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RESEARCH ARTICLE

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Classification bias and impact of COVID-19 vaccination on all-cause mortality: the case of the Italian region Emilia-Romagna

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ABSTRACT

Real-world studies on vaccine effectiveness may suffer from several biases, typically distorting their results. A previous article on the population of an Italian province, correcting the "immortal time bias", showed worse results for the all-cause death of the vaccinated compared to the unvaccinated. This article highlights the "case counting window bias", that considers the vaccine recipients "unvaccinated" usually for 14 days, a time interval reputed necessary to express the vaccine immune response. We aim to document this bias in an Italian region, calculating the daily death incidence for each age class of vaccinated and unvaccinated and checking their all-cause mortality difference within the considered time window. Indeed, in this window the two groups showed huge differences in all-cause deaths, that cannot be attributed only to COVID-19 deaths (in the absence of reasons to expect significant vaccine effects on non-COVID-19 deaths). In conclusion, analyzing the data of an Italian Region, we found evidence of the 'case counting window bias', which artificially increases the 'unvaccinated' mortality and reduces the mortality in the vaccinated.

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COVID-19 vaccination; 14-days-mortality-shift; case counting window bias; miscategorization bias; vaccine status miscategorization

1. Introduction

During the SARS-CoV-2 pandemic, a significant number of studies have been conducted to establish the effectiveness and safety of various treatments, particularly of mRNA vaccines, in real-world settings. However, it has been noted that studies on vaccine effectiveness may present different biases—common in observational research—that could distort the validity of the results[1]. To highlight the impact on the results of one of the biases listed in the aforementioned review, e.g. the Immortal Time Bias (ITB), in a previous article we corrected the data of a study on the effectiveness of COVID-19 vaccines [2]. Such study was conducted on the entire population of the province of Pescara. Correcting the ITB it was suffering from, we obtained much worse results than the original article for the all-cause death of vaccinated compared to the unvaccinated. However, ITB was not the only bias highlighted in the review cited above [1]. Among them, we have already hypothesized and explained the "healthy-adherer bias", not easy to quantify in observational studies, but well documented in the medical literature [3,4]. The current article, in particular, will address and document the so-called "case counting windows bias", which could significantly alter the association estimates, as has been shown with a theoretical model [5]. This bias, theorized by Fung et al. [5], is a differential misclassification bias, which acts asymmetrically on the groups being compared. It considers as "unvaccinated" the subjects in the period between the vaccine administration and the moment in which the immune response is believed to be fully established (usually 14 days, but in some countries even 21). Therefore, it attributes to the

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This article has been corrected with minor changes. These changes do not impact the academic content of the article.

unvaccinated any event (infection, hospitalization, or death) occurring in the aforementioned time window. Differential misclassification leads to substantial biases in association estimates that are unpredictable and it occurs when subjects are assigned into a category other than the one to which it should be assigned; in fact, it can shift the estimate either toward or away from the null value [6]. However, if the misclassification occurs in only one direction (for example, by only moving subjects from the treated group to the control group), an asymmetry occurs that cancels out the cases in the group exposed to the treatment and makes the effect of the treatment itself appear to be effective [5]. Specifically, people who got COVID-19 within 14 days after their first vaccine dose, or who had other problems related to the disease or vaccine, were "immortalized". This means their COVID-19 cases or other events were not counted in the total cases for the vaccinated group, but they were still included in the group used to measure vaccine effectiveness [7]. This bias also applies to any other event occurring within 14 days that affects the safety of the vaccine, and the cases are referred to as unrelated incidents in a so-called "unvaccinated person" [8,9]. Consequently, this bias may have prevented the attribution of numerous adverse effects occurring within the post-vaccination period to the vaccine itself, including acute cardiovascular events, severe allergic reactions (anaphylaxis), thrombosis with thrombocytopenia syndrome (TTS), and several forms of autoimmune reactions [10,11]. Furthermore, failure to recognize and correct for this bias can lead to policy makers providing incorrect information about the observed phenomenon due to incorrect conclusions about the impact of measurement error on estimates [8,12].

In Italy, according to an instruction of the National Institute of Health (ISS) [13], it is is common practice to consider as unvaccinated those vaccinated for less than 15 days and to repeat the same shift for every further dose administration.

The aim of this study is to show the impact of the case counting window bias in a population of the Italian region Emilia Romagna, examining the relationship between the trend of administration of the first doses and all-cause deaths in the unvaccinated population for each age group. Furthermore, we want to verify whether there is a temporal correspondence with or without a gap between the trend of vaccinations and all-cause deaths in the unvaccinated.

We hypothesize that the presence of the case counting window bias may be the cause of misattribution of all-cause deaths in the unvaccinated group and to explore whether a temporal gap can be observed between the two trends that approximately overlaps across the age groups.

2. Materials and methods

2.1. Data sources

In this study we collected data regarding the Emilia-Romagna region from three different institutional sources: all causes mortality data and region population from ISTAT (Italian National Institute of Statistics), COVID-19 vaccines administration from ANV (Anagrafe Nazionale Vaccini, managed by the Italian Ministry of Health), COVID-19 mortality of vaccinated people and vaccines administration data from the Regione Emilia-Romagna obtained through a FOIA request by lawyer Lorenzo Melacarne, which were released already fully anonymized and in accordance with the art. 5, comma 2 of the Italian Legislative Decree No. 33/2013.

The data we have worked on is strictly what has been provided by the public institutions above, we did not collected or measured anything by other sources or by ourselves.

The collected data concerns the entire population of the Region: both sexes, all ages. The data about vaccines administration and vaccinated mortality is about just the vaccinated people of both sexes and all ages.

From ISTAT we collected the number of daily all-cause deaths for each decennial age class in Emilia-Romagna region from 27 December 2020 (launch of the COVID-19 vaccination campaign in Italy) to 31 December 2021. These data are publicly available and updated monthly on the ISTAT website [14], released under Creative Commons 4.0 license.

From ISTAT we got also the region's population size on January 1st, 2021 and January 1st, 2022, for each decennial age class. The daily total population for each age class has been estimated as linear interpolation from the ISTAT population on January 1st, 2021 and the population on January 1st, 2022.

From ANV we collected the number of daily administered first doses to get, for each day, the size of the vaccinated population for each quinquennial age class (then aggregated in decennial age classes to match ISTAT data), from 27 December 2020 to 31 December 2021. The daily size of the unvaccinated population has been calculated by subtracting the vaccinated population from the total population. These data are publicly available on the GitHub repository [15], released under Creative Commons 4.0 license by the Italian Ministry of Health.

