Review 1: "Soft drinks can be misused to give false "false positive" SARS-CoV-2 lateral flow device results"

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RR:C19 Evidence Scale rating by reviewer:

- **Potentially informative.** The main claims made are not strongly justified by the methods and data, but may yield some insight. The results and conclusions of the study may resemble those from the hypothetical ideal study, but there is substantial room for doubt. Decision-makers should consider this evidence only with a thorough understanding of its weaknesses, alongside other evidence and theory. Decision-makers should not consider this actionable, unless the weaknesses are clearly understood and there is other theory and evidence to further support it.

Review:

This paper shows the results of an in vitro experiment dealing with the performance of a lateral flow assay (LFA) device authorized to diagnose SARS-CoV-2 infection in the United Kingdom. The main aim of this study is to verify whether some very common soft drinks or sweeteners can cause a false positive result when carrying out a Covid test, thus raising significant issues about this screening method.

The manuscript' s introduction section contextualizes the topic referring to a recent episode of students reporting false-positive results with the LFA in question after drinking flavored juice drinks or misusing them as analytes.

The methodology described in the study is clear and conducted with a rigorous approach.

Fourteen brands of commonly available soft drinks and four sweeteners were tested with the Innova SARS-CoV-2 antigen rapid qualitative test. First, each specimen was evaluated for pH, sugar content, and ingredients. Then, the specimen was applied to the LFA while the researchers recorded the result.

However, it should be stated that the two outcome assessors were not completely blinded. Only one of the outcome assessors did not know the sample type applied to the nitrocellulose membrane.

The results section shows outcomes consistent with the initial hypothesis, demonstrating that most of the specimens provided a false positive result when applied to the LFA.

In my opinion, the overall quality of the manuscript is acceptable and provides new knowledge that should be considered when employing rapid antigen tests in mass

screening programs for SARS-CoV-2.

However, the main limitation of this study is that it was carried out only with non-organic specimens directly applied to the LFA. Therefore, we cannot know the real incidence of false-positive results when a biological sample is applied to the nitrocellulose membrane. For example, biological samples may include saliva or respiratory samples. Another critical issue is that the specimens were tested on a single lateral flow assay type, one of the most commonly used in the UK for school testing. This feature does not allow us to understand whether the presence of false-positive results is a consequence of the application of soft drinks in general or a result of the interaction of the specimens with the specific reagents of this LFA device.

Therefore, the findings of this study do not provide fresh evidence for decision-makers and cannot be put into clinical practice before further well-structured clinical studies are performed, recruiting human subjects, analyzing biological samples, and different LFA devices.

These limitations should be highlighted in the discussion section.