PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Beyond Deaths per Capita: Comparative CoViD-19 Mortality Indicators
AUTHORS	Heuveline, Patrick; Tzen, Michael

VERSION 1 – REVIEW

REVIEWER	Enrique Acosta Max Planck Institute for Demographic Research Germany
REVIEW RETURNED	06-Oct-2020

GENERAL COMMENTS	General comments The article proposes two main objectives: 1) an indirect standardization of COVID-19 death rates in any population (country or subdivision), without the need to account for the age distribution of COVID-19 deaths, and 2) estimate the impact of COVID-19 mortality on the reduction in life expectancy during 2020. In the current context of the COVID-19 pandemic, indirect methods for estimating COVID-19 mortality and its impact on the population are much needed. The two methods proposed in the article are very interesting approaches for this purpose. However, I do not find that the implicit assumptions in the construction of the indicators are well-founded or supported in the text. Also, the assumptions behind both methods are not consistent with each other. These issues should definitely be addressed. On the other hand, among the massive amount of research about COVID-19 mortality by researchers from all domains, it is very encouraging to see a proper estimation of rates as it is done in this analysis, using person-years instead of population size. Main issues - Indirect standardized COVID-19 Death Rate (ISCDR) The assumptions behind the imputation of U.S. age-specific COVID-19 death rates to all populations are too strong and not well funded in the manuscript. The imposition of U.S. age-specific COVID-19 death rates implies that age-specific infection rates and age-specific infection fatality rates are the same in all populations. Differences in social dynamics driving the spread of the virus, in non-pharmaceutical policies, in testing capacity, in intergenerational contacts, and in the age pattern of chronic disease prevalences, make this assumption improvable. The selection of the U.S. as the reference population is not well supported. The authors justify the selection of the U.S. as the reference "because this is to date the largest number of CoViD-19 deaths distributed by age and sex” (Page 8, line 38). Although

	magnitude is important, in this case, an important reason for the large counts is that the U.S. has one of the largest populations where this information is available. The criteria for selecting the reference population must include the size of the sample and the quality of the testing regime, which would lead to better identification of deaths from COVID-19. To support the consistency of the ISCDR, the authors present a sensitivity check comparing the indirect and direct standardizations in several populations (Figure 5). However, all the populations compared are western and predominantly White populations (7 European countries and 6 U.S. states) with similar socioeconomic contexts and health profiles. Thus, it is not surprising to find a relatively similar age pattern of COVID-19 mortality. It is more pertinent to examine the differences and consistency of the ISCDR for those less similar populations, which also have the most considerable impact on mortality, which according to this analysis, are the Latin American countries and regions. It is stated in the manuscript that the sensitivity check was done on these populations because European countries and the U.S. states have data on age disaggregation of COVID deaths (page 12, line 33). However, for almost all countries in Latin America, these data are also available. An example of this data is the COVerAGE database (https://osf.io/mpwjq/), which also has the advantage of being age-harmonized. For the sake of transparency, I must say that I am co-leading this database project. Although I usually do not self-reference while reviewing, in this specific case, these data are pertinent for testing the accuracy of the proposed ISCDR when applied to populations that have a very different socioeconomic and health profiles. - Projected reductions in life expectancy The age-specific deaths for each country are estimated “by multiplying the total for the Country in (1.2) by the ratio of deaths in the age group to total deaths in the U.S.A. in (2.1)” (Page 25, line 30). The assumption behind this imputation is not consistent with the assumption that is implicit in the ISCDR. Instead of supposing an equal infection fatality rate - as was the case of the ISCDR -, it is assumed an identical age structure of COVID-19 deaths among populations. However, the age structure of COVID-19 deaths is highly dependent on the age structure of the population. It is expected that “the ratio of deaths in the age group to total deaths in the U.S.A." would increase if the exposure within that age group increases. When imposing this U.S. age-structure of mortality to populations older than the U.S., the age structure of mortality is artificially shifted – i.e., biased –toward younger ages, and the opposite is true for populations that are younger than the U.S. In order to assess the degree of bias from imputing the U.S. age structure of COVID-19 mortality to other countries, it would be required to perform a sensitivity check that compares these indirect estimates with those obtained when using the observed age-structure of COVID-19 mortality for the populations where this information is available. Note that Minor Issues - When describing the formula 1, it should be more evident that the denominator is not the “total population size at time tm between time t1 and time t” (page 6, line 26), but the total person-years lived between time t1 and time t, as it is clearly explained later in the text.

	- The population taken from the W.P.P. is in thousands, and the estimates are obtained from these values. Thus, this information is essential for an accurate description and interpretation of the results in the text. There is mention that “the CCDR is expressed in deaths per person-year” (line 42, page 6) when it is in deaths per thousand person-years. - According to the content discussed in the text, references 10 and 11 seem to be switched. - It is not clear the correspondence of estimating the ISCDR by “multiplying a population CCMR [in Eq 2] by the US CCDR [in Eq 1]” (line 47, page 7) with what is presented in Equation 3. It is not clear why Equation 3 is equal to US CCDR * CCMR. In case I was missing something, I tried with an example, but the results I obtained were quite different when multiplying and applying Equation 3. If Equation 3 is correct, it should be more clear to the average reader of B.M.J. Open how to obtain that formula from multiplying US CCDR by CCMR. - In figure 4, to see that "CoViD-19 is projected to reduce U.S. life expectancy at birth in 2020 to its lowest level since 2008", there is a need to be able to observe the life expectancy at least since 2008. - When describing the results on page 10, lines 17-27, it was difficult to understand the distinction between “with the highest CCDR currently in New Jersey” and “The highest CCDR value to date has been reached in New York.” Maybe, in the latter, it should say something like, "The highest CCDR value at any given time was reached in New York on April 25th.”

REVIEWER	Lars Ängquist Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Denmark.
REVIEW RETURNED	10-Nov-2020

GENERAL COMMENTS	---------- General comments: ---------- [Scope and content] Well-written and ambitious article with an important topic of high current interest to a wide audience - both the general public and various representatives of society in general and research in particular. [Potential update] Since some time has now passed since the last update, would it be possible to produce yet another data-update before publication (if accepted)? Since the pandemic has now been running for a much longer period (than into June/July), this would clearly enrich the underlying foundation with quite important data? [Indicators] It would be instructive and facilitate a deeper understanding if the various assumptions underlying the various indicators (with respect to their equations)could be discussed at greater length. For example, for CCMR, the given formula seems to assume that the distribution of the reference sex-age death rates is (approximately) valid also for other countries and areas. Similarly, an inherent assumption seems to made of 'similar spread-distribution' among the age-sex groups - compared to the reference population - for other areas since one uses given strata populations as weights, etc. (This comment also goes generally for the other equations; see related comments below.)

