stage of this research, as described in JAMDA [13], the team will translate the definition into each of the languages of the national groups participating, and operationalize its various sub-terms, such as 'bio-psychosocial factor' or the 'social network'. This step is on-going, with a forward-backward translation, based on a Delphi procedure [71][72]. Following this, the team will be able to do qualitative research, using that definition as a deductive model. FPs will be interviewed (using semi-structured interviews and focus groups) to ensure the definition is clear and useful for Family Medicine. It is anticipated that those studies will be completed by winter 2012. The research group will record that definition on primary care databases to calculate its internal validity (consistency, reproducibility and feasibility). However, current databases in Family Medicine are not designed to record multimorbidity. When this has been achieved, a new ICPC [73] code or code combination, or an International Resident Assessment Instrument (interRAI) [74], must



be established for the implementation of multimorbidity. With this new coding or coding combination, quantitative research into multimorbidity and, in particular, its links with frailty, will take place. Quality assessment in Family Medicine, with regard to Long-Term Care, will be one final task for the research team, now that the link between quality assessment in Family Medicine and multimorbidity is being highlighted[75].

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# Chapter 5

## **The European General Practice Research Network presents the translations of its comprehensive definition of Multimorbidity in Family Medicine in ten European languages.**

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**Abstract:**

Background: Multimorbidity, according to the World Health Organization, exists when there are two or more chronic conditions in one patient. This definition seems inaccurate for the holistic approach to Family Medicine (FM) and long-term care. To avoid this pitfall the European General Practitioners Research Network (EGPRN) designed a comprehensive definition of multimorbidity using a systematic literature review.

Objective: To translate that English definition into European languages and to validate the semantic, conceptual and cultural homogeneity of the translations for further research.

Method: Forward translation of the EGPRN's definition of multimorbidity followed by a Delphi consensus procedure assessment, a backward translation and a cultural check with all teams to ensure the homogeneity of the translations in their national context. Consensus was defined as 70 % of the scores being higher than 6. Delphi rounds were repeated in each country until a consensus was reached

Results: 229 European medical expert FPs participated in the study. Ten consensual translations of the EGPRN comprehensive definition of multimorbidity were achieved.

Conclusion: A comprehensive definition of multimorbidity is now available in English and ten European languages for further collaborative research in FM and long-term care.

**Key words:** Geriatrics – Long-term care - Family Medicine- multimorbidity- linguistics – research.

**Introduction:**

The concept of multimorbidity was first published in 1976 [1] in Germany and remained almost entirely restricted to German publications for 14 years. Between 1976 and 1990 only 72 articles used the term multimorbidity in their text, of which 66 were written in German. In 1990 the concept became internationally recognized through research [2].

The concept of multimorbidity was an addition to the concept of comorbidity. Comorbidity was defined as any disease or risk factors that could interact with one main disease with the effect of making it worse [3][4][5]. Multimorbidity has been defined by the World Health Organisation (WHO) as people being affected by two or more chronic health conditions [6]. The intention of the WHO was to look at all conditions in one individual that could impact on that individual's global health status. However the word 'condition' was not sufficiently clear for practical purposes (for instance, whether a treated disease was a 'condition' in this sense), and could lead to numerous interpretations.

Multimorbidity is a very interesting and challenging concept particularly for Family Medicine and long term care, given the increasing prevalence of chronic illness in an aging population across all developed countries. It is closely related to a global or comprehensive view of the patient, which is a core competency of Family Medicine (FM), as defined for instance by the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) [7]. It is a global 'functional' view (useful for Long-Term Care) versus a 'disease' centered point of view (useful for acute care) [8]. It is also a very interesting concept, when applied to patients, as it gives a global overview of all the factors that could lead to frailty [9][10]. Frailty is a new concept, formulated to help physicians identify decompensating patients. Its link with multimorbidity has already been discussed [11] and a call to action for a consensus on Frailty has been formulated[12].

The European General Practice Research Network (EGPRN) is committed to concepts that could advance research in primary care throughout Europe. The EGPRN has created a research agenda specifically designed for methodological and instrumental research, which includes the development of primary care epidemiology, focusing on patient-centered health [13]. A clear definition of the concept of multimorbidity (ie one which is both understandable and usable for further collaborative research) is an important objective for a research network

of this type. It will help researchers in FM to investigate the complexity of patients' conditions and their overall impact on patients' health. This definition of multimorbidity could be an additional tool for Family Physicians (FPs), enabling them to identify frail patients and prevent decompensation.

A research team, including 9 national groups, all active within the EGPRN, has created a research community for the purpose of clarifying the concept of multimorbidity for FM throughout Europe [14]. An initial review, presented in an EGPRN meeting in spring 2011 [15], identified more than one hundred different definitions used by academic researchers. Such a large number of definitions added more confusion than clarification to the discussion and led the group to the production of a comprehensive definition of multimorbidity [16].

This definition had then to be translated into most European languages for use in further collaborative research. It has been previously demonstrated that translating definitions, index or scales is a risky task in medical science[17]. The challenge is to establish a cultural homogeneity between the translations in order to ensure a qualitative transfer of content and that task is as difficult in the medical sciences as it is in literature[18]. The purpose of this research was to translate the exhaustive definition of multimorbidity into ten European languages with the help of a multinational team, with the objective of maintaining a strong homogeneity across those translations.

### **Material and Methods:**

Maintaining homogeneity between translations needed a cautious and step by step method [19][20][21]. For all participating countries (Bosnia, Bulgaria, Croatia, France, Germany, Greece, Italy, Poland, Spain) the forward and backward translation of the original English definition has been assessed using a Delphi consensus procedure [22].

### *Ethics Statement*

The study was approved by the ethic committee of the University de Bretagne Occidentale. The participants provided their written informed consent to participate in the study. The ethic committee approved the consent procedure.

### *Research team*

First, a research team (including several medical researchers and official translators for each country) was asked to translate the definition from English into their native language. For Spain and Catalonia, a double-language team was used as Catalan is a regional language of Spain.

### *Participant selection*

The next stage was to send the English multimorbidity definition and its native translation by email to a group of at least 10 and, if possible, 30 national expert FPs. Those changes in the sample size were due to the limited number of such experts in small countries and the need to have a larger purposive sample, if possible, allowing a less tentative interpretation of results. [23]. Those expert FPs had to be known as English-speaking and to be involved in research or teaching activities. Each participant was contacted separately using emails to avoid contamination, according to the methodology for Delphi procedure [24].

### *Data collection*

From May 2012 to December 2012 all experts were then asked to assess the equivalence of the translations on a scale from 1 (absolutely no agreement) to 9 (full agreement) and had to write down their remarks and opinions for each ranked below 7. Consensus was defined as at least 70 % of the participants rating the consensual definition at 7 or above. This process, called a Delphi round, had to go on until a consensus was achieved. Between each round all discordances had to be taken into account. All suggestions and remarks made by the experts were incorporated into the translation with the objective of defining a new version for the next round. Once the consensual definition in the native language had been established, two other translators did a backward translation from the native language into English.

### *Data Analysis*

Those English consensual back translations had to be examined in order to ensure their semantic and conceptual homogeneity by the study's scientific committee (4 professors of Family Medicine, one associate professor in public health and one associate professor in Family Medicine drawn from Belgium, France and The Netherlands). Changes could be instigated at that point, depending on the advice of the scientific committee.

To ensure cultural homogeneity, they were then analysed by the research group by employing a cultural check [25][26]. It was an iterative procedure including a physical meeting in May 2013 during the EGPRN meeting in Kusadasi (Turkey) and exchanges by e-mail before and after the meeting to prepare data and validate the results. The group was composed of all team leaders and an English linguist from the university of Torun (Poland). The cultural check needed to take into account that some language conventions (affirmative or passive voice, for example) could express the same meaning within two languages. It had to be very cautious about:

- The control of the study quality within the complete follow-up to the research process which was confirmed by the national team's leaders and the scientific committee of the study
- The decision to look carefully at changes in meaning and especially at concepts within the translations using tables to help comparison between translations
- The control of the quality of each final translation as the expression of all the concepts in the original language, using tables to record discordances and each participant's comment.
- The synthesis of all the translations in order to compare them. Their presentation to the research group used tables for all translations, all changes and all comments.

Depending on the result of the cultural check, some changes in the definition's phrasing were undertaken to ensure homogeneity within the definitions. Then all final translations and their backward translations had to be sent for agreement to the study's scientific committee.

## **Results:**

### Sample

#### *Participants*

The nine teams in the different countries consisted of 12 to 30 members. In total there was a good gender distribution, having a mean age of 48 years and on average 18 years of practice experience. All team members had reasonable experience of English usage (spoken read and written). Their number of publications in English averaged 5,91. (See table 1).

Table 1: Expert Panel Characteristics

	COUNTRY	Gender		Average Age in years	Average years of practice	English Level			Average English publications	Other publications
	Total N=229	M	F			Read	Spoken	Written		
1	Bosnia N=14	5	9	43,29	16,71	All	All	All	2,79	8,43
2	Bulgaria N=30	11	19	47,03	21,8	All	All	All	0,27	1
3	Croatia N=23	3	20	50,13	23,43	All	All	All	14,57	51,3
4	France N=30	18	12	47,43	19,17	All	All	All	3,23	16,57
5	Germany N=30	21	9	56,46	18,97	All	All	All	1,5	6,37
6	Greece N=30	18	12	45,67	12,63	All	All	All	10,2	61,22
7	Italy N=30	19	11	50,7	24,17	All	All	All	4,38	19
8	Poland N=30	15	15	43,67	12,2	All	All	All	1,75	6,27
9	Spain N=12	8	4	48,33	22,58	All	All	All	15,33	6
Global Average		50,69 %	49,31 %	48,26	18,82	100%			5,91	20,45

### *Number of rounds*

Countries needed one to two Delphi rounds to achieve their translations. When two rounds were needed, it was mainly the result of experts' confusion. In those countries the experts thought they could discuss the definition itself. After a formal explanation of their task, the rounds were successful. Even where all the consensus scores were high, the lower they were, the more comments were expressed, as expected by this method. Comments were numerous expressing the richness of the exchanges.

Table 2: Number of Delphi Rounds and Number of Comments in Each Country

Country	Number of Delphi rounds	Mean consensus score for final Round	Number of score>6 as percentage	Total number of comments
Bosnia	2	7,8	100 %	27
Bulgaria	1	8,2	96,67 %	6
Croatia	1	8,5	100,00 %	7
France	2	7,4	80.00 %	63
Germany	2	7,8	81,00 %	23
Greece	1	8,3	100,00 %	6
Italy	1	7,6	80.00 %	18
Poland	1	7,56	83.33 %	9
Spain	1	7,08	75.00 %	12
Catalonia	1	7,25	75.00 %	12
Mean for Europe	1.3	7,895	96%	18,3

### Analysis

#### *Challenged terms*

The terms which were challenged the most within Europe during translation were:

- Social network
- Burden of disease
- Health care consumption
- Modifiers
- Health outcomes
- Frailty
- Biopsychosocial factors

Grammatical rewording suggestions were frequent. All comments were carefully recorded, even if consensus had been obtained, in order to help the cultural check.

#### *Backward translation*

Backward translations were finalized and sent to the original authors of the definition. The authors validated the translated definitions using the backward translations to check that there were no semantic or conceptual changes in comparison with the original English definition.

#### *Cultural check*

The final phase was the cultural check to ensure the transculturality and homogeneity of the translated definitions.

For Bosnia, the translated definition was not different with the original one despite the fact that the phrases often involved the inversion of subject and complement. Some articles were added to the original definition (“a chronic disease” instead of “chronic disease”) with a little more stress placed on the presence of one chronic disease in a multimorbid patient. The group concluded that there was no change in meaning.

For Bulgaria, some articles were added to the original translation (“a chronic disease” instead of “chronic disease”) with the same meaning as the Bosnian changes. The group concluded that there was no change in meaning. There was a change concerning ‘connection’ instead of ‘association’ (bio psychosocial factors “connected or not with the disease” instead of “associated or not with the disease”). But there is only one word in Bulgarian to express those two meanings and the group concluded that there was no change of meaning. The “somatic risk factors” were changed to “risk factors” as risk factors are always understood as somatic by Bulgarian FPs. The Bulgarians changed ‘network’ into ‘social network’, when describing the patient’s environment, to be sure the concept was as broad as in the original English definition. In this way, they encompassed, in Bulgarian, not only family and friends (which is the meaning of network in Bulgarian) but also the social infrastructures surrounding the patient, as was intended in English. They modified « may modify the health outcomes » to “Multimorbidity can lead to a change in the health outcomes “ This phrasing is less emphatic than the original. Nevertheless, the research group did not think that the meaning was radically changed and kept the Bulgarian version.



For Catalonia there was the same difference as in Bulgaria, regarding the use of articles. There was no difference in meaning.

For Croatia, the “somatic” risk factor was present in the first sentence of the definition but not in the second. The explanation was different from Bulgarian, as the Croatians did not want to repeat the same item twice, seeing it as an underlying factor. All the articles in the second paragraph were omitted as the Croatians wanted to simplify the definition, the way it should be in their language. The group concluded that there were no differences in meaning.

For France, there was the same difference as in Bulgaria, regarding the use of articles, and turning the second paragraph the other way round, with the same explanations. “The effects of multimorbidity may be modified by” instead of “may function as modifiers (of the effects of Multimorbidity).” There was no difference in meaning.

For Germany, there were some significant changes as the backward translation did not reflect the German Version. As an example, the word ‘condition’ appears in the first sentence of the backward translation and “Erkrankung” which means ‘disease’ is the only one used in the German version. The back translation was corrected by another team of linguists and the only difference was the affirmative phrasing in German with no use of the conditional tense. This loss of the conditional tense is cultural in spoken German so this was accepted because this definition is intended to be understood by everyone, including patients. There was a final difference between “reduced quality of life” instead of “decreased quality of life” which seemed unchanged in meaning for the research group.

For Greece, there were many differences in relation to an affirmative phrasing in the Greek language (even more so than in German) with the use of “can” instead of “may” which was accepted as it there is no difference in meaning in Modern Greek. The “health service use” occurred instead of the “health service consumption” due to the fact that in Greek the word consumption has the meaning of spending or expenditure and was better encompassed by “use”.

For Italy, the use of “can be defined” instead of “is defined” comes from the fact that Italians did not use “is defined”, preferring to express this idea by using ‘can be defined’ or “may be defined” with the verb “potere” (being able to). The use of “chronic illness” instead of “chronic disease” came from the point that “malattia” in Italian carries both meanings. The same difficulty with the use of articles was observed as in Bulgaria and in France. The word “ogni” in Italian could be translated as ‘any’ or ‘every,’ with no change in meaning, and defines a more global point of view which does not change the meaning of the sentence. A

“worsening quality of life” occurred instead of a “decreased quality of life” which encompassed a more affirmative idea or greater fear about multimorbidity in Italy. This seems to be due to the greater presence of multimorbidity in Italian practice which leads to a more active phrasing.

For Poland, the same difference with the use of articles was observed as in Bulgaria, France and Italy. The use of “related” instead of “associated” looked stronger but did not change the meaning and was accepted. There was the same difficulty with ‘risk factor’ instead of ‘somatic risk factors’ as in Bulgaria, with the same underlying meaning pointing to the same conclusion. The “use of health care services” instead of the ‘health care consumption.’ as in Greece, but for a different reason which is the lack of available medication, an additional factor in health services in Poland. The Polish translators forgot the second part of the sentence at the end of the second paragraph (‘of the effects of multimorbidity’) but this was added in the final definition. Then ‘weakness’ replaced ‘frailty’ as there is only one word for the two concepts in Polish.

For Spain and Catalonia there was the same difference as in Bulgaria, regarding the use of the articles. There was no difference in meaning.

The necessary changes were integrated into the final definitions and proposed to the study’s scientific committee. The committee found no semantic, conceptual or cultural changes compared with the original definition and so the translations obtained were validated for all the countries concerned. (See table 3)

Key points

Table 3: English Original and final translation for each country

English original	Bosnia	Bulgaria	Croatia
<p>Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.</p> <p>Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of Multimorbidity).</p> <p>Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.</p>	<p>Multimorbidnost (pacijent sa više bolesti u isto vrijeme) je definisana kao svaka kombinacija bolesti sa najmanje još jednom nekom bolešću (akutnom ili hroničnom) ili bio-psihosocijalnim faktorom koji je udružen ili ne) ili somatskim faktorom rizika.</p> <p>Svaki bio-psiho-socijalni faktor, svaki faktor rizika, socijalna podrška, raširenost bolesti, korištenje zdravstvene zaštite i način kako se sam pacijent nosi sa bolešću, može dovesti do promjene (efekata multimorbidnosti).</p> <p>Multimorbidnost - višebolesnost može mijenjati ishode zdravlja i voditi povećanoj nesposobnosti ili sniženom kvalitetu života ili povećanoj osjetljivosti.</p>	<p>Полиморбидност се определя като всяка комбинация от хронично заболяване, с поне едно друго заболяване (остро или хронично) или свързан или не със заболяването био-психо-социален фактор или друг соматичен рисков фактор.</p> <p>Всеки био-психо-социален фактор, всеки рисков фактор, социалната среда, тежестта на заболяванията, използването на здравни услуги и стратегии на пациента за справяне могат да оказват влияние върху ефектите на полиморбидността.</p> <p>Полиморбидността може да доведе до промяна на очакваните резултати и до висока степен на инвалидност, понижено качество на живот или слабост.</p>	<p>Multimorbiditet označava bilo koju kombinaciju kronične bolesti s barem još jednom bolesti (akutnom ili kroničnom), ili s biopsihosocijalnim čimbenikom (pridruženim ili nepridruženim) ili sa somatskim čimbenikom rizika.</p> <p>Bilo koji biopsihosocijalni čimbenik, bilo koji čimbenik rizika, društveno okruženje, teret bolesti, korištenje zdravstvene zaštite te načini bolesnikova nošenja s bolešću, mogu djelovati kao modifikatori (na učinke multimorbiditeta).</p> <p>Multimorbiditet može utjecati na zdravstvene ishode te dovesti do povećanja nesposobnosti ili do smanjenja kvalitete života ili do nemoći.</p>

France	Germany	Greece	Italy
<p>La multimorbidité est définie comme toute combinaison d'une maladie chronique avec au moins : une autre maladie (aiguë ou chronique) ou un facteur biopsychosocial (associé ou non) ou un facteur de risque somatique.</p> <p>Les effets de la multimorbidité peuvent être modifiés par : tout facteur biopsychosocial, tout facteur de risque somatique, le réseau social, le poids des maladies, la consommation de soins de santé et les stratégies adaptatives du patient.</p> <p>La multimorbidité peut modifier les résultats de santé et mener à une augmentation du handicap ou à une diminution de la qualité de vie ou à la fragilité. »</p>	<p>Definiert als jegliche Kombination einer chronischen Erkrankung mit zumindest einer weiteren Erkrankung (akut oder chronisch), oder einem bio-psycho-sozialen Faktor(assoziiert oder nicht) oder einem somatischen Risikofaktor.</p> <p>Jeglicher bio-psycho-soziale Faktor, jeglicher Risikofaktor, das soziale Netzwerk, die Krankheitslast, die Inanspruchnahme des Gesundheitssystems sowie persönliche Bewältigungsstrategien können die Auswirkungen von Multimorbidität beeinflussen.</p> <p>Multimorbidität kann Gesundheitsparameter beeinflussen und Funktionseinbußen verstärken. Sie kann auch die Lebensqualität reduzieren oder zu Gebrechlichkeit führen.</p>	<p>Ως πολυνοσηρότητα ορίζεται κάθε συνδιασμός οξέων ή χρόνιων νοσημάτων με ή χωρίς συσχετιζόμενους ή μη συσχετιζόμενους βιοψυχοκοινωνικούς παράγοντες ή σωματικούς παράγοντες κινδύνου.</p> <p>Αυτοί οι παράγοντες μπορούν επίσης να λειτουργήσουν ως τροποποιητές, παράλληλα με τον κοινωνικό ιστό, τη χρήση υπηρεσιών υγείας και τις στρατηγικές αντιμετώπισης του ασθενούς.</p> <p>Μπορεί να τροποποιήσει τα αποτελέσματα στην υγεία και να οδηγήσει σε μια αυξημένη ανικανότητα, μια μειωμένη ποιότητα ζωής ή ευθραστότητα.</p>	<p>Si definisce multimorbidità ogni combinazione di una malattia cronica con almeno un'altra malattia (acuta o cronica), o un fattore bio-psicosociale (associato o meno), o un fattore di rischio somatico.</p> <p>Ogni fattore bio-psicosociale, ogni fattore di rischio somatico, la rete sociale, il carico delle malattie, l'uso dei servizi sanitari e le strategie con cui i pazienti affrontano i loro problemi possono fungere da agenti modificanti (degli effetti di multimorbidità).</p> <p>La multimorbidità può modificare i risultati di salute e portare ad un incremento della disabilità o ad un peggioramento della qualità della vita o a fragilità.</p>

Poland	Spain (Castilian)	Spain (Catalan)
<p>Wielochorobowość jest definiowana jako jakiegokolwiek połączenie choroby przewlekłej z przynajmniej jeszcze jedną chorobą (ostrą lub przewlekłą) lub z czynnikami bio-psycho-społecznymi (związanymi z nią lub nie) lub z czynnikami ryzyka.</p> <p>Jakikolwiek czynnik bio-psycho-społeczny, czynnik ryzyka, sieć społeczna, obciążenie chorobami, korzystanie z opieki zdrowotnej i strategie radzenia sobie przez pacjenta mogą funkcjonować jako modyfikatory.</p> <p>Wielochorobowość może modyfikować wyniki zdrowotne i prowadzić do zwiększonej niepełnosprawności lub obniżenia jakości życia lub osłabienia.</p>	<p>Se define multimorbilidad como cualquier combinación de una enfermedad crónica con al menos otra enfermedad (aguda o crónica) o un factor biopsicosocial (asociado o no) o un factor de riesgo.</p> <p>Cualquier determinante bio-psicosocial, cualquier factor de riesgo, la red social, la carga producida por las enfermedades, el uso de recursos sanitarios y las estrategias de afrontamiento del paciente pueden actuar como modificadores del efectos de la multimorbilidad.</p> <p>La multimorbilidad puede modificar los resultados en salud y conducir a una mayor discapacidad o una menor calidad de vida o fragilidad.</p>	<p>Es defineix multimorbiditat com qualsevol combinació d'una malaltia crònica amb com a mínim una altra malaltia (aguda o crònica) o un determinant biopsicosocial (associat o no) o un factor de risc.</p> <p>Qualsevol determinant psicosocial, qualsevol factor de risc, la xarxa social, la càrrega generada per les malalties, l'ús de recursos sanitaris i les estratègies d'afrontament del pacient poden funcionar com a modificadors dels efectes de multimorbiditat.</p> <p>La multimorbiditat pot modificar els resultats en salut i conduir cap a una major discapacitat o una menor qualitat de vida o fragilitat.</p>

## **Discussion.**

### Main Results

These studies are a consecutive stage of the EGPRN project, which aims to provide a comprehensive definition of Multimorbidity throughout Europe [16]. The main findings are the translations of the English definition of multimorbidity into ten European languages (Table 3). The homogeneity of the translations is of importance for further collaborative research within EGPRN. The homogeneity of the translations has been evaluated in a semantic, conceptual and cultural way which confirms that these translations make provision

for the cultural background in which FPs cope with problems in their practices, and demand a holistic approach to the patient.

