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Original Research

Investigating mortality trends in Italy during the COVID-19 pandemic: life expectancy changes within provinces and vaccination campaign impact up to December 2022

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ABSTRACT

Objectives: We used publicly available population data from 1 January 2019 up to 31 December 2022, to investigate mortality trends in Italy during the COVID-19 pandemic, evaluating changes in life expectancy (LE) at birth within provinces and the impact of COVID-19 vaccinations.
Study design: Aggregate data analysis.
Methods: Annual period life tables were used to estimate sex-specific LEs within provinces from 2019 to 2022. We used Arriaga decomposition to analyze the contribution of age groups (<60 years and ≥60 years) to annual LE changes. We implemented a Quasi-Poisson regression model to estimate the number of averted deaths by the achieved COVID-19 vaccination rates from January 2021 up to December 2022, simulating a counterfactual scenario where vaccine doses were not administered.
Results: The results revealed geographical heterogeneity in annual LE changes across Italian provinces during the pandemic. By the end of 2022, LE was below the prepandemic levels in 88% of provinces for females and in 76% for males. In addition, we estimated that the achieved vaccination rates averted 460,831 deaths (95% confidence interval: 250,976–707,920), corresponding to a 25% reduction in expected all-cause mortality.
Conclusions: Overall, the study highlighted the significant role of COVID-19 vaccinations in averting a considerable number of deaths and improving LE. However, by the end of 2022, LE had not fully recovered to prepandemic levels in many provinces. This could be attributed to concurrent factors, including enduring COVID-19 pandemic effects, intense summer heat waves and early onset of seasonal flu. Further research and continuous monitoring are essential to fully comprehend long-term mortality trends and optimize public health strategies.

Introduction

The SARS-CoV-2 outbreak and COVID-19 pandemic greatly affected public health, welfare, and global economy. Italy, as an early European outbreak epicenter, experienced a sudden and alarming increase in mortality rates.[1] COVID-19 infections showed notable variation across different Italian regions. Northern regions experienced a rapid rise in COVID-19 cases after the first diagnosis in February 2020, leading to one of the highest mortality rates globally during the first wave (February to May 2020).[1–3] In contrast, the quick implementation of national lockdowns on March 11, 2020, helped to maintain a low SARS-CoV-2 spread in Center-Southern regions, limiting COVID-19 burden.[4–6] From the second wave (October to December 2020) onward, SARS-CoV-2 spread became more uniform across the country due to relaxed restrictions.[7] In 2020, the national life expectancy (LE) at birth experienced a decline of approximately one year, indicating a significant impact on overall population health.[8] To counter the pandemic, a large vaccination campaign was launched on December 27, 2020.[9] Initially, healthcare personnel, elderly people, and vulnerable individuals were prioritized, followed by the general population.[9] Overall, 86 % of the Italian population received at least one vaccine dose on December 31, 2022,[10,11] reaching one of the highest vaccination rates in Europe. The vaccination campaign played a crucial role in reducing COVID-19 hospitalizations and deaths,[9,12–17] contributing to a partial

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national LE recovery in 2021.[8] This success was achieved despite fears and skepticism in the population, fueled by misleading and conflicting information from media sources,[18–20] comprising mistrust in the government, COVID-19 severity underestimation, doubts about vaccine efficacy,[19] and concerns about short-/long-term rare side-effects.[21–23] In 2022, social restrictions were almost completely removed,[24] moving toward prepandemic normalcy. However, a large SARS-CoV-2 Omicron variant spread,[25–27] intense summer heat waves,[28] and early seasonal flu[29] contributed to persistent excess mortality.[26]

This article aims to examine Italian population mortality trends throughout COVID-19 pandemic, assessing two key aspects. First, we studied LE changes within provinces from 2019 up to 2022. We used publicly available aggregated data at provincial (NUTS-3, 107 provinces), regional (NUTS-2, 20 regions), and macroregion level (NUTS-1, four macroregions)[30] to consider the geographical variations in COVID-19 infections and in territories characteristics. This approach allows to go beyond national estimates, providing a more accurate assessment of mortality changes. It also helps to highlight territories experiencing increases in mortality and which could deserve further investigations. In addition, we evaluated whether LE in 2022 has recovered to prepandemic levels to compare the population health status. Second, using COVID-19 vaccination data aggregated at regional level,[31] we evaluated the vaccination campaign effectiveness in reducing mortality up to December 2022. We provided an estimate for the number of averted deaths, expanding on the latest official Italian health authorities report that covered January 2021 to January 2022.[17]

