## **Conclusions**

In spite of the rapid development of effective vaccines, there is still a worldwide crisis as highly transmissible delta variant is replacing other circulating variants

Public funding of profitable vaccines entitles the public to share in the benefits of vaccines, and creative solutions could increase the opportunity for more people to be vaccinated

While immunology of protection is complex, protection may be predicted by antibody responses as measured directly after vaccination. Key questions include absolute correlate, role of anamnestic response, contribution of T cells, platform dependence of conclusions

Animal studies model delta variant pathogenesis in humans, including higher viral loads, greater shedding





Randomized data are lacking for delta variant with most vaccines. Vaccine efficacy for beta variant is variable, but VE against severe disease remains. Drops in VE vs. symptomatic disease may not predict drops in VE vs. severe disease.

Reductions in vaccine neutralizing titers to delta variant are not as great as some other variants. Variants may not escape T cell responses. Durability in elderly may be lower. Efficacy against severe disease may be less dependent on neutralizing antibodies.

Observational studies may not yield accurate assessments of vaccine efficacy over time.

So far, observational studies have not detected waning of vaccine efficacy against severe disease.

Neutralizing titers fall faster than vaccine efficacy after mRNA vaccination. Overall, clinical evidence of need for boosting is sparse. The fact that reduced neutralizing antibodies can be boosted implies that vaccines induce robust memory immune responses.





Importance of safety infrastructure and follow-up if boosting is implemented. Importance of global coordination of vaccine safety surveillance. Potential for collection of more data if boosting is gradually implemented, importance of looking at currently available data. Considerations for special populations, including pediatrics. Consider cumulative effect of repeated immunizations and lipid nanoparticles. Be open and transparent, communication. Mechanisms of AEs.

There still are gaps in understanding optimal vaccination doses and regimens and (if additional doses are needed) what antigens or platforms should/can be used in different situations.

Ability to predict protection against severe disease would facilitate decision-making. Dose adjustment, even if antibody responses were lower, could make more vaccines available and may thus save lives. Studies of adjusted doses, including in boosting, could make a large public health difference.





Value of coordinating use of surveillance systems to target interventions. Importance of research to develop strategies for vaccine use in the context of other interventions Importance of collecting and sharing data as vaccines are deployed. Importance of considering new vaccines that may be more readily deployable.





## Final thoughts

We have effective vaccines, and so far they are doing what they need to do.

There is no reason to panic, or to allow fear to drive policy decisions.

We need to find ways to vaccinate more people in all countries, regardless of wealth.

Implementation of a coordinated research agenda will allow us all, working together, to bring the world closer to ending the pandemic for everybody.