#### Strengths and limitations of the study

The Delphi technique for translation had its own strengths and weaknesses. Nevertheless, it is seen as an accurate consensus technique in health research [27] [28]. There was no information bias in this study as all data was sent to all experts and group members. There was no selection bias either. Even though the scientific committee was concerned about the small size of the Bosnian and Spanish-Catalan groups, it was reassured by the homogeneity of their definitions, which were also the most obvious. In some countries (France and Germany), during the first round, some of the participants believed they had to evaluate the accuracy of the definition which led to a confusion bias. This bias was disentangled at the beginning of the second round while emphasizing the role of translation as the only goal of the study. The sample's characteristics were very carefully followed up in every country to ensure that it was composed of genuine experts, both in Family Medicine and in use of English.

#### Key points

A standardized and reproducible definition of multimorbidity is of importance in developed countries where a larger proportion of the population is elderly. This comprehensive definition is helpful for targeting resources in a far more accurate way than the WHO definition [6]. In addition it gives more focused prognoses for individuals and improves risk management. It improves clinical decision making, in terms of risk/benefit evaluation. It could help decision-making when considering the position of an individual on the spectrum of palliative versus aggressive care.

When considering the previous definitions, most authors agreed to reject any concept which was too vague or insufficiently discriminating for the selection of patients with the diseases mentioned. Those caused problems of interpretation and inclusion of patients and induced a lack of power and confounding factors [29] [30] [31] [32]. This comprehensive definition and its translation into ten European languages encompasses all definitions of multimorbidity found in literature [16] and will override previous limitations.

The holistic approach and the patient centered care core competencies of family medicine, according to WONCA, [7] promote a concept of multimorbidity which is closer to the result of this study than any other.

#### Implications for practice and future research

The purposes of a standardized and reproducible definition of multimorbidity are numerous and its translation into ten European languages is of great value for further research. A more comprehensive and homogeneous definition leads to better focused research, especially for quality of care and cost of care. This study is included in an EGPRN project, which aims to define the best possible intervention to prevent depression for multimorbid patients. For inclusion a comprehensive and homogeneous definition of multimorbidity within 11 European languages (including English) was essential.

#### **Conclusion:**

This study has finalized ten European translations of the published English Multimorbidity definition from the EGPRN. In the light of an increasing number of elderly patients across Europe, [33] [34] introducing these translations and their semantic, conceptual and cultural homogeneity was a necessary and relevant step, especially for further research.

The implementation of the new definition is intended to help European FPs to identify multimorbid patients. It is also important for other Long-Term Care Physicians (geriatrists for example), as well as policy makers, to plan an optimal management of patients, and to lower the burden of multimorbidity [35].

The European translations enable the research team to proceed to the next step, which is qualitative research, in order to find the value added by FPs to the concept of multimorbidity. This will be achieved by using a grounded theory analysis and a deductive analysis from the translated definitions of multimorbidity. Then the study's scientific committee will be able to discuss which means could be used to ensure the implementations

of Multimorbidity into databases and registers. Eventually an International Classification Primary Care code will be put forward to the ICPC committee of the WONCA [36].

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Le Reste JY designed the whole study for every country, collected data for all countries, wrote the article,

Nabbe P designed the whole study for every country, collected data for France, reviewed the article,

Rivet C collected data for Bosnia, Bulgaria, Croatia, Greece, Germany, Italy and Poland, reviewed the article,

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Van Marwijk H designed the whole study and reviewed the article,

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Van Royen P designed the whole study and reviewed the article.



**Ethical issues.** The Ethical Committee of the “Université de Bretagne Occidentale” has accepted the project. All participants gave their written informed consent.

**Conflict of Interest statement:** All Authors confirm that they have no conflict of interest in this article.

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# Chapter 6

## **How do General Practitioners recognize the definition of Multimorbidity? A European qualitative study.**

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**Abstract:**

**Background:** Multimorbidity is a challenging concept for General Practice. An EGPRN working group has published a comprehensive definition of the concept of multimorbidity. As multimorbidity could be a way to explore complexity in General Practice, it was of importance to explore if European General Practitioners (GPs) recognize this concept and whether they would change it.

**Objective:** To investigate if European GPs recognize the EGPRN concept of multimorbidity and whether they would change it.

**Methods:** Focus group meetings and semi-structured interviews as data collection techniques with a purposive sample of practicing GPs from every country. Data collection continued until saturation was reached in every country. Analysis was undertaken using a grounded theory based method. In each national team, four independent researchers, working blind and pooling data, carried out the analysis. To ensure the internationalization of the data, an international team of 10 researchers pooled the axial and selective coding of all national teams to check the concept and highlight emerging themes.

**Results:** The maximal variation and saturation of the sample were reached in all countries with 211 selected GPs. The EGPRN definition was recognized in all countries. Two additional ideas emerged: the use of the Wonca's core competencies of General Practice and the dynamics of the doctor-patient relationship for detecting and managing multimorbidity and patient's complexity.

**Conclusion:** European GPs recognized and enhanced the EGPRN concept of multimorbidity. These results open new perspectives regarding the management of complexity using the concept of multimorbidity in General Practice.

**Key words:** Multimorbidity, qualitative research, competencies.

**Key message:**

European General Practitioners recognize the EGPRN enhanced, comprehensive concept of Multimorbidity

They add the use of the Wonca's core competencies and the patient's doctor relationship dynamics for detecting and managing multimorbidity.

The EGPRN concept of Multimorbidity leads to new perspectives for the management of complexity.



## **Introduction**

The concept of multimorbidity was first described in the 1970s [1]. It was an addition to the concept of comorbidity with the intention of looking at all conditions in one individual [2-4]. Nevertheless, the concept stayed unclear, especially for research and practical purpose[3][4]. In 2008 the World Health Organisation (WHO) tried to clarify the concept with the intention to focus on the individual's global health status. It defined multimorbidity as 'being affected by two or more chronic health conditions' [5]. However, the word 'condition' was not sufficiently clear and could lead to numerous interpretations.

Despite those interpretations, multimorbidity seemed an interesting and challenging concept for general practice and long-term care. It seemed closely related to a global or comprehensive view of the patient, which is a core competency of general practice [6]. It is a global 'functional' view (useful for Long-Term Care) versus a 'disease' centred point of view (useful for acute care) [7].

The European General Practice Research Network (EGPRN) is fully committed to concepts that could advance research in general practice throughout Europe with a research agenda focusing on patient-centred health [8]. Therefore, the EGPRN was specifically interested in the development of an understandable and usable in collaborative research definition of the concept of multimorbidity. It will help researchers in general practice to investigate the complexity of patients and their overall impact on patients' health and their use of health services [9]. It could be an additional tool for general practitioners(GPs), enabling them to identify frail patients and prevent decompensation[10].

A research group, including nine national groups from EGPRN, has created a research community for the purpose of clarifying the concept of multimorbidity for general practice throughout Europe [11]. An initial review [12] identified more than one hundred definitions.

Such a large number of definitions added more confusion than clarification to the discussion and led the group to the production of an enhanced concept of multimorbidity supported by a systematic review of literature [13]. This concept is as follows: *multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor. Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of multimorbidity). Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.* There are three distinctive parts in this definition. The first sentence describes what multimorbidity is, the second which factors could modify multimorbidity and the third what the outcomes of multimorbidity are.

This raised the question whether practicing GPs recognize this concept as developed from medical research, and use the same or different criteria for their complex patients [14]. It would be plausible to assume that they have different criteria of definition from researchers, because GPs seem more in line with patient expectations than other specialists [15]. In order to assess this for GPs in different European countries, the enhanced definition of multimorbidity was carefully translated into 10 European languages using a Delphi consensus methodology [16] in a previous work. It was then necessary to present the translated definitions to practicing GPs to check if they recognize the developed concept of multimorbidity. The current survey was designed to answer the following questions: Do European GPs recognize the enhanced concept of multimorbidity and would they want to change it?

## **Methods,**

### *Study design*

The study consisted of a set of 13 studies, involving 7 European countries (Bulgaria, Croatia, France, Germany, Greece, Italy and Poland). France, as the pilot team, carried out 6 studies, Germany 2 and the other countries 1. Each national team approached GPs selected from a local panel by phone. Some of them declined the invitation and the following GP in the panel list was subsequently approached. Reasons for declining were prior engagements, illness and heavy workload. None of them declined because of lack of interest in the study. The samples for each country and for each study were carefully constructed to achieve maximum variation in age, gender, experience, practice type and practice setting.

### *Ethical approval*

Ethical approval was given by the ethical committee of the “université de Bretagne occidentale”.

### *Data collection*

The translated definitions were presented to all participating GPs. Both individual and focus groups interviews were used as data collection techniques. Interviews were used in order to find a more personal, in depth, perspective of GPs as individuals [17] and to balance the group perspective provided by focus groups of GPs as a social group [18][19]. As the objective was the same the interview guide for both focus groups and individual interviews was similar and was translated into the national language of each country (see Table 1). Using the same interview guide gave the opportunity to use a comparable framework for analysis even if it was expected that results could differ from a personal or a social group perspective.

**Table 1.** Interview guide

Interview guide	
Question 1	We have defined multimorbidity. Could you describe one case of a multimorbid patient which has arisen in your practice?
Question 2	Do these patients need managing in a particular/specific way?
Question 3	How do you identify these patients?
Question 4	What is your perception of these patients?
Question 5	These patients are difficult to spot or locate. Which additional means could help you to do so?

### *Data Analysis*

As the research group was looking at what GPs might think about the enhanced concept of multimorbidity, a critical theory paradigm appeared to be the best possible research perspective [20]. The data analysis technique was based on grounded theory with an open coding followed by an axial coding and a selective coding [21]. For each study, a pair of national researchers working blind, coded the transcripts independently and compared the results at the end of the open coding and at the end of the axial coding. When all the countries

had completed the axial coding, they had to translate between one and three verbatim accounts for each axial code to provide clear examples. Those translations were used to establish the international codebook during the EGPRN meeting in Malta (October 2013). The international codebook was designed using a comparison between the axial coding and the criteria of the enhanced concept of multimorbidity. Any axial code that was not comparable to the criteria of the concept of multimorbidity, would define the definition's enhancement for GPs. Then each national team applied the international codebook to the whole coding process, using two pairs of two researchers (one pair from the pilot team and one pair from the national team) working blind and pooling data at each step. This was undertaken to ensure the completeness and the consistency of the coding process. A selective coding was subsequently proposed. That selective coding was finalized with a physical meeting during the EGPRN meeting in Barcelona (May 2014). Before and during this meeting the whole team used an interactive process of data pooling, summarizations and explanations to finalize the process between researchers, pairs of researchers and team. That iterative and interactive process was conducted with the help of team meetings in each country and interaction between the national researchers and the international ones by mails and skype meetings. In addition, the quality of the data was checked to verify the coherence between the native verbatim and the open coding by another team of two researchers for each country's coding.

#### *Result's internationalization check*

A final step was undertaken to ensure the internationalisation of the coding. Six physical international workshops were conducted during the EGPRN meetings from 2012 to 2014 with all team leaders (10 international researchers) to ensure the internationalization of the coding and the analysis. The final agreement was that an axial code identified by at least five

countries out of seven would be considered international. An axial code identified by four countries or fewer would be considered nationally specific. An upgraded definition would be issued if new international codes appeared.

## Results

### *Participants*

Two hundred and eleven GPs were interviewed within Europe. The maximal variation in age, gender, experience, practice type and practice setting was ensured for each study and is shown in Table 2.

**Table 2.** Sample data for maximal variation

		Germany	Bulgaria	Croatia	Greece	Italy	France	Poland	Total
<b>Total Sample</b>		32	30	19	19	17	83	11	211
<b>Setting Type</b>	Rural	3	3	3	4	3	23	1	40
	S Rural	9	3	2	7	3	20	3	47
	Urban	20	24	14	8	11	40	7	124
<b>Gender</b>	Male	16	11	3	10	9	51	3	103
	Female	16	19	16	9	8	32	8	108
<b>Years in Practice</b>	< 20 years	22	10	11	19	6	33	11	111
	> 20 years	9	20	8	0	11	50	0	98
	Unknown	1	0	0	0	0	0	0	1
<b>Practice Type</b>	Single	12	23	17	8	2	21	3	86
	Group	20	7	2	11	11	62	8	121
	Others	0	0	0	0	4	0	0	4

One German GP refused to report his “Years in Practice” but, since he gave his informed consent, his data was kept. Some Italian GPs had mixed activities (others had various types of Practice) as they were working in different settings (Single on some days and in a group on other days).

### *Data extraction and analysis*

A total of 10,999 codes were extracted from the data highlighting the implication, comprehension and diversity of the GPs experience throughout Europe. The use of an international codebook with its iterative and interactive process of coding and recoding within all teams permitted the aggregation of this massive amount of codes into 61 sub-themes and consecutively 13 themes. Those sub-themes and themes were compared to those of the enhanced concept of multimorbidity as detailed in Table 3 below to understand whether they were covering the same meanings or new ones appeared.

**Table 3.** Comparison between academic criteria for multimorbidity based on the literature review and the criteria defined as main codes from the interviews – ranked in the different themes

THEMES	Academic criteria	GPs' criteria	International criteria
Chronic disease	Chronic condition	Chronic condition/complaints symptoms signs	✓
Chronic disease	Chronic disease	Chronic disease	✓
Chronic disease	Psychosomatic diseases/physical implications	Psychosomatic disease	✓
Chronic disease	Complexity characteristics of chronic disease	Complexity characteristics of chronic disease	✓
Acute disease	Acute condition	Acute condition/complaints symptoms signs	✓
Acute disease	Acute disease	Acute disease	✓
Acute disease	Reaction to severe stress and acute disorders	Reaction to severe stress and acute disorders	✓
Acute disease	Complexity characteristics of acute disease	Complexity characteristics of acute disease	✓
Biopsychosocial factors and somatic risk factors	Somatic risk factors	Somatic risk factors	✓
Biopsychosocial factors and somatic risk factors	Psychological risk factors	Psychological risk factors	✓
Biopsychosocial factors and somatic risk factors	Psychosocial risk factors	Psychosocial risk factors	✓
Biopsychosocial factors and somatic risk factors	Lifestyle	Lifestyle	✓
Biopsychosocial factors and somatic risk factors	Demographic risk factor	Demographic risk factor	✓



Biopsychosocial factors and somatic risk factors	Deleted: Psychological distress	Classified in psychological risk factors et coping strategies	deleted
Biopsychosocial factors and somatic risk factors	Socio-demographic characteristics	Socio-demographic characteristics	✓
Biopsychosocial factors and somatic risk factors	Deleted: Aging	Classified in demographic risk factor et socio demographic characteristics	deleted
Biopsychosocial factors and somatic risk factors	Patients' beliefs/expectations	Patients' beliefs/ expectations/culture	✓
Biopsychosocial factors and somatic risk factors	Deleted: Physiology	Classified in physiopathology	deleted
Biopsychosocial factors and somatic risk factors	Physiopathology	Physiopathology	✓
Coping	Patients' coping strategies	(Behavioral and psychological) coping strategies	✓
Coping	Not described	Patients' basic compliance	✓
Burden of diseases	Disease complication	Disease complication	✓
Burden of diseases	Disease morbidity	Disease comorbidity / patient perception about his own multimorbidity level	✓
Healthcare consumption	Use of caregivers	Use of caregivers	✓
Healthcare consumption	Treatment or medication	Treatment	✓
Healthcare consumption	Management	Management	✓
Healthcare consumption	Disease management	(Multidisciplinary) disease management	✓
Healthcare consumption	Medical procedure	Medical procedure	✓
Healthcare consumption	Malpractice	Malpractice	✓
Healthcare consumption	Health care services	Health care services	✓
Healthcare consumption	Health care	Health care	✓
Healthcare consumption	Health care policy	Health care policy	✓
Healthcare consumption	Medical history	Medical history	✓
Healthcare consumption	Deleted: Family history	Classified into others consumption codes	deleted
Healthcare consumption	Deleted: Assessment	Classified medical procedure or health care policy	deleted
Healthcare consumption	Prevention	Prevention/education/ detection	✓
Healthcare consumption	Pain	Pain	✓
Healthcare consumption	Health services/setting/treatment	Health services/setting/treatment	✓
Healthcare consumption	Symptoms/signs/ complaints	Symptoms/signs/complaints (not pain)	✓
Healthcare consumption	Cost of care	Cost of care	✓
Healthcare consumption	Polypharmacy	Polypharmacy (including polymedication)	✓
Disability	Handicap	Handicap	✓
Disability	Functional impairments	Impairments	✓
Quality of life	Quality of life	Quality of life	✓
Quality of life	Health status	Health status	✓
Quality of life	Impairment implication	Impairment/morbidity implications	✓

Frailty	Frailty	Frailty	✓
Social network	Social network	Social Isolation	✓
Social network	Social network	Support from the network	✓
Social network	Social network	Dependence on the network	✓
Social network	Social network	Family's coping strategies	✓
Social network	Social network	Carers' protection	✓
Health outcomes	Mortality	Mortality	✓
Health outcomes	Deleted: Indicator	Classified in health outcomes	deleted
Health outcomes	Outcome	Health outcome	✓
Health outcomes	Medical research/ epidemiology/ instruments/level of multimorbidity	Medical research, epidemiology	✓
Health outcomes	Classification of morbidity statistics	Classification of morbidity statistics	✓
<b>FP's expertise</b>	Not described	<b>Holistic approach</b>	✓
<b>FP's expertise</b>	Not described	<b>Primary care management</b>	✓
<b>FP's expertise</b>	Not described	<b>Person centered care</b>	✓
<b>FP's expertise</b>	Not described	<b>Comprehensive approach</b>	✓
<b>FP's expertise</b>	Not described	<b>Specific problem solving skills</b>	✓
<b>FP's expertise</b>	Not described	<b>Intuition/gut feeling</b>	✓
<b>Doctor-patient relationship dynamics</b>	Not described	<b>Communication challenge</b>	✓
<b>Doctor-patient relationship dynamics</b>	Not described	<b>GP's and patient's experience</b>	✓

Themes are the themes developed in the concept of multimorbidity and/or by the GPs. Academic criteria are those used in the EGPRN concept of multimorbidity., GPs' Criteria are the criteria described by GPs. International criteria means that those criteria have been described in at least five out of seven countries.

All sub-themes and themes of the enhanced concept of multimorbidity were identified by GPs.

#### *GPs additions and simplifications*

GPs felt necessary to add one sub-theme: the patient's basic compliance in addition to the theme coping strategies. This theme was mainly focused on acceptance or denial of an illness and not on compliance, which was of importance for them.

They simplified, however, by classifying six sub-themes into previously known categories as the verbatim extracts all fitted into that categorization. Those reclassified sub themes appeared repetitious and unsuitable for the final definition of multimorbidity. They were as follows:

- Psychological distress was reclassified under coping strategies or psychological risk factors as GPs described them as inefficient coping strategies and psychological risk factors.
- Aging was reclassified under demographic risk factors or socio demographic characteristics.
- Physiology, which GPs obviously perceived as a repetition of physiopathology, was reclassified in that category.
- Family History (a part of the health care consumption theme) was reclassified within several health care consumption criteria (medical history, management and disease management) as these criteria were clearer for GPs.
- Assessment in health care consumption was reclassified under medical procedure or health care policy.
- Indicator had obviously to be reclassified under health outcomes for GPs.

### *Description of subthemes and themes*

As it was impossible to describe all the qualitative data the most innovative themes and sub-themes are described in detail while more common ones are briefly described. Where the themes and sub-themes that emerged have been described in detail, they are illustrated by selected verbatim accounts drawn from all the countries involved. The countries are described

at the beginning of each verbatim account with the method of data collection (I for individual interviews and F for focus groups interviews). Countries and verbatim accounts are in italic.

The core of the enhanced concept of multimorbidity is represented by its first sentence showing interaction between chronic diseases, acute diseases, bio-psychosocial and somatic risk factors. It was of importance that GPs recognize those themes and their interaction and they did:

The chronic diseases were precisely and comprehensively described. Most of the chronic diseases from the ICD 10 could be retrieved in the verbatim accounts describing the completeness of selected GPs clinical experience. The GPs described chronic conditions as addictions, overweight, atopy. The Psychosomatic diseases/physical implications were also of importance especially with somatizations of psychological distress; *Greece: "a patient who was developing more and more depressive symptoms, which were mostly somatized" (F)*. Finally the Complexity characteristics of chronic diseases was accurately described especially with the accumulation of diseases or the follow up complexity and complications for *Italy: "the balance is very delicate when compensating, maintaining the circulatory compensation, the renal problem, also maintaining the hemoglobin level, the weight" (F)*; or with the sudden appearance or rapid succession of problems; *France: "we managed to resolve a problem due to smoking and then another one shows up" (I)*...

The acute diseases were exhaustively described with an exhaustive description as according to ICD 10. The GPs were also careful with the Acute condition. They could be symptoms for *Greece: "chest pain" (F)*, or complaints; *France: "It is true that he's always turning up, as soon as he starts coughing you see him" (I)*; or acute medical conditions with no diagnosis; *Germany: "blood in the urine" (F)*. GPs also described Reaction to severe stress and acute

disorders with reactional anxiety; *France: "sometimes he starts crying: "I've had it, doctor""* (I). Then the Complexity characteristics of acute disease was frequent recurrence and their complications; *Bulgaria: "she had an acute heart attack last month and coronary stent had been put in" (F)*; *Croatia: "with some ugly hemoptysis" (F)*...

The Bio-psychosocial factors and the somatic risk factors were underlined by Somatic risk factors. Psychological risk factors were also mentioned as psychological frailty. The psychosocial risk factors were shown as professional, familial or as financial difficulties. Lifestyle was of importance. Demographic risk factors were described as both ends of life. In addition Socio-demographic characteristics like professional status; *Poland: "a priest" (I)* and familial or couple status were described. The Patient's beliefs/expectations like optimism; *Greece: "they were not worried" (F)*; faith; *Poland: "this patient doesn't believe" (I)*; expectations. Finally Physiopathology like physiological frailty; *France: "it makes me think of the morphology, someone who is a weakling, all shrunken" (I)*...

The modifiers of multimorbidity were described as bio-psychosocial factor, somatic risk factor (already described upper), social network, burden of diseases, health care consumption and patient's coping strategies enhanced with the Patient's basic compliance which was added to coping strategies; *Croatia: "it depends whether he is coping well with his disease or not" (F)* "you've mentioned frustration... but we still have patients with multimorbidity, coping well" (F) and adherence; *Greece: "adherence to treatment" (F)*. (see additional file)

The outcomes of multimorbidity were the third part of the definition and were important for the comprehension of the consequences of Mutimorbidity. They were described as health outcomes, disability, quality of life and frailty (see additional file).

Two additional themes were identified. They are of help to detect and manage multimorbidity. The international team decided to classify them as modifiers.

