IMPACT VAN DE VACCINATIESTRATEGIE OP DE GELDENDE MAATREGELEN ROND TESTEN EN QUARANTAINE IN INITIËLE FASE – 2e UPDATE.

RAG vergadering 20/04/2021

Eind december werd een eerste advies afgeleverd in verband met **eventuele wijzigingen aan de huidige geldende procedures met betrekking tot quarantaine en testen van personen die gevaccineerd zijn**. Een eerste update werd uitgebracht eind februari. Omwille van een initiële lage vaccinatiegraad bij risicogroepen en onvoldoende gegevens rond het effect op transmissie werden slechts erg beperkte wijzigingen aan de geldende richtlijnen aangeraden. Het huidige document bevat de 2e herziening. De RAG maakte in zijn eerdere adviezen reeds gewag van mogelijke problemen rond billijkheid zolang niet iedereen toegang heeft gehad tot vaccinatie en zolang er geen vrije keuze is van het type vaccin. Momenteel buigt een groep experten van de GEMS aangevuld met juridische, ethische en sociologische experten zich over deze meer ethische en maatschappelijke vraagstukken (bv. wat mogen gevaccineerde personen onderling wel/niet doen?).

1. Aanbevelingen :

- **De eerste resultaten uit andere landen bevestigen dat vaccinatie een sleutelrol speelt in de terugkeer naar het normale leven. Het is daarom uitermate belangrijk de bevolking te motiveren om zich te laten vaccineren. Correcte informatie en doelgerichte communicatie zijn daarbij onontbeerlijk, waarbij zowel de voordelen voor het individu (bescherming tegen ernstige ziekte) als voor de samenleving (bescherming gezondheidszorgsysteem, vermindering viruscirculatie) benadrukt moeten worden.**
- Gezien de beperkte beschikbaarheid van vaccins gebeurt de uitrol echter gradueel. De vaccinatiegraad neemt de laatste tijd sterk toe maar ligt momenteel nog laag bij risicogroepen. In die omstandigheden blijven niet-farmaceutische interventies (zoals het dragen van mondmaskers, testen en quarantaine) bijzonder belangrijk. In welk ritme versoepelingen voor de volledige populatie kunnen gebeuren, vormt het onderwerp van politieke beslissingen, rekening houdend met een wetenschappelijk advies dat voorbereid wordt door de GEMS.
- De verschillende aspecten die een invloed hebben op dit advies, namelijk de epidemiologische situatie in België (in het bijzonder de hospitalisaties), de vaccinatiegraad, circulatie van VOCs, en de wetenschappelijke kennis rond vaccins (in het bijzonder wat betreft het risico op transmissie na vaccinatie) zullen nauw opgevolgd worden. Een herziening van dit advies is daarom voorzien binnen één maand.
- Zowel uit praktische overwegingen (controleerbaarheid) als omwille van het onvolledige effect van vaccinatie op transmissie, blijven de algemene preventieve maatregelen zoals physical distancing en het dragen van mondmaskers in openbare ruimtes ook gelden voor personen die al gevaccineerd zijn.
- Voor de aanbevelingen in dit document betekent “gevaccineerd” dat personen volledig gevaccineerd zijn, dat wil zeggen:
    - voor Comirnaty® (Pfizer-BioNTech): ≥7 dagen na de tweede dosis
    - voor COVID-19 Moderna vaccin (Moderna): ≥14 dagen na de tweede dosis
    - voor Vaxzevria® (AstraZeneca-Oxford): ≥15 dagen na de tweede dosis
    - voor Janssen COVID-19 vaccine: ≥14 days na de eerste dosis

Voor personen die partieel gevaccineerd zijn, gelden dezelfde regels als voor personen die nog niet gevaccineerd werden.

