

### Answering Reviewer #1

1. The authors can use more figures and tables to summarize their findings, making it easier for readers to understand.

Thank you for this suggestion. We have included a new figure (Figure 1: SARS-CoV-2 infection induces microbial dysbiosis and intestinal inflammation) to introduce the inter-relationship between microbial dysbiosis and the pro-inflammatory response, including infiltration of lymphocytes. We highlight the increase in *Bacteroides* and *Ruminococcus* and loss of *Bifidobacterium* and *Faecalibacterium*. We also show the growth of opportunistic fungal infections observed in some individuals.

2. Some parts of the review needs to be readjusted to make the structure clearer, "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in the Gut", "Gut Inflammation and SARS-CoV-2", and "SARS-CoV-2 infection results in Microbial Dysbiosis in the Gut" are all about SARS-CoV-2 and gut. "Utility of Vitamin D as an Alternative Therapy for SARS-CoV-2 and IBD therapy" can be put in the last part.

We appreciate this feedback and made changes to the structure to better clarify the relationships of these sections. The structure of our review starts with infection of the gut, proceeds to the impact to the gut immune and microbial diversity, and finally describes the effect of this infection on the CNS and the gut-brain axis. We agree that the section of Vitamin D did not fit with this flow. In order to rectify this discrepancy without disrupting the structure of the paper, we incorporated the section of Th17 and Vitamin D into the discussion on gut inflammation since Th17 cells are the primary cells lymphocytes involved in the destructive inflammatory response in the gut.

#### Minor comments:

1. In the core tip part, "In this review, we summarize recent findings on COVID-19 pathogenesis in the gut-brain axis and offer therapeutic interventions to improve clinical outcomes." gut-brain axis or gut-brain-lung axis, please confirm it.

We have corrected this by changing it to "gut-brain-lung axis" in the core tip.

2. In the introduction part, "The pandemic has taken countless lives (approximately 2 million worldwide as of 01/15/2021) and unprecedented socio-economic losses." By 18 April 2021, the Confirmed deaths is 3,003,794, please update the number.

We have updated the deaths and infection numbers.

3. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the abbreviation should be used for the first time it appears.

We have corrected the abbreviations to introduce them the first time they are used.

### Answering the Science Editor

(1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

We have uploaded evidence of our NIH Grant Funding as requested

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor

We have uploaded our original figures as a PowerPoint file as requested. These figures were generated with BioRender which requires the figure to be exported in its entirety, including arrows and text.

(3) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights.

Thank you for pointing out this oversight. We have included this information in an acknowledgement at the end of the paper outlining the source (BioRender.com) according to their instructions. All figures were originally created by authors of this paper and not modified from templates, which would require a different citation method. All figures were exported as outlined in our agreement with BioRender, including the text added in this process.