The Core competencies of GP (GPs' expertise) including a Holistic approach: *Poland: "a holistic approach is necessary... it's impossible to treat any of these diseases (conditions) separately" (I)*. The Primary care management; *Italy: "Coordinate a multidisciplinary assistance" (F)*. The Person centred care; *Germany: "that's why it is important, that you try as a GP, to find out as much as possible about the patient's overall background and, of necessity, take it into account." (F)*, *Poland: "a tailor-made approach" (I)*. The need for a Comprehensive approach was valued; *Croatia: "both children have asthma, girl has hyperthyroidism. Whole family is complex. Under the surface are the social circumstances" (F)*. Specific problem-solving skills were of importance; *Croatia: "summing up problems for patients and viewing the situation objectively makes intervention much more effective..."*. The Intuition/gut feeling of the FP was recognized as a specific expertise of the FP for multimorbidity detection and described as a kind of non-hypothetical-deductive analysis; *Greece: "sixth sense" (F)*, *Italy: "it can be recognized with intuition" (F)*.

The doctor-patient relationship dynamics, including the challenge of clear communication, seemed important in detecting multimorbidity; *France: "You have to convince them. We can't force the people" (I)* and the FP's and patient's experience described as positive or negative feelings about their relationship; *Germany "I have to say that I feel good with most of those patients" (F)* or *Croatia "sometimes we feel compassion for them, but then they become a source of frustration for us" (F)* that could make them less inclined to follow up the patient'.

Then, a final enhanced concept of multimorbidity was issued which integrated those two additional themes. This definition is shown in Table 4

Table 4. Comparison between original and final definition of multimorbidity

Original definition	Final definition
<p>Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.</p> <p>Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption and the patient’s coping strategies may function as modifiers (of the effects of Multimorbidity).</p> <p>Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.</p>	<p>Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.</p> <p>Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption, the patient’s coping strategies, <i>the FP’s expertise and the doctor-patient relationship dynamics</i> may function as modifiers (of the effects of Multimorbidity).</p> <p>Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.</p>

*Internationalisation of the data*

No nationally specific codes were found. All codes or criteria were identified as international.

More details are described in a supplemental web only file.

## **Discussion:**

### *Main findings*

European GPs recognized the 11 themes of the EGPRN enhanced concept of multimorbidity. They removed six sub-themes (psychological distress, aging, physiology, family history, assessment, indicator) as it became obvious that they duplicated existing criteria. One subtheme was added (patient's basic compliance) to enhance the coping strategies of the patient. Two new themes emerged as modulating factors of multimorbidity: the GPs' expertise (including the GPs' gut feeling) and the dynamic of the doctor-patient relationship.

### *Strengths and limitations*

The main strength of this study is the fact that a set of 13 homogeneous studies was conducted throughout Europe with an international collaborative team. 211 GPs were interviewed. They were drawn from a broad geographic area of Europe, from the full range of European health systems (primary care centred, secondary care centred or hospital centred), from a spectrum of European cultures (Former Communist countries, Catholic, Protestant, Muslim) and most European linguistic groups (Latin Germanic, Slavic and Greek).

There was no information bias as exactly the same care was taken to provide all the necessary information to all participants. The data was recorded and all records and verbatim accounts were collected by the pilot team for quality control. There was little selection bias as all the studies followed the protocol for maximum variation sampling with precision. Nevertheless, for Poland and Greece it was impossible to select GPs who had had more than 20 years of



practice experience as the specialty had only been created in the late 1990s'. Subsequently it was impossible to avoid this bias in those countries. A pitfall of qualitative research can be confusion bias due to researchers' personal interpretations. However, this was highly unlikely in this case as two pairs of two independent researchers working independently were involved at each step of the coding process and group consensus meetings took place which included all the teams. The researchers' personal interpretations were always discussed, at each coding step, with three other researchers and then in a group consensus meeting. The sample's characteristics are always debatable. Those were age, gender, experience, setting type and practice type. The research team assumed that there was sufficient diversity because the sample included the broadest possible range of GPs.

#### *Discussion of the literature*

The two new themes that emerged as modulating factors of multimorbidity are of importance for GPs. The first one is the GPs' expertise. It is based on the Wonca core competencies of GP[6] including the GP's gut feeling [22]. The Wonca core competencies enhance GPs' detection and management of multimorbidity. The second theme is the dynamic of the doctor-patient relationship in terms of quality of communication and mutual experience. This is important, as this relationship is seen, by GPs, not only as a mean of developing skills for communication or comprehension of the patient's point of view, but as a global and mutual experience both for the patient and for themselves.

Those new themes highlight the solutions to known difficulties in the management of patients with multimorbidity. Those difficulties, described in a systematic review in 2013, and including meta-ethnographic syntheses, [23] were as follows:

Lack of organization within healthcare, challenges in delivering patient-centred care and inadequate guidelines. The EGPRN concept of multimorbidity has broken down

those difficulties while using the Wonca core competencies.

Barriers to the sharing of decision-making which are broken down by the dynamic of the doctor-patient relationship.

The enhanced concept of multimorbidity has been confirmed and enriched by this study. The term “condition” defining multimorbidity is now clearer and could be operationalized in research and possibly in practice. Some additions to previous definitions have been developed. For example, acute diseases are important for GPs like in other studies [24][25]. The presence of biopsychosocial factors (including somatic risk factors but adding patients’ beliefs and expectations, psychosocial factors...) is highlighted too and that is a key point for the exploration of complexity in GP. [26] [9] [27].

The effects of multimorbidity could be modified to enhance the role of carers, caregivers and patients. The importance of the coping strategies of the patient are well defined by GPs and the link with therapeutic alliance is important, as in previous publications [28]. The burden of diseases has also been taken into account by GPs well aware of the difficulties of scoring it in an homogeneous way [29]. The role of health care consumption in dealing with multimorbidity is important and could lead to new health cost indicators, as was shown in previous studies [2][30]. The importance of the social network of the patient (and of its failures) is highlighted, as has already been demonstrated [31]. Finally, frailty, disability and quality of life are in the balance as it was already demonstrated [10][32].

These findings and confirmations could lead to new research focused on complexity, which is one of the major tasks of health systems throughout the developed countries. Policy makers need new indicators, synthesis and research about complexity in order to be able to handle it

[33]. The EGPRN enhanced concept of multimorbidity focuses on a conceptual understanding of all the criteria that contributes to multimorbidity. Work of this kind has never been achieved in such a complete way until now. Most of the expert literature focused on the accumulation of illnesses and attempts to find prevalent patterns of multimorbidity[34][35]. The main pitfall of that approach was that complexity was omitted from research and that primary care physicians would not be able to recognize their complex patients by using such studies[36][37]. This pitfall could lead to less effective care compared with patient-centred approaches to complexity[38].

### *Implications*

European GPs recognized the EGPRN enhanced concept of multimorbidity. They added greater significance for complexity. Previous definitions were probably too concise, in a conceptual way, leading to a misunderstanding of the key role of complexity in General Practice. Simplification could be helpful for research but could also be a major drawback in the assessment of complexity[8][39]. This concept focuses more on a conceptual understanding of all the criteria that contribute to multimorbidity. It now needs to be operationalized in research. The research team will undertake a European consensus survey to design a research agenda for multimorbidity throughout Europe.

### **Conclusion:**

European GPs recognized the EGPRN enhanced concept of multimorbidity. They did not change it but added greater significance for complexity. It will now be operationalized in research to determine which criteria are effective in detecting, preventing and managing multimorbidity.

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# Chapter 7

## **What research agenda could be generated from the European General Practice Research Network concept of Multimorbidity in Family Practice? (A nominal group survey).**

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**Abstract :**

Background: Multimorbidity is an intuitively appealing, yet challenging, concept for Family Medicine (FM). An EGPRN working group has published a comprehensive definition of the concept based on a systematic review of the literature which is closely linked to patient complexity and to the biopsychosocial model. This concept was identified by European Family Physicians (FPs) throughout Europe using 13 qualitative surveys. To further our understanding of the issues around multimorbidity, we needed to do innovative research to clarify this concept. The research question for this survey was: what research agenda could be generated for Family Medicine from the EGPRN concept of Multimorbidity?

Method: Nominal group design with a purposive panel of experts in the field of multimorbidity. The nominal group worked through four phases: ideas generation phase, ideas recording phase, evaluation and analysis phase and a prioritization phase.

Results: 15 international experts participated. A research agenda was established, featuring 6 topics and 11 themes with their corresponding study designs. The highest priorities were given to the following topics: measuring multimorbidity and the impact of multimorbidity. In addition the experts stressed that the concept should be simplified. This would be best achieved by working in reverse: starting with the outcomes and working back to find the useful variables within the concept.

Conclusion: The highest priority for future research on multimorbidity should be given to measuring multimorbidity and to simplifying the EGPRN model, using a pragmatic approach to determine the useful variables within the concept from its outcomes.

Key words: Multimorbidity, nominal group, research, family medicine.

## **Background,**

The number of people suffering from multiple conditions (multimorbidity) is rising rapidly especially in family medicine (FM)[1]. The concept of multimorbidity was first described in the 1970s [2]. It was, at that time, an addition to the concept of comorbidity, with the intention of looking at all the conditions in one individual [3][4][5]. Nevertheless, the concept remained unclear, especially for research and practical purposes[6][7]. The World Health Organisation (WHO), in 2008, tried to clarify the concept and defined Multimorbidity as people being affected by two or more chronic health conditions [8]. The intention of the WHO was to look at all conditions in one individual that could impact on that individual's global health status. However the word 'condition' was not sufficiently clear for research or practical purposes (for instance, whether a treated disease was a 'condition' in this sense), and could lead to numerous interpretations.

Despite those interpretations, multimorbidity is a very interesting and challenging concept, particularly for FM and long-term care, given the increasing prevalence of chronic illness in an aging population across all countries. It is closely related to a global or comprehensive view of the patient, which is a core competency of FM, as defined for instance by the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) [9]. It is also a global 'functional' or 'goal-oriented' view (useful for Long-Term Care) versus a 'disease' centered point of view (useful for acute care). Nevertheless, the disease centered point of view remains the basis of most clinical guidelines even if it is not fully applicable in FM [10][11].

The European General Practice Research Network (EGPRN) was very interested in the concept of multimorbidity as this network is committed to concepts that could advance research and practice in primary care throughout Europe. The EGPRN has created a research agenda specifically designed for methodological and instrumental research, which includes the development of primary care epidemiology, focusing on patient-centered health [12]. A clear definition of the concept of multimorbidity (i.e. one which is both understandable and usable for further collaborative research) is an important objective for a research network of this type. It aims to help researchers in FM to investigate the complexity of patients' conditions and their overall impact on patients' health. A clear definition of multimorbidity

could be an additional tool for Family Physicians (FPs), enabling them to identify frail patients and prevent decompensation[13]. A specific research agenda could be developed for multimorbidity.

A research group, including 9 national groups, all active within the EGPRN, has created a research community for the purpose of clarifying the concept of multimorbidity for FM throughout Europe [14]. An initial review, presented in an EGPRN meeting in spring 2011 [15], identified more than one hundred different definitions used by academic researchers. Such a large number of definitions added more confusion than clarification to the discussion and led the group to the production of a comprehensive definition of the concept of multimorbidity with the help of a systematic review of literature [16].

It was then necessary to assess whether Family Physicians (FPs) recognized this concept, which had emerged from medical research, as applicable to their complex patients. FPs are well-placed to identify this concept as they aim to be more aware of their patients' expectations than other specialists [17] and they are used to dealing with complex patients[18] [19]. In order to make this assessment, the comprehensive definition of Multimorbidity was carefully translated into 10 European languages with the help of a forward-backward translation procedure using a Delphi consensus methodology [20]. Those translated definitions were presented to European FPs with 13 consecutive qualitative surveys, designed to check how the FPs experienced and worked with the developed concept of multimorbidity and whether this was fully consistent with the definition. European FPs clarified the concept and added the role of gut feelings, core competencies of FM, and patient and doctor experience, to the management of Multimorbidity. A comprehensive concept of multimorbidity for FM was then established.

Researchers in the field of multimorbidity explored innovative research topics, themes, questions and appropriate design formats in relation to the concept of Multimorbidity for FM, leading to the question: what research agenda could be generated for Family Medicine from the EGPRN concept of Multimorbidity?

## Methods,

For this study we used a qualitative research method, i.e. a nominal group technique (NGT) [21]. This technique was chosen because multimorbidity is conceptually complex. The NGT enables researchers to gather information from relevant experts[22][23]. NGT facilitates creative problem solving by means of judgmental decision making in situations where routine answers are inadequate[24]. With an NGT, it is possible to plan research through group meetings or by email [25]. The ethical committee of the “université de Bretagne occidentale” gave the ethical approval for the whole process as this university led the study. Informed consent was obtained from all participants even if it was a non-interventional study. NGT is a well-known technique that has already been used by members of the research group [26]. With an international group, adaptations were needed and an email system was used as it had already been successfully employed in several earlier studies [27][28][29]. An NGT involves four phases: *ideas generation phase*, *ideas recording phase*, *evaluation and analysis phase* and a *prioritization phase*.

Type of participants and selection of experts:

An international panel of experts in the field of multimorbidity was purposively sampled. The NGT does not require a fixed number of experts in order to be valid but does require relevant experts. To be relevant, those experts should have prior experience in the field of the research in question (multimorbidity, FM, patient-centered care). The group was selected from three backgrounds: The EGPRN, the Threads and Yarns network members (a group designed for research into the field of multimorbidity), and researchers in multimorbidity from Polish, Dutch and British Universities. The group was made up of FM clinicians, researchers in FM and linguistics, methodologists and epidemiologists. Some individuals were involved in two different groups. 18 experts were approached by email. 18 were willing to cooperate and received written information. We invited them to participate and 15 accepted. Reasons for declining were prior engagements and illness.

NGT sessions:

For *ideas generation*, experts were asked to read the publications about the concept of Multimorbidity produced by the EGPRN (protocol[14], systematic review[16], translations [20] and qualitative surveys). Then they were asked to take time and write down what they regarded as the main research questions relating to the “concept of Multimorbidity issued by the EGPRN”. At the same time, they were asked to present an appropriate design for each research question, with a commentary to make it easily understandable by each participant. Each expert could produce a maximum of five propositions, arising from that definition, with a design and a commentary for each. The aim was to leave this process wide open in order to elicit the widest possible variety of responses.

In the *ideas recording* phase participants were engaged in a round-robin feedback system by email. All the propositions were sorted, with their designs and commentaries, and classified to detect duplicates. Duplicates were summarized and sent back to the planners to check that they were compatible with the planners’ initial intentions. Where necessary, corrections were made to the questions, designs and commentaries.

The *evaluation and analysis* phase was undertaken to identify and clarify research topics and themes and to develop designs. All the propositions were classified into research topics and themes and then summarized by an independent group of 6 researchers from the SPURBO research team (Université de Bretagne Occidentale). These 6 researchers’ propositions were sent to all participants for agreement before any further development. Then designs were developed, for each research theme and topic, by their proposers. The designs were sent back to all the participants for analysis. Where necessary, it was possible to have open discussions, by email, between members so that submitted propositions could be clarified. These emails were sent out to all the participants so that all the members received clarification on each proposition.

The intention of the *prioritization* phase was to aggregate the judgment of the experts in order to determine the relative importance of the research questions, and corresponding designs for future research relating to the concept of Multimorbidity produced by the EGPRN. All participants were asked to rank the propositions, according to the level of importance they attached to them, for FM and patient centered care. They had the opportunity to apply 3 scores: a score of 5 points for one proposition, a score of 3 points for another and a score of 1 point for the final proposition. A prioritized list of all the propositions was drawn up from these scores. This prioritized list was sent back to all the participants in order to evaluate the procedure and the outcomes and to collect objections, should any arise.

## **Results,**

### *Description of participants:*

In total, 15 experts participated in the study, 7 men and 8 women from different countries, including Bulgaria, Croatia, France, Germany, Greece, Italy, Poland, Spain and the UK. Their average age was 49 years (ranging from 35 to 62 years). All clinicians (14 out of 15) had an average of 19.8 years' practice experience (ranging from 4 to 33 years), with 10 working in group practices, mostly in urban areas. Methodologists, linguists and epidemiologists were also experienced, with an average of 38.5 published articles. They all had experience of publishing articles, with an average of 34 published articles (ranging from 6 to 70), of which an average of 16 were in English (ranging from 3 to 65). Participants had had an average of 5 articles published with multimorbidity as a major topic (ranging from 1 to 15).

### *Description of Results:*

The ideas generation and ideas recording phase produced 61 research questions and study designs after duplicates had been withdrawn. Although there was considerable overlap in the ideas, the evaluation and analysis phase aggregated those 61 research questions into 11 themes, including 6 major topics, with their attached research questions and designs. The prioritization phase produced a consensual ranking of the topics and themes. The total score possible, by adding up the points of all 15 experts, was 135. Topics, themes and study design, with their ranking, are described in Table 1 below.

Table 1 Topics, Themes and design ranked by participants' votes

<b>Topics, themes and designs for multimorbidity Agenda</b>				
Topics	Themes	Study design formats	Points per theme	Points per topic
Measuring multimorbidity	Developing or finding measurement tool of multimorbidity	Expert consensus and cross sectional	31	49
	Epidemiology of Multimorbidity	Expert consensus or cross sectional or cohort	18	
Impact of (or on) Multimorbidity	Impact of multimorbidity on frailty or health outcomes, or cost of care, or health service utilization, or depression.	Cohort	38	40
	Impact of socioeconomic status on multimorbidity	Cross sectional or cohort	2	
Management of multimorbidity	Multimorbidity management in General Practice	Expert consensus or cross sectional	16	24
	Patient Doctor relationship evaluation in the management of multimorbidity	Cross sectional	5	
	FP workload and burden of multimorbidity	Cross sectional	3	
Patient perspective	Multimorbid patient's perspective	Qualitative study (semi directed interviews or focus groups)	8	13
	Burden of diseases effect on multimorbidity from patient's perspective	Qualitative study and expert consensus	5	
Links between complexity and multimorbidity	Multimorbidity definition as a help to detect complexity	Cross sectional	6	6
Stakeholders' perspective	Consensus for multimorbidity research according to stakeholders' interest	Expert consensus	3	3
Total Votes			135	135

*Experts had 9 points to allocate (5 for their first top theme, 3 for the second, 1 for the third). They were 15 experts with a maximum of 135 points to allocate. Top three research themes are the first three. All the others are secondary research themes.*

The research questions suggested for the multimorbidity research agenda are listed, by topic, in Table 2 below.

Table 2 Proposed research questions for the different topics and themes

Proposed research questions for the different topics and themes		
Topics	Themes	Research question examples
Measuring multimorbidity	Developing or finding measurement tool for multimorbidity	What tool could be designed using the definition of multimorbidity to enhance medical decision making (including shared decision-making)? Then design an application to be implemented in electronic medical records and evaluate that tool's effectiveness in decision-making.
	Epidemiology of multimorbidity	Are there clear trends in the development of multimorbidity at the individual (patient) level? What are the predictors of multimorbidity and are there any specific patterns of accumulation? Are there specific patterns and conditions which are likely to accelerate the development of multimorbidity? Evaluation of MM in EU countries? Would it be possible to measure the different levels of multimorbidity in order to describe the patient's complexity?
Impact of Multimorbidity	Impact of multimorbidity on patient or health service outcomes.	Have the different criteria included in the definition of multimorbidity different predictive powers in terms of patient outcomes (Mortality, health status, frailty, health outcomes decline, poly-pharmacy, depression) or health system outcomes (cost of care or poly-pharmacy or health services utilization)? With an additional question for depression: is depression a specific factor or is it related to Pain in Multimorbidity measurement?
	Impact of socioeconomic status on multimorbidity	What is the Impact of multimorbidity on particular groups (low socioeconomic status, addictive persons, societies in economic crisis)? What is the role of socioeconomic differences in multimorbidity?
Management of multimorbidity	Multimorbidity management in General Practice	What are the methods to promote medical audit in patients with multimorbidity? How does multimorbidity influence FP management? How can medical records of co-morbid patients be improved?
	Patient Doctor relationship evaluation in the management of multimorbidity	Is the doctor- patient relationship a modifying factor in the concept of multimorbidity? This study will take into account communicative challenges, including, not only FPs' communicative skills/ communicative competence, but in particular, FPs' ability to cope with their own emotions and the patients' emotions.
	FP workload and burden of multimorbidity	Do FPs of multimorbid patients have an unchanged quality of life when their patients' multimorbidity increases? Selecting groups of FPs according to their patients' multimorbidity, using the definition of multimorbidity and comparing their quality of life.
Patient perspective	Multimorbid patient's perspective	How do patients conceptualize the multimorbidity condition using their own language, concepts, metaphors, and expectations? With the intention of looking at the impact of multimorbidity on patients' experiences of self-management and health care
	Burden of diseases effect on multimorbidity (from patient's perspective) and prevention strategies	What is the role of the patient perceived burden of diseases into the multimorbidity definition? Is the burden of disease, as perceived by the patient, a modifier of multimorbidity or should it be included in the defining illnesses? Is it possible to assert that only diseases with a burden should be considered to contribute to multimorbidity? (For example, not a healed cataract or stabilized hypertension).
Links between complexity and multimorbidity	Multimorbidity definition as a help in detecting complexity	How could the concept of multimorbidity improve the ability to detect complex patients in family medicine? As risk factors, guidelines and recommendation for secondary prevention are well defined for cardiovascular diseases and diabetes mellitus, the aim of the study might be to identify the level of comorbidity (in terms of complexity) in these patients, to define barriers, to follow preventive activities which are well defined by European associations of cardiologists and diabetologists. It can be measured from the FP's perspective, and specific diseases perspective and from the patient's perspective), with the aim of formulating more specific recommendation for the preventive and curative care of multimorbid patients with cardiovascular diseases.
Stakeholders' perspective	Consensus for multimorbidity research according to stakeholders' interest	Are stakeholders interested in the patient's perspective (multimorbidity: perceived severity and grading, self-management and individualized patient-centered plan) or health professional's perspective (operational definition of MM, improvement of clinical decision support, practice-based guidelines in multimorbidity and poly-pharmacy) or in research perspective (gaps in multimorbidity research, consensus-based set of recommendations for inclusion and reporting of multimorbid patients in Randomized Controlled Trials, and for addressing multimorbidity in Clinical Practice Guidelines)



## **Discussion:**

*Main findings:* With the help of a nominal group technique, the research team was able to establish a research agenda on Multimorbidity in Family Practice. 6 topics and 11 themes were listed with their corresponding designs (see Table 1). Overall, the highest priorities were given to the following topics: measuring Multimorbidity and the impact of Multimorbidity (see Table 2).

The measurement of Multimorbidity is seen as the most important topic when totaling the votes for the different themes included. The impact of Multimorbidity on patient or health outcomes is seen by the research group as the most important theme for future research, even if it is included in the second topic to research (Impact of Multimorbidity). The management of multimorbidity in practice is seen as the third most important topic.

*Interpretation:* The measurement of Multimorbidity has been explored considerably over the past 10 years and has often been divergent as the authors did not use the same definition of this concept [7][30]. With the EGPRN concept of multimorbidity, this pitfall could be avoided, especially if an expert consensus could be obtained on the effect of the burden of diseases on multimorbidity (see Table 1). The effect of the burden of diseases on multimorbidity was a secondary research theme in this survey (7<sup>th</sup> theme to be researched) but could also be of major importance for the measurement of Multimorbidity. Although it has already been the subject of many studies, [30][31] practitioner input has, so far, been limited. Most of our experts are also practicing FPs and confirm the importance of this topic.