The data obtained from Emilia-Romagna region consist of a database with date of birth, date of all-cause death, and dates of each inoculation event of the sole people who received at least the first dose of COVID-19 vaccine. This allowed us to calculate the daily number of deaths of the vaccinated people, for each age class. Then we calculated the daily number of deaths of the unvaccinated population, subtracting the daily vaccinated deaths from the ISTAT total daily deaths. The Emilia-Romagna region provided data from 27 December 2020 to 31 December 2021. These data have been obtained on December 2023 by lawyer Lorenzo Melacarne, who submitted a request for access to public documents to the Emilia-Romagna region.

The vaccines administration and vaccinated mortality data contain the dates of 1st, 2nd and all further vaccine doses. In the present study we used the date of the first dose to identify "vaccinated" and "unvaccinated" people: we considered "vaccinated" those who received at least the first dose of a COVID-19 vaccine and "unvaccinated" who did not receive any dose.

Having all these data for each day, we have been able to calculate the daily death incidence for each age class of the vaccinated and the unvaccinated people. We could not study the two sexes separately because the dataset provided by Region Emilia Romagna does not provide this information.

The daily death incidences are calculated by dividing the vaccinated/unvaccinated daily death number by the vaccinated/unvaccinated daily population. All the rates have been calculated per 100.000 people.

After observing trends in administrations and the incidence of all-cause deaths in the vaccinated and unvaccinated groups, we have established the time windows in which to collect the data for statistical analysis. Specifically, we decided that the beginning of the time window under consideration should coincide with the beginning of the surge in the administration graph, while the end should coincide with the plateau of the trend. Data on all-cause deaths in the two groups were collected within this time window.

We excluded from the analysis the age groups whose change in slope of cumulative vaccination trends did not correspond to a similar change in slope of mortality rates in the unvaccinated groups.

Therefore, only the age groups 50–59, 60–69 and 70–79 were analyzed. Specifically, the time windows considered are as follows:

1. for the 70–79 age group, the start of the time window was set for March 15, 2021 and the end for May 24, 2021;
2. for the 60–69 age group, the start of the time window was set for April 19, 2021 and the end for June 23, 2021;
3. for the 50–59 age group, the start of the time window was set for May 7, 2021 and the end for July 12, 2021.

2.2. Statistical analysis

After establishing the reference period and observing the trend of the administrations, unvaccinated and vaccinated variables, we decided to check whether there was a significant difference in the all-cause mortality incidence between the groups, to verify the presence of statistically plausible reasons to motivate further analysis. In this regard, the U Mann-Whitney test was used to compare the all-cause mortality incidence between the groups after their distribution was checked with the Shapiro-Wilk normality test.

After testing this assumption, we determined the regression model that best fits the data between the linear and exponential models by the comparison of the R^2, taking the administrations as the independent variable and the incidence of all-cause deaths in the unvaccinated group as the dependent variable. For all age groups considered, exponential regression showed the best fit to the data. After calculating the coefficient of the exponential regression, we plotted the gaussian Kernel density for pattern recognition by density estimation in the distribution of administrations. To find out in which time period the peaks observed in the graph occurred, we then plotted the trend of the number of administrations over time, to see in which weeks the number of administrations was concentrated. The same procedure was performed for the variable all-cause death incidence in the unvaccinated group. This allowed us to verify the time gap between the doses administered and the deaths in the unvaccinated group.

α level was fixed to 0.05, the $p < 0.05$ were considered significant and the data were processed using R studio (version 2023.09.0).

3. Results

3.1. Differences in all-cause mortality incidence between vaccinated and unvaccinated groups within the time window considered

The U Mann-Whitney test revealed significant differences in all age groups within the time windows considered: (i) 70–79 years age group ($W = 4.731$, $p < .0001$); (ii) 60–69 years age group ($W = 3.866$, $p < .0001$); (iii) 50–59 years age group ($W = 3.023$, $p < .0001$) (Figure 1).

3.2. 70–79 Years age group (time window: March 15, 2021–May 24, 2021)

The trends of administration of the first doses and deaths from all causes in the vaccinated and unvaccinated groups are shown in Figure 2.

The exponential regression model showed coefficient of determination $R^2 = .659$ and a p-value < .0001 (Figure 3).

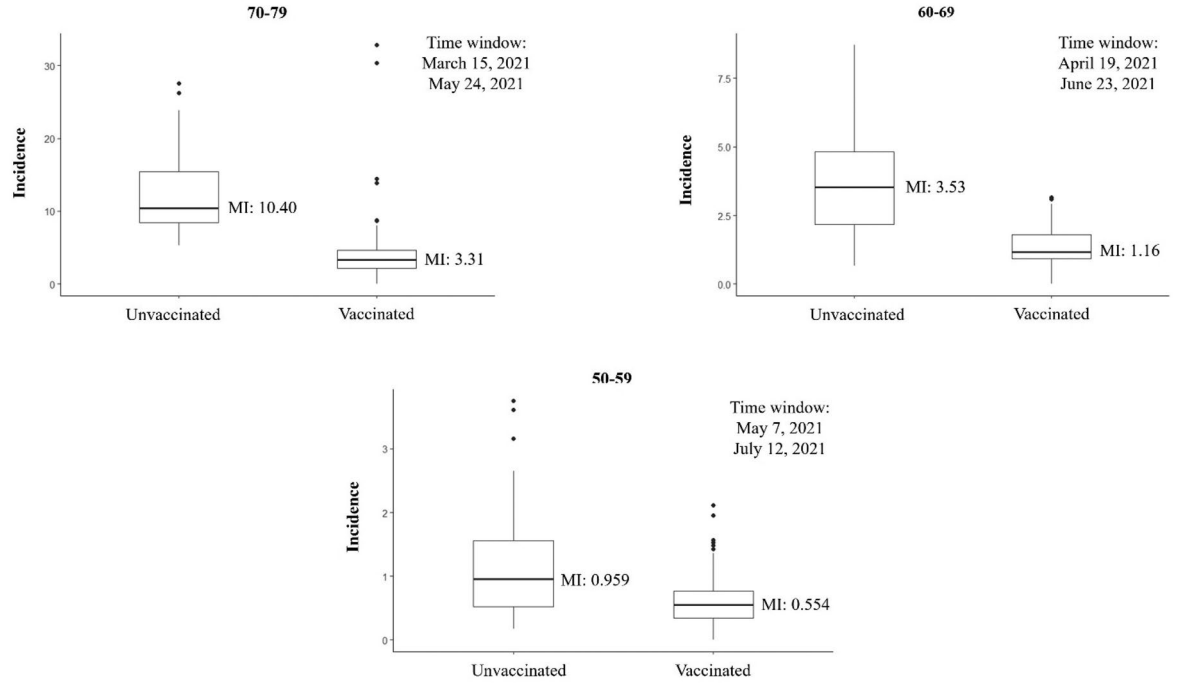

Figure 1. Difference in median mortality incidence per 100,000 by age groups between unvaccinated and vaccinated groups within the time window under consideration. MI: median incidence and its value.

