Analysis of intra-annual mortality fluctuations by causes of death in Italy

Introduction

Mortality patterns are often influenced by seasonal variations, with distinct peaks in death rates observed during winter or summer months. These seasonal fluctuations are closely tied to various causes of death, such as respiratory and cardiovascular conditions, which exhibit pronounced temporal patterns[1,2]. For instance, during cold winter months and summer heat waves, deaths related to respiratory illnesses and cardiovascular events tend to increase[2–4], intensifying pre-existing health conditions. Since intra-annual fluctuations in mortality have a strong impact on life expectancy estimates[5,6], it is important to understand the underlying patterns in cause-specific mortality. This insight is essential for accurately identifying the mechanisms through which these fluctuations affect overall mortality and life expectancy.

Two main external factors trigger higher mortality during winter and summer months, especially for circulatory diseases and respiratory diseases: temperature and virus spread. The first one relates to higher mortality during low temperature shocks during wintertime[7,8] and prolonged extremely hot days during summer. Interestingly, in Europe, countries with milder winters have higher excess winter mortality rates than those with much colder temperatures[9,10], suggesting that seasonal mortality may be more likely due to inefficient temperature protections, linked to a lower socio-economic advantage, than to the direct influence of colder weather[9]. The second factor is mainly linked to virus spread throughout the year, which might aggravate already pre-existing comorbidities[11,12]. Despite the wide literature on the mortality mechanism of these two drivers, current knowledge remains limited when it comes to understanding cause-specific contributions to intra-annual excess mortality trends.
In fact, the majority of the studies have analysed specific causes of death trends within the year[13–15], mainly relying on annual estimates, using data from specific high-mortality burden weeks or specific causes of death. A comprehensive epidemiological analysis of the mortality fluctuations by causes of death is still lacking. In this context, Italy is one of the European countries most affected by heat waves and flu epidemics[2,16] in recent years. Over the last decades, the country has experienced several fluctuations in life expectancy at birth due to short-term events, such as the economic crisis[17], heatwaves[18], and extreme winter temperatures[11]. Some studies revealed similar cause-specific patterns as in the rest of Europe, with excess mortality mainly driven by cardiovascular and respiratory diseases[10,13,19].

This study provides a comprehensive analysis of intra-annual mortality fluctuations by cause of death in Italy between 2004 and 2019. Using the excess mortality framework, we quantify both the absolute and relative contributions of causes of death to intra-annual excess mortality. Specifically, we want to understand which causes of death are affected by intra-annual mortality fluctuations, calculate their impact by cause of death, and quantify the relative contribution of each cause of death to intra-annual excess mortality. In doing so, we offer new insights into the mechanisms driving short-term mortality shocks in Italy and highlight the leading contributors to excess mortality across different seasons. This analysis provides a deeper understanding of how specific causes of death shape temporal mortality patterns and their implications for overall life expectancy.

Data and Methods

Data

We employed monthly death count data from the Italian National Institute of Statistics (ISTAT), disaggregated by cause of death (ICD-10), sex, and 5-year age groups from 0 to 90+, covering the period from 2004 to 2019. Annual population data by sex and age group were also obtained from ISTAT for the same reference period. The causes of death were grouped into: Acute respiratory diseases, Other respiratory diseases, Infectious diseases, Neoplasm, Congenital malformations, Diseases of the digestive system, Endocrine diseases, Heart (or Cardiovascular) diseases (CVD), Other disorders of the circulatory system, Cerebrovascular diseases, Nervous system, Neurodegenerative Diseases (Alzheimer, Parkinson and Dementia), Mental disorders, External, Accidents, Suicide, Other (see Table S1 in Supplementary Material for a complete list of the ICD-10 codes). We define seasons based on calendar years (Winter: January, February, December; Spring: March, April, May; Summer: June, July, August; Autumn, September, October, November).

