

**DOCTORAL THESIS**

**Gender differences in the  
association between disability  
and mortality in the elderly**

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# **Gender differences in the association between disability and mortality in the elderly**

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in order to obtain the title of doctor by  
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*To Ricard whose unconditional support and motivation was essential in making a dream a reality. He gave me the strength to overcome all the external difficulties that arose along the way.*



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## **PREFACE**

This thesis is presented as a set of original research articles published in scientific journals, according to the current regulations on doctoral theses at the Department of Experimental and Health Sciences of the Universitat Pompeu Fabra approved in June 2001.

The thesis is mainly aimed at assessing whether or not there are gender differences in the relationship between disability and mortality. In doing so the methodological aspects of the survival analysis in ageing research have turned into a key role. Therefore, it has been considered more appropriate to classify the research articles as ‘thesis papers’ or ‘support papers’. The first ones are the core papers focussing on the association between mortality and disability by gender in which the leading author is the doctoral candidate; the latter ones correspond to those research papers whose findings give an answer to some relevant issues, that emerged at some stage in the development of this work and mainly contributed to the elaboration of the second thesis paper. For that reason, the thesis is mostly focused on the two core papers.

The thesis is structured in eight chapters. Chapter 1 provides an introduction to two of the three key concepts in the development of this thesis: population ageing and disability. Providing the context which the scientific question relies on, and covering significant aspects of disability. Chapters 2 and 3 state the rationale and the objectives of the research, respectively. Chapter 4 presents the statistical methodology used in the thesis with special emphasis to the survival analysis approach using counting processes, the third key concept, when dealing with right-censored, left-truncated data, and time-dependent covariates. In

chapter 5, the study sample is described by means of baseline and follow-up characteristics with the purpose of giving the necessary background to the reader to be able to set findings of the thesis. A summary of the results derived from the validity analysis of the disability measure is also provided in this chapter. Furthermore, it includes the thesis and support papers together with a brief description of the main results of the thesis papers. In chapter 6, the relevant findings of the research are presented and discussed in light of the current knowledge. In chapter 7, the conclusions of this research are listed. Bibliographic notes and comments are given as footnotes to facilitate the reading, nevertheless all references are listed alphabetically in chapter 8. The principal concepts of the counting process, an approach that has substantial impact on the survival analysis methodology, are presented in the Appendix.

It is necessary to note that the time elapsed from the first to the last thesis paper is quite long. This was mainly due to the existing rules, which do not allow enrolling in a doctoral programme those students with a Bachelor degree. Unfortunately, it was impossible to get a higher degree in Statistics at that time because it didn't exist; but the new university degree emerged at the Universitat Politècnica de Catalunya in 1999-2000. Therefore, the real research period, that began in 1994, was longer than the ones experienced by other doctoral candidates, as a result I was able to be involved in other projects besides ageing research during this period and cover other interesting topics. I also had the opportunity to be a guest researcher at the University of Copenhagen, where I learnt about counting processes, and to do MSc in Applied Statistics at Sheffield Hallam University. In the end, it has been a long and enjoyable journey that has allowed me to meet excellent people at the Institut Municipal d'Investigació Mèdica (IMIM), and has been an unforgettable period of my life.

### **Funding and support**

The first and second waves of the cohort were funded by grants from the Spanish Fondo de Investigación Sanitaria (FIS, Expte.:89/0450 and 91/0629).

The graduand as doctor was supported by a grant from Institut Municipal d'Investigació Mèdica and from Instituto de Salud Carlos III (Expte.:97/4364).

Mortality data of the cohort were provided by the Regional Mortality Register of the Generalitat de Catalunya.

Mortality rates of Barcelona population stratified by gender and age were provided by the Institut Municipal de la Salut de Barcelona.

### **Presentations**

Part of this thesis was presented at 5th Spanish Conference of Biometry (Valencia 1995), XIV Meeting of the Spanish Society of Epidemiology (Zaragoza 1996), and the 52nd Annual Scientific Meeting of the Gerontological Society of America (San Francisco 1999).

### **Prizes**

Part of this work was awarded with the following prizes: a) to the best student oral presentation in the 5th Spanish Conference of Biometry (Valencia 1995), b) to the best 10 communications in the Meeting of the Spanish Society of Epidemiology (Zaragoza 1996), and c) to best paper published on the gerontology field in 1999, Prize 'Agrupación Mutua'.



## **ACKNOWLEDGEMENTS**

I am very grateful to all the people who contributed to the performance of this thesis. It is a long list and at the top of it there are those anonymous elderly individuals who were so kind to participate in the project, being so patient to answer such a long questionnaire in the re-assessment and perform the associated physical examination. I would like to thank Dr. Jordi Alonso, the director of this thesis, who initiated this project and other colleagues who also worked on it: other fellowships, interviewers, computing, and unit assistants, among others. Also, I want to express my gratitude to Dra. Lupe Gómez for reviewing the statistical sections and providing many worthy comments; and Dr. Jordi Sunyer who kindly accepted to be my tutor. Finally, I am indebted to the Institut Municipal d'Investigació Mèdica, in particular to the Health Services Research Unit and those institutions that gave financial support to both the project and myself. While this is undoubtedly not a complete list, unfortunately, it was not feasible to mention all of them.



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## **SUMMARY**

### **BACKGROUND**

It is estimated that the spectacular growth of the elderly population will lead to an increase in the number of old people with disabilities. This will result in an important economic burden, since disability increases the risk for need of home help, hospitalisation, nursing home admission and premature death. Despite the fact that women experience a higher burden of morbidity and disability, men die earlier; the reasons for such premature mortality are not entirely explained.

### **OBJECTIVES**

This thesis evaluated the existence of gender differences in the relationship between disability and mortality by using the disability life history and taking into account other risk factors. To this end, the evolution of disability prevalence over 8 years was assessed in a sample of non-institutionalised elderly. Also, the use of age as time scale in the survival analyses for elderly studies was examined.

### **METHODS**

Data from the Health Interview Survey of Barcelona (HISB) in 1986 and the oversample of subjects aged 65 years and older was used to evaluate the health of non-institutionalised elderly population living in Barcelona (n=1,315). They were then re-evaluated 8 years later to assess the evolution of their health and functional status and the relationship between baseline factors and the development of new conditions and mortality. Self-reported difficulty to perform basic activities of daily living was used to assess disability. Survival

analysis with delayed entry was formulated in the counting process framework to study time from aged 65 years to death or exit from the study. The semi-parametric Cox model with age as time scale and disability as time-dependent variable was applied to mortality data by sex.

## RESULTS

The proportion of subjects who were dependent or who had difficulties was higher among women than men both at baseline (42% vs. 30%, respectively) and at follow-up (60.0% vs. 48.7%, respectively). Disability status showed a dynamic pattern over time, being the group of elderly people with difficulties at baseline the most variable (only 20.0% among men and 30.2% among women remained in the same disability category group after eight years of follow-up, among those with follow-up information). Also, a subset of those who had some degree of disability ('difficulty' or 'dependency') at baseline improved their disability status (26.6% for men, and 26.9% for women). The risk of mortality associated with disability varied with gender and age. The adjusted relative risk of dying for those with basic ADLs dependency ranged from 3.5 for women and 1.8 at age 80 for men, to 1.9 and 1.2, respectively, at age 90. Also, multivariate analyses showed that a low body mass index (RR= 2.2), and either former or current smoking (RR= 1.6 and 2.4, respectively) were independently associated with mortality among elderly men.

Age as time scale facilitated the interpretation of the results derived from the survival analysis since inferences were based on the ageing process instead of time-on study. Thus, the graphical comparison of the survival function between men and women could be performed by using just one figure. This was in contraposition to the more elaborated approach when using time-on-study,

where it is necessary to carry out several figures and join the different pieces of the survival curves implementing an additional method. It was possible to estimate more percentiles of the survival time, such as the second and third quartiles for those subjects not disabled (16.9 and 22.5, respectively) that couldn't be obtained with the time-on-study scale. It also overcame the confusing role of age since a substantial number of risk factors correlate with age. The statistical models were more parsimonious since they avoided the inclusion of interaction terms (i.e., age\*time-on-study) due to the inherent assumption of linearity between the independent variables and the outcome in the semi-parametric Cox model. Although the results derived from both approaches were similar in the multivariate context, the estimates were slightly attenuated in the analysis of age as time scale, RR= 1.84 vs. 1.77 for males and RR= 2.10 vs. 1.92 for females. This attenuation is most likely due to the fact that adjustment by age was more tight using age as time scale.

## CONCLUSIONS

In 8 years disability in the elderly evolves over time worsening with age, but a non-negligible proportion of subjects are able to recover. There are gender differences in the evolution of disability: women are less able to regain functional capacity once they become disabled.

The strength of the association between disability and mortality also varies with time among the elderly: the relative risk of dying for disabled elderly decreases as they grow older. This association also varies with gender: dependent elderly women show a higher risk of dying compared to men at any given age. The results showed that smoking and a low body mass index are independent risk factors of mortality among elderly men. This excess risk of smoking has been

mainly attributed to cancers, heart and respiratory diseases. However, the association between low weight and mortality is less consistent, on the one hand it is likely to be a symptom of underlying diseases such as cancer or a poor nutritional status, and on the other, it may reflect individuals who are physically less active.

Health and social care policies focusing on disabled women should be implemented, due to the higher proportion of disabled women than disabled men, the lower probability of regaining functional capacity, and their higher risk of dying compared to disabled men.

Age should be considered the natural time-scale for the survival analysis in the elderly population. In doing so, the interpretation of the results is more straightforward because the estimates get rid of the confounding effect of age, the survival plots are then meaningful, and the risk factors are considered at the age time that they were measured. Moreover, the available information of the subjects is handled in a more efficient way allowing us to estimate more percentiles. Also, the multivariate models are simpler because the proportional hazards assumption of the semi-parametric Cox's model does not hold for those risk factors whose exposition tend to decrease with age, which are not rare in the elderly population.

The dynamic nature of disability should be considered when designing studies to capture its variations along the ageing process. To do so, longitudinal studies of older people with periodical disability assessments should be performed. Disability should be considered as a time-dependent variable to avoid possible underestimations of its relationship with mortality.

# **CHAPTER 1**

# **INTRODUCTION**



## 1. Introduction

### 1.1. *Population ageing*

#### 1.1.1. Demographic transition

World population is growing as a consequence of several factors such as improvements in nutrition, in public health and hygiene, technology and medical advances that yield a reduction of both mortality and fertility rates. This phenomenon is known as the ‘Demographic transition’, the transition from a society with high mortality and fertility rates to a society with increasing longevity due to low mortality and fertility rates. At the beginning of this process, a decline in the infant and childhood mortality rate is observed and later on the fertility rate drops<sup>1</sup>. As a consequence, the population besides growing also ages and life expectancy increases.

Population age structure depends mainly on three factors: fertility, mortality and net migration levels. With the purpose of simplifying the description of demographic transition the latter will be omitted<sup>2</sup>. As is shown in Figure 1, a population can be in one of three demographic phases<sup>3</sup>: a) early: where the age structure follows a pyramid pattern, the weight of each age stratum of the

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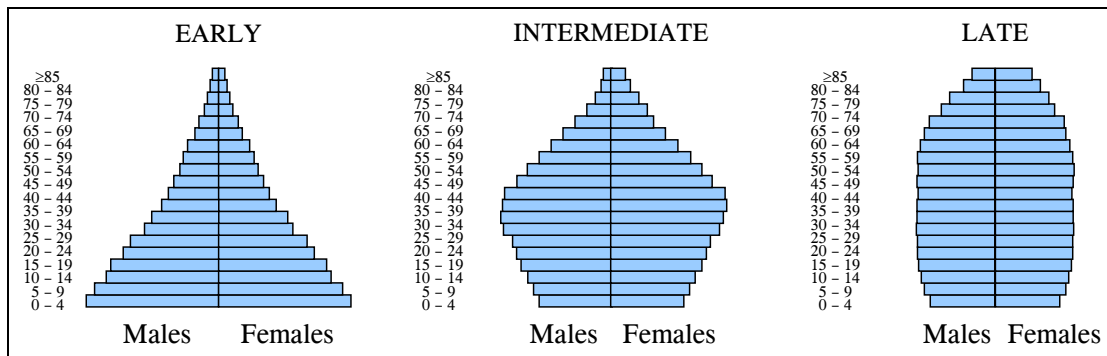
<sup>1</sup> Although there are a few exceptions in the reverse order, where the fertility declined first and then the mortality rate as the United States and France.

<sup>2</sup> The effect of the migration levels on the population age structure is not well established. R. Lee (2003) defined it as modest because the immigrants also get old and tend their fertility rates to the ones of the receptor country. The United Nations is in agreement with this argument unless the migration flows would be very large, i.e., millions annually.

<sup>3</sup> Other authors as R.P. Cincotta, R. Engelman and D. Anastasion (2003) describe the demographic transition process with five consecutive phases: pre-transition, early-transition, middle-transition, late-transition and post-transition. The pre-transition phase comprises the major part of the human history, and none country is currently in this phase. The early-transition will correspond with the early phase; a combination of the middle-transition and late transition will be similar to the intermediate phase and the post-transition to the late phase.

population being smaller than the subsequent one, overall a rapid population growth characterise this phase, b) intermediate: where the middle-age stratum groups have the largest weight on population and a slight asymmetry between men and women is observed in the age pyramid, and c) late: where a rectangular shape is observed, except in the oldest and youngest age stratum, with an increase in the proportion of elderly population<sup>4</sup>, with women showing the largest survival rates. It leads to population ageing and a possible population reduction.

Figure 1: Age pyramids for early, intermediate and late phases of the demographic transition.



However, there are marked differences in how far countries have progressed all along the demographic transition. While the transition began in Europe in 1800 and expanded around the world<sup>5</sup>, in most Asian, Caribbean and Latin American countries the infant and childhood mortality rate did not decrease until the early to mid 20<sup>th</sup> century. Industrialized countries, the ones in a late phase, are experiencing further reductions in mortality rates as a result of a decrease in fatality rates of some illnesses such as cancer and heart disease and

<sup>4</sup> Elderly population is defined as those subjects aged 65 years old or over.

<sup>5</sup> Lee R. The demographic transition: three centuries of fundamental change. *Journal of Economic Perspectives* 2003;17:167-90.



improvements in living conditions<sup>6</sup>. In contrast, the countries with more delay in the transition are experiencing a more rapid decline in mortality than was observed in industrialized countries before, although not without difficulties. Indeed, the mortality trend has been modified by the HIV/AIDS epidemic in some countries, especially those belonging to sub-Saharan Africa<sup>7</sup>.

The fertility rate started to decrease in Europe in the first decade of the 20<sup>th</sup> century and in most Asian, Caribbean and Latin American countries this decrease took place in the 1960s and 1970s<sup>8</sup>. In 2000, the fertility rate was below the replacement rate (2.1 children per woman) in the majority of industrialized countries, and in some Asiatic countries other than Japan (Singapore 1.2, South Korea 1.7, China 1.8, Thailand 1.9 and Sri Lanka 2.0)<sup>9</sup>.

The behaviour of mortality and fertility rates is leading the world population to an unprecedented ageing process. Among the 25 countries<sup>10</sup> with the largest proportion of elderly population in 2000, only one does not belong to Europe (Japan). The list is headed by Italy (18.1%) while Spain is in 5<sup>th</sup> position (16.9%), and the United States is not included due to its moderate proportion (13%) compared to most industrialized countries.

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<sup>6</sup> Riley J.C. *Rising life expectancy: a global history*. Cambridge;Cambridge University Press: New York, 2001. Quoted in page 171 of Lee R. *The demographic transition: three centuries of fundamental change*. *Journal of Economic Perspectives* 2003;17:167-90.

<sup>7</sup> Cincotta R.P., Engelman R. and Anastasion D. *The Security Demographic*. In: *Population and civil conflict after the cold war*. Population Action International: Washington, 2003: pp. 24-41.

<sup>8</sup> Cincotta R.P., Engelman R. and Anastasion D. *The Security Demographic*. *Population and civil conflict after the cold war*. In: *Population Action International: Washington, 2003: pp. 24-41*.

<sup>9</sup> Kinsella K. and Velkoff V.A. U.S. Census Bureau, Series P95/01-1, *An Aging World: 2001*, U.S. Government Printing Office, Washington, DC, 2001.

<sup>10</sup> The list is composed by world's major nations, so small areas as Monaco were omitted.

Among the elderly population, the eldest ( $\geq 80$  years) are the fastest growing of all population groups. In 2000, more than half of them lived in China, the United States, India, Japan, Germany and Russia<sup>11</sup>. It has been estimated that, in general, the number of elderly people aged from 90 to 99 years will rise from the current 8 million to 60 million by 2050, whereas the number of centenarians will increase from 190,000 to 2.5 million<sup>12</sup>. It is worth mentioning that although industrialized countries have the highest proportion of elderly population; around sixty percent of the world's elderly lived in developing countries in 2000. It is precisely in these countries where there are more room to grow, projections describe an increase in the elderly population of up to seventy one percent by 2030<sup>13</sup>.

The effects of the demographic change described above can be illustrated in the trend of life expectancy at birth and at the age of 65 in six European countries (Denmark, France, Italy, Spain, Sweden and United Kingdom) using data from Eurostat<sup>14</sup> and comparing them with those from the United States and Japan.

Continuing gains in life expectancy at birth have been experienced in both females and males from 1950 to the present, see Figures 2 and 3. A sustained sex differential in life expectancy at birth is observed along time in the 4.7-7.4 year range in 2000. Also, a rise in life expectancy at age 65 is observed in both sexes, see Figure 4. An average gap of around 3 years between the sexes in

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<sup>11</sup> Kinsella K. and Velkoff V.A. U.S. Census Bureau, Series P95/01-1, An Aging World: 2001, U.S. Government Printing Office, Washington, DC, 2001.

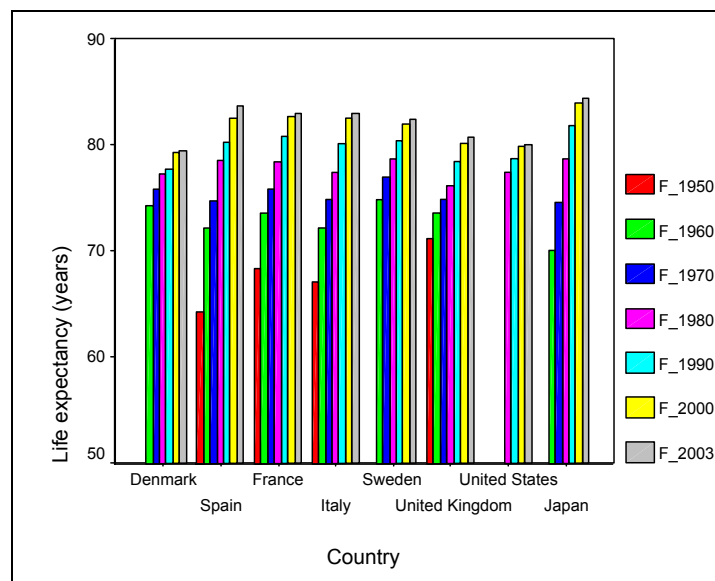
<sup>12</sup> Kalache A., Aboderin I. and Hoskins I. Compression of morbidity and active aging: key priorities for public health policy in the 21st century. Bull World Health Organ 2002;80:243-4.

<sup>13</sup> Kinsella K. and Velkoff V.A. U.S. Census Bureau, Series P95/01-1, An Aging World: 2001, U.S. Government Printing Office, Washington, DC, 2001.

<sup>14</sup> Statistical office of the European Communities.

favour of females is observed in 2000 with the exception of France that increased up to 4.5 years. This pattern of life expectancy is consistent with the observed low rates of infant and children mortality, since it implies that the decline in mortality can only come from a reduction of the mortality in the eldest group.

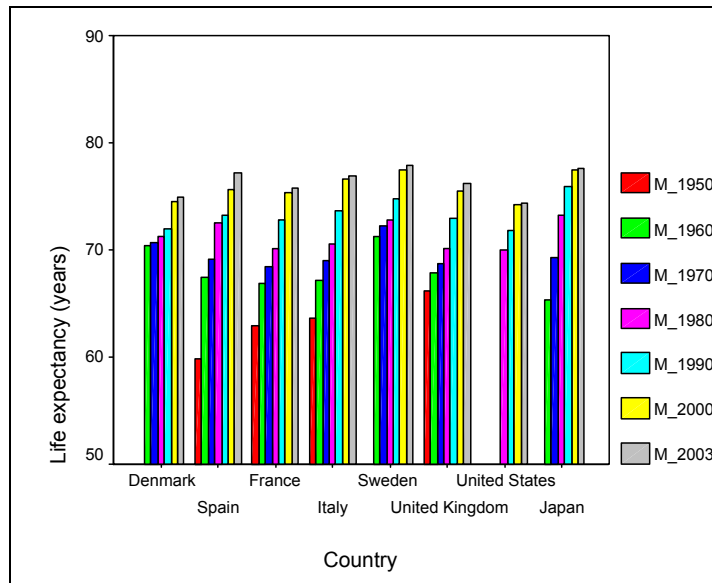
Figure 2: Life expectancy by time period. Females.



Source: Eurostat Feb 2005.

The behaviour of the United States and Japan is similar to that observed in the selected European countries. Although, life expectancy in the United States from 1980 to 2003 is among the lowest and life expectancy in Japan is always the highest over this period with the exception of Sweden in 2003 for females.

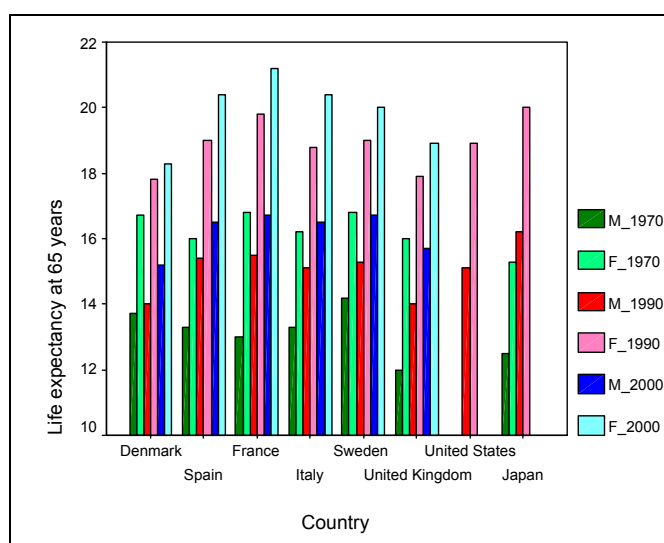
Figure 3: Life expectancy by time period. Males.



Source: Eurostat Feb 2005.

In Spain, life expectancy increased by 26.6 and 28.3 percent, respectively, in males and females. That is, from 59.8 to 75.7 years in males and from 64.3 to 82.5 years in females between 1950 and 2000. In addition, the average number of years remaining at 65 years also augmented by 39.8 and 51.1 percent in males and females, respectively, between 1950 and 2000. In the same time period, the former European Union (EU) compounded by 15 countries experienced an increase from 67.4 to 75.5 years (12.0%) in males and from 72.9 to 81.4 years in females (11.7%). These figures<sup>15</sup> decrease slightly with the incorporation of the additional 10 countries that currently make up the EU, being from 67.1 to 74.4 years (10.9%) in males and from 72.6 to 80.8 years in females (11.3%).

Figure 4: Life expectancy at 65 years old by gender and time period.



Source: Eurostat Feb 2005.

Data from the ‘Institut d’Estadística de Catalunya’ show how life expectancy has also increased in Catalonia by around 2 years in the decade from 1992 to 2002 in both sexes, being similar to the pattern in Spain according to data from the ‘Instituto Nacional de Estadística’ (see Table 1).

Table 1: Evolution of life expectancy in Catalonia and Spain (1992-2002).

	1992		1995		2000		2002	
	Males	Females	Males	Females	Males	Females	Males	Females
Catalonia <sup>1</sup>	74.0	81.4	74.8	82.2	76.5	83.2	76.9	83.4
Spain <sup>2</sup>	73.8	81.1	74.4	81.6	75.7	82.5	75.7	83.1

<sup>1</sup> Departament de Salut de la Generalitat de Catalunya.

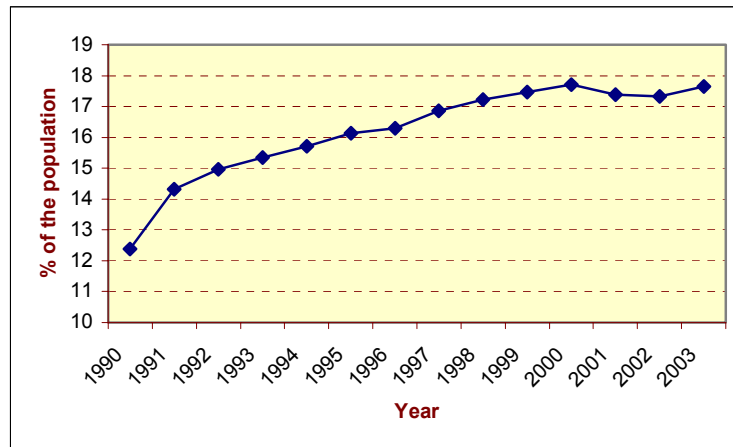
<sup>2</sup> Instituto Nacional de Estadística.

In addition, the number of people over 65 years old has also grown. The elderly accounted for 12.4% of the overall Catalan population in 1990, but this figure increased steadily until 2000 where it seemed to level off at around 17.7% from 2000-2003 (see Figure 5). This change in the age structure of the Catalan population is reflected in the increasing average age of the whole population

<sup>15</sup> The values for the current European Union (25 countries) have been estimated by Eurostat.

from 34.2 years in 1981 to 40.8 years in 2002, as well as the ageing index<sup>16</sup> from 44.0% in 1981 to 123.7% in 2002.

Figure 5: People aged over 65 years old as the percentage of the total population of Catalonia.



Source: Institut d'Estadística de Catalunya.  
Estructura en grans grups d'edat de la població.

### 1.1.2. Theories about the population health status changes due to ageing

There is controversy about whether population ageing will imply a change in overall health status. In the following sections, the principal theories about population health change are presented. However, to understand the health changes in the elderly population, it is important to note that there are normal age-related changes in the organism, which are being approached by the Theories of Ageing (genetic<sup>17</sup>, cellular<sup>18</sup>, problems in homeostasis<sup>19</sup>, and 'wear and tear'<sup>20</sup> theories, among others) and are out of the scope of this thesis.

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<sup>16</sup> Individuals aged 65 years or over per 100 individuals younger than 15 years old.

<sup>17</sup> Among other genetic theories, it has been argued that the number of times that a cell can replicate without error is limited and there may be a relationship between the number of cell replications and lifespan. Hayflick L. How and why we age. Ballantine Books. New York. 1996.

<sup>18</sup> The free radical theory is one of the leading cellular theories. The free radicals are produced during the oxidation process within cells. The theory states that the cell damage increases with

In general, it must be considered that human ageing is a process that involves biological changes that occur with age (e.g., decline in cellular activity). An additional aspect that should be highlighted is the existence of a high variability between elderly people: some individuals are disabled in their 70's, while others are able to run marathons at the same age.

#### *1.1.2.1. Compression of morbidity*

When presenting his Compression of Morbidity theory in 1980, J.M. Fries postulated that, at the population level, the disability state will be compressed in a shorter period in the later stages of life<sup>21,22,23,24</sup>. That is, an increase in life expectancy will be associated with a diminution of disability. The theory is based on the following assumptions<sup>25</sup>: a) the increase in life expectancy will be smaller than the postponed onset of disability, b) the capacity to postpone or avoid disability by preventive activities, and c) the increase in survival as a result of removing life-threatening conditions will not counterbalance the gains

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age as more free radicals are generated in the cell. Sohal S.S. and Weindruch R. Oxidative stress, caloric restriction, and aging. *Science* 1996;273:63-7.

<sup>19</sup> The homeostatis maintains intra and extracellular environmental conditions, such as temperature, pH balance, and heart rate, among others. There is evidence that it is more difficult to sustain homeostatis as people age. Taffett G.E. Age-related physiologic changes. In: Reuben D.B., Yoshikawa T.T. and Besdine R.W. (eds.). *Geriatrics review syllabus*. Kendall/Hunt. Dubuke. 1996.

<sup>20</sup> The theory proposes that the organism wears out after extended use.

<sup>21</sup> Fries J.F. Aging, natural death, and the compression of morbidity. *N Engl J Med* 1980;303:130-5.

<sup>22</sup> Fries J.F. The compression of morbidity. *Milbank Mem Fund Q Health Soc* 1983;61:397-419.

<sup>23</sup> Fries J.F. Compression of morbidity in the elderly. *Vaccine* 2000;18:1584-9.

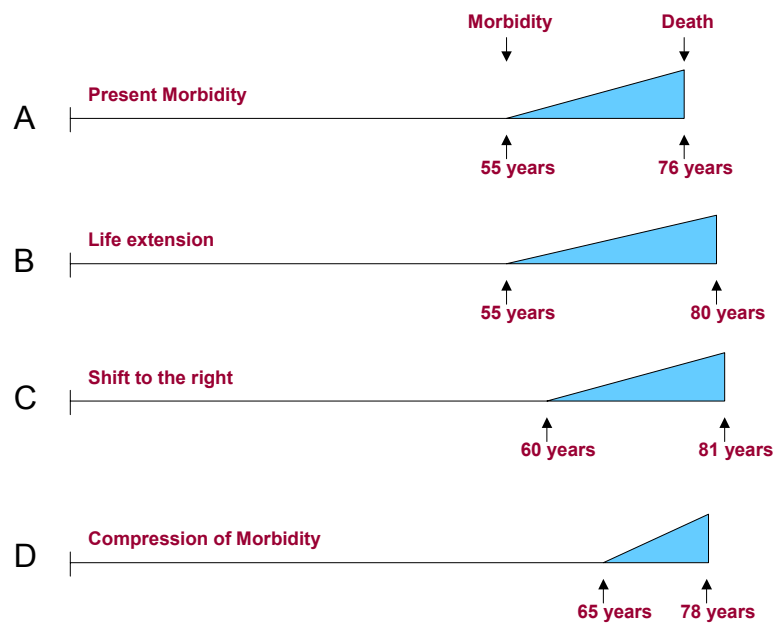
<sup>24</sup> Fries J.F. Measuring and monitoring success in compressing morbidity. *Ann Intern Med* 2003;139:455-9.

<sup>25</sup> Kane R.L., Evans J.G. and Macfadyen D. Improving the health of older people. A world view. Oxford University Press on behalf of the World Health Organization. New York. 1990. Chapter 4 'Compression of morbidity: issues and irrelevancies'. Kane R.L., Radosevich D.M. and Vaupel J.W.

achieved by this elimination. As shown in the scenario D of Figure 6, Compression of Morbidity will imply a deferred onset of morbidity from 55 to 65 years in the illustration, while longevity will increase from 76 to 78 years. Thus, the gain in the postponement of morbidity is larger than the gain in life expectancy, yielding as a result a compression of the period of time with morbidity.

The policy implication of this rather optimistic theory is that health resources should be shifted to the later stages of life and for a shorter period of time.

Figure 6: Current status and three possible scenarios for future morbidity and mortality.



Source: Adapted from Fries J.F. (2003)<sup>26</sup>.

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<sup>26</sup> Fries J.F. Measuring and monitoring success in compressing morbidity. *Ann Intern Med* 2003;139:455-9.



### 1.1.2.2. *Expansion of morbidity*

E.M. Gruenberg (1977)<sup>27</sup> and M. Kramer (1980)<sup>28</sup> introduced the Expansion of Morbidity theory also known as the Failure of Success theory. They postulated that the gain in years lived as a result of the increase in life expectancy, would be spent in a poorer health condition because the life being extended is that of individuals with disease and disability. As illustrated in the scenario B (Figure 6), if the age at death is postponed (from 76 to 80 years old) but the age of onset of morbidity remains constant (55 years old) then the period of time with morbidity will increase. Under this pessimistic theory, the demand for health resources will rise dramatically due to the expansion for morbidity.

### 1.1.2.3. *Dynamic equilibrium*

K.G. Manton (1982)<sup>29</sup> proposed a theory that contains elements from both the compression and expansion theories. In this one, the decrease in mortality rates will come from a reduction in the rate of chronic disease evolution. According to this approach, the number of years lived with disability will increase but the severity of the disability will decrease. Thus, the period of life with severe illnesses or disability will decrease or stabilise, whereas the period with moderate illnesses or disability will increase leading all together to a dynamic equilibrium.

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<sup>27</sup> Gruenberg E.M. The failures of success. *Milbank Mem Fund Q Health Soc* 1977;55:3-24.

<sup>28</sup> Kramer M. The rising pandemic of mental disorders and associated chronic diseases and disabilities. *Acta Psychiatrica Scandinavica* 1980;62:282-97.

<sup>29</sup> Manton K.G. Changing concepts of morbidity and mortality in the elderly population. *Milbank Mem Fund Q Health Soc* 1982;60:183-244.

#### *1.1.2.4. General theory of population ageing*

Recently, J.P. Michel and J.M. Robine (2004)<sup>30,31</sup> proposed the basis for a new theory that comprises the ‘Compression of morbidity’, ‘Expansion of morbidity’ and ‘Dynamic equilibrium’ theories in an attempt to explain the current contradictory findings on chronic conditions, disability and functional limitations research taking into account the demographic change.

The theory relies on a cyclical movement: The decline in mortality at old ages in the demographic transition leads to the possibility of sick people surviving into old age supporting the ‘Expansion of morbidity’ because the prevalence of chronic conditions and disability rates increases. Then, medical improvements slow down the evolution of chronic conditions achieving certain equilibrium thus supporting the ‘Dynamic equilibrium’ theory. Afterwards, a new status will follow where new cohorts enter into the elderly process. Given that these people will be healthier due to predominantly better health habits and living conditions, then the ‘Compression of Morbidity’ will apply at this stage. Finally, the emergence of very old populations will imply the need to deal with frail people burdened by multiple chronic diseases in their last years of life. Therefore, the scenario about population ageing will vary depending on the demographic transition phase where the country is positioned.

#### *1.1.2.5. Current situation*

Apart from the recent General Theory of Population Ageing still under discussion, to date there is no conclusive evidence about the true health status

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<sup>30</sup> Robine J.M. and Michel J.P. Looking forward to a general theory on population aging. *J Gerontol Med Sci* 2004;59A:M590-M597.

<sup>31</sup> Michel J.P. and Robine J.M. A new general theory of population aging. *The Geneva papers on risk and insurance* 2004;29:667-78.

change, although the current dominant view is that an initial Compression of morbidity will be followed by a Dynamic Equilibrium in industrialised countries, there is, however, no sign of compression of morbidity in developing countries<sup>32</sup>.

J.F. Fries stated that some compression of comorbidity has occurred during the last 20 years<sup>33</sup> and is being experienced nowadays in the population of the United States<sup>34</sup>: the U.S. elderly adult mortality decline is about 1% per year and the disability decline about 2% per year<sup>35</sup>. K.G. Manton and colleagues<sup>36,37,38,39</sup> showed a decrease of chronic diseases and disability over time using data from the National Long Term Surveys (NLTS)<sup>40</sup>. B.H. Singer and K.G. Manton estimated that a 1.5% decline in chronic disability per year within the period 1995-2070 would be possible if the correct health policies were applied (appropriate public health programs and increasing biomedical research

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<sup>32</sup> Kalache A., Aboderin I. and Hoskins I. Compression of morbidity and active aging: key priorities for public health policy in the 21st century. *Bull World Health Organ* 2002;80:243-4.

<sup>33</sup> Fries J.F. Compression of morbidity in the elderly. *Vaccine* 2000;18:1584-9.

<sup>34</sup> Fries J.F. Measuring and monitoring success in compressing morbidity. *Ann Intern Med* 2003;139:455-9.

<sup>35</sup> Fries J.F. Reducing disability in older age. *JAMA* 2002;288:3164-6.

<sup>36</sup> Manton K.G., Corder L.S. and Stallard E. Estimates of change in chronic disability and institutional incidence and prevalence rates in the U.S. elderly population from the 1982, 1984, and 1989 National Long Term Care Survey. *J Gerontol Soc Sci* 1993;48:S153-S166.

<sup>37</sup> Manton K.G., Corder L.S. and Stallard E. Chronic disability trends in elderly United States populations: 1982-1994. *Proc Natl Acad Sci USA* 1997;94:2593-98.

<sup>38</sup> Manton K.G., Stallard E. and Corder L.S. The dynamics of dimensions of age-related disability 1982 to 1994 in the U.S. elderly population. *J Gerontol Bio Sci* 1998;53:B59-B70.

<sup>39</sup> Manton K.G. and Gu X. Changes in the prevalence of chronic disability in the United States black and nonblack population above age 65 from 1982 to 1999. *Proc Natl Acad Sci USA* 2001;98:6354-9.

<sup>40</sup> National representative longitudinal surveys from U.S. population.

investments)<sup>41</sup>. Using data from the National Institute on Ageing Established Populations for Epidemiological Studies of the Elderly, L.A. Beckett et al.<sup>42</sup> showed a decline in physical function (Katz ADL scale, Nagi scale and the Rosow-Breslau Functional scale) that increased with age. V.A. Freedman and L.G. Martin<sup>43</sup> also observed declines from 1984 to 1993 in the prevalence of difficulty in four functions (seeing, lifting and carrying, climbing and walking) among participants in the U.S. Bureau of the Census's Survey of Income and Program Participation. Recently, V.A. Freedman, L.G. Martin and R.F. Shoeni (2002)<sup>44</sup> conducted a systematic review of studies about self-reported disability and functioning among older adults in the United States that were performed in the late 1980s and early 1990s. The authors concluded, based on 8 studies, that there was a decrease in the prevalence of any disability during the 1990s. However, contradictory results were available about the trend in Activities of Daily Living (BADLs) in contraposition to the clear decline pattern observed in the Instrumental Activities of Daily Living (IADLs)<sup>45</sup>.

Nevertheless, the postponement of morbidity could be larger if health policies focus on diminishing/eliminating unhealthy behavioural factors, such as smoking, sedentary lifestyle, and diet (specially saturated fat) since they are among the major contributors to chronic diseases. Findings from the University

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<sup>41</sup> Singer B.H. and Manton K.G. The effects of health changes on projections of health service needs for the elderly population of the United States. *Proc Natl Acad Sci USA* 1998;95:15618-22.

<sup>42</sup> Beckett L.A., Brock D.B., Lemke J.H., Mendes de Leon C.F., Guralnik J.M., Fillenbaum G.G., Branch L.G., Wetle T.T. and Evans D.A. Analysis of change in self-reported physical function among older persons in four population studies. *Am J Epidemiol* 1996;143:766-78.

<sup>43</sup> Freedman V.A. and Martin L.G. Understanding trends in functional limitations among older Americans. *Am J Public Health* 1998;88:1457-62.

<sup>44</sup> Freedman V.A., Martin L.G. and Shoeni R.F. Recent trends in disability and functioning among older adults in the United States. A systematic review. *JAMA* 2002;288:3137-46.

<sup>45</sup> The reader is derived to section 1.2.2 for a definition of BADLs and IADLs.

of Pennsylvania Study<sup>46</sup> and the Precursors of Arthritis Study<sup>47</sup> support this fact by showing that subjects with healthier habits were associated with lower rates of disability and that the onset of disability emerged at an older age.

A widespread implementation of the use of health expectancy indicators<sup>48</sup>, that combine information from current health status (quality) and remaining life (quantity), will help monitor the evolution of population health and clarify whether or not the aforementioned theories are correct.