An alternative way of measuring multimorbidity, for this study's experts, was to determine the impact of multimorbidity on negative health outcomes (such as frailty, depression, cost of care, health service use). The impact of multimorbidity was, according to the experts in this study, for the patient, the clinical, negative result of being Multimorbid. It is a reverse way of determining multimorbidity. The burden of diseases could determine whether a patient is multimorbid and the impact of multimorbidity will determine the effect of multimorbidity on a patient's life. This alternative route could lead a research team to define the most effective variables that contribute to the concept of multimorbidity to help prevent those negative

outcomes. In addition, it could simplify the concept when it is aimed at a specific outcome, to help clinicians in everyday practice. This was an attractive issue for most experts. It could resolve the debate about measuring a concept as broad as multimorbidity seems to be. Many studies have been conducted to assess the relationship between multimorbidity and health outcomes but without solving the problem of the meaning and the intensity of that relationship [32][33].

The results underline the usefulness of the patient's perception of his/her own multimorbidity which could be an alternative way to weigh and measure multimorbidity. This perception has rarely been explored[34]. The experts emphasized this fourth topic for future research and its importance for them. They were stimulated by their own practice experience and by their need to integrate the patients' perspective as a key element of the decision making process. They felt that the patient's perception was one way to enhance the coping strategies of the patient which is of importance in the EGPRN definition of multimorbidity: to lower the level of multimorbidity.

How to improve the management of multimorbidity in everyday practice seemed of importance to our experts, as a research theme, and this management focus could be linked to patient complexity, as both are important issues for family medicine. Using the concept of multimorbidity as an aid for detecting and managing patient complexity may be a new pathway for research.

The final topic took into account all the stakeholders' perspectives, which should be incorporated into all the research, as stakeholders reflect population needs [4].

*Strengths and limitations:* Nominal group technique has already been used as a method to generate ideas for study designs[35]. It is an efficient technique to gather specific ideas about difficult research questions. The benefit of nominal group technique is that all experts have an equal opportunity to participate and influence the decision. It reduces the conforming common influence of face-to-face group meetings.

The study team tried to be as open as possible in the data collection. Information bias was limited as all the experts had open access to all the information. This bias was still possible because their prior researches in the field of multimorbidity could influence their

prioritization. To handle that possible bias, throughout the entire process, the research team stimulated open discussion and interaction through regular face-to-face meetings. Selection bias was limited by the use of a pan-European panel of researchers, with real experience of multimorbidity research, assessed by specific publications, as well as experience in practicing as FPs.

*Implications:* Results allow researchers to start relevant and, it is hoped, high-quality studies using the EGPRN concept of multimorbidity, avoiding difficulties previously encountered in research into multimorbidity, to detect and measure it in practice. They highlight the connection between multimorbidity and complexity which could lead to specific recommendations for the complex patients, often seen in Family Medicine, whose situation has rarely been explored in research up to now. They increase the possibility of using reverse methods, starting from the outcomes, or the patient's perspective, or the stakeholder's perspective, and working back to the variables in the concept which are useful for research, in order to create pragmatic models for multimorbidity.

They also open up a new aim for practitioners: multimorbidity could help them in managing patients, by using a more holistic and goal-oriented approach as the EGPRN concept of multimorbidity is closely related to the biopsychosocial model[36]. The aim would be to place the exchange with the patient at the center of the clinical consultation process rather than allocate it a supporting role [37].

They also open new perspectives in medical education, focusing on the patient's perspective which is a core competency for Family Practice, as specified in the WONCA Family Practice competencies[9].

**Conclusion:**

Using a Nominal Group technique, a research agenda is now available for further research into Multimorbidity. The highest priority should be given to measuring multimorbidity and to simplifying this model, using the outcomes of a pragmatic approach to determine the useful variables of this concept.

**List of abbreviations:**

FM - Family Medicine

FPs - Family Physicians

EGPRN - European General Practice Research Network.

NGT - Nominal Group Technique

WONCA - World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians

**Competing Interest:**

The study had a Grant of 8000 Euros from the EGPRN.

No non-financial competing interest to declare.

**Author's contributions:**

LRJY designed the study, collected data, led meetings, drafted the article and submitted it for publication. NP designed the study, collected data, led meetings and reviewed the article. LH collected data and reviewed the article. KLD collected data and reviewed the article. RA collected data and reviewed the article. MM collected data and reviewed the article. SA collected data and reviewed the article. LC collected data and reviewed the article. DC collected data and reviewed the article. CS collected data and reviewed the article. AS collected data and reviewed the article. VJ collected data and reviewed the article. LFB designed the study, assembled themes and topics and reviewed the article. DJ, designed the study, assembled themes and topics and reviewed the article. JT, collected data, assembled themes and topics and reviewed the article. ME, collected data, assembled themes and topics and reviewed the article. BP, collected data, assembled themes and topics and reviewed the article. OM, collected data, assembled themes and topics and reviewed the article. LC designed the study and reviewed the article. VRP

designed the study and reviewed the article. VMH designed the study and reviewed the article.

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# **Chapter 8**

## **General Discussion**

In this chapter, the findings of the thesis are summarized, a critical comparison with existing literature is provided, strong and weak points are displayed and a general perspective is designed. Implications for practice, health system policy, medical education and future research are discussed.

The aim of this thesis was to conceptualize the concept of multimorbidity for academic researchers and for European FPs and to define what research could be issued from that concept. The specific objectives were

- To create a European research team and to design a research protocol acceptable by all the members of the team. The hypothesis was that it would be of help to manage and to motivate the European research team.
- To define the concept of multimorbidity in the academic literature. The hypothesis was that academic researchers should have used inclusion criteria in their studies that could describe multimorbidity in an exhaustive way.
- To translate the defined concept of multimorbidity in the languages of the international team. The hypothesis was that cultural and linguistic differences could be of importance and lead to misunderstanding in the defined concept of multimorbidity.
- To assess if European FPs recognized the defined concept of multimorbidity throughout Europe and to check if they would add factors to this concept. The hypothesis was that FPs are more in line with patients than other specialists and academic researchers and that they could input an added value to the concept.
- To establish a research agenda about the concept of Multimorbidity in family medicine (FM). The hypothesis was that researchers in the field of Multimorbidity could assess if the concept of multimorbidity was useful for research in FM.

We first describe the main findings from the four studies in this part. Secondly a critical comparison with existing literature is provided. Thirdly weak and strong points are described, Fourthly the implications for FM and future research are discussed.

**What this thesis adds: A comprehensive definition of the concept of Multimorbidity issued from academic research.**

Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.

Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of Multimorbidity).

Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.

This result of the systematic literature review gave an overview of multimorbidity.

First the core components defining multimorbidity explaining what was underlied behind the word "condition":

Chronic diseases were attended as described by the WHO and many authors[1][2].

Acute diseases were an addition to the concept, which was mainly centered on chronic conditions. Nevertheless, that result was partly speculated, as some acute diseases are the way to enter in a chronic disease (ie a myocardial infraction reveals a systemic arteriopathy).

Biopsychosocial factors were of importance and that was an important addition to the concept even if it was also speculated with the possible links between multimorbidity and complexity [3].

Somatic risk factors were also mentioned as conditions and that was already described as conditions [4].

Second the modifying factors of multimorbidity were comprehensively expressed giving physicians some effective tools to manage multimorbidity. This aspect of management and modifying factors for multimorbidity were never expressed in such a comprehensive way. Even if the burden of disease, the somatic risk factors and the health care consumption were already expressed in several studies as of importance to modify the global burden of multimorbidity [5] [6][7]. The presence of the biopsychosocial factors, the social network and the patient's coping strategies were never expressed with such strength in order to modify multimorbidity.

Thirdly the effects of Multimorbidity were vague in literature and its effect on health outcomes, quality of life, disability and frailty are described with more clarity with this study.

With those eleven themes to describe or modify multimorbidity and to describe its effect on patients, new perspectives were offered to go on with this thesis.

**What this thesis adds: ten translation of the comprehensive definition of the concept of multimorbidity.**

English Original and final translation for each country

English original	Bosnia	Bulgaria	Croatia
<p>Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psycho-social factor (associated or not) or somatic risk factor.</p> <p>Any bio-psycho-social factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of Multimorbidity).</p> <p>Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.</p>	<p>Multimorbidnost (pacijent sa više bolesti u isto vrijeme) je definisana kao svaka kombinacija bolesti sa najmanje još jednom nekom bolešću (akutnom ili hroničnom) ili bio-psihosocijalnim faktorom koji je udružen ili ne) ili somatskim faktorom rizika.</p> <p>Svaki bio-psiho-socijalni faktor, svaki faktor rizika, socijalna podrška, raširenost bolesti, korištenje zdravstvene zaštite i način kako se sam pacijent nosi sa bolešću, može dovesti do promjene. (efekata multimorbidnosti).</p> <p>Multimorbidnost-višebolesnost može mijenjati ishode zdravlja i voditi povećanoj nesposobnosti ili sniženom kvalitetu života ili povećanoj osjetljivosti.</p>	<p>Полиморбидност се определя като всяка комбинация от хронично заболяване, с поне едно друго заболяване (остро или хронично) или свързан или не със заболяването био-психо-социален фактор или друг соматичен рисков фактор.</p> <p>Всеки био-психо-социален фактор, всеки рисков фактор, социалната среда, тежестта на заболяванията, използването на здравни услуги и стратегии на пациента за справяне могат да оказват влияние върху ефектите на полиморбидността.</p> <p>Полиморбидността може да доведе до промяна на очакваните резултати и до по-висока степен на инвалидност, понижено качество на живот или слабост.</p>	<p>Multimorbiditet označava bilo koju kombinaciju kronične bolesti s barem još jednom bolesti (akutnom ili kroničnom), ili s biopsihosocijalnim čimbenikom (pridruženim ili nepridruženim) ili sa somatskim čimbenikom rizika.</p> <p>Bilo koji biopsihosocijalni čimbenik, bilo koji čimbenik rizika, društveno okruženje, teret bolesti, korištenje zdravstvene zaštite te načini bolesnikova nošenja s bolešću, mogu djelovati kao modifikatori (na učinke multimorbiditeta).</p> <p>Multimorbiditet može utjecati na zdravstvene ishode te dovesti do povećanja nesposobnosti ili do smanjenja kvalitete života ili do nemoći.</p>

France	Germany	Greece	Italy
<p>La multimorbidité est définie comme toute combinaison d'une maladie chronique avec au moins : une autre maladie (aiguë ou chronique) ou un facteur biopsychosocial (associé ou non) ou un facteur de risque somatique.</p>	<p>Definiert als jegliche Kombination einer chronischen Erkrankung mit zumindest einer weiteren Erkrankung (akut oder chronisch), oder einem bio-psycho-sozialen Faktor(assoziiert oder nicht) oder einem somatischen Risikofaktor.</p>	<p>Ως πολυνοσηρότητα ορίζεται κάθε συνδιασμός οξέων ή χρόνιων νοσημάτων με ή χωρίς συσχετιζόμενους ή μη συσχετιζόμενους βιοψυχοκοινωνικούς παράγοντες ή σωματικούς παράγοντες κινδύνου.</p>	<p>Si definisce multimorbidità ogni combinazione di una malattia cronica con almeno un'altra malattia (acuta o cronica), o un fattore bio-psicosociale (associato o meno), o un fattore di rischio somatico.</p>
<p>Les effets de la multimorbidité peuvent être modifiés par : tout facteur biopsychosocial, tout facteur de risque somatique, le réseau social, le poids des maladies, la consommation de soins de santé et les stratégies adaptatives du patient.</p>	<p>Jeglicher bio-psycho-soziale Faktor, jeglicher Risikofaktor, das soziale Netzwerk, die Krankheitslast, die Inanspruchnahme des Gesundheitssystems sowie persönliche Bewältigungsstrategien können die Auswirkungen von Multimorbidität beeinflussen.</p>	<p>Αυτοί οι παράγοντες μπορούν επίσης να λειτουργήσουν ως τροποποιητές, παράλληλα με τον κοινωνικό ιστό, τη χρήση υπηρεσιών υγείας και τις στρατηγικές αντιμετώπισης του ασθενούς.</p>	<p>Ogni fattore bio-psicosociale, ogni fattore di rischio somatico, la rete sociale, il carico delle malattie, l'uso dei servizi sanitari e le strategie con cui i pazienti affrontano i loro problemi possono fungere da agenti modificanti (degli effetti di multimorbidità).</p>
<p>La multimorbidité peut modifier les résultats de santé et mener à une augmentation du handicap ou à une diminution de la qualité de vie ou à la fragilité. »</p>	<p>Multimorbidität kann Gesundheitsparameter beeinflussen und Funktionseinbußen verstärken. Sie kann auch die Lebensqualität reduzieren oder zu Gebrechlichkeit führen.</p>	<p>Μπορεί να τροποποιήσει τα αποτελέσματα στην υγεία και να οδηγήσει σε μια αυξημένη ανικανότητα, μια μειωμένη ποιότητα ζωής ή ευθραστότητα.</p>	<p>La multimorbidità può modificare i risultati di salute e portare ad un incremento della disabilità o ad un peggioramento della qualità della vita o a fragilità.</p>

Poland	Spain (Castilian)	Spain (Catalan)
<p>Wielochorobowość jest definiowana jako jakiegokolwiek połączenie choroby przewlekłej z przynajmniej jeszcze jedną chorobą (ostrą lub przewlekłą) lub z czynnikami bio-psycho-społecznymi (związanymi z nią lub nie) lub z czynnikami ryzyka.</p> <p>akikolwiek czynnik bio-psycho-społeczny, czynnik ryzyka, sieć społeczna, obciążenie chorobami, korzystanie z opieki zdrowotnej i strategie radzenia sobie przez pacjenta mogą funkcjonować jako modyfikatory.</p> <p>Wielochorobowość może modyfikować wyniki zdrowotne i prowadzić do zwiększonej niepełnosprawności lub obniżenia jakości życia lub osłabienia.</p>	<p>Se define multimorbilidad como cualquier combinación de una enfermedad crónica con al menos otra enfermedad (aguda o crónica) o un factor biopsicosocial (asociado o no) o un factor de riesgo.</p> <p>Cualquier determinante bio-psiicosocial, cualquier factor de riesgo, la red social, la carga producida por las enfermedades, el uso de recursos sanitarios y las estrategias de afrontamiento del paciente pueden actuar como modificadores del efectos de la multimorbilidad.</p> <p>La multimorbilidad puede modificar los resultados en salud y conducir a una mayor discapacidad o una menor calidad de vida o fragilidad.</p>	<p>Es defineix multimorbiditat com qualsevol combinació d'una malaltia crònica amb com a mínim una altra malaltia (aguda o crònica) o un determinant biopsicosocial (associat o no) o un factor de risc.</p> <p>Qualsevol determinant psicosocial, qualsevol factor de risc, la xarxa social, la càrrega generada per les malalties, l'ús de recursos sanitaris i les estratègies d'afrontament del pacient poden funcionar com a modificadors dels efectes de multimorbiditat.</p> <p>La multimorbiditat pot modificar els resultats en salut i conduir cap a una major discapacitat o una menor qualitat de vida o fragilitat.</p>

Those translations were entirely new. They were carefully designed in order to maintain homogeneity between them. This aspect was of importance as literal translations tend to lose meaning, and to confound concepts [8][9][10]. That homogeneity was tested with a careful cultural check and the research group assumes that those definitions are stable.

It was then possible to use the translations for inclusion of patients in collaborative research throughout 11 European countries (including Ireland and the United Kingdom with the English version).

It was also possible to use them as a basis to check whether family physicians (FPs) will recognize the concept of multimorbidity developed in that thesis throughout Europe.



In addition the research protocol for translation is available and will lead to new translations (A Portuguese translation was finalized for Brazil and Portugal and published in Biomed research international in November 2015 [11]).

**What this thesis adds: the recognition of the concept of Multimorbidity and the definition of each theme and subthemes that nominate multimorbidity throughout Europe for FPs.**

THEMES	Academic criteria	FPs' criteria	International criteria
Chronic disease	Chronic condition	Chronic condition/complaints symptoms signs	✓
Chronic disease	Chronic disease	Chronic disease	✓
Chronic disease	Psychosomatic diseases/physical implications	Psychosomatic disease	✓
Chronic disease	Complexity characteristics of chronic disease	Complexity characteristics of chronic disease	✓
Acute disease	Acute condition	Acute condition/complaints symptoms signs	✓
Acute disease	Acute disease	Acute disease	✓
Acute disease	Reaction to severe stress and acute disorders	Reaction to severe stress and acute disorders	✓
Acute disease	Complexity characteristics of acute disease	Complexity characteristics of acute disease	✓
Biopsychosocial factors and somatic risk factors	Somatic risk factors	Somatic risk factors	✓
Biopsychosocial factors and somatic risk factors	Psychological risk factors	Psychological risk factors	✓
Biopsychosocial factors and somatic risk factors	Psychosocial risk factors	Psychosocial risk factors	✓
Biopsychosocial factors and somatic risk factors	Lifestyle	Lifestyle	✓
Biopsychosocial factors and somatic risk factors	Demographic risk factor	Demographic risk factor	✓
Biopsychosocial factors and somatic risk factors	Deleted: Psychological distress	Classified in psychological risk factors et coping strategies	deleted
Biopsychosocial factors and somatic risk factors	Socio-demographic characteristics	Socio-demographic characteristics	✓
Biopsychosocial factors and somatic risk factors	Deleted: Aging	Classified in demographic risk factor et socio demographic characteristics	deleted
Biopsychosocial factors and somatic risk factors	Patients' beliefs/expectations	Patients' beliefs/ expectations/culture	✓
Biopsychosocial factors and somatic risk factors	Deleted: Physiology	Classified in physiopathology	deleted
Biopsychosocial factors and somatic risk factors	Physiopathology	Physiopathology	✓
Coping	Patients' coping strategies	(Behavioral and psychological) coping strategies	✓
Coping	Not described	Patients' basic compliance	✓
Burden of diseases	Disease complication	Disease complication	✓

Burden of diseases	Disease morbidity	Disease comorbidity / patient perception about his own multimorbidity level	✓
Healthcare consumption	Use of caregivers	Use of caregivers	✓
Healthcare consumption	Treatment or medication	Treatment	✓
Healthcare consumption	Management	Management	✓
Healthcare consumption	Disease management	(Multidisciplinary) disease management	✓
Healthcare consumption	Medical procedure	Medical procedure	✓
Healthcare consumption	Malpractice	Malpractice	✓
Healthcare consumption	Health care services	Health care services	✓
Healthcare consumption	Health care	Health care	✓
Healthcare consumption	Health care policy	Health care policy	✓
Healthcare consumption	Medical history	Medical history	✓
Healthcare consumption	Deleted: Family history	Classified into others consumption codes	deleted
Healthcare consumption	Deleted: Assessment	Classified medical procedure or health care policy	deleted
Healthcare consumption	Prevention	Prevention/education/ detection	✓
Healthcare consumption	Pain	Pain	✓
Healthcare consumption	Health services/setting/treatment	Health services/setting/treatment	✓
Healthcare consumption	Symptoms/signs/ complaints	Symptoms/signs/complaints (not pain)	✓
Healthcare consumption	Cost of care	Cost of care	✓
Healthcare consumption	Polypharmacy	Polypharmacy (including polymedication)	✓
Disability	Handicap	Handicap	✓
Disability	Functional impairments	Impairments	✓
Quality of life	Quality of life	Quality of life	✓
Quality of life	Health status	Health status	✓
Quality of life	Impairment implication	Impairment/morbidity implications	✓
Frailty	Frailty	Frailty	✓
Social network	Social network	Social Isolation	✓
Social network	Social network	Support from the network	✓
Social network	Social network	Dependence on the network	✓
Social network	Social network	Family's coping strategies	✓
Social network	Social network	Carers' protection	✓
Health outcomes	Mortality	Mortality	✓
Health outcomes	Deleted: Indicator	Classified in health outcomes	deleted
Health outcomes	Outcome	Health outcome	✓
Health outcomes	Medical research/ epidemiology/ instruments/level of multimorbidity	Medical research, epidemiology	✓

Health outcomes	Classification of morbidity statistics	Classification of morbidity statistics	✓
<b>FP's expertise</b>	Not described	<b>Holistic approach</b>	✓
<b>FP's expertise</b>	Not described	<b>Primary care management</b>	✓
<b>FP's expertise</b>	Not described	<b>Person centered care</b>	✓
<b>FP's expertise</b>	Not described	<b>Comprehensive approach</b>	✓
<b>FP's expertise</b>	Not described	<b>Specific problem solving skills</b>	✓
<b>FP's expertise</b>	Not described	<b>Intuition/gut feeling</b>	✓
<b>Doctor-patient relationship dynamics</b>	Not described	<b>Communication challenge</b>	✓
<b>Doctor-patient relationship dynamics</b>	Not described	<b>GP's and patient's experience</b>	✓

Themes are the themes developed in the concept of multimorbidity and/or by the FPs. Academic criteria are those used in the EGPRN concept of multimorbidity., FPs' Criteria are the criteria described by FPs. International criteria means that those criteria have been described in at least five out of seven countries.

The concept of multimorbidity was issued from academic research. The systematic review of literature showed a huge amount of different definitions (132 different definitions) and a great diversity in those definitions (with 1631 distinct single criteria). The comprehensive definition of the concept of multimorbidity issued from the systematic literature review was a relevant step as it gave an overview and a merging of all those definitions in one (with 57 criteria). Still some criteria remained difficult to define and this step of the research had for primary aim to understand if FPs will recognize them, and they did. The secondary aim was to check if they defined those criteria in a clearer way than academic researchers did. FPs did it also:

They emphasized that six criteria were duplicates. This was showed by the redundancies of the verbatims in two criteria. The main criterion was the one that encompassed the other.

They added one criterion in the coping strategies of the patient emphasizing the role of patient's compliance.

They added 8 criteria to explain the role of five core competencies of FM, of gut feeling, of communication challenge in patient's doctor relationship and of mutual experience of patients and doctors useful to manage multimorbidity in FM.

For all other criteria they issued an international codebook that explain precisely every criteria (Appendix) for FM and that is an important addition to our knowledge about multimorbidity.

Nevertheless the concept is still moving as some criteria could change in the near future like Frailty. Frailty was defined by FPs as the risk that the patient had a decompensation in the near future. That definition is not the one of the “Frail elderly” [12], which is a geriatric concept that is not stabilized yet [13]. This criterion label could be changed because of future changes.

Some other criterion like “health status” were very precisely designated by FPs as the way the patient feels his health status, which is exactly the definition of the English form of “health status”. That was not as clear for all academic researchers as this concept has moved during the 20 years that were searched by the review.

The comprehensive definition of the concept of multimorbidity was enriched by those new criteria and that explicitation of each criterion and is now comprehensible for FM. With those additions the definition of the concept is:

Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.

Any bio-psychosocial factor, any somatic risk factor, the social network, the burden of diseases, the health care consumption, the patient’s coping strategies, the FP’s expertise and the doctor-patient relationship dynamics may function as modifiers (of the effects of Multimorbidity).

Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.

Then a final question was popping out what to do with the concept of multimorbidity in FM?

**What this thesis adds: a research agenda about Multimorbidity in European FM.**

6 topics and 11 themes were listed with their corresponding designs. The highest priorities were given to the following topics: measure of Multimorbidity and to the impact of Multimorbidity (see table below).

<b>Topics, themes and designs for multimorbidity Agenda</b>				
Topics	Themes	Study design formats	Points per theme	Points per topic
Measuring multimorbidity	Developing or finding measurement tool of multimorbidity	Expert consensus and cross sectional	31	49
	Epidemiology of Multimorbidity	Expert consensus or cross sectional or cohort	18	
Impact of (or on) Multimorbidity	Impact of multimorbidity on frailty or health outcomes, or cost of care, or health service utilization, or depression.	Cohort	38	40
	Impact of socioeconomic status on multimorbidity	Cross sectional or cohort	2	
Management of multimorbidity	Multimorbidity management in General Practice	Expert consensus or cross sectional	16	24
	Patient Doctor relationship evaluation in the management of multimorbidity	Cross sectional	5	
	FP workload and burden of multimorbidity	Cross sectional	3	
Patient perspective	Multimorbid patient's perspective	Qualitative study (semi directed interviews or focus groups)	8	13
	Burden of diseases effect on multimorbidity from patient's perspective	Qualitative study and expert consensus	5	
Links between complexity and multimorbidity	Multimorbidity definition as a help to detect complexity	Cross sectional	6	6
Stakeholders' perspective	Consensus for multimorbidity research according to stakeholders' interest	Expert consensus	3	3
Total Votes			135	135

The measure of Multimorbidity has been considerably explored during the past 10 years and was often divergent as the authors did not use the same definition of this concept [14][15]. With the EGPRN concept of multimorbidity this pitfall could be overlapped especially if an expert consensus could be obtained on the burden of multimorbidity. Burden was a secondary research theme for this survey but could also be of major importance for the measurement of Multimorbidity. Although it has already been the subject of many studies, [15][3] practitioner input was limited so far. Most of our experts were also practicing FPs and confirmed the importance of this topic for practicing FPs.

An alternative way of measuring multimorbidity for this study's experts was to determine the impact of multimorbidity on negative health outcomes (such as frailty or others such as cost of care, health service use, depression). This alternative way could lead a research team to define the most efficient variables that contribute to the concept of multimorbidity, to help prevent deterioration of those outcomes and could simplify the concept when it is aimed at a specific outcome to help clinician in everyday practice. This was an attractive issue for most experts. It could close the discussions about the measure of a too wide concept, as multimorbidity seems to be. Many studies have been conducted to assess a relation between multimorbidity and health outcomes but without solving the problem of the sense and the intensity of that relation[5][16].

The results underline the usefulness of the patient's perception of their own multimorbidity that could be an alternative way to weigh and measure multimorbidity. This perception has rarely be explored[17].

How to improve the management of Multimorbidity in everyday practice seemed of importance to our experts as a research theme and this management focus could be linked with the patient's complexity, as both are important issues for FM. Using the concept of multimorbidity as a patient complexity's detection and management helper may be a new path for research.

A last topic was to take account of all stakeholders' perspectives. Stakeholders like active politicians or high administrative responsables are accounters of an efficient use of a country income. Their perspective should be incorporated into all primary care research as, in democratic states, stakeholders reflect population needs [18].

## **Critical comparison with existing literature**

There are several important issues to note about the concept of Multimorbidity as it was issued. The research team anticipated some themes. The burden of disease appeared on the Cumulative Illness Rating Scale (CIRS) [20] in spite of the fact that it is not in the WHO definition[1]. Indeed mild hypertension does not seem too complicated to handle whereas very aggressive cancer is a far greater cause for concern. The health care consumption was also predictable, as it makes sense to look at cost and patient uptake [3]. The health outcomes were less obvious but seemed as important as the conditions leading to them [21]. Frailty[22], increased disability [23] or reduction in quality of life [24] were already described as the consequences of multimorbidity.

Nevertheless the research team did not anticipate some of the themes. The WHO definition was limited to two or more chronic conditions in one individual [1]. The data identified in the review used acute disease to define multimorbid patients. It seems logical to concentrate on acute disease that may lead to chronic conditions in the patient, such as when myocardial infarction leads to chronic cardiac ischemia [25]. However, purely acute disease, such as infectious diseases [26] or surgical abdominal pathologies [25] were also included by researchers themselves, or through the use of classifications such as the International Classification of Primary Care (ICPC). Somatic risk factors were also included in the term ‘conditions’ by researchers. Somatic risk factors are not illnesses and were not anticipated by the research team. The inclusion of risk factors in multimorbidity is of importance as it leads to shift multimorbidity from a special characteristic of some human beings or groups of human beings to a common condition of human being. However, it is pragmatic for FPs or other Long-Term Care physicians to take them into account when considering the



management of their patients. The bio-psychosocial model [27] posits that biological, psychological (encompassing thoughts, emotions, and behaviors), and social factors, all play a significant role in human functioning in the context of disease or illness. This model is promoted, as an appropriate model for FM, nevertheless its importance, in this instance, was not anticipated by the team. The social network of the patient was included as a modifier to cope with multimorbidity. It is apparent that FPs should take into account the patient's social network (family, friends, relatives) to help the patient adapt his lifestyle to the situation. Also included were the coping strategies of the patient. Coping strategies were differentiated from social networks and the bio-psychosocial model because the patients' coping strategies were sometimes described independently of these factors in the articles examined. Those emerging themes lead to the recent concept of goal oriented care [28] using the importance of information, empowerment of the patient and the definition of process and outcomes indicators that may contribute to the monitoring of care [29]. They give body for the need to shift from disease-oriented care to goal-oriented care for multimorbid patients.

The purposes of a standardized and reproducible definition of the concept of multimorbidity are numerous and its translation into ten European languages is of great value for further research. A more comprehensive and homogeneous concept leads to better focused research, especially for quality of care and cost of care. For inclusion of patient in a research process a comprehensive and homogeneous concept of multimorbidity within 10 European languages (including English) was essential. The homogeneity of the translations was of importance for further collaborative research within EGPRN as it has been showed for literature[30].The homogeneity of the translations has been evaluated in a semantic, conceptual and cultural way which confirmed that these translations make provision for the cultural background in which FPs cope with problems in their practices, and demand a holistic approach to the patient.

Carefull translation is rarely undertaken in medical research and could lead to numerous difficulties while promoting confusion, misunderstanding and loss of the cultural background of the language[31].

When considering the previous definitions, most authors agreed to reject any concept, which was too vague or insufficiently discriminating for the selection of patients with the diseases mentioned. Those caused problems of interpretation and inclusion of patients and induced a lack of power and confounding factors [32] [25] [33] [34]. This concept of multimorbidity and its translation into ten European languages encompasses all definitions of multimorbidity found in literature [35] and will override previous limitations. Nevertheless the EGPRN concept of Multimorbidity stays, like more authors, on the cooccurrence of two or more medical conditions. A major pitfall is that most of the population after 50 could be considered as multimorbid[36]. In consequences future research could focus on the burden of multimorbidity or on what some authors describe as “intensive forms of multimorbidity” and others to an increasing complexity in multimorbidity[37][38].

The recognition of all the themes, by FPs, of the concept of multimorbidity issued by the EGPRN was very important for the research team. Three new themes emerged as modulating factors of Multimorbidity. One of them was the FP’s expertise; this theme is based on the Wonca core competencies of FM [39] and is hardly described in scientific literature. This is a new pathway for future research as FPs experience themselves as experts in the field of managing multimorbidity and complex patients. The FP’s gut feeling was also a new modulating factor that was already known. But its link to complexity and multimorbidity management was not assessed till this study [40][41]. Those competencies enhance FPs’ detection and management of multimorbidity. The other theme was the dynamic of doctor’s

patient relationship in term of quality of communication and mutual experience. The quality of FPs communication with their patient is already known as extremely important for therapeutic alliance[42][43]. But what was even more important was the interactive and mutual experience of FPs with their patients. It enhanced the importance of the reflexive physician model [27] [44] and highlighted that FPs in the field of practice integrated this skill to their practice in order to help their multimorbid patients. They tried to be aware of their patient's point of view as a global and mutual experience on both the patient and themselves. The FPs' expertise, the FP's gut feeling and the dynamic of the doctor's patient relationship lead to a more integrated care system. FPs are taking care of function and of the functional status of each individual, they use information and empowerment of the patient. They also listen to their intuition and furthermore use the mutual interaction with their patient to enhance their understanding of complexity. These possibilities were in James Mackenzie lecture in 2011 [45] and this thesis confirmed that analysis.

As a comparison with existing literature the developed concept of multimorbidity was confirmed and enhanced with this thesis. The term "condition" defining multimorbidity is now clearer and could be operationalized in research and possibly in practice. Some additions to previous definitions have been developed for the term conditions in addition to chronic diseases. For example acute diseases are of importance for FPs. This was also found in other studies [46][5]. The presence of biopsychosocial factors (including somatic risk factors but adding patient's beliefs and expectations, psychosocial factors...) is highlighted too and that is a key point for the exploration of complexity in daily FM [47] [3] [48].

The effects of Multimorbidity could be modified with what the concept calls "modifiers of multimorbidity". They enhance the role of carers, caregivers and patients and globally the role

of context for multimorbidity as it has been described in the Ariadne principles for handling primary care consultations for multimorbid patient [49]. This is also linked with Mackenzie outlook [45] and the importance for realistic goals in order to help patients instead of exhausting them with unfeasible tasks. The importance of the coping strategies of the patient are well defined by FPs and the link with therapeutic alliance is of importance as it has been shown in previous publications [43]. The burden of diseases is also taken into account by FPs with difficulties to score it in an homogeneous way [15]. The role of health care consumption in dealing with multimorbidity is of importance and could lead to new health costs indicators as it was suggested or shown in previous studies [50][51]. The importance of the social network of the patient (and of its failures) is highlighted as it was already demonstrated [52]. The results of Multimorbidity are shown by FPs, Frailty, Disability, Quality of life are in the balance as it was previously demonstrated [53][54]. Those findings and confirmations could lead to new research focused on complexity, which is one of the major task of the health systems throughout Europe. Policy makers need new indicators, synthesis and research about complexity in order to be able to handle it [55].

With the EGPRN concept of multimorbidity complexity is taken into account. Previous definitions were probably too concise in a conceptual way, leading to a misunderstanding of the key role of complexity in FM. Simplification could be of help in research but could be also a major pitfall to assess complexity[56][57]. The survey enhances the fact that, if for academic researchers it could be complicated to define precisely what a chronic or an acute disease is, it is not for FPs on the field. Academic researchers tend to use complex combinations of existing classification like ICPC 2 [58] or ICD 10 [59] and tend to complexify definitions. FPs in this study cited more than 2500 codes of chronic and acute diseases and had no difficulties to use them in practice. Their extensive use of ICD 10 in the

verbatim has to be emphasized.

The EGPRN concept is a conceptual understanding of all the criteria that deal with multimorbidity. Nevertheless we should admit that it stays broad and that most of patients in FM are multimorbid. This stays as the major pitfall of the research process at this stage. We tried to override this trouble with a research agenda.

This research agenda on multimorbidity for FM was established with a nominal group technique: 6 topics and 11 themes were listed with their corresponding designs. Overall the highest priorities were given to the following topics: measure of Multimorbidity and to the impact of Multimorbidity. The measure of Multimorbidity has been considerably explored during the past 10 years and was often divergent as the authors did not use the same definition of this concept [14][15]. With the EGPRN concept of multimorbidity this pitfall could be overlapped especially if an expert consensus could be obtained on the burden of multimorbidity. Burden was a secondary research theme for this survey but could also be of major importance for the measurement of Multimorbidity. Although it has already been the subject of many studies, [3] [15] practitioner input was limited so far. Most of our experts were also practicing FPs and confirmed the importance of this topic for practicing FPs.

An alternative way of measuring multimorbidity for this study's experts was to determine the impact of multimorbidity on negative health outcomes (such as frailty, depression, cost of care, health service use). This alternative way could lead a research team to define the most efficient variables that contribute to the concept of multimorbidity, to help prevent deterioration of those outcomes and could simplify the concept when it is aimed at a specific outcome to help clinicians in everyday practice. This was an attractive issue for most experts.

It could close the discussions about the measure of a too wide concept, as multimorbidity seems to be. Many studies have been conducted to assess a relation between multimorbidity and health outcomes but without solving the problem of the sense and the intensity of that relation[5][16]. The results underline the usefulness of the patient's perception of their own multimorbidity that could be an alternative way to weigh and measure multimorbidity. This perception has rarely been explored[17] and seems appealing [60].

How to improve the management of Multimorbidity in everyday practice seemed of importance to our experts as a research theme and this management focus could be linked with the patient's complexity, as both are important issues for FM. Using the concept of multimorbidity as a patient complexity's detection and management helper may be a new path for research.

A last topic was to take account of all stakeholders' perspectives, which should be incorporated into all research, as stakeholders reflect population needs [18].

## **Weak and strong points of the research process**

For the concept issued from the systematic literature review the strong points are as follows:

a more comprehensive definition leads to better focused research, especially for quality of care and cost of care. This comprehensive definition is helpful for targeting resources in a far more accurate way than the WHO definition as it describes what lies behind the term condition. In addition it gives more focused prognoses for individuals and improves risk management. It improves clinical decision making, in terms of risk/benefit evaluation. It could help decision-making when considering the position of an individual on the spectrum of palliative versus aggressive care.

The 21-year time span applied to the sourcing of documents could be seen as a limitation but, in fact, multimorbidity is rarely described before that period [61].

The selection process was very broad in order to avoid losing information and was following the PRISMA statement for systematic reviews [62]. The three main medical databases were screened in order to avoid any information bias.

The use of the single keyword multimorbidity provided a protection against conflation with related terms such as “comorbidity, morbidity, multiple morbidity...”, as it was felt that the literature around those terms was already diverse.

For the concept issued from the systematic literature review the weak points are as follows:

There was a voluntary selection bias (looking only at medical databases) as the object was to find a pre-existing model (ie multimorbidity) in medical studies. And subsequently the team did not look at the way other scientists could look at the concept.

The analysis and coding of the data extracted from literature were undertaken as carefully as possible with the help of native speakers and linguists. The use of different

researchers working blind and pooling data at each step of coding was performed to lower the loss of data. Nevertheless it is still possible to have loss some information even if the research team assumes that it is unlikely.

Confronting the differences between conditions, disease, risk factors could have been clarified using the ICF-framework [63]. The ICF Framework allows to integrate patient perception and permits health professional's thinking and reaction about functioning, disability and health [64]. Nevertheless the article was complicated enough and the research team choosed to keep a thematic analysis. That could be a limitation to interpret data leading to some confusion bias.

Starting from a systematic literature review of published scientific work could be a limitation as this method eliminates grey literature, lectures, opinion articles and unpublished works and lead to an information bias. The research team anticipated this pitfall by using in the following steps a qualitative survey with practicing FPs. Qualitative research was undertaken in order to enrich the research process.

Finally at the end of the systematic review contacts were taken to produce a new ICPC code or an international resident assessment instrument (interRAI) using multimorbidity definition. For the ICPC code the concept of multimorbidity was complicated to integrate for the ICPC committee as it encoumpassed reason of encounters (including point of view of the patient), diagnosed health conditions and care, which are the three pillars of ICPC. Discussions are still ungoing with some participants of the WONCA committee for ICPC. For the interRAI the complexity and the price of the procedure to achieve an integrated instrument prevented the research team to go further.



*For the translations' studys the weak points are as follow:*

In some countries (France and Germany), during the first round, some of the participants believed they had to evaluate the accuracy of the concept, which led to a confusion bias. This bias was disentangled at the beginning of the second round while emphasizing the role of translation as the only goal of the study. The scientific committee was concerned about the small size of the Bosnian and Spanish-Catalan groups, it was reassured by the homogeneity of their translations.

*For the translations' studys the strong points are as follow:*

The Delphi technique for translation had its own strengths and weaknesses. Nevertheless, it is seen as an accurate consensus technique in health research [65] [66]. There was no information bias in this study as all data was sent to all experts and group members. There was no selection bias either. The sample's characteristics were very carefully followed up in every country to ensure that it was composed of genuine experts, both in FM and in use of English. The cultural check was complete with the help of native speakers, all team leaders some linguists and English native speakers.

*For the qualitative survey about the perception of the concept by European FPs possible weak points were:*

A pitfall of qualitative research could be confusion due to personal interpretation. This was very unlikely here as two pairs of two independent researchers working blind were involved at each step of the coding process and group consensus meeting with all teams were executed. The sample's characteristics are always debatable. Those were on age, gender, experience, setting type and practice type. The research team assumed that it gave diversity enough to explore all kind of FPs throughout Europe.

*For the qualitative survey about the perception of the concept by European FPs the strong points were:*

There was no lack of information as exactly the same data was sent to all participants and all needed translations were carefully executed.

There was no selection bias as all studies paid great attention to follow the protocol for maximum variation sampling

The main strength was in the set of 13 homogeneous qualitative studies conducted throughout Europe with an international collaborative team from the EGPRN. 211 FPs were interviewed coming from all geographic parts of Europe, all type of European health system (primary care centered, secondary care centered or hospital centered), all type of European culture (Former Communist countries, Catholic, Protestant, Muslim) and most of European linguistic groups (Romance, Germanic, Slavic and Greek). The richness and completeness of the data with a massive amount of codes (10999) and the full internationalization of the themes of the definition highlight the accuracy and interest of the concept for FPs in the field of practice.

*For the research agenda the weak points were:*

The research process was undertaken by mail and has been complicated to handle. Physical meetings were scheduled to override that difficulty.

*For the research agenda the strong points were:*

Nominal group technique was already used as a method to generate ideas for study designs[19]. It is an efficient technique to gather specific ideas about difficult research questions. The benefit of nominal group technique is that all experts get equal opportunities to participate and influence the decision. It reduces the conforming common influence of face-to-face group meetings.

The research team tried to be as open as possible in the data collection. Information bias was limited as all experts had open access to all information. Selection bias was limited by the use of a pan European panel of researchers with real experience of multimorbidity research assessed by specific publications and also experience in practice as FPs. Confusion bias was as constraint as possible as experts were involved into open mail group discussions and face to face meeting and the research team enhanced discussion and interaction all through the process.

## **What this thesis adds: the research perspectives about Multimorbidity in European FM.**

### *Implications*

Results allow researchers to start relevant and hopefully high-quality studies using the EGPRN concept of multimorbidity, overlapping preceding difficulties encountered in research about multimorbidity to detect and measure it in practice. They highlight the connection between multimorbidity and complexity. They could lead to specific recommendations for the complex patients (often seen in FM) who are hardly explored in research up to now even if that specific need is recognized[67][68]. They enhance the possibility to use reverse methods starting from the outcomes, or the patients' perspective of the stakeholders' perspective to lead to the useful variables in the concept for research to describe pragmatic models for multimorbidity.

They also open a new perspective for practitioners as multimorbidity could help them in managing patients with a more holistic approach as the EGPRN concept of multimorbidity is highly related with the biopsychosocial model[44]. This means that we could place the consultation with the patient at the centre of the clinical universe, and not an index condition.

They also open new perspective in medical education with the opening on the patient's perspective which is a core competency for Family Practice as the WONCA designed Family Practice competencies[39] .

### Relevance for the clinical perspective

FPs often faces complex patient[57]. Their awareness of that complexity is sometimes vague [41]. The concept of multimorbidity could help them in different ways:

- **Detection:** a consensual definition of what a multimorbid patient is was issued (Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor). That definition allows FPs to detect multimorbid patients and to evaluate the severity and the complexity of the patient. This enhanced awareness will be of help for practice.
- **Management:** what this concept of multimorbidity adds is that not only burden of disease has to be managed but also bio-psychosocial factor, somatic risk factor, social network, health care consumption and patient's coping strategies. This open new means for FPs to help their multimorbid patients or to enhance medical, social familial help around them. It gives also a new perspective with the possibility to enhance the coping strategies of the patient. Finally it assesses the importance of collaborative care around the patient. The aim of FM is not to be on the center of the follow up but to organize and manage it. This is precisely what multimorbid patient needs according to the concept of multimorbidity.
- **Outcomes:** this concept leads FPs to be aware of the results of multimorbidity in terms of health cost, quality of life and disability. This is of importance to manage them in an enhanced way to prevent those difficulties or to accompany them when they will occur. This is very often cited in literature since Engel [27] described the bio psycho social model but no conceptual model was issued till now to help physicians to be aware of those difficulties and to try to anticipate them in everyday practice. What was informal could now start to be formal.

### Relevance for Health care organization and policy

This concept of multimorbidity could help developing innovative models to handle multimorbid patients not aimed only on medicine but also on social services for stakeholders. The balance of needs of those patients between health care consumption and social services consumption is now evaluable in term of final outcomes (morbidity, quality of life, disability).

New indicators could be issued to predict health cost for multimorbid patients. This is of importance as those patients are the most expensive for all developed countries health systems [51][69]. Being aware of the evolution of that specific population could lead the health systems to a better cost's prevision. This could be of great help to help the populations to a better comprehension of the burden of health cost and the needs for specific fundings. This is true also for developing countries as the incidence of multimorbidity and non communicable diseases is raising in those countries [70].

This concept leads to collaborative care and to goal oriented care [29][49] [71][72][73]. It is another suggestion, for stakeholders, to enhance these types of care. The concept of multimorbidity has the possibility to make them understand the necessity to develop cares aimed at patient centeredness, with a holistic approach and with negotiated goals. It should make them understand that all caregivers should have the place they deserve in the follow up of those patients. In addition education turned on collaborative care, patient centeredness and holistic approach should be promoted, by stakeholders, in all caregivers or social workers educational programs according to this concept.

### Relevance for medical education

This concept of multimorbidity added the idea that for an optimal management FPs should be competent in the terms of the core competencies of FM developed by the Wonca [39]. This is of importance as a competence-based curriculum with the constructivist perspective of building competencies is not the rule in most countries. Teachers in FM are in a fierce struggle in many countries to achieve that essential task. This concept of multimorbidity should give them new arguments to develop such a training perspective and curriculum.

This concept of multimorbidity emphasizes the importance of a fair relation between patients and doctors. That relation is not only what was called patient doctor relationship mostly aimed at therapeutic alliance or adherence to treatment [74]. It is an in depth relation where the mutual experience could lower or raise the burden of multimorbidity. FPs are experts to that peculiar communication that leads to truthfulness from and to their patients and to the acceptance of their feelings' role in practice. That in depth relationship should be explained and trained in pre graduate education as an added tool for person centered care.

### Relevance for future research

Results allow researchers to start relevant and hopefully high-quality studies using the EGPRN concept of multimorbidity, overlapping preceding difficulties encountered in research to detect and measure multimorbidity. They focus the needs into the measure of multimorbidity and the impact of multimorbidity. They highlight the connection between

multimorbidity and complexity and could lead to specific recommendations for the complex patients often seen in FM who are hardly explored in research up to now. They enhance the possibility to use reverse methods starting from the outcomes, or the patients' perspective of the stakeholders' perspective to lead to the useful variables in the concept for research to describe pragmatic models for multimorbidity.



