Appendix A

Table A.1. Sources of data

Indicator	**data**	**Web, if available**
Excess deaths	Weekly mortality data from first week of 2019 to week 24 of 2021	https://www.ine.es/jaxiT3/Tabla.htm?t=35179
Excess deaths	Weekly mortality data by region, age and sex for 2015-2018	From National Institute of Statistics upon request
Life expectancy	We grouped monthly mortality data by five-year age group (including infant mortality), sex and region between January 2010 and December 2020	The National Epidemiology Centre receives anonymised data on all deaths with months of birth and death from the National Institute of Statistics annually. These data are available on request.
Annual populations	By age, sex, and region from the continuous census, 1 July estimates, except for 2021, when 1 January estimates	https://www.ine.es/jaxiT3/Tabla.htm?t=10262&L=1
COVID-19 deaths	By day, age, sex and region	National Epidemiology Centre (Institute of Health Carlos III, SiViES): https://cnecovid.isciii.es/covid19/#documentaci%C3%B3n-y-datos

Statistical analysis

Estimation of excess deaths

Assuming that Yr,s,a (t), the number of deaths at week t for individuals in region r of sex s and age group a, is ~Poisson($\mu_{r,s,a}(t)$), our mean model is

$$\mu_{r,s,a}(t) = N_{r,s,a}(t)\exp\{\beta t + g_{r,s,a}(w_t)\} \text{ for } t \in I_r \qquad \text{EQ (A.1)}$$

Here, $\mu_{r,s,a}(t)$ is the expected number of deaths at region r, sex s, age group a at week t. $N_{r,s,a}(t)$ is an offset term for the population size, β represents an estimated linear effect of time to account for slow-moving changes in mortality, $g_{r,s,a}(w_t)$ is a function to account for seasonal trends, where $w_t \in \{1, \dots, 52\}$ represents the weeks of the year, and I_r is a region-specific reference interval (here, 2015-2019 for all regions) used to fit the model.

We calculated the smooth estimates of weekly percent change using:

$$\lambda_{r,s,a}(t') = \hat{\mu}_{r,s,a}(t')\exp\{f_{r,s,a}(t')\} \qquad \text{EQ (A.2)}$$

In equation (2), $\lambda_{r,s,a}(t')$ and $\hat{\mu}_{s,c,a}(t')$ represent the average number of observed and counterfactual deaths at the respective stratum in week t', respectively, and $f_{r,s,a}(t')$ is a natural cubic spline with 3 internal knots per calendar year (which returned the lowest median of the median absolute deviation in the reference period). The smooth estimate of weekly percent change from average at t', $\hat{\gamma}_{r,s,a}(t') = \hat{\lambda}_{r,s,a}(t') / \hat{\mu}_{r,s,a}(t') - 1$. We used excessmort R package to fit our modelling scheme, and additional details, including the smooth estimates of the weekly percent change and the estimation of the uncertainty around the point estimates, have been described extensively elsewhere.[1,2]

To avoid a false sense of precision,[1,3] numbers <1000, between 1000 and <100,000, and those ≥100,000 were rounded to the nearest ten, hundred, and thousand, respectively. Excess deaths were directly standardised using the 2013 European Standard Population.[4]

The estimated number of excess deaths was compared with the reported number of confirmed COVID-19 deaths in each region reported by the autonomous region to the National Epidemiology Centre as of 30 June 2021.

Calculation of life expectancy and YLL in 2020 and 2021

We have obtained annual data by granular age (including infant mortality) and sex groups for each region for 2010-2020. The data we have obtained for 2021 had similar granularity except that the death counts were available for 0-4 age groups without further disaggregation into <1, and 1-4 as required for the calculation of life expectancy. Using a similar approach, we have applied the following method to split the first age group. First, we split population exposures using proportions from previous years:

$${}_1P_0(y) = w_1 \cdot {}_5P_0(y),\ {}_4P_1(y) = {}_5P_0(y) - {}_1P_0(y).$$

Here ${}_aP_b(y)$ denotes population exposures in year y in age interval $[b;b+a)$ and w_1 is average proportion of age group <1:

$$w_1 = \frac{1}{N} \sum_{i=y-N}^{y-1} w_1(y)\ , w_1(y) = \frac{{}_1P_0(y)}{{}_4P_1(y) + {}_1P_0(y)}\ .$$

At the next step, we estimate infant mortality rate (IMR) in year y using linear regression fitted using IMRs from N previous years. The number of deaths in the first year of life ${}_{1}\mathrm{D}_{0}$ is calculated as follows:

$$
{}_{1}\mathrm{D}_{0}(\mathrm{y}) = \begin{cases} \widehat{\mathrm{IMR}}(\mathrm{y}) \cdot {}_{1}\mathrm{P}_{0}, \text{if } \mathrm{IMR}(\mathrm{y}) \cdot {}_{1}\mathrm{P}_{0} < {}_{5}\mathrm{D}_{0} \\ \mathrm{IMR}(\mathrm{y}-1) \cdot {}_{1}\mathrm{P}_{0}, \text{if } \mathrm{IMR}(\mathrm{y}-1) \cdot {}_{1}\mathrm{P}_{0} < {}_{5}\mathrm{D}_{0} \text{ and } \mathrm{IMR}(\mathrm{y}) \cdot {}_{1}\mathrm{P}_{0} \geq {}_{5}\mathrm{D}_{0} \\ {}_{5}\mathrm{D}_{0}, \text{else} \end{cases}
$$

And the number of deaths in age interval $(1,5)$ is

$$
{}_{4}\mathrm{D}_{1}(\mathrm{y}) = {}_{5}\mathrm{D}_{0}(\mathrm{y}) - {}_{1}\mathrm{D}_{0}(\mathrm{y}).
$$

We applied this algorithm separately to each sex in each region.

