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## Excess mortality during the first 2 years of the COVID-19 pandemic (2020-2021) in the Netherlands: Overall and across demographic subgroups

Camila Caram-Deelder<sup>1</sup>, Astrid van Hylckama Vlieg<sup>1</sup>, Rolf H.H. Groenwold<sup>1,2</sup>, Qingui Chen<sup>1</sup>, Dennis O. Mook-Kanamori<sup>1,3</sup>, Olaf M. Dekkers<sup>1,4</sup>, Eva A.S. Koster<sup>2</sup>, Liesbeth C. de Wreede<sup>2</sup>, Cees van Nieuwkoop<sup>3,5</sup>, Dimitar D. Toshkov<sup>6</sup>, Frits R. Rosendaal<sup>1,\*</sup>

<sup>1</sup> Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands

<sup>2</sup> Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands

<sup>3</sup> Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands

<sup>4</sup> Department of Endocrinology and Metabolism, Leiden University Medical Center, Leiden, The Netherlands

<sup>5</sup> Haga Hospital, The Hague, The Netherlands

<sup>6</sup> Faculty of Governance and Global Affairs, Leiden University, Leiden, The Netherlands

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### ABSTRACT

**Objectives:** The overall impact of the COVID-19 pandemic on mortality can be estimated by the assessment of excess deaths from all causes because the reported number of deaths due to COVID-19 do not accurately reflect the true death toll. We assessed excess mortality in 2020 and 2021 in the Netherlands.

**Methods:** All analyses were performed on data from comprehensive nationwide registers provided by Statistics Netherlands (Centraal Bureau voor de Statistiek), including demographic characteristics and mortality. All-cause mortality incidence rates were calculated per calendar month and compared against COVID-19 infections and preventive strategies. The all-cause mortality incidence rate ratios (IRRs) with 95% confidence intervals (95% CIs) were estimated per calendar year using Poisson regression (overall and for subgroups).

**Results:** Compared with predicted mortality based on 2019 rates, the overall excess mortality was 8.9% (IRR 1.089, 95% CI 1.081-1.097) in 2020 and 8.5% (IRR 1.085, 95% CI 1.077-1.092) in 2021. Relative excess mortality was higher for men, people with low household income, first-generation immigrants, and individuals living in extremely urbanized areas. In 2020, excess mortality was highest in age groups above 75 years (over 10%); in 2021, it was clearly present even in the 20-39 years age group (6.6%).

**Conclusions:** Our results quantify excess mortality during the first 2 years of the COVID-19 pandemic in the Netherlands. We show that the extent of excess mortality varies considerably across demographic groups, which may help in identifying target groups for preventive strategies during future health crises.

### Introduction

Since the first patient was diagnosed with COVID-19 in December 2019, over half a billion cases and 7 million deaths worldwide have been reported [1]. In the first semester of 2023, the World Health Organization declared the end of the pandemic. Still, by the middle of that same year, over 21 million patients were reported as active cases of the disease [2].

As we and others have pointed out [3,4], the overall impact of the pandemic on mortality can be estimated by the overall excess death toll, i.e. the number of deaths from all causes in excess of the number

expected based on historical data [5]. Obviously, a major cause of excess death will be deaths from COVID-19. These will be captured by overall mortality but not in all cases by assessment of deaths registered as attributable to COVID-19 because not all will have been coded as such. In addition, the pandemic and the measures introduced to contain it also affected others besides those infected with SARS-CoV-2, and this may also have introduced excess deaths.

When hospital wards were fully occupied, care for patients with other, mainly, chronic, disorders was postponed. Patients also sought less medical care. Such shifts in use and access of health care were also evident for patients with COVID-19, as we have shown that the duration

\* Corresponding author.

E-mail address: [f.r.rosendaal@lumc.nl](mailto:f.r.rosendaal@lumc.nl) (F.R. Rosendaal).

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of hospital admission for patients with COVID-19 was inversely associated with the number of patients admitted, i.e. with an increasing number of admissions patients with COVID-19 were discharged at an earlier stage [6]. Another major effect of the intense pressure of the pandemic on the health care system was an almost complete discontinuation of solid organ transplantations [7]. Furthermore, measures enacted to contain the pandemic also may have impacted individual health directly, for instance, for individuals with psychiatric disorders [8,9]. Some indirect effects might have been positive, e.g. because of fewer traffic accidents and fewer cases of influenza during lockdown periods [10,11].

Some of the deleterious effects did not happen only during the early and strongest waves of the pandemic. This may be related to delayed effects of COVID-19, such as an elevated risk of cardiovascular events (e.g. for influenza) [12]. Furthermore, delayed care is also likely to have long-lasting effects. Therefore, to assess the impact of the pandemic in full, it is not only crucial to evaluate its consequences on all-cause mortality but also to look at a longer period than the first months of the pandemic. This applies to the direct effects of COVID-19 and to the indirect effects of the pandemic and the related containment measures, e.g. lockdowns. Looking at the overall excess mortality, we observe direct and indirect effects (positive and negative) of the pandemic; hence, specific deleterious effects may be worse than the net overall figures suggest [13].

Finally, the reported numbers of deaths due to COVID-19 do not accurately reflect the true death toll because infections were not always diagnosed as COVID-19, and an infection may have been a contributing cause but not have been coded as such. Moreover, comparing COVID-19 death rates between countries is hampered by differences in definitions and reporting methods (e.g. in some countries, a COVID-19 infection had to be proven by polymerase chain reaction test, whereas in other countries, a clinical suspicion was sufficient). Several large, collaborative studies assessed excess mortality in 2020 and 2021 compared with data from previous years in several countries. All reported excess mortality in most countries, including the Netherlands [14–17]. Furthermore, the life expectancy during the COVID-19 pandemic (2020–2021) was compared with pre-COVID-19 years in several studies. All showed a decrease in life expectancy in most of the included countries, including the Netherlands [18–20]. The effect, however, varied between countries, from little change in life expectancy to over 2 years [14,20] and reported excess death rates ranging from 47 to 87 per 100,000 per year [16].

