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Direct and indirect burden of COVID-19 on mortality in Spain (2020 to 2022)

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Abstract

Background Life expectancy in high-income countries remained lower in 2022 compared to pre-pandemic levels in 2019. This study explores the deficit of life expectancy and excess of years of life lost (YLL) in Spain from 2020 to 2022, assessing both direct effects of infectious diseases and indirect effects of other causes of death.

Methods Data on life expectancy and YLL from 2010 to 2022 were obtained from the Spanish Institute for Statistics (INE). Using linear regression, we estimated expected life expectancy and YLL for 2020–2022 under the assumption that pre-pandemic trends (2010–2019) had continued.

Results During the first year of the pandemic, Spanish women lost 1.10 years and men lost 1.40 years in life expectancy. By 2022, life expectancy remained lower than in 2019 for both sexes. The excess YLL was similar across 2020 (2.40 million YLL and 5.3 YLL/100 people), 2021 (2.35 million YLL, 5.1 YLL/100 people), and 2022 (2.35 million YLL, 5.0 YLL/100 people). Approximately 70% of this excess was attributable to infectious diseases (87% in 2020, 78% in 2021, and 43% in 2022). Other major contributors to excess YLL included external causes, circulatory diseases, digestive diseases, and endocrine, nutritional, and metabolic diseases, while cancer mortality did not show an excess during the pandemic period.

Conclusions Mortality in Spain in 2022 remained elevated compared to pre-pandemic expectations. The contribution of non-infectious diseases to excess mortality increased over time.

Trial registration Not applicable.

Keywords Life expectancy, Years of life lost, COVID-19, Excess mortality, Pandemic mortality chronic diseases, Infectious diseases, Non-infectious diseases

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Introduction

COVID-19 pandemic led to strong increases in mortality and decreases in life expectancy in most countries in 2020 [1–4]. The World Health Organization (WHO) estimated the global excess deaths in 2020–2021 at 14.83 million deaths, 3.18 million of which were in the European region [5]. Other studies have reported even higher figures [3, 4]. Data recently reported by Eurostat indicate that European Union countries had not fully recovered their pre-pandemic life expectancy by 2022 [6].

Excess mortality in the pandemic cannot be restricted to deaths registered as due to COVID-19. The ratio between total excess deaths and reported COVID-19 deaths ranged between 1.08 in high-income countries and 16.64 in low-income countries [5]. This is due to two reasons: firstly, deaths directly caused by COVID-19 were strongly under-reported. Secondly, deaths indirectly caused -or influenced by- COVID-19 as the pandemic disrupted normal society functioning, including that of health services. In this way, concerns were raised on whether the pandemic could deteriorate the care for chronic diseases [7, 8] as well as cancer screening programs [9, 10], eventually leading to further increases in mortality due to cardiovascular diseases, cancer, or other chronic conditions [9, 11–13]. Moreover, as compulsory measures -such as lockdown, stay-at-home orders, or prohibition of social events- were enforced, the issue of mental health deterioration was discussed both in specialised journals [14, 15] and mass media [16–19].

Data are still sparse when it comes to excess deaths due to causes other than COVID-19. A recent study of cause-specific excess of death in 30 countries in 2020 reported 7.3% excess deaths from ischemic heart diseases, although with high inter-country variability ranging – 11.7% in Estonia to 38.8% in Mexico. Similar heterogeneity was reported regarding mortality by cerebrovascular diseases and diabetes [20].

Spain was among the European countries more affected by the pandemic, with about 160,000 excess deaths in 2020–2021 [3, 4] and ratio between excess mortality rate and reported COVID-19 mortality rate about 1.62 [3, 4], meaning that 38% of excess deaths in the two first years of the pandemic were not registered as COVID-19.

As official data regarding mortality in 2022 have recently been published, in this paper, we describe the impact of COVID-19 pandemic on life expectancy at birth (LE) in Spain, from 2020 to 2022; we estimate the direct effect in term of the number of YLL due to infectious diseases and the indirect effect as the number of years of life lost due to other diseases.

Methods

Setting and main government measures against COVID-19 pandemic

Spain had 47.3 million inhabitants (51% women) by 1st January, 2020. It is administratively organized into 17 regions and 2 autonomous cities. Regions have executive power, including competences on public health and health care.

