FILLING GAPS IN FEMALE GOUT: A CROSS-SECTIONAL STUDY OF 192,000 PATIENTS HOSPITALIZED WITH GOUT FROM 2005 TO 2015

AUTOR: RODRÍGUEZ SOSA, ENRIQUE

TUTOR: DR. ANDRÉS COLLADO, MARIANO

COTUTOR: DR. DE MIGUEL MENDIETA, EUGENIO

Departamento y Área: MEDICINA

Curso académico: 2022-2023

Convocatoria de: Febrero 2023

1 INDEX

ABSTRACT

Introduction: Patients with gout suffer from several comorbidities. Female gout has received little attention in the published literature, although our experience and some studies suggest different clinical presentation, comorbidity profile and higher mortality rates than men.

Objective: To compare distribution of comorbidities by sex in hospitalized patients with gout in Spain.

Methods: The Minimal Basic Data Set from all Spanish hospitalizations with gout (ICD-9 coding) from 2005 to 2015 was analyzed. The comorbidities of interest were obesity, dyslipidemia, chronic kidney disease, diabetes mellitus and chronic heart failure, among others. Comparative analyses were carried out by sex. Then, stratification by age was performed and the population was divided into six subgroups. A logistic regression analysis was built for the total population and two subgroups. A decision tree was constructed to assess the accuracy of a sex prediction algorithm.

Results: 192,037 admissions were analyzed. 158,646 cases were in men, significantly younger than women (64.0±14.4 vs 73.9±13.7 years; p<0.001). Female predominant comorbidities were obesity, dyslipidemia, chronic kidney disease, diabetes mellitus, heart failure, dementia, urinary tract infection and concurrent rheumatic disease. Variables independently linked to females in logistic regression analysis were age, heart failure, obesity, urinary tract infection, diabetes mellitus, rheumatic disease, dyslipidemia, chronic kidney disease and venous thromboembolism. Accuracy of the decision tree algorithm was 74.44%.

Conclusions: A nation-wide analysis of 11years of hospitalizations with gout confirm a different comorbidity profile between men and women. A different approach for female gout is needed, to reduce gender blindness.

RESUMEN

Introducción: Los pacientes con gota asocian varias comorbilidades. La gota en mujeres ha recibido poca atención en la literatura, pese a que nuestra experiencia y algunos estudios sugieren manifestaciones y comorbilidades distintas a las de los hombres y mayores tasas de mortalidad.

Objetivo: Comparar la distribución de comorbilidades por sexo en pacientes hospitalizados con gota en España.

Métodos: Se analizó el Conjunto Mínimo Básico de Datos de todos los pacientes hospitalizados en España con gota (según la codificación de CIE-9) desde 2005 hasta 2015. Las comorbilidades analizadas fueron obesidad, dislipemia, enfermedad renal crónica, diabetes mellitus e insuficiencia cardíaca crónica, entre otras. Se realizó un análisis comparativo por sexos. A continuación, se estratificó a la población en seis subgrupos de edad. Posteriormente se creó un modelo de regresión logística para la muestra total y para dos subgrupos. Se confeccionó un árbol de decisiones para contar con un algoritmo predictor de sexo.

Resultados: Se analizaron 192.037 hospitalizaciones. 158.646 casos se dieron en hombres, significativamente más jóvenes que las mujeres (64,0±14,4 vs. 73,9±13,7 años; p<0,001). Las comorbilidades más prevalentes en mujeres fueron obesidad, dislipemia, enfermedad renal crónica, diabetes mellitus, insuficiencia cardíaca crónica, demencia, infección del tracto urinario y enfermedad reumatológica concomitante. El análisis de regresión logística mostró coeficientes positivos (relacionados con sexo femenino) para edad, insuficiencia cardíaca crónica, obesidad, infección del tracto urinario, diabetes mellitus, enfermedad reumatológica, dislipemia,

enfermedad renal crónica y enfermedad tromboembólica venosa. La precisión del árbol de decisiones fue del 74,44%.

Conclusiones: Un análisis nacional de 11 años de hospitalizaciones de pacientes con gota corrobora un perfil de comorbilidad diferencial entre hombres y mujeres. Es necesario un enfoque distinto para la gota en la mujer, en aras de reducir el sesgo de género.

Palabras clave: GOTA, SEXO, COMORBILIDADES, ALTAS HOSPITALARIAS, CONJUNTO MÍNIMO BÁSICO DE DATOS.

2 INTRODUCTION

In health, there are differences between men and women that can be attributed to biological sex (for example, those related to testosterone and estrogens blood levels) or gender (that is, the social conception of man and woman). Whereas the first ones are ineluctable, the second ones respond to human biases that can and must be addressed. In 1991, Doctor Healy coined the term "Yentl syndrome" to illustrate that women with symptoms of myocardial infarction were less likely to be tested and treated in comparison with men (1).

Although initially described for cardiovascular diseases, Yentl syndrome extends to many other pathologies of different areas and specialties. Our impression is that there is gender blindness as well in gout, a rheumatic condition that consists on the deposition of monosodium urate crystals in joints and surrounding structures. This deposition leads to an inflammatory state with acute local pain, but also systemic, long-term consequences, such as accelerated arteriosclerosis or risk of renal function decrease. This disease is more prevalent in men, who intrinsically have higher serum urate levels; after menopause the difference between men and women diminishes, though usually it never overlaps.

Patients with gout associate with a myriad of comorbidities, especially cardiovascular, renal and endocrine-metabolic diseases, many already present at the time of diagnosis and involved in developing hyperuricemia and gout, such as renal failure (2). Moreover, the odds of developing new comorbidities increase progressively since the first attack of gout, with a higher risk than the general population (3). Furthermore, the incidence of gout and its associated comorbidities has increased over the last years (4). Recent studies have identified different phenotypes of gouty patients, based on the aggrupation of certain comorbidities (5–7). These studies also revealed that the accompanying comorbidities vary with time. For instance, women with gout and type 2 diabetes develop stroke earlier than men (7). Gout-related hospital admissions have risen over the last decades (8), and it is unknown whether some comorbidities play a role here.

Gout in women has received little attention in the published literature, and is notably underrepresented in phenotype evaluation studies and clinical trials (5,9). Our clinical experience and some studies suggest affecting at elder stages of life, with more accompanying conditions (higher use of diuretics, higher prevalence of chronic kidney disease and heart failure) and different clinical manifestations that hamper gout identification (subtle, vague joint pain, often migratory, not fulfilling flare criteria, or persistent low-grade arthritis) and delay the proper management, with larger disability and higher urate levels (10). A prospective study conducted in China with 52,322 people revealed that, after a mean follow-up period of 8.1 years, gout-related mortality risk estimates were higher in women though only numerically (11).

Therefore, there is room for progress in the knowledge of female gout. The purpose of this study, focused on analyzing differences in comorbidities, was to advance in this characterization and help to reduce the existing gender bias in this pathology.

3 HYPOTHESES AND OBJECTIVES

3.1 HYPOTHESES

- Women with gout would show a notably different comorbidity profile compared to men.

- Differences in the prevalence of comorbidities would not be completely explained by different age.

- There would be some comorbidities closely linked to each sex.

- The pattern of comorbidities for women with gout would be specific enough to be able to predict the sex of a certain subject only considering to his/her comorbidities.

3.2 OBJECTIVES

Primary objective: To compare the distribution of comorbidities between sexes on Spanish hospitalized patients with gout.

Secondary objectives:

- To assess the influence of age on the distribution of comorbidities as a potential confounder.

- To evaluate the strength of association between each comorbidity and sex.

- To study the consistency of findings according to having gout as primary or secondary diagnosis.

- To build an automatic algorithm able to accurately predict gouty sufferer's sex just considering comorbidities.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN, POPULATION AND STUDY VARIABLES

An observational, multicenter cross-sectional study was performed. The study used the Minimal Basic Data Set (MBDS) of all patients ≥18 years admitted to Spanish hospitals with a gout diagnosis, either as a primary or secondary diagnosis. The MBDS contains relevant information (age, sex, primary and secondary diagnoses, and diagnostic and therapeutic procedures, among others) of all admissions in private and public Spanish hospitals, extracted from discharge reports. Gout was coded using the ninth version of the International Classification of Diseases - ICD-9- as 274.0, 274.00, 274.01, 274.02, 274.03, 274.1, 274.10, 274.11, 274.19, 274.8, 274.81, 274.82, 274.89 or 274.9. The study period comprised from January 1st, 2005, to December 31st, 2015. Later years were not analyzed due to the introduction of new ICD-10. Data was provided by the National Statistics Institute and a first report assessing trends of gout hospitalizations had been previously published (12). The present analysis focused on age and presence of comorbidities of inpatients comparing between sexes.

The primary explanatory variable was sex (man/woman). Other variables were age at admission, gout as main diagnosis or secondary diagnosis and comorbidities (according to their ICD-9): obesity, dyslipidemia, chronic kidney disease, diabetes mellitus, coronary heart disease, chronic heart failure, peripheral vascular disease, arrhythmia, venous thromboembolism, cerebrovascular disease, dementia, urinary tract infection, pneumonia, sepsis, obstructive pulmonary disease, liver disease, and rheumatic disease.

4.2 STATISTICAL ANALYSIS

Quantitative variables (age) were expressed as arithmetic mean with standard deviation, and qualitative variables (sex, comorbidities) as frequencies and percentages. In order to compare between sexes, Student's t-test was used for quantitative variables, and chi-square test was

used for qualitative variables. Age could act as a potential confounding factor, so the population was divided into sextets with a similar size (≤70 years, 71-80 years, 81-85 years, 86-90 years, 91-95 years and >95 years) to perform comparative analyses.

In order to assess the strength of association between each comorbidity and sex, a multiple logistic regression analysis was carried out. To avoid the potential role of having largely more men than women in the population, a sample of men (n=33,394) with the same size as that of women (n=33,394) was randomly selected. Comorbidities were used as independent variables, whereas sex was assigned as the dependent variable. Results were expressed as coefficients ranged from -1 to +1 (where negative coefficients were related to men and positive coefficients to women) and *odds ratio*, with their corresponding 95% confidence intervals (CI) and p-values. To discern if comorbidities would behave similarly in younger and older patients, the models were performed after dividing the population into two subgroups (≤60 years and >60 years) and also by sextets of age. Moreover, the model was also run stratifying by gout as primary or secondary diagnosis in MBDS.

A decision tree algorithm was constructed using the aforementioned comorbidities to identify the sex of individual cases with gout just considering their age and comorbidities.

For both regression model and decision tree, the accuracy, defined as the rate of population whose sex was correctly guessed by the model, was estimated.

Google Colab®, which allows execution of Python, was utilized to analyze the data (packages *matplotlib* 3.2.2, *pandas* 1.3.5, *scikit-learn* 1.0.2 and *statsmodels* 0.12.2). Statistical significance was set at an error probability of less than 5% (p < 0.050).

4.3 ETHICAL ASPECTS

The study was approved by the ethics committee of the Dr. Balmis General University Hospital of Alicante, following the principles of the Declaration of Helsinki, on September 29th, 2022 (Supplementary Material). The Responsible Investigation Office of Miguel Hernandez University

also authorized the study (TFG.GME.MAC.ERS.221005). As data is retrospective and was provided pseudonymized, no informed consent from participants was needed.

5 RESULTS

The data of 192,037 hospital admissions was included, 158,646 of which were men (82.6%). Mean age was 64.0±14.4 years in men and 73.9±13.7 years in women (p<0.001). The group with gout as the primary diagnosis (n=10,512; 5.5%) consisted of 9,027 men (85.9%) and 1,485 women (14.1%), whereas the group with gout as a secondary diagnosis (n=181,518; 94.5%) included 149,619 men (82.4%) and 31,899 women (17.6%). The sum of both groups results in 192,030; the remaining 7 people were classified as "undetermined sex" and were excluded from the analysis.

The distribution of comorbidities is given in **Tables 1, 2** and **3**. **Figure 1** illustrates the global prevalence of comorbidities, without stratification by age. Comorbidities significantly more prevalent in women than in men were obesity (16.3% of women vs 10.8% of men), dyslipidemia (31.8% vs 30.7%), chronic kidney disease (33.8% vs 25.1%), diabetes mellitus (36.2% vs 26.0%), heart failure (31.8% vs 16.6%), dementia (2.1% vs 1.2%), urinary tract infection (12.0% vs 5.4%), and concurrent rheumatic disease (2.6% vs 1.4%). Conversely, male predominant comorbidities were coronary heart disease (21.8% of men vs 16.9% of women), peripheral vascular disease (3.8% vs 1.2%), pneumonia (4.5% vs 3.8%), obstructive pulmonary disease (8.9% vs 2.3%) and liver disease (2.2% vs 1.3%). No differences were observed in arrhythmia (p=0.532), venous thromboembolism (p=0.969), cerebrovascular disease (p=0.742) and sepsis (p=0.341).