It is important to assess excess mortality not only for the total population but also across specific demographic groups. A study by Weinberger *et al.* using individual-level data showed that in the US veterans' excess mortality differed by age, sex, ethnicity, and residence type [21]. Others have also reported differential excess mortality per age, sex, and minorities (i.e. immigrants and ethnic minorities) [22,23].

Therefore, this study aimed to assess the death toll of the COVID-19 pandemic in the Netherlands by estimating excess mortality during the 2 first years of the pandemic (2020–2021), overall, and across specific subpopulations based on sex, age, socio-economic status, immigration background, and place of residence. Of note, vaccination campaigns began in January 2021, indicating that our study period includes 1 year without and 1 year with the (partial) impact of vaccination [24], albeit that the first population-wide vaccination campaign lasted until September 2021 when close to 90% of all individuals aged 12 years and older were vaccinated.

## Methods

### Data source

All analyses were performed using comprehensive nationwide data registers provided by Statistics Netherlands (Centraal Bureau voor de Statistiek [CBS]). These data include demographic characteristics, e.g. age, sex, immigration background, household income, and place of res-

idence (province and degree of urbanization), and mortality. The study was approved by the Scientific Committee of the Department of Clinical Epidemiology of the Leiden University Medical Center (protocol A0199), with a waiver of participant consent because it used exclusively preexisting de-identified data, which the CBS is allowed to process by law (Wet op het Centraal Bureau voor de Statistiek, i.e. law for the CBS). Full information about the CBS data sets and variables used in the analyses can be found in the supplemental material (Table S1).

### Study population

For each calendar year, the population at risk was defined as all registered individuals living in the Netherlands on the first day of the year. Thus, new immigrants and expatriates returning to the country in the course of a year were not counted during that same year but were included in the next calendar year. Illegal immigrants, estimated to be between 23,000 and 58,000 people in the Netherlands (0.01–0.03%), are, by definition, not registered and, as a result, were not included in the population at risk nor in the death counts [25]. The numbers of newly arriving immigrants, expatriates, and illegal immigrants are small compared with the general Dutch population [26].

To calculate the incidence rates per month, for each calendar month, the population at risk was defined as the population at the beginning of the year minus the people who died in the previous months. For each calendar year, the number of person-years was calculated based on the number of people at risk at the beginning of the year and taking into account if (and when) people died. The technical details about population at risk are in the supplemental material (Figure S1).

The population at risk was further characterized by sex, age at the beginning of the calendar year, immigration background (native; first-generation immigrant, defined as a person born abroad with at least one foreign-born parent; and second-generation immigrant, defined as a person born in the Netherlands with at least one foreign-born parent), and household income based on the percentile of the standardized household disposable income in the previous year, i.e. the disposable income adjusted for differences in household size and composition (categories: low =  $\leq 25^{\text{th}}$  percentile of the population, lower-middle =  $> 25^{\text{th}}$  to  $\leq 50^{\text{th}}$  percentile of the population, higher-middle =  $> 50^{\text{th}}$  to  $\leq 75^{\text{th}}$  percentile of the population, and high =  $> 75^{\text{th}}$  percentile of the population).

The population was also classified according to the characteristics of the place of residence on the first day of the year, i.e. province and degree of urbanization [27] (categories: extremely urbanized = 2500 addresses or more per km<sup>2</sup>, strongly urbanized = 1500–2500 addresses per km<sup>2</sup>, moderately urbanized: 1000–1500 addresses per km<sup>2</sup>, hardly urbanized: 500–1000 addresses per km<sup>2</sup>, not urbanized = fewer than 500 addresses per km<sup>2</sup>).

### Statistical analysis

Population characteristics are described by providing percentages of the total population for sex, age groups, immigration background, household income, and degree of urbanization. All-cause mortality rates were calculated per calendar month by dividing the number of deaths in that month by the total population at risk. To illustrate possible trends in mortality over time, mortality rates per 10,000 individuals were plotted against events of interest, i.e. COVID-19 peaks, lockdown periods, and main vaccination program.

Poisson regression analysis was used to estimate conditional excess mortality using incidence rate ratios (IRRs) for 2020 and 2021 compared with the reference year (2019). Unless specified differently, all available socio-economic factors (age, sex, immigration background, and household income) were included as covariates in the models. IRRs were estimated for the total population and per subgroups, which were based on sex, age categories, immigration background, household income, urbanization degree, and regions and provinces of the country.

We focused on relative excess mortality rather than estimating an absolute number of deaths. The latter is heavily dependent on the size of the group it refers to and, hence, not appropriate to identify vulnerable groups (if a small subsegment of the population is hit extraordinarily hard, the relative excess mortality will be high, whereas the number of excess deaths will remain small). However, based on estimates of (relative) excess mortality, we calculated the numbers of absolute excess mortality.

For the main analysis, we used 2019 as the reference period. To probe the robustness of our results, we also used all years between 2015 and 2019 (separately and in combinations) as the reference periods. These additional analyses illustrate the extent to which our estimates of excess mortality are sensitive to using a single year (2019) as the reference period. Using a longer reference period (2015-2019) smooths incidental mortality peaks in certain years preceding 2020, yet years that are longer ago may provide a less-valid comparison because of changes in, for example, unmeasured demographics and health care.

To estimate the IRR of each population subgroup of interest per year, an interaction term between the subgroup and the variable “year” was added to the models. For each subgroup, the reference year (i.e. 2019) was indicated as the baseline. This method, in contrast to stratification, allows the full population to be used to estimate the IRR rather than the subgroup only.

Because we used the same reference category within each subgroup of the population and the same matrix of associations (models with the same covariates), the excess mortality for 2020 and 2021, within subgroups, can be directly compared.