Methods

To understand whether the causes of death trends followed a seasonal pattern, we computed age-standardised death rates (ASDR) using the direct method of standardisation and the 2013 European Standard Population[20], for each month, year, cause of death, and sex. We applied time series analysis (Kruskal-Wallis test) by cause-specific ASDR to check for seasonality patterns. Subsequently, to estimate the cause-specific excess deaths due to intra-annual fluctuations in mortality, we also computed the baseline ASDR (i.e., the counterfactual mortality rate in the absence of excess mortality), calculated as explained below. For both the observed and baseline ASDR, all deaths were first analysed collectively (all causes combined) and then disaggregated by cause of death to evaluate their specific contributions to overall mortality dynamics. We computed both the absolute and relative contribution because, while absolute excess deaths reveal the largest contributors to seasonal mortality in terms of volume, relative excess deaths highlight causes disproportionately affected by intra-annual variation.

Absolute values analysis: Cause-specific excess deaths due to intra-annual fluctuations in mortality

We conceptualised the baseline ASDR as the mortality rate in the absence of excess mortality, as the mortality rate based on the three months in each year with the lowest death counts, all ages combined.

$$ASDR^{baseline} = \sum_x m_x^{baseline} \cdot \frac{P_x^S}{\sum_x P_x^S},$$

Where P_x^s is the European Standard Population 2013 at age x, while $m_x^{baseline}$ is the counterfactual mortality age at age x, based on the three months for each year with the lowest death counts at all ages (following the same rationale as in Marinetti et al.[5]). We quantified excess mortality as the difference between observed and baseline ASDR, both for all causes combined and separately by cause of death, sex, and year. The difference between observed and baseline ASDR was multiplied by the relevant population exposure to estimate the number of excess deaths.

Relative values analysis: Cause-specific excess deaths ratio due to intra-annual fluctuations in mortality

Finally, to understand which causes of death were relatively more affected by excess mortality, we computed the ratio of excess deaths (Fig S1, Supplementary material) to baseline deaths (Fig S2, Supplementary material) for each cause of death, sex, month and year. This indicator allowed us to compare how much more affected each cause was, relative to its own baseline level, revealing causes particularly vulnerable to short-term mortality shocks. Moreover, we performed a simple regression analysis of death counts by months (after the removal of the baseline death counts). We considered months as a dummy variable, September as the reference category (month with the lowest mortality throughout the year), following a negative binomial distribution. This analysis showed us which months had a statistical impact on the cause-specific mortality in the study period. The analyses were conducted in R version 4.2.3.