### 1.1.3. Implications on health, social and economical systems

Increased longevity can be considered a success and a sign of progress. However, this demographic change has an impact on public expenditure, particularly health care systems and social (pension) care costs: those increased costs are more importantly due to the change in the age structure of the population than the population growth itself. There are two major issues: the population of working age has shrunk and the elderly population has grown. Those societies with a large proportion of elderly people are likely to devote a high proportion of resources to their care, which may inhibit economic growth since there are not enough individuals in the working age group to support it, challenging the sustainability of welfare states.

Some economists have expressed their concern that the population ageing together with inefficient public policies may jeopardise long-term growth<sup>49</sup>.

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<sup>46</sup> Vita A.J., Terry R.B., Hubert H.B. and Fries J.F. Aging, health risks and cumulative disability. *N. Engl J Med* 1998;338:1035-41.

<sup>47</sup> Fries J.F., Singh G, Morfeld D, Hubert H.B., Lane N.E. and Brown B.W. Running and the development of disability with age. *Ann Intern Med* 1994;121:502-9.

<sup>48</sup> Among the health expectancy indicators are found the Health-Adjusted Life Expectancy (HALEs) and Disability-Adjusted Life Expectancy (DALEs).

<sup>49</sup> Palacios R. The future of global aging. *Int J Epidemiol* 2002;31:786-91.

They point out two reasons to support their position: first, personal savings of the elderly may diminish since people may rely either on the public pension system or on their descendents; provoking both a burden on the working age population directly by means of family transfers or indirectly by means of taxes and secondly, the decrease in productivity in industrialized countries due to reduced labour working years, mainly in the stratum of males aged between 55 and 64 years. In Catalonia, for instance, 8,130 out of the 8,700 million Euros devoted to the ageing population in 2000 (excluding health services) were devoted to pensions. The economic resources used for pensions have doubled in the 1990-2000 period<sup>50</sup>.

In Europe there are differing approaches to pension regimens, while some countries combine basic social insurance with pay-as-you-go (PAYG) in which people currently working support retired individuals, others prefer privatisation and funding<sup>51</sup>. The first system fails when successive generations are of different sizes, whereas the second one may put people from lower socio-economic levels at risk.

A positive discrimination towards women should be evaluated because women live longer and are less likely to have full contribution records in employment. Therefore, they are more likely than men to not receive complete pensions and to be poor at old age. Moreover, if we consider the existing gender inequalities in salary income during the working years, women should be targeted in public policies.

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<sup>50</sup> Data from the Institut d'Estadística de Catalunya.

<sup>51</sup> Walker A. Aging in Europe: policies in harmony or discord?. *Int J Epidemiol*;31:758-61.

Another aspect to be considered is the growing contribution of women in the labour force that has changed traditional values, which ensured that ‘women will cope with the care of elderly’. In addition, fertility rates have dropped and family size has diminished; therefore the number of potential informal carers has also been reduced. In our country, the number of children per woman has dropped from 2.80 in 1975 to 1.27 in 2002 in Spain<sup>52</sup> (2.86 in 1975 to 1.33 in 2002 in Catalonia<sup>53</sup>). As a consequence, the family-based care system needs to be revised, especially if we consider that family structure has varied in recent decades (due to factors such as the rise in the divorce rates, the number of people living alone, among others). Therefore, social policies need to be updated or transformed to face this situation.

The evolution of health spending will depend on whether or not morbidity will decline in relation with mortality. The gain life expectancy by diminishing mortality rates may also imply an increase in the number of disabled elderly people. Alternatively, the functional status of elderly people may be good, with a resulting gain in healthy years. The chances of increasing the proportion of disabled people were discussed in section 1.1.2. Beyond the disability rate, the fall in the mortality rates may imply that other diseases that may be more costly in terms of care are replacing some diseases. For instance, Alzheimer’s disease may replace heart diseases, as a consequence of the competing mortality behaviour. Those individuals who have not died from a previous disease due to medical improvements are then susceptible to suffer a more demanding (in terms of health care) disease.

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<sup>52</sup> Data from the Instituto Nacional de Estadística.

<sup>53</sup> Data from the Institut d’Estadística de Catalunya.

In relation to the use of hospital resources, a previous study<sup>54</sup> describes that it was 4.5 times higher in those subjects aged between 65 and 74 years old than in those aged between 5 and 54 years old, and it increased up to 6 times for the age stratum of individuals older than 74 years old in our setting. Concerning drugs expenditure, pensioners consumed 10 times more than the remaining population in our setting<sup>55</sup>. In 2000, 77.4% and 78.0% of the pharmaceutical expenses came from pensioners (who may include people below 65 years) in Spain and Catalonia, respectively<sup>56</sup>.

Some strategies adopted by European policymakers to preserve economic growth are: to accept a larger influx of immigrants, extend the retirement age and incorporate more women into the labour market by trying to make it compatible with their family activities<sup>57</sup> (including direct economic incentives for additional children). In contrast, Japan replaces low-skilled jobs with technology, and out-sources less innovative, labour-intensive industries overseas and increases its investment in research and development<sup>58</sup>.

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<sup>54</sup> Casado D. and López G. Vellea, dependència i atencions de llarga durada. Situació actual i perspectives de futur, Col·lecció d'estudis socials, num. 6. Fundació La Caixa, 2001, page 12.

<sup>55</sup> Casado D. and López G. Vellea, dependència i atencions de llarga durada. Situació actual i perspectives de futur, Col·lecció d'estudis socials, num. 6. Fundació La Caixa, 2001, page 12.

<sup>56</sup> Abellán A. Longevidad y estado de salud. In: Las personas mayores en España. Informe 2002. Volumen I, Ministerio de Trabajo y Asuntos Sociales, 2002, page 113.

<sup>57</sup> Cincotta R.P., Engelman R. and Anastasion D. The Security Demographic. In: Population and civil conflict after the cold war. Population Action International: Washington, 2003: pp. 24-41.

<sup>58</sup> Cincotta R.P., Engelman R. and Anastasion D. The Security Demographic. In: Population and civil conflict after the cold war. Population Action International: Washington, 2003: pp. 24-41.



## **1.2. Disability**

### 1.2.1. Conceptual framework

In order to understand and evaluate disability, it is important to have an understanding of the progression ending with a loss of functionality. Unfortunately, there is no consensus and differing viewpoints of the underlying frameworks of disability exist. Indeed, the magnitude of such confusion is so significant that the same terms may have different meanings depending on the conceptual framework.

The present work is based on the model proposed by L.M. Verbrugge and A.M. Jette<sup>59</sup> called the Disablement Process. It is a development of the initial model conceived by the sociologist S.Z. Nagi<sup>60,61,62</sup>. Other frameworks to describe the disability process include the International Classification of Impairments, Disabilities and Handicaps (ICIDH) and its current revision the International Classification of Functioning, Disability and Health (ICF). The three major disability frameworks, as well as the definition of the term disability under each conceptual framework, are discussed below.

Nagi's model, developed in 1965, attempted to incorporate social and physical environment aspects into the medical perspective of disability. Disability is seen as a gap between a person's capabilities and the demands of the social and

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<sup>59</sup> Verbrugge L.M. and Jette A.M. The disablement process. *Soc Sci Med* 1994;38:1-14.

<sup>60</sup> Nagi S.Z. Some conceptual issues in disability and rehabilitation. In: Sussman M.B. (ed). *Sociology and rehabilitation*. Washington D.C. American Sociological Association, 1965: pp. 110-13.

<sup>61</sup> Nagi S.Z. An epidemiology of disability among adults in the United States. *Milbank Mem Fund Q Health Soc* 1976;54:439-67.

<sup>62</sup> Nagi S.Z. Disability concepts revisited: implications for prevention. In *Disability in America: toward a National agenda for prevention*. Institute of Medicine, National Academy Press, Washington, DC, 1991: pp. 309-27.

physical environment that causes cessation or restriction in performing the activities of daily living. Therefore, disability is not intrinsic to a person but reflects the interaction between the individual and her/his environment. It follows that an individual limitation may lead to different patterns of disability or no-disability at all, depending on how the subject experiences a situation and reacts to it within their environment, and how others (for example relatives and friends,) view such a situation. For instance, a decrease in visual acuity may disable a pilot because he/she will be unable to operate a plane. However, the same impairment may not have any major limitation on a lawyer to perform her/his activities. Further, a distinction between intrinsic and actual disability is made. The first refers to disability when the individual has no access to assistance (personal or equipment) and the second, when such assistance is available.

Nagi's disability model<sup>63</sup> is based on four related concepts that compound the main pathway: pathology, impairment, functional limitation and disability in performing social roles and activities, see Figure 7. Nagi defined the first three terms as<sup>64</sup>: a) pathology: the interruption of normal cellular processes and the efforts of the organism to regain a normal state, b) impairment: anatomical, physiological, intellectual or emotional loss or abnormality at the tissue, organ, and body system level, c) functional limitations: restrictions in the basic physical or cognitive performance of the person.

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<sup>63</sup> Nagi S.Z. Disability concepts revisited: implications for prevention. In *Disability in America: toward a National agenda for prevention*. Institute of Medicine, National Academy Press, Washington, DC, 1991: pp. 309-27.

Figure 7: Nagi's disability model (1965).

PATHOLOGY ⇒ IMPAIRMENT ⇒ FUNCTIONAL LIMITATION ⇒ DISABILITY

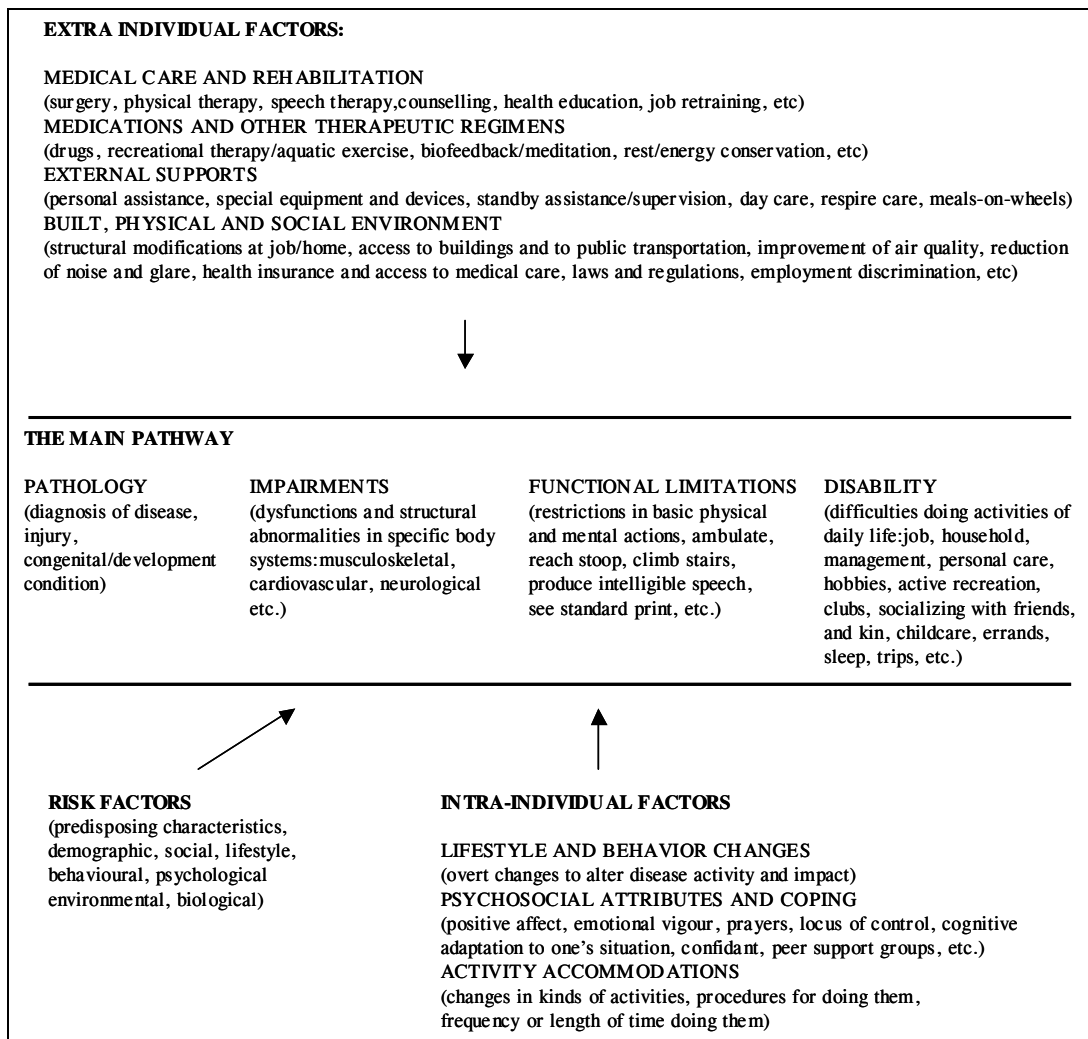
L.M. Verbrugge and A.M. Jette<sup>65</sup> extended Nagi's model to include a complete sociomedical perspective taking into account personal and environmental factors that influence the evolution of the disablement process, see Figure 8. The model emphasizes the dynamic aspect of disablement focusing on the process itself that leads to disability, that is, the factors that affect its evolution over time (direction, pace and pattern of change). The extraindividual factors, predisposing risk factors and intraindividual factors may modify the relationship of the four concepts in the main pathway.

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<sup>64</sup> Jette A.M. and Keysor J.J. Disability models: implications for arthritis exercise and physical activity interventions. *Arthritis Rheum* 2003;49:114-20.

<sup>65</sup> Verbrugge L.M. and Jette A.M. The disablement process. *Soc Sci Med* 1994;38:1-14.

Figure 8: The disablement process (1994).

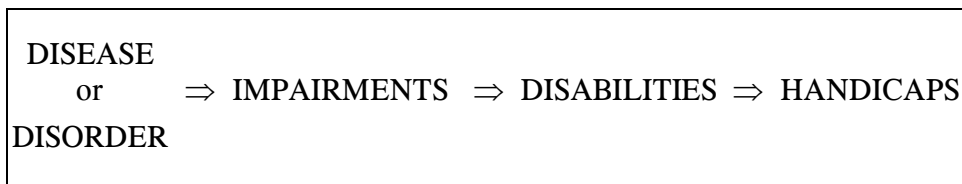


Source: Adapted from Verbrugge L.M. and Jette A.M.(1994)<sup>66</sup>.

In 1980 the World Health Organisation (WHO) proposed a theoretical framework to describe the sequence from disease/disorder to impairment, disability and handicap named International Classification of Impairments, Disabilities and Handicaps (ICIDH). The WHO developed the ICIDH focusing on disability in contrast to the available tool, the International Classification of Diseases (ICD), a system for coding diseases and health conditions from a medical perspective.

The ICIDH was aimed at describing the impact of disease/disorder on functioning. It describes a process that starts with an underlying cause, which results in an impairment that may produce disability, and may end in a handicap, see Figure 9.

Figure 9: The International Classification of Impairments, Disabilities and Handicaps model (ICIDH), (1980).



It is not mandatory that a subject will complete the whole pathway, that is, disability does not necessarily evolve into handicap, or impairment into disability; in this sense they are relatively independent concepts. Impairment refers to an organ level, disability to a personal level and handicap to a social level. Impairment is defined as any loss or abnormality of physiological, psychological or anatomical structural or function. Disability is viewed as a restriction in the ability to perform an activity considered as ‘normal’ due to impairment. Handicap is seen as a disadvantage that limits the ‘normal’ role of the individual.

This approach raised some controversies such as: being too medically-oriented, ignoring the social and the psychological dimensions; the negative connotation of the term ‘handicap’; assuming a linear casual connection between impairment to handicaps; omitting environmental factors; and being too complex from an operational point of view to distinguish unequivocally the three concepts.

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<sup>66</sup> Verbrugge L.M. and Jette A.M. The disablement process. Soc Sci Med 1994;38:1-14.

The ICDIH model in comparison with Nagi's disablement model presents some similarities in the definition of the four concepts. The disease and impairment terms in the ICDIH model are comparable to the pathology and impairment terms in Nagi's model. Whereas, the concepts of disability and handicap may be comparable to functional limitation and disability, respectively<sup>67</sup>.

In 2001, the WHO presented a revision of the classification in response to the ICIDH's criticism<sup>68</sup>: the International Classification of Functioning, Disability and Health (ICF)<sup>69</sup>, see Figure 10. The new conceptual framework for health and disability was originated by putting major emphasis on health and functioning instead of disability as they did in the past, ICF focuses on 'components of health as human functioning' instead of 'disabilities as consequences of disease'. The criticism about the linear link between impairment, disability and handicap is sorted out by the inclusion of bi-directional arrows, which allow all the components to be connected.

The ICF has a broader coverage than its predecessor, and allows its use in different sectors, besides health research and clinical setting, for example in insurance, economics, and education, among others.

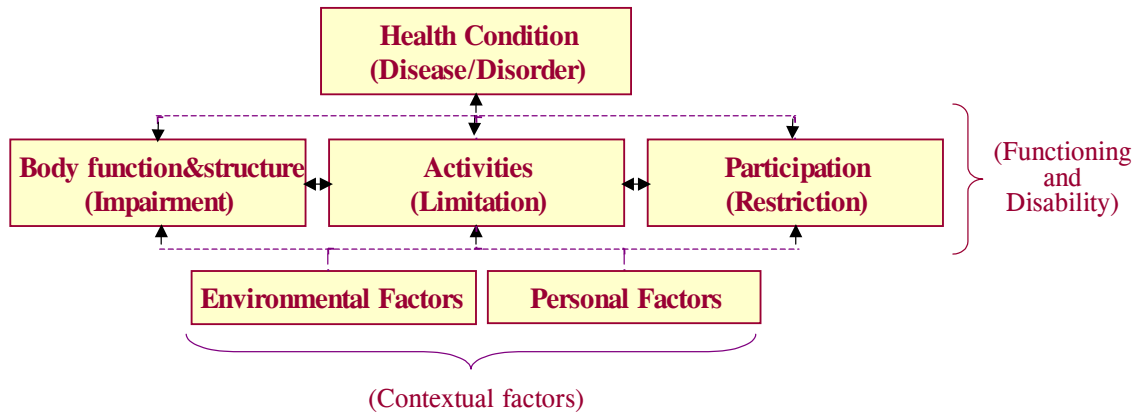
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<sup>67</sup> Pope A.M. and Tarlov A.R. (eds). A model for disability and disability prevention. In: *Disability in America: toward a National agenda for prevention*. Institute of Medicine, National Academy Press, Washington, DC, 1991: pp.76-108.

<sup>68</sup> Before the release of the ICF model, WHO also developed a new version of the ICIDH model in 1997; it was called ICIDH-2 and took into consideration participation and environmental factors.

<sup>69</sup> World Health Organisation. ICF Introduction. Accessed on February 2005. URL: [www3.who.int/icf/intros/ICF-Eng-Intro.pdf](http://www3.who.int/icf/intros/ICF-Eng-Intro.pdf).

Figure 10: The International Classification of Functioning, Disability and Health model (ICF), (2001).



Source: Adapted from WHO<sup>70</sup>.

Instead of describing impairment, disability, and handicap, the ICF describes body structure, functioning, activities and participation. The goal of this approach was to focus on health components instead of disease consequences, classifying the status of a person in an array of health or health-related domains<sup>71</sup>. The definitions of the key terms used in the ICF framework are displayed in Table 2.

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<sup>70</sup> World Health Organisation. Towards a common language for functioning, disability and health ICF. Geneva 2002. Accessed on February 2005. URL: [www3.who.int/icf/beginners/bg.pdf](http://www3.who.int/icf/beginners/bg.pdf).

<sup>71</sup> Health domains are vision, hearing, speech, digestion, bodily excretion, fertility, sexual activity, skin and disfigurement, breathing, pain, affect, sleep, energy/vitality, cognition, communication, mobility and dexterity. Health-related domains are: self-care (including eating), usual activities (household and work or school activities), social functioning (interpersonal relations), and participation (societal participation including discrimination/stigma).

Table 2: ICF definitions in the context of health.

<p><b>Body functions:</b> physiological functions of body systems (including psychological functions) <i>example: seeing</i></p> <p><b>Body structures:</b> anatomical parts of the body such as organs, limbs and their components <i>example: eye and related structures</i></p> <p><b>Impairments:</b> problems in body function or structure such as significant deviation or loss <i>example: loss of vision</i></p> <p><b>Activity:</b> execution of a task or action by an individual <i>example: reading</i></p> <p><b>Participation:</b> involvement in a life situation <i>example: reading performance</i></p> <p><b>Activity limitations:</b> difficulties an individual may experience in involvement in life situations <i>example: attend the University without the use of any assistance</i></p> <p><b>Environmental factors:</b> make up the physical, social and attitudinal environment in which people live and conduct their lives <i>example: light or transportation services</i></p>
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Source: Adapted from 'ICF introduction'<sup>72</sup>.

The ICF follows a hierarchical structure. In the first level two parts are differentiated, then each part has two components and each component is made up of domains and then categories. As is shown in Table 3, the two parts are: a) functioning and disability and b) contextual factors. The first part contains two components: body functions and structures (changes in body function and body structure), and activities and participation (capacity and performance), it measures what a person with a specific health condition can do in a standard environment and what they can actually do in their usual environment. The components of the second part are environmental factors (barriers and facilitators) and personal factors. Environmental factors include social norms, cultural and political factors, among others, whereas personal factors refer to characteristics of the individual such as gender, age, education, other health conditions, coping style and social background, among others. Therefore, the

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<sup>72</sup> World Health Organisation. ICF Introduction. Accessed on February 2005. URL: [www3.who.int/icf/intros/ICF-Eng-Intro.pdf](http://www3.who.int/icf/intros/ICF-Eng-Intro.pdf).



person's functioning and disability comes from the interaction between health conditions and contextual factors, therefore disability may be caused by a health condition or an existing disability may change a health condition.

Table 3: ICF overview.

	<b>Part 1: Functioning and Disability</b>		<b>Part 2: Contextual Factors</b>	
Components	body functions and structures	activities and participation	environmental factors	personal factors
Domains	body functions body structures	Life areas (tasks, actions)	external influences on functioning and disability	internal influences on functioning and disability
Constructs	change in body functions (physiological)  change in body structures (anatomical)	Capacity executing tasks in a standard environment Performance executing tasks in a current environment	Facilitating or hindering impact of features of the physical, social and attitudinal world	Impact of attributes of the person
Positive aspect	functional and structural integrity	activities participation	facilitators	not applicable
	functioning			
Negative aspect	impairment	activity limitation participation restriction	barriers/hindrances	not applicable
	disability			

Source: Adapted from 'ICF introduction'.

In Table 4, it is compared Verbrugge and Jette's disablement model and the ICF model: whereas pathology and impairment correspond to body function and structures in the ICF model, functional limitations and disability correspond to activities and participation.

Table 4: The disablement model and the International Classification of Functioning, Disability and Health model (ICF).

	<b>Anatomical body parts</b>	<b>Physiological functions of the body</b>	<b>Task performance</b>	<b>Involvement in life roles</b>
<b>Disablement Model</b>	Pathology	Impairment	Functional Limitations	Disability
	Disease, injury, congenital condition	Dysfunctions and structural abnormalities	Restrictions in basic physical and mental actions	The expression of a physical or mental limitation in a social context
<b>ICF</b>	Body Functions and Structures		Activities and Participation	
	Physiological functions of body systems and anatomical parts of body		Activity: execution of a task or action Participation: involvement in a life situation	

Source: Adapted from Jette A.M. and Keysor J.J.<sup>73</sup>

The disablement model of L.M. Verbrugge and A.M. Jette has been used as a conceptual frame in this work. Although the ICF model has implied a significant step further as a classification tool, the disablement model is more useful for disability research in the elderly population. In the epidemiological studies, it facilitates distinguishing and studying the different factors that contribute to the development of disability.

### 1.2.2. Measures of disability

Disability is typically assessed by means of self-reported measures that evaluate the ability to perform a set of tasks needed to maintain one's lifestyle in order to live independently<sup>74</sup>. These tasks are known as 'activities of daily living' (ADLs) classified in: basic (BADLs<sup>75</sup>) developed by S. Katz and colleagues in

<sup>73</sup> Jette A.M. and Keysor J.J. Disability models: implications for arthritis exercise and physical activity interventions. *Arthritis Rheum* 2003; 49:114-20.

<sup>74</sup> Verbrugge L.M. and Jette A.M. The disablement process. *Soc Sci Med* 1994;38:1-14.

<sup>75</sup> They are also called physical activities of daily living (PADLs).

1963<sup>76</sup> and instrumental activities (IADLs) developed by M.P. Lawton and E.M. Browdy in 1969<sup>77</sup>. The BADLs refer to everyday life tasks of personal care, whereas IADLs refer to more complex tasks needed to live in the community. S. Katz highlighted that the loss of function takes place in a specific order so the ability to perform the most complex activities are lost first, which are also the last acquired in the learning process due to their difficulty. Besides these two measures, disability can also be assessed through mobility performance, objective measures that evaluate standardized tasks, such as standing balance, walking distances, climbing stairs, and chair stand tests, among others by means of counting repetitions or timing the task.

Measures of disability such as ADLs are important because they provide an appraisal of the burden caused by suboptimal health by taking into consideration other factors (e.g., underlying diseases, psychological and social factors). Moreover, in the elderly population, impairment in ADLs has been found to be predictor of all-cause mortality<sup>78</sup>, institutionalisation<sup>79</sup>, nursing home

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<sup>76</sup> Katz S., Ford A.B., Moskowitz R.W., Jackson B. and Jaffe M.W. Studies of illness in the aged. The Index of ADL: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 1963;185:914-9;

Katz S. Assessing self-maintenance: activities of daily living, mobility and instrumental activities of daily living. *J Am Geriatr Soc* 1983;31:721-6.

<sup>77</sup> Lawton M.P. and Browdy E.M. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9:179-89.

<sup>78</sup> Scott W.K., Macera C.A., Cornman C.B. and Sharpe P.A. Functional health status as a predictor of mortality in men and women over 65. *J Clin Epidemiol* 1997;50:291-6; Mor V., Wilcox V., Rakowski W. and Hiris J. Functional transitions among the elderly: patterns, predictors, and related hospital use. *Am J Public Health* 1994;84:1274-80; Ruigómez A., Alonso J. and Antó J.M. Functional capacity and five-year mortality in a sample of urban community elderly. *Eur J Public Health* 1993;3:165-71; Pijls L.T., Feskens E.J. and Kromhout D. Self-rated health, mortality, and chronic diseases in elderly men. The Zutphen Study, 1985-1990. *Am J Epidemiol* 1993;138:840-8; Manton K.G. A longitudinal study of functional change and mortality in the United States. *J Gerontol* 1988;43:S153-S161; Wolinsky F.D., Callahan C.M., Fitzgerald J.F. and Johnson R. Changes in functional status and the

placement<sup>80</sup>, increase the use of hospital services<sup>81</sup> and associated to higher costs<sup>82</sup>, and be used as eligibility criteria for long-term care in the States<sup>83</sup>. However, ADL measures in elderly research to improve in some areas such as: a) the number of activities considered differ across studies creating difficulties in comparing their findings, and b) the validity of these measures in different cultural settings beyond industrialised countries needs to be more thoroughly evaluated.

### 1.2.3. Evolution of disability

There is some degree of variability among elderly people in the evolution of disability. The average pattern is defined by a considerable proportion of elderly persons who are able to live with a good functional ability during several years, whereas some elderly people experience a functional decline over time, and a small proportion of elderly people recover from disability over time<sup>84</sup>. This

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risks of subsequent nursing home placement and death. *J Gerontol B Psychol Sci Soc Sci* 1993;48:S93-S101.

<sup>79</sup> Mor V., Wilcox V., Rakowski W. and Hiris J. Functional transitions among the elderly: patterns, predictors, and related hospital use. *Am J Public Health* 1994;84:1274-80.

<sup>80</sup> Wolinsky F.D., Callahan C.M., Fitzgerald J.F. and Johnson R.J. Changes in functional status and the risks of subsequent nursing home placement and death. *J Gerontol B Psychol Sci Soc Sci* 1993;48:S93-S101.

<sup>81</sup> Ferrucci L., Guralnik J.M., Pahor M, Corti M.C. and Havlik R.J. *JAMA* 1997;227:728-34.

<sup>82</sup> Mor V., Wilcox V., Rakowski W. and Hiris J. Functional transitions among the elderly: patterns, predictors, and related hospital use. *Am J Public Health* 1994;84:1274-80.

<sup>83</sup> Spector W.D. and Fleishman J.A. Combining activities of daily living with instrumental activities of daily living to measure functional disability. *J Gerontol B Psychol Sci Soc Sci* 1998; 53:S46-57; Stone R.I. and Murtaugh C.M. The elderly population with chronic functional disability: implications for home care eligibility. *Gerontologist* 1990;30:491-6.

<sup>84</sup> Fried L.P and Guralnik J.M. Disability in older adults: evidence regarding significance, etiology and risk. *J Am Geriatr Soc* 1997 ;45:92-100.

evolution may be altered by social, environmental and behavioural factors, such as vigorous running that slows the development of disability<sup>85</sup>.

#### 1.2.4. Risk factors of disability

The risk factors can be categorised into two groups: non-modifiable and modifiable factors. Among the non-modifiable risk factors, chronological age is the foremost factor causing disability, increasing the prevalence of disability with advancing age. J.M. Guralnik et al.<sup>86</sup> reported that each 10 year increase of age has an impact on augmenting by about 2.0 the relative risk of functional status decline. The importance of age relies also on the confounding role that it plays with other risk factors of functional decline<sup>87</sup>. Moreover, heterogeneity in the relationship between disability and age has been found. Indeed, E. von Strauss et al.<sup>88</sup> proposed to stratify the elderly population into age groups to account for this variability because they reflect diverse severity levels of functional capacity. The female sex has been consistently found to be associated with highest rates of disability (see section 1.2.5).

Among the modifiable risk factors, those which are behavioural may be differentiated from those that are not. The first include: a) nutritional habits with an excess fat intake contributing to premature death at middle age and

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<sup>85</sup> Fries J.M., Singh G., Morfeld D., Hubert H.B., Lane N.E. and Brown B.W. Running and the development of disability with age. *Ann Intern Med* 1994;121:502-9.

<sup>86</sup> Guralnik J.M., LaCroix A.Z., Abbott R.D., Berkman L.F., Satterfield S., Evans D.A. and Wallace R.B. Maintaining mobility in late life I. Demographic characteristics and chronic conditions. *Am J Epidemiol* 1993;137:845-57.

<sup>87</sup> Avlund K. Disability in old age. *Danish Medical Bulletin* 2004;51:315-49.

<sup>88</sup> von Strauss E., Agüero-Torres H., Kåreholt I., Winbland B. and Fratiglioni L. Women are more disabled in basic activities of daily living than men only in very advanced ages: a study on disability, morbidity, and mortality from the Kungsholmen project. *J Clin Epidemiol* 2003;56:669-77.

mortality and disability among survivors at older ages<sup>89,90</sup>; b) underweight and overweight people have been associated to be at higher risk of disability than those of normal weight; c) no alcohol consumption compared to moderate use; d) lack of physical activity is associated with an increase in the prevalence of disability, whereas physical exercise has been shown to reduce the risk of losing mobility<sup>91</sup>; and e) tobacco is a preventable cause of disability since many health problems associated with smoking may cause disability such as respiratory disorders (lung cancer and chronic obstructive pulmonary disease), circulatory (stroke), and cardiovascular diseases<sup>92</sup> (heart attacks), among others. Findings from the cohort studied in this thesis also support the benefits of stopping smoking for heart and respiratory health problems. However, the lack of statistical differences in the disability prevalence observed between the smoking status groups was explained by the fact that smokers were somewhat healthier than expected due to survival bias (see supporting paper 1). W.J. Nusselder et al.<sup>93</sup> concluded that by eliminating smoking, the length of disability-free lifetime will be extended and disability will be compressed into a shorter period. They found that non-smokers spent fewer years with disability than the mixed smoking-non-smoking population. Non-smokers were exposed to disability over a longer period because of lower mortality rates; however, their length of

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<sup>89</sup> Cutler D.M. The reduction of disability among the elderly. *Proc Natl Acad Sci* 2001;98:6546-7.

<sup>90</sup> Guralnik J.M. and Kaplan G.A. Predictors of healthy aging: prospective evidence from the Alameda County study. *Am J Public Health* 1989;79:703-8.

<sup>91</sup> LaCroix A.Z., Guralnik J., Berkman L.F., Wallace R.B. and Satterfield S. Maintaining mobility in late life II. Smoking, alcohol consumption, physical activity and body mass index. *Am J Epidemiol* 1993;137:858-69.

<sup>92</sup> Larson M.G. Assessment of cardiovascular risk factors in the elderly: the Framingham heart study. *Stat Med* 1995;14:1745-56.

<sup>93</sup> Nusselder W.J., Looman C.W.N., Marang-van de Mheen P.J., van de Mheen H. and Mackenbach J.P. Smoking and the compression of comorbidity. *J Epidemiol Community Health* 2000;54:566-74.

disability-free lifetime is longer due to their capacity to keep a good health status and to recover from health losses.

Among the non-behavioural factors, characteristics of the environment, low social contacts<sup>94</sup> and poor self-perceived health have been also associated with an increase of disability in some studies.

In addition, a number of chronic conditions have been found to be associated with disability: arthritis, hip fracture, cardiopulmonary conditions (heart disease and chronic obstructive pulmonary disease), stroke, diabetes, visual impairment, low cognitive performance, musculoskeletal conditions, and high depressive symptoms<sup>95</sup>. Among them, arthritis has the highest population impact due to its high prevalence in the population. It is important to stress that the co-existence of more than one chronic condition put people at greater risk of disability.

The World Health Organisation, based on the review performed by A.B. Stuck and colleagues<sup>96</sup>, generated a summary table of modifiable risk factors of disability, indicating their relevance at population level (see table 5).

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<sup>94</sup> Avlund K. Disability in old age. Danish Medical Bulletin 2004;51:315-49; World Health Organisation. Men ageing and health. Achieving health across the life span. Geneva 2001.

<sup>95</sup> Fried L.P and Guralnik J.M. Disability in older adults: evidence regarding significance, etiology and risk. J Am GeriatrSoc 1997 ;45:92-100. Wray L.A. and Blaum C.S. Explaining the role of sex on disability: a population-based study. Gerontologist 2001;41:499-510.

<sup>96</sup> Stuck A.E., Walthert J.M., Nikolaus T., Büla C.J., Hohmann C. and Beck J.C. Risks factors for functional status decline in community-living elderly people: a systematic literature review. Soc Sci Med 1999;48:445-69.

Table 5: Modifiable risks factors for disability in elderly people.

Factor	Risk for disability confirmed?	Importance of risk factor at population level?	Effect on disability confirmed through intervention or other evidence
Cognitive impairment	+++	++	0
Depression	+++	++	0
Disease burden	+++	+++	++
Increased and decreased body mass index	++	++	0
Lower extremity functional limitations	+++	++	++
Low frequency of social contacts	+	++	+
Low level of physical activity	+++	++	+++
No alcohol use compared to moderate use	+	++	?
Poor self-perceived health	++	++	0
Smoking	+++	++	+
Vision impairment	+++	++	+

Source: Adapted from WHO.<sup>97</sup>, based on work by Stuck A.E. et al. in 1999.

+, ++, +++: the level of reliability; 0: the question has not been studied thoroughly; ?:the scientific evidence is contradictory.

### 1.2.5. Gender differences

The prevalence of disability is consistently higher among women than men at all ages in this stratum of the population. This gap between men and women is well substantiated in literature. Several factors have been suggested to explain this gender difference. First, the morbidity pattern differs by sex: women experience more nonfatal but disabling diseases (e.g., osteoarthritis of the knee) while men suffer from lethal diseases in the short term (e.g., heart attack)<sup>98</sup>. A.B. Newman

<sup>97</sup> World Health Organisation. What are the main factors for disability in old age and how can be disability prevented? 2003.

<sup>98</sup> Ettinger W.H., Fried L.P., Harris T., Shemanski L., Schulz R. and Robbins J. Self-reported causes of physical disability in older people: the Cardiovascular Health Study. CHS Collaborative Research Group. J Am Geriatr Soc 1994; 42:1035-44.



and J.S. Branch<sup>99</sup> reviewed the most relevant diseases causing differences in gender disability. Among nonfatal diseases, arthritis (knee and generalized osteoarthritis), depression, dementia, falls, body composition (higher percentage of body fat in women) are more common in women than in men. Among fatal diseases, cardiovascular diseases, and stroke are more prevalent in men; however, they do not contribute substantially to the gender differences in disability because the cardiovascular diseases gap become smaller with increasing age, and strokes account for a small proportion of disability. With respect to heart disease and chronic obstructive pulmonary disease, the authors relied on the aforementioned study of W.H. Ettinger et al. where heart disease was more often reported as cause of disability in women and chronic obstructive pulmonary disease in men. Beyond this issue, it should be stressed that women tend to experience medical comorbidity more often than men do. This fact also leads to a greater percentage of disabled women because of the positive correlation between the number of chronic conditions and disability, as well as the synergy of the combination of certain chronic conditions that causes an excess of disability compared to the sum of their effects alone.

Second, life expectancy is consistently higher for women than men and, as a consequence, women spend more time disabled than men do. Also, women are more likely to become disabled since disability increases with age. Third, recent studies conclude that disability incidence is higher among women<sup>100,101</sup>, although

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<sup>99</sup> Newman A.B. and Branch J.S. Gender gap in longevity and disability in older persons. *Epidemiol Rev* 2001;23:343-51.

<sup>100</sup> Leveille S.G., Penninx B.W.J.H., Melzer D., Izmirlian G. and Guralnik J.M. Sex differences in the prevalence of mobility disability in old age: the dynamics of incidence, recovery, and mortality. *J Gerontol B Psychol Sci Soc Sci* 2000;55:S41-S50.

<sup>101</sup> Dunlop D.D., Hughes D.S.W. and Manheim L.M. Disability in activities of daily living: patterns of change and a hierarchy of disability. *Am J Public Health* 1997;87:378-83.

not the age of onset of disability, that was found to be similar for both men and women<sup>102</sup>. S.G. Leveille et al. (2000)<sup>103</sup> addressed the uncertainty of gender differences in the prevalence of disability by examining the role of disability incidence, recovery from disability and mortality. It was found that disability incidence played a key role showing the largest contribution to the gender differences among the three factors. This result contradicts previous findings showing that mortality explains the highest disability prevalence among women rather than disability incidence. The two remaining factors were also related to disability prevalence but to a lower extent. Indeed, recovery from disability is only relevant after age 80. Fourth, it has also been suggested that women are less likely to recover from disability<sup>104</sup>.

Fifth, gender differences may be partially related to the measures used to assess disability. It has been observed that the gender gap is usually more likely in mobility activities or IADLs than in BADLs<sup>105</sup>. Among other plausible explanations this may be due to the fact that women are at greater risk of mobility loss related to age-associated strength declines. L.A. Wray and C.S. Blaum (2001)<sup>106</sup> also suggested that the relationship between gender and disability depends on the evaluation tool. While chronic conditions and

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<sup>102</sup> Ferrucci L., Turchi A., Fumagalli S., Di Bari M., Silvestrini G., Zacchei S., Nesti A., Magherini L., Tarantini F., Pini R., Antonini E., Masotti G. and Marchionni N. Sex-related differences in the length of disability prior to death in older persons. *Aging Clin Exp Res* 2003;15:310-4.

<sup>103</sup> Leveille S.G., Penninx B.W.J.H., Melzer D., Izmirlian G. and Guralnik J.M. Sex differences in the prevalence of mobility disability in old age: the dynamics of incidence, recovery, and mortality. *J Gerontol B Psychol Sci Soc Sci* 2000;55:S41-S50.

