Peer Review Report

Review Report on The role of COVID-19 in excess mortality in Slovakia: A novel approach based on healthcare billing records

Original Article, Int J Public Health

Reviewer: Reviewer 1
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EVALUATION

Q 1 **Please summarize the main findings of the study.**

Using healthcare administrative data a "COVID-associated" deaths category is defined for Slovakia, which much more closely matched the excess mortality.

Q 2 **Please highlight the limitations and strengths.**

Important contribution to better capture COVID-related deaths, with slight problems (rooms for improvement) in the statistical methodology.

Q 3 **Please provide your detailed review report to the authors. The editors prefer to receive your review structured in major and minor comments. Please consider in your review the methods (statistical methods valid and correctly applied (e.g. sample size, choice of test), is the study replicable based on the method description?), results, data interpretation and references. If there are any objective errors, or if the conclusions are not supported, you should detail your concerns.**

I consider this manuscript to be very relevant, interesting and practically useful. However, I have a few problems that should be addressed in my opinion before publication.

Major remarks:

- While the Authors clearly state the difference, and that they're aware of it, the manuscript sometimes nevertheless suggests that excess mortality should be somehow equal to the reported mortality. (In reality, excess mortality includes not only the direct effects of the epidemic, but also the indirect effects (which, to complicate matters, might be both positive and negative), so there is neither theoretically, nor practically any requirement that the two should be the same.) Here are a few examples:

* To begin with, the Authors suggest that the the officially reported mortality is "too low", but the one obtained with the Authors' method is "better", because -- and that's the crucial point! -- it is closer to the excess mortality. Saying that something is better because it is closer implies that they should be the same (or at least similar).
* "there is a 32.4% underestimation of COVID-19 impact." That's not an "under"estimation, as they estimate *different* things!
* The confusion is clearly indicated by the fact that at one point the Authors contradict themselves: "the methodology allows for a closer study of deaths, which occurred due to COVID-19-related restrictions but were not directly caused by a COVID-19 infection, for example deaths related to reduced access to healthcare". The Authors are entirely correct, but this phenomenon means that the reported deaths and excess deaths SHOULD differ, so the difference in this respect is something expected, and a lack of difference would be a problem...!

To be clear, I completely agree that 21 thousand is likely too low, and that the Authors' number is likely more realistic (that's actually the primary reason why I consider this study to be important!), but the above distinction should be nevertheless made very clear.

- As for the determination of the timeframe, it'd have been crucial to include a plot on the number of deaths vs. timeframe length. Not only as a supplementary material: I believe that it is so important that it should be included in the main text. (I assume that these are presented in SM5, but again, this should be given in the main text, and with a plot.)
- I also have problems with the statistical methodology of the determination of the timeframe length. This is what the Authors write: "We tested the slope coefficient of the simple linear regressions between the number of deaths added by lengthening the timeframe by 7 days from the previous length and the length of the timeframe performed iteratively on sets generated by removing the shortest length of the timeframe. The last set with the slope coefficient statistically significant at the level of 0.1% (P-value of 0.001) determined the length of timeframe – the shortest timeframe in the set (SM4)". First of all, to be honest, while the overall English of the paper is good, but I simply don't really understand what is written here, I can't surely reconstruct the Authors' method. With that said, I am pretty sure that it is not what should have been done. Here is the correct approach in my view:
1) First, there should be no hard threshold to define the timeframe (i.e. within which deaths are counted as "COVID-associated"). When plotting SM5 -- I hope these are really the raw data -- it is clear that there is an asymptote, so I would avoid finding "the" optimal cut-off and simply fit the asymptote! This completely solves the problem of how to find the optimal cut-off, as there is no cut-off needed.
2) Second, there is not only a statistical consideration, but also a theoratical flaw with the Authors' approach. The problem is that the background rate of deaths (for instance, around 110 in Interval-1) should be subtracted EVEN within the timeframe! (The Authors' methodology assumes -- correctly -- that these are deaths that only incidentally follow a contact -- but this is possible even a week after the contact!) It is important to note that this problem is immediately resolved by fitting the asymptote. (This, by the way, somewhat alleviates Limitation #2...!)