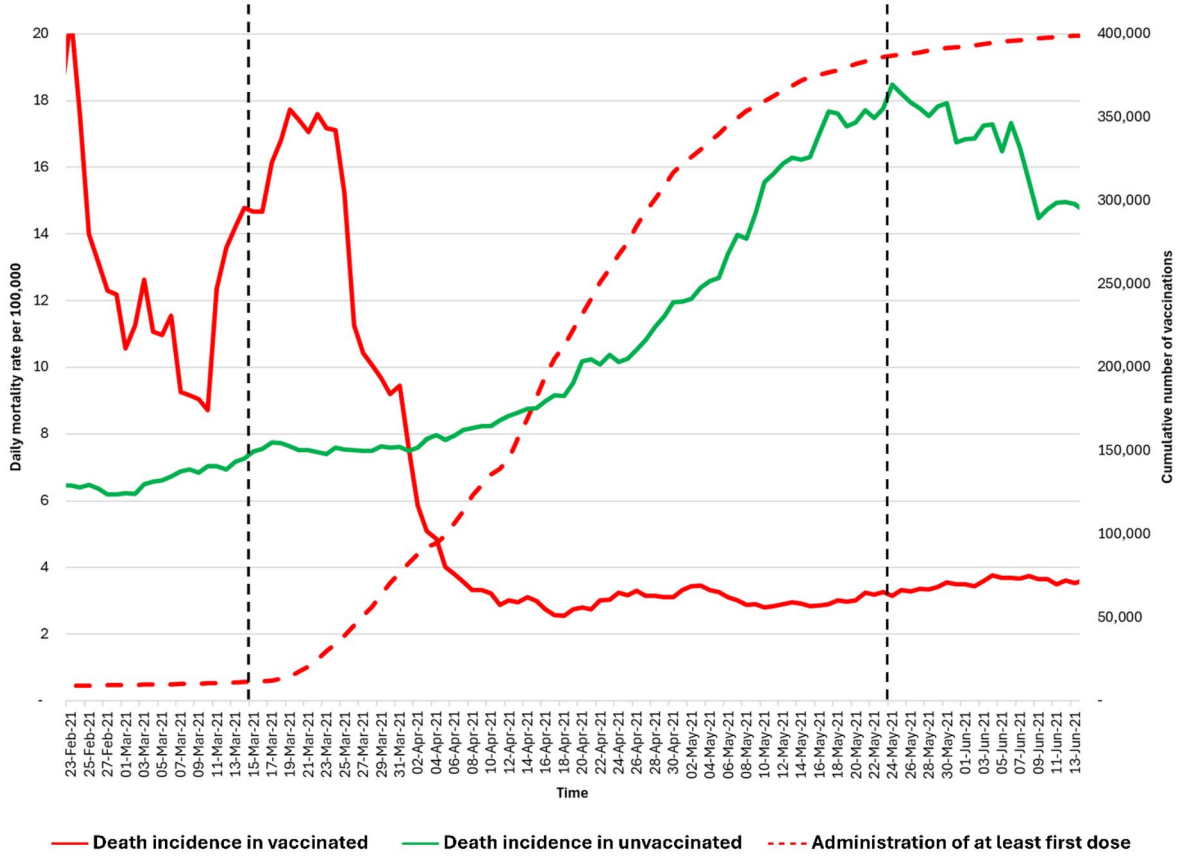

Figure 2. Age group 70–79; daily mortality rate per 100,000 vaccinated (red line), unvaccinated (green line) and cumulative number of vaccinations with at least 1 dose (red dotted line) for 70–79 years old (males + females). Death incidence lines are shown as 15 days moving average.

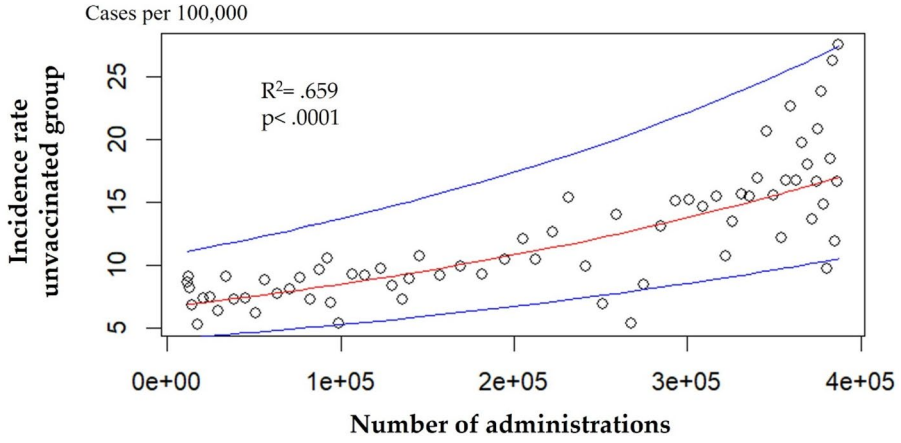

Figure 3. Age group 70–79; exponential regression line (red line) and confidence intervals (blue lines).

The kernel density estimate for vaccine administration shows two peaks: the first within 10 days after mid-March '21 and the second in end-May '21, while for the variable "all-cause death incidence" in the unvaccinated group the peak occurs between mid-March and mid-April '21 (Figure 4).

3.3. 60–69 Years age group (time window: April 19, 2021–June 23, 2021)

The trends of administration of the first doses and deaths from all causes in the vaccinated and unvaccinated groups are shown in Figure 5.