<sup>104</sup> Oman D., Reed D. and Ferrara A. Do elderly women have more physical disability than men do? *Am J Epidemiol* 1999;150:834-42.

<sup>105</sup> Beckett L.A., Brock D.B., Lemke J.H., Mendes de Leon C.F., Guralnik J.M., Fillenbaum G.G., Branch L.G., Wetle T.T. and Evans D.A. Analysis of change in self-reported physical function among older persons in four population studies. *Am J Epidemiol* 1996;143:766-78.

sociodemographic variables largely explained the association of gender and ADL difficulties, these variables could not explain the relationship of gender with mobility and strength difficulties. Moreover, different interactions with gender were found depending on the measure, as well as the magnitude of such interaction and the main factors involved. For ADL difficulties, the interactions with gender were musculoskeletal conditions (aOR<sup>107</sup>=1.46) and depressive symptoms (aOR=0.68). For difficulties in mobility activities, there was a joint effect of gender and musculoskeletal (aOR=1.40) conditions and body mass index (aOR=1.57). For difficulties with strength activities, there was only one interaction: gender and body mass index (aOR=1.38).

Finally, gender differences in disability prevalence have been attributed to inaccurate reporting by women, who tend to overreport symptoms due to their greater perception of physical discomfort. However, the latter hypothesis is under discussion since available studies that carried out a comparison between self-reported function of activities of daily living and performance of physical tasks showed an agreement between both measures<sup>108,109,110</sup>, concluding that there are no gender differences in the reporting of disability. One of these studies used data from the same cohort HISB that the present thesis, and supported the validity of the selected activities of daily living (see supporting paper 2).

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<sup>106</sup> Wray L.A. and Blaum C.S. Explaining the role of sex on disability: a population-based study. *Gerontologist* 2001;41:499-510.

<sup>107</sup> aOR stands for adjusted odds ratio.

<sup>108</sup> Ferrer M., Lamarca R., Orfila F. and Alonso J. Comparison of performance-based and self-rated functional capacity in Spanish elderly. *Am J Epidemiol* 1999;149:228-35.

<sup>109</sup> Merrill S.S., Seeman T.E., Kasl S.V. and Berkman L.F. Gender differences in the comparison of self-reported disability and performance measures. *J Gerontol A Biol Sci Med Sci* 1997;52:M19-M26.

<sup>110</sup> Kelly-Hayes M., Jette A.M., Wolf P.A. and Odell P.M. Functional limitations and disability among elders in the Framingham Study. *Am J Public Health* 1992;82:841-5.



## **CHAPTER 2**

# **JUSTIFICATION**



## 2. Justification

The population of Spain, as an industrialized country, is ageing significantly and the number of octogenarians is increasing. The increase in the number of elderly people will probably bring with it an increase of old people with disabilities in absolute numbers, irrespectively of the theory of population health change that will be valid. Consequently, this stratum of the population will generate new needs for healthcare as well as a rise in the consumption of resources already in place, since disability is associated with institutionalisation, an increase of the use of hospital services and of premature death, among others. To ascertain those needs and to allocate the available resources efficiently, the policy makers require information about disability among the elderly population. In particular, knowledge about gender differences in the impact of disability on mortality. Differences in health between elderly men and women are a consistent finding in numerous studies. Women report more morbidity, are more likely to suffer from non-lethal but disabling diseases, show higher rates of disability and lower mortality rates. It has been suggested that men's health is strongly related with their social role, that is, the way that men are expected to behave which determines the male perception of health and their own features such as less contact with the health care system<sup>111</sup> and a lack of ability to built social networks and family ties<sup>112</sup>. However, the extent to which disability and mortality interrelate as people age needs to be fully explored in both men and women. The hypothesis is that there will be a gender

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<sup>111</sup> Verbrugge L.M. Women and men: mortality and health of older people. In: Aging in society: selected reviews of recent research. Hillsdale, N.J., Erlbaum, 1983.

<sup>112</sup> World Health Organisation. Men ageing and health. Achieving health across the life span. Geneva 2001.

difference in the relationship between disability and mortality<sup>113</sup>. Specifically, the impact of disability on mortality is expected to be greater for women than men, because the male population is a selected one composed of survivors; fragile individuals die at early ages due to lethal diseases, such as coronary heart disease, cardiovascular diseases and lung cancer, among others.

The statistical methodology applied to studies of the elderly should also be reviewed and improved whenever possible. The answer to these questions is becoming more urgent because the increase in the number of elderly people has been notable in the last decade and the advantage in absolute number of women increases with age. Thus, it is crucial to be aware if there is any gender difference, since a population imbalance in favour of women exists.

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<sup>113</sup> This hypothesis needs to be revisited for future cohorts evaluating the impact of the change of some behavioural risk factors in women population, which may contribute to decrease the gender gap. For example, the increase in the prevalence of smoking among middle-aged women is currently contributing to a raise of related diseases, such as cancer and chronic pulmonary obstructive disease.



## **CHAPTER 3**

# **OBJECTIVES**



### **3. Objectives**

The objectives of this thesis are both methodological and substantive. The primary objectives are to:

- *Improve the estimation of the relationship between disability and mortality by using age as time scale in the survival analyses for studies of the elderly population.*
- *Model the survival probability in the elderly by using the disability life history and risk factors and to investigate whether or not there are differences by sexes in this model.*

As a secondary objective supporting the above main objectives:

- *Describe the evolution of the disability prevalence over an 8 year period.*



# **CHAPTER 4**

# **METHODS**



## 4. Methods

### 4.1. Study design

Data comes from the Health Interview Survey of Barcelona (HISB) in 1986<sup>114,115</sup>, a cross-sectional study of residents in Barcelona city with 6,894 participants. With the purpose of evaluating the health of elderly people, an oversample of non-institutionalised subjects equal or older than 65 years old was performed<sup>116</sup> to obtain a representative sample of non-institutionalised elderly population living in Barcelona. They were first interviewed to assess their health status (wave 1), and were then followed up to evaluate the evolution of the health status and the relationship between baseline factors and the development of new conditions and mortality (wave 2). The present work is based on waves 1 and 2 of the sample of elderly people.

The sampling frame was derived from the update of the 1981 Local Census Register of Barcelona at October 1<sup>st</sup> 1985. A non-proportional stratified random sample in two stages (district and size of the family) was conducted. The household<sup>117</sup> was defined as the primary sampling unit, and the secondary unit was all the individuals aged 65 or over that were registered in the 3,062 selected households.

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<sup>114</sup> Alonso J. and Antó J.M. *Enquesta de Salut de Barcelona 1986*, Barcelona: Ajuntament de Barcelona, Àrea de Salut Pública, 1989.

<sup>115</sup> The first edition of the Health Interview Survey of Barcelona in 1983 was the first Health Interview carried out in Spain (Antó J.M., Company A. and Domingo A. *Enquesta de Salut de Barcelona*, Barcelona: Ajuntament de Barcelona, Subàrea de Salut Pública, 1985). Followed two years later by the first national health interview named 'Encuesta Nacional de Salud' (ENS-1).

<sup>116</sup> An individual was considered as institutionalized if he/she was living in a nursing home, pension, hotel, hospital or any other centre beyond the household.

<sup>117</sup> A household was defined as a set of individuals who live in the same home and have a common home economy.

A sample size of 1,632 individuals, 1,100 coming from the original sample and 522 from the oversampling, comprised the first wave. It represented a 6.5‰ of the total population aged 65 or over of Barcelona. The sample size was calculated assuming that the expected proportion of elderly subjects needing help in bathing was 0.7%.

In wave 1, participants filled the general HISB questionnaire and received a supplementary questionnaire to gather specific information about chronic conditions, visual impairment, hearing disorders, dental status, basic and instrumental activities of daily living, devices used such as wheelchairs, contacts with relatives, pensions and services use.

In wave 2, the members of the study group were interviewed face to face by trained health personnel at their homes. They provided different information depending on the following scenarios:

A) Individuals who were alive at the time of the re-assessment

- Individuals willing to participate:
  - A cognitive evaluation through the Mini-Mental State Examination.
  - A standard questionnaire: sociodemographic data (including social and relative contacts), self-perceived health status, physical activity, tobacco, alcohol consumption, morbidity, health services use, visual impairment, hearing disorders, dental status, mobility, basic and instrumental activities of daily living, incontinence, devices use, social services use, and pensions.
  - A standardised physical examination (static equilibrium, walking speed test walking over a course of 4 meters, chair stand test,



ophthalmologic test, weight and height, additional anthropometrical measures, and dental examination).

- Two quality of life questionnaires (the Nottingham Health Profile and the Medical Outcome Study).
  
- Individuals Institutionalised at the time of the second interview:
  - A shortened version of the standard questionnaire including: sociodemographic data, tobacco, alcohol consumption, chronic conditions, institutionalisations, visual impairment, hearing disorders, dental status, basic and instrumental activities of daily living, and incontinence.
  - One quality of life questionnaire (the Medical Outcome Study).
  
- Individuals who refused to participate to the interview:
  - A shortened version of the standard questionnaire collecting key data on self-perceived health status, tobacco, chronic conditions, basic and instrumental activities of daily living, number of physician visits, hospital admissions and institutionalisations, and devices use.

#### B) Deceased Individuals

- A proxy interview was carried out gathering information on basic and instrumental activities of daily living, living arrangements with relatives before dying, institutionalisations, incontinency, and devices use.

Vital status on October 30<sup>th</sup> 1994 was ascertained by a confidential linkage with the Regional Mortality Register of the 'Generalitat de Catalunya'. An additional search was conducted for those subjects not traced by means of linkage with the Local Census Register of Barcelona. For a small number of subjects who were not traced after the two linkages, a telephone contact was carried out.

#### 4.1.1. Disability

In the present study, the self-reported disability indicators come from an adaptation of the Supplement of Aging (SOA) integrated in the 1984 National Health Interview Survey<sup>118</sup>. It was measured on ten BADLs and four IADLs. The BADLs were: *walking, brushing hair/shaving, sitting, bathing, using the toilet, dressing, eating, going up/down stairs, cutting their toenails, and going outside*; whereas the IADLs were: *cooking their own meals, managing money, using the telephone, and shopping*. Individuals were asked about their difficulty in carrying out each activity of daily living (none, a little, moderate and unable to perform without help). Overall measures for BADLs and IADLs, respectively, were derived by combining the responses of the corresponding activities as: "Independent" if they were able to perform all the activities without difficulty, "With difficulty" if they reported to have little or moderate difficulties in any of the activities, and "Dependent" if they were unable to perform at least one activity without assistance.

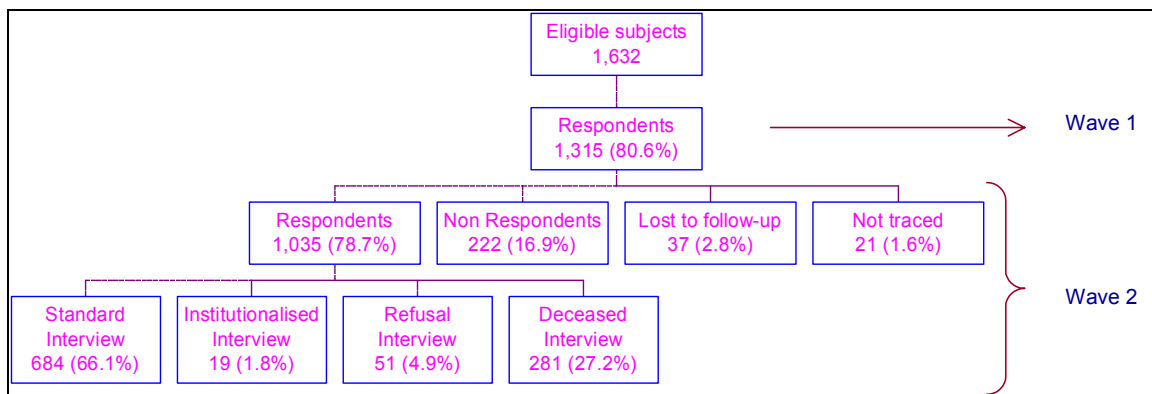
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<sup>118</sup> Fitty J.E. and Kovar M.G. The Supplement of Aging to the 1984 National Health Interview Survey. National Center for Health Statistics. Vital and Health Statistics. Series 1 No 21 DHHS Publ No (PHS) 87-1323. Public Health Service. Washington: U.S. Government Printing Office.

#### 4.2. Data collection

Figure 11 shows the participation in the survey in each wave. Baseline interviews were completed for 1,315 individuals between January 1986 and January 1987, representing 80.6 percent of the subjects comprising the sample. The second wave of the survey took place between June 1993 and June 1994. Information was collected from 1,035 (78.7%) subjects or proxies. Among these, 684 underwent the standard interviewed, 19 the institutionalised interview, 51 the refusal interview, and 281 the deceased interview. A total of 382 interviews were answered by proxies, 101 corresponding to living participants and 281 to deceased participants during the follow-up period. Around 20 percent of the subjects were not interviewed, 37 were lost to follow-up due to emigration, and 21 of them had been lost immediately after baseline interview.

Figure 11: Participation into the survey (waves 1 and 2).



With respect to the vital status at the closing date, 842 were alive, 452 had died and 21 could not be traced. Twenty-nine deceased cases came from living subjects successfully interviewed at the time of the second wave. The mortality rate after 8-years of follow-up was higher for men (41.8%) than women (30.6%). Comparisons between the mortality experience of the cohort and the

entire elderly population of Barcelona were performed to ensure the validity of the results. To do so, standard mortality ratios (SMR) were calculated by age and gender groups. The expected survival probabilities were computed using the population mortality rates by gender and age categories provided by the ‘Institut Municipal de la Salut’. No deviations from the population were observed supporting that no bias in the gathered data may limit the validity of the findings.

### **4.3. Statistical methods**

#### 4.3.1. Multiple Correspondence Analysis

A Multiple Correspondence Analysis was carried out to ascertain the underlying structure of the ADLs as well as the existing relationships between ADLs and a set of illustrative variables. This multivariate method produces geometric representations that enable us to understand intuitively the behaviour of the variables.

This approach reduces the dimensionality of the data matrix in subspaces, in such a way that they are interpretable and retain the maximum information of the initial data. To do so, algebra developments are performed on the initial data matrix that is transformed into a symmetric matrix, which minimise the overlapping of the projected points on the factorial axes of the geometric representations. The data matrix is defined by subjects (rows) and variables (columns); whereas the symmetric matrix is a matrix of distances between the categories of the variables. The latter matrix is used to get the eigenvalues that will define the number of significant factorial axes, and the eigenvectors that will define the projections of the categories of each variable and the subjects on

the selected axes. In our case, the factorial axes were defined by the BADLs and IADLs. In the resulting graphical representations of the factorial axis, the projected categories of each variable represent gravity centres corresponding to the average behaviour of the individuals with such characteristic.

#### 4.3.2. Survival analysis

The survival analysis to study the time exposed to the ageing process was based on the counting process theory, where 65 years old was chosen as the time origin and chronological age as the time scale. This approach permits dealing with left-truncated data and time-dependent variables. The Nelson-Aalen estimator of the cumulative hazard function and an extension of Cox's proportional hazards model were used. Plots of the hazard function were smoothed by the Kernel method<sup>119</sup> using a bandwidth of 6 years to display the instantaneous risk of dying at any age.

##### 4.3.2.1. *Left-truncated data*

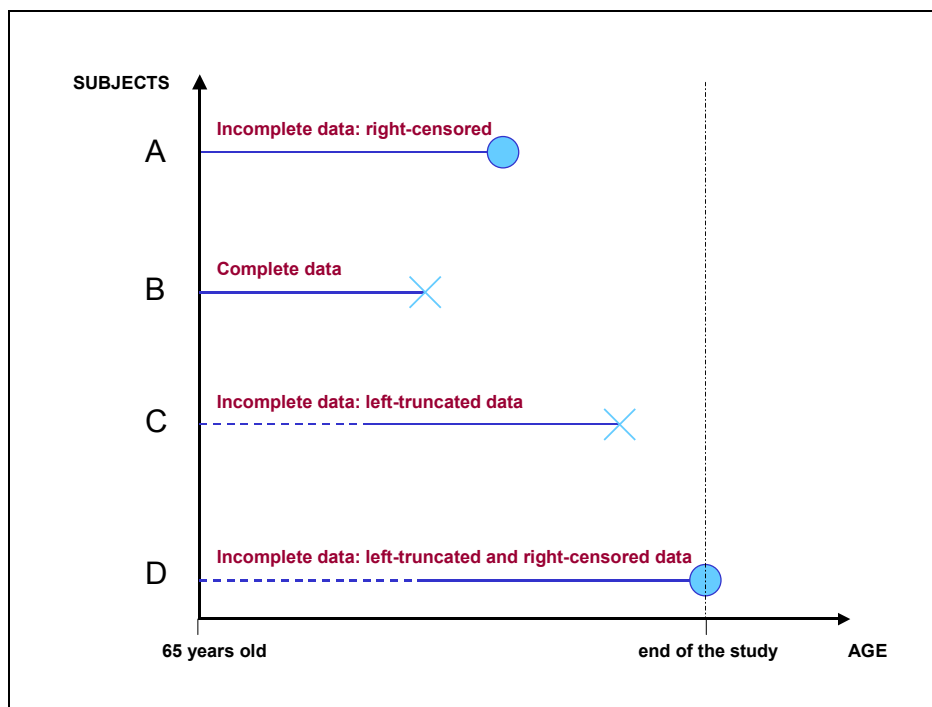
In this cohort, a substantial number of subjects provided partial information on mortality data due to a random left-truncation process and/or a right-censored process. The first process is less common and it is characterised by entering late into the study, thus once the origin time point has already occurred. As a consequence, a period of time exists, from the origin time to the real time of entering the study, where there is no information available. In this case, it will be subjects older than 65 years old, such as subjects C and D depicted in figure 12. This is noteworthy, because it implies that the survival estimates will be biased since we ignore those subjects who have not survived long enough to be

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<sup>119</sup> Hess K.R., Serachitopol D.M. and Brown B.W. Hazard function estimators: a simulation study. *Stat in Med* 1999;18:3075-88.

under observation, as a result the sample is incomplete; moreover, those survivors with longer survival times are more likely to be included in the sample<sup>120</sup>. In the present cohort, we refer to those elderly subjects who died before 1986 and they were then not included in the cohort, so the risk of dying is underestimated since we are omitting these subjects at higher risk.

Figure 12: Left-truncated data.



O: alive or lost to follow-up, and X: died during the follow-up.

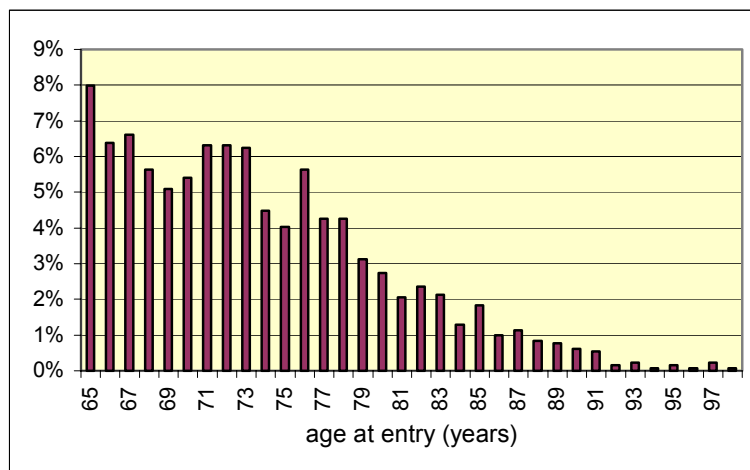
It is essential to know the length of time that the subject has been exposed to the ageing process without being under observation in order to do the appropriate corrections. In the present cohort it is straightforward because it depends on the age at entry, and this information was collected in the interview. Therefore, the

<sup>120</sup> Guo G. Event-history analysis for left-truncated data. *Sociol Methodol* 1993;23:213-33; Hoover D.R., Muñoz A., Carey V., Odaka N., Taylor J.M., Chmiel J.S., Armstrong J. and Vermund S.H. The unseen sample in cohort studies: estimation of its size and effect. *Multicenter AIDS Cohort Study. Stat Med* 1991;10:1993-2003.

length of time will be the gap between the age at entry and 65 years old<sup>121</sup>. The correction is to consider the subject at risk upon entry into the study and not before, and the bias of not observing those individuals who have not survived long enough is overcome. In addition, the subject's covariates are considered at the time they enter into the study, thus when they were assessed and not before.

Left-truncation was present in the majority of participants into the HISB, thus the origin time point was observed only in 8 percent of the subjects as it is shown in Figure 13. The age at entry into the study was 73.6 years on average (SD= 6.6 years) with an observed range between 65 and 99 years.

Figure 13: Distribution of age at entry into the study.



<sup>121</sup> Usually, it is not so easy to calculate the length of time that the subject has been exposed to the process of interest and not observed. For example, A. Muñoz et al. split the cohort in two: the incident cohort and the prevalent cohort. The origin time is known for the first but not for the second. They use the first cohort to get estimations that allow them to impute the missing origin time in the subjects that belong to the second cohort. Muñoz A., Carey V., Taylor J.M., Chmiel J.S., Kingsley L., Van Raden M. and Hoover D.R. Estimation of time since exposure for a prevalent cohort. *Stat Med* 1992;11:939-52.

#### 4.3.2.2. *Counting processes in the survival analysis framework*

The relevant results of the counting processes in the survival analysis setting are introduced in this section.

##### 4.3.2.2.1. *The Nelson-Aalen estimator of the cumulative hazard function*

The study of the time to a certain event may be approached through the estimation of the survival function, Kaplan-Meier estimator, or by means of the cumulative hazard function estimation. In the latter case, the existing relationship between both functions,  $\Lambda(t) = -\log S(t)$ , is then used to obtain an estimate of the survival function. The cumulative hazard function is defined from the hazard function  $\lambda(u)$  as follows:

$$\Lambda(t) = \int_0^t \lambda(u) du, \quad \text{where } \lambda(u) \text{ denotes the hazard function.}$$

The interpretation of the cumulative hazard function is quite complex, since it represents the sum of conditional probabilities on different sampling spaces. T.M. Therneau and P.M. Grambsch<sup>122</sup> describe it as the average number of events that would be observed within a time period for a subject perpetually at risk. If the subject dies then he/she is replaced by another subject presenting the same characteristics (equal exposition time and mortality prognostic factors). Nevertheless, it has been shown to be useful for the selection of parametric models. For example, a plot of  $\hat{\Lambda}(t)$  vs.  $t$  showing a linear pattern suggests that the exponential model is plausible to fit the data. It is also utilized to get an estimation of the hazard function  $\lambda(t)$  from its slope, and to verify the proportionality assumption of the Cox's proportional hazards model.

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<sup>122</sup> Therneau T.M. and Grambsch P.M. Modelling survival data. Extending the Cox model. Springer-Verlag: New York, 2000, page 10.



W. Nelson (1972)<sup>123</sup> proposed an estimator of the cumulative risk function that was formulated in the counting process framework by O.O. Aalen in 1978<sup>124</sup>. The latter estimator is known as the Nelson or the Nelson-Aalen estimator and it is defined as:

$$\hat{\Lambda}_{NA}(t) = \begin{cases} 0 & \text{if } t \leq t_1 \\ \sum_{i=1, t_i < t}^n \frac{d(t_i)}{r(t_i)} & \text{if } t > t_1 \end{cases}$$

where  $t_1$  represents the first failure time observed in the sample.

It can be re-written using the counting process notation as:

$$\hat{\Lambda}_{NA}(t) = \int_0^t \frac{d\bar{N}(u)}{\bar{Y}(u)}, \quad \text{where } \bar{Y}(u) = \sum_i Y_i(u) \text{ and } \bar{N}(u) = \sum_i N_i(u)$$

The indicator function  $Y_i(t)$  determines whether or not the subject  $i$  was under observation at time  $t$  ( $\mathbb{I}\{T_i \geq t\}$ ), whereas  $N_i(t)$  is a function that counts the number of failures of the subject  $i$ <sup>125</sup>; whereas the first term of the expression  $d\bar{N}(t) = \Delta\bar{N}(t) + n(t)dt$  denotes the number of events that have occurred up to time  $t$  and the second term defines the continuous part of the change. In this

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<sup>123</sup> Nelson W. Hazard plotting for incomplete failure data. *J Qual Technol* 1968;1:27-52; and Nelson W. Theory and applications of hazard plotting for censored failure. *Technometrics* 1972;14:945-65.

<sup>124</sup> Aalen O.O. Non parametric inference for family of counting process. *Ann Statist* 1978;6:701-26.

<sup>125</sup> The counting process approach is a general framework allowing that a subject may experience more than one event. For example, a subject may suffer several relapses in cancer progression. In the present work, the event of interest is an absorbent state, death; therefore  $N_i(t)$  can only take values 0 or 1.

case, the counting process jumps, hence there is no continuous part, and so  $d\bar{N}(t) = \Delta\bar{N}(t)$ . The Nelson-Aalen estimator can be re-formulated as:

$$\hat{\Lambda}_{NA}(t) = \sum_{i:t_i \leq t} \frac{\Delta\bar{N}(t_i)}{\bar{Y}(t_i)}$$

This expression becomes familiar because it represents the rate between the number of observed events and the number of subjects at risk.

The Nelson-Aalen estimator can be derived from the method of moments and its variance can be estimated consistently as:

$$\text{var}[\hat{\Lambda}_{NA}(t)] = \int_0^t \frac{d\bar{N}(u)}{[\bar{Y}(u)]^2} = \sum_{i:t_i \leq t} \frac{\Delta\bar{N}(t_i)}{\bar{Y}^2(t_i)}$$

Tsiatis developed the above variance estimate, but there are others available such as Greenwood and Klein<sup>126,127</sup>. All of them are based on the fact that the Nelson-Aalen estimator can be interpreted as the independent sum of the following increments  $\Delta\bar{N}(u)/\bar{Y}(u)$ .

The properties of the Nelson-Aalen estimator come from the fact that under certain regularity conditions  $\hat{\Lambda}_{NA}(t) - \Lambda(t)$  it behaves as a martingale<sup>128</sup>. The estimator: a) is uniformly consistent, b) its variance estimator is also uniformly

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<sup>126</sup> S-Plus 6.0 Guide to Statistics, Volume 2, Data analysis division, MathSoft, Seattle WA, page 320.

<sup>127</sup> Properties of the variance estimator of the Nelson-Aalen estimator for small samples can be found in: Klein J.P. Small sample moments of the estimators of the variance of the Kaplan-Meier and Nelson-Aalen estimators. Scandinavian Journal of Statistics 1991;18:333-40.

<sup>128</sup> Therneau T.M. and Grambsch P.M. Modelling survival data: Extending the Cox model, Springer-Verlag: New York, 2000, pp: 26-8.

consistent, and c) converges weakly to a Gaussian process when  $n$  goes to infinity.

Finally, the Fleming-Harrington estimator of the survival function can be derived from the Nelson-Aalen estimator of the cumulative hazard:

$$\hat{S}_{FH}(t_j) = e^{-\hat{\Lambda}_{NA}(t_j)}$$

It is very similar to the Kaplan-Meier when the sample is large enough.

The main reason to start estimating the cumulative hazard function instead of the survival function is its link with the counting processes that allow us to use this formulation. Also, the Nelson-Aalen estimator behaves better than the Kaplan-Meier estimator when dealing with small samples<sup>129</sup>. Nevertheless, the Kaplan-Meier estimator presents advantages over the Nelson-Aalen estimator such as its non sensitivity to tied data<sup>130</sup>; so it is possible to start with it if the problem faced does not require the use of the counting processes formulation. It is interesting to note that the Nelson-Aalen estimator is the first term of Taylor's series development of minus the logarithm of the Kaplan-Meier estimator.

#### 4.3.2.2.2. *The Cox's proportional hazards model*

In 1972 D.R. Cox<sup>131</sup> proposed Cox's model, also known as the proportional hazards model, as well as a new estimation method that later on was named

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<sup>129</sup> Klein J.P. and Moeschberger M.L. Survival analysis. Techniques for censored and truncated data, Springer-Verlag: New-York, 1997, page 86.

<sup>130</sup> A modification of the Nelson-Aalen estimator has been proposed to overcome its sensitivity to ties. It is implemented in S-plus: type="fh2". Fleming T.R. and Harrington D.P. Non parametric estimation of the survival distribution in censored data. Communications in Statistics 1984;13:2469-86.

<sup>131</sup> Cox D.R. Regression models and life tables (with discussion). J Roy Statist Soc B 1972;34:187-220.

maximum partial likelihood. Due to its straightforward interpretation, the effect of a factor comes from the risk (hazard) multiplied by a constant, and the easy manner to incorporate the censoring processes onto the model, Cox's model has become one of the most popular models. It is defined as follows:

$$\lambda_i(t) = \exp(\beta' Z_i) \lambda_0(t)$$

where  $\lambda_0(t)$  denotes the baseline hazard function,  $\beta$  the regression coefficients vector, and  $Z_i$  the covariates vector with values corresponding to the subject  $i$ . It is a semi-parametric model because the baseline hazard function is not specified. It is also important to note that it is not necessary to formulate the model through the exponential function, other functions can be used, and the only condition is that it cannot be negative.

To draw inferences about  $\beta$ , the likelihood function is factorised in two parts, the first depends on the baseline hazard function and beta, whereas the second part only depends on beta. In the shake of simplicity, it is worked only on the section of the likelihood function coming from the second part, that is the partial likelihood function. The estimation of the  $\beta$  parameters is then based on the following partial likelihood function:

$$PL(\beta) = \prod_{i=1}^n \prod_{t \geq 0} \left\{ \frac{Y_i(t) \exp[Z_i(t)\beta]}{\sum_j Y_j(t) \exp[Z_j(t)\beta]} \right\}^{dN_i(t)}$$

The loss of efficiency for not working with the full likelihood function is small (the standard errors are a bit larger than they should be)<sup>132</sup>. The  $\beta$  estimator is consistent being asymptotically normally distributed with mean  $\beta$  and variance  $\{EI(\beta)\}^{-1}$ , where  $I(\beta)$  is the information matrix. Instead of calculating the inverse of the expected information matrix it is computed the inverse of the observed information matrix,  $I^{-1}(\beta)$ , because the first requires knowledge about the distribution of the censoring process, which is usually not available. P.K. Andersen and R.D. Gill (1982) showed the consistency and the asymptotically normal distribution of the beta estimator when the Cox's model was formulated in the counting process framework<sup>133</sup>. In the counting process context, a subject can be represented as an observation coming from a very slow Poisson process. A censored subject is viewed as someone whose counting events indicator is still zero, instead of someone who provides incomplete information<sup>134</sup>.

The Newton-Raphson algorithm is used to find out the maximum of the partial likelihood function because it is robust and it is strange to experience convergence difficulties starting with  $\beta(0)=0$  as initial value.

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<sup>132</sup> Effron B. The efficiency of Cox's likelihood function for censored data. *J Am Stat Assoc* 1977;72:557-65.

<sup>133</sup> Andersen P.K. and Gill R.D. Cox regression model for counting processes: a large sample study. *Ann Statist* 1982;4:1100-20.

<sup>134</sup> Therneau T.M. Extending the Cox model. Technical report number 58. Mayo Foundation 1996, page 3.



# **CHAPTER 5**

# **RESULTS**





## 5. Results

### 5.1. *Sample characteristics*

#### 5.1.1. Baseline data

The sample was compounded mainly by women (61.5%), with a predominant age range of 65 to 74 years (60.5%). Around half of them were married, the majority lived with someone else (80.7%), sixty percent had only studied at primary school level and nearly half of them were from low social class backgrounds<sup>135</sup> (46.8%) (see Table 6). A statistically significant gender differential was observed in the aforementioned sociodemographic variables.

Table 7 presents the health services use and health-related behaviours distribution of men and women in the sample. With respect to the health services use, the average number of doctor's visits was 6.1 (SD=9.9), with no differences between men and women; whereas the percentage of elderly people who had been hospitalised at least once in the past year was 9%, being statistically higher for men. It is remarkable that just a small proportion of respondents smoked (11.8% smokers), mostly due to the low prevalence among women. About two thirds of the sample were of normal weight, the women being more overweight and obese than the men. Nearly 50% of the participants reported having consumed some alcohol over the last year, this figure increased up to 61.5% for men. The majority of the subjects reported sleeping between 7 and 9 hours per day with differences between men and women: a quarter of the latter devoted less than 7 hours to the night rest.

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<sup>135</sup> Domingo A. and Marcos J. Propuesta de un indicador de "clase social" basado en la ocupación. Gac Sanit 1989;3:320-6.

Table 6: Sociodemographic characteristics by sex.

	All (n=1,315) %	Men (n=506) %	Women (n=809) %
Sex		38.5	61.5
Age			
65-74 years	60.5	63.6	58.5*
75-84 years	31.9	32.2	31.6
85+ years	7.7	4.2	9.9
Marital status			
Single	7.9	4.5	10.0*
Married	54.4	80.0	38.3
Widowed	35.8	14.0	49.4
Divorced / Separated	1.3	1.0	1.3
Living alone	19.2	8.3	26.0*
Level of education			
High school / University	24.2	35.4	17.1*
Primary school	60.3	56.1	62.9
Unable to read or write	14.2	7.9	18.2
Social Class <sup>†</sup>			
I-II	17.0	19.6	15.3*
III	18.4	26.1	13.6
IV-V	46.8	44.7	48.1

\* Statistical significant differences between men and women ( $p < 0.05$ ).

<sup>†</sup> Social class was based on the occupational labour of the family head: Class I= Professional occupations; Class II= Intermediate occupations; Class III= Skilled non-manual occupations; Class IV= Qualified or Semi-qualified manual occupations; Class V= Non-qualified manual occupations.

Participants reported having a good health status; around 55% reported a 'very good' or 'good' health status, while only 6% of the subjects described their health status as 'poor' or 'very poor'. There were differences in the self-reported health status between men and women ( $p < 0.001$ ), women showing a worst health status (see Figure 14).

Table 7: Health services use and health behaviours by sex.

	All (n=1,315) %	Men (n=506) %	Women (n=809) %
<i>Health services use</i>			
Number of physician visits (last 12 months)	6.1 (9.9)	6.3 (10.7)	6.0 (9.3)
Hospitalised (last 12 months)	9.0	11.3	7.7*
<i>Health-related behaviours</i>			
Body mass index <sup>†</sup>			
Overweight / Obese	19.5	5.5	28.2*
Normal	64.9	76.9	57.5
Underweight	6.0	9.7	3.5
Smoking status			
Smoker	11.8	26.3	2.7*
Former smoker	17.8	42.7	2.2
Never smoker	61.3	21.7	86.0
Physical activity			
Active	38.5	37.7	38.9
Sedentary	50.9	51.0	50.8
Any alcohol consumption (last 12 months)	48.6	61.5	40.5*
Daily hours of sleep			
< 7 hours	22.1	16.0	25.8*
7 to 9 hours	59.3	64.6	56.0
More than 10 hours	11.3	12.3	10.6

\* Statistical significant differences between men and women ( $p < 0.05$ ).

<sup>†</sup> Body mass index is the result of dividing weight (Kg) by height ( $m^2$ ).

Figure 15 shows that comorbidity was more prevalent among women than among men, 74% vs. 63%, respectively ( $p < 0.001$ ). It is important to note that 54% of the women reported to suffer three or more chronic conditions, this percentage being 42% among men.

Figure 14: Self-reported health status by sex.

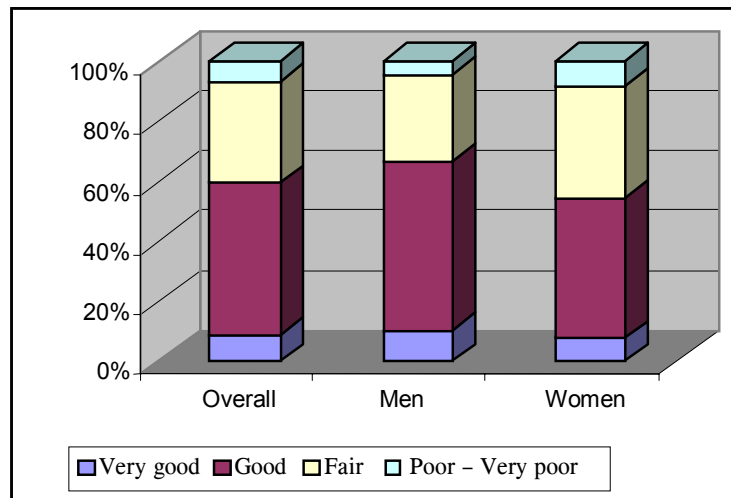


Figure 15: Distribution of the number of chronic conditions by sex.

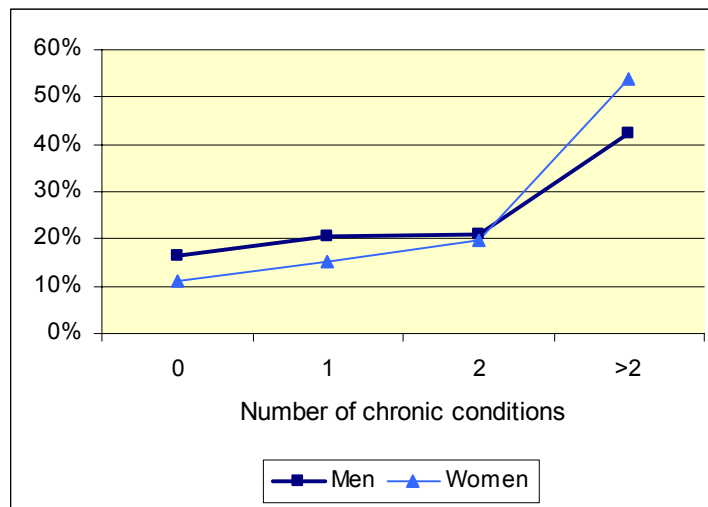


Table 8 displays the ten leading chronic conditions among the participants for the entire sample, men and women. As the number of conditions differed between men and women, the prevalence of specific chronic conditions also varied. In the majority of cases a statistically significant higher prevalence was found in women, except for bronchitis and asthma where the smoking habit plays a key role.

Table 8: Prevalence of the ten leading chronic conditions among participants by sex.

	All (n = 1,315)	Men (n = 506)	Women (n = 809)
Arthritis	51.3	32.2	63.3*
Circulatory disorders	31.4	21.1	37.8*
Hypertension	20.5	17.2	22.6*
Deafness	19.2	20.8	18.3
Varicose veins	16.4	9.1	21.0*
Cataracts	13.9	13.4	14.2
Heart diseases	12.7	12.3	13.0
Back pain	12.1	4.9	16.6*
Bronchitis / Asthma	11.4	16.8	8.0*
Depression	9.4	7.1	10.9*

\* Statistical significant differences between men and women ( $p < 0.05$ ).

### 5.1.2. Follow-up data

Tables 9 and 10 summarize the characteristics of the participants traced at follow-up for their vital status. In both sex groups, survivors and those who died over the follow-up period differed in the distribution of the following variables: age, body mass index, physical activity, and hospitalisation. The oldest subjects showed the highest proportion of deaths. A higher percentage of subjects with low body mass index was found among the deceased subjects. Also, a larger number of sedentary subjects was observed among those deceased, as well as a higher proportion of individuals who had been hospitalised 12 months before the baseline interview.

Table 9: Baseline characteristics according to vital status in 1994, by gender.

