HSC Public Health Agency

Trends in Excess Mortality in Northern Ireland in 2022 and 2023

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Contents

1. Lay Summary

The COVID-19 pandemic caused many deaths worldwide, both directly from infection and indirectly through its effects on healthcare and society. One way to understand the overall impact of the pandemic on deaths is to compare the number of deaths that actually happened with the number of deaths that would have been expected if the pandemic had not occurred. This is called ‘excess mortality’.

In the UK, the Office for National Statistics (ONS) has introduced in 2024 a new method to measure excess mortality. This approach improves on previous methods but it is not considered a definitive ‘gold standard’ as it still remains "Official Statistics in Development" and is expected to be refined further. Using this method, the ONS estimated that in the UK, there were over 43,000 more deaths than expected in 2022, and nearly 11,000 more in 2023. These additional deaths were linked to a mix of causes, including COVID-19 itself, other infections, long-term health effects, and changes in access to healthcare.

We carried out three studies to investigate excess deaths in Northern Ireland:

- We compared weekly death registrations with the number expected from the past trends, broken down by age, sex, cause of death, and place of death.
- We looked at how the pandemic affected cancer care, including waiting times for diagnosis and treatment, and short-term cancer survival.
- We investigated whether there was any link between excess deaths, COVID-19 deaths, and COVID-19 vaccination.

We found:

- In 2022, there were 320 more deaths than expected (about 2% higher), while in 2023 there were 523 fewer deaths than expected (about 3% lower). Excess deaths were higher in older people. In 2022, the greatest excess deaths, compared with what would have been expected without the pandemic, were due to influenza, pneumonia, dementia, cerebrovascular diseases, and cancer. Some differences from official figures arise due to incomplete linkage of deaths across datasets, resulting in lower registered death counts in this study. Both these lower counts and population estimates used contributed to differences in overall, age-specific, and sex-specific excess death calculations.

- Waiting times for cancer diagnosis and treatment became longer during the pandemic. Survival also declined for people newly diagnosed with some cancers, such as lymphoma, oesophageal and ovarian cancers. Our findings may differ from other studies due to variations in data sources, study periods, and follow-up durations.
- COVID-19 vaccinations were not linked to excess deaths. Instead, excess deaths closely tracked the number of COVID-19 deaths, showing that the disease itself was the main driver of excess mortality during this period.

2. Executive summary

2.1. Background

The COVID-19 pandemic led to deaths worldwide, directly with infection with SARS-CoV-2 and indirectly through its broader societal impacts. Accurately measuring the impact is complex due to underreporting of COVID-19 deaths, indirect deaths from disrupted healthcare, and shifts in the timing of deaths. To address this, *excess mortality* is estimated, comparing reported deaths to the number of deaths expected by a statistical model. These estimates vary depending on the statistical models and timeframes used. A standardised approach to estimating excess mortality was adopted following a review by the Office for Statistics Regulation. Using this method, the Office for National Statistics reported 43,456 excess deaths in 2022 and 10,994 in 2023 across the UK. The causes of these excess deaths include early and long-term effects of COVID-19, other infections, consequences of societal changes during the pandemic, and changes in healthcare use and system performance.

2.2. Methods

We undertook three studies, two of them using the HSC Honest Broker Service (HBS) for provision of pseudonymised data:

1. To estimate the expected weekly number of deaths for each set of analyses (all-cause, cause-specific, and place-of-death), a quasi-Poisson regression model was used, based on historical death registration data aggregated by unique combinations of demographic characteristics. The number of actual death registrations was subtracted to estimate excess deaths, with analysis by sex and age, cause of death and location of death. Our approach follows the method adopted by the ONS in 2024. It is important to note that this method is still classified as 'Official Statistic in Development', and therefore subject to future refinement.
2. We examined the impact of the pandemic on various aspects of cancer care, including short-term survival and key waiting times throughout the treatment process. These included: i) the time between the decision-to-treat and the start of the first treatment, ii) the time between the referral date and the start of the first treatment, and iii) the time between the referral and diagnosis dates.

3. To examine the temporal relationship between COVID-19 vaccination and all-cause excess mortality, we conducted linear regression analyses using weekly mortality data. The analyses covered 5 December 2020 to the week ending Friday, 29 December 2023. Weekly excess deaths were regressed on i) weekly COVID-19 deaths and ii) weekly administered first-dose COVID-19 vaccinations, incorporated via a distributed lag non-linear model framework to capture potential lagged effects.

2.3. Results

- In 2022, there were an estimated 320 excess deaths, representing 1.9% more deaths than expected. In 2023, this shifted to an overall mortality deficit of 523 deaths (-3.1%), with the highest excess mortality occurring in January, followed by deficits in subsequent months. Incomplete linkage of deaths across datasets led to lower weekly registered death counts in our study, and differences in population estimates used here compared with NISRA further contributed to discrepancies in overall, age-specific, and sex-specific excess death calculations between this study and official statistics.
- The model produced significant sex disparities in mortality for both 2022 and 2023. Of the total 320 excess deaths in 2022, 535 were in females, while males experienced a mortality deficit of 213 deaths. In 2023, this pattern persisted, with males showing a substantial deficit of 686 deaths (-7.8%), while females recorded an excess of 169 deaths, 2.1% higher than expected. However, sensitivity analyses showed that the use of a single pooled model for both sexes using the ONS approach systematically underestimated expected deaths for females and overestimated them for males, resulting in inflated excess mortality for women and artificial mortality deficits for men. Modelling expected deaths separately by sex would allow for better detection of diverging mortality trajectories.
- In 2022, excess mortality was highest for influenza and pneumonia (10.3%), dementia and Alzheimer's disease (4.3%), cerebrovascular diseases (3.9%), and primary cancers (2.3%). Most excess deaths for influenza, pneumonia, circulatory diseases, and chronic lower respiratory diseases occurred in individuals aged 75 and older, while cancers accounted for excess deaths primarily in the 50–64 age group.
- In 2023, influenza and pneumonia showed the greatest excess mortality overall (1.4%), though much lower than in 2022. A distinct peak in early 2023 (58.9% excess in the first seven weeks)

was followed by a majority of weeks with deficit mortality, except for a small rise toward the end of the year. Mortality deficits were recorded for most other causes, including chronic lower respiratory diseases (-2.8%), circulatory diseases (-2.9%), and cancers (-3.0%).

- There were significant differences between survival functions for individuals diagnosed with cancer in 2019, 2020, and 2021 ($p < 0.001$). Overall, for all cancers, 1-year survival decreased from 81% in 2019 to 78% in 2020 while 2-year survival decreased from 74% in 2019 to 71% in 2020.
- The median time from referral to cancer diagnosis increased from 24 days in 2019 to 37 days in 2023 – a 54.2% increase. Similarly, the median time from referral to the first treatment rose from 49 days in 2019 to 65 days in 2023, representing a 32.7% increase.
- Significant declines between short-term cancer survival rates were observed for lymphoma, oesophageal, and ovarian cancers.
- Short-term survival rates for breast and prostate cancer remained the same for individuals diagnosed in 2019 and 2020, with an improvement observed for breast cancer in 2021.
- Our analysis confirmed a significant association between COVID-19 deaths and excess mortality, reaffirming that COVID-19 itself was the main driver of excess mortality during the study period.
- We found no statistically significant association between COVID-19 vaccination (either first-dose or cumulative) and excess mortality, aligning with international studies that similarly reported no increase in mortality following vaccination.

3. Introduction

The COVID-19 pandemic caused many deaths worldwide, directly and indirectly [1]. Measuring the full mortality impact of the pandemic over any time period is complicated for many reasons, including that: (a) not all deaths that were caused by COVID-19 will have been correctly identified as such, especially earlier in the pandemic; (b) deaths that were *indirectly* caused by the pandemic and factors related to society's response to it generally cannot be specifically identified and counted; and (c) the pandemic changed the time and cause of death for many people, meaning that they will be absent from death records when they would otherwise have died, had the pandemic not occurred [2,3]. To estimate the impact of events like the COVID-19 pandemic, epidemiologists and national statistical authorities use methods to estimate *excess mortality.* This means counting the total number of actual deaths recorded in a time period and subtracting the number of expected deaths that a statistical model predicts would have occurred in the absence of the pandemic [3]. A variety of statistical approaches have been used by different groups to do this at different times, and the estimates produced by the models are affected by technical factors in building the model, like the selection of the time period from which expected mortality is projected [4].

In the United Kingdom (UK), the range of approaches taken to excess mortality was reviewed by the Office for Statistics Regulation [5] and subsequently, statistical authorities agreed on a shared approach, which they published [6]. Using the new common approach, the Office for National Statistics (ONS) estimated 43,456 excess deaths in 2022 across the UK [7]. In 2023, there were 10,994 more deaths than expected [7]. At the time of writing, this methodology is classified as "Official Statistics in Development", meaning that it is expected to undergo further changes. Although it represents an advance on earlier approaches, it is not considered a definitive 'gold standard'.

The causes of excess deaths are mixed, and numerous factors may have contributed. Contributing factors may include:

- deaths caused directly by COVID-19;
- the return of other infectious diseases, including influenza, after a period of absence associated with reduced transmission during the pandemic period;

- longer-term harms from COVID-19 infection. For example, Xie et al. [8] showed that survivors of acute COVID-19 faced increased risks for 20 cardiovascular conditions, including myocardial infarction and stroke, in the year after SARS-CoV-2 infection;
- Reduced attendance at healthcare services for acute health problems and for issues that would normally have resulted in earlier diagnosis of disease [9];
- During this time period, indicators of time-to-healthcare in emergency departments, ambulance services and outpatient clinics showed increasing delays [10,11], which would be expected to result in worse outcomes for patients.

Excess mortality has, in some public discussion, been attributed to COVID-19 vaccination, often involving misinterpretation of scientific evidence [12-15]. We therefore investigated whether there was any statistical relationship between population COVID-19 vaccination and excess mortality in Northern Ireland.

4. Aim and objectives

The aim of this study was to investigate excess mortality in Northern Ireland during 2022 and 2023 and explore the association between the number of deaths and demographic, clinical, and healthcare-related factors.

The specific objectives of this project were to:

1) To estimate the number of excess deaths by week of registration, age, sex, place of death, and cause of death in 2022 and 2023.
2) To examine the impact of the COVID-19 pandemic on cancer deaths.
3) To investigate whether there was any relationship between COVID-19 vaccination and excess deaths

We conducted three separate studies, one to address each of these objectives, which are reported in chapters 6, 7 and 8 of this report.

5. Acknowledgements

Studies 1 and 2 were conducted through the Business Services Organisation's Honest Broker Service. The Honest Broker Service is the main Trusted Research Environment for accessing healthcare-related service user data for analysis in Northern Ireland. The Honest Broker Service provides access to de-identified data via a safe setting for approved health and social care related research.

The authors would like to acknowledge the help provided by the staff of the Honest Broker Service (HBS) within the Business Services Organisation Northern Ireland (BSO). The HBS is funded by the BSO and the Department of Health (DoH). The authors alone are responsible for the interpretation of the data and any views or opinions presented are solely those of the author and do not necessarily represent those of the BSO.

6. Excess deaths by week of registration, age, sex, cause of death, and place of death

6.1. Context

Excess mortality is analysed by week of death, sex, age, cause of death, and place of death, to understand variation across demographic, clinical, and temporal factors, and to compare outcomes between hospitals, hospices, nursing homes, and other places of death.

6.2. Methods

Mortality data, covering the period from January 2015 to December 2023, were provided by the Northern Ireland Statistics and Research Agency (NISRA) and accessed via HSC HBS; NISRA compiles these data from daily extracts of death registration records held in the NI General Register Office's (GRO) Registration System (NIROS). These records include the date of death, date of registration, cause of death, and place of death. The mortality data were matched with individual GP registration records from the National Health Application and Infrastructure Services (NHAIS) system to obtain information on patient age and sex. Registration and cause of death information were only available for GRO records successfully matched to NHAIS records. As a result, some deceased individuals without matching records lacked information on the date of death registration, and these records (n = 2,746) were excluded from the analysis.

Three separate sets of analyses were conducted: 1) excess deaths from all causes, broken down by age group and sex; 2) excess deaths from specific causes, identified by underlying cause of death; and 3) excess deaths categorized by place of death. For the all-cause mortality analyses, a single model was applied to ensure consistency across results. For the cause-specific analyses, separate models were constructed for each cause of death listed on the death certificate, whether primary or secondary cause, since groups of causes are not necessarily mutually exclusive. Deaths were classified using the International Classification of Diseases (version 10; ICD-10) codes. These included cancer (C00 to C97), dementia and Alzheimer's disease (F01, F03, and G30), circulatory diseases (I00 to I99), ischaemic heart diseases (I20 to I25), cerebrovascular diseases (I60 to I69), influenza and pneumonia (J09 to J18), chronic lower respiratory diseases (J40 to J47), and cirrhosis and other liver diseases

(K70 to K76). The causes of death were selected based on their contribution to a significant number of deaths or their specific policy relevance [16]. For the place-of-death analyses, separate models were run for each location (hospitals, hospices and nursing homes, and ‘other places’) to account for the different factors influencing mortality in each setting.

To estimate the expected weekly number of deaths for each set of analyses (all-cause, cause-specific, and place-of-death), a quasi-Poisson regression model was used, based on historical death registration data aggregated by unique combinations of demographic characteristics. This approach follows the new Office for National Statistics (ONS) methodology for estimating excess mortality [7]. Although this methodology is still an "Official Statistics in Development", it represents an advance on earlier approaches and it is expected to undergo further changes and refinements.

Age was grouped into six age bands: 0 to 24, 25 to 49, 50 to 64, 65 to 74, 75 to 84, and 85 and over, while sex (male or female) was based on the sex reported in the NHAIS record. Expected deaths for each age-sex stratum were calculated using variables for age group, sex, a linear time trend, and a seasonal component modelled by week number. A linear trend was included to account for changes in mortality over time that are not explained by the shifts in the age structure of the population, while the seasonal component accounted for variations in mortality rates, which are typically higher in winter. The sex, trend, and seasonal terms were also interacted with the age group variable for the all-cause mortality and place of death analyses, allowing these effects to vary by age. This approach enabled more precise estimation of expected mortality by accounting for how different age groups might respond to trends and seasonal variations in mortality. For the cause of death analysis, the interaction between the seasonal term and age group was excluded, as it did not improve the fit of the model.

Additionally, population size estimates were included in the model as an offset term. These population values were derived from mid-year population data and then linearly interpolated to generate weekly estimates for each age-sex stratum [17]. Where mid-year estimates were not available (2023), the mid-year population estimates were extrapolated with population projections in each age-sex-geography stratum. For the cause of death and place of death analyses, the entire population was used as the denominator, serving as a proxy due to the unavailability of population size for specific cohorts (such as individuals with cancer or those in hospitals).

All models (all-cause, cause-specific, and place-of-death) were fitted to five years of mortality data, with a one-year lag between the end of the fitting period and the current period. This ensured that the expected number of deaths in each week was based on its own five-year baseline period. For example, to estimate the expected number of deaths in Week 1 2022, the model was fitted to data from Week 2 2016 to Week 1 2021. Individual weeks that were significantly affected by the immediate mortality impact of the COVID-19 pandemic were removed from the data when estimating expected deaths in subsequent weeks. Periods significantly impacted by pandemic-related mortality were defined as those in which COVID-19 was listed as the underlying cause of death for at least 15% of all deaths registered across the UK [7], including Weeks 14 to 22 of 2020, and Week 45 of 2020 to Week 8 of 2021. Following NISRA's approach, these periods were excluded to maintain consistency with regional mortality reporting practices. Any instances of Week 53 were re-labelled as Week 52 during model fitting and when estimating expected numbers of deaths. It was assumed that the mortality rate in a typical Week 53 would be similar to that of a Week 52. Given that Week 53 occurs roughly every five years, estimating a separate seasonal term for it was not considered practical when fitting models to five years of data.

Excess (or deficit) mortality was calculated as the difference between observed and expected deaths in each age-sex stratum for each week, with a 95% confidence interval (95% CI). The estimated total number of excess deaths for 2022 and 2023 was obtained by summing excess (and deficit) deaths across all age groups and sexes.

It is important to note that differences exist between the official excess death figures reported by NISRA and the estimates presented in this report. These variations arise from differences in data samples and sources. Firstly, the date of death information used in this study was sourced from both the GP registration system and GRO data. However, registration and cause of death details were only available for GRO records that successfully matched to the GP register. As a result, some deceased individuals may have lacked matching records and were therefore excluded from this analysis. Secondly, the 2023 mid-year population and migration estimates (MYEs) for NI, published in September 2024, were incorporated into NISRA's calculations of expected deaths. In contrast, this report uses mid-year population estimates that were extrapolated from population projections for each age-sex-geography stratum, as the official 2023 MYEs were not available at the start of the project.

6.3. Results

6.3.1. Excess all-cause mortality

Weekly number of observed and expected deaths are presented in Figure 1. Estimates of excess all-cause mortality are presented separately for 2022 and 2023, broken down by population subgroups (age and sex). The results show variations in excess (i.e., expected deaths < observed deaths) and deficit (i.e., expected deaths > observed deaths) mortality over the observed period (Figure 2).

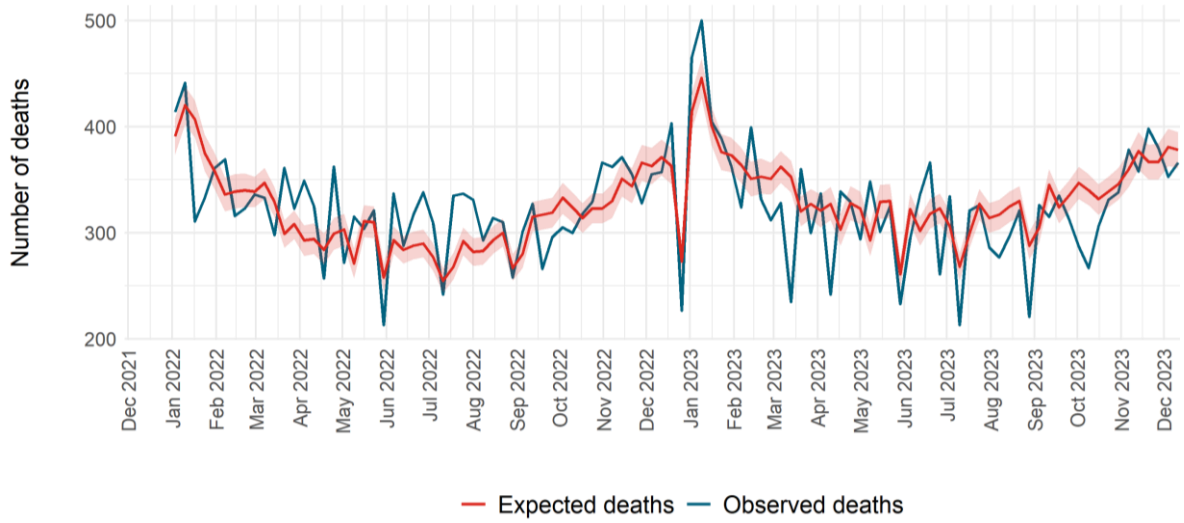


Figure 1. Weekly number of observed and expected deaths during the period 2022-23.

