Author reply

Manuscript ID BMJ-2021-064535 entitled "Hospitalisation and mortality rates in Denmark during the Covid-19 pandemic: a nationwide population-based cohort study"

Comments from Reviewers

Reviewer: 1

Recommendation:

Comments:
This is a study on hospitalization rates in Denmark at different time periods. While the paper is concise (which is welcome), I find that it lacks sufficient details in important areas.

Author reply: Thank you for reviewing our manuscript. Of note, we have re-computed the entire dataset by extending the follow-up until January 27, 2021 in order to include the 2nd national lockdown in Denmark effective as of December 16, 2020. Furthermore, a table of summary statistics of the study population has also been included (now Table 1).

In particular, I did not have a strong sense of how they accounted for COVID hospitalizations and mortality from COVID. If the overall hospitalization rate they quote during lockdown is inclusive of COVID (147.5), which is less than baseline hospitalization rate, this deserves far greater discussion. I also would have liked to see a more nuanced analysis of pneumonia hospitalizations given the close relation to COVID.

Author reply: Excellent points. We have clarified overall hospitalisation and 30-day mortality rates with and without Covid-19:

P 7, line 22:” All non-Covid-19 hospitalisations since March 13, 2019 through January 27, 2021 were identified by principal diagnosis codes in the Danish National Patient Registry and grouped according to major ICD-10 diagnosis group (Supplementary Table 1) identified by the first primary code given within the listed chapters. However, if a patient was assigned a diagnosis code for Covid-19 within five days of admission, the hospitalisation was categorised as Covid-19”

and

P. 8, line 11:” Overall hospitalisation rates were examined with and without Covid-19 admissions and stratified by major disease groups”

and
Mortality risk at 30 days from non-Covid-19 hospitalisation was assessed by the cumulative incidence function with censoring at emigration, diagnosis of Covid-19, or end of follow-up (February 28, 2021), whichever occurred first.

Tables 2 and 3 have also been updated accordingly with rows indicating overall hospitalisation rates and 30-day mortality risks with and without Covid-19 admissions.

The diagnosis codes for categorising patients with pneumonia did not include Covid-19 diagnosis codes (B342A or B972A) as described in Suppl. Table 1. In addition, patients were categorised as Covid-19 if assigned such diagnosis codes within five days of admission as detailed above.

P. 9, line 1: “530,420,002 weeks of observation”. I think you mean “530,420,002 person-weeks of observation”. That’s a big difference.

Author reply: You are absolutely right, revised as suggested.

P. 3, line 39: what is the comparison group for this RR?

Author reply: The comparison was the pre-pandemic baseline period (March 13, 2019 through March 10, 2020). This has been clarified.

P. 3, line 46: does “respiratory diseases” include COVID?

Author reply: Covid-19 patients were not included in this category. This has been clarified.

P. 3, results abstract: there is no mention of COVID hospitalization rates, which is odd

Author reply: In this study, the focus is on non-Covid-19 hospitalisations and we feel that word restrictions preclude the addition of Covid-19 hospitalisation rates in the abstract. However, data on overall hospitalisation rates with and without Covid-19 have been added to Table 2 and Covid-19 hospitalisation rates are depicted in Figure 1.

P. 4, lines 15-17: “increased attention” under what circumstances? When COVID pandemic is done? During the ongoing COVID pandemic? during the next pandemic?

Author reply: This has been specified.
P 6, line 30: is the age range listed of “<1 year” for children correct? Shouldn’t it be “<18”?

Author reply: Thank you for bringing this to our attention. We also included children. Age limits have been aligned in the abstract and throughout the manuscript, e.g. p. 6, line 20: “Data were excluded for children (<1 year of age) and for individuals with recent migration status or inconsistent vital data (Supplementary Figure 2).”

P 7, line 34: more detail should be provide don how 30 day mortality was determined. Was there a match with a death registry? Etc

Author reply: Data on mortality rates were obtained from the Danish Civil Registry System. This registry was established in 1968, primarily for taxation purposes, and it keeps track of the migration and vital status of all Danish residents. The registry is updated daily (not including weekends) and loss to follow-up is <0.3%. Please see reference #4 for additional details.