	Men		Women	
	Alive (n=291) %	Dead (n=209) %	Alive (n=551) %	Dead (n=243) %
Age				
65-74 years	75.6	46.4*	71.2	30.0*
75-84 years	22.7	45.9	26.1	44.1
85+ years	1.7	7.7	2.7	25.9
Marital status				
Single	3.4	6.2	9.3	11.1*
Married	83.5	75.6	45.6	23.0
Widowed	11.7	17.2	42.8	64.6
Divorced / Separated	1.0	1.0	1.8	0.4
Living alone	8.2	8.7	25.2	27.6
Level of education				
High school / University	33.3	38.3	18.3	14.0
Primary school	57.7	54.5	62.8	64.6
Unable to read or write	8.2	7.2	17.6	19.3
Social class <sup>†</sup>				
I-II	19.6	19.1	15.4	14.8
III	25.8	27.3	14.3	12.3
IV-V	44.7	45.0	49.0	46.5

\* Statistical significant differences between alive and dead groups ( $p < 0.05$ ).

<sup>†</sup> Social class was based on the occupational labour of the family head: Class I= Professional occupations; Class II= Intermediate occupations; Class III= Skilled non-manual occupations; Class IV= Qualified or Semi-qualified manual occupations; Class V= Non-qualified manual occupations.

However, there were factors associated with mortality in only one of the sex groups. For men, a higher prevalence of smokers was observed among those who would subsequently die. For women, the deceased were more frequently widows with a poorer self-reported health status, with more chronic conditions, and sleeping more than 10 hours per day.

Table 10: Baseline characteristics according to vital status in 1994, by gender.

	Men		Women	
	Alive (n=291)	Dead (n=209)	Alive (n=551)	Dead (n=243)
Self-reported health status				
Very good	11.3	7.7	7.6	5.3*
Good	55.0	49.3	48.3	32.1
Fair	27.1	25.4	34.5	34.6
Poor / Very poor	2.7	6.2	5.1	13.6
Chronic conditions				
0	22.0	17.2	14.0	10.3*
1	23.7	20.1	18.3	14.4
2	23.4	21.5	22.5	17.7
≥ 3	30.9	41.1	45.2	57.6
Body mass index <sup>†</sup>				
Overweight / Obese	7.2	3.3*	31.0	21.8*
Normal	80.4	72.7	59.3	54.3
Underweight	7.2	13.4	3.3	4.9
Smoking status				
Smoker	23.7	30.1*	2.9	2.1
Former smoker	44.0	41.6	2.7	1.2
Never smoker	25.4	16.7	88.7	81.5
Physical activity				
Active	44.3	29.2*	46.1	23.5*
Sedentary	46.7	57.4	47.7	58.4
Alcohol consumption (last 12 months)				
	67.7	53.6	46.3	27.6
Daily hours of sleep				
< 7 hours	15.1	17.7	27.2	23.9*
7 to 9 hours	68.4	59.8	59.9	47.3
More than 10 hours	12.7	12.0	8.5	15.6
Hospitalised (last 12 months)				
	5.8	18.7*	4.7	14.4*

\* Statistical significant differences between alive and dead groups ( $p < 0.05$ ).

<sup>†</sup> Body mass index is the result of dividing weight (Kg) by height (m<sup>2</sup>).

Table 11 presents the distribution of disability status at baseline by vital status in 1994 for men and women. Differences were found between those who were alive and those who died, those who died showing more difficulties and dependency in both men and women.

Table 11: Disability status at baseline according to vital status in 1994, by gender.

	Men		Women	
	Alive (n=551)	Dead (n=243)	Alive (n=291)	Dead (n=209)
Disability status at baseline				
Independent	77.0	57.4*	64.4	37.0*
Difficulty	19.6	33.0	30.1	41.6
Dependent	1.7	7.7	2.5	16.9

\* Statistical significant differences between alive and dead groups ( $p < 0.05$ ).

With respect to survival data, it is interesting to observe the behaviour of the group at risk when there are both right-censored and left-truncated data (see Figures 16 and 17). The observed dynamic pattern due to the staggered entries into the study increases the group at risk, in contrast to the right-censored data scenario where the group can only diminish over time due to the elimination of those individuals who die.

Figure 16: Group at risk: Men.

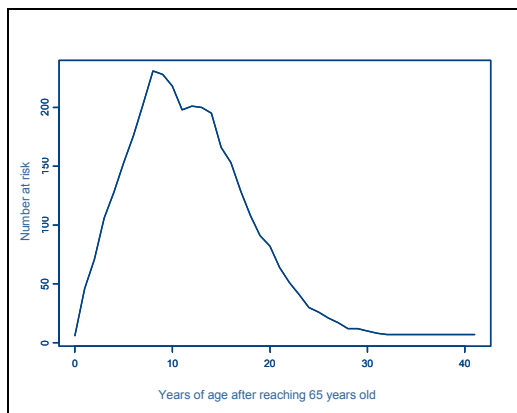
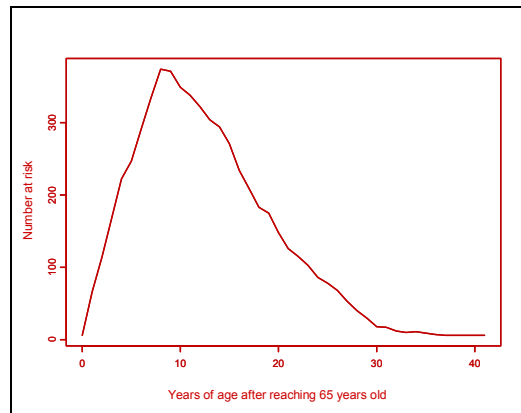


Figure 17: Group at risk: Women.



## 5.2. Empirical validity of the disability indicators

As a first step in this work, the validity of the underlying hierarchical pattern between basic and instrumental activities of daily living in our environment was evaluated. It was hypothesized that the hierarchy of the BADLs will differ with respect to IADLs due to the differences in the biological/physiological process.



In general, an individual is able to perform the BADLs before that IADLs, and he/she also loses first the ability to perform the BADLs.

Table 12 presents the ADLs distribution for the entire sample, men and women at baseline. The rank of basic and instrumental activities of daily living was the same, irrespectively of sex. Surprisingly, a BADL, cutting their toenails, showed the higher rate of impairment (11.8% of the participants reported to be unable to do the activity without assistance).

Figure 18 shows the graph with the two main factorial axis and the ADLs projected on them<sup>136</sup>. The first Axis separated those who reported information from those who did not. The second Axis represented a gradient of functional capacity, distinguishing those who had no difficulties from those who had difficulties, and from those who were unable to perform the activities. Thus, descending along the Axis 2 increased the level of impairment in ADLs. BADLs and IADLs showed a similar pattern, the activities were grouped into three different sets (independent, with difficulty, and dependent), irrespectively whether they are basic or instrumental. The IADLs were frequently situated in the second half of the group, which means a higher level of impairment; with the exception of the activity 'cutting their nails' that showed a different behaviour that the other ADLs, difficulty in cutting their nails is placed near to the 'independent group' whereas, unable to cut their nails is located in the 'with difficulty' group. The results derived from the analysis supported the hierarchical structure pattern between basic and instrumental ADLs and the lack of validity of the activity 'cutting their toenails'. Also, disability of activities

depending on lower-extremity functions seemed to be greater than from activities related to upper-extremity functions. It may be explained by the hypothesis that lower-extremity disability precedes upper-extremity disability in elderly people.<sup>137</sup>

Shopping showed to be the most severe IADL whereas cooking the less severe. This result contradicts the finding of a previous study<sup>138</sup>, although it is consistent with the cultural behaviour of the Spanish elderly men at that time when almost exclusively women carried out household tasks. Also, the low prevalence of impairment in cooking for men since they did not cook; as a consequence they do not report any difficulty in cooking since they are not aware of them. This reflects that activities relevant to elderly men and women in one culture may not be so in another culture.

As a result of the findings of the multiple correspondence analysis, the disability assessment is based only on the BADLs, specifically on nine of them omitting the activity 'cutting their toenails'.

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<sup>136</sup> The screen plot of the first 32 eigenvalues pointed out the existence of two significant factorial axis, which retained 55% of the variability of the data. Similar contribution of the categories of each ADL to the construction of the factorial axis was observed.

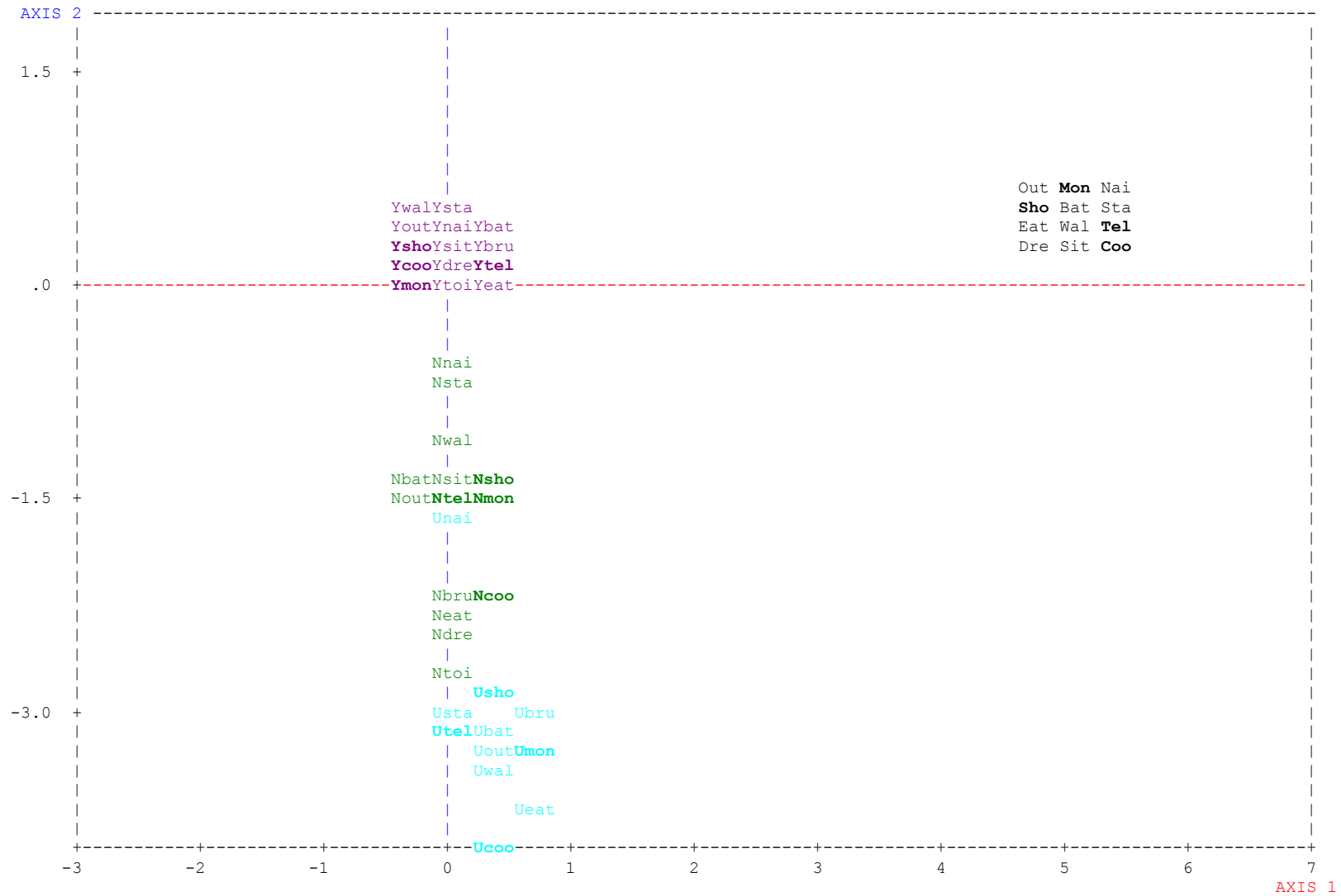
<sup>137</sup> Dunlop D.D., Hughes D.S.W. and Manheim L.M. Disability in activities of daily living: patterns of change and a hierarchy of disability. *Am J Public Health* 1997;87:378-83.

<sup>138</sup> Finch M., Kane R.L. and Philip I. Developing a new metric for ADLs. *JAGS* 1995;43:833-40.

Table 12: Distribution of the activities of daily living (ADLs) at baseline stratified by sex.

Activities of daily living	All (n=1,315)				Men (n=506)				Women (n=809)			
	No difficulty %	Difficulty %	Unable %	Non- response %	No difficulty %	Difficulty %	Unable %	Non- response %	No difficulty %	Difficulty %	Unable %	Non- response %
<b>Basic ADLs</b>												
Using the toilet (toi)	93.6	2.0	0.8	3.7	95.3	1.4	0.6	2.8	92.6	2.3	0.9	4.2
Eating (eat)	92.9	2.9	0.5	3.7	94.3	2.6	0.4	2.8	92.1	3.1	0.5	4.3
Brushing hair/ shaving (bru)	91.9	3.6	0.9	3.7	93.7	2.8	0.8	2.8	90.7	4.1	1.0	4.2
Dressing (dre)	90.8	4.9	0.7	3.7	92.9	3.4	1.0	2.8	89.5	5.8	0.5	4.2
Going outside (out)	84.8	8.5	3.2	3.5	89.5	5.1	2.6	2.8	81.8	10.6	3.6	4.0
Bathing (bat)	84.1	9.3	3.3	3.3	89.7	5.3	2.2	2.8	80.6	11.7	4.1	3.6
Sitting (sit)	80.5	15.2	0.8	3.4	87.7	8.9	0.8	2.6	76.0	19.2	0.9	4.0
Walking (wal)	73.9	21.4	1.3	3.4	78.7	17.8	1.0	2.6	71.0	23.6	1.5	4.0
Going up/down stairs (sta)	68.3	25.2	3.3	3.3	74.9	20.4	2.0	2.8	64.2	28.2	4.1	3.6
Cutting their toenails (nai)	66.7	18.3	11.8	3.2	74.7	15.0	7.7	2.6	61.7	20.4	14.3	3.6
<b>Instrumental ADLs</b>												
Cooking (coo)	92.9	1.7	1.7	3.7	92.9	1.7	1.7	3.7	91.1	2.5	2.2	4.2
Managing money (mon)	92.0	1.8	2.7	3.5	92.0	1.8	2.7	3.5	91.0	1.9	3.1	4.1
Using the telephone (tel)	90.6	3.4	2.4	3.5	90.6	3.4	2.4	3.5	89.9	3.5	2.6	4.1
Shopping (sho)	88.8	3.4	4.3	3.5	88.8	3.4	4.3	2.1	85.0	5.1	6.1	3.8

Figure 18: Hierarchical pattern of the activities of daily living: Multiple Correspondence Analysis.



### 5.3. Thesis papers

Paper	Objective	Finding
<p>1. <b>Lamarca R.</b>, Alonso J., Gómez G. and Muñoz A. <i>Left-truncated data with age as the time-scale: an alternative for survival analysis in the elderly population.</i> <u>J Gerontol Med Sci</u> 1998; 53A:M337-M343.</p>	<p>To illustrate the usefulness of taking age 65 as the origin point for the analysis of survival time in the elderly, instead of the date when the study was started.</p>	<p>The use of age as time scale is deemed more appropriate for survival analysis of the elderly: inferences are easier to interpret and final models are simpler.</p>
<p>2. <b>Lamarca R.</b>, Ferrer M., Andersen P.K., Liestol K., Keiding N. and Alonso J. <i>Changing relationship between disability and survival among the elderly at different ages.</i> <u>J Clin Epidemiol</u> 2003; 56:1192-201.</p>	<p>To describe the relationship of disability with mortality at different ages, allowing for changes in disability status during the follow-up period</p>	<ul style="list-style-type: none"> <li>• Disability increases monotonically over time while the risk of mortality associated with disability varies with gender and age.</li> <li>• Elderly disabled women show higher rates of disability and are less likely to recover from disability. They should be considered a target group for intervention.</li> <li>• It is necessary to consider disability status as a time-dependent variable, to avoid an underestimation of its association with mortality.</li> </ul>

PAPER 1: Left-truncated data with age as the time-scale: an alternative for survival analysis in the elderly population.

**Lamarca R.**, Alonso J., Gómez G. and Muñoz A. *Journal of Gerontology Medical Sciences* 1998; 53A:M337-M343. Copyright © The Gerontological Society of America. Reproduced by permission of the publisher

The definition of age as time-scale in the survival analysis made the comparison of mortality between men and women easier. It was performed by using only a graphical display and a log-rank or Wilcoxon test. However, it was necessary to draw three graphs to carry out a similar comparison when using the time-on-study as scale (one per each age group: 65-74 years old, 75-84 years old, and more than 85 years old), because it was not possible to account for the effect of age in a continuous fashion. Further, an additional method was then needed to link the survival curves from the different graphs and perform also an overall test. It was also possible to estimate more percentiles of the survival time, such as the second and third quartiles for those subjects not disabled (16.9 and 22.5, respectively) that couldn't be provided with the time-on-study scale.

It also overcame the confusing role of age since a substantial number of risk factors correlate with age. The statistical models were more parsimonious since they avoided the inclusion of interaction terms (i.e., age\*time-on-study) due to the inherent assumption of linearity between the independent variables and the outcome in the semi-parametric Cox model. Although the results derived from both approaches were similar in the multivariate context, the estimates were slightly attenuated in the analysis of age as time scale, RR= 1.84 vs. 1.77 for males and RR= 2.10 vs. 1.92 for females in time-on study and age as time scales, respectively, because the adjustment by age was tighter using age as time scale.

Moreover, the estimates derived from the multivariate semi-parametric Cox models were finer since the adjustment by age was more efficient: RR= 1.84 vs. 1.77 for males and RR= 2.10 vs. 1.92 for females in time-on study and age as time scales, respectively (see, Table 13).

In addition, the shape of the hazard curves matched that of the population, an increasing risk of dying as people age, since we were studying the ageing process instead of the time-on-study. Finally, the multivariate models were potentially more parsimonious because the number of interaction terms due to the assumption of linearity is diminished.

Table 13: Semi-parametric Cox model stratified by gender for both time-on study and age as time scales.

	Men		Women	
	Time-on-study Relative Risk (95% CI*)	Age Relative Risk (95% CI)	Time-on-study Relative Risk (95% CI)	Age Relative Risk (95% CI)
Age				
65 – 74 years	1 (—)		1 (—)	
75 – 84 years	2.25 (1.68-3.00)		2.80 (2.06-3.82)	
≥ 85 years	3.24 (1.39-7.59)		6.33 (3.64-11.01)	
Basic ADLs <sup>†</sup>				
No disability	1 (—)	1 (—)	1 (—)	1 (—)
Disability	1.84 (1.38-2.46)	1.77 (1.32-2.36)	1.84 (1.38-2.46)	1.77 (1.32-2.36)

\* Confidence Interval

<sup>†</sup> Activities of Daily Living

# Left-truncated Data With Age as Time Scale: An Alternative for Survival Analysis in the Elderly Population

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**Background.** The standard approach for survival analysis of the elderly population is to define the survival time as the elapsed time from entry into the study until death, and to adjust by age using stratification and regression procedures. However, the interest is in the study of the aging process and the risk factors related to it, not in the use of time-on-study as the time scale. Here, we present methods to use age as the time scale and compare inferences and interpretations with those obtained using the standard approach.

**Methods.** A total of 1,315 individuals aged 65 years or older from the city of Barcelona, Spain, were interviewed in 1986 (baseline). The vital status of the cohort was assessed in October 1994. To illustrate the usefulness of age as time scale (alternative approach) instead of time-on-study in the survival analysis of the elderly population, both methods were used to assess the relationship between baseline functional capacity and mortality.

**Results.** Using the alternative approach, we observed that 50% of the sample died at age 80.6 years; this information could not be estimated with the standard approach. Using age as a covariate in the standard analysis with time-on-study as the time scale and using age as the time scale in the alternative analysis, the association of functional capacity at baseline and mortality was of similar magnitude under both analyses. Nevertheless, using the alternative approach, relative risks were slightly lower, and the adjustment by age was tight and was not subject to the inherent assumptions in regression models of the functional relationship of independent variables with outcome. We illustrated the methods with fixed covariates (i.e., gender) and baseline values of time-dependent covariates (i.e., functional capacity), but we discussed the extension of our methods for the analysis of time-dependent covariates measured at several visits in a cohort study. Methods proposed here are easily implemented with widely available statistical software packages.

**Conclusions.** Although the use of standard survival analysis generally produces correct estimates, the use of age as time scale is deemed more appropriate for survival analysis of the elderly: Inferences are easier to interpret and final models are simpler. We therefore recommend the use of age as time scale for survival analysis of the elderly population.

THE stratum of population older than 65 years is growing considerably faster than the rest of the population. The projections for the period 2000–2025 are that the elderly population will increase an average rate of 2.6%, compared to 1.2% for the overall population (1). As a consequence, aging of the elderly population itself is expected (2). The aging process may be associated with a higher risk for chronic diseases and mortality (3). Therefore, older adults have become a very important focus of interest for clinical and epidemiological research.

Cohort studies have been useful for the identification and understanding of how different risk factors may lead to premature mortality or loss of functional capacity at older ages (3). Typically, the putative risk factors are assessed at baseline, and individuals are followed with "dead" as the endpoint. The standard, "time-on-study" approach for the analysis of this type of data is to define survival time as the elapsed time from entry into the study until death. However, the entry time into the study as origin point lacks the characteristics of a meaningful interpretation that other

points may have (e.g., the moment when an intervention is carried out, a point of change in the disease or when a disease begins, or even when a person is classified as an "elder"). In studies of the elderly population the interest is in the study of the aging process, and this process has been conventionally considered to begin when the individual is age 65 and not when the subject enters the study cohort. Study subjects therefore are included in the sample if they are alive at the date that the study started and if they have reached age 65 at the entry time, that is, if their survival time exceeded that age. As a matter of fact, we are not truly interested in the mortality rate as a function of time since recruitment, because this is a function of the study duration, instead of the mortality rate as a function of the aging process duration. In addition, age per se is associated with survival and with the risk factors of interest; there is a high correlation of many of the risk factors with increasing age, such as blood pressure and cholesterol (4), among others, and therefore age acts as a confounder factor. The standard statistical procedures partially overcome



this fact by means of adjusting by age (5), stratifying by age (6), or by computing age-adjusted incidence rates (7); however, it is necessary to take into account at what ages the risk factors are measured (8), because, for example, to be disabled at age 90 is not the same as to be disabled at age 67.

An alternative approach is to consider the survival time as the elapsed time from age 65 until the event of interest. In this approach, the time scale is age and not the time in the cohort. Thus, this approach directly takes into account the age effect on mortality, adjusting automatically for the confounding effect of age. This approach will allow us to draw individual inferences at specific ages (i.e., the survival probability will be based on an individual aged  $x$  years instead of an individual who has spent  $y$  years in the study cohort), and it would provide a more understandable interpretation (9). These and other related issues were discussed recently by Korn and colleagues (10).

The alternative approach is more appropriate for survival studies of elderly populations where the interest is in describing the factors that modify the hazard of death after a specific age, say, 65 years. In observational studies, individuals enter the study at different ages, but those who have entered the study after the origin point (older than 65 years) enter "late" into the observation (left-truncation) and their peers who died before the study started are not observed. Usually, the data are right-censored; that is, the event of interest (death) is not observed at the end of the study (either because the individual was lost to follow-up or was alive at the end of the study). In these situations, where the observed data are left-truncated and right-censored, one needs to use the extension of the standard proportional hazards model by incorporating the delayed entries.

The aim of this research is to illustrate the usefulness of taking age 65 as the origin point for the analysis of survival time in elders, instead of the date when the study was started.

The time scale of the analysis is age, which is the canonical scale in a study that attempts to identify factors that increase the risk of death after controlling for the aging process. The results of an 8-year study of elderly people living in the city of Barcelona, Spain, are used to implement this alternative approach for right-censored and left-truncated data. Here, we compare the inferences regarding the relationship of baseline functional capacity and mortality, when using as time scale the time since entry into the study (time-on-study) and the time elapsed since age 65 years (age as time scale). Although the methods have been used to describe incidence of AIDS in cohorts of young homosexual men infected with HIV (11), there is not, to our knowledge, a report explaining the methods using age as time scale in the elderly population, for which this is of prime importance.

## METHODS

### *Subjects*

The data are based on a longitudinal study of a sample of persons age 65 and older from Barcelona, Spain. The aim of the study was to assess the relationship between health status, health-related behaviors, the use of health services,

and functional capacity with subsequent mortality. Among these factors, we chose functional capacity to assess the relationship with mortality. Details of the design and sampling methods of this study have been previously published (12,13). Briefly, a total of 1,315 individuals, 809 females and 506 males, were interviewed at their homes between January 1986 and January 1987. A second home interview was carried out between July 1993 and July 1994. After approximately 8 years of follow-up (October 1994), the vital status of the whole cohort was assessed using the Local Census Register of Barcelona and the Regional Mortality Register of the Generalitat de Catalunya by a confidential record linkage. If the participant did not appear in registers because he or she had moved away from the area, an active search was carried out.

Among the 1,315 participants, 805 (61.2%) were documented to be alive at the end of the follow-up in October 1994; 452 (34.4%) had died, 37 (2.8%) were lost to the follow-up, and 21 (1.6%) could not be traced. We have restricted our analysis to those individuals for whom information on vital status at the end of the follow-up was available ( $n = 1,294$ ), and those subjects who were lost to follow-up were considered as right-censored at the age they were considered lost from follow-up.

Furthermore, because the main interest was to describe the relationship between functional capacity and mortality in individuals between 65 and 90 years of age, we further restricted our analysis to those who were younger than 90 years at the time of entry into the study ( $n = 1,275$ ).

Functional capacity was measured based on the difficulty or need of help in carrying out nine basic activities of daily living (ADLs). These activities were: walking, going up/down stairs, bathing, using the toilet, brushing hair/shaving, dressing, sitting, going outside, and eating. Individuals were defined as "disabled" if they reported being unable to perform one or more of the activities without assistance or having difficulty in performing them and "not disabled" when they reported being able to perform all the activities without any difficulty. The survival patterns after 8 years were compared in these two groups of elders defined by their functional capacity. In the standard analysis, when time in the study is taken as the time scale, age was categorized in three groups: younger than 74 years, between 75 and 84 years, and older than or equal to 85 years. The multivariate analysis using Cox regression was performed, stratifying by gender.

### *Statistical Methods*

To assess the relationship between functional capacity and mortality, we analyzed these data using two different approaches. In the standard approach, time since entering the study was considered as the time scale; in the alternative approach, age minus 65 was taken as the time scale. Some minimal notation required for the analysis is described briefly below.

Let  $Y$  be a variable measuring the exposure time in years or longevity process, that is, the time from entry into the study (when the cohort is selected) until death or emigration if it occurred before October 1994. Let  $W$  be the delayed entry (14), that is, the elapsed time (in years) from

reaching age 65 until the individual was recruited. Let  $T$  be the complete longevity process, a random variable denoting the residual survival time since turning 65 until death or exit from the study:  $T = W + Y$ . We define  $\delta$  as the censoring indicator, that is,  $\delta = 1$  if we observe the event of interest (death) during the follow-up, and  $\delta = 0$  otherwise. We assumed that the delayed entry process and the censoring mechanism are independent of the longevity distribution.

The Kaplan-Meier standard approach for right-censored data (15,16) is based on the observable data  $(Y, \delta)$  and estimates the survival function by:

$$\hat{S}_1(y) = \prod_{j|y_j \leq y} \left\{ 1 - \frac{d(y_j)}{r(y_j)} \right\}, \quad (1)$$

where  $d(y_j)$  is the number of deaths at time  $y_j$ , and  $r(y_j)$  is the number of individuals at risk of dying at time  $y_j$ .

If age is taken as the alternative time scale, the estimator for the survival function when data are both right-censored and left-truncated (16,17), is based on the observable data  $(W, Y, \delta)$ . This estimator is given by:

$$\hat{S}_2(t) = P(T \geq t) = \prod_{j|t_j \leq t} \left\{ 1 - \frac{d(t_j)}{r(t_j)} \right\}, \quad (2)$$

where, as before,  $d(t_j)$  is the number of deaths at time  $t_j$ , but the number of individuals at risk at time  $t_j$ ,  $r(t_j)$ , only includes those individuals who have entered the study at an age younger than  $t_j + 65$ . Note that, in contrast to the standard situation, where  $r(y_j)$  decreases monotonically, the number of individuals at risk  $r(t_j)$  may fluctuate dynamically with time  $t$ .

Figure 1 illustrates the above variables ( $W, Y, T$ , and  $\delta$ ) for four different individuals. Individuals A and B entered the study at 65 years of age, thus  $w = 0$  for both of them. Individual A died during the study at age  $65 + y$ , thus  $\delta = 1$ , and individual B was alive at the end of the study when she was  $65 + y$  years old, thus  $\delta = 0$ . On the other hand, individuals C and D entered the study at age  $65 + w$ , thus  $w \neq 0$  for both of them. Individual C died during the study at age  $65 + y + w$ , thus  $\delta = 1$ , and individual D was alive at the end of the study, when he was  $65 + y + w$  years old and  $\delta = 0$ .

An important feature of the proposed methods is that individuals are not considered at risk prior to the age at which they entered the study. Specifically, individual C does not contribute to the estimation and hypothesis testing at the time that individual A develops the event of interest.

Parallel to the extension of the Kaplan-Meier methods presented here, the methods of the proportional hazards model can also be extended for the estimation and hypothesis testing of relative hazards measuring the association between risk factors and survival with age as the time scale (15).

The methods presented here can be implemented with several statistical packages including S-plus, SAS, STATA, and EGRET. The Appendix includes the commands used to implement the proposed methods.

**RESULTS**

The distribution of the main variables of the study cohort at baseline is shown in Table 1. Among the male popula-

tion, 198 died and 297 were alive or were lost during the follow-up. The median age at entry was 75 years among those who died during the study and 71 years for the censored ones. Note that there is a large proportion of individuals who entered the study when older than 74 years. The median follow-up time for the censored individuals was 8.3 years. The median of the survival time was similar for both genders. Concerning the functional capacity, we observed that those individuals alive at the end of the study were significantly less disabled than those who died during the study ( $p < .001$ ). Among women, an analogous pattern for age at entry and for the follow-up time was observed. The median age at entry was slightly higher for the uncensored group. Concerning the basic activities of daily living,

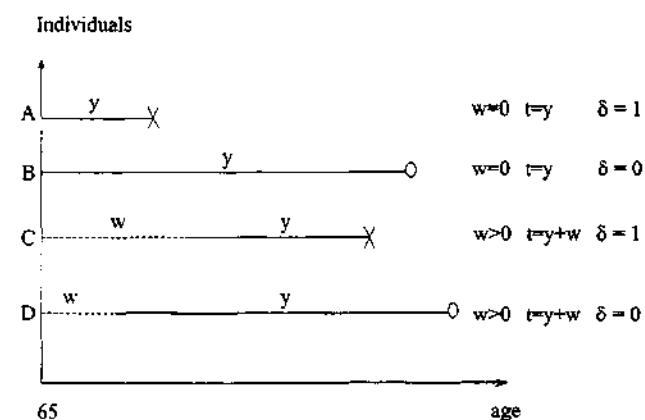


Figure 1. Definition of survival time.  $y$  = time from entering the study until death or emigration;  $w$  = time from reaching age 65 until the recruitment into the study.

Table 1. Age, Follow-up, Survival Time, and Functional Capacity of the Elderly Cohort

	Men		Women	
	Uncensored (n = 198)	Censored (n = 297)	Uncensored (n = 194)	Censored (n = 586)
Age at Entry				
Median	75	71	76	71
Range	65-87	65-90	65-89	65-90
65-74	49.0%	74.1%	37.6%	66.9%
75-84	47.5%	22.9%	52.6%	25.4%
> 85	3.5%	3%	9.8%	7.7%
Follow-up (y)				
Median	4.1	8.3	4.4	8.3
Range	0.1-8.5	0.4-8.9	0.1-8.7	0.4-8.9
Survival Time (T = W + Y)				
Median	14.1	14.0	16.2	14.5
Range	0.2-24.7	1.4-25.0	1.5-24.7	0.4-25.0
Basic ADLs				
No Disability	57.6%	76.8%	39.7%	62.5%

Notes: Uncensored = died during the study; Censored = alive or lost to follow-up; ADLs = activities of daily living.

women presented a lower level of no disability than men ( $p < .001$ ).

In order to compare mortality of men and women using the standard survival approach, we split the sample into age categories (65–74 years, 75–84 years, and  $\geq 85$  years) and present the corresponding survival curves (Figure 2). A worse survival experience was observed for men in each age stratum. Because age is taken care of by definition (Figure 3), the alternative approach may be represented in one graph. We were able to assess the differences, when they existed, between men and women by performing a log-rank or Wilcoxon test. In contrast, using the standard approach we had to use some technique that allowed us to join the three different survival curves and then carried out an overall log-rank or Wilcoxon test.

To illustrate, Table 2 presents the estimation of the median and the first and third quartiles of the survival time for the male group using the two approaches. While in the standard case we could only estimate up to the first quartile, in the alternative approach the three quartiles were estimable from the data. Among men older than 65 years, 50% lived to over 80.56 years (i.e.,  $80.56 = 65 + 15.56$ ). Analogously, among those who were functionally free of disability, 75% survived 74.39 years, 50% survived 81.9 years, and 25% survived 87.45 years. In contrast, among functionally disabled individuals, 50% died before age 76.11. Figure 4 shows the survival curves by baseline basic ADL categories, when using the alternative method.

It is important to note that the Kaplan-Meier curves shown in Figures 3 and 4 correspond to fixed (i.e., gender) and time-varying (i.e., disability) risk factors, respectively. The interpretation for a fixed covariate is straightforward, but for a time-varying covariate the survival functions correspond to those while the disability status remains stable. Later in this article, we indicate how to extend the proposed methods to incorporate measures of time-varying covariates beyond those obtained at baseline as presented here (see Discussion).

To assess how functional capacity predicts survival, we carried out a multivariate Cox proportional hazards model for both survival approaches. Table 3 gives the estimates of the relative hazard of age and functional capacity. Note that age is taken into account in the definition of the time scale and thus was not entered in the alternative model. Both methods show that the risk of death of a functionally disabled man is approximately 1.8 times higher than the risk of a functionally nondisabled man, irrespective of which methodology was used. Similarly, functionally disabled women had approximately 2.0 times higher risk than functionally nondisabled women. However, we observed that the estimated risks were attenuated in the alternative approach for both (male and female) models.

## DISCUSSION

The aim of this research was to show that the use of age instead of time-on-study as the time scale is an appropriate way to handle survival analyses of the elderly population. An advantage of the methods proposed is that they provide the juxtaposition of all the different periods provided by different individuals, and in doing so one obtains estimates

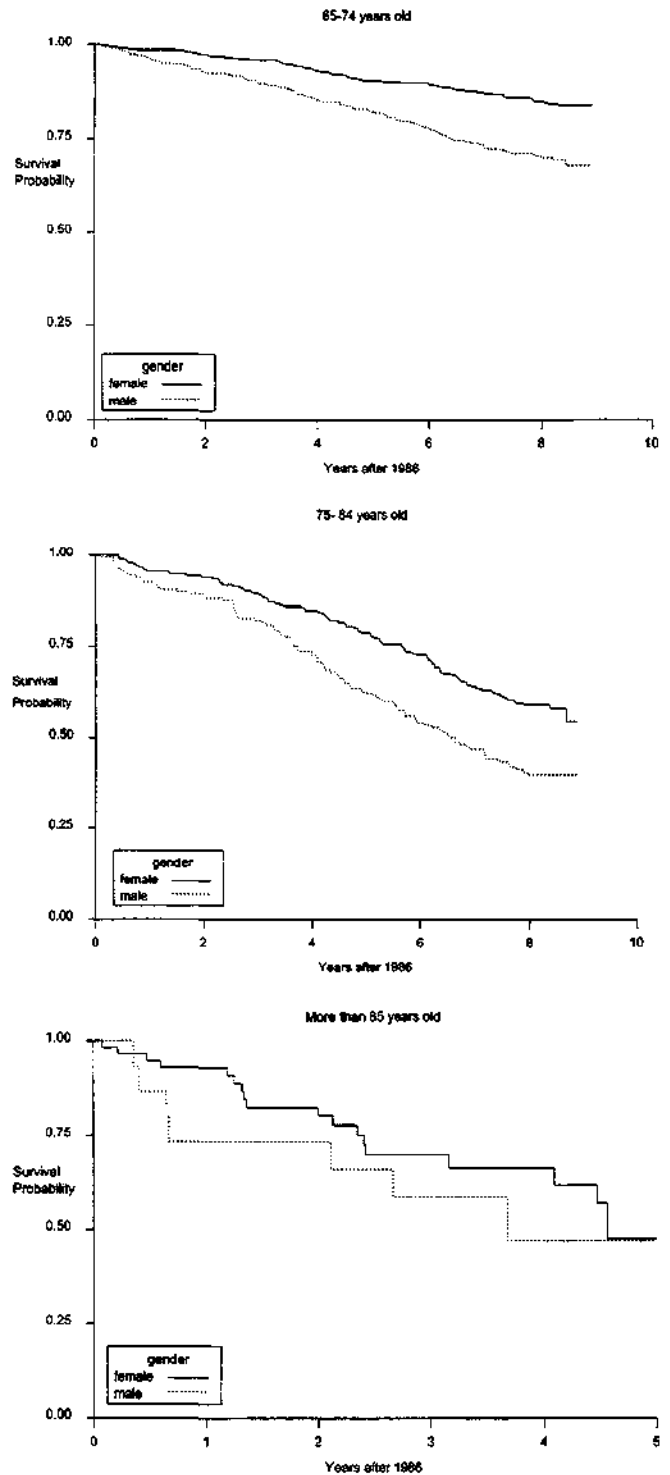


Figure 2. Survival curves by gender stratifying by age (standard approach: time-on-study as time scale).

of the survival probabilities at every age in groups that are homogeneous according to the risk factors considered in a given analysis. Another advantage of the proposed alternative approach is that it has a more straightforward interpretation of mortality, as it is free of the confounding effect of age, which is automatically taken into account as the mea-

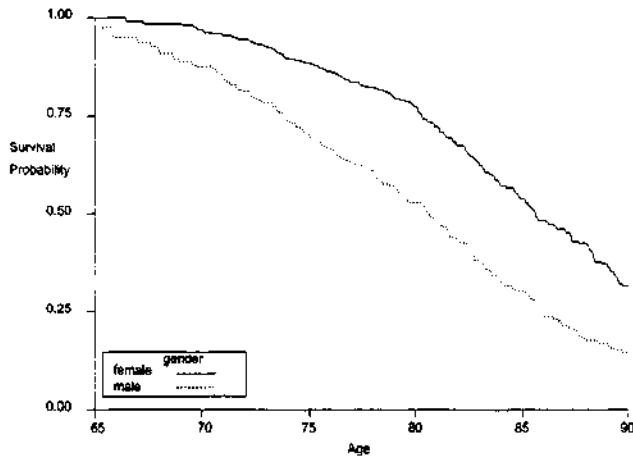


Figure 3. Survival curves by gender (alternative approach: age as time scale).

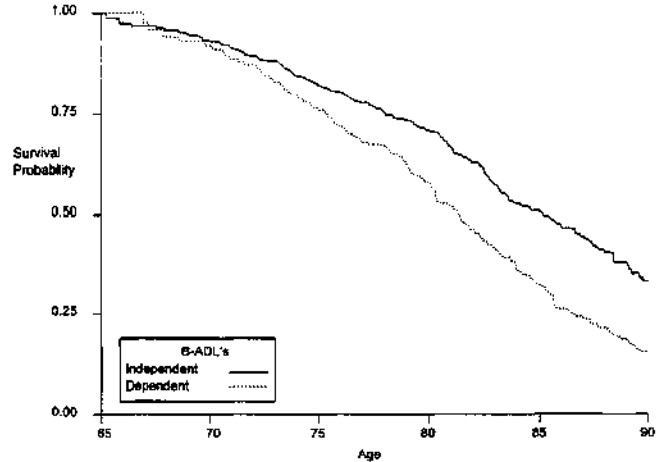


Figure 4. Survival curves by functional capacity using age as time scale. B-ADLs = basic activities of daily living.

