All-Cause Mortality During Covid-19 Vaccinations in European Active Populations

Patrick E. Meyer
Patrick.Meyer@Uliege.be
Bioinformatics and Systems Biology Lab
Liege University
Belgium

Pierre Chaillot
National Institute of Statistics and Economic Studies
INSEE
France

ABSTRACT

The question whether Covid-19 vaccination campaigns could have had an immediate negative impact on excess deaths continues to be debated two years later, in particular in the less than 45 years old. When the age-stratified (anonymized) vaccination status of deceased will be publicly available, the debate should come to an end. In the meantime, this paper provides three new statistical analyses that further shed light on the matter. Two of them connect the temporality of all-cause mortality data with injection data. Another analysis, using internet search trends, investigates possible alternative explanations. We deem that taken together, as it is done in this paper, those three analyses reinforce our previous conclusions suggesting caution when it comes to vaccinating/boosting young European populations.

KEYWORDS

All-cause mortality, excess deaths, Covid-19 vaccination, concordance statistics, google trends

1 INTRODUCTION

Several papers have noticed an unusually high all-cause mortality in 2021 in a majority of European countries [24, 35]. This can be difficult to explain in lower age groups since their Covid-19 fatality rate is known to be low [32]. Furthermore one of their main cause of deaths, i.e. accidents, might have been strongly reduced due to various mobility restrictive measures. The fact that Covid-19 vaccinations could have been responsible for some of the observed excess deaths continues to this day to be debated [19]. However, the crux of the matter in this debate lies in determining if a statistical association is causal or not. Indeed, traditional methods for determining causality in those circumstances consists in performing a survival analysis comparing two groups, namely a control one and a treatment one. However, to do so in mortality studies requires (anonymized) data concerning the vaccination status of the deceased. Unfortunately, despite researchers requesting those data [10], to our knowledge, those are still unavailable everywhere in EU thereby preventing traditional approaches [11]. The only country releasing data around the vaccination status of the deceased has been the UK but unfortunately the provided data might have been prone to miscategorization [27]. For this reason, in a previous work, a causal network has been provided in order to detect a possible connection between excess mortality and anti-covid injection campaigns using data from 18 European countries [24]. In some of those countries injection campaigns were extremely fast. Every interested person could directly take the first dose no matter the age group or the comorbodities. This was for example the case in Hungary. In other ones, the rollout were much more progressive such as, for example, Belgium. In the latter case, each age group could access injections at a different period of the year. Those temporal and spatial drifts in injections both across countries and age groups constitute a precious information when it comes to infer dependencies. Indeed, the number of vaccine doses delivered each month in each country (irrespective of the type of vaccine used) has been a more relevant variable in order to predict all-cause mortality than both the covid case rate and the covid death rate, at least for the two lower age categories (i.e. those below 45 years old). In other words, vaccines appear to have contributed (directly or indirectly) to an increase in other causes of death (than covid), in young populations. Those previous conclusions are now consistent with statistical results brought by a dozen of preprints and papers [1, 3, 5, 16, 19, 20, 28, 30, 33, 34, 38]. However, they are seemingly in contradiction with several major papers such as [26, 42] as well as [6, 21, 22, 41] that defend (based on all-cause mortality) a positive benefit/risk balance. It is worth noting that the latter four papers focus either explicitly or implicitly (by aggregating all age groups) on the mortality of the 60+ (as opposed to the less than 45 years old), [42] focus on populations having received a flu shot (hence a bias toward young adults with comorbidities [24]) and finally [26] analyses excess deaths at twelve weeks after vaccination (as opposed to before and after injections). As a result, none of these six papers are formally in contradiction with our previous statistical results. When the requested data will finally be released, this debate around the benefit/risk balance for young adults should come to an end. In the meantime, it is fundamental to release as much statistical analyses on the matter. Due to the very high numbers of vaccinated individuals, if there is even a slight toxicity related to the injection, as also suggested by recent biomedical papers [31], we should be able to observe statistics hinting in that direction. In the following subsections, we describe three new analyses focusing on active populations of Europe. First we show a statistically significant increase of all-cause mortality post-injection compared to pre-injection in several age groups and countries. Second, we show via internet search trends in France that the usual suspects for the younger age groups, such as accidents and suicides are not allowing us to explain the observed signal. On the contrary there is a clear increase of death-, emergency- and cardiac-related searches in correlation with (independent) vaccination queries. Obviously, those search trends could reflect some fear of vaccination rather than an underlying truth. When it comes to cardiac related fears, it should not come as surprise since the Center for Disease Control and Prevention (CDC) itself had stated early in the crisis that there were rare cardiac events associated with vaccinations [9]. Nonetheless, those search trends are very consistent with the increase of cardiac events reported in Israel in the less than 40 years old [37], in adolescents in Thailand [23], and that cannot be easily attributed to the disease itself [39]. In order to check if there might be more than fear at play when it comes to mortality, we deliver a third statistical analysis that reaches significant association between periods with unusually high excess deaths and periods with maximal injection rates. As a consequence, all our new analyses reinforce our previous conclusion that is, caution should be encouraged when it comes to vaccinating and/or boosting young populations, at the very least until innocuity becomes a proven fact, in particular, via analyses of the requested anonymized vaccination status of the deceased.