Materials and methods

Geographical sex-specific LE estimation and its Arriaga decomposition by age group

To investigate LE at birth, daily counts on all-cause deaths and estimated resident population on January 1 from 2019 through 2022 were retrieved from the Italian National Institute of Statistics database.[32,33] Daily death counts were aggregated into sex- and age-specific five year classes from ‘0’ to ‘≥100.’ Annual life tables were calculated via standard demographic techniques[34] and used to estimate sex-specific LE at birth from 2019 to 2022 within each province and region. We then estimated (1) the deviation between LEs and the national LE mean in 2022 (this latter obtained by weighting each sex- and province-specific LE using population size), (2) annual LE changes from 2019 to 2022, and (3) overall LE changes from 2019 to 2022. Ninety-five percent confidence intervals around estimates were derived from 1000 Poisson simulations of death counts to account for potential uncertainty in data collection, although our data represent the study population and not a random sample. We tested the null hypothesis of null LE deviation from national mean as well as null LE recovery to prepandemic levels fixing a two-sided $\alpha = 0.05$. Using Arriaga decomposition,[35] we calculated the contribution to annual changes in LE by individuals aged <60 years and ≥60 years, providing insightful measures for the pandemic's impact.

COVID-19 vaccination campaign impact on mortality

COVID-19 vaccination campaign impact on mortality was investigated from 4 January 2021 to 31 December 2022. Following literature's recommendations, we considered all-cause mortality as a better outcome to reflect the pandemic's true impact compared with reported COVID-19 mortality.[36,37] Weekly all-cause mortality and population data for the years 2021–2022 were obtained from Italian National Institute of Statistics database.[32] COVID-19 vaccine administration data were retrieved from,[31] and were aggregated by region, sex, and age groups ‘5–19’, ‘20–29’, ‘30–39’, ‘40–49’, ‘50–59’, ‘60–69’, ‘70–79’, ‘80–89’, ‘≥90’. Vaccines administered were of two types: (1) ‘two-dose vaccines,’ that is, BNT162b2, mRNA-1273, NVX-CoV2373, ChAdOx1-S, and (2) ‘one-dose vaccine,’ that is, Ad26.COV2.S. We calculated regional weekly age- and sex-specific vaccination rates for:

a) partially vaccinated (one dose from ‘two-dose vaccines’);
b) fully vaccinated (two doses from ‘two-dose vaccines’ or one dose from ‘one-dose vaccines’ or one dose from ‘two-dose vaccines’ after 3–6 months from COVID-19 infection);
c) fully vaccinated plus one booster dose;
d) fully vaccinated plus two booster doses.

The denominator was represented by the number of individuals, specific to region, sex, and age group, eligible for vaccination in the analyzed calendar years, regardless of their life status in the study period. A seven day delay was assumed between vaccination day and development of immunity.[38] In addition, a 14-day interval was considered between COVID-19 infection and death.[39] Therefore, the term ‘vaccination week’ was defined with a three week delay compared with the study week, and the term ‘immunization week’ was defined with a two week delay compared with the study week. Vaccination rates at each study week then referred to the proportion of individuals who received vaccine doses during the ‘vaccination week’ and the proportion of individuals who achieved COVID-19 immunity during the ‘immunization week’.

