Clarify whether for CFR calculation, the number of case and death being taken are from same day or different days (it appears to be from same week, which will only minimize the effect of reporting bias/delay, not other inherent issues, see latter). The day from symptoms appearance to outcome (resolution or mortality) takes upwards of 10 days. So for comparative analysis as presented in the paper, where the CFR of different communities are being compared at a same time point could erroneously make conclusions non dependable for any purpose if done during the wave of infections unless incubation period approximation is taken into consideration (e.g., Cases at day X, then deaths on day X+14 day, if 14 day average time is expected for the disease outcome). The non dependability could stem from different communities/regions may be at different phases of the pandemic for a variety of reasons, differential stringency of measures in place, people behavior, season etc. Therefore, author should make the description as clear as possible and include the incubation period consideration in the CFR calculation or alternatively present analysis of the data when all infections had an outcome (i.e., post wave of infections).

The data collected come from the Spanish Ministry of Health and are harmonized for all Spanish Regions. Since these data are retrospective, we understand that they are not affected by the clinical course, including the incubation period. In this case, the effect would be the same on all Regions, given that during the first wave, all the Regions followed the guidelines of the Spanish central government and did not have independence of actions. This aspect is highlighted in Material and Methods section, where we also point out that the data are collected within a window of one week, in order to minimize the possible bias in the report of cases and deaths by the Regions.

The general guidelines of the Spanish Health System (SNS) regarding vaccination, prevention protocols, and public health measures are agreed by the Interterritorial Board of the SNS, which includes the Ministry of Health and the Regional Health Departments. Therefore, as regards vaccination plans (such as BCG) or the prevalence of tuberculosis infection, although potential differences among Regions cannot be excluded, we believe that since there is a national program, these differences do not significantly change the objectives of the study concerning comparisons between Regions. As for other protective variables such as Vitamin D, there is not enough scientific information from the pandemic period to analyze the differences.

| Question | Answer |
|----------|--------|
| Clarify whether for CFR calculation, the number of case and death being taken are from same day or different days (it appears to be from same week, which will only minimize the effect of reporting bias/delay, not other inherent issues, see latter). The day from symptoms appearance to outcome (resolution or mortality) takes upwards of 10 days. So for comparative analysis as presented in the paper, where the CFR of different communities are being compared at a same time point could erroneously make conclusions non dependable for any purpose if done during the wave of infections unless incubation period approximation is taken into consideration (e.g., Cases at day X, then deaths on day X+14 day, if 14 day average time is expected for the disease outcome). The non dependability could stem from different communities/regions may be at different phases of the pandemic for a variety of reasons, differential stringency of measures in place, people behavior, season etc. Therefore, author should make the description as clear as possible and include the incubation period consideration in the CFR calculation or alternatively present analysis of the data when all infections had an outcome (i.e., post wave of infections). | The data collected come from the Spanish Ministry of Health and are harmonized for all Spanish Regions. Since these data are retrospective, we understand that they are not affected by the clinical course, including the incubation period. In this case, the effect would be the same on all Regions, given that during the first wave, all the Regions followed the guidelines of the Spanish central government and did not have independence of actions. This aspect is highlighted in Material and Methods section, where we also point out that the data are collected within a window of one week, in order to minimize the possible bias in the report of cases and deaths by the Regions. |

) Include background information about different protective variables ("more background information related to the determinates of outcome") being discussed in the literature [e.g., Global Health Security index (Health care access/ setup/ capacity, prevention practices etc.), COVID-19 stringency index (stringency of measures in place to prevent infections in different regions during the study period), Vitamin D status, BCG vaccination, prevalence of Latent Tuberculosis infection (LTBI)/TST positivity, etc.] that may have varied in these regions. | The general guidelines of the Spanish Health System (SNS) regarding vaccination, prevention protocols, and public health measures are agreed by the Interterritorial Board of the SNS, which includes the Ministry of Health and the Regional Health Departments. Therefore, as regards vaccination plans (such as BCG) or the prevalence of tuberculosis infection, although potential differences among Regions cannot be excluded, we believe that since there is a national program, these differences do not significantly change the objectives of the study concerning comparisons between Regions. As for other protective variables such as Vitamin D, there is not enough scientific information from the pandemic period to analyze the differences |
| Task                                                                 | Comment                                                                 |
|----------------------------------------------------------------------|-------------------------------------------------------------------------|
| Briefly, discuss how the protective variables (indicated in #2) may be impacting the observation/conclusions made in the current study. Wherever possible, make an attempt to correlate the study observations with supposed protective variables. | The answer is related to the previous point. In any case, we include this limitation to the manuscript. |
| Enhance referencing for facts which are not commonly known (provide references for the global audience as specifics of the study area are not known widely). | The main objective of the study is to analyze if there are differences in case fatality rates, by comparing the “official” register of the Ministry of Health and the MoMo mortality register, as well as to compare if there are differences between Regions between both register systems. From the data obtained, a number of options are considered as possible causes of the differences observed. In the ‘Discussion’ section, we consider such factors as population dispersion, the distribution and ageing of population in the different Regions, and the accessibility to hospital care and emergency care services, among others. To what extent these and other factors are responsible for the differences found should be addressed by another study. |
| The statistical methods used in the paper were adequately presented; however, there is no Statistical Analysis Section in this paper. In the current version, all the statistical methods, such as Spearman’s Rho Coefficient, linear regression, etc., were spread out in the manuscript. This paper would have been strengthened by centralizing all the statistical inputs in one section – Statistical Analysis Section. | We agree with the reviewer’s suggestion and make the corresponding correction. |
| Abstract: ENE and R2 need to be defined | We make the changes suggested by the reviewer. |
| Introduction: The second paragraph, the first sentence needs reference | The sentence’s reference is a previous reference from Lancet 2020: (2). |
| Method: The reliability of data is not known. | In the ‘Material and Methods’ section, we refer to the reliability of data, which come from the official publications of the Ministry |
of Health and the Regional Health Departments. Analyzed from a current perspective, the data used have been verified and confirmed by the official national and regional bodies.

