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Managing chronic care: how to decrease exacerbations

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Managing chronic care: how to decrease exacerbations

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Als meus pares, Joan i Lídia, a la meva germana Laura i a l'Adrià.

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CHAPTER 1.

INTRODUCTION, JUSTIFICATION AND OBJECTIVES

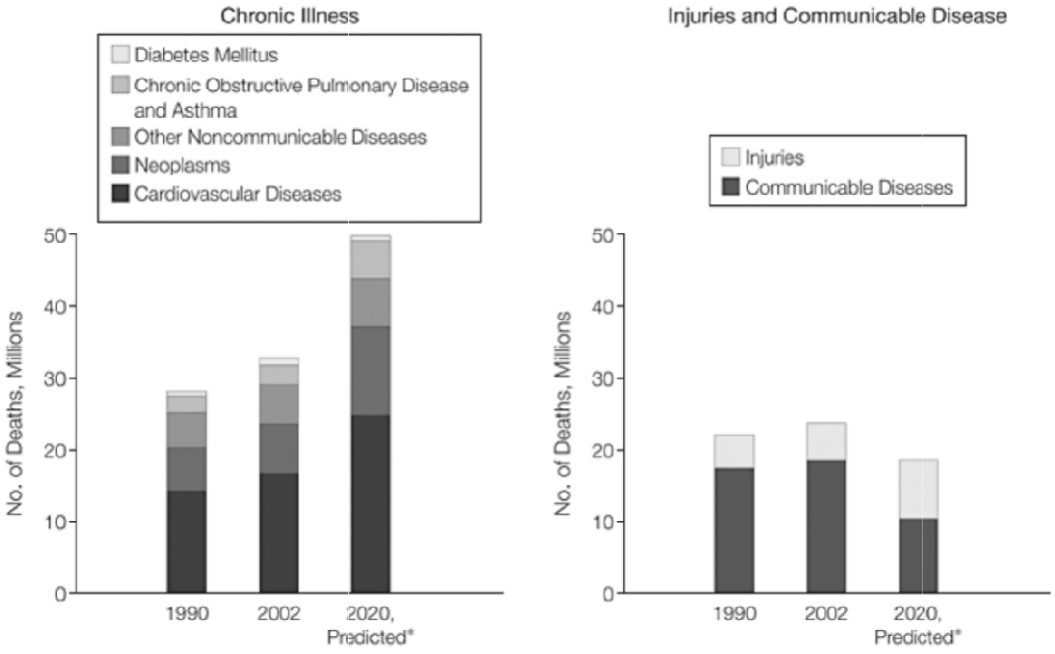
1.1. PRESENTATION AND JUSTIFICATION

Chronic patients are becoming a huge problem for today's governments. They are responsible for 70% of the deaths[1], for 81% of hospital admissions; 91% of all prescriptions filled; and 76% of all physician visits[2]. In relation with the health care spending, more than 75% of the total spending is on people with chronic conditions [3].

Among chronic patients, there are two types of diseases, non-communicable and communicable diseases. Non-communicable diseases are diseases that are not passed from person to person[4]. They are the largest cause of death worldwide. The first one is cardiovascular disease (17 million deaths in 2002, mainly from ischemic heart disease and stroke), followed by cancer (7 million deaths), chronic lung diseases (4 million), and diabetes mellitus (almost 1 million)[5].

In the following figure (figure 1.1) it can be observed the difference in number of deaths caused by communicable and non-communicable diseases.

Figure 1.1. Number of deaths caused by communicable and non-communicable diseases.



Source: World Health Report and Murray and Lopez[5-6].

It is also important to mention that a big part of the patients that suffer from chronic diseases are the elderly patients. At least 80% of people older than 60 are living with one chronic illness[7], but 68% older than 64 are living with two chronic illnesses[8]. This is very important because this population range is expected to grow exponentially in the following years. In 2014, the population that was 64 years or older, account for 17.90% of the total population in Spain. In year 2050, this same population will account for 27.50% [9].

1.2. OBJECTIVES OF THE RESEARCH

The main purpose of this study is to improve the care received by chronic patients by decreasing the number of exacerbations that complex chronic patients have in order to help them achieve a better health state and reduce cost. The study is divided in four objectives all related with this purpose.

The first objective is related with the role of Nurse Case Managers and its patient's identification. Care management programs for all patients focus just on single conditions[10], for this reason, most chronic patients receive unplanned care and poorly coordinated among specialists[11]. In order to improve the care received by chronic patients, some health care systems have created the role of Nurse Case Manager. They are responsible for the care of those patients. They try to offer them the best care possible and at the same time, rationalize the use of the public resources. In order to be able to affirm that the role of Nurse Case Manager has a positive effect on the resource consumption, it is necessary to identify a treatment group and a control group. To identify this control group is necessary to create a model that finds possible patients of Nurse Case Managers, otherwise, there it would be difficult to know which patients would have a Nurse Case Manager and currently they do not. In order to overcome this problem, the first objective of this study is to create a patient identification model for Nurse Case. In addition, having a model like this could be used as an alarm method, so whenever a patient needs a Nurse Case Manager and does not have it, it could be used as an advice or alert.

The second objective is to identify the main factors that influence a patient to be attended by a Nurse Case Manager. The main difference between being a chronic patient and having or not a Nurse Case Manager is the fact that the patient is

having an exacerbation. For this reason, knowing which factors identify patients of Nurse Case Managers is like, among other things, identifying factors of having an exacerbation. This would allow the health agencies to improve the care received by chronic patients because it would help them know when there is an exacerbation, so they can study what happened before and create policies to avoid it. In addition, it would help reducing cost, because most of the costs are due to the exacerbations.

When identifying the factors that influenced a chronic patient to become a Nurse Case Manager one, several factors came up to light. One of the most important factors was that most chronic patients had a low rate of adherence. This observation is related with the fact that chronic patients are polimedicated. On average, they were taking more than nine drugs per patient. If this is linked with the fact that elder patients have some kind of cognitive impairment and a lack of support, it seems a predictable ending.

So following with the main purpose of the study that is reducing exacerbations, the last two objectives were settled. These objectives were focus in targeting the preventable facts related with having exacerbations. The number of drugs that a patient is taking or if he/she has cognitive impairment are non-preventable facts, but there are others that can be improved. Following this path, the third objective was settled. The third objective was to reduce the rate of non-adherence. To achieve such goal, an intervention to reduce non-adherence among chronic patients was proposed and evaluated it.

The fourth and last objective of this study was to target the lack of support. Most of old patients are living alone or without support, meaning that although they might be living with his wife or her husband, they are impaired so they are not of any help. As most of the studies are done on isolation or living alone, the fourth objective was to know a little bit more on the real consequences that living without support has on elder complex chronic patients.

1.3. RESEARCH STRUCTURE

In order to achieve the objectives settled, three main contributions have been proposed that form the central chapters of this research work. For this reason, the PhD thesis is presented as a summary of academic contributions send for

publication to international journals included in Elservier's SCOPUS and in Journal of Citation Reports (JCR). It is important to mention that a previous version of the the first contribution, was presented in the national congress "VII Congreso de Atención Sanitaria al Paciente Crónico", from which valuable suggestions from external reviewers were taken (see appendix 5).

It is also interesting to mention that this thesis has been done under a collaboration agreement with two health institutions: Institut IDIAP-Jordi Gol (institute for the development and research on Primary Care) and also with Institut Català de la Salut. They have provided this study with a big database and also with several meetings with different health professionals related with the field of study, to provide the author with field knowledge. More information on the agreement can be find in the appendixes 3 and 4.

The academic contributions that form the body of this study are under the line and objectives of this research. Each of the three contributions is focus in achieving the proposed objectives, under three different methodological strategies. The contributions, although they were elaborated following a sequential path in time, are strictly interrelated among them, in agreement with the objectives initially settled. Below, you can find the structure of the study work (figure 1.2)

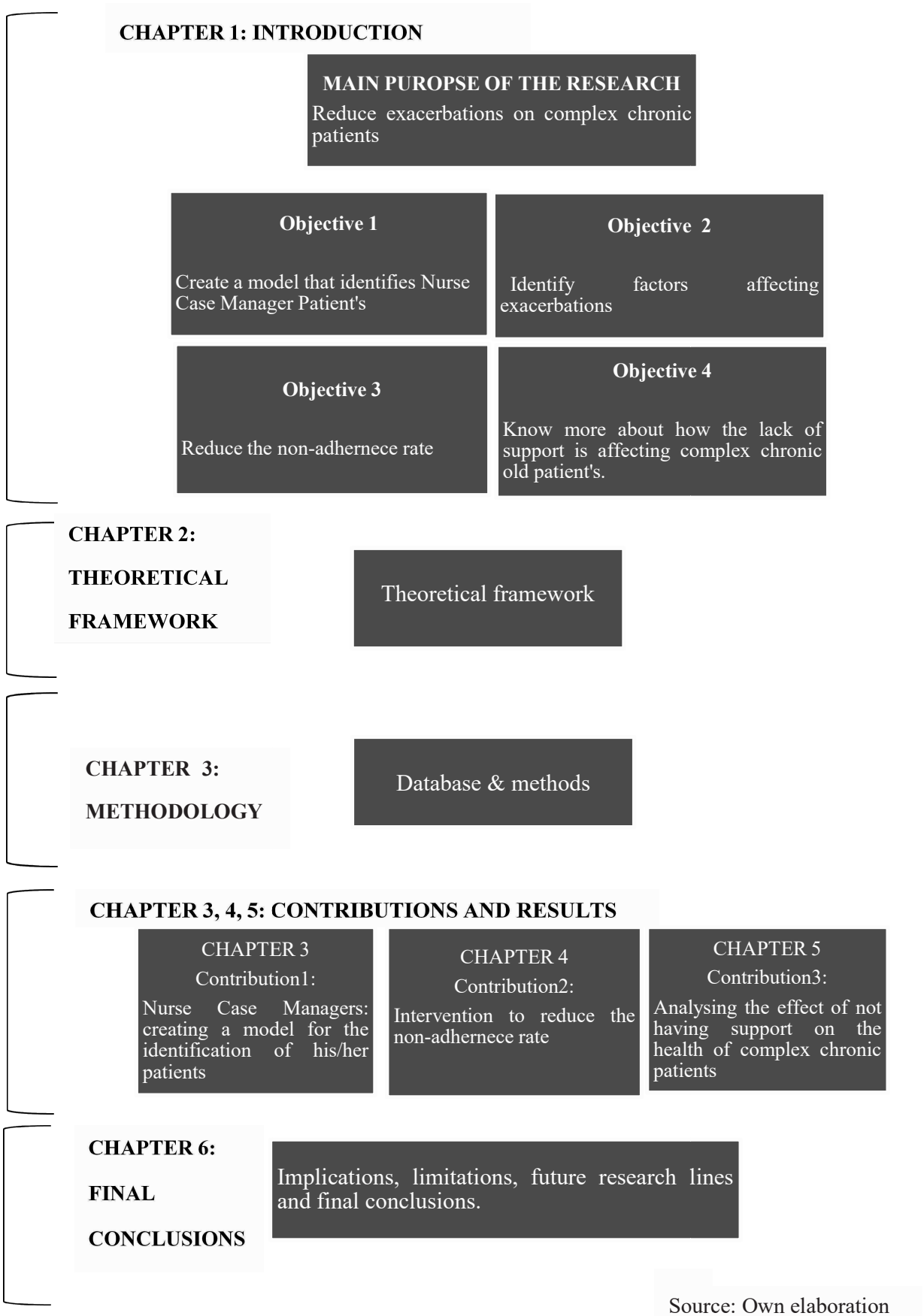
As it is shown in figure 1.2, the study is divided in 7 chapters:

The first chapter is an introduction to the topic of this study, which is managing chronic care among elder and reducing exacerbations. In this chapter there is also explained the reason why this topic has been chosen, settled the four objectives in which this study is subdivided, and explained the research structure.

The second chapter is a brief explanation of the main topic of this study. The chapter starts defining and explaining chronic diseases and care among elderly, the current situation and how it is expected to evolve. Also the role of the Nurse Case Managers as instrument to identify exacerbations. Then it goes more in deep explaining two of the main factors affecting exacerbations, which are non-adherence and social risk.

The third chapter is a review of the four methodologies used to pursue with the objectives of this study, but also there is explained the database used for two of the three contributions.

Figure 1.2: Thesis structure.



Source: Own elaboration

The next three chapters are the contributions of this study:

Chapter 4: Contribution I: An empirical model for a nurse case manager patient identification.

Chapter 5: Contribution II: Potential cost and savings of a proposed intervention to reduce non-adherence of advanced chronic patients.

Chapter 6: contribution III: Analysis of the effect of living without support in chronic old patients.

In the seventh chapter, there are explained the main conclusions of the three contributions, together with the implications, limitations and future research lines.

At the end of the study there is also attached an appendix that includes a list with all the abbreviations used, a glossary of the medical tests that appear as variables in the database, the agreement between the University of Barcelona and the Catalan Health Agency to share and analyze the database, and annex of this agreement where it is said that the author of this study is authorized to use the data from the database, and lastly the poster presented together with the oral presentation to the Congreso de Atención al Paciente Crónico Avanzado.

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CHAPTER 2.

THEORETICAL FRAMEWORK

2.1. NON-COMUNICABLE DISEASES

Non-communicable diseases (NCDs), or also known as chronic diseases, are diseases that are not passed from person to person. Their duration is long and generally they have a slow progression. There are four main types of non-communicable diseases, which are: cardiovascular diseases (for example heart attacks and stroke), cancers, chronic respiratory diseases (such as chronic obstructed pulmonary disease) and diabetes[1].

2.1.1. People are at risk of such diseases.

Although NCDs are often associated with older age groups, they affect all range groups. Evidence shows that 16 million of all deaths around the world attributed to non-communicable diseases (NCDs) occur before the age of 70. Children, adults and the elderly are all vulnerable to the risk factors that contribute to non-communicable diseases, due to unhealthy diets, physical inactivity, exposure to tobacco smoke or the effects of the harmful use of alcohol[2].

The risk factors could be divided in two main groups: modifiable behavioral risk factors and Metabolic/physiological risk factors:

Modifiable behavioral risk factors:

They are tobacco use, physical inactivity, unhealthy diet and the harmful use of alcohol:

- Tobacco accounts for around 6 million deaths every year (including from the effects of exposure to second-hand smoke), and is projected to increase to 8 million by 2030[2].
- About 3.2 million deaths annually can be attributed to insufficient physical activity[2].
- More than half of the 3.3 million annual deaths from harmful drinking are from NCDs[3].
- In 2010, 1.7 million annual deaths from cardiovascular causes have been attributed to excess salt/sodium intake[4].

Metabolic/physiological risk factors:

The leading metabolic risk factor and also one of the main leader to death is elevated blood pressure (to which 18% of global deaths are attributed)[2] followed by overweight and obesity and hyperglycemia (high blood glucose levels) and hyperlipidemia (high levels of fat in the blood).

2.1.2. Socioeconomic impact of Non-Communicable Diseases

Chronic non-communicable diseases are reaching epidemic proportions worldwide[5-7].

Over the coming decades, the burden from NCDs is projected to rise particularly fast in the developing world. Without taking further actions, 388 million people worldwide will die of one or more NCDs in the next 10 years. With an action plan, it would be possible to avoid at least 36 million premature deaths in the near future[8].

NCDs have a huge negative economic impact[9]. Health-care costs for cardiovascular diseases, cancers, diabetes or chronic lung diseases can quickly drain household resources, driving families into poverty. NCDs cost are normally high because of the lengthy and expensive treatment and loss of breadwinners, which forces many families into poverty[1]. In the next 10 years, China, India and the United Kingdom are projected to lose $558 billion, $237 billion and $33 billion, respectively, in national income as a result of heart disease, stroke and diabetes, partly as a result of reduced economic productivity[6].

Fortunately, NCDs are largely preventable[10]. Up to 80% of premature deaths from cardiovascular diseases and diabetes can be avoided with behavioral and pharmaceutical interventions[6]

2.1.3. Chronic Care

Patients with chronic advanced conditions are very common users of the health services that are often unplanned and poorly coordinated care in response to a crisis or exacerbation. To fight this, the role of the nurse case manager has been identified as a central measure to improve the care of these patients[11]. If he/she is

able to identify complex chronic patients, it is easier to plan resource consumption and structure them in a more efficient way, thus arriving to meet the needs of society in a more efficiently.

Nowadays in Spain, there is a change in the chronic patients care model. This change redirects the way services have been provided, promoting cooperation environment between health care areas and social services and between organizations and professionals working with patients themselves, evolving towards an integrated model[12].