To investigate the relationship between vaccination rates and all-cause mortality, we stratified the analysis for age groups ‘5–39’, ‘40–59’, ‘60–69’, ‘70–79’, ‘80–89’, and ‘≥90’. We formulated a Quasi-Poisson regression model, including a set of potential confounders, for example, variables related to demographics, seasonality, social influence on vaccine uptake, SARS-CoV-2 spread, and variants prevalence (see Supplementary Material for additional information). To assess the impact of achieved vaccination rates on mortality, we estimated the weekly expected number of all-cause deaths in a counterfactual scenario where vaccination rates were fixed to zero. We then obtained an estimate of the number of deaths averted by achieved vaccination rates as the difference between expected and observed deaths. We calculated the averted deaths fraction as the ratio between number of deaths averted and expected.[40] Ninety-five percent confidence intervals for both expected and averted number of deaths were obtained assuming asymptotic normal distribution. Models' parameters were exponentiated to obtain incidence rate ratios (IRRs). To assess the effectiveness of vaccination rates, we tested the null hypothesis of IRR = 1 fixing a two-sided $\alpha = 0.05$. All analyses were conducted using RStudio 2023.06.0+421.

Results

LE at birth deviation from the national mean in 2022

Fig. 1 displays sex-specific LEs deviation from the national mean (i.e. 84.88 for females and 80.69 for males) in 2022. A spatial heterogeneity is observed, with higher LEs in North-East and Center and lower LEs in North-West and, to a greater extent, in the South and Islands. For each investigated year, sex-specific LEs at birth, along with their deviation from the national mean and the contribution of individuals aged <60 and ≥60 years, are reported in Supplementary Tables 1–3, respectively, for provinces, regions, and chief towns/provinces with at least 500,000 inhabitants. As fully reported in Supplementary Table 1, in South and Islands, 73% and 88% of the provinces had a negative LE deviation from the national

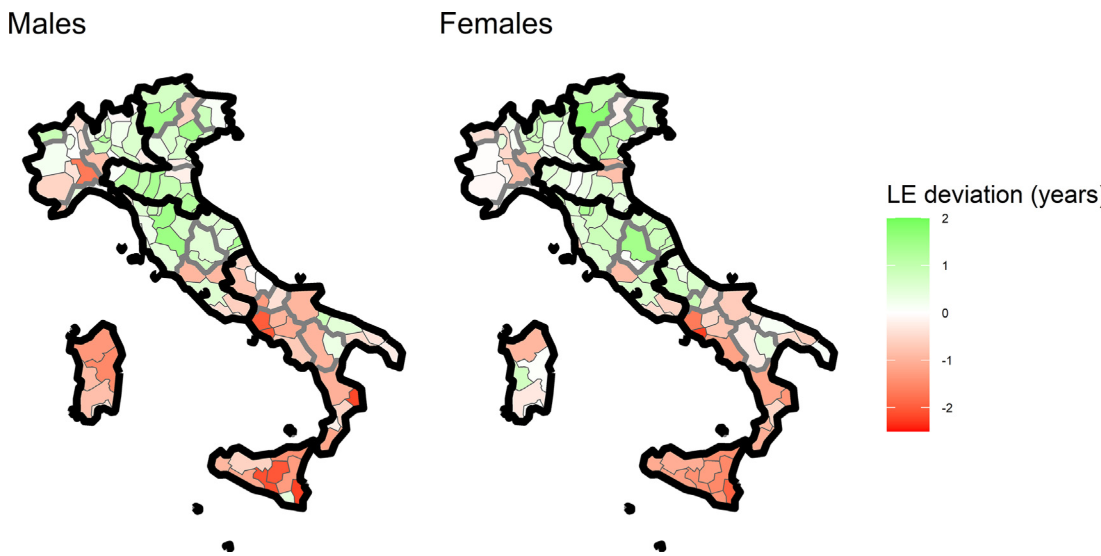

Fig. 1. Heat maps of sex-specific life expectancy (LE) at birth deviations (in years) from national mean (i.e., 84.88 for females and 80.69 for males) within Italian provinces (NUTS-3) in 2022.

mean, respectively, for females and males; in North-West, these percentages were 36% and 40%. On the other hand, North-East and Center had the highest proportions of provinces with positive LE deviations: 72% for both sexes in North-East, and 72% (males) and 68% (females) in Center. Supplementary Table 4 reported the 10 provinces with highest and lowest sex-specific LEs in 2022 along with their deviations from the national mean.