Information on vital status has been detailed further, p. 8 line 2: “Using the Civil Registration System, 30-day mortalities were computed for hospitalised patients, overall and according to selected major disease groups.”

P 9, line 9: same comment as up above about “weeks”. I think what is meant is “person-weeks”

Author reply: You are right, thank you. Corrected, p. 9, line 20. “The study included 5,753,179 Danish residents during 567.8 million person-weeks of observation yielding a total of 1,113,705 hospitalisations distributed among 675,447 individuals (Table 1).”

P 9, line 32: does “infectious diseases” include COVID? That should be made more clear

Author reply: Good point. Please see reply to your first question, where this has been clarified in the methods section, Tables 2 and 3, and in the results, p. 10, line 11: “Compared with infectious diseases hospitalisations during the pre-pandemic baseline period, hospitalisation RR for non-Covid-19 infectious diseases was 0.73 (95% CI 0.70 to 0.76) during the 1st national lockdown (Table 2).”

P 9, line 32: it’s not clear what the comparison group is for the RR. Is it all hospitalizations during the baseline period? Or just infectious disease hospitalizations during the baseline period?

Author reply: The comparison group was infectious disease hospitalisation during the pre-Covid-19 baseline period. Please see reply above with the quote from p. 10, line 11.

P 9, line 46: same comment as up above, not clear what the comparison group is

Author reply: We have revised the sentence, now page 10, line 18: “For all other major diagnosis groups, hospitalisation RRs also attenuated markedly during the 1st and 2nd national lockdowns compared with the hospitalisations rate of each group during the baseline period ranging from 0.34
(95% CI 0.25 to 0.46) for bone, muscle, and connective tissue diseases to 0.86 (95% CI 0.80 to 0.91) for cancer during the 1st national lockdown.”

P 10, line 36: how have the authors determined that “pneumonia” as used here is unrelated to COVID?

Author reply: Please see previous reply to your first comment. Patients categorised with pneumonia excluded those assigned a diagnosis code of B342A or B972A within five days of admission. Risk of misclassification of hospitalised patients assigned non-Covid-19 diagnosis codes is discussed on p. 16, line 3: “Danish healthcare and administrative registries have been shown to be of very high quality,[14,16,32] but differential misclassification of conditions with a similar clinical presentation as Covid-19 cannot be excluded and may introduce bias in an unpredictable direction.”

P 11’s mortality section: authors should make clear throughout this paragraph if they are referring to 30-day mortality or to in-hospital mortality. I think it’s clear from the methods that the focus is on 30 days, but one would not know that by reading this paragraph alone.

Author reply: Revised as suggested. Mortality is described as “30-day mortality” throughout the paragraph starting on p. 12, line 8.

Please enter your name: Neil Vora

Job Title: Medical Epidemiologist

Institution: NYC Health Department/CDC

Reviewer: 2

Recommendation:

Comments:
This peer review was conducted as a part of the Peer Review and Biomedical Editing Training Initiative (Peerspectives), which has been developed by the Institute of Public Health at the Charité - Universitätsmedizin Berlin in cooperation with the BMJ.

Summary:
The paper reports the incidences of hospitalisations for other medical conditions than Covid-19 and associated mortality rates during the Covid-19 pandemic using population-based healthcare registries in Denmark from 11 March through 30 November 2020. The authors compare these measures with the pre-pandemic baseline from 1 March 2019 through 10 March 2020. They show, using data from 5,960,934 Danish residents, that the overall hospitalisation rate decreased during national lockdown and returned to baseline levels at the end of the study conclusion. Moreover, the authors find that this pattern is reflected for all major diagnosis groups except for respiratory diseases, nervous system diseases, circulatory diseases, cancer and non-Covid-19 infections, which remained lower at the end of the observation period. They also show that in many major diagnosis
groups, e.g. sepsis, urinary tract infections and respiratory diseases, the mortality during the pandemic was higher than pre-pandemic and remained higher for sepsis and respiratory diseases at the end of follow-up. Thus, the authors draw the conclusion that an increased attention towards management of serious non-Covid-19 medical conditions may be needed.

