

**Associations between Cataract and Multimorbidity: A Cross-Sectional Study of 23,089 adults
from Spain**

Running title: Cataract and Multimorbidity

Louis Jacob, PhD^{1,2}; Guillermo F. López-Sánchez, PhD^{3*}; Lin Yang, PhD^{4,5}; Josep Maria Haro, MD-PhD²; Jae Il Shin, MD-PhD⁶; Nicola Veronese, MD-PhD⁷; Pinar Soysal, MD-PhD⁸; Trish Gorely, PhD⁹; Ai Koyanagi, MD-PhD^{2,10}; Lee Smith, PhD¹¹

¹ Faculty of Medicine, University of Versailles Saint-Quentin-en-Yvelines, Montigny-le-Bretonneux 78180, France

² Research and Development Unit, Parc Sanitari Sant Joan de Déu, CIBERSAM, Dr. Antoni Pujadas, 42, Sant Boi de Llobregat, Barcelona 08830, Spain

³ Faculty of Sport Sciences, University of Murcia, Murcia, Spain

⁴ Department of Cancer Epidemiology and Prevention Research, Cancer Control Alberta, Alberta Health Services, Calgary, AB, Canada

⁵ Departments of Oncology and Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

⁶ Department of Pediatrics, Yonsei University College of Medicine, Seoul, Republic of Korea

⁷ National Research Council Neuroscience Institute Padua, Italy

⁸ Department of Geriatric Medicine, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey

⁹ Department of Nursing and Midwifery, University of the Highlands and Islands, Inverness, UK.

¹⁰ ICREA, Pg. Lluís Companys 23, Barcelona, Spain

¹¹ The Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University,
Cambridge, CB1 1PT, UK

*** Corresponding author:** Dr. Guillermo F. López-Sánchez. Faculty of Sport Sciences,
University of Murcia, Murcia, Spain. gfls@um.es

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Conflict of interests

All authors declare that they have no conflicts of interest.

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Abstract

Background: Little is known about the association between cataract and multimorbidity.

Therefore, the aim of the present study was to examine the relationship between cataract and chronic conditions and multimorbidity in a large representative sample of Spanish adults.

Methods: This study used data from the Spanish National Health Survey 2017, a cross-sectional sample of 23,089 adults aged ≥ 15 years from Spain [54.1% female; mean (standard deviation) age 53.4 (18.9) years]. Cataract and 30 other physical and mental chronic conditions were self-reported. Multimorbidity was defined as the presence of at least two physical and/or mental chronic conditions (excluding cataract). Control variables included sex, age, marital status, education, smoking, and alcohol consumption. Multivariable logistic and negative binomial regression analyses were conducted to assess associations.

Results: The prevalence of cataract and multimorbidity was 12.5% and 56.5%, respectively. All chronic conditions were significantly more frequent in individuals with than in those without cataract. Overall, there was a positive relationship between cataract and multimorbidity [odds ratio (OR)=2.77; 95% confidence interval (CI): 2.39-3.21]. In addition, cataract was significantly associated with the number of chronic conditions in the whole population [incidence rate ratio (IRR)=1.34; 95% CI: 1.29-1.38].

Conclusions: Cataract is positively associated with chronic conditions and multimorbidity in adults. Interventions specifically designed for those with cataract to reduce or manage co-occurring chronic conditions and multimorbidity are urgently required .

Keywords: cataract; chronic conditions; multimorbidity; adults; Spain

1. Introduction

Cataract is defined as clouding of the lens of the eye which prevents clear vision [1]. Importantly, cataract is responsible for 51% of world blindness [2]. Worldwide women have a higher cataract burden than men [3], and most cases of cataract are related to the ageing process [4]. However, it should be noted that congenital forms of cataract also exist and that cataract can also develop as a consequence of eye injury, inflammation, and other diseases, such as rubella [2].

Multimorbidity may be defined as the simultaneous occurrence of two or more chronic diseases in one person and can include both physical and mental health complications. Ageing populations and an increase in chronic conditions mean that the number of people with multiple health conditions is set to rise [5]. Indeed, it has been found that in developed countries more than 40% of the population have at least one chronic condition and approximately 25% have greater than one condition [6]. Importantly, multimorbidity is associated with high mortality [7], reduced functional status [8], and increased use of both inpatient and ambulatory health care [9, 10]. Finally, previous studies have shown that multimorbidity tends to be more prevalent in women than men [11]. This difference might be related to biological, sociocultural, environmental or economic factors [12].