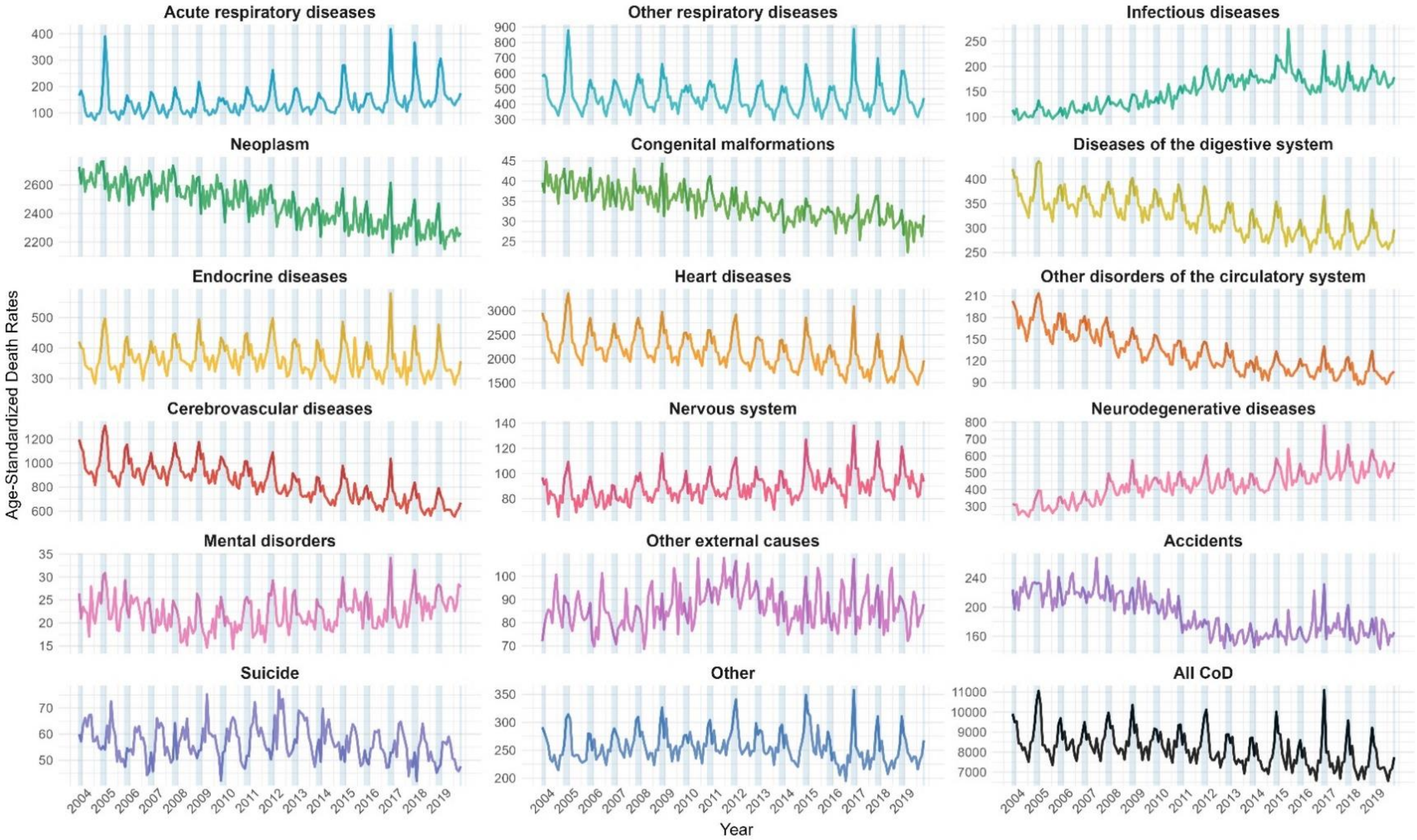
Results

Intra-annual fluctuations of causes of death in Italy

In Italy, during the period 2004–2019, all-cause mortality declined. However, this decrease was not uniform across all causes of death. In fact, mortality due to infectious diseases, diseases of the nervous system, neurodegenerative diseases, and mental disorders increased over time, while mortality from respiratory diseases (including acute and other respiratory conditions), endocrine diseases, suicide, and other external causes remained relatively stable. Conversely, causes such as neoplasms, heart diseases, cerebrovascular diseases, and accidents showed a clear declining trend (Figure 1).

Moreover, all-cause mortality followed a statistically significant seasonal pattern, as did the majority of cause-specific mortality rates. Most causes of death displayed marked peaks during the winter months (Figure 1), particularly those related to circulatory and respiratory conditions. In contrast, deaths due to suicide, other external causes, and accidents tended to be higher during the spring and summer months. Notably, congenital malformations did not exhibit any consistent seasonal pattern.

Figure 1. Age-standardized death rates (per 10.000) by month and cause of death, total population (in blue winter months), 2004-2019