After age stratification (**Tables 1-3**), differences in dementia were lost. For dyslipidemia, differences started to be statistically significant at 81-85 years. In the case of chronic kidney disease, there was a descendent trend, as in the oldest subgroup (>95 years), prevalence was significantly higher in men. Differences remained statistically significant for all subgroups in the rest of analyzed comorbidities.

Table 1. Prevalence of obesity, dyslipidemia, chronic kidney disease (CKD), diabetes mellitus and coronary heart disease (CHD) in men and women, for the whole population and stratified by age.

	Number of men (%)	Number of women (%)	p-value
Obesity			
Total	17,084 (10.8)	5,444 (16.3)	< 0.001
< 70 years (28,214/1,912)	4,496 (15.9)	373 (19.5)	0.031
71-80 years (33,673/3,319)	4,623 (13.7)	786 (23.7)	< 0.001
81-85 years (20,771/3,179)	2,410 (11.6)	779 (24.6)	< 0.001
86-90 years (27,521/6,089)	2,800 (10.2)	1,229 (20.2)	< 0.001
91-95 years (25,032/7,374)	1,795 (7.2)	1,192 (16.2)	< 0.001
> 95 years (23,407/11,521)	960 (4.1)	1,085 (9.4)	< 0.001
Dyslipidemia			
Total	48,634 (30.7)	10,624 (31.8)	0.020
< 70 years (28,214/1,912)	9,126 (32.3)	631 (33.0)	0.570
71-80 years (33,673/3,319)	12,347 (36.7)	1,241 (37.4)	0.420
81-85 years (20,771/3,179)	7,092 (34.1)	1,219 (38.4)	0.009
86-90 years (27,521/6,089)	8,840 (32.1)	2,217 (36.4)	< 0.001
91-95 years (25,032/7,374)	6,866 (27.4)	2,465 (33.4)	< 0.001
> 95 years (23,407/11,521)	4,363 (18.6)	2,851 (24.8)	< 0.001
CKD			
Total	39,817 (25.1)	11,291 (33.8)	< 0.001
< 70 years (28,214/1,912)	3,772 (13.4)	539 (28.2)	< 0.001
71-80 years (33,673/3,319)	6,381 (18.9)	959 (28.9)	< 0.001
81-85 years (20,771/3,179)	5,120 (24.7)	922 (29.0)	0.001
86-90 years (27,521/6,089)	7,850 (28.5)	2,197 (36.1)	< 0.001
91-95 years (25,032/7,374)	8,386 (33.5)	2,729 (37.0)	< 0.001
> 95 years (23,407/11,521)	8,307 (35.5)	3,945 (34.2)	0.022
Diabetes mellitus			
Total	41,185 (26.0)	12,073 (36.2)	< 0.001
< 70 years (28,214/1,912)	4,759 (16.9)	440 (23.0)	< 0.001
71-80 years (33,673/3,319)	9,206 (27.3)	1,286 (38.8)	< 0.001
81-85 years (20,771/3,179)	6,393 (30.8)	1,314 (41.3)	< 0.001
86-90 years (27,521/6,089)	8,349 (30.3)	2,583 (42.4)	< 0.001
91-95 years (25,032/7,374)	7,108 (28.4)	2,937 (39.8)	< 0.001
> 95 years (23,407/11,521)	5,360 (22.9)	3,507 (30.4)	< 0.001
CHD			
Total	34,507 (21.8)	5,633 (16.9)	< 0.001
< 70 years (28,214/1,912)	3,764 (13.3)	116 (6.1)	< 0.001
71-80 years (33,673/3,319)	7,115 (21.1)	407 (12.3)	< 0.001
81-85 years (20,771/3,179)	4,715 (22.7)	456 (14.3)	< 0.001
86-90 years (27,521/6,089)	6,883 (25.0)	1,067 (17.5)	< 0.001
91-95 years (25,032/7,374)	6,226 (24.9)	1,333 (18.1)	< 0.001
> 95 years (23,407/11,521)	5,804 (24.8)	2,254 (19.6)	< 0.001

Table 2. Prevalence of chronic heart failure (CHF), peripheral vascular disease (PVD), arrhythmia, venous thromboembolism (VTE), cerebrovascular disease (CVD) and dementia in men and women, for the whole population and stratified by age.

	Number of men (%)	Number of women (%)	p-value
CHF			
Total	26,406 (16.6)	10,631 (31.8)	< 0.001
< 70 years (28,214/1,912)	1,648 (5.8)	169 (8.8)	< 0.001
71-80 years (33,673/3,319)	3,505 (10.4)	578 (17.4)	< 0.001
81-85 years (20,771/3,179)	3,050 (14.7)	780 (24.5)	< 0.001
86-90 years (27,521/6,089)	5,414 (19.6)	1,818 (29.9)	< 0.001
91-95 years (25,032/7,374)	6,054 (24.2)	2,657 (36.0)	< 0.001
> 95 years (23,407/11,521)	6,735 (28.8)	4,629 (40.2)	< 0.001
PVD			
Total	5,980 (3.8)	385 (1.2)	< 0.001
< 70 years (28,214/1,912)	417 (1.5)	9 (0.5)	< 0.001
71-80 years (33,673/3,319)	1,206 (3.6)	42 (1.3)	< 0.001
81-85 years (20,771/3,179)	887 (4.3)	32 (1.0)	< 0.001
86-90 years (27,521/6,089)	1,333 (4.8)	76 (1.3)	< 0.001
91-95 years (25,032/7,374)	1,133 (4.5)	106 (1.4)	< 0.001
> 95 years (23,407/11,521)	1,004 (4.3)	120 (1.0)	< 0.001
Arrhythmia			
Total	1,950 (1.2)	396 (1.2)	0.532
< 70 years (28,214/1,912)	260 (0.9)	6 (0.3)	0.009
71-80 years (33,673/3,319)	429 (1.3)	54 (1.6)	0.103
81-85 years (20,771/3,179)	309 (1.5)	47 (1.5)	1.000
86-90 years (27,521/6,089)	371 (1.4)	90 (1.5)	0.457
91-95 years (25,032/7,374)	337 (1.4)	89 (1.2)	0.387
> 95 years (23,407/11,521)	244 (1.0)	110 (1.0)	0.476
VTE			
Total	4,087 (2.6)	862 (2.6)	0.969
< 70 years (28,214/1,912)	816 (2.9)	33 (1.7)	0.004
71-80 years (33,673/3,319)	874 (2.6)	76 (2.3)	0.315
81-85 years (20,771/3,179)	549 (2.6)	78 (2.5)	0.573
86-90 years (27,521/6,089)	690 (2.5)	182 (3.0)	0.034
91-95 years (25,032/7,374)	613 (2.5)	210 (2.9)	0.061
> 95 years (23,407/11,521)	545 (2.3)	283 (2.5)	0.483
CVD			
Total	5,620 (3.5)	1,170 (3.5)	0.742
< 70 years (28,214/1,912)	629 (2.2)	36 (1.9)	0.359
71-80 years (33,673/3,319)	1,108 (3.3)	102 (3.1)	0.535
81-85 years (20,771/3,179)	782 (3.8)	102 (3.2)	0.134
86-90 years (27,521/6,089)	1,079 (3.9)	219 (3.6)	0.260
91-95 years (25,032/7,374)	1,054 (4.2)	271 (3.7)	0.045
> 95 years (23,407/11,521)	968 (4.1)	440 (3.8)	0.166
Dementia			
Total	1,903 (1.2)	709 (2.1)	< 0.001
< 70 years (28,214/1,912)	15 (0.1)	1 (0.1)	1.000
71-80 years (33,673/3,319)	88 (0.3)	3 (0.1)	0.087
81-85 years (20,771/3,179)	149 (0.7)	25 (0.8)	0.753
86-90 years (27,521/6,089)	372 (1.4)	87 (1.4)	0.672
91-95 years (25,032/7,374)	460 (1.8)	149 (2.0)	0.333
> 95 years (23,407/11,521)	819 (3.5)	444 (3.9)	0.101

Table 3. Prevalence of urinary tract infection (UTI), pneumonia, sepsis, obstructive pulmonary disease (OPD), liver disease and rheumatic disease in men and women, for the whole population and stratified by age.

|	Number of men (%)	Number of women (%)	p-value
UTI			
Total	8,480 (5.4)	4,017 (12.0)	< 0.001
< 70 years (28,214/1,912)	916 (3.3)	188 (9.8)	< 0.001
71-80 years (33,673/3,319)	1,289 (3.8)	343 (10.3)	< 0.001
81-85 years (20,771/3,179)	1,036 (5.0)	319 (10.0)	< 0.001
86-90 years (27,521/6,089)	1,531 (5.6)	658 (10.8)	< 0.001
91-95 years (25,032/7,374)	1,631 (6.5)	887 (12.0)	< 0.001
> 95 years (23,407/11,521)	2,077 (8.9)	1,622 (14.1)	< 0.001
Pneumonia			
Total	7,068 (4.5)	1,273 (3.8)	< 0.001
< 70 years (28,214/1,912)	607 (2.2)	37 (1.9)	0.582
71-80 years (33,673/3,319)	1,116 (3.3)	85 (2.6)	0.022
81-85 years (20,771/3,179)	881 (4.2)	103 (3.2)	0.009
86-90 years (27,521/6,089)	1,376 (5.0)	184 (3.0)	< 0.001
91-95 years (25,032/7,374)	1,455 (5.8)	319 (4.3)	0.009
> 95 years (23,407/11,521)	1,633 (7.0)	545 (4.7)	< 0.001
Sepsis			
Total	2,399 (1.5)	481 (1.4)	0.341
< 70 years (28,214/1,912)	332 (1.2)	33 (1.7)	0.044
71-80 years (33,673/3,319)	461 (1.4)	53 (1.6)	0.321
81-85 years (20,771/3,179)	333 (1.6)	47 (1.5)	0.654
86-90 years (27,521/6,089)	423 (1.5)	97 (1.6)	0.780
91-95 years (25,032/7,374)	452 (1.8)	105 (1.4)	0.030
> 95 years (23,407/11,521)	398 (1.7)	146 (1.3)	0.002
OPD			
Total	14,080 (8.9)	761 (2.3)	< 0.001
< 70 years (28,214/1,912)	844 (3.0)	40 (2.1)	0.029
71-80 years (33,673/3,319)	2,379 (7.1)	51 (1.5)	< 0.001
81-85 years (20,771/3,179)	1,953 (9.4)	74 (2.3)	< 0.001
86-90 years (27,521/6,089)	3,144 (11.4)	127 (2.1)	< 0.001
91-95 years (25,032/7,374)	2,957 (11.8)	184 (2.5)	< 0.001
> 95 years (23,407/11,521)	2,803 (12.0)	285 (2.5)	< 0.001
Liver disease			
Total	3,547 (2.2)	427 (1.3)	< 0.001
< 70 years (28,214/1,912)	988 (3.5)	68 (3.6)	0.951
71-80 years (33,673/3,319)	1,029 (3.1)	85 (2.8)	0.124
81-85 years (20,771/3,179)	565 (2.7)	58 (1.8)	0.004
86-90 years (27,521/6,089)	461 (1.7)	91 (1.5)	0.352
91-95 years (25,032/7,374)	327 (1.3)	66 (0.9)	0.006
> 95 years (23,407/11,521)	177 (0.8)	59 (0.5)	0.011
Rheumatic disease			
Total	2,283 (1.4)	874 (2.6)	< 0.001
< 70 years (28,214/1,912)	271 (1.0)	85 (4.5)	< 0.001
71-80 years (33,673/3,319)	423 (1.3)	111 (3.3)	< 0.001
81-85 years (20,771/3,179)	281 (1.4)	96 (3.0)	< 0.001
86-90 years (27,521/6,089)	451 (1.6)	142 (2.3)	< 0.001
91-95 years (25,032/7,374)	471 (1.2)	214 (2.9)	< 0.001
> 95 years (23,407/11,521)	386 (1.7)	226 (2.0)	0.040
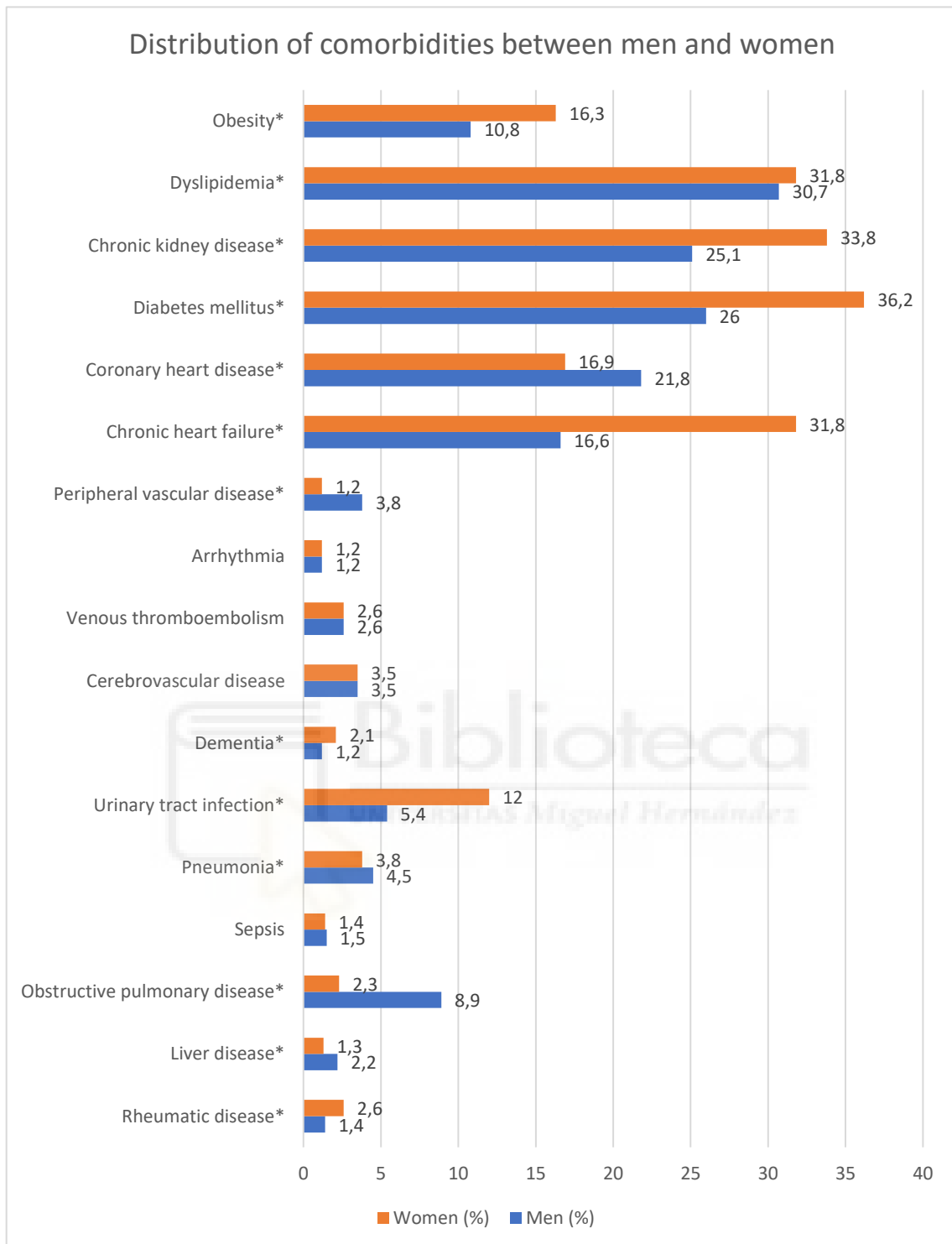
*Figure 1. Distribution of comorbidities between men and women. Prevalence is expressed as percentage of population with each comorbidity. Statistical significance is marked with ***