One previous study investigated the relationship between visual impairment per se and multimorbidity in a Spanish population and found that arthritis, stroke and the co-occurrence of various chronic physical diseases were associated with higher visual impairment [13]. Moreover, visual impairment was associated with higher prevalence of depression and poorer cognitive function [13]. Other studies have found similar findings in other countries (e.g., the

US) [14]. Visual impairment is defined as partial sight or blindness in the better seeing eye [15], and can be a consequence of many different eye conditions (e.g. cataract, macular degeneration, retinopathy, etc.). To inform practice and targeted interventions to reduce or manage multimorbidity it would be beneficial to investigate the relationship between specific eye conditions (such as cataract) and multimorbidity. It should be noted that some research has been carried out to identify common comorbidities in those who suffer from cataracts *per se*. For example, in a sample of 773 cataract surgical patients angina, previous myocardial infarct, diabetes and hypertension were found to be the most common comorbidities [16].

The aim of the present study was to examine the relationship between cataract and chronic conditions and multimorbidity (at least two physical and/or mental chronic conditions) in a large representative sample of Spanish adults. Moreover, owing to the higher prevalence of cataract and multimorbidity in women it is important to also investigate sex-specific associations. Finally, it is important to carry out age-stratified analyses owing to cataracts mainly being present in older adults, resulting from aging of the tissue of the eye lens. However, younger adults can also develop cataract, resulting from pathways such as injury, diabetes, smoking, previous eye surgery, amongst others.

2. Methods

2.1. The survey

Data from the Spanish National Health Survey 2017 were analyzed. This survey was undertaken in Spain between October 2016 and October 2017. Details of the survey method have been already published [17]. In brief, for the data collection, a stratified three-stage sampling was used in which the census sections were first considered, then the family

150 dwellings, and then an adult (15 years or more) was selected within each dwelling. The
151 dwellings were selected by systematic sampling and to select the person who had to complete
152 the Adult Questionnaire, the random Kish method was used. The sample was representative
153 of the adult population residing in Spain and consisted of 23,089 adults aged 15-103 years.
154 The method of data collection used was computer-assisted personal interviewing (CAPI),
155 conducted in the homes of the selected participants. The interviewers, previously trained,
156 completed the questionnaires with the information provided by the participants. All of them
157 signed an informed consent form before responding to the survey questions. This research
158 was conducted in accordance with the Declaration of Helsinki of 1961 (revised in Tokyo in
159 1989 and in Edinburgh in 2000).

161 2.2. *Cataract (Exposure)*

162 The interviewer asked the participants the following question: “Have you ever been
163 diagnosed with cataracts?”. Those who answered affirmatively to the question were
164 considered to have cataract. The interviewer was also in charge of solving the possible doubts
165 that the participants had. Previous research has confirmed the validity and high accuracy of
166 self-reported diagnosis of cataract [18].

168 2.3. *Multimorbidity (Outcome)*

169 Multimorbidity was defined as the presence of two or more chronic conditions (excluding
170 cataract). The interviewer asked the participants the following question: “Have you ever been
171 diagnosed with ‘*chronic condition*’?” and read a list of chronic conditions. Those who
172 answered affirmatively to the question were considered to have the specific chronic condition.
173 The interviewer was also in charge of solving the possible doubts that the participants had.
174 Previous research has confirmed the validity and high accuracy of self-reported diagnosis of

chronic conditions [19]. Chronic conditions included obesity, hypertension, myocardial infarction, angina pectoris and other coronary diseases, other cardiac diseases, varicose veins of lower extremities, osteoarthritis, chronic neck pain, chronic low back pain, chronic allergy (excluding allergic asthma), asthma (including allergic asthma), chronic bronchitis, emphysema or chronic obstructive pulmonary disease (COPD), diabetes, peptic ulcer disease, urinary incontinence, hypercholesterolemia, chronic skin disease, chronic constipation, liver cirrhosis and other hepatic disorders, depression, anxiety disorder, other psychiatric disorders, stroke, migraine and other frequent headaches, hemorrhoids, cancer, osteoporosis, thyroid disease, renal disease, and injury.

2.4. Control variables

The selection of the control variables was based on past literature [20]. Sociodemographic variables included sex, age, marital status, and education. Marital status was categorized as married and not married (single/widowed/divorced/separated). Education was based on the highest educational level achieved and was categorized as \leq primary, secondary, and \geq tertiary. Smoking status was self-reported and categorized as never, past and current smoking. Alcohol consumption in the last 12 months was self-reported and categorized as yes (any) and no (none).

