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MPIDR Working Paper WP 2025-036 | December 2025  
<https://doi.org/10.4054/MPIDR-WP-2025-036>

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# **Analysis of intra-annual mortality fluctuations by cause of death in Italy**

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## **Abstract**

**Background:** Seasonal fluctuations in mortality significantly affect population health and remain an important public health challenge. As climate change increases temperature extremes and ageing populations heighten vulnerability, understanding the cause-specific drivers of these mortality fluctuations is increasingly urgent. Yet, detailed evidence on how different causes of death shape these mortality patterns remains limited.

**Data and Methods:** We analysed monthly mortality data from the Italian National Institute of Statistics, disaggregated by cause of death, sex, and 5-year age groups, 2004-2019. Excess mortality for 17 major causes of death was quantified by comparing the observed age-standardised death rate (SDR) with the baseline SDR, defined as the average of the three months with the lowest mortality each year. We estimated both the absolute and relative impact of cause-specific mortality on overall seasonal mortality.

**Results:** Heart and respiratory diseases were the leading contributors to excess mortality, accounting for approximately 40% and 15% of the intra-annual burden, respectively. The summer months exhibited significantly smaller excess mortality. Respiratory diseases showed the highest relative impact compared to the other causes of death. While baseline mortality decreased over time, the relative intra-annual burden remained stable or increased for specific causes, indicating persistent or growing seasonal vulnerabilities.

**Conclusion:** Intra-annual mortality fluctuations in Italy were mainly driven by cardiovascular and respiratory diseases and have remained stable over time despite improvements in overall mortality. These persistent patterns highlight unmet seasonal vulnerabilities and the importance of integrating cause-specific seasonality into health planning, particularly in light of ageing populations and climate change challenges.

**Keywords:** Seasonal mortality; Causes of death; Excess mortality; Italy

# 1. Introduction

Mortality patterns are often influenced by seasonal variations, particularly in temperate regions, where death rates tend to peak, predominantly, in the winter and, to a lesser extent, during summer heatwaves [1–4]. These intra-annual fluctuations not only reflect environmental and social stressors, such as cold temperatures, extreme heat, or infectious disease spread, but also healthcare system capacity and public health planning. Moreover, these seasonal variations contribute to short-term changes in overall mortality and can influence life expectancy levels [5]. When analysing all-cause seasonal mortality patterns, we are essentially observing the combined effect of the underlying cause-specific curves. Therefore, understanding the underlying patterns in cause-specific mortality is essential to accurately identifying the mechanisms through which these fluctuations affect overall mortality and life expectancy. However, an analytical approach to estimate the main cause-of-death drivers of mortality within the year is still lacking.

Indeed, specific causes of death respond in various ways to seasonal risks. Respiratory diseases, such as influenza and pneumonia, typically peak in winter due to cold temperatures and the spread of seasonal viruses [6,7]. Cardiovascular diseases also show seasonal variation, with increased risks during both cold spells and heatwaves [8,9]. In contrast, neoplasms tend to exhibit little to no seasonality, showing stable mortality rates throughout the year [10], but the results may depend on the country analysed [11]. External causes of death, such as accidents or suicides, display reverse seasonal trends, with some studies reporting peaks in spring or summer [12,13]. These differences underscore the importance of analysing seasonal mortality from a cause-specific perspective, as the timing, magnitude, and direction of fluctuations vary substantially across causes.

In this context, Italy is one of the European countries most affected by heat waves and flu epidemics in recent years [6,14]. Life expectancy at birth showed several fluctuations attributable to short-term events, including the economic crisis in 2008-2010 [15], heatwaves in 2003 and 2015 [16–18], extreme winter temperatures in 2005, 2012 and 2017, and flu epidemics in 2015 and 2017 [7,8,19]. The few cause-specific studies in Italy suggest similar cause-specific patterns as observed in other European countries, with high excess mortality for cardiovascular and respiratory diseases [8,17,20], and peaks in external mortality during spring and summer [21–23]. However, the mentioned studies have mainly focused on specific high-burden years or specific causes of death analysis, while an overall formal assessment of the actual intra-annual impact for a wide range of different causes of death is still lacking.

Such an assessment requires a novel methodological framework to intra-annual mortality variations, for which use can be made of the excess mortality framework. This method is commonly used to assess mortality impacts during exceptional events, such as pandemics or flu epidemics. When applied to seasonal mortality, it allows for a more detailed understanding of the mechanisms behind short-term mortality changes.