Between Week 1 2022 (ending 7 January 2022) and Week 52 2022 (ending 30 December 2022), there were an estimated 320 (95% CI: 214 to 426) excess deaths in NI. The highest numbers of excess deaths occurred from mid-March to mid-April, June to August, and in November 2022 (Figure 2). Of the total 320 excess deaths, 535 (95% CI: 465 to 605) were in females, while males experienced a mortality deficit of 213 (95% CI: -292 to -134), representing 213 fewer deaths than expected.

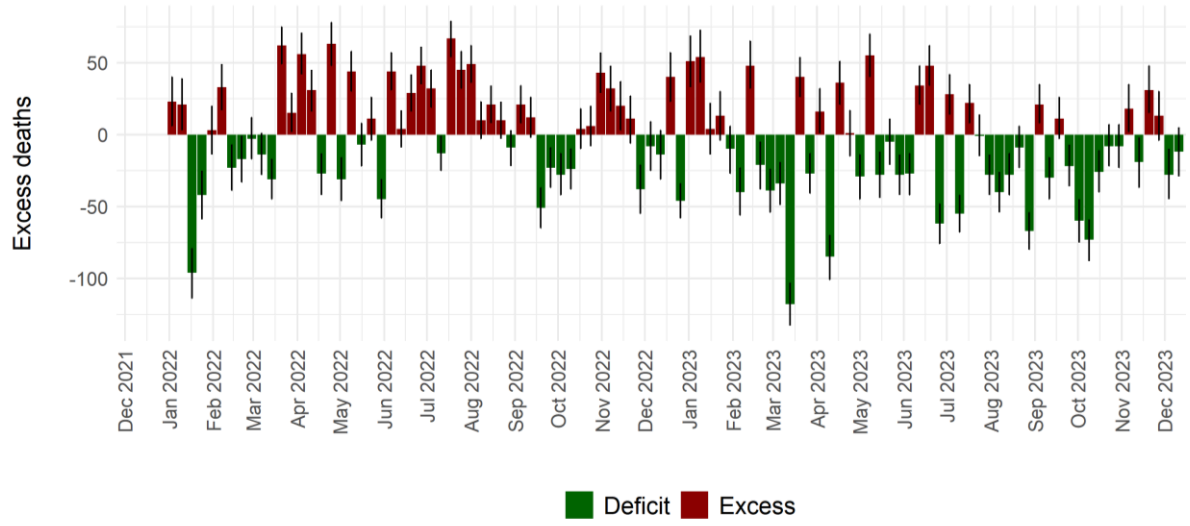


Figure 2. Weekly number of excess deaths during the period 2022-23.

There was a steep upward gradient in the death count with increasing age: estimated excess deaths ranged from -111 (95% CI: -136 to -86) for ages 15-24 to 219 (95% CI: 155 to 283) for ages 85 years and over (Figure 3). All-cause mortality was reported at 3.8% (95% CI: 2.0% to 5.7%) above expected levels for those aged 65-74 and 3.6% (95% CI: 2.3% to 4.9%) for 75-84-year-olds. When considering both sex and age, the highest excess mortality, 8.7% higher than expected, was observed among females over 65. In contrast, males aged 75 and older experienced a mortality deficit of -206 (95% CI: -262 to -150), 3.5% below expected levels.

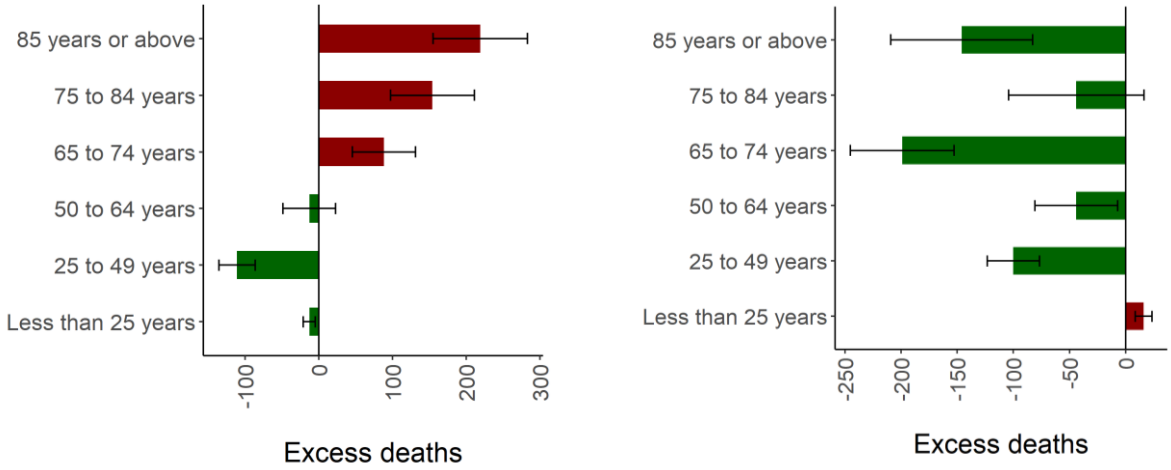


Figure 3. Total number of excess deaths by age in: a) 2022 (Weeks 1–52) and b) 2023 (Weeks 1–50).

Between Week 1 2023 (ending 7th January 2023) and Week 50 2023 (ending 15th December 2023), the highest mortality excess was observed in January. In contrast, mortality deficits were observed in the following months (Figure 2). The estimated all-cause excess death counts were negative at -523 (95% CI: -631 to -414) for both sexes combined, -686 (95% CI: -767 to -605) for males, and positive at 169 (95% CI: 98 to 240) for females. This represents -3.1% and -7.8% below the expected levels overall and for males, respectively, while being 2.1% higher than expected for females. Figure 4 shows sex differences in excess mortality over time.

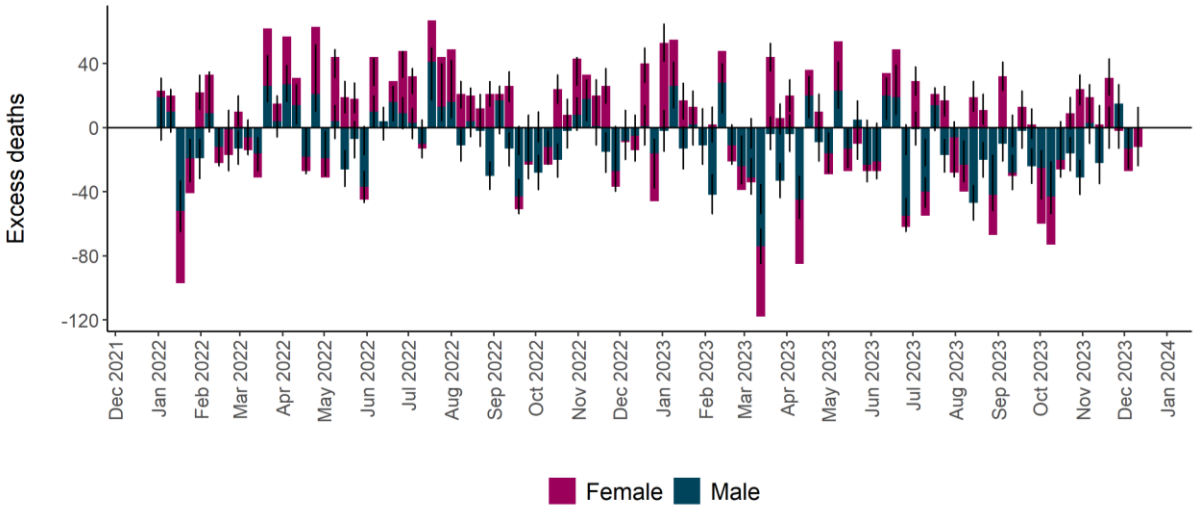


Figure 4. Weekly excess deaths by sex during the period 2022-23.

When considering both sex and age, there was no statistically significant excess mortality in males or females under 25 years of age (9 excess deaths overall, 11.7% higher than expected) (Table 1). In the older age groups, sex differences in excess mortality were observed and had contrasting patterns. In the 75-84 and 85+ age groups, sex differences in excess mortality were particularly evident. Among females, excess deaths were estimated at 104 (95% CI: 67 to 141) for those aged 75-84 (5.2% higher than expected) and 119 (95% CI: 70 to 168) for those aged 85 and older (3% higher than expected). In contrast, males experienced a deficit in all-cause mortality, with estimates of -142 (95% CI: -190 to -94) for ages 75-84 (5.4% lower than expected) and -268 (95% CI: -308 to -228) for ages 85 years and over (8.3% lower than expected).

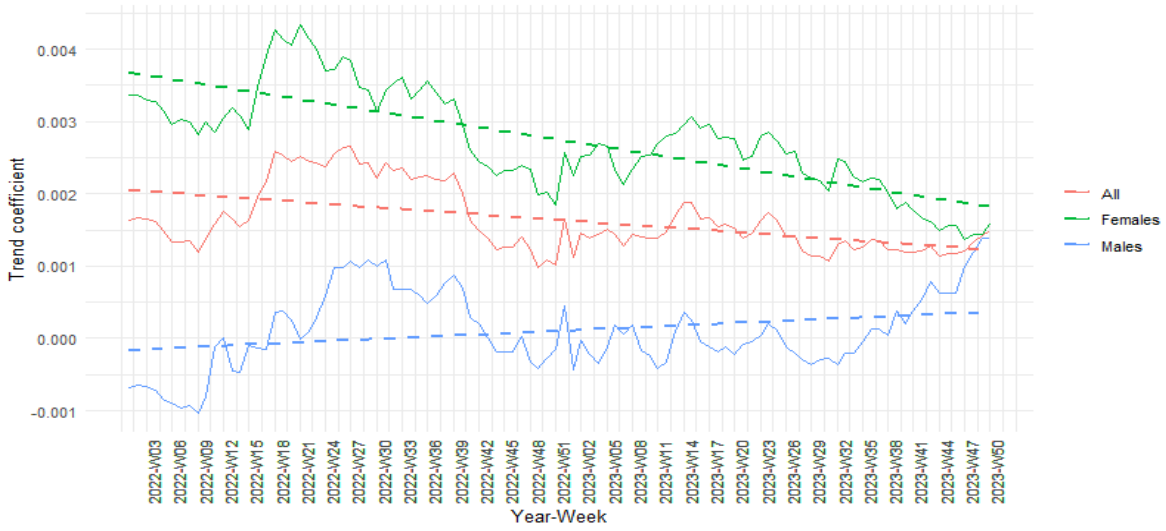


Figure 5. Trend coefficients of expected deaths by week, estimated separately for males and females.

To explore the reason behind this difference in sex-specific excess mortality, we examined the linear trend component of our model, which captures gradual changes in baseline mortality over time (Figure 5). Because the model predicts expected deaths on a weekly basis, it is fitted separately for each week, meaning the trend coefficient is not fixed, but varies week by week. By capturing these evolving patterns, the trend helps refine estimates of expected deaths beyond what can be explained by seasonal fluctuations or demographic structure. In line with the updated ONS methodology, the trend coefficient in our pooled model is applied uniformly across both sexes, under the assumption that men and women share the same underlying trajectory in mortality risk over time.

To test whether this trajectory differs between males and females, we conducted additional analyses by fitting separate models for each sex, allowing the trend coefficients to vary independently. This approach allowed us to examine whether there were distinct trends in mortality risk for each sex, providing a more detailed understanding of potential differences over time and their implications for excess mortality estimates. Throughout the study period, trend coefficients for females were consistently higher than those observed in the pooled model. They ranged from 0.0019 to 0.0043 in 2022, and from 0.0014 to 0.0031 in 2023, corresponding to weekly changes in expected mortality ranging from a 0.19% to 0.43% increase in 2022, and from a 0.14% to 0.31% increase in 2023. It is important to note that these values represent the observed minimum and maximum for each year, rather than a linear change from the beginning to the end of the study period. For males, the weekly trend coefficients ranged from -0.001 to 0.0011 in 2022, and from -0.0004 to 0.0014 in 2023, corresponding

to a 0.1% weekly decrease to a 0.11% weekly increase in expected deaths in 2022, and a 0.04% decrease to a 0.14% increase in expected deaths in 2023.

Trend coefficients for the pooled model were consistently lower for females and higher for males. In 2022, they ranged from 0.001 to 0.0027, corresponding to a 0.1% to 0.27% weekly increase in expected deaths. In 2023, they ranged from -0.0011 to 0.0019, corresponding to a 0.11% decrease to a 0.19% weekly increase in expected deaths. As a result, the pooled model *underestimated* expected deaths for females, inflating estimates of excess mortality, while for males, it *overestimated* expected deaths, which likely led to deficit mortality estimates. Such diverging patterns are likely, at least in part, due to the discrepancy between the pooled trend and the sex-specific trends.

To better assess the overall direction of change in the trend coefficients, we applied smoothing to the weekly estimates from each of the three models, i.e. pooled, female-only, and male-only. This approach helped reveal broader patterns beyond short-term week-to-week variation. To formally evaluate these differences, we fitted a linear regression model in which the trend coefficient was the outcome, and time and model type were included as predictors, along with their interaction. This allowed us to test for differences in both the baseline level and the evolution of the trend coefficients over time across the three models. The results confirmed that the female-only model had a significantly higher baseline trend coefficient than the pooled model ($p < 0.0001$) and a more pronounced downward slope ($p < 0.0001$), indicating a decelerating trend in expected mortality. In contrast, the male-only model showed a significantly lower baseline ($p < 0.0001$) and a significant upward trajectory ($p < 0.0001$), pointing to a gradually increasing trend in male mortality risk over time. These findings confirm that the assumption of a common time trend across sexes, as used in the pooled model, may obscure important sex-specific mortality dynamics.

Table 1. Excess all-cause number of deaths and relative mortality in % (95% confidence limits shown in brackets) for males and females by age group in 2022 (Weeks 1–52) and 2023 (Weeks 1–50). Numbers in the table highlighted in red or green indicate statistically significant excess or deficit deaths, respectively.

	2022				2023			
Age	**Male**		**Female**		**Male**		**Female**	
0 to 24	-7 (-14 to -0.4)	-15.2% (-30% to -1%)	-11 (-16 to -6)	-30% (-43% to -17%)	7 (1 to 13)	16% (2% to 30%)	2 (-2 to 6)	6% (-7% to 19%)
25 to 49	-91 (-113 to -69)	-20.0% (-25% to -15%)	-29 (-40 to -18)	-13% (-18% to -8%)	-90 (-111 to -69)	-21% (-26% to -16%)	-15 (-25 to -5)	-7% (-12% to -2%)
50 to 64	26 (-3 to 55)	3% (-0.3% to 6%)	-43 (-64 to -22)	-6% (-10% to -3%)	-44 (-74 to -14)	-4% (-7% to -1%)	5 (-17 to 27)	1% (-2% to 4%)
65 to 74	52 (17 to 87)	4% (1% to 6%)	33 (8 to 58)	3% (1% to 6%)	-150 (-188 to -112)	-10% (-12% to -7%)	-46 (-73 to -19)	-4% (-7% to -2%)
75 to 85	-37 (-82 to 8)	-2% (-3% to 0.3%)	192 (158 to 226)	10% (9% to 12%)	-142 (-190 to -94)	-5% (-7% to -4%)	104 (67 to 141)	5% (3% to 7%)
85+	-169 (-209 to -129)	-5.0% (-6% to -4%)	384 (334 to 434)	9% (8% to 10%)	-268 (-308 to -228)	-8% (-10% to -7%)	119 (70 to 168)	3% (2% to 4%)

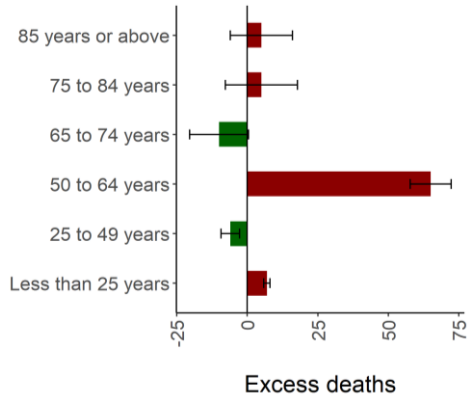
6.3.2. Excess mortality by cause of death

Excess mortality by cause of death was investigated, focusing on cancer, influenza and pneumonia, chronic lower respiratory diseases, liver diseases, dementia and Alzheimer's disease, circulatory diseases, including ischaemic heart diseases and cerebrovascular diseases which are subsets of circulatory diseases. For cancer, two separate analyses of excess mortality were performed. The first analysis encompassed all cancers (C00-C97), providing an overview of cancer-related mortality, including primary, metastatic, and unspecified cancers. The second analysis focused specifically on primary cancers categorized by their anatomical origin (ICD10 codes C00 to C75) that typically follow distinct clinical pathways. This distinction allows for a more detailed investigation of excess mortality directly attributable to primary cancers, excluding the potential confounding effects of cancer spread or other systemic complications.