Finally, we estimated excess mortality as rates and absolute numbers, overall and for each of the subgroups, as a measure of impact, e.g. 10% excess mortality in a large subgroup indicates more deaths than in a small subgroup. Per subgroup and for the total population, we estimated the absolute number of deaths in the observation year (product of the IRR of the Poisson regression model, with only age and sex as covariates, and the population size of that subgroup) and subtracted the expected number of deaths in the observation year, under the assumption that the mortality rate was similar to that in the reference year (i.e. the product of the incidence ratio in 2019 and the population size). As a result, zero represents no excess mortality and negative value represent fewer than expected deaths. To simplify the interpretation, the estimated absolute number of deaths were rounded to the nearest multiple of 10.

We performed several additional analyses. First, to demonstrate the effect of adjustment for different covariates, we present the crude excess mortality (no covariates) and models with different covariates. Second, we investigated the influence of removing household income from the set of covariates on the effect of immigration origin. Third, excess mortality was quantified for the different provinces and regions (aggregates of provinces) in the Netherlands and for different countries of origin of the immigrants [28] (based on the country where the person was born to first-generation immigrants and on the country where the person's parents were born to second-generation immigrants). Countries were grouped according to geographic and economic characteristics.

The number of reported COVID-19–positive tests and vaccination coverage were extracted from the Dutch reporting system [29,30]. All analyses were performed in Stata (StataCorp, College Station, Texas) [31]. For graphs, RStudio and GraphPad Prism (GraphPad Software, San Diego, California) were used [32,33].

## Results

Table 1 shows the population characteristics in 2019, 2020, and 2021. During these years, the Netherlands had over 17 million inhabitants and the population size increased from 17.2 to 17.4 million. The ratio of men to women remained the same over the years, with 50.3% women and 49.7% men. The population aged slightly during these years, i.e. the percentage of individuals aged under 60 years was 74.4% in 2019 and 73.6% in 2021. Approximately 24% of the population were

**Table 1**  
Dutch population characteristics in the studied years.

	2019	2020	2021
<b>Population</b>	17,196,092	17,299,904	17,407,509
<b>Sex</b>			
Women	50.3%	50.3%	50.3%
Men	49.7%	49.7%	49.7%
<b>Age</b>			
0 to 19	21.9%	21.6%	21.4%
20 to 39	24.8%	25.0%	25.2%
40 to 59	27.7%	27.3%	27.0%
60 to 64	6.4%	6.5%	6.5%
65 to 69	5.8%	5.8%	5.8%
70 to 74	5.3%	5.4%	5.6%
75 to 79	3.5%	3.7%	3.7%
80 to 84	2.5%	2.5%	2.6%
85 to 89	1.5%	1.5%	1.5%
90+	0.7%	0.8%	0.8%
<b>Immigration background<sup>a</sup></b>			
Native Dutch	76.7%	76.2%	75.6%
First-generation immigrant	12.0%	12.4%	12.9%
Second-generation immigrant	11.2%	11.4%	11.5%
<b>Household income<sup>b</sup></b>			
Low	12.4%	12.4%	12.4%
Lower-middle	16.8%	16.8%	16.8%
Higher-middle	22.0%	22.0%	22.0%
High	27.6%	27.8%	28.0%
Institutional household <sup>§</sup>	1.2%	1.2%	1.2%
Unknown <sup>c</sup>	0.6%	0.6%	0.6%
Children <sup>c</sup>	19.4%	19.2%	18.9%
<b>Urbanization degree<sup>d</sup></b>			
Extremely urbanized	25.5%	25.6%	25.6%
Strongly urbanized	30.4%	30.4%	30.3%
Moderately urbanized	14.9%	14.9%	14.9%
Hardly urbanized	21.8%	21.8%	21.7%
Not urbanized	7.4%	7.4%	7.3%
Unknown <sup>c</sup>	0.0%	0.0%	0.0%
<b>Deaths (per 10,000)</b>	87.8	97.0	97.7

<sup>a</sup> **Immigration background:** Native: both parents born in the Netherlands; first-generation immigrant: born abroad with at least one foreign-born parent; second-generation immigrant: born in the Netherlands with at least one foreign-born parent.