We have validated this approach extensively,[5] and found that the difference was <0.01 years for all ages below 80 (maximum absolute difference was 0.02). In this analysis, we have validated our approach for 2020 data, and found that the mean difference was 0.10 years (median: 0.10, maximum: 0.19).

We used standard life table methodology to estimate life expectancy at birth and at age 65.[6,7] The details of the methodology have been published elsewhere.[5] In summary,

we converted the death rates, ${}_{\mathrm{n}}\mathrm{m}_{\mathrm{x}}$, into probabilities of death, ${}_{\mathrm{n}}\mathrm{q}_{\mathrm{x}}$, where index n refers to the length of the interval, and x denotes the beginning of the age interval. For example, ${}_{\mathrm{n}}\mathrm{q}_{\mathrm{x}}$ denotes the probability of death in age interval $[\mathrm{x}, \mathrm{x}+\mathrm{n})$.

Let, ${}_{\mathrm{n}}\mathrm{a}_{\mathrm{x}}$ be the average number of years lived within the age interval $[\mathrm{x}, \mathrm{x}+\mathrm{n})$ for people dying at that age. We assume that $\mathrm{a}_{\mathrm{x}} = \frac{\mathrm{n}}{2}$ for all single-year ages except age 0 (see below). We then compute ${}_{\mathrm{n}}\mathrm{q}_{\mathrm{x}}$ from ${}_{\mathrm{n}}\mathrm{m}_{\mathrm{x}}$ and ${}_{\mathrm{n}}\mathrm{a}_{\mathrm{x}}$ according to the formula:

$$
{}_{n}q_{x} = \frac{{}_{n}m_{x}}{1+(1-{}_{n}a_{x})\cdot {}_{n}m_{x}} \qquad \text{EQ (A.3)}
$$

for $x = 0, 1, 5, 10, \ldots, 85$. For the open age interval (90+), we set ${}_{\infty}a_{90} = \frac{1}{{}_{\infty}m_{90}}$ and ${}_{\infty}q_{90} = 1$.

For infants <1 year of age, we used the formulas for a_0 suggested by Preston et al.,[6] which are adapted from the Coale-Demeny model life tables.[7] Thus, if $m_0 \geq 0.107$:

$$a_0 = \begin{cases} 0.350 & \text{for women} \\ 0.330 & \text{for men} \end{cases}$$

On the other hand, if $m_0 < 0.107$:

$$a_0 = \begin{cases} 0.053 + 2.800 \cdot m_0 & \text{for women} \\ 0.045 + 2.684 \cdot m_0 & \text{for men} \end{cases}$$

To complete the life table calculation, let ${}_{n}p_{x}$ be the probability of surviving from age x to $x + n$. Therefore,

$$ {}_{n}p_{x} = 1 - {}_{n}q_{x} \qquad \text{EQ (A.4)}$$

for all ages x. Let the radix (the starting number of new-borns) of the life table be $l_0 = 100{,}000$. Then, the number of survivors (out of 100,000) at age x is

$$l_x = l_0 \cdot \prod_{i=0}^{i<x} {}_{n}p_{i} \qquad \text{EQ (A.5)}$$

The distribution of deaths by age in the life-table population is

$$ {}_{n}d_{x} = l_{x} \cdot {}_{n}q_{x} \qquad \text{EQ (A.6)} $$

for $x = 0, 1, 5, \dots, 85$. For the open age category, ${}_{\infty}d_{x90} = l_{90}$.

The person-years lived by the life-table population in the age interval $[x, x + n)$ are

$$ {}_{n}L_{x} = l_{x} - (n - {}_{n}a_{x}) \cdot {}_{n}d_{x} \qquad \text{EQ (A.7)} $$

for $x = 0, 1, 5, \dots, 85$. For the open age category, ${}_{\infty}L_{90} = l_{90} \cdot a_{90}$. The person-years remaining for individuals of age x equal

$$ T_{x} = \sum_{i=x}^{85} L_{i} + {}_{\infty}L_{90} \qquad \text{EQ(A.8)} $$

for $x = 0, 1, 5, \dots, 85$. Remaining life expectancy at age x is

$$ e_{x} = \frac{T_{x}}{l_{x}} \qquad \text{EQ (A.9)} $$

for $x = 0, 1, 5, \dots, 85, e_{90} = 1/ {}_{\infty}m_{90}$

To attribute an equal loss of lifetime produced by deaths at the same age across the regions,[8, 9] we calculated the YLL using World Health Organization (WHO) standard life table, as is used in the Global Burden of Disease, Injuries and Risk Factor (GBD) study.[9, 10] We estimated the YLL with the following equation:

$$ \mathrm{YLL}_{r,s,a,t} = \mathrm{D}_{r,s,a,t} \times \mathrm{SLE}_{a}, $$

where $D_{r,s,a,t}$ is the number of deaths in region r, sex s, age a, and calendar year t, and SLE_a is the WHO Global Health Estimates standard life expectancy at age a.[9]

Calculation of changes in life expectancy and YLL in 2020 and up to the 24th week of 2021

We applied bootstrap methods to estimate the statistical uncertainty from the sample of 5000 iterations. Once a distribution of age-and-sex-specific forecasted mortality rates has been derived, we generated a random set of death rates and calculated our parameters of interest (LE, YLL, and changes in LE and YLL). The 2.5th and the 97.5th quantile of the bootstrap distribution were used as the 95% confidence intervals for each region and sex strata.

We have used the same methodology to also estimate the changes in LE and YLL for 2021 using data up to the 24th week of 2021. Statistical analyses were conducted using R (version 4.1.0). The Lee Carter forecast was performed using the R-package demography.[8]

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