Dear Kamran,

Thank you for reviewing our paper. Please see below for our responses to your comments.

1. There is some new evidence – summarized here, that you may wish to consider

https://twitter.com/mac_puck/status/1541329319330553856?s=20&t=lkwxJzaP3j-XaJJwJxLssQ

This Twitter thread by Jim Grace is entirely unreferenced, and contains numerous misleading statements. For example, Grace states that "*The reason we approved Pfizer and AZ faster than the EU initially was we took a gamble on safety and gave a waiver on liability. The AZ blood clot thing shone a very harsh light on all that*." The MHRA decisions on approving covid-19 vaccines for use in the UK were made with the evidence available at the time. Rare adverse events – such as clotting problems following the AZ vaccine or myocarditis following mRNA vaccines – can't be detected until a vaccine is in widespread use. This is discussed in one of our previous articles and is the reason why studies were set up in the UK and elsewhere to identify and quantify any rare but serious side effects of covid-19 vaccines (see **Majeed A, Papaluca M, Molokhia M. Assessing the long-term safety and efficacy of COVID-19 vaccines. J R Soc Med. 2021 Jul;114(7):337-340**). Giving the AZ vaccine a prominent role in the UK's Covid-19 vaccination programme was a rational decision based on the available evidence in late 2020 on safety and efficacy, and because of the lower cost and simpler storage requirements of viral vector vaccines compared to mRNA vaccines. When problems were identified with the AZ vaccine, appropriate action was taken by the UK government. Finally, although viral vector vaccines are now no longer widely used in many developed countries (including the UK), they did play a key role in reducing global mortality from Covid-19 (see **Which covid-19 vaccine saved the most lives in 2021?** https://www.economist.com/graphic-detail/2022/07/13/which-covid-19-vaccine-saved-the-most-lives-in-2021).

Grave states "*Adopting the Tory philosophy of "lie first and hope nobody notices" our vaccine rollout was slowed to a crawl and soon we were overtaken by Italy, Spain, France, Germany, Ireland, Denmark etc.*" The graph used to illustrate this statement is for vaccine uptake in 12-17 year olds between January to August 2021. As Covid-19 vaccines were not approved for general use in children aged 12 and over until September 2021, the graph show exactly what we would expect – a very low take-up of vaccines in the UK in this group compared to countries that approved Covid-19 vaccines for use in this group earlier in the year. The correct graph to have shown would have been for vaccine uptake in adults. Also vaccine uptake was not uniform across Europe and many countries (particularly those in the Eastern part of the EU) continued to have a slow uptake of vaccines, illustrating that public attitudes towards vaccination – as well as vaccine supply – are an important determinant of vaccine uptake.

In conclusion, there is nothing new in this Twitter thread. That the UK's vaccine programme was constrained by supply issues during early 2021 was well known at the time, and was commented on by numerous people (including Majeed and Hodes). One factor that Grace does not consider is that part of the reason for the slowdown in vaccination rates for first doses in mid-2021 was that by then, the UK vaccination programme was targeting groups that were vaccine hesitant and less likely to come forwards for vaccination (see **Where are we with covid-19 vaccination in the United Kingdom?** https://blogs.bmj.com/bmj/2021/07/09/where-are-we-with-covid-19-vaccination-in-the-united-kingdom/). In the second half of 2021, vaccine supply in the UK improved considerably as shown by the very high daily vaccination rates seen during the booster programme in late 2021.

2. *There does seem to be a bit of a mismatch between the questions in the box and the text and we do think the comments on JCVI and childhood vaccination are much more restrained than is justified, especially as we now have their most recent minutes. Summary here:*

https://twitter.com/profcolindavis/status/1454577561808297989?s=21&t=uDcjMBkmxkDxZRxHFV__0A

https://twitter.com/sgriffin_lab/status/1454944267219132419?s=21&t=uDcjMBkmxkDxZRxHFV__0A

https://twitter.com/chrischirp/status/1537125049077055491?s=21&t=uDcjMBkmxkDxZRxHFV__0A

https://twitter.com/karamballes/status/1454235882400145414?s=21&t=uDcjMBkmxkDxZRxHFV__0A

We think our comments about the JCVI are reasonable and balanced. The JCVI took a more cautious view about implementing Covid-19 vaccination in children than some other countries, based on the lower absolute benefits compared to vaccination in older people and because of the potential risks from myocarditis, which made the decision about approval more finely balanced for children. Although many people disagreed with this decision, it was not an extreme position. For example, it was supported by the two main medical royal colleges for doctors responsible for the health care of children and for vaccine delivery in the UK, the RCPCH and the RCGP (see https://www.rcpch.ac.uk/resources/covid-19-vaccination-children-young-people and https://rcgp.org.uk/news/covid-vaccines-children-young-people). Some other countries also delayed the decision of the use of vaccines in children; and recently, the government in Denmark has announced it will stop covid-19 vaccination for most under 18-yeara olds.

We haven't critiqued the twitter threads above in detail but the language in them is often intemperate, using terms such as **gaslit** and **FFS**, and has no place in academic discourse. For example, Karam Bales states that "*Looks like I was right, JCVI mainly only looked at PHE's own studies, the ones they've gaslit us with for over 18 months*." Covid-19 vaccine research is an area where the UK has played a leading role and data from the UK has helped guide vaccine policies globally (see **Majeed A, Tessier E, Stowe J, Mokdad A H. How data from the United Kingdom has guided covid-19 vaccine policies BMJ 2022; 376 :o839**).

3. *Simply because it is so widely misrepresented, it would be good to note that the EUA was given while the UK was still working under EU law.*

We have added a statement on this on page 5 in the paragraph about MHRA approval of vaccines.

"The UK became the first country in Europe to grant an Emergency Use Authorisation for a covid-19 vaccine when the MHRA gave approval for use of the Pfizer-BioNTech vaccine in adults in the UK on 2 December 2020. The AstraZeneca vaccine was approved for use in adults on 30 December 2020. ***Both these decisions took place when the UK was still operating under EU law and were therefore entirely unrelated to Brexit****."*

4. *A few more key messages are contained in the last 2 paras (lessons for the future) – e.g. investment in UK scientific infrastructure (though this is a bit general); we think a key message about transparency of decision making by JCVI would be a good thing to highlight too.*

We have added a key message about the importance of transparency in the decision-making by the JCVI on page 12.

Greater transparency about the work of the JCVI and a level of public dialogue that is appropriate for the 21st century world we now live in are essential to maintain public confidence in the decisions made by the JCVI, reduce levels of vaccine hesitancy, and maintain high vaccine uptake in the UK.

We have also added a comment and reference on page 11 on the recent announcement of the partnership between the UK government and Moderna, which will start to address one of our key messages; that the UK is currently very reliant on overseas manufactured mRNA vaccines for its Covid-19 vaccination programme.

7. Would there be merit in adding a question for the inquiry about procurement and the over-procurement of vaccines (and impact on availability for other countries)?

We have added two questions on this. Developed countries did over-procure vaccines and this would have reduced the availability of vaccines for lower income countries. This is now less of an issue for Covid-19 vaccines because production globally has increased substantially but could arise again in the future for a vaccine for a different pandemic or if an updated vaccine was required for a new variant of SARS-CoV-2.

Q11. Did the UK government take the correct decisions about vaccine procurement? Was the UK correct to work alone on procurement or should there have been greater collaboration with the EU?

Q12. What impact did the over-procurement of vaccines by developed countries such as the UK have on vaccine equity and on the supply of vaccines for lower income countries early in the pandemic?