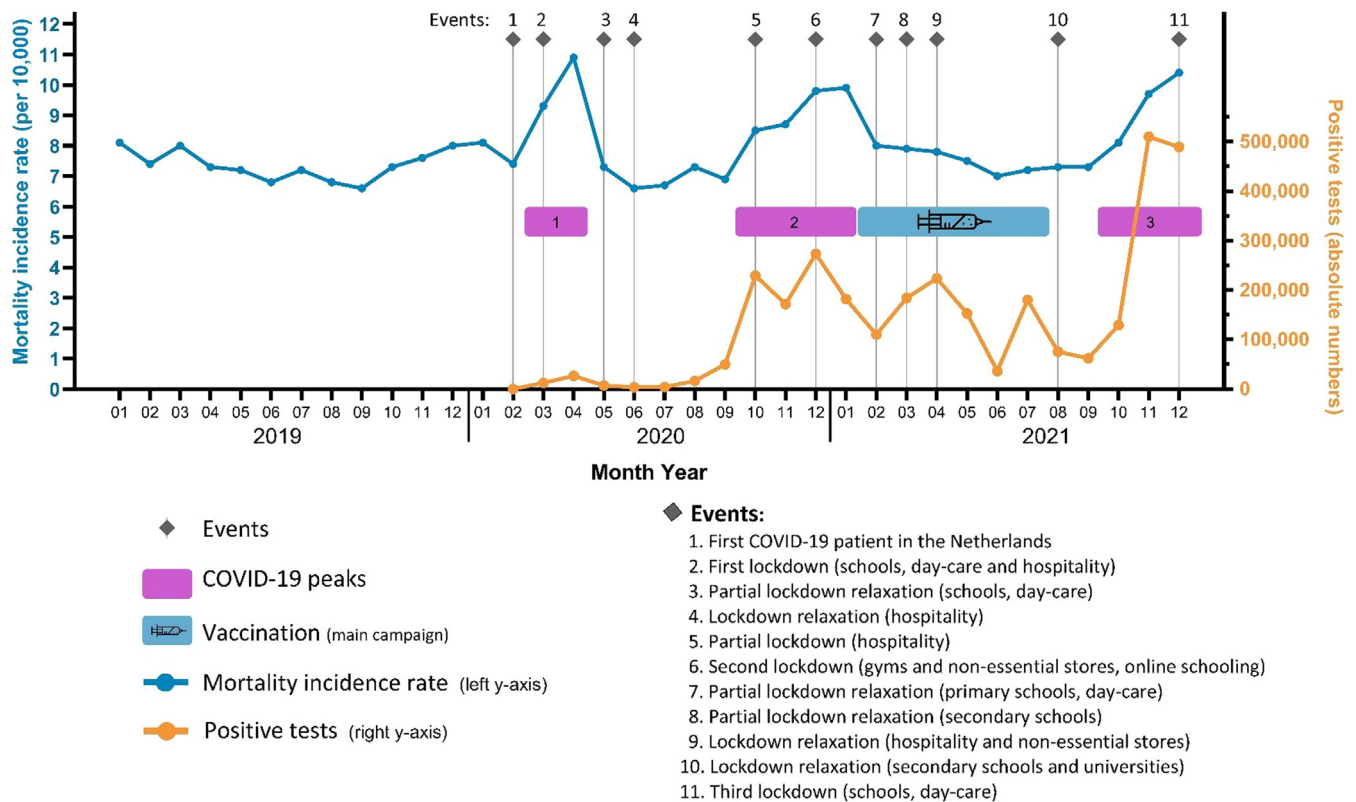
<sup>b</sup> **Household income:** Based on the percentile of the standardized household disposable income, i.e. the disposable income of a household corrected for the size and composition of a household. Categories: Low: up to percentile 25 (inclusive) of the population; lower-middle: from percentile 25 to percentile 50 (inclusive) of the population; higher-middle: from percentile 50 to percentile 75 (inclusive) of the population; and high: higher than percentile 75 of the population.

<sup>c</sup> **Impertinent categories:** Results of these categories are not relevant as a separate subpopulation group.

<sup>d</sup> **Urbanization degree:** Extremely urbanized: 2500 addresses or more per km<sup>2</sup>, strongly urbanized: 1500 to 2500 addresses per km<sup>2</sup>, moderately urbanized: 1000 to 1500 addresses per km<sup>2</sup>, hardly urbanized: 500 to 1000 addresses per km<sup>2</sup>, not urbanized: fewer than 500 addresses per km<sup>2</sup>.

first- or second-generation immigrants and more than half of the population lived in strongly or extremely urbanized areas (>1500 addresses per km<sup>2</sup>); these two population characteristics were stable over time. The absolute mortality rate in the total population was 87.8 per 10,000 in 2019, 97.0 per 10,000 in 2020, and 97.7 per 10,000 in 2021. The absolute difference was 9.2 and 9.9 deaths per 10,000 inhabitants in 2020 and 2021 and relative excess mortality of 10.4% and 11.2%, respectively.

Figure 1 shows the monthly all-cause mortality rates per 10,000 individuals for the period 2019-2021 plotted against events of interest, i.e. COVID-19 peaks, lockdown periods, and vaccination campaign. In 2019, the mortality rate fluctuated slightly, with higher mortality rates during the winter months than in summer, but no major peaks were observed. Mortality rates were highest in March and April 2020, between September 2020 and January 2021, and between September 2021 and



**Figure 1.** The incidence rate of mortality per month per 10,000 inhabitants in the Netherlands, along with the COVID-19 timeline, including COVID-19 peaks, lockdown periods, and the vaccination program.

December 2021 (end of study period). These increases in mortality rates roughly follow the dynamic of the COVID-19 pandemic in the Netherlands. Mortality rates decreased during medical and non-medical preventive strategies, such as lockdown periods and vaccination campaigns. We did not observe an increase in excess mortality during or soon after the vaccination campaign in the Netherlands. During the main campaign (January to July 2021), 75% of the adult population (aged 18+ years) was fully vaccinated and more than 80% received at least one dose. By the end of 2021, 86% of the adult population was fully vaccinated and 89% had received at least one dose.

Figure 2 shows the excess mortality measured as IRRs with 95% confidence interval (CI) for 2020 and 2021, compared with 2019, after adjustment for all covariates. In the total Dutch population, excess mortality was 8.9% in 2020 (IRR 1.089, 95% CI 1.081-1.097) and 8.5% for 2021 (IRR 1.085, 95% CI 1.077-1.092). Excess mortality was higher for men than for women in 2020 and in 2021. For men, excess mortality was 10.2% in 2020 (IRR 1.102, 95% CI 1.091-1.112) and 9.5% in 2021 (IRR 1.095, 95% CI 1.084-1.106). For women, these figures were 7.7% (IRR 1.077, 95% CI 1.066-1.087) in 2020 and 7.5% (IRR 1.075, 95% CI 1.065-1.086) in 2021. Excess mortality by age categories varied from approximately zero (IRR = 1, i.e. no excess mortality during the pandemic years) in the age category 0-19 years to relative excess rates of 12.0% for the age category 75-79 years in 2020 (IRR 1.120, 95% CI 1.099-1.142). Excess mortality was consistently higher in the first year of the pandemic (2020) than in the second year for individuals aged 75 years and older, although this was reversed for those aged 20-75 years, where excess mortality was higher in 2021 (i.e. the second year of the pandemic).