All in all, in our study, we will assess cause-specific patterns of seasonal mortality and their contribution to overall seasonal mortality in Italy between 2004 and 2019. We will use a comprehensive approach and apply a novel methodological framework to formally quantify both the absolute and relative contributions of 17 main groups of causes of death to intra-annual excess mortality, overall and both in winter and summer, over a long period of time, using high-quality national monthly mortality data. By doing so, we deepen the existing literature by attributing all-cause excess mortality to specific causes of death, uncovering how different causes contribute to the observed seasonal fluctuations and to what extent they shape overall mortality trends throughout the year.

## **2. Data and Methods**

### **2.1 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 diseases, other disorders of the circulatory system, cerebrovascular diseases, nervous system, neurodegenerative diseases (Alzheimer, Parkinson and dementia), mental disorders, other external causes, accidents, suicide, other (see Table S1 in Supplementary Material for a complete list of the ICD-10 codes). Cardiovascular diseases (heart and cerebrovascular diseases) are by far the largest group of causes of death in Italy, on average in the analysed period (56% of total mortality), followed by neoplasms (30%), acute and other respiratory diseases (7%), and neurodegenerative diseases (5%) (see Table S1 in Supplementary Material for the other causes of death). For the sake of visualisation, the results presented are the monthly unweighted average for the period analysed (2004-2019). In the Supplementary Material, the time trend and specific-month results are available. Appendix A, Supplementary Material, provides a detailed analysis of the causes of death handling.

### **2.2 Methods**

To understand whether the causes of death trends followed a seasonal pattern, we computed age-standardised death rates (SDR) using the direct method of standardisation and the 2013 European Standard Population,[24] for each month, year, cause of death, and sex. Subsequently,

to estimate the cause-specific excess deaths due to intra-annual fluctuations in mortality, we also computed the baseline SDR (i.e., the counterfactual mortality rate in the absence of excess mortality), calculated as explained below.

For both the observed and baseline SDR, 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.

### ***2.2.1 Absolute impacts: cause-specific excess deaths due to intra-annual fluctuations in mortality***

We conceptualised the baseline SDR 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 by sex and cause of death, all ages combined.

$$SDR^{baseline} = \sum_x m_x^{baseline} \cdot \frac{P_x^s}{\sum_x P_x^s}$$

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 [5]). We quantified excess mortality as the difference between observed and baseline SDR, both for all causes combined and separately by cause of death, sex, month and year. The difference between observed and baseline SDR was multiplied by the relevant population exposure ( $P_x$ ) to estimate the number of excess deaths.

$$Excess\ Deaths = (SDR^{observed} - SDR^{baseline}) \cdot P_x$$

To then compare the excess deaths values by cause of death, we have computed a percentage contribution calculated as the ratio between the cause-specific contribution and the all-cause mortality contribution in that month. We also present the values for only winter and summer months as their monthly sum.

### ***2.2.2 Relative impacts: cause-specific excess mortality 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 difference between observed (Fig. S1, Supplementary Material) and baseline (Fig. S2, Supplementary Material) SDR divided by the baseline SDR for each cause of death, sex, month and year. This indicator allowed us to compare how much each cause was affected by seasonality, relative to its own baseline level, revealing causes particularly vulnerable to short-term mortality shocks.

$$\text{Relative Excess Deaths} = \frac{SDR^{observed} - SDR^{baseline}}{SDR^{baseline}}$$