Annual LE changes from 2019 to 2022

Fig. 2 shows annual sex-specific LE changes within provinces from 2019 to 2022 (a detailed representation is provided in Supplementary Figs. 1–5). Table 1 reported the number and proportion of provinces with non-negative or negative annual sex-specific LE changes within macroregions (results within regions are also reported in Supplementary Table 5). A marked geographic pattern in LE changes from 2019 to 2021, similar for both sexes, can be observed from Fig. 2 (panels A to D). LE losses from 2019 to 2020 affected all macroregions, particularly provinces in North, primarily driven by individuals aged ≥60 years (Supplementary Table 1). Lombard provinces experienced the highest LE losses (>2 years) for both sexes, for example, ≈3 and ≈5 years in Cremona province, for males and females respectively (Fig. 2, panels A–B and Supplementary Table 1). In 2021, LE recovery was particularly observed in North-West provinces (i.e. 96% for females and 100% for males), while in Center-South and Islands, LE losses were observed in about 70% of provinces, although less severe than in the previous year (Fig. 2, panels C–D). LE changes from 2021 to 2022 revealed interesting patterns (Fig. 2, panels E–F). Center and Southern provinces generally experienced LE recoveries, while Northern provinces showed more frequent LE losses in females. Sardinian provinces also had high LE losses (>1 year), primarily driven by individuals aged ≥60 years (Supplementary Table 1).

Both Table 1 and Fig. 2 (panels G–H) suggest that LEs at the end of 2022 have not completely returned to prepandemic levels of 2019. In Supplementary Table 6, the 10 highest overall sex-specific LE losses within provinces in each macroregion, along with age group contributions, are reported. Provinces with LE reductions were more frequent in females (24%) compared with males (10%). Among females, the Center had the highest proportion of provinces with non-negative LE changes (27%) compared with other macroregions (<10%). Notably, Fig. 2 (panels G) and Supplementary Table 6 reveal that Sardinia region experienced the most drastic overall LE losses, e.g.for example, provinces of Nuoro, Sassari, and Cagliari, ranging from ≈1 to 2 years. Among males, North-West and North-East had a higher proportion of provinces with non-negative LE change, that is, 28% and 41%, compared with Center and South and Island, that is, 18% and 16%. As shown in Supplementary Table 6, provinces in the Center experienced the highest LE losses in males, for example, provinces of Rieti (Lazio), Arezzo (Tuscany) and Perugia (Umbria). In general, a negative contribution to overall LE change was observed in almost all provinces for individuals aged ≥60 years, i.e., 97% and 87% for females and males, respectively, but was also frequent for individuals aged <60 years, that is, 51% and 54% for females and males, respectively (see Supplementary Table 1).

Estimated number of averted deaths by achieved vaccination rates

From 4 January 2021 to 31 December 2022, more than 90% of individuals aged 40–89 years received at least one vaccine dose, while lower rates (≈80%) were observed for individuals aged 5–39 or ≥90 years (Supplementary Fig. 6). However, vaccination rates for those aged ≥90 years might be underestimated due to potential deaths, given their shorter LE, before having the chance to obtain a vaccine dose administration. Supplementary Figs. 7 and 8 display, respectively, the weekly changes, within macroregions, in SARS-CoV-2 spread (weekly new positive and currently positive COVID-19 cases)[41] and variants prevalence[42] (for additional information, refer to Supplementary Material). Both trends had similar patterns across macroregions, with peaks of COVID-19 cases between January and July 2022. In Supplementary Table 7, full results of Quasi-Poisson models for estimating the number of expected weekly all-cause deaths are reported. For individuals of any age, increases in partial vaccination, full vaccination, and full vaccination plus one booster dose rate always resulted in a decreased mortality in the population (IRR <1). Except for individuals aged 5–39 years (where statistical power was reduced due to low number of deaths), these associations were also statistically significant (P < 0.05). Nevertheless, IRR estimates were consistent among all age groups (see Supplementary Table 7). Finally, an increase in full vaccination plus two booster doses rate had a