- De bescherming die de vaccins bieden is hoog, maar geen 100%. **Gevaccineerde personen die mogelijke symptomen vertonen van COVID-19 moeten daarom net als niet-gevaccineerde personen contact nemen met een arts om een test te ondergaan**. Er wordt herhaald dat zelftesten NIET gebruikt kunnen worden bij symptomatische personen (gevaccineerd of ongevaccineerd.)
- Personen die ondanks vaccinatie toch een COVID-19 besmetting oplopen, moeten net als ongevaccineerde personen in isolatie, ook al vertonen ze geen symptomen. Er zijn aanwijzingen dat deze personen over het algemeen minder besmettelijk zijn, maar besmettelijkheid is zeker niet uitgesloten. Dit geldt óók voor bewoners van WZC waar een hoge vaccinatiegraad behaald is bij de medebewoners.
- Er is toenemend bewijs dat vaccinatie ook een effect heeft op transmissie. De bescherming is echter onvolledig en mogelijk afhankelijk van het type vaccin, leeftijd en onderliggende aandoeningen van de gevaccineerde en circulerende virus-varianten. **Zolang de vaccinatiegraad in risicogroepen laag ligt, betekent dit dat er slechts in onderstaande situaties uitzonderingen op de quarantaine toegestaan kunnen worden** voor personen die reeds gevaccineerd werden. De vaccinatiegraad in de algemene bevolking zou de komende weken sterk moeten stijgen, waarbij er verwacht wordt dat tegen midden juni elke inwoner ≥45 jaar minstens een eerste dosis aangeboden heeft gekregen. Zoals hoger vermeld zal dit advies binnen één maand geherevalueerd worden, waarbij rekening gehouden zal worden met eventuele nieuwe gegevens rond transmissie na vaccinatie, de algemene epidemiologische situatie en de stijgende vaccinatiegraad.
    - Die hoge vaccinatiegraad in risicogroepen wordt nu reeds bereikt in vele woonzorgcentra. **Asymptomatische gevaccineerde personeelsleden van WZC mogen blijven werken na een hoog-risico contact indien de vaccinatiegraad bij bewoners ≥90% is en ≥70% bij personeelsleden**. Ze dienen wel nog steeds getest te worden zoals andere HRC.
    - Gevaccineerde zorgverleners die niet onder de hogervermelde situatie vallen, moeten in principe wel in quarantaine na een hoog-risico contact. Een **uitzondering hierop is enkel toegestaan indien noodzakelijk voor de continuïteit van de zorg**, onder de reeds bestaande voorwaarden (zie procedures).
- Bij preventieve screening is de pre-test probabiliteit lager dan in andere indicaties. Bij gevaccineerde personen is het a priori risico op besmetting nog lager, zodat preventieve screening enkel dient te gebeuren indien het risico in geval van onopgemerkte infectie bijzonder groot is. Dat is bv. het geval pre-transplant (risico voor receptor) of bij ziekenhuisopname (risico voor ongevaccineerde medepatiënten). Bij beslissingen rond preventieve screening in woonzorgcentra moet steeds rekening gehouden worden met de vaccinatiegraad van zowel personeel als bewoners.
- In woon-zorgcentra of andere residentiële collectiviteiten die een hoge vaccinatiegraad hebben bereikt, is het risico op een uitbraak onder de bewoners beperkter dan in de algemene samenleving. WZC zijn echter geen eilanden die geïsoleerd zijn van de bredere samenleving: er is nog interactie via bezoekers en personeelsleden. Bepaalde maatregelen, zoals het dragen van mondneusmaskers door de personeelsleden, moeten dan ook blijven gelden.

- **De aanbevelingen worden samengevat in de tabel op volgende bladzijde.**

2. Overzicht mogelijke impact en aanbevelingen

Onderwerp	Hoofdpunten huidige procedure (link)	Aanbeveling voor gevaccineerden
Mogelijke gevallen van COVID-19	Elk mogelijk geval wordt getest Antigen-test mogelijk als symptomen ≤5 dagen	Zelfde indicaties voor testen **Sterke voorkeur voor PCR-test** Indien positief: melden + sequencing
Isolatie van bevestigde gevallen	10 dagen waarvan minstens 3d koortsvrij Speciale regels in ziekenhuizen, immunogecompromitteerden, ernstige ziekte.	Geen wijzigingen.
Contact tracing		
Indexgeval	HRC identificeren vanaf 2d vóór symptoombegin → quarantaine	Geen wijzigingen.
Hoogrisicocontact (HRC)	Test en 7-10 dagen quarantaine Werken uitzonderlijk toegestaan voor zorgverleners indien noodzakelijk	Personeel WZC: werken toegestaan (wel test) indien asymptomatisch en vaccinatiegraad bewoners ≥90% EN personeel ≥70%. Geen wijzigingen zolang vaccinatiegraad in risicogroepen laag ligt. Indien werken uitzonderlijk noodzakelijk voor continuïteit zorg: voorrang aan gevaccineerde werknemers.
Cluster	Niet-WZC: uitgebreidere testing van laag-risico contacten met antigen-test WZC: uitgebreide testing personeel/bewoners met PCR	Geen wijzigingen.
Reizigers		
Niet-Belgische residenten	Verplichte negatieve test en quarantaine in bepaalde omstandigheden	Geen wijzigingen.
Terugkerende inwoners	Quarantaine en test verplicht in bepaalde omstandigheden	Geen wijzigingen.
Preventieve screening		
Personeel WZC	Overweeg regelmatige screening met PCR op speekselstaal	Geen screening indien vaccinatiegraad bewoners ≥90% en personeel ≥70%
Bezoekers WZC	Overweeg om snelle antigentesten in te zetten vóór bezoek	Geen screening indien vaccinatiegraad bewoners ≥90% en personeel ≥70%
Ziekenhuisopname	Systematische screening bij hoge prevalentie / risicoafdeling	Screening indien risico op overdracht naar ongevaccineerde medepatiënten.
Nieuwe bewoners residentiële collectiviteit (opname vanuit thuis-setting)	Systematische screening & kamerisolatie in afwachting resultaat	Systematische testing. Geen isolatie op kamer noodzakelijk in afwachting van resultaat tenzij vaccinatiegraad bewoners <90% of personeel <70%
Andere beroepen (bv. leerkrachten)	Arbeidsarts kan beslissen tot systematische screening	Geen nut van screening bij gevaccineerde zonder contact risicopopulatie
Pre-transplant screening donor	Systematische screening	Geen wijzigingen (omwille van hoog risico voor acceptor)