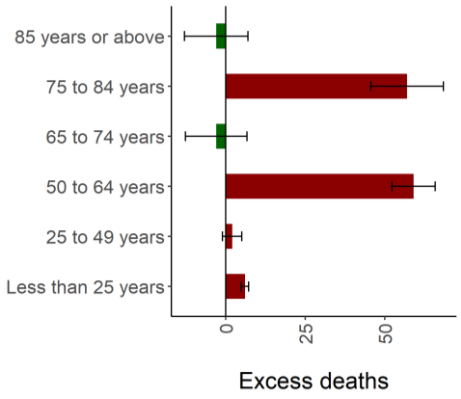
In 2022, several causes showed a relative excess greater than that seen in deaths from all-causes (1.9%) over the same period (week ending 7 January 2022 – week ending 30 December 2022), namely: influenza and pneumonia (10.3%, (95% CI: 9.7% to 10.9%)), cerebrovascular diseases (3.9%, (95% CI: 3.2% to 4.6%)), dementia and Alzheimer's disease (4.3%, (95% CI: 3.8% to 4.8%)), and primary cancers (2.3%, (95% CI: 1.9 to 2.7)). Excess deaths were also reported for chronic lower respiratory diseases (1.2%, (95% CI: 0.6% to 1.9%)), circulatory diseases (1.8%, (95% CI: 1.4% to 2.2%)), ischaemic heart diseases (1.6%, (95% CI: 1.1% to 2.0%)), and all cancers including primary, metastatic, systemic, and unspecified cancers (1%, (95% CI: 0.6 to 1.4)). Relative mortality deficits of -7.6%, (95% CI: -8.7% to -6.4%) were observed for cirrhosis and other liver diseases.

Excess deaths for influenza and pneumonia, chronic lower respiratory diseases, circulatory diseases, including ischaemic heart diseases and cerebrovascular diseases, and dementia and Alzheimer's disease were highest among individuals aged 75 years old and older, while cancers, including primary cancers, accounted for most excess deaths in the 50-64 age group (Figure 6). There were significant sex differences in excess/deficit deaths observed (Table 2). Among females, excess deaths were recorded across all causes of deaths, except liver diseases, with the highest excess in influenza and pneumonia at 13.6% (nearly double that of men), cerebrovascular disease at 5.3% (five times higher than males), chronic lower respiratory diseases at 7.4% (a deficit of -4.3% in males), circulatory

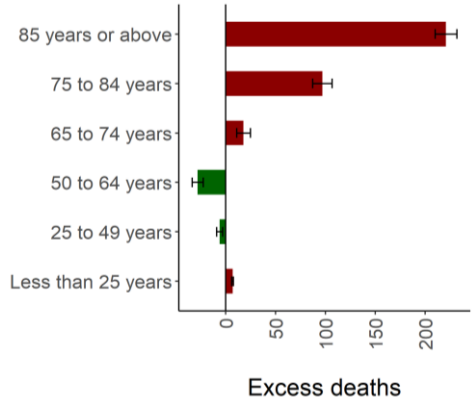
a) All cancers



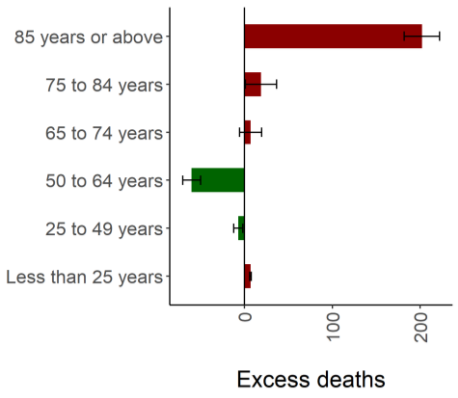
b) Primary cancers



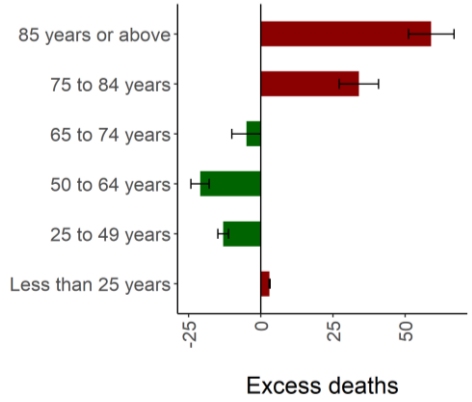
c) Influenza and pneumonia



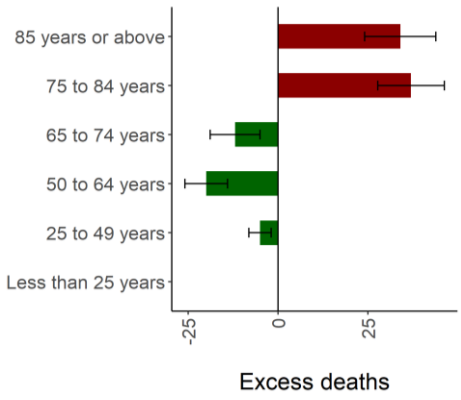
d) Circulatory diseases



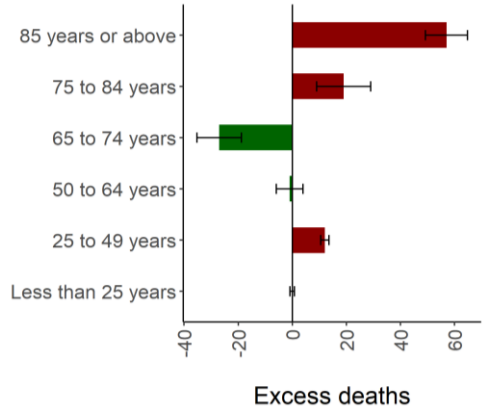
e) Cerebrovascular diseases



f) Ischaemic heart diseases



g) Chronic lower respiratory diseases



h) Dementia and Alzheimer's disease

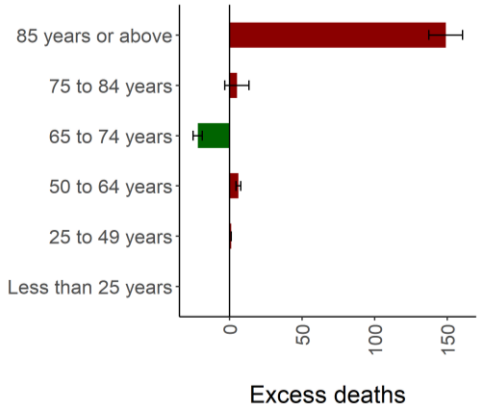


Figure 6. Excess mortality by cause of death in 2022.

Table 2. Excess number of deaths and relative mortality in % (95% confidence limits shown in brackets) by cause of death in 2022 and 2023. The 2022 data cover Weeks 1 to 52, while the 2023 data correspond to Weeks 1 to 50.

	2022				2023			
Underlying cause of death	**Female**		**Male**		**Female**		**Male**	
All cancers	38 (24 to 52)	1.5% (1.0% to 2.1%)	15 (1 to 31)	0.5% (0.04% to 1.1%)	45 (32 to 58)	1.8% (1.3% to 2.4%)	-202 (-217 to -187)	-6.8% (-7.3% to -6.3%)
Primary cancers	53 (40 to 66)	2.5% (1.9% to 3.1%)	45 (30 to 60)	1.8% (1.2% to 2.4%)	38 (26 to 50)	1.8% (1.2% to 2.3%)	-145 (-159 to -131)	-5.7 (-6.2% to -5.1%)
Circulatory diseases	352 (332 to 372)	8.7% (8.2% to 9.2%)	-190 (-215 to -165)	-4.0% (-4.5% to -3.4%)	180 (161 to 199)	4.4% (3.9% to 4.8%)	-448 (-471 to -425)	-9% (-9.4% to -8.5%)
Ischaemic heart diseases	115 (107 to 123)	9.4% (8.8% to 10.1%)	-68 (-83 to -54)	-3.2% (-3.9% to -2.5%)	-31 (-39 to -23)	-2.6% (-3.2% to -1.9%)	-240 (-254 to -226)	-11% (-11.5% to -10.3%)
Cerebrovascular diseases	49 (41 to 58)	5.3% (4.4% to 6.3%)	9 (0.4 to 18)	1.0% (0.04% to 2.0%)	37 (29 to 45)	4% (3.2% to 4.9%)	-67 (-75 to -59)	-7.3% (-8.3% to -6.4%)
Influenza and pneumonia	186 (174 to 198)	13.6% (12.7% to 14.4%)	116 (103 to 129)	7.8% (6.9% to 8.7%)	101 (90 to 112)	7.3% (6.5% to 8.1%)	-66 (-79 to -53)	-4.2% (-5.0% to -3.4%)
Chronic lower respiratory diseases	86 (75 to 97)	7.4% (6.4% to 8.3%)	-57 (-69 to -45)	-4.3% (-5.2% to-3.4 %)	15 (5 to 25)	1.2% (0.4% to 2.0%)	-92 (-103 to -81)	-6.7% (-7.5% to -5.9%)
Cirrhosis and other liver diseases	-7 (-11 to -3)	-2.6 (-4.1% to -1.0%)	-45 (-52 to -39)	-11.2 (-12.8% to -9.6%)	-15 (-19 to -11)	-5.3% (-6.7% to -3.9%)	-35 (-41 to -29)	-8.7% (-10.1% to -7.3%)

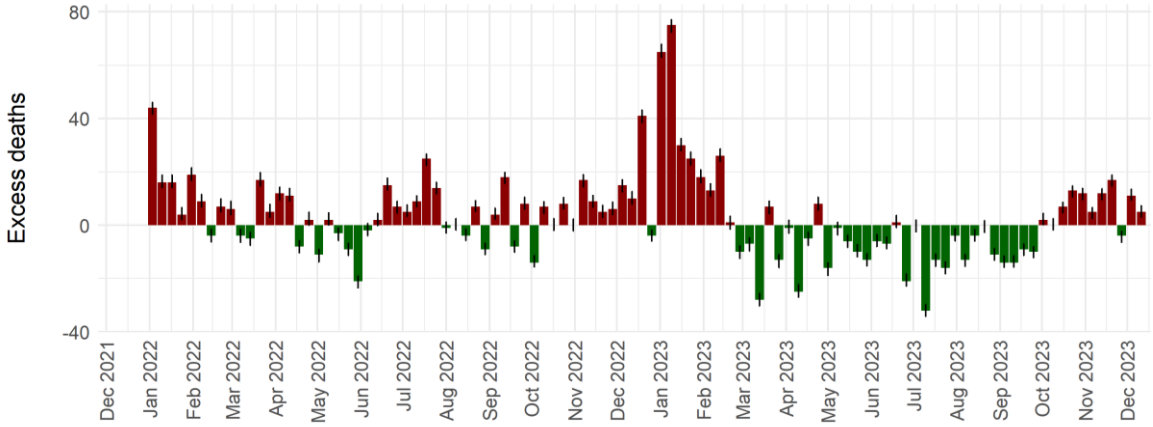
diseases at 8.7% (double that of men), and ischaemic heart disease at 9.4%, compared to a deficit of -3.2% in males.

Considering 2023 overall, deaths due to influenza and pneumonia had the greatest number of deaths above expected (1.4%, (95% CI: 0.8% to 1.9%)), though it was significantly lower compared to 2022 (10.3%). However, a distinctive pattern was observed at the beginning of 2023, with significant relative excess mortality of 58.9% in the first seven weeks of the year (equivalent to 252 excess deaths), followed by deficit deaths during most of the subsequent weeks (Figure 7). Toward the end of 2023, there were additional weeks of excess deaths, although these were less substantial compared to the earlier peak. The relative deficits were observed for other causes of death, including chronic lower respiratory diseases (-2.8%, (95% CI: -3.3% to -2.2%)), circulatory diseases (-2.9%, (95% CI: -3.2% to -2.6%)), ischaemic heart diseases (-8.0%, (95% CI: -8.5% to -7.5%)), cerebrovascular diseases (-1.3%, (95% CI: -1.9% to -0.6), and all cancers (-3.0%, (95% CI: -3.4% to -2.6%)). For chronic lower respiratory diseases and circulatory diseases, including ischaemic heart diseases, the pattern of excess deaths through the year was similar to that for influenza and pneumonia: higher excess at the start of the year, reducing through the first seven weeks of 2023 and several weeks of excess deaths at the end of the year, with deficit mortality reported in the majority of the intervening weeks (Figure 7).

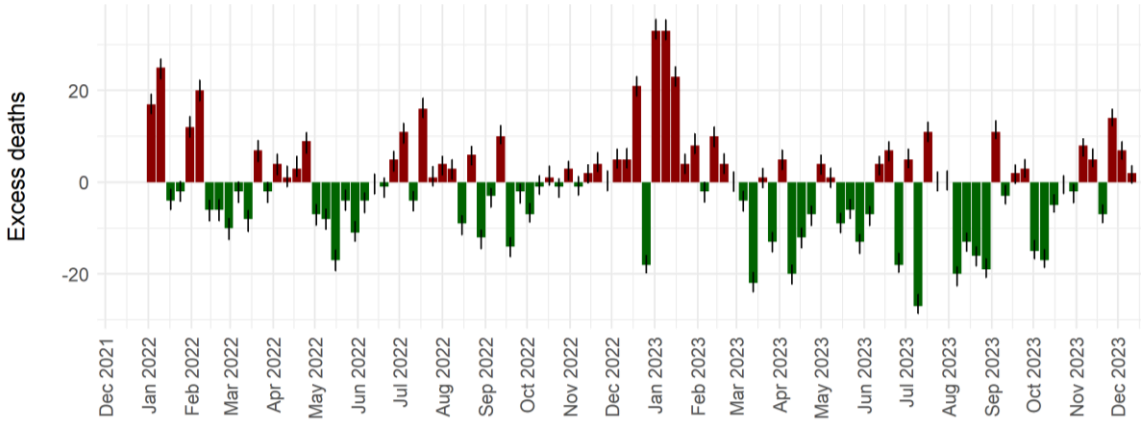
In 2023, as in 2022, excess deaths from all cancers and primary cancers, were again most pronounced in the 50-64 age group and among those less than 25 years old (Figure 8). For influenza and pneumonia, circulatory diseases, and cerebrovascular diseases, excess mortality was observed among individuals aged 85 years and older, while the most significant deficit in deaths occurred in those aged 50-74 years. For ischaemic heart disease, deficit mortality was recorded across all age groups. For liver disease, deficits were noted among individuals aged 50 years and older, while excess deaths were seen in the 25-49-year age group.

Sex differences in excess mortality remained substantial in 2023, with estimates of deficit deaths across all cancers, circulatory diseases, cerebrovascular diseases, and influenza and pneumonia for males, while females experienced excess deaths for these same causes (Table 2).

a) Influenza and pneumonia



b) Chronic lower respiratory diseases



c) Ischemic heart diseases

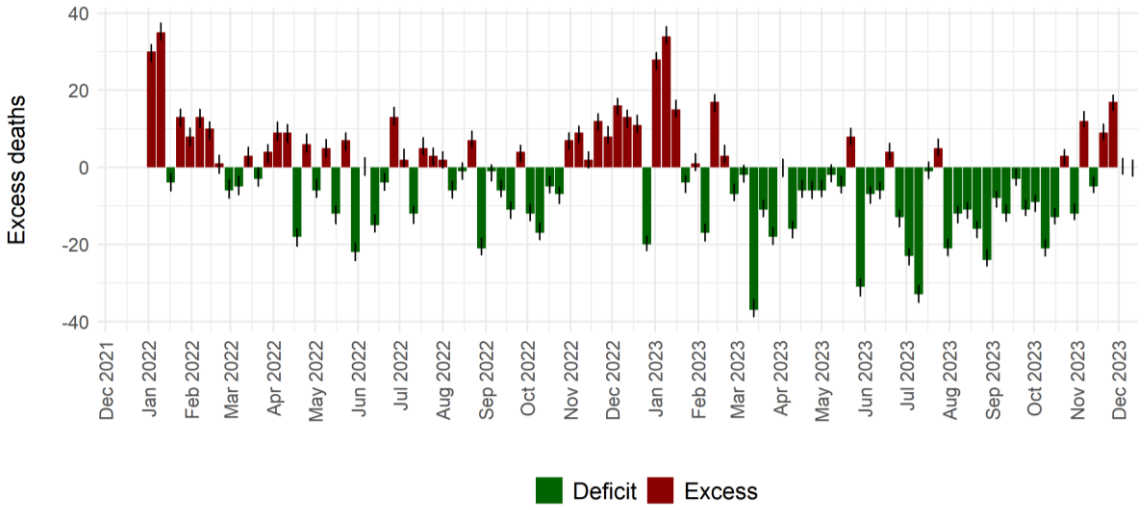


Figure 7. Excess deaths due to a) influenza and pneumonia, b) chronic lower respiratory diseases, and c) ischaemic heart diseases in the period 2022-2023. The 2022 data cover Weeks 1 to 52, while the 2023 data correspond to Weeks 1 to 50.