Table 2. Median, First, and Third Quartile of Elderly Men by Baseline Functional Capacity and Type of Survival Analysis Approach

	Time Scale: Time-on-Study (standard)			Time Scale: Age (alternative)		
	Q1	Median	Q3	Q1	Median	Q3
Overall	4.92	—	—	8.82	15.56	20.67
Basic ADLs						
No disability	5.90	—	—	9.39	16.90	22.45
Disability	3.29	6.64	—	6.32	11.11	17.10

Notes: Q1 = First quartile; Q3 = Third quartile; ADLs = activities of daily living.

sure of survival time. In fact, the survival curves with this method are more similar to those describing general population mortality.

A drawback of the standard approach is that it did not allow us to estimate either the median or the third quartile for the survival time of the functionally nondisabled individuals. This happened because the standard approach does not maximize the available information of the subjects. For instance, if an individual age 70 years was alive at entry into the study, then the individual was alive at the beginning of the aging process, that is, at age 65. As a consequence, the survival time considered by the standard method is shorter than the one used by the alternative approach. In our case, although the cohort was followed for 8 years, this was not enough time to estimate the median and the third quartile. Therefore, possible trends in the data for each level of functional capacity could not be observed. However, the alternative approach makes optimal use of the data by means of extending the follow-up time for each individual who enters into the study older than 65 years (Table 2). It is necessary to point out that the inferences reported by each method require different interpretation. The median computed using the standard approach describes the mor-

Table 3. Proportional Hazard Regression Stratified by Gender for Both Analytical Approaches: Standard (Time-on-Study as Time Scale) and Alternative (Age as Time Scale)

Covariate	Men		Women	
	Standard RH (95% CI)	Alternative RH (95% CI)	Standard RH (95% CI)	Alternative RH (95% CI)
Age				
65-74 years	1		1	
75-84 years	2.25 (1.68-3.00)		2.80 (2.06-3.82)	
>85 years	3.24 (1.39-7.59)		6.33 (3.64-11.01)	
Basic ADLs				
No disability	1	1	1	1
Disability	1.84 (1.38-2.46)	1.77 (1.32-2.36)	2.10 (1.56-2.83)	1.92 (1.43-2.59)

Notes: RH = relative hazard; ADLs = activities of daily living.

tality rate as a function of study duration, in this case the time elapsed since January 1986. On the other hand, because we are interested in studying mortality of the elderly population, the alternative approach provides the median age at death that was computed as a function of time since the onset of the elderly process (65 years). The medians under the alternative approach have a straightforward interpretation for a fixed covariate (e.g., gender), but they are interpreted as those obtained under stable conditions for a time-varying covariate (e.g., disability).

To overcome the problems mentioned for the standard approach, other authors have suggested building age-specific curves for each age group (7). This strategy is, however, less efficient than the use of the proposed time scale, because it reduces the information provided by age as a continuous variable. Other alternatives have also been proposed; for example, the computation of adjusted conditional probabilities of the event at each failure time (18), the average covariate method (18), and the corrected group prognosis (19,20).

Although it is necessary to break down the age group into categories for the estimation of the survival functions, this is not the case for the Cox regression. Specifically, in the regression setting one can use smaller age groups and even continuous terms if the association is linear. In doing so, one would obtain relative hazards of the exposure of interest adjusted by age as precise as in the alternative approach using age as the time scale. Indeed, we carried out the analysis using the standard approach with age as a continuous variable, and the relative hazards of disability were 1.77 and 1.96 for men and women, respectively. These values are very close to those obtained using the alternative approach. However, using age as an independent covariate with time-on-study as the time scale imposed a structure (e.g., logarithm of hazard is linear in age) that the alternative approach avoids because the underlying hazard of the Cox model with age as time scale is completely unrestricted (i.e., the nonparametric component of the regression approach).

Because data of studies of elderly adults are right-censored (i.e., some individuals are lost to follow-up or alive at the end of the study) and left-truncated (i.e., individuals entered into the study at different ages), an alternative, more appropriate methodology—namely, the extended-Kaplan-Meier estimator—was used. This estimator differs from the standard Kaplan-Meier estimator in that not all the subjects are considered at risk at time 0; that is, those individuals entering at age  $A_0$  (older than 65) will not be included in the definition of the risk set for values  $t < A_0$ . Then, the covariables of each individual will contribute at the age that they have been recorded, and not before, avoiding the mixture of information of individuals who have different ages. This prevents the confounding effect of age.

Left-truncation is a situation characterized by the fact that the study cohort does not include those subjects who have not survived long enough to be observed. Consequently, the cohort that is observed is an incomplete sample (21,22). This fact must be taken into account in the statistical analysis. In fact, not including individuals who have previously died results in an underestimation of the mortality risk, because the individuals at the highest risk are not observed. To adjust or to compensate this bias, the survival analysis with delayed entry is needed (9). With large enough samples this estimator has similar properties to the standard product-limit estimator; that is, it is consistent and its distribution is approximately normal (23). However, the left-truncated approach is not free of difficulties. In studies where the sample size is small, there is the possibility that the survival estimator may be zero for some  $t_i$ , resulting in not having any individual at risk in a given moment. Then, the survival estimator becomes zero for some  $t > t_i$ . Approaches to avoid this problem are given by Lynden-Bell (24).

We have shown the advantages of using age as the time scale, and how to use methods of survival analysis for delayed entries to carry out estimation and regression analyses. Here, we have restricted our analysis to fixed covariates (e.g., gender), and time-varying covariates measured only at one time point (i.e., disability measured at baseline). Because disability is strongly related with age, it is possible that a person who is not disabled at baseline could become

disabled at a later age under follow-up; and by simply considering the disability at baseline, we will be biasing the comparison toward the null hypothesis. Even though we found strongly significant results using disability at baseline, it is important to incorporate the time-varying nature of disability, if available.

The methods presented here can naturally be extended, so as to partition each individual in as many individual periods corresponding to updates of the disability status. The records for the data analysis will contain: (a) the years after 65 an individual entered into a certain value of the disability status; (b) the years after 65 when that individual ceased to have that status; and (c) the vital status at the time the individual ceased to have that status (i.e.,  $\delta = 0$  if alive and move to another status,  $\delta = 1$  if dead). In studies where updates of time-varying covariates are not available, it is recommended that total follow-up of an individual be restricted to a reasonable length of time when it is expected that the exposure will not likely change substantially.

It has been postulated that the importance of traditional risk factors, such as hypertension or smoking, tends to decrease with age. In the standard approach, this calls for the introduction of interactions between age and the risk factor of interest. In the alternative approach, because age is the time scale, this will correspond to a risk factor not fulfilling the usual assumption of proportional hazards in Cox regression. Therefore, in order to allow for a risk factor to have different levels of association with the outcome at different ages, all the methods developed to incorporate departures from proportional hazards are directly applicable to the alternative methods proposed here (25).

As we have shown, the alternative approach gives a more intuitively understandable interpretation of the survival curves, makes possible a juxtaposition of the available information, and indicates that age is the right time scale to build adequate inferences. In conclusion, we recommend the use of age as the time scale in the survival analysis when dealing with data from observational studies in elderly subjects.

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## Appendix

### Commands in S-plus, SAS, STATA, and EGRET

Using the notation introduced in the Methods section, W represents the years after 65 when an individual enters the study, T represents the years after 65 when an individual exits the study, and delta ( $\delta$ ) is the vital status of the individual at exit. Let X denote the disability variable (= 0 if no, = 1 if yes).

#### Estimation of the Survival Functions (Figure 3)

S-plus: plot(survfit(coxph(Surv(W,T,delta) ~ +strata(X))))  
 SAS: proc phreg;  
 model (W,T) \* delta(0)=;  
 strata X;  
 baseline out=estimate survival=peralive;  
 proc print;  
 var T peralive X;  
 STATA: stset T delta, t0(W)  
 sts graph, by (X)  
 EGRET: failure-time variable: T  
 censoring indicator variable: delta  
 entry-time variable: W  
 stratify: X

#### Regression (Alternative Models in Table 3)

S-plus: summary(coxph(Surv(W,T,delta) - X))  
 SAS: proc phreg;  
 model (W,T)\*delta(0)=X;  
 STATA: stset T delta, t0(W)  
 stcox X  
 EGRET: definitions as in (I)  
 regression terms: X

PAPER 2: Changing relationship between disability and survival among the elderly at different ages.

**Lamarca R.**, Ferrer M., Andersen P.K., Liestol K., Keiding N. and Alonso J. Journal of Clinical Epidemiology 2003; 56: 1192-201. Erratum

The proportion of subjects who were dependent or who had difficulties was higher among women than men at baseline and at the end of the study (42.0% vs. 30.0%, and 60.0 vs. 48.7%, respectively). It was observed that a subset of subjects with disability or experiencing difficulties were able to improve somewhat their disability status over the follow-up (26.9% for women, and 26.6% for men). Further, a small percentage recovered from the dependent status.

Among elderly men, low weight was significantly associated with an increased risk of dying compared to those subjects with a normal weight, RR=2.16. Former and current smokers had a significantly higher risk of dying than non-smokers, RR= 1.63 and 2.41, respectively. Among elderly women, no other variable, apart from disability status, was statistically significant in the multivariate model.

The effect of disability on mortality varied with age in both men and women as it was shown by the significant interaction terms between disability and age (the time scale). To further illustrate the interaction effect, the relative risks by disability status are graphically displayed for men and women (see Figures 19 and 20, respectively). It was observed that the impact of being dependent on mortality decreased as subjects aged in both sexes. Also, the relative risk of dying was higher for women than men at any given time and the differences in

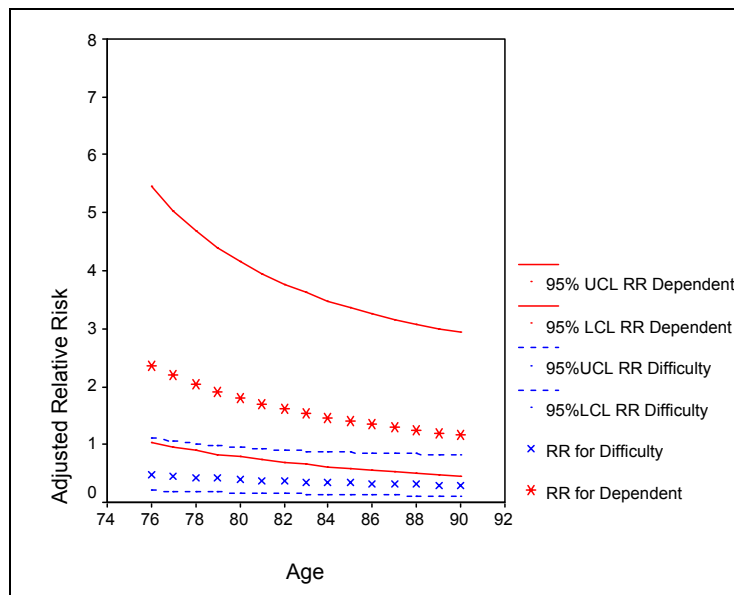
survival across disability status were greater among women than men. For instance, the risk was 3.5 for women and 1.8 for men at 80 years, while it was 1.9 and 1.2 at 90 years, respectively.

Table 14: Semi-parametric Cox model for both men and women.

	$\hat{\beta}$	Standard Error	p-value	Relative Risk (95% CI)
<b>Men</b>				
Body mass index				
Normal	0	—	—	1 (—)
Low	0.77	0.218	< 0.001	2.16 (1.41-3.31)
Overweight or Obese	-0.56	0.388	0.146	0.57 (0.27-1.22)
Smoking habit				
Nonsmoker	0	—	—	1 (—)
Former smoker	0.49	0.208	0.018	1.63 (1.09-2.46)
Current smoker	0.88	0.219	< 0.001	2.41 (1.57-3.70)
Disability status				
Independent	0	—	—	1 (—)
Difficulty	-0.08	0.204	0.695	0.92 (0.62-1.38)
Dependent	1.47	0.175	< 0.001	4.35 (3.09-6.14)
Disability status * log(time;age)				
Difficulty* log(time;age)	-0.57	0.392	0.142	0.56 (0.26-1.21)
Dependent* log(time;age)	-0.87	0.332	0.009	0.42 (0.22-0.80)
<b>Women</b>				
Disability status				
Independent	0	—	—	1 (—)
Difficulty	-0.20	0.201	0.308	0.81 (0.55-1.21)
Dependent	1.34	0.165	< 0.001	3.83 (2.77-5.29)
Disability status * log(time;age)				
Difficulty * log(time;age)	0.61	0.443	0.167	1.85 (0.77-4.40)
Dependent* log(time;age)	-1.25	0.340	< 0.001	0.29 (0.15-0.56)

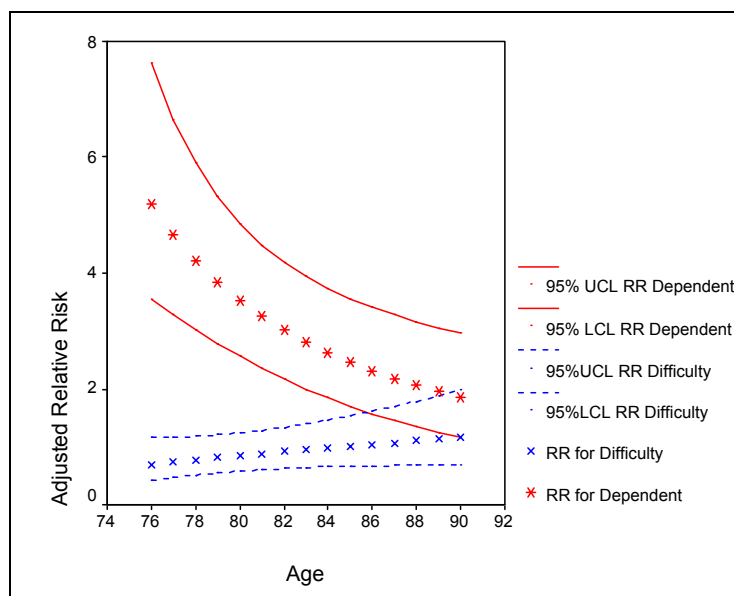


Figure 19: Relative risk of dying by disability status for Men.



Notes: UCL: Upper Confidence Level, LCL: Lower Confidence Level, and RR: Relative Risk.

Figure 20: Relative risk of dying by disability status for Women.



Notes: UCL: Upper Confidence Level, LCL: Lower Confidence Level, and RR: Relative Risk.

## A changing relationship between disability and survival in the elderly population: differences by age

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### Abstract

**Background:** Longitudinal studies estimating the association between disability and mortality in the elderly population have typically assumed disability constant through the follow-up study period. Current knowledge indicates that such assumptions may not be appropriate. Our purpose was to examine this association (disability and mortality) taking into account the transitions in the disablement process.

**Methods:** 1,294 participants (aged 65 and over) in the Health Interview Survey of Barcelona were followed up for a median of 8 years. Nine basic activities of daily living (ADLs) were measured at baseline and at the end of follow-up. Individuals were defined as “dependent” if they reported not being able to perform one or more of the activities without assistance. Survival analysis with delayed entry, age as the time variable, and disability as a time-dependent variable was performed.

**Results:** The rates of disability had increased by the end of the follow-up (from 42.0 to 60.0% among women and from 30.0 to 48.0%, among men); 7.5% of disabled women at baseline and 28.5% of men recovered from disability. The adjusted relative risk of dying for those with basic ADLs dependency varied with age: at 80 years of age it was 3.5 for women and 1.8 for men, while at 90 years it was 1.9 and 1.2, respectively.

**Conclusions:** Disability increases monotonically over time while the risk of mortality associated with disability varies with gender and age. Elderly disabled women should be considered a target group for intervention because they show higher rates of disability and are less likely to recover from disability. Our results illustrate the need to consider disability status as a time-dependent variable, to avoid an underestimation of its association with mortality. © 2003 Elsevier Inc. All rights reserved.

**Keywords:** Aging; Activities of daily living; Disability; Follow-up studies; Survival; Proportional hazards model

### 1. Introduction

Disability is an important indicator of health status of the elderly people that has been shown to be strongly associated with mortality [1–5]. The importance of disability measured by limitations in performing certain activities of daily living (ADLs) relies on the fact that it provides a measure of the burden caused by suboptimal health. It is the result of a large number of factors such as underlying diseases, coexisting chronic conditions, psychologic aspects, and social and environmental factors [6]. ADLs have been exten-

sively used for assessing the need for health services [7] and as eligibility criteria for long-term care [6,8].

The relationship between disability and mortality has often been analyzed by means of logistic regression, with the main outcome being vital status. That is, the association has been assessed ignoring possible changes in the risk of death over time. Some studies overcame this limitation by taking into account the time elapsed from entry into the study until death or emigration or the end of the study using survival techniques. However, as far as we know, these studies have considered disability as a time-fixed variable, not taking changes into account during the follow-up period.

Wallace and Colsher [9] have pointed out that when considering disability and chronic illnesses, the change over time of exposures and their differential impact must be considered. This suggestion is consistent with previous studies that have shown that disability follows a dynamic

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pattern, with an increasing prevalence of dependence with age, but also with a small subset of individuals who are able to regain independence [10,11]. As a consequence, the association between mortality and disability found with a long follow-up period and a fixed measure of disability may be misleading. Typically, the estimated association will be too weak. Moreover, there is little information about the changes in disability that elderly people experience over time and the effect of such changes on survival.

The objective of the present study was to describe the relationship of disability with mortality at different ages, allowing for changes in disability status during the follow-up period.

## 2. Methods

### 2.1. Sample

Data come from the Health Interview Survey of Barcelona, a longitudinal study of the noninstitutionalized elderly population, aged 65 and over, and resident in Barcelona (Mediterranean city with about 1,500,000 inhabitants [12] located in the north-east of Spain). The study was conducted to examine the relationship between health-related characteristics, the use and need of health services, and subsequent mortality. The used was derived from an adaptation of the supplement on aging in the 1984 U.S. National Health Interview Survey [13].

The sampling design has been described in detail elsewhere [2,14–16]. A representative sample from the elderly population of Barcelona was drawn ( $n = 1,632$  of eligible individuals). Among them, 1,315 elderly people were initially interviewed face to face at home between January 1986 and January 1987, representing a response rate of 80.6%. However, we restricted our analyses to 1,294 traced subjects because 21 participants were lost immediately after the baseline interview.

Reassessment was performed between June 1993 and June 1994: we obtained information from 754 subjects who were alive at the evaluation period and 281 subjects who died before the follow-up evaluation; and no reassessment information was available for 259 subjects, of whom 117 were confirmed alive and 142 were confirmed dead. A total of 382 interviews (30%) were answered by proxies, 101 corresponding to alive individuals and 281 corresponding to participants who had died during the follow-up period. In both cases, the profile of the proxy was similar: the majority of them were close relatives (around 84 and 93%, respectively), lived in the same house (83 and 72%, respectively) and knew very well the participant (95 and 91%, respectively). We collected information on sociodemographic factors, self-rated health, disabilities, chronic diseases, and life style among others, in both evaluations. Among those with a follow-up evaluation (1,035), all except one provided information on disability at baseline and at follow-up. For the

remaining 259 with only baseline disability information, the latter was assumed to remain stable throughout the follow-up period, except for 12 individuals with missing data on disability at baseline. These 13 individuals, who did not report information on disability status either at baseline or at follow-up, were excluded from the survival analysis (1.0% of the whole cohort).

The vital status and causes of death were ascertained for the whole cohort in October 1994, after a median of 8.1 years of follow-up. The information was collected from the Local Census register of Barcelona and the Regional Mortality Register of the Generalitat de Catalunya by confidential record linkage. Causes of death were classified according to the 9th revision of the International Classification of Diseases [17].

### 2.2. Measures of disability

Disability was measured by questions on nine basic activities of daily living (B-ADL) derived from the Katz scale: walking, going up/down stairs, bathing, using the toilet, brushing hair/shaving, dressing, sitting, going outside, and eating. Subjects were asked about their difficulty to carry out the activity (none, a little, moderate, and unable to perform without help) [13]. The combination of the responses to each activity yielded an overall categoric measurement grouped into three categories: *Independent*, those with no difficulties in performing the nine activities; *With difficulty*, those with difficulties (a little or moderate) in at least one of the activities; and *Dependent*, those needing help in performing at least one of the activities.

To account for the effect of change in disability status on the risk of death over time, some additional information on the nine activities during the follow-up was retrospectively collected. Change in disability status was defined as a change of category (independent, with difficulty, dependent) in any B-ADL that could affect the variable derived from the combination of the nine B-ADLs. The variable was constructed as follows: (1) subjects who reported having difficulties in the reassessment were asked “how long have you experienced any difficulty in performing *activity*?”; (2) the subjects who rated themselves in the reassessment as dependent were asked “how long have you needed help to perform *activity*?” and “how long did you have any difficulty in performing *activity* before needing help?”; (3) for those individuals reporting a new disability status at the reassessment but no information on the duration ( $n = 116$ ), a duration of 1 year in this status prior to the measurement was assumed; (4) in a few individuals ( $n = 70$ ) for whom a discrepancy between the first and the second evaluations was found, the first disability status was assumed to have a duration of 0.1 years; (5) for those individuals not reinterviewed and with baseline information on disability status ( $n = 247$ ), their disability was assumed to remain equal to the baseline during the whole

follow-up period; and (6) finally, for those individuals who had died and had become impaired during the last year of their life or did not report the duration, the cause of death and the cause of disability were compared ( $n = 90$ ). If both causes were the same, only the baseline information was used to avoid an overestimation of the association between disability and mortality ( $n = 65$ ).

For the present analysis, we used the following information obtained at baseline to adjust the estimates of the relation between disability and mortality: age, gender, marital status (married, widowed, and separated-single-divorced), education level (none completed, primary, and secondary, or tertiary), living arrangements (with others, alone), self-rated health status (very good, good, fair, poor, very poor), comorbidity ( $\leq 1$ ,  $> 1$  chronic conditions), sleep hours per day ( $< 7$ ,  $7-9$ ,  $> 9$  hr), smoking status (never, former, current), alcohol intake (no, yes), body mass index (BMI), chronic limitation of activity, and physical activity.

Due to the differences observed in the distributions between males and females, BMI was categorized by using the quartile values specific to each gender and grouping the two highest groups: low weight  $\leq 21.35$ , and  $\leq 18.88$ ; normal  $21.36-30.24$ , and  $18.89-26.66$ ; overweight-obese  $\geq 30.25$ , and  $\geq 26.67$  kg/meter<sup>2</sup>, respectively, for men and women. Chronic limitation was ascertained using the following question: "Do you have any obstacle or difficulty to perform your principal activity (principal activity could be paid work or house work or usual activity for those retired) during the last 12 months?" Daily physical activity was assessed by asking the interviewees to grade their total physical activity during the day in four categories. Those declaring "doing a job that requires a great deal or extra effort" or "walking frequently during the day" were classified as "active," while those "expending most part of their daytime standing up but not walking" or "sitting most of the day" were classified as "sedentary."

### 2.3. Statistical analysis

The survival analyses were formulated in the counting process framework [18]. Age was used as the time variable, with 65 years old as the point of origin for the survival time with the purpose of studying the association of disability with the ageing process [19].

Graphs of the crude hazard function were smoothed using a kernel method with a bandwidth of 6 years to describe the instantaneous death rate at each age.

To estimate the effect of disability on mortality controlling for covariates, the semiparametric Cox model for delayed entry and time-varying covariates was applied [18,20,21]. The inclusion of the disability status as a time-dependent variable in the Cox model allowed us to use all the information provided by the subject (baseline and follow-up) to study the relationship between disability and mortality at different ages. Interaction terms between each covariate and age were explored, as well as interaction terms between

covariates. Several plausible relationships between age and disability were considered to define the interaction, and finally, the logarithm of age was used, although the obtained estimates for different functions were quite similar.

Separate models were built for each gender, because the way of experiencing disability has been described to be different for men and women [22]. In addition, women consistently show a higher prevalence of chronic conditions than men, and different types of diseases [23]. The PROC PHREG routine of SAS was used to fit the aforementioned models [24].

### 3. Results

The distribution of the main variables of the study cohort at baseline is shown in Table 1. More than 60% of the subjects were women ( $n = 794$ ); the mean age at entry into the study was 74.4 (SD = 7.0) for women and 73.5 (SD = 5.9) for men. The majority of men were married (80.2%), and were living with others (91.4%). Women were less educated (18.1% with no studies completed), mainly widowed (49.5%) or married (38.7%), and about a quarter of them lived alone. Only 5.6% of the men had overweight or obesity, while this proportion was of 28.2% among women. Conversely, the proportion of current and former

Table 1  
Description of the characteristics of the sample at baseline (1986)  
by gender

	Men ( $n = 500$ )	Women ( $n = 794$ )	<i>P</i> -value
Age (mean, SD)	73.5 (5.9)	74.4 (7.0)	<.001
Marital status (%)			
Married	80.2	38.7	
Widow	14.0	49.5	<.001
Single/divorced/separated	5.6	11.2	
Education level (%)			
Tertiary or secondary	35.4	17.0	
Primary completed	56.4	63.4	<.001
None completed	7.8	18.1	
Living arrangements (%)			
With others	91.4	73.9	<.001
Alone	8.4	25.9	
Body mass index (%)			
Low	9.8	3.8	
Normal	77.2	57.8	<.001
Overweight-obese	5.6	28.2	
Smoking status (%)			
Never smoked	21.8	86.5	
Former smoker	43.0	2.3	<.001
Current smoker	26.4	2.6	
Self-rated health status (%)			
Very good	9.8	6.9	
Good	52.6	43.3	<.001
Fair	26.4	34.5	
Poor-Very poor	4.2	7.7	
Vital status (October 1994) (%)			
Dead	41.8	30.6	<.001

Table 2  
Evolution of disability status during the follow-up period in men ( $n = 500$ )

	Disability status at follow-up (1993–1994)				All $n$ (%)	Total with information <sup>a</sup>
	Independent	Difficulty	Dependent	Missing		
Disability status at baseline (1986)						
Independent	169	46	59 <sup>c</sup>	70	344 (68.8%)	344 (70.0%)
Difficulty	25	19	51	31	126 (25.2%)	126 (25.7%)
Dependent	3	1	10	7	21 (4.2%)	21 (4.3%)
Missing	2	1	2	4	9 (1.8%)	n.a. <sup>d</sup>
ALL $n$ (%)	199 (39.8%)	67 (13.4%)	122 (24.4%)	112 (22.4%)	500 (100%)	n.a. <sup>d</sup>
Total with Information <sup>b</sup>	199 (51.3%)	67 (17.3%)	122 (31.4%)	n.a. <sup>d</sup>	n.a. <sup>d</sup>	n.a. <sup>d</sup>

<sup>a</sup> Those subjects without missing data on disability at baseline (Independent + Difficulty + Dependent).

<sup>b</sup> Those subjects without missing data on disability at follow-up (Independent + Difficulty + Dependent).

<sup>c</sup> Seventeen individuals had difficulties in performing B-ADLs before becoming “dependent.”

<sup>d</sup> Not applicable.

smokers was high among men (26.4 and 43.0%, respectively) but very low among women (2.6 and 2.3%, respectively). At baseline, 50.2% of women rated their health as very good or good, while that proportion increased to 62.4% among men. However, the proportion of deaths during the follow-up period was higher for men than women (41.8 vs. 30.6%). All gender differences were statistically significant at a  $P$ -level  $< .001$ .

Tables 2 and 3 show the transitions between the different disability status (independent, having difficulties, and dependent) for male and females, respectively. Figures about transitions of disability status were calculated for those with available information at follow-up. At baseline, the proportion of subjects who were dependent or who had difficulties was higher among women than men 42 vs. 30%. Women also showed higher rates of disability than men at the end of the 8 years of follow-up: 60.0 vs. 48.7%.

Almost half of the men who were independent at baseline remained independent at the time of the second assessment, while this proportion was somewhat lower among women (61.7 and 49.2%, respectively). The most unstable group was that formed by the elderly people, who reported at baseline to have difficulties when performing the activities: only 20.0% among men and 30.2% among women remained

in the same group after 8 years of follow-up, among those with follow-up information. The majority of those who were dependent at baseline were also dependent at follow-up. Recovery from being dependent was less likely among women than among men: three women (7.5%) and four men (28.5%) improved their disability status. A subset of those who had some degree of disability (difficulty or dependent) at baseline improved their disability status (26.6% for men, and 26.9% for women).

Table 4 presents descriptive survival data stratified by gender. Both for men and women a strong gradient in mortality with disability status at baseline was observed.

Survival analyses showed that elderly individuals with disability had higher mortality risks than those who were independent. Fig. 1 shows the smoothed intensity curves of death by gender and disability. They show an increased death intensity with increasing age in all groups, except for those men who were dependent, for whom the concave shape of the curve indicates that the risk of dying decreased with age for high values of age. This suggests that dependent younger males make up a selected group a very high risk.

In addition to disability, the following factors were significantly ( $P \leq .01$  level) associated with all-cause mortality among males in the univariate analyses: smoking habit,

Table 3  
Evolution of disability status during the follow-up period in women ( $n = 794$ )

	Disability status at follow-up (1993–1994)				All $n$ (%)	Total with information <sup>a</sup>
	Independent	Difficulty	Dependent	Missing		
Disability status at baseline (1986)						
Independent	181	105	82 <sup>c</sup>	77	445 (56.0%)	445 (58.0%)
Difficulty	62	61	79	65	267 (33.6%)	267 (34.8%)
Dependent	1	2	37	15	55 (6.9%)	55 (7.2%)
Missing	7	3	8	9	27 (3.4%)	n.a. <sup>d</sup>
All $n$ (%)	251 (31.6%)	171 (21.5%)	206 (25.9%)	166 (20.9%)	794 (100%)	n.a. <sup>d</sup>
Total with Information <sup>b</sup>	251 (40.0%)	171 (27.2%)	206 (32.8%)	n.a. <sup>d</sup>	n.a. <sup>d</sup>	n.a. <sup>d</sup>

<sup>a</sup> Those subjects without missing data on disability at baseline (Independent + Difficulty + Dependent).

<sup>b</sup> Those subjects without missing data on disability at follow-up (Independent + Difficulty + Dependent).

<sup>c</sup> Twenty-seven individuals had difficulties in performing B-ADLs before becoming “dependent.”

<sup>d</sup> Not applicable.

Table 4  
Baseline disability status of the sample and survival status at follow-up, stratified by gender

	Male (n = 500)				Female (n = 794)			
	Person-years		Deaths		Person-years		Deaths	
	n	Total	n	(%)	n	Total	n	(%)
Overall	500 <sup>a</sup>	7,491	209	(41.8%)	794 <sup>a</sup>	13,065	243	(30.6%)
Disability status at baseline 1986								
Independent	344	4,966	120	(34.9%)	445	6,747	91	(20.4%)
Difficulty	126	2,011	69	(54.8%)	267	4,688	101	(37.8%)
Dependent	21	359	16	(76.2%)	55	1,185	41	(74.5%)

<sup>a</sup> Nine men and 27 women did not report disability status at baseline.

level of physical activity, bodymass index, comorbidity, and chronic limitation of activity. For women, the factors that showed a significant relationship with mortality were, in addition to disability status, level of physical activity, chronic limitation, self-rated health status, and alcohol consumption.

In the multivariate analysis, only body mass index and cigarette smoking remained statistically associated with survival among men (Table 5, left column). Compared to elderly individuals with normal weight, the relative risk of mortality (RR) was 2.16 (95% CI = 1.41–3.31) for those who reported a low weight, and an RR of 0.57 (95% CI = 0.27–1.22) for those who were overweight or obese. Relative to nonsmokers, the risk of dying was significantly higher for former and current smokers: RR = 1.63 (95% CI = 1.09–2.46), and RR = 2.41 (95% CI = 1.57–3.70), respectively. The association of disability status with mortality varied with age, as shown by the statistical significance of the interaction between logarithm of time (age) and disability. Also among women, the relationship between disability and mortality was modeled by means of a nonproportional Cox model (Table 5, right column). Disability status remained statistically significant associated with survival time, as did the interaction between logarithm of time (age) and disability.

The estimated relative risks by level of disability at different ages are displayed in Fig. 2. All the curves indicate a nonconstant relationship of disability and mortality with age. The relative risk of death among those elderly men who were dependent diminished over age-time compared to those who were independent. However, at age 82, those men who were still dependent had a 50% higher risk of dying compared to those who were independent. Compared to independent women, the relative risk of death slowly increased for those women who reported having difficulties, while the risk decreased for those who were dependent.

#### 4. Discussion

The purpose of the present study was to examine the association between disability and mortality in the elderly population taking into account the possible changes in the disability status. We wanted also to evaluate the intensity of functional loss and its impact on mortality at different ages.

Compared to predominant survival analysis strategies for the elderly population, which define the survival time as the elapsed time from entry into the study until death, our approach via survival analysis with age as the basic time variable and delayed entry [18,19,25,26] offered several advantages. First, the methodology for delayed entry assured that the estimated survival experience from the sample matched that of the study base. Second, the calendar time approach considered all the risk factors in the same time moment at the starting of the follow-up. This heterogeneity lead to survival curves more flat than expected due to the confounding effect of age. However, any confounding by age was directly handled using age as time variable, and by using age-dependent covariates allowance might be made for age-dependent exposure variables and for age as an effect modifier.

The most important characteristic of the analytical approach presented here is that it allowed individuals to change their disability status during the period under observation. In the standard approach, an individual independent at baseline is considered independent until the end of follow-up, even if she/he has become dependent during this period. Taking into account that elderly people are more likely to worsen their disability status than to improve it, this standard approach would tend to consider as independent individuals who would be actually dependent. As a consequence, the association between disability and the outcome variable, in this case death, is usually underestimated. There is controversy in studies assessing disability trends on aging. These uncertainties may be partially explained by this misclassification problem. Whether disability status will decline in parallel with mortality or whether the decline will be faster or slower is a key policy question for health services planning. This issue is better approached from a longitudinal point of view.

Two findings are noteworthy in the current study. The first is that disability status did not show the same pattern of decline for all individuals, but rather a dynamic pattern in which a small subset of individuals regained independence. The proportion of recovery estimated in our study is similar to that reported in previous studies [4,27,28], although comparability is limited due to differences in design, in definition of disability and in the length of follow-up. Recovery from being dependent in basic ADLs was less likely among

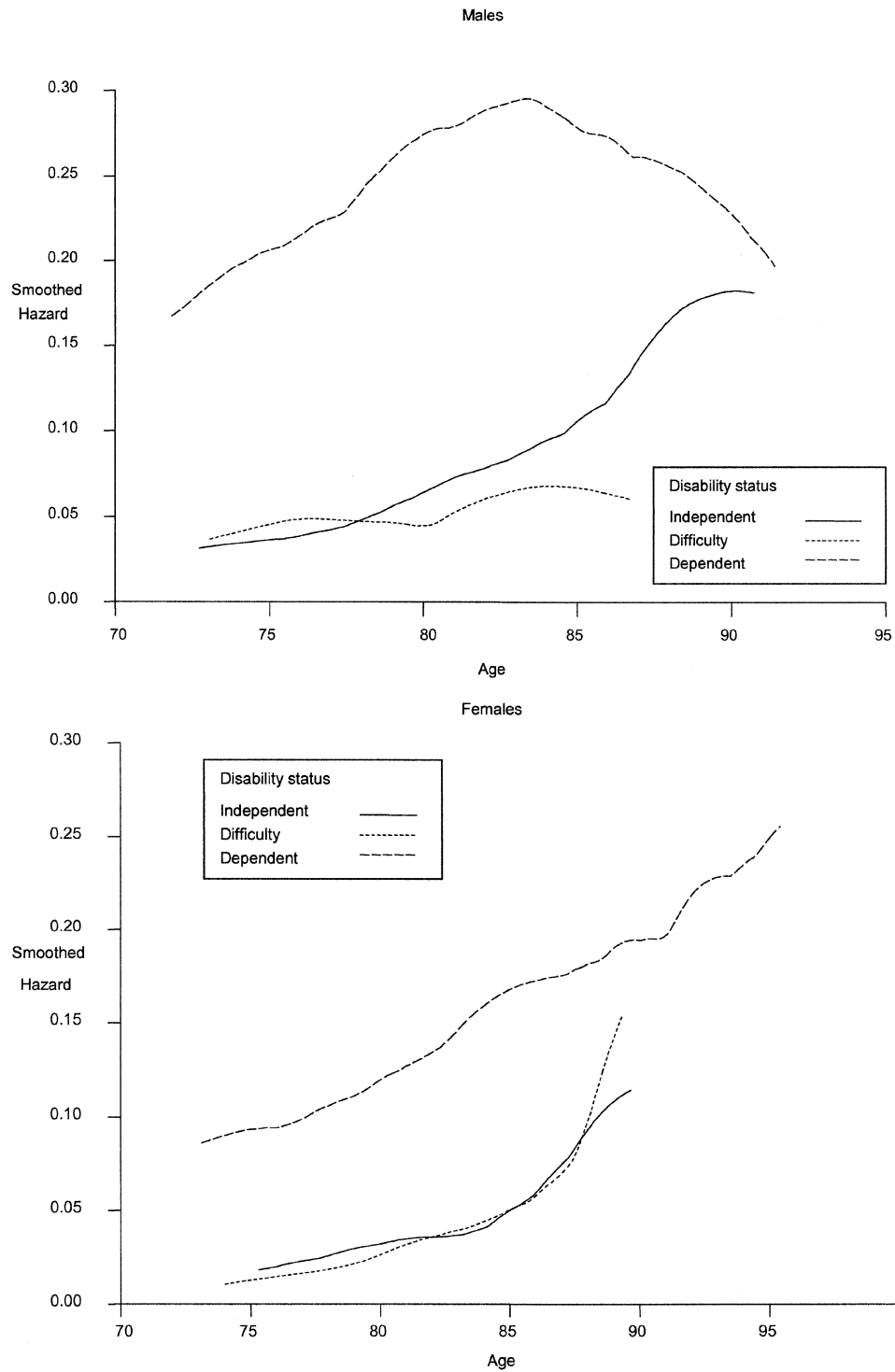


Fig. 1. Smoothed hazard curves by disability status according to gender (bandwidth of 6 years).

women than among men, as previously observed by Beckett et al. [10]. Nevertheless, we should be cautious due to the small numbers in the group of dependent elderly people in our study.