3. Situatie

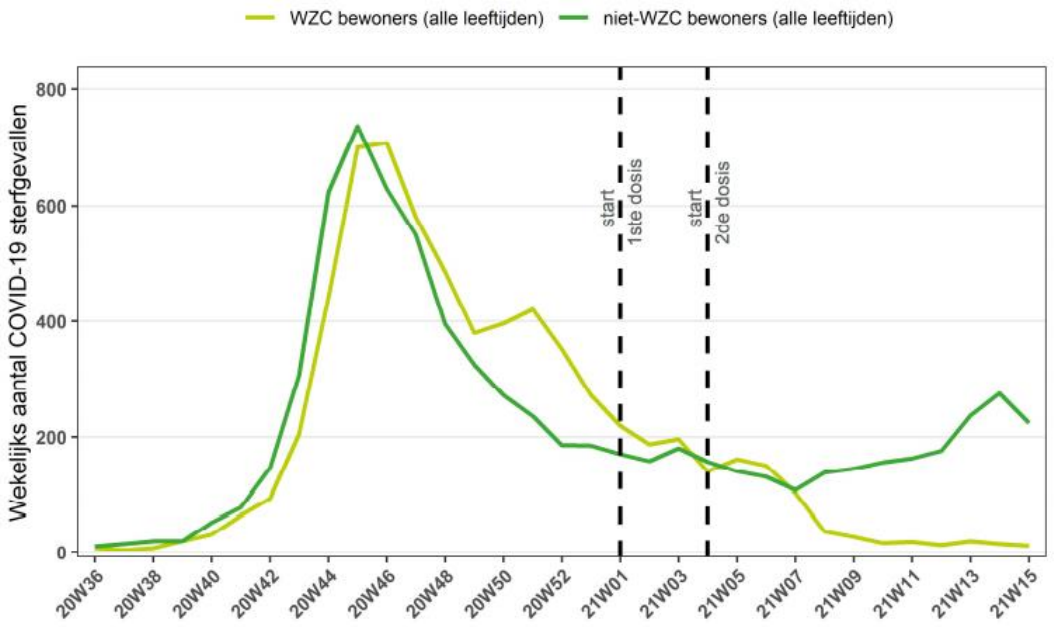
- Op 20/4/2021 bedroeg de cumulatieve 14-daagse incidentie van nieuwe gevallen 424/100 000 inwoners en bedroeg het wekelijks gemiddelde 233 nieuwe ziekenhuisopnames per dag.