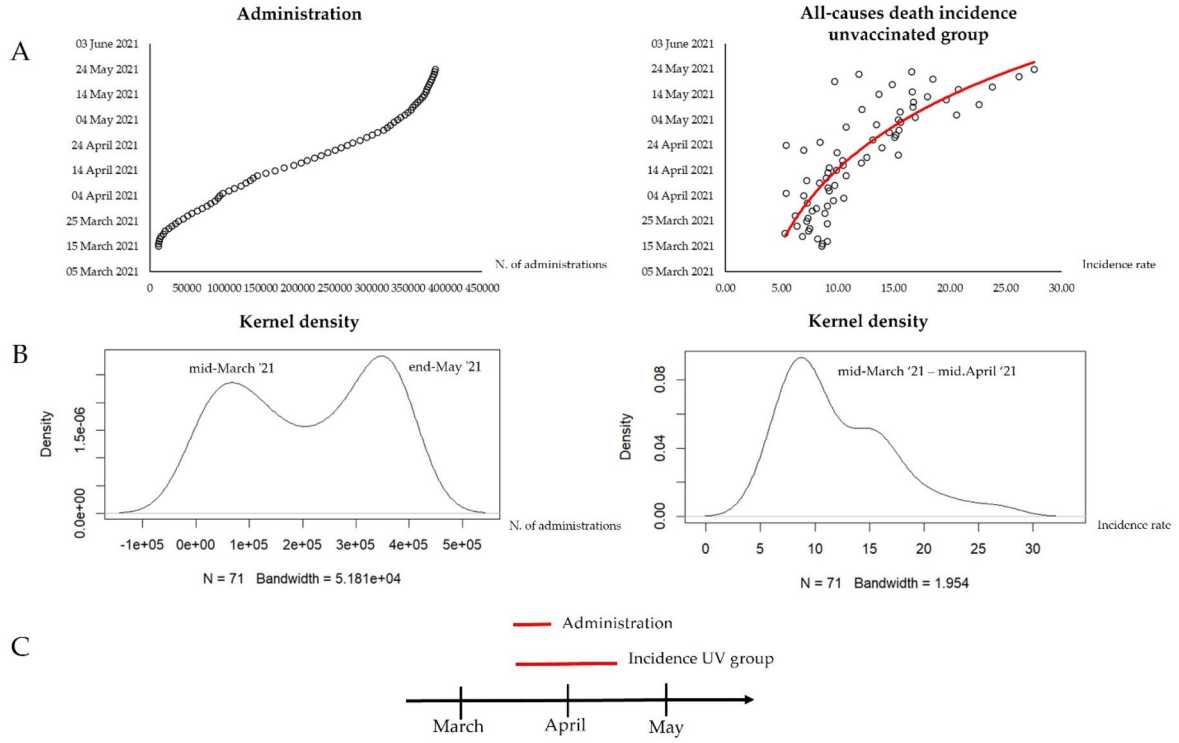

Figure 4. Age group 70–79; (A) trend of the number of vaccine administrations over time and all-cause death incidence of the time window under consideration; (B) Kernel density estimate; (C) Temporal distribution of the peaks of the two variables. N: number of observations.

The exponential regression model showed coefficient of determination R^2= .317 and a p-value < .0001 (Figure 6).

The kernel density estimate for vaccine administration shows two peaks: the first within 10 days after mid-April '21 and the second in end-June '21, while for the variable "all-cause death incidence" in the unvaccinated group the peak occurs between mid-April and mid-May '21 (Figure 7).

3.4. 50–59 Years age group (time window: May 7, 2021–July 12, 2021)

The trends of administration of the first doses and deaths from all causes in the vaccinated and unvaccinated groups are shown in Figure 8.

The exponential regression model showed coefficient of determination R^2= .290 and a p-value < .0001 (Figure 9).

The kernel density estimate for vaccine administration shows two peaks: the first within the first half of May '21 and the second in July '21, while for the variable "all-cause death incidence" in the unvaccinated group the peak occurs between mid-May and early June '21 (Figure 10).

4. Discussion

The aim of this study was to use population data from Emilia Romagna to test the effects of differential misclassification in real-world data and to determine whether there was a temporal relationship between the administration of the first doses and the increase in all-cause deaths in different age groups. We hypothesized that this bias might affect the incidence of deaths for all cases in the unvaccinated group and that a temporal gap might be observed between these two variables. The first step of the analysis was to identify a time window in which there was a clear overlap between the trend of vaccination and the incidence of deaths from all causes in the unvaccinated group. Subsequently, our analysis showed that within this time window there was a