2.5. Statistical analysis

The statistical analysis was performed with R 3.5.2 (The R Foundation) [21]. Differences in the sample characteristics and in the prevalence of chronic conditions by cataract status were assessed by chi-squared tests for all variables except age (t-test), while effect size was calculated using the phi coefficient. The relationship of cataract (independent variable) with multimorbidity and the number of chronic conditions (dependent variables) was assessed

using multivariable logistic regression models and multivariable negative binomial regression models, respectively. Multivariable negative binomial regression models were used instead of multivariable Poisson regression models because the number of chronic conditions was over-dispersed (i.e., conditional variance exceeded conditional mean). The associations were investigated in the overall population and in sex- (i.e., men, women) and age- (i.e., age \leq 40 years, age 41-65 years, age >65 years) stratified samples. Interaction analyses were conducted by including the product term of cataract X sex or cataract X age into the regression models. Independent variables were included in the models as categorical variables with the exception of age which was included as a continuous variable. Multimorbidity and the number of chronic conditions were included in the models as dichotomous and count variables. Models were adjusted for sex (apart from the sex-stratified analyses), age, marital status, education, smoking, and alcohol consumption. There were missing data only for the following variables: marital status (n=39, 0.17%), smoking (n=22, 0.10%), alcohol consumption (n=26, 0.11%), and obesity (n=1070, 4.63%). Complete-case analysis was carried out. Results from the logistic regression analyses are presented as odds ratios (ORs) and 95% confidence intervals (CIs), while results from the negative binomial regression analyses are presented as incidence rate ratios (IRRs) and 95% CIs. Confidence intervals and p-values were corrected using the Benjamini-Yekutieli and the Benjamini-Hochberg adjustment method, respectively. The level of statistical significance was set at $p < 0.05$.

3. Results

This study included 23,089 individuals residing in Spain [54.1% female; mean (standard deviation) age 53.4 (18.9) years; **Table 1**]. The prevalence of cataract and multimorbidity was 12.5% and 56.5%, respectively. Female gender, single/widowed/divorced/separated, \leq primary

education, never smoking, and no alcohol consumption were more frequent in participants with than in those without cataract, while age was significantly higher in the cataract than in the no cataract group. All chronic conditions were significantly more frequent in individuals with than in those without cataract, and size effects were the highest for osteoarthritis (phi coefficient=0.32), hypertension (0.27) and urinary incontinence (0.24; **Table 2**). Finally, the results of the regression models are displayed in **Table 3**. Overall, there was a positive association between cataract and multimorbidity (OR=2.77; 95% CI: 2.39-3.21), and this association was significant in the different sex and age subgroups. In addition, cataract was significantly associated with the number of chronic conditions in the whole population (IRR=1.34; 95% CI: 1.29-1.38), and all sensitivity analyses were significant. Finally, there was a significant interaction between cataract and age in both the logistic and the negative binomial regression models, with the relationship between cataract and the number of chronic conditions being more pronounced in participants aged ≤ 40 years (IRR=2.16; 95% CI: 1.23-3.79).

4. Discussion

To the best of our knowledge this is the first study to investigate the relationship between cataract and multimorbidity. The present study found that the prevalence of cataract was 12.5%, while the prevalence of multimorbidity was 56.5% in the general population. Importantly, all chronic conditions were more prevalent in those participants with cataract compared to those without. Those with cataract were found to be at a 2.77 higher odds of experiencing multimorbidity than those without. Moreover, the present study found that the number of chronic diseases increases by a factor of 1.34 in patients with cataract compared to

those without cataract. Taken together these findings suggest that those with cataract residing in Spain have a poorer health profile than those without cataract.

Findings from the present study are in agreement with other previous studies investigating visual impairment per se [13, 14], and these studies found those with visual impairment are at greater risk of several chronic conditions and multimorbidity. Moreover, the present findings add to this body of knowledge by showing that such associations also exist specifically in relation to cataract. Several plausible pathways may explain the observed relationships. First, those with several chronic conditions, such as cardiovascular conditions, diabetes or arthritis, may have cumulative risk for cataract due to vascular, neurodegenerative, biochemical or inflammatory pathways [13, 22]. Second, those with cataract may exhibit a higher prevalence of harmful lifestyle behaviors. For example, it has been shown that those who are visually impaired have much lower levels of physical activity than those without [15, 23, 24]. Moreover, a diet with nutrient deficiencies is associated with several chronic conditions [25, 26] and potentially cataract [27]. Third, those with cataract are likely to experience a lower quality of life (QOL) [28] and QOL has been found to be associated with several physical and mental health complications [29-31]. Moreover, poor ocular health is associated with social isolation [32] and loneliness [33], while social isolation [34] and loneliness [35] are risk factors for multimorbidity. In line with this hypothesis, cataract may be a risk factor for several mental conditions such as depression [36]. Fourth, cataract increases the risk of falls [37], and falls are associated with fractures, pain and functional decline [38]. Finally, cataract and multimorbidity may also share common risk factors that were not assessed in this study (e.g., income).