Tabel 1: Cumulatief aantal personen die een eerste en tweede dosis van het COVID-19 vaccin kregen, volgens leeftijdsgroep, status op 20/04/2021 *Bron: Vaccinnet+, dagelijks epidemiologisch rapport Sciensano*

		Totale bevolking [1]	Bevolking van 18 jaar en ouder [1,2]	Bevolking van 65 jaar en ouder [1,2]
Vaccinatiegraad minstens 1 dosis	België	19,9%	24,9%	64,4%
	Brussel [3]	14,8%	19,2%	66,0%
	Vlaanderen [3]	20,7%	25,6%	64,0%
	Wallonië [3,4]	20,0%	25,2%	64,1%
	Duitstalige Gemeenschap [3]	20,8%	25,7%	78,1%
Vaccinatiegraad volledig gevaccineerd	België	6,2%	7,7%	12,7%
	Brussel [3]	4,1%	5,2%	14,5%
	Vlaanderen [3]	6,4%	8,0%	11,8%
	Wallonië [3,4]	6,3%	7,9%	13,8%
	Duitstalige Gemeenschap [3]	7,2%	9,0%	19,9%

- Gedetailleerde informatie in verband met de vaccinatiegraad in WZC is beschikbaar in een apart rapport. Op basis van een bevraging waaraan > 85% van de Belgische WZC heeft deelgenomen, was **de bereikte vaccinatiegraad onder de bewoners van de WZC zeer hoog in al deze instellingen, met een nationaal gemiddelde van 89,4%.** De eerste tekenen van het gunstige effect van deze massale vaccinatie op de COVID-19- epidemie beginnen zichtbaar te worden, met een daling van het aantal clusters van bevestigde gevallen in WZC, maar ook van het aantal ziekenhuisopnames en sterfgevallen onder de Belgische WZC bewoners. Daarentegen is de **vaccinatiegraad van het WZC personeel lager**. Op 24 maart 2021 lag deze tussen de 47 % en 65 % in de Brusselse, de Duitstalige en Waalse WZC, en bereikte deze 86,5 % in de Vlaamse WZC.

Figuur 1: Vergelijking van de mortaliteit in twee groepen met sterk verschillende vaccinatiegraad: bewoners van woonzorgcentra en algemene bevolking. *Bron: thematisch rapport COVID-19 vaccinatie in WZC, Sciensano*



4. Overwegingen

- Er is toenemend bewijs dat vaccinatie ook een effect heeft op transmissie. De bescherming is echter onvolledig en mogelijk afhankelijk van het type vaccin, leeftijd en onderliggende aandoeningen van de gevaccineerde en circulerende virus-varianten.
- Eventuele wijzigingen in de bestaande procedures vragen voldoende tijd voor implementatie op het terrein (informatie stakeholders, opleiding medewerkers call center, technische implementatie…) en zijn bij voorkeur niet al te complex. Inmiddels zijn verschillende vaccins op de markt die onderling verschillen in kenmerken. Er is geen vrije keuze van type vaccin door het individu. Richtlijnen die alle gevaccineerde personen (onafhankelijk van het type vaccin) op dezelfde manier behandelen, zijn het eenvoudigste qua logistieke implicaties en qua duidelijkheid in communicatie naar de bevolking.
- De RAG leden uitten reeds vroeger hun bezorgdheid over mogelijke ongelijke behandeling:
    - Vanuit motivationeel oogpunt zou het verbinden van bepaalde voordelen aan vaccinatie (bv. geen of verkorte quarantaine) de bereidheid tot vaccineren kunnen verhogen. Daar staat tegenover dat tot dusver steeds een beleid gehanteerd is dat gebaseerd is op solidariteit en op het beperken van transmissie: er is steeds geëist dat ook personen met een laag persoonlijk risico op ernstige ziekte (zoals jongeren) de maatregelen respecteren.
    - Het verbinden van bepaalde voordelen aan vaccinatie stelt mogelijk een probleem van billijkheid zolang er geen gelijke toegang tot vaccins is voor iedereen. Bovendien is het interval vanaf de 1e dosis tot volledige vaccinatie verschillend naargelang het vaccin (2 weken na 1e dosis voor Johnson&Johnson vs. 12 weken voor AstraZeneca-Oxford vs. 3 weken voor Pfizer-BioNTech) zodat ook personen die behoren tot dezelfde groep, zoals zorgverleners in 1e lijn, niet op hetzelfde moment volledig gevaccineerd zullen zijn.

  De RAG noteert dat deze bezorgdheden momenteel het onderwerp uitmaken van een multidisciplinair advies dat door een aparte werkgroep voorbereid wordt en waarover uiteindelijk

een politieke beslissing genomen zal moeten worden. De RAG heeft daarom de voorgelegde vragen rond mogelijke uitzonderingen op quarantaine vanuit een wetenschappelijk invalshoek benaderd: slechts beperkte gegevens rond effect op transmissie die een reëel maar onvolledig effect suggereren, binnen de huidige context van hoge viruscirculatie en sterke druk op het gezondheidszorgsysteem, met toenemende maar nog lage vaccinatiegraad en nog onduidelijkheid over effecten van VOCs.