We hereby describe the main government measures against COVID-19 pandemic. On 14th March, 2020, the Spanish government declared the so-called State of Alarm, including a partial lockdown with severe restrictions to mobility. On 29th March, the lockdown was reinforced, halting all non-essential activities. The lockdown was eased on 12th April and the State of Alarm ended on 21st June. A second State of Alarm was decreed from 25th October, 2020 to 9th May, 2021. In this occasion, the only restrictive measure applied to all people in Spain was the prohibition of travelling between -but not within- regions, while other restrictive measures in that period were ruled by regional rather than national government, so differently applying to people according to the region they were living in.

From 14th March, 2020, use of face mask was compulsory in any public space. It was not required in open spaces from 10th February, 2022, in interior spaces from 19th April, 2022, and in public transport from 7th February, 2023.

Vaccination against COVID-19 began on 7th January, 2021. By 1st July, 2021, 60.8% people had received at least one dose and 42.7% had received the complete primary series. By 1st January, 2022, these figures were 87.2% (at least one dose) and 83.3% (complete primary series) [21].

Source of mortality data

We obtained data from the Spanish National Institute for Statistics (INE) website [22], which publishes estimates of LE as well as number and rate of YLL for the whole Spanish population and for each of the main ICD-10 groups for years 2010–2022 (Supplementary Table 1). In this regard, the "infectious diseases" group includes codes relative to COVID-19: U04.9 (severe acute respiratory syndrome [SARS], unspecified), U07.1 (COVID-19, virus confirmed), U07.2 (virus not identified) and U10.9 (multisystem inflammatory syndrome associated with COVID-19, unspecified). INE estimates YLL as the number of years lost by deaths between the first and the 80th birthday. For instance, if a person died being 55, they would account for 80–55 = 35 YLL. INE estimates rates of YLL standardized to the 2011 standard European population as published by Eurostat [23]. From here on, we denote INE estimates as "observed LE" or "observed YLL number/rate".

Estimation of expected LE and YLL

In order to estimate the expected LE if the pandemic had not occurred, we carried out linear regression models of observed LE (Y variable) on year (X variable), for years 2010–2019. Then, we used those models to extrapolate for years 2020–2022, obtaining expected LE. Finally, we consider the difference expected minus observed as the impact of COVID-19 pandemic and we construct its 95% confidence interval as the difference ± 1.96*standard error of the predictions. The same procedure was used to estimate the expected YLL for all causes and for each ICD-10 group, although excluding data from 2010, as INE changed the reference population in 2011, making YLL figures in 2010 not comparable to those in 2011–2022. Long-run trends of LE and YLL are not expected to be linear. The rational of using linear regression in our analyses is, however, based in both theoretical and practical considerations. Ten-year trends could be considered short-term. Theoretically, any smooth function can be locally approached with a linear model (for instance, first-order Taylor's series). We would consider LE and YLL trends as "smooth" in the absence of any trend disruption (e.g., a war, a pandemic). The practical consideration is the actual trends we found were about linear. For instance, LE 2010–2019 linear regression has $R^2 = 0.90$ and all-causes YLL rate linear regression has $R^2 = 0.94$.

Results are here displayed as LE in years and YLL in number of years or rate per 100,000 people. YLL results are presented by all causes of death and by each ICD-10 group. All results are displayed for both sexes together and for women and men, separately. We did not carry out any hypothesis tests, so p-values are not displayed.

All data we used are in the public domain. Therefore, we did not ask for authorization of any ethics committee.

Results

Life expectancy

LE in years 2010–2022 and estimated LE lost in years 2020–2022 appear in Table 1; Fig. 1. Before the pandemic, LE was steadily increasing in both women and men, reaching 80.78 for men and 86.19 years for women in 2019. During the first year of the pandemic, Spanish women lost 1.10 years and men lost 1.40 years in their LE. By year 2022, LE for both sexes remained not only lower than that of the last pre-pandemic year of 2019, but also lower than that of 2018. LE was 1.30, 0.70 and 0.79 years lower than expected in 2020, 2021 and 2022, respectively. Each year, LE lost was higher in men than in women, with ratio of men to women equal 1.3 in 2020, 1.8 in 2021 and 1.3 in 2022.