**Conclusion:**

Using a step-by-step careful research process this thesis created a European research team to design its research protocol. It defined the concept of multimorbidity using academic literature. It translated this defined concept of multimorbidity in ten European languages to use it in qualitative research throughout Europe. It assessed that European FPs recognized the defined concept of multimorbidity all over Europe. It highlighted that European FPs added to the concept the use of the Wonca's core competencies of FM and the dynamics of the doctor-patient relationship for detecting and managing multimorbidity. Finally it established a research agenda about the concept of Multimorbidity in FM focused on the measurement of multimorbidity and its impact on patient. It also enhanced the need for the simplification of this concept using a pragmatic approach to determine the useful variables of the concept on its outcomes and its link to complexity.

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# Abbreviations

EGPRN : European General Practice Research Network

FM : Family Medicine

FP: Family Physician

WHO : World Health organization

Wonca : WOrld family doctors. CARing for People





# Summary

This chapter provides a short English summary of this research project.

Multimorbidity is a concept encompassing all the medical conditions of an individual patient. The concept links into the European definition of Family Medicine and its core competencies. However, the definition of multimorbidity and its subsequent operationalization were unclear. There was a great lack of data about what multimorbidity was and what its usefulness could be. For the World Health Organization people with multimorbidity are “people being affected by two or more chronic health conditions”. The WHO highlighted the need for research and practice to take into account complexity and that multimorbidity was an efficient concept to understand and then manage complexity. However the word “condition” was broad but not that manifest for research or practical purpose. “Conditions” has led to numerous interpretations and gave great diversities for the inclusion of patients in research. Multimorbidity is a very challenged concept for Family Medicine. A lack of knowledge is persistent for the usefulness of the concept of multimorbidity in family medicine. Some authors linked Multimorbidity with cost of care, health related quality of life, depression, frailty, patient’s complexity... The links with complexity could be of high interest for the implementation of usable recommendations in practice. The European General Practice Research Network (EGPRN) was concerned with the concept of Multimorbidity and constituted a research group to produce, translate and check the accuracy of a comprehensive definition of multimorbidity. The management of that research group was one of the challenges of this thesis.

The research question of this thesis was: How can we better formulate the concept of Multimorbidity, translate and validate it (conceptualization) for academic researchers and for European Family Physicians? What research could be issued from that reformulated concept?

The first study aim was to produce a comprehensive definition of multimorbidity. The method was a systematic review of literature involving eight EGPRN national teams. The databases searched were Pubmed, Embase and Cochrane (1990-2010). Only articles containing descriptions of multimorbidity criteria were selected for inclusion. The multi-national team undertook a methodic data extraction, according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.

The results identified 416 documents, selected 68 abstracts, included 54 articles and found 132 definitions with 1631 different criteria. These criteria were aggregated into 11 themes which led to the following definition:

Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor. Any bio-psychosocial factor, any risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of multimorbidity). Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.

This first study produced a comprehensive definition of multimorbidity. The resulting improvements in the management of multimorbidity, and its usefulness in Long-Term Care and in Family Medicine, will have to be assessed in future studies.

The second study objective was to translate that comprehensive definition into European languages and to validate the semantic, conceptual and cultural homogeneity of the translations for further research. The method was a forward backward translation of the EGPRN's definition of multimorbidity followed by a Delphi consensus procedure assessment, a backward translation and a cultural check for all translations. This design was achieved to ensure the homogeneity of the translations in their national context. Consensus was defined as 70 % of the scores being higher than 6. Delphi rounds were repeated in each country until a consensus was reached.

The results were drawn by 229 European medical expert FPs that participated in the study. Ten consensual translations of the EGPRN comprehensive definition of multimorbidity were achieved.

This second study produced a comprehensive definition of multimorbidity available in English and ten European languages for further collaborative research in FM and long-term care.

The third study objective was to explore how European Family Physicians (FPs) perceived and worked with this concept of multimorbidity and whether they would add new themes to it. The method was qualitative survey using focus groups or semi structured interviews as data collection techniques with a purposive sample of practicing FPs from each country. Data collection continued in each country until saturation was reached. Analysis was undertaken using a grounded theory based method. In each national team, the analysis was carried out by four researchers, working independently on the coded data and pooling them afterwards. Finally, an international team of 10 researchers pooled the axial and selective coding of all the national teams to check the concept of multimorbidity and highlight emerging themes.

The results highlighted the maximal variation and saturation of the sample that were reached

in each country with 211 FPs selected for inclusion. The 11 themes which describe multimorbidity in the EGPRN definition were identified in each country. Two additional themes emerged from this survey: the use of the Wonca's core competencies of FM and the dynamics of the doctor-patient relationship in detecting and managing Multimorbidity.

The third study underlined that European FPs recognized the enhanced concept of multimorbidity and added the two previously mentioned themes. These results open new perspectives regarding the dealing with complexity through the use of the concept of Multimorbidity in FM. It also highlighted the complexity of the concept of multimorbidity and its main weakness: what is the burden of multimorbidity that needs an intervention from carers? This issue led to a need for simplification.

The fourth study wanted to achieve a research agenda in order to detail new paths for the simplification of the concept in FM. The research question was: What research themes help our understanding of the concept of multimorbidity in family medicine?

The method was a nominal group design by e-mail with a purposive panel of 15 experts in the field of multimorbidity coming from three groups of researchers: the EGPRN working group, the Threads and Yarns multimorbidity group and academic researchers in the field of multimorbidity from Polish, UK and Dutch universities. The Nominal group followed four phases: ideas generation phase, ideas recording phase, evaluation and analysis phase and a prioritization phase. A research agenda was established with 6 topics and 11 themes with their corresponding designs. The highest priorities were given to the following topics: measure of Multimorbidity and to the impact of Multimorbidity. Reverse methods starting from the outcomes of multimorbidity to lead to the useful variables in the pragmatic concept for research on multimorbidity, should also be used to simplify the concept

Using a step-by-step careful research process this thesis created a European research team to design its research protocol.

The systematic review of literature showed a huge amount of different definitions (132 different definitions) and a great diversity in those definitions (with 1631 distinct single criteria). The comprehensive definition of the concept of multimorbidity issued from the systematic literature review was a relevant step.

The translations of the concept were finalized for Bulgarian, Castellan, Catalan, Croatian, French, Galician, German, Greek, Italian and Polish.

The qualitative studies confirmed the concept for FPs and added two modifiers of Multimorbidity with the Wonca's core competencies of FM and the doctor-patient relationship dynamics as a help to detect and manage multimorbidity.

The research agenda focused future research needs on the measurement of multimorbidity and its impact on patient. It also enhanced the need for the simplification of this concept using a pragmatic approach to determine the useful variables of the concept on its outcomes and its link to complexity.



# Samenvatting

Dit hoofdstuk geeft een korte samenvatting van dit doctoraatsonderzoek.

Multimorbiditeit is een concept dat alle medische aandoeningen omvat van een individuele patiënt. Het concept sluit aan bij de Europese definitie van de Huisartsgeneeskunde en bij de kerncompetenties van de huisarts. De definitie van multimorbiditeit en de toepassing ervan bleven de laatste jaren echter onduidelijk. Er was een groot gebrek aan gegevens over wat multimorbiditeit precies betekende en hoe men dit kon gebruiken. Voor de Wereldgezondheidsorganisatie (WGO) is multimorbiditeit “het gelijktijdig optreden van twee of meer chronische ziekten en medische condities bij één persoon”. De WGO benadrukte de noodzaak dat men zowel in onderzoek als de klinische praktijk meer rekening zou moeten houden met complexiteit en dat multimorbiditeit een efficiënt concept is om complexiteit te begrijpen en aan te pakken. Echter het begrip “conditie” is te breed geformuleerd en niet zo herkenbaar voor gebruik in onderzoek en praktijk. “Conditie” heeft geleid tot talrijke verschillende interpretaties en tot grote verschillen in te includeren patiënten voor onderzoek. Multimorbiditeit is een erg uitdagend concept voor de huisartsgeneeskunde. Er blijft echter gebrek aan kennis om het concept goed te gebruiken binnen de huisartsgeneeskunde. Sommige auteurs brachten multimorbiditeit in verband met kosten van zorg gezondheidsgerelateerde levenskwaliteit, depressie, kwetsbaarheid (frailty), de complexiteit van de patiënt, ... Het verband met complexiteit zou erg interessant kunnen zijn voor het implementeren van bruikbare aanbevelingen in de praktijk. De European General Practice Research Network (EGPRN) vond het concept multimorbiditeit belangrijk en richtte een



onderzoeksgroep op om een allesomvattende definitie van multimorbiditeit te formuleren, te vertalen en na te kijken op zijn nauwkeurigheid. Het aansturen van deze onderzoeksgroep was één van de uitdagingen voor dit doctoraat.

De onderzoeksvraag voor deze thesis was: Hoe kunnen we het concept multimorbiditeit beter omschrijven, vertalen en valideren voor academische onderzoekers en voor de Europese huisartsen? Welk onderzoek kan men formuleren vanuit dit geherformuleerde concept?

Het eerste doel was om een allesomvattende definitie van multimorbiditeit te formuleren. De gebruikte methode was een systematisch literatuuronderzoek met acht EGPRN nationale teams. De databases die doorzocht werden waren Pubmed, Embase en Cochrane (1990-2010). Enkel artikels die beschrijvingen bevatten van multimorbiditeit criteria werden geselecteerd voor inclusie. Het multinationale team deed een data-extractie, volgende de methode van de PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) richtlijnen. Het onderzoek vond 416 documenten, selecteerde 68 abstracts, includeerde 54 artikels en vond uiteindelijk 132 definities met 1631 verschillende criteria. Deze criteria werden samengevoegd in 11 thema's die leidde tot de volgende definitie: Multimorbiditeit wordt gedefinieerd als elke combinatie van een chronische ziekte met tenminste één andere ziekte (acuut of chronisch) of bio-psychosociale factor (geassocieerd of niet) of somatische risicofactor. Elke bio-psychosociale factor, elke risicofactor, het sociaal netwerk, de ziektelast, de gezondheidszorgconsumptie en de coping-strategieën van de patiënt kunnen functioneren als modifiers (van de effecten van multimorbiditeit). Multimorbiditeit kunnen de gezondheidsuitkomsten modificeren en leiden tot een verhoogde beperktheid, een verlaagde levenskwaliteit of kwetsbaarheid.

Deze eerste studie produceerde een allesomvattende definitie van multimorbiditeit. In de toekomst zullen studies moeten beoordelen of deze definitie de aanpak van multimorbiditeit kan verbeteren, en of het concept nuttig kan zijn voor chronische zorg en in de huisartsgeneeskunde.

De tweede doelstelling van het onderzoek was om deze allesomvattende definitie te vertalen in verschillende Europese talen en de semantische, conceptuele en culturele homogeniteit van de vertalingen te valideren voor verder onderzoek. De vertaling van de definitie gebeurde volgens de forward-backward translation-methode. Dit werd gevolgd door een Delphi consensus procedure beoordeling, een backward vertaling en een culturele check van alle vertalingen. Dit verzekerde de homogeniteit van alle vertalingen in hun nationale context. Consensus werd gedefinieerd wanneer 70 % van de scores hoger waren dan 6. In elk land werden de Delphi rondes herhaald totdat consensus werd bereikt.

We verkregen onze resultaten door deelname van 229 Europese medische expert-huisartsen. Aldus werden op basis van consensus tien vertalingen van de EGPRN allesomvattende definitie van multimorbiditeit ontwikkeld.

Deze tweede studie gaf als resultaat een allesomvattende definitie van multimorbiditeit in het Engels en in tien Europese talen, beschikbaar voor verder collaboratief onderzoek in de huisartsgeneeskunde en chronische zorg.

Als derde doelstelling wilde het onderzoek exploreren hoe Europese huisartsen het concept multimorbiditeit ervaren en hiermee werken en of zij nieuwe thema's wensten toe te voegen. Men gebruikte een kwalitatieve onderzoeksmethode met focusgroepen en semi-gestructureerde interviews als dataverzamelingstechniek en met een doelgerichte steekproef van actieve huisartsen in elk land. Dataverzameling werd in elk land verdergezet tot

datasaturatie werd bereikt. Voor de analyse werd een grounded theory gebaseerde methode gebruikt. In elk nationaal team, werd de analyse uitgevoerd door vier onderzoekers, die onafhankelijk van elkaar de gecodeerde gegevens analyseerden en ze nadien samenbrachten. Tenslotte bracht een internationaal team van 10 onderzoekers alle axiaal en selectief gecodeerde gegevens van alle nationale teams bij elkaar, met de bedoeling om deze te vergelijken met het concept multimorbiditeit en de opvallende thema's aan te duiden.

De bereikte resultaten bewijzen de maximale variatie en saturatie van de steekproef in elk land met 211 geselecteerde huisartsen voor inclusie. In elk land werden alle 11 thema's geïdentificeerd die multimorbiditeit in de EGPRN definitie beschrijven. Er kwamen twee bijkomende thema's uit dit onderzoek: het gebruik van de kerncompetenties van WONCA definitie van huisartsgeneeskunde en de dynamiek van de arts-patiëntrelatie om multimorbiditeit op te sporen en aan te pakken.

De derde studie bevestigde dat de Europese huisartsen het uitgebreide concept van multimorbiditeit herkenden evenals de twee toegevoegde thema's. Deze resultaten openen nieuwe perspectieven voor het omgaan met complexiteit door het gebruik van het concept multimorbiditeit in de huisartsgeneeskunde. Het toonde ook de complexiteit van het concept multimorbiditeit aan alsook de belangrijkste beperking ervan: welke last van multimorbiditeit heeft juist een interventie vanuit verzorgers nodig? Dit aspect bracht naar voren dat er noodzaak is voor vereenvoudiging.

De vierde studie wenste een onderzoeksagenda op te stellen om nieuwe paden voor vereenvoudiging van het concept in de huisartsgeneeskunde te omschrijven. De onderzoeksvraag was: welke onderzoeksthema's kunnen helpen om het concept van multimorbiditeit in de huisartsgeneeskunde beter te begrijpen?

Een nominale groepsmethode werd gebruikt op basis van een e-maildiscussie met een doelgericht samengesteld panel van 15 experts in het domein van multimorbiditeit vanuit drie groepen onderzoekers: de EGPRN werkgroep, de Threads en Yarns multimorbiditeit groep en academische onderzoekers in het domein multimorbiditeit vanuit universiteiten in Polen, Groot-Brittannië en Nederland. De nominale groep methode verliep in vier fases: ideeën genereren, er een lijst van maken, de ideeën evalueren en analyseren en tenslotte prioriteren. Een onderzoeksagenda werd opgesteld met 6 topics en 11 thema's en de daaraan gekoppelde designs. De hoogste prioriteit werd gegeven aan de volgende topics: meting van multimorbiditeit en de impact ervan. Om het concept te vereenvoudigen zou men ook omgekeerde methodes moeten gebruiken die starten vanuit de gevolgen van multimorbiditeit om te komen tot de bruikbare variabelen binnen het pragmatisch concept voor onderzoek over multimorbiditeit.

Door een stapsgewijs en zorgvuldig onderzoeksproces heeft dit doctoraatsonderzoek een Europees onderzoeksteam gevormd om het onderzoeksprotocol gestalte te geven. Het systematische literatuuronderzoek toonde de enorme hoeveelheid aan verschillende definities (132 verschillende definities) en een grote diversiteit in deze definities (met 1631 verschillende enkele criteria). De allesomvattende definitie voor het concept multimorbiditeit opgesteld op basis van een systematische literatuuronderzoek was een relevante stap. De vertalingen van het concept werden gerealiseerd in de volgende talen: Bulgaars, Spaans, Catalaans, Croatisch, Frans, Portugees, Duits, Grieks, Italiaans en Pools.

Het kwalitatief onderzoek bevestigde het concept voor de huisartsen en voegde twee modificatoren toe met name WONCA's kerncompetenties van de huisartsgeneeskunde en de arts-patiëntrelatie dynamiek als een hulpmiddel om multimorbiditeit op te sporen en aan te pakken.

De onderzoeksagenda gaf aan dat er behoefte is aan onderzoek over het meten van multimorbiditeit en de impact ervan op de patiënt. Het concept moet ook vereenvoudigd worden door het gebruik van een pragmatische benadering om die variabelen van het concept te definiëren die nuttig zijn voor relevante uitkomsten voor de patient en de relatie tot complexiteit.

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The love, forgiveness and understanding of my six children and wife were essential. The thoughts of an often absent father and husband are with them. Real life is when dreams meet reality and is finally dedicated to Nathalie, my wife and life companion, without her help that work would never start.

# Curriculum Vitae

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## Education

- 1991  
Diplôme universitaire de médecine urgente – Faculté de médecine de Brest – Université de Bretagne Occidentale.
- 1992  
Diplôme universitaire de réparation juridique du dommage corporel – Institut médico-légal de Paris – Université René Descartes Paris.
- 1994  
Diplôme d'état de docteur en médecine – Faculté de médecine Broussais Hôtel Dieu Université Pierre et Marie Curie, Paris. Médaille de bronze (Prix de Thèse). Lauréat de la faculté de médecine de Paris.
- Diplôme universitaire de prévention de la santé de l'enfant – Faculté de médecine de Brest - Université de Bretagne Occidentale.
- 1998  
Diplôme universitaire d'immunologie clinique – Faculté de médecine de Brest - Université de Bretagne Occidentale.
- 2006  
Diplôme Inter Universitaire de Pédagogie médicale – Faculté de médecine de Brest – Université de Bretagne Occidentale – Avec mention.
- 2010  
Diplôme inter universitaire d'échographie médicale 2010 – Faculté de médecine de Rennes. Université de Rennes 1.
- Qualitative research in primary Health Care september 2010: Antwerp university, (Belgium).
- International course on research in primary health care : UMC Amsterdam, (Netherlands), september 2010.
- 2011  
International summer course on research in primary health care , second year: Maastricht University (Netherlands), september 2011,.
- 2012  
International Spring course on research in primary health care, second year: Marburg University (Germany), June 2012.
- International Summer course on primary Health care, Antwerp University (Belgium), October 2012 second year.
- PhD student at university of Antwerp, Belgium and Université de Bretagne occidentale, France. Tutors Paul Van Royen, MD, PhD, Dean, Claire Lietard, PhD, HDR. Topic : How can we better formulate the concept of Multimorbidity, translate and validate it (conceptualization) for academic researchers and for European Family Physicians? What research could be issued from that reformulated concept?



### **Professional Practice**

- 1994 Family Physician, group practice in Lanmeur (Finistère, France)
- 1994 Member of the medical staff of Lanmeur's Hospital
- 1995 In charge of the medical information department of Lanmeur's Hospital
- 2007 Animator of the peer group of FPs of Lanmeur
- 2010 In charge of the medicine and palliative care ward of Lanmeur's Hospital
- 2011 Member of the directory of Lanmeur's Hospital

### **University Titles**

- 1999 Lecturer at university of medicine Brest.
- 2001 clinical teacher at university of medicine Brest.
- 2002 Tutor at university of medicine Brest.
- 2004 in charge of Lanmeur 's university primary care clinic.
- 2005 Senior lecturer in Family medicine at university of medicine Brest.
- 2008 Associate professor in Family medicine at university of medicine Brest
- 2008 Director of the département de médecine générale at university of medicine Brest
- 2011 Committee member of the department of continuous medical education at university of medicine Brest
- 2011 Committee member of the pedagogic department at university of medicine Brest
- 2011 Committee member of the scientific department at university of medicine Brest
- 2013 professor in family medicine at university of medicine Brest
- 2014 Director at ERCR SPURBO (Labelled research team in Family Medicine and Public Health)

## Scientific Work

### 21 Original articles in French or other national languages in national publications

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13. Le Reste JY, Le Lez N, Le Floch B, Barraine P, Cadier S, Nabbe P. Infections broncho pulmonaires nosocomiales en EHPAD. *Le suivi des recommandations suffit pour le traitement*. *exercer* 2011;95:25-9.
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4. Le Reste JY, Bail Ph, Jouquan J. Un portfolio électronique peut-il faciliter ou contribuer à améliorer l'évaluation des étudiants à la faculté de médecine de Brest ? Communication orale au 6<sup>ème</sup> Congrès National du CNGE, Dijon, 24 et 25 novembre 2005.
5. Le Reste JY, Jeffredo P, Bail P. Evolution à Brest vers un portfolio plus sélectif. Pourquoi ? Comment ? Communication orale au 7<sup>ème</sup> Congrès National du CNGE, Poitiers, 23 et 24 novembre 2006.
6. Le Reste JY, Bail P. Comment augmenter la recherche clinique dans un département d'enseignement de médecine générale ? Une expérience brestoïse. Communication orale au 7<sup>ème</sup> Congrès National du CNGE, Poitiers, 23 et 24 novembre 2006.
7. Lucas-Barbré C, Le Reste JY, Bail P. Surveillance biologique des AVK. Une étude de pratique et de coordination entre patients et professionnels de santé dans le nord Finistère. Communication orale au 7<sup>ème</sup> Congrès National du CNGE, Poitiers, 23 et 24 novembre 2006.
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9. Le Bivic G, Cadier S, Bail P, Le Reste JY. Pertinence de la maison médicale de garde de Lannion (22) dans le dispositif de permanence des soins. Communication orale 2<sup>ème</sup> congrès de la médecine générale Lyon, 12-14 juin 2008.
10. Cadier S, Hummers Pradier E, Nowak E, Le Reste JY. Décision médicale : transmission des données cliniques et paracliniques concernant les patients Alzheimer lors de l'institutionnalisation. Communication orale 2<sup>ème</sup> congrès de la médecine générale Lyon, 12-14 juin 2008.
11. Cadier S, Le Roux V, Nabbe P, Le Reste JY. Description de la population de l'hôpital local de Lanmeur étude démographique et de l'activité médicale. Poster 2<sup>ème</sup> congrès de la médecine générale Lyon, 12-14 juin 2008.
12. Bail P, Barraine P, Le Floch B, Cadier S, Le Reste JY, Nabbe P. Comment faire face aux contraintes du DES de MG en conservant le cadre pédagogique du tutorat ? Réflexions au terme de 10 ans de mise en place du tutorat à Brest. Communication orale au congrès du CNGE Angers Novembre 2008
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# Appendix A



## MULTIMORBIDITY DEFINITION FOR GENERAL PRACTICE RESEARCH PROTOCOL

## Summary

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# Background

## What we know:

The Multimorbidity concept was first published in 1976 [2] in Germany and remained almost entirely German and confidential for 14 years. Between 1976 and 1990 only 72 articles had multimorbidity in their corpus of which 66 were written in German. In 1990 the concept began its internationalisation through research [86]. It was an addition to the concept of comorbidity. Comorbidity was defined as any disease or risk factors that could play on one main disease with the effect of making it worse [4][87][5]. Multimorbidity has been defined by the World Health Organisation as people being affected by two or more chronic conditions [14]. The intention of the definers was to look at all conditions in one individual that could change his global health status. However the word “condition” is not sufficiently clear and could lead to numerous interpretations.

