Vraag 1. Het interval tussen eerste en tweede dosis Pfizer bij 80+

- Nauwelijks data (het wachten is op de UK), slechts **1 preprint** die enige aanwijzing geeft: https://www.medrxiv.org/content/10.1101/2021.02.03.21251054v1

Studie in <80 vs. 80+ subjects (n=26, median age 82y, 30% female, geen info comorbiditeiten) gevaccineerd volgens 3-weekse interval.

We observed poor neutralisation activity exclusively in participants over the age of 80 (7/15) as compared to those under 80 (0/11) after the first dose. Geometric mean neutralisation titres in the over 80 years group after the first dose were almost an order of magnitude lower than in younger individuals. Three weeks after the second dose, the vaccine sera exhibited an increase in neutralizing titres against the wild-type pseudoviruses between first and second doses. The seven poor responders now demonstrated neutralisation activity comparable to those who responded to the first dose and there was no statistically significant difference in neutralizing titres between participants above and below the age of 80.

➔ Dus: significante aanwijzingen voor inadequate virus neutralisatie bij 80+'ers na 1e prik, welke om die reden baat lijken te hebben bij een 2e dosis. Hoewel geen correlaten van bescherming bekend, zou afgeleid hiervan een langer interval ongunstig zijn in deze groep, met name in het licht van kans op infectie en, waar mogelijk, immune escape mutations. Maar, kleine studie dus, en er is niet naar een langer interval dan 3 weken gekeken, dus onbekend hoe de response na de 1e dosis nog verder uit rijpt in deze oudere groep. De UK data gaat ons hopelijk snel aanwijzingen geven.

Vraag 2. Een of twee vaccinaties na doorgemaakt infectie:

- **Publicatie in Eurosurveillance** (11 feb 2021) https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.6.2100096?emailalert=true.

Vaccine data (Pfizer) uit Israël onder HCW (n=514, 19-77y, 62% female) na 1e prik.

Among all vaccinated HCWs, 475 (92%) had detectable anti-SARS-CoV-2 spike IgG antibodies and among these, GMC was 68.6 AU/mL (95% CI: 64–73.6). The 39 HCWs who did not respond to the first dose were older (median age 57 vs 45 in other, p < 0.001) and more likely to be Jewish (31/38 non-responders of known ethnicity, 82% vs 291/459 responders of known ethnicity; 63%; p = 0.01). Among responders, there was no statistically significant difference in antibody titres between males and females and between different ethnicities, but titres decreased with increasing age (p < 0.001). The trend persisted when previously infected individuals were excluded (p < 0.001).

➔ Verschillen zijn overigens wel klein tussen leeftijden en in het licht van ontbreken van correlate of protection niet bekend of dit klinische relevant is (want efficacy data suggereert immers geen verschillen tussen age groups)

➔ The sample is relatively small and therefore did not allow for adjusted analyses. In addition, information on co-morbidities was not available and since the study population only includes HCWs, it may not be representative of the wider population: elderly individuals in particular are under-represented.

Compared with HCWs with no evidence of previous infection, post-vaccination IgG levels among those with previous evidence of infection were much higher (GMC 573 vs 61.5). IgG titres among those with previous evidence of infection were at least one order of magnitude higher than those without, regardless of whether IgG antibodies were detectable before being vaccination

- ➔ Kortom: Low numbers of previous infected people included (n=17), but a single dose of vaccine in these individuals seems to boost the response, although the optimal timing between infection and vaccination as well as the ensuing duration of protection remain to be determined.

- **Preprint** (1 feb 2021), by Kramer et al (New York)

https://www.medrxiv.org/content/10.1101/2021.01.29.21250653v1.full.pdf.

Data aangaande mRNA vaccines van Pfizer en Moderna (geen specifieke aantallen bekend per vaccine): n=109 individuals, waarvan 41 met previous infection. Niets beschreven qua gender, age, severity of previous infection, maar gezien de titerverschillen in pre-samples lijkt het te gaan om een brede range vwb ernst ziekte.

*In this short report, we show that the antibody response to the **first vaccine dose** in individuals with pre-existing immunity is equal to or even exceeds the titers found in naïve individuals after the **second dose**. We also show that the reactogenicity is significantly higher in individuals who have been infected with SARS-CoV-2 in the past. Changing the policy to give these individuals only one dose of vaccine would not negatively impact on their antibody titers, spare them from unnecessary pain and free up many urgently needed vaccine doses.*

- ➔ *The antibody titers of vaccinees with pre-existing immunity are not only 10-20 times higher than those of naïve vaccines at the same time points, but also exceed the median antibody titers measured in naïve individuals after the second vaccine dose by more than 10-fold.*
- ➔ *To note: Vaccine recipients with pre-existing immunity experience systemic side effects with a significantly higher frequency than antibody naïve vaccines (e.g., fatigue, headache, chills, fever, muscle or join pains, in order of decreasing frequency, $P < 0.001$ for all listed symptoms).*

- **Preprint:**

https://www.medrxiv.org/content/10.1101/2021.02.07.21251311v1.full

Klein studie, n=32, 13 previous infected (mild/asymptomatic, waarvan 11 zes maanden geleden geinfecteerd), 19 naïve, age range: 24-62.

Here, we evaluated immune responses in 32 subjects who received two-dose BNT162b2 mRNA vaccination. In individuals naive to SARS-CoV-2, we observed robust increases in humoral and antigen-specific antibody-secreting cell (ASC) responses following each dose of vaccine, whereas individuals with prior exposure to SARS-CoV-2 demonstrated strong humoral and antigen-specific ASC responses to the first dose but muted responses to the second dose of the vaccine for the time points studied.

- ➔ Respons was na de twee prik voor beide groepen even hoog, vooral omdat de tweede prik bij de naive deelnemers enorme boosted, en bij de pre-exposed een stuk minder. Voor neutraliserende antistoffen gold hetzelfde (hoewel getest in een kleine subset).