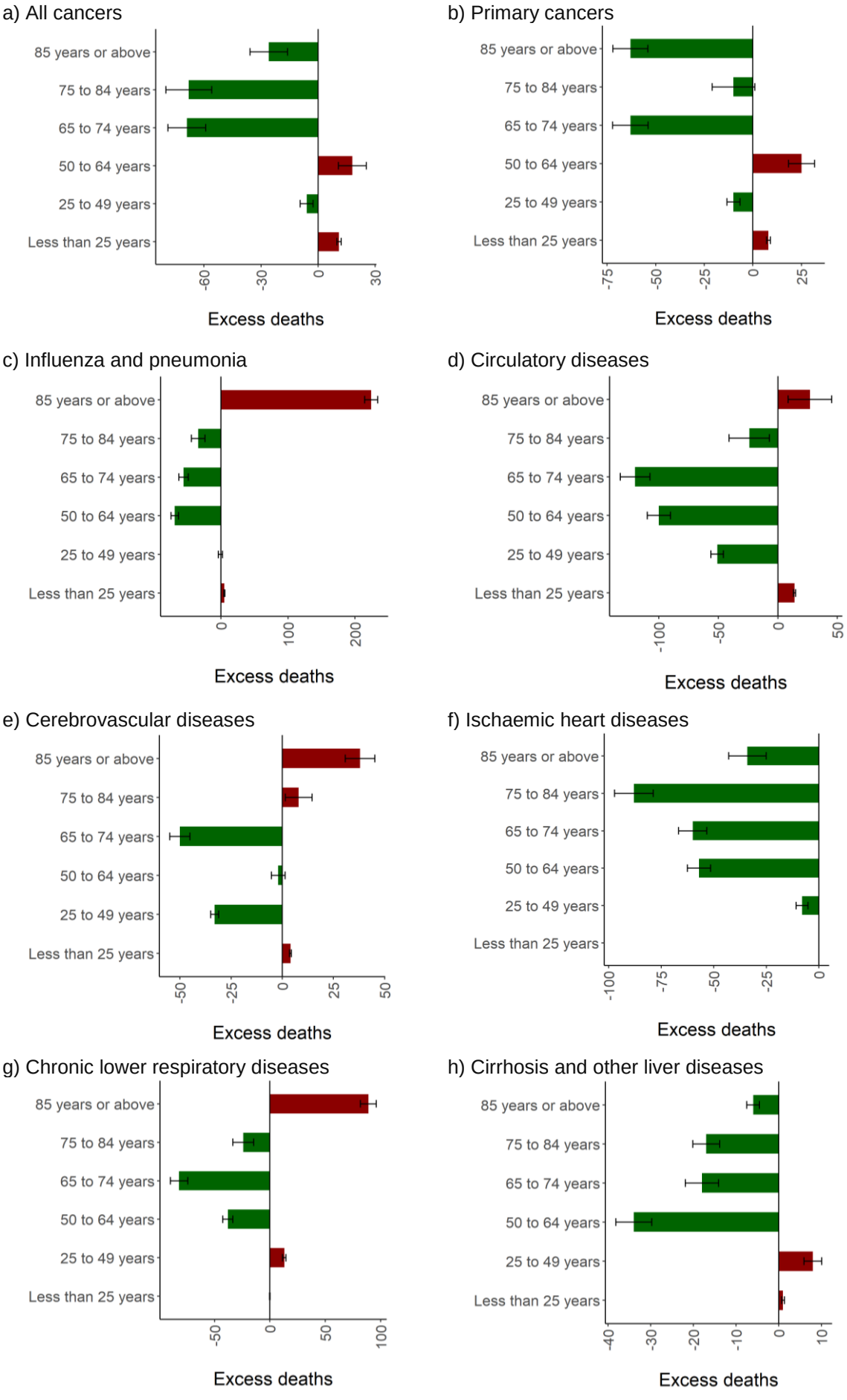


Figure 8. Excess mortality by cause of death in 2023

6.3.3. Excess mortality by place of death

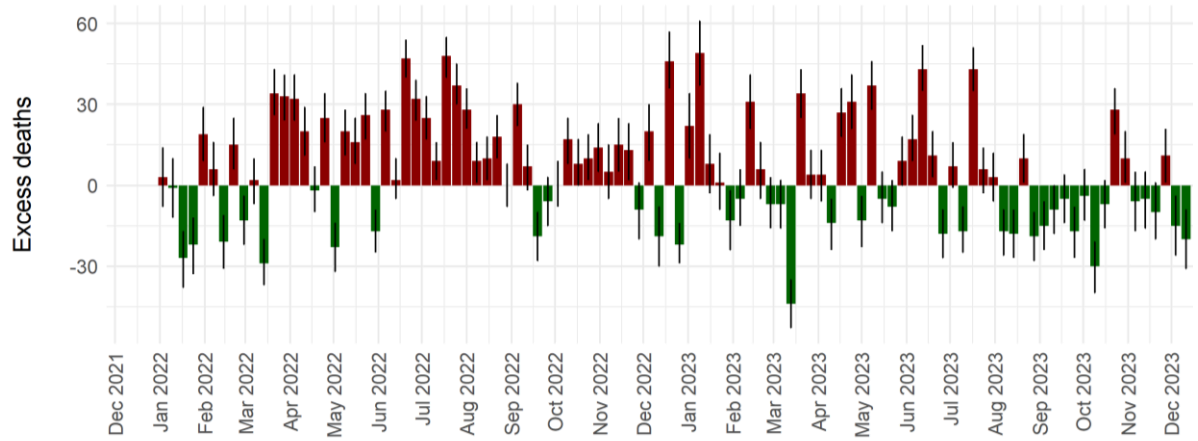
In 2022, most deaths occurred in hospitals (7,793), followed by 'other places' (5,725), and nursing homes/hospices (3,294). Excess mortality was observed in hospitals (6.8% (95% CI: 6.0% to 7.7%)) and in hospices and nursing homes (2.9% (95% CI: 1.7% to 4.1%)), while 'other places' experienced deficit mortality of -5.5% (95% CI: -6.6% to -4.4%) (Figure 9).

Excess mortality in hospitals was 4.5% (95% CI: 3.2% to 5.7%) for males and 9.6% (95% CI: 8.3% to 10.8%) for females, with females aged 65 and older experiencing over 3 time more excess deaths than males (Figure 10). This was significantly different from the sex-specific mortality observed in nursing homes/hospices. Here, males experienced a deficit in mortality, with -1.3% (95% CI: -3.0% to 0.4%) fewer deaths than expected, while females had excess mortality of 5.9% (95% CI: 4.3% to 7.5%). In particular, the most significant excess mortality for females was observed in the 85 and older age group at 4.8% (95% CI: 3% to 6.6%), whereas males in the same age group had the highest deficit mortality, at -6.4% (95% CI: -8.2% to -4.5%).

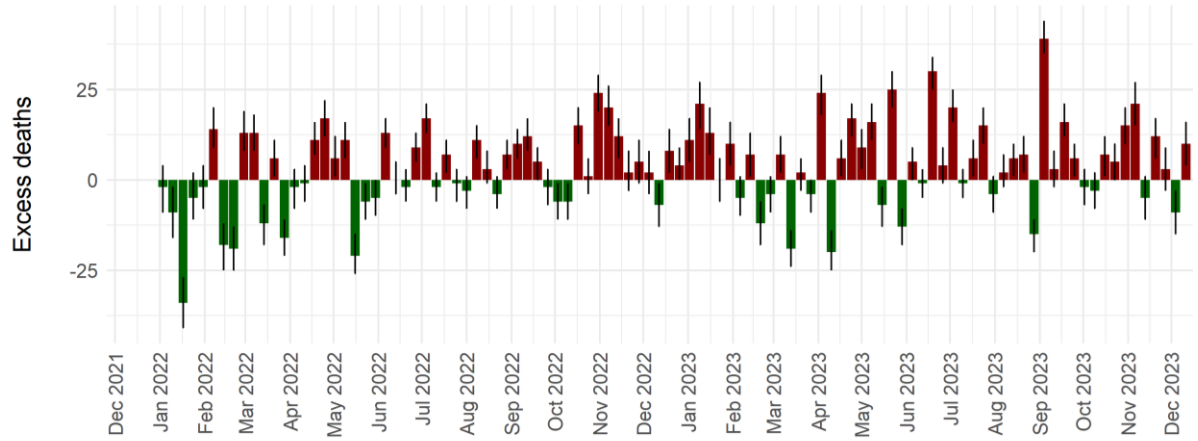
While over two-thirds of deaths in 2022 occurred in hospitals and nursing homes/hospices, the sex distribution of excess deaths in each setting differed significantly. While females experienced excess mortality in both hospitals and nursing homes/hospices, males had excess mortality only in hospitals, and at significantly lower rates than females (Figure 11). The pattern in ‘other places’ mirrors the sex-specific distribution of excess (deficit) deaths observed in nursing homes/hospices. In both settings, females experienced more deaths than expected, while males reported a deficit mortality. Accordingly, males experienced a deficit in mortality of -11.8% (95% CI: -13.3% to -10.3%) in ‘other places’, while females had excess mortality of 3.1% (95% CI: 1.6% to 4.5%), driven predominantly by excess mortality in female age groups 75 years and older (Figure 11).

In 2023, most deaths occurred in hospitals (7,671), followed by ‘other places’ (5,400), and nursing homes/hospices (3,294). Excess mortality was highest in nursing homes/hospices at 9.1% (95% CI: 7.9% to 10.4%), compared to a more modest 1.4% (95% CI: 0.5% to 2.3%) in hospitals, while ‘other places’ experienced a notable deficit mortality of -15.2% (95% CI: -16.2% to -14.1%) (Figure 9).

a) Hospitals



b) Hospices and Nursing Homes



c) Other Places

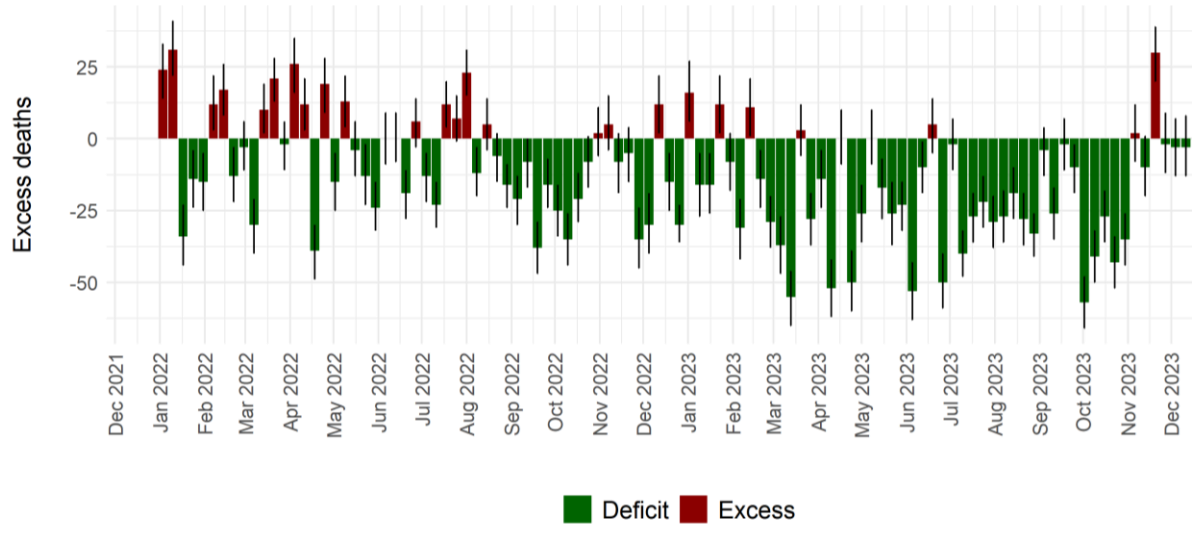
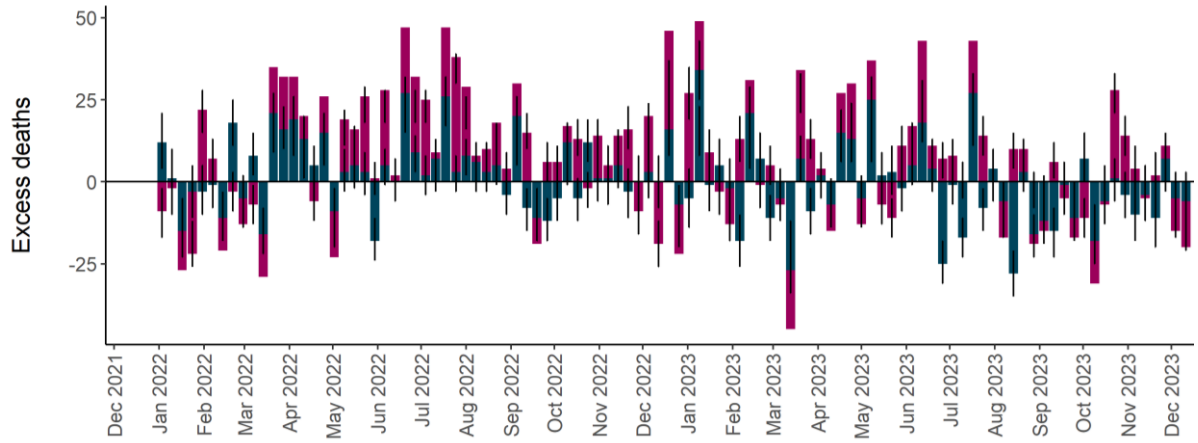
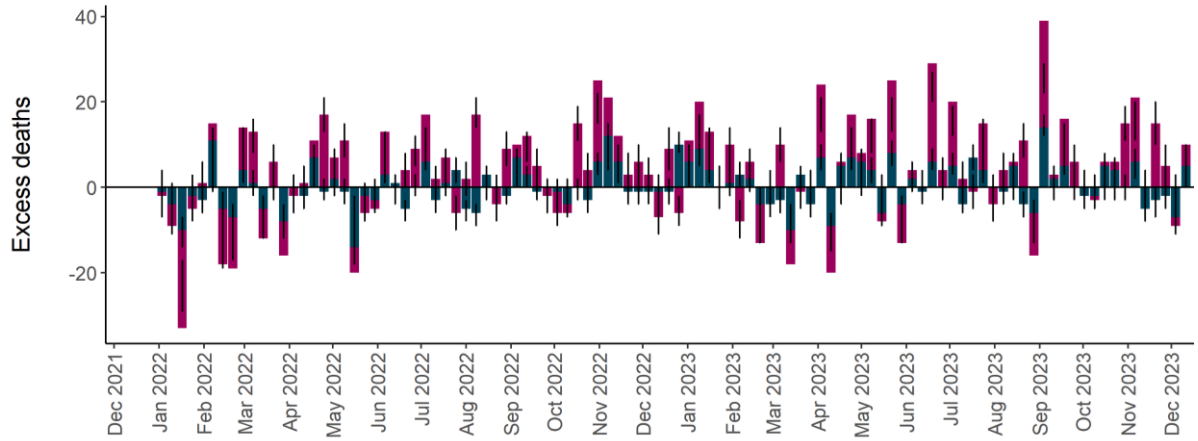


Figure 9. Excess death counts by place of death categorized as a) 'Hospitals', b) 'Hospices and Nursing Homes', and c) 'Other Places' in the period 2022-2023. The 2022 data cover Weeks 1 to 52, while the 2023 data correspond to Weeks 1 to 50.

a) Hospitals



b) Hospices and Nursing Homes



c) Other Places

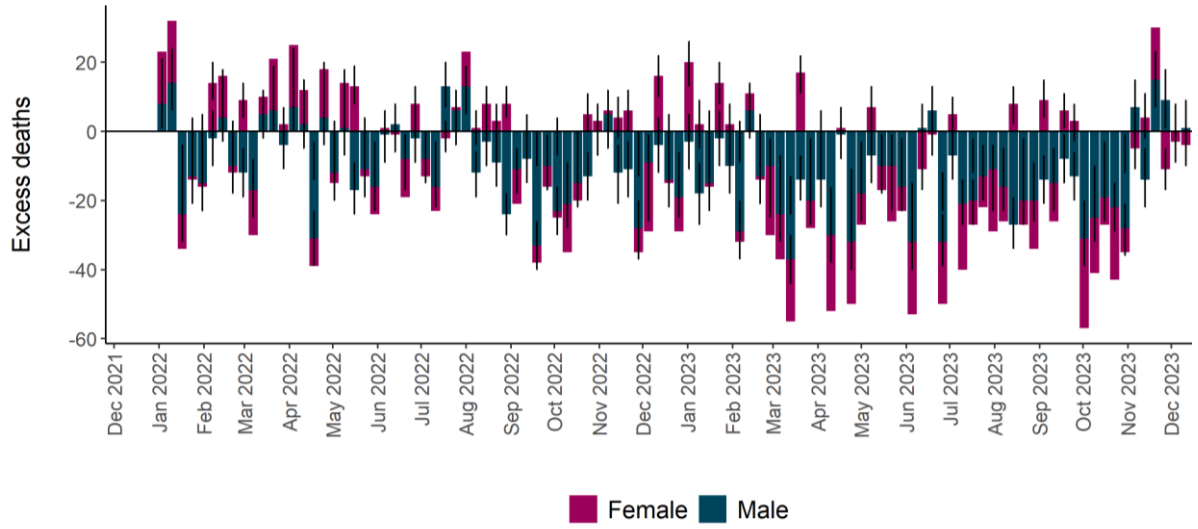
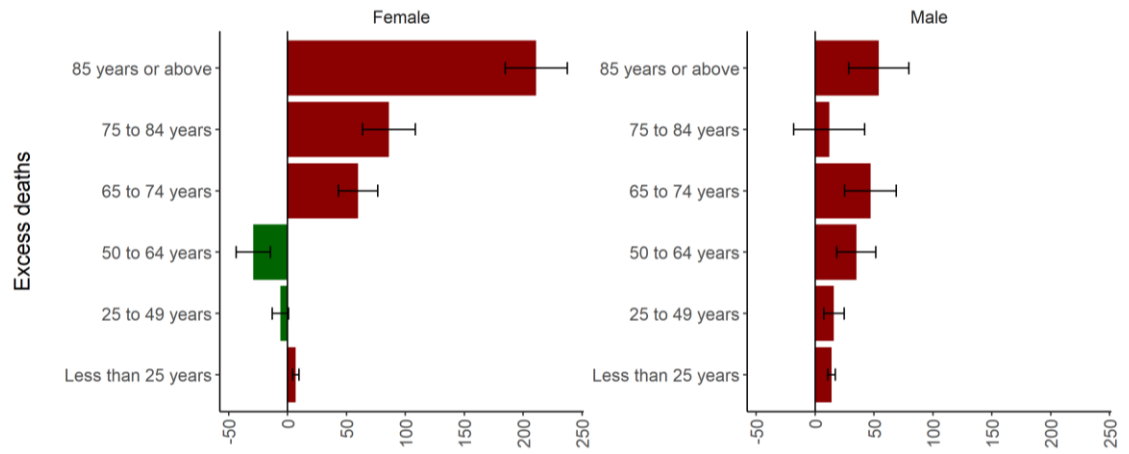


Figure 10. Sex differences in excess mortality rate by place of death categorized as a) 'Hospitals', b) 'Hospices and Nursing Homes', and c) 'Other Places' in the period 2022-2023. The 2022 data cover Weeks 1 to 52, while the 2023 data correspond to Weeks 1 to 50.