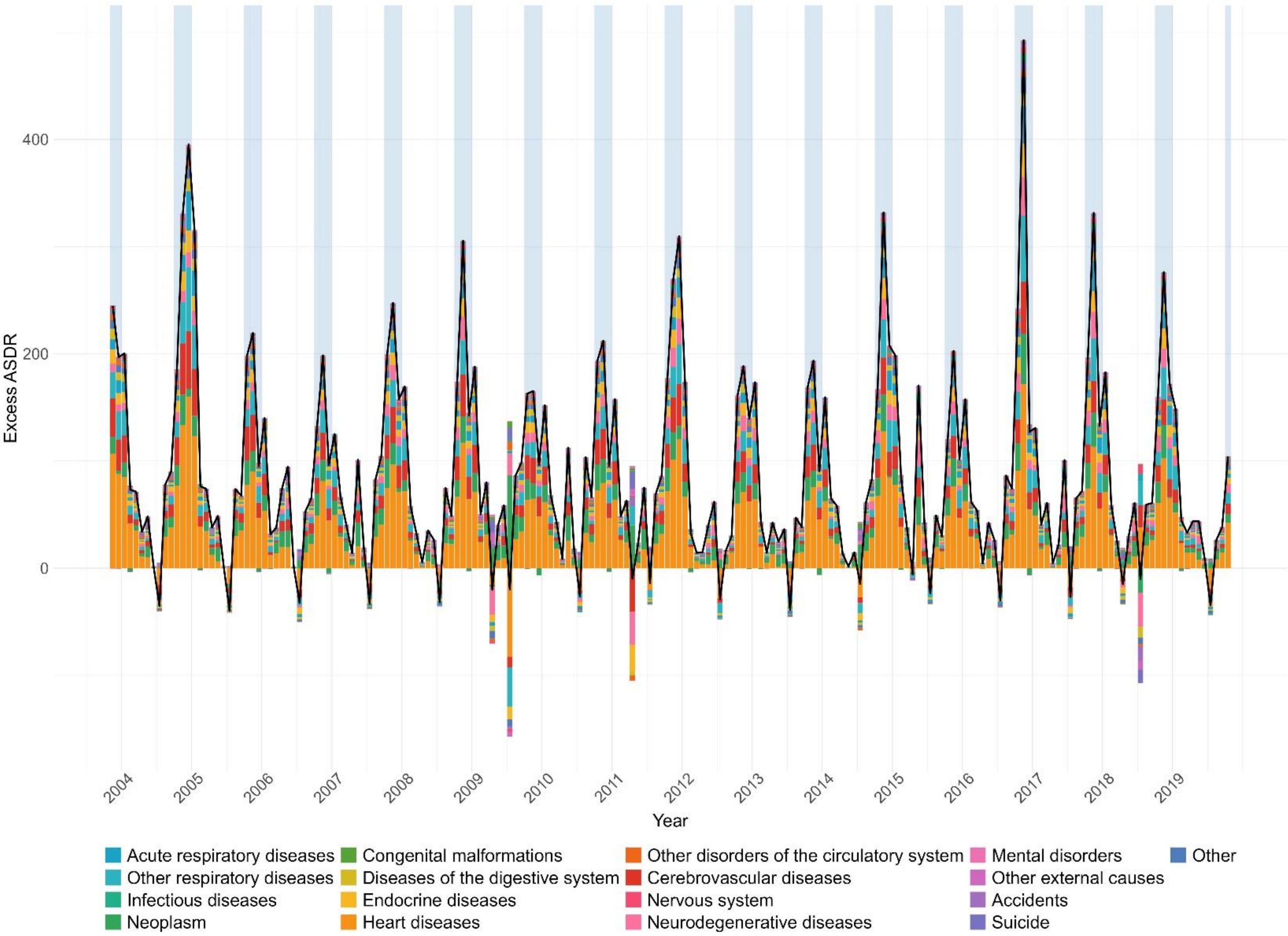


Excess mortality by cause of death in Italy

Analysing excess mortality trends for all causes of death (black line in Figure 2), the strongest intra-annual fluctuations consistently occurred during the winter months (highlighted with blue background shading), reflecting a clear seasonal pattern. When decomposing this trend by cause of death, we identified the specific contributions of each cause to overall excess mortality. During peak mortality months, the dominant contributor was cardiovascular diseases (CVD), accounting for approximately 40% of total excess mortality. Additional significant contributors included cerebrovascular diseases and respiratory diseases, particularly acute respiratory infections, which together contributed between 10% and 15%. As seen in the graph, negative values for cause-specific contributions occasionally emerged during periods of low mortality, especially in May, June, and September. These fluctuations are likely due to unstable estimates caused by small death counts during those months.

Interestingly, in the last years of the study period, we observed an increasing contribution from certain causes of death. For example, neurodegenerative diseases rose from contributing around 3% of the total excess mortality in 2004 to about 8% by 2019. Similarly, the contribution of acute respiratory diseases increased from approximately 4% to 7%, indicating their growing role in seasonal mortality patterns (Figure S1, Supplementary Material).