2 DATA AND METHODS

Similarly to [24], we extracted datasets with 9 variables in each, namely *ZscoresCurrent* (i.e. all-cause mortality of the investigated period), *ZscoresPast1Y* (i.e. one year before), *ZscoresPast2Y* (i.e. two years before), *When* (i.e. the period of interest) , *Who* (i.e. age-category), *Where* (i.e. country), *DoseRate* (i.e. reflecting the administered doses in that age group during the investigated period), *CaseRate* (i.e. average 14-day-positivity-rate in the country during the period) and *CovDeathRate* (i.e. average 14-day-deaths-rate in the country during the period). The three first Zscores variables are coming from the European MOrtality MOnitoring project (EuroMOMO) [14] whereas the *DoseRate,* which is simply the sum of the four first doses administered divided by the targeted population, the case-positivity-rate and the covid-death-rate are all extracted from the European Center for Disease Control and Prevention (ECDC) data [13]. Each of the data source provides a weekly monitoring of their respective variables but we have averaged those over periods of 4 weeks in order to have a time-interval large enough to capture time-delayed effects. The produced datasets start at week 24 of 2022 and goes down to week 50 of 2020 by groups of 4 weeks, that is for each variable. Other choices of starting and ending week could be chosen but 24 is the last week of 2022 where the ECDC monitored the covid case-rate and death-rate worldwide while the last weeks of 2020 correspond to the early beginning of most vaccination campaigns in the countries investigated.

Unfortunately the list of countries and the list of age groups are not a perfect fit between our two data sources. Hence, we have focused on the countries and age categories where an intersection of the data sources has been possible. As a result, 17 EU countries are present in our resulting datasets. In terms of age categories, we grouped the 0-18, the 18-49 and the 50-69 from ECDC, in order to match (with a less than 5 years difference) the 0-14, the 15-44 and the 45-64 categories of EuroMOMO. In the end, three datasets have been produced, one for each age category investigated (i.e. 0-14, 15-44, 45-64), all with 20 periods (of 4 weeks) times 17 countries, that is 340 samples. Our R script to produce those datasets as well as the script to compute the following statistical analyses are all publicly available [25].

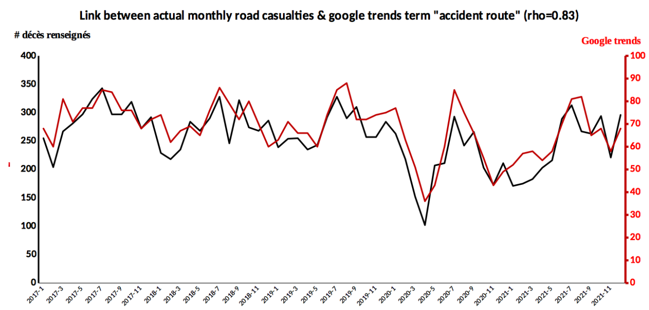

Figure 2.1: Google trends "accident route" (road accident) vs actual number of road deaths in the five years preceding 2022 in France. Pearson's correlation is 0.83.

