Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Surveillance Information System (SIVEP-GRIPE) dataset.

Second, the authors should have mentioned that the risk factors included in SIVEP-GRIPE were self-reported (provided by the patients themselves or their families). Therefore, the analysis could be biased by the patients' knowledge regarding their medical condition. Additionally, some variables could be incorrectly coded in the electronic records; for instance, we identified in the current SIVEP-GRIPE platform at least 14 puerperal individuals younger than 10 years, which was probably a data entry error (leading to outliers).

Finally, the author did not mention any effort to test the regression model assumptions (eg, non-linearity relationship and residual analysis). The inclusion of the variables in the final multivariate model was based on a univariate parameter, which could have suppressed other important variables that should be included in the model. There was also no internal validation or cross-validation. Therefore, we believe that our concerns should affect how the data presented by Oliveira and colleagues[1] should be interpreted.

We declare no competing interests.

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1 Oliveira EA, Colosimo EA, Simões e Silva AC, et al. Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database. *Lancet Child Adolesc Health* 2021; **5:** 559–68.

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We read the Article by Eduardo Oliveira and colleagues[1] with great interest and believe the findings from this cohort study are important, given that they directly investigated the risk factors associated with COVID-19 in children and adolescents.

In their study, patients were roughly evenly distributed among the three age groups, and risk of death was increased in infants younger than age 2 years and in adolescents aged 12–19 years, relative to children aged 2–11 years. However, the authors did not provide a rationale for the age groupings. The lower age limit of adolescence is generally defined as 10 years,[2] including by the UN and WHO.[3] Additionally, a study of COVID-19 trends between March 1, 2020, and Dec 12, 2020, in young people aged 0–24 years in the USA found that more than 81% of patients were older than 10 years.[4] Therefore, we are interested to know how a different age stratification (<2 years, 2–9 years, and 10–19 years) would affect the study findings, and we believe that comparison between these age groups could provide further insight on the COVID-19 mortality risk in adolescents.

It is important to present the median and mean ages in the three age groups, given that this information will help readers understand how mortality risk is influenced by age within the broad age bands. Having data related to symptoms, comorbidities, admission to intensive care units, and death rate by age groups will also provide a basis for understanding the disparity in death risk among age groups.

The upper-age definition of adolescence has long posed a conundrum and varies across countries. Defining adolescence as age 10–24 years has been proposed to align more closely with adolescents' biological growth and social-role transitions,[2] and some studies on COVID-19 have included patients aged 0–24 years.[4] The study by Oliveira and colleagues[1] included patients younger than 20 years, and the inclusion of patients aged 21–24 years might provide a more comprehensive understanding of COVID-19 in adolescence.

We declare no competing interests.

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Authors' reply

We thank Jonas Carneiro Cruz and colleagues and Siyu Chen and Yong Shao for their interest in our study in *The Lancet Child & Adolescent Health*.[1] Here, we further discuss some findings and methodological aspects, specifically the question of the effect of age and comorbidities in the prognosis of paediatric COVID-19.

Cruz and colleagues raised concerns about grouping different clinical disorders in a single categorical variable. This issue is interesting from both clinical and methodological points of view. We tested various models that included the variable comorbidities, as dichotomous, categorical, or continuous, and also models including the main chronic pre-existing conditions as separate covariates. In this regard, we did not observe any superiority in clinical contribution among the different

models tested. Moreover, in the appendix of our Article,[1] we also showed that the presence of any clinical condition, including obesity, significantly increased the risk of death (except asthma, as also found by de Souza and colleagues).[2]

In their Correspondence, Chen and Shao asked why we used a cutoff of 11 years for adolescents, arguing that adolescence is defined by WHO as the period starting from 10 years of age. Although the definition of adolescence varies across different countries and societies, we believe that this reanalysis might contribute to a relevant clinical issue.[3] Our reanalysis (appendix p 1) shows the distribution of covariates according to the redefined age groups and the corresponding competing-risk survival analysis. The cumulative incidence of death was 9·2% for infants younger than 2 years, 4·9% for children aged 2–10 years, and 9·5% for adolescents aged 10–20 years (appendix p 3); the cumulative incidence of death after adjustment by the Fine-Gray model is also shown in the appendix (p 4). The hazard of death for infants and adolescents was about 2·5 times higher than in those aged 2·0–9·9 years. The results are similar to our original analysis.[1] In a preprint meta-analysis of 57 studies, which did not include our data, Harwood and colleagues[4] also showed a similar result—the odds of poor outcomes were 1·6–2·0 times higher for infants (aged <1 year), and adolescents (aged >10 years) had elevated odds of severe COVID-19 (an increase of 1·4–2·2 times greater odds) and particularly multisystem inflammatory syndrome (2·5–8·0 times greater odds), compared with children aged 1–4 years. In this regard, we considered clinically relevant the issue raised by Cruz and colleagues, that differences in mortality in the age groups might be confounded by the distribution of the comorbidities. Our reanalysis shows a significant difference in the prevalence of comorbidities among the age groups ($p<0·0001$; appendix p 1). Nevertheless, the lowest prevalence of comorbidities was in children younger than 2 years, who had a higher hazard of death in our analysis. Both age and the number of comorbidities retained significance in the final model after adjustment by competing-risk analysis (appendix p 2). These findings suggest that the increased risk of death, which presents as a U shape with infants and adolescents at higher risk, might have other underlying factors beyond the uneven distribution of comorbidities among different age groups.

Furthermore, we disagree with Cruz and colleagues that we completely ignored the variable of other comorbidities available in the Influenza Epidemiological Surveillance Information System (SIVEP-GRIPE) dataset. On the contrary, as we stated in Methods section of our Article,[1] we carefully reviewed all text fields, especially the MORB_DESC field. This field is open ended, and relevant clinical information was included within it, especially relating to comorbidities and other risk factors. Cruz and colleagues also stated that some variables could be incorrectly coded in SIVEP-GRIPE. We agree that registry errors are inherent to databases such as SIVEP-GRIPE. To overcome this issue, we exhaustively searched for inconsistencies in the information provided by crosschecking variables of interest before the recoding process.

We agree that the self-reporting of risk factors included in SIVEP-GRIPE is a limitation. In this regard, we believe that the effect is mainly related to possible family omissions in reporting relevant conditions. However, the most important issue is the impossibility to access detailed clinical information of the cases for further analysis. Therefore, we suggest that further versions of SIVEP-GRIPE should include a link in the database to permit access to the laboratory or imaging results and detail of the treatment during hospital admission.

Finally, regarding Cruz and colleagues' point about checking regression-model assumptions, we agree that failure of model adequacy might lead to biased parameter estimation. The main assumption of the Fine-Gray model is the proportionality of hazard ratios. A visual inspection of the relevant figure in our Article[1] shows no substantial crossing curves that could be an indication in favour of the proportionality assumption. A non-linearity relationship does not apply to our analysis given that all covariates are categorical. Model building was based on a univariate model. We agree that there is a risk of excluding important covariates from the final model. However, our statistical inference was based on a unique cohort, both in terms of the number of events (deaths and discharges) and of the sample size. We believe that under these conditions, the risk of excluding important covariates is very small, and the sex variable was the only factor excluded. Unlike adult cohorts, sex has not been associated with severe disease or death in paediatric cohorts.[4] Finally, internal and cross-validation are essential for calibration and discrimination in prediction models, not for an estimation study, such as ours.

See **Online** for appendix

We declare no competing interests.

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