Rate of potential years of life lost

Figure 2 and Supplementary Table 2 present excess of age-standardized rate of YLL. Excess rate was 525, 450 and 455 per 100,000 people in 2020, 2021 and 2022, respectively. Each year, excess rate in men more than double that of in women. Excess rate due to infectious diseases (including COVID-19) accounted for 99% of total excess rate in 2020, 88% in 2021, and 55% in 2022. Apart from infectious diseases, the ICD-10 group with higher excess rates was that of external causes (16, 59 and 102 more YLL per 100,000 people in 2020–2022, respectively). Results on external causes of death were very different in men and in women: +39 YLL per 100,000 men vs. -14 YLL per 100,000 women in 2020; +97 per 100,000 men vs. +11.8 per 100,000 women in 2021; and + 152 per 100,000 men vs. +40 per 100,000 women in 2022.

Other ICD-10 groups with excess rates were circulatory system (+ 28, + 41 and + 79 YLL per 100,000 people

Table 1 Actual life expectancy, 2010–2022, and estimated life expectancy lost in the pandemic, 2020–2022

Year	Observed life expectancy	Estimated life expectancy lost*	Observed life expectancy	Estimated life expectancy lost*	Observed life expectancy	Estimated life expectancy lost*	Estimated life expectancy lost– ratio men: women
	Both sexes		**Men**		**Women**		
2010	82.07		79.05		85.03		
2011	82.25		79.30		85.13		
2012	82.26		79.36		85.10		
2013	82.77		79.92		85.53		
2014	82.91		80.10		85.63		
2015	82.67		79.89		85.39		
2016	83.08		80.26		85.82		
2017	83.05		80.32		85.71		
2018	83.15		80.40		85.83		
2019	83.53		80.78		86.19		
2020	82.28	-1.30 (-1.70, -0.93)	79.52	-1.40 (-1.80, -1.00)	85.04	-1.10 (-1.50, -0.79)	1.27
2021	83.03	-0.70 (-1.10, -0.32)	80.20	-0.88 (-1.30, -0.49)	85.81	-0.48 (-0.84, -0.11)	1.83
2022	83.08	-0.79 (-1.02, -0.39)	80.36	-0.89 (-1.30, -0.47)	85.74	-0.67 (-1.00, -0.28)	1.33