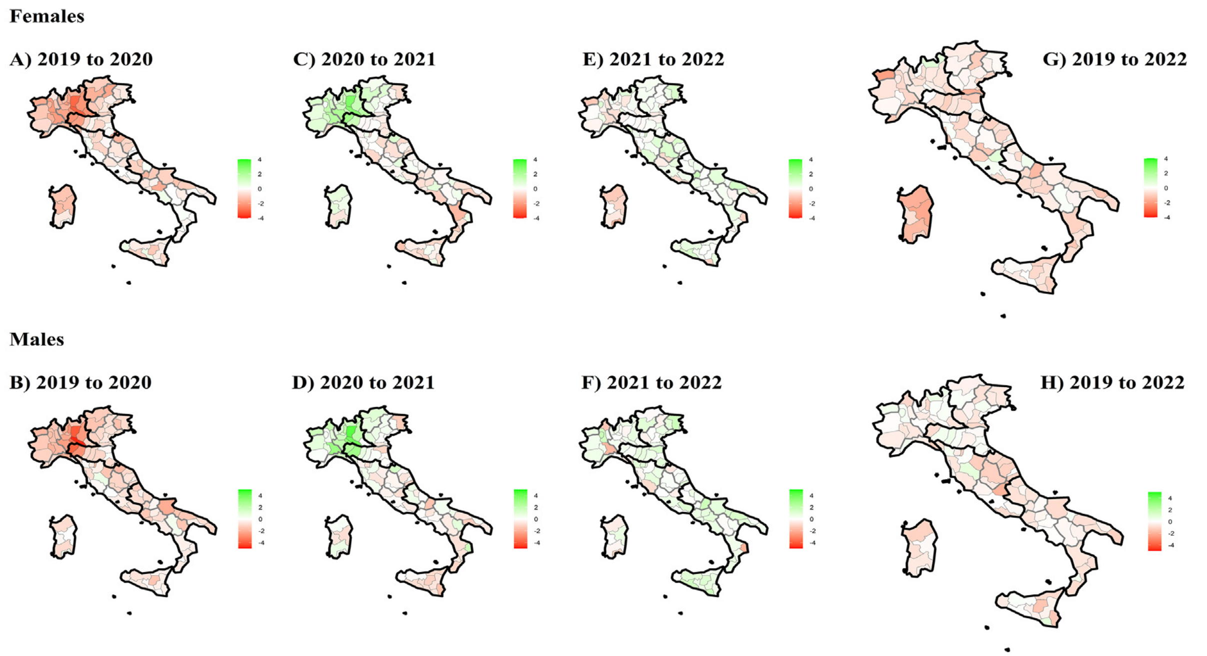

Fig. 2. Heat maps of sex-specific life expectancy (LE) at birth annual changes (in years) from 2019 to 2022, within Italian provinces (NUTS-3).

statistically significant protective effect only for individuals aged 80–89 years (IRR = 0.84, $P < 0.05$).

Table 2 reports estimates for the expected number of all-cause deaths, in a counterfactual scenario where vaccination rates were assumed to be zero, and the number of deaths averted by achieved vaccination rates by age group. Overall, the number of averted deaths was estimated as 460,831 across all age groups, representing 25% of expected all-cause deaths in the absence of vaccinations. Among the averted deaths, 92.5% were in individuals aged ≥60 years, and 77% were in 2022. This is more evident in Fig. 3, which compares observed weekly number of all-cause deaths with expected number in the counterfactual scenario. Averted death fractions were similar across age groups, with the highest observed in individuals aged 60–69 years (31%) and the lowest in those aged ≥90 years (18 %). Supplementary Table 8 and Supplementary Fig. 9 provide estimates and plots within macroregions.

Table 1
Number and proportion of provinces with non-negative or negative annual sex-specific life expectancy (LE) changes from 2019 to 2022 by macroregion (NUTS-1).