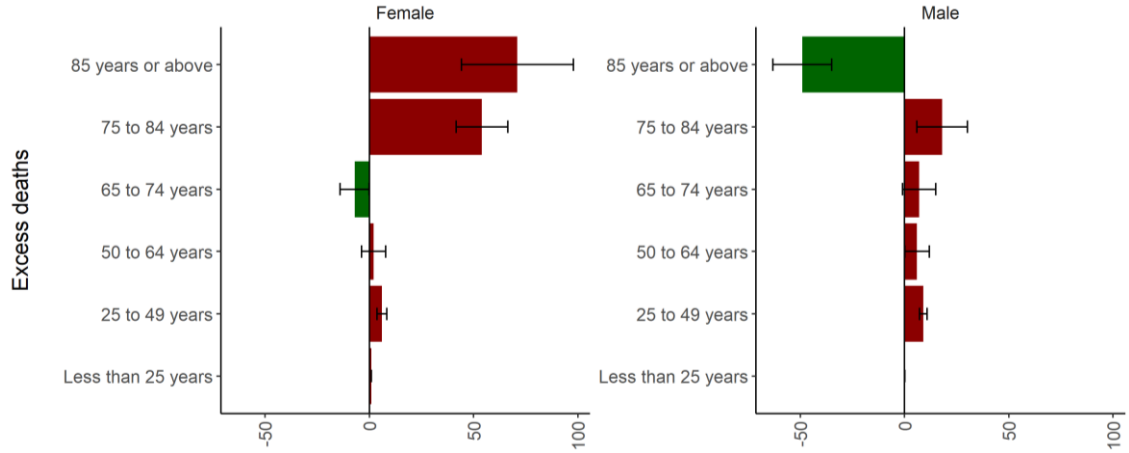
In hospitals, excess mortality trends varied across the year, with most weeks of excess deaths observed until the end of August (Figure 9), predominantly in older age groups (75–84 and 85+ years). When both age and sex were considered, females aged 75 years and older accounted for the highest excess mortality (9.5%) (Figure 12). In nursing homes/hospices, excess deaths were reported for all age groups except those under 25 years. Females experienced four times more excess deaths than males in this setting, with the highest relative excess mortality again observed among females aged 75 and older (11.5%) (Figure 12).

In contrast, the 'other places' category recorded deficit mortality across all age groups, with the highest deficits occurring in individuals aged 75 and older (-17% (95% CI: -18.6% to -15.4%) lower than expected). Only six weeks in 2023 saw excess deaths in this setting, four of which were in winter months (Figure 9). By sex, both males and females experienced deficit mortality, though the deficit for males was 2.5 times greater than that for females. Age-sex patterns in mortality showed that deficit mortality increased with age for both males and females, however for females, deficits were most pronounced from age 75 onward (Figure 12).

a) Hospitals



b) Hospices and Nursing Homes



c) Other Places

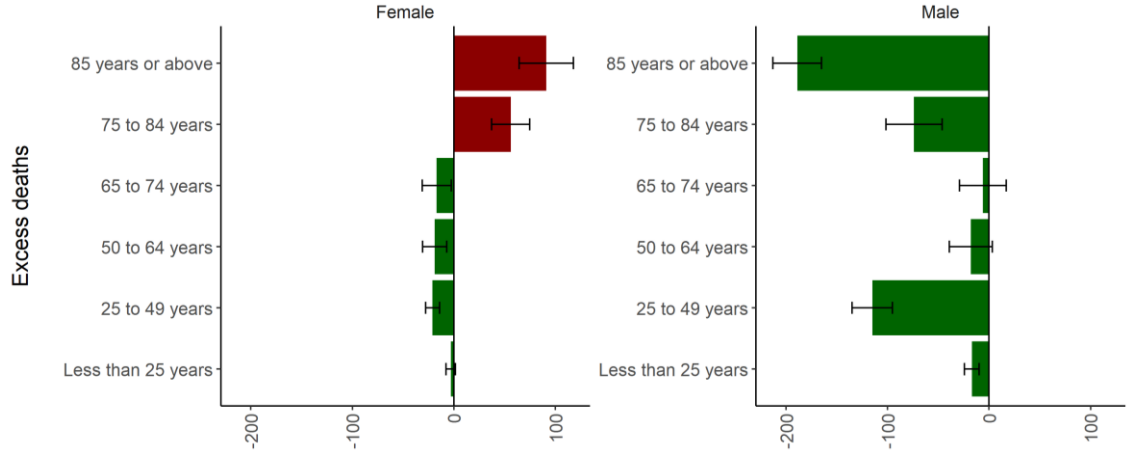
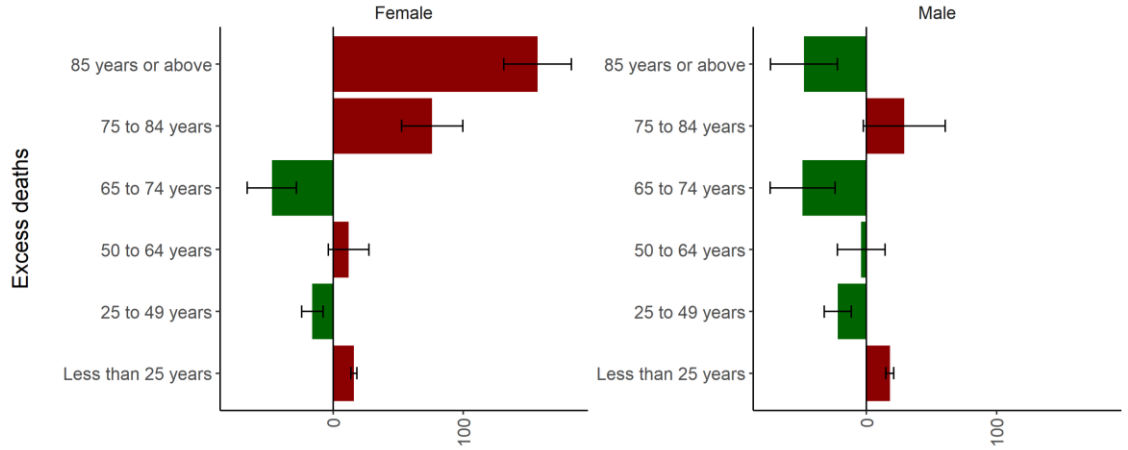
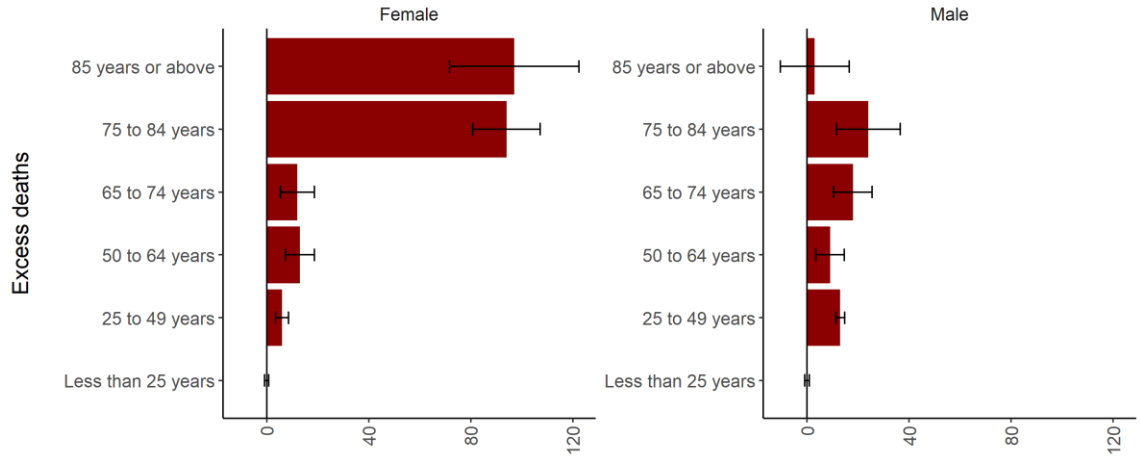


Figure 11. Excess mortality by sex and age for a) 'Hospitals', b) 'Hospices and Nursing Homes', and c) 'Other Places' in 2022 (Weeks 1 to 52).

a) Hospitals



b) Hospices and Nursing Homes



c) Other Places

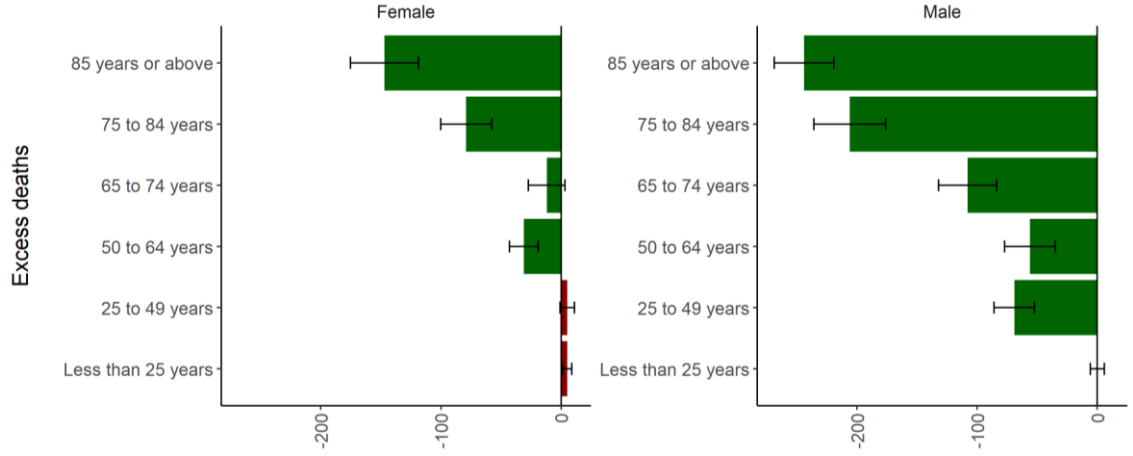


Figure 12. Excess mortality by sex and age for a) 'Hospitals', b) 'Hospices and Nursing Homes', and c) 'Other Places' in 2023 (Weeks 1 to 50).

7. The impact of the COVID-19 pandemic on cancer deaths

7.1. Context

The COVID-19 pandemic disrupted healthcare systems worldwide, with potential implications for cancer diagnosis, treatment, and survival [18]. A reduction in referrals for urgent cancer diagnoses was reported in April 2020, which likely resulted in delayed diagnoses and missed opportunities for earlier treatment [19,20]. This analysis examines short-term survival in patients with cancer to understand the pandemic's impact on cancer outcomes and assess whether disruptions in care led to significant variations in survival rates across cancer types.

7.2. Method

The analysis was conducted using data from the Cancer Patient Pathway System (CaPPS), covering the period from January 2019 to December 2023. The study cohort consisted of individuals with a diagnosed cancer. We examined the impact of the pandemic on various aspects of cancer care, including short-term survival and key waiting times throughout the treatment process. These included: i) the time between the decision-to-treat and the start of the first treatment, ii) the time between the referral date and the start of the first treatment, and iii) the time between the referral and diagnosis dates. The 'decision-to-treat' date corresponded to the date on which it was determined that the patient should receive cancer treatment. The 'first definitive treatment' date referred to the first intervention intended to remove or shrink the tumour that took place. The date of cancer diagnosis was defined as the first histological or cytological confirmation of malignancy, in accordance with the European Network of Cancer Registries recommendations [21].

ICD-10 diagnostic codes were used to identify incident cancer events, including bladder cancer (C67), brain and central nervous system cancers (C70-C72, C75.1-C75.3), breast cancer (C50), cervical cancer (C53), colorectal cancer (C18-C20), gallbladder cancer (C23-C24), head and neck cancers (C00-C14, C30-C32), kidney cancer (C64), leukaemia (C91-C95), liver cancer (C22), lung cancer (C33-C34), lymphoma (C81-C86), oesophageal cancer (C15), ovarian cancer (C56-C57.4), pancreatic cancer (C25), prostate cancer (C61), and stomach cancer (C16). Diagnostic codes indicative of either non-malignant cancer or metastasis were excluded. Metastases were excluded since we intended to

analyse the impact of the pandemic on patients with incident cancer diagnoses that had not yet entered a clinical care pathway.

The waiting times were summarised for each calendar year (2019-2023), with median and interquartile range (IQR). In the primary analysis presented in this chapter, survival was estimated based on cancer-specific mortality, meaning only deaths with an ICD-10 code indicating cancer on the death certificate were included. Sensitivity analyses using all-cause mortality, which includes deaths from any cause, were performed to assess the robustness of the primary findings. Accordingly, individuals were followed up from the date of their cancer diagnosis to either date of death or end of the study period. Patients whose date of death and date of cancer diagnosis were identical were excluded from the survival analysis. Instances of patients diagnosed with two different cancers, as indicated by ICD-10 codes, either on the same date or with the same or different types of cancer on different dates, were considered unique records. All outcomes included both sexes, except for breast cancer (females only) and prostate cancer (males only). To evaluate changes in survival patterns over time, we stratified analyses by calendar time of cancer diagnosis (2019, 2020, and 2021), enabling comparisons between pre-pandemic and pandemic periods. Short-term survival at one and two years was estimated using the Kaplan-Meier (KM) method.

7.3. Results

The number of patients diagnosed with cancer increased from 12,647 in 2019 to 13,821 in 2023. In 2020, the total number of diagnoses dropped to 11,378. In the following years, the number of diagnoses returned to, and eventually exceeded, pre-pandemic levels.

In 2019, the median time from referral to diagnosis was 24 days [IQR: 6 to 55 days]. This remained at 24 days [IQR: 7 to 55 days] in 2020. However, the median time rose significantly in subsequent years, reaching 29 days [IQR: 8 to 63 days] in 2021, 36 days [IQR: 10 to 78 days] in 2022, and 37 days [IQR: 9 to 75 days] in 2023 - an increase of 54.2% compared to 2019. In addition, the IQR showed a slight expansion from 6-55 days in 2019 to 9-75 days in 2023. This widening IQR indicates growing disparities in how quickly patients progressed from referral to diagnosis. While some patients continued to be diagnosed relatively quickly (near the lower bound of the IQR), others experienced much longer delays (as seen in the upper bound's increase).

The median time from referral to the first treatment decreased from 49 days [IQR: 24 to 88 days] in 2019 to 47 days [IQR: 23 to 85 days] in 2020. However, this decline was followed by a steady increase in subsequent years, with the median time rising to 55 days [IQR: 28 to 98 days] in 2021, 62 days [IQR: 30 to 114 days] in 2022, and 65 days [IQR: 34 to 115 days] in 2023. Overall, this represents a 32.7% increase compared to the pre-pandemic level. Furthermore, the widening IQR suggests that while some patients still accessed treatment relatively quickly, a growing number faced increasingly longer delays.

The median time from the decision-to-treat date to the first treatment remained at 5 days from 2019 to 2020, increased to 7 days in 2021, and then returned to 5 days in 2023. The IQR also remained narrow and relatively stable, moving from 0-19 days in 2019 to 0-16 days in 2020, then slightly expanding to 0–21 days in 2021 and staying at that level through 2023.

Short-term survival at 1-year and 2-years was estimated for people diagnosed with cancer in 2019, 2020, and 2021, with 1-year survival indicating the percentage of patients who survived at least one-year post-diagnosis, and 2-year survival representing those who survived at least two years after diagnosis. As such, the 1-year survival in 2019 reflects patients diagnosed with cancer in 2019 who survived at least one year, while the 2-year survival in 2019 corresponds to those diagnosed in 2019 who survived at least two years. This methodology applies similarly to subsequent years.

We found significant differences between survival functions for individuals diagnosed with cancer in 2019, 2020, and 2021 ($p < 0.001$). Table 3 shows the observed 1-year and 2-year cancer-specific survival rates for patients diagnosed in 2019, 2020, and 2021, along with p-values indicating the statistical significance of differences in survival between patients diagnosed in 2019 (baseline year) and those diagnosed in 2020 or 2021. Only *p*-values below 0.05 indicate that the differences in survival rates between years are statistically significant, meaning the changes are unlikely to be due to chance and suggest a real change in patient outcomes over time. Overall, 1-year survival for all cancers decreased from 81% (95% CI: 79% to 83%) in 2019 to 78% (95% CI: 77% to 83%) in 2020 (Table 3). A decline in 1-year survival rates in 2020 was observed for several tumour sites (bladder, head and neck, brain, oesophageal, lung, lymphoma, stomach), with gallbladder cancer experiencing a further drop in 2021 – a total decrease of 11% between 2019 and 2021, as survival rates fell from 43% (95% CI: 34% to 54%) in 2019 to 36% (95% CI: 27% to 49%) in 2020, and then to 32% (95% CI: 23% to 43%) in 2021. Oesophageal cancer showed a 15% drop in survival from 57% (95% CI: 51% to 64%) in 2019

to 42% (95% CI: 36% to 49%) in 2020, followed by 3% increase in survival to 45% (95% CI: 39% to 51%) in 2021. The observed decline in survival for oesophageal cancer may be attributed to stage migration, with patients presenting later with more advanced disease [22]. For bladder cancer, the 1-year survival dropped from 88% (95% CI: 85% to 91%) in 2019 to 80% (95% CI: 76% to 85%) in 2020, and while it slightly improved to 82% (95% CI: 78% to 86%) in 2021, it remained lower than the 2019 level. Brain and other CNS tumours saw a substantial drop in survival, with the 1-year survival rate falling from 41% (95% CI: 35% to 49%) in 2019 to 34% (95% CI: 28% to 42%) in 2020, before increasing to 37% (95% CI: 31% to 45%) in 2021, but still remaining below the pre-pandemic level.

Head and neck cancers saw a decrease in 1-year survival from 80% (95% CI: 75% to 84%) in 2019 to 74% (95% CI: 69% to 79%) in 2020, followed by a 3% increase in survival increase to 77% (95% CI: 73% to 82%) in 2021, still lower than the pre-pandemic survival rate. Reduced access and a 60% drop in adult dental visits in NI during 2020/21, compared to 2019/20, may have contributed to later-stage diagnoses and poorer survival in head and neck cancer [23]. Previous studies have shown that regular dental visits reduce the odds of late-stage diagnosis for oral and pharyngeal cancers [24]. Ovarian cancer also recorded a 12% reduction in survival rate from 87% (95% CI: 81% to 94%) in 2019 to 75% (95% CI: 67% to 85%) in 2020, with a subsequent increase to 84% (95% CI: 77% to 91%) in 2021. The pandemic has caused significant disruption to both. Women with ovarian cancer reported having their surgery postponed and having additional cycles of chemotherapy while waiting for surgery [25]. The overall 1-year survival rate for lung cancers declined, with survival falling from 46% (95% CI: 44% to 49%) in 2019 to 42% (95% CI: 40% to 45%) in 2020, and then slightly recovering to 43% (95% CI: 41% to 46%) in 2021.