The second finding is that not only the disability status changed with age, but also the strength of its association with mortality varied. Thus, the relative risk of death among

those elderly people who were dependent decreased with age in both genders. This variation may reflect that disability has a different impact at different ages, as previously suggested by Ferrucci et al. [29]. These authors reported that elderly people developing severe disability at older ages were more likely to suffer from a longer disabling process than those at younger ages. Conversely, it has been suggested that

Table 5  
Risk of death by disability status: estimates derived from a multivariate Cox model

	Males				Females			
	$\beta$	Standard error	P-Value	Relative risk (95% confidence interval)	$\beta$	Standard error	P-Value	Relative risk (95% confidence interval)
Body-mass index								
Normal	0	—	—	1 (—)				
Low	0.77	0.218	<.001	2.16 (1.41–3.31)				
Overweight—obese	–0.56	0.388	.146	0.57 (0.27–1.22)				
Smoking habit								
Never smoked	0	—	—	1 (—)				
Former smoker	0.49	0.208	.018	1.63 (1.09–2.46)				
Current smoker	0.88	0.219	<.001	2.41 (1.57–3.70)				
Disability status								
Independent	0	—	—	1 (—)	0	—	—	1 (—)
Difficulty	–0.08	0.204	.695	0.92 (0.62–1.38)	–0.20	0.201	.308	0.81 (0.55–1.21)
Dependent	1.47	0.175	<.001	4.35 (3.09–6.14)	1.34	0.165	<.001	3.83 (2.77–5.29)
Disability* log(age-time)								
Difficulty* log (age-time)	–0.57	0.392	.142	0.56 (0.26–1.21)	0.61	0.443	.167	1.85 (0.77–4.40)
Dependent* log(age-time)	–0.87	0.332	.009	0.42 (0.22–0.80)	–1.25	0.340	<.001	0.29 (0.15–0.56)

those who are dependent at younger ages are more frail because the strategies that they would typically use to compensate for their disability would have already failed [30]. This difference in coping with disability by age could partly explain the observed variation in the strength of the association between disability and mortality.

The shape of the hazard rate curve for men shows that disability is influencing the mortality process, in the sense that disability status is measuring how far or close the subject is to death. Those subjects closer to death (the dependent group) showed a declining hazard ratio of mortality from the eighties, whereas those subjects with difficulties or independent showed an increasing ratio. It is important to note that although the hazard rate is a measure of the development of risk in a single subject, it is influenced by selection effects among individuals (i.e., the weakest subjects die first, which results in survival bias). However, this age-related pattern is not observed among women, because their absorption point (death) is further away than that for men, due to the differences in life expectancy by gender. This age-related effect of disability on mortality is well in agreement with the interpretation of the shape of the hazard ratio made by Aalen and Gjessing [31].

Women presented higher rates of disability, and their disability had a stronger association with mortality than men. This is consistent with the study of Merrill et al. [32], who showed that the excess of disability reported by women truly reflects a higher level of functional limitation. This would also be consistent with a previous finding in this cohort comparing the performance of a walking speed test and the chair stand test with their corresponding self-reports in two basic ADLs [33]. We found a higher rate of reported disability among women compared to men, and that it was accompanied with a higher rate of observed functional limitation. The lack of perfect agreement between self-reports and performance of tests was not influenced by gender. In addition, more elderly men than women would recover

from disability in our study. Thus, we can conclude that disability among elderly women is both more prevalent, and more strongly associated to mortality.

Several methodologic limitations of the present study must be taken into account. First, the fact that the time history of disability was assessed retrospectively may imply recall bias mainly due to erroneous recollection of when transitions between disability status took place. For instance, if most people overreported the disability length, the association between disability and mortality would have been underestimated. If the contrary, it would have been overestimated. Ideally, studies should contain repeated evaluations of ADLs to minimize this type of error. Nevertheless, the proportion of subjects who improved their disability status was similar to previous studies [4,27,28], which would support the validity of the approach used. On the other hand, to perform a validation, the information collected at the time of the second assessment (retrospective information) was compared with the disability status at baseline. Only a small number of discrepancies were observed (70 subjects) supporting the validity of the data. Such validation was not possible for some cases (116 individuals) where the beginning of a new disability status was missing. For these individuals, an arbitrary duration of 1 year in this status prior to the measurement was assumed. In selecting that arbitrary duration we tried to bias the comparisons towards our null hypothesis (i.e., no differences in mortality according to disability status). Given that the global tendency is to worsen health status, our assumption very likely led us to consider an individual as dependent or with difficulties less often than was really the case.

Second, the assessment of changes in disability status was not possible for those subjects who did not participate in the second assessment ( $n = 259$ ). Among those, 115 subjects showed difficulties or dependency at baseline, contributing with a short survival time (3.9 years). The assumption of no changes in their disability status may not have a great



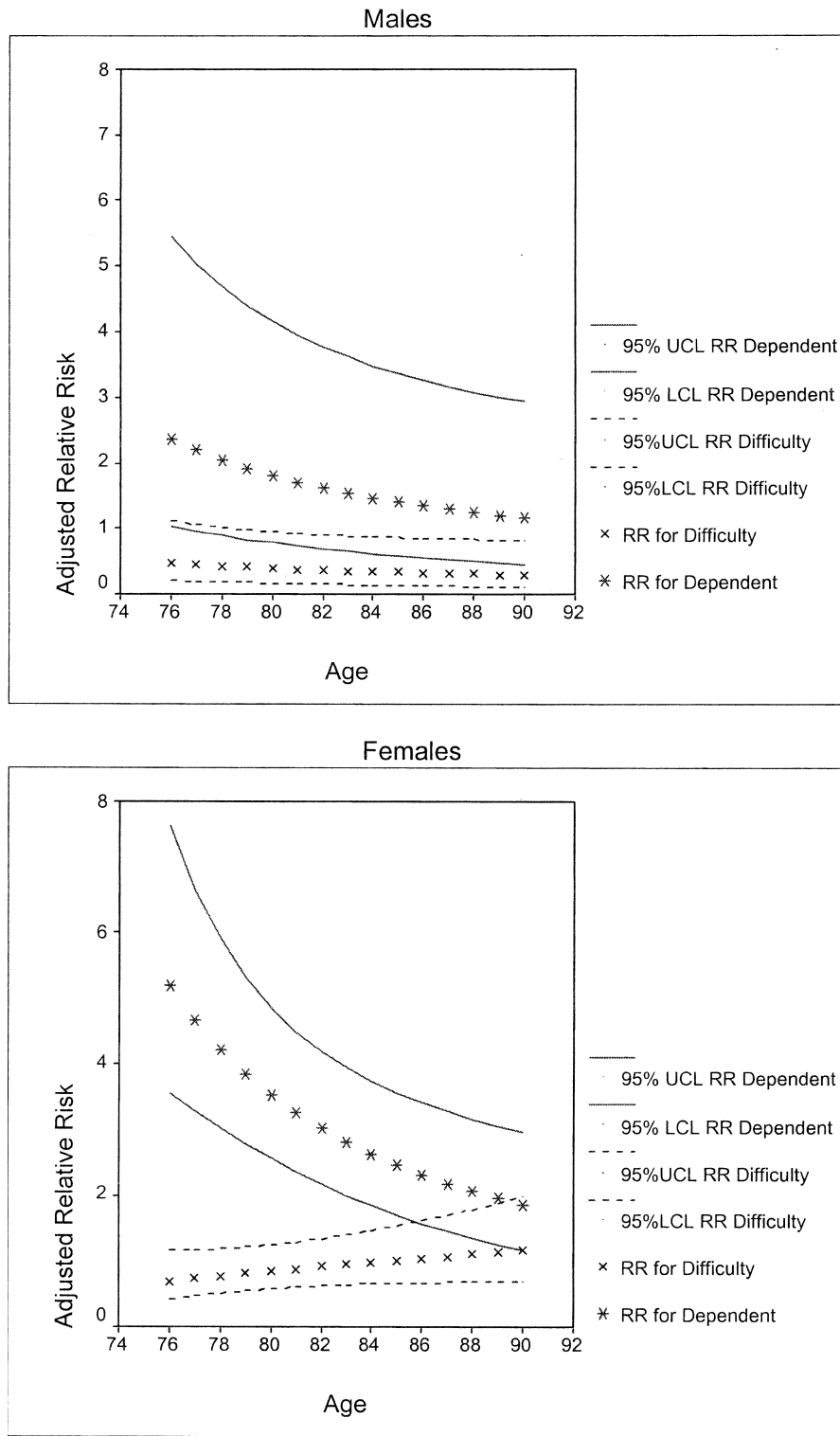


Fig. 2. Relative risk of mortality for disability in basic ADLs at different ages, by gender. 95% UCL = 95% upper confidence limit; 95% LCL = 95% lower confidence limit; RR = relative risk.

impact on the subsequent inferences for this subgroup due to the short follow-up time. On the other hand, considering those subjects who were independent at baseline as independent through the entire follow-up period may have led to

some underestimation of the association between disability status and mortality.

A third limitation of our study is that the information on disability status for those who had died before the second

assessment was obtained from proxies. If proxy respondents overreported disability of the deceased individual, as some authors have suggested [34–36], then an underestimation of the mortality risk may have resulted. However, in a previous study of the same sample comparing reported disability and performance tests, no significant differences by informant source (self or proxy) were found [33]. Thus, we believe that this has not influenced the results obtained.

Finally, if disability is caused by the presence of a fatal disease leading to death in a short time, an overestimation of the association between disability and mortality will be observed. To minimize this bias, the cause of death and the cause of disability were compared in those individuals who died during the study period and had become impaired during the last year of their life ( $n = 90$ ). If both causes were the same, only the baseline information on disability was used ( $n = 65$ ). A sensitivity analysis was carried out including the follow-up disability information provided for these subjects, the estimated relative risk for the dependent group increased more than 10 times (data not shown).

In this article we applied nonstandard survival methods to describe the association between disability and mortality in elderly people. Despite the limitations of the study, these methods allowed us to extend prior findings showing that the effect of disability on mortality changes with age, among elderly individuals. Thus, disability at younger ages was associated with increased relative risk of death compared to that for older ages (RR = 1.80 at 80 years old and RR = 1.15 at 90 years old, for men and RR = 3.53 at 80 years old and RR = 1.86 at 90 years old, for women). According to our results, disabled elderly women should be considered a target population group when planning health services, because they show higher rates of disability and seem less likely to recover from disability. Moreover, disability among women is associated with a higher risk of dying than among men. On the other hand, it is important to point out that disability should be considered a time-dependent variable to avoid a possible underestimation when analyzing its association with the outcome variable.

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#### 5.4. Support papers

Paper	Objective	Finding
<p>S1. Sunyer J., <b>Lamarca R.</b> and Alonso J. <i>Smoking after 65 years of age and mortality in Barcelona-city.</i> <u>Am J Epidemiol</u> 1998; 148:575-80.</p>	<ul style="list-style-type: none"> <li>• To study the hazard of dying associated with long term smoking among persons who survive to the age of 65 years</li> <li>• To study the benefits of quitting smoking in the elderly population, taking into account baseline health status.</li> </ul>	<ul style="list-style-type: none"> <li>• The study confirms that the effects of smoking extend to later life. That is, an excess of all cause and cancer mortality: aRR* = 2.11 (95% CI†: 1.4-3.3) and aRR = 3.11 (95% CI: 1.4-7.0), respectively. Also the risk of dying due to cardiovascular and respiratory diseases were in the expected direction although not statistically significant (aRR = 1.33 and 3.36, respectively).</li> <li>• Stopping smoking after age 65 reduces the risk of dying. aRR = 1.53 (95% CI: 1.0-2.3)</li> </ul>
<p>S2. Ferrer M., <b>Lamarca R.</b>, Orfila F. and Alonso J. <i>Comparison of performance-based and self-rated functional capacity in Spanish elderly.</i> <u>Am J Epidemiol</u> 1999; 149(3):228-35.</p>	<ul style="list-style-type: none"> <li>• To evaluate the agreement between self-report of disability and performance-based measures for some basic mobility tasks in the community-dwelling elderly of a Mediterranean country.</li> <li>• To examine the factors which may influence self-report independently of physical function.</li> </ul>	<ul style="list-style-type: none"> <li>• There is moderate agreement between self-report and performance-based measures.</li> <li>• The direction of the differences is not systematic.</li> <li>• Disagreement between both measures is influenced by the level of perceived health status (those with worst health status tended to overreport functional limitations).</li> </ul>
<p>S3. Orfila F., Ferrer M., <b>Lamarca R.</b> and Alonso J. <i>Evolution of self-rated health status in the elderly: cross-sectional vs. longitudinal estimates.</i> <u>J Clin Epidemiol</u> 2000; 53:563-70.</p>	<ul style="list-style-type: none"> <li>• To assess self-reported health status evolution.</li> <li>• To assess the differences in the estimation of age-related changes in reported health status cross-sectionally and longitudinally.</li> </ul>	<ul style="list-style-type: none"> <li>• Ageing is associated with an increased deterioration in perceived health status.</li> <li>• The use of longitudinal studies to understand the evolution of perceived health in the elderly is recommended (the estimate of perceived health changes inferred from a cross-sectional analysis of the data undervalued the level to which deterioration in perceived health is associated with ageing by a factor of 8.7).</li> </ul>

\* aRR: adjusted relative risk

† CI: confidence interval

PAPER S1: Smoking after 65 years of age and mortality in Barcelona-city.

Sunyer J., Lamarca R. and Alonso J. American Journal of Epidemiology 1998;  
148:575-80. Oxford University Press



## Smoking after Age 65 Years and Mortality in Barcelona, Spain

Jordi Sunyer,<sup>1</sup> Rosa Lamarca,<sup>2</sup> and Jordi Alonso<sup>2</sup>

The objective of this study was to assess the risk of dying associated with smoking after the age of 65 years and the benefits of quitting smoking, taking into account baseline health status. The study was carried out in Barcelona, Spain, a southern European city with an increase in smoking prevalence and lifestyle different from those of other areas where hazards of smoking have been studied. A follow-up study begun in 1986 was carried out in 477 males (94.3% of the original cohort) who were randomly selected by census from members of the Barcelona general population aged  $\geq 65$  years. Vital status as of October 1994 and, where applicable, cause of death (cardiovascular disease, cancer, or respiratory disease) were assessed. The relative risk of dying was 2.11 (95% confidence interval (CI) 1.37–3.26) times higher in current smokers and 1.53 (95% CI 1.03–2.27) times higher in former smokers than in never smokers. Quitting smoking after the age of 65 years reduced the relative risk of dying to 0.77 (95% CI 0.51–1.16) in comparison with continuing to smoke, although persons who stopped smoking had poorer self-perceived health and were more frequently reported to suffer from cardiovascular disease ( $p < 0.05$ ). This study confirms that the effects of smoking extend to later life in this elderly general population, with a magnitude as great as that seen in previous studies with different populations. In addition, it indicates that stopping smoking after age 65 reduces the risk of dying. *Am J Epidemiol* 1998;148:575–80.

aged; mortality; smoking; survival

Recent prospective studies have shown that the effect of smoking on survival extends to later life (1, 2). Previously it had been suspected that smokers who survived to old age had a risk of death similar to that of never smokers (3). Furthermore, a recent report showed that the impact of smoking in absolute terms (the difference between smokers and nonsmokers in risk of dying) increases with age (4). A related observation of studies carried out in the elderly has been that stopping smoking after the age of 65 years probably reduces the risk of death (1, 2). Since persons who stop smoking in later life are likely to do so because of ill health (5), and because health status affects fatality from chronic diseases (6) as well as the hazard due to smoking (7), the benefit of quitting smoking in this age group has probably been underestimated.

Most of the currently available prospective information on mortality and smoking was based on a UK

cohort of physicians (1) and on general population cohorts followed in the United States (2, 8, 9). However, temporal variations in smoking patterns vary widely according to geographic area. In Spain, smoking was mainly limited to males until recently; and increased smoking of manufactured cigarettes among Spanish males started in the late 1940s and reached a peak during the mid-1980s, some 25 years later than in the United Kingdom and the United States (10). This could account in part for the lower incidence of lung cancer in Spain during the late 1970s and 1980s (approximately two times lower) (10, 11). Geographic differences in other lifestyle factors, such as alcohol consumption (12), could also imply geographic differences in the effects of smoking on risks of cancer and cardiovascular disease (13, 14).

We had the opportunity to follow a general population-based cohort of elderly people in Barcelona, Spain, with reported information on perceived health and chronic diseases. Our objective was to study the hazard of dying associated with long term smoking among persons who survive to the age of 65 years and the benefits of quitting smoking after that age, taking into account baseline health status. This information may contribute to a better assessment of the worldwide epidemic of smoking-related deaths.

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Abbreviations: CI, confidence interval; ICD-9, *International Classification of Diseases, Ninth Revision*; RR, relative risk.

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## MATERIALS AND METHODS

A cohort of 1,315 individuals (506 males and 809 females) aged 65 years or older was interviewed in 1986, as part of the Health Interview Survey of Barcelona (15). Briefly, a nonproportional random sample of all households in the city of Barcelona, stratified by district and family size, was drawn from the local 1985 census (16). The sample comprised 1,632 (638 males and 994 females) noninstitutionalized elderly people. The analyses described in this paper were based only on the 506 males aged  $\geq 65$  years (79 percent of those selected) who responded. Females were excluded, because almost all of them (94 percent) had never smoked (15).

The variables studied have been described elsewhere (15, 17). Briefly, information on self-perceived health ("How would you rate your overall health: very good, good, fair, poor, or very poor?"), basic activities of daily living (measured by the self-reported ability to perform nine basic activities of daily living), chronic conditions (using a checklist with 14 conditions common among the elderly, including asthma or chronic bronchitis and heart diseases), total physical activity (in four graded categories), alcohol consumption during the previous 12 months (based on a quantity/frequency scale), and cigarette smoking (never, former, or current smoking and age at quitting, but not type of tobacco) was collected through a face-to-face home interview. Among surviving individuals, the same variables were assessed in 1993–1994.

Vital status in October 1994 was obtained for 500 (98.8 percent) of the original 506 men, 209 (41.8 percent) of whom had died, using confidential record linkage with the regional mortality register. A telephone survey was carried out for those not listed in the mortality register, which allowed validation of vital status. All subjects but six were contacted. For 23 subjects, information on smoking was missing. Hence, we studied 477 individuals (94.3 percent of the original cohort). Table 1 shows the ages at entry of these

individuals and the mean follow-up time for each age group.

Smoking status was defined by the category in which subjects placed themselves in 1986. In addition, former smokers were categorized according to the age at which they had stopped smoking, the median age being approximately 64 years. No individual classified as a current smoker in 1986 reported being a never smoker in 1994. Similarly, none of the never smokers in 1986 reported being current smokers in 1994.

Mortality hazards were estimated for lifelong non-smokers and for former and current smokers. Causes of death were classified according to the Ninth Revision of the *International Classification of Diseases* (ICD-9) (18) on the basis of the underlying cause recorded in the death register. Mortality rates for each smoking category were calculated by dividing the numbers of deaths from all causes and from cardiovascular disease (ICD-9 codes 390–459), lung cancer (ICD-9 code 162), all cancers (ICD-9 codes 140–239), and respiratory disease (ICD-9 codes 460–519) by the accumulated person-years of follow-up (19). Rates were standardized by age in years. Rate differences for specific causes of death by smoking status were assessed using Poisson regression (19), since cause-specific mortality rates followed a Poisson distribution. Poisson regression allowed adjustment for other risk factors for death at baseline in addition to age, such as perceived health, reported chronic conditions, current alcohol intake, basic activities of daily living, and current physical activity.

Mortality from all causes was assessed using survival methods, which are based on a much finer division of time than Poisson regression methods. The survival function for all causes of death by smoking status, using age as the time scale and entries at different ages, was estimated by means of the Kaplan-Meier method and the Cox proportional hazards model (20). The latter allowed us to calculate the relative risk of dying among current smokers in relation to that among never or former smokers, adjusting for the other risk factors. Using age as the time scale allows comparisons between the hazards of death in groups of comparable ages but in different calendar periods. Since individuals entered into observation at different ages, the survival methods used here were those for cohort studies with staggered entry times. An individual subject contributed to the risk sets only at ages where he could have been observed. Comparisons carried out did not violate the assumption of constant proportionality of the hazards. The inclusion of interaction terms in the model allowed assessment of whether the relative risk associated with smoking varied according to baseline health status.

TABLE 1. Distribution of 477 men aged  $\geq 65$  years by age at study entry in 1986 and vital status in 1994, Health Interview Survey of Barcelona, Barcelona, Spain

Age (years) at study entry (1986)	No.	% of deaths	Mean years of follow-up
65–74	310	29.4	7.1 (2.3)*
75–84	150	56.7	5.8 (2.6)
>84	17	70.6	4.4 (3.1)
All ages	477	39.4	6.6 (2.5)

\* Numbers in parentheses, standard deviation.



TABLE 2. Baseline health status (%) of 477 men aged  $\geq 65$  years, according to cigarette smoking, Health Interview Survey of Barcelona, Barcelona, Spain, 1986

Health status at study entry	Baseline smoking status		
	Never smoker (n = 120)	Former smoker (n = 222)	Current smoker (n = 135)
Fair, poor, or very poor self-rated health	32.8	38.7	23.7
Difficulty or dependence in basic activities of daily life	26.9	34.4	22.6
Heart disease	9.2	17.1	8.2
Respiratory disease	7.5	20.7*	18.5*
Poor baseline health (any of the above)	55.0	64.9*	51.1

\*  $p < 0.05$  in comparison with never smokers (logistic regression analysis with adjustment for age).

## RESULTS

Only 120 (25.2 percent) of the 477 men were never smokers. Two hundred and twenty-two men (46.5 percent) had stopped smoking, and 135 (28.3 percent) were current smokers. The average duration of smoking was 42.6 years in former smokers and 53.4 years in current smokers. Among the former smokers, 47.8 percent had stopped smoking after the age of 65 years.

Individuals who had stopped smoking (former smokers) reported poorer baseline health than never smokers and a higher frequency of cardiac and respiratory conditions (table 2). Health status was worse among men who had stopped smoking after the age of 65 years (38 percent of them reported having difficulty in activities of daily living and 23 percent had respiratory diseases). Current smokers reported being in better health than never smokers and less frequently having difficulty or dependence in activities of daily living; however, the differences were not statistically significant ( $p > 0.1$ ), except for the prevalence of respiratory diseases ( $p < 0.05$ ).

The age-adjusted rates of specific and all-cause

mortality are shown in table 3. Current smokers had higher risks of dying from any type of cancer (age-adjusted relative risk (RR) = 3.11, 95 percent confidence interval (CI) 1.38–7.01), from cardiovascular disease (RR = 1.33, 95 percent CI 0.71–2.50), and from respiratory disease (RR = 3.36, 95 percent CI 0.64–17.4) than never smokers, though the difference was statistically significant only for cancer ( $p < 0.05$ ). Adjustment for self-perceived health, activities of daily living, cardiac or respiratory diseases, alcohol intake, and physical activity did not confound or modify these risks.

The yearly excess mortality attributed to the persistence of smoking was 38.4 deaths per 1,000 persons aged  $\geq 65$  years. The highest proportion of the excess mortality was due to cancer (26.9 – 9.2 = 17.7 (see table 3), which accounts for 46.1 percent of the excess), followed by cardiovascular diseases (14.8 percent) and respiratory diseases (10.9 percent).

Figure 1 depicts the survival function after age 65 years for never, former, and current smokers, by age. Half of the never smokers died before reaching age 84, whereas half of the current smokers died before reaching age 78. The age-adjusted relative risk for current smoking was 2.11 (95 percent CI 1.37–3.26). This higher risk was maintained after adjustment for self-reported health status, basic activities of daily living, and cardiac or respiratory diseases. We did not find any interaction between smoking and alcohol consumption; the preventive effect of alcohol intake among never smokers was also observed among smokers.

Among former smokers, the relative risk for all-cause mortality was significantly higher than that in never smokers (RR = 1.53, 95 percent CI 1.03–2.27) but was lower than that in current smokers (RR = 0.73, 95 percent CI 0.52–1.02), coinciding with the survival function depicted in figure 1. After adjustment for baseline health status, the relative risk of

TABLE 3. Average annual age-adjusted mortality per 1,000 person-years of observation for major causes of death, by smoking status at baseline: Health Interview Survey of Barcelona, Barcelona, Spain, 1986–1994

Cause of death (ICD-9† codes)	Age-adjusted mortality rate (deaths per 1,000 person-years)					
	Never smokers (37/83)‡		Former smokers (88/134)		Current smokers (63/72)	
	Rate	95% CI†	Rate	95% CI	Rate	95% CI
Cancer (140–239)	9.2	4.6–18.5	12.2	7.7–19.4	26.9*	17.9–40.5
Cardiovascular disease (390–459)	18.1	11.3–28.9	25.3	18.3–34.9	23.8	11.4–30.4
Respiratory disease (460–519)	1.7	0.4–7.1	6.0	3.2–11.8	5.9	2.4–14.1
All causes	37.7	27.1–52.5	60.4*	49.0–74.5	76.1*	59.4–97.4

\*  $p < 0.05$  in comparison with never smokers, assuming a Poisson distribution.

† ICD-9, *International Classification of Diseases*, Ninth Revision; CI, confidence interval.

‡ Numbers of persons (dead/alive).

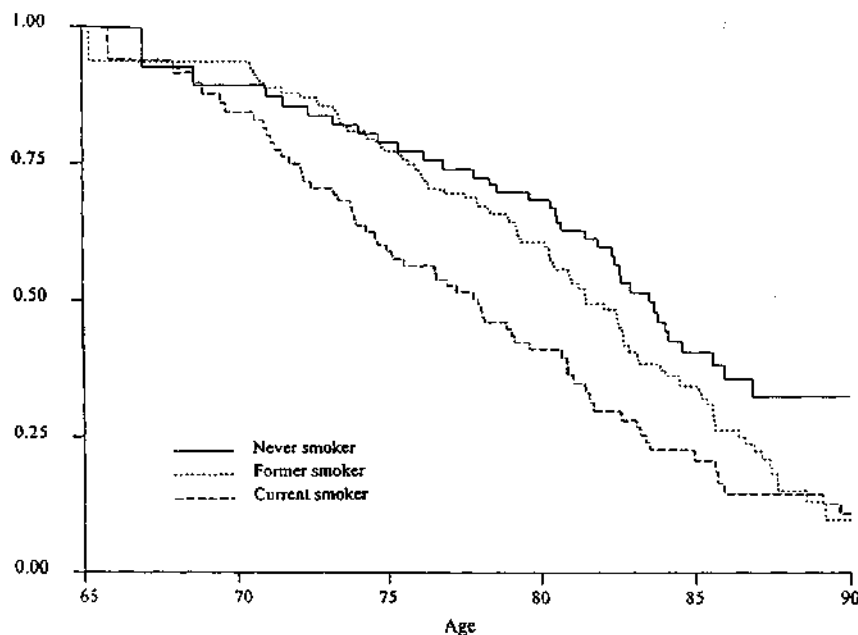


FIGURE 1. Survival (proportion) after age 65 years according to smoking status, Barcelona, Spain, 1986-1994. —, never smokers; ····, former smokers; ---, current smokers.

dying among individuals who had quit smoking in comparison with current smokers decreased to 0.69 (95 percent CI 0.49-0.97). After adjustment for baseline health, quitting smoking after age 65 years was associated with a decreased risk of death in comparison with persisting in smoking (age-adjusted mortality from all causes = 69.0 deaths per 1,000 person-years; RR = 0.77, 95 percent CI 0.51-1.16), although this reduction was not statistically significant.

## DISCUSSION

This study found that smokers who survived to old age had a higher risk of dying than did never smokers, while those who stopped smoking, even after age 65 years, had an intermediate risk. These results confirm the findings of previous studies carried out in the United Kingdom and the United States (1, 2, 8, 9). A second finding was that former smokers reported more cardiac and respiratory diseases than never smokers, which is consistent with results from the Framingham cohort (4). This suggests that poorer health was one reason for quitting smoking.

This study contributes to the ongoing assessment of the worldwide epidemic of smoking-related deaths in several ways: 1) it provides data from a specific area with a relatively late onset of cigarette smoking and with dietary factors that differ from those of other studies, including different patterns of alcohol consumption (12); 2) the data analyzed were based on a representative sample of the noninstitutionalized el-

derly population; and 3) we were able, at least partially, to avoid the confounding effect of a worse health status associated with stopping smoking in evaluating the benefit of quitting smoking after age 65.

It is important to note that the tobacco consumed in Spain during the 1960s and 1970s was mainly the black type, which differed from the mainly blond tobacco consumed in the United Kingdom and the United States. Blended tobacco was introduced in Spain in the 1960s, and its use increased until 1988, when it constituted half of all tobacco sold in Spain (21). However, we could not assess the effect of tobacco type in our study.

The magnitudes of the risk ratio and risk difference for all-cause mortality were somewhat greater in our study (RR = 2.1) than in a US study (2) (RR = 1.9) and in a UK study (1) among persons aged 65 years or older (RR = 1.7). Doll et al. (1) reported a decrease with age in the risk of dying due to smoking, which they explained by a reduction in the proportion of deaths caused by cancer and the reduction in intensity of smoking among the elderly. In our study, most of the excess mortality attributed to tobacco use was due mainly to cancer (46 percent of the excess deaths), not to cardiovascular conditions as in previous studies (1, 2). Similarly, in the mortality statistics of Barcelona (22), the proportion of mortality due to cancer at ages 65-74 years was higher (38 percent) than that in the United Kingdom (24 percent) and the United States (26 percent) (1, 2). Since misclassification of diag-

noses is unlikely to occur when causes of death are combined into a few large groups, as a previous validity study conducted in Barcelona showed (23), a likely explanation is that the cancer epidemic due to smoking in Barcelona was postponed, appearing in persons of older ages because of a delay in the introduction of mass cigarette smoking.

We found a benefit of stopping smoking in this elderly Barcelona cohort that was consistent with findings from other cohorts. An improvement in survival was observed, even though persons who had stopped smoking had poorer self-perceived health and were more frequently reported to suffer from cardiac and respiratory diseases. Those who stopped smoking after age 65 also showed a reduction in the mortality hazard (though it was not statistically significant, probably because of the reduced number of subjects who quit after age 65).

Alcohol could confound some of the association between smoking and premature death, because of its protective effect against cardiovascular disease (13, 14) and because smoking and alcohol use are highly correlated. Alcohol consumption is common in Spain (74 percent of our males drank alcohol), but most of our subjects (81 percent) reported moderate consumption (<40 g/day). However, for both all-cause and cardiovascular mortality, we found similar relative risks associated with smoking in alcohol consumers and abstainers, as well as similar protective effects of alcohol in smokers and nonsmokers.

Misclassification of smoking status could have biased our results. However, use of repeated information on smoking allows assessment of and improvement in the quality of data. When we took as "never" smokers and "current" smokers only those individuals who reported being such in both interviews (i.e., in both 1986 and 1993-1994), the hazard ratio for smoking became even higher (RR = 2.49). The lower relative risk found when we defined smoking only by the information obtained in 1986 can probably be explained by the misclassification, as current smokers, of subjects who stopped smoking between 1986 and the year of death. Unfortunately, the short time interval between the second interview and the end of follow-up precluded the use of this secondary information on smoking to more accurately define exposure. The group with less consistent data was the former smokers, since this group could have included persistent smokers who, because of embarrassment, did not accurately report their actual smoking status. However, when we defined smoking only by the men who reported being former smokers on both questionnaires, we still found a beneficial effect of stopping smoking.

In summary, the present study found that smoking

reduced life expectancy by approximately 6 years among persons alive at age 65 in a Mediterranean city. We estimated that almost 38 deaths per 1,000 males aged  $\geq 65$  per year could be attributed to smoking—the same number of deaths that could be attributed to all of the other causes (table 3). In addition, the findings suggested that quitting smoking was beneficial even after health had deteriorated (probably in association with previous smoking). The resulting estimates of public health impact are of a similar magnitude as, if not higher than, those reported by prospective studies carried out in countries with an earlier peak in tobacco smoking prevalence and different lifestyle patterns. These results support the prediction made by other investigators (24, 25) that a rise in mortality will follow the recent massive introduction of smoking in developing countries.

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PAPER S2: Comparison of performance-based and self-rated functional capacity in Spanish elderly.

Ferrer M., Lamarca R., Orfila F. and Alonso J. American Journal of Epidemiology 1999; 149(3):228-35. Oxford University Press



## Comparison of Performance-based and Self-rated Functional Capacity in Spanish Elderly

Montserrat Ferrer, Rosa Lamarca, Francesc Orfila, and Jordi Alonso

Recent data have shown differences between Spain and the United States in the prevalence of reported disability among community elderly. Differences in reporting functional capacity by culture may contribute to these observed differences. The purpose of this study was to estimate the agreement between self-report of disability and performance-based measures for some basic mobility tasks in the community-dwelling elderly of a Mediterranean country. Interviews containing questions about difficulty for walking and rising from a chair, and performance-based measures (walking speed and chair stand tests) were carried out in 626 individuals aged 72 years and older in Barcelona, Spain. Kappa statistics were calculated, and logistic regression models were constructed to identify possible factors associated with under- and overreporting functional capacity. Moderate kappas (0.41–0.55) were found between self-report and performance-based measures. Patients who rated their health as "poor or very poor" were less likely to underreport disability (adjusted odds ratio (OR) = 0.2, 0.4) but more likely to overreport it (adjusted OR = 23.4, 9.9). No significant agreement differences by sex or informant source were found. These findings suggest that Spanish elderly self-report functional capacity accurately and that, contrary to previous results among US elderly, the direction of the observed disagreement is not systematic. *Am J Epidemiol* 1999;149:228–35.

activities of daily living; aged; aging; disability; geriatric assessment

In the past two decades, assessment of disability has been increasingly used to characterize the health status and health service needs of older populations. Disability in older persons has been generally assessed through self-reported indicators of functioning on different activities of daily living. However, it is only recently that physical performance measures have been developed. Performance-based measures consist of objective observations of functional capacity and are claimed to be applicable cross-culturally because they seem less likely to be as influenced by culture, language, and educational level as are self-reported measures (1–3). A few comparisons between self-reports and performance test results conducted in the United States (4–8) and Canada (9) have been published, but with no consistent conclusions. However, good correspondence (overall agreement >80 percent)

has been found in US studies conducted among community-dwelling elderly (7, 8).

In Spain, recent data (10) have shown that prevalence of reported disability in community elderly is somewhat lower than that reported in the US studies (11–13), but comparability may be limited due to differences in methods and definitions. A potential source of this difference is that the Spanish elderly underreport disability. This could be due to a lower availability of long-term care and social services and/or a different cultural approach to aging (for instance, a much higher proportion of Spanish elderly live with their family (10) and institutionalization rates among the elderly are much lower in Spain than in the United States).

While performance-based measures are not a gold standard of disability nor functional capacity, they seem reliable enough and are probably less culturally dependent than self-reports in order to make comparisons across countries (8, 14). For instance, if prevalence of functional limitations as assessed by performance-based measures are similar, differences of prevalences based on self-reports are more likely to be due to cultural or environmental factors.

The purpose of this paper was: 1) to evaluate the agreement between self-report of disability and performance-based measures for some basic mobility tasks

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Abbreviations: CI, confidence interval; EPESE, Established Populations for the Epidemiologic Study of the Elderly; OR, odds ratio.

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in the community-dwelling elderly of a Mediterranean country; and 2) to examine the factors which may influence self-report independently of physical function.

## MATERIALS AND METHODS

### Population sample

A cohort of elderly adults included in the "Health Interview Survey of Barcelona" (15) was studied. Details about the study have been described elsewhere (10, 16, 17). Briefly, from a total sample of 1,632 eligible individuals aged 65 years or older who resided in the city of Barcelona (population = 1.5 million inhabitants), 1,315 (80.6 percent) participated in the baseline interview in 1986 and constituted the study cohort (15). Survivors were considered eligible for a reinterview and physical examination conducted between June 1993 and June 1994, after a median of 7.5 years of follow-up. The analyses presented here are based on the 1993–1994 reinterview data, because this was the only wave on which performance-based and self-report measures were included.

At the moment of the reassessment, from the 1,315 individuals of the initial cohort, 424 had died and 19 were institutionalized. From the 872 individuals alive and living in the community, 735 (84.3 percent) were interviewed (68 refused the interview and 69 could not be contacted). Compared with participants, persons who had no second interview were similar in terms of age, sex, and level of education, and also reported similar perceived health and functional capacity to perform nine basic activities of daily living at the baseline interview. Participants were interviewed at their homes, and performance-based measures were assessed after the interview. Performance-based data were missing for 109 of the interviewees (86 were refusals, 18 did not live in Barcelona, and five presented cognitive incapacity) and thus were excluded from the analyses. The final sample size for this analysis was 626.

### Interview

Variables recorded in the interview included: perceived health status, functional capacity, health-related practices, and health-services utilization, as well as sociodemographic and other information. Self-perceived health was assessed by the question, "In general, how would you rate your health: very good, good, fair, poor, or very poor?" (15). Functional capacity was assessed by asking the participants to rate their level of difficulty to carry out nine basic activities of daily living ("What level of difficulty do you have to perform

the activity without help or devices? none, a little, moderate or unable to perform the function"). Only the two activities corresponding with performance measures (see below) were chosen for the comparison ("walking" and "standing up and sitting down from a chair"). Two dichotomous variables were created: individuals were first classified as having "self-reported difficulty" if they had reported any level of difficulty, or "without difficulty" otherwise; subsequently, they were considered as having "self-reported need for help" if they had reported being unable to perform the activity without help or devices, or "without need for help" otherwise. Thus, both variables assessed disability, with "self-reported need for help" reflecting a more severe level.

### Physical performance measures

Performance measures were adapted from the Established Populations for the Epidemiologic Study of the Elderly (EPESE) performance test, a short battery of tests to assess lower extremity function, which has been used widely in the United States (1, 18) and more recently in the Netherlands (19) to assess functions needed to perform routine daily activities. The measures were designed to be applied by lay examiners in a home setting with limited space (1). Interviewers were specially trained in the administration of the performance measures used in the study. To ensure uniformity of administration, in training interviewers, we used the videotape produced for the EPESE with detailed instructions for administering and scoring the tests, as well as instructions on maintaining the safety of the subjects.

Walking speed test followed procedures used by the EPESE, with the exception of the distance: rather than a course of 8 ft (2.44 m), we used 4 m, as in another study (20). The walking speed test therefore consisted of having the participant walk over a course of 4 m and recording the time needed to complete the entire path. The test was repeated twice and the shortest time was used in the analysis. Participants were instructed to "walk at their usual speed, just as if they were walking down the street to go to the store," and they could use assistive devices if they needed them.

The chair stand test was carried out by having the participant stand up and sit down from a chair five times as quickly as possible and recording the total time required. Chairs were those at the interviewees' homes.

For both performance measures, a three-level ordinal variable was constructed, ranging in score from 0 to 2: 0 = individuals who could not complete the task or the task was not attempted; 1 = slower times (>1st quartile time); and 2 = quicker times ( $\leq$ 1st quartile time).

## Analysis

Differences in sociodemographic characteristics and functional status by sex were tested using the chi-square test for proportions.

Comparisons were made between self-reported function measures and similar physical performance tests: 1) reported difficulty to walk was compared with the observed ability to walk 4 m; 2) reported difficulty to stand up and sit down from a chair was compared with the observed ability to rise five times from a chair. Crude agreement and Kappa coefficients were calculated to estimate the agreement between interview and physical examination data (21, 22). To determine accuracy of reported functional problems, sensitivity and specificity (23) were calculated for each comparison. For these analyses, physical performance tests were considered the "true positive," although this is clearly an arguable assumption. Confidence intervals for these proportions were calculated using the exact binomial formula. Analyses were performed using the statistical package Epi Info (USD Inc., Stone Mountain, Georgia). All *p* values are two-tailed.

In addition to agreement, analyses examined the percent of bias in subject self-reports compared with observed performance (14, 24). Percent bias was calculated as the ratio of the difference between the proportion of reported disability and the proportion of observed limitation to perform the task, expressed as percent of the proportion of subjects with observed limitation. A positive percent bias indicates that subjects reported disability more often than functional limitation to perform the task was observed. Bias was tested for statistically significant departures from zero using McNemar's test (25).

Logistic regression models were constructed to identify possible factors associated with under- and overestimation of functional limitation from reported disability. Subject's sex, age, perceived health, level of education, type of informant (self- or proxy-report), number of chronic conditions, and health-related practices (smoking, alcohol consumption, and physical activity) were included as independent variables. Analyses were performed using the statistical package SPSS-PC (SPSS, Inc., Chicago, Illinois).