*Central estimates and 95% confidence intervals

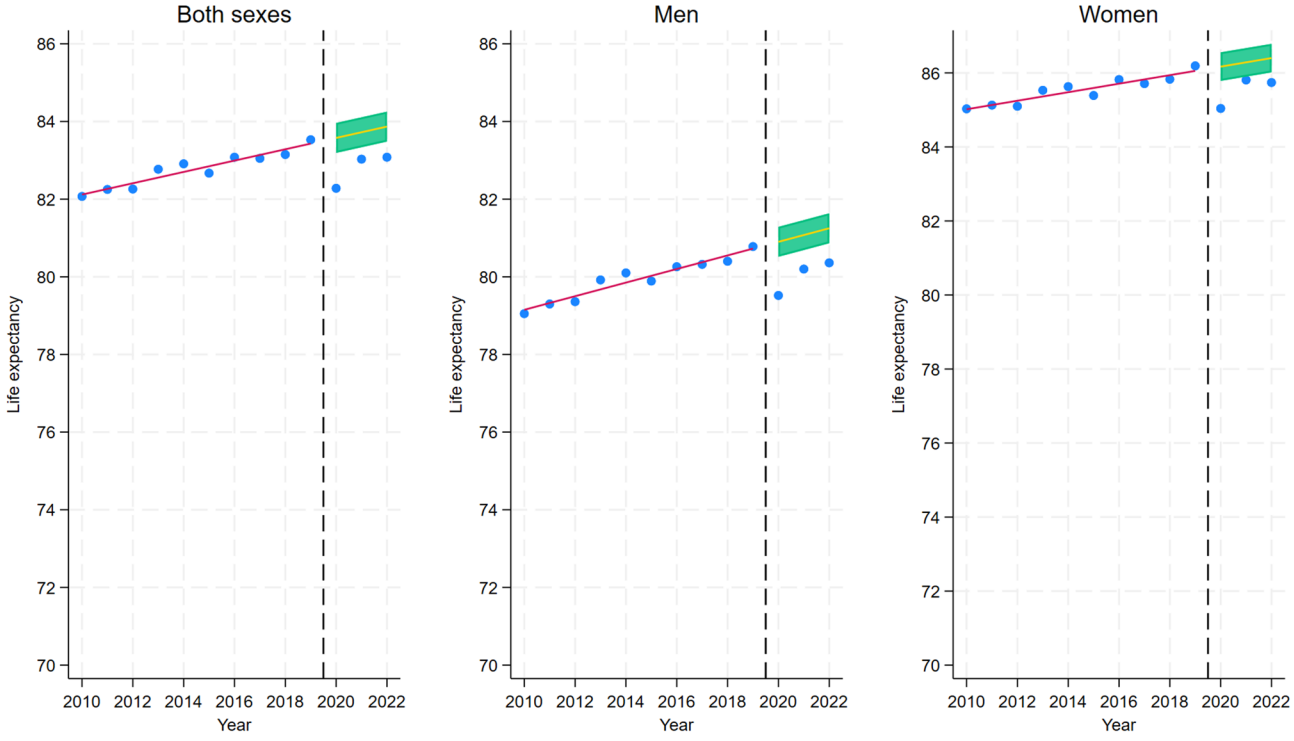

Fig. 1 Life expectancy in Spain. Dots represent the actual estimates. Lines represent the trend line from 2010 to 2019 and its extrapolation to 2020–2022. A vertical line between 2019 and 2020 divides the graph by the beginning of the pandemic. Green area represents the 95% prediction interval in the pandemic years

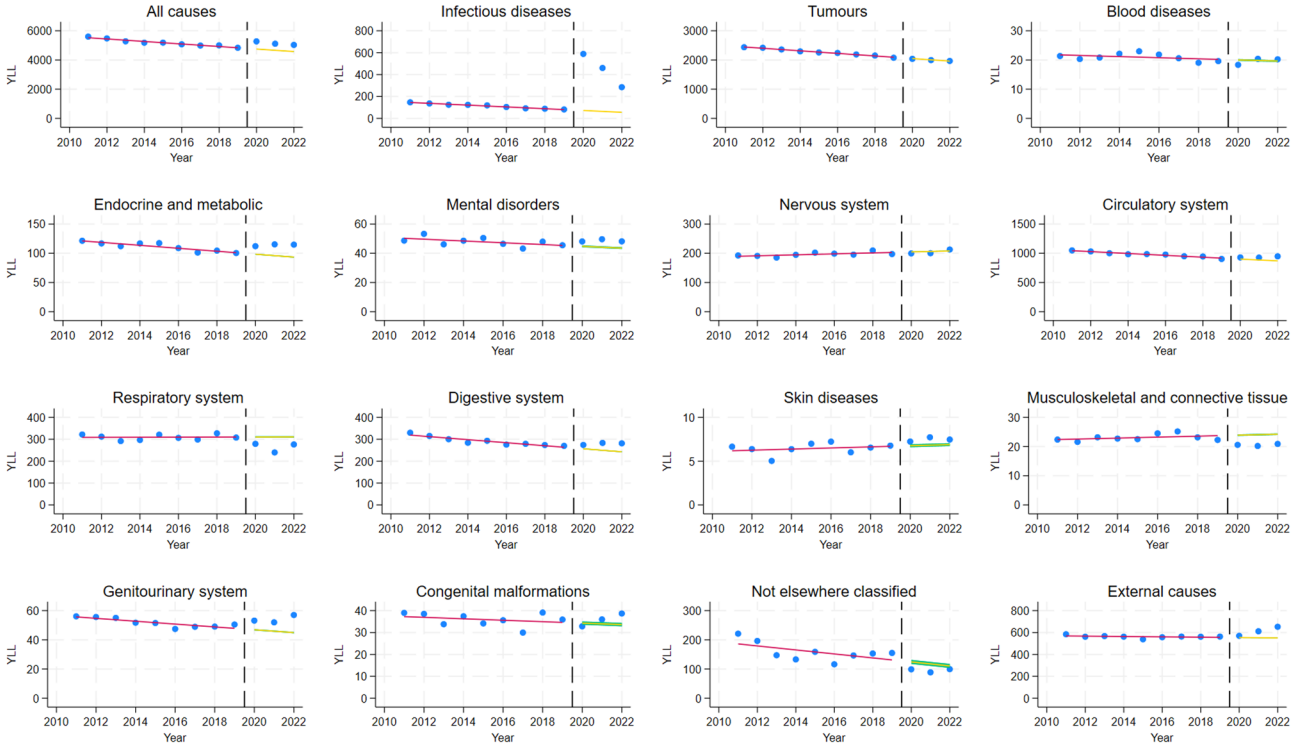

Fig. 2 Rates of years of life lost per 100,000 people by all causes and each ICD-10 group, both sexes. Blue dots represent the actual estimates. Red line is the trend line between 2010 and 2019. Yellow line is the extrapolation of that trend to 2020–2022. Geen line is the 95% prediction interval in the pandemic years