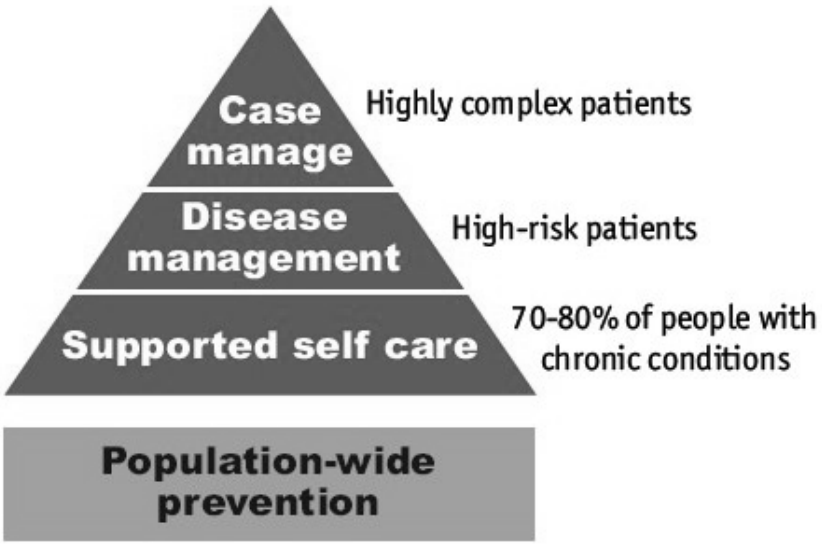
Case management is based on a proactive approach that involves detection of cases, assessment, care planning and coordination[16]. It has been demonstrated that case management provides a more efficient care in many cases, such as in the case of heart disease[13] and diabetes[14].

With this purpose, the Spanish system can take as reference other systems that have already applied this model of integrated care. Good examples are the English Health System (NHS) or Kaiser Permanente (US).

Taking a deeper look at this last example, it is possible to observe a model that stratifies individuals according to their needs. It is based on the idea that everyone is not equal, and therefore not all have the same chronic care needs. The model has a pyramid shape, where it can be distinguished different population segments, and for each of them the approach used is different. The following figure (figure 2.1) explains the model.

The base of the pyramid is formed with the general population, who do not have special needs. The best strategy that can be applied to them is prevention and promotion of health. Going up through the pyramid, there are the chronic patients who need a bit more specialized care and clinical trajectories cross paths. Finally, on the top of the pyramid there are the complex chronic patients, who need proactive care to improve their health and reduce the use of high-cost resources[15].

Figure 2.1. Kaiser Permanente management model.



Source: Bodenheimer and Wagner[15]

Nurse Case Managers is another step used to transform the current system into a more stratified one, individualizing care depending on the needs of the patients. The health system should be developing interventions oriented towards a specific strata in the population, as Nurse Case managers are oriented towards complex chronic patients, so specific needs could be covered and thus patients' health improved.

2.1.4. The role of Nurse Case Managers

Patients with long term conditions are high users of health services, as said before, but they do not receive the care they need because programs focus on single conditions[16]. To fight this problem, the administration has been changing its care models, evolving to an integrated care model that promotes cooperation environments between care areas, health and social services, and between organizations and professionals who work with the same patients. Continuity of care (CC) focuses on the patient and its family care as the main element, with a bidirectional relationship between healthcare and social care services. Its objective is to avoid the lack of coordination between the different levels of care which could be negative for patients[17].

As nurses are the main health care professionals involved in caring for individuals with long term care[18-19], they are normally used as key workers to help manage and prevent these potential problems in several countries[19-20]. Nurses usually have more contact with chronic patients in community settings, are responsible for liaising with other members of the health care team and are also closely involved in care of recently discharged patients[21].

As said before, nurses have become an essential part in this change[22]. In concrete, the one pursuing this role is called "Nurse Case Manager" (NCM). NCM are responsible to[23]:

1. Optimize and rationalize the use of services and of resources to prevent admissions due to clinical worsening of people with chronic diseases, that is, avoiding unnecessary transfers to hospital
2. Decrease visits to the emergency department by people with complex conditions, as well as their number of admissions and, if admitted, the length of their hospital stay
3. Empower family members by providing them with the necessary tools to avoid clinical worsening and manage risky situations.

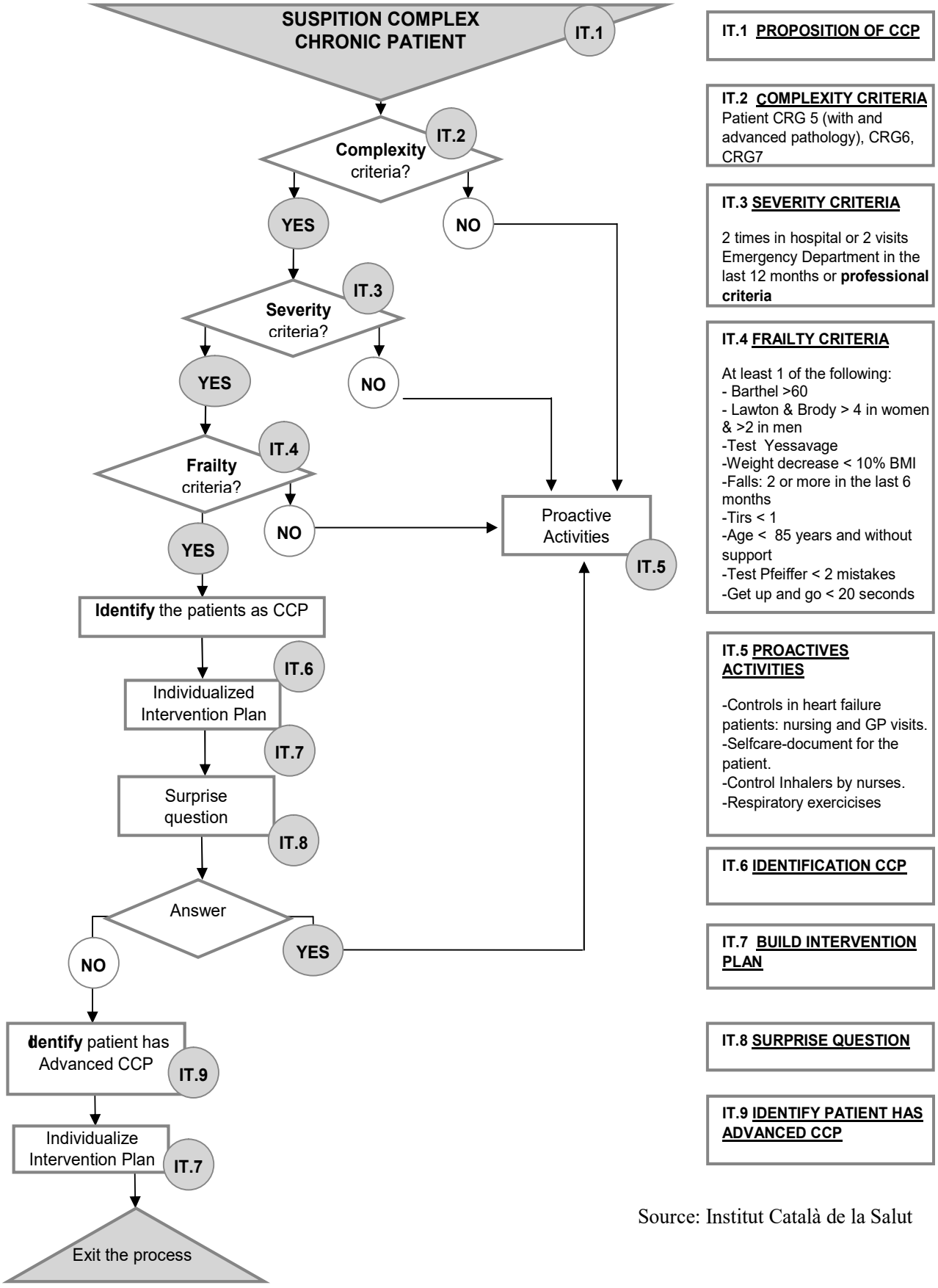
2.1.5. Identification of Nurse Case Manager Patients.

To be identified as an advanced chronic patient's, the patient has to fulfill several criteria. On the following figure (figure 2.2), it is shown the labeling and registration process followed to be identified as a Complex Chronic Patient susceptible of having a Nurse Case Manager. The problem is, as it is possible to observe, that the final decision is based on a human perception.

First criteria: To be a Complex Chronic patient.

Patients are identified and categorized depending on its health status. Clinical Risk Groups (CRG) were developed in the year 1999 and are used to classify people into mutually exclusive clinical categories in any health care setting. The CRG can be used, among other possible applications for the following purposes: a) monitoring the prevalence rates of chronic diseases; b) understand patterns of use and consumption of services; c) develop risk adjustment applications and prices and d) relate consumer satisfaction and measures of quality of care from

Figure 2.2. Labeling and registration process



Source: Institut Català de la Salut

the point of view of the patient[24-25] .If focusing on Complex Chronic patients, they are identified with CRG 5, 6 and 7.

In table 2.1 it is described the CRGs and given an example for each of them.

Table 2.1. CRG description.

CRG level	Health status	Example
9	Catastrophic	History of major organ transplant
8	Dominant/Metastatic malignancy	Metastatic colon malignancy
7	Dominant chronic disease in 3 or more organ systems	Diabetes mellitus, (CHF) and chronic obstructive pulmonary disease (COPD)
6	Significant chronic diseases in multiple organ systems	Diabetes mellitus and CHF
5	Significant chronic disease	Diabetes mellitus
4	Minor chronic diseases congestive heart failure in multiple organ	Migraine and benign prostatic hyperplasia (BPH)
3	Single minor chronic disease	Migraine
2	History of significant acute disease	Chest pains
1	Healthy	No chronic health problems

Source: 3M ™ Clinical Risk Groups: Measuring Risk, Managing Care. 3M HIS. 2011[26]

Second criteria: Severity Criteria

The second criterion is the called Severity Criteria, which means that on the last 12 months, the patient has been two times at the Emergency Department or also has been twice hospitalized.

Third Criteria: Frailty Criterion

Frailty is a syndrome associated with functional loss, physiological impairment, and reduced ability to recover after a stressful, destabilizing event. Frail persons have a high risk of accelerated physical, cognitive, and functional decline, disability, and death[27-28].

Frailty has been defined in several ways. Fried et al. (2001) defined it as a clinical syndrome, separate but partly overlapping with the concepts of chronic disease and disability[28]. Rockwood and Mitnitski (2011) defined it as an state, resulting from the accumulation of several deficits[29].

It is important to identify frail people in an early stage because interventions may, potentially, prevent or delay its clinical consequences[30].

Below, in table 2.2, there are some of the variables used to define if a patient is frail.

Table 2.2. Description of the variables of the frailty criteria.

Area	Variable	Limit
Functional decline	Barthel test	> 60
	Lawton test (Women)	> 4
	Lawton test (Men)	> 2
Physical decline	"Getupandgo" test	< 20
	Falls	< 2
	Weight loss	≤10% BMI
Cognitive decline	Pfeiffer test	< 2
Emotional decline	Yesavage test	≤ 3
Social risk	TIRS	< 1
	"Agealone" test	

Source: Institut Català de la Salut

Functional status was assessed by means of the 10-item ordinal scale for the basic activities of daily living (BADL) (Katz, Downs, Cash, & Grotz, 1970 with a Cronbach's reliability between 0.84 y 0.97[31]) and the instrumental activities of

daily living (IADL) (Lawton & Brody, 1969 Lawton & Brody, 1969 with a Cronbach's reliability of 0.90[32]), physical status by the number of falls during the last two years and the "Get-Up and Go" Test (Mathias et al, 1986 with a Cronbach's reliability of 0.91[33]),cognitive status by means of the Spanish Version of Short Portable Mental Status Questionnaire (SPMSQ) (Peiffer et al.; 1975 1975 with a Cronbach's reliability of 0.92[34]), emotional status by means of the 5-item Spanish Version of the Geriatric Depression Scale (GDS) (Yesavage et al., 1983 with a Cronbach's reliability of 0.82[35]). Social risk is assessed by means of "Age-alone" Test and other indicators summarized in the TIRS test (obtain from interviews with Institut Català de la Salut). On the appendix 2 the specifications for every test are explained.

Fourth criteria: To have an exacerbation

Nurse Case Managers appear just when the patient is having an exacerbation, in order to bring him/her back to its regular state. There are several factors that indicate that a patient is having or is going to have in a short period of time a crisis. Some of the factors are:

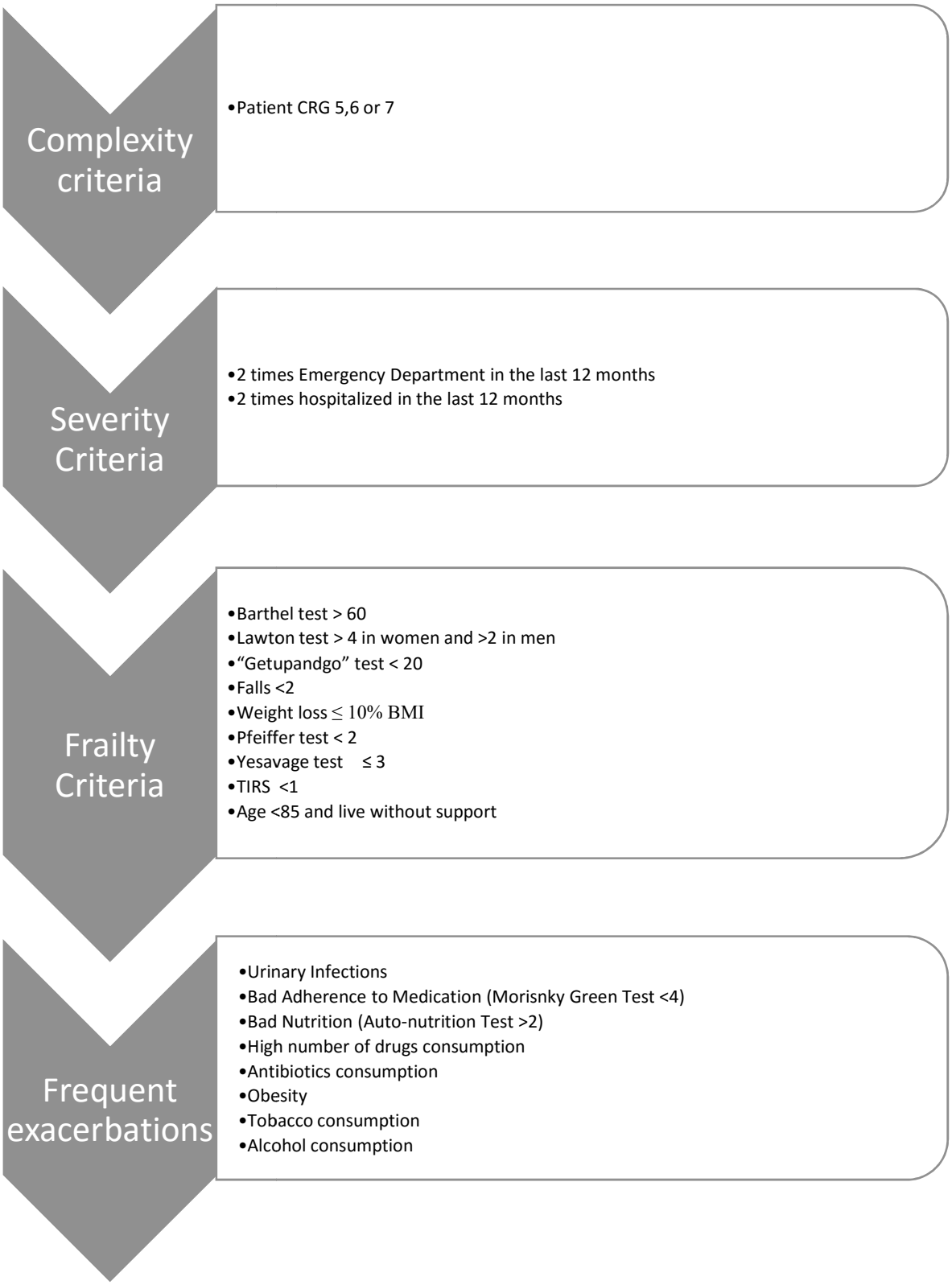
- Urinary Infections
- Bad Adherence to medication (Morinsky Green Test <4: Morinsky DE, Green LW, Levine DM, 1986 with Cronbach's reliability's of 0.82[36])
- Bad nutrition (Auto-nutrition Test >2: Nutrition Screening Test used by CatSalut)
- High number of drugs consumption
- Antibiotics consumption
- Obesity
- Tobacco consumption
- Alcohol consumption

More information on these variables is available in the appendix 2.

A sum up of the different criteria can be found in figure 2.3.

Those are the factors that will be used to build the model for the first objective.

Figure 2.3. Defining a NCM patient.



Source: Own elaboration

2.2. NON-ADHERENCE

Poor medication adherence is a common fact nowadays. Studies show that on average, the non-adherence rate is between 20 to 30%. Adherence is defined as the extent to which a patient's behavior (in terms of taking medication, following a diet, modifying habits, or attending clinics) coincides with medical or health advice, and it represents a large limitation for the healthcare agencies. Adherence to treatment has shown to be a problem for today's health agencies, especially for chronic patients, with more than 50 percent of medications not taken as prescribed by the healthcare provider[37-38].

There is a significant association between medication adherence and clinical outcomes: better medication adherence is correlated with improved outcomes[39].

As said before, adherence rates are typically higher among patients with acute conditions, as compared with those with chronic conditions; persistence among patients with chronic conditions is disappointingly low, dropping most dramatically after the first six months of therapy[40]. This is becoming a problem because chronic conditions account for big percentage of the total expenditure in health care[41], and poor adherence to medication regimens accounts for substantial worsening of disease, death, and increased health care costs[42], which keeps increasing the budget for chronic conditions for the healthcare agencies. Not only this, but the number of chronic patients is expected to grow a lot in the following years, because every day medicine is saving more and more patient's life's, but leaving them in chronic conditions. Thus, the impact of poor adherence grows as the burden of chronic disease grows worldwide[14].