2.1 Comparing post-injection with pre-injection excess deaths

In order to check if there are differences between excess deaths pre- and post-injection campaigns, we have compared the zscores of excess deaths during 11 periods of 4 weeks after 5% of the targeted population had received at least one shot (i.e. a starting date in 2021 that differs for each age group and each country), with the zscores of the same periods but the year before (i.e. mainly in 2020). Those 11 periods corresponds to the maximal consecutive number of periods available in our dataset for all the age groups/countries (i.e. given by the age group/country vaccinated the latest). Also it is worth noting that comparing to the year before makes sense since Covid-19 waves were already striking and mobility restrictive measures were already implemented. As a result, vaccination is likely one of the major discriminating variables between the two investigated periods. In Table 1 we report both non-statistically significant increases of excess deaths with respect to the reference year (with + symbol) as well as statistically significantly higher zscores (with a ++ symbol). Paired t.tests are used to compare the zscores post- and pre-injection in each country/age group. No correction for multiple testing are applied here because all the tests are independent (each pair age-group/country is compared to its own values of the year before). It is worth noting that zscores differences between two Covid years (i.e. 2021 vs 2020) should in theory average at a close zero value, that is assuming the vaccine had zero benefit. In such case, we would expect, as much (-) than (+) and at most two (++) by chance alone. Unfortunately, we observe a much higher number of pluses than expected. The differences among countries could be explained by differing health-care systems, overall health and wealth in the population, government measures or even some batch effects from vaccine production.

2.2 Google trends in France

It is sometimes argued that excess deaths waves following injection campaigns could simply be due to concomitant Covid-19 waves, suicides due to government measures such as lockdowns or even accidents coming from the recovery of freedoms. As we have shown in the past, identifying causal variables in diseases from statistical dependencies is a difficult task [7]. It usually requires to investigate as much variables as possible. In this section, we address several

VS 2020	AT	BE	CY	DK	EE	EL	ES	FI	FR	HU	IE	IT	LU	MT	PT	SE	SI
0-14	-	+	+	+	+	++	++	++	++	++	+	-	-	+	+	+	-
15-44	+	+	++	-	++	++	-	-	++	++	-	+	-	-	-	-	+
45-64	++	-	+	+	+	++	-	-	+	++	+	+	+	+	-	-	++

Table 1: Increases of excess deaths in the 11 periods of 4 weeks post-injection (after 5% of the population received a shot) with respect to the same periods the previous year (mainly in 2020). Non significant increases are reported with (+) and statistically significant increases (using a paired t.test) are reported with a (++). Age groups in bold have the highest number of (++).

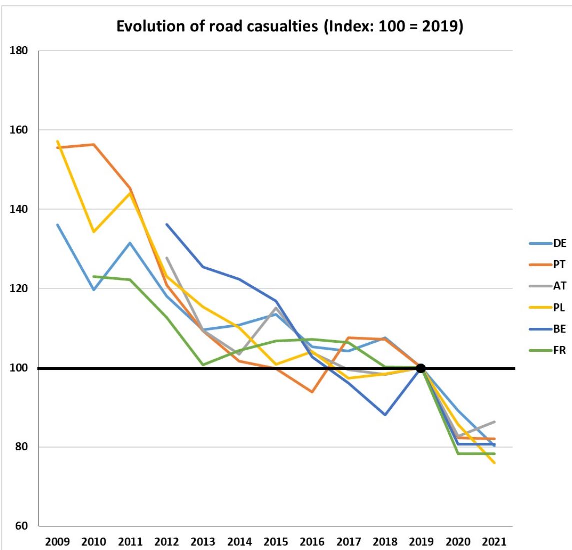

Figure 2.2: Evolution of road casualties across 10 years in 6 European countries

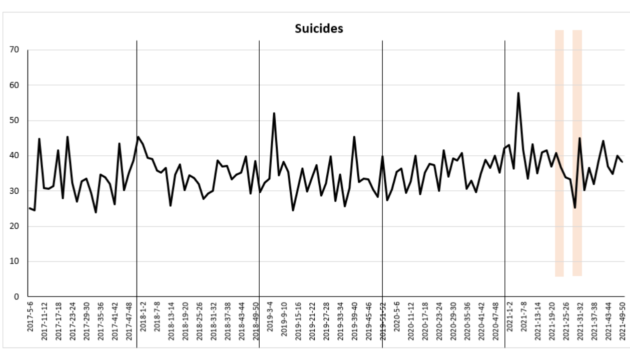

Figure 2.3: Google trends aggregating various suicide related search terms from 2017 to 2022. Vertical bars indicate injection campaigns in France in that age group.

of them using internet search trends. Internet search trends have already been used in many scientific fields, in fact a search of the terms "Google trends" [18] in PubMed already returns several thousands hits. For example, it has been used successfully to predict epidemics [12], crimes [17] or even suicides [2]. We have little information on the link between search trends and age groups except for a 2021 study that identified that 75% of internet users worldwide