Figure 2. Excess mortality by month and cause of death, total population (in blue winter months), legend arranged by absolute relevance of CoD, 2004-2019



Relative impact of intra-annual fluctuations in mortality by causes of death in Italy

To evaluate the relative burden of intra-annual mortality fluctuations, we examined the ratio between cause-specific excess mortality (Figure 2 and S1, Supplementary Material) and the corresponding baseline mortality levels (Figure S2, Supplementary Material). This ratio captures the relative impact of seasonal mortality excess for each cause of death. Respiratory diseases, especially acute respiratory infections, stood out with a ratio substantially above 1, reaching on average 2.5 times the baseline level during peak months, with some years reaching 4 times higher values (Figure 3). This finding indicates that, although cardiovascular diseases remain the largest contributors to overall excess mortality in absolute terms, respiratory diseases are the most sensitive to seasonal fluctuations, particularly during winter.

Despite a general decline in baseline mortality levels across most causes of death over the study period (Figure S2, Supplementary Material), the relative excess (i.e. the fluctuation compared to baseline) remained stable. This suggests that the seasonal burden has not diminished proportionally and may be increasing for certain causes, such as neurodegenerative and respiratory diseases, highlighting a growing sensitivity to seasonal stressors in specific subpopulations.

To further explore the relative seasonal impact of mortality by cause, we conducted a regression analysis to identify the most and second-most relevant contributors to excess mortality for each month between 2004 and 2019 (Table 1). As expected, CVD was the leading cause of death for most months in the total population as well as in both sexes. However, the summer months showed distinct patterns: in June and July, accidents and neoplasms had the highest impact on excess mortality in the total population, while in August, neoplasms and neurodegenerative diseases. These patterns were similar in the male population. On the other side, among females, other external causes, CVD, and neurodegenerative diseases were more prominent in the summer. Regarding the second-highest contributors by month, cerebrovascular and respiratory diseases frequently ranked second in the colder months, while causes such as suicide, CVD, and neurodegenerative diseases became more relevant during summer.

Figure 3. Ratio of excess ASDR (Figure 2) and baseline ASDR (Figure S2) by month and cause of death, 2004-2019