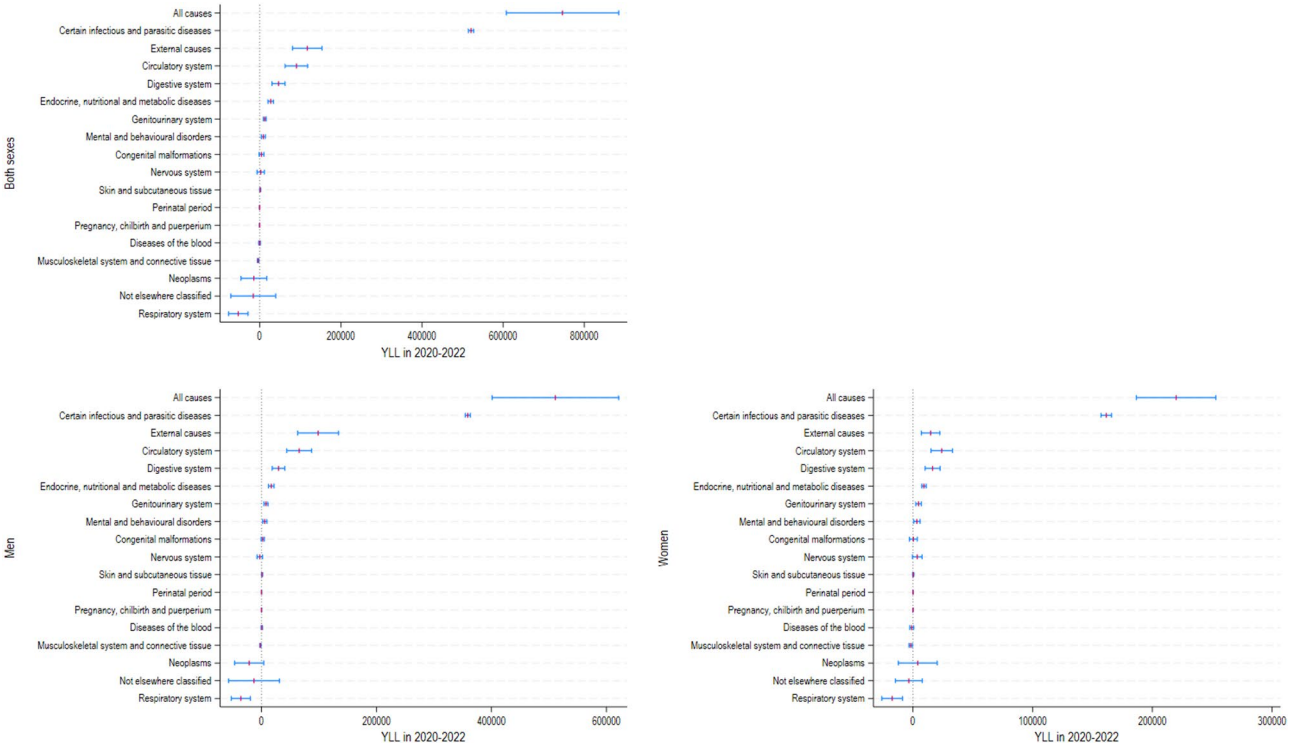

Fig. 3 Increase in years of life lost by ICD-10 group in the 2020–2022 period, both sexes. Central estimates and 95% confidence intervals. Note: the group "Certain infectious and parasitic diseases" includes COVID-19 (see Supplementary Table 1)

in 2020–2022, respectively), digestive system (+18, +34 and +39 YLL per 100,000 people in 2020–2022) and endocrine diseases (+14, +19 and +21 YLL per 100,000 people in 2020–2022). ICD-10 groups with lower-than-expected rates were respiratory system (-31, -71 and −35 YLL per 100,000 people) and causes not elsewhere classified (-25, -29 and −11 YLL per 100,000 people in 2020–2022). Neoplasms had lower-than-expected rates in 2020 and 2021 (-10 and −8 YLL per 100,000 people, respectively) but excess rate in 2022 (+6 YLL per 100,000 people).