- Het dragen van mondneusmaskers en andere verstrengde maatregelen van infectiepreventie hebben ook een aantoonbaar gunstig effect gehad op andere respiratoire aandoeningen, zoals Influenza, wat een bijkomend argument is om ook in WZC met hoge vaccinatiegraad verder mondmaskers aan te bevelen voor personeelsleden.

5. Update scientific evidence

5.1. VACCINE EFFECTIVENESS (PROTECTION AGAINST SYMPTOMATIC DISEASE)

Clinical trials have reported high efficacy of currently available vaccines (1–3). As opposed to clinical trials, which evaluate vaccines in highly-controlled settings, vaccine effectiveness studies report on vaccine outcomes in real-life settings.

First results of vaccine effectiveness (VE) studies are highly promising, with results mainly available for Comirnaty® (Pfizer-BioNTech) and Vaxzevria® (AstraZeneca-Oxford). In general, a good protection against symptomatic disease (4–11), hospitalization (5,6,11,12) and death (5,6) are found. Furthermore, a majority of these studies show substantial protection after the first dose, which further increases after the second dose (4–8,10).

If VE has been found to decline mildly but significantly with age (10), several studies have now shown that **high effectiveness is still achieved in the elderly** (5,6,12). In a study from Israel, effectiveness of Comirnaty® against symptomatic COVID-19 in individuals of 70 years and older was slightly lower after the first dose but similar after the second dose, when compared to the general population (6). In an English pre-print focusing on people ≥70 years old, very high effectiveness against symptomatic infection was achieved with both Comirnaty® and Vaxzevria®. In those ≥80 years old with a positive test ≥14 days after the first dose, a substantial reduction was noted in risk for hospitalisation (>37%) and death (51% for Comirnaty®, insufficient data to assess Vaxzevria®) (5). A Scottish pre-print, focusing on VE of the first dose against hospitalisation, found that effectiveness in those ≥80 years old was 81% (95% CI: 65–90) (combined Comirnaty®/Vaxzevria® effect, no separate estimates available). Of note, in this study, peak effectiveness (for all age groups combined) was found at 28-34 days after the first dose (85% (95% CI: 76–91) for Comirnaty® and 94% (95% CI: 73–99) for Vaxzevria®) (12). Interestingly, a Danish pre-print looking at residents (median age 84 years) and staff of long term care facilities found close to no protective effect against laboratory confirmed SARS-CoV-2 14-25 days after the first dose of Comirnaty®, but VE >7 days after the second dose increased to 64% (95% CI: 14–84) in residents and 90% (95% CI: 82–95) in staff. The authors suggest that this may be due to increased testing (and therefore increased detection of asymptomatic cases) (9). However, other studies have found higher VE despite incorporated data from regular testing schemes (4,8), so the exact reason for this difference remains to be elucidated. **In general, direct comparison of the referred articles is hard due to differences in test strategies, dosage schemes, vaccines, outcomes, time points, study populations and epidemic context.**

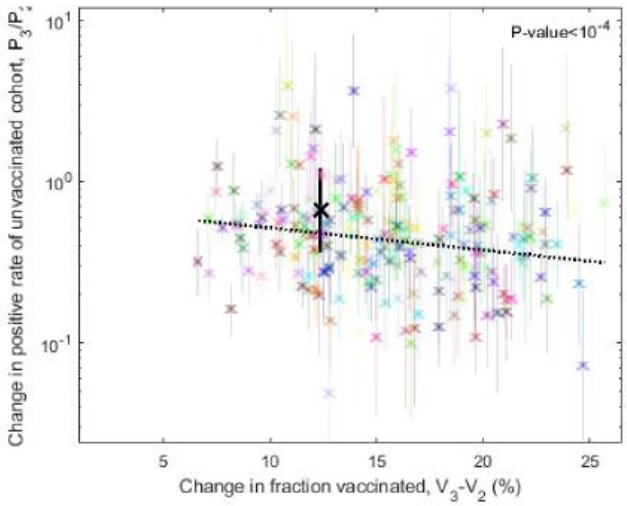
5.2. EFFECT ON TRANSMISSION

Interventions like quarantine and testing seek not to minimize the risk for the individual, but rather aim to protect the community by preventing onwards transmission. Since there is evidence that **truly asymptomatic infections are less contagious than symptomatic disease** (13–16), a vaccine that is effective in preventing symptomatic disease might automatically have some impact on transmission. Additionally, several studies have suggested a lower viral load in infected individuals after the first dose of an mRNA vaccine (17,18). Since viral load seems related to the risk of transmission (19,20), these breakthrough cases might be less transmissible. However, if a vaccinated individual is unaware of his/her asymptomatic infection and no longer complies with non-pharmaceutical interventions, he/she might unknowingly contribute more to the spread of the disease. Studies that assess the risk of transmission and asymptomatic infection are therefore key.