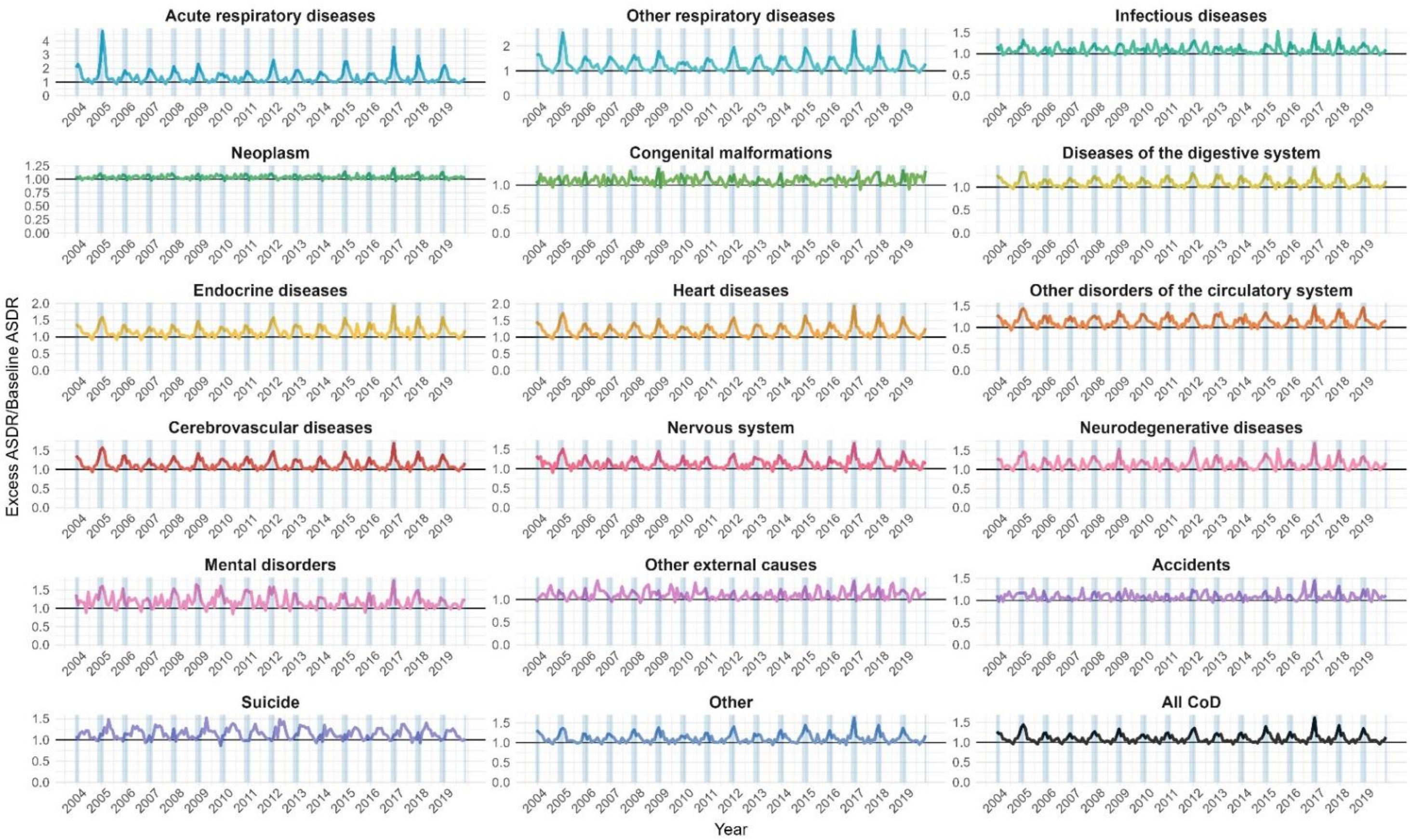


Table 1. Main two cause-of-death contributors to relative excess deaths in Italy, by sex and month (2004-2019)

Month	**Main cause(s) of death**					
	Total		**Females**		**Males**	
	First	**Second**	**First**	**Second**	**First**	**Second**
January	CVD	Cerebrovascular	CVD	Cerebrovascular	CVD	Respiratory
February	CVD	Respiratory	CVD	Cerebrovascular	CVD	Respiratory
March	CVD	Respiratory	CVD	Cerebrovascular	CVD	Respiratory
April	CVD	Respiratory	CVD	Respiratory	CVD	Respiratory
May	CVD	Respiratory	CVD	Respiratory	CVD	Neoplasm
June	Accidents	Suicide	External	Nervous system	Accidents	Suicide
July	Neoplasm	CVD	CVD	Neoplasm	Neoplasm	Cerebrovascular
August	Neoplasm	Neurodegenerative	Neurodegenerative	Neoplasm	Neoplasm	Neurodegenerative
October	CVD	Neoplasm	CVD	Neoplasm	CVD	Neoplasm
November	CVD	Cerebrovascular	CVD	Cerebrovascular	CVD	Neoplasm
December	CVD	Cerebrovascular	CVD	Cerebrovascular	CVD	Neoplasm

Discussion

Main Findings

This study provides a comprehensive analysis of intra-annual fluctuations in cause-specific mortality in Italy between 2004 and 2019. By using high-quality monthly mortality data and computing absolute and relative excess mortality by causes of death, we identified significant cause-specific seasonal patterns that influence overall mortality rates. The results revealed that excess mortality was not evenly distributed throughout the year and that especially specific causes exhibit pronounced seasonal patterns.

The highest impact on mortality was observed during winter months. Cardiovascular and respiratory diseases emerged as the main drivers of winter excess mortality (40% and 15%, respectively). While cardiovascular diseases accounted for the largest proportion of absolute excess deaths, respiratory mortality also displayed the highest relative deviations from baseline levels, reaching more than twice the expected monthly rates. Importantly, these seasonal peaks remained persistent over time, even as overall baseline mortality declined, indicating a growing or unmitigated seasonal burden for specific causes.

Despite the seasonal impact being lower during summer months compared to winter months, we observed a different seasonal epidemiological profile. Neoplasms, accidents, and neurodegenerative diseases played a more prominent role in the summer. For instance, external causes and neurodegenerative conditions were more relevant among females, while accidents and neoplasms had greater influence in the male population. These findings highlight that both the magnitude and composition of excess mortality vary considerably across the calendar year and by sex.