The multiple logistic regression model (**Figure 2**) showed an accuracy score of 68.51%. Comorbidities with positive coefficients (related to female sex) were age (+0.701), chronic heart failure (+0.242), obesity (+0.214), urinary tract infection (+0.199), diabetes mellitus (+0.186), rheumatic disease (+0.102), dyslipidemia (+0.087), chronic kidney disease (+0.080) and venous thromboembolism (+0.007). Comorbidities with negative coefficients (related to male sex) were obstructive pulmonary disease (-0.386), coronary heart disease (-0.229), peripheral vascular disease (-0.197), pneumonia (-0.068), liver disease (-0.028), cerebrovascular disease (-0.025), sepsis (-0.023) and arrhythmia (-0.005). Odds ratio with 95% CI and p-values are expressed in **Table 4**; all were statistically significant.

The logistic regressions performed after stratifying the whole population into two subgroups (≤60 years and >60 years) showed an accuracy of 61.62% and 62.93%, respectively (**Figure 3**). Some differences were found between the two of them: for example, in the first subgroup, chronic heart failure and dyslipidemia were associated with male sex, while cerebrovascular disease and obstructive pulmonary disease were associated with female sex.
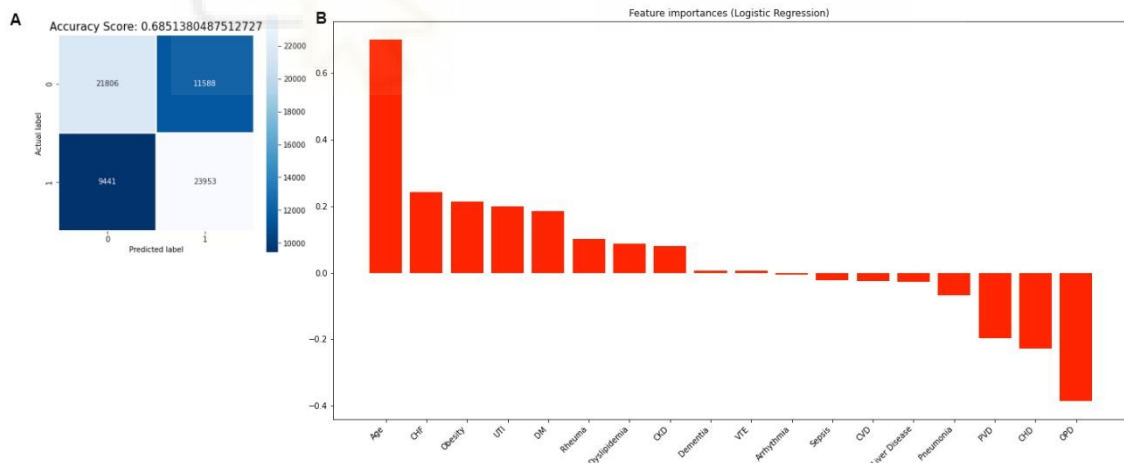
Figure 2. A) accuracy of logistic regression, where male sex is represented as 0 and female sex as 1. B) Coefficients of each comorbidity. Positive coefficients associate with women with gout, negative ones otherwise. Legend: CHF: chronic heart failure; UTI: urinary tract infection; DM: diabetes mellitus; Rheuma: rheumatological disease; CKD: chronic kidney disease; VTE: venous thromboembolism; CVD: cerebrovascular disease; PVD: peripheral vascular disease; CHD: coronary heart disease; OPD: obstructive pulmonary disease.

Table 4. Coefficients, odds ratio with 95% confidence intervals (CI) and p-values of each comorbidity for the whole population in the logistic regression.

	Coefficient	Odds ratio	95% CI	p-value
Obesity	0.21	1.24	1.23-1.24	< 0.001
Dyslipidemia	0.09	1.09	1.09-1.09	< 0.001
CKD	0.08	1.08	1.08-1.09	< 0.001
Diabetes mellitus	0.19	1.20	1.20-1.21	< 0.001
CHD	-0.23	0.80	0.79-0.80	< 0.001
CHF	0.24	1.27	1.27-1.28	< 0.001
PVD	-0.20	0.82	0.82-0.82	< 0.001
Arrhythmia	-0.01	1.00	0.99-1.00	0.011
VTE	0.01	1.01	1.00-1.01	0.002
CVD	-0.03	0.98	0.97-0.98	< 0.001
Dementia	0.01	1.01	1.00-1.01	< 0.001
UTI	0.20	1.22	1.22-1.22	< 0.001
Pneumonia	-0.07	0.93	0.93-0.94	< 0.001
Sepsis	-0.02	0.98	0.97-0.98	< 0.001
OPD	-0.39	0.68	0.68-0.68	< 0.001
Liver disease	-0.03	0.97	0.97-0.98	< 0.001
Rheumatic disease	0.10	1.11	1.10-1.11	< 0.001
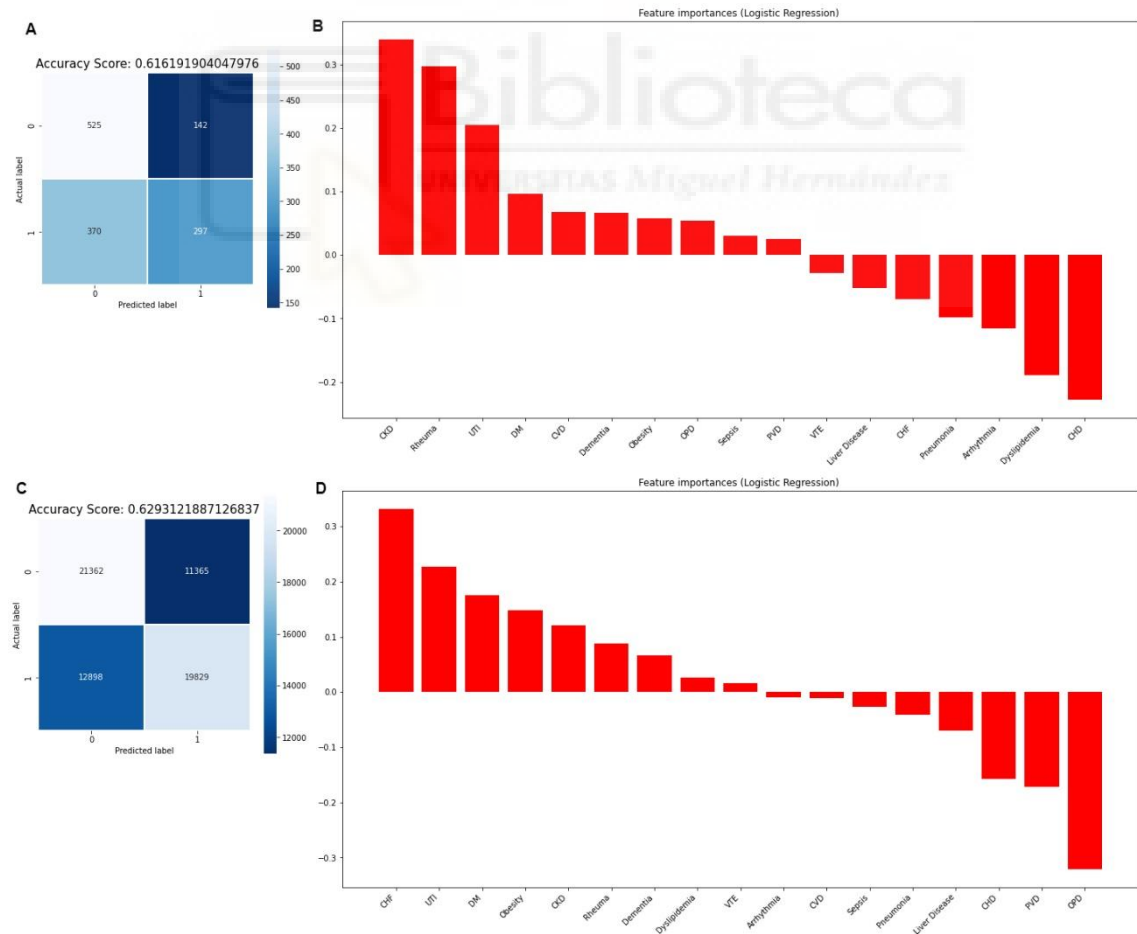
Figure 3. Logistic regression stratified by age. A-B) Accuracy of logistic regression of population ≤60 years and coefficients of each comorbidity C-D) Accuracy of logistic regression of population >60 years and coefficients for each comorbidity.

Logistic regressions for gout as primary or secondary diagnosis and for population divided into sextets can be found at Supplementary Material (**Figures S1-S3**).