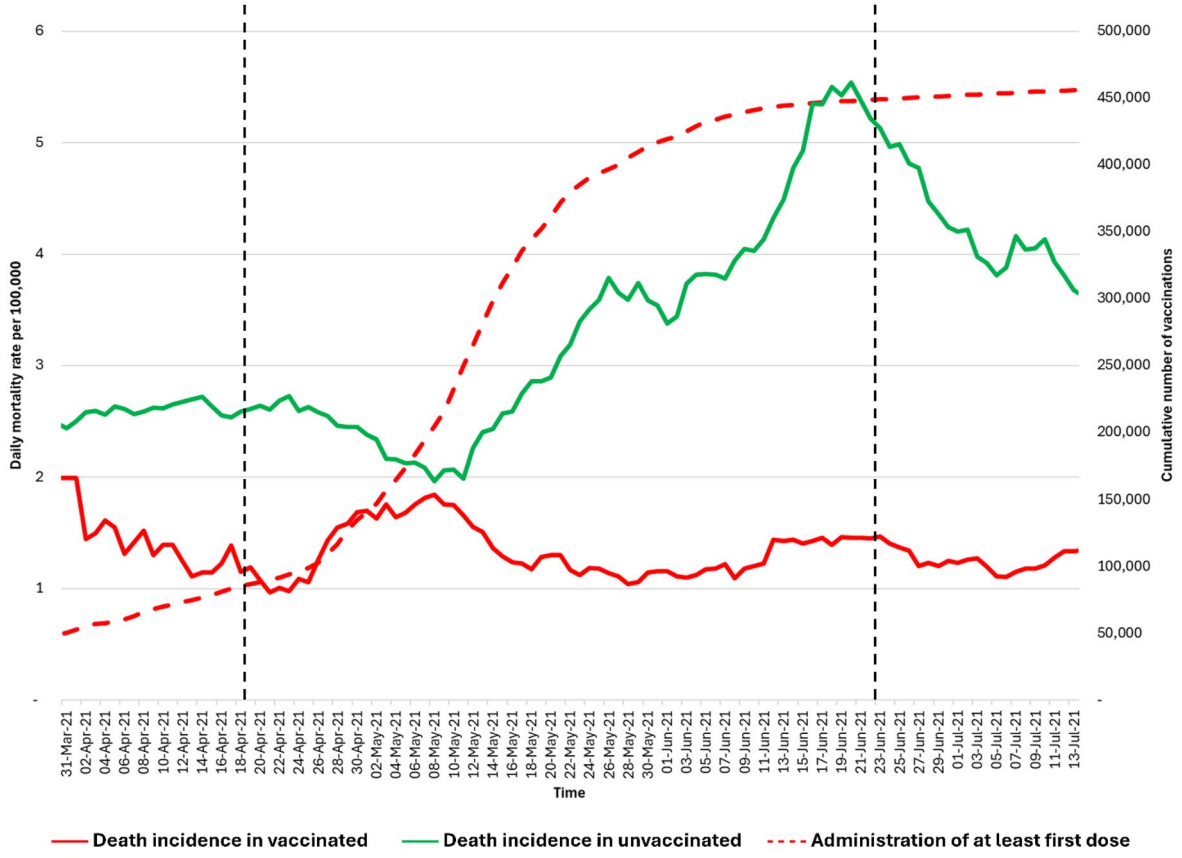

Figure 5. Age group 60–69; daily mortality rate per 100,000 vaccinated (red line), unvaccinated (green line) and cumulative number of vaccinations with at least 1 dose (red dotted line) for 60–69 years old (males + females). Death incidence lines are shown as 15 days moving average.

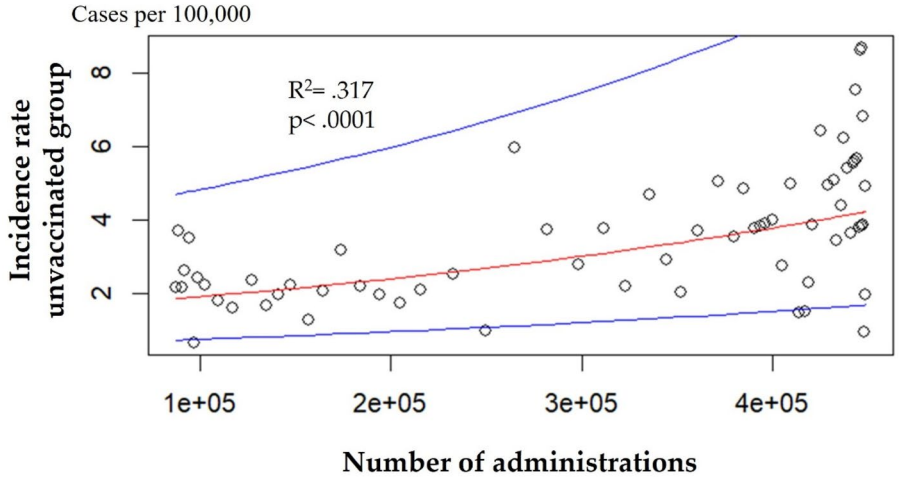

Figure 6. Age group 60–69; exponential regression line (red line) and confidence intervals (blue lines).

significant difference between the incidence of deaths from all causes in vaccinated and unvaccinated individuals. This difference cannot be attributed solely to the impact of COVID-19 deaths for at least two reasons:

i. In Italy, the percentage of COVID-19 deaths on total deaths was 9% in the year 2021 [16]. Thus, even if we wanted to attribute entirely these COVID-19 deaths to the unvaccinated

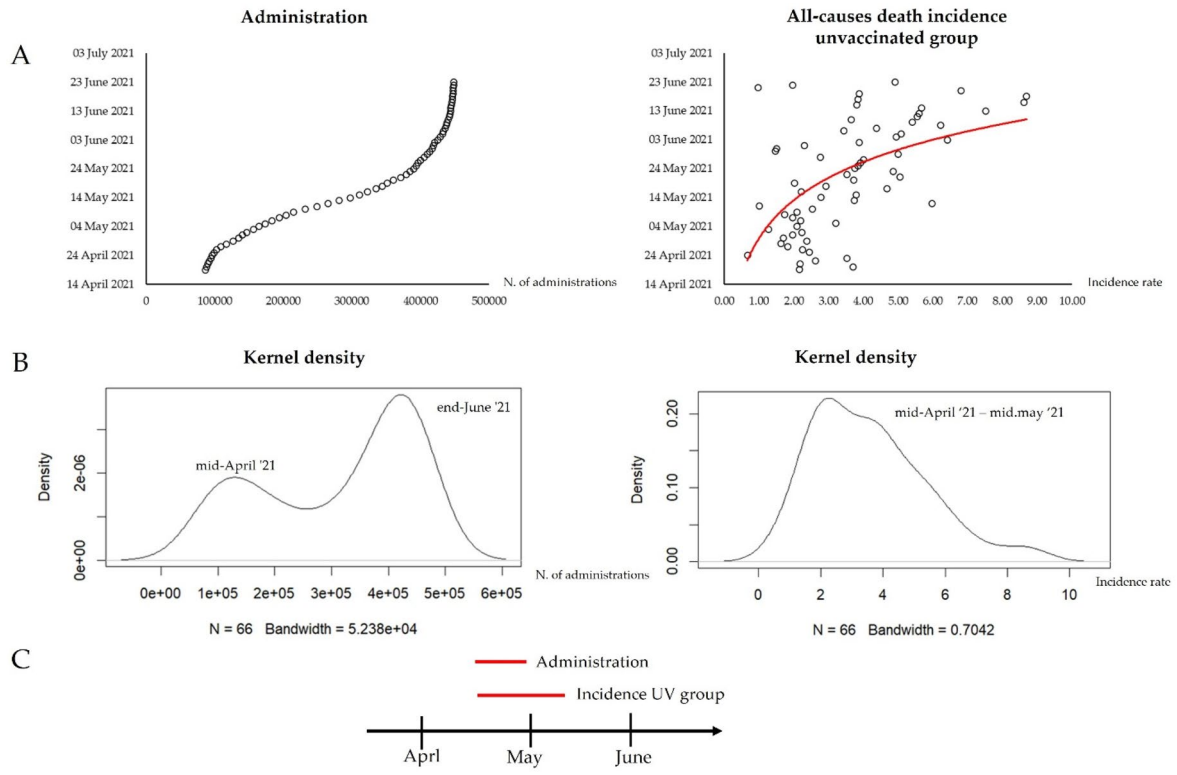

Figure 7. Age group 60–69; **A**: trend of the number of vaccine administrations over time and all-cause death incidence of the time window under consideration; **B**: Kernel density estimate; **C**: Temporal distribution of the peaks of the two variables. N: number of observations.

group, and subtract them, we would still have found a significant difference between the groups within the time window considered, given the distance between the medians (see Figure 1).

ii. We are not aware of biologically plausible reasons that could demonstrate a real, substantial effectiveness of the vaccine also for off-target deadly pathologies (in reality, the healthy-adherer bias, was widely discussed in our previous paper [2], and it can explain an artificial advantage of health intervention adherers, in the short-medium term [17–21], but also in the long term [22,23]).