Macroregion (NUTS-1)	N° Provinces	Females		Males	
		N° Provinces (%) with LE change ≥0	N° Provinces (%) with LE change <0	N° Provinces (%) with LE change ≥0	N° Provinces (%) with LE change <0
		From 2019 to 2020			
North-West	25	0 (0%)	25 (100%)	0 (0%)	25 (100%)
North-East	22	2 (9%)	20 (91%)	1 (5%)	21 (95%)
Center	22	4 (18%)	18 (82%)	2 (9%)	20 (91%)
South and Islands	38	7 (18%)	31 (82%)	4 (11%)	34 (89%)
Italy	107	13 (12%)	94 (88%)	7 (7%)	101 (94%)
		From 2020 to 2021			
North-West	25	24 (96%)	1 (4%)	25 (100%)	0 (0%)
North-East	22	12 (55%)	10 (45%)	15 (68%)	7 (32%)
Center	22	6 (27%)	16 (73%)	6 (27%)	16 (73%)
South and Islands	38	10 (26%)	28 (74%)	11 (29%)	27 (71%)
Italy	107	52 (49%)	55 (51%)	57 (53%)	50 (47%)
		From 2021 to 2022			
North-West	25	11 (44%)	14 (56%)	18 (72%)	7 (28%)
North-East	22	13 (59%)	9 (41%)	19 (86%)	3 (14%)
Center	22	16 (73%)	6 (27%)	16 (73%)	6 (27%)
South and Islands	38	29 (76%)	9 (24%)	31 (82%)	7 (18%)
Italy	107	69 (64%)	38 (36%)	84 (79%)	23 (21%)
		From 2019 to 2022			
North-West	25	1 (4%)	24 (96%)	7 (28%)	18 (72%)
North-East	22	2 (9%)	20 (91%)	9 (41%)	13 (59%)
Center	22	6 (27%)	16 (73%)	4 (18%)	18 (82%)
South and Islands	38	2 (5%)	36 (95%)	6 (16%)	32 (84%)
Italy	107	11 (10%)	94 (88%)	26 (24%)	81 (76%)

Table 2
Comparison between observed and expected number of all-cause deaths in the absence of vaccination campaign by age group in 2021 and 2022, along with number of averted deaths and averted fraction.

Age group	Observed number of all-cause deaths			Expected number of all-cause deaths			Number of averted deaths			
	2021[a]	2022[a]	Total	2021[a]	2022[a]	Total (95% CI)	2021[a]	2022[a]	Total (95% CI)	Averted fraction[b] (95% CI)
5–39	6151	5907	12,058	6984	8297	15,281 (11,291 to 20,997)	833	2390	3223 (−767 to 8939)	21% (−7% to 43%)
45–59	41,706	39,196	80,902	47,866	64,291	112,158 (91,092 to 139,092)	6160	25,095	31,256 (10,190 to 58,190)	28% (11% to 42%)
60–69	64,522	60,556	125,078	71,703	108,572	180,275 (145,434 to 225,173)	7181	48,016	55,197 (20,356 to 100,095)	31% (14% to 44%)
70–79	139,397	134,155	273,552	158,455	210,744	369,200 (320,900 to 426,171)	19,058	76,589	95,648 (47,348 to 152,619)	26% (15% to 36%)
80–89	271,468	272,688	544,156	320,572	417,051	737,622 (677,180 to 804,338)	49,104	144,363	193,466 (133,024 to 260,182)	26% (20% to 32%)
≥90	181,792	195,508	377,300	207,640	251,701	459,342 (418,126 to 505,195)	25,848	56,193	82,042 (40,826 to 127,895)	18% (10% to 25%)
Total	706,250	709,078	1,4153,28	813,220	1,060,656	1,873,877 (1,664,022 to 2,120,966)	108,184	352,646	460,831 (250,976 to 707,920)	25% (15% to 33%)

CI, confidence interval; IRR, incidence rate ratio.
[a] 2021 = study weeks 1–52, 2022 = study weeks 53–104.
[b] Averted fraction = number of averted deaths/expected number of all-cause deaths.