The decision tree algorithm was constructed (**Figure 4**) (13). The accuracy score of the algorithm was 74.43%. The first cut-off point was an age of 85.5 years, as it had the greatest discriminative value. The presence or absence of certain comorbidities led the algorithm to conclude male sex (orange boxes) or female sex (blue boxes).
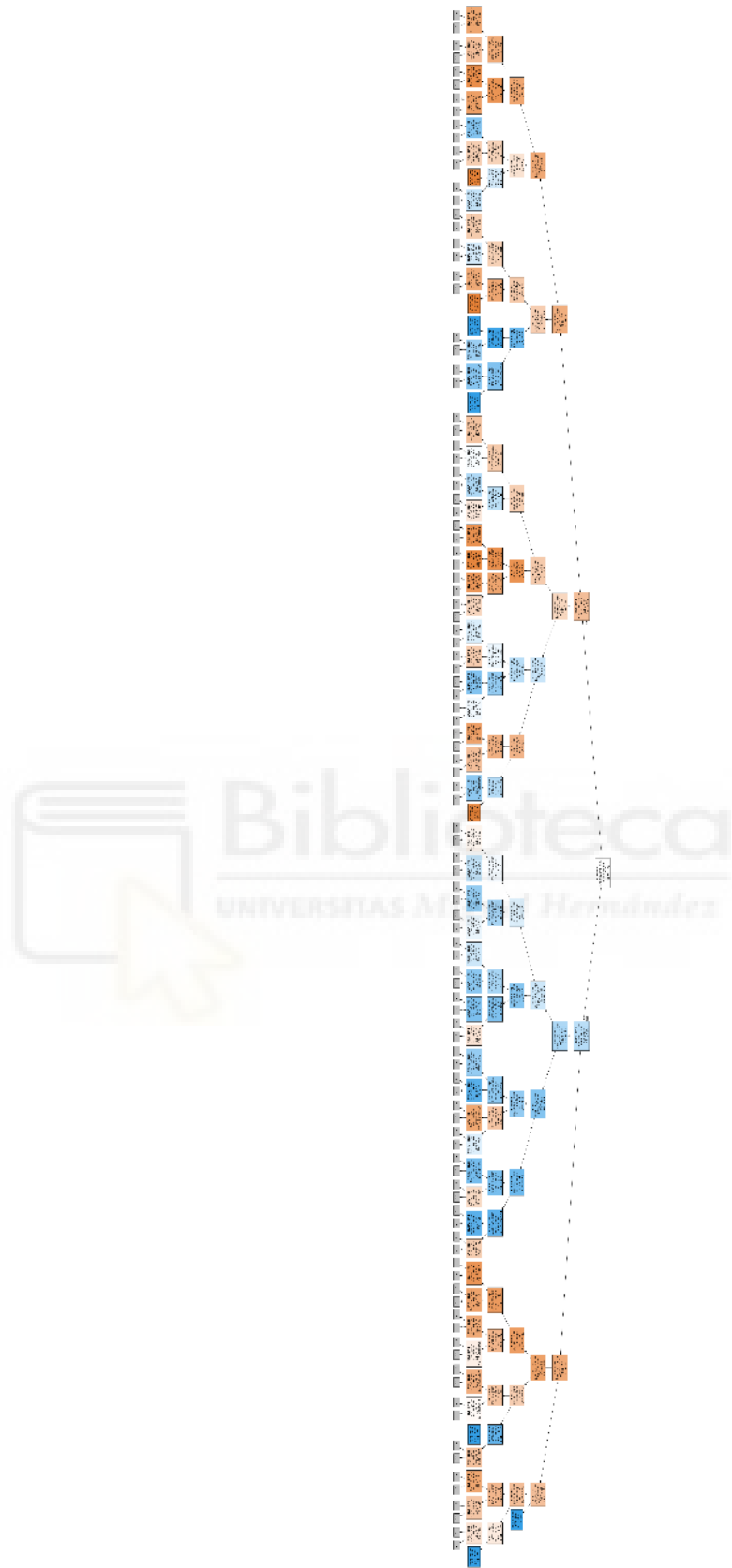
Figure 4. Decision tree. Orange and blue boxes are associated with males and females, respectively, while the colour intensity is related to the strength of association. For an image at higher resolution, please see reference 13.

6 DISCUSSION

To our knowledge, this is the first study to assess comorbidities in female gout in Spain using a large, hospitalized population. Using the national hospital database (MBDS), we have found that, compared to men, women with gout are almost 10 years older and at higher risk of heart failure, obesity, diabetes mellitus, dyslipidemia and chronic kidney disease, with clinically significant differences of even more than 10% in some cases. By multiple logistic regression analysis, we identified separate comorbidity profiles for women and men with gout, even after stratifying by age. We were able to design a decision tree algorithm capable of predicting the sex of the individuals solely using age and comorbidities with an accuracy of almost 75%. These findings imply that age and comorbidities play a major role in the development of gout, especially in women. The 25% of inaccuracy of models could rely on the existence of other contributors to gout, such as diet, drugs and genetics, which may be more prevalent in men (14).

Some studies have previously addressed the differences on comorbidities between men and women with gout, but in outpatient clinics. The CACTUS Study, a multicenter study run in France, proved that hypertension, metabolic syndrome, heart failure and renal failure were more prevalent in women, which were almost 10 years older (71±12 in women vs 62±11 years in men) (5). Similarly, Harrold et al. analyzed 1012 men and 262 women with gout in the USA, and found that women were older and had higher rates of hypertension, diabetes, renal failure and obesity (10). In addition, a latent transition analysis by Huang et al. found that women with gout and type 2 diabetes were more likely than men to suffer stroke in the follow-up (7). Our results, though based on hospitalizations, are in line with the previous ones, and confirm that women with gout are older and have more risk of developing certain comorbidities, mainly of cardiovascular, renal and endocrine-metabolic type. Particular attention to these conditions is thus needed when treating women with gout.

As pointed out in the results, hospitalized women with gout in Spain were almost 10 years older than men, and age might be influencing the comorbidities profiles. However, the majority of results remained unaltered after age stratification, with some interesting exceptions. For instance, the prevalence of dementia was no longer increased in women. In the case of chronic kidney disease, its prevalence starts at younger subgroups being higher in women and progressively inverts. Similarly, the strength of association of renal disease and female sex is maximal in those aged below 60 years and in the first sextet, while the influence reduces with increasing age and other comorbidities, such as heart failure, take the leading role. Gout in young women, especially before menopause, is unusual and most cases are related to reduced renal excretion of urate because of chronic kidney disease and use of diuretics; whereas, in younger men, hyperuricemia tends to be more related to genetic causes or metabolic syndrome (15). At later stages of life, renal diseases are common and not able to discriminate between women and men with gout.

The behavior of cardiovascular comorbidities -coronary heart disease, cerebrovascular disease, peripheral vascular disease and heart failure- in our study is particular and should be discussed. The first three conditions, closely derived from atherosclerosis, were associated with male sex, as occurs in the general population, likely in relation to diet, risk habits such as smoking, or lacking the cardioprotective role of estrogens. On the other hand, heart failure was associated with female sex; it has been stated in some studies that women tend to use diuretics (known for rising serum urate levels) more frequently than men, and one of the most common causes of diuretic prescription is heart failure (9). Unfortunately, pharmacological therapies are not coded in MBDS, so the role of diuretics could not be assessed in the present study. Interestingly, a study published in 2010 reported a 1.3-fold risk of acute myocardial infarction in elderly women with gout compared to women without gout, after adjusting for age, comorbidities and medication use, while the relative risk for men with gout was of 1.11 (16). Little is known why gout could impact more in women than in men. It has been proposed that, as women have lower serum

urate levels during most of their life, the effect of developing hyperuricemia could be more harmful, because homeostatic mechanisms are less developed than in men (16). Nevertheless, evidence is lacking in this subject and further research in this topic is warranted.

The relationship between sex and comorbidities in gout studied here may have direct consequences for general practitioners and rheumatologists. When a healthcare professional deals with a gouty patient, they should pay attention to sex and serve as a first and direct indicator of concurrent diseases: a woman with gout is probably about 74 years old and suffers from obesity, chronic kidney disease, diabetes mellitus or chronic heart failure. On the other hand, a male gout sufferer is expected to be at his sixties and present with respiratory problems, coronary heart disease and peripheral vascular involvement. Therefore, sex may guide the search of comorbidities and provide a tailored management of gout.

Our study holds several strengths. First, the sample size (192,037 cases, with more than 30,000 women) is considerably greater than that of similar studies, allows to build robust multivariable models to rule out confound and it grants differences of less than 1% to be statistically significant; it is also representative of Spanish population and can be generalized by similarity to European patients with gout, though probably not to North Americans, with different comorbidity numbers (17). Second, it uses the MBDS, which has shown similar results to other field studies (18). It relies on ICD coding, extensively used for gout-related investigations using population-based datasets (19).

Some limitations should be noted. The cross-sectional nature impedes any temporal evaluation that could label comorbidities as cause or consequence of gout. As earlier indicated, no treatment data was available, nor was the ethnicity of the participants; a majority of European whites is expected, so our findings may need verification in other populations. Gout cases are included in the MDBS if they were registered in discharge records. Subsequently, there could be some variability in the diagnosis of gout of our population, as it covers the clinical practice of

hundreds of specialists who might use different criteria (serum urate levels, identification of monosodium urate crystals, typical symptoms of gout, etc.). Moreover, some gout cases may be missed as the disease is often under-registered in discharge reports, although available numbers seem sufficient to perform robust analyses (20). Comorbidities of interest, such as arterial hypertension and urinary lithiasis, were excluded since their prevalence was substantially lower than expected according to our practice and other studies, suggesting under-registration. Other comorbidities evaluated in previous studies, like anemia, cancer and psoriasis, were not analyzed (7). The study period was selected until 2015, as in 2016 the diagnosis coding in MBDS was substituted by ICD-10, and discrepancies could have occurred.

7 CONCLUSION

A nation-wide analysis of 11 years of hospitalizations of patients with gout confirm a different comorbidity profile between men and women. Women with gout were older and had higher prevalence of several diseases (obesity, dyslipidemia, chronic kidney disease, diabetes, chronic heart failure, urinary tract infection and concurrent rheumatic disease). Association between sex and certain comorbidities is intense enough for sex prediction by an algorithm with considerable accuracy. Therefore, these results confirm the need of addressing gout in women with special considerations. They usually are older and have several comorbidities that differ from those of men. Consequently, management of female gout must be performed carefully, evaluating drug interactions, drug-related adverse events (e.g., nephrotoxicity of non-steroidal anti-inflammatory drugs), etc., in order to reduce gender blindness and guarantee the best attention from healthcare professionals.

8 REFERENCES

1.   Healy B. The Yentl Syndrome. N Engl J Med [Internet]. 1991 Jan 14 [cited 2022 Jul

      16];325(4):274–6. Available from:

      https://www.nejm.org/doi/10.1056/NEJM199107253250408 DOI:

      10.1056/NEJM199107253250408

2.   Kanbay M, Solak Y, Dogan E, Lanaspa MA, Covic A. Uric Acid in Hypertension and Renal

      Disease: The Chicken or the Egg. Blood Purif [Internet]. 2010 [cited 2023 Jan

      02;30(4):288–95. Available from: https://www.karger.com/Article/FullText/321074

      DOI: 10.1159/000321074

3.   Kuo CF, Grainge MJ, Mallen C, Zhang W, Doherty M. Comorbidities in patients with gout

      prior to and following diagnosis: case-control study. Ann Rheum Dis [Internet]. 2016 Jan

      [cited 2022 Jul 21];75;(1):210-7. Available from:

      https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4717388 DOI: 10.1136/annrheumdis-

      2014-206410

4.   Elfishawi MM, Zleik N, Kvrgic Z, Michet CJ, Crowson CS, Matteson EL, et al. The Rising

      Incidence of Gout and the Increasing Burden of Comorbidities: A Population-based

      Study over 20 Years. J Rheumatol [Internet]. 2018 Apr 1 [cited 2022 Sep 25];45(4):574–

      9. Available from: https://pubmed.ncbi.nlm.nih.gov/29247151/

      DOI:10.3899/jrheum.170806

5.   R Richette P, Clerson P, Périssin L, Flipo RM, Bardin T. Revisiting comorbidities in gout: A

      cluster analysis. Ann Rheum Dis [Internet]. 2015 [cited 2022 Sep 17];74(1):142–7.

      Available from: https://pubmed.ncbi.nlm.nih.gov/24107981/ DOI:

      10.1136/annrheumdis-2013-203779

6.   Bevis M, Blagojevic-Bucknall M, Mallen C, Hider S, Roddy E. Comorbidity clusters in people with gout: an observational cohort study with linked medical record review. Rheumatology (Oxford) [Internet]. 2018 Aug 1 [cited 2022 Sep 17];57(8):1358–63. Available from: https://pubmed.ncbi.nlm.nih.gov/29672754/ DOI: 10.1093/rheumatology/key096

7.   Huang HC, Chiang HP, Hsu NW, Huang CF, Chang SH, Lin KC. Differential risk group of developing stroke among older women with gouty arthritis: A latent transition analysis. Eur J Clin Invest [Internet]. 2019 [cited 2022 Oct 12];49(5):1–8. Available from: https://pubmed.ncbi.nlm.nih.gov/30912848/ DOI: 0.1111/eci.13090

8.   Kiadaliri AA, Englund M. Temporal trends and regional disparity in rheumatoid arthritis and gout hospitalizations in Sweden, 1998–2015. Clin Rheumatol [Internet]. 2018 [cited 2022 Dec 21];37(3):825–30. Available from: https://pubmed.ncbi.nlm.nih.gov/29359231/ DOI: 10.1007/s10067-018-3983-8

9.   O'Dell JR, Brophy MT, Pillinger MH, Neogi T, Palevsky PM, Wu H, et al. Comparative Effectiveness of Allopurinol and Febuxostat in Gout Management. NEJM Evid [Internet]. 2022 Feb 22 [cited 2022 Dec 27];1(3). Available from: https://evidence.nejm.org/doi/10.1056/EVIDoa2100028 DOI: 10.1056/EVIDoa2100028

10.   Harrold LR, Etzel CJ, Gibofsky A, Kremer JM, Pillinger MH, Saag KG, et al. Sex differences in gout characteristics: Tailoring care for women and men. BMC Musculoskelet Disord [Internet]. 2017 [cited 2022 Jul 11];18(1):1–6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5351188/ DOI: 10.1186/s12891-017-1465-9