	[Covid19-deaths] This is discussed to some extent while it would still be interesting with a richer discussion on various potential sources for differences between Covid19-deaths measurements and reporting over areas: e.g. regarding requirements for being defined as a Covid19-death with respect to actual causality on death (e.g. all dead with positive Covid19-tests or just some group with obvious death-cause implications of this very diagnosis, etc.); general underreporting of cases (lack of registration of causes-for-deaths or unregistered deaths; situations where, for example, only related deaths at hospitals and related centers are registered as potential Covid19-cases, areas where it is unlikely to get to healthcare-centers before death, where Covid19-testing is unlikely or testing capacity is restricted or nonexisting, etc.); possibly also - with reverse implications - cases where some kinds of deaths might be automatically counted as a Covid19-death without actual positive testing results (for example solely based on some symptoms, etc.). Apart from discussing such sources it would be useful to discuss their implications for the validity of the results (comparisons made) and how that likely might have been affected - in practice, in the actual data at hand - by such differences. [Indicators] With respect to the given indicators, personally I here find it more informative to put more emphasis on the first two (CCDR and CCMR) - although they are methodologically quite simple and standard (this is not indicated to be a bad thing) - while the third more involved indicator is less well described but also seemingly based on future projections where it appears possible that such predictions could possibly be linked to very uncertain assumptions (given the varying unpredictable nature of the disease and unclear timing of future availability of general vaccination programs, etc.). [Time perspective] Rather than putting much emphasis on the third indicator, one could suggestively focus more on the distinction between long-term and short-term indicators. Briefly, the former seems to mainly be the one currently discussed in the article where this measure gives some information on a 'general disease burden' (through death rates) over a longer period of time; the latter would then instead rather give similar measures over shorter periods (e.g. as weekly or monthly), which then could be followed over time, and perhaps often might be of more interest regarding the 'current situation' within an area (or at least being of complementary interest, where the two time-perspectives would complement each other to facilitate full understanding and interpretation of the status). [Third indicator] If still to be included, and used, this part needs to be much more clearly described (both in the main text and in supplementary). All steps needs to be explained and the actual definition and interpretation of the indicator fully, and clearly, introduced, motivated, explained and discussed. [References] Since some time has passed since the given submission date, it might be important to yet again perform some publication search to see whether similar global (or relevant regional) reporting on Covid19-deaths data now has been published and, if so, to take that into account with respect to the article-update (in any way needed).

	[Technical appendix] This part is, in my opinion, unnecessarily hard to follow. I would here suggest a full rewrite with the core parts more fully described in words, where the notation is simplified (to the extent possible) and always introduced in detail and all steps are clearly explained, motivated and derived. Further, one could complement this with adding-on a simple and single numerical example running through all steps (see more comments below). In my opinion, this fine article - and important topic - deserves a sufficiently clear presentation also with respect to these fine and somewhat technical details since this is indeed of utter importance to fully grasp the nature of the indicators, their interpretation and range of validity (of importance to the readers with such an interest). ---------- Specific comments: ---------- [X:Y; page X, row Y] [X --> Y; suggestively replace Y with X] (Abstract) 3:7 'than' --> 'that'? (Background) 6:8 Related to the note above regarding delayed reporting etc., does this correspond to the numbers actually reported by this date (as observed by the end of this very day) or does it also include 'delayed' reported cases, originating from later dates-reporting, corresponding to events within this date limit? 6:10 Why regions corresponding to these specific countries? (Methods and Data) 6:49 Should 'estimated' here just refer to the actual 'registered' number or does this involve some model-based extrapolation, etc.? 6:56 How accurate are such projections expected to be? (Now, in November, that could perhaps actually be observed, evaluated and reported on.) This given that the changes in rates around the world at least seemingly appears to be quite irregular and hard to closely predict? 7:48 This combined formula (stated to be created by multiplication) should preferably be derived and explained in more detail. Though the final formula seems to clearly make sense, it is perhaps not immediately clear how it is formed based on a multiplication step involving the stated CCDR and CCMR formulas (using the given notation for the respective formulas)? (Results)

	9:6 How does this date (July 3rd) relate e.g. to the mentioned June 12th date above? (Perhaps some more related details on exactly which period one here will use actually observed data from, etc.?) 9:6-19 Given the outline, it still appears a bit unclear to me which time period that is used for these CCDR:s, i.e. e.g. cumulative data from the first respective observed death to June 12th (or to July 3rd), or data from just a single week, or something else? (Though I would guess the first alternative with respect to one of these two dates, since the highest observed death rates in this part of Europe likely occurred earlier on, in springtime, as I recall it.) 9:12 Per thousand what? Please preferably refer back to the given formula and detail how this number was found based on that notation (and hence explain the given rate unit). This said, I guess that it should be interpreted as something like: if this death rate would have been observed throughout a full year, then the yearly death rate would be 2.78/1000 individuals where the involved population size, N(t_m) in the CCDR-formula, would be estimated either some time within the year (e.g. in the very beginning of the year) or as some estimated mean population representing the year? 9:15-17 Perhaps suggestively in text here as 'four Spanish...' and 'six US...'? 9:27 Again, is this (New York-number) based on e.g. just a single week or does it correspond to a cumulative measure (up until a specified point)? 9:31-35 As I interpret it, when comparing it to the numbers from a standard non-Covid19 year (as for the described compared-to number). With respect to this specific period, perhaps many of the Covid19-deceased individuals would still have been among the set of overall-deceased individuals if the pandemic (contrafactually) did not have existed, i.e. the mortality from other causes could potentially be lower than usual for this period? 10:19 (Figure 2 caption) Does the country-requirement above go also for the subnational units? For example, on p.6 China is mentioned as contributing with subnational statistics whereas I cannot find any (the largest) subnational rate for this country in Figure 2? 10:24-27 (Also above in Methods and also below) Preferably elaborate a bit more on what this would more exactly correspond to in practice (and on the underlying exact definition). For example, what is 'reduction at birth' here, in more details, related to, i.e. does it vaguely, relate to something like and/or related to a mean reduction in remaining life expectancy of the individuals in the population, or to some hypothetical populations being born at this very point (then, vaguely, assuming Covid19 would either stay present to the same extent as for this period also throughout their full life or according to some quite uncertain projections throughout some time - until the disease having become extinct - or something else, etc.)?