One finding of the present study that needs to be interpreted with caution is the lack of significant interaction between cataract and sex in the cataract-multimorbidity relationship. Indeed, previous work has shown that the prevalence of cataract and the prevalence of multimorbidity is higher in females than in males [3, 11]. This difference might be related to biological, sociocultural, environmental or economic factors [12]. It may also be owing to the fact that generally QOL is lower in older women than men [39]. Taking these data together, further research is now required to elucidate the question about the role played by sex in the association between cataract and multimorbidity.

Finally, the high prevalence of cataract (12.5%) in the present study should also be noted. Owing to such a high prevalence, interventions to either prevent cataract or allow for early detection are warranted in Spain. To aid in the prevention of cataract development, interventions should focus on smoking cessation, reducing sunlight exposure by wearing ultraviolet A and B protective eyewear and wide-brimmed hats, optimal management of diabetes, and consuming a balanced diet [40]. To aid in early detection of cataracts, Spanish adults should be encouraged to undergo regular eye examinations.

This is the first study to investigate the relationship between cataract, chronic conditions, and multimorbidity. The large sample size and the stratification by sex and age are clear strengths. However, findings from this study must be interpreted in light of its limitations. Both cataract and all chronic conditions were self-reported, potentially introducing bias. Moreover, it is not known whether the person was operated on for cataracts. Indeed, if the person was operated on it is highly likely that the person no longer has visual problems. In addition, the survey did not include information about specific diagnostic criteria, while there was a lack of data on the onset, severity and duration of the diseases, underlying the need for further surveys with

more detailed questions. Finally, the cross-sectional nature of the study means the direction of observed associations is not known. Therefore, future longitudinal studies are warranted to clarify the direction of causality. Nevertheless, the mere coexisting presence of cataract with chronic conditions and multimorbidity highlights an important health priority and informs targeted intervention.

In conclusion, in this large sample of Spanish residents, those with cataract were at greater risk of chronic physical and mental health complications and multimorbidity. Interventions specifically designed for those with cataract to reduce or manage co-occurring chronic conditions and multimorbidity are urgently required. Such interventions may consist of group exercise to favor physical activity, adaptation of the home environment to reduce fall risk, and use of low vision devices to improve social participation. Finally, ophthalmologists should be aware that individuals with cataracts are at high risk of multimorbidity.

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Tables

Table 1. Sample characteristics (overall and by cataract status)

Characteristics	Category	Overall (N=23,089)	Cataract		P-value ^a
			No (N=20,211)	Yes (N=2,878)	
Sex	Male	45.9	47.4	35.1	<0.001
	Female	54.1	52.6	64.9	
Age (years)	Mean (SD)	53.4 (18.9)	50.2 (17.6)	76.0 (10.3)	<0.001
Marital status	Single/widowed/divorced/separated	45.9	44.8	53.6	<0.001
	Married	54.1	55.2	46.4	
Education	≤Primary	31.2	25.9	68.8	<0.001
	Secondary	43.0	46.3	20.3	
	≥Tertiary	25.8	27.9	11.0	
Smoking	Never	50.8	48.7	65.0	<0.001
	Past	25.8	25.8	26.1	
	Current	23.4	25.5	9.0	
Alcohol consumption	No	35.8	33.2	54.5	<0.001
	Yes	64.2	66.8	45.5	

Abbreviation: SD standard deviation.

Cataract was assessed with a question with “yes” and “no” options.

^a P-values were based on chi-squared tests except for age (t-test), and were corrected using the Benjamini and Hochberg procedure.

The results are expressed as percentage (%) except age.