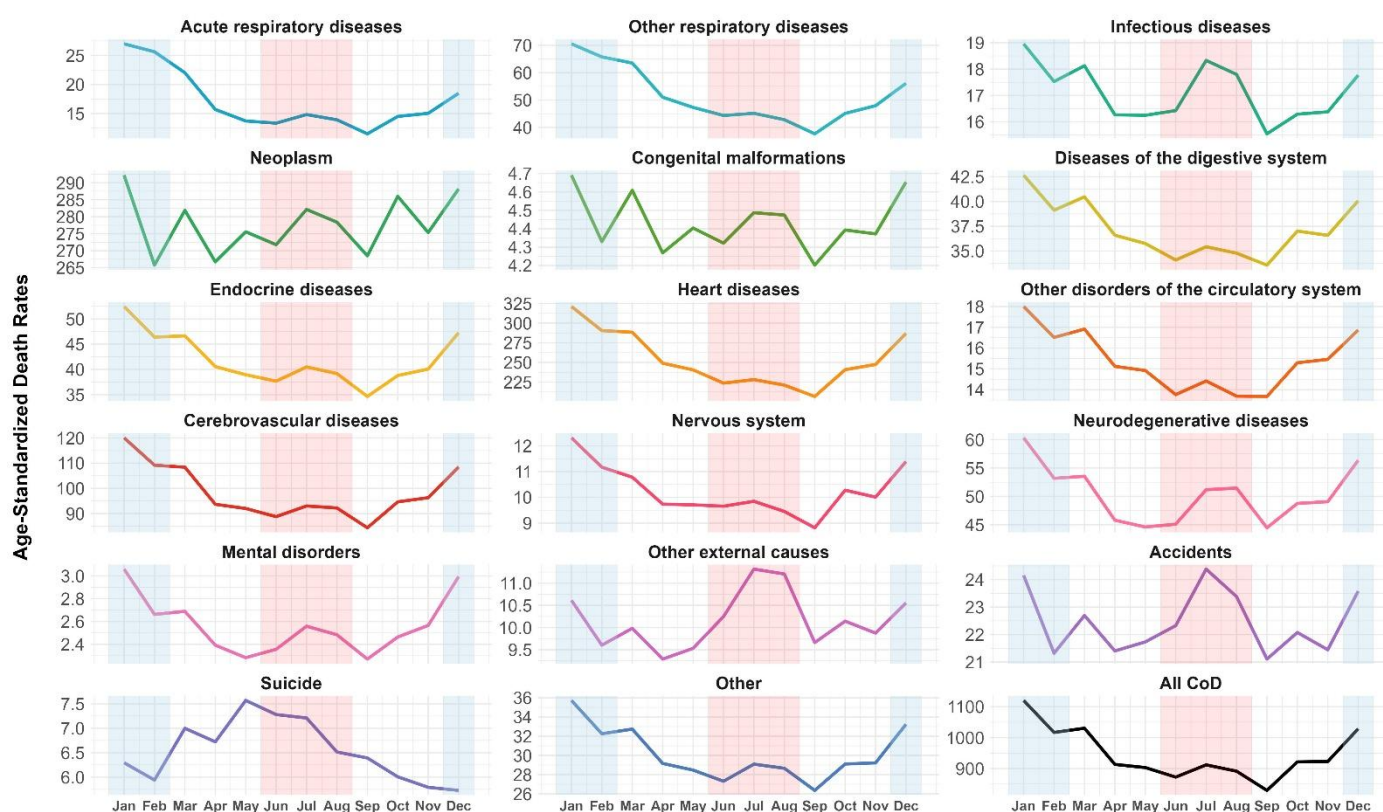
The analyses were conducted in R version 4.2.3.

## **3. Results**

### **3.1 Intra-annual fluctuations of causes of death in Italy**

All-cause mortality followed a statistically significant seasonal pattern, as did the majority of cause-specific mortality rates (Figure 1). Both all-cause mortality and most causes of death displayed marked peaks during the winter months (blue shadow), particularly those related to circulatory and respiratory conditions, with slight increases also during summer months (red

shadow). In contrast, deaths due to suicide, other external causes, and accidents showed a reversal seasonal pattern, with peaks during summer months and lower mortality rates during colder months. Notably, congenital malformations did not exhibit any consistent seasonal pattern.



**Figure 1.** Age-standardized death rates (per 100.000) by month (blue shadow: winter, red shadow: summer) and cause of death, total Italian population, average 2004-2019

Causes of Death	Winter			Summer			Annual		
	Total	Female	Male	Total	Female	Male	Total	Female	Male
<b>All Causes of Death</b>	593.4	522.5	709.6	106.6	102.1	108.6	1071.7	942.0	1286.4
Acute respiratory	5.4%	5.6%	5.0%	3.5%	4.0%	4.1%	4.7%	5%	4.0%
Other respiratory	11.0%	9.5%	12.8%	7.9%	6.5%	6.8%	10.2%	9%	11.3%