Disease management programs have proliferated recently as a means of improving quality and efficiency of care for patients with chronic illness[42]. There have been several interventions framed in these programs, oriented to increase the adherence rate to treatment. Most of those interventions are efficient and increase the quality of life of the patients, but they are also quite expensive to develop, implement, and evaluate for the health care sector[43].

2.2.1. Causes of non-adherence

There are several possible causes of non-adherence and ways of grouping them, although most of them have a weak influence on it[43].The World Health Organization recognizes two distinct categories of non-adherence: preventable

(e.g., patient forgets, misunderstands) and no-preventable (e.g., life-threatening side effects), and recommends targeting tailored treatment interventions for the former[44].

Another definition is provided by Marinker et al. (1997), who divides the causes in two possibilities: (1) the role of patients' health beliefs and (2) the barriers to treatment and the role of non-intentional lapses. The first one, the role of patients' health beliefs, is defined by Marinker like *"The most salient and prevalent influences on medicine taking are the beliefs that people hold about their medication and about medicines in general (...). For the prescriber simply to reaffirm the views of medical science, and to dismiss or ignore these beliefs, is to fail to prescribe effectively"*[45].

For the second one, the barriers to treatment and the role of non-intentional lapses, there are two things that have to be taken into account: characteristics of the patient and their environment and characteristics of the treatment.

Characteristics of the patient

Most of non-adherence interventions target complex chronic patients, because they are causing a big part of the expenses in health care cost and its growing rate is exponential[37-38], but also because they have higher rates of non-adherence compare to other patients, which increases the possibility of improvement[8].

Complex Chronic patients are mostly old people suffering from multiple comorbidities, so it is quite possible that they are physically or psychologically impaired (characteristics of the patient)[46]. Not only this, but it is also relevant that most of them live in a situation of social risk, which means that they live alone or without support (characteristics of the environment).

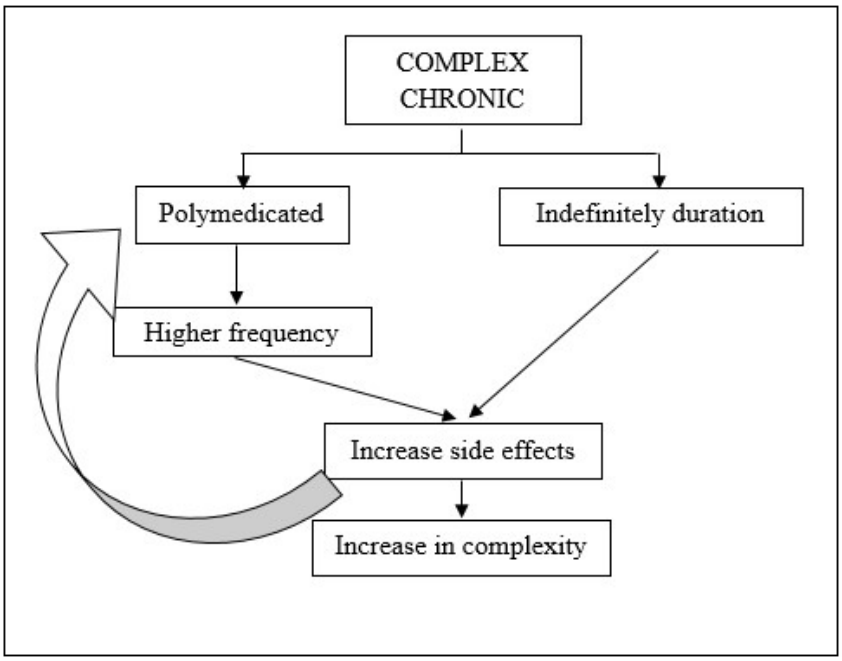
Characteristics of the treatment

There are several variables that have to be taken into account because they can affect the adherence to treatment, as for example number of pills, frequency of treatment, duration, complexity of the regime, side effects, etc. Generally, the higher the levels of these factors, the lower the level of compliance[47-48].

Figure 2.4 illustrates the situation of complex chronic patients related with the characteristics of the treatment. The figure starts showing the relation between complex chronic patient and adherence. Complex chronic patients are typically polymedicated and they will have to be for the rest of their live as they are chronic patients. Due to its high index of comorbidities[46], the number of pills and

thus its frequency increases, which increases the side effects and as a consequence, the number of pills they are taking to mitigate the side effects.

Figure 2.4. Scheme from complex chronic patient.



Source: own elaboration

All those facts, specially being polymedicated, added to the fact that they normally live under social risk and are physically or psychologically impaired, could lead to non-intentional lapses. To support this statement, it has been observed that just around 30% of patients older than 54 years old that are taking 8 drug treatments at the same time, was able to remember the physicians instructions and just 20% of them recognized that was taking the drugs correctly[49].

2.2.2. Types of intervention for the treatment of non-adherence

The following table summarizes types of interventions that have been already done in order to reduce non-adherence targeting beliefs but also barriers to treatment and non-intentional lapses; and the results they have obtained. It is based on the most recent study found, from Perterson et al.[50]. Based on this

study, reported adherence-related interventions and its results were grouped into four categories that are explained in table 2.3.

Table 2.3. Adherence related interventions

Intervention	Explanation	What does it target?	Effect size in increase adherence
Patient education	More instructions for patients (oral and written material and programmed learning).	Beliefs	N=22 0.11 (95% CI = 0.06–0.15)
Simplification of dosing	Increase the convenience of care (provision at the work- site, simplified dosing)	Treatment characteristics and non-intentional lapses.	N=6 0.12 (95% CI = 0.20–0.04)
Motivation	Reinforcement or rewards (i.e. economic incentives)	Treatment characteristics and non-intentional lapses.	N=2 0.08 (95% CI = 0.22–-0.06)
Communication and counseling	Manual follow-up	Treatment characteristics and non-intentional lapses.	By mail: N=2 0.38 (95% CI = 0.54–0.22) By telephone: N=4 0.07 (95% CI = 0.17–-0.03)
	Monitoring: tailoring the regimen to daily habits; special reminder pill packaging.	Treatment characteristics and non-intentional lapses.	Packaging: N=6 0.14 (95% CI = 0.22–0.06)

N: Number of individuals in the study
CI: Confidence Interval

Source: Peterson, Takiya, Finley[50]

Based on the table 2.3, all interventions have proven to increase adherence, in special communication and counseling interventions which on average has demonstrated to be the one with the highest effect (0.14 packaging and 0.38 mail intervention, although the sample size of this last one is quite small).

2.3. SOCIAL RISK

Loneliness has a great influence on physical and mental health. Some studies have investigated a possible association between loneliness and mortality risk in men and women[51]. It has been demonstrated that pursuing social activities is associated with a reduction in the risk of mortality and institutionalization in older people[52].

2.3.1. Demographic trends

Between one-third and one-fourth of people age 60 years old or more live at home alone[53].

During the last 50 years, patterns of household composition have changed. The marriage rate has decreased[54], and if it is combined with the fact that most women have nowadays also a paid job[55], and that everyday people is having less and less children[56], this leaves elderly with fewer family members to provide company and care[57].

When added to the fact that longevity has risen sharply in OCDE countries, due to a fall in mortality at advanced ages, and to the fact that most of them are left in a chronic state[1], with the increase in health expenses that it implies; it seems urgent to take care of this matter.

In the United States, 11 million people live alone or what is the same, 28% of the people 65 and older. Living alone and living without support is not the same. Many persons who live alone have effective social support, while many who live with others have poor social support[58-59]. There is a very little amount of the literature on the effects of living without support, for this reason, this revision has focus on the literature on living alone. Another reviewed fact in the literature is the effects of isolation, which is a real risk when a person starts living alone. Both, although they are not the same as living without support, are the best

approximation. Social isolation could be defined as not having contact with family and friends and participation in civic organizations. Social relations are related with the maintenance of health, especially at older ages, because there is a decrease in economic resources, but also a decline in mobility, which could limit the access to care and thus to the maintenance of health[60].

2.3.2. Description of the elderly

Common conditions in older age include hearing loss, cataracts and refractive errors, back and neck pain and osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression, and dementia. Furthermore, as people age, they are more likely to experience several conditions at the same time[61].

As said, another characteristic of old people is that they have several complex health states and that do not fall into discrete disease categories. These syndromes are often the consequence of multiple underlying factors and include frailty, urinary incontinence, falls, delirium and pressure ulcers[62].

2.3.3. Consequences of living without support and isolation

Older patients living alone have a higher risk of admissions to hospital[63], dementia64, depression[65-66] and loneliness[50, 67]. At the same time, these factors are associated with increased mortality, poor physical health, difficulties to pursue with the daily activities but not with an emotional or cognitive decline compared to patients living with support[68-69].

At the same time, elderly living in isolation have a higher risk of cardiovascular disease, infectious illness, cognitive deterioration, and mortality[70].

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CHAPTER 3.

METHODOLOGY

The following chapter reviews the methodology used in the thesis. The first part is about the database, it explains the sampling system, who has done it, the period of data collection and also there is a statistical description of the variables from the database. The second part is a review of the methodology used.

3.1. DATABASE

For the first and third contributions, samples of a database were used. The database was provided by the Catalan Health Institute and Institut IDIAP-Jordi Gol. The database is formed from data of all the patients from the Catalan Health Institute of the North Metropolitan Area of Barcelona (Badalona, Sant Adrià, Santa Coloma de Gramanet, Terrassa, Sabadell, Cerdanyola) older than 65 years old. In total are 9,336 patients. For all those patients the database includes demographic, clinic diagnostics, tests and other variables explained below in table 3.1 from the period between December 2012 and December 2013.

Table 3.1. Variables database.

Variable	Description of the variable	Observations	Mean	Stand. Dev.	Min	Max	% yes
Demographic variables:							
Date of birth	date						
Sex	male/female						58.18 (male)
Living alone	yes/no						4.47
Clinic diagnostics							
Chronic Cardiovascular Diseases	yes/no						5.31
Severity of CVD	num	1154	2.44	0.70	0	4	
Ejection fraction	num	386	56.02	15.66	0	88	
Dyspnea level	num	615	2.25	0.46	0	4	

Chronic Respiratory Disease	yes/no						9.16
Severity of CRD	num	1474	2.25	0.40	0	4	
Inhalers	yes/no						12.63
Diabetes	yes/no						25.04
Glycated hemoglobin	num	2561	6.42	7.21	0	1144	
Obesity	yes/no						27.26
Tests							
Barthel Test	num	16929	83.02	25.44	0	100	
Lawton and Brody Test	num	6007	3.79	2.68	0	8	
Yesavage Test	num	949	1.89	1.42	0	5	
TIRS Test	num	6610	0.73	1.08	0	6	
Pfeiffer Test	num	10451	2.51	2.94	0	10	
“Get up and go” Test	num	1438	3.45	5.99	0	60	
Zarit	num	1638	51.76	18.96	0	110	
Morinsky Green Test	num	714	3.69	1.07	0	4	
Auto-Nutrition Test	num	1329	2.87	2.68	0	18.5	
Other variables							
Complex chronic patient	yes/no						3.65
MACA*	yes/no						0.42
Nurse Case Manager	yes/no						0.55
CRG	num	62968	5.82	1.13	0	9	
Visits to hospital	num	65023	0.11	0.44	0	11	

Ambulances used	num	122	1.29	0.67	0	5	
Drugs	num	57801	6.06	3.45	0	29	
Antibiotics	num	1328	1.06	0.26	0	4	
Alcohol use	num	59860	0.28	0.48	0	3	
Tobacco	yes/no						14.43
Falls	num	3501	0.29	0.80	0	5	
Urinary infections	Num	3703	1.10	0.36	0	4	

*MACA: is a patient that has been forecasted with less than one year of life.

Source: own elaboration. Data provided by the Catalan Health Institute (ICS)

More information about these variables can be found in the appendixes.

Reviewing the information given in table 3.1 it is possible to observe that on average, patients from the database are men (58.18%), aged 75 years old. Most of the patients from the sample are not suffering from chronic cardiovascular diseases (94.69%), nor chronic respiratory diseases (90.84%), but it is not happening the same with diabetes and obesity, due to the fact that more than a quarter of the patients are suffering from one of them at least.

Just 3.65% of the patients are considered Complex Chronic Patients, and the percentage corresponding to patients that have been forecasted with less than a year of life is 0.42%.

As it is observable, because of the values of skweness and kurtosis, the data seems to be normally distributed in most of the cases.

Some of the results seem a little bit biased from what literature states, this is due to the fact that there are some missing values. For example, the number of ambulances used, as it is observable, there are just 122 records. In order to solve this problem, different statistical methods have been used in each contribution.

The database has been use for contributions one and three, although it has not been used in its total, but just a part of it depending on the topic of study.

3.2. METHODS

3.2.1. Logistic Regression Model with Maximum Likelihood Parameter Estimation

When the dependent variable is categorical, the use linear regression is not advised because the response values are not measured on a ratio scale and the error terms are not normally distributed. In this case, logistic regression is what is normally used. For logistic regression, least squares estimation (that is what it is used for linear regression) is not capable of producing minimum variance unbiased estimators. To solve it for the parameters that best fit the data, maximum likelihood estimation is used[1].
This method is used in the third contribution.

3.2.2. Propensity Score Matching with random effects

The propensity score method is used to build from the set of observed and measured variables a function of all them to estimate the probability ("propensity") that patients have to be assigned to treatment or intervention.
(Propensity Score: conditional probability of receiving treatment based on a set of observed variables)
It allows designing and analyzing some of the particular characteristics of a randomized study.
This method is used in the first contribution.

Assumptions:

1. Conditional Independence Assumption (Unconfoundedness):

The identification strategy assumes that given a set of observable covariates “X”, which are not affected by treatment, potential outcomes are independent of treatment assignment.
This implies that selection is only based on observable characteristics and that the researcher can observes all the variables that influence treatment assignment and potential outcomes at the same time[2].

2. Common Support: also called the overlap condition. It ensures that persons with the same "X" values have a positive probability of being both participants and non-participants[3].

Estimating the Propensity Score:

There have to be made two choices in order to estimate the Propensity Score. The first one is related with the model that will be used for the estimation, and the second one with the variables to be included in this model.

Focusing on the model choice, any discrete choice model could be used. Compared to linear probability models, logit or probit models have less deficiencies, especially the unlikeliness of the functional form when the response variable is highly skewed and predictions that are outside the [0, 1] bounds of probabilities. For a binary treatment case, where the probability of participation vs. non-participation is estimated, logit and probit models usually yield similar results.

Regarding the inclusion (or exclusion) of covariates in the propensity score model, the matching strategy requires that the outcome variable must be independent of treatment conditional on the propensity score. This means that using matching requires choosing a set of variables "X" that satisfy this condition.

A critical factor is not to omit important variables, which could increase the bias of the estimates.

Another factor to be taken into account is that the matching strategy should only include variables that are not affected by participation. To ensure this, variables should either be fixed over time or measured before participation.

The method used in this study for the selection of the variables is the "statistical significance". In order to choose the variables, the process begins with the specification of the model and then it should be 'tested up' by iteratively adding variables to the specification. A new variable is kept if it is statistically significant. Once significance is tested, the second method to be used is the "hit or miss" method, where variables are kept if they are statistically significant and increase the prediction rates by a substantial amount[4].

Matching algorithm

Matching estimators contrast the outcome of a treated individual with outcomes of comparison group members. Two different methods were used in the different contributions:

Nearest Neighbor Matching: it is the most straightforward matching estimator. An individual from the control group is chosen as a matching partner for another individual from the treated group, who in terms of propensity score, is the closest. This method was used in the third contribution.

Caliper: an individual from the control group is chosen as a matching partner for an individual from the treated group that is very near in terms of propensity score, and compare to the Nearest Neighbor, it also has to lie within a propensity range (caliper). If the closest neighbor is far away, the Nearest Neighbor method faces the risk of bad matches, this is what is avoided with this method by fixing a maximum propensity score distance (caliper). Imposing a caliper works in the same direction as allowing for replacement, by avoiding bad matches quality is risen. There is also a danger with this method, and it appears when a fewer matches can be performed. In this case the variance of the estimates would increase[1]. This method was used in the first contribution.

3.2.3. Cost-Benefit Analysis (CBA)

It is a systematic process for calculating and comparing benefits and costs of a project, decision or government policy. This technique provides the best approach to choose the option that best suits the situation for the adoption in terms of benefits in labor, time and cost savings[5-7]. For this reason it was used in the second contribution.

Below can be found a list with the steps that have to be followed to perform a Cost-Benefit Analysis[6]:

1. List the different alternative project options.
2. Measure all cost/benefit elements.
3. Predict the outcome of cost and benefits over relevant period.
4. Transform the costs and benefits into a common currency.
5. Apply discount rate.
6. Bring to the present the different project options (calculate the net present value)
7. Perform a sensitivity analysis.

3.2.4. Mixed Effects

The third method used is the Mixed Effects model. The term mixed model refers to the use of both fixed and random effects in the same analysis. Fixed effects analyses different primary levels of interest. Random effects have levels that are not of primary interest, but that are a random selection from a much larger set of levels. The effects related with the individual are usually random effects, while treatment levels are usually fixed effects[8]. This method was used in the third contribution.