Number of potential years of life lost

Excess of YLL is displayed in Supplementary Table 3. Regarding all causes of death, excess of YLL was 265,768, 232,070 and 248,676 in 2020, 2021 and 2022, respectively. About two thirds of the excess of YLL occurred in men, with ratios excess YLL in men: women equal to 2.2 in 2020, 2.7 in 2021 and 2.2 in 2022. When it comes to ICD-10 groups, 70% of all excess of YLL could be attributed to infectious diseases (including COVID-19), with decreasing figures from 2020 to 2022 (87% in 2020, 78% in 2021 and 43% in 2022). Other groups with high excess of YLL are external causes with increasing figures from 2020 to 2022 (7%, 16% and 25% of all excess YLL attributed to this condition respectively), diseases of circulatory system (7.5%, 11% and 18%), diseases of digestive system (3.6%, 7.4% and 7.9%), endocrine, nutritional and metabolic diseases (2.6%, 4% and 4.4%), diseases of genitourinary system (1.2%, 1.4% and 2.4%), and mental and behavioural disorders (0.9%, 1.5% and 1.3%).

It is worth noting that all groups here indicated but mental and behavioural disorders account for increasing excess of YLL as time goes by. Conversely, diseases of the respiratory system, as well as neoplasms and causes of death not elsewhere classified, account for negative excess YLL (i.e., less observed YLL than expected).

Figure 3 shows the estimated excess of YLL adding up all three years studied. The pattern looks quite similar for men and women with some remarkable differences: in men, the four most important groups were: first, infectious diseases; second, external causes of death; third, diseases of the circulatory system, and fourth, diseases of the digestive system. In women, the order of these main groups changed: first, infectious diseases; second, diseases of the circulatory system; third, diseases of the digestive system, and fourth, external causes of death. Neoplasms behaved differently in men -negative excess of YLL- than in women -positive excess of YLL, in both sexes being one of the ICD-10 groups with lower changes in YLL during the pandemic.

Discussion

In this study on excess mortality in Spain in 2020–2022, we found that, three years after the beginning of the pandemic, mortality continued to be higher than expected and higher than pre-pandemic levels. The impact of the pandemic was higher in men than in women, with YLL in men doubling YLL in women. Of note, increasing in LE in most Western European countries in the pre-pandemic period (2011–2019) had been slowly than that of 1990–2011. Then, in the 2019–2021 pandemic period, only Denmark, Belgium, Ireland, Norway, Sweden and Iceland avoid decreasing in LE [24].Proportion of excess mortality due to infectious diseases -thus, directly attributable to COVID-19- progressively decreased from 87% in 2020 to 43% in 2022.

The fact that LE in 2022 is still lower and YLL are still higher than in 2018 and 2019 shows that impact of COVID-19 pandemic remains even after the main compulsory control measures had been waived: as noted in the Methods– Setting section, travelling restrictions were removed in May 2021 and compulsory face mask use was progressively stopped from February 2022. The explanation of excess mortality in 2022 is not straightforward. On one hand, mortality due to infectious diseases continued to be higher than expected in 2022, although its contribution to the excess mortality about halved that of 2021, while other causes of death -namely cardiovascular diseases and external causes- increased their contribution from 2020 to 2022. On the other hand, coding of causes of death could have suffered of some temporal variations. For instance, in 2020 and the beginning of 2021, when most government and society efforts were centred on the pandemic, people dying with COVID-19 and having previous chronic medical conditions could have been classified as dying by COVID-19, while from middle 2021 on -where the pandemic was no more in the headlines, so to speak- they could have been codified as dying by their background disease (so, dying "with COVID", not "out of COVID") [25].

Apart from infectious diseases, two ICD-10 groups account for most of the increases in YLL from 2019 to 2022: external causes of death (62409 excess YLL in 2022, after progressive increases in 2020 and 2021), and diseases of circulatory system (45279 excess YLL if 2022, again after progressive increases from 2020 to 2022) (Supplementary Table 3). To further clarify the progressively increase in mortality due to external causes, we explore the INE web page in order to obtain the number of deaths for specific external causes. The number of deaths from external causes rose by about 2,500, from 16,141 in 2019 to 18,574 in 2022. Significant increases in external causes included accidental drowning and submersion (3,248 deaths in 2019 vs. 4,108 in 2022), suicide (3,671 vs. 4,227), and accidental falls (3,297 vs. 3,788). There were no remarkable increases in deaths from traffic accidents or homicides [25].

Although health authorities repeatedly expressed their concerns on mental health during the pandemic [26, 27], some authors have reported positive changes in health risk behaviours in adolescents during lockdown [28]. This could eventually impact on the number of suicides. In this way, the number of suicidal attempts stepped-up in six European countries, most of them in the Mediterranean area, about ten months after the beginning of the pandemic [29], while no increase in suicide rates was detected in the first 15 months of the pandemic [30, 31]. However, a wide study on European Union countries found heterogeneous changes in suicide number when comparing rates in 2020 with those in 2019, with increasing rates in Ireland, Hungary, Spain or France, and decreasing rates in Lithuania, Sweden or Austria [32].