The distance between the medians (even after subtracting COVID-19 deaths, attributed only to the unvaccinated group) should not remain significantly different: in the absence of bias, we would expect a difference close to zero. Furthermore, Figure 1 also clearly shows that the distance between the medians of the two groups decreases with increasing age. We hypothesize that this phenomenon may be due to the greater number of comorbidities in the older age groups [24], which may make these individuals more susceptible to the risk of death from all causes. Alessandria et al. showed that subjects with more comorbidities had a higher risk of death from all causes compared to subjects without comorbidities with the same number of vaccine doses received [2]. This phenomenon could be related to both direct damage (adverse events) and indirect damage, i.e. to the immune system [24–26]. We note that also in Italy, at the beginning of the vaccination campaign, the highest risk individuals, both in terms of age and comorbidities, were considered priority groups for access to vaccination. These hypotheses could also explain the value of R^2 observed in the age groups considered. Indeed, the model fits better for the age groups 70–79 (R^2= .659) than for the age groups 60–69 and 50–59 (R^2= .317 and .290, respectively).

Another interesting result of the kernel density estimation is the difference in the number of peaks observed in the graphs between the administrations and the incidences of total deaths in the unvaccinated group. In the administration graph we always observe two peaks about 2 months apart for all age groups, while in the incidence graphs, we always observe only one peak. Among the possible

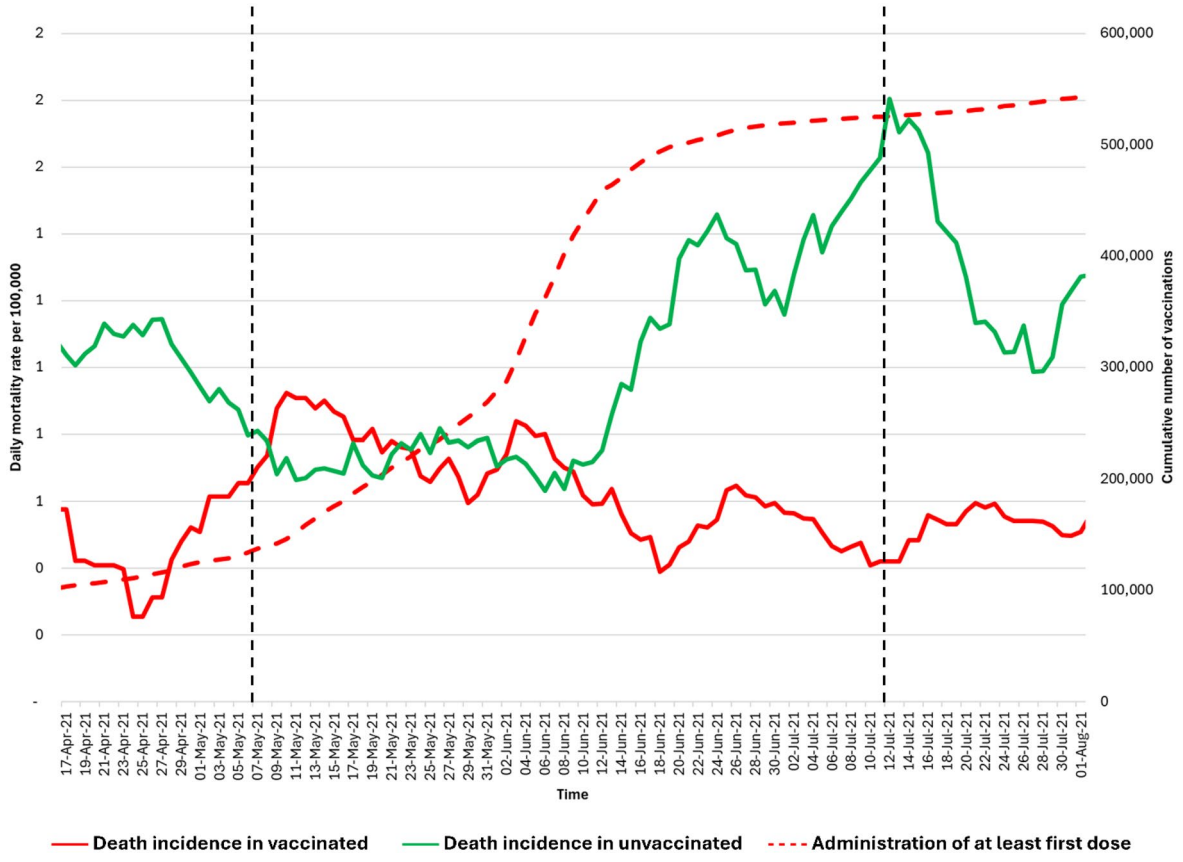

Figure 8. Age group 50–59; daily mortality rate per 100,000 vaccinated (red line), unvaccinated (green line) and cumulative number of vaccinations with at least 1 dose (red dotted line) for 50–59 years old (males + females). Death incidence lines are shown as 15 days moving average.