11. Teng GG, Ang LW, Saag KG, Yu MC, Yuan JM, Koh WP. Mortality due to coronary heart disease and kidney disease among middle-aged and elderly men and women with gout in the Singapore Chinese Health Study. Ann Rheum Dis [Internet]. 2012 Jun [cited 2022 Sep 17];71(6):924–8. Available from: https://pubmed.ncbi.nlm.nih.gov/22172492/ DOI: 10.1136/ard.2011.200523

12. Benavent D, Peiteado D, Martinez-Huedo MÁ, Hernandez-Hurtado M, Balsa A, de Miguel E. Healthcare-related impact of gout in hospitalized patients in Spain. Sci Rep [Internet]. 2021 Dec 1 [cited 2022 Sep 25];11(1). Available from: https://pubmed.ncbi.nlm.nih.gov/34168227/ DOI: 10.1038/s41598-021-92673-3

13. Andrés M, Rodríguez-Sosa E, De-Miguel E, Borrás, F. Decision Tree Algorithm - Sex and Comorbidities in gout. Mendeley Data V1 [Internet]. 2023 Jan 23 [cited 2023 Jan 25]. Available from: https://data.mendeley.com/datasets/j4vf42jhkw DOI: 10.17632/j4vf42jhkw.1

14. Merriman TR. An update on the genetic architecture of hyperuricemia and gout. Arthritis Res Ther [Internet]. 2015 Apr 10 [cited 2023 Jan 25];17(1). Available from: /pmc/articles/PMC4392805/ DOI: 10.1186/s13075-015-0609-2

15. Hak AE, Curhan GC, Grodstein F, Choi HK. Menopause, postmenopausal hormone use and risk of incident gout. Ann Rheum Dis [Internet]. 2010 Jul 1 [cited 2022 Nov 09];69(7):1305–9. Available from: https://ard.bmj.com/lookup/doi/10.1136/ard.2009.109884 DOI: 10.1136/ard.2009.109884

16.   De Vera MA, Rahman MM, Bhole V, Kopec JA, Choi HK. The Independent Impact of Gout on the Risk of Acute Myocardial Infarction Among Elderly Women: A Population-Based Study. Ann Rheum Dis [Internet]. 2010 Jun [cited 2022 Sep 17];69(6):1162. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3142935/ DOI: 10.1136/ard.2009.122770

17.   Zhu Y, Pandya BJ, Choi HK. Comorbidities of Gout and Hyperuricemia in the US General Population: NHANES 2007-2008. Am J Med [Internet]. 2012 Jul [cited 2022 Nov 13];125(7):679-687.e1. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0002934312001891 DOI: 10.1016/j.amjmed.2011.09.033

18.   Andrés M, Bernal JA, Sivera F, Quilis N, Carmona L, Vela P, et al. Cardiovascular risk of patients with gout seen at rheumatology clinics following a structured assessment. Ann Rheum Dis [Internet]. 2017 Jul 1 [cited 2023 Jan 26];76(7):1263–8. Available from: https://ard.bmj.com/content/76/7/1263 DOI: 10.1136/annrheumdis-2016-210357

19.   Singh JA. Veterans Affairs databases are accurate for gout-related health care utilization: a validation study. Arthritis Res Ther [Internet]. 2013 Dec 31 [cited 2023 Jan 04];15(6):R224. Available from: https://pubmed.ncbi.nlm.nih.gov/24377421/ DOI: 10.1186/ar4425

20.   Calabuig I, Gómez-Garberí M, Andrés M. Gout Is Prevalent but Under-Registered Among Patients With Cardiovascular Events: A Field Study. Front Med [Internet]. 2020 Sep 29 [cited 2022 Dec 09];7:560. Available from: https://pubmed.ncbi.nlm.nih.gov/33117824/ DOI: 10.3389/fmed.2020.00560

9.1   MULTIPLE LOGISTIC REGRESSION WITH GOUT AS PRIMARY AND SECONDARY DIAGNOSIS
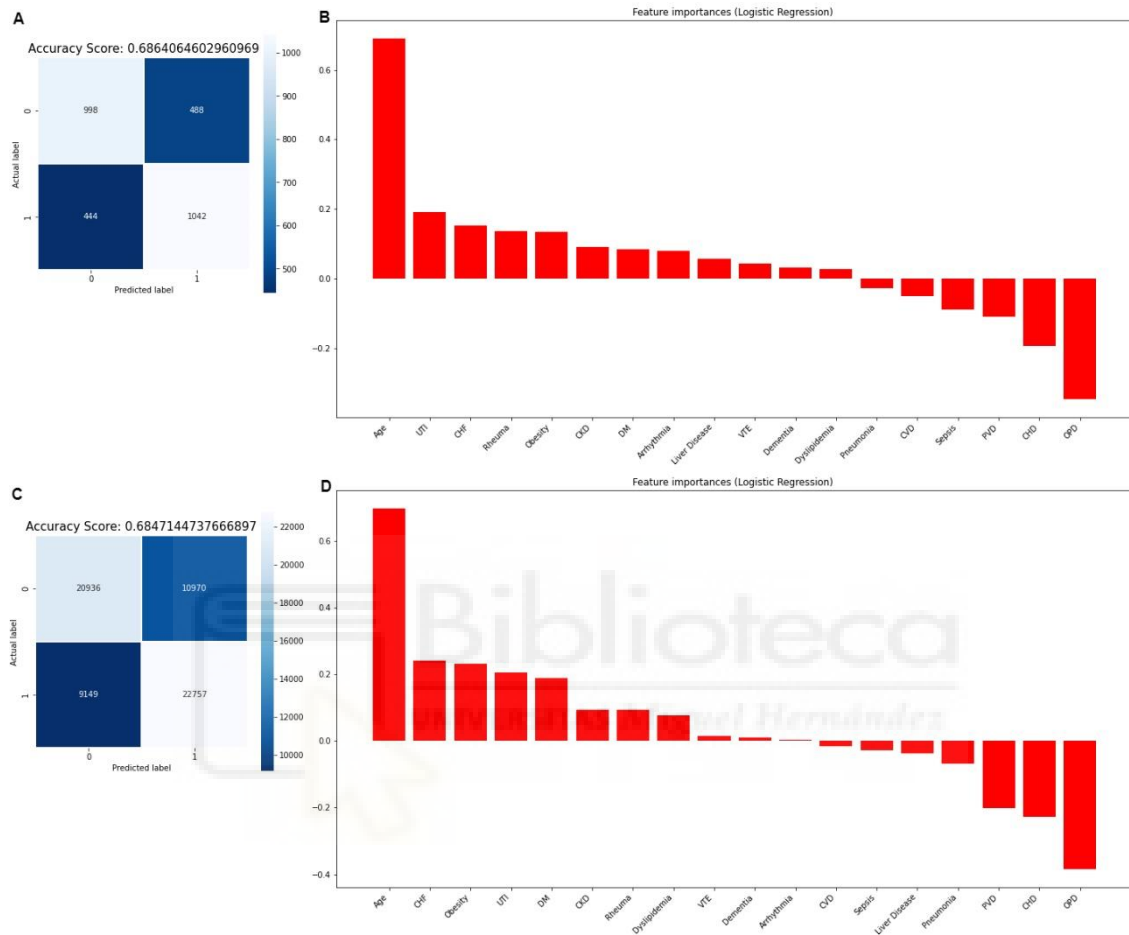

Figure S1. Logistic regression for gout as primary and secondary diagnosis. A-B) Accuracy of logistic regression of population with gout as main diagnosis and coefficients of each comorbidity C-D) Accuracy of logistic regression of population with gout as secondary diagnosis and coefficients for each comorbidity.

