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Reply

We thank Dr. Duan for the interest in our paper that reported the association between postvaccination and overall and coronavirus disease 2019 (COVID-19)–related mortality among participants with cirrhosis. We adjusted for the etiology of alcohol-associated liver disease versus others based on studies that showed a worse prognosis of COVID-19 associated with alcohol.[1–4] However, as suggested, we now include the various etiologies of liver disease in the baseline characteristics (Table S1). The most common cause of cirrhosis in both the postvaccination and unvaccinated COVID-19 cohorts was NAFLD (28.7% and 28.2%, respectively), and the two groups were well matched with respect to liver disease etiology. We agree that exposure to proton pump inhibitors (PPIs) may be a potential confounder. Participants with postvaccination COVID-19 were more likely to be exposed to PPIs than those with unvaccinated COVID-19 (80.3 vs. 65.8%; $p < 0.0001$). Third, Dr. Duan suggests socioeconomic status as a potential confounder. Although we did not have data on individual income levels, we examined the socioeconomic status by identifying participant locations using residential zip codes and the median household income associated with these locations. Median household incomes were similar between the two groups ($47,400 vs. 47,100; $p = 0.64$).

We repeated the analysis by including these three variables in the multivariable model (Table 1). Compared with NAFLD cirrhosis, alcohol and HCV cirrhosis were not associated with an increase in overall or COVID-19-related death. We observed no association between the median household income and overall (per $1000 change in household income; adjusted HR [aHR] 0.98, 95% CI 0.93–1.07; $p = 0.16$) or COVID-19-related death (aHR 0.99, 95% CI 0.97–1.03; $p = 0.11$). However, PPI exposure was associated with an increase in overall mortality (aHR 1.61, 95% CI 1.06–2.15; $p = 0.001$), but not COVID-19-related death (aHR 1.08, 95% CI 0.55–1.54; $p = 0.75$). After inclusion of these variables, postvaccination COVID-19 continued to be associated with a decrease in overall (aHR 0.25, 95% CI 0.12–0.49; $p < 0.0001$) and COVID-19-related death (aHR 0.27, 95% CI 0.13–0.60; $p = 0.001$).

These analyses reveal similar associations described in our original estimates, indicating that postvaccination COVID-19 is associated with consistent reductions in overall and COVID-19-related death.

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DISCLAIMER

The authors prepared this work in their personal capacity. The opinions expressed in this article are the authors' own and do not reflect the view of the Department of Veterans Affairs or the US government.

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TABLE 1 Multivariable HRs for the risk of overall death or COVID-19-related death in patients with postvaccination COVID-19 versus unvaccinated COVID-19

	Overall death		COVID-19-related death	
Variable	**aHR (95% CI)**	***p*-Value**	**aHR (95% CI)**	***p*-Value**
Number of patients	762	–	762	–
Number of events	87	–	64	–
Group				
Control	REF		REF	
Vaccine	0.25 (0.12, 0.49)	**<0.0001**	0.27 (0.13, 0.60)	**0.0011**
Location, n (%)				
Northeast	REF		REF	
Southeast	1.13 (0.51, 2.53)	0.7606	1.42 (0.55, 3.65)	0.4726
Midwest	1.30 (0.64, 2.64)	0.4759	1.46 (0.61, 3.48)	0.3914
South	0.61 (0.26, 1.42)	0.2528	0.87 (0.32, 2.38)	0.7897
Northwest	2.47 (0.98, 6.23)	0.0557	2.53 (0.82, 7.81)	0.1067
Southwest	1.54 (0.68, 3.49)	0.2992	2.29 (0.91, 5.80)	0.0801
Age	1.05 (1.02, 1.08)	**0.0015**	1.06 (1.02, 1.10)	**0.0012**
BMI	1.00 (0.97, 1.02)	0.6657	1.01 (0.98, 1.03)	0.6598
Diabetes				
No	REF		REF	
Yes	0.92 (0.56, 1.53)	0.9894	0.78 (0.45, 1.34)	0.3673
Etiology at cirrhosis				
NAFLD	REF		REF	
Alcohol	1.01 (0.49, 2.08)	0.9894	1.41 (0.64, 3.12)	0.3942
HCV+Alcohol	0.68 (0.32, 1.43)	0.3043	0.51 (0.20, 1.29)	0.1544
HCV	0.85 (0.45, 1.59)	0.6024	0.93 (0.52, 2.17)	0.8666
Others	0.29 (0.07, 1.18)	0.0841	NA	NA
AUDIT-C score				
Low	REF		REF	
High	1.17 (0.53, 2.57)	0.6902	1.21 (0.47, 3.06)	0.6959
eCTP				
A	REF		REF	
B	1.06 (0.60, 1.89)	0.8335	0.83 (0.42, 1.62)	0.5747
C	1.28 (0.11, 4.17)	0.6659	N/A	N/A
Dexamethasone				
No	REF		REF	
Yes	4.25 (2.08, 8.69)	**<0.0001**	3.78 (1.55, 9.22)	**0.0035**
Remdesivir				
No	REF		REF	
Yes	0.75 (0.33, 1.70)	0.4926	1.41 (0.55, 3.62)	0.4778
MELD-Na	1.03 (0.99, 1.08)	0.1183	1.04 (0.99, 1.09)	0.1661
PPI exposure				
No	REF		REF	
Yes	1.61 (1.06, 2.15)	**0.0007**	1.08 (0.55, 1.54)	0.7511
Median household income per $1000	0.98 (0.93, 1.07)	0.1567	0.99 (0.97, 1.03)	0.1078

Abbreviations: aHR, adjusted HR; AUDIT-C, Alcohol Use Disorders Identification Test–Concise; BMI, body mass index; COVID-19, coronavirus disease 2019; eCTP, electronic Child Turcotte Pugh; MELD-Na, Model for End-Stage Liver Disease–Sodium; NA, not available; PPI, proton pump inhibitor.

Bold indicates $p < 0.05$.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.