Correlation	translation	covid	vaccine
perte gout	taste loss	0.47	0.01
migraine	migraine	0.11	-0.16
hopital urgence	emergency hospital	-0.19	0.26
medecin garde	emergency doctor	-0.08	0.21
arret cardiaque	cardiac arrest	-0.04	0.22
caillot	(blood) clot	-0.01	0.26
decede jeune	died young	0.01	0.12
retrouve mort	found dead	0.1	0.26
pericardite	pericarditis	0.08	0.52
myocardite	myocarditis	0.11	0.6

Table 2: Pearson's correlations between weekly scores of search terms from January 1st 2020 to December 31th 2021.

are aged 18-44 years old and a 2015 marketing study that showed that the 18-44 are most likely to be using Google to search the web [36, 40]. As a consequence, it appears quite reasonable to assume that the various search trends presented below are dominated by one of our age groups of interest. We focused on France since it is both, one of the most populated country in our list but also because of its results in Table 1.

In order to confirm that those search trends can be used in the French population during the targeted period, we have plotted the signal returned by the search "accident route" (road accident in French) with the official numbers of road deaths over the previous five years as reported by the French national institute of road surveillance [29].

As can be seen in Fig. 2.1, (with a correlation of 0.83) search trends can provide efficient proxy variables. This figure also shows that there are no abnormal spike post-injection in our data. Also, using statistics from six different EU road institutes [29], we can observe that the global numbers of road casualties were much lower than expected in 2021 (see Fig 2.2). This is probably due to the various mobility restrictive measures adopted. It might be argued that a lower incidence of accidents is compensated by an increase in Covid deaths but Covid-19 is known to have a close to zero fatality in that age-group [32]. However suicide, being the third cause of deaths in the 15-49 in France [15], it remains a potential candidate variable for explaining partly at least our previous p-values. Using internet search trends, we observe that in the months following the injections, aggregated search terms that have been shown to be good precursors of an increase in suicides [2] containing "depression" (depressed), "comment se suicider" (how to kill yourself),

	AT	BE	CY	DK	EE	EL	ES	FI	FR	HU	IE	IT	LU	MT	PT	SE	SI
0-14	+	-	-	++	-	+	++	-	++	+	-	-	-	-	-	+	+
15-44	++	++	-	+	++	+	++	-	++	++	-	-	-	-	++	+	++
45-64	++	++	-	+	++	++	++	++	++	++	-	++	+	+	+	+	+

Table 3: Concordance between high excess deaths and maximal injection rate. Zscores exceeding 0.675 (that is a probability of 0.25 of happening) are reported with a (++). Positive zscores not reaching the threshold are denoted with a symbol (+). The age groups in bold are those reaching statistically significant concordance (using a binomial test) with at least 8(++) out of 17.

”se pendre” (hang oneself) are not increasing post-injection (contrarily to a spike happening during lockdowns, before injection campaigns), see Fig. 2.3.

Finally, we correlated (using Pearson’s method) the weekly scores of various search trends to the corresponding weekly scores of both “covid” and “vaccine” searches. Not surprisingly, side effects of the disease such as “perte gout” (taste loss) have a much higher correlation with the search term “covid” than with the search term “vaccine” and, on the other hand, search terms such as “pericarditis” and “myocarditis” have much stronger correlation with the search term “vaccine” than with the search term “covid”. Those side effects trends thereby provide us with a scale to compare various searches. Interestingly, searches such as “hopital urgence” (hospital emergency), “retrouve mort” (found dead), “decede jeune” (died young) have a much stronger correlation to the search term “vaccine” than “covid” (see Table 2). The latter results could of course be due to a fear of vaccination rather than to the vaccination itself but it should be emphasized that these queries have been searched independently and not jointly. Hence, it is the temporality of those queries that is correlated. Nonetheless, in order to assess if correlations between search terms are entirely fear-related or if those trends may have some solid ground, we perform in the next subsection a concordance analysis between periods with excess deaths spike and periods with maximal dose rates. These search trends already suggest that suicides, road accidents and Covid waves (at the very least in France) do not offer any explanation to the post-injection excess deaths observed in Table 1.