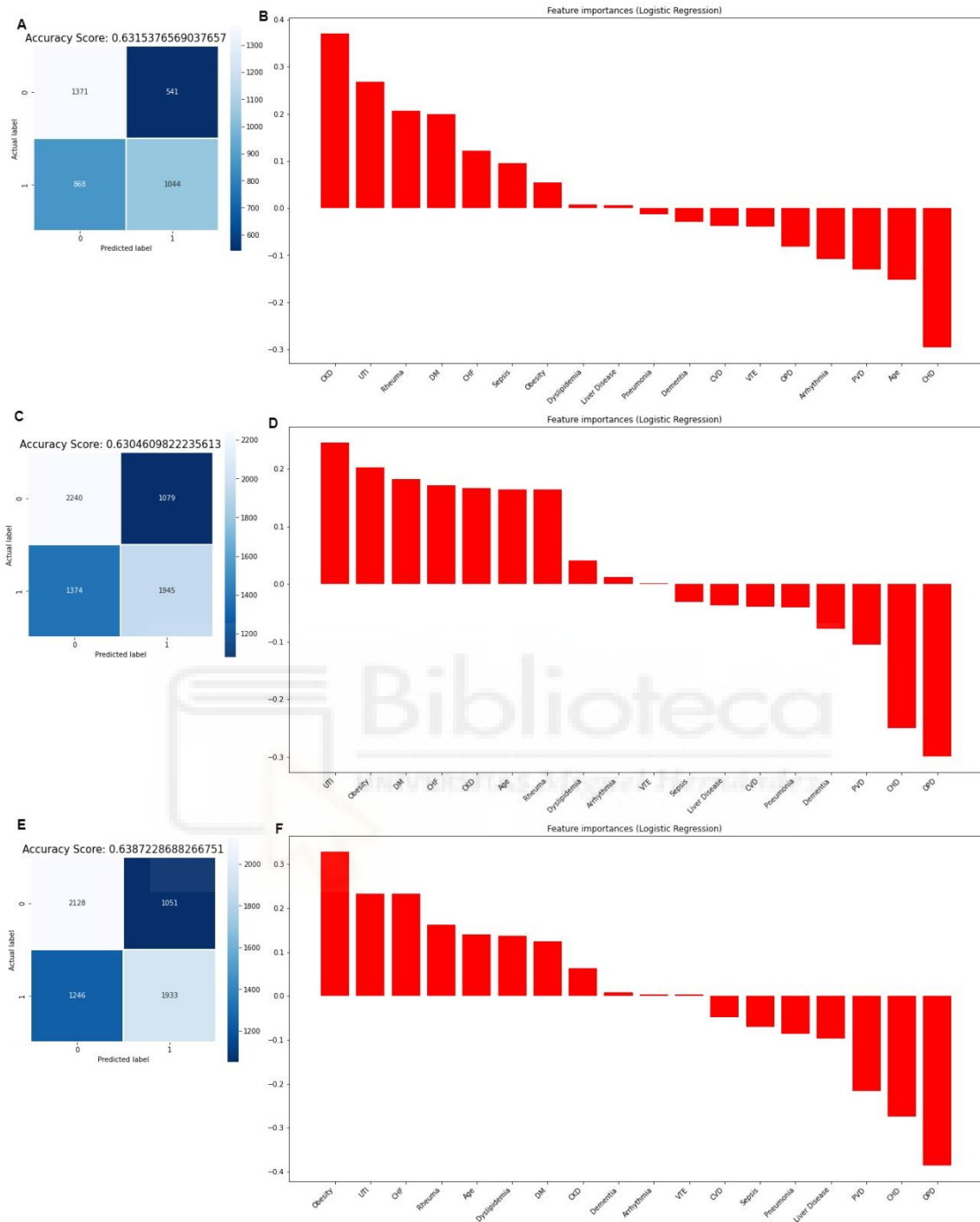## 9.2 MULTIPLE LOGISTIC REGRESSION STRATIFIED BY SEXTETS OF AGE

Figure S2. Logistic regression stratified by age. A-B) Accuracy of logistic regression of population ≤70 years and coefficients of each comorbidity C-D) Accuracy of logistic regression of population of 71-80 years and coefficients for each comorbidity E-F) Accuracy of logistic regression of population of 81-85 years and coefficients for each comorbidity.
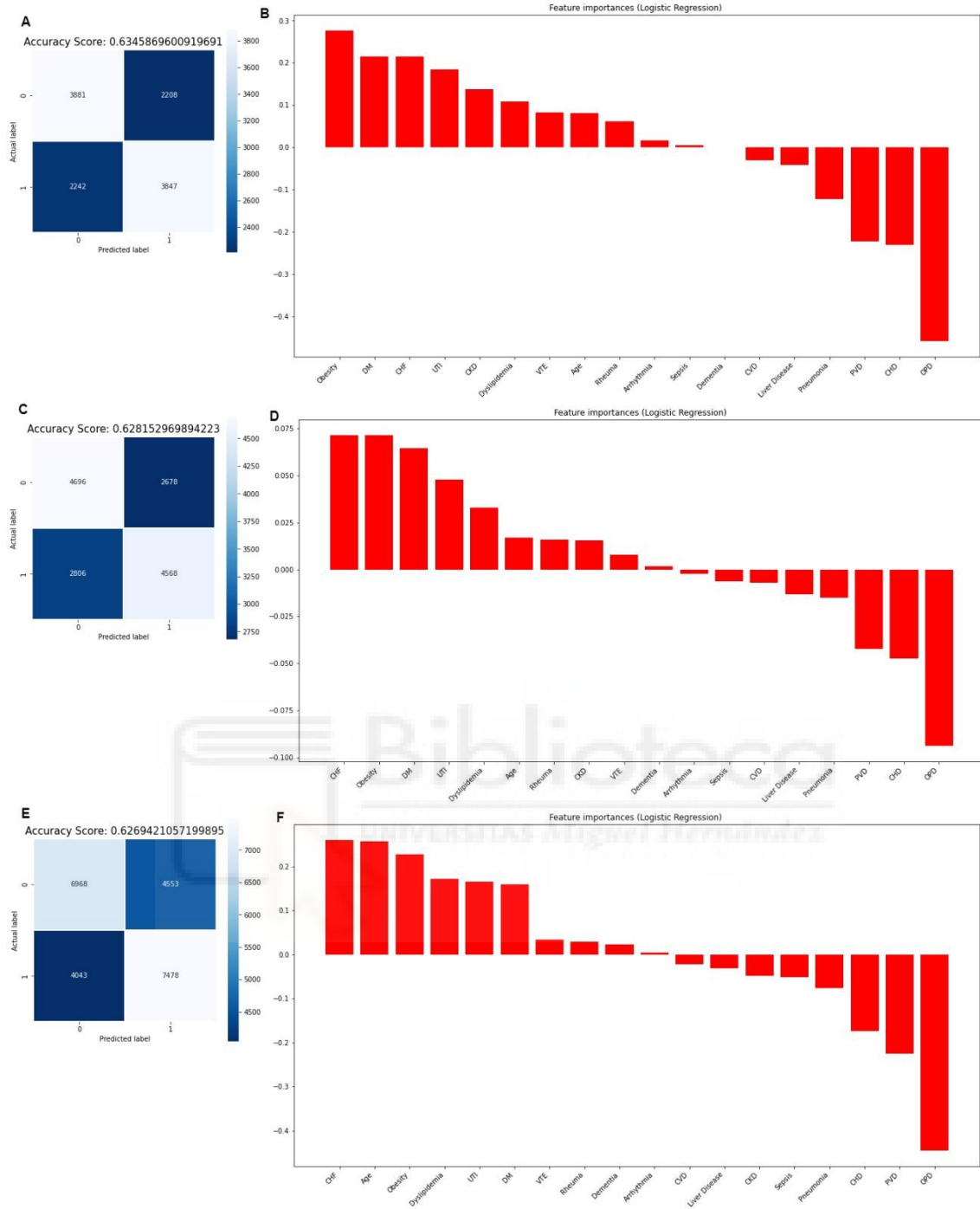
Figure S3. Logistic regression stratified by age. A-B) Accuracy of logistic regression of population 86-90 years and coefficients of each comorbidity C-D) Accuracy of logistic regression of population of 91-95 years and coefficients for each comorbidity E-F) Accuracy of logistic regression of population of >95 years and coefficients for each comorbidity.

9.3 APPROVAL FROM ETHICS COMMITTEE OF DR. BALMIS GENERAL UNIVERSITY HOSPITAL OF ALICANTE

GENERALITAT VALENCIANA
CONSELLERIA DE SANITAT

ALACANT HOSPITAL GENERAL
DEPARTAMENT DE SALUT

COMITÉ DE ÉTICA PARA LA INVESTIGACIÓN CON MEDICAMENTOS DEL DEPARTAMENTO DE SALUD DE ALICANTE - HOSPITAL GENERAL
C/. Pintor Baeza, 12 – 03010 Alicante
http://www.dep19.san.gva.es
Teléfono: 965-913-921
Correo electrónico: ceim_hgua@gva.es

Ref. CEIm: PI2022-113 - Ref. ISABIAL: 2022-0388

INFORME DEL COMITE DE ETICA PARA LA INVESTIGACION CON MEDICAMENTOS

Reunidos los miembros del Comité de Ética para la Investigación con medicamentos del Departamento de Salud de Alicante – Hospital General, en su sesión del día 28 de septiembre de 2022 (Acta 2022-08), y una vez estudiada la documentación presentada por **D. Mariano Andrés Collado** del Servicio de Reumatología del Hospital General Universitario Dr. Balmis, tiene bien a informar que el proyecto de investigación titulado **"Conociendo mejor la gota en la mujer: análisis de comorbilidades a través de las altas hospitalarias españolas (2005-2015)"**, se ajusta a las normas deontológicas establecidas para tales casos. Se informa a su vez de que este estudio ha solicitado la exención del Consentimiento Informado.

Y para que conste a los efectos oportunos, firmo la presente en Alicante con fecha 29 de septiembre de 2022.

Firmado por Luis Manuel Hernandez Blasco - 21424371D el 05/10/2022 09:20:04
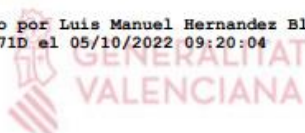
Fdo. Dr. Luis Manuel Hernández Blasco
Secretario Técnico CEIm Departamento de Salud de Alicante – Hospital General

9.4 APPROVAL FROM RESPONSIBLE INVESTIGATION OFFICE

INFORME DE EVALUACIÓN DE INVESTIGACIÓN RESPONSABLE DE 1. TFG (Trabajo Fin de Grado)

Elche, a 05 de octubre del 2022

Nombre del tutor/a	MARIANO-NICOLÁS ANDRÉS COLLADO
Nombre del alumno/a	ENRIQUE RODRÍGUEZ SOSA
Tipo de actividad	Adherido a proyecto
Título del 1. TFG (Trabajo Fin de Grado)	Conociendo mejor la gota en la mujer: análisis de comorbilidades a través de las altas hospitalarias españolas (2005-2015).
Código/s GIS estancias	
Evaluación Riesgos Laborales	No procede
Evaluación Ética	No procede
Registro provisional	221005113829
Código de Investigación Responsable	**TFG.GME.MAC.ERS.221005**
Caducidad	2 años

Se considera que el presente proyecto carece de riesgos laborales significativos para las personas que participan en el mismo, ya sean de la UMH o de otras organizaciones.

La necesidad de evaluación ética del trabajo titulado: **Conociendo mejor la gota en la mujer: análisis de comorbilidades a través de las altas hospitalarias españolas (2005-2015).** ha sido realizada de manera automática en base a la información aportada en el formulario online: "TFG/TFM: Solicitud Código de Investigación Responsable (COIR)", habiéndose determinado que no requiere someterse a dicha evaluación. Dicha información se adjunta en el presente informe. Es importante destacar que si la información aportada en dicho formulario no es correcta este informe no tiene validez.

Por todo lo anterior, **se autoriza** la realización de la presente actividad.

Atentamente,

Alberto Pastor Campos
Secretario del CEII
Vicerrectorado de Investigación

Domingo L. Orozco Beltrán
Presidente del CEII
Vicerrectorado de Investigación

Información adicional:

- En caso de que la presente actividad se desarrolle total o parcialmente en otras instituciones es responsabilidad del investigador principal solicitar cuantas autorizaciones sean pertinentes, de manera que se garantice, al menos, que los responsables de las mismas están informados.
- Le recordamos que durante la realización de este trabajo debe cumplir con las exigencias en materia de prevención de riesgos laborales. En concreto: las recogidas en el plan de prevención de la UMH y en las planificaciones preventivas de las unidades en las que se integra la investigación. Igualmente, debe promover la realización de reconocimientos médicos periódicos entre su personal; cumplir con los procedimientos sobre coordinación de actividades empresariales en el caso de que trabaje en el centro de trabajo de otra empresa o que personal de otra empresa se desplace a las instalaciones de la UMH; y atender a las obligaciones formativas del personal en materia de

Página **1** de **2**

COMITÉ DE ÉTICA E INTEGRIDAD EN LA INVESTIGACIÓN
VICERRECTORADO DE INVESTIGACIÓN
UNIVERSIDAD MIGUEL HERNÁNDEZ DE ELCHE

prevención de riesgos laborales. Le indicamos que tiene a su disposición al Servicio de Prevención de la UMH para asesorarle en esta materia.

La información descriptiva básica del presente trabajo será incorporada al repositorio público de Trabajos fin de Grado y Trabajos Fin de Máster autorizados por la Oficina de Investigación Responsable de la Universidad Miguel Hernández en el curso académico 2020/2021. También se puede acceder a través de https://oir.umh.es/tfg-tfm/

9.5 ICD-9 CODES OF COMORBIDITIES INCLUDED

- 274 Gout:

  - 274.0   Gouty arthropathy

    - 274.00 Gouty arthropathy, unspecified

    - 274.01 Acute gouty arthropathy

    - 274.02 Chronic gouty arthropathy without mention of tophus (tophi)

    - 274.03 Chronic gouty arthropathy with tophus (tophi)

  - 274.1   Gouty nephropathy

    - 274.10 Gouty nephropathy, unspecified

    - 274.11 Uric acid nephrolithiasis

    - 274.19 Other

  - 274.8   Gout with other specified manifestations

    - 274.81 Gouty tophi of ear

    - 274.82 Gouty tophi of other sites

    - 274.89 Other

  - 274.9   Gout, unspecified

- 250 Diabetes mellitus

  - 250.0   Diabetes mellitus without mention of complication

    - 250.00 Type II or unspecified type, not stated as uncontrolled

    - 250.01 Type I [juvenile type], not stated as uncontrolled

    - 250.02 Type II or unspecified type, uncontrolled

    - 250.03 Type I [juvenile type], uncontrolled

  - 250.1   Diabetes with ketoacidosis

    - 250.10 Type II or unspecified type, not stated as uncontrolled

    - 250.11 Type I [juvenile type], not stated as uncontrolled

    - 250.12 Type II or unspecified type, uncontrolled

    - 250.13 Type I [juvenile type], uncontrolled

  - 250.2   Diabetes with hyperosmolarity

- 250.20 Type II or unspecified type, not stated as uncontrolled

- 250.21 Type I [juvenile type], not stated as uncontrolled

- 250.22 Type II or unspecified type, uncontrolled

- 250.23 Type I [juvenile type], uncontrolled

- 250.3 Diabetes with other coma

  - 250.30 Type II or unspecified type, not stated as uncontrolled

  - 250.31 Type I [juvenile type], not stated as uncontrolled

  - 250.32 Type II or unspecified type, uncontrolled

  - 250.33 Type I [juvenile type], uncontrolled

- 250.4 Diabetes with renal manifestations

  - 250.40 Type II or unspecified type, not stated as uncontrolled

  - 250.41 Type I [juvenile type], not stated as uncontrolled

  - 250.42 Type II or unspecified type, uncontrolled

  - 250.43 Type I [juvenile type], uncontrolled

- 250.5 Diabetes with ophthalmic manifestations

  - 250.50 Type II or unspecified type, not stated as uncontrolled

  - 250.51 Type I [juvenile type], not stated as uncontrolled

  - 250.52 Type II or unspecified type, uncontrolled

  - 250.53 Type I [juvenile type], uncontrolled

- 250.6 Diabetes with neurological manifestations

  - 250.60 Type II or unspecified type, not stated as uncontrolled

  - 250.61 Type I [juvenile type], not stated as uncontrolled

  - 250.62 Type II or unspecified type, uncontrolled

  - 250.63 Type I [juvenile type], uncontrolled

- 250.7 Diabetes with peripheral circulatory disorders

  - 250.70 Type II or unspecified type, not stated as uncontrolled

  - 250.71 Type I [juvenile type], not stated as uncontrolled

  - 250.72 Type II or unspecified type, uncontrolled

  - 250.73 Type I [juvenile type], uncontrolled

- 250.8 Diabetes with other specified manifestations

- 250.80 Type II or unspecified type, not stated as uncontrolled

- 250.81 Type I [juvenile type], not stated as uncontrolled

- 250.82 Type II or unspecified type, uncontrolled

- 250.83 Type I [juvenile type], uncontrolled

  o 250.9 Diabetes with unspecified complication

- 250.90 Type II or unspecified type, not stated as uncontrolled

- 250.91 Type I [juvenile type], not stated as uncontrolled

- 250.92 Type II or unspecified type, uncontrolled

- 250.93 Type I [juvenile type], uncontrolled

- 272 Dyslipidemia:

  o 272.0 Pure hypercholesterolemia

  o 272.1 Pure hyperglyceridemia

  o 272.2 Mixed hyperlipidemia

  o 272.3 Hyperchylomicronemia

  o 272.4 Other and unspecified hyperlipidemia

  o 272.9 Unspecified disorder of lipoid metabolism

- 278 Obesity:

  o 278.0 Overweight and obesity

- 278.00 Obesity, unspecified

- 278.01 Morbid obesity

- 278.02 Overweight

- 278.03 Obesity hypoventilation syndrome

  o 278.1 Localized adiposity

  o 278.8 Other hyperalimentation

- Dementia

  o 290 Dementias

- 290.0 Senile dementia, uncomplicated

- 290.1 Presenile dementia

  - 290.10 Presenile dementia, uncomplicated

- 290.11 Presenile dementia with delirium

- 290.12 Presenile dementia with delusional features

- 290.13 Presenile dementia with depressive features

- 290.2 Senile dementia with delusional or depressive features

  - 290.20 Senile dementia with delusional features

  - 290.21 Senile dementia with depressive features

- 290.3 Senile dementia with delirium

- 290.4 Vascular dementia

  - 290.40 Vascular dementia, uncomplicated

  - 290.41 Vascular dementia with delirium

  - 290.42 Vascular dementia with delusions

  - 290.43 Vascular dementia with depressed mood

- 290.8 Other specified senile psychotic conditions

- 290.9 Unspecified senile psychotic condition

o 294 Persistent mental disorders due to conditions classified elsewhere

- 294.0 Amnestic disorder in conditions classified elsewhere

- 294.1 Dementia in conditions classified elsewhere

  - 294.10 Dementia in conditions classified elsewhere without behavioral disturbance