Explanation of the findings

The observed winter peaks in cardiovascular and respiratory mortality are consistent with a large body of literature documenting the adverse effects of cold temperatures and seasonal infections on cardiorespiratory outcomes[2,3,21]. These effects are well-established and are often linked to increased incidence of influenza-like illnesses, reduced indoor air quality, and physiological stress induced by cold exposure. Of particular note is the finding that, despite steady improvements in overall mortality over the analysed period, the relative burden of intra-annual mortality fluctuations has remained stable. This suggests that while general health outcomes have improved, the seasonal vulnerability causes of death have not followed the same trajectory.

The sex-specific differences in cause-of-death patterns during the summer months provide a more nuanced view of intra-annual mortality dynamics. Female mortality was more affected by neurodegenerative diseases and external causes, while male mortality was more sensitive to accidents and neoplasms. These patterns may reflect a combination of behavioural, biological, and structural risk factors, including differential exposure to heat stress, occupational hazards, and access to healthcare. Prior studies have suggested that women may be more vulnerable to the effects of heat on neurocognitive health[22], while men are disproportionately affected by risk-taking behaviour and occupational exposure[23,24] during warmer months.

Strengths and limitations of the study

A key strength of this study lies in its use of monthly, cause-specific mortality data from official statistics produced by the Italian National Statistical Institute. These data allowed for the computation of a precise estimation of seasonal mortality patterns and impacts by causes of death, often impossible to achieve in annual analysis or relying on less detailed data. Our methodological approach allowed for a standardised comparison of intra-annual fluctuations across time and causes. This approach improves on traditional metrics by estimating the actual impact of intra-annual mortality fluctuations on observed cause-specific mortality trends.

Nevertheless, several limitations must be acknowledged. First, the analysis assumes intra-month homogeneity in mortality patterns, which may overlook extreme short-term events such as heatwaves or flu outbreaks concentrated within a few days. Second, while we attempted to mitigate the influence of long-term trends and counterbalancing seasonal effects by selecting appropriate baselines (validated through sensitivity analyses in previous work[5,6]), the choice of baseline months is still arbitrary. Third, the study analysed causes of death grouped in specific categories, based on previous literature[25] and knowledge of the mortality patterns by causes of death in Italy. Finally, despite working with national data, low death counts in specific months and causes may introduce random variation, particularly for less frequent causes like mental disorders or congenital conditions.

Conclusion

This study shows that cause-specific mortality in Italy is shaped by clear and persistent seasonal patterns. While overall mortality has decreased over time, certain causes of death, especially cardiovascular and respiratory diseases, continue to be strongly affected by winter excess mortality. These patterns have remained stable over time for all causes of death, suggesting that seasonal vulnerabilities have not improved in the same way as general mortality. These results highlight the importance of taking seasonal dynamics into account when planning public health measures. Interventions such as targeted wintertime prevention campaigns for respiratory and cardiovascular conditions, or summer safety efforts focused on accidents and heat-related risks, could help reduce avoidable deaths. This will become even more relevant in the coming years, as ageing populations and climate change are likely to increase the health risks associated with extreme temperatures[26–28] and seasonal variation.

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Supplementary Material

Table S1. List of ICD-10 codes used in the analysis

Causes of death	ICD-10 code
Acute respiratory diseases	J00-J22, U04-U07
Other respiratory diseases	J30-J98
Infectious diseases	A00-A99, B00-B99
Neoplasm	C00-C99, D00-D48
Congenital malformations	P00-P99, Q00-Q99, R95
Diseases of the digestive system	K00-K63, K65-K92
Endocrine diseases	E00-E88
Heart diseases	I00-I51
Other disorders of the circulatory system	I70-I99, K64
Cerebrovascular diseases	G45, I60-I69
Nervous system	G00-G19, G24-G29, G33-G44, G47-G93
Neurodegenerative Diseases	F00-F03, G20-G23, G30-G32
Mental disorders	F04-F99
External	W00-W99, Y00-Y99
Accident	V00-V99, X00-X59
Suicide	X60-X84
Ill-defined	R00-R94, R96-R99
Other	D50-D89, E89-E90, H00-H95, L00-L98, M00-M99, N00-N99, O00-O99, S00-S99, T00-T98, U00-U49, U82-U85, Z00-Z99