Importance and originality:
Investigating the potential collateral effect of the Covid-19 pandemic on several aspects of healthcare is of high relevance since previous studies indicated that hospitalisation rates are substantially lower during the pandemic than pre-pandemic. However, these studies focused mostly on one single non-Covid-19 acute medical condition. The strength of this present paper is that it includes data based on a whole population and investigates the hospitalisation and mortality rates of all major diagnosis groups. Overall, the paper has a clear structure, is well written and gives new insight into a highly relevant topic.

Author reply: Thank you all for reviewing our manuscript. Of note, we have re-computed the entire dataset by extending the follow-up until January 27, 2021 in order to include the 2nd national lockdown in Denmark effective as of December 16, 2020. Furthermore, a table of summary statistics of the study population has also been included (now Table 1).

Major comments:
1. Data processing and analyses: The flow of participants, groups characteristics and handling of multiple diagnoses/hospital stays is not clear. Please extend the method section to address the following points:

   a. Please provide a second flow chart for the overall population showing the removal of patients (age, due to inconsistent vital status, immigration, Covid-19 and loss to follow up). Please also clarify the baseline exclusion and censoring due to migration/emigration in the manuscript.

   Author reply: Supplementary Figure 2 has been updated accordingly and details on baseline characteristics of the study population have been added as a new Table 1 and in the results p. 9, line 20: “The study included 5,753,179 Danish residents during 567.8 million person-weeks of observation yielding a total of 1,113,705 hospitalisations distributed among 675,447 individuals (Table 1). Of these hospitalised persons, 68.5% were admitted once, 17.5% were admitted twice, and 14% had three or more admissions during the study period.”

   b. P. 3: l. 16 and P:6: l. 30: Please clarify your inclusion criterion for age (first, “>17 years” is stated, later “>1 years”).

   Author reply: Thank you for bringing this to our attention. We also included children older than one year of age. Age limits have been aligned in the abstract and throughout the manuscript, p. 6, line 20: “Data were excluded for children (<1 year of age) and for individuals with recent migration status or inconsistent vital data (Supplementary Figure 2).”

   c. Please clarify, how many people were hospitalized for how many times.
Author reply: Good point. Details on re-admissions of individual patients during the study period have been detailed, p. 9, line 20: “The study included 5,753,179 Danish residents during 567.8 million person-weeks of observation yielding a total of 1,113,705 hospitalisations distributed among 675,447 individuals (Table 1). Of these hospitalised persons, 68.5% were admitted once, 17.5% were admitted twice, and 14% had three or more admissions during the study period.”

d. Please clarify, if the absence of missing data (P. 8: l. 30) is due to the prior removal of patients with inconsistent vital status and overall loss to follow up.

Author reply: This has been clarified, p. 9, line 5: “Due to exclusion of individuals with inconsistent vital status, there were no missing data for hospitalisation or death.”

e. Please present a table with summary statistics of the variables evaluated within the general population and the hospitalized sample (e.g. sex, age and vital status) to aid with the generalization of the present findings to other comparable populations or countries.

Author reply: Included as suggested (now Table 1).

f. Please clarify how overlaps in diagnoses of patients were handled (P. 3: l. 58 and P. 7: l. 41). For example, patients with urinary infections and subsequent sepsis due to the urinary infections - were these patients included in both mortality rates? The same applies to myocardial infarction and heart failure. Please comment or discuss the potential limitations of this procedure.

Author reply: This has been clarified in the methods section p. 7, line 22: “All non-Covid-19 hospitalisations since March 13, 2019 through January 27, 2021 were identified by principal diagnosis codes in the Danish National Patient Registry and grouped according to major ICD-10 diagnosis group (Supplementary Table 1) identified by the first primary code given within the listed chapters. However, if a patient was assigned a diagnosis code for Covid-19 within five days of admission, the hospitalisation was categorised as Covid-19. Using the Civil Registration System, 30-day mortalities were computed for non-Covid-19 hospitalisations, overall and according to selected major disease groups.”

and discussion p. 16, line 3: “Danish healthcare and administrative registries have been shown to be of very high quality,[14,16,32] but differential misclassification of conditions with a similar clinical presentation as Covid-19 cannot be excluded and may introduce bias in an unpredictable direction.”