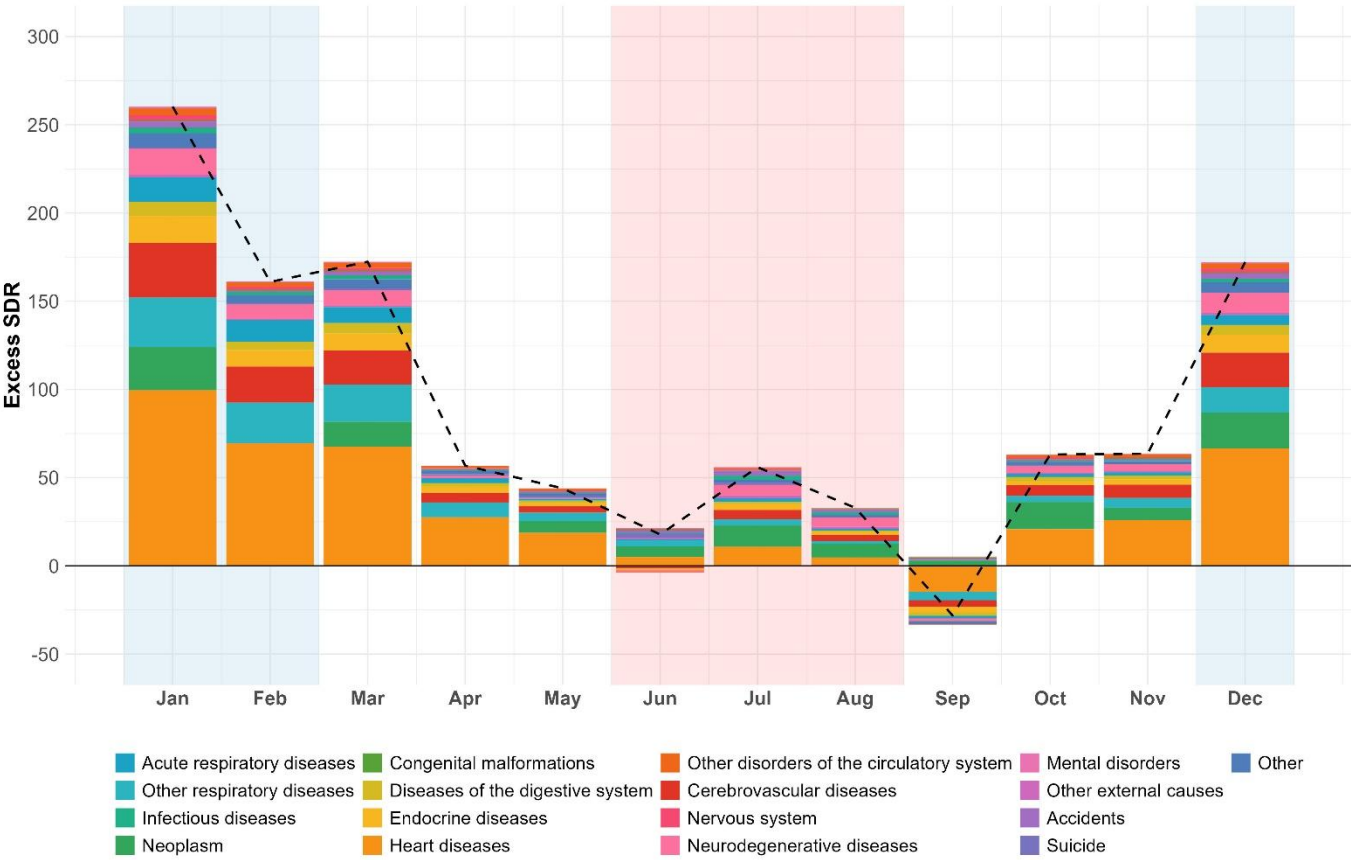
Infectious	1.2%	1.3%	1.2%	4.0%	4.4%	3.3%	1.5%	2%	1.4%
Neoplasm	7.5%	6.5%	8.8%	24.2%	19.8%	21.8%	11.5%	10%	12.1%
Congenital	0.2%	0.3%	0.3%	1.0%	1.1%	-0.1%	0.5%	1%	0.4%
Digestive system	3.1%	2.8%	3.4%	1.5%	1.9%	2.5%	3.0%	3%	3.3%
Endocrine	5.8%	6.2%	5.4%	4.2%	6.4%	6.3%	5.1%	6%	4.9%
Heart	39.7%	39.7%	38.7%	19.3%	20.5%	19.7%	37.0%	37%	37.0%
Other circulatory	1.6%	1.5%	1.8%	0.6%	1.1%	1.0%	1.8%	2%	2.1%
Cerebrovascular	12.0%	12.6%	11.2%	7.1%	10.2%	11.2%	11.0%	11%	10.4%
Nervous system	1.2%	1.3%	1.2%	1.4%	1.3%	0.6%	1.2%	1%	1.1%
Neurodegenerative	5.9%	6.6%	4.9%	9.3%	12.9%	9.5%	5.7%	7%	4.9%
Mental disorders	0.3%	0.3%	0.4%	0.8%	0.7%	-0.1%	0.4%	0%	0.3%
Other external causes	0.5%	0.6%	0.5%	3.5%	1.9%	3.2%	0.9%	1%	1.0%
Accidents	1.2%	1.8%	0.8%	5.7%	3.2%	5.4%	1.7%	2%	1.9%
Suicide	0.1%	0.1%	0.2%	3.4%	1.3%	1.0%	0.9%	1%	0.8%
Other	3.2%	3.2%	3.3%	2.7%	2.9%	3.7%	2.8%	3%	3.2%