Excess mortality was strongly associated with immigration background. Excess mortality was highest for first-generation immigrants: 15.4% (IRR 1.154, 95% CI 1.126-1.182) in 2020 and 17.7% (IRR 1.177, 95% CI 1.149-1.205) in 2021 (relative to mortality in first-generation

immigrants in 2019). For second-generation immigrants, excess mortality in 2020 and 2021 was largely similar to that of the native Dutch population. These estimates for people with different immigration background were fully adjusted, including adjustment for household income. Importantly, in the model without adjustment for household income, excess mortality by immigration status was largely similar (15.0% excess mortality for first-generation immigrants in 2020 and 17.1% in 2021), indicating that household income and immigration status had separate effects on mortality (Table S2).

Household income had a graded inverse relation with excess mortality during the pandemic, with the highest excess mortality in the lowest income groups. Excess mortality was estimated to be 8.0% (2020) and 9.5% (2021) among people with low household income and 5.8% (2020) and 4.3% (2021) among people with a high household income. Excess mortality was highest in extremely urbanized areas: IRR 1.113 (95% CI 1.096-1.129) for 2020 and IRR 1.093 (95% CI 1.077-1.110) for 2021.

Table 2 shows the absolute all-cause mortality rates and the projected excess mortality rates and absolute numbers for the total Dutch population, as well as for the various subpopulations. For the overall Dutch population, the projected absolute number of excess deaths was 12,860 in 2020 and 11,780 in 2021. There were more excess deaths among men than women in both years, and there was a strong age effect: in those aged under 60 years, fewer than 1500 excess deaths occurred in both years combined, whereas over 18,000 excess deaths occurred for those aged over 75 years in both years combined. In absolute terms, excess mortality was particularly prominent in those with low or lower-middle household incomes (15,000 excess deaths in both years combined). Absolute excess mortality was also clearly higher among those living in more urbanized areas than other parts of the country.

The results of additional analyses are presented in the supplement. In short, Table S3 shows the excess mortality estimates based on different sets of covariates included in the models. The crude excess mortality



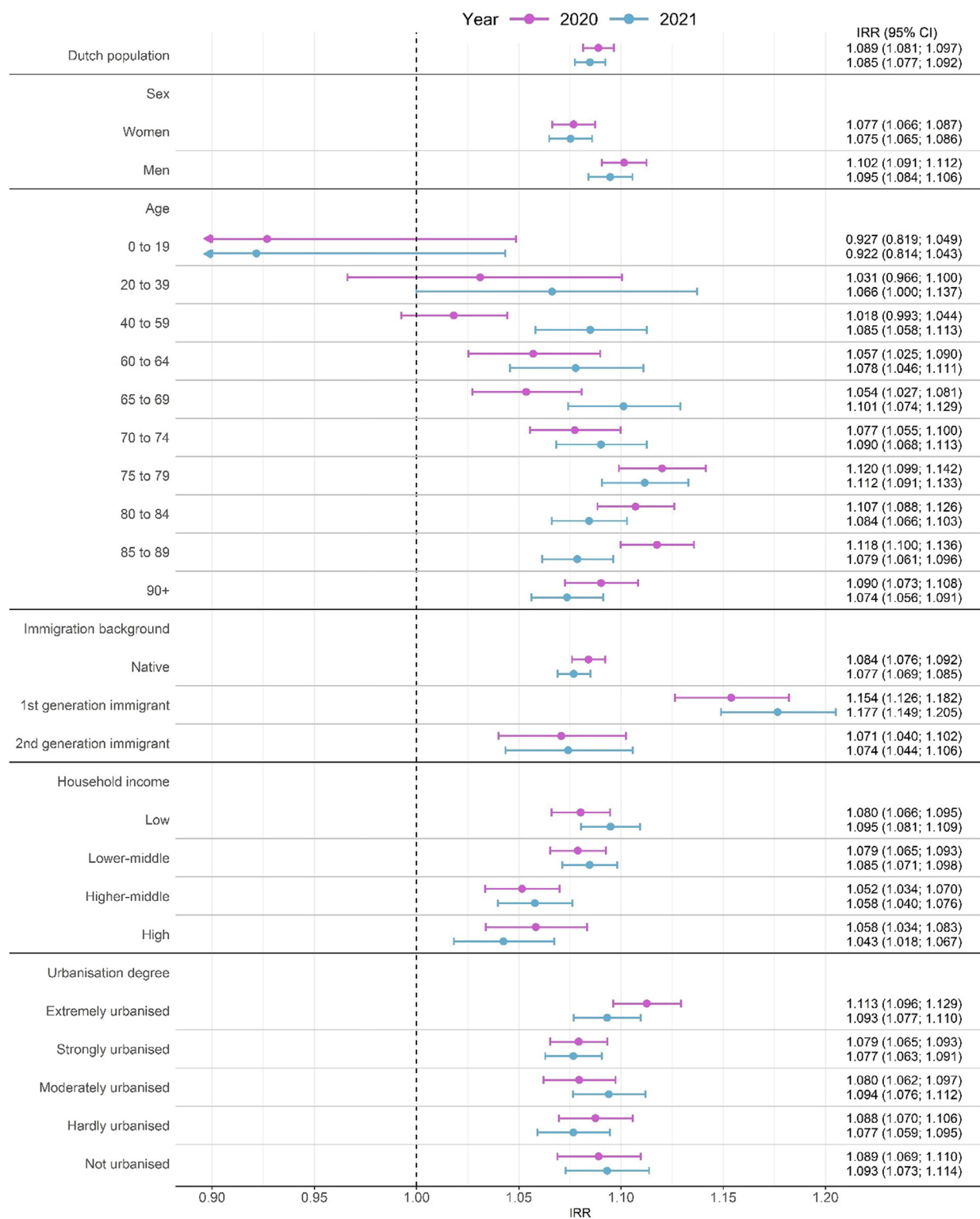


Figure 2. All-cause excess mortality in the Netherlands in 2020 and 2021: IRR, reference year 2019.