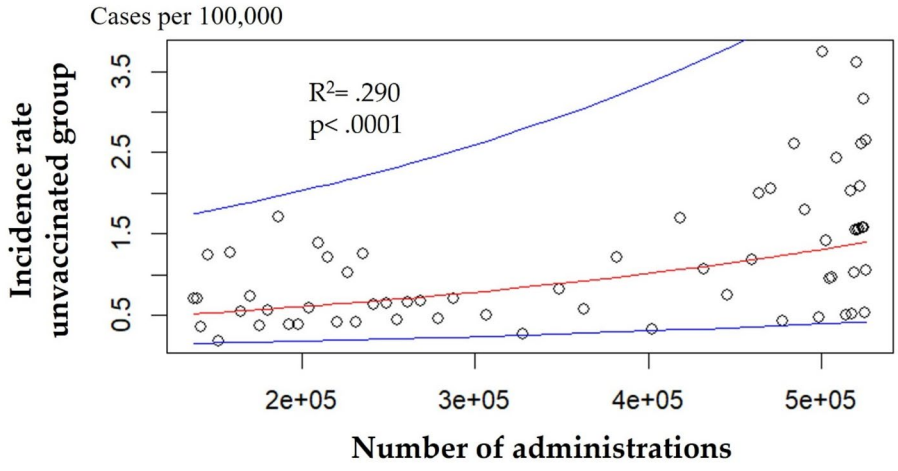

Figure 9. Age group 50–59; exponential regression line (red line) and confidence intervals (blue lines).

explanations for this phenomenon, we highlight the non-negligible harvesting effect, which is considered in the natural sciences as a stabilizing factor leading to the absence of disease [27] and which suggests that exposure to a certain factor particularly affects those whose health was already compromised, being therefore more susceptible to fatal outcomes. A similar finding was highlighted by Alessandria et al. where HRs for the all-cause death variable were higher in subjects with one dose compared to two or three doses [2].

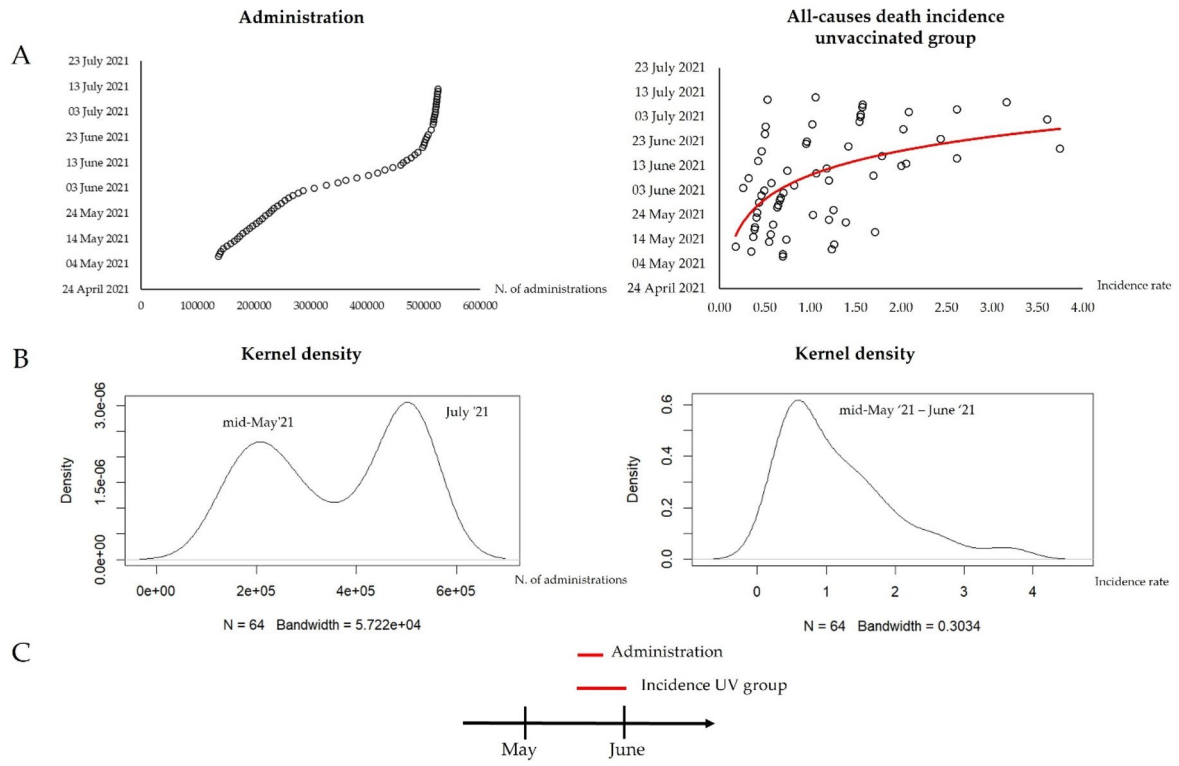

Figure 10. Age group 50–59; (A) trend of the number of vaccine administrations over time and all-cause deaths incidence of the time window under consideration; (B) Kernel density estimate; (C) Temporal distribution of the peaks of the two variables. N: number of observations.

We are not able to confirm the hypothesis of a temporal gap between the peaks in the administration of vaccines and the peaks in the incidence of total deaths. In fact, at the beginning of the observation of the phenomenon, we observe an almost temporal correspondence between the two variables, but a greater temporal dispersion in the incidence of total deaths in the unvaccinated group. This "tail" lasts about a month for the 70–79 and 60–69 age groups and about 2 weeks for the 50–59 age group. Among some possible explanations for this phenomenon, we might hypothesize the following. It is known that the recombinant mRNA administered as a vaccine encodes the SARS-CoV-2 spike protein. Castruita et al. [28] emphasized the partial to complete presence of the mRNA sequence in the blood of the tested subjects up to 28 days after vaccine administration and hypothesized that the half-life of the lipid nanoparticles (LNPs) was underestimated because the vaccine mRNA detected in them and released into the plasma of the recipients is contained in the LNPs. Röltgen et al. [29] found that both mRNA and free spike proteins persist in the cytoplasm and nuclei of germ cells in axillary lymph nodes ipsilateral to the injection site in the deltoid muscle for up to 60 days after vaccination. The "longevity" of the mRNA appears to be due to the presence of the N1-methylpseudouridine, which makes the synthetic mRNA excessively stable for a prolonged period of time [30,31]. Subsequently, Brogna et al. [32] demonstrated that the time at which this protein can be detected in the body of the vaccinated person varies between 69 and 187 days after the administration of the drug. Numerous definitive histopathological studies have demonstrated prolonged synthesis of the vaccine-derived spike protein in several tissues [11], causing severe autoimmune inflammatory reactions, with evidence showing spike protein production persisting up to 15 months after vaccination [33].

The review by Parry et al. [34] focuses on the pathogenic and toxic role of both the spike protein and the LNPs carrying the mRNA. The authors emphasize that the persistence of the spike protein causes persistent inflammation (chronic inflammation), which can potentially lead the immune system into a state of immune tolerance (strong relative increase in IgG4). This exposes the vaccinated individual to potential effects on the cardiovascular system (i.e. thrombosis, myocarditis, pericarditis), on the neurovascular system with neurodegenerative effects due to the formation of prions and

dysautonomia, on immune surveillance with a possible reduced effectiveness in fighting infections and cancer cells. In addition, there is the proinflammatory role of LNPs [35] able to induce significant secretion of inflammatory cytokines and macrophage inflammatory proteins leading to cell death [36].