	10:45 (Figure 3 caption) Several European countries mentioned on p.9 to have high CCDRs seem not to be part of Figure 3? Please make the selection process more clear here. 10:60 Minor: Page numbers from 10+ appears only as '1'? (Discussion) 11:35 Perhaps 'three important...' --> '3 important...' ? 12:3-7 As I read it, this is not exactly what is shown in Figure 1? Early on, the rate is just lower (as long as the spread is low and the time-to-death after infection is not very short) while, of course, any early estimates might tend to be a bit more uncertain given the corresponding lower number of events? 12:8-24 This seems a bit vague to me. First, one notes on comparing ISCDRs while at the end of the paragraph one rather refers to CCDRs. Second, what is really referred to with 'effects of scale' here? The later explanation rather just indicates that the rates may vary quite a lot within countries (especially if the countries are large with largely within-country varying circumstances)? 12:33-43 Perhaps noting on that this potentially could get affected by here using countries likely being quite nicely represented by the US-standard, while larger differences - I guess - might perhaps be seen for countries not being as well-represented by the standard? 13:24-31 Since a second wave in - at least - Europe has already entered the arena, this might call for yet another update of the data (see comment above) and also perhaps that any forecasts far into the future might still be attached with very high uncertainty (and hence being in many cases of quite limited validity and practical use at this point)? 13:45-49 On the other hand, mortality from other causes could also potentially decrease if a large enough set of individuals, vaguely, that would have died anyway now instead died of Covid-19. (See comment above - this said, I guess that complementary mortality might in some cases also increase - short-term or long-term - according to the effects of heavy Covid19 pressure on healthcare-systems, etc.) (Tables) No main tables. (Figures) Figure 2 Minor: the width of boxes appears to vary a bit over the cases and, relatedly, sometimes the box-pair seem to have some space between them and sometimes not? Figure 2 For the x-axis labels: Perhaps preferably consistently use something like only giving the name for countries and giving the region followed by country in parentheses for subnational units?

	(Examples: 'Belgium', 'Brazil', 'Rio de Janeiro (Brazil)', 'Michigan (USA)', etc.; further sometimes as U.S.A. and sometimes as USA and, in text, sometimes as US - perhaps preferably make it consistent throughout?) Figure 3: For y-axis labels: See label-comments to Figure 2 above. Figure 5 Minor: the width of boxes appears to vary a bit over the cases and, relatedly, sometimes the box-pair seem to have some space between them and sometimes not? (As for Figure 2, perhaps slightly less so here.) Figure 5: For x-axis labels: See label-comments to Figure 2-3 above. (Supplementary) Excel-based data: Preferably include some brief introduction to the material and make some initial sort e.g. based on country and, within-countries, either on name or population size? From the Excel-sheet, it seems that it might currently be sorted by CCMR/ISCDR while - as a starting point - it might be easier to get an overview based on the alternative sorting procedure, I think. (Relatedly, note that the pdf-version available for review does initially only hold the six left-most columns of the material shown in the corresponding Excel-sheet; the later columns seem to follow after all such related pages which makes it hard to read/combine while using this pdf-file.) [Part A] S1.1-S1.2 Sometimes as 'covid-19' and sometimes as 'CoViD-19', etc. Perhaps preferably aim at consistency throughout. Potentially many related cases throughout the supplementary (and possibly even within the main text). S1.1-S1.3 Sometimes as '&' and sometimes as 'and', etc. Perhaps preferably aim at consistency throughout. Potentially many cases throughout the supplementary, etc. S2.2 As 'Part B' - and not 'part B' - above. Aim at consistency. Possibly several cases throughout. S2.3 As 'U.S.' - and not 'U.S.A' above. Aim at consistency. Possibly several cases throughout. S3.4 To facilitate an enhanced intuitive understanding - and implicitly to make the validity more transparent - I think this part (and also the supplementary technical appendix in general) would favor from describing the steps in more detail (making all steps in the derivations fully clear). Specifically, for this item, I am a bit uncertain that q_x has been introduced and it is also quite hard to follow the argument for performing these very steps and how it all connects. Generally, especially S3 seems very hard to follow through the details - with lots of notation without sufficient explanation - while

	this is also to some degree the case also for S2 (and to a lesser degree for S1). Relatedly, it would help - in my opinion - if complementing the description with a small example corresponding to one, or a few, actual cases where each step is detailed in full numerical transparency. [Part B] S1 Links etc. in italics? (Potentially many cases throughout.) S1.1 For Mexico, this reference year - 2010 - is much longer ago than for the other countries? Perhaps some related notes on this and on the corresponding expected validity related to whether the distribution over groups might likely have been constant over these ten years or whether some, vaguely, bias might have likely been introduced in this sense? S1.3 In S1.1, the subitems (here a-e) were indented - perhaps also so for this case? S1.3c Seems a bit unclear, but as I read it shouldn't the combined ten year group - as 5-14y - rather be found by merging two five year groups (as 5-9 and 10-14)? S2.1. In S1.1, the subitems (here a-b) were indented - perhaps also so for this case? S2.2. In S1.1, the subitems (here a-d) were indented - perhaps also so for this case?

VERSION 1 – AUTHOR RESPONSE

Reviewer Comments to Author:

Reviewer: 1

Rev1#01
General comments
The article proposes two main objectives: 1) an indirect standardization of COVID-19 death rates in any population (country or subdivision), without the need to account for the age distribution of COVID-19 deaths, and 2) estimate the impact of COVID-19 mortality on the reduction in life expectancy during 2020. In the current context of the COVID-19 pandemic, indirect methods for estimating COVID-19 mortality and its impact on the population are much needed.
The two methods proposed in the article are very interesting approaches for this purpose. However, I do not find that the implicit assumptions in the construction of the indicators are well-founded or supported in the text. Also, the assumptions behind both methods are not consistent with each other. These issues should definitely be addressed.