2. From Figure 1 it seems that the number of hospitalizations and the 30-days-mortality drops already prior to onset of the lockdown on 11 March 2020. Is this due to a time window averaging of the plot, or is this indeed observable in the raw data? If there is indeed a drop before the lockdown, this might systematically underestimate the baseline rate of hospitalizations and mortality and we would recommend to use a shorter baseline, e.g. only until 1 March 2020 to avoid this dip prior to lockdown or even until 30 November 2019 to match the time periods under investigation in 2019 and 2020.

Author reply: We have carefully reflected on the Reviewer’s comment. Any point in the plots are
placed in the beginning of each period and the connected plot may thus occasionally give rise to small artefacts – in this case, the impression of a gradual drop within the timeframe between to plot points. On the other hand, the plot highlights fluctuations over time. We think that it is important to visualize these changes as different restrictions were imposed and lifted, often within few days, during the first 11 months of the Covid-19 pandemic in Denmark. Therefore, we respectfully prefer not to change the baseline.

Minor Comments:
1. We suggest the authors change or append their title of the paper to indicate that the hospitalisation and mortality rates are related to non-Covid-19 diseases. For example: “Hospitalisation and mortality rates for non-Covid-19 diseases in Denmark during the Covid-19 pandemic:…”

Author reply: We agree that the focus of the paper is on non-Covid-19 diseases. Revised as suggested.

2. The introduction is quite short. We suggest the authors add more original research articles, for example cite studies which are mentioned later in the discussion to put the study into context of recent research and help with the text flow here.

Author reply: Thank you for this suggestion. The following sentence has been moved from the discussion to the introduction p. 5, line 11: "Previous studies examining hospitalisation rates during the pandemic have mainly focused on a single non-Covid-19 acute medical condition, and most have been restricted to one or a few hospitals within a certain healthcare program or geographical region during a relative short period of time.[12–22]"

3. P. 2, l. 11: The first sentence of the summary box is quite long. We would therefore recommend to split it into two sentences.

Author reply: Revised as suggested: “Early observations during the Covid-19 pandemic suggested that patients may not seek help for cardiovascular or neurological diseases. Some hospitals, overwhelmed by the pandemic, may also have been incapable of providing timely care for other serious and acute non-Covid-19 medical conditions.”

4. P. 2: l. 30: Earlier in the sentence, the authors speak only about non-infectious diseases and later they state “...and non-Covid-19 infections”. We suggest to simply write “In this study, hospitalisations for all major non-covid disease groups…”.

Author reply: Revised as suggested, p. 4, line 3: “In this study, hospitalisations for all major non-Covid-19 disease groups declined during national lockdowns compared with the pre-pandemic baseline and mortality was higher, overall and for patients hospitalised with e.g. respiratory diseases, cancer, pneumonia, and sepsis”

5. P. 2: l. 34: “Mortality was higher for patients …”. Please indicate compared to what the mortality was higher.
Author reply: Comparator group has been added, please see revision in reply to minor comment #4.

6. P. 3: l. 39 and P. 9: l. 9: We suggest the authors include a summary statistic, e.g. median and first/third quartile, for the weeks of observations per resident and put the total number of weeks of observations in brackets for readability in the abstract and results.

Author reply: Summary statistics have been included as a new Table 1.

7. P. 3: l. 44: Please add the missing space in the confidence interval.

Author reply: Added as suggested.


Author reply: The sentence has been revised and RRs for each major disease group have been omitted due to word limitations and for improved readability.

9. P. 7: l. 55: Please explain if the authors checked for overdispersion and zero inflation regarding the Poisson Regression.

Author reply: All analyses were executed with specification of robust estimation of the covariance in order to allow for potential deviation from the model assumptions. This has been added to methods, p. 8, line 17:”Hospitalisation rate ratios (RR) with 95% confidence intervals (CI) were computed using the pre-Covid-19 baseline period as reference. A sandwich estimator for robust estimation of covariances was used to account for potential overdispersion”.

10. P. 8: l. 4: We suggest the authors add a short explanation why and how the weekly hospitalisation rates were adjusted for the number of working days per week and public holidays.

Author reply: Each time period was adjusted for number of working days per week, since most hospital contacts occur during regular weekdays and the number of working days may vary between examined time periods. Reasons and procedure for computation of weekly hospitalisation rates have been expanded, p. 8, line 13:”Using a Poisson regression model with log of the population size as offset, standardised weekly hospitalisation rates were estimated. The rates were adjusted for number of working days per week and public holidays since elective hospital contacts are mainly scheduled during regular weekdays.”