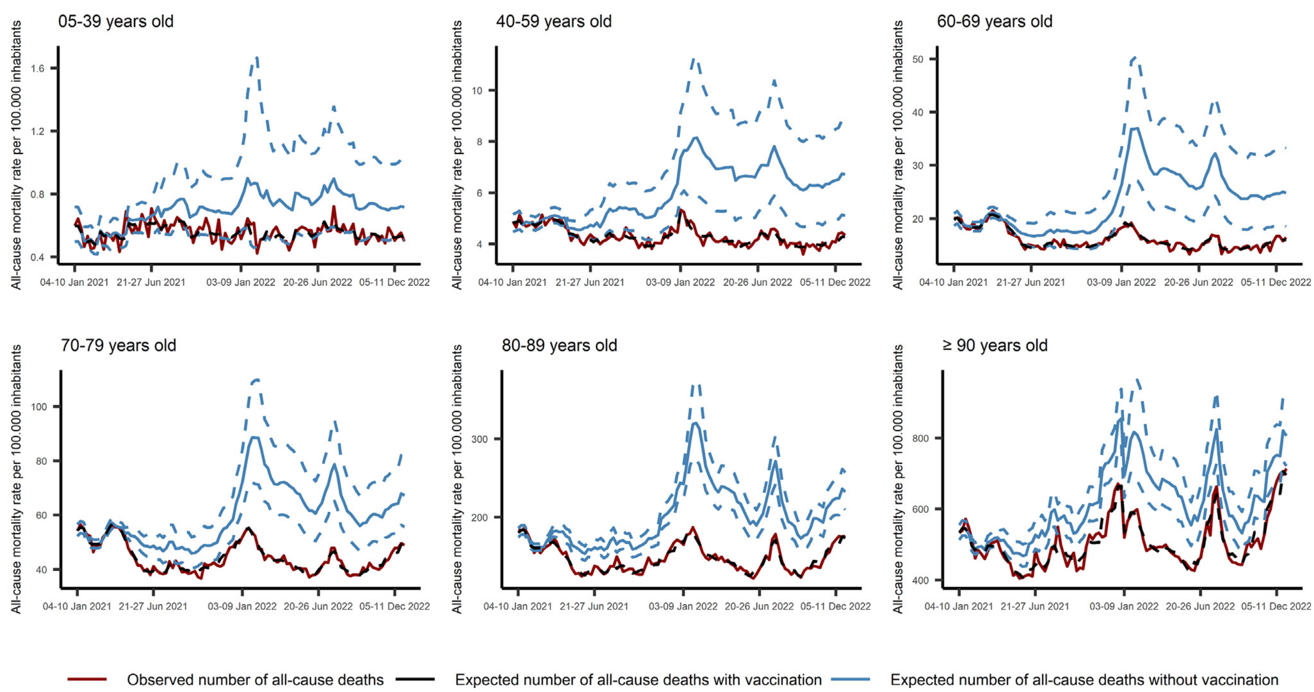

Fig. 3. Comparison between observed and expected number of all-cause deaths in absence of vaccination campaign by age group in 2021 and 2022.

Discussion

This study investigated the mortality trends observed in Italy throughout the COVID-19 pandemic, evaluating annual changes in LE at birth within provinces and the COVID-19 vaccination campaign's effectiveness in reducing mortality. In the first analysis, publicly available population data were used to estimate sex-specific LEs at birth from 2019 to 2022 within provinces. As expected, LE in 2022 showed a North-South gradient with lower LEs in South, reflecting socio-economic, healthcare, and lifestyle disparities.[43–47] Interestingly, LEs in North-West provinces were lower than those in North-East and Center, suggesting the presence of additional risk factors for mortality. Considering LE annual changes, in 2020, significant LE losses were observed in Northern provinces, with substantial decreases in around 2–5 years in Lombardy. Instead, Center-South provinces experienced smaller LE reductions (around 8 months on average). This geographical variation was shaped by a different cumulative COVID-19 incidence and the prompt lockdown implementation in March 2020. Northern regions, being the outbreak epicenter, reached a high cumulative COVID-19 incidence before lockdowns implementation, resulting in the observed significant mortality burden. Additional factors as pollution and local climate conditions might have worsened COVID-19 impact in the North, particularly around Po Valley and Milan area.[7,48–52] On the contrary, the lockdowns were crucial to maintain the low cumulative COVID-19 incidence in Center-South regions, therefore limiting COVID-19 mortality.[4–6,53] In 2021, the Northern provinces heavily impacted in 2020 experienced a bounce back in LE, nearing or surpassing 2019 levels. This observed LE recovery can be attributed to the advent of COVID-19 vaccinations, ongoing monitoring of SARS-CoV-2 spread, implementation of focused restriction measures, improved COVID-19 treatment, and loss of individuals in poorer health status in 2020 (e.g. due to comorbidities).[54] Conversely, Center-South provinces still experienced LE losses, although less frequent and less severe than in 2020, likely due to increased SARS-CoV-2 spread after the relaxation of lockdowns in May 2020.[55]