The inconsistency noted here resulted from an error in the description of our approach in the technical appendix. In fact, the sex- and age-distribution of CoViD-19 produced while estimating
the ISCDR (product of the vectors of a population distribution by age and sex and the US sex- and age-specific CoViD-19 death rates) is the same as the distribution used in the life-table to estimate

the life-expectancy reduction. Thank you for noticing this; the text in the technical appendix has been corrected to properly describe the corresponding step in our estimation of life-expectancy reductions. With respect to the implicit assumptions in the construction of the indicators, we find that the point is more relevant to the estimation of life-expectancy reductions than to the estimation of the ISCDR. Reasoning for this is provided in response to the next few comments below.

Rev1#02
On the other hand, among the massive amount of research about COVID-19 mortality by researchers from all domains, it is very encouraging to see a proper estimation of rates as it is done in this analysis, using person-years instead of population size.
Main issues
- Indirect standardized COVID-19 Death Rate (ISCDR)
The assumptions behind the imputation of U.S. age-specific COVID-19 death rates to all populations are too strong and not well funded in the manuscript.
The imposition of U.S. age-specific COVID-19 death rates implies that age-specific infection rates and age-specific infection fatality rates are the same in all populations. Differences in social dynamics driving the spread of the virus, in non-pharmaceutical policies, in testing capacity, in intergenerational contacts, and in the age pattern of chronic disease prevalences, make this assumption improvable.

While we agree that the sex and age patterns of CoViD-19 mortality may differ across populations—a point we return to with respect to another comment below—the validity of comparisons of CoViD-19 mortality levels across populations through the “imposition” of the US age-specific CoViD-19 death rates on the age structures of all other populations does not rest on the assumption that the sex and age patterns are identical in all populations.

Standardization techniques rest on a counterfactual assumption: what if a population had the age distribution of a different population (direct standardization) or the age-specific death rates of a different population (indirect standardization)? In the case of indirect standardization, this allows for a comparison between the counterfactual number of deaths obtained so and the actual number of deaths in the population. If the counterfactual number of deaths with the “borrowed” rates is higher than the actual number of deaths with the prevailing (but unobserved) rates, the conclusion is that mortality in this population is lower overall than in the population that provided the counterfactual rates.

A classic example of indirect standardization techniques is Coale’s set of fertility indices (Preston et al. 2001, pp.97-99). In this case, applying the age-specific marital fertility rates of the Hutterites to the age-distribution of married women in a population and comparing the result to the actual number of legitimate births is intended to detect the departure from natural fertility. There is no assumption that the age-specific marital fertility rates in the population be identical or proportional to those of the Hutterites and in general they are not since departure from natural fertility typically changes the age pattern of marital fertility from convex to concave.

Rev1#03
The selection of the U.S. as the reference population is not well supported. The authors justify the selection of the U.S. as the reference "because this is to date the largest number of CoViD-19 deaths distributed by age and sex” (Page 8, line 38). Although magnitude is important, in this case, an important reason for the large counts is that the U.S. has one of the largest populations where this information is available. The criteria for selecting the reference population must include the size of the sample and the quality of the testing regime, which would lead to better identification of deaths from COVID-19.

This is a valid concern, since the choice of a standard may affect the amount of difference between (directly or indirectly) standardized rates and even, though made unlikely in this case by empirical regularities in age distribution and mortality patterns, the direction of that difference. It is a regrettable feature of standardization techniques that there is no simple rule for the selection of a standard distribution or set of specific rates and that these techniques inevitably involve an element of arbitrariness. Whichever manner one selects a standard, the paramount principle should be that the criteria be as objective as possible rather than guided by an attempt to obtain particular results (Preston et al. 2001, p.26)

In our case, we decided when we started this work in April 2020 to choose one of the populations with reliable data and, among those, the one with the largest number of CoViD-19 deaths. The quality of the data is obviously the most important criterion. While we agree some under-reporting of CoViD-19 deaths in the US is likely, only differential under-reporting by age would distort the age pattern of CoViD-19 mortality. The size of the sample is also important because it provides robustness to the estimated age-specific rates. Data are now available from a larger set of nations than in April 2020. In a November-2020 conference paper, Christophe Guilmoto culled together a sample of 792,000 CoViD-19 deaths by age and sex in 24 countries. The USA continues to make the largest contribution to that sample (217,000). While some different, objective criteria could be invoked to constitute a different standard pattern, we believe the choice of the US age-specific CoVid-19 death rates continues to be defensible on objective grounds.

Rev1#04
To support the consistency of the ISCDR, the authors present a sensitivity check comparing the indirect and direct standardizations in several populations (Figure 5). However, all the populations compared are western and predominantly White populations (7 European countries and 6 U.S. states) with similar socioeconomic contexts and health profiles. Thus, it is not surprising to find a relatively similar age pattern of COVID-19 mortality. It is more pertinent to examine the differences and consistency of the ISCDR for those less similar populations, which also have the most considerable impact on mortality, which according to this analysis, are the Latin American countries and regions. It is stated in the manuscript that the sensitivity check was done on these populations because European countries and the U.S. states have data on age disaggregation of COVID deaths (page 12, line 33). However, for almost all countries in Latin America, these data are also available. An example of this data is the COVerAGE database (https://osf.io/mpwjq/), which also has the advantage of being age-harmonized. For the sake of transparency, I must say that I am co-leading this database project. Although I usually do not self-reference while reviewing, in this specific case, these data are pertinent for testing the accuracy of the proposed ISCDR when applied to populations that have a very different socioeconomic and health profiles.
To many researchers only familiar with direct standardization, indirect standardization is not an intuitive procedure. The main objective of Figure 5 is thus to illustrate that directly or indirectly standardization the crude rates operate in a similar fashion (say, decrease the rate of the populations that have an older age structure). When data limitations prevent the computation of directly standardized rates, indirectly standardized rates would provide corrections of the unstandardized rate similar to those of directly standardized rates, and provide a better basis for comparisons across populations.