Using a standard linear regression model it only takes into account the fixed effects, so when the variation among individuals is compared through several measurements, the errors for those measurements will almost surely be correlated.

The mixed effects model is the solution for this problem, Seltman explains it this way:

"*The solution to the problem of correlated within-subject errors is to estimate a single variance parameter which represents how spreads out the random intercepts are around the common intercept of each group. This is the mixed models approach. […] From another point of view, in a mixed model we have a hierarchy of levels. At the top level the units are often subjects. At the lower level we could have repeated measurements within subjects. The lower level measurements that are within the same upper level unit are correlated, when all of their measurements are compared to the mean of all measurements for a given treatment, but often uncorrelated when compared to a personal (or class level) mean or regression line. […] We also expect that there are various measured and unmeasured aspects of the upper level units that affect all of the lower level measurements similarly for a given unit.*"[8]

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CHAPTER 4.

CONTRIBUTION I: AN EMPIRICAL MODEL FOR NURSE CASE MANAGER PATIENT IDENTIFICATION

- An adaptation of this chapter has already been submitted to the Journal BMC Health Services Research.

On the following contribution, the first and second objectives (stated in section 1.3) are answered. This contribution is done in collaboration with Institute IDIAP-Jordi Gol and Institut Català de la Salut (ICS).

4.1. INTRODUCTION

Chronic (non-communicable) health conditions (NCDs), are responsible for a major part of the budget of the health care systems[1-2]. Their growth and impact is alarming[3-5]. Five of these conditions, diabetes, cardiovascular diseases, cancer, chronic respiratory diseases and mental disorders, account alone for an 86% of the deaths and a 77% of burden diseases[2]. Non-communicable diseases are linked by common risk factors, underlying opportunities for intervention, which are hugely increased by lifestyle and demographic changes[6]. Long-term patients are high users of health services, but they receive unplanned, poorly coordinated, ad-hoc care in response to an exacerbation or crisis[7], because in most of the cases, management programs just focus on single conditions[8], which leads to an increase in costs.

To fight this problem, the administration has been changing its care models, evolving to an integrated care model that promotes cooperation environments between care areas, health and social services, and between organizations and professionals who work with the same patients. The role of the nurse case manager (NCM) has become an essential part in this change[9]. NCM are responsible of optimizing and rationalizing the use of services and resources and to prevent admissions due to clinical worsening of people with chronic diseases[10].

This paper aims to identify the main factors that distinguish a person as a nurse case manager's patient, and finally to be able to build a model that identifies if an individual should become one of them. To the best of our knowledge, this is one of the first papers proposing an empirical model for a NCM's patient identification.

4.2. METHODOLOGY

4.2.1. Register-based data

The data used was a sample of the database provided by the Catalan Health Institute and Institut IDIAP-Jordi Gol. A total sample of 6393 patients was used. From it, 3209 patients were used to build the model and 3184 out-of-sample patients were used to validate it, to assess the accuracy of the model in predicting behavior. Data extraction was done from December 2012 to December 2013.
The sample is formed by all the patients from the Catalan Health Institute of the North Metropolitan Area of Barcelona, older than 65 years old and classified with Clinical Risks Group (CRG) of at least 5, which means that he/she will have and advanced pathology, or two chronic conditions or more. As not all the variables that are studied in this paper have a mandatory register, it was decided to focus just on the chronic complex patients because register rate is higher, thus this will give more realistic results due to the fact that there is less missing data for those patients.

4.2.2. Significant factors in having a Nurse Case Manager

In order to find the factors defining a NCM's patient, a review of the literature was done searching what defines them. It was found out that patients under the supervision of NCM have to be first identified as advanced chronic patients.
What differentiates an advanced chronic patient from a NCM's patient is the fact that the advanced chronic patient is having an exacerbation. It is important to remember that NCM appears only as a punctual help, meaning that the NCM will take care of the patient while he/she has an exacerbation. In order to identify the main factors in the process of having an exacerbation, a literature review was done as well as several interviews with NCM and physician.

4.2.2.1. Factors defining an Advanced Chronic Patient.

The theoretical framework used as baseline to define an advanced chronic patient is the one from the Catalan Health Institute, and it is formed by three criteria: (a) Fulfilling the Complexity Criterion, (b) Fulfilling the Severity Criterion and (c) Fulfilling the Frailty Criterion.

First of all, the patient has to be a Complex Chronic Patient with an advanced pathology (CRG 5), two chronic conditions (CRG6) or more (CRG 7). This is known as the Complexity Criterion. As the sample is built with people that accomplish it, this criterion was excluded from the model.
Second, the patient also needs to fulfill the Severity Criterion, which means that at least this patient has been twice hospitalized or has visited twice the emergency unit in the last twelve months. Due to data limitations, it was impossible to obtain registers from the variable number of hospitalizations for this study.
Third, the patient has to fulfill the Frailty Criterion. There are several definitions of what a frail patient is, for example Fried's definition based on data from the Cardiovascular Health Study defines it as a: weight loss, weakness, exhaustion, low activity level, and slow gait speed[11]. In order to find the most accurate definition, other studies were searched in the literature and come up with the most common components and outcomes[12-15]. Most of the variables found are tests; for this reason, limits used by the Catalan Health Institute are going to be used for this contribution. Variables were group in different categories. The 10-item ordinal scale for the basic activities of daily living (BADL) (Katz, Downs, Cash, & Grotz, 1970 with a Cronbach's reliability between 0.84 y 0.97[16]) and the instrumental activities of daily living (IADL) (Lawton & Brody, 1969 with a Cronbach's reliability of 0.90[17]) determined the functional status. The number of falls during the last two years and the "Get-Up and Go" Test (Mathias et al, 1986 with a Cronbach's reliability of 0.91[18]) determined the physical status. The Spanish Version of Short Portable Mental Status Questionnaire (SPMSQ) (Peiffer et al.; 1975 with a Cronbach's reliability of 0.92[19]) determined the cognitive status. The 5-item Spanish Version of the Geriatric Depression Scale (GDS) (Yesavage et al., 1983 with a Cronbach's reliability of 0.82[20]) determined the emotional status. And finally, "Age-alone" Test and TIRS Test (current instruments used by the Catalan Health System) they were used to determine if there was social risk.

4.2.2.2. Factors defining probability of exacerbation.

As mentioned previously, just five of the chronic conditions, namely diabetes, cardiovascular diseases, cancer, chronic respiratory diseases and mental disorders, account for most of deaths. Due to the importance of these pathologies,

it was decided to include them as factors causing exacerbations. For this reason, this section has been divided in two parts; one for factors common in all illnesses, and the other one for factors from 3 of the pathologies mentioned: cardiovascular diseases (CVD), chronic respiratory diseases (CRD) and diabetes. Cancer and mental disorders have not been included due to its disparity of origins and consequences. For choosing the variables to be included, a literature review was done as weel as some interviews to NCM and primary care physicians.

4.2.3. Statistical method

First of all, individual and conjoint significance were tested in order to choose which variables should be included in the model.
Once the significance test was done, the significant variables were taken and a model using Propensity Score Matching (PSM) with random effects[21] was build. In order to do the matching, the caliper method is used, which defines a tolerated radius or neighborhood around the propensity score for treated individuals. In this case, the caliper used was equal to 0.5 of the standard deviation of the probit of the propensity score.

The propensity score is the probability of treatment assignment conditional on observed baseline characteristics. It allows designing and analyzing some of the particular characteristics of a randomized study. In particular, the propensity score is a balancing score: conditional on the propensity score, the distribution of observed baseline covariates will be similar between treated and untreated subjects[22-23]. As the assignation of a Nurse Case Manager can vary from one hospital to another, the study is facing a 2-level structure. For this reason, if running a regular PSM, it is possible that several control units have the same value of the propensity score within the caliper, thus the ATT estimator would be biased. In order to solve for this situation, random effects to represent unmeasured cluster variables were used. After matching, the effect meaning the individual's propensity to receive treatment had been estimated through a propensity score regression including the propensity score variable instead of the fictitious variable indicative of treatment[24-25].

In order to verify the robustness and validity of the model, the second sample mentioned before was used. It was evaluated if the model was also valid for that sample. This was done by calculating the expected probability and comparing it with the one from the first sample.

4.3. RESULTS

Table 4.1 summarizes all the descriptive results from the variables chosen related with the frailty criterion. It can be observed that for the frailty criterion, most of the variables are under the accepted limits, although very close to them. The exceptions is the variable Pfeiffer test (3.09), which is over the limit, implying that patients have some kind of cognitive impairment which is quite normal because the mean age of the sample is between 81 and 82 years old.

Table 4.2 shows the descriptive results for the variables related with the probability of exacerbation. Results from the variables common to all illnesses overcome in some cases the limits, especially the number of drugs (9.42), which is very high as well as adherence to treatment (3.30) and the nutrition test (3.70). The only variables that are within limits are alcohol consumption (just 1.40 % of the patients are consumers), tobacco consumption (just 11.55% are smokers) and obesity (10.81% of them are obese).

Table 4.1. Statistics for variables from the frailty criterion.

Area	Variable	Obs (%)	Mean	Std. Dev.	Skewness	Kurtosis	Limit
Functional decline	Barthel test	82.01	69.92	29.50	-1.69	5.03	> 60
	Lawton test (Women)	30.91	3.29	2.55	0.13	1.77	> 4
	Lawton test (Men)	17.91	2.88	2.06	0.13	1.77	> 2
Physical decline	"Getupandgo" test	10.62	4.06	6.68	6.62	53.18	< 20
	Falls	16.98	0.47	0.94	4.67	37.73	<2
Cognitive decline	Pfeiffer test	66.74	3.09	3.12	1.16	3.27	<2
Emotional decline	Yesavage test	14.58	1.76	1.37	0.42	2.25	≤ 3
Social risk	TIRS test	52.50	0.78	1.14	1.98	7.67	< 1
	"Age-alone" test (yes)	10.81			4.16	18.30	

Table 4.2. Statistics for variables related with having an exacerbation.

Variable	Obs (%)	Mean	Std. Dev.	Skewness	Kurtosis	Limit
Variables common in all illnesses						
Urinary Infections	0.10	1.13	0.39	3.60	17.71	
Morisnky Green Test	6.70	3.30	1.07	17.72	318.72	<4
Auto-nutrition Test	9.30	3.70	3.15	1.75	7.14	>2
Number of drugs	98.72	9.42	3.88	0.78	3.69	
Number of antibiotics	3.46	1.11	0.34	4.63	28.97	
Obesity (yes)	10.81			0.88	1.79	
Tobacco consumption (yes)	3.70			3.18	11.14	
Alcohol consumption* (yes)	1.40			1.47	4.17	
1	1.30					
2	0.06					
3	0.03					

Variables for specific illnesses							
Chronic Cardiovascular Diseases (CVD)	**Severity CVD**	8.91	2.44	0.72	.12	2.62	>2
	Ejection fraction	2.64	54.54	9.13	-0.55	2.75	<50
	Dyspnea	3.24	2.22	0 .44	0.77	2.87	>2
Chronic Respiratory Diseases (CRD)	**Severity CRD**	5.54	2.5	0.36	0.47	2.83	>2
	Inhalers (yes)	34.25			2.19	5.82	
Diabetes	**Severity Diabetes****	61.48	6.73	3.77	28.62	1178.61	≥8

*Alcohol consumption: 1 means is a low risk drinker, 2 means is a risk drinker, and 3 means the patient has dependency on alcohol.

**Severity Diabetes: for which is used the level of glycated hemoglobin (average plasma glucose concentration (%)).

Relative to results from specific illnesses, results are not considered conclusive for chronic cardiovascular diseases due to the low record level. For respiratory diseases and diabetes, the percentage of observations is a little bit higher, (around 61% for severity diabetes), and levels are around the limit.

On the following tables (tables 4.3 and 4.4) are shown the results from the study of the individual impact on the probability of having a NCM.
Results from severity criteria as well as most of the other variables showed significant and positive if individually tested. These tables show how much will increase the probability of having a NCM, for an increase of 1 unit of that variable.

Table 4.3. Individual significance for variables related with being a chronic patient.

Variable		**% Variation in the probability of having a NCM**	**Std. Error**
Complexity		Not included	
Severity		162.07**	4.92
Frailty	**Barthel Test**	1.07***	0.00
	Lawton Test	9.94*	0.02
	GetUpAndGo test	1.86***	0.01
	Number falls	1.83***	0.10
	Pfeiffer Test	1.43**	0.02
	Yesavage Test	6.88***	0.05
	TIRS Test	9.38***	0.05
	Age-alone Test	1.64**	0.25

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Analyzing the results from table 4.3, it can be observed that all the variables from the frailty criterion are significant and have a positive relation with the fact of having an NCM. Once the individual significance was tested, it was decided to

used the "hit or miss" method, where variables are kept if they are statistically significant and increase the prediction rates. It was found that prediction rate was higher if Barthel Test, Yesavage Test and TIRS Test were not included.

Table 4.4. Individual significance for variables related with exacerbations.

Variable		**% Variation in the probability of having a NCM**	**Std. Error**
Common variables in all illnesses			
Urinary Infections		4.45	0.15
Morisnky Green Test		1.16***	0.04
Auto-nutrition Test		1.75***	0.03
Number of drugs		1.80**	0.07
Number of antibiotics		9.45	0.19
Obesity (yes)		7.61**	0.15
Tobacco consumption		1.37	0.01
Alcohol consumption		4.50**	0.18
Variables for specific illnesses			
Chronic Cardiovascular Diseases (CVD)	**Severity CVD**	5.29	0.01
	Ejection fraction	9.45	0.01
	Dyspnea	1.39	1.86
Chronic Respiratory Diseases (CRD)	**Severity CRD**	9.97*	2.66
	Inhalers	3.61	6.03
Diabetes	**Severity Diabetes**	3.13	0.48

Significant codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

About the common variables of exacerbation (table 4.4), as urinary infections, antibiotics and tobacco are not significant, a new group variable called "Commonexacerbations" was generated, which was significant. In order to make it more accurate, following Rockwood and Mitnitski criterion of frailty[17] which states that as deficits accumulate, people become more susceptible to adverse health outcomes; therefore it was decided to increase the number of variables to fulfill. It was found that fulfilling at least four of them was more predictive.

Also in table the same table 4.4 , variables related with specific illnesses are also studied. Taking a look at the variables from the CVD group, none of them was significant. It may be due to the fact that there are not many registers of them. For this reason, it was created a new variable grouping all the CVD variables together called "CVDexacerbations", which was significant. For CRD exacerbations, only the variable severity level was significant, so it was taken as a representative variable for the illness, and left inhalers out. We could not do the same for diabetes, because the only variable related was the severity level, and it was not significant, so diabetes was removed from the final model.

Below, there is a list of the variables finally included in the model:

- Severity (S_1): if the number of hospitalizations was bigger or equal to two, the variable was 1, if not 0.
- To evaluate frailty the following variables were included: Lawton Test (F_1), Getupandgo Test (F_2), Number of falls (F_3), Pfeiffer Test (F_4), Agealone Test (F_5), all them were 1 if the test was positive, 0 if not.
- "Commonexacerbations" (C_1): if the patient fulfilled at least 6 criteria, the variable was 1, 0 if not.
- "CVDexacerbations" (V_1): this variable was 1 if at least one of the variables that form it was different than 0, 0 if not.
- "CRDexacerbations" (R_1): this variable was 1 if the variable severity level was different than 0, 0 if not.

After choosing the variables to be included in the model, Propensity Score Matching with random effects was estimated. The final empirical model is the following one:

$$\eta_{ij}=\alpha+ \beta_1*S_1+ \beta_2*C_1+ \beta_3*V_1+ \beta_4 I*(R_1==1) + \beta_5* I*(R_1 ==2) +\beta_6* I*(R_1 ==3) + \beta_7*I*(R_1==4) + \beta_8*F_1 + \beta_9*F_2 + \beta_{10}*F_3+ \beta_{11}*F_4 + \beta_{12}*F_5$$

Table 4.5. Coefficients from the variables of the model.

Coefficient	Estimate	Std. Error
α	-1.64***	0.18
β_1	1.02***	0.14
β_2	1.28***	0.12
β_3	0.88***	0.15
β_4	-13.93	0.53
β_5	-0.96*	0.46
β_6	-0.60	0.42
β_7	0.13	0.47
β_8	0.78***	0.14
β_9	-0.46**	0.16
β_{10}	-0.61***	0.14
β_{11}	-1.03***	0.13
β_{12}	0.17	0.24

Significant codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Null deviance: 2198.8 on 3208 degrees of freedom
Residual deviance: 1809.7 on 3196 degrees of freedom

$$\text{Prob}_i(\text{NCM}=1) = e^{\eta_i} / (1 + e^{\eta_i})$$

As specified in table 4.5, some coefficients per se do not predict the fact of having a NCM. This means that on their own, they are not sufficient, but when adding all them together they are. It is a conjunction of factors that predict it. It can be observed that when the variables are combined, they are significant, but when they are left alone, they are not significant or even in some cases they are negative by balance. Those variables have to be included in the model because if not, there is the risk of overweighting the significant variables.

The prediction power of the model is 64%, which means that the final model predicts 64% of the cases in which a patient will have a Nurse Case Manager.

When comparing the null deviance with the residual deviance, it is possible to affirm that there has been a significant reduction in deviance, so the model has improved its prediction value.