  - 294.11 Dementia in conditions classified elsewhere with behavioral disturbance

- 294.2 Dementia, unspecified

  - 294.20 Dementia, unspecified, without behavioral disturbance

  - 294.21 Dementia, unspecified, with behavioral disturbance

- 294.8 Other persistent mental disorders due to conditions classified elsewhere

- 294.9 Unspecified persistent mental disorders due to conditions classified elsewhere

- Hypertension:

  o 401 Essential hypertension

  - 401.0 Malignant

  - 401.1 Benign

- 401.9 Unspecified

o 402 Hypertensive heart disease

- 402.0 Malignant

    - 402.00 Without heart failure

    - 402.01 With heart failure

- 402.1 Benign

    - 402.10 Without heart failure

    - 402.11 With heart failure

- 402.9 Unspecified

    - 402.90 Without heart failure

    - 402.91 With heart failure

o 403 Hypertensive chronic kidney disease

- 403.0 Malignant

    - 403.00 With chronic kidney disease stage I through stage IV, or unspecified

    - 403.01 With chronic kidney disease stage V or end stage renal disease

- 403.1 Benign

    - 403.10 With chronic kidney disease stage I through stage IV, or unspecified

    - 403.11 With chronic kidney disease stage V or end stage renal disease

- 403.9 Unspecified

    - 403.90 With chronic kidney disease stage I through stage IV, or unspecified

    - 403.91 With chronic kidney disease stage V or end stage renal disease

o 404 Hypertensive heart and chronic kidney disease

- 404.0 Malignant

    - 404.00 Without heart failure and with chronic kidney disease stage I through stage IV, or unspecified

    - 404.01 With heart failure and with chronic kidney disease stage I through stage IV, or unspecified

    - 404.02 Without heart failure and with chronic kidney disease stage V or end stage renal disease

    - 404.03 With heart failure and chronic kidney disease stage V or end stage renal disease

- 404.1 Benign

  - 404.10 Without heart failure and with chronic kidney disease stage I through stage IV, or unspecified

  - 404.11 With heart failure and with chronic kidney disease stage I through stage IV, or unspecified

  - 404.12 Without heart failure and with chronic kidney disease stage V or end stage renal disease

  - 404.13 With heart failure and chronic kidney disease stage V or end stage renal disease

- 404.9 Unspecified

  - 404.90 Without heart failure and with chronic kidney disease stage I through stage IV, or unspecified

  - 404.91 With heart failure and with chronic kidney disease stage I through stage IV, or unspecified

  - 404.92 Without heart failure and with chronic kidney disease stage V or end stage renal disease

  - 404.93 With heart failure and chronic kidney disease stage V or end stage renal disease

- 405 Secondary hypertension

  - 405.0 Malignant

    - 405.01 Renovascular

    - 405.09 Other

  - 405.1 Benign

    - 405.11 Renovascular

    - 405.19 Other

  - 405.9 Unspecified

    - 405.91 Renovascular

    - 405.99 Other

- Coronary heart disease

  - 410 Acute myocardial infarction

    - 410.0 Of anterolateral wall

      - 410.00 Episode of care unspecified

      - 410.01 Initial episode of care

- 410.02 Subsequent episode of care

- 410.1 Of other anterior wall

  - 410.10 Episode of care unspecified

  - 410.11 Initial episode of care

  - 410.12 Subsequent episode of care

- 410.2 Of inferolateral wall

  - 410.20 Episode of care unspecified

  - 410.21 Initial episode of care

  - 410.22 Subsequent episode of care

- 410.3 Of inferoposterior wall

  - 410.30 Episode of care unspecified

  - 410.31 Initial episode of care

  - 410.32 Subsequent episode of care

- 410.4 Of other inferior wall

  - 410.40 Episode of care unspecified

  - 410.41 Initial episode of care

  - 410.42 Subsequent episode of care

- 410.5 Of other lateral wall

  - 410.50 Episode of care unspecified

  - 410.51 Initial episode of care

  - 410.52 Subsequent episode of care

- 410.6 True posterior wall infarction

  - 410.60 Episode of care unspecified

  - 410.61 Initial episode of care

  - 410.62 Subsequent episode of care

- 410.7 Subendocardial infarction

  - 410.70 Episode of care unspecified

  - 410.71 Initial episode of care

  - 410.72 Subsequent episode of care

- 410.8 Of other specified sites
  - 410.80 Episode of care unspecified
  - 410.81 Initial episode of care
  - 410.82 Subsequent episode of care
- 410.9 Unspecified site
  - 410.90 Episode of care unspecified
  - 410.91 Initial episode of care
  - 410.92 Subsequent episode of care

- 411 Other acute and subacute forms of ischemic heart disease
  - 411.0 Postmyocardial infarction syndrome
  - 411.1 Intermediate coronary syndrome
  - 411.8 Other
    - 411.81 Acute coronary occlusion without myocardial infarction
    - 411.89 Other

- 412 Old myocardial infarction

- 413 Angina pectoris
  - 413.0 Angina decubitus
  - 413.1 Prinzmetal angina
  - 413.9 Other and unspecified angina pectoris

- 414 Other forms of chronic ischemic heart disease
  - 414.0 Coronary atherosclerosis
    - 414.00 Of unspecified type of vessel, native or graft
    - 414.01 Of native coronary artery
    - 414.02 Of autologous biological bypass graft
    - 414.03 Of nonautologous biological bypass graft
    - 414.04 Of artery bypass graft
    - 414.05 Of unspecified type of bypass graft
    - 414.06 Of native coronary artery of transplanted heart
    - 414.07 Of bypass graft (artery) (vein) of transplanted heart

- 414.1 Aneurysm and dissection of heart

  - 414.10 Aneurysm of heart (wall)

  - 414.11 Aneurysm of coronary vessels

  - 414.12 Dissection of coronary artery

  - 414.19 Other aneurysm of heart

- 414.2 Chronic total occlusion of coronary artery

- 414.3 Coronary atherosclerosis due to lipid rich plaque

- 414.4 Coronary atherosclerosis due to calcified coronary lesion

- 414.8 Other specified forms of chronic ischemic heart disease

- 414.9 Chronic ischemic heart disease, unspecified

- 427 Arrhythmia:

  - 427.0 Paroxysmal supraventricular tachycardia

  - 427.1 Paroxysmal ventricular tachycardia

  - 427.2 Paroxysmal tachycardia, unspecified

  - 427.3 Atrial fibrillation and flutter

    - 427.31 Atrial fibrillation

    - 427.32 Atrial flutter

  - 427.4 Ventricular fibrillation and flutter

    - 427.41 Ventricular fibrillation

    - 427.42 Ventricular flutter

  - 427.5 Cardiac arrest

  - 427.6 Premature beats

    - 427.60 Premature beats, unspecified

    - 427.61 Supraventricular premature beats

    - 427.69 Other

  - 427.8 Other specified cardiac dysrhythmias

    - 427.81 Sinoatrial node dysfunction

    - 427.89 Other

  - 427.9 Cardiac dysrhythmia, unspecified

- 428 Heart failure

- 428.0   Congestive heart failure, unspecified

- 428.1   Left heart failure

- 428.2   Systolic heart failure

  - 428.20 Unspecified

  - 428.21 Acute

  - 428.22 Chronic

  - 428.23 Acute on chronic

- 428.3   Diastolic heart failure

  - 428.30 Unspecified

  - 428.31 Acute

  - 428.32 Chronic

  - 428.33 Acute on chronic

- 428.4   Combined systolic and diastolic heart failure

  - 428.40 Unspecified

  - 428.41 Acute

  - 428.42 Chronic

  - 428.43 Acute on chronic

- 428.9   Heart failure, unspecified

- Cerebrovascular disease:

  - 430 Subarachnoid hemorrhage

  - 431 Intracerebral hemorrhage

  - 432 Other and unspecified intracranial hemorrhage

    - 432.0 Nontraumatic extradural hemorrhage

    - 432.1 Subdural hemorrhage

    - 432.9 Unspecified intracranial hemorrhage

  - 433 Occlusion and stenosis of precerebral arteries

    - 433.0 Basilar artery

      - 433.00 Without mention of cerebral infarction

      - 433.01 With cerebral infarction

    - 433.1 Carotid artery

- 433.10 Without mention of cerebral infarction

- 433.11 With cerebral infarction

- 433.2 Vertebral artery

  - 433.20 Without mention of cerebral infarction

  - 433.21 With cerebral infarction

- 433.3 Multiple and bilateral

  - 433.30 Without mention of cerebral infarction

  - 433.31 With cerebral infarction

- 433.8 Other specified precerebral artery

  - 433.80 Without mention of cerebral infarction

  - 433.81 With cerebral infarction

- 433.9 Unspecified precerebral artery

  - 433.90 Without mention of cerebral infarction

  - 433.91 With cerebral infarction

- 434 Occlusion of cerebral arteries

  - 434.0 Cerebral thrombosis

    - 434.00 Without mention of cerebral infarction

    - 434.01 With cerebral infarction

  - 434.1 Cerebral embolism

    - 434.10 Without mention of cerebral infarction

    - 434.11 With cerebral infarction

  - 434.9 Cerebral artery occlusion, unspecified

    - 434.90 Without mention of cerebral infarction

    - 434.91 With cerebral infarction

- 435 Transient cerebral ischemia

  - 435.0 Basilar artery syndrome

  - 435.1 Vertebral artery syndrome

  - 435.2 Subclavian steal syndrome

  - 435.3 Vertebrobasilar artery syndrome

- 435.8 Other specified transient cerebral ischemias

- 435.9 Unspecified transient cerebral ischemia

o 436 Acute, but ill-defined, cerebrovascular disease

o 437 Other and ill-defined cerebrovascular disease

- 437.0 Cerebral atherosclerosis

- 437.1 Other generalized ischemic cerebrovascular disease

- 437.2 Hypertensive encephalopathy

- 437.3 Cerebral aneurysm, nonruptured

- 437.4 Cerebral arteritis

- 437.5 Moyamoya disease

- 437.6 Nonpyogenic thrombosis of intracranial venous sinus

- 437.7 Transient global amnesia

- 437.8 Other

- 437.9 Unspecified

o 438 Late effects of cerebrovascular disease

- 438.0 Cognitive deficits

- 438.1 Speech and language deficits

  - 438.10 Speech and language deficit, unspecified

  - 438.11 Aphasia

  - 438.12 Dysphasia

  - 438.13 Dysarthria

  - 438.14 Fluency disorder

  - 438.19 Other speech and language deficits

- 438.2 Hemiplegia/hemiparesis

  - 438.20 Hemiplegia affecting unspecified side

  - 438.21 Hemiplegia affecting dominant side

  - 438.22 Hemiplegia affecting nondominant side

- 438.3 Monoplegia of upper limb

  - 438.30 Monoplegia of upper limb affecting unspecified side

- 438.31 Monoplegia of upper limb affecting dominant side

- 438.32 Monoplegia of upper limb affecting nondominant side

  - 438.4 Monoplegia of lower limb

    - 438.40 Monoplegia of lower limb affecting unspecified side

    - 438.41 Monoplegia of lower limb affecting dominant side

    - 438.42 Monoplegia of lower limb affecting nondominant side

  - 438.5 Other paralytic syndrome

    - 438.50 Other paralytic syndrome affecting unspecified side

    - 438.51 Other paralytic syndrome affecting dominant side

    - 438.52 Other paralytic syndrome affecting nondominant side

    - 438.53 Other paralytic syndrome, bilateral

  - 438.6 Alterations of sensations

  - 438.7 Disturbances of vision

  - 438.8 Other late effects of cerebrovascular disease

    - 438.81 Apraxia

    - 438.82 Dysphagia

    - 438.83 Facial weakness

    - 438.84 Ataxia

    - 438.85 Vertigo

    - 438.89 Other late effects of cerebrovascular disease

  - 438.9 Unspecified late effects of cerebrovascular disease

- 443 Peripheral vascular disease

  - 443.0 Raynaud's syndrome

  - 443.1 Thromboangiitis obliterans [Buerger's disease]