As pointed out in this comment, the directly and indirectly standardized rates might differ by a greater amount for a population whose age-pattern of CoViD-19 mortality deviates from the US pattern. The COVerAGE database is a wonderful contribution to the scientific community and indeed allows for analyses of differences in the sex- and age-structure of CoViD-19 mortality. Such analyses are undoubtedly important and worthy of publication on their own right, but we feel that conducting them would take us too far astray from what we trying to illustrate here, namely, that indirect standardization is preferable to no standardization. According to several articles on CoViD-19

mortality across populations cited in the paper, the increase of CoViD-19 death rates with age looks quite similar across populations, with a possible exception of differences in the slope of that increase at the oldest ages. It follows that indirect standardization, albeit with a “borrowed” pattern that does not quite have the same upward slope as the pattern prevailing in the population, would capture most of the age-dependency of CoViD-19 mortality across populations. In a new appendix, we calculate the directly standardized rate of CoViD-19 mortality for Brazil, the country with the largest number of CoViD-19 deaths. The result, 1.89 CoViD-19 deaths per 1,000 person-years is again much closer to the indirectly standardized rate, 1.96, than from the unstandardized rate, 1.15 CoViD-19 deaths per 1,000 person-years.
In other words, what has been shown so far about variation in age-patterns of CoViD-19 mortality does not appear susceptible to invalidate the main message in Figure 5, that is, that indirect standardized rates provide a better basis than unstandardized rate to compare CoViD-19 mortality levels across populations.

Rev1#05
- Projected reductions in life expectancy
The age-specific deaths for each country are estimated “by multiplying the total for the Country in (1.2) by the ratio of deaths in the age group to total deaths in the U.S.A. in (2.1)” (Page 25, line 30). The assumption behind this imputation is not consistent with the assumption that is implicit in the ISCDR. Instead of supposing an equal infection fatality rate - as was the case of the ISCDR -, it is assumed an identical age structure of COVID-19 deaths among populations. However, the age structure of COVID-19 deaths is highly dependent on the age structure of the population. It is expected that “the ratio of deaths in the age group to total deaths in the U.S.A." would increase if the exposure within that age group increases. When imposing this U.S. age-structure of mortality to populations older than the U.S., the age structure of mortality is artificially shifted – i.e., biased – toward younger ages, and the opposite is true for populations that are younger than the U.S.
In order to assess the degree of bias from imputing the U.S. age structure of COVID-19 mortality to other countries, it would be required to perform a sensitivity check that compares these indirect estimates with those obtained when using the observed age-structure of COVID-19 mortality for the populations where this information is available. Note that [sic]

As noted above (comment Rev1#01), this was indeed an error in the write-up of the technical appendix. The US age structure of CoViD-19 is not used; the age-specific CoViD-19 death rates are. The age structure of CoViD-19 deaths in other populations is thus derived by multiplying these rates and the actual age distribution of the population.

It remains true that the corresponding age distribution of deaths may differ from the actual distribution and bias the estimate of life-expectancy reduction. But as noted above (comment Rev1#04), while sex- and age-patterns of CoViD-19 mortality vary across populations, they share substantial similarities and the difference induced by using a given age-pattern of CoViD-19 mortality instead of the one that prevails in a specific population is likely to be small (relative to other uncertainties in assessing this difference). To illustrate this, we calculated the difference in life expectancy at birth for Brazil using the actual sex- and age-pattern reported in the country (chosen for this illustration as it is second to the USA in terms of deaths from CoViD-19). The result, 1.67 years, is indeed relatively close to the one calculated initially with the US sex- and age-specific rates, 1.62 years. As noted in the text, this 3% difference should not be a main concern given likely larger, other sources of uncertainty.

Rev1#06
Minor Issues
- When describing the formula 1, it should be more evident that the denominator is not the “total

population size at time tm between time t1 and time t" (page 6, line 26), but the total person-years lived between time t1 and time t, as it is clearly explained later in the text.

A sentence was added before equation 1.

Rev1#07
- The population taken from the W.P.P. is in thousands, and the estimates are obtained from these values. Thus, this information is essential for an accurate description and interpretation of the results in the text. There is mention that "the CCDR is expressed in deaths per person-year" (line 42, page 6) when it is in deaths per thousand person-years.

This is true of the UN population estimates but not of all the subnational units. As the text attempts to present the indicators in the most general terms, this point was made in the supplementary information describing one particular set of estimates based on the UN numbers instead.

Rev1#08
- According to the content discussed in the text, references 10 and 11 seem to be switched.

Quite, thank you for picking this up.

Rev1#09
- It is not clear the correspondence of estimating the ISCDR by "multiplying a population CCMR [in Eq 2] by the US CCDR [in Eq 1]" (line 47, page 7) with what is presented in Equation 3. It is not clear why Equation 3 is equal to US CCDR * CCMR. In case I was missing something, I tried with an example, but the results I obtained were quite different when multiplying and applying Equation 3. If Equation 3 is correct, it should be more clear to the average reader of B.M.J. Open how to obtain that formula from multiplying US CCDR by CCMR.

The formula was incorrect and has been corrected.

Rev1#10
- In figure 4, to see that "CoViD-19 is projected to reduce U.S. life expectancy at birth in 2020 to its lowest level since 2008", there is a need to be able to observe the life expectancy at least since 2008.

Figure 4 has been edited to include the most recent year with a lower life expectancy than estimated for 2020.

Rev1#11
- When describing the results on page 10, lines 17-27, it was difficult to understand the distinction between "with the highest CCDR currently in New Jersey" and "The highest CCDR value to date has been reached in New York." Maybe, in the latter, it should say something like, "The highest CCDR value at any given time was reached in New York on April 25th."

Indeed, the sentence has been edited for clarity.

Reviewer: 2

Rev2#01

General comments:

[Scope and content] Well-written and ambitious article with an important topic of high current interest to a wide audience - both the general public and various representatives of society in general and research in particular.

[Potential update] Since some time has now passed since the last update, would it be possible to produce yet another data-update before publication (if accepted)? Since the pandemic has now been running for a much longer period (than into June/July), this would clearly enrich the underlying foundation with quite important data?

The results discussed in the paper have been updated based on the latest data (January 1st, 2021).

Rev2#02
[Indicators] It would be instructive and facilitate a deeper understanding if the various assumptions underlying the various indicators (with respect to their equations)could be discussed at greater length. For example, for CCMR, the given formula seems to assume that the distribution of the reference sex-age death rates is (approximately) valid also for other countries and areas. Similarly, an inherent assumption seems to made of 'similar spread-distribution' among the age-sex groups - compared to the reference population - for other areas since one uses given strata populations as weights, etc. (This comment also goes generally for the other equations; see related comments below.)

As mentioned with reference to comment Rev1#02, there is no implicit assumption in the calculation of the CCMR, other than in the sense of a counterfactual assumption (what if?). Additional comments on specific equations follow.