A validation of the power of the model was done with another sample with the same characteristics. In order to do the validation, the coeficients from sample one have been used and the predictive power of the model has been verified with the new data. The result from the validation process showed a probability similar to the one obtained in the previous sample. Thus, it is possible to conclude that the model is robust.

4.4. CONCLUSIONS

To know the factors that influence a patient to be attended by a nurse case manager allows identifying opportunities for intervention. If we are able to point out which are the main factors, this can promote the creation of policies to change them and increase the quality of life of chronic patients. In addition, it can also reduce costs.

Chronic patients under exacerbations are big care consumers, thus are responsible for a huge part of its cost. Identifying which factors determine that a patient has to be attended by a nurse case manager, means also determining how to reduce exacerbations, and less exacerbation leads to less costs. This is the case of the number of drugs and adherence to treatment. As results show, the situation related with the number of drugs or "polymedication" is alarming. Although a point from which it can be stated that the patient is polymedicated is not widely and uniquely accepted, more than five medications generates a higher risk of adverse effects and negatives consequences in health[24]. The average number of drugs taken by the patients in the investigated sample is more than nine, which clearly exceeds the limit considered. This variable could be related with another alarming factor, i.e., adherence to treatment. The average sample's age is quite high, so taking into account that most of them are polymedicated and have some kind of cognitive impairment and a lack of support, a decrease in the level of adherence seems within the limits. Other studies show similar results related with the low level of adherence in chronic patients[25-26]. So there is the possibility for an intervention, which could consist in aligning health care policies in order to increase adherence, increasing quality of life for patients and reducing costs.

Finally, regarding the model, it could be used as a method of alert for the health agencies, thus it is a way of stopping exacerbations. Another important advantage of this model is the simplicity of the model and the variables used, which will allow almost any agency or entity to use it.

Some limitations of the current study arise due to the use of clinical records. Clinical records are sometimes incomplete, and this could lead to bias the results. This problem was improved with the used of the different methodology used.

One of the main objectives of this model is that it had to be repeatable by other centers or agencies. For this reason, data needed have to be easy to obtain so other forms of replications in different agencies and countries can be done.

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CHAPTER 5.

CONTRIBUTION II: POTENTIAL COST AND SAVINGS OF A PROPOSED INTERVENTION TO REDUCE NON-ADHERENCE OF ADVANCED CHRONIC PATIENTS.

- An adaptation of this chapter has already been submitted and accepted for publication with changes in the Journal PharmacoEconomics Spanish Research Articles

On the following contribution, the third objective (stated in section 1.3) is answered. This contribution is a follow up of the first one, were it is studied more in deep the relation between non-adherence and patients' health.

5.1. INTRODUCTION

Adherence to treatment is a problem for today's health agencies due to the fact that more than 50 percent of medications are not taken as prescribed by the healthcare provider[1-2]. There is a significant association between medication adherence and clinical outcomes: better medication adherence is correlated with improved outcomes[3].
Adherence rate among patients with chronic conditions is disappointingly low compared to other patients[4]. This is becoming a problem because chronic conditions account for big percentage of the total expenditure in health care[5], and poor adherence to medication regimens accounts for substantial worsening of disease, death, and increased health care costs[6], which keeps increasing the budget for chronic conditions for the healthcare agencies.

Disease management programs have proliferated recently as a means of improving quality and efficiency of care for patients with chronic illness[7]. There have been several interventions framed in these programs, oriented to increase the adherence rate to treatment. Most of those interventions are efficient and increase the quality of life of the patients, but they also tend to be exceedingly complex, labor intensive and costly[7-8]. For this reason, this study has proposed an intervention as simple as possible. The intervention chosen is a patient focus intervention, which plans to reduce the preventable rate of non-adherence by monitoring patients' medication use regularly in order to avoid misunderstoods related with medication use. In particular, the intervention consist in reviewing the way medication has been taken in every visit that advanced chronic patients do to their primary care centers. This kind of intervention is already partially done in many medical systems, but it is has not been widely implemented in Spain.

The objective of this article is estimating the potential net benefits from the proposed intervention to reduce non-adherence.

5.2. METHODOLOGY

This contribution is an economic evaluation where they are compared cost and benefits of applying the intervention just explained to reduce non-adherence to a population of 7.5 million inhabitants (Catalan population) with and effectiveness of 10%. The applied perspective was from the society point of view, the reference year was from October 2014 to October 2015, and the discount ratio used to update cost and benefits was 4%. A sensibility analysis is also done, using lower effectiveness rates.

5.2.1. Sample selection

For this simulation, Catalan population has been chosen. The main reason is that monitoring patient's use is just recommended once a year by the Catalan Health Agency[9], so it has not yet been implemented.
The release of this article is the frequency at which this intervention is proposed. For this reason, chronic patients have been chosen as main recipient, because they attend quite often to primary care. In Catalonia, the average number of visits to the primary care center by patients 65 years old and older is 14[10].
Another important reason why this population has been chosen is that non-adherence interventions tend to target non-intentional lapses, which are related with the characteristics of the treatment and of the patient. Complex chronic patients are mostly old people suffering from multiple comorbidities, so it is quite possible that they are physically or psychologically impaired, and for this reason, patients are typically polymedicated[1, 11].
Therefore, the population chosen would be Complex Chronic patients older than 65 years old. Assuming than in Catalonia there are 1.3 million inhabitants older than 64 years old (IDESCAT) and that from those 66.98% are multimorbid[12], the final number of participants would be of 893,715 patients. The profile of this type of patient in Catalonia corresponds to a person of 82 years old, in 52% of the cases women, with a medical history of hypertension (82.2%), chronic cardiovascular problems (67.8%), chronic respiratory problems (43.3%), diabetes (42%), and under social risk in 53.7% of the cases[13].

5.2.2. Estimating potential costs

Once the participation is estimated, the cost of the intervention is calculated.
As there are no adquisition nor maintenance cost for the hospital, the only direct cost is the cost of the time added to the visit. To calculate the cost of added time per visit, this study uses the article form Seguí et al[14], who study primary care visits and state how much time is devoted to each step in the visit. The mean time per problem attended in a primary care visit is of 7.4 minutes. Taken into account that to review adherence the physician or nurse will need a little bit more time, the mean time devoted to the exposition of the problem and to the interrogation of the patient to know how the medication is taken (which is in total 1.16 minutes), is added to the visit, because those are the ones that are more similar to the process of reviewing adherence. Assuming a cost per visit to primary care of 14.78 Euros[14] and that during the year on average a chronic patient older than 65 years goes 14 times to the primary care, the extra time would represent an increase of 31.94 Euros/ patient/year.

Because depending on the illnesses the efficiency of this intervention may vary, the cost is estimated for three illnesses: Chronic Obstructive Pulmonary Disease (COPD), Chronic Heart Failure (CHF) and Diabetes. The reason why these illnesses are chosen is because they are part of the most frequent combinations of multimorbidity[15], but also because as Di Matteo et al. [16] state, the adherence average for these three illnesses is in the range between 60% and 80%, and thus there is still room to improve it.
Medical cost and drug cost used are: for CHF data from Delgado et al. [17] using as base year 2010; for COPD data from Izquierdo et al. [18], using as base year data from 2004; and for diabetes data from Mata et al. [19], using as base year 2002. It is important to mention that these were the most recent studies found specifying costs for those illnesses in Spain. Medical costs included outpatient services, emergency room services, and hospitalization. Drug costs included all ambulatory prescriptions. Due to the fact that those costs are from different years from the past, they were updated applying the increase in the Spanish Price Index (IPC). For those in 2002 was of 30.8%, for 2004 was of 23.1% and for 2010 was of 6.4%. This increase in the Spanish Price Index was obtained from the data published by the Spanish Statistics National Institute (INE).

5.2.3. Estimating potential benefits

Due to the increase in adherence, medical costs were expected to decrease, thus benefits are calculated as the reduction in health consumption assuming an effectiveness of the intervention of 10%. Because the population is 65 years old or older, there is no need to calculated potential increase in productivity, thus there are not going to be indirect benefits.

To calculate the direct benefits, again data from Di Matteo[16] is used. Knowing that the average adherence for these three illnesses is in the range between 60% and 80%, the difference in cost between this range of adherence and a next higher one is calculated, simmulating the jump in the adherence range that would be achieved by pursuing with the intervention, and then applying to that difference the Spanish cost per illness using data from Delado et.[17] Izquierdo et al.[18] and Mata et al.[19]. Taking into account that the expected life for a multimorbid patient is of 81.4 years old[20] and that the intervention starts when the patient is 65 years old, total direct benefit per patient is calculated. To establish direct benefits, future benefits are subtracted with an annual discount rate of 4%.

5.2.4. Sensibility Analysis

For the previous calculations, it was assumed and average effectiveness rate of 10%. For the sensibility analysis, other rates of effectiveness will be calculated from a more pessimistic approach. To value the efficiency of the intervention, the net cost-benefit result using as base year 2014 for each of the efficiency rates is going to be calculated taking into account future costs and benefits.

5.3. RESULTS

In the following table (table 5.1) it is showed the cost before and after the implementation of the intervention, so the costs before and after the intervention.

Table 5.1. Cost per disease before and after treatment.

Diseases		Cost before treatment (€)	Cost after treatment (€)
Diabetes	**Average Cost**	1887.36	1739.02
	Medical cost	1263.39	1014.02
	Drug cost	592.03	725
CHF [a]	**Average cost**	6335.28	5203.09
	Medical cost	4735.64	3764.03
	Drug cost	1567.69	1439.06
COPD [b]	**Average cost**	2770.11	2568.99
	Medical cost	1982,36	1602,65
	Drug cost	755,80	966,34

[a] CHF: Chronic Heart Failure
[b] COPD: Chronic Obstructive Pulmonary Disease

Source: based on Delgado et al. [17], Izquierdo et al. [18]and Mata et al. [19].

Although drug costs in some cases increases due to the increase in adherence, in the three cases final average cost is lower after the treatment, meaning that this intervention would be saving money to the health systems, although the difference is especially significant in the case of Chronic Heart Failure.

Table 5.2 shows the benefits from applying the treatment.

Table 5.2. Benefits from the intervention.

CONCEPT	Base year 2014	Base year 2014	Base year 2050
Avoided healthcare cost/year	525.78€	525.8€	
Total benefit per patient	525.78€	4532.16€	
Total benefit of the intervention	469,903,114€	405,0469,884€	6,206,283,015€
Total cost of the intervention	28,551,621€	246,109,211€	377,097,833€
Net Benefit of the intervention	44,1351,492€	3,804,360,673€	5,829,185,181€
Cost-benefit ratio	16.45€	16.45€	16.45€

Source: own elaboration

The first column explains the annual cost having as base year 2014, which means that it is just taken into account the cost and benefit for this year. The second column takes also into account the future cost and benefits, and subtracts them from the direct cost. This can be observed by comparing total benefit per patient between both columns. This second column has a higher total benefit per patient than the first one, because future cost and benefits are also taken into account. In both cases, the net cost-benefit analysis is positive, meaning the situation after the intervention is better than before. The last column is the same than the second one, but for the year 2050. As benefit is calculated from the difference in costs, an assuming that there is not going to be inflation, costs from 2014 have been used to do these calculations. It is observable that the result for the net cost-benefit analysis has increased; this can only be due to the increase in population for that age range. As Sanchez (2015) stays, the current population older than 65 years old is 17%, but it is expected to grow until 27, 5% in 2050[21], which means that this intervention would generate high benefits for the society nowadays, but specially in the future because the population range targeted is going to increase.

The results from the sensitivity analysis are shown in table 5.3.

Table 5.3. Sensitivity analysis.

Concept	Cost effectiveness (€) 2%	Cost effectiveness (€) 5%	Cost effectiveness (€) 10%
Avoided healthcare cost/year	98.77	246.92	525.78
Total benefit per patient	851.37	2128.43	4532.17
Total benefit of the intervention	760,883,054	1,902,207,635	4,050,469,884
Total cost of the intervention	246,109,211	246,109,211	246,109,211
Net Cost-benefit of the intervention	514,773,842	1,656,098,424	3,804,360,672
Cost-benefit ratio	3.09	7.73	16.46

Source**:** own elaboration

In table 5.3 it can be observed that whereas the cost does not increase, the benefit does. Cost-benefit ratio increases if effectiveness increases, but not in a proportional way. Even though the cost-benefit ratio is very low for an efficacy rate of 2%, the net cost-benefit of the intervention is 51,4773,842€, which is a very important figure in terms of savings. This means that although the cost-benefit ratio is low, society would be saving lots of money.

5.4. CONCLUSIONS

The aim of this study was to propose a possible solution to the current situation about non-adherence, especially for the advanced chronic community and to asses if it was worth implementing it.

As results show, total savings from applying this intervention would currently be very important, but are going to be even more important in the future due to the exponential growth of the targeted population.
This intervention is easily generalizable, because it does not vary depending on the concentration of the population or its size. The patient does not have to change its habits, so aside from a little extra time need for the revision of the way medication is taken, nothing else is needed.
It is also important to mention that even if effectiveness was very low, the savings would be very significant (as the sensibility analysis is showing). This means that targeting adherence should be a very important point on the agenda of the health agency, because even with a small improvement, the benefits would be huge.

The study has several limitations. First of all, it focuses on three pathologies, Diabetes, Chronic Obstructive Pulmonary Diseases, Chronic Heart Failure, which could bias the results; but they have been chosen because they are three of the most common pathologies[9] and also they are part of the most frequent combinations of multimorbidity[22]. Second, results cannot be applied to developing countries, because its population pyramid is different, thus the percentage of advanced chronic patient is different and results would vary.
Complex chronic patients are causing a big part of the expenses in health care cost and its growing rate is exponential[2-3]. The intervention proposed, not only would mean a decrease in the expenditure on public health budget, but it also would be increasing patients' health and thus, quality of life.

5.5. REFERENCES

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CHAPTER 6.

CONTRIBUTION III: ANALYSIS OF THE EFFECT OF LIVING WITHOUT SUPPORT IN CHRONIC OLD PATIENTS.

On the following contribution, objective four (stated in section 1.3) is answered. This contribution is a follow up of the first one, were it is studied more in deep the relation between living without support and patients' health.
This contribution, as well as the first one, is done with the database offered by Institute IDIAP-Jordi Gol and Institut Català de la Salut (ICS).

6.1. INTRODUCTION

Older people living alone or without support are seen as a potential at-risk group worthy of further intervention[1]. On average people aged 60 and older make up 12.3% of the global population, and between one-third and one-fourth live at home alone[2]. This prevalence is predicted to further increase over the next 20 years[3-4], in some cases like United States, it is even going to be duplicated at the end of 2050[5]. In Spain, 12.5% of old people live alone, which in absolute numbers means 8 million people[6].

When following the demographic patterns, it is possible to observe that during the last 50 years, patterns of household composition have changed. The marriage rate has decreased[7-8], if combined with the fact that most women nowadays have also a paid job[9], and that everyday people is having less and less children[7], this leaves elderly with fewer family members to provide company and care[8]. This is more important when added to the fact that longevity has risen sharply in most developed countries, due to a fall in mortality at advanced ages. It is also important to mention that as people gets older, they are more likely to experience several illnesses at the same time[10], which added to the fact that thanks to the health advances most of them are left in a chronic state, with the increase in health expenses that it implies. For this reason, it seems urgent to take care of this matter.

Living alone in older patients is associated with a higher rate of admissions to hospital[11-12], dementia[13], depression[14-15] social isolation and loneliness[16-17]. The last factors are indeed strongly interdependent[18] and are associated with increased mortality, poor physical health and difficulties to pursue with the daily activities. However, they have also reported no difference in terms of emotional health decline compared to patients living alone[1-2] and also a better cognitive status[2].

The perception of living alone or without support drives policymakers and thus primary care practitioners to use the lone or living without support status as a

trigger for further attention. The aim of this study was to calculate the statistical effect of living without support among advanced chronic older patients on their health. This study focus on living without support instead of living alone because many patients of the latter group have effective social support, while many patients of the former have poor social support[19-20]. Focusing on old chronic patients allows isolating the effect of not having support on the health status. To the best of our knowledge, this is one of the first papers studying the effect of living without support on health. In addition, it is one of the first papers using clinical data to do so.

6.2. METHODOLOGY

6.3.1. Sample selection

The data used was issued by the Catalan Health Agency (Spain) and Institut IDIAP-Jordi Gol. A sample of 6168 patients was used, it is a part of a bigger database. The database is formed from data of all the patients from the Catalan Health Institute of the North Metropolitan Area of Barcelona (Badalona, Sant Adrià, Santa Coloma de Gramanet, Terrassa, Sabadell, Cerdanyola) older than 65 years old from the period between December 2012 and December 2013. In this case the sample was created by restricting the patients to just those that were CRG 5, 6 and 7, in total are 9,336 patients.
The data set contains information regarding the functional, physical, cognitive and emotional health, information about the chronic illnesses of the patient (CRG), information of the patient about living without support, age and sex. These are the variables that are used throughout the analysis. The data set also contains information about clinical diagnosis of patients (cancer…), habits (smoking, drinking…), if they have been assigned a nurse, number of entrances in the hospital, among others.