Table 2. Prevalence of chronic conditions by cataract status in adults residing in Spain

Chronic condition	Cataract		Effect size ^a	P-value ^b
	No	Yes		
Obesity	16.8	24.7	0.07	<0.001
Hypertension	22.4	59.3	0.27	<0.001
Myocardial infarction	1.8	5.9	0.09	<0.001
Angina pectoris and other coronary diseases	1.5	6.7	0.12	<0.001
Other cardiac diseases	5.1	18.3	0.17	<0.001
Varicose veins of lower extremities	10.1	28.2	0.18	<0.001
Osteoarthritis	17.6	58.5	0.32	<0.001
Chronic neck pain	14.2	34.9	0.18	<0.001
Chronic low back pain	19.1	42.5	0.19	<0.001
Chronic allergy (excluding allergic asthma)	16.0	17.9	0.02	0.009
Asthma (including allergic asthma)	5.6	8.9	0.05	<0.001
Chronic bronchitis, emphysema or chronic obstructive pulmonary disease (COPD)	3.8	13.3	0.14	<0.001
Diabetes	7.4	26.7	0.21	<0.001
Peptic ulcer disease	3.5	10.8	0.12	<0.001
Urinary incontinence	3.8	20.8	0.24	<0.001
Hypercholesterolemia	20.4	46.2	0.20	<0.001
Chronic skin disease	5.3	11.4	0.08	<0.001
Chronic constipation	3.3	12.9	0.15	<0.001
Liver cirrhosis and other hepatic disorders	1.3	2.7	0.04	<0.001
Depression	8.8	23.7	0.16	<0.001
Anxiety disorder	8.2	14.5	0.07	<0.001
Other psychiatric disorders	1.9	4.4	0.06	<0.001
Stroke	1.5	6.2	0.11	<0.001
Migraine and other frequent headaches	9.4	14.8	0.06	<0.001
Hemorrhoids	6.1	17.0	0.14	<0.001
Cancer	4.1	10.7	0.10	<0.001
Osteoporosis	3.5	16.5	0.19	<0.001
Thyroid disease	6.3	12.0	0.07	<0.001
Renal disease	3.9	12.2	0.13	<0.001
Injury	5.8	9.3	0.05	<0.001

Cataract and other chronic conditions were assessed with questions with “yes” and “no” options.

^a Effect size was calculated using phi coefficient.

^b P-values were based on Chi-squared tests and were corrected using the Benjamini and Hochberg adjustment method.

The prevalence of chronic conditions is expressed as percentage (%).

Table 3. The relationship of cataract (independent variable) with multimorbidity and the number of chronic conditions (dependent variables) in adults residing in Spain

	Multimorbidity			Number of chronic conditions		
	Odds ratio	95% confidence interval	P-value	Incidence rate ratio	95% confidence interval	P-value
Overall (N=23,089)	2.77	2.39-3.21	<0.001	1.34	1.29-1.38	<0.001
Men (N=10,595)	2.82	2.27-3.55	<0.001	1.33	1.26-1.41	<0.001
Women (N=12,494)	2.69	2.21-3.30	<0.001	1.33	1.28-1.40	<0.001
Participants aged ≤ 40 years (N=6,271)	2.97	1.08-8.50	0.035	2.16	1.23-3.79	0.008
Participants aged 41-65 years (N=10,129)	2.72	2.07-3.62	<0.001	1.54	1.41-1.68	<0.001
Participants aged >65 years (N=6,689)	3.22	2.69-3.88	<0.001	1.42	1.38-1.47	<0.001

Cataract and other chronic conditions were assessed with questions with “yes” and “no” options.

Chronic conditions included obesity, hypertension, myocardial infarction, angina pectoris and other coronary diseases, other cardiac diseases, varicose veins of lower extremities, osteoarthritis, chronic neck pain, chronic low back pain, chronic allergy (excluding allergic asthma), asthma (including allergic asthma), chronic bronchitis, emphysema or chronic obstructive pulmonary disease (COPD), diabetes, peptic ulcer disease, urinary incontinence, hypercholesterolemia, chronic skin disease, chronic constipation, liver cirrhosis and other hepatic disorders, depression, anxiety disorder, other psychiatric disorders, stroke, migraine and other frequent headaches, hemorrhoids, cancer, osteoporosis, thyroid disease, renal disease, and injury.

Multimorbidity was defined as the presence of two or more chronic conditions.

The relationship of cataract (independent variable) with multimorbidity and the number of chronic conditions (dependent variables) was assessed using multivariable logistic regression and multivariable negative binomial regression models, respectively. The associations were investigated in the overall population, males, females, and different age groups (i.e., age ≤ 40 years, age 41-65 years, age >65 years). Multimorbidity and the number of chronic conditions were included in the models as dichotomous and count variables.

Models were adjusted for sex (apart from the sex-stratified analyses), age, marital status, education, smoking, and alcohol consumption.

Confidence intervals were corrected using the Benjamini-Yekutieli adjustment method, while p-values were corrected using the Benjamini-Hochberg adjustment method.