A further analysis on Spain's data showed also an increase in suicide in 2021 [33]. The increase in the number of deaths by suicide in Spain we are describing goes beyond the main phases of the pandemic and reaches 2022. This increase is not enough to explain the whole increase in external causes of death. However, Spain has usually had low rates of suicide, ranking 137 in WHO statistics in 2019 [34]. It has been noted that a relevant proportion of actual suicides in Spain could have been historically hidden as deaths due to suffocation or accidental poisoning [35], which are precisely the other external causes of death increasing in 2020–2022.

The number of deaths due to diseases of the circulatory system stepped up from 116,615 in 2019 to 121,341 in 2022 [25]. During the pandemic, some debate happened about the impact that disrupting health care system could have on both acute and chronic diseases. Of note, most in Spanish hospitals is oriented to attending acute diseases [36]. Therefore, if the disruption of normal functioning of Spanish hospitals during the pandemic have had affected cardiovascular mortality, it would have produced an increase in mortality due to acute infarction or other ischaemic heart diseases, as well as to cerebrovascular diseases as they have highly effective procedures for acute/emergency situations, such as angioplasty, stent implant and tissue plasminogen activator. But this is not what happened. The number of deaths by ischemic heart diseases (ICD-10 code I20-I25) was 29,247 in 2019 vs. 29,068 in 2022, and deaths by cerebrovascular diseases (ICD-10 code I60-I69) were 25,712 in 2019 vs. 24,688 deaths in 2022. Rises in cardiovascular mortality were mainly due to hypertensive diseases (ICD-10 code I10-I1A) (11854 deaths in 2019 vs. 14865 in 2022) and cardiac failure (ICD-10 code I50) (19040 and 20584 deaths in 2019 and 2022, respectively). They both are chronic diseases, which mortality depends more on continuing

attention in the whole health system (i.e., primary and hospital care) than on attention to acute cases [37–39].

During the COVID pandemic, the majority of financial and human resources were redirected toward hospitals, leading to the closure of many primary health care centres and a shift to remote medical assistance. This, combined with mobility restrictions following the state of alarm declared in March 2020, overwhelmed phone lines and severely limited access to primary care services [40]. As a result, the ability of primary care physicians to detect and prevent chronic conditions diminished. Several studies have confirmed a significant reduction in new diagnoses of common conditions, with hypertension being one of the most affected [41, 42].

The COVID pandemic also negatively affected the quality of chronic disease monitoring and management in Primary Care [43], which could partly explain the increase in cardiovascular disease mortality observed from 2021 onward.

Mortality from cardiovascular diseases progressively increased in Norway, with 3.4% excess mortality in 2020 to 42.8% in 2022 [44], while in the US, 73% excess of mortality from heart diseases and 26% from cerebrovascular diseases [45]. A recent population-based study found increases in mortality due to cardiovascular diseases in 11 out of 16 countries for 2020 and 2021; those increases were higher than 5% in seven countries for 2020 and nine countries for 2021 [46]. A study carried out in Czechia showed that cardiovascular diseases contribution to LE was −0.18, +0.15 and +0.20 years in 2020, 2021 and 2022, respectively. In the same years, changes in LE were −0.97, -1.03 and +1.76 years [47]. A decline in deaths due to ischaemic heart disease was described few months after the beginning of the pandemic, which was explained as frail individuals, who may have died from their cardiovascular conditions, actually died from COVID-19 early in the pandemic [48].

Diabetes mellitus could be responsible for most excess deaths in the Endocrine, nutritional and metabolic diseases ICD-10 group. Early in the pandemic, it was described that diabetes mellitus was associated with about twice the mortality in patients with COVID-19 pneumonia [49], a result later confirmed in a large meta-analysis, which also shows great heterogeneity in mortality [50]. Excess mortality due to diabetes mellitus in the US (2020-21) was 34% in men and 38% in women, COVID-19 being reported as underlying cause of death in more than 50% and as contributing cause in about 7% [51]. Excess deaths due to diabetes mellitus was also reported in most of 16 countries analysed for 2020–2021 [46].