**Table 1.** Excess mortality by month and cause of death, total Italian population, (blue shadow: winter, red shadow: summer), average 2004-2019

### 3.2 Absolute impact of causes of death on excess all-cause mortality

Analysing excess mortality from all causes of death (black line in Figure 2), we observed a clear seasonal pattern, with the strongest intra-annual fluctuations consistently occurring during the winter months (highlighted by the blue background shading). During the winter months, the dominant contributors were heart diseases, accounting for approximately 40% of total excess mortality (Figure 2 and Table 1). Additional significant contributors included cerebrovascular diseases and respiratory diseases, particularly acute respiratory infections, which together contributed between 12% and 16% to the overall excess intra-annual mortality. Summer excess mortality was composed not only of heart mortality (20.6% on average), but also of neoplasms

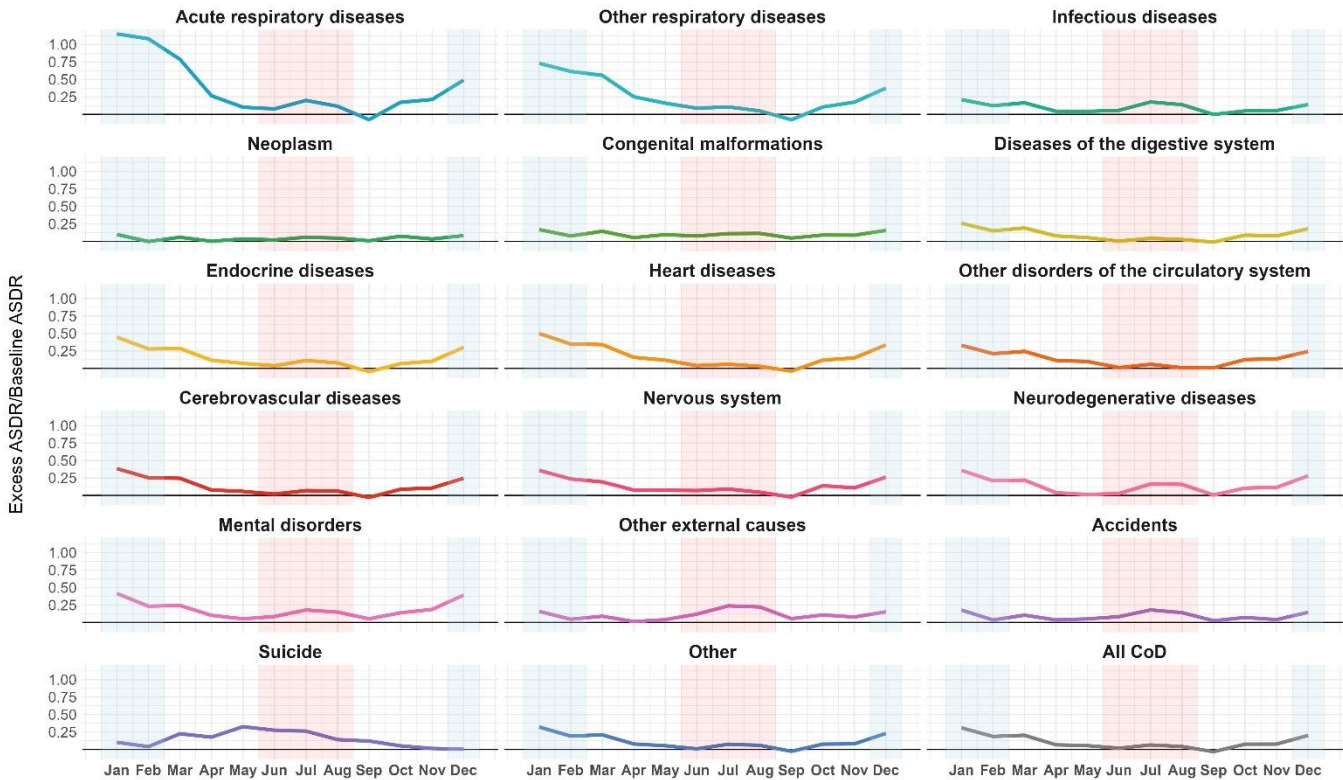
(26.4% on average), neurodegenerative diseases (6.5% in total, but 13% when considering only July and August, see Table S2 in Supplementary Material for month-specific results), and suicides (17% in June). However, since the total number of excess deaths during the summer months averaged only around 50 excess deaths, these percentage contributions correspond to relatively small absolute numbers.