Rev2#03
[Covid19-deaths] This is discussed to some extent while it would still be interesting with a richer discussion on various potential sources for differences between Covid19-deaths measurements and reporting over areas: e.g. regarding requirements for being defined as a Covid19-death with respect to actual causality on death (e.g. all dead with positive Covid19-tests or just some group with obvious death-cause implications of this very diagnosis, etc.); general underreporting of cases (lack of registration of causes-for-deaths or unregistered deaths; situations where, for example, only related deaths at hospitals and related centers are registered as potential Covid19-cases, areas where it is unlikely to get to healthcare-centers before death, where Covid19-testing is unlikely or testing capacity is restricted or nonexisting, etc.); possibly also - with reverse implications - cases where some kinds of deaths might be automatically counted as a Covid19-death without actual positive testing results (for example solely based on some symptoms, etc.). Apart from discussing such sources it would be useful to discuss their implications for the validity of the results (comparisons made) and how that likely might have been affected - in practice, in the actual data at hand - by such differences.

This issue is returned to in the discussion section. Differences between Covid19-deaths measurements and reporting is also mentioned in the “Strength and limitations” section.

Rev2#04
[Indicators] With respect to the given indicators, personally I here find it more informative to put more emphasis on the first two (CCDR and CCMR) - although they are methodologically quite simple and standard (this is not indicated to be a bad thing) - while the third more involved indicator is less well described but also seemingly based on future projections where it appears possible that such predictions could possibly be linked to very uncertain assumptions (given the varying unpredictable nature of the disease and unclear timing of future availability of general vaccination programs, etc.).

As the updated data pertain to January 1st, 2021, they provide estimates of CoViD-19 deaths for the year 2020 and projections are no longer necessary to estimate the impact on life expectancy at birth in 2020.

Rev2#05
[Time perspective] Rather than putting much emphasis on the third indicator, one could suggestively focus more on the distinction between long-term and short-term indicators. Briefly, the former seems to mainly be the one currently discussed in the article where this measure gives some information on a 'general disease burden' (through death rates) over a longer period of time; the latter would then instead rather give similar measures over shorter periods (e.g. as weekly or monthly), which then could be followed over time, and perhaps often might be of more interest regarding the 'current situation' within an area (or at least being of complementary interest, where the two time-perspectives would complement each other to facilitate full understanding and interpretation of the status).

The discussion section now mentions the fact that the rates could be estimated for shorter period of times, whereas it might not be appropriate for life expectancy at birth.

Rev2#06
[Third indicator] If still to be included, and used, this part needs to be much more clearly described (both in the main text and in supplementary). All steps needs to be explained and the actual definition and interpretation of the indicator fully, and clearly, introduced, motivated, explained and discussed.

As suggested, we now include a spreadsheet that illustrate the step by step calculation of each indicator.

Rev2#07
[References] Since some time has passed since the given submission date, it might be important to yet again perform some publication search to see whether similar global (or relevant regional) reporting on Covid19-deaths data now has been published and, if so, to take that into account with respect to the article-update (in any way needed).

We now note in the text that data are available from a more diverse set of populations that at the time of the original writing. In a new appendix, we repeat the calculations for Brazil using data from this country as opposed to imputed using the CDC data for the USA.

Rev2#08
[Technical appendix] This part is, in my opinion, unnecessarily hard to follow. I would here suggest a full rewrite with the core parts more fully described in words, where the notation is simplified (to the extent possible) and always introduced in detail and all steps are clearly explained, motivated and derived. Further, one could complement this with adding-on a simple and single numerical example running through all steps (see more comments below). In my opinion, this fine article - and important topic - deserves a sufficiently clear presentation also with respect to these fine and somewhat technical details since this is indeed of utter importance to fully grasp the nature of the indicators, their interpretation and range of validity (of importance to the readers with such an interest).

Thank you for this suggestion. We have added an appendix that illustrate the calculations for Brazil (both in a text document and in a spreadsheet)

Rev2#09

Specific comments:

[X:Y; page X, row Y] [X --> Y; suggestively replace Y with X]

(Abstract)

3:7 'than' --> 'that'?

Correction has been made

Rev2#10
(Background)

6:8 Related to the note above regarding delayed reporting etc., does this correspond to the numbers actually reported by this date (as observed by the end of this very day) or does it also include 'delayed' reported cases, originating from later dates-reporting,
corresponding to events within this date limit?

Reference to a paper by Havers et al. (2020) was added to provide further details on the methodology on the cited estimates.

Rev2#11
6:10 Why regions corresponding to these specific countries?

These were the largest countries in the successive “epicenters” of the pandemic over time (clarification added in the text).

Rev2#12
(Methods and Data)

6:49 Should 'estimated' here just refer to the actual 'registered' number or does this involve some model-based extrapolation, etc.?

Text was clarified to indicate numbers are cumulative cases reported by various administrative entities and tallied by Johns Hopkins University. Further details about the methodology are available in the cited paper.

Rev2#13
6:56 How accurate are such projections expected to be? (Now, in November, that could perhaps actually be observed, evaluated and reported on.) This given that the changes in rates around the world at least seemingly appears to be quite irregular and hard to closely predict?

Projections are no longer used in this updated version.

Rev2#14
7:48 This combined formula (stated to be created by multiplication) should preferably be derived and explained in more detail. Though the final formula seems to clearly make sense, it is perhaps not immediately clear how it is formed based on a multiplication step involving the stated CCDR and CCMR formulas (using the given notation for the respective formulas)?

The derivation of the combined formula has been added.

Rev2#15
(Results)

9:6 How does this date (July 3rd) relate e.g. to the mentioned June 12th date above? (Perhaps some more related details on exactly whichperiod one here will use actually observed data from, etc.?)

Results have been updated with January 1st, 2021 numbers.

Rev2#16
9:6-19 Given the outline, it still appears a bit unclear to me which time period that is used for these CCDR:s, i.e. e.g. cumulative data from the first respective observed death to June 12th (or to July 3rd), or data from just a single week, or something else?
(Though I would guess the first alternative with respect to one of these two dates, since the highest observed death rates in this part of Europe likely occurred earlier on, in springtime, as I recall it.)

The first interpretation is indeed correct, but a sentence has been added in the text to clarify.

Rev2#17
9:12 Per thousand what? Please preferably refer back to the given formula and detail how this number was found based on that notation (and hence explain the given rate unit). This said, I guess that it should be interpreted as something like: if this death rate would have been observed throughout a full year, then the yearly death rate would be 2.78/1000 individuals where the involved population size, N(t_m) in the CCDR-formula, would be estimated either some time within the year (e.g. in the very beginning of the year) or as some estimated mean population representing the year?