## RESULTS

The mean age of participants was 79 years (standard deviation (SD) = 5.16). Their sociodemographic characteristics, perceived health status, and both self-report and performance-based measurements of functional capacity are shown in table 1. The proportion of individuals who reported disability was relatively low even when considering the less restrictive definition

(31 percent reported "difficulty" for walking and 19 percent "difficulty" for standing up). Women reported more disability than men and also obtained significantly worse scores on the physical performance measures. Individuals with and without physical performance data were of similar age and level of education, and reported similar perceived health and disability, although information for individuals with missing performance test was more frequently provided in interview responses by a proxy.

The comparison between reported "need of help" to walk and the ability to walk 4 m is presented in the top portion of table 2. Specificity (98 percent) was high and kappa was moderate (0.55), indicating that reported disability to walk is acceptably accurate. Nevertheless, false negatives were quite frequent: 42 percent of participants who were unable to complete the walk 4 m in the performance test did not report need for help. For the comparison between reported "difficulty" and the proportion of subjects who walked slowly (table 2, middle third), specificity was again quite high, kappa was moderate, and false negatives were fairly frequent (40 percent of participants who walked slowly did not report difficulty).

The bottom third of table 2 presents the comparison between reported difficulty to stand up or sit down from a chair and observed times to perform five consecutive rises from a chair. For this comparison, specificity (92 percent) was again high and kappa was moderate (0.55), indicating that reported disability to stand up is accurate. Nevertheless, false negatives were moderately frequent (37 percent of participants who were unable to rise five times from a chair did not report difficulty).

For each of the comparisons, although false positive rates were higher than false negative rates, a lack of systematic direction of the disagreement was observed (bias was less than 25 percent and was not statistically significant), indicating that around 50 percent of subjects overreported their limitation (52 percent for "need of help to walk," 57 percent for "difficulty to walk," and 49 percent for "difficulty to rise from a chair" (table 2)) while the other half underreported it.

Multiple logistic regression analysis (table 3) showed that perceived health was the variable most strongly and consistently associated with disagreement between performance and self-reports. Those patients who rated their health as "fair," "poor," or "very poor" were less likely to underreport but more likely to overreport disability than patients who perceived health as "very good" or "good." In addition, proxy respondents, subjects in the older age groups, and educated subjects tended to underreport significantly less "difficulty" in walking (table 3, first column).



**TABLE 1. Percent distribution of sociodemographic characteristics and functional status among 626 elderly adults, Barcelona, Spain, 1993-1994**

Characteristic	Study sample			Missing performance test (n = 109)	p value†	
	Males (n = 217)	Females (n = 409)	p value*			Total (n = 626)
Females				65.3	70.6	0.280
Age (years)						
72-74	22.1	22.5		22.4	22.9	
75-79	38.2	37.9		38.0	29.4	
80-84	26.3	25.7		25.9	25.7	
≥85	13.4	13.9	0.996	13.7	22.0	0.104
Level of education						
Unable to read or write	2.3	7.8		5.9	10.3	
Incomplete primary school	16.7	29.1		24.8	15.5	
Complete primary school	51.6	51.1		51.3	56.9	
High school or university	29.3	12.0	<0.001	17.9	17.2	0.273
Source of information proxy	5.1	8.8	0.092	7.5	38.5	<0.001
Perceived health						
Very good or good	51.4	40.8		44.5	47.7	
Fair	38.9	44.5		42.6	35.8	
Poor or very poor	9.7	14.7	0.027	13.0	16.5	0.348
Reported functional capacity						
Difficulty for walking	22.9	34.4	0.003	31.1	38.5	0.127
Need of help for walking	2.3	5.6	0.064	4.7	7.3	0.243
Difficulty for standing up	7.5	24.2	<0.001	18.5	19.3	0.847
Need of help for standing up	1.4	4.3	0.057	3.2	4.6	0.403
4 meters walking speed test						
Unable	3.2	4.8		4.2		
Slow	16.2	27.6		23.6		
Quick (≤7.5 seconds)	80.6	67.7	0.003	72.2		
5 times chair stand test						
Unable	14.4	20.6		18.4		
Slow	14.4	23.6		20.4		
Quick (≤16.5 seconds)	71.2	55.8	<0.001	61.2		

\* Chi-square test of gender differences.

† Chi-square test of interview differences between those participants with performance test available and not available.

In table 4, results from physical performance tests for the sample studied in this paper ("Spanish sample") are compared with those in a previous US study (1) ("US sample") which used exactly the same procedures with exception of the distance assessed for the walking speed test (2.44 m instead of 4 m). Both samples showed a similar prevalence of individuals who were unable to perform these tests and required a similar time to complete the chair stand test. Nevertheless, US elderly performed somewhat more poorly than Spanish elderly in the walking speed test.

## DISCUSSION

The purpose of this study was to examine the agreement between self-report of disability and perfor-

mance-based measures in the community-dwelling elderly of a Mediterranean community. Although performance measures were considered as the standard criterion for this comparison, some conceptual differences between the two measures exist: while subject self-reports are closer to the concept of disability because they reflect subjective performance within a sociocultural context, the assessment of an external observer is closer to objective functional limitation. An individual with a limitation in a specific task might have adapted to his/her environment and may not perceive this limitation as a disability. Also, a limitation may not translate into disability if the specific activity is not very relevant for the individual in his/her daily life. Therefore, perfect agreement was not expected

**TABLE 2. Agreement between reported disability and observed performance among 626 elderly adults, Barcelona, Spain, 1993-1994**

Reported performance	Observed performance		Sensitivity* (95% CI)†	Specificity* (95% CI)†	% Agreement (95% CI)†	Kappa (SE)†	% bias	p value‡
	4 meters walk							
"Need of help" to walk	No. unable	No. able						
Unable	15	12	0.58	0.98	96	0.55	4.0	1.0
Able	11	571	(0.37-0.77)	(0.96-0.99)	(94-98)	(0.04)		
Total	26	583						
	4 meters walk							
"Difficulty" to walk	No. slow§	No. quick§						
Difficulty	85	75	0.60	0.83	78	0.41	13.4	0.116
No difficulty	56	367	(0.52-0.68)	(0.79-0.86)	(74-81)	(0.04)		
Total	141	442						
	5 rises from chair							
"Difficulty" to stand up from chair	No. unable	No. able						
Difficulty	71	41	0.63	0.92	86	0.55	-0.9	1.0
No difficulty	42	455	(0.53-0.72)	(0.89-0.94)	(83-89)	(0.04)		
Total	113	496						

\* Sensitivity and specificity were calculated considering the physical performance test as the gold standard.

† CI, confidence interval; SE, standard error.

‡ p value for a test of zero bias (McNemar's test).

§ Slow = subjects who spent >7.5 seconds to walk 4 m; quick = subjects who spent ≤7.5 seconds to walk 4 m.

although comparisons between the two measures were considered informative in order to improve the assessment of disability in the elderly (8, 14).

We found moderate agreement between performance-based and self-report measures (kappa ranging from 0.41 to 0.55). Percent agreement (ranging from 78 to 96 percent) is well in accordance with that reported in comparable studies published in the United States (7, 8). Nevertheless, while the direction of the differences observed in those studies was systematic (most of the time when a disagreement was identified, the reported disability was greater than the functional limitations observed), in our sample, the direction of the differences was not systematic. Around 50 percent of the time when a disagreement between self-report and performance was identified, the reported disability was higher than the functional limitation observed and the opposite was found for the other half. Thus, the level of overreporting of disability observed in our sample was lower than that observed in the US studies. These results, together with the fact that there seems to be no relevant differences in performance-based functional capacity between Spanish and US elderly, suggest that Spanish elderly are truly as functionally limited as their US peers. Therefore, the lower prevalence of self-report disability among Spanish elderly may be attributed to their lower tendency to overreport observed limitations.

Detailed discussion of the causes of a cultural effect when reporting disability in basic mobility activities is beyond the scope of this article. Nevertheless, it may be speculated that different expectations, and differences in the availability and access to health services may contribute to differences in disability reporting for a similar level of objective functional limitation. In any case, our results do support the conclusion that both self-report and performance-based measures of functional limitation provide quite similar aggregate information of non-institutionalized elderly in our culture. This is useful in planning health services. On the other hand, our results also indicate that information based on self-reported disability should be used cautiously for individual assessments.

As in previous studies (7, 26), disagreement between self-report and performance-based measures was influenced by the level of perceived health status. Subjects who rated their health as poor ("fair," "poor," or "very poor") were more likely to overreport functional limitation while subjects who perceived their health as "very good" or "good" tended to underreport limitations. A possible explanation is that individuals with illnesses that affect their general health status may perceive physical symptoms (pain or discomfort) as functional limitation. Nevertheless, the influence of perceived health status remained after adjusting by the number of chronic conditions. Our results suggest that subjects

**TABLE 3. Association of informant, demographic characteristics, and health status with underestimation and overestimation of functional limitation from reported disability (adjusted by smoking, alcohol consumption, number of chronic conditions, and physical activity) among 626 elderly adults, Barcelona, Spain, 1993-1994**

Characteristic or health status	Underestimation (only participants with functional limitation)				Overestimation (only participants without functional limitation)			
	Walking slowly* (n = 141)		Unable to rise 5 times† (n = 113)		Walking quickly‡ (n = 442)		Able to rise 5 times§ (n = 496)	
	OR¶	95% CI¶	OR	95% CI	OR	95% CI	OR	95% CI
Informant								
Self	1.0		1.0		1.0		1.0	
Proxy	0.1	0.02-0.56	0.3	0.10-1.23	1.6	0.32-8.38	3.8	0.75-19.1
Sex								
Men	1.0		1.0		1.0		1.0	
Women	2.4	0.56-10.0	0.9	0.20-4.11	1.6	0.57-4.70	6.1	0.83-44.5
Age (years)								
72-74	1.0		1.0		1.0		1.0	
75-79	0.2	0.04-0.95	1.5	0.26-8.83	1.6	0.69-3.60	0.8	0.32-1.80
80-84	0.6	0.13-2.71	0.5	0.07-3.00	3.5	1.42-8.39	0.4	0.12-1.17
≥85	0.4	0.09-1.96	0.9	0.13-6.75	2.9	0.85-10.1	0.8	0.19-3.17
Level of education								
Unable to read or write	1.0		1.0		1.0		1.0	
Incomplete primary school	0.2	0.03-0.94	1.9	0.17-21.1	0.3	0.10-1.19	0.4	0.11-1.43
Complete primary school	0.1	0.02-0.66	3.1	0.28-34.8	0.4	0.12-1.16	0.5	0.15-1.54
High school or university	0.1	0.01-0.65	9.2	0.59-141.1	0.6	0.17-2.06	0.5	0.11-2.32
Perceived health								
Very good or good	1.0		1.0		1.0		1.0	
Fair	0.8	0.30-2.19	0.4	0.12-1.59	3.0	1.47-6.03	2.4	0.92-6.00
Poor or very poor	0.2	0.06-1.04	0.4	0.09-1.75	23.4	7.71-70.9	9.9	3.03-32.3

\* Multivariate logistic regressions with the dependent variable coded as: 0 = agreement (reporting difficulty to walk) and 1 = disagreement (reporting no difficulty to walk).

† Multivariate logistic regressions with the dependent variable coded as: 0 = agreement (reporting difficulty to rise from a chair) and 1 = disagreement (reporting no difficulty to rise from a chair).

‡ Multivariate logistic regressions with the dependent variable coded as: 0 = agreement (reporting no difficulty to walk) and 1 = disagreement (reporting difficulty to walk).

§ Multivariate logistic regressions with the dependent variable coded as: 0 = agreement (reporting no difficulty to rise from a chair) and 1 = disagreement (reporting difficulty to rise from a chair).

¶ OR, odds ratio; CI, confidence interval.

with a negative perception of health tended to rate their functional capacity negatively independently of their "true" health status. Because a strong and robust association between self-rated health and mortality that cannot be explained by measures of physical health obtained in a more objective manner has been consistently shown (27-32), this is a group with increased care needs.

Although it is well known that prevalence of reported disability is higher among elderly women than among men, to our knowledge, only one study, by Myers et al. (8), has compared self-reports and performance of tasks and addressed sex differences. The higher rate of reported disability among women in our study is accompanied by a higher rate of observed functional limitation. Furthermore, disagreement between self-report and performance-based measures was not influenced by sex. Thus, consistent with the study by Myers et al. (8), our results support the evidence that the higher prevalence of reported disability among older women truly reflects a higher level of functional limitation.

Whether proxy reports can be used interchangeably with self-reports is an important issue in community elderly surveys. In our study, proxy respondents were less likely to underreport functional limitation than self-respondents, but they did not present significant differences for overreporting. This finding is in contrast to previous studies (4, 6, 14, 33) which have shown that proxy-reports were less accurate. Although cultural differences could explain the higher accuracy of proxy respondents found in our study, a methodological issue should be taken into account. Our study differs from the works mentioned above because instead of comparing the information of the same individual from two sources (proxy and self-report), we obtained information from a proxy only when the eligible participant was unable to self-respond (7.5 percent of the sample). In fact, Corder et al. (34), who also obtained their data from a unique information source, found small differences by proxy respondent in the accuracy of reporting service use. Proxy respondents are probably individuals who are very involved with the subject's care,

**TABLE 4. Comparison of Spanish and US elderly in observed walking speed and 5-times chair stand performance tests\***

Age or test	Men			Women		
	Spanish	US	<i>P</i> value†	Spanish	US	<i>P</i> value†
Age (years)						
71-79	60.3	69.4		60.4	61.3	
≥80	39.7	30.6	0.007	39.6	38.7	0.724
5-times chair stand test						
Unable (%)	14.3	17.7	0.231	20.6	23.7	0.167
Mean time (seconds)	13.3	13.7		15.2	14.9	
95% CI‡	12.7-13.9			14.6-15.8		
Walking speed test						
Unable (%)	3.2	4.2	0.501	4.8	5.3	0.641
Mean speed (m/seconds)	0.66	0.55		0.55	0.42	
95% CI	0.60-0.72			0.52-0.59		

\* Spanish data from present study of 626 elderly adults in Barcelona, 1993-1994, and US data extracted from the study by Guralnik et al. (1) of over 5,000 elderly adults in three US communities.

† Chi-square test of differences between Spanish and US elderly.

‡ CI, confidence interval.

because the majority of proxy responses were due to the difficulty of obtaining a response from the eligible participant because of health problems, and therefore, they are likely to better know the participant's functional capacity. This finding is important since it suggests that in severely impaired individuals the proxy responses are valid.

Some limitations of our study should be discussed. First, only agreement for two specific mobility tasks has been examined. Because functional capacity is typically assessed through a global score obtained from several tasks and agreement could differ by specific tasks and by the manner in which measures are scored (14), our results are limited and inferences have to be made cautiously. Second, comparisons with observed functional ability to perform a task among US elderly are based on point estimations. Nevertheless, for ability to rise from a chair, estimations were similar, with the US means being included in the Spanish confidence intervals; and for walking speed, although US means were lower and lay outside the Spanish confidence intervals, it should be pointed out that observed speeds were not directly comparable because walked distances were different. Finally, with regard to the representativeness of our results, despite the fact that the percent of subjects with missing performance-based data was large (15 percent), these subjects reported similar disability levels to those who completed physical performance tests and it is unlikely that their level of agreement was different.

Despite these limitations, our findings suggest that Spanish elderly self-report functional capacity accurately and, contrary to previous results among US elderly (7, 8), the direction of the observed disagree-

ment is not systematic. Our study has also shown that women were not more likely to overreport disability, suggesting that the higher prevalence of reported disability among women reflects a higher rate of functional limitation instead of differences in reporting by sex.

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PAPER S3: Evolution of self-rated health status in the elderly: cross-sectional vs. longitudinal estimates.

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## Evolution of self-rated health status in the elderly: Cross-sectional vs. longitudinal estimates

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### Abstract

We assessed the perceived health status evolution among elderly subjects and examined the age-related differences in perceived health when comparing estimates obtained from cross-sectional and longitudinal approaches. Data come from a cohort of non-institutionalized individuals aged 65 years or older, living in Barcelona, Spain. One thousand three hundred fifteen (1315) elderly were successfully interviewed at baseline in 1986 and 754 (84.6% of the eligible) at the re-assessment (1993–1994). Estimates of change in perceived health status were calculated based on cross-sectional and longitudinal approaches. Cross-sectionally, no significant differences in the proportion of individuals with poor self-rated health were found (40.5 vs. 42.5%,  $P = 0.90$ ). Among survivors, the proportion of individuals with poor health increased from 37.8% to 55.1% ( $P < 0.01$ ), an 8.7-fold decline of perceived health when compared with the cross-sectional estimates. Comorbidity (aOR 2.1; 95%CI: 1.4–3.3) and no education (aOR 1.9; 95%CI: 1.1–3.2) were associated with a decline in health status after adjusting by baseline health status. We recommend the use of longitudinal studies to understand the evolution of perceived health in the elderly. © 2000 Elsevier Science Inc. All rights reserved.

**Keywords:** Aging; Perceived health; Longitudinal studies; Cross-sectional studies; Health surveys

### 1. Introduction

The elderly population is increasing, both in absolute and relative terms. This effect is due to a decrease in fertility as well as a lower mortality rate, including mortality in the oldest groups [1]. As a consequence, there is increasing interest in the evaluation of health and health services needs of the elderly [2].

Until recently, the planning of social and health care services for the elderly was based on demographic projections. However, health and social services utilization is more closely related to the perceived health or functional status of the individuals than to demographic characteristics [3,4]. Chronological age itself may be less associated with physical limitations than it was previously assumed [5]. Moreover, there is growing evidence of the heterogeneous nature of the aging process, suggesting that although it is associated to a higher risk of disability, the relationship is neither inevitable nor uniform [6–8].

Two different perspectives have been adopted when considering the need of health services in an aging population: one “optimistic” and another “pessimistic.” The latter is based on the assumption that a life-expectancy increase will lead to a larger proportion of individuals living more years with sickness and disability, and therefore, to an increased need for health services [9,10]. From the optimistic perspective, a life-expectancy increase should go along with the compression of morbidity, and therefore, there will not be an increased demand for health services [11,12].

Most of the studies estimating the relationship of functional capacity or health-related quality of life with aging are cross-sectional in nature. This type of study does not allow to distinguish properly the effects of age, due to the many coexisting processes contributing to the differences between age groups [13]. These processes include those related to selection bias, as for instance, differential characteristics of surviving individuals as well as their different life experiences. On the other hand, longitudinal studies have focused more on disability or mortality. Yet, there is little information on self-rated health and its evolution as people age. Recently conflicting findings have been reported. Beckett et al. [14] found physical function to worsen as people got older, more so than would be expected from cross-sectional designs. While Denning et al. [15] showed an im-

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provement of perceived health with aging, especially when data were analyzed longitudinally.

We present results from the cohort of elderly adults of the “Elderly Health Interview Survey of Barcelona” that originally was created to describe the health status of the elderly population and to identify factors associated with mortality and functional status deterioration. The aim of this study is to assess self-reported health status evolution and to illustrate the need of longitudinal data to properly estimate age-related changes in reported health status. We compare the inferences regarding the relationship of reported health status and aging, when using cross-sectional data and longitudinal data.

## 2. Methods

Data come from a cohort of individuals aged 65 years or older, non-institutionalized, and residents in the city of Barcelona (population = 1.7 million inhabitants), who participated in a Health Interview Survey in 1986 and were re-interviewed in 1993–1994. More details have been reported previously [16–18].

### 2.1. Sample

A non-proportionally stratified random sample of 3062 households was drawn from the 1985 Local Census Register, stratifying by district and family size. The household was the sampling unit and all members of the household

were considered eligible for the general study. Households with individuals 65 or older were over sampled to get a total of 1632 individuals of this age group.

### 2.2. Study design

The eligible subjects were initially interviewed at home between January 1986 and January 1987 by trained non-medical interviewers, using a precoded questionnaire. Of 1632 individuals, 1315 (80.6%) were successfully interviewed in the baseline study. Some 14% of the interviews were answered by a “proxy,” mainly because the eligible participant had difficulty responding and, to a much lesser extent, because he/she was not at home after three visits at different times. Higher mortality rates, worse reported health status and older age were observed for those participants whose interview was responded by proxy.

The follow-up interview (re-assessment) was carried out between June 1993 and June 1994, after a median of 7.5 years of follow-up. The vital status of the whole cohort was ascertained from the Local Census Register by a confidential record linkage.

Variables recorded in both interviews included among others: perceived health status, functional capacity, comorbidity, as well as socio-demographic variables. Self-rated health was assessed by the question “In general, how would you rate your health: very good, good, fair, poor or very poor?” [16]. Information on social class was based on the occupation of the head of the household [19].

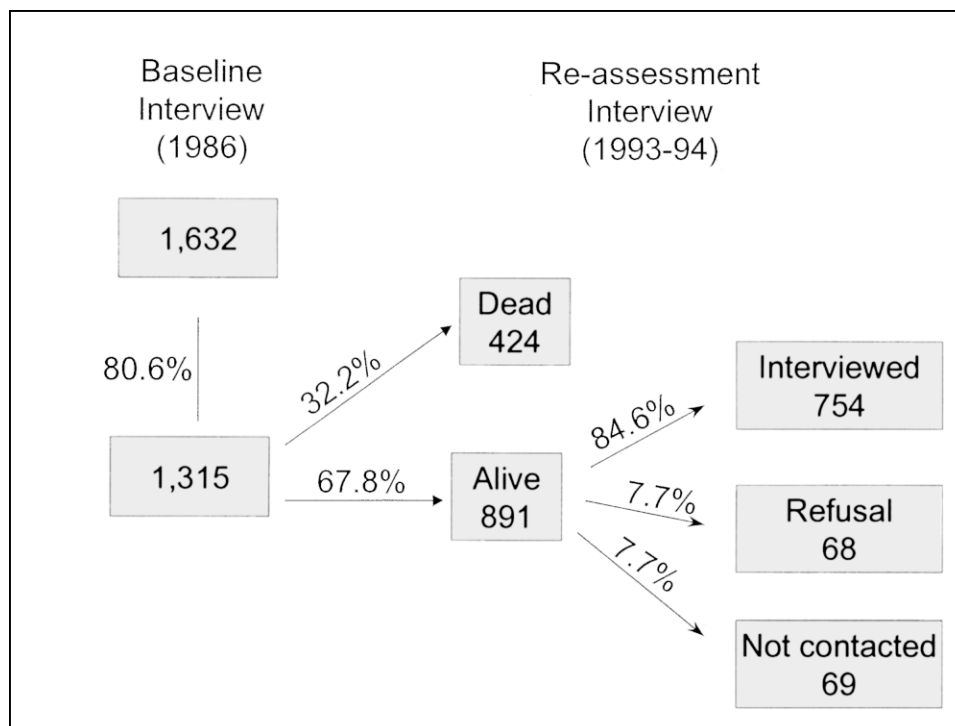


Fig. 1. Participation in the different stages of the Elderly Health Interview Survey of Barcelona.



### 2.3. Enrollment and vital status at the end of follow-up

At the second interview, of the 1315 individuals of the initial cohort, 424 (32.2%) had died (Fig. 1). From the 891 individuals alive, 69 could not be contacted (7.7%), and 68 refused the interview (7.7%). Thirteen point four percent (13.4%) of the re-interviews were answered by a “proxy” respondent.

### 2.4. Analysis

The characteristics of the baseline and the re-assessment samples were assessed by means of computing percentages and compared by means of the chi-square ( $\chi^2$ ) statistic.

A multinomial logistic regression was performed to compare the characteristics of those individuals who were successfully re-interviewed with those who died during the follow-up period and those who refused to participate or were

not traced. Between-individuals (cross-sectional) differences and within-individuals (longitudinal) changes in self-reported health status were compared. Cross-sectionally, comparisons of self-rated health were made between age subgroups at baseline (1986). For these comparisons, we used only data from the baseline interview. After the follow-up period, we compared the baseline (1986) and follow-up (1993) self-rated health status of the same individual, (longitudinal approach). In order to make comparable cross-sectional and longitudinal estimates, we assessed differences in self-rated health status between groups of individuals that differed by on average 8 years of age (length of follow-up time).

Participants in the baseline interview were stratified in age groups of two years (65–66, 67–68, 69–70, and so on) in order to avoid age confusion within age groups. Cross-sectional comparisons of health were established between

Table 1  
Characteristics of the sample studied at baseline (1986) and at the re-assessment interview (1993–1994) Elderly Health Interview Survey of Barcelona

	Baseline interview (1986)			Re-assessment interview (1993–1994)		
	Total ( <i>n</i> = 1.315)	65–74 years ( <i>n</i> = 795)	75+ years ( <i>n</i> = 520)	Total ( <i>n</i> = 754)	72–79 years ( <i>n</i> = 437)	80+ years ( <i>n</i> = 317)
Gender						
Female	61.5 <sup>a</sup>	59.5	64.6	66.3	65.4	67.5
Marital status						
Single	8.0	7.2	9.1	7.1	8.2	5.7
Married	54.7 <sup>a</sup>	66.2 <sup>b</sup>	37.1	44.9	52.2 <sup>b</sup>	34.8
Widow	36.1 <sup>a</sup>	24.8 <sup>b</sup>	53.4	47.0	37.9 <sup>b</sup>	59.5
Divorced/separated	1.3 <sup>a</sup>	1.7 <sup>b</sup>	0.4	1.0	1.7	0.0
Living alone						
Yes	19.2 <sup>a</sup>	18.5	20.3	23.0	25.1	19.9
Social class						
I–II	20.6	21.3	19.6	21.3	20.0	23.1
III	22.4	23.4	20.8	24.2	28.0 <sup>b</sup>	18.9
IV–V	56.9	55.3	59.7	54.5	52.0	58.0
Level of education						
High school or university	24.5 <sup>a</sup>	26.5 <sup>b</sup>	21.4	17.9	20.9 <sup>b</sup>	13.6
Primary school	61.1 <sup>a</sup>	61.9	59.9	75.8	72.9 <sup>b</sup>	79.7
Unable to read or write	14.4 <sup>a</sup>	11.7 <sup>b</sup>	18.7	6.4	6.2	6.8
Self-rated health						
Very good	8.7	7.9	9.9	7.4	6.7	8.3
Good	50.6 <sup>a</sup>	52.3	47.7	37.6	40.8 <sup>b</sup>	33.0
Fair	34.0	33.5	34.9	41.6	38.9	45.3
Poor/very poor	6.8 <sup>a</sup>	6.3	7.5	13.5	13.6	13.3
Comorbidity						
No	30.4 <sup>a</sup>	32.5 <sup>b</sup>	27.3	13.3	16.0 <sup>b</sup>	9.5
Body mass index (BMI)						
Underweight	6.8 <sup>a</sup>	5.5 <sup>b</sup>	9.2	3.9	2.0 <sup>b</sup>	7.0
Normal	65.0 <sup>a</sup>	62.1 <sup>b</sup>	70.1	52.1	49.6	56.1
Overweight	28.1 <sup>a</sup>	32.4 <sup>b</sup>	20.7	44.0	48.4 <sup>b</sup>	36.9
Smoking habit						
Never smoker	67.4	63.7 <sup>b</sup>	73.8	69.4	65.0 <sup>b</sup>	75.4
Former smoker	19.6 <sup>a</sup>	21.1	17.0	23.4	25.7	20.2
Smoker	13.0 <sup>a</sup>	15.2 <sup>b</sup>	9.2	7.2	9.3 <sup>b</sup>	4.4
Physical activity						
Yes	43.1 <sup>a</sup>	48.9 <sup>b</sup>	33.3	36.2	43.4 <sup>b</sup>	23.3
Proxy respondents						
Yes	14.2	10.4 <sup>b</sup>	20.0	13.4	6.2 <sup>b</sup>	23.3

<sup>a</sup> Statistically significant differences between total percentages from 1986 and 1993–1994, column 1 and 4 ( $P < 0.05$ ).

<sup>b</sup> Statistically significant differences between both age groups (column 2 vs. column 3 and column 5 vs. column 6) ( $P < 0.05$ ).

the groups differing by on average 8 years at baseline (65–66 vs. 73–74; 67–68 vs. 75–76; 69–70 vs. 77–78, and so on). For the longitudinal estimates, we selected those individuals who were alive at the time of the second interview, then we directly assessed the change in 8 years as the difference between the health status reported in the baseline interview and the health status reported in the re-assessment. Thus, we compared self-rated health of the same individuals. Differences in health status and other variables were tested using the  $\chi^2$  tests for proportions.

Associations of independent variables with a decline in self-reported health status were ascertained by means of a logistic regression model. The health status of the subjects was considered to decline if they had moved towards a lower (worse) category in the response choice (very good or good, fair, poor, and very poor) in the 1993 re-assessment as compared with the 1986 baseline survey. The data-splitting strategy was used to assess the accuracy of the model: 80%

of the subjects were randomly selected to estimate the model, and with the remaining 20% we ascertained the ability of the model to discriminate outcomes. Once the accuracy of the model had been satisfactorily evaluated, we refitted the model with the whole data set to obtain the final estimates (coefficients). The performance of the final model was assessed comparing the predictions obtained from the model and the observed outcomes.

Analyses were performed using the following statistical packages: SPSS-PC [20] and STATA [21]. All P-values are two-tailed.

### 3. Results

At the re-assessment, after an average period of 7.5 years of follow-up, 561 subjects could not be re-interviewed (Fig. 1). The majority of them had died, the global mortality rate

Table 2

Multinomial logistic regression model assessing the association between baseline characteristics and dead (compared to those successfully re-interviewed) and refusal/not traced (compared to those successfully re-interviewed) Elderly Health Interview Survey of Barcelona

	Dead ( <i>n</i> = 424)		Refusal/not contacted ( <i>n</i> = 137)	
	OR	95% Confidence Interval	OR	95% Confidence Interval
Gender				
Female	1	—	1	—
Male	2.00	1.24–3.21	1.05	0.53–2.07
Age (years)				
65–74	1	—	1	—
75–84	4.07	2.91–5.71	1.19	0.72–1.94
≥85	15.55	7.71–31.33	0.41	0.05–3.27
Level of education				
Primary school	1	—	1	—
High school or university	1.25	0.85–1.82	1.09	0.64–1.84
Unable to read or write	0.79	0.49–1.28	0.85	0.44–1.65
Living alone				
No	1	—	1	—
Yes	0.95	0.62–1.45	0.66	0.39–1.11
Self-rated health status				
Very good/good	1	—	1	—
Fair	1.23	0.88–1.73	1.25	0.78–1.99
Poor/very poor	2.76	1.46–5.22	1.79	0.71–4.49
Comorbidity				
No	1	—	1	—
Yes	1.36	0.93–1.99	0.74	0.45–1.20
Body mass index (BMI)				
Normal	1	—	1	—
Underweight	2.74	1.54–4.90	1.08	0.43–2.75
Overweight	0.93	0.64–1.33	0.61	0.36–1.03
Smoking habit				
Never smoker	1	—	1	—
Former smoker	1.52	0.90–2.59	1.09	0.50–2.38
Smoker	2.40	1.37–4.22	1.38	0.61–3.09
Physical activity				
Yes	1	—	1	—
No	1.70	1.22–2.37	1.39	0.89–2.16
Proxy respondent in 1986				
No	1	—	1	—
Yes	1.25	0.70–2.24	0.64	0.38–1.09

Table 3

Differences in self-rated health (% with fair, poor, or very poor health) at 8 years: comparison between cross-sectional and longitudinal estimates

Cross-sectional					Longitudinal			
Age (1986)	% Fair, poor/very poor health	Age (1986)	% Fair, poor/very poor health	Difference	Initial age (1986)	% Fair, poor/very poor health (1986)	% Fair, poor/very poor health (1993–94)	Difference
65–66	40.7	73–74	41.2	0.5	65–66	38.5	51.9	13.4 <sup>a</sup>
67–68	40.4	75–76	43.2	2.8	67–68	40.0	47.6	7.6
69–70	34.1	77–78	42.7	8.6	69–70	31.9	45.7	13.8
71–72	41.8	79–80	44.3	2.5	71–72	37.7	60.5	22.8 <sup>b</sup>
73–74	41.2	81–82	40.8	−0.4	73–74	34.7	62.7	28.0 <sup>b</sup>
75–76	43.2	83–84	39.5	−3.7	75–76	43.9	63.2	19.3 <sup>a</sup>
77–78	42.7	85–86	48.3	5.6	77–78	40.4	63.5	23.1 <sup>a</sup>
Average	40.5		42.5	2.0		37.8	55.1	17.3 <sup>b</sup>

<sup>a</sup>P < 0.05 y <sup>b</sup>P < 0.01 when proportions were compared using X<sup>2</sup>; all other comparisons non significant.

for the cohort being 32%, with a higher rate amongst men (39%) than women (28%) (P < 0.001). A small proportion of the initial cohort (15%) could not be traced or refused to participate. From the 754 participants of the second assessment, most of them were living in the community, with only 19 institutionalized. Information was obtained from proxies for 101 individuals (13.4%). The latter presented worse reported health status and older ages when compared to those who responded by themselves.

The characteristics of the cohort at both evaluations (baseline and re-assessment) are shown in Table 1. The average age was 73.6 in 1986, and 79.2 at the re-assessment (1993–1994). The proportion of women rose from 61.5% to 66.3%, with a consequently higher number of widows at the second evaluation. A greater number of illiterate individuals

was found among the older elderly at baseline, the proportion decreasing at re-assessment. At the first evaluation, 70% of the individuals reported chronic conditions and 87% at reassessment. While in 1986 the majority of the group assessed their general health as “good” or “very good” (59%), at the re-assessment the proportion of the survivors who stated the same decreased to 45% (P < 0.001). However, no significant differences in self-rated health were found when comparing the two age groups within the two evaluations separately (65–74 vs. 75 or over, and 72–79 vs. 80 or over, respectively). The proportion of proxy respondents remained stable in both evaluations, around 14%.

The factors associated with a higher probability of dying compared to those who were successfully interviewed (Table 2, left side) were: gender (aOR 2.0; 95%CI: 1.2–3.2),

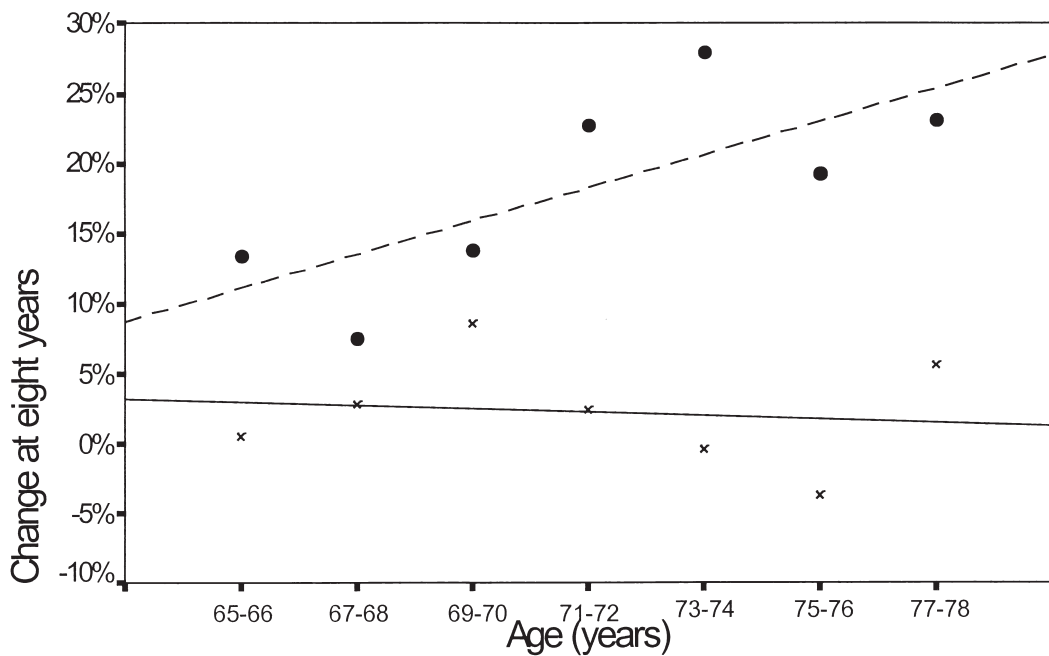


Fig. 2. Cross-sectional (x) and longitudinal (•) estimates of an 8-year difference in self-rated health (% with fair, poor, or very poor health). The solid line fits the means of the proportions estimated from the cross-sectional data and the dashed line fits the means estimated from the longitudinal data.

older ages (75–84 years old, aOR 4.1; 95%CI: 2.9–5.7 and older than 85 years aOR 15.6; 95%CI: 7.7–31.3), reporting very poor or poor health status (aOR 2.8; 95%CI: 1.5–5.2), underweight (aOR 2.7; 95%CI: 1.5–4.9), being a smoker (aOR 2.4; 95%CI: 1.4–4.2), and sedentary lifestyle (aOR 1.7; 95%CI: 1.2–2.4). There were no factors associated to the failure to re-interview (refused or not traced) compared to the successfully re-interviewed group (Table 2, right side).

Differences between cross-sectional and longitudinal estimates of change in perceived health are shown in Table 3. The left side of the table is based on data from the initial evaluation (cross-sectional estimates), and it shows the percentages of “fair,” “poor,” or “very poor” self-rated health for groups of individuals whose age differed on average by 8 years. Differences ranged from –3.7% to 8.6%, with an average of 2.0%, but none of them were statistically significant.

The right side of Table 3 is based on data from both evaluations (longitudinal estimates), and it shows the evolution of self-rated health in surviving individuals. When responses of the survivors of the cohort were compared with their previous responses 7.5 years earlier, there was a significant increase in the proportion of “fair,” “poor,” or “very poor” self-rated health (an average of 17.3%,  $P < 0.01$ ). Therefore, the average longitudinal estimate of change in self-rated health was 8.7 times higher than in the cross-sectional analysis (17.3 over 2.0).

The cross-sectional estimates of change did not increase with age, while the longitudinal analysis showed that the average pattern of decline accelerates with increasing age (Fig. 2). Cross-sectional estimates were more homogenous along age groups, ranging from –3.7 to 8.6, compared to those obtained from the longitudinal analysis (7.6–28.8). Differences between both estimates were slightly larger at older ages.

The probability of experiencing a decline in health status was higher for those who had more than 1 chronic condition (aOR 2.1; 95%CI: 1.4–3.3), and for those who were illiterate (aOR 1.9; 95%CI: 1.1–3.2) (Table 4). Proxy respondents did not show any association with a declining health. With respect to the accuracy of the model, 83.6% subjects with no decline in health status at re-assessment were correctly predicted by the model. Similarly, 44.8% subjects with decline were correctly classified. Overall, 69.6% of the subjects were correctly predicted by the model.

#### 4. Discussion

The aim of the present paper was to assess health status evolution and to examine to what extent it was affected by using cross-sectional or longitudinal data. Our results show that, in addition to an increased probability of dying, aging is also associated with an increased deterioration in perceived health status. The association between age and health status decline loses its statistical significance when comorbidity is considered, suggesting that health status decline may be attributed to suffering from chronic conditions

rather than to chronological age itself. In addition, we found that education was associated with decline. Low education levels have been shown to be associated with longer waiting times for hospital admission, as well as to lower dentist and gynaecologist consultation rates [22]. These findings would suggest that chronic conditions and barriers to health services, such as low educational level, are important contributors to health status decline in the elderly. On the other hand, predictors of death in the elderly are well-established [23–26] and our data confirm age, gender, health status, smoking habit, underweight, and sedentary lifestyle as main risk factors of dying.