**Figure 2.** Excess mortality by month and cause of death, total Italian population (blue shadow: winter, red shadow: summer), average 2004-2019. *Note: Negative values for cause-specific contributions occasionally emerged during periods of low mortality and are likely due to unstable estimates caused by small death counts.*

### 3.3 Relative impact of causes of death on excess all-cause mortality

To evaluate the relative burden of intra-annual mortality fluctuations, we examined the relative ratio between cause-specific observed mortality and the corresponding baseline mortality levels. This ratio captures the relative impact of intra-annual mortality excess deaths for each cause of death. Respiratory diseases, especially acute respiratory infections, stood out with a ratio substantially above 0, reaching, on average, 90% more than the baseline level during January and February (Figure 3). This finding indicates that, although heart diseases remain the largest contributors to overall excess mortality in absolute terms, respiratory diseases are the most sensitive to seasonal fluctuations, particularly during winter.



**Figure 3.** Relative ratio of observed SDR and baseline SDR by month and cause of death (blue shadow: winter, red shadow: summer), total Italian population, 2004-2019 average

### **3.4 Sex differences in the cause-specific contributions**

Furthermore, analysing the results by sex (Figure S3 and S4, Supplementary Material and Table 1), we observed a larger impact of intra-annual mortality on male mortality both during winter months and summer months (respectively 710 excess deaths and 110 excess deaths) than in the female population (520 and 100). We also found similar patterns in excess mortality by causes of death during winter, but not during summer. In fact, in the female population, we observed a larger contribution of neurodegenerative diseases, while in the male population, a higher contribution of accidents and other external causes. Looking at the results for the relative impacts, we found that females had a relatively higher burden of mortality by respiratory disease than males during the winter months (Figures S5-S6 in Supplementary Material).

### **3.5 Trends over time in intra-annual mortality fluctuations by causes of death**

In Italy, all-cause mortality declined between 2004 and 2019, though trends varied by cause of death. Mortality from infectious diseases, nervous system and neurodegenerative conditions, and mental disorders increased, while respiratory and endocrine diseases, suicide, and other external causes remained stable. In contrast, neoplasms, heart disease, cerebrovascular disease, and accidents showed clear declines (Figure S1, Supplementary Material). Both the absolute and the relative impact of different causes of death on excess mortality remained largely unchanged over time (Figures S7-S8 and S9 in the Supplementary Material). This suggests that the seasonal burden has not diminished proportionally and the relative impact may even be rising for specific causes, such as neurodegenerative (from 3% in 2004 to 8% in 2019) and respiratory diseases (from 4% in 2004 to 7% in 2019), pointing to an increasing vulnerability of certain subpopulations to seasonal stressors.

## **Discussion**

### **Main Findings**

This study assesses cause-specific patterns of seasonal mortality and their contribution to overall seasonal mortality in Italy between 2004 and 2019. Using monthly mortality data, we computed absolute and relative excess mortality by cause of death and identified significant cause-specific seasonal patterns that shape overall mortality rates, patterns that are essential for understanding the mechanisms through which these fluctuations affect overall mortality and life expectancy. The results revealed that excess mortality varies by cause of death and that particular causes exhibit pronounced seasonal patterns.