Functional, physical, cognitive and emotional healths were described according to medical tests carried out by specialists. Functional status was assessed by means of the 10-item ordinal scale for the basic activities of daily living (BADL) (Katz, Downs, Cash, & Grotz, 1970 with a Cronbach's reliability between 0.84 and 0.97[21]) and the instrumental activities of daily living (IADL) (Lawton & Brody, 1969 with a Cronbach's reliability of 0.90[22]), physical status by the number of falls during the last two years and the "Get-Up and Go" Test (Mathias

et al, 1986 with a Cronbach's reliability of 0.91[23]), cognitive status by means of the Spanish Version of Short Portable Mental Status Questionnaire (SPMSQ) (Peiffer et al.; 1975 with a Cronbach's reliability of 0.92[24]), and emotional status by means of the 5-item Spanish Version of the Geriatric Depression Scale (GDS) (Yesavage et al., 1983 with a Cronbach's reliability of 0.82[25]).

The following table (table 6.1) describes the different tests that are used throughout the paper. The limits denote the boundaries where it is considered the patient has a decline. For instance, the Barthel test specifies that the patient has a functional decline if the results are below 60. It is assumed that a patient has a functional or physical decline in case one of the tests gets positive.

Table 6.1. Classification criteria.

Area	Variable	Limit
Functional decline	Barthel test	> 60
	Lawton & Brody (Women)	> 4
	Lawton & Brody (Men)	> 2
Physical decline	"Getupandgo" test	< 20
	Number of Falls	<2
Cognitive decline	Pfeiffer test	≤3
Emotional decline	Yesavage test	< 1

Source: Institut Català de la Salut

The main exogenous variable of study is living without support. Living alone or without support is not the same. Many persons who live alone have effective social support, while many who live with others have poor social support[19-20]. For this reason, living without support is used instead of living alone, because it includes all the alternatives. In this case, the chosen variable used is a called "TIRS (Test Indicador de Risc Social)". This test assesses the rate of social risk of the patient. A patient is under social risk if living alone or with a caregiver who can only provide a limited amount of support. The test consists in a

questionnaire where the patient has to answer “yes” or “no” to several questions related with living alone, personal hygiene, accommodation or lack of financial resources[26]. For further information, see Appendix 2. In the analysis, value 1 is given to variable TIRS whenever the patient lives with support and 0 otherwise.

All observations are from chronic complex patients. That is, they have a CRG between 5 and 7. These patients are stable within their severity. Thus, they may still live alone or without support. Patients with CRG higher than 7 are not considered. These patients need constant care and may not develop day-to-day life activities on their own. CRG is the second exogenous variable that is used in this study. The values that CRG takes is 5, 6 and 7.

The rest of exogenous variables are sex and age. Sex takes value 1 if the patient is a man and 0 otherwise. Age takes the numerical variable of the real age of the patient.

There are four criteria variables used in different regressions: Physical Decline, Functional Decline, Cognitive Decline and Emotional Decline.

The sample information is described as follows in the following table (table 6.2). Since from the whole sample there is not information of all patients of all tests, for each of the regressions we eliminate those observations that information was not provided. Thus, the sample is reduced for each of the regressions that are carried out.

From the table, it can be observed that on average 68% has functional decline, 8% has physical decline, 52% have emotional decline and 30% has cognitive decline. It should also be taken in consideration that these percentages could be upward biased because most of the tests are run if there is the suspect that the patient is in risk of suffering this decline. The average age for all the subsamples is between 83 and 84 years old, around 30% are men and its average CRG is 6. As it is observable, because of the values of skewness and kurtosis, the data seems to be distributed normally.

Table 6.2. Samples description.

Variable	Mean	St. Dev	Skewness	Kurtosis
Sample 1 (N=4591)				
Functional Decline	0.688	0.464	-0.810	1.656
TIRS Test	0.434	0.496	0.268	1.071
Age	84.692	7.086	-0.349	2.954
Sex	0.298	0.458	0.881	1.776
CRG	6.136	0.456	-0.228	2.783
Sample 2 (N=1994)				
Physical Decline	0.083	0.276	3.017	10.103
TIRS Test	0.444	0.497	0.226	1.051
Age	84.663	7.153	-0.312	2.889
Sex	0.311	0.463	0.814	1.663
CRG	6.139	0.436	-0.203	2.854
Sample 3 (N=5504)				
Cognitive Decline	0.308	0.462	0.833	1.694
TIRS Test	0.434	0.496	0.268	1.072
Age	84.433	7.116	-0.314	2.891
Sex	0.310	0.463	0.822	1.675
CRG	6.137	0.456	-0.237	2.799
Sample 4 (N= 632)				
Emotional Decline	0.521	0.500	-0.082	1.007
TIRS Test	0.456	0.498	0.178	1.032
Age	83.585	7.007	-0.251	2.832
Sex	0.345	0.476	0.652	1.423
CRG	6.211	0.496	-0.146	2.327

6.3.2. Empirical methods

To provide a robust analysis, two empirical methods are used.

The first method used is the Mixed Effects model. Since the health data used in this study is objective and provided by a health agency, personal data such as income or education was not provided. This method is useful to overcome this limitation. Using the Mixed Effects model we account both for fixed and unknown random effects. The specification of the model is the following:

$$Decline_j = X\beta + Z\gamma + \varepsilon,$$

being j each of the four possible declines: functional, physical, emotional and cognitive. When using this method, and for the forthcoming analysis, all the mentioned dependent variables are dichotomous, and they take value 1 if the patient has the decline. The X matrix contains information regarding the known covariates used in the analysis: information about the chronic illnesses of the patient (CRG), information of the patient about living without support, age and sex. Sex and living without support are dichotomous variable that takes value 1 if the patient is a male or if the patient lives without support respectively. The vector of fixed effects β includes the parameter under study that determines the effect of living without support in the different declines. Matrix Z is a design matrix that accounts for random effects and γ its associated vector of random effects.

The second method used is a Logistic Regression Model with Maximum Likelihood Parameter Estimation. As the dependent variable was categorical, the use of linear regression is not advised because the response values are not measured on a ratio scale and the error terms are not normally distributed. For this reason it was used logistic estimation. Then to have the best fitted data, maximum likelihood estimation was used because least squares estimation would provide biased estimators.

In order to check for the significance of the model and its fit, χ^2 and R^2 were also calculated. Also to verify the normal distribution assumed of the residuals, so that there is not heteroskedasticity, a skewness and kurtosis analysis was done.

6.3. RESULTS

Table 6.3. Results Mixed Effects Model

Mixed Effects	Functional decline		Physical decline		Cognitive decline		Emotional decline	
	Coefficient	**P-value**	**Coefficient**	**P-value**	**Coefficient**	**P-value**	**Coefficient**	**P-value**
Tirs	-0.038	0.004	0.030	0.017	-0.008	0.504	0.115	0.004
Sex	-0.085	0.000	0.005	0.728	-0.074	0.000	-0.135	0.001
Age	0.013	0.000	-0.001	0.402	0.011	0.000	-0.004	0.170
CRG	0.130	0.000	0.000	0.000	0.000	0.000	-0.000	0.194
Constant	-1.233	0.000	0.073	0.353	-0.634	0.000	0.906	0.000

Table 6.4. Results Logistic Regression Model

Mixed Effects	Functional decline		Physical decline		Cognitive decline		Emotional decline	
	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value
Tirs	-0.197	0.003	0.389	0.017	-0.033	0.580	0.470	0.004
Sex	-0.338	0.000	0.052	0.769	-0.380	0.000	-0.552	0.002
Age	0.062	0.000	-0.009	0.40	0.053	0.000	-0.016	0.171
CRG	0.001	0.002	0.003	0.000	0.001	0.000	-0.001	0.194
R2	0.041		0.010		0.031		0.013	
Chi2	242.57		21.04		221.71		21.29	
Skweness	-0.848		3.175		0.907		-0.083	
Kurtosis	2.017		11.61		2.116		1.154	
AIC (Intercept only)	1.191		0.568		1.196		1.367	
AIC (Full model)	5469.160		1132.059		6583.631		863.773	
BIC (Intercept only)	-33209.318		-13990.160		-40790.523		-3189.680	
BIC (Full model)	-208.843		9.348		-187.262		4.501	

The direction of the results of the Mixed Effects Model and the Maximum Likelihood Model are the same as can be checked in tables 6.3 and 6.4.

Table 6.3 shows the average effect that living without support has for the different declines and table 6.4 shows the raw coefficient, which is easier to interpret than the odd ratio. The values in parenthesis show the p-value.

Living with support affects patients positively in the functional and cognitive declines, though the latter seems not be significant in none of the models. The analysis says that living with support worsens physical and emotional health, though this result may be due to the fact of an existing problem of omitted variables.

Some other interesting results can be seen. Men seem to be healthier at a functional, cognitive and emotional level. Also it seems that age worsens the functional and cognitive health and that CRG almost do not affect health, except that a higher CRG worsens the functional health.

For the Maximum Likelihood model, it was also done a study of different measures of fit for each models studied: χ^2 and R^2. For all health categories, it can be said that the model is significant with a 95% Confidence Interval. Statistic χ^2 for each of the declines is the following one: FD=242.57, PD= 21.04, CD=221.71, ED=21.29. Although the model is significant, the effect explained in every case is not quite high (FD= 4.1%, PD= 1%, CD=3.1%, ED=1.3%). The highest effect that can be explained is for functional decline, for which the model stated represents a 4.1% of the effect. For this reason, the possible omission of variables was also checked. In each case, the Ramsey Reset Test shown that there is omission of variables.

A residual analysis for each of the regressions was done too. In order to check for heteroskedasticity, a skewness and kurtosis analysis run. Reviewing the results from that analysis, it is possible to state that in all cases there is a normal distribution, except for physical decline.

To finish with the revision of the results, it should also be mentioned that the Akaike Criterion and the Bayesian Criteria (were also reviewed to measure the predictive accuracy of the models). For every single model, the results for full model compare to the one for only the intercept were bigger, which indicates that the model proposed in each case is a better-fitting model.

6.4. CONCLUSIONS

Two statistical methods were used to analyze the effects of living without support in four different declines: functional, physical, cognitive and emotional. In all of them, the results were very similar, which gives robustness to the analysis.

Living without support affects patient's positively functional and cognitive declines. The results are similar when using both methods. It can also be seen that age worsens the functional and cognitive health, but as it has been found that there is an omission of variables, so results could be biased. For this reason, it could be stated that this article points the direction of the effect, which in this case is positive for functional and cognitive declines. In order to immprove this situation, other significant variables should be included in the model, but due to the nature of the data, it was not possible. As said before, the data used comes from a database provided by the Catalan health agency, and does not include socio-demographic variables such as wealth and education.

If reviewing the existing literature, it can be observed that there are no many studies on the effect of having support on health. Two studies were found, Kharicha et al (2015) and Bilotta et al (2010), and were focusing on the effects of living alone. Living alone or without support is not the same. Many persons who live alone have effective social support, while many who live with others have poor social support[19-20]. For this reason, living without support is used instead of living alone, because it includes all the alternatives. Since to the best of our knowledge, this is the first study to analyze the effects of living without support. If reviewing the variables used for those studies, it is found that they used as exogenous variables income and educational attainment too. So in order to increase the predictor effect of the model, for future researches, those variables should also be included.

If comparing results with "popular knowledge", they support the acquire idea that having support would benefit functional and cognitive health of the old population. It also shows that age worsens the health.

If comparing the results with the existing literature, they found a positive effect on emotional decline but worse cognitive and functional health[1-2]. It can be observed that their results differ from the ones from this article. This might be caused for three reasons.

First, they are two different phenomena. When studying the effects of living alone on health, it is not being considered the effects of the attendance that the patient receives to develop their day-to-day life activities. That is, some patients could be living alone and having support or not. The same happens for patients not living alone. However, when studying the effects of having support, it is isolated the true effect of the attendance received by patients from others, independently of living alone or not. This variable is more efficient to determine the searched effect.

Second, the studies carried out by the mentioned authors were developed using self-reported health data, while in this contribution the data of the medical tests are objective, since they have been determined by a specialist.

And third, they do not adjust for CRG level, while this article does it. This may cause the results to be biased.

It is worthy to comment how health is affected by CRG. In special, it can be seen that functional health is affected by the degree of CRG, whereas the other health categories are not. For this reason, it should be implemented that for higher levels of CRG, patients should be having support. This should be translated into different political interventions targeting this population, in order to help them with the activities of the daily living.

The main limitation of this study contribution comes from the dataset. Due to the type of dataset used, it has many missings. For this reason results could be biased. In order to avoid so, the authors tried to generate smaller datasets for which the number of missings was smaller, so the biased was smaller too.

Future research should target the effect of living alone when adjusting for specific illnesses, in special the ones that are more common and caused the biggest percentage of exacerbations in old chronic advanced patients. Also future research should be oriented towards studying and proposing different interventions that could help improve the situation of advanced chronic patients living without support.

6.5. REFERENCES

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CHAPTER 7.

CONCLUSIONS, LIMITATIONS, IMPLICATIONS AND FUTURE RESEARCH LINES

7.1. CONCLUSIONS

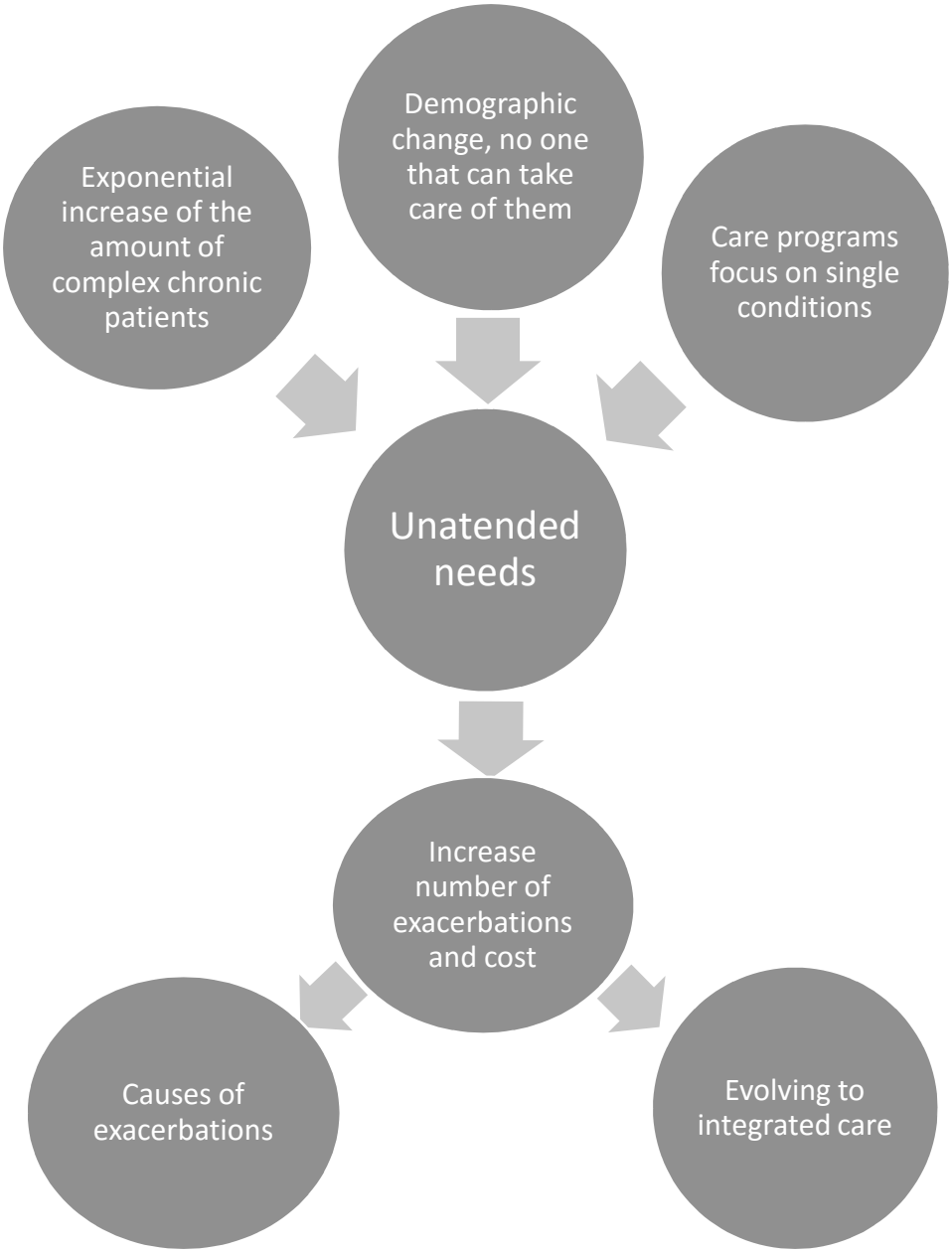
The number of complex chronic patients has been increasing and is going to continue increasing in the following years. Due to the demographic change, and to the empowerment of women who leave their work at home to have a paid job somewhere else, there is no one at home who can take care of them.

Health care programs focus on just single conditions, making it difficult to cover the needs from complex chronic patient, who by definition, have more than one dominant illness at the same time.

Nowadays, the three circumstances are happening at the same time, leading to a problem that has to be solved (figure 7.1). If it is not solved, it is going to mean an increase in the number of exacerbations, and thus an increase in health care cost and a worsening in the health of the complex chronic patients. This study seeks to improve this situation following two paths. The first one focuses on studying the care management model and proposing a possible change towards an integrated method, which would imply the introduction of the role of the Nurse Case Manager (first objective). The second one focuses on studying which factors could causes exacerbations in order to reduce them (second, third and fourth objective).