11. P. 8: l. 21: We suggest the authors provide Cumulative Incidence Functions instead of Kaplan Meier estimation since it overestimates event probabilities in competing risks settings.

Author reply: We agree with the reviewers that the Kaplan Meier estimator can lead to overestimation in competing risk settings such as estimating the risk of a non-death event or cause-specific death (in which case death of other causes would be a competing event). The current study
examines all-cause 30-day mortality risk and competing risks are not present - only independent, mainly administrative censoring. Thus, we suggest keeping the analyses as they are.

12. P. 8: l. 27: Please clarify if the computation of the Cox model for competing risks was based on Fine and Gray’s proportional subdistribution hazards model or which alternative method was used.

Author reply: As discussed in our previous answer (minor comment, question #11), competing risks are not present and the Cox proportional hazards model is valid for the analysis.

13. P. 16: Figure 1: The curve for positive Covid-19 admitted patients is difficult to see, please consider using another color or making the curve thicker. Moreover, the caption is not sufficient to explain the displayed diagram. The labels are inconsistent with the classification of the phases of the pandemic (the phase of regional lockdowns started in October). Please clarify what the lines reflect; are these raw or standardized rates? Why does the mortality rate end earlier than the hospitalization rate?

Author reply: Good points. A thicker line has been used for Covid-19 hospitalisations, the caption has been expanded, and labels have been aligned with the classifications in the manuscript. The hospitalisation rates were standardised which has been incorporated in the expanded figure legend and follow-up for hospitalisation and mortality rates has been harmonised.

14. P. 17: Table 1 and P. 20: Table 2: As the font size is very small, we suggest the authors add some spaces between the two categories.

Author reply: We have re-formatted the tables to include a column for the 2nd national lockdown and – hopefully - for improved readability.

15. P. 18: Figure 2 and P. 19: Figure 3: Since there is still some space on the pages and the plots are very small, please consider making them bigger and reformat the pages. Moreover, we suggest the authors use the same diagnosis names as in Table 1.

Author reply: Revised as suggested.

16. Supplementary Figure 1: Please add additional information into a caption and clarify what “index date” and “concurrent medication” mean since these terms have not been used in the manuscript.

Author reply: Clarified as suggested.

17. P. 26: Supplementary Figure 2: Please check the numbers. The number of hospitalizations in Denmark from 13 March 2019 through 30 November 2020 minus the number of excluded hospitalisations is 1,035,914 instead of 1,025,914, which is probably a typo. Also, the period under investigation starts 1 March 2019 according to the paper, but has a different date here?
Author reply: Supplementary Table 2 has been updated and corrected using follow-up until January 27, 2021. Thank you.

PhD Students:
Melina Engelhardt
Jean Tori Pantel
Kerstin Rubarth
Pimrapat Gebert

Mentors (take responsibility for the review):
Toivo Glatz
Dr. Maarten van Smeden

Job Title: Assistant professor

Institution: University Medical Center Utrecht

Reviewer: 3

Recommendation:

Comments:
In this original research article, the authors sought to examine the incidence of hospitalizations for medical conditions other than coronavirus disease 2019 (COVID-19) – and subsequent mortality – during the COVID-19 pandemic using the well-known Danish nationwide. Specifically, the authors compared hospitalization rates – and subsequent 30-day mortality rates – during the COVID-19 pandemic (defined as March 11 through November 30, 2020) with the pre-pandemic period (defined as March 1, 2019 through March 10, 2020). The authors found that hospitalizations for all major non-infectious disease groups declined during national lockdown, and mortality was higher for patients hospitalized with non-COVID-19 medical conditions including respiratory diseases, sepsis, and urinary tract infections.

The main strengths of this study are 1) the inclusion of a large, nationwide, and unselected cohort; 2) completeness of data; and 3) contemporary data until the end of November 2020. The authors address an important question and present some interesting data in this well-written manuscript. Nonetheless, the conclusions and clinical implications are not that novel, given that many studies, including several Danish studies, have examined this question as well (although these have mainly looked at specific cardiovascular diseases and included less contemporary data). Moreover, I have some concerns regarding the statistical analyses, and I would therefore recommend the BMJ to obtain a statistical review.