As expected, heart and respiratory diseases emerged as the main drivers of winter excess mortality (40% and 16%, respectively). While heart diseases accounted for the largest proportion of absolute excess deaths, respiratory mortality displayed the highest relative deviations from baseline levels. Importantly, these seasonal peaks remained persistent over time, even as overall baseline mortality declined, indicating a growing or unmitigated seasonal burden for specific causes of death. We found that excess heart mortality not only shaped the total excess mortality but also had one of the highest winter excess mortality levels, while only minor excess mortality occurred in summer.

Despite the seasonal impact being lower during summer months compared to winter months, we found different contributing causes of death compared to winter. In fact, neoplasms, accidents, and neurodegenerative diseases played a more prominent role in excess mortality during summer. Furthermore, the male population was more affected by the intra-annual mortality fluctuations, considering all-cause mortality and each specific cause of death;

nevertheless, neurodegenerative conditions were more relevant among females, especially in summer.

Furthermore, although we observed a general decline in baseline mortality levels across most causes of death over the study period, the relative excess mortality remained stable for almost all causes.

## **Explanation of the findings**

The observed impact of intra-annual fluctuations on mortality in Italy was driven by heart and respiratory diseases. The observed winter peaks in heart (absolute terms) and respiratory mortality (relative terms) were consistent with a large body of literature documenting the adverse effects of cold temperatures and seasonal infections on cardiorespiratory outcomes [6,25,26]. 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.

We found that the impact of summer on mortality was considerably smaller than that of winter. While heart diseases remained important contributors, other causes, such as neoplasms, neurodegenerative diseases, and suicides, also played a role. Although summer excess mortality is markedly lower than in winter, it may be driven by similar underlying mechanisms. These differences likely arise from a mix of behavioural, biological, and structural risk factors, such as varying exposure to heat stress and unequal access to healthcare. Such vulnerabilities may also interact with underlying disparities in the leading causes of death. For example, neurocognitive disorders, which are more common among older women [27], can increase their susceptibility to heat-related mortality [27]. It is also important to note that our analysis does not cover the major 2003 heatwave, which caused more than 20,000 excess deaths in Italy [28],

nor the recent heatwaves in 2022 [29] and 2023 [30]. Within the period studied, however, the observed summer mortality patterns suggest that typical seasonal heat and low-intensity heatwaves have not substantially affected excess mortality in Italy.

Of particular note is the finding that, despite steady improvements in overall mortality over the analysed period in Italy [31,32], the relative burden of intra-annual mortality fluctuations has remained persistent, similar to other European countries [5]. Moreover, the composition of absolute excess mortality by cause has remained stable over time, suggesting that the seasonal burden has not diminished in step with overall mortality improvements. It may even be increasing for certain causes, such as neurodegenerative and respiratory diseases, pointing to growing vulnerability to seasonal stressors in specific subpopulations. In contrast, relative excess mortality showed little change over time, likely because observed and baseline mortality followed similar temporal patterns.

A closer look at age-specific patterns reveals who is most affected. Although our analysis relies on a standardised measure of mortality, which limits direct interpretation of age-specific contributions, we further examined cause- and age-specific death rates (Figure S10, Supplementary Material). As expected, mainly the oldest age groups (75-89 and 90+) exhibited a clear seasonal pattern in mortality, particularly for respiratory and cardiovascular mortality. In contrast, younger age groups showed relatively stable mortality throughout the year, with minimal seasonal fluctuations. These findings suggest that intra-annual excess mortality, especially during winter months, is largely driven by older individuals, highlighting their higher vulnerability to seasonal and environmental stressors.

The patterns observed in Italy likely reflect broader dynamics seen across Southern and Central Europe. In our previous work [5], we found that seasonal fluctuations in mortality and their impact on life expectancy share common features across European countries, particularly those

with similar climatic conditions and population age structures. However, the contribution of specific causes of death to these seasonal patterns can differ markedly between countries. For example, multi-country research has shown that cold weather tends to increase cardiovascular and respiratory mortality, especially from heart failure [33,34], yet the relative weight of these causes varies depending on national profiles. Factors such as population age structure, health system capacity, and housing conditions (e.g., thermal insulation, air conditioning) can shape both the magnitude and composition of seasonal excess mortality. This underscores that while the seasonal mechanisms we identify in Italy may be relevant elsewhere, targeted interventions must account for country-specific cause-of-death patterns and vulnerabilities.