A sentence was added to clarify the unit (deaths per thousand person-years).

Rev2#18
9:15-17 Perhaps suggestively in text here as 'four Spanish...' and 'six US...'?

The results were updated and the comment no longer applies.

Rev2#19
9:27 Again, is this (New York-number) based on e.g. just a single week or does it correspond to a cumulative measure (up until a specified point)?

It corresponds to a cumulative measure; a sentence has been added in the text to clarify.

Rev2#20
9:31-35 As I interpret it, when comparing it to the numbers from a standard non-Covid19 yar (as for the described compared-to number). With respect to this specific period, perhaps many of the Covid19-deceased individuals would still have been among the set of overall-deceased individuals if the pandemic (contrafactually) did not have existed, i.e. the mortality from other causes could potentially be lower than usual for this period?

A sentence was added to clarify that this possibility, known as “competing risks” (individuals cannot succumb to both the risk of death from other causes and the risk of death from CoViD-19 was ignored here. While some adjustment should indeed be performed (and it is, through a life table, in estimating the effect of CoViD-19 on life expectancy at birth), the goal in this section is merely to compare order of magnitude and show the CCDR in New York surpassed the CDR. This would be even more so if the number of deaths from other causes were reduced by CoViD-19 deaths.

Rev2#21
10:19 (Figure 2 caption) Does the country-requirement above go also for the subnational units? For example, on p.6 China is mentioned as contributing with subnational statistics whereas I cannot find any (the largest) subnational rate for this country in Figure 2?

Figure 2 included units with the highest ISCDR values among units with a population of 10 million or more, but the population-size requirement was dropped for units that had the highest value of all subnational units in their respective nations. This was meant to increase the range of values, but clarifying this in the legend would be cumbersome. Instead, Figure 2 was simplified by only including the highest ISCDR values for units with a population size of 5 million or more.

Rev2#22
10:24-27 (Also above in Methods and also below) Preferably elaborate a bit more on what this would more exactly correspond to in practice (and on the underlying exact definition). For example, what is 'reduction at birth' here, in more details, related to, i.e. does it vaguely, relate to something like and/or related to a mean reduction in remaining life expectancy of the individuals in the population, or to some hypothetical populations being born at this very point (then, vaguely, assuming Covid19 would either stay present to the same extent as for this period also throughout their full life or according to some quite uncertain projections throughout some time - until the disease having become extinct - or something else, etc.)?

This is an important clarification, which is addressed in the discussion section.

Rev2#23
10:45 (Figure 3 caption) Several European countries mentioned on p.9 to have high CCDRs seem not to be part of Figure 3? Please make the selection process more clear here.

The selection was simplified and is now based on the largest values for national and subnational units with population size of 5 millions or more. The reason several European countries are not among those with the largest values, however, is due to the fact that reductions in life expectancy at birth are based on age-specific death rates, whereas the CCDRs are based on numbers of death. For a given set of age-specific death rates, the age distribution of European countries contributes to larger numbers of deaths than in non-European countries.

Rev2#24
10:60 Minor: Page numbers from 10+ appears only as '1'?

The page numbers are fine on our Word document. The issue may emerge during the conversion to pdf, but we’re not sure how to address it.

Rev2#25
(Discussion)

11:35 Perhaps 'three important...' --> '3 important...' ?

Change was made.

Rev2#26
12:3-7 As I read it, this is not exactly what is shown in Figure 1? Early on, the rate is just lower (as long as the spread is low and the time-to-death after infection is not very short) while, of course, any

early estimates might tend to be a bit more uncertain given the corresponding lower number of events?

With apologies, we might be missing the point made in this comment, but the sentence in the text is correct. The period CCDR and ISCDR are based on the average number of deaths per day since the first death begin to decline (when the period starts on the day of the first death). Early in the pandemic, the daily numbers of deaths tend to increase, which will lead to higher values of the period CCDR and ISCDR. In more mature epidemics, when the daily average is calculated over a longer period, the period CCDR and ISCDR are less sensitive to these daily changes. Comparing populations at, say, day 40 and day 50 of the pandemic is thus less problematic than comparing them at day 10 and 20.

Rev2#27
12:8-24 This seems a bit vague to me. First, one notes on comparing ISCDRs while at the end of the paragraph one rather refers to CCDRs. Second, what is really referred to with 'effects of scale' here? The later explanation rather just indicates that the rates may vary quite a lot within countries (especially if the countries are large with largely within-country varying circumstances)?

First, we now refer to ISCDRs through the paragraph. Second, a sentence was added to clarify that indeed it is the within-country variations that might create some issues when comparing large (presumably more heterogeneous in rates) and small populations.

Rev2#28
12:33-43 Perhaps noting on that this potentially could get affected by here using countries likely being quite nicely represented by the US-standard, while larger differences - I guess - might perhaps be seen for countries not being as well-represented by the standard?

A paragraph was added after Figure 5 to discuss the impact of differences in sex ratios and age patterns of death rates, and emphasize that the aim of indirect standardization is not to precisely represent the age structure of mortality across populations. It is to determine whether the total number of deaths in a population is higher or lower than the counterfactual total number of deaths had standard sex- and age-specific death rates prevailed, and indicate whether overall mortality is thus higher or lower than in the population that provides the standard. While it is theoretically possible that rates would vary across populations in such a manner that the choice of a standard would affect the assessment of which population has higher mortality, empirically regularities in age distribution and mortality patterns make it quite unlikely, however.

Rev2#29
13:24-31 Since a second wave in - at least - Europe has already entered the arena, this might call for yet another update of the data (see comment above) and also perhaps that any forecasts far into the future might still be attached with very high uncertainty (and hence being in many cases of quite limited validity and practical use at this point)?

Since estimates have been updated to the end of 2020, projections are no longer used to estimate reductions in life expectancy at birth.

Rev2#30
13:45-49 On the other hand, mortality from other causes could also potentially decrease if a large enough set of individuals, vaguely, that would have died anyway now instead died of Covid-19. (See comment above - this said, I guess that complementary mortality might in some cases also increase - short-term or long-term - according to the effects of heavy Covid19 pressure on healthcare-systems, etc.)