Our results show no relevant excess mortality due to cancer. Similar results were reported in the US [45] and Northern Italy [52], while a 2.3% excess mortality was reported in Norway in 2022, but not in 2020 [44]. Results in an analysis of 16 countries mortality for 2020–2021 show less deaths due to cancer than expected in most of them, with no country suffering excess deaths over 5% [46]. Delays in cancer-specific diagnostic have been reported on colorectal, urological, gastric, and head and neck cancer. Results on breast cancer were contradictory, while lung cancer diagnostic was reported as not delayed [10]. Of note, delays in cancer diagnosis would eventually lead to increases in cancer-specific mortality, although for most cancers this would require more than two years to be measurable. In this respect, Maringe et al. (2020) [9, 53] analysed the expected impact of delaying cancer diagnosis during the pandemic, according to three increasingly disruptive scenarios of referral patterns. According to their projections, progressively increasing excess number of deaths are to be expected 1, 3 or 5 years after breast or colorectal cancer diagnosis, while the excess number of deaths due to lung or oesophageal cancers could reach its maximum only 1 year after the diagnosis.

Higher pandemic-associated mortality in men has been observed in other high-income countries [3]. It has been suggested that oestrogens may play a protective role in women by modulating the immune response, while androgens in men may have immunosuppressive effects [54]. Women have higher levels of T-cell activity, which is key in the adaptive immune response, eventually helping women better control SARS-CoV-2 infection, leading to lower hospitalization and mortality rates [55]. Men tend to have higher rates of smoking and alcohol consumption, both known risk factors for severe COVID-19 complications [56]. Moreover, men are more likely to suffer from serious comorbidities, such as cardiovascular and chronic respiratory diseases, which significantly increase the risk of death from COVID-19 [57, 58].

This article has some limitations. Firstly, cancer, ischemic heart disease and chronic kidney disease are among the main risk factors of dying by COVID-19 [59–63]. Therefore, it could have happened that COVID-19 anticipated to 2020 or 2021 deaths that, otherwise, would only occur a bit later. If this "harvest effect", which have been described as produced by influenza epidemics [64] or heat waves [65] had actually happened with COVID-19, then we cannot discard the possibility that actual trends in cause-specific mortality be veiled by COVID-19 as, in the main pandemic waves, these deaths could have been attributed to COVID-19 rather than to the background condition. Secondly, ascribing causes of death could have been heterogeneous in the studied period: if in 2020, most people dying with a background condition -say, cancer- and COVID-19 could have been ascribed to COVID-19 as cause of death, in 2022 -when the concern for the pandemic stepped down- they could have been ascribed to their background condition. This could

make 2022 figures less comparable to those from 2020 to 2021. Thirdly, we are analysed the impact of pandemic on mortality via YLL and LE. It is noteworthy that mortality in people over 80 years-old, which was most remarkable in the pandemic, does not account for YLL and has little impact on LE. Fourthly, we modelled the expected LE and YLL using linear models. In fact, YLL depend on the population age structure, so they are not expected to be linear in the long term. In the short term, however, a linear approach could approximate well as shown in studying life expectancy in European countries 1990–2021 [24]. Fifthly, when presenting excess deaths as direct (infectious diseases) /indirect (any other ICD-10 group) effects of COVID-19 we are simplifying. For instance, low influenza virus circulation in 2020/2021 followed by its high circulation in 2022, which in 2022/2023 reaches almost pre-pandemic levels in European Union countries [66] would sensibly be considered an indirect effect of COVID-19 as lockdown at the pandemic beginning could have prevented influenza virus circulation at the cost of decreasing people natural immunity.

In conclusion, mortality in 2022 in Spain remained higher than expected according to pre-pandemic trends. Excess mortality due to non-infectious diseases gained importance from 2020 to 2022, especially regarding suicide and other external causes of death, as well as some cardiovascular diseases. Cancer mortality, however, was not in excess in the pandemic period.

Abbreviations

INE	Spanish Institute for Statistics
LE	Life expectancy
YLL	Years of life lost

Supplementary Information

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Supplementary Material 1

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Author contributions

J.L. contributed to the conception and design of the study. All authors were involved in data acquisition and contributed to drafting the manuscript. The first draft was written by J.L., I.G.A., J.A.M., M.D.R., and T.D.S. All authors reviewed and provided input on the final version of the manuscript.

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Data availability

All data analysed in this study are in the public domain. All data generated during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate

All data we used are in the public domain. Therefore, we did not ask for authorization of any ethics committee.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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