The 2-year cancer survival rate decreased from 74% (95% CI: 72% to 76%) for individuals diagnosed in 2019 to 71% (95% CI: 69% to 73%) for those diagnosed in 2020, with the differences driven by tumour type (Table 3). Brain and CNS cancers saw a sharp drop, with 2-year survival falling from 31% (95% CI: 25% to 29%) in 2019 to 25% (95% CI: 20% to 33%) in 2020, and then to 23% (95% CI: 18% to 30%) in 2021. Lung cancer also showed a decline, with 2-year survival dropping from 33% (95% CI: 30% to 35%) in 2019 to 30% (95% CI: 28% to 33%) in 2020, and remaining at 30% (95% CI: 28% to 33%) in 2021. Ovarian cancer recorded a 12% decline in 2-year survival from 84% (95% CI: 77% to 91%) in 2019 to 72% (95% CI: 63% to 82%) in 2020 while for oesophageal the 2-year survival dropped by 9% from 38% (95% CI: 32% to 44%) in 2019 to 29% (95% CI: 23% to 35%) in 2020. For lymphoma,

the 2-year survival rate fell from 78% (95% CI: 74% to 82%) in 2019 to 72% (95% CI: 68% to 76%) in 2020.

Some tumour types did not show a decline in 2-year survival rates for patients diagnosed in 2020 and 2021 compared to 2019, with some even showing improvements. For kidney cancer, 2-year survival remained stable at 83% (95% CI: 79% to 88%) for 2019 and 2020 diagnoses and increased to 86% (95% CI: 82% to 90%) for those diagnosed in 2021, though this change was not statistically significant. Similarly, leukaemia exhibited an improvement in 2-year survival from 73% (95% CI: 69% to 78%) for 2019 diagnoses to 78% (95% CI: 73% to 82%) in 2021.

For breast cancer, the survival at 1 year was 95% (95% CI: 94% to 96%) in both 2019 and 2020, and increased to 97% (95% CI: 96% to 98%) in 2021. The survival at 2 years was 92% (95% CI: 90% to 93%) in 2019, 92% (95% CI: 91% to 93%) in 2020, and 93% (95% CI: 92% to 95%) in 2021. For prostate cancer, survival rates were also consistent, with 96% (95% CI: 95% to 97%) in 2019, 95% (95% CI: 94% to 97%) in 2020, and 96% (95% CI: 95% to 97%) in 2021 at 1 year, and 91% (95% CI: 89% to 92%) in 2019, 90% (95% CI: 88% to 92%) in 2020, and 92% (95% CI: 90% to 93%) in 2021 at 2 years.

The results of sensitivity analysis are shown in Table S1 (Appendix 1). Across most cancer types and years, survival rates estimated using all-cause mortality were generally lower than those estimated using cancer-specific mortality. This reflects the inclusion of deaths from causes unrelated to the cancers of interest in the all-cause mortality estimates.

Table 3. Observed 1- and 2-year survival rates (%) by cancer type with 95% confidence intervals in brackets. *P*-values indicate statistical significance of differences in survival rates between patients diagnosed in 2019 (baseline year) and those diagnosed in 2020 or 2021 for each cancer type. Mortality was defined as cancer-specific mortality, meaning only deaths where the ICD-10 code indicates the cancer on the death certificate were considered.

Cancer type	ICD-10 code	Year	1-year survival [%]	2-year survival [%]	*p-value*
Bladder	C67	2019	88 (85-91)	80 (76-84)	-
		2020	80 (76-85)	74 (69-79)	0.2
		2021	82 (78-86)	75 (71-80)	0.1
		2019	41 (35-49)	31 (25-39)	-

Brain (inc CNS)	C70-C72, C75.1-C75.3	2020	34 (28-42)	25 (20-33)	0.7
		2021	37 (31-45)	23 (18-30)	0.3
Colorectal	C18-C20	2019	80 (78-83)	73 (70-75)	-
		2020	80 (78-83)	70 (67-73)	0.3
		2021	80 (78-82)	73 (70-75)	0.8
Breast	C50	2019	95 (94-96)	92 (90-93)	-
		2020	95 (94-96)	92 (91-93)	0.2
		2021	97 (96-98)	93 (92-95)	0.06
Gallbladder	C23-C24	2019	43 (34-54)	22 (15-32)	-
		2020	36 (27-49)	26 (17-38)	0.7
		2021	32 (23-43)	20 (14-31)	0.4
Head and Neck	C00-C14, C30-C32	2019	80 (75-84)	67 (62-72)	-
		2020	74 (69-79)	65 (60-71)	0.7
		2021	77 (73-82)	71 (66-76)	0.7
Kidney	C64	2019	88 (84-93)	83 (79-88)	-
		2020	90 (87-94)	83 (79-88)	0.8
		2021	89 (85-93)	86 (82-90)	0.5
Leukaemia	C91-C95	2019	83 (79-87)	73 (69-78)	-
		2020	84 (79-88)	78 (74-83)	**0.049***
		2021	87 (83-91)	78 (73-82)	0.1
Liver	C22	2019	39 (32-48)	27 (21-35)	-
		2020	45 (38-53)	34 (27-41)	0.3
		2021	46 (39-54)	30 (24-37)	0.5
Lung	C33-C34	2019	46 (44-49)	33 (30-35)	-
		2020	42 (40-45)	30 (28-33)	0.07
		2021	43 (41-46)	30 (28-33)	0.09
Lymphoma	C81-C86	2019	83 (79-86)	78 (74-82)	-
		2020	79 (75-83)	72 (68-76)	**0.03***
		2021	81 (78-85)	74 (70-78)	0.2
Oesophageal	C15	2019	57 (51-64)	38 (32-44)	-
		2020	42 (36-49)	29 (23-35)	**0.01***
		2021	45 (39-51)	34 (29-40)	0.2
Ovarian	C56-C57.4	2019	87 (81-94)	84 (77-91)	-
		2020	75 (67-85)	72 (63-82)	**0.049***
		2021	84 (77-91)	76 (68-84)	0.06
Pancreatic	C25	2019	33 (27-39)	20 (16-26)	-
		2020	34 (29-40)	19 (15-24)	0.8
		2021	37 (31-43)	24 (19-30)	0.2
Prostate	C61	2019	96 (95-97)	91 (89-92)	-
		2020	95 (94-97)	90 (88-92)	0.8
		2021	96 (95-97)	92 (90-93)	0.3
Stomach	C16	2019	53 (46-62)	35 (29-44)	-
		2020	51 (44-60)	39 (32-48)	0.5
		2021	57 (50-65)	48 (41-56)	**0.02***

* statistically significant at the 0.05 significance level

8. Investigation of whether there is any statistical relationship between COVID-19 vaccination and excess deaths

8.1. Context

On December 8, 2020, the United Kingdom launched its COVID-19 vaccination program, prioritising groups identified by the Joint Committee on Vaccination and Immunisation (JCVI). While clinical trials initially focused on the short-term efficacy of the COVID-19 vaccine against symptomatic infection [26, 27], real-world data has shown that the vaccine provides more sustained protection against severe disease and death caused by COVID-19 [28-30]. Despite this, some have claimed that COVID-19 vaccination caused excess mortality. To investigate this claim, we analysed whether all-cause excess mortality in NI during the pandemic was temporally associated with COVID-19 vaccination.

8.2. Method

Aggregate weekly mortality data were obtained from NISRA, the official source of vital events statistics based on GRO information [31]. Weekly vaccination data were sourced from the NI Vaccine Management System (VMS) published via Open Data NI [32]. The all-cause excess mortality was estimated using a quasi-Poisson regression model applied to weekly death registration data. The model incorporated historical death registration records, aggregated by unique combinations of demographic characteristics, and adjusted for time trends, seasonal variations, and changes in population size. This approach follows the new ONS methodology for estimating excess mortality [7]. Further details on model specification can be found in Section 5.2.

To examine the temporal relationship between COVID-19 vaccination and all-cause excess mortality, we conducted linear regression analyses using weekly mortality data. The analyses covered the period from the week beginning Saturday, 5 December 2020 – when first vaccine doses were administered in NI – through to the week ending Friday, 29 December 2023, in accordance with the NISRA definition of weeks (Saturday to Friday). Weekly excess deaths were regressed on i) weekly COVID-19 deaths and ii) weekly administered first-dose COVID-19 vaccinations, incorporated via distributed lag non-linear model framework to capture potential lagged effects [33]. Two distinct modelling scenarios were performed using different definitions of COVID-19 deaths based on ICD-10 codes: 1) deaths involving

COVID-19; and 2) deaths due to COVID-19. Deaths involving COVID-19 were identified where any of the ICD-10 codes – U07.1, U07.2, U09.9, U10.9 – were listed among the full list of causes, regardless of whether they were listed as underlying or contributory causes. Deaths due to COVID-19 were defined as those where the underlying cause of death was any of the relevant ICD-10 codes, specifically U07.1, U07.2, U09.9, U10.9. In both analyses, we applied two cross-basis matrices to model the lagged effect of vaccination. The short-term matrix assumed vaccination influenced mortality risk only within the first 8 weeks post-vaccination. The lag-response relationship was stratified, with one indicator per week for up to 8 weeks, allowing us to measure the specific effect of vaccination each week (short-term model). The long-term matrix extended the analysis to assess potential effects over a six-month period (long-term model). The lag-response relationship was modelled using a natural cubic spline with three knots, allowing the relationship between vaccination and mortality to change across different segments of the 26-week period. Lag-specific effects of vaccination on excess deaths were evaluated by comparing performance of each model against a null model (which included only COVID-19 deaths) using the Akaike Information Criterion (AIC) and Likelihood Ratio Tests (LRT) to determine whether including vaccination improved model fit. AIC is a measure of model quality that balances goodness of fit with model complexity; lower AIC values indicate a better fitting. The LRT compares two nested models to assess whether the more complex model provides a significantly better fit to the data. An LRT $p < 0.05$ suggests that the additional variables in the more complex model improve model fit beyond what would be expected by chance.

8.3. Results

The estimated excess all-cause mortality, vaccination doses, and deaths involving or due to COVID-19 are shown in Figure 13 and 14 respectively. Figures 15 and 16 illustrate the cumulative and lag-specific effects of first and all COVID-19 vaccine doses on weekly excess deaths, with models adjusted for deaths involving COVID-19 and deaths due to COVID-19, respectively. The comparison of second-stage model fits, which further evaluates the relationship between vaccination and mortality, is presented in Table 4.

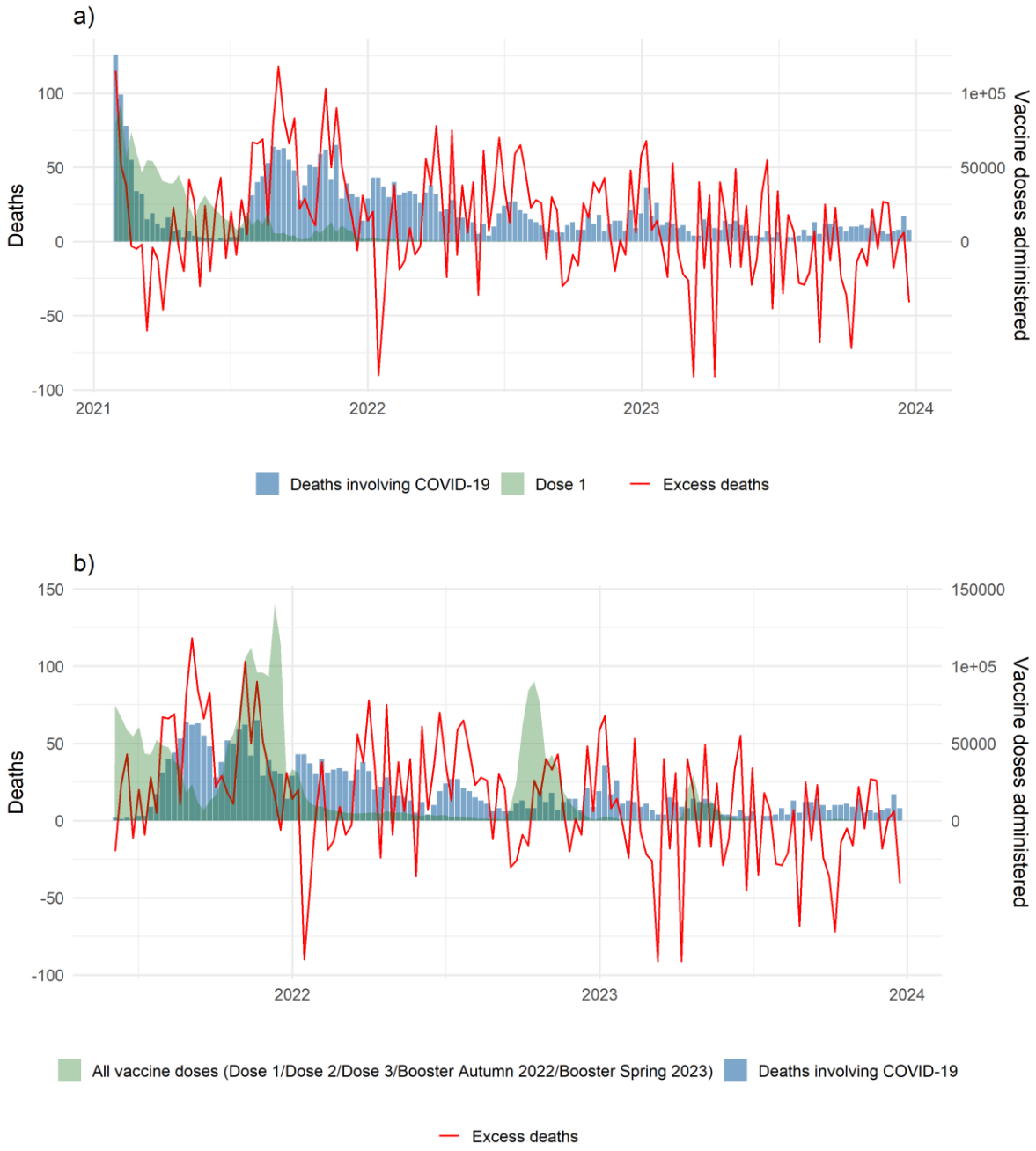


Figure 13. Weekly excess mortality, deaths involving COVID-19 and a) first vaccine doses administered and b) all vaccine doses administered in NI over the study period (05/12/2020 to 29/12/2023). Deaths involving COVID-19 are defined as those where any of the ICD-10 codes, U07.1, U07.2, U09.9, U10.9, appeared among the full list of causes, regardless of whether they were listed as underlying or contributory causes.

8.3.1. Deaths involving COVID-19

In the short-term model (with lags up to 8 weeks), COVID-19 deaths were significantly associated with excess mortality ($p < 0.001$), but no significant association was found between excess mortality and first-dose vaccination across the 8 lag periods examined. The individual lag coefficients for vaccination were small and non-significant. The inclusion of vaccination in the short-term model did not improve model fit, as indicated by the higher AIC value for the model with vaccination compared to the model with only COVID-19 deaths (AIC = 1511 vs 1505). The LRT comparing the short-term model to the null model yielded a *p*-value of 0.27, further supporting no significant improvement in model fit with the addition of vaccination.

In the long-term model, which considered vaccination effects over 26 weeks, COVID-19 deaths again showed a significant effect on excess mortality ($p < 0.001$), but the lagged vaccination terms remained non-significant. The inclusion of vaccination did not improve model fit, as reflected by the higher AIC value for the model with vaccination compared to the model with only COVID-19 deaths (AIC = 1329 vs 1326, $p = 0.41$).

Table 4. Model fit comparison for short- and long-lag cross-basis functions of COVID-19 vaccination against a null model including only COVID-19 deaths using likelihood ratio tests (LRT). LRT *p*-values above 0.05 indicate no temporal association between excess deaths and COVID-19 vaccination.

	Deaths involving COVID-19	Deaths due to COVID-19
	p-value	*p*-value
Dose 1		
Null	-	-
Short term	0.27	0.24
Long-term	0.41	0.54
*All doses**		
Null	-	-
Short term	0.18	0.18
Long-term	0.65	0.78

* Include first, second, third doses as well as 2022 and 2023 booster doses of COVID-19 vaccine

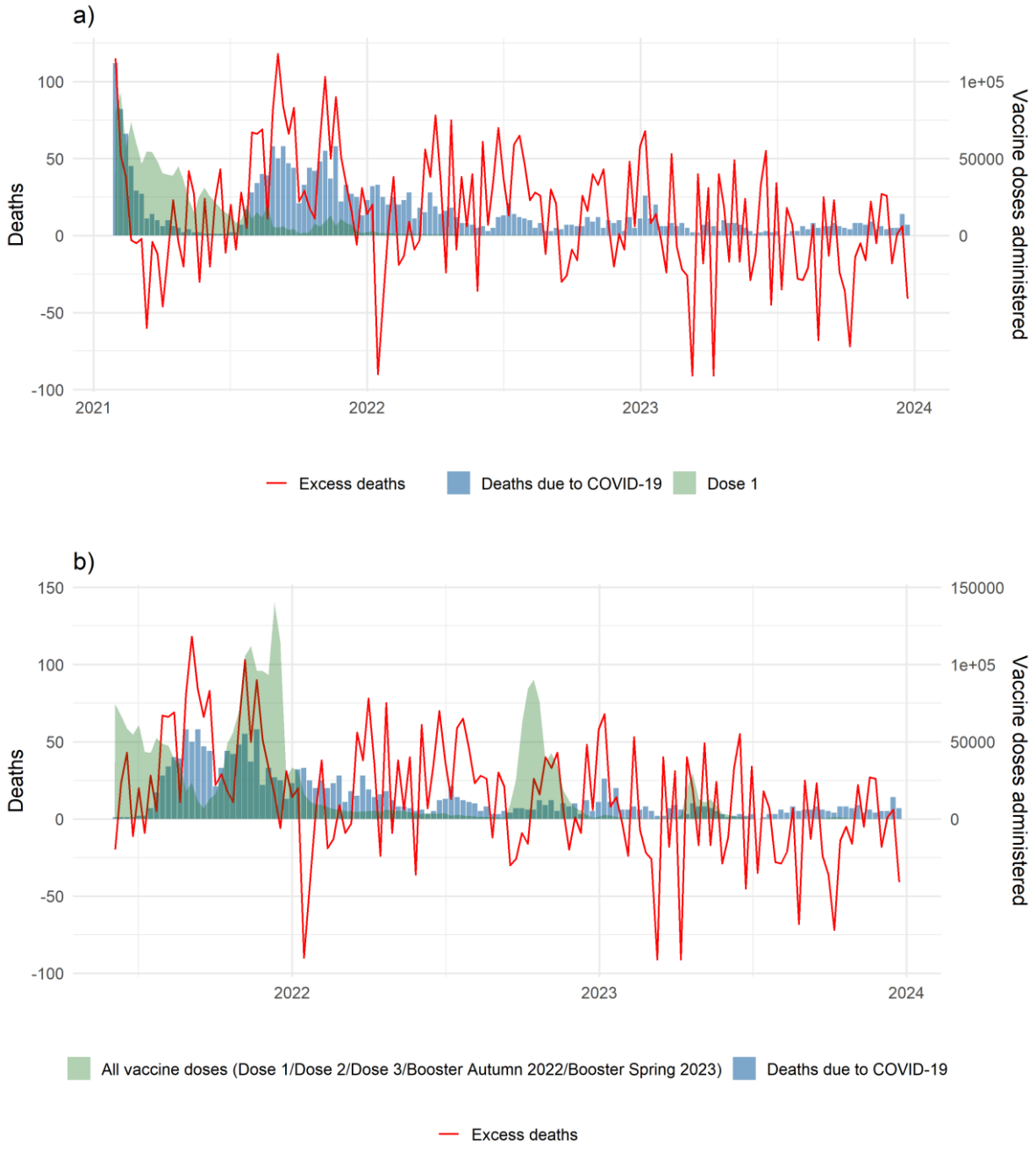


Figure 14. Weekly excess mortality, deaths due to COVID-19 and a) first vaccine doses administered and b) all vaccine doses administered in NI over the study period (05/12/2020 to 29/12/2023). Deaths due to COVID-19 were defined as those where the underlying cause of death was any of the relevant ICD-10 codes, specifically U07.1, U07.2, U09.9, U10.9.