Figure S1. Excess mortality by month and cause of death, total population (in blue winter months), 2004-2019

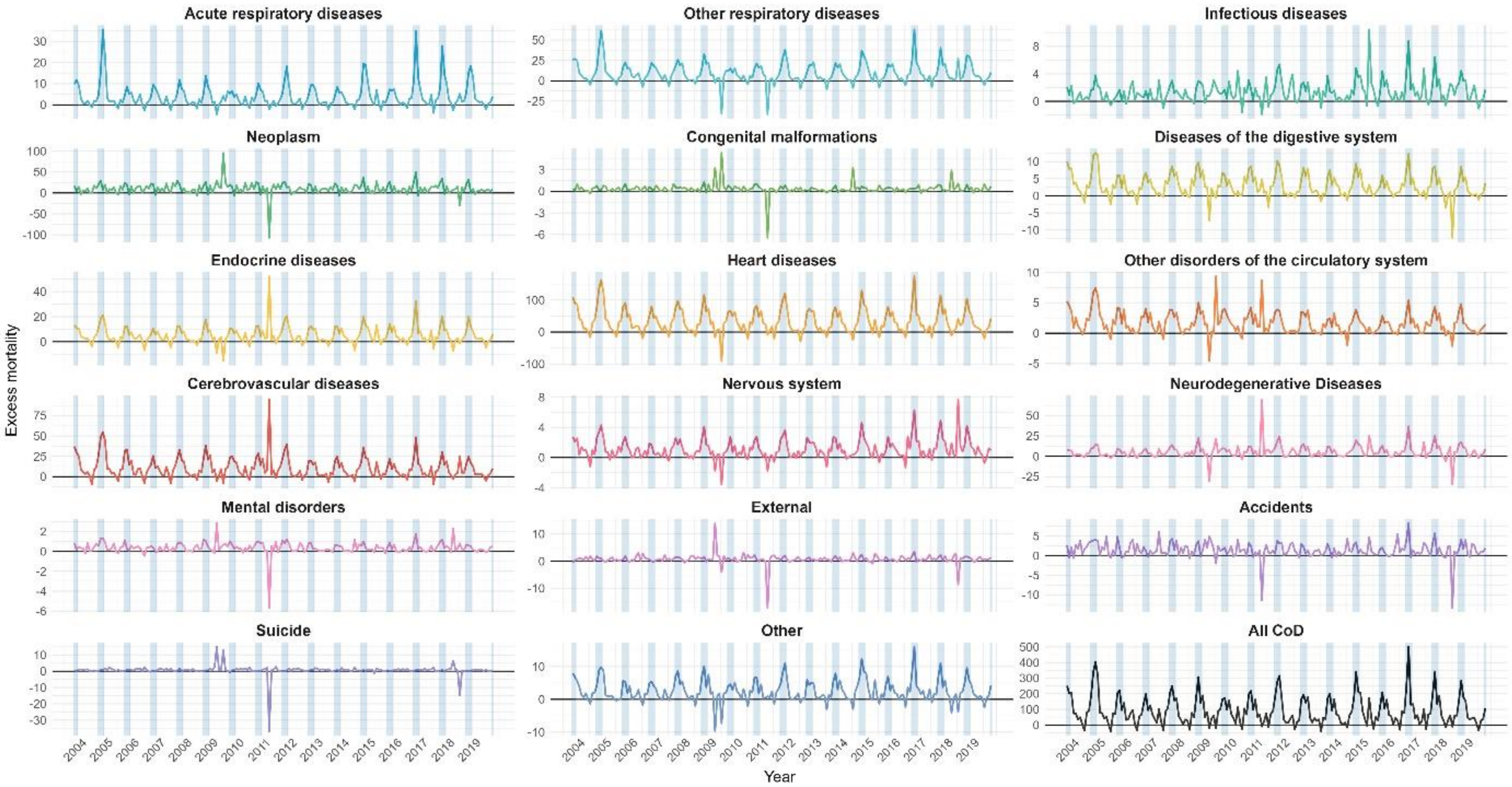

Figure S2. Baseline age-standardized death rates (per 10.000) used for the computation of excess ASDR, by month and cause of death, total population, 2004-2019