IRR (95% CI): incidence rate ratio and 95% confidence interval.

All models include as covariates: age, sex, household income, and immigration background.

**Immigration background:** Native: both parents born in the Netherlands; first-generation immigrant: born abroad with at least one foreign-born parent; second-generation immigrant: born in the Netherlands with at least one foreign-born parent. **Household income:** Based on the percentile of the standardized household disposable income, i.e. the disposable income of a household corrected for the size and composition of a household. Categories: Low: up to percentile 25 (inclusive) of the population, lower-middle: from percentile 25 to percentile 50 (inclusive) of the population, higher-middle: from percentile 50 to percentile 75 (inclusive) of the population, and high: higher than percentile 75 of the population. **Urbanization degree:** Extremely urbanized: 2500 addresses or more per km<sup>2</sup>, strongly urbanized, 1500 to 2500 addresses per km<sup>2</sup>, moderately urbanized: 1000 to 1500 addresses per km<sup>2</sup>, hardly urbanized: 500 to 1000 addresses per km<sup>2</sup>, not urbanized: fewer than 500 addresses per km<sup>2</sup>.

**Table 2**  
All-cause mortality rates and projected excess mortality.

	Absolute mortality rates (per 1000) <sup>a</sup>			Projected excess mortality			
	2019	2020	2021	Rates (per 1000)		n	
				2020	2021	2020	2021
<b>Population</b>	8.8	9.5	9.5	0.7	0.7	12,860	11,790
<b>Sex</b>							
Women	8.9	9.5	9.5	0.6	0.6	5400	4970
Men	8.7	9.5	9.4	0.9	0.8	7450	6820
<b>Age (years)</b>							
0 to 19	0.1	0.1	0.1	0.0	0.0	−40	−40
20 to 39	0.4	0.4	0.4	0.0	0.0	50	110
40 to 59	2.5	2.5	2.7	0.1	0.2	270	1110
60 to 64	7.2	7.6	7.8	0.4	0.5	440	620
65 to 69	11.8	12.4	12.9	0.6	1.2	600	1160
70 to 74	18.7	20.3	20.9	1.6	2.2	1510	2100
75 to 79	32.5	36.2	36.0	3.7	3.5	2360	2230
80 to 84	59.3	65.4	63.9	6.1	4.6	2650	2060
85 to 89	111.9	124.7	119.3	12.8	7.4	3280	1910
90+	216.9	234.8	229.5	18.0	12.6	2330	1660
<b>Immigration background<sup>b</sup></b>							
Native Dutch	9.9	10.7	10.6	0.8	0.7	10,340	8890
First-generation immigrant	5.8	6.7	6.8	0.9	1.0	1870	2240
Second-generation immigrant	4.5	4.8	4.8	0.3	0.3	620	630
<b>Household income<sup>c</sup></b>							
Low	19.4	20.9	21.2	1.6	1.8	3340	3970
Lower-middle	16.0	17.3	17.4	1.3	1.4	3670	3950
Higher-middle	6.5	6.9	6.9	0.3	0.4	1270	1450
High	2.8	3.0	2.9	0.2	0.1	790	580
<b>Urbanization degree<sup>d</sup></b>							
Extremely urbanized	8.2	9.0	8.9	0.9	0.7	3570	2850
Strongly urbanized	9.2	9.9	9.9	0.6	0.6	3090	2980
Moderately urbanized	8.9	9.5	9.6	0.6	0.7	2000	2340
Hardly urbanized	9.3	10.1	10.0	0.8	0.7	2260	1900
Not urbanized	8.2	8.9	9.0	0.7	0.7	1790	1870

<sup>a</sup> **Absolute rates:** 2019 observed. 2020 and 2021 are estimated by the Poisson regression models with age and sex as covariates.

<sup>b</sup> **Immigration background:** Native: both parents born in the Netherlands; first-generation immigrant: born abroad with at least one foreign-born parent; second-generation immigrant: born in the Netherlands with at least one foreign-born parent.

<sup>c</sup> **Household income:** Based on the percentile of the standardized household disposable income, i.e. the disposable income of a household corrected for the size and composition of a household. Categories: Low: up to percentile 25 (inclusive) of the population, lower-middle: from percentile 25 to percentile 50 (inclusive) of the population, higher-middle: from percentile 50 to percentile 75 (inclusive) of the population, and high: higher than percentile 75 of the population.

<sup>d</sup> **Urbanization degree:** Extremely urbanized: 2500 addresses or more per km<sup>2</sup>, strongly urbanized: 1500 to 2500 addresses per km<sup>2</sup>, moderately urbanized: 1000 to 1500 addresses per km<sup>2</sup>, hardly urbanized: 500 to 1000 addresses per km<sup>2</sup>, not urbanized: fewer than 500 addresses per km<sup>2</sup>.

rates are slightly higher than the adjusted estimates. Age had a strong effect on the reported IRRs, which can be explained by the aging of the population over the years.

Table S3 also shows the IRR estimated using different reference years (2015-2019), individually and in combination. Regardless of the reference period used, excess mortality is clearly visible in 2020 and 2021. The exact magnitude of the excess, however, varies depending on the reference period used. Using 1 year as reference the lowest estimates were from the models with 2016 and 2018 as the reference (2020 had 4.7% excess mortality and 2021 had 4.3% excess mortality). Using group of years as reference, the IRR magnitude decreases with the number of years included. For example, the excess mortality in 2020 using 1 year (2019) as reference was 8.9%; using 3 reference years (2017-2019), it was 6.5%; and finally, using 5 years as reference (2015 to 2019), the excess mortality in 2020 was 5.8%. All estimates suggest substantial excess mortality in 2020 and 2021, and it is reasonable to expect that using the most recent years as reference periods is the most appropriate, given the changes in the population structure that cannot be accounted for by the variables we adjust for. Figure S2 shows the results for all subgroups of interests, similar to Figure 1, but using the years 2015-2019 as a reference period.