| Figure: MoMo??                  | We made the correction |
|--------------------------------|------------------------|
| In your abstract, you stated that the objective of this paper is to compare COVID-19 case fatality rates across the Spanish CC.AA. It obvious to find discrepancy for the same outcome across different communities characterized by different socio-economic and demographic features. However, I think the paper aims do detect differences in CFR for Covid-19 in the Spanish Autonomous Communities (CC.AA) when using different methods of the official records and the daily mortality record. Moreover, if your primary outcome is to estimate the CFR, then the prevalence of infection for COVID-19 will be treated as a secondary outcome that necessary to estimate CFR. - Please clarify your study question, whether to correlate the estimated prevalence of infection with CFR or to compare CFR across different methods of CFR-PCR+ and CFR-Mo. | We agree with the reviewer that the objective of the study may not be clearly defined in the ‘Abstract’. According with your accurate comment, the main objective is to detect whether there are any differences in case fatality rates between Spanish Regions using two different register systems, i.e., the official register of the Ministry of Health and the MoMo; and secondarily, to analyze whether the prevalence of infection can explain those differences. We make the necessary corrections. |

| Introduction: • Please mention any variation in preventive measures across the State Administration and the Autonomous Communities (CC.AA.) in your background information; such as health services, social distancing, closure of public transport, workplaces, and schools, and termination of public gatherings and events. You can move some background information about the official records and the daily mortality record from introduction to methods and material section. | The key feature of the first wave in Spain was the comprehensive lockdown for all the population, without differences between Regions. This is an excellent opportunity for another study to compare the effect of a single strategy as opposed to different strategies, as happened later on in Spain during the subsequent waves. The data collection system of the Ministry of Health and of the mortality register is specified in the ‘Materials and Methods’ section. During the pandemic, there was a logical oversaturation of information, which however, looking back, did not affect its accuracy and reliability. |
Material and Methods:

- Although the number of deaths for the calculation of CFR-PCR+ was obtained from the information provided by the Ministry of Health during the week of 11 to 16 May 2020, the period for data collection on the infection prevalence was not identified. Due to the rapid spread of pandemic, inconsistency between the period of collecting the data on infection prevalence and the period of estimating CFR may affect the study results.

The date of collection of data on cases and deaths was chosen on purpose to make it coincide with the completion of ENE-Covid19, and therefore, with the highest infection incidence known at that time. Although there may be some discrepancy, given that the data are so consecutive, we believe that this does not affect the data analysis. The dates of data collection are specified in the ‘Materials and Methods’ section, which is considered as a possible limitation in the corresponding section.

Please identify the period for the data collection on the prevalence of positive IgG antibody tests of the ENE-COVID-19 to estimate the infection prevalence.

The dates of data collection of ENE-Covid19 are clarified in ‘Materials and Methods’.

You concluded, “It is preferable to consider the daily mortality records to estimate case fatality rate because the official records underestimate the case fatality rate of the SARS-CoV-2 virus pandemic”. However, more information about the validity and process of collecting the data in both methods is required.

This dates are clarified in ‘Materials and Methods’ with more information.

Please clarify any auditory methods or measures taken to classify deaths in CFR data, such as ICD-10, with clear exclusion and inclusion criteria and specific identification for the main cause and underlying cause of death.

In the Spanish register system, every person who dies with a positive diagnostic result for SARS-CoV-2 is considered a death attributable to covid19, and that is how it has been considered for the analysis. Obviously, this implies some classification bias, which is commented on in the ‘Discussion’ and in a previous article by the same group of authors.

Reviewer #4: It would be appropriate if few of the sentences are rephrased and checked for grammatical errors.

We review the paper in order to make the necessary corrections according to the reviewer’s comment.