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**From:** 5.1.2e 5.1.2e  
**Sent:** Tue 3/2/2021 9:06:08 PM  
**Subject:** Preprint test negative design study - and comments on VE against infectiousness  
**Received:** Tue 3/2/2021 9:06:08 PM  
[Report Early effectiveness of COVID vaccines.pdf](#)

Hi 5.1.2e

Yes, the VE against infectiousness is a super relevant question. I know the epicconcept people are trying to study this with health care workers, and their households.

A complicating factor is that you also need asymptotically infected indexes (vaccinated and unvaccinated), to also assess their role in onward transmission. It is too limited to only assess it amongst symptomatic infected people.

This requires intensive testing of a group at high risk of exposure, to find infected people, and then to follow up their households.

Of course proxy measures such as viral load and whether people carry virus that can be cultured is also useful – but again you need this also in asymptomatics.

5.1.2e 5.1.2e did a sample size calculation – she concluded we would need to follow up a few thousand people with a weekly test – and then f/u their household contacts in case someone is positive – for the moment we decided this is too labour and cost intensive.

An outbreak investigation would be a good opportunity to document VE against infectiousness, but it would need to be a large outbreak in a relatively closed setting where contact between people can be tracked well – challenging!

We tried a study on mumps vaccine effect against infectiousness - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5223546/> - which failed, not enough asymptomatic infections detected – too few participants...

I suspect the answer about whether the vaccine protects against onward transmission will depend on inference from case reports where people got it from a vaccinated person, in some special situation where they could have not acquired it from someone else. And then the key thing is whether the index had primary or secondary vaccine failure: primary occurs in a know proportion, and is likely to be infectious; whereas secondary vaccine failure is uncertain in terms of incidence and whether they can transmit...

Attached a nice preprint of a TND case control – also very useful data for action: hopefully we will start to use the Astra Zeneca vaccine soon in elderly here in the Netherlands.

Best wishes,

5.1.2e