Table S4 shows the rates and IRR for all-cause mortality for the total Dutch population, as well as for the various subpopulations, after stratification for urbanization degree. IRR within subgroups of age, sex, and household income were not affected by the degree of urbanization. The

higher overall excess mortality observed in first-generation immigrants and the lower overall excess mortality in second-generation immigrants was mostly driven by the effect in individuals from urbanized areas.

Figure S3 shows the results per regions and provinces of the Netherlands and per (grouped) country of origin of immigrants. Clear regional differences could be observed: the provinces in the south of the country were clearly more affected in 2020, whereas the north/east and most densely populated central (Randstad) provinces were more affected in 2021. Regarding immigrants' countries of origin, people who originated from Indonesia and Morocco had a significantly higher excess mortality. For immigrants from Suriname, the Dutch Caribbean, and Turkey, estimates higher than 10% excess mortality were observed as well. Immigrants from western Europe experienced excess mortality similar to the native Dutch population, which also held true for immigrants from central and eastern Europe. Figure S4 is a visualization of the absolute numbers presented in Table 2.

## Discussion

In this study, based on nationwide data and including over 17 million residents of the Netherlands, we compared mortality in 2020 and 2021 after appropriate adjustments, with mortality in 2019 to estimate excess mortality during the COVID-19 pandemic. We assessed whether there were specific demographic subgroups who were at a particularly high risk of excess death during the COVID-19 pandemic. During 2020

and 2021, we found approximately 9% overall excess mortality, amounting to almost 25,000 extra deaths in 2020 and 2021 combined compared with 2019. During the first 2 pandemic years, excess mortality was greater in men than in women, in older vs younger individuals, in those living in high vs low urbanized areas, in those with low vs higher income, and in first-generation immigrants vs native Dutch or second-generation immigrants.

When we compared the mortality rates in 2020 and 2021, excess mortality was highest in 2020 for older people (aged 75 years and above). For younger adults (aged 20-75 years), excess mortality was higher in 2021 than in 2020. For all other demographic subgroups, i.e. by sex, immigration background, household income, and urbanization degree, only minor differences in excess mortality were found between 2020 and 2021, albeit with different trends in time, e.g. somewhat higher excess mortality in 2021 than 2020 for first-generation immigrants and somewhat higher excess mortality in 2020 than in 2021 for high household income groups.

Although relative excess mortality is an appropriate way to compare the mortality in the overall population in the years of the pandemic with the year before and, subsequently, individuals with specific demographic characteristics, e.g. older age or low household income, during the pandemic years with individuals with the same characteristics in the pre-pandemic year, this comparison shows relative excess mortality in a group during COVID-19, superimposed on differences in mortality that are also present between these subgroups in any year. Nonetheless, when this is compared between levels of the demographic characteristics or with the overall figures, it shows whether certain characteristics were associated with a large relative impact of the pandemic. However, this does not show the impact in absolute terms: because older individuals have higher baseline death rates than younger individuals, the same excess mortality (IRR) will yield a much larger impact in the actual number of deaths in older than younger individuals. A high impact in absolute numbers was also seen in people with a low household income and those living in extremely urbanized areas.

In the literature, excess mortality during the COVID-19 pandemic has been reported in several countries over different periods of the pandemic, using different methods and reference periods. Despite these major differences, these studies consistently reported the presence of excess mortality during the COVID-19 pandemic [15,21,22]. Stratified analysis has also shown differences in excess mortality in demographic subgroups, e.g. men had higher excess mortality than women, highest relative excess mortality was reported in older age groups, and some studies found higher relative excess mortality in urban than rural areas [21,22,34]. Alicandro *et al.* assessed all-cause mortality in 30 countries during the year 2020 using mortality and population data downloaded from the World Health Organization mortality database [35]. They reported excess mortality in 2020 compared with the period 2011-2019 in 22 of 30 countries, with the majority of countries experiencing more than 10% excess mortality. Shang *et al.* performed a systematic review to assess all-cause excess mortality during the COVID-19 pandemic [34]. Consistent with our results, this meta-analysis concluded that men had a higher excess mortality than women and excess mortality was highest in individuals aged 60 years and older. These researchers postulate several explanations for these findings, including a worse prognosis after COVID-19 infection in men and a lower physical function and immunity in the elderly.

In line with our results, high excess mortality in subgroups with different immigration origin was previously reported in several studies [36-40]. Here, we show that the excess mortality was highest for first-generation immigrants (after full adjustment, including age and sex) but that the second-generation immigrants' excess mortality during COVID-19 was largely similar to that of native Dutch. We also show that the high excess mortality among first-generation immigrants cannot be explained by their generally lower household income and that excess mortality was highest among people with their origin in Indonesia, Morocco, Turkey, Suriname, and the Dutch Caribbean islands.

Several authors have reported on methodological difficulties in analyzing excess mortality that allows comparisons between countries [41,42]. Estimates of excess mortality strongly depend on methodological choices, and, particularly, not taking into account the aging of the population could lead to an overestimation of the excess mortality. Furthermore, the choice of the reference period can affect the results. We explored the influence of different modeling choices on the estimates of excess mortality. Indeed, our results showed that the crude estimates of excess mortality were higher than the fully (including age) adjusted estimates and that the choice of reference period led to somewhat different estimates of excess mortality but did not alter the conclusions.

We performed several analyses which are specific for the Netherlands and were, therefore, reported in the supplemental material only. Although these results are mainly of interest to describe excess mortality in the Netherlands, they do emphasize that major regional differences occur within a country, even one as small as the Netherlands. Furthermore, these results show that not only immigration background, but, more specifically, the country of origin, affects the magnitude of excess mortality during the pandemic.