Cumulative estimates from distributed lag nonlinear models indicated a negative association between COVID-19 vaccination and excess mortality, although this was not statistically significant (Figures 15a and 15b). The cumulative effect reflects the overall impact of vaccination on mortality over time, incorporating both immediate and delayed effects. The lag effect, on the other hand, captures the delay

between receiving the vaccine and the observed impact on mortality, recognising that the effects may unfold over time. This includes both short-term reductions in mortality and potential longer-term effects, which may emerge at different time lags. In the short-term model, first doses of COVID-19 vaccine were associated with a deficit of 32.3 deaths (95% CI: -65.9 to 1.3), and in the long-term model, with a mortality deficit of 72 deaths (95% CI: -349.4 to 205.3). The lag-response curves were erratic, showing both excess and deficit mortality at varying lags, in a manner that is unlikely to indicate a casual association.

8.3.2. Deaths due to COVID-19

For deaths where COVID-19 was the underlying cause, the short-term model also found a significant effect of COVID-19 deaths on excess mortality ($p < 0.001$), but vaccination showed no significant association with excess deaths. None of the lagged vaccination coefficients were statistically significant. The inclusion of vaccination in the short-term model did not improve model fit, as shown by the higher AIC value for the model with vaccination compared to the model with only COVID-19 deaths. The LRT comparing the short-term model to the null model resulted in a *p*-value of 0.24, further indicating no significant improvement in model fit with vaccination.

The long-term model for deaths due to COVID-19 produced similar results. COVID-19 deaths were significantly associated with excess mortality ($p < 0.001$), while there was no significant association with vaccination over the 26-week period (Table 4). The inclusion of vaccination did not improve model fit, as reflected by the higher AIC value for the model with vaccination compared to the model with only COVID-19 deaths.

The cumulative effect of vaccination on mortality over time revealed that the first dose in the short-term model was associated with a mortality deficit of -37.3 deaths (95% CI: -71.8 to -2.9) (Figures 16a). In contrast, the long-term model indicated a deficit of -109.5 deaths (95% CI: −396.3 to 177.4), though this result was not statistically significant (Figures 16b). The lag-response curves exhibited an inconsistent pattern.

Across both definitions of COVID-19 mortality, COVID-19 deaths remained a consistent predictor of excess mortality, while COVID-19 vaccination showed no association with excess mortality at either short or extended lags (with one exception when the model was adjusted for deaths due to COVID-19, where vaccination was associated with a deficit in mortality). Model comparisons using AIC and LRT further reinforced that the inclusion of vaccination did not significantly improve model fit in either case.

While the confidence intervals overlap with zero, the consistent direction toward a mortality deficit across multiple models tend towards demonstrating a protective effect of vaccination, though this effect is not statistically significant. This ecological study design does not measure vaccine effectiveness, and these results do not measure vaccine effectiveness against harm from COVID-19 infection.

8.3.3. Sensitivity analysis

To assess the robustness of our findings, we conducted a sensitivity analysis in which we considered the combined weekly number of all vaccine doses administered – including first, second, third doses of COVID-19 vaccine as well as 2022 and 2023 booster doses of COVID-19 vaccine, rather than first doses alone. This approach aimed to capture the total vaccine exposure in the population more comprehensively, as both doses are relevant to the full immunological response. Results from both the short-term and long-term models using this combined vaccination measure were consistent with the main analyses. In the short-term model based on deaths involving COVID-19, the inclusion of vaccination terms did not improve model fit (AIC = 1510 vs 1505), and LRT was not statistically significant (p = 0.18). Similarly, in the long-term model, LRT also indicated no significant improvement (p = 0.65). When considering deaths due to COVID-19, the short-term model again showed no improvement in fit with vaccination terms included (AIC = 1511 vs 1506; p = 0.17), nor did the long-term model (AIC = 1332 vs 1327; p = 0.78). Coefficients for vaccination-related terms remained statistically non-significant across all models. Across both definitions of COVID-19 mortality, the cumulative estimates of the total impact of vaccination on mortality over time, for both the short-term and long-term models, were not statistically significant (Figures 15c, 15d, 16c, 16d). These findings further reinforce the conclusion that there was no evidence of an association between COVID-19 vaccination – whether first doses alone or combined doses – and all-cause excess mortality during the study period. Again, this investigation of any relationship between COVID-19 vaccination and *excess* mortality does not investigate vaccine effectiveness against death with COVID-19 infection and does not provide evidence about this.

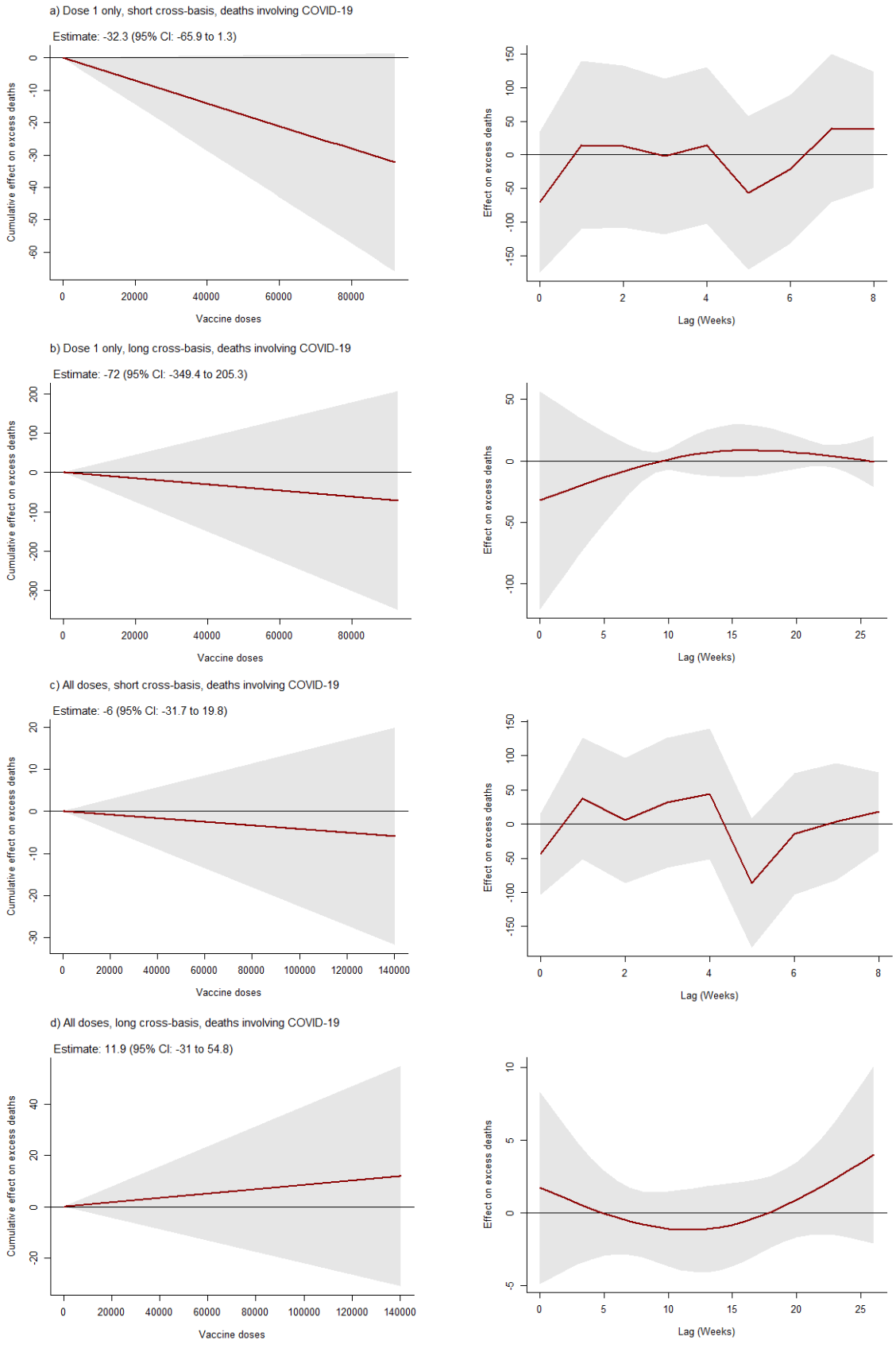


Figure 15. Cumulative and lag-specific effects of first (a & b) and all (c & d) COVID-19 vaccine doses on weekly excess deaths. Estimates are based on distributed lag nonlinear models adjusted for deaths involving COVID-19.

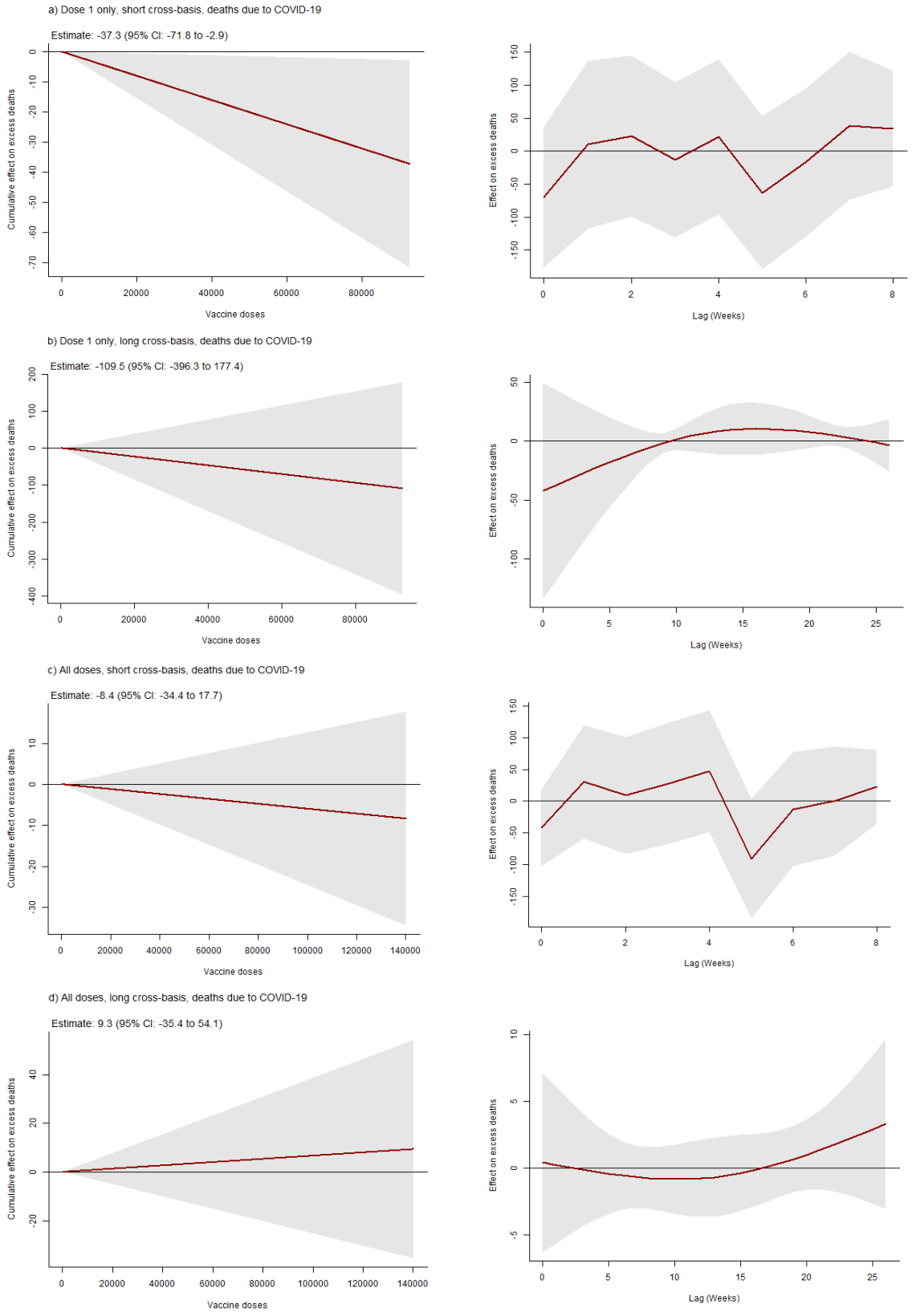


Figure 16. Cumulative and lag-specific effects of first (a & b) and all (c & d) COVID-19 vaccine doses on weekly excess deaths. Estimates are based on distributed lag nonlinear models adjusted for deaths due to COVID-19.

9. Discussion

This study aimed to address three objectives: (1) to estimate the number of excess deaths by week of registration, age, sex, place of death, and cause of death in 2022-23, using the new ONS methodology for estimating excess mortality; (2) to examine the impact of the COVID-19 pandemic on cancer deaths; and (3) to evaluate any statistical relationship between COVID-19 vaccination and excess deaths. The findings are consistent with broader international research but also reveal distinct local variations, reflecting the distinct socio-health contexts in NI.

Objective 1: To estimate the number of excess deaths by week of registration, age, sex, place of death, and cause of death in 2022 and 2023.

The excess mortality trends observed in NI during 2022 and 2023 provide insight into the evolving public health impact of the COVID-19 pandemic. In 2022, there were an estimated 320 excess deaths, representing 1.9% more deaths than expected. In 2023, this shifted to an overall mortality deficit of 523 deaths (-3.1%), with the highest excess mortality occurring in January, followed by deficits in subsequent months. Significant sex disparities were observed: females experienced excess mortality in both years, particularly in older age groups (75+), while males exhibited a mortality deficit, especially in 2023.

It is important to note that differences exist between the official excess death figures reported by NISRA and the estimates presented in this study. Our study included 16,812 deaths in 2022 and 16,365 in 2023, whereas NISRA reported 17,158 and 17,255 deaths, respectively. Discrepancies were modest in 2022 (~2%) but more pronounced in 2023 (~5%). These differences affected the calculation of excess deaths: NISRA estimated 837 excess deaths in 2022 and a deficit of 139 deaths in 2023, while our study produced 320 excess deaths in 2022 and a deficit of 523 in 2023. These differences stem from incomplete linkage across datasets, which led to lower weekly registered death counts in our analysis. Because our study relied on linked administrative data, deaths that could not be matched (due to incomplete information) were excluded. Such gaps can bias sex-specific analyses if linkage rates differed by sex, potentially underestimating male mortality while inflating apparent female excess. These methodological factors may explain why our estimates diverge from NISRA's, and why patterns of sex-specific mortality should be interpreted with caution. Furthermore, pooled models that assume a

common underlying mortality trend for both sexes may distort excess mortality estimates, underestimating excess in one group while overstating it in another. Using sex-specific trend models may provide a clearer and more accurate understanding of distinct mortality trajectories for different population groups.

Methodological improvements in estimating expected deaths also affected excess mortality estimates. The earlier approach relied on a simple five-year average to estimate expected deaths, often resulting in higher excess mortality figures [7]. In contrast, the new ONS methodology uses age-specific mortality rates and adjusts for changes in population size. This provides a better estimate of expected deaths by incorporating demographic changes, long-term trends, and seasonal patterns. For example, the previous ONS method estimated 38,960 excess deaths in the UK in 2022, whereas the new method produced a slightly higher figure of 43,456 [7]. In contrast, for 2023, the difference between the two methods was much greater: the previous ONS method estimated 31,442 excess deaths, while the new model reported 10,994 excess deaths [7]. While both methods report similar peaks during the height of the pandemic, the new approach consistently provides lower estimates for more recent periods, such as 2023. It should be noted that the new ONS methodology remains classified as "Official Statistics in Development" but represents a significant improvement on earlier methods.

Placed in a wider context, UK-wide data highlight both similarities and differences with NI's experience. In 2022, excess mortality in the UK was more than 7% above expected for both males and females, suggesting NI experienced a relatively lower mortality burden that year. In 2023, when NI recorded a mortality deficit, England still reported excess deaths among both females (5,828) and males (5,064), each representing a 2% increase over expected levels [34]. Cause-specific mortality data show that in 2022, NI recorded increases in deaths from influenza and pneumonia (10.3%), dementia and Alzheimer's disease (4.3%), and cerebrovascular disease (3.9%). A significant increase in respiratory deaths occurred in early 2023, with a 58.9% increase in the first seven weeks, coinciding with seasonal virus circulation. This trend aligns with ONS findings, where influenza and pneumonia were the leading causes of excess deaths in England, accounting for 1,802 excess deaths, 59.2% above the five-year average in January 2023 [35].

International comparisons also highlight how distinctive NI's recent mortality patterns are. Across Italy and the Nordic countries, men typically experienced higher excess mortality than women during the pandemic, particularly in older age groups [36-38].