Here is an R code that illustrates my calculation (using both the cumulative and the incremental data -- giving of course almost identical results):

```
library(data.table)
library(ggplot2)

RawData <- fread("SM5.csv")
RawData <- melt(RawData, id.vars = "dt", value.name = "TotalDeath", variable.name = "Interval")
RawData[ , DeathIncrement := c(TotalDeath[1], diff(TotalDeath)), .(Interval)]

ggplot(RawData, aes(x = dt, y = TotalDeath, group = Interval, color = Interval)) +
geom_point() + geom_line()
ggplot(RawData[dt > 14], aes(x = dt, y = DeathIncrement, group = Interval, color = Interval)) +
geom_point() + geom_line()

fitTotalDeaths <- setNames(lapply(unique(RawData$Interval), function(int)
lm(TotalDeath ~ dt, data = RawData[Interval == int & dt > 100])), unique(RawData$Interval))

lapply(fitTotalDeaths, summary)

predTotalDeaths <- rbindlist(lapply(1:length(fitTotalDeaths), function(i)
data.table(Interval = names(fitTotalDeaths)[i], dt = 14:200,
TotalDeath = predict(fitTotalDeaths[[i]], newdata = data.frame(dt = 14:200)))))

ggplot(RawData, aes(x = dt, y = TotalDeath, group = Interval, color = Interval)) +
geom_point() + geom_line() + geom_line(data = predTotalDeaths, linetype = "dashed")

fitDeathIncrements <- setNames(lapply(unique(RawData$Interval), function(int)
lm(DeathIncrement ~ 1, data = RawData[Interval == int & dt > 100])),
unique(RawData$Interval))
```

```
lapply(fitDeathIncrements, summary)

predDeathIncrements <- rbindlist(lapply(1:length(fitDeathIncrements), function(i)
data.table(Interval = names(fitDeathIncrements)[i], dt = 14:200,
DeathIncrement = predict(fitDeathIncrements[[i]], newdata = data.frame(dt = 14:200)))))

ggplot(RawData[dt > 14], aes(x = dt, y = DeathIncrement, group = Interval, color = Interval)) +
geom_point() + geom_line() + geom_line(data = predDeathIncrements, linetype = "dashed")

sapply(fitTotalDeaths, predict, newdata = data.frame(dt = 0))

sapply(1:length(fitDeathIncrements), function(i)
sum(RawData[Interval == names(fitDeathIncrements)[i]]$DeathIncrement -
predict(fitDeathIncrements[[i]], RawData[Interval == names(fitDeathIncrements)[i]])))
```

Minor remarks:

- "Moreover, the methodology allows for a closer study of deaths, which occurred due to COVID-19-related restrictions but were not directly caused by a COVID-19 infection, for example deaths related to reduced access to healthcare" I don't understand this statement, the Authors' method does not even aim to capture deaths related to reduced access to healthcare.
- "in 31,789 excess deaths" My problem with such phrasings is that it handles the number of excess deaths as if they're a fixed, known number, while in reality, several methods exist to calculate it, and they might result in -- sometimes substantially -- different estimates (see 10.1186/s12874-023-02061-w or 10.1111/eci.14008).
- The Abstract states the there were 21,395 reported deaths, but Table 1 (and the associated text) gives 21,496.
- The program used for statistical analysis should be documented.
- Figure should have a standalone caption.
- The caption of SM7 is pretty unfortunate: it actually includes (luckily!) information on _all_ age groups.
- Table headers of SM8 and SM9 should be readable, and not only abbreviations.

PLEASE COMMENT

Q 4 **Is the title appropriate, concise, attractive?**

Yes.

Q 5 **Are the keywords appropriate?**

Yes.

Q 6 **Is the English language of sufficient quality?**

Ye.

Q 7 **Is the quality of the figures and tables satisfactory?**

Yes.

Q 8 **Does the reference list cover the relevant literature adequately and in an unbiased manner?)**

Yes.

QUALITY ASSESSMENT

Q 9	Originality	■■■■□
Q 10	Rigor	■■■□□
Q 11	Significance to the field	■■■■□
Q 12	Interest to a general audience	■■■■□
Q 13	Quality of the writing	■■■■□
Q 14	Overall scientific quality of the study	■■■■□

REVISION LEVEL

Q 15 Please make a recommendation based on your comments:

Major revisions.