2.3 Spike concordance analysis

In 2019 and 2020, excess mortality waves tend to be synchronous between neighboring age groups in the same country, as well as between neighboring countries in the same age group, simply because excess deaths spikes are often caused by events that cross both age groups and frontiers such as for example heat waves, floods or epidemics,... However in 2021, excess mortality waves appear to present larger delays across age groups (for example the 25-49 and 70-79 years old in Belgium, a densely populated country with a radius of less than 150km) as well as across neighboring countries in the same age group (for example the 15-24 years old in Austria and in Croatia, two countries separated by at most 1000km from each other) [8]. In order to formalize those spatio-temporal drifts, we have performed a spike concordance analysis connecting maximal dose rates and excess-mortality spikes, using the extracted datasets involved in Table 1. It should be noted that spike concordance analyses have typically been used in the field of neural connectomics [4]. In Table 3, we report (with a ++ symbol) when the average excess mortality at the maximal injection period (of 4 weeks) reaches an unusual value (a zscore above 0.675 which corresponds to a probability below 0.25 of happening by chance, using the theoretical quantile function for normally distributed variable). The Table 3 displays all the EU countries where such spike happens coincidentally in the period with maximal injection rate. From this table, a p-value is computed using a binomial test, that is the probability of having as many (++) out of 17. This computation leads to statistically significant results for the 15-44 and the 45-64 (with respective p-values of 0.047 and 0.02).

2.4 Validations

Due to our results, it has been important to double check that we might not be facing inaccurate data from EuroMOMO. As a result, we have downloaded raw mortality data from Eurostat [15] and we have computed age-standardized mortality rate (ASMR) using 52 linear models, that is one per week, using six data points from years 2013 to 2018 (for each country and three age-groups between 15 and 60 years old). Linear models are a logical choice of model to capture increasing and decreasing trends across several years. On the other hand, the use of weekly models allows us to capture seasonal trends, for example, it can be observed that before 2020, the 15-24 year old Polish population tends to have spikes of excess deaths in the summer when road accidents are more numerous whereas the 70-79 years old Danish population tends to have excess deaths spikes in the winter during flu seasons. Unfortunately injections campaigns have happened precisely at those periods in those age groups and countries. This could lead to an underestimate of excess deaths because the main cause of deaths (respectively accidents and flus) have been shown to be strongly reduced by the various restrictive measures during vaccination campaigns. Despite this, we have also reached statistical significance for one age group (i.e. 25-49), that is over 16 EU countries investigated. This result has been obtained with slight differences in country sets, age-categories and methodology [8, 10]. This not only suggests the relevance of EuroMOMO zscores (for the investigated period) but also the robustness of our results. Models and predictions based on Eurostat are also publicly available [10].

It is also worth noting that the various machine learning analyses presented in [24], that have been performed on the same data but stopping at week 46 of 2021, still show similar trends on the updated data used in this paper (and stopping at week 24 of 2022). More precisely, the numbers continue to support the causal model where the variable DoseRate had not only a positive effect (i.e. reducing) on the covid death rate variable but also a negative effect on the all-cause mortality variable (i.e. suggesting concomitant increases of other causes of death in young populations). Hence, this confirms the consistency of both the methodology that have been used previously but also of the updated data that have been used in this paper.

3 CONCLUSION

When human health is at stake, it is of fundamental importance for data scientists to contribute to shedding light on public debates, especially when important follow-up data remain unavailable nearly two years after it has been requested. Those vaccines may have contributed to reduce covid related deaths during vaccination campaigns but if this happens at the expense of contributing to an increase of other causes of death, then a benefit/risk balance automatically appears. In this paper, we have provided three different statistical analyses. We deem that each one of them provides a separate piece of a puzzle but taken together, those reinforce our previous machine learning study that suggested a negative benefit/risk balance for the less than 45 years old. Indeed in the 15-44 age group, we have shown in this paper statistically significant concordance between high excess deaths and maximal injection rate periods, as well as abnormally high excess deaths in the following ten months (i.e. 11 periods of 4 weeks when compared to the same period of the previous year). Finally no other obvious explanation to the observed statistics pops up when using a well-known tool such as Google trends, on the contrary high cardiac- and emergency-correlated searches are observed. Transparency and falsifiability are fundamental in this debate, that is why we have provided all the data and codes to reproduce our results. Nonetheless, we hope that when the vaccination status of the deceased (of 2021 and 2022) will finally be released, those will demonstrate a positive benefit/risk balance of these injection campaigns also for the less than 45 years old.

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As for every paper, our results do not in any way, shape or form reflect any belief of our respective institutions.
None of us have any conflicts of interest.

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