Indeed, the indirect effect of CoViD-19 on other causes of death, both positive and negative, are still largely a matter of speculation at this point. The aggregate effects on excess deaths are discussed rather than the separate positive and negative potential effects.

Rev2#31
(Tables)

No main tables.

(Figures)

Figure 2 Minor: the width of boxes appears to vary a bit over the cases and, relatedly, sometimes the box-pair seem to have some space between themand sometimes not?

Adjustment has been made.

Rev2#32
Figure 2 For the x-axis labels: Perhaps preferably consistently use something like only giving the name for countries and giving the region followed by country in parentheses for subnational units? (Examples: 'Belgium', 'Brazil', 'Rio de Janeiro (Brazil)', 'Michigan (USA)', etc.; further sometimes as U.S.A. and sometimes as and, in text, sometimes as US - perhaps preferably make it consistent throughout?)

Adjustment has been made to the labelling of populations in Figure 2. As for USA v. US, we try to consistently use the USA for the country and the US as the adjective thereof (e.g., mortality in the USA, but the US mortality rates).

Rev2#33
Figure 3: For y-axis labels: See label-comments to Figure 2 above.

Adjustment has been made to the labelling of populations in Figure 3.

Rev2#34
Figure 5 Minor: the width of boxes appears to vary a bit over the cases and, relatedly, sometimes the box-pair seem to have some space between them and sometimes not? (As for Figure 2, perhaps slightly less so here.)

Adjustment has been made.

Rev2#35
Figure 5: For x-axis labels: See label-comments to Figure 2-3 above.

Adjustment has been made.

Rev2#36
(Supplementary)

Excel-based data: Preferably include some brief introduction to the material and make some initial sort e.g. based on country and, within-countries, either on name or population size? From the Excel-sheet, it seems that it might currently be sorted by CCMR/ISCDR while - as a starting point - it might

be easier to get an overview based on the alternative sorting procedure, I think. (Relatedly, note that the pdf-version available for review does initially only hold the six left-most columns of the material shown in the corresponding Excel-sheet; the later columns seem to follow after all such related pages which makes it hard to read/combine while using this pdf-file.)

The Excel-based data is now sorted on location type (first UN country/territories, then subnational units for Brazil, China, etc…), then in alphabetic order within these types.

Rev2#37
[Part A]

S1.1-S1.2 Sometimes as 'covid-19' and sometimes as 'CoViD-19', etc. Perhaps preferably aim at consistency throughout. Potentially many related cases throughout the supplementary (and possibly even within the main text).

The main text and supplementary text have been checked for consistency.

Rev2#38
S1.1-S1.3 Sometimes as '&' and sometimes as 'and', etc. Perhaps preferably aim at consistency throughout. Potentially many cases throughout the supplementary, etc.

Use of ‘&’ was limited to between numbers referring to steps (as in (1.1) & (1.2) for example)

Rev2#39
S2.2 As 'Part B' - and not 'part B' - above. Aim at consistency. Possibly several cases throughout.

Change has been made to ‘part B’.

Rev2#40
S2.3 As 'U.S.' - and not 'U.S.A' above. Aim at consistency. Possibly several cases throughout.

See response to comment Rev2#32 above.

Rev2#41
S3.4 To facilitate an enhanced intuitive understanding - and implicitly to make the validity more transparent - I think this part (and also the supplementary technical appendix in general) would favor from describing the steps in more detail (making all steps in the derivations fully clear).

A fully worked-out spreadsheet example has been added as suggested below (Rev2#44).

Rev2#42
Specifically, for this item, I am a bit uncertain that q_x has been introduced and it is also quite hard to follow the argument for performing these very steps and how it all connects.

Definition has been added.

Rev2#43
Generally, especially S3 seems very hard to follow through the details - with lots of notation without sufficient explanation - while this is also to some degree the case also for S2 (and to a lesser degree for S1).

Additional text has been added for steps 3.2 and 3.4, as well as reference in the main text that describe the estimation of how a single cause of death impacts life expectancy at birth.

Rev2#44
Relatedly, it would help - in my opinion - if complementing the description with a small example corresponding to one, or a few, actual cases where each step is detailed in full numerical transparency.

A fully worked-out spreadsheet example has been added.

Rev2#45
[Part B]

S1 Links etc. in italics? (Potentially many cases throughout.)

Unclear about the suggestion here: is it that links should be in italics?

Rev2#46
S1.1 For Mexico, this reference year - 2010 - is much longer ago than for the other countries? Perhaps some related notes on this and on the corresponding expected validity related to whether the distribution over groups might likely have been constant over these ten years or whether some, vaguely, bias might have likely been introduced in this sense?

This comment made us realize that the description of the proration of the age groups for subnational populations was probably misleading. The age distribution of each subnational unit is not assumed to remain constant, in the case of Mexico from 2010 to 2020. Instead, in each age group, the proportion of the national population that lives in a subnational unit is assumed to remain constant. Of course, there is still an assumption of fixed ratio that is less likely to hold the longer the interval, but the age distribution of each subnational is allowed to change over time (at the same pace as the age distribution of the national population).

Rev2#47
S1.3 In S1.1, the subitems (here a-e) were indented - perhaps also so for this case?

Change has been made.

Rev2#48
S1.3c Seems a bit unclear, but as I read it shouldn't the combined ten year group - as 5-14y - rather be found by merging two five year groups (as 5-9 and 10-14)?

Yes, absolutely, thank you for this. Change has been made.

Rev2#49
S2.1. In S1.1, the subitems (here a-b) were indented - perhaps also so for this case?

Change has been made.

Rev2#50
S2.2. In S1.1, the subitems (here a-d) were indented - perhaps also so for this case?

Change has been made.

VERSION 2 – REVIEW

REVIEWER	Enrique Acosta Max Planck Institute for Demographic Research, Germany
REVIEW RETURNED	12-Feb-2021

GENERAL COMMENTS	I congratulate the authors for a great job. This paper is a valuable contribution for two reasons: First, it proposes a method that allows for an adequate measurement and comparison of the impact of the pandemic across populations with very different population sizes and sex-age-structures, even in the absence of detailed information. Second, it offers a broad picture of the massive impacts of the pandemic on mortality in a bast amount of populations. I consider that all the concerns expressed during the first review were appropriately addressed by the authors, the potential limitations were discussed adequately, and pertinent sensibility analyses were added. A very minor issue is the format of the labels in the horizontal axis in Figure 1, which should be dates instead of numbers.