Multimorbidity is a very interesting and challenging concept for general practice as it is closely related to the global vision of the patient, which is a core competency of general practice as defined by WONCA [29]. It is also a very interesting concept when applied to patients as it gives a global overview of all the factors that could lead him to frailty (ie decompensating) [23]. Frailty is also a new concept formulated to help physicians detecting decompensating patients. Its link with Multimorbidity has already been discussed [24].

The European General Practitioner Research Network (EGPRN) is very interested in concepts that could help research in primary care throughout Europe. The concept of multimorbidity and a clear definition (ie understandable and usable for further collaborative research) is a leading concept for such a network. It will help researchers in General Practice investigate the complexity of patients’ conditions and their overall impact on global health. Multimorbidity could be an additional tool for GPs working in the field to detect frail patients with the intention of preventing decompensation. However the word “conditions” remains unclear and not easily usable and therefore multiple definitions of multimorbidity are coexisting [99] and the misunderstanding of the concept is obvious in literature [178][7]. The European General Practitioner research network (EGPRN) is interested as a support and dissemination network for Multimorbidity definition. That type of modelling (making Multilanguage’s definitions and validation) is necessary for collaborative research. It provides translated concept for collaborative research protocols between countries. EGPRN will support the study in each of its meetings by booking rooms and presentation devices (twice a year).

As a synthesis Gps are not comfortable with actual definition and furthermore operationalisation of multimorbidity but their core competency and daily task need to model that concept.

## What we need:

The primary care carer's community needs a clear and validated definition of Multimorbidity that could be usable in daily practice. In addition it is highly probable that GPs use conceptualization of multimorbidity that differ from those of other second line specialists. They are justified in doing so because they seem more in line with patient expectations [89]. We assume that there is an added value with the general practitioner's point of view. That added value has to be researched and conceptualized.

## Aim

The aim of this study is to make and validate a definition of Multimorbidity for General Practice.

The results of this research will be helpful for future collaborative research throughout Europe while providing a clear, consensual, consistent definition of Multimorbidity in various European languages.

## Partners in the project

Miguel-Angel Munoz from Idiap Jordi Gol Barcelona (Spain)

Jean Yves Le Reste, Claire Lietard and Patrice Nabbe from Brest university department of General Practice (France)

Stella Argyriadou from University of Thessaloniki (Greece)

Harris Argyriadou from the Italian association of Family Medicine (Italy)

Harm Van Marjwijk from the Free University of Amsterdam (VUMC) (Nederland)

Eva Hummers Pradier and Heidrun Lingner from Hannover University department of General Practice (Germany).

Slawomir Czachowsky from University of Torun (Poland)

Djurdjica Lazic from medical school, University of Zagreb dept. of Family Medicine (Croatia)

Melida Hasaganic from Sarajevo University Bosnia

# Methodology

## Daily Board:

Jean Yves Le Reste, Harm Van Marwijk, Patrice Nabbe, Paul Van Royen, Claire Lietard.

## Global summary of the study

### First phase:

What arguments support the utility of multimorbidity in general practice?

Additional and important question for EGPRN and the dissemination of the results: is that concept usable all across Europe?

Systematic review of literature for definition of multimorbidity in primary care?

### Second Phase:

How GPs recognize Multimorbidity in general practice?

Consensus procedure to validate the translation of Multimorbidity definition in all teams native language.

Qualitative study on GPs to find new topics about GP's multimorbidity definition and the added value, in the concept, by GP across Europe.

### Third Phase:

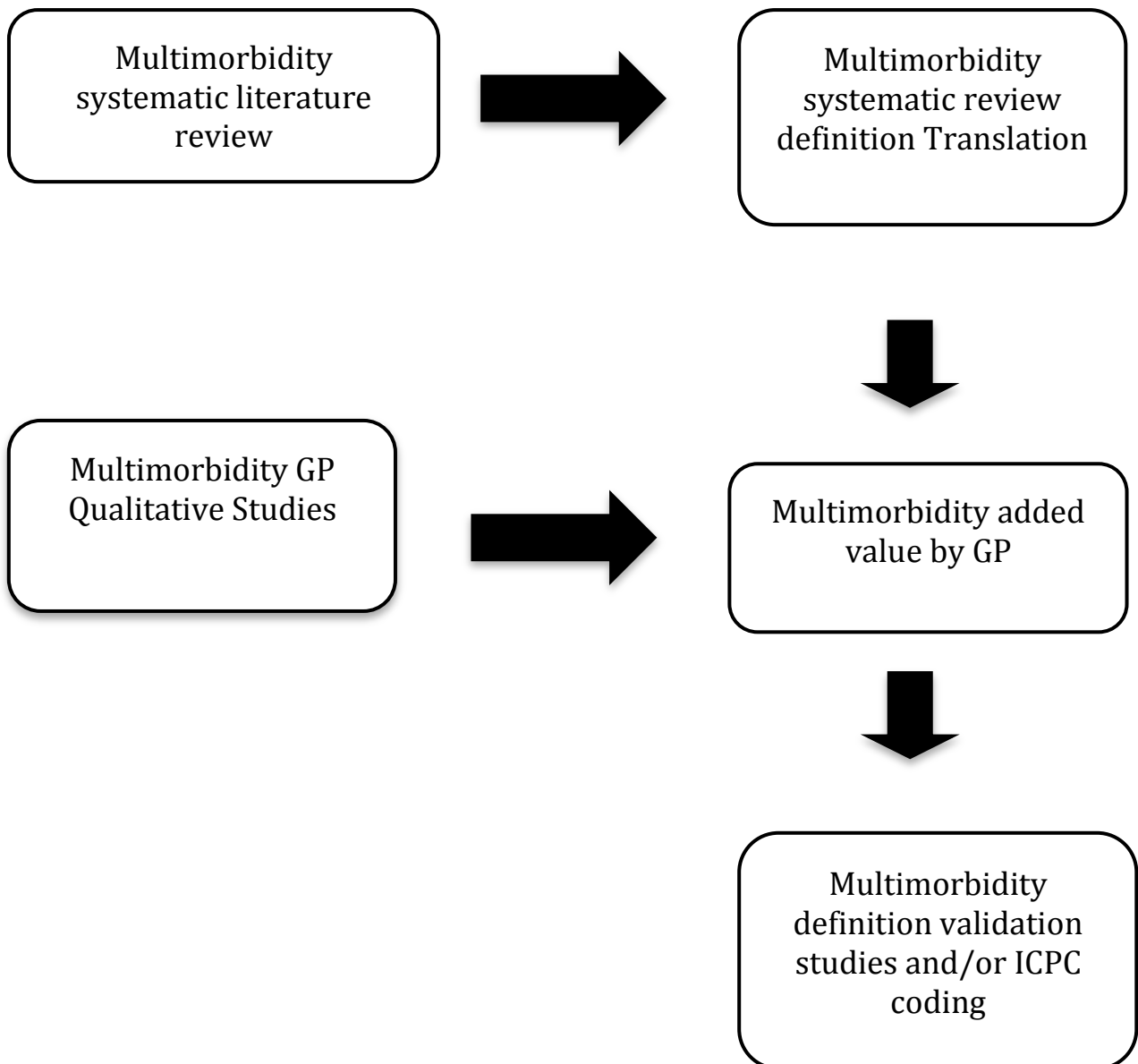
What are the specifics GP's themes into the whole multimorbidity concept? A comparison between the systematic reviews results and the qualitative studies results will be realized to define the value added by GPs. That phase will incorporate the new items into the definition of Multimorbidity.

### Fourth Phase:

Find the usefulness of the definition of multimorbidity in general practice research for its validation and/or a formulation of an ICPC (international classification of primary care) code produced in order to explore GP databases for the screening of multimorbid patient and dissemination of that code.



## Multimorbidity Study Map.



## Materials and design

### What we need:

We need a multinational team for each step (language for literature validation, richness of found topics for qualitative studies and triangulation of those studies, robust validation for quantitative validation part).

Meeting and check point at every EGPRN meeting as a pre conference workshop. Every team presents its work, troubleshooting and questions during this session (one complete day, at least half day). Each national team presentation is in English, must be followed by a word document arguing the presentation. Presentation must be held in 15 minutes, questions for 15 minutes. Selection of trouble points for discussion and solution with all groups if needed.

### Design for each step:

#### First phase: **systematic** review for multimorbidity definition:

Research question: what are the definitions and criteria of multimorbidity  
Secondary question: What tools could be useful in general practice to evaluate multimorbidity?

Keywords: Multimorbidity

Bases: pubmed, embase, Cochrane

#### **Abstracts selection:**

The French team will do the databases research for abstract. They will send to each national team its national language abstract plus its part of the English abstracts.

Each national team will do inclusion or exclusion of its abstracts. The French team will include or exclude all abstracts (in order to give more reliability). All team will use those criterias:

- Inclusion criteria for abstract selection: The study is about multimorbidity as a major topic (ie multimorbidity should be named in the article and some criteria of its definition should be present), the study is in English or in one's team mother language (English, Dutch, German, Polish, Greek, Italian, Spanish, French, Portuguese)

- Exclusion criteria for abstract selection: no abstract, no IMRAD format, no English abstract, older than 20 years.

Validate list of abstract is send back to the French team, which will compare them with their own finding.

In case of discordance, Paul Van Royen and Harm Van Marjwick will judge the final inclusion.

### ***Articles selection methodology:***

The validated list of abstracts will be cut for each national team (its mother language validated abstract plus its part of English abstracts). The French team will do this work. Each national team will receive his mother language articles plus a 9<sup>th</sup> of the English articles if there is not too many mother language articles. Each team will have to include or exclude the articles after reading according to the inclusion exclusion criteria.

The French team will include or exclude all articles, using the same criterias.

Exclusion/exclusion criterias: (using two reading grids, one for qualitative and one for quantitative research)

- Inclusion criteria for articles: the study is about multimorbidity as a major topic, criteria and definition are present in background (introduction), methodology, results or conclusion. Reading grid has a mean score greater than or equal to 14. .
- Exclusion criteria for articles: not on the definition of the topic, not in English or not in one national team language (English, Dutch, German, Polish, Greek, Italian, Spanish, French, Portuguese), Reading grid has a mean score lower than 14. Article is not a scientific article (for example editorials, opinion articles...)

Two local researchers in each team will do this inclusion/exclusion system separately using two reading grids (one for qualitative articles and the other one for quantitative articles). They will agree at the end on their final inclusion list. They will send back to the French team their reading grids and a list of all included articles. In case of persistent disagreement they will send the final list plus the troubleshooting articles to Jean Yves Le Reste and Patrice Nabbe. Those two persons will do the final judgment.

At the same time the French group will include or exclude all articles with two separate researchers. They will agree at the end on their final inclusion list. In case of persistent disagreement they will send the final list plus the troubleshooting articles to Paul Van Royen and Harm Van Marjwick who will judge the disagreement.

Jean Yves Le Reste and Patrice Nabbe will collate the two inclusion lists separately (the French complete list versus each national list). If they have some disagreement they will

send their disagreement(s) to the national team involved and will see if a consensus is findable. If not they will send them to Paul Van Royen and Harm Van Marjwick for final agreement.

At the end of this process we will have a new article lists that will be send to each national team according to the same partition (for each team all is mother language article plus a ninth of the English included articles).

### ***Coding:***

Each team will have to code the articles with two researchers coding separately. They will first focus on the first question what are the definitions and criteria of multimorbidity for coding. They will differentiate coding for general practice and other specialities. Then they will look in those articles for tools that could be useful in general practice to evaluate multimorbidity.

The French team will code all articles. This will be a phenomenological open coding first and each team will have to make agreement or disagreement with his two researchers for the coding book.

All the national coding books will be send back to the French team after local agreement. The French team will ensure a complete version of the coding book while comparing all books with his book. All the codes will have to be in English.

In case of disagreement on the codes the French team will call and talk with each national team concerned to find an agreement. In case of persistent disagreement the disturbing codes will be send to Paul Van Royen and Harm Van Marjwick for final decision.

After agreement on the complete book it will be send back to three volunteer teams for axial coding (Italian, French and German). Some metacodes will be the result of that part after a complete agreement following the same process.

Then the three volunteers teams will perform a selective coding in order to give a complete systematic review of Multimorbidity (academic because it is a definition issued from literature with research protocols).

## **Second phase: How GP recognize the concept of multimorbidity, will they add new criteria?**

For the second phase each national team should complete the two following parts:

- 1/ forward backward translation of the academic multimorbidity definition using a Delphi procedure
- 2/ qualitative studies to find how GPs recognize the concept of multimorbidity and if they will add new criteria.

## **Consensus procedure for translation of multimorbidity systematic review definition:**

Translation should respect all the rules of forward backward translation.

### Research question (for each translation):

What is the translation of the multimorbidity systematic review definition in our native language?

Research population: native expert GPs, English speakers, still in Gp practice and having teaching or research activities and not involved in the research.

Methodology: Forward backward translation using a Delphi consensus procedure. [157][179][135][80][73][74][139]

The forward translation will be done from English to native language by two translators (one medical and one official translator).

The Delphi consensus procedure will be held with 20 to 30 expert Gps. We will propose them the English definition and its translation into our native language. This proposition will be done using emails (each participant should be contacted separately to avoid contamination which is the basic methodology for Delphi procedure: so **no mailing list**). As many as needed Delphi round will be conducted to reach consensus.

Participants will rank translation from 1 (absolutely no agreement) to 9 (fully agreement). The participant should explain each rank under 7.

Consensus is defined as at least 70 % of the participants rating 7 or above the consensual definition.

With the consensual definition in native language two other native/English translators will do a backward translation from native language to English. It will be submitted to

the daily board of the study for final validation (Jean Yves Le Reste, Harm Van Marwijk, Patrice Nabbe, Paul Van Royen, Claire Lietard).

## **Qualitative studies to find how GPs recognize the concept of multimorbidity and if they will add new criteria**

Then we will perform qualitative studies on GPs to find new topics about GP's multimorbidity definition and the added value, in the concept, by GP across Europe. The multimorbidity systematic review definition will be the model to perform the analysis.

Focus groups and interviews (for triangulation):

- For each national team
- Groups participants: more than 5 less than 10
- One investigator, one moderator
- Audio recording (video use is allowed)
- Data collection until saturation
- Coding and Analysis with two reviewers
- Using thematic analysis (with or without specific tools like Nvivo)
- Analysis framework will be made in English and as to be translated (and back translated) by each national team for its own language codes.

The focus will show what GP thinks about multimorbidity as a professional group. The interviews will show, in addition, what GP thinks about multimorbidity as individuals.

Research question:

how GPs recognize the concept of multimorbidity and will they add new criteria?

Research Population:

European GPs selected with a purposive sampling strategy in each country in order to assume maximal variation of the population.

Methodology:

- Focus groups (one study for each participating and volunteer team) to saturation
- Semi structured Interviews (one study for each participating and volunteer team) to saturation
- Aim: add group effect to individual point of view
- Samples: maximum variation with addition of variation about multi-morbidity (Gp's with more elderly patients in practice)
- Audio recording of interviews and focus groups.

- Analysis is done according to grounded theory methodology and using the definition of multimorbidity as a frame.
- Separate analysis for each study with two different researchers for each national team based on phenomenology.
- Open coding and axial coding using a heuristic tool (NVivo 8) or excel ® with two separate researchers in each team.

### Interview or focus guide:

Setting: Doctor's practice or any place he will feel suitable for an interview. Appointment is made by phone. They have to be scheduled in order for the interviewee to be available and open-minded.

Contractual framework: The researchers present themselves. They explain the goal of the research project. They give information about anonymity. They assume that the work will consist in a few questions and that there is no good or bad answer. The systematic review definition of multimorbidity is exposed to the interviewee(s). The informed consent is asked and signed (if not this is the end of the process for that peculiar interviewee) (annex C). To begin the interview and gain the confidence of the interviewee it starts with question about demographic, practice type and expectations. All data concerning the test of maximal variation sample are collected at that moment.

Intervention of the interviewers: during the interview the interviewer puts himself in a listening strategy. He will only restart the conversation with the next question, or if his "in field" analysis of the data collection allows to go more in depth he will ask open question like (could you precise a little bit more that idea? What do you mean more precisely with this concept? Certainly could you go further?...). He always tries not to induce the answers by close-ended questions.

He follows the interview guide and when the interview is finished thanks the doctor for his help. He tells him that he will receive the transcription of the interview to validate it (or to correct it if needed) and that he will be glad to have it back accepted for definitive utilization. (Annex E: letter for verbatim acceptance)

### Interview Guide:

First Question: we have described what multimorbidity definition is. Could you describe one case of a multimorbid patient that comes from your practice?

Second Question: What kind of peculiar management could they need?

Third question: How do you identify those patients?

Fourth question: How do you feel those patients?

Fifth question: those patients could be difficult to spot or locate. What additional means could help you to do so?

### Remarks about the Coding book:

The coding will be done according to grounded theory[180][62]. The research will focus on themes that could explain what define a multimorbid patient in general practice.

Open coding books of multimorbidity will be done in English by each team. It will be send to the French team for integration of all books. The final book will be send back to each national team for final completion and validation of the open coding.

Then we will do an axial coding with three volunteer teams and we will do a final comparison of that axial coding to be sure it is as complete as possible and consensual.

Triangulation of both analysis from focus groups and interviews will be completed at the end of the open and axial coding.

The final outcome of the complete study will be a list of topics coming from the axial coding with all its sub codes.

<p><b>Third phase: a comparison between the results of the systematic review of literature and the results of the qualitative studies for multimorbidity definition.</b></p>
--

After the 1st and 2nd phase, we will have two lists of codes coming from both literature and qualitative studies. We will only keep the additional codes founded in the GP's qualitative studies comparatively with the literature definition of multimorbidity. With this list of specific GP's codes we will be able to add, or not, specific GP's themes.

### Research question:

What are the specifics GP's themes that could be added to the systematic review definition of multimorbidity?

### Setting:

Axial coding books (themes) of qualitative studies and systematic review definition of multimorbidity.

### Methodology:

comparison between the systematic reviews definition of multimorbidity and the themes book of the qualitative studies. Results will define the value added by GPs.

### Final outcome:



Incorporation of new items into the systematic review Multimorbidity definition leading us to a pragmatic and academic based GP definition of Multimorbidity.

### **Fourth Phase Dissemination:**

Find the usefulness of the definition of multimorbidity in general practice research for its validation and/or a formulation of an ICPC (international classification of primary care) code produced in order to explore GP databases for the screening of multimorbid patient and dissemination of that code.

EGPRN, WONCA and publications will ensure dissemination.

## **Timescales:**

### **Review:**

Agreement on databases and key words by mail: September 2010  
Search abstracts: January 2011  
Articles selection: march 2011  
Articles scoring: May 2011  
Open coding: August 2011  
Axial Coding: November 2011  
Multimorbidity systematic review definition: end 2011.  
International redaction and submission: December 2011

### **Qualitative studies:**

Delphi procedure: January 2012  
Group selection: February 2012  
End of national inclusion: February 2012  
End of national analysis: September 2012  
End of international analysis: December 2012  
Unweighted Multimorbidity definition February 2013.  
International articles redaction and submission: April 2013

# Deliverable and expected output:

This project has the potential of adding knowledge to a core competency of General practice. It has also the potential to begin research modeling throughout Europe and to build a reliable basis for collaborative research throughout Europe.

The output of the project comprises:

## international reports and publications:

- Short report of team's creation and troubleshooting about international team management to EGJP (1 article)
- Systematic review one article proposed to BMJ (1 article)
- Consensus procedure to validate the translation of the academic multimorbidity definition in each team language (1 to 9 articles)
- Qualitative study one article for the GP added value into the definition of Multimorbidity. (1 article plus articles in national press for each national team)

**Dissemination** of findings will take place at international meetings and conferences.

One of the researchers will make a doctoral thesis on this research with a cooperative tutoring between Antwerp University and Brest University.

## Financing

Grant from Brest department of general practice (4000 € a year plus 6 master students a year)

# Appendix B



MULTIMORBIDITY DEFINITION FOR GENERAL PRACTICE  
AND  
TOOLS TO DIAGNOSE DEPRESSION IN GENERAL PRACTICE

**Expected Publications and Rules for publication and authorship within the FPDM team.**

Overview

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## General information

### Publication rank:

Authorship credit is based only on substantial contribution to: conception and design, or analysis and interpretation of data drafting the article or revising it critically for important intellectual content and final approval of the version to be published (from BMJ criteria). Participation solely in the acquisition of funding or the collection of data does not justify authorship. The final decision rests with the daily board. The order of the authors depends further on the number of investigators and PhD student in every site.

### Publication acceptations by the daily board:

Each proposal for a publication with FPDM study data will be submitted to the daily board as an IMRAD abstract of 300 words. The daily board will check the proposal for overlap with other plans and potential combined or conflicting interests. These interests can concern the submitted publication plans or the use of data to which certain persons are explicitly involved. If there is no overlap or there are no conflicting interests, the proposal will, with a positive advise from the board, be accepted. When there is a possibility of overlap or when there are (possible) conflicting interests, the submitter of the proposal will be informed about this, with the request to adjust the plans.

The submission of a proposal implies concrete plans for a publication, etc. At which will be worked on a short time basis. When within half a year after submitting a proposal there is no provable activities in that direction, or when after a year no publication has been submitted to a journal, the subject can be released for other interested parties.

There is a maximum of two proposals that can be submitted as first author at the same time. Only after the presentation of the paper to a journal, a new proposal can be submitted.

Senior researchers who acquire extra funds have priority at the submission of publication plans on the theme of the extra fund.

Researchers who are not part of the study can, after consultation by the board taking advice with the most involved researchers, submit a proposal for data-analysis and publications. A senior researcher of the study will always be a member of this research group and will be co-author of the publications.

## **Authorship**

- The one who “pulls” the article and has the most important role in writing it, is the first author. He/she is responsible for the contents of the article.
- The first author determines in consultation with the board who the co-authors are and in which order. The board considers the investments and contributions of the study members, like authorship of the original proposal and local coordination. When the first author is a PhD-student, this happens in consultation with the (co-) promoters. Possible conflicts will be put before the board.
- (Co) promoter(s) who are primarily responsible for the supervision of PhD-students are (also) responsible for the integrity of the work as a whole, from inception to published article.
- Other co-authors should have made an important contribution to the design of the study, data collection and/or writing of the paper. Consider the three conditions of the Requirements for Authorship sometimes an acknowledgement is more suitable than a co-authorship.
- All authors get to inspect the article at least twice before it is forwarded to a magazine.
- It is the responsibility of the first author that the guide-lines according authorship are followed, that the sample and the research-methodology are described correctly and that references to former relevant study publications are made. To anticipate carelessness in this, the board should see every manuscript before presented for publication.
- The international study team (named as “FPDM Team”) will always be in the author list of any publication as the last name of authors.

## **Particular circumstances**

- 
- If in publication plans study data are used in combination with data collected by other research groups, both the study board and the board of the other research group will judge the publication plan.
- 
- Every member of the team is free to publish his own national results (after board reviewing) but for the systematic reviews and for the final articles at each step all the national teams have to be named.

## **Overview of publications**

An overview of all publications and publication plans, as well as publications in journals as chapters in books, is kept by the board. Changes in publications and publication plans (as mentioned under a.), are to be communicated to the secretary - preferably by e-mail.