The exposure to the components of vaccine products and their persistence in the body of the vaccinated might explain the observed "tail".

The case of Emilia-Romagna, however, is not isolated in Italy. Following the indication of the ISS [13], the practice of considering those vaccinated with one dose as "unvaccinated" in the first 14 days and, similarly, those vaccinated with two doses within the same time interval, as "vaccinated with one dose", and so on, has also been followed in other settings. In Pescara, for example, the study [2] already noted that, in the original study under review, all the follow-up of those vaccinated with any dose started from the 15th day after vaccination, while those of the unvaccinated all started from the first day of observation. Therefore, there was certainly a differential misclassification of deaths from all causes between vaccinated and unvaccinated people, because it is unquestionable that the deaths occurring in the first 14 days after vaccination were omitted. Unfortunately, it was not possible to establish whether they had been attributed to the previous vaccination category or to quantify the impact of this bias on the results, since it was not possible to trace the number of deaths omitted or attributed to the previous category.

However, there is evidence that the same practice has been adopted in other countries, and some observational studies conducted there, evaluating the effect of COVID-19 vaccinations on different outcomes, such as hospitalizations or deaths, may be affected by the same type of bias, as already highlighted by Lataster (2024) [8]. For example, the methodological notes of a study [37] conducted by the UK Office for National Statistics (ONS) contain a statement very similar to that of the ISS: "*Data for COVID-19 vaccination were retrieved from the National Immunization Management Service (NIMS). Vaccination status (unvaccinated, single-vaccinated or double-vaccinated) was defined as the number of doses received at least 14 days before the index date*".

Another ONS study [38] on the effectiveness of COVID-19 vaccinations on COVID-19-related hospitalizations and deaths even uses a 21-day case counting time window, according to the following statements: "*The vaccination statuses used were: unvaccinated (those with no vaccination or who were vaccinated with a first dose less than 21 days ago) first dose (those who were vaccinated with a first dose at least 21 days ago to earliest of less than 91 days after first dose or less than 21 days after second dose) over three months after first dose (those vaccinated with a first dose at least 91 days ago to less than 21 days after the second dose) second dose (those who were vaccinated with a second dose at least 21 days ago to earliest of less than 91 days after second dose or less than 21 days after third dose) [… omissis].*"

This latest study appears interesting, because in addition to COVID-19-related deaths it also considers non-COVID-19 deaths and therefore, indirectly, also deaths from all causes.

This seems to confirm that ONS applies - depending on the case - a time window of 14 or 21 days from vaccination with a given dose, during which not only COVID-19 infections or hospitalizations, but also deaths from any cause are attributed to the previous vaccination status, as already highlighted in a previous study [8].

5. Limitations of study

The region's daily population size has been estimated with a linear interpolation between 1st Jan 2021 and 1st Jan 2022 sizes, since ISTAT is providing this information only on 1st Jan of every year.

The unvaccinated population has been calculated by subtracting the vaccinated population from the general population. Different criteria of data collection between ANV, ISTAT and Emilia-Romagna region may lead to errors, due to counting or not counting nonresident population. The Emilia-Romagna vaccinated people mortality data has been provided for the resident population only, in line with what is done by ISTAT, but ANV administrations database records the vaccine delivery region instead of the region of residence. This implies that a person resident in another region but vaccinated in Emilia-Romagna is counted in the ANV database for Emilia-Romagna, but her/his possible death

would be counted in the database of the region of residence. Vice-versa, a resident in Emilia-Romagna vaccinated elsewhere will not be counted in the Emilia-Romagna ANV database, but her/his possible death would be counted in the ISTAT database for Emilia-Romagna. We assume that this kind of error can be compensated between the Italian regions, in the hypothesis that the number of Italian nonresident people vaccinated in Emilia-Romagna is similar to the Emilia-Romagna residents vaccinated elsewhere in Italy.

Moreover, foreign nonresident people are counted in the ANV data but are not counted in the ISTAT and mortality of vaccinated people data. This might lead to an overestimation of the vaccinated population, that could cause an underestimation of the daily death rate of that population and a consequent overestimation of the unvaccinated daily death rate. A study published on Bollettino Epidemiologico Nazionale (ISS, Istituto Superiore di Sanità) has estimated the foreign population vaccinated in Italy as the 0,38% of the total [39].

These different data collection methods are constant during all the study periods, so we suppose that they don't affect the dynamic comparison between the daily death rates of the two populations of vaccinated and unvaccinated, and the evaluation of their very different trends.

To date, the number of the daily unvaccinated deaths is not yet available, despite a specific request submitted to the Emilia Romagna region authorities.

6. Future research directions

Very few countries in the world have so far published their mortality data by COVID-19 vaccination status, and even some of them that have done so have stopped making them public (e.g. the United Kingdom stopped doing it in June 2023).

However, it is clear that many countries have such data, including Italy, at least for several Italian regions. We therefore intend to replicate this study with other Italian regions, and it would also be valuable if the international scientific community pushed to obtain the publication by the United Kingdom of the ONS data for the last two years. The same could be hoped for other countries.

7. Conclusions

Despite potential sources of error arising from data collection by various Italian authorities, the results of this study highlight the existence of a "case counting window bias" in the real-world data, which was already suspected by previous authors based on simulations. This bias could artificially increase the mortality of the unvaccinated and decrease that of the vaccinated by shifting deaths that occur in the first 14 days after vaccination to unvaccinated status, on the grounds that this time interval is necessary for the full expression of the immune response. The systematic repetition of this shift can distort the epidemiologic results of an event and lead to erroneous public health decisions.

Author contribution statement

CRediT: **Marco Alessandria**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **Giovanni Trambusti**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **Giovanni Maria Malatesta**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **Panagis Polykretis**: Formal analysis, Validation, Visualization, Writing – review & editing; **Alberto Donzelli**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Disclosure statement

The authors declare the absence of financial or non-financial competing interests. The study was based exclusively on anonymous data, released under the Italian Freedom of Information Act (Legislative Decree No. 33/2013, art. 5, comma 2).

Ethics statement

The study was based exclusively on anonymous data released under the Italian Freedom of Information Act (Legislative Decree No. 33/2013, art. 5, comma 2). Ethical review and informed consent were not required.

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Data availability statement

The data are available upon reasonable request.

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