The first objective of the study consists in creating a model that could determine the probability of a patient of having a Nurse Case Manager. As said before, Nurse Case Managers are in charge of the management of complex chronic patients that are suffering from an exacerbation[1-3]. This model could be used as a way of stopping exacerbations, as an alert method for the health agencies because they can check if everybody who needs a nurse case manager, has it. One of the main advantages of this model, and one of the main objectives for which it was created, is that is has to be a very simple model to replicate. For this reason, the variables used are simple to find, which will allow almost any agency or entity to use it, thus objective one was met.

Figure 7.1. Objective of the study



Source: own elaboration

The second objective consists in identifying the factors that influence a patient to have a Nurse Case Manager.

Factors affecting the probability of having a Nurse Case Manager were divided in 4 categories: complexity (CRG 5, 6 and 7), severity (more than two visits to the emergency unit in the last twelve months), frailty (accumulation of deficits) and the factors affecting the probability of having an exacerbation itself.

Complexity criteria was excluded because all the data was already CRG 5, 6 and 7. The severity criterion was demonstrated to highly affect the probability of having a Nurse Case Manager. About the frailty criteria, the variables number of falls and social risk (TIRS test and Age Alone test) also were proven to be the ones that affected more the probability of having a Nurse Case Manager. Finally, the factors causing exacerbation itself were divided in two: general factors affecting all illnesses and factors related with specific illnesses. The general factors affecting all illnesses that give a higher probability to the patient of having a Nurse Case Manager are there adherence to the treatment (Morinsky Green Test) and the number of drugs.

By knowing the factors that affect a patient to be attended by a Nurse Case Manager allows identifying opportunities for intervention. It is possible to create new interventions targeting the variables that have a higher effect on the probability of chronic patients of having an exacerbation and thus increasing their health and reducing cost for the health care agency due to the reduction in exacerbations. These were the first and second objective, and were included in the first contribution.

Following the results from this second objective on some of the main factors affecting the probability of having a Nurse Case Manager, the second and third contributions were settled. As said before, two of the factors having more relevance on the probability of having a Nurse Case Manager were the low adherence rate and being under social risk. It can be stated from the second objective, that the average number of drugs taken by the patients from the sample is more than nine, which clearly exceeds the limit considered. If it is added that sample's age is quite high (so they may have some kind of cognitive impairment) and also that it is quite probable that they have a lack of support (social risk), a decrease in the level of adherence seems quite probable. For this reason, each factor was studied in deep building the second and third contributions.

In the second contribution a new intervention to increase adherence is proposed. The level of adherence to treatment is really low, specially among chronic patients[4-5]. Increasing the level not only would increase patient's health, but also

it would decrease cost due to the decrease in exacerbations. The proposed intervention consist in targeting non-intentional lapses when taking the medication by revising, in each visit to primary care, the process of taking the medication. This intervention would mean a big improvement for patients and health agencies, taking into account other interventions targeting non-adherence, and using similar efficiency rates, the result would be very encouraging. Even taking lower rate of efficiency, the result would imply a big improvement.
The main benefit of this intervention is the fact that the extra cost added is small. Whereas most of the interventions targeting non-adherence imply a high amount of human resource factor, or high cost for the patient (like transportation and time costs)[6-7], this one does not.
Also, and as a consequence of the latest benefit, the proposed intervention pretends to be easy and feasible to implement. Because of the small effort from physicians and patients required to implement it, it would be much more feasible to implement than other proposed and implemented interventions.
So as a conclusion, reducing the levels of non-adherence among old chronic advanced patients would mean a big benefit for the society because of the health improvements, but also because the pool of patients targeted is so big that in terms of potential savings society would be saving a lot of money that can be invested somewhere else.

The third and last contribution analyses the effect of living without support on chronic patients. Results support the idea that living with support benefits functional and cognitive health. It also partially contradicts the existing literature. The existing literature shows a negative effect on functional and cognitive decline[8-9]. Accepting the results from the third contribution would mean that day-to-day activities are harder to follow for advanced chronic patients that live without support. Also it would mean that it is hard for them to think and remember. This contribution helps to know better the health behavior of the elder patients with advanced chronic illnesses. By knowing better their health behavior, it is possible to build more precise interventions to help them improve their health, and make their daily life better and easier.

As final conclusion, complex chronic patients are the biggest consumer group of health care resources[10]. Also, they have been growing in number and they are expected to grow much more in the near future[11-13]. For this reason, any policy targeting these same individuals will imply a future benefit, even if the individual benefit is very small. So it is worth the effort to study and develop policies

related with chronic patients, first of all to improve their health, but also the decrease in the future cost that are expected to be high.

7.2. IMPLICATIONS

This section is divided in two, depending if the implications are regarding to management and professionals or patients.

7.2.1. Implications for Management & Health Professionals

Advanced chronic patients received poorly coordinated care, and the reason is the care model. The Spanish care model is oriented towards the treatment of a single illness. The problem is that nowadays, the biggest consumers of the health resources are old patients that tend to suffer from more than one chronic illness.

For this reason, advanced chronic patients receive unplanned care, because there is not a coordinator or a manager that, from a global perspective, reviews their needs and organize their care.

The Catalan and Spanish healthcare system should be oriented towards an integrated care model, that best fits and faster answers the new and increasing needs from the market.

In order to try to solve this problem, the role of the nurse case manager has been identified as a central measure to improve the care of these patients[14]. By identifying complex chronic patients, it is easier to plan resource consumption and structure them in a more efficient way, thus arriving to meet the needs of society in a more efficiently.

The care model has to evolve, to change the way services have been provided, creating an environment of cooperation between health care areas and social services and between organizations and professionals[15], because case management provides more efficient care[16-18].

The decrease in number of exacerbations of the chronic patients, could lead to a decrease in the health expenditure, which would mean two different things. On one side, less expenditure means more money to invest in the health systems,

which could mean money to invest in innovative technologies, new drugs or more physicians per patient for example.

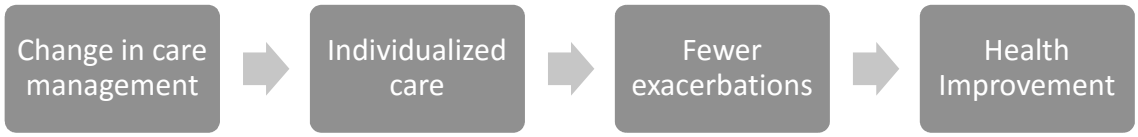
On the other side, it is true that the time devoted per patient would be longer, but at the same time if there are fewer exacerbations, this implies fewer visits to the emergency departments, hospitals and physicians. Therefore, it is expected that the second effect will overcome the first one, reducing the cues to access to some health test and to the physician visits, so patients will have to wait less. This would mean a change in the staff structure, meaning more primary care physicians due to the longer visits, but at the same time less physicians in the hospitals and in the emergency departments due to the decrease in exacerbations.

Regarding the effect of living without support on advanced old chronic patients, knowing the direction of the effect on them implies that health interventions could be more efficient. If taking into account the result from the last contribution, this would imply that health and social interventions should be oriented to improve the activities of the daily living of these patients, helping them with the regular activities related with the house and personal hygiene.

7.2.2. Implications for Patients

Due to the change in the management care system, chronic care patients should receive a more individualized care. This should translate into an increase of the health results, meaning fewer exacerbations, so a better health (figure 7.2 shows the implications).

Figure 7.2. Implications for patients



Source: Own elaboration

As said before, fewer exacerbations would mean healthier people, less visits to emergency rooms, fewer cues to access health tests, etc. At the same time the healthcare system would be saving money, so more money to invest in order

health interventions or research, meaning more future benefits in terms of health for those patients.

Regarding the effect of knowing the direction of how advanced old chronic patients are affected by the fact of living without support, it could mean generating more efficient policies towards the improvement of this issue. For example if it is observed a negative relation between living alone and functional health, they could be receiving help regarding daily activities like preparing the meals, cleaning the house, own hygiene, etc, so it would make their lives easier at the same time that improves their health and the contributors money is spent in a more efficient way.

7.3. LIMITATIONS

Below there are some of the main limitations regarding the contributions.

First of all, it should be mentioned that due to the use of clinical records the results may be a little biased. Clinical records are sometimes incomplete, what could lead to bias the results. This has been tried to be avoid with the different methodologies applied, by grouping the variables, or by using the fact of having records as an indicator of having the illness and not its level.
Also, due to the fact that these are all clinical records shared from Institute Català de la Salut, some data regarding the number of visits to the hospital or socio-demographic variables could not be obtained. Having these variables would have helped the authors make the thesis more accurate, but it was not possible to have it as normally socio-demographic data is obtained from surveys, which are subjective. In this case, data, as said, was obtained from the health agency, so they do not used to have data on the level of education or wealth of the patients. On the other side, data used is much more objective and health can be observed from different angles as for example physical or emotional health.

Focusing on the second contribution, some pathologies due to its adherence level or its specifications, and as a consequence of the increase in the pharmacy rate, could have less savings or even costs. Every pathology has a different average level of adherence and the costs associated to each of them are different and thus, the calculated savings could decrease if applied to a single pathology. In order to

compensate for this, the three most common pathologies and also the ones that are most frequently combinations of multimorbidity, Diabetes, Chronic Obstructive Pulmonary Diseases and Chronic Heart Failure, have been chosen to calculate the final savings. About this second article too, although this intervention could be applied to almost every developed country because they share the same population pyramid, it cannot be applied to developing countries, because its population pyramid is different, thus the percentage of advanced chronic patient is different and results would vary.

7.4. FUTURE RESEARCH LINES

This research topic has a big potential due to the number of people targeted and also due to the big cost they cause[10-13]. For this reason, any kind of research on this topic is interesting, because the potential benefits from it are huge.

In the field of complex chronic patients, and specially targeting exacerbations, there is still a lot to study and to improve. Future research could consist in validating the model created to identify potential patients from Nurse Case Managers. The next step could be to study which and why patients have been left out from the model and should be included and the opposite, which patients that have been included should not be there. From this research, it could be obtained a more precise model and a better understanding of what causes exacerbations on those patients.
Also on the same line, future research could just focus on one illness and determine what causes exacerbations, especially for illnesses that are very common and also for illnesses that have a high rate of morbidity. A good starting point would be studying the variable "severity" from patients with Chronic Obstructive Pulmonary Disease, because it has been demonstrated to highly affect the probability of having a Nurse Case Manager.

Also it would be beneficial to study the variables affecting functional status and how this one is related with living without support. To study more in deep the relation between living alone and living without support and find if the difference in results are due to the data or external causes. To study the relation among the different health declines. In addition, research should be directed towards the development and implementation of health interventions oriented to improve the

functional status of the old chronic population and to see if and how functional status is related with the rest of the health categories.

On the same direction, it could be studied other variables affecting exacerbations. For example the variable nutrition. It has been demonstrated that nutrition affects the probability of having exacerbations[19]. For this reason, the relation between nutrition and health could be a future research topic. Also, studying the relation between living without support and the level of nutrition would be a good starting point, because it have been proven that ones an old person is left alone or without support, the levels of nutrition fall down. So by studying it, and knowing more about how is the current nutritional situation among old chronic patients, several interventions could be develop to improve their health.

7.5. REFERENCES

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APPENDIXES

APPENDIX 1. ABBREVIATIONS

BPH: Benign Prostatic Hyperplasia

CBA: Cost-Benefit Analysis

CC: Continuity of Care

CCP: Complex Chronic Patient

CHF: Congestive Health Failure

CI: Confidence Interval

COPD: Chronic Obstructive Pulmonary Disease

CRG: Clinical Risks Group

CVD: Chronic Cardiovascular Diseases

CRD: Chronic Respiratory Diseases

GP: General practitioner

IDESCAT: Institut D'Estadíctica de Catalunya

INE: Instituto Nacional de Estadística

IT: Item

JCR: Journal of Citation Reports

N: Number of individual in the sample

NCDs: Non- Communicable Diseases

NCM: Nurse Case Manager

NHS: National Health System

OECD: Organitsation for Economic Co-operation and Development

PSM: Propensity Score Martching

APPENDIX 2. GLOSSARY OF MEDICAL TEST

- **Barthel Test** (Katz, Downs, Cash, & Grotz, 1970)

The Barthel is a 10-item ordinal scale that measures functional independence in the domains of personal care and mobility (evaluation of the basic activities of the daily living). Specifically, it measures self-care, self-management, transfers and locomotion . Cronbach's reliability's was between 0.84 y 0.97 depending on the study.

Score:

< 20: Total dependency
From 20 to 35: Severe dependency
From 40 to 55: Moderate dependency
≥ 60: Low dependency
100: autonomous

References:

Cid-Ruzafa J, Damián-Moreno. Valoración de la discapacidad física: el indice de Barthel. J. *Rev. Esp. Salud Publica* . 1997 Mar; 71(2): 127-137.

- **Lawton and Brody Test** (Lawton & Brody, 1969)

The Instrumental Activities of Daily Living (IADL) Scale is used to assess independent living skills of an individual and measures functional ability as well as declines and improvements over time. The test attempts to assess everyday functional competence in the elderly. This is done by evaluating a more complex set of behaviors like telephoning, shopping, food preparation, housekeeping, laundering, use of transportation, use of medicine, and financial behavior.
A summary score ranges from 0 (low function, dependent) to 8 (high function, independent) for women, and 0 through 5 for men. The higher the score, the greater the person's abilities. Women are scored on all 8 areas of function, but, for men, the areas of food preparation, housekeeping, laundering are excluded. Clients are scored according to their highest level of functioning in that category.
The Cronbach's reliability's was 0.90, 95% Confidence Interval (CI) 0.88-0.97

References:

Martín Lesende M, Quintana Cantero S, Urzay Atucha V, et al. Reliability of the VIDA questionnaire for assessing instrumental activities of daily living (iADL) in the elderly. *Atención Primaria* 2012. Vol. *44*. Num. *06*.

- **Yesavage Test (Geriatric Depression Scale)** (Yesavage et al., 1983).

Scale of geriatric depression, it is use to evaluate if an old patient has depression. Version 5 questions used. Cronbach's reliability's was 0.82 with an standard deviation of 0.082.

Score:

From 0 to 1: no depression
>1: depression

References:

Ortega Orcos R, Salinero Fort M.A., Kazemzadeh Khajoui A, Vidal Aparicio S, De Dios del Valle. Validation of 5 and 15 items Spanish version of the geriatric depression scale in elderly subjects in Primary Health Care setting. *R. Rev Clin Esp*.2007; 207:559-62 - Vol. 207 Num.11

Rinaldi P,Mecocci P,Benedetti Ph.D,Ercolani S,Bregnocchi M,Menculini G,et al. Development and testing of a five-item version of the Geriatric Depression Scale. *Am Geriatr Soc*.1999;47:873-8.

De Dios R,Hernández AM,Rexach LI,Cruz AJ. Validación de una versión de cinco ítems de la Escala de Depresión Geriátrica de Yesavage en población española. *Rev Esp Geriatr Gerontol*. 2001. 36, pp. 276-80

Martínez J, Onís MC, Dueñas R, Aguado C, Albert C, Luque R. Versión española del cuestionario de Yesavage abreviado (GDS) para el cribado de depresión en mayores de 65 años. Adaptación y validación. *Medifam*,2002. 12, pp. 620-30

- **Indicadors de Risc Social (TIRS) "Social Risk Indicators"** (Catalan Health System)

The following questionnaire is done to patients to evaluate the possibility that this patient is under a situation of social risk.

Questionnaire

1. **Living alone or with family with little capacity to provide support:** an individual who lives on their own or with people who have some level of disability (for reasons of age, illness or impairment)	YES	NO
2. **Problematic family relationships:** where this refers to any type of family conflict (from disagreements to broken relationships)	YES	NO
3. **Family are not readily able to take on responsibility for caring for the patient:** where this refers to work commitments, other dependent relatives, exhaustion and other personal limitations.	YES	NO
4. **Unsatisfactory or poor personal hygiene:** as stated	YES	NO
5. **The accommodation does not meet patient needs:** where this refers to architectural barriers, lack of space, damp, lack of basic utilities (running water, electricity, etc.)	YES	NO
6. **An apparent lack of financial resources:** this refers to statements by the family and also the impression of professionals (by observation)	YES	NO

Score: 'Yes' response to 1 or more item=Social risk.

References:

El treball social sanitari en l'atenció del pacient crònic. Institut Català de la Salut. 2013

- **"Age-alone" Test** (Catalan Health System)

It is a measure used by the Catalan Health System to evaluate is a patient is in risk of isolation. It is 1 if the person is older than 84 years old and lives alone and 0 otherwise.

References:

El treball social sanitari en l'atenció del pacient crònic. Institut Català de la Salut. 2013

- **Pfeiffer Test** (Peiffer et al.; 1975)

The version used is the Spanish Version of Short Portable Mental Status Questionnaire (SPMSQ) from Peiffer. Screening tool for detecting cognitive impairment in patients suspected it may exist.

From 0 to 2 mistakes: normal
From 3 to 4 mistakes: low cognitive decline
From 5 to 7 mistakes: moderate cognitive decline
From 8 to 10 mistakes: important cognitive decline

Cronbach's reliability's was 0.92 with an standard deviation of 0.082.