### **Strengths and limitations of the study**

A key strength of this study lies in its use of monthly, cause-specific population-level mortality data from official statistics produced by the Italian National Statistical Institute (ISTAT). Our methodological approach allowed for a standardised comparison of intra-annual fluctuations across time and causes of death. This approach allows the estimation of 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 concentrated within a few days and compensated by the following harvesting effect. Second, while we attempted to mitigate the influence of long-term trends and counterbalance seasonal effects by selecting a consistent reference mortality level (validated through sensitivity analyses in previous work [5,35]), the choice of baseline is still suboptimal. Another baseline might be proposed under different assumptions, but the result will probably not be significantly changed if the assumptions are reasonable. Third, although mortality data in Italy are of high quality [36], the high level of detail required for our analysis (monthly data

by cause of death) limited our ability to examine smaller, more specific causes, such as heatstroke or dehydration, which may have important implications for interpreting seasonal mortality patterns. Fourth, our results may partially reflect underlying differences in the distribution of causes of death between men and women. Since seasonal mortality is driven primarily by specific causes, sex differences in the prevalence of these causes may contribute to observed patterns. Therefore, the magnitude and shape of seasonal mortality by sex could be sensitive to the composition of cause-specific mortality, rather than to sex alone.

## **Conclusion**

This study offers new evidence on the persistent and cause-specific nature of seasonal mortality fluctuations in Italy, revealing patterns that have remained stable over time despite improvements in overall mortality. These findings underscore that seasonal vulnerabilities, particularly for cardiovascular and respiratory diseases in winter, continue to have a strong influence on short-term mortality risks, especially among the oldest age groups. The seasonal composition of excess mortality has also remained consistent, suggesting that health system adaptations or behavioural changes have not substantially altered these patterns.

As populations age and climate variability intensifies, the relevance of these findings will likely grow. Understanding how specific causes of death and demographic groups respond to seasonal stressors can help inform more targeted and adaptive public health strategies. For example, winter interventions could be prioritised for older adults and individuals with cardiorespiratory conditions, while summer campaigns might address risks linked to neurodegenerative diseases, external causes, and heat exposure.

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 (heatstroke, dehydration), could help reduce avoidable deaths [14]. This challenge will become even more relevant in the coming years, as climate change associated with extreme temperatures is likely to increase the health risks in rapidly ageing societies. Reliable evidence about specific subpopulations at risk is also a precondition for addressing emerging health threats and healthcare system planning [37–39].

## Statements and Declarations

**Competing Interests:** The authors have no relevant financial or non-financial interests to disclose.

**Funding:** FJ has received funding from the Netherlands Organisation for Scientific Research (NWO) (grant no. VIC.191.019).

**Data Availability:** Monthly death counts by causes of death are available upon request to the ISTAT contact centre, while population exposures are openly available on the National Italian Statistical Institute (ISTAT) website (<https://www.istat.it/en/>).

**Authors' contributions:** IM, DAJ and FJ conceived the study. IM, DAJ, FJ and FM designed the study. IM conducted the statistical analysis and drafted the manuscript. DAJ and FJ provided critical input and revisions to the draft manuscript. DJ, FM and provided scientific advice for the interpretation and framing of the analysis. All authors revised the final draft and approved the final version of the manuscript.

**Acknowledgements:** IM gratefully acknowledges the resources provided by the International Max Planck Research School for Population, Health and Data Science (IMPRS-PHDS).

## **Key-points:**

- Seasonal mortality patterns are known in Europe, with peaks in winter (flu-related) and smaller peaks in summer (heatwaves), but no comprehensive long-term analysis exists on how different causes of death shape these fluctuations.
- This study applies a novel framework to quantify absolute and relative contributions of 17 cause-of-death groups to seasonal mortality in Italy (2004–2019)
- We found that winter mortality, due to excess mortality from heart and respiratory diseases, is the key driver of excess seasonal mortality, highlighting persistent vulnerabilities despite overall mortality improvements.
- Seasonal mortality remains a significant, cause-specific public health challenge; public health policy should prioritise targeted, cause- and season-specific prevention strategies to reduce excess mortality and strengthen resilience to short-term risk factors.

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