In this study, we observed that the estimate of perceived health changes among elderly subjects inferred from a cross-sectional analysis of the data undervalued the level to which deterioration in perceived health is associated with aging by a factor of 8.7. This underestimation could be due to several methodological issues of cross-sectional analysis.

First, the differences in the perception of health at different ages could have been masked by a “cohort effect.” In aging re-

Table 4  
Factors associated with decline in self-rated health after 7 years of follow-up

	aOR*	95% Confidence Interval
Gender		
Female	1	
Male	1.28	0.70–2.33
Age (years)		
65–74	1	
75–84	0.67	0.42–1.08
≥85	0.92	0.20–4.25
Level of education		
Primary school	1	
High school or university	0.79	0.49–1.28
Unable to read or write	1.87	1.09–3.20
Living alone		
No	1	
Yes	1.16	0.71–1.89
Comorbidity		
No	1	
Yes	2.14	1.39–3.30
Body mass index (BMI)		
Normal	1	
Underweight	1.23	0.51–2.93
Overweight	1.46	0.97–2.19
Smoking habit		
Never smoker	1	
Former smoker	1.12	0.56–2.21
Smoker	0.45	0.20–1.01
Physical activity		
Yes	1	
No	0.90	0.62–1.31
Proxy respondent in 1986		
No	1	
Yes	0.51	0.21–1.26
Proxy respondent in 1993–1994		
No	1	
Yes	1.74	0.96–3.17

\* Odds ratios adjusted by baseline health status.

search, a fundamental assumption of the cross-sectional design to estimate change is that the individuals in the study are equivalent in all aspects other than age. Cohort effects refer to differences that may affect people born of different generations [27]. For example, differences between persons aged 70 and those aged 80 may not result from the age gap alone, but instead reflect that the younger group was born in 1923 whereas the older group was born in 1913, and they benefited from different education and environment. These differences in life experiences or in the expectations of the younger cohort may have caused the older cohort to perceive their health more positively, as was recently reported by Spiers and colleagues in a UK cohort [28]. There are also a number of examples in the literature concerning the effects of cohort differences to define the pattern of intellectual abilities with aging [29].

Second, when the older elderly are compared to younger elderly groups in the cross-sectional analysis, a survival bias is introduced. The older elderly are a more selected group in terms of health, given that they are the group within their generation that survived longest and thus showed least health problems. In contrast, younger groups included not only those individuals who will survive, but also individuals who will die shortly and thus with more health problems.

Third, cross-sectional community-based studies of health status are subject to under-representation of persons with poor health status and poor function living in the community and elderly individuals placed in long-term care institutions are selectively removed from the population [14]. These in themselves lead to an overestimation of the general health status of the older elderly group. Thus, the selection bias could also explain part of the differences between the two types of estimates presented here, since those elderly who were institutionalized during the follow-up were not excluded. However, the institutionalization rate observed in our sample was very low (2.5%).

Our results differ from recently published data reporting improvements in self-rated health with age, both cross-sectionally and longitudinally [15]. A likely explanation of this inconsistency is the different wording of the health status questions used. In our study, the elderly were asked to rate their health “in general” while in the above mentioned study participants rated their health “comparing with others of the same age.” The concept underlying the two self-rated health questions are clearly different. For example, a 70-year-old man claimed in 1986 to be in good general health and also in good health comparing himself with others of the same age; seven years later, in 1993, (77 years old) this man could claim to be in poor general health while he still could assess his health with respect to others of the same age as good. It simply reflects the aging process, his health is worsening at the same rate as other elderly of his age. It should be highlighted that both questions are valid, but they have different uses.

Some methodological issues affect longitudinal studies and must be taken into account in order to interpret the findings presented here. Longitudinal studies rely on subjects

returning for assessment, which can lead to other biases due to the differential loss of individuals during the follow-up period [27]. In our study the drop-out rate was low (15%) and is very unlikely to have caused the results found. When included as one of the outcomes of the multinomial regression, the fact of being lost to follow-up showed no significant associations with any baseline variables. Considering that individuals lost to follow-up are usually those with the poorest health status, if they had been re-interviewed the health decline would have been larger than that observed. Therefore, if any, attrition bias would be acting towards the null hypothesis, that is, against finding significant health status decline and diminishing differences between longitudinal and cross-sectional estimates.

Another issue to consider is the effect of proxy respondents because it has been suggested that it may bias the results due to a plausible overestimation of health problems. Proxy responses were included as an adjusting factor in all the analyses performed, and no significant associations with the outcomes were found. In addition, a sensitivity analysis (including and excluding proxy responses from the analysis) was performed and we are sure that our main findings were not due to a proxy effect. Furthermore, high accuracy has been shown for proxy responses when comparing reported and observed functional capacity in our study [30].

Our results suggest a worsening of the self-rated health of the elderly over time, greater than that which may be inferred from cross-sectional data. If this deterioration persists in future generations it very likely will be associated with a greater need for health care services in the western societies. More people will experience poor perceived health and disability during their lives than cross-sectional projections may have anticipated. This may contradict the optimistic hypotheses of certain authors regarding the compression of morbidity [11,12], indicating a significant decline in perceived health amongst the older elderly (75 or over).

## Acknowledgments

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# **CHAPTER 6**

# **DISCUSSION**





## **6. Discussion**

The present longitudinal data, coming from a population-based sample, provided an opportunity to study the evolution of disability among the elderly as they age; and to compare its association with mortality according to gender in a Mediterranean population. It also allows us to review the statistical approach for the survival analysis in elderly studies.

The main findings of this thesis can be summarised as follows. First, although disability tends to increase as people age, the thesis provides evidence that there are a small proportion of elderly people who can recover their health status, supporting the notion that the elderly population is a heterogeneous group. Second, the findings indicate a gender difference in the impact of disability on mortality, being dependent women at higher risk of dying at any given age. Third, the association between disability and mortality changes over time, being stronger at earlier ages than at advanced ages for both men and women. Fourth, our findings show that the inclusion of age as time scale is more efficient than the traditional time-on-study, because the comparison of survival functions is more straightforward, as well as the multivariate models, which are more parsimonious. It also facilitates the interpretation of the results derived from the survival analysis since inferences are based on the ageing process instead of time-on-study.

## **6.1. Contributions**

### 6.1.1. Evolution of disability and changes in the relationship between disability and mortality as elderly people age

The present study showed that the disability status evolves during the ageing process, questioning the validity of the sentence ‘once disabled, always disabled’. Although the overall trend is to worsen functional capacity, a subset of those who had some degree of disability (difficulty or dependent) at baseline improved their disability status (26.6% for men, and 26.9% for women). The most unstable group was that formed by the elderly people with difficulties at baseline: only 20.0 percent among men and 30.2 percent among women remained in the same group after eight years of follow-up, among those with follow-up information. Even though, the dynamic nature of disability has been previously suggested in few studies, to our knowledge, none of them was carried out in a south European population<sup>139</sup>.

Moreover, we found that not only the disability status of the elderly varies with age, supporting the dynamic disability process hypothesis, but also the strength of the relationship between disability and mortality changes with age. The impact of disability on mortality is smallest at older ages relative to the observed at younger ages, so there is no linearity in age (RR=1.80 and 3.53 at age 80 and RR=1.15 and 1.86 at age 90 among men and women, respectively).

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<sup>139</sup> Manton K.G. A longitudinal study of functional change and mortality in the United States. *J Gerontol* 1988;43:S153-61. Sonn U. Longitudinal studies of dependence in daily life activities among elderly persons. *Scand J Rehabil Med Suppl* 1996;34:1-35. Strawbridge W.J., Kaplan G.A., Camacho T., Cohen R.D. The dynamics of disability and functional change in an elderly cohort: results from the Alameda County Study. *J Am Geriatr Soc* 1992;40:799-806. Beckett L.A., Brock D.B., Lemke J.H., Mendes de Leon C.F., Guralnik J.M., Fillenbaum G.G., Branch L.G., Wetle T.T., Evans D.A. Analysis of change in self-reported physical

Failing to take age into account together with the growth of the oldest old group<sup>140</sup> may produce an underestimation of the impact of disability on mortality, since combining young and old elderly subjects diminishes the effect of disability.

This result may reflect that disability at different ages has different connotations as L. Ferrucci and colleagues<sup>141</sup> have previously commented. These authors pointed out that elderly people who develop a severe disability at older ages were more likely to suffer a long disabling process than those at early ages. It was suggested that elderly subjects who become disabled at younger ages are frailer, since all the strategies to cope with their disability have failed<sup>142</sup>.

#### 6.1.2. Differences between women and men

Our findings indicate that older women experience higher disability rates with longer retention of disability, but have lower mortality rates than older men. The proportion of subjects who were dependent or who had difficulties was higher among women than men both at baseline (42% vs. 30%, respectively) and at follow-up (60.0% vs. 48.7%, respectively). Higher disability and survival rates among elderly women are a common result in epidemiological studies. The survival gap among men and women results in women having a higher chance of becoming disabled because disability increases with age, and

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function among older persons in four population studies. *Am J Epidemiol* 1996;143:766-78. Avlund K. Disability in old age. *Danish Medical Bulletin* 2004;51:315-49.

<sup>140</sup> Those elderly subjects aged over 85 years old.

<sup>141</sup> Ferrucci L., Guralnik J.M., Simonsick E., Salive M.E., Corti C. and Langlois J. Progressive versus catastrophic disability: a longitudinal view of the disablement process. *J Gerontol A Biol Sci Med* 1996;51:M123-30.

<sup>142</sup> Fried L.P., Herdman S.J., Kuhn K.E., Rubin G. and Turano K. Preclinical disability hypothesis about bottom of the iceberg. *J Aging Health* 1991;3:285-300.

they are exposed to disability for longer periods of time. Also, gender differences in the underlying causes leading to disability contribute to a higher disability prevalence, women are more likely to suffer arthritis and musculoskeletal conditions; while heart disease, lung cancer and stroke, among others, are more common in men (see section 1.2.5). This issue is noteworthy in that it may explain the excess of disability among women, since the prevalence of the first conditions is higher than the second ones and also less lethal<sup>143,144</sup>. In this direction, J. R. Lunney et al.<sup>145</sup> recently showed that the pattern of functional decline varies with different illnesses (cancer, sudden death, organ failure, and frailty) in the last years of life. It was found that the average number of impaired BADLs 12 months before death differed by illnesses. Also, their evolution depended on the illnesses, whereas this number remained stable for those who suffered a sudden death, it increased over the last 3-months for those who died from cancer. The results presented here also support a previous study<sup>146</sup> that found that women were less likely to recover from disability than men; although this finding should be viewed cautiously in our study due to the small numbers.

The current work builds on previous findings by showing a stronger association between disability and mortality for women. Disabled women are at higher risk

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<sup>143</sup> Guralnik J.M., Leveille S.G., Hirsch R., Ferrucci L. and Fried L.P. The impact of disability in older women. *JAWMA* 1997;52:113-20.

<sup>144</sup> The number of chronic conditions is higher among women than men. Guralnik J.M., LaCroix A.Z. and Everett D.F. Comorbidity of chronic conditions and disability among older persons-United States, 1984. *JAMA* 1990;263:209-10; Verbrugge L.M. Gender and health: an update on hypotheses and evidence. *J Health Soc Behav* 1985;26:156-82.

<sup>145</sup> Lunney J.R., Lynn J., Foley D.J., Lipson S. and Guralnik J.M. Patterns of functional decline at the end of life. *JAMA* 2003;289:2387-92.

<sup>146</sup> Beckett L.A., Brock D.B., Lemke J.H., Mendes de Leon C.F., Guralnik J.M., Fillenbaum G.G., Branch L.G., Wetle T.T. and Evans D.A. Analysis of change in self-reported physical function among older persons in four population studies. *Am J Epidemiol* 1996;143:766-78.

of mortality compared to their peers' disabled men, hence other factors besides disability should also explain the longer life expectancy at 65 years old for females. On the other hand, a plausible survival bias for men should be also explored: a) men suffer more frequently from lethal diseases at middle age, which does not allow them to survive long enough to reach the age of 65. This is more accentuated in this cohort since women were not exposed to smoking but men were. Therefore there were diseases uncommon among women such as chronic obstructive pulmonary disease and lung cancer; and b) gender differences in the use of resources to deal with disability; men were found to be more likely to receive no help, such as informal assistance by relatives or devices, in a previous study<sup>147</sup>. Also, the authors noted that resources, which are useful for women might not be appropriate for men and viceversa. For example, they found that elderly disabled men who received personal assistance showed lower levels of subjective well-being; by contrast, elderly disabled women who use devices or technical aids<sup>148</sup> showed lower levels of subjective well-being. This difference in the way of handling disability by age may partially justify the observed variation of the strength of the association between disability and mortality.

### 6.1.3. Relationship between mortality and other factors

With respect to the relationship between mortality and other factors, the results are in the expected direction giving validity to the findings of the present study. Among men, smoking (former and current smoker) was found to be a risk of

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<sup>147</sup> Penning M.J. and Strain L.A. Gender differences in disability, assistance, and subjective well-being in later life. *J Gerontol Soc Sci* 1994;49:S202-S208.

<sup>148</sup> Examples of technical aids or devices are: canes, wheelchairs, walkers, specialized handrails, grab bars, raised toilet seats, among others.

dying factor<sup>149</sup>, supporting paper 1. In a previous study, L. Ferrucci et al.<sup>150</sup> estimated the effect of smoking on life expectancy reporting an increase in life expectancy, ranging from 1.6 to 3.9 years, for non-smokers compared to smokers for elderly men. As expected, former smokers had a lower risk than current smokers, since smoking cessation reduces the risk of premature death in the elderly population, as it does in the general population. C.L. Jajich et al.<sup>151</sup> suggested that the benefits of stopping smoking start within one to five years later. In the literature, the excess risk of smoking has been mainly attributed to cancers, heart and respiratory diseases. Also, body mass index (low weight) increased the risk of dying among men, although this association is less consistent than smoking and mortality in the literature. The role of low weight is complex, on one hand it is likely to be a symptom of underlying diseases such as cancer or a poor nutritional status<sup>152</sup>, and on the other hand it may reflect individuals who are physically active. Among women, all the factors become not statistically significant when including disability status. It should be noted, that smoking was not incorporated into the women's model due to the small number of smokers and former smokers (around 5%). The smoking factor was

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<sup>149</sup> Simons L.A., McCallum J., Friedlander Y. and Simons J., Diabetes, mortality and coronary heart disease in the prospective Dubbo study of Australian elderly. *Aust N Z J Med* 1996;26:66-74; Kaplan G.A., Seeman T.E., Cohen R.D., Knudsen L.P. and Guralnik J.M. Mortality among the elderly in the Alameda County Study: behavioral and demographic risk factors. *Am J Public Health* 1987;77:307-12.

<sup>150</sup> Ferrucci L., Izmirlan G., Leveille S., Philips C.L., Corti M.C., Brock D.B. and Guralnik J.M. Smoking, physical activity, and life expectancy. *Am J Epidemiol* 1999;149:645-53.

<sup>151</sup> C.L. Jajich, A.M. Ostfeld and D.H.Freeman. Smoking and coronary heart disease mortality in the elderly. *JAMA* 1984;252:2831-4.

<sup>152</sup> Losonczy K.G., Harris T.B., Cornoni-Huntley J., Simonsick E.M., Wallace R.B., Cook N.R., Ostfeld A.M. and Blazer D.G. Does weight loss from middle age to old explain the inverse weight mortality relation in old age?. *Am J Epidemiol* 1995;141:312-21; Harris T., Cook E.F., Garrison R., Higgins M., Kannel W. and Goldman L. Body mass index and mortality among nonsmoking older persons. The Framingham Heart Study. *JAMA* 1988;259:1520-24; Diehr P., Bild D.E., Harris T.B., Duxbury A., Siscovick D. and Rossi M.

restricted to males for the study cohort due to the delay in the smoking epidemic compared to other countries, such as the United Kingdom<sup>153</sup>, and cultural behaviours during this period; unfortunately, this pattern has changed in new generations, this habit being more prevalent among young Spanish women.

#### 6.1.4. Methodological issues

With respect to the methodological issues, age should be the time scale instead of calendar time in the survival analysis. Otherwise, the association between disability and mortality is confusing because all the inferences will be based on time since recruitment (function of the study duration, arbitrary period of time), instead of the ageing process duration. It is important to highlight that the study design used to ensure representativity of the sample unfortunately induces to a selection of the population (left-truncated data). On one hand, allowing enrolling those subjects older than 65 years we omit their peers who died before and are not then eligible for the study. In addition, those subjects over 65 years at entry into the study have already been exposed to the ageing process for a certain period of time. In studies of the elderly this is an important issue because age is the most important risk factor of mortality, functional decline, and it is also related to some of their corresponding risk factors. Using age as time scale in the survival analysis and extending the standard survival methods to deal with left-truncated data overcome these limitations.

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Body mass index and mortality in nonsmoking older adults: the Cardiovascular Health Study. *Am J Public Health* 1998;88:623-9.

<sup>153</sup> Rodríguez-Artalejo F., Hernández-Vecino R., Graciani A., Banegas J.R. and del Rey Catero J. La contribución del tabaco y de otros hábitos de vida a la mortalidad por cáncer de pulmón en España de 1940 a 1988, *Gac. Sanit* 1994;8:272-9.

In addition, there is a potential bias inherent in studies of the elderly: a substantial number of factors are correlated with age. But, the confusing role of age is dealt with by the inclusion of age as time scale. Although the calendar time estimates will be adjusted by age, the data obtained is handled in a more efficient way with age as time scale. The age at which covariates were measured is used in the analysis; this information is taken into consideration at the corresponding age and not before. For example, information about the disability status of an 80-year-old subject contributes to the estimation of the survival function at this age; whereas calendar time combines the information of all the subjects at the starting point of the study, irrespective of the age of the participants. The latter ignores the age-related changes of body function that cause certain values to be normal at certain ages but abnormal at other ages; such as oxygen uptake and exchange that decreases over time due to the loss of elasticity of the lung tissue. Moreover, the survival models with calendar time as time-scale are more complex due to the inclusion of interaction terms needed as a result of the existing non linear relationship between age and mortality (several studies have shown a dose-response effect in both males and females<sup>154</sup>). Even though, the estimates derived from both survival models are similar, the use of age as time scale allows for a finer adjustment of the estimates by age.

Furthermore, calendar time does not reflect the behaviour of the underlying population because the study's survival curves do not match with the reference population ones. The population hazard function has a bathtub shape and it shows an exponential pattern at later ages, however the study hazard function

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<sup>154</sup> Scott W.K., Macera C.A., Cornman C.B. and Sharpe P.A. Functional health status as a predictor of mortality in men and women over 65. *J Clin Epidemiol* 1997;50:291-6.



has the flattest growth with the calendar time approach. This pattern comes as a result of the combination of all the individuals at origin (time zero) in this approach, yielding a heterogeneous group of different ages.

It should also be noted that treating disability as a fixed variable, thus a fixed characteristic of the individuals, is misleading. It ignores the dynamic aspect of disability, and so this approach will consider as independent an individual who has become disabled during the follow-up time. As a consequence, it lessens the impact of disability on mortality since disability rates tend to increase with advancing age. Moreover, the estimates of the association between disability and mortality have become more accurate by using the disability time history over the follow-up time, allowing us to observe the changeable relationship between disability and mortality along the ageing process for both men and women.

## **6.2. Limitations**

Limitations of the study regarding the data should be underlined. Firstly, it may not be completely representative of the elderly because elderly people living in institutions were not eligible in the first wave. This issue may lead to an underestimation of the disability rates since institutionalised subjects tend to have a poorer health status.

With respect to the information on disability, data from the two waves were used to define the evolution of disability for each member in the cohort. Participants were asked to report their disability evolution since the first interview at the time of the second wave. This approach may lead to a recall

bias because the time at which the transitions between disability status took place may be recalled inaccurately. Ideally, studies should be designed with frequent reassessments to track changes in disability more accurately. The implications of such a bias will be to underestimate the relationship between disability and mortality if people tend to overreport the disability length, and to overestimate it, otherwise. However, the proportion of people who improved their disability status in our cohort is similar to the reported in previous studies<sup>155</sup>. In addition, we examined whether the information collected in the second wave agreed with the information coming from the first wave. Discrepancies were found in only 70 (5.9%) subjects supporting the validity of the data. For the 116 subjects who did not report the beginning of a new disability status and therefore the above-mentioned validation was not applicable, we assumed one-year duration prior to the disability status reported at the second wave. The selection of the arbitrary duration was performed deliberately biasing the results towards the null hypothesis (i.e., no differences in the mortality experience according to the disability status). Thus, having in mind that elderly people's health status tends to worsen over time, this cut-off point will lead to considering a subject as disabled or with difficulties less often than most likely, was really the case.

In addition, for those subjects who did not take part in the second wave (n=259), it was considered that the disability status that they declared at the

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<sup>155</sup> Manton K.G. A longitudinal study of functional change and mortality in the United States. *J Gerontol* 1988; 43:S153-S161. Sonn U. Longitudinal studies of dependence in daily life activities among elderly persons. *Scand J Rehabil Med Suppl* 1996;34:1-35. Strawbridge W.J., Kaplan G.A., Camacho T. and Cohen R.D. The dynamics of disability and functional change in an elderly cohort: results from the Alameda County Study. *J Am Geriatr Soc* 1992; 40:799-806.

first wave was constant along time. Among these, 115 subjects reported difficulties or dependency at first wave, contributing to the survival time with a short period (3.9 years). It was considered unlikely that these subjects affect the inferences drawn from the study due to the short survival time and the percentage of recovery observed. On the other hand, this approach may have led to an underestimation of the relationship between the disability status and mortality in the cases where the subjects were independent at first wave.

Selective mortality between the 2 assessments might have caused us to overestimate the association between disability and mortality if disability was caused by a fatal disease leading to death in a relatively short period. In this situation, it is assessed the mortality process itself instead of the impact of disability on mortality and attributing then to disability an effect that it doesn't have. In order to evaluate the magnitude of this issue in our cohort, we compared the cause of death and the cause of disability for those subjects who died during the follow-up and became impaired in the last year of their life (n=90). A sensitivity analysis was then performed: first using all the available information and second using only the disability information provided in the first wave. The results showed that a bias was present since the risk of dying for the dependent group was 10 times higher when using all the disability information. Therefore, to avoid this bias only information about disability status in the first wave was used if the causes of death and disability coincided in those who became impaired in the last year of life.

It has been suggested that there may be potential gender differences in self-reported disability when evaluating different activities of daily living. This might bias the results towards an excess of disability rates in women. In this

study, we examined the reported disability in sitting and walking and the corresponding performance of physical tasks (chair stand test and walking speed test). The results did not support the existence of an overreporting of disability among elderly women (supporting paper 2).

On the other hand, it is inherent to the longitudinal design of the study that some elderly people die during the follow-up period. In the case of death, the evolution of the disability status was ascertained through proxies. Previous studies suggest that proxy respondents tend to overreport the disability of the deceased participants<sup>156</sup>, which would lead to underestimating the risk of dying. Proxy behaviour was explored in the present study and no significant differences of overreporting between the informant sources were found in two tasks (sitting and walking). Proxies were less likely to underreport functional limitation in one of the two tasks (walking slowly) (supporting paper 2). Therefore no relevant bias may have been introduced by the use of proxies in our results.

### **6.3. Implications**

From a public health perspective, our findings have important implications for health and social interventions aimed at maintaining independence among elderly people: women should be considered a priority for such interventions. Since, it was found that elderly women once they become disable are at higher

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<sup>156</sup> Rubenstein L.Z., Scharier C., Wieland G.D. and Kane R. Systematic biases in functional status assessment of elderly adults: effects of different data sources. *J Gerontol* 1984;39:686-91; Magaziner J., Zimmerman S.I., Gruber-Baldini A.L., Hebel J.R. and Fox K.M. Proxy reporting in five areas of functional status. Comparison with self-reports and observations of performance. *Am J Epidemiol* 1997;146:418-28; Dorevitch M.I., Cossar R.M., Bailey F.J., Bisset T., Lewis S.J., Wise L.A. and MacLennan W.J. The accuracy of self and informant ratings of physical functional capacity in the elderly. *J Clin Epidemiol* 1992;45:791-8.

risk of dying at any age and they have less chance to regain independence compared to their counterparts' elderly men. Also, elderly women showed higher rates of disability, and higher comorbidity burden in the ten leading chronic conditions except bronchitis/asthma<sup>157</sup>. As noted earlier, women are also a population group with limited economic resources at those ages. Therefore, elderly women are less likely to get equipment to help them performing the activities of daily living and to receive paid human help. In addition, women with disability are at high risk of diseases such as depression and coronary heart disease, as well as, falls and hip fractures<sup>158</sup>. The latter risk is critical since European women are menopausal for a third of their lives, during which time osteoporosis is a common disease leading to a dramatic increase in the risk of fractures.

Finally, actions to promote healthier lifestyles should be planned and developed, such as health programs to help older smokers stop. Most campaigns aimed at preventing smoking have been traditionally targeted at the young and middle aged, not the elderly. Indeed, these policies are becoming more relevant since, up to now, the majority of the smokers were men in the elderly population in our environment, but this situation is changing in the new generations for whom smoking consumption is common among women.

With respect to methodological issues, the results also have implications for study design of elderly people and its statistical analysis. Firstly, longitudinal data with repeated disability assessments over time will be ideal to study the

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<sup>157</sup> The lower prevalence of bronchitis/asthma among women compared to men is well in agreement with the proportion of current/former smokers (4.9% vs. 69.0%, respectively) in the present cohort.

association between disability and mortality in order to capture the dynamic disability process. The frequency of such measurements should be determined by the ability to detect those whose disability is intermittent, as well as the study sample size because frequent assessments may prove too costly to conduct with large studies.

Secondly, age should be the standard time scale in the survival analysis of data obtained from elderly people. In doing so, the survival models will be more parsimonious, the association of several risk factors with age can be handled, the information can be considered at the age-time that it was measured, and the comparison of the survival curves from different studies will be more straightforward.

Thirdly, disability should be treated as a time dependent variable, whenever possible, to account for the dynamic process of disability and avoid the plausible underestimation of the association between disability and mortality. Furthermore, it allows for the evaluation of the effect of disability on mortality at any given age.

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<sup>158</sup> Guralnik J.M., Leveille S.G., Hirsch R., Ferrucci L. and Fried L.P. The impact of disability in older women. *JAMWA* 1997;52:113-20.

# **CHAPTER 7**

# **CONCLUSIONS**





## 7. Conclusions

This thesis has been targeted at assessing the gender differentials in the relationship between disability and mortality along the ageing process, paying special attention to survival analysis methodology. It has contributed new knowledge to the relationship between disability and mortality and the factors that affect it in a Southern-European city, as well as the appropriate statistical approach to address survival analysis in studies of the elderly. The conclusions of this thesis are the following

- Disability in the elderly evolves over time, it is not fixed. Overall, disability tends to worsen with age, but a sizeable proportion of disabled subjects are able to recover after 8 years.
- There are gender differences in the changes of functional capacity among the elderly: women are less able to regain functional capacity once they become disable.
- The strength of the association between disability and mortality among the elderly varies over time. The relative risk of dying for disabled elderly people at older ages decreases.
- Body mass index and smoking habit are independently associated with mortality among elderly men.
- Health and social care policies focusing on disabled women should be implemented, due to the higher proportion of disabled women than

disabled men, their lower probability of regaining functional capacity and their higher risk of dying compared to disabled men.

- Age should be considered the time-scale for the survival analysis in the elderly population.
- The dynamic nature of disability should be considered when designing studies to capture its variations along the ageing process. To do so, longitudinal studies of older people with periodical disability assessments should be performed.
- Disability should be considered as a time-dependent variable to avoid possible underestimations of its relationship with mortality.

## **CHAPTER 8**

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# APPENDIX



## **Appendix: Introduction to the counting processes**

In the latest 70s, a major theoretical development in the survival analysis framework took place, however its relevance was not acknowledged until the earliest 90s. O.O. Aalen<sup>159</sup> formulated the statistical models through counting processes; jump processes that evolves over time and count the number of events occurred up to any moment in time. Specifically, he introduced the multiplicative intensity model for counting processes.

The main advantage of the counting process formulation is its close link with the stochastic processes called martingales<sup>160</sup>. The mathematical development set up for the theory of martingales allows deriving in an elegant and easy manner the first and second order moment of the statistics<sup>161</sup>, as well as, their asymptotic distribution.

Traditionally, the Kaplan-Meier estimator has been used to estimate the survival curves without covariates, which extends the empirical survival function to censored data. With respect to the comparison of different populations, the k-sampling tests that are applied are mostly generalizations of classical non-parametric tests such as the Wilcoxon statistic. The use of counting processes provided the tools to proof the asymptotic properties in a simple mode and to incorporate more complex censoring and truncation processes. In addition, the more general setting allowed dealing with repeated measures within the Cox

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<sup>159</sup> Aalen O.O. Non parametric inference for family of counting process. *Ann Statist* 1978;6:701-26.

<sup>160</sup> The difference between a counting process and the integrated intensity process result to be a martingale.

<sup>161</sup> The first and second order moment of the statistics are used to calculate the expected value and the standard error of the statistic.

model, multiple events, recurrent events, non-stationary Poisson process, semi-Markov processes, etc.

The application of counting processes to time-dependent variables lead to a substantial simplification in their formulation in the survival analysis context, as well as, in the treatment of censored and left-truncated data. For this reason, this methodology was employed in this work.

### ***Counting processes and martingales***

This section is aimed to give an intuitive view of the counting processes and martingales. The reader is referred to the following texts for a formal approach: D.P. Heyman - M.J. Sobel (1990)<sup>162</sup>, S. Karlin - H.M. Taylor (1975)<sup>163</sup>, J.L. Doob (1953)<sup>162</sup> and D. Pollard (1984)<sup>164</sup>. The application of these processes to the survival analyses framework can be found in the following references: O.O. Aalen (1978)<sup>165</sup>, R.D. Gill (1980), T.R. Fleming - D.P. Harrington (1991) and P.K. Andersen et al. (1993).

A stochastic process is defined as a random process that evolves over time and follows probabilistic laws<sup>166</sup>. A counting process is then a stochastic process

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<sup>162</sup> The authors address both counting processes and martingales.

<sup>163</sup> In both books, the authors define the martingales and describe them by means of giving examples of stochastic processes that behave as martingales.

<sup>164</sup> The author describes the central limit theorem for martingales in chapter 8 (page 170 and the followings). Also, it can be found the construction of the Kaplan-Meier estimator for censored data using martingales (page 182 and the followings).

<sup>165</sup> Aalen O.O. Non parametric inference for family of counting process. *Ann Statist* 1978;6:701-26.

<sup>166</sup> Doob J.L. *Stochastic processes*, John Wiley and Sons Inc.: New York, 1953: page 46;  $X=(x_t, t \in T)$ , a set of random variables defined on a probabilistic space  $(\Omega, \mathfrak{F}, \varphi)$  that takes values on the real space. Syski R. *Stochastic process*. *Encyclopedia of Statistical Sciences* vol. 8. Editors in chief: Kotz S. and Johnson N.L.; Executive editor: Campbell B.R. John Wiley and Sons Inc.: New York, 1988: pp. 836-58.

$\{N(t):t \geq 0\}$  non-decreasing and right-continuous, defined as an indicator function with jumps of size one, taking the values 0 or 1, whether or not a condition is satisfied. The counting processes can be decomposed as the sum of a martingale and a process called compensator (Doob-Meyer decomposition).

The term Martingale comes from the Provençal name of a French community called Martingues<sup>167</sup>. Originally, this name was used in the game theory context to define a gambling strategy, which consisted of doubling the bet upon experiencing a loss. Specifically, we consider the game of tossing a coin where the gambler wins a certain amount of money if head, and loses the same quantity if tail. Then, repeating the game n-times, the accumulated gains of the gambler behave as a discrete martingale<sup>168</sup>. To put into notation,  $N_t$  denotes the process that takes the value +1 if the gambler wins at time t and value -1 if loses; assuming then that the game is fair, thus  $P(N_t=1) = P(N_t=-1) = 0.5$ ,  $\bar{N}_t = \sum_{s=1}^{\infty} N_s$  represents the gambler's accumulated gains verifying:

$$E[\bar{N}_t | N_1, N_2, \dots, N_s] = \bar{N}_s, \quad 0 \leq s \leq t$$

or equivalent,  $E[\bar{N}_t - \bar{N}_s | N_1, N_2, \dots, N_s] = 0, \quad 0 \leq s \leq t$

This is the key property that characterizes a martingale: the best prediction of a value in the future, taking into account its previous history, is the current value of the process.

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<sup>167</sup> Hall P. Martingales. Encyclopedia of Statistical Science, vol. 5. Editors in chief: Kotz S. and Johnson N.L.; Executive editor: Campbell B.R. John Wiley and Sons Inc.: New York, 1985, page 278.

<sup>168</sup> Gordon Lan K.K. and Lachin J.M. Martingales without tears. Lifetime Data Analysis 1995;1:361-75.

In the case that the game is unfair,  $P(N_t=1) \neq P(N_t=-1)$ , the expected value will differ from zero, then it is necessary to modify the game by means of an easy approach. If the game favours the gambler, the conditional expectation is positive, then the process  $\bar{N}_t$  behaves as a submartingale, otherwise – negative conditional expectation -  $\bar{N}_t$  behaves as a supermartingale. To keep the game fair in the first scenario, the gambler should pay the quantity that the expectation exceeds from zero before each tossing. The new process will be defined as follows:  $\tilde{N}_t = \sum_{s=1}^t (N_s - E_s)$ . The cumulative payments  $A_t = \sum_{s=1}^t E_s$  is called the compensator of the submartingale.

The martingale processes imply a substantial advance in the theory of statistics, mainly, for the following results:

1. The theorem of martingale transformation
2. The martingales' inequalities
3. The convergence theorems (Martingale Central Limit Theorem)

The first states, under certain conditions, that the process resulting from the transformation of martingales can be represented as a martingale. For example, if a sequence of partial sums behaves as a martingale, then the new sequence defined as the summatory of the partial sums,

$Y(t+1) = \sum_{i=0}^t X(t+1)f(X(0), X(i))$ , will be also represented as a martingale.

The second result allows relaxing the martingale property leading to the supermartingales and submartingales processes:

$$\begin{array}{lll}
 E[\bar{N}_t | N_1, N_2, \dots, N_s] = \bar{N}_s & 0 \leq s \leq t & \\
 \mapsto E[\bar{N}_t | N_1, N_2, \dots, N_s] > \bar{N}_s & 0 \leq s \leq t & \textit{Supermartingale} \\
 \mapsto E[\bar{N}_t | N_1, N_2, \dots, N_s] < \bar{N}_s & 0 \leq s \leq t & \textit{Submartingale}
 \end{array}$$

As it has been described previously, the martingales approach can be used frequently, since it is possible to find often a compensator for the inequalities through the Doob-Meyer decomposition.

Finally, the result with the largest impact on the inferential theory has been the Martingale Central Limit Theorem<sup>169</sup>. It is used to establish asymptotic normality for sequence of martingales, and it can be interpreted as the convergence rate in the Law of large numbers<sup>170</sup>. Moreover, the asymptotic distribution is frequently a good approximation for small samples.

The rationales behind the martingales approach are very similar to the classical Theorems of the Central Limit, as it is the Lindeberg's proof of the Central Limit Theorem. The key point relies on the martingale property that allows to weakly factorising the conditional expectations to their previous history, and the conditional variances become then variances of independent sums. Although the majority of the classical theorems have the corresponding martingale approximation, the latter ones are superior in elegance and the wider spectrum of situations where they are applicable.

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<sup>169</sup> The development of the Central Limit Theorem can be found in chapter 5: '*A martingale central limit theorem*', pp: 201-28, and the results needed along the development are described in the Appendix C: '*The martingale central limit theorem: some preliminaries*', pp: 343-58; Fleming T.R. and Harrington D.P. Counting processes and survival analysis. John Wiley and Sons Inc.: New York, 1991.

<sup>170</sup> Karr A.F. Stochastic process. Encyclopedia of Statistical Sciences, vol. 8. Editors in chief: Kotz S. and Johnson N.L.; Executive editor: Campbell B.R. John Wiley and Sons Inc.: New York, 1988, pp: 853-4.

A counting process is a submartingale that can be decomposed, under certain conditions, as the sum of a martingale  $M$  and a no decreasing predictable process “ $A$ ” called compensator.

$$N_j(t) = M_j(t) + A_j(t) \quad (\text{Doob – Meyer Decomposition})^{171}$$

“ $A$ ” represents the cumulative intensity associated with the counting process  $N(t)$ , it is unique and depends on the past history called filtration  $\{\mathfrak{F}(t):t \geq 0\}$ . The filtration process ( $\sigma$ -algebras family) contains all the available information for a specific subject collected until the moment  $t$ , for example: vital status, gender, age, functional capacity, etc.  $\mathfrak{F}$  is an increasing process if  $s \geq t$  then  $\mathfrak{F}(s) \geq \mathfrak{F}(t)$ . Therefore, information about the subjects that compound the sample increases over time. The main restriction on the process  $A$  is that it has to be predictable; consequently its behaviour at time  $t$  is completely fixed by its previous behaviour along the interval  $[0,t]$  for any  $t$ . In other words, for each  $t \geq 0$  given  $\mathfrak{F}(t)$ , the increments  $\Delta N_1(t), \Delta N_2(t), \dots, \Delta N_n(t)$  are independent random variables  $(0, 1)$ , mathematically equivalent to say that  $N(t)$  has to be  $\mathfrak{F}(t)$  measurable.

In the survival analysis framework,  $N(t)$  registers the number of events (e.g., dead) observed over the period  $[0,t]$ . For a specific subject  $i$ ,  $N_i(t)$  is defined in such a way that takes the value zero until he/she dies and then the function jump and takes the value 1.

For right-censored data, the function is defined as follows:

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<sup>171</sup> The authors describe the conditions in which the Doob-Meyer Decomposition is feasible. Fleming T.R. and Harrington D.P. Counting processes and survival analysis, John Wiley and Sons Inc.: New York, 1991, pp: 31-42.



$$N_s(t) = \sum_{s=0}^t \sum_{i=1}^n I(T_i \leq t, \delta_i = 1) \quad , \text{ where } N(0) = 0 \quad \text{and} \quad N(t) < \infty$$

In this context, the compensator  $A$  comes defined by the integral  $\lambda(t) = Y(t)h(t)$ , called intensity process of the counting process, being also a stochastic process that depends on the information contained in the natural history of the process  $\mathfrak{F}(t)$  by means of  $Y(t)$ . With probability  $\lambda(t)dt$  (hazard function), the subject will die within the tiny interval  $t$  and  $t+dt$ , then  $N_i(t)$  will be equal to 1.

$$M_j(t) = N_j(t) - \int_0^t h(u)Y(u)du \quad , \quad t \geq 0$$

The new predictable counting process,  $Y(t)$ , together with  $N(t)$  may be considered the pillars of the survival analysis methodology. It defines the risk set, thus the number of subjects at risk for dying at time  $t$ , and can also allow to deal with left-truncated data, if needed. The indicator function of the subjects at risk is defined as:

$$Y_i(t) = \begin{cases} 1 & \text{\underline{i} is under observation and at risk at time t} \\ 0 & \text{otherwise} \end{cases}$$

The cumulative intensity process  $\Lambda(t) = \int_0^t h(u)Y(u)du \quad , \quad t \geq 0$  is characterized by the following property:

$$\begin{aligned} E[N(t) | \mathfrak{F}(t)] &= E[M(t) + \Lambda(t) | \mathfrak{F}(t)] = E[M(t) | \mathfrak{F}(t)] + E[\Lambda(t) | \mathfrak{F}(t)] = 0 + \Lambda(t) \\ &= \Lambda(t) \end{aligned}$$