Author reply: Thank you for reviewing our manuscript. Of note, we have re-computed the entire dataset by extending the follow-up until January 27, 2021 in order to include a 2nd national lockdown in Denmark effective as of December 16, 2020. Furthermore, a table of summary statistics of the study population has also been included (now Table 1).
Specific comments below:
- Summary box: Cardiological should perhaps be replaced by cardiac or cardiovascular.

Author reply: Revised as suggested.

- In the abstract, the authors state that only Danish citizens 18 years of age or older are included. In the Methods section, the authors state that all Danish citizens are included (apart from those < 1 year of age).

Author reply: Thank you for bringing this to our attention. We also included children above 1 year of age. Age limits have been aligned in the abstract and throughout the manuscript, p. 6, line 20: “Data were excluded for children (<1 year of age) and for individuals with recent migration status or inconsistent vital data (Supplementary Figure 2).”

- In the Methods section, the authors state that “On March 11, 2020 the Danish government issued a comprehensive lockdown in Denmark with closure of schools and most workplaces, implementation of quarantines, border closings, and restriction on public gatherings”. This is now entirely correct. The Prime Minister in Denmark announced these restrictions on March 11, 2020, but most of these were implemented on March 12 or March 13.

Author reply: The study examined hospitalisation rates and 30-day mortality risks among hospitalised individuals during the Covid-19 pandemic in Denmark. Hospitalisation rates depend on ill patients seeking help and being admitted (either by referral from a doctor or by calling an ambulance). Thus, in order to capture the potential impact of behavioural aspects of patients and doctors as well as for practical purposes (i.e. a date has to be set), we suggest keeping the categorisation as it is.

- The structure of the Danish National Patient Registry changed substantially with the introduction of the 3rd version in February/March 2019. In the previous version, a variable indicated if a hospital contact was a hospital admission, an outpatient visit, or an emergency department visit, but this variable is not included in the 3rd version. How did the authors define a hospitalization in the absence of this variable?

Author reply: Good question. A description of the algorithm used has been provided in the methods section, p. 6, line 18: “Hospitalisations less than 12 hours apart were considered as one continued contact. Next, inpatient hospitalisations were defined as hospital contacts crossing midnight and of at least 12 hours duration.”

- I presume that the authors look at all hospitalizations and not only the first for a given patient. This should be stated more clearly.

Author reply: This has been clarified, e.g. in the results p. 9, line 20: “The study included 5,753,179 Danish residents during 567.8 million person-weeks of observation yielding a total of 1,113,705 hospitalisations distributed among 675,447 individuals (Table 1). Of these hospitalised persons, 68.5% were admitted once, 17.5% were admitted twice, and 14% had three or more admissions during the study period.”
- How many patients had more than one hospitalization, overall and within 30 days? Potentially, a patient could be included twice in the same Cox model assessing the 30-day mortality if the patient had more than one admission within 30 days and this would violate the assumption of independent observations.

Author reply: Please see reply just above concerning the number of persons with several admissions during the study period. You are right about potential violation of the assumption of independent observations and therefore robust methods for handling covariances have been employed. This has been added to the methods section, p. 8, line 17: “Hospitalisation rate ratios (RR) with 95% confidence intervals (CI) were computed using the pre-Covid-19 baseline period as reference. A sandwich estimator for robust estimation of covariances was used to account for potential overdispersion”, and p. 9, line 3:” Mortality risk ratios (MRR) with robust 95% CI were calculated using Cox proportional regression models adjusted for age and sex, and using a diagnosis of Covid-19 within 30 days after the index date as competing risk.”

Please enter your name: Jawad Haider Butt

Job Title: MD

Institution: Rigshospitalet

**Report from The BMJ’s manuscript committee meeting**

Members of the committee were: John Fletcher (Chair), Jon Deeks (Statistical advisor), Timothy Feeney, Nazrul Islam, Jessica Kimpton, Elizabeth Loder, David Ludwig, Joseph Ross, Tiago Villanueva, Wim Weber.

Detailed comments from the meeting:

We thought your study addresses an interesting and important research question. We had the following concerns.