  - 443.2 Other arterial dissection

    - 443.21 Dissection of carotid artery

    - 443.22 Dissection of iliac artery

    - 443.23 Dissection of renal artery

    - 443.24 Dissection of vertebral artery

- 443.29 Dissection of other artery

o 443.8 Other specified peripheral vascular diseases

- 443.81 Peripheral angiopathy in diseases classified elsewhere

- 443.82 Erythromelalgia

- 443.89 Other

o 443.9 Peripheral vascular disease, unspecified

- Venous thromboembolism:

o 415 Acute pulmonary heart disease

- 415.1 Pulmonary embolism and infarction

- 415.11 Iatrogenic pulmonary embolism and infarction

- 415.13 Saddle embolus of pulmonary artery

- 415.19 Other

o 416 Chronic pulmonary heart disease

- 416.2 Chronic pulmonary embolism

o 451 Phlebitis and thrombophlebitis

- 451.0 Of superficial vessels of lower extremities

- 451.1 Of deep vessels of lower extremities

- 451.11 Femoral vein (deep) (superficial)

- 451.19 Other

- 451.2 Of lower extremities, unspecified

- 451.8 Of other sites

- 451.81 Iliac vein

- 451.82 Of superficial veins of upper extremities

- 451.83 Of deep veins of upper extremities

- 451.84 Of upper extremities, unspecified

- 451.89 Other

- 451.9 Of unspecified site

o 452 Portal vein thrombosis

o 453 Other venous embolism and thrombosis

- 453.0 Budd-Chiari syndrome

- 453.1 Thrombophlebitis migrans

- 453.2 Of inferior vena cava

- 453.3 Of renal vein

- 453.4 Acute venous embolism and thrombosis of deep vessels of lower extremity

  - 453.40 Acute venous embolism and thrombosis of unspecified deep vessels of lower extremity

  - 453.41 Acute venous embolism and thrombosis of deep vessels of proximal lower extremity

  - 453.42 Acute venous embolism and thrombosis of deep vessels of distal lower extremity

- 453.5 Chronic venous embolism and thrombosis of deep vessels of lower extremity

  - 453.50 Chronic venous embolism and thrombosis of unspecified deep vessels of lower extremity

  - 453.51 Chronic venous embolism and thrombosis of deep vessels of proximal lower extremity

  - 453.52 Chronic venous embolism and thrombosis of deep vessels of distal lower extremity

- 453.6 Venous embolism and thrombosis of superficial vessels of lower extremity

- 453.7 Chronic venous embolism and thrombosis of other specified vessels

  - 453.71 Chronic venous embolism and thrombosis of superficial veins of upper extremity

  - 453.72 Chronic venous embolism and thrombosis of deep veins of upper extremity

  - 453.73 Chronic venous embolism and thrombosis of upper extremity, unspecified

  - 453.74 Chronic venous embolism and thrombosis of axillary veins

  - 453.75 Chronic venous embolism and thrombosis of subclavian veins

  - 453.76 Chronic venous embolism and thrombosis of internal jugular veins

  - 453.77 Chronic venous embolism and thrombosis of other thoracic veins

  - 453.79 Chronic venous embolism and thrombosis of other specified veins

- 453.8 Acute venous embolism and thrombosis of other specified veins

- 453.81 Acute venous embolism and thrombosis of superficial veins of upper extremity

- 453.82 Acute venous embolism and thrombosis of deep veins of upper extremity

- 453.83 Acute venous embolism and thrombosis of upper extremity, unspecified

- 453.84 Acute venous embolism and thrombosis of axillary veins

- 453.85 Acute venous embolism and thrombosis of subclavian veins

- 453.86 Acute venous embolism and thrombosis of internal jugular veins

- 453.87 Acute venous embolism and thrombosis of other thoracic veins

- 453.89 Acute venous embolism and thrombosis of other specified veins

- 453.9 Of unspecified site

- 459 Other disorders of circulatory system

  - 459.1 Postphlebitic syndrome

    - 459.10 Postphlebitic syndrome without complications

    - 459.11 Postphlebitic syndrome with ulcer

    - 459.12 Postphlebitic syndrome with inflammation

    - 459.13 Postphlebitic syndrome with ulcer and inflammation

    - 459.19 Postphlebitic syndrome with other complication

- Pneumonia:

  - 480 Viral pneumonia

    - 480.0 Pneumonia due to adenovirus

    - 480.1 Pneumonia due to respiratory syncytial virus

    - 480.2 Pneumonia due to parainfluenza virus

    - 480.3 Pneumonia due to SARS-associated coronavirus

    - 480.8 Pneumonia due to other virus not elsewhere classified

    - 480.9 Viral pneumonia, unspecified

  - 481 Pneumococcal pneumonia

  - 482 Other bacterial pneumonia

    - 482.0 Pneumonia due to Klebsiella pneumoniae

    - 482.1 Pneumonia due to Pseudomonas

- 482.2 Pneumonia due to Hemophilus influenzae [H. influenzae]

- 482.3 Pneumonia due to Streptococcus

  - 482.30 Streptococcus, unspecified

  - 482.31 Group A

  - 482.32 Group B

  - 482.39 Other Streptococcus

- 482.4 Pneumonia due to Staphylococcus

  - 482.40 Pneumonia due to Staphylococcus, unspecified

  - 482.41 Methicillin susceptible pneumonia due to Staphylococcus aureus

  - 482.42 Methicillin resistant pneumonia due to Staphylococcus aureus

  - 482.49 Other Staphylococcus pneumonia

- 482.8 Pneumonia due to other specified bacteria

  - 482.81 Anaerobes

  - 482.82 Escherichia coli [E. coli]

  - 482.83 Other gram-negative bacteria

  - 482.84 Legionnaires' disease

  - 482.89 Other specified bacteria

- 482.9 Bacterial pneumonia unspecified

o 483 Pneumonia due to other specified organism

- 483.0 Mycoplasma pneumoniae

- 483.1 Chlamydia

- 483.8 Other specified organism

o 484 Pneumonia in infectious diseases classified elsewhere

- 484.1 Pneumonia in cytomegalic inclusion disease

- 484.3 Pneumonia in whooping cough

- 484.5 Pneumonia in anthrax

- 484.6 Pneumonia in aspergillosis

- 484.7 Pneumonia in other systemic mycoses

- 484.8 Pneumonia in other infectious diseases classified elsewhere

- 485 Bronchopneumonia, organism unspecified

- 486 Pneumonia, organism unspecified

- Obstructive pulmonary disease:

  - 490 Bronchitis, not specified as acute or chronic

  - 491 Chronic bronchitis

    - 491.0 Simple chronic bronchitis

    - 491.1 Mucopurulent chronic bronchitis

    - 491.2 Obstructive chronic bronchitis

    - 491.20 Without exacerbation

      - 491.21 With (acute) exacerbation

      - 491.22 With acute bronchitis

    - 491.8 Other chronic bronchitis

    - 491.9 Unspecified chronic bronchitis

  - 492 Emphysema

    - 492.0 Emphysematous bleb

    - 492.8 Other emphysema

  - 493 Asthma

    - 493.0 Extrinsic asthma

      - 493.00 Unspecified

      - 493.01 With status asthmaticus

      - 493.02 With (acute) exacerbation

    - 493.1 Intrinsic asthma

      - 493.10 Unspecified

      - 493.11 With status asthmaticus

      - 493.12 With (acute) exacerbation

    - 493.2 Chronic obstructive asthma

      - 493.20 Unspecified

      - 493.21 With status asthmaticus

      - 493.22 With (acute) exacerbation

o 494 Bronchiectasis

- 494.0 Bronchiectasis without acute exacerbation

- 494.1 Bronchiectasis with acute exacerbation

o 495 Extrinsic allergic alveolitis

- 495.0 Farmers' lung

- 495.1 Bagassosis

- 495.2 Bird-fanciers' lung

- 495.3 Suberosis

- 495.4 Malt workers' lung

- 495.5 Mushroom workers' lung

- 495.6 Maple bark-strippers' lung

- 495.7 "Ventilation" pneumonitis

- 495.8 Other specified allergic alveolitis and pneumonitis

- 495.9 Unspecified allergic alveolitis and pneumonitis

o 496 Chronic airway obstruction, not elsewhere classified

- Liver disease:

o 571 Chronic liver disease and cirrhosis

- 571.0 Alcoholic fatty liver

- 571.1 Acute alcoholic hepatitis

- 571.2 Alcoholic cirrhosis of liver

- 571.3 Alcoholic liver damage, unspecified

- 571.4 Chronic hepatitis

- 571.40 Chronic hepatitis, unspecified

- 571.41 Chronic persistent hepatitis

- 571.42 Autoimmune hepatitis

- 571.49 Other

- 571.5 Cirrhosis of liver without mention of alcohol

- 571.6 Biliary cirrhosis

- 571.8 Other chronic nonalcoholic liver disease

- 571.9 Unspecified chronic liver disease without mention of alcohol

- o 572 Liver abscess and sequelae of chronic liver disease

  - 572.2 Hepatic encephalopathy

  - 572.3 Portal hypertension

  - 572.4 Hepatorenal syndrome

  - 572.8 Other sequelae of chronic liver disease

- o 573 Other disorders of liver

  - 573.0 Chronic passive congestion of liver

  - 573.5 Hepatopulmonary syndrome

  - 573.8 Other specified disorders of liver

  - 573.9 Unspecified disorder of liver

- 585 Chronic kidney disease

  - o 585.1   Chronic kidney disease, Stage I

  - o 585.2   Chronic kidney disease, Stage II (mild)

  - o 585.3   Chronic kidney disease, Stage III (moderate)

  - o 585.4   Chronic kidney disease, Stage IV (severe)

  - o 585.5   Chronic kidney disease, Stage V

  - o 585.6   End stage renal disease

  - o 585.9   Chronic kidney disease, unspecified

- Urinary tract infection:

  - o 590 Infections of kidney

    - 590.0 Chronic pyelonephritis

      - 590.00 Without lesion of renal medullary necrosis

      - 590.01 With lesion of renal medullary necrosis

    - 590.1 Acute pyelonephritis

      - 590.10 Without lesion of renal medullary necrosis

      - 590.11 With lesion of renal medullary necrosis

    - 590.2 Renal and perinephric abscess

    - 590.3 Pyeloureteritis cystica

    - 590.8 Other pyelonephritis or pyonephrosis, not specified as acute or chronic

      - 590.80 Pyelonephritis, unspecified

- •590.81 Pyelitis or pyelonephritis in diseases classified elsewhere
  - ▪ 590.9 Infection of kidney, unspecified
- o 595 Cystitis
  - ▪ 595.0 Acute cystitis
  - ▪ 595.1 Chronic interstitial cystitis
  - ▪ 595.2 Other chronic cystitis
  - ▪ 595.3 Trigonitis
  - ▪ 595.4 Cystitis in diseases classified elsewhere
  - ▪ 595.8 Other specified types of cystitis
    - •595.81 Cystitis cystica
    - •595.89 Other
  - ▪ 595.9 Cystitis, unspecified
- o 597 Urethritis, not sexually transmitted, and urethral syndrome
  - ▪ 597.0 Urethral abscess
  - ▪ 597.8 Other urethritis
  - ▪597.80 Urethritis, unspecified
    - •597.81 Urethral syndrome NOS
    - •597.89 Other
- o 599 Other disorders of urethra and urinary tract
  - ▪ 599.0 Urinary tract infection, site not specified
- • Urinary lithiasis
  - o 591 Hydronephrosis
  - o 592 Calculus of kidney and ureter
    - ▪ 592.0 Calculus of kidney
    - ▪ 592.1 Calculus of ureter
    - ▪ 592.9 Urinary calculus, unspecified
  - o 594 Calculus of lower urinary tract
    - ▪ 594.0 Calculus in diverticulum of bladder
    - ▪ 594.1 Other calculus in bladder
    - ▪ 594.2 Calculus in urethra

- 594.8 Other lower urinary tract calculus
- 594.9 Calculus of lower urinary tract, unspecified

- Rheumatological disease
  - 710 Diffuse diseases of connective tissue
    - 710.0 Systemic lupus erythematosus
    - 710.1 Systemic sclerosis
    - 710.2 Sicca syndrome
    - 710.3 Dermatomyositis
    - 710.4 Polymyositis
    - 710.5 Eosinophilia myalgia syndrome
    - 710.8 Other specified diffuse diseases of connective tissue
    - 710.9 Unspecified diffuse connective tissue disease
  - 714 Rheumatoid arthritis and other inflammatory polyarthropathies
    - 714.0 Rheumatoid arthritis
    - 714.1 Felty's syndrome
    - 714.2 Other rheumatoid arthritis with visceral or systemic involvement
    - 714.3 Juvenile chronic polyarthritis
      - 714.30 Polyarticular juvenile rheumatoid arthritis, chronic or unspecified
      - 714.31 Polyarticular juvenile rheumatoid arthritis, acute
      - 714.32 Pauciarticular juvenile rheumatoid arthritis
      - 714.33 Monoarticular juvenile rheumatoid arthritis
    - 714.4 Chronic postrheumatic arthropathy
    - 714.8 Other specified inflammatory polyarthropathies
      - 714.81 Rheumatoid lung
      - 714.89 Other
    - 714.9 Unspecified inflammatory polyarthropathy

- 995 Sepsis
  - 995.91 Sepsis
  - 995.92 Severe sepsis