The following information is needed:

- a. Date of sending the manuscript and name of the journal, including possible changes
- b. Changes in authors or title
- c. Date of acceptance
- d. At publication: full reference
- e. Withdrawal (decision not to publish)

From the moment of presentation and after being inserted in the overview, all manuscripts are kept in an archive. As soon as a paper is send to a journal, the first author will send a (digital or paper) copy of this to the board. After publication a reprint of the final article will be send to the board.

Abstracts of congress papers should also be sended to the board.

### **Timescales for multimorbidity:**

#### **Review:**

Agreement on databases and key words by mail: September 2010  
Search abstracts: January 2011  
Articles selection: march 2011  
Articles scoring: August 2011  
Open coding: November 2011  
Axial Coding: March 2012  
Multimorbidity systematic review definition: end 2012  
International redaction and submission: beginning 2013

#### **Qualitative studies:**

Delphi procedure for translation : January to October 2012  
Group or interview inclusion: Till end 2012  
End of national analysis: February 2013  
End of international analysis: April 2013  
Validation of analysis: May 2013 (EGPRN)  
Unweighted Multimorbidity definition July 2013.  
International article redaction and submission: September 2013

## **Deliverable and expected output:**

This project has the potential of adding knowledge to a core competency of General practice. It has also the potential to begin research modelling throughout Europe and to build a reliable basis for collaborative research throughout Europe.

The output of the project comprises:

## **International and national reports and publications:**

- As scheduled upper.

**Dissemination** of findings will take place at international meetings and conferences.

One of the researchers will make a doctoral thesis on this research with a cooperative tutoring between Antwerp University and Brest University.



# Appendix C



## Methodology for qualitative studies

**How GP recognize the concept of multimorbidity, will they add new criteria?**

Summary

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**What are the new topics for multimorbidity in general practice ?**

# **How GP recognize the concept of multimorbidity, will they add new criteria?**

**First: you have to select your populations, and researchers**

This part is to support you to decide what the next step will be (focus, interviews or both) and in order to find the population you need and the researchers to recruit.

You will perform qualitative studies with GPs to explore the full range of meaning of the concept of multimorbidity to GPs and to find How European GP experience the concept of multimorbidity and the new criteria they will add to the concept. The multimorbidity academic definition (translated into your language) will be the model to perform the analysis in a deductive way.

Focus groups and interviews (for triangulation):

- For each national team
- Groups participants: more than 5 less than 10
- One investigator, one moderator
- Audio recording (video use should be done too)
- Data collection until saturation
- Coding and Analysis with two reviewers
- Using thematic analysis (with or without specific tools like Nvivo or the provided excel file)
- Analysis framework will be made in English and as to be translated by each national team for its own language codes.

**Research question:**

How GP recognize the concept of multimorbidity, will they add new criteria?

**Research Population:**

European GPs selected with a purposive sampling strategy in each country in order to assume maximal variation of the population.

### **Methodology:**

- Focus groups to saturation
- Semi structured Interviews to saturation
- Each national team has to choose whether he wants to do both interviews and focus or only one method.
- Aim: add group effect to individual point of view for the whole international team
- Samples: maximum variation with addition of variation about multi-morbidity (Gp's with more elderly patients in practice)
- Audio recording of interviews and focus groups
- Separate analysis for each study with two different researchers for each national team based on phenomenology.
- Open coding and axial coding using a heuristic tool (NVivo 8) or excel ® with two separate researchers in each team.

### **Interview or focus guide:**

**Setting:** Doctor's practice or any place he/she will feel is suitable for an interview. Appointment is made by phone. They have to be scheduled in order for the interviewee to be available and open-minded.

**Contractual framework:** The researchers present themselves. They explain the goal of the research project. They give information about anonymity. They assume that the work will consist in a few questions and that there is no good or bad answer. The academic definition of multimorbidity is exposed to the interviewee(s) (annex A). The informed consent is asked and signed (if not this is the end of the process for that peculiar interviewee) (annex B). To begin the interview and gain the confidence of the interviewee it starts with question about demographic, practice type and expectations. All data concerning the test of maximal variation sample are collected at that moment (Annex C).

**Intervention of the interviewers:** during the interview the interviewer puts himself in a listening strategy. He will only restart the conversation with the next question, or if his "in field" analysis of the data collection allows to go more in depth he will ask open question like (could you precise a little bit more that idea? What do you mean more precisely with this concept? Certainly could you go further?...). He always tries not to induce the answers by close-ended questions.

He follows the interview guide and when the interview is finished thanks the doctor for his help. He tells him that he will receive the transcription of the interview to validate it (or to correct it if needed) and that he will be glad to have it back accepted for definitive utilization. (Annex E: letter for verbatim acceptance)

## **Interview Guide:**

First Question: we have described what multimorbidity definition is. Could you describe one case of a multimorbid patient that comes from your practice?

Second Question: Do those patients need a peculiar management?

Third question: how do you identify those patients?

Fourth question: How do you feel those patients?

Fifth question: those patients are difficult to spot or locate. What additional means could help you to do so?

## **Remarks about the Coding book:**

First level of codebooks (very close to the verbatim) of multimorbidity will be done first in native language. For this first coding at least one text should be coded- but it is not necessary to code all the texts. It will be sent to the French team for data collection of all codebooks.

Then taking into account all this first level of coding, each national team will ensure a second level of coding aimed to have a minimum of 40 and a maximum of 100 codes. Each code from that second level has to be related to one or several identical concepts in the verbatim. Each team will have to translate that level of coding and send it back to the French team as a first coding book. Each team also sends for each corresponding code, one (and only one) text fragment (quote) (translated in English) and/or explain in English what is understood by the code. This is necessary to validate the coding process.

The French team will merge all books and finalize a coding book following this cautious procedure:

- Merging all related codes in one book with categories and sub-codes
- Finding analogies in different team's coding (looking carefully to concordance and discordance)

Proposing by consensus and by mail a first coding book with three categories:

- Common (universally emerging) codes for all nations
- Some nation specific codes- that are not universal
- Doubtful codes (where the team is not sure if they are universal or not)

The French team will look carefully to concordance and discordance and will propose a categorisation into common codes, doubtful codes or national specific ones. Mail

consensus between the French and all national teams would achieve validation of common and national specific codes first.

Doubtful codes will be transmitted for thinking and categorize (to common or national specific codes) to each team thinking about the idea that those codes could fit into the common or national specific ones.

The remaining doubtful codes will then be again explained by each team in English and sent back to the French Team with one text fragment (a segment of one verbatim from which it was extracted it) translated to English.

These codes have to be explained and categorized in a physical meeting in EGPRN Malta meeting (October 2013) or quicker if it is possible. The final coding book will be finalized and validated for all teams at this precise time.

## **This is where we are now:**

The final coding book (International coding book) is sent back to each national team. They will recode all verbatim with that book changing their codes (second level) with the corresponding international codes and looking carefully at all codes to be sure they find them or not in their verbatim. They will propose eventually extra codes after that final check. The international coding book is now your basis for the rest of the analysis. Stick on it and propose only new emerging codes together with three translated text fragments for each new code to ensure the quality of coding.

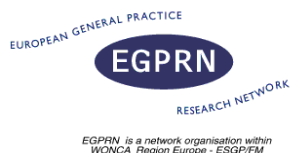
Please send back your complete coding using the international coding book with themes and sub themes in English and your first level of coding in native language to ensure the quality of the whole survey.

### **Then wait for us for the international selective coding.**

The French team will propose a selective coding for the new themes and will include those new themes into the definition of Multimorbidity. This selective coding will be sent to each team to discuss it and see if it is conform with their native coding. Corrections will be made if needed. Then a physical meeting in Next EGPRN meeting (Barcelona 8 to 11 may 2014) will achieve the selective coding and validate it for the whole team.

**The final outcome** of the complete study will be an English list of topics coming from the several levels of coding with its links to the native sub codes and a selective coding explaining the definition of Multimorbidity.

## Annex A: Academic definition of multimorbidity:



### Département Universitaire de Médecine Générale

22, avenue Camille Desmoulins CS 93837 – 29238 – Brest CEDEX 3

Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

### FPDM Study, Qualitative research for Multimorbidity definition in general Practice

#### Multimorbidity Definition:

Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factor (associated or not) or somatic risk factor.

Any bio-psychosocial factor, any risk factor, the social network, the burden of diseases, the health care consumption and the patient's coping strategies may function as modifiers (of the effects of Multimorbidity).

Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty.

## Annex B: informed consent



# Département Universitaire de Médecine Générale

22, avenue Camille Desmoulins CS 93837 – 29238 – Brest CEDEX 3  
Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

## INFORMATION NOTICE

### **International Investigator Senior Coordinator**

Name: Le Reste Jean Yves

Address: Département de médecine générale, Faculté de Médecine de Brest, 22, avenue Camille Desmoulins, 29238 Brest cedex 3

### **International Developer**

Département Universitaire de Médecine Générale – 22 avenue Camille Desmoulins - 29238 Brest Cedex 3

National investigator senior coordinator:

Name:

Address:

National developer:

Dear Madam or Sir

You are invited to participate in a survey by ..... (trainee in general practice, GP...). The department of general practice from ..... is the national developer of that survey. He is responsible for it and assume its organization.

Mrs/Mr ..... will explain his/her work to you. If you decide to participate you will be asked to sign a consent form. This signature will confirm that you did agree to participate.

### **1- Course of study**

One interview or focus group. This interview or focus group will be fully anonymised and it will be impossible for a study reader to identify you.

### **2- Potential risk of study**

There are no risks associated with your participation in this study



### **3- Potential benefits of the study**

There is no potential benefit to this study

### **4- Voluntary participation**

Your participation to this study is entirely voluntary.

You are free to refuse to participate and to terminate your participation in the study at any time and without incurring any liability or any injury of this fact and without causing consequences.

In this case you must inform the investigator of your decision

In the event that you withdraw your consent, we will conduct a computer processing of your personal data unless written objection on your part.

During the study, your investigator will notify you, if new facts might affect your willingness to participate in the study.

### **5- Obtaining complementary informations**

If desired, Professor Le Reste or local national investigator (phone number), who can be reached at telephone number: 00 33 298 016 552 at any time can answer all your questions about the study.

At the end of the study, and at your request, your investigator will inform you of the overall results of this research.

### **6- Confidentiality and use of medical or personal data**

As part of biomedical research in which the DUMG Brest, Professor Le Reste and your national investigator offer to participate, a treatment of your personal data will be used to analyse the results of research in light of the objective of that study which was presented to you.

To this end, the data collected, including any survey and the data on your lifestyle will be forwarded to the promoter of the research where the data will be processed in this study.

Those data will be anonymized and their identification will be held with a code number.

Staff involved in the study is subject to professional secrecy.

These data may also, under conditions ensuring their confidentiality be transmitted to the national or European health authorities.

Under the provisions of Law you have the right to access and modify. You also have the right to object to the transmission of data covered by professional secrecy.

<p>If you agree to participate in this study, thank you to complete and sign the consent form. You will keep a copy of it.</p>
--

**Consent Form**

**Promoter** : Département Universitaire de Médecine Générale – 22 avenue Camille Desmoulins -  
29238 Brest Cedex 3

Dr:.....  
Address: .....

**Local investigator name**  
Address: .....  
University:

**Asked me to participate in an interview (a focus group)**

I had time to reflect on my involvement in this study. I am aware that my participation is completely voluntary and that the study will entail no additional cost to my charge.

I can, at any time, decide to leave the study without giving reasons for my decision and that it does without consequences.

I understood that the data collected during the research would be protected in accordance to confidentiality. They can only be accessed by persons subject to professional secrecy belonging to the team-investigating physician, mandated by the promoter.

I accept the computerized processing of personal data in accordance with the data protection act. I have been informed of my right to access and rectify data concerning me.

My consent does not absolve the responsibilities of the organizers of this research. I retain all my rights guaranteed by Law.

Done in two originals  
at....., the dd/mm/yyyy

Name, first name of investigator:

Name, first name of the interviewee:

Signature:

## Annex C: data for maximal variation sampling

EUROPEAN GENERAL PRACTICE

EGPRN

RESEARCH NETWORK

EGPRN is a network organisation within  
WONCA Region Europe - ESGP/PM



## Département Universitaire de Médecine Générale

22, avenue Camille Desmoulins CS 93837 – 29238 – Brest CEDEX 3

Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

Birth date:

Gender:

Number of year in practice

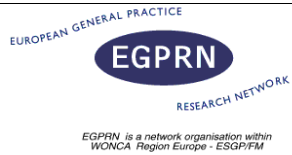
Practice type (single, group, others)

Setting type (rural (less than 2000 inhabitants), semi rural (between 2000 and 5000, urban (more than 5000 inhabitants):

Annual income level: changed to teaching activities

Subspecialty: changed to solo or group practice.

**Annex D: Letter sent with the verbatim for acceptance**



## Département Universitaire de Médecine Générale

22, avenue Camille Desmoulins CS 93837 – 29238 – Brest CEDEX 3  
Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

Dear colleague,

Following our recent interview/focus related to my research, I send you the transcript corresponding to the record made. As you can see everything has been anonymized. I'll let you read it and note your remarks there. If you agree to its use, I ask you to please sign it and send it to me.

I would like again to thank you for agreeing to participate in this research. This interview/focus was very helpful.

I enclose an envelope pre-filled in my address and postage for returning the signed transcript.

With my kindest regards.

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# Appendix D

## Nominal group to find the usefulness of the concept of multimorbidity in FM research.

Brest July 24th 2014.

*Equipe Reconnue  
par la Commission  
Recherche de  
l'Université de  
Bretagne  
Occidentale :  
SPURBO.*

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Director  
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Jean Baptiste NOUSBAUM  
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Claire LIETARD  
Morgane GUILLOU  
Bernard LE FLOCH  
Pierre BARRAINE  
Patrice NABBE  
Benoit CHIRON  
Marie BARAIS  
Jeremy DERIENNIC*

*Thomas Jan  
International junior investigator  
Tél. : 02 98 01 65 52  
[thomas.jan56@hotmail.fr](mailto:thomas.jan56@hotmail.fr)*

Dear researcher,

My Name is Thomas Jan and I am a trainee in General Practice in Brest (France). In the name of the Family Practice Depression and Multimorbidity (FPDM) study group I am in charge of a nominal group survey by mail. The research question of that survey is: what are the research themes that should be explored according to the EGPRN definition of Multimorbidity?

The EGPRN published in the Journal of the American Medical Directors Association in 2013, an exhaustive definition of Multimorbidity issued from a systematic review of literature:

Multimorbidity is defined as any combination of chronic disease with at least one other disease (acute or chronic) or biopsychosocial factor (associated or not) or somatic risk factor. Any biopsychosocial factor, any risk factor, the social network, the burden of diseases, the health care consumption, and the patient's coping strategies may function as modifiers (of the effects of multimorbidity).

Multimorbidity may modify the health outcomes and lead to an increased disability or a decreased quality of life or frailty

Though establishing this exhaustive definition was an essential step to carry on working on the concept of multimorbidity, European General Practice Research Network (EGPRN) members also considered that Family Physicians (FPs), facing multimorbid patients on a day-to-day basis, might define multimorbidity through other criteria. French, Italian, Greek, Polish, Bulgarian, Croatian and German teams worked during one year on that subject using qualitative surveys with 211 European FPS. By this way, two new themes were found: "FP's expertise in detecting and following multimorbid patients" and "the doctor-patient relationship dynamics". These have to be considered as mediating factors of multimorbidity.

We would like to develop new perspectives from this definition. As an expert in the field of multimorbidity we would be very proud if you could formulate a maximum of five proposals of research departing from that definition. Each proposal should have a short explanation on how you will use that definition for research perspective. All propositions will be anonymized. Your informed consent is needed. The complete process will take very little time.

To familiarize you to this concept you will find attached a mind map (FPDM Multimorbidity mind map.pdf) and an excel file with all the themes of the definition and their sub themes with some verbatim drowned from the qualitative surveys (FPDM Multimorbidity themes.xlsx).

We will aggregate duplicates and send those proposals back to all of you with the intention to rate them. Then we will be able to achieve a research agenda with your rating.

If you accept to participate in this nominal group please send back your filled in informed consent (page 3), the data for inclusion (page 4) and your propositions (page 5) using the "FPDM Multimorbidity files.docx".

If you experience any trouble with the files please feel free to call us or e-mail us.

Thanks for your collaboration to this project, sincerely yours.

Thomas Jan and Jean Yves Le Reste



# Informed consent



## Département Universitaire de Médecine Générale

22, avenue Camille Desmoulins CS 93837 – 29238 – Brest CEDEX 3  
Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

### INFORMATION NOTICE

#### **International Investigator Senior Coordinator**

Name: Le Reste Jean Yves

Address: Département de médecine générale, Faculté de Médecine de Brest, 22, avenue Camille Desmoulins, 29238 Brest cedex 3

#### **International Developer**

Département Universitaire de Médecine Générale – 22 avenue Camille Desmoulins - 29238 Brest Cedex 3

International junior investigator: Thomas Jan

Dear Madam or Sir

You are invited to participate in a survey by Thomas JAN (trainee in general practice). The department of general practice from Brest France is the national developer of that survey. He is responsible for it and assumes its organization.

Mrs/Mr ..... will explain his/her work to you. If you decide to participate you will be asked to sign a consent form. This signature will confirm that you did agree to participate.

#### **7- Course of study**

One nominal group by mail, this nominal group will be fully anonymized and it will be impossible for a study reader to identify you.

#### **8- Potential risk of study**

There are no risks associated with your participation in this study

**9- Potential benefits of the study**

There is no potential benefit to this study

**10- Voluntary participation**

Your participation to this study is entirely voluntary.

You are free to refuse to participate and to terminate your participation in the study at any time and without incurring any liability or any injury of this fact and without causing consequences.

In this case you will be kind to inform the investigator of your decision

In the event that you withdraw your consent, we will conduct a computer processing of your personal data unless written objection on your part.

During the study, your investigator will notify you, if new facts might affect your willingness to participate in the study.

**11- Obtaining complementary informations**

If desired, Professor Jean Yves LE RESTE or Thomas JAN who can be reached at telephone number: 00 33 298 016 552 at any time can answer all your questions about the study.

At the end of the study, and at your request, your junior investigator will inform you of the overall results of this research.

**12- Confidentiality and use of medical or personal data**

As part of biomedical research in which the DUMG Brest, Professor Le Reste and your junior investigator offer to participate, a treatment of your personal data will be used to analyse the results of research in light of the objective of that study which was presented to you.

To this end, the data collected, including any survey and the data on your lifestyle will be forwarded to the promoter of the research where the data will be processed in this study.

Those data will be anonymized and their identification will be held with a code number.

Staff involved in the study is subject to professional secrecy.

These data may also, under conditions ensuring their confidentiality be transmitted to the national or European health authorities.

Under the provisions of Law you have the right to access and modify. You also have the right to object to the transmission of data covered by professional secrecy.

If you agree to participate in this study, thank you to complete and sign the consent form. You will keep a copy of it.
---

**Consent Form**

**Promoter** : Département Universitaire de Médecine Générale – 22 avenue Camille Desmoulins -  
29238 Brest Cedex 3

**The international junior investigator Thomas JAN**

**Asked me to participate in an interview (a focus group)**

I had time to reflect on my involvement in this study. I am aware that my participation is completely voluntary and that the study will entail no additional cost to my charge.

I can, at any time, decide to leave the study without giving reasons for my decision and that it does without consequences.

I understood that the data collected during the research would be protected in accordance to confidentiality. They can only be accessed by persons subject to professional secrecy belonging to the team-investigating physician, mandated by the promoter.

I accept the computerized processing of personal data in accordance with the data protection act. I have been informed of my right to access and rectify data concerning me.

My consent does not absolve the responsibilities of the organizers of this research. I retain all my rights guaranteed by Law.

Done in two originals

at....., the ..../....

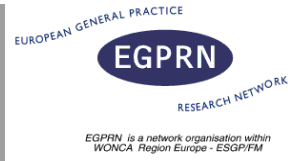
Name, first name of investigator:

JAN, Thomas

Signature:

Name, first name:

# Data for sampling



## Département Universitaire de Médecine Générale

22, avenue Camille Desmoulins CS 93837 – 29238 – Brest CEDEX 3  
Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

Birth date:

Gender:

Number of year in practice (if appropriate)

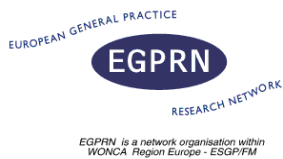
Practice type (if appropriate) (single, group, others)

Setting type (rural (less than 2000 inhabitants), semi rural (between 2000 and 5000, urban (more than 5000 inhabitants):

Number of published articles in English:

Number of published articles all languages:

Number of published articles with multimorbidity as major theme (all languages):



## Département Universitaire de Médecine Générale

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Tél : 02 98 01 65 52 – fax : 02 98 01 64 74

Research proposition	Comment

# Appendix F

International coding book with link to verbatims to be found on mendeley  
([www.mendeley.com](http://www.mendeley.com))

Working group: multimorbidity data for JY Le Reste Thesis

Invitation on request at the following email: [lereste@univ-brest.fr](mailto:lereste@univ-brest.fr)

All other working files will be send on request to the same email

# La Multimorbidité: un concept pour la médecine familiale en Europe

Jean Yves Le Reste

## Résumé

En utilisant un processus de recherche minutieux étape par étape, cette thèse a créé une équipe de recherche européenne pour concevoir son protocole de recherche. L'examen systématique de la littérature a montré une énorme quantité de définitions différentes (132 définitions différentes) et une grande diversité dans ces définitions (avec 1631 critères uniques distincts). La définition globale du concept de multimorbidité découlant de la revue systématique de la littérature est une étape pertinente. Les traductions du concept ont été finalisées pour le bulgare, le castellan, le catalan, le croate, le français, le galicien, l'allemand, le grec, l'italien et le polonais. Les études qualitatives ont confirmé le concept en MG et ont ajouté deux modificateurs de la Multimorbidité aux compétences fondamentales de la Wonca et la dynamique des relations médecin-patient comme aide à la détection et à la gestion de la multimorbidité. Le programme de recherche a porté sur les besoins futurs de recherche sur la mesure de la multimorbidité et son impact sur le patient. Elle a également renforcé la nécessité de simplifier ce concept en utilisant une approche pragmatique pour déterminer les variables utiles du concept sur ses résultats et son lien avec la complexité.

**Mots Clés** : multimorbidité, médecine générale

## Multimorbidity a concept for Family Medicine within Europe

### Abstract

Using a step-by-step careful research process this thesis created a European research team to design its research protocol. The systematic review of literature showed a huge amount of different definitions (132 different definitions) and a great diversity in those definitions (with 1631 distinct single criteria). The comprehensive definition of the concept of multimorbidity issued from the systematic literature review was a relevant step.

The translations of the concept were finalized for Bulgarian, Castellan, Catalan, Croatian, French, Galician, German, Greek, Italian and Polish.

The qualitative studies confirmed the concept for FPs and added two modifiers of Multimorbidity with the Wonca's core competencies of FM and the doctor-patient relationship dynamics as a help to detect and manage multimorbidity.

The research agenda focused future research needs on the measurement of multimorbidity and its impact on patient. It also enhanced the need for the simplification of this concept using a pragmatic approach to determine the useful variables of the concept on its outcomes and its link to complexity.

**Key words** : multimorbidity, general medicine