Author reply: Thank you for considering our manuscript and for providing us with helpful comments.

You only present data up to November 30, which was just before the major surge in cases during the 2nd wave (on November 30th you had roughly 217 cases per million and peaked on December 18th at 610 per 1 million), so hospitalizations and deaths must have followed accordingly afterwards. Before November 30th the number of cases was not that high, so the healthcare system could not have been that overwhelmed and show things like excess mortality. We would appreciate
to see at least 2 more months of data.

Author reply: The follow-up has been extended until January 27, 2021 and data on the 2\textsuperscript{nd} national lockdown has been added. This has led to a major revision of the results (incl. tables and figures to accommodate the new data) and the discussion, since there was an excess mortality on a national level during the 2\textsuperscript{nd} national lockdown in December 2020. In addition, we have also included a table with summary statistics of the study population (now Table 1 in the revised manuscript).

This study is just hospital admissions and deaths following hospital admissions. Primary care data on consults and deaths are missing.

Author reply: Unfortunately, we do not have access to diagnoses made in primary care and no such registry exists in Denmark.

The lower numbers of people going to hospital may be due to lower disease burden; may be due to avoidance of health care contact; or may be due to shift of care from hospital to primary care.

Author reply: We agree. Considerations on genuine lower disease burden or avoidance of health care contacts have been further emphasized on p. 14, line 15:” In general, fewer hospital admissions could represent genuine lower incidences of diseases because of lifestyle and behavioural changes during lockdown. Still, patient reluctance to seek care due to perceived risks of contracting the infection at hospital or negligence of symptoms as well as decreased hospital capacity to manage these patients remains a concern.”

Aspects of potential shift from hospital to primary care has also been addressed on p. 14, line 6: “Reports on the productivity of general practitioners by the Danish Board of Health observed that physical consultations also dropped markedly during the early stages of the Covid-19 pandemic and were only partially replaced by telephone consultations, video calls, and e-mail.[23,24] This decrease was especially pronounced for children 0-4 years of age, adults > 70 years of age, and immigrants. By late April 2020, consultations had returned to baseline levels suggesting that there was no major shift in management of serious diseases from hospital to primary care.”

The higher 30 mortality following hospitalisation may be due to delayed presentation and progression to more severe disease; may be due to suboptimal care in a stressed system (primary or secondary care); may be due to appropriate self care and primary care leading to admission of only the severe cases (and a drop in the denominator as above).

Author reply: We agree. These considerations have been incorporated into the discussion section on p. 15, line 13: “This could be due to delayed presentation and progression to more severe disease in some patients. In addition, the implementation of isolation precautions in a burdened healthcare system (primary and hospital care) may further hinder appropriate examinations and time-dependent treatments. Importantly, these results should be interpreted with caution and further studies are needed to clarify whether this represents a significantly higher mortality adjusted for disease severity, or whether the observations merely reflect increased self- or primary care management of less severe cases.”.
You acknowledge that primary care data are absent, but speculate that there were restrictions on primary care, so you feel there was no shift. Might you have data to support this?

Author reply: The Danish Board of Health have published several reports on the productivity in general practice in Denmark during the Covid-19 pandemic (in Danish):

- https://sundhedsdatastyrelsen.dk/da/nyheder/2020/laegekontakt_covid_19_131120

These data are based on billings from general practitioners and are limited to an indication of whether the consultation was a usual physical consultation or consisted of contact by telephone, video calls, and e-mail. Thus, the data does not contain any information on diagnosis, diagnostic tests performed, or action taken on the basis of the consult. The status reports clearly show that physical consultations dropped markedly during the early stages of the pandemic and did not exceed usual productivity afterwards.

This has been included in the discussion (including references), p. 14, line 6: “Reports on the productivity of general practitioners by the Danish Board of Health observed that physical consultations also dropped markedly during the early stages of the Covid-19 pandemic and were partially replaced by telephone consultations, video calls, and e-mail.[23,24] This decrease was especially pronounced for children 0-4 years of age, adults > 70 years of age, and immigrants. By late April 2020, consultations had returned to baseline levels suggesting that there was no major shift in management of serious diseases from secondary to primary care.”