Our study has several strengths. These include the use of a comprehensive nationwide database, on individual level, of the Dutch population, with complete information on mortality and a rich set of demographic characteristics. The size of the population allows precise estimations of the mortality rates and detailed subgroup analyses based on demographic factors. Furthermore, we assessed excess all-cause mortality, by which we estimate the direct and indirect impacts of the pandemic. For the estimation of the IRRs, we provide models without covariates (crude) and with different sets of covariates, providing readers the opportunity to assess the influence of different methodological choices. Estimates of excess mortality are highly dependent on the choice of the reference, i.e. what is the predicted mortality. The most suitable benchmark depends on several assumptions. When mortality rates are declining over time due to other causes than COVID-19, extrapolation of rates of previous years to the years of the pandemic would lead to an overestimation of the expected mortality and, hence, an underestimation of the excess mortality. However, there was no major trend in mortality rates during the last decade in the Netherlands, so the effects of any trends are trivial [43]. We considered 2019 an appropriate reference because it is the year closest to 2020 and, hence, the measured and unmeasured characteristics of the Dutch population are likely similar. Nevertheless, to show the possible impact of other assumptions regarding what is considered the most appropriate reference, we also included 2015-2019 as a reference (in the form of a sensitivity analysis). This provides valuable insight into patterns of mortality since mortality rates were not constant also in pre-COVID-19 years. Aging of the population and other morbidities varying over time (e.g. intensities of influenza seasons) may have influenced the variability in mortality rates in non-COVID-19 years. Nonetheless, all analyses consistently indicate excess mortality during the first 2 years of the COVID-19 pandemic. Because of our model structure, the results shown as excess mortality for 2020 and 2021 within subgroups can be directly compared.

Our study also has several limitations. Only people registered in the Dutch Municipal Basic Administration database are included in the analyses. This means that illegal immigrants are not included in our analyses. However, this number of unregistered people is small in relation to the overall population and constant over time [25]. Because we assessed all-cause mortality, we show the direct and the indirect effects, i.e. effects on mortality due to other causes related to, for instance, limited use of health care facilities or resulting from the containment measures of the COVID-19 pandemic combined, and we cannot disentangle these direct and indirect effects. Importantly, the excess mortality we report on occurred within the framework of reactions to the pandemic on the individual, societal, and governmental level, and we cannot evaluate what would have happened within another hypothetical framework, i.e. with alternative containment policies. Therefore, we cannot draw conclusions regarding the effects (or the lack thereof) of different measures.

However, some important signals emerge from these results. There was substantial excess mortality in two specific groups, i.e. in individuals with an immigration background and in those with low household income. Although these two factors will often go together, we also noticed that the excess mortality in first-generation immigrants was not fully explained by household income. The explanation for these finding may be found in poor health, low access to care due to language barriers and an accompanying information disadvantage, and low vaccination grade. Vaccinations started in the Netherlands in 2021, and acceptance of SARS-CoV-2 vaccination in the Netherlands was substantially lower in individuals with an immigration background other than native Dutch and lowest among those with a Moroccan background [44]. Similar findings resulted from studies in other countries [45]. The vaccination prevalence was also positively associated with income [46]. This may have resulted from a lack of information and mistrust in the government in specific groups. Although a reduced willingness to vaccinate will have contributed to mortality in 2021, it did not in 2020. Low income has consistently been associated with higher death rates than high income. This is related to a web of causes which vary among countries in their relative importance but have commonalities in a high frequency of poor and crowded housing conditions, limited access to preventive and curative medicine, and unfamiliarity with and lack of funds to afford a healthy diet and physical exercise, which are reflected, among others in an increased prevalence of smoking and obesity [47,48]. Although efforts to improve public health go back to Rudolf Virchow in the 19<sup>th</sup> century and are beyond the scope of this report, the finding that an acute health crisis such as COVID-19 has hit these traditionally most vulnerable groups the hardest transcends the specific circumstances of this pandemic and emphasizes the need for continuous governmental efforts in the field of public health, with an emphasis on filling information and knowledge gaps in certain groups in the population.

In conclusion, our results robustly show excess mortality during the COVID-19 pandemic (2020 and 2021) compared with preceding years, regardless of the reference period used. We found different effects in various demographic subgroups of the population which represent vulnerable groups in various aspects that often go together, i.e. may help in the identification of target groups for medical and non-medical preventive strategies during future health pandemics. Future research will focus further on the identification of vulnerable groups in the population which were affected the most by the COVID-19 pandemic. It should also uncover the mechanisms that explain why certain groups, such as first-generation immigrants from particular countries of origin or lower-income individuals, had significantly higher risks of excess mortality during the pandemic.

#### Declarations of competing interest

The authors have no competing interests to declare.

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#### Ethical approval

This study was approved by the Scientific Committee of the Department of Clinical Epidemiology of the Leiden University Medical Center (protocol A0199) with a waiver of participant consent, because it used exclusively pre-existing, de-identified data, which the CBS is allowed to process by law (Wet op het Centraal Bureau voor de Statistiek, i.e. Law for the CBS).

#### Author contributions

Conceptualization: CCD, AvHV, DOMK, OMD, CvN and FRR. Data curation: CCD and QC. Formal Analysis: CCD, AvHV, RHHG and FRR. Funding acquisition: CCD, AvHV, QC, DOMK, OMD, CvN and FRR. Methodology: CCD, AvHV, QC, DOMK, OMD, EASK, LCdW, DDT, CvN, RHHG and FRR. Project administration: CCD, AvHV and FRR. Supervision: RHHG and FRR. Validation: AvHV and QC. Visualization: CCD and AvHV. Writing original draft: CCD, AvHV and FRR. Writing review & editing: CCD, AvHV, QC, DOMK, OMD, EASK, LCdW, DDT, CvN, RHHG and FRR. Investigation, Resources and Software: not applicable.

#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2024.100500.

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