In 2022, most Italian provinces showed LE improvements, especially in males and Center-South provinces. On the contrary, LE losses were noticeable in females, Northern provinces, and Sardinia region. These mortality increases were influenced by factors both related and unrelated to COVID-19. Among the firsts, SARS-CoV-2 Omicron variant's higher transmission,[27,56–58] together with relaxed restrictions,[24] led to wider virus spread and persistent COVID-19 mortality risk.[26] Nonetheless, this risk was limited by the reduced Omicron's lethality[27] and high vaccination rates in the population.[59] Long-term cardiovascular effects from previous COVID-19 infections[60,61] and indirect pandemic effects,[45,62–65] for example, reduced healthcare access, might also have increased mortality. However, the factors unrelated to COVID-19 likely played a greater role.[26] Strong summer heat waves were estimated to cause 18,000 deaths in Italy, affecting women and North-West provinces more severely, especially around Po Valley.[28,66,67] This aligns with observed LE losses in the Po Valley area, particularly in females (see Fig. 2). Furthermore, an earlier and harsher winter flu has been linked to excess mortality in late 2022.[26,29]

Overall, Italian LE at birth in 2022 generally remained below prepandemic levels, prompting questions on future LE trends, mortality risk factors, and health prevention strategies. Our provincial-level analysis provides insights for investigating hypotheses concerning specific territories.

Nevertheless, in the second analysis, we demonstrated the significant impact of COVID-19 vaccination campaign in reducing mortality rates. This not only alleviated the burden on public health and economy but also contributed to improve LE. An important strength of this analysis was the availability of vaccination data aggregated by sex, age group, and region, as well as the inclusion of several potential confounders in the model, helping to limit spurious associations. In agreement with previous literature,[9,12–17] we highlighted the protective impact of increasing vaccination rates in the population, leading to a decrease in mortality across all age groups. The vaccination rates achieved by the population averted, according to our model, 460,831 deaths (95% CI: 250,976–707,920) up to December 31, 2022. This estimate corresponded to a 25% reduction in expected all-cause mortality without vaccinations. A higher number of deaths were averted in 2022 (352,646) due to higher vaccination rates and wider SARS-CoV-2 spread. Finally, our averted deaths estimate until January 2022 (142,376) closely aligns with Italian health authorities' latest report (151,532), although using differing data and methods.[17] These findings can assist in mitigating doubts and instilling confidence in the general population regarding the vaccination campaign effectiveness, offering clear evidence derived from real-world data.

Despite its strengths, this study has several limitations. First, the assumptions made regarding time lags between vaccine administration-immunization and COVID-19 infection-death may not accurately reflect individual characteristics. Second, the lack of age- and sex-specific data for regional-positive COVID-19 cases may have introduced residual confounding. In addition, underestimation of COVID-19 cases due to asymptomatic individuals could have influenced results. Third, as an observational study, not all potential confounders could be addressed due to limited data availability. Fourth, the counterfactual scenario assumed that the absence of vaccination campaign did not influence other measured and unmeasured variables, which may not reflect the real-world scenario. Despite these limitations, our findings align with previous research, providing further support for the vaccination program success. However, it is still important to continue monitoring and surveillance of vaccination safety using individual data.

Author statements

Ethical approval

The present study is based on aggregated data publicly available from the Italian National Institute of Statistics and from the Ministry of Health of Italy. This study did not involve experiments on humans and/or human tissue samples; therefore, ethics approval and consent to participate were not required.

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Competing interests

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.09.031.

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