There is a lack of actual numbers - there are lots of rates. We would appreciate data on how many deaths, how many cases? Some of these diseases are rare, others are common, so the absolute impact would be good to see.

Author reply: Good point, thank you for this suggestion. We have included summary statistics (number of individuals, age groups, sex distributions) as well as absolute numbers of hospital admissions and observation time (person-weeks), overall and within each time period, as a new Table 1 shown below:
<table>
<thead>
<tr>
<th>Overall population demographics</th>
<th>Baseline</th>
<th>1st national lockdown</th>
<th>Gradual re-opening</th>
<th>Few restrictions</th>
<th>Regional lockdowns</th>
<th>2nd national lockdown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of individuals</td>
<td>5,753,179</td>
<td>416,034</td>
<td>46,362</td>
<td>151,824</td>
<td>98,410</td>
<td>58,706</td>
</tr>
<tr>
<td>Age (years), mean (sd)</td>
<td>41.8 (23.4)*</td>
<td>59.9 (22.4)</td>
<td>60.5 (22.2)</td>
<td>60.2 (22.4)</td>
<td>60.6 (22.1)</td>
<td>61.8 (21.9)</td>
</tr>
<tr>
<td>0-20</td>
<td>21.4 (1,231,783)*</td>
<td>5.7 (35,152)</td>
<td>5.2 (3,852)</td>
<td>5.4 (10,281)</td>
<td>5.3 (6,091)</td>
<td>4.4 (2,931)</td>
</tr>
<tr>
<td>21-40</td>
<td>25.4 (1,463,171)*</td>
<td>15.8 (97,329)</td>
<td>15.6 (11,472)</td>
<td>16.2 (30,851)</td>
<td>15.4 (17,805)</td>
<td>15.3 (10,183)</td>
</tr>
<tr>
<td>41-60</td>
<td>27.0 (1,553,768)*</td>
<td>18.8 (115,783)</td>
<td>18.4 (13,476)</td>
<td>18.2 (34,704)</td>
<td>18.4 (21,296)</td>
<td>17.5 (11,683)</td>
</tr>
<tr>
<td>61-80</td>
<td>21.4 (1,230,024)*</td>
<td>40.3 (248,065)</td>
<td>40.5 (29,732)</td>
<td>40.2 (76,564)</td>
<td>40.9 (47,390)</td>
<td>40.4 (26,950)</td>
</tr>
<tr>
<td>81-</td>
<td>4.8 (274,433)*</td>
<td>19.3 (118,877)</td>
<td>20.3 (14,885)</td>
<td>20.0 (38,077)</td>
<td>20.1 (23,269)</td>
<td>22.4 (14,962)</td>
</tr>
<tr>
<td>Females</td>
<td>50.3 (2,892,854)*</td>
<td>53.6 (329,970)</td>
<td>53.3 (39,141)</td>
<td>53.8 (102,384)</td>
<td>53.6 (62,086)</td>
<td>53.0 (35,327)</td>
</tr>
<tr>
<td>Number of hospitalisations</td>
<td>1,113,705</td>
<td>615,206</td>
<td>52,045</td>
<td>73,417</td>
<td>190,477</td>
<td>115,851</td>
</tr>
<tr>
<td>Weeks of observation/10⁶ individuals</td>
<td>567.8</td>
<td>299.2</td>
<td>29.6</td>
<td>44.4</td>
<td>94.0</td>
<td>62.7</td>
</tr>
<tr>
<td>Absolute number of deaths</td>
<td>N/A</td>
<td>30,966</td>
<td>3,323</td>
<td>3,847</td>
<td>9,569</td>
<td>6,075</td>
</tr>
</tbody>
</table>

However, we are concerned about including the absolute number of deaths as they may easily be misinterpreted if not considering differences in duration of observation and number of individuals/hospitalisations within each time period. Naturally, if the editors prefer it, we are happy to provide the data (shown here as an extra row compared with Table 1 in the current manuscript).
In the abstract you include those > 17 years but in the methods you only exclude children < 1 year.

Author reply: Thank you for bringing this to our attention. We also included children above one year of age. Age limits have been aligned in the abstract and throughout the manuscript, p. 6, line 20: “Data were excluded for children (<1 year of age) and for individuals with recent migration status or inconsistent vital data (Supplementary Figure 2).”