References:

Martínez de la Iglesia J.,Dueñas Herrero R., Onís Vilches M.C. Cross-cultural adaptation and validation of Pfeiffer's test (Short Portable Mental Status Questionnaire [SPMSQ]) to screen cognitive impairment in general population aged 65 or older. *Medicina Clínica*. Junio 2001. Vol. *117*. Núm. *04*. 30 .

- **"Get up and go" Test** (Mathias et al, 1986)

It assesses if the patient has gait disturbance. The Cronbach's reliability's was 0.91, 95% Confidence Interval (CI) 0.86–.094.
Score:

<10 seconds: normal
From 10 to 19 seconds: slightly altered
From 20 to 29 seconds: moderately altered

>30 seconds: severely altered

References:

Nordin E , Rosendahl E., and Lundin-Olsson L. Timed “Up & Go” Test: Reliability in Older People Dependent in Activities of Daily Living— Focus on Cognitive State. *Physical Therapy* 2006. 86, no. 5 : 646-655.

- **Zarit Test (**Zarit, Rever y Bach-Peterson, 1980**)**

Caregivers are asked to indicate the extent of burden experienced while providing care to a loved one.

- Burden is defined as the extent to which a caregiver perceives emotional, physical health, social life, and financial consequences that impairs one’s ability to provide care
- Responses range from "not at all" to "extremely
- Total score are obtained by summing all items endorsed

Score:

≤46: no overload
From 47 to 55: Slightly overload
≥56: extremely overload

The version used is the original one, having a Cronbach's reliability's of 0.71-0.85 internationaly validated.

References:

Breinbauer K, Vásquez V, Mayanz S, Guerra C, & Millán K,. Validación en Chile de la Escala de Sobrecarga del Cuidador de Zarit en sus versiones original y abreviada. *Revista médica de Chile*, 2009.137*(*5), 657-665.

- **Morinsky Green Test** (Morinsky DE, Green LW, Levine DM, 1986)

The Morisky Medication Adherence 4 items Scale (MMAS-4) is a generic self-reported, medication-taking behavior scale, used for a wide variety of medical conditions.
Score:

<4 points: noncompliant suspect
= 4 points: compliant

The Cronbach's reliability's of this 4 item test is of 0.82.

References:

Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986;24:67–74.

Culig J. and Leppée M.: Scales for Measuring Adherence, Coll. *Antropol.* 2014. 38 1: 55–62

- **Nutrition Screening Test (Auto-nutrition Test)**

It is an auto-nutrition test done by the patient.
Score:

<2 points: no risk
From 3 to 5 points: moderate risk
>6 points: high risk

Scale provided by CatSalut during one of the several interviews done.

APPENDIX 3. AGREEMENT BETWEEN UNIVERSITAT DE BARCELONAAND IDIAP

CONVENI MARC ENTRE LA UNIVERSITAT DE BARCELONA I L'IDIAP Jordi Gol

REUNITS

D'una part el Senyor Didac Ramirez i Sarrió, Rector magnífic de la Universitat de Barcelona, en virtut del nomenament per Decret 160/2012, d'11 de desembre (DOGC núm. 6272, de 12 de desembre), com a representant legal d'aquesta institució en virtut de les competències que estan previstes en l'Estatut de la Universitat de Barcelona aprovat per Decret 246/2003, de 8 d'octubre (DOGC núm. 3993, de 22 d'octubre).

I de l'altra, l'Institut d'Investigació en Atenció Primària. Fundació Jordi Gol (en endavant IDIAP), amb domicili social a l'avinguda Gran Via de les Corts Catalanes, 587, 08007 Barcelona, CIF: G-60954104, representat per la senyora Concepció Violan i Fors, amb DNI: 46.326.530-E, en nom i representació de l'esmentada Fundació en virtut del nomenament del Patronat de 14 d'abril de 2004.

Ambdues parts, en l'exercici de les funcions que els hi estan legalment atribuïdes, reconeixent-se recíprocament la capacitat legal necessària,

MANIFESTEN

Que la Universitat de Barcelona, com a corporació de dret públic, té atribuïda, entre d'altres, la funció de col·laborar amb les administracions públiques, institucions i entitats privades amb la finalitat d'elaborar, participar i desenvolupar plans i accions que contribueixin al progrés de la ciència, de la difusió de la cultura i el desenvolupament de la societat

Que l'IDIAP és una fundació sense ànim de lucre, creada amb la finalitat d'impulsar, promoure i dur a terme tasques d'investigació, docència, formació i difusió dels coneixements generats per la recerca a l'atenció primària de salut a Catalunya. Que l'IDIAP posa a l'abast dels investigador/es els mitjans de què disposa, donant-los-hi el suport logístic i metodològic que precisen per a l'òptim desenvolupament dels seus projectes com es preveu a l'article 5 dels seus estatuts.

Que ambdues institucions estan interessades en col·laborar en estudiar els procediments de gestió i els costos dels pacients crònics complexos

I, és per tot això que ambdues parts, conclouen en signar aquest acord marc que es basarà en les següents

CLÀUSULES

Primera
L'objecte d'aquest conveni és l'establiment d'una col·laboració entre la Universitat de Barcelona, mitjançant el Departament d'Economia i Organització d'Empreses, i l'IDIAP Jordi Gol en relació al programa de pacients crònics que es porta a terme a diverses àrees de la Unitat de Suport a la Recerca (USR) Metropolitana Nord.

Segona
El desenvolupament d'aquesta col·laboració inicial haurà d'establir-se a través d'una programació anual i específica que s'elaborarà de comú acord entre ambdues parts. Aquesta programació anual serà sotmesa a l'aprovació de les autoritats competents d'acord amb els

procediments establerts per cadascuna de les parts i serà objecte, si s'escau, dels convenis específics oportuns.

Tercera
El marc de col·laboració s'estendrà a les activitats següents:

- Anàlisi de les dades relatives al programa de pacients crònics que es porta a terme a diverses àrees de la USR Metropolitana Nord. Presentació dels resultats de l'anàlisi.
- Publicació dels resultats del l'anàlisi.

Quarta
Els coordinador encarregat de supervisar el desenvolupament d'aquest conveni marc, seran per part de la UB, la professora Mercè Bernardo del Departament d'Economia i Organització d'Empreses. Per part de l'IDIAP Jordi Gol serà Pere Torán Monserrat, coordinador de la Unitat de Suport a la Recerca Metropolitana Nord.

Conjuntament, els coordinadors designats per les parts elaboraran, proposaran i activaran els convenis específics que calguin d'acord amb el programa d'activitats que es proposin impulsar.

Cinquena

Qualsevol dels projectes que sorgeixin d'aquesta col·laboració hauran de ser presentats al comitè científic i al comitè d'investigació clínica de l'IDIAPJGol per la seva aprovació.

Sisena

El desenvolupament de les activitats serà objecte de tractament confidencial per part de la UB.
Els aspectes en que es basa la relació, com ara la temporalitat, les contraprestacions econòmiques generals, la propietat industrial i/o intel·lectual i la gestió d'aquesta, la visualització i la comptabilització dels resultats, la gestió dels projectes, les contraprestacions econòmiques per aspectes específics (overheads, afiliació i autoria utilització dels serveis entre ambdues institucions). Seran establerts en un conveni específic.

Els investigadors del projecte hauran de signar la declaració de bones pràctiques que s'adjunta en l'annex 1.

Setena

La signatura del present conveni no implica cap compromís econòmic per cap de les dues parts.

Tanmateix, les parts podran sol·licitar subvencions i projectes de recerca a altres organismes nacionals, regionals i internacionals que donin cobertura a les activitats programades.

Novena

Les qüestions litigioses que puguin sorgir en la interpretació i compliment del conveni seran resoltes per acord d'ambdues parts i, si no fos possible aquest acord, les parts es comprometen a sotmetre's a mediació abans d'iniciar qualsevol reclamació davant de la jurisdicció que pertoqui.

Desena

Aquest conveni iniciarà la seva vigència a partir de la data de la seva signatura i tindrà una durada de tres anys. Abans de la seva finalització, les parts podran prorrogar el present conveni,

per escrit i de forma expressa, per períodes de igual durada. No obstant, qualsevol de les parts pot comunicar amb un avís previ de sis mesos i per escrit la seva voluntat de rescindir l'acord.

I en prova de conformitat, les parts signen aquest conveni per duplicat en el lloc i la data que figuren a continuació.

Barcelona, 16 de febrer de 2015

Per la UNIVERSITAT DE BARCELONA

Didac Ramirez Sarrió
Rector

Per IDIAP Jordi Gol

Concepció Violán Fors
Gerent

UNIVERSITAT DE BARCELONA

APPENDIX 4. ANNEX OF THE PREVIOUS AGREEMENT

Declaració de bones pràctiques en l'ús d'informació

Barcelona, a 12 de Març de 2015.

Nom i cognoms: Gemma Seda Gombau

NIF: 43562941K

Centre de treball i Institució: Universitat de Barcelona

Correu electrònic: gemma.seda@ub.edu

Que actua com Investigador Principal (IP) ó investigador col·laborador del projecte: Procediments de gestió i costos dels pacients crònics complexos

CLÀUSULES

PRIMERA.- OBJECTE

1.1. L'investigador principal ha sol·licitat la col·laboració al IDIAP i l'ICS per el desenvolupament del projecte de recerca mencionat prèviament.

1.2. Si en relació a aquest projecte de recerca existís un acord de col·laboració amb organització externa, s'haurien de respectar els acords marcats per aquest acord.

SEGON.- TITULARITATI MANEIG DE LES DADES

2.1. El maneig de les dades es realitzarà a la unitat de la Metropolitana Nord de l'IDIAP Jordi Gol. El seu objectiu es garantir que la qualitat de les dades que

s'obtinguin sigui la millor possible a partir de es dades de la història clínica d'atenció primària i de les altres fonts de dades necessàries.

2.2. Los dades són propietat del'IDIAP Jordi Gol el qual les cedirà al'equip investigador per a la seva utilització exclusivament pel projecte mencionat en aquest acord per al seu posterior anàlisis.

2.3. Si fos necessàriala seva utilització per un fi diferent a l'exposat en el present acord, s'haurà de demanar autorització prèvia al propietari de les dades (IDIAP Jordi Gol), exposant clarament els motius que justifiquen aquesta petició.

TERCER.- MANTENIMENT DE LA INFORMACIÓ DEL GIR

3.1. L'investigador principal és responsable de mantenir la seva informació personal actualitzada al GIR.

3.2. Tanmateix, haurà d'actualitzar aquella informació relativa al projecte que sigui de la seva competència, com per exemple, el compliment de les memòries o informes a realitzar i l'apartat relatiu al disseny del projecte.

QUART.- TITULARITATDELS DRETS SOBRE ELS RESULTATATS DE LA INVESTIGACIÓ I PUBLICACIONS

4.1. S'haurà d'informar al'IDIAP Jordi Gol de qualsevol difusió de resultats, ja siguin articles científics, comunicacions a congressos, etc. enviant una copia en PDF del mateix o entrant directament la informació i el documento annex a l'aplicatiu de gestió del'IDIAP Jordi Gol, GIR, al qual s'hi accedeix a través de la pàgina web de l'IDIAP (www.idiapjgol.org).

Aquests, només seran utilitzats per l'IDIAP Jordi Gol per a difusió interna, i només s'utilitzarà el material no protegit dels mateixos (autors, títol, lloc de difusió i abstract) per a comunicacions externes (presentacions, pàgina web, etc.).

4.2. En qualsevol mitjà de difusió dels resultats obtinguts a l'apartat de *material y mètodes*s'haurà d'especificar la font d'obtenció de les dades.

4.3. A l'apartat*agraïments* també haurà de constar l'ICS i l'IDIAP. En el cas que s'haguessin utilitzat altres fonts de dades (CMBD, facturació de farmàcia, mortalitat), també haurà d'aparèixer en aquesta secció l'entitat propietària d'aquestes bases de dades.

4.4. En cap cas s'utilitzarà la imatge o nom del' ICS o IDIAP Jordi Gol per a la difusió de resultatssense el consentiment d'aquestes institucions.

CINQUÈ.- CANVIS I MODIFICACIONS

5.1. Les dades es donaran d'acord al protocol operatiu acordat. Qualsevol modificació al respecte requerirà d'una nova aprovació del Comitè Científic seguint el formulari establert per aquests casos.

5.2. No obstant a allò establert en el punt anterior, es podran fer modificacions menors en un termini de 3 mesos.

SISÈ.- CONFIDENCIALITAT

6.1. L'IP o l'equip col·laborador del projecte, s'abstindran de cedir o prestar a tercers les dades resultants del'estudi.

6.2. Qualsevol informació serà utilitzada exclusivament per a la realització de la investigació indicada en el present acord.

Gemma Seda

_____

Barcelona, 12/03/2015

En compliment de la Llei Orgànica 15/1999 de 14 de desembre, de Protecció de Dades de Caràcter Personal, s'informa a la persona interessada que les dades de caràcter personal que facilita, inclosa l'adreça electrònica i que resulten necessàries per a la gestió administrativa, així com a l'execució i el desenvolupament de tota activitat institucional pròpia de l'IDIAP Jordi Gol, seran incorporades al fitxer automatitzat GIR, la titularitat i responsabilitat del qual és ostentada per l'IDIAP.

La persona interessada, n'autoritza expressament la utilització a efectes de comunicacions, incloent expressament les que es puguin realitzar entre l'IDIAP i l'ICS sempre amb finalitats relacionades amb l'activitat institucional que s'hi desenvolupa.
La persona interessada es **compromet a**: Respectar i complir les normes ètiques, així com vetllar per la confidencialitat de les dades a les que tingui accés. I a respectar l'autoria i propietat intel·lectual de les idees i projectes als que tingui accés.

La persona interessada podrà exercir els drets d'accés, rectificació, cancel·lació i oposició sobre les seves dades a l'adreça electrònica gir@idiapjgol.org.

APPENDIX 5. POSTER CONGRESS: ATENCION SANITARIA AL PACIENTE CRONICO

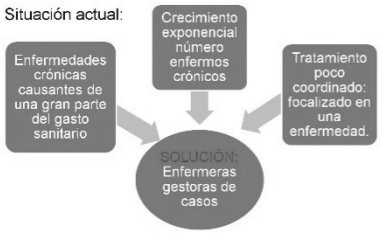
PROPUESTA METODOLÓGICA PARA UN MODELO DE IDENTIFICACIÓN DE PACIENTES DE LAS ENFERMERAS GESTORAS DE CASOS.

G. Seda Gombau [2], R. Hervás Pérez [1], M. Figuerola Batista [1], M. Isnard Blanchar [1], M.D. Reina Rodríguez [1], J.A. De La Fuente Cadenas [1]

[1]SAP Barcelonès Nord i Maresme (Institut Català de la Salut).
[2]Universitat de Barcelona. Universidad de Barcelona. Barcelona

Introducción:

Situación actual:



Objetivos:

1. Identificar los factores más importantes que incrementan la posibilidad de tener una enfermera gestora de casos.
2. Crear un modelo para la identificación de pacientes de la enfermera gestora de casos. Debe ser simple para poderse utilizar desde las diferentes agencias.

Material y métodos:

Material:
Pacientes mayores de 64 años y con CRG 5, 6 y 7.

Muestra dividida en dos:

- Construcción del modelo: Santa Coloma, Sant Adrià, El Masnou, Premià, Vilassar, Mataró, Arenys y Llavaneres.
- Validación modelo: Montcada, Cerdanyola, Badia, Ripollet, Sabadell, Sant Quirze, Polinyà, Sentmenat, Castellar y Terrassa.

Metodología:

1. Búsqueda en la literatura de variables.
2. Validación de la significación de las variables para su inclusión en el modelo.
3. Propensity Score Matching con efectos aleatorios.
4. Validación de la robustez del modelo comparando si la probabilidad esperada es igual a la real.

Resultados:

Significación de la variables en relación con la variable gestora de casos:

Tabla 1. Significación variables paciente crónico		
Variable		% Variación en la probabilidad de tener EGC
Complejidad		No incluida
Severidad		162.07
Fragilidad	Test Barthel	1.07
	Test Lawton	23.52
	TGetUpAndGo	1.86
	Número caídas	135.72
	Test Pfeiffer	8.14
	Test Yesavage	37.83
	Test TIRS	69.07
	TAgeAlone	70.13

Tabla 2. Significación variables descompensación		
Variable		% Variación en la probabilidad de tener EGC
Variables comunes en todas las enfermedades		
Infecciones Urinarias		No significativa
Test Morinsky Green		105.23
Test Nutrición		26.33
Polimedicación		107.61
Antibióticos		No significativa
Obesidad		-30.63
Alcohol		-55.69
Tabaco		-0.05
Variables específicas para enfermedades		
Enfermedades Cardiovasculares Crónicas	Severidad	No significativa
	Fracción eyección	No significativa
	Disnea	No significativa
Enfermedades respiratorias crónicas	Severidad	700.10
	Inhaladores	No significativa
Diabetes	Severidad	No significativa

Modelo:

$$\eta_i = -2.7558 + 0.9663 * \text{severidad} - 0.5355 * \text{fragilidad} + 1.1399 * \text{descom.comunas} + 0.8353 * \text{descom.ECC} - 0.1469 * \text{descom.ERC}$$

$$\text{Prob}_i(\text{NCM}=1) = \frac{e^{\eta_i}}{(1+e^{\eta_i})}$$