Another plausible explanation, beyond incomplete linkage and pooled modelling, is mortality displacement. Periods of elevated mortality (e.g. during the pandemic or severe winters) are often followed by below-expected deaths, as some of the most vulnerable individuals die earlier than they otherwise would have [39]. COVID-19 accelerated mortality among frailer individuals [40-42], while pandemic-related disruptions (e.g. suppressed influenza circulation, reduced healthcare use) also altered longer-term trends [43,44]. These dynamics may have unfolded differently by sex: men in NI experienced higher excess mortality earlier in the pandemic (2020-2021) [45], suggesting an earlier displacement effect, while women showed delayed displacement, with excess deaths persisting into 2022 and 2023.

Supporting this interpretation, Holleyman [46] demonstrated that standard models may overestimate expected deaths following a pandemic or other major public health disruption. This is because many deaths projected for the post-event period may have actually occurred during earlier surges. This phenomenon is not unique to COVID-19. For instance, Armstrong et al. [47], after analysing data from 278 locations across 12 countries, found that many deaths related to extreme heat and cold were brought forward by at least one year. Such evidence underscores that mortality deficits often reflect earlier excesses, rather than genuine improvements in survival.

Objective 2: To examine the impact of the COVID-19 pandemic on cancer deaths.

Our findings demonstrate a notable and immediate drop in cancer diagnoses in 2020, accompanied by substantial increases in waiting times for diagnosis and treatment in the subsequent years. These delays, though initially subtle, became more apparent by 2022 and 2023, particularly in the time from referral to diagnosis, which increased by 54.2% from 2019 to 2023. The time between referral and first treatment also rose, though to a lesser extent, by 32.7% compared to levels before the pandemic. This is in line with existing evidence highlighting the broad, indirect effects of the COVID-19 pandemic on healthcare delivery. Numerous studies have reported significant reductions in cancer screening, diagnostic procedures, and elective surgeries, particularly during the initial period of the pandemic [48-50]. In England, urgent cancer referrals dropped by 60% during the early phase of the pandemic [50].

This drop in diagnostic activity likely contributed to delayed detection, a shift toward more advanced stages at presentation, and ultimately, poorer survival outcomes for certain cancers. In NI, Bennett et al. [48] reported a 13% overall reduction in new cancer diagnoses, with variation across tumour types. Melanoma experienced the steepest decline at 39%, while other cancers, such as lung (7.5%), female breast (11%), colorectal (12%), and prostate (14.5%), showed more moderate reductions. These findings are consistent with broader international trends; a systematic review of 245 studies across 46 countries revealed an even more substantial overall decline, including a 39% decrease in screening participation, a 23% drop in diagnoses, and a 28% reduction in treatment during the pandemic [51].

We observed significant differences in survival functions among individuals diagnosed with cancer in 2019, 2020, and 2021 ($p < 0.001$). Overall, 1-year survival for all cancers declined from 81% in 2019 to 78% in 2020. These findings align with those of Hong et al. [52], who reported a similar decrease in 1-year relative survival for all cancers – from 82.3% in Q2 2018 to 77.5% in Q2 2020. In our study, short-term survival rates decreased for several cancer types during the first and second years of the pandemic, particularly for oesophageal, bladder, lung, lymphoma, ovarian, gallbladder, head and neck, and brain cancers. Although statistically significant differences were observed only for lymphoma, oesophageal, and ovarian cancers ($p < 0.05$). For example, 1-year survival for gallbladder cancer dropped sharply from 43% in 2019 to 32% in 2021. In contrast, breast and prostate cancer, showed stable short-term survival during the pandemic period. Our findings are consistent with existing UK-based evidence [53,54]. Official statistics from Public Health Wales [53] reported a decrease in 1-year survival for all cancers combined, from 76% in 2019 to 72% in 2020, attributing the decline to pandemic-related disruptions in care. Survival was consistently lower for patients diagnosed at later stages; for example, over half of bowel cancer cases in 2020 were diagnosed at stage three or four. Similarly, a UK population-based cohort study comparing cancers diagnosed between 2000-2019 and 2020-2022 found significant drops in 1-year survival for several tumour types, including colorectal (78.8% to 77%), head and neck (81.2% to 77.6%), oesophageal (45.3% to 42.4%), and pancreatic (28.4% to 25.9%) cancers [54]. One-year survival remained stable for liver, breast, and prostate cancers, consistent with our findings regarding differences in the pandemic's effect across tumour types.

When comparing our findings to Bennett et al. [48], the only other Northern Ireland study on pandemic-related cancer survival, results broadly align, although differences in statistical significance were

observed for some tumour types. These differences likely reflect methodological factors: our study used 2019 as a baseline and included all diagnoses in 2020-2021, capturing pre-pandemic months, whereas Bennett et al. [48] compared April-December 2018-2019 with April-December 2020. Follow-up duration also differed: we estimated 1- and 2-year survival, while their shorter observation window limited ascertainment of deaths. Data sources differed, with our analysis based on CaPPS and Bennett's et al. [48] on the Northern Ireland Cancer Registry (NICR), potentially affecting case capture. Sample size, cancer incidence, and censoring patterns further influence statistical significance, particularly for less common cancers.

The absence of statistically significant differences ($p > 0.05$) in some cancer types, despite these observed declines in survival, can be attributed to several factors. One key issue is the relatively small sample sizes for certain tumour types, which reduced statistical power and limited the ability to detect significant differences. Additionally, the high number of censored cases, where patients were still alive at the time of the last follow-up, introduced complexity to the analysis. As a result, survival curves mainly represented individuals who had not yet experienced the outcome event of interest, which limited our ability to assess the longer-term impact of pandemic-related delays. The high level of censoring reduced the effective sample size at later follow-up points, lowering the likelihood of detecting statistically significant differences [55].

Our results also align with prior modelling work predicting additional cancer deaths in the coming decade due to pandemic-related care disruptions [56]. Projections suggest that diagnostic delays during the COVID-19 pandemic in the UK could lead to a 15.3-16.6% increase in deaths from colorectal cancer, a 4.8-5.3% increase for lung cancer, and a 5.8-6.0% increase for oesophageal cancer over the next five years. Our findings, specifically the decline in 1- and 2-year survival among those diagnosed with cancer in 2020 and 2021 across multiple tumour types, provide empirical support for these projections, underscoring the long-term consequences of short-term disruptions in the healthcare system.

Objective 3: To evaluate the association between COVID-19 vaccination and excess deaths

Our results showed a significant association between COVID-19 deaths and excess mortality, reaffirming that COVID-19 itself was a primary driver of excess mortality during the study period. In contrast, we found no statistically significant association between either first-dose or cumulative COVID-

19 vaccination and excess mortality across both short and extended lag periods. Our distributed lag nonlinear models also suggested a potentially protective, though not statistically significant, association between vaccination and all-cause excess mortality. This study design does not measure vaccine effectiveness and should not be interpreted as an indication of low effectiveness.

These findings align broadly with international evidence. For example, Lytras et al. [57] found no consistent association between COVID-19 vaccination and all-cause mortality in Cyprus. Their results suggested that COVID-19 disease accounted for changes in population mortality. While a short-term increase in mortality following first-dose vaccination was initially observed among individuals aged 18–49 years in Cyprus, further investigation attributed this to a type I error rather than a true causal effect [57]. These conclusions are consistent with data from the ONS, which reported no increase in excess mortality among young adults following COVID-19 vaccination [58].

Further supporting this, multiple studies have demonstrated that vaccinated individuals had a substantially lower risk of hospitalisation and death due to COVID-19 [59]. De Gier et al. [59] specifically assessed the short-term risk of non-COVID-19 mortality following vaccination and found no evidence of increased risk. In fact, the risk of non-COVID-19 death in the 5 to 8 weeks post-vaccination was generally similar to or lower than in unvaccinated individuals across all age groups and long-term care populations. Hazard ratios for non-COVID-19 mortality were consistently below 1 – regardless of vaccine type or timing – indicating a neutral or protective effect. Throughout most of the study period, unvaccinated individuals exhibited the highest incidence of non-COVID-19 deaths [59]. These findings are consistent with other research showing lower non-COVID-19 mortality rates among vaccinated individuals [60-62]. De Gier et al. [59] also observed some temporary increases in mortality among vaccinated individuals during specific periods of the vaccination rollout, particularly at the start and during the booster phase. However, these patterns likely reflect the prioritisation of the most vulnerable groups, such as the very elderly or those with significant underlying health conditions, for early vaccination. As a result, deaths occurring shortly after vaccination in these populations are more plausibly attributed to pre-existing health risks rather than the vaccines themselves. This observation is supported by work by Xu et al. [63], which showed that when mortality rates were adjusted for age, vaccinated individuals consistently had a lower risk of death compared to their unvaccinated peers. The initial appearance of higher mortality among vaccinated groups was largely attributable to the earlier vaccination of older and frailer individuals, rather than a causal effect of the vaccine.

Taken together, the evidence demonstrates the robustness of the conclusion that COVID-19 vaccines did not contribute to excess mortality.

Evidence from multiple studies has consistently shown that COVID-19 vaccines were highly effective in preventing severe disease and death. De Gier et al. [59] found that COVID-19 vaccines were highly effective in preventing COVID-19 mortality, with vaccine effectiveness (VE) exceeding 90% shortly after completion of the primary series. Importantly, booster doses restored VE to over 85% across all groups. These results are consistent with other studies that demonstrated high VE in preventing severe illness, hospitalisation, and death following both primary and booster vaccinations, alongside more rapid waning among long-term care populations [64-68].

10. Limitations

While this study offers valuable insights into excess mortality trends in NI during the COVID-19 pandemic and places these patterns within UK-wide and international contexts, several limitations should be considered when interpreting the findings across Objectives 1, 2, and 3.

Objective 1: To estimate the number of excess deaths by week of registration, age, sex, place of death, and cause of death in 2022 and 2023.

- The study's reliance on a pooled model, which assumes a common mortality trend across males and females, may have masked important sex-specific differences in mortality trajectories. Our separate analyses for males and females revealed significant disparities in trend coefficients, which the pooled model failed to capture. This limitation may have led to inaccurate estimates of excess mortality, particularly inflating figures for females and underestimating deficits for males.
- Comparisons with other UK nations and European countries provide important context but must be interpreted with caution due to underlying differences in healthcare systems, baseline population health, and demographic structures, all of which can influence mortality outcomes. Additionally, the statistical methods used to estimate excess mortality vary across jurisdictions and over time, creating potential inconsistencies in reported figures. In the UK, for example, a wide range of methods has been used to calculate excess deaths since the beginning of the COVID-19 pandemic. These include five-year averages, relative age-standardised mortality rates, segmented regression, time series models, neural networks, and institutional frameworks such as the Continuous Mortality Investigation (CMI) projections and pandemic monitor, EuroMOMO, the World Health Organization (WHO) pandemic excess mortality method, the UK Health Security Agency (UKHSA) daily mortality model, and the Office for Health Improvement and Disparities (OHID) excess deaths model. Each method has unique strengths and limitations, which can produce different excess mortality estimates and should be considered when interpreting findings.
- Mortality data are subject to delays in death registration. These delays disproportionately affect certain causes of death, particularly those requiring investigation or coroner involvement,

potentially leading to underestimation of short-term excess deaths and introducing bias into temporal trend analysis.

- The date of death registration was used (rather than the actual date of death) to ensure consistency with the NISRA methodology for calculating excess mortality. While this ensures data consistency, delays in death registration, especially for causes requiring investigation or coroner involvement, can create a temporal mismatch between when deaths actually occur and when they are recorded. This can obscure short-term fluctuations in mortality, artificially dampening or inflating week-to-week death counts. Such delays may introduce bias into the analysis of temporal trends, especially during periods of rapid change, and may limit the precision of time-sensitive assessments of excess mortality. Registration dates, however, are more reliably and uniformly recorded, and are less affected by retrospective updates or delays in medical certification.
- Our estimates of excess deaths are based on linked administrative data, which exclude deaths that could not be matched between the GRO and GP systems. As a result, observed totals are lower than the official NISRA counts, and the degree of under-ascertainment may vary by sex, age, and geography. Differences in population denominators further contribute to discrepancies, particularly for 2023, meaning that overall excess-death figures as well as age- and sex-specific comparisons should be interpreted with caution.

Objective 2: To examine the impact of the COVID-19 pandemic on cancer deaths.

- By limiting the analysis to incident, non-metastatic cancer cases, the study focuses on patients diagnosed at earlier stages of disease progression. This approach, while useful for isolating changes in diagnostic and early treatment pathways, excludes individuals who presented with metastatic cancers during the pandemic – a group that might have been affected by delays in diagnosis and healthcare access. As a result, their exclusion limits the generalisability of the findings to the wider group of people who have cancer, particularly in understanding how care disruptions may have shifted the disease burden toward more advanced stages.
- The restriction of survival analysis to cancer diagnoses up to the end of 2021 means that for the most recent cases, especially those diagnosed in 2022 and 2023, the available follow-up

time is insufficient to evaluate 1-year and especially 2-year survival outcomes. This truncated follow-up introduces censoring that limits insights into medium- and long-term trends in survival.

- The study does not adjust for several key variables known to influence cancer survival, such as comorbidities (e.g., cardiovascular disease, diabetes), tumour stage at diagnosis, and socioeconomic status. These unmeasured confounders may have varied significantly during the pandemic, affecting both the likelihood of diagnosis and the outcomes of treatment. For example, a patient with significant comorbid conditions may have had poorer survival irrespective of cancer care delays, while those diagnosed at later stages due to pandemic-related disruptions may show worse outcomes not captured in this analysis.

Objective 3: To evaluate the association between COVID-19 vaccination and excess deaths

- The analysis examined the relationship between vaccination and excess deaths based on estimated expected deaths for all age groups combined, rather than separately for distinct age categories. In the UK, different age groups were vaccinated at different times and within varying priority groups, which could introduce heterogeneity not fully addressed in this analysis.
- The associations between vaccination and mortality were measured at the population level rather than the individual level. This can limit the ability to draw causal inferences, as conclusions drawn about group-level data do not necessarily hold for individuals within those groups.
- Vaccination status was not linked to individual death records, making it impossible to directly assess whether the individuals who died had been vaccinated or not. This study cannot investigate protective effects of vaccination influenced mortality outcomes in a specific way, such as reducing the likelihood of death among those who had been recently vaccinated versus those who were not. The lack of individual-level data on vaccination status means the study relies on the assumption that general population-level vaccination trends apply consistently across all individuals.
- The lag structures used to model potential delayed effects of vaccination – 8 weeks for short-term and 26 weeks for long-term – may not have captured more complex or delayed temporal relationships.

- While sensitivity analyses incorporated all vaccine doses, the analysis did not differentiate between different vaccine products

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Appendix 1

Table S1. Observed 1- and 2-year survival rates (%) by cancer type with 95% confidence intervals in brackets. *P*-values indicate statistical significance of differences in survival rates between patients diagnosed in 2019 (baseline year) and those diagnosed in 2020 or 2021 for each cancer type. Mortality was defined as all-cause mortality, meaning that all deaths were considered regardless of the cause listed on the death certificate.

Cancer type	ICD-10 code	Year	1-year survival [%]	2-year survival [%]	*p*-value
Bladder	C67	2019	87 (84-90)	77 (73-81)	-
		2020	78 (74-83)	71 (66-76)	0.16
		2021	80 (77-84)	73 (69-78)	0.16
Brain (inc CNS)	C70-C72, C75.1-C75.3	2019	39 (33-47)	27 (22-35)	-
		2020	31 (25-39)	22 (17-29)	0.58
		2021	31 (25-39)	16 (12-23)	**0.04***
Colorectal	C18-C20	2019	79 (77-82)	71 (69-74)	
		2020	79 (77-82)	69 (66-71)	0.45
		2021	79 (77-81)	70 (68-73)	0.8
Breast	C50	2019	95 (94-96)	91 (89-92)	-
		2020	95 (94-96)	91 (90-93)	0.2
		2021	96 (95-97)	92 (90-93)	0.38
Gallbladder	C23-C24	2019	42 (33-53)	20 (13-30)	-
		2020	36 (27-49)	26 (17-38)	0.99
		2021	31 (22-42)	17 (11-27)	0.36
Head and Neck	C00-C14, C30-C32	2019	79 (75-83)	66 (61-71)	-
		2020	71 (66-77)	61 (56-67)	0.26
		2021	77 (72-81)	69 (64-74)	0.83
Kidney	C64	2019	87 (82-91)	81 (76-87)	-
		2020	88 (85-92)	80 (76-85)	0.9
		2021	88 (84-92)	83 (78-87)	0.6
Leukaemia	C91-C95	2019	80 (76-84)	69 (64-74)	-
		2020	79 (75-84)	73 (68-78)	0.06
		2021	83 (79-87)	70 (65-75)	0.53
Liver	C22	2019	38 (31-47)	25 (19-33)	-
		2020	41 (35-49)	29 (23-37)	0.5
		2021	43 (36-51)	27 (21-34)	0.68
Lung	C33-C34	2019	45 (42-47)	31 (28-33)	-
		2020	42 (39-45)	29 (26-31)	0.12
		2021	42 (39-45)	28 (26-31)	0.06
Lymphoma	C81-C86	2019	82 (78-86)	76 (72-80)	-
		2020	78 (75-82)	71 (67-75)	0.09
		2021	81 (77-84)	74 (70-78)	0.25

		2019	56 (50-63)	36 (30-42)	-
Oesophageal	C15	2020	42 (36-48)	27 (22-34)	**0.01***
		2021	44 (39-50)	32 (27-39)	0.14
		2019	86 (80-93)	81 (74-89)	-
Ovarian	C56-C57.4	2020	74 (65-84)	71 (62-81)	0.08
		2021	84 (77-91)	76 (68-84)	0.16
		2019	31 (26-38)	19 (15-24)	-
Pancreatic	C25	2020	33 (28-39)	18 (14-23)	0.88
		2021	36 (31-42)	22 (17-27)	0.2
		2019	95 (94-96)	89 (88-91)	-
Prostate	C61	2020	95 (94-96)	89 (87-91)	0.83
		2021	96 (95-97)	90 (88-92)	0.38
		2019	52 (45-60)	34 (27-42)	-
Stomach	C16	2020	50 (42-58)	37 (29-45)	0.76
		2021	56 (49-64)	45 (38-53)	**0.04***

* statistically significant at the 0.05 significance level