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# Journal Pre-proof

Increased mortality risk associated with statins in the CORONADO study

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Dear Editor,

23 February, 2021

Concerning our revision, we do not know what to do. We got reviewer comments, which were not about our letter to the Editor. I have sent emails about this to you, but got no answer.

Please advice.

Sincerely,

Timo Strandberg, MD

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## Increased mortality risk associated with statins in the CORONADO study

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1 The Coronavirus SARS-CoV-2 and Diabetes Outcomes (CORONADO) study investigators  
2 reported an increase in mortality associated with ongoing statin treatment in 2449 inpatients  
3 with type 2 diabetes (T2D) during the coronavirus disease 2019 (COVID-19) pandemic [1].  
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5 Crude 7-day mortality rates were 12.8% among statin users and 9.8% among non-users ( $P =$   
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10 0.02), with the corresponding percentages for 28-day mortality being 23.9% and 18.2%,  
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12 respectively ( $P < 0.001$ ). Calculated unadjusted odds ratios (ORs) based on these figures were  
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14 1.36 [95% confidence interval (CI): 1.06–1.76] and 1.41 (95% CI: 1.15–1.72).  
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18 This difference in mortality was not unexpected as the statin users were older (mean age: 72  
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20 and 70 years, respectively), had diabetes of longer duration (15 and 12 years, respectively), and  
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22 more hypertension (87% and 74%, respectively), heart failure (14% and 10%, respectively) and  
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24 chronic obstructive pulmonary disease (COPD; 12% and 8%, respectively), as well as more  
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26 macrovascular (54% and 27%, respectively) and microvascular (50% and 41%, respectively)  
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28 complications than non-users of statins. After propensity score matching, the reported 7-day  
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30 and 28-day ORs for mortality risk were 1.74 (95% CI: 1.13–2.65) and 1.46 (95% CI: 1.08–  
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32 1.95), respectively. Nevertheless, it is rather surprising that the mortality risk prevails, even  
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34 despite higher point estimates after adjusting for patients who had more factors associated with  
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36 poor COVID-19 prognosis.  
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44 Statin treatment has been shown to be beneficial in randomized controlled trials of particular  
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46 patient groups, such as patients with diabetes, who are most at risk of COVID-19. In addition,  
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48 the majority of analyses concerning mortality risk during COVID-19 have thus far indicated a  
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50 beneficial or neutral effect of statin use [2]. Large studies from China [3] and the US [4,5], for  
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52 example, indicated a 12–46% reduced mortality risk among statin users, including those with  
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54 diabetes, and a UK-wide analysis of 2.9 million patients with T2D (mean age: 70 years) found  
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56 that the risk of death due to COVID-19 was 28% lower among statin users [5].  
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Thus, the unexpected statin mortality results so far from CORONADO may represent outlier findings and call for more detailed analyses of underlying factors.

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