Direct evidence on the risk of transmission from vaccinated individuals is currently only available from one Scottish pre-print study. In the study, based on routinely available national registry data, the risk of infection is assessed in household members (N= 194,362) of healthcare workers (N=144,525). Infection rates are corrected for calendar time, socio-demographic, occupational and comorbidity variants. The main outcome is 'risk of documented COVID-19 infection' in household members of healthcare workers that have received at least one dose of Comirnaty® or Vaxzevria® vs. household members of unvaccinated household members. **The risk of documented COVID-19 infection in household members was 30% lower (hazard ratio: 0.70, 95% CI: 0.63–0.78) ≥14 days after first dose and 50% lower after full vaccination (HR: 0.46, 95% CI 0.3-0.7).** The authors further estimate that a 30% reduction in infection rates amongst household members equals a 60% reduction of transmission through the vaccinated healthcare workers, since the household members are also exposed to other potential sources of infection (11).

Another pre-print study, from Israel, evaluates the risk of infection in (unvaccinated) children <16y old as a function of vaccine coverage in the population (21). They first identify 223 geographically different communities with similar temporal patterns of infection rate prior to vaccination onset. They then capitalize on the different vaccination coverage rates in those regions to evaluate the relative changes in infection rate at fixed time intervals of 3 weeks. The changes in vaccine coverage are compared to changes in infection rates for children 35 days later, to allow time for the potential protective effect of vaccination on the unvaccinated cohort. **The risk of infection in the unvaccinated cohort decreased in proportion to the rate of vaccination in each community**, with an overall strongly significant negative association, although heterogeneity between communities is large (see figure 1).

Figure 1: Correlation between change in infection rates in unvaccinated cohort and change in vaccination coverage rate for 223 communities in Israel *Source: Milman et al.*
For each community, the change in positive rate between consecutive time intervals (*P*3/*P*2) is shown as a function of the change in vaccinated fraction in the corresponding time intervals (*V*3-*V*2). Dash line shows linear fit (P-value<10-4;)



A pre-print study from Spain estimated the indirect protection of unvaccinated residents in long-term care facilities at 81.2% [80.2-82%] after the vaccination campaign with Comirnaty® (22). The indirect protective effect was in identical to direct vaccine effectiveness >28d after the first dose (as a proxy for effectiveness >7d after the second dose). It has to be noted though, that this was in the context of very high vaccination coverage (>99%) amongst all residents, which might be hard to obtain outside this closed setting.

5.3. ASYMPTOMATIC INFECTION (SEE ALSO ANNEX 1)

In order to be able to transmit, people need first to become infected. Therefore, vaccine effectiveness studies that have all infections (including asymptomatic infections) as an outcome, are extremely relevant. Preferably, these studies have a clearly identified testing strategy existing of repeated screening. Annex 1 lists an overview of key studies identified to date.

Two prospective cohort studies (from the US (8) and from the UK (4)) have found **effectiveness against all types of infection (including asymptomatic) of 70-80% after the first dose and 85-90% after the second dose of the Comirnaty® vaccine.** Similarly, Jones et al report that the test-positivity rate of a weekly screening programme of asymptomatic healthcare staff in the UK dropped from 0.8% in unvaccinated healthcare workers to 0.2% in those having received at least 1 dose of Comirnaty® ≥12 days ago (23) and comparable results have been reported from the US (24). The abovementioned **studies include mainly healthy adults, and effects might not be the same in other groups**. Interesting therefore is the retrospective cohort of Tande et al. using data from screening pre-procedural patients (25). They conclude that the risk of asymptomatic SARS-CoV-2 infection, as compared to unvaccinated individuals, was markedly lower among those >10 days after first dose (RR=0.21; 95% CI: 0.12–0.37) and among those >0 days after second dose (RR=0.20; 95% CI: 0.09-0.44) of either Comirnaty® or Moderna). In contrast, Britton et al. report results from weekly screening of residents of a long-term care facility and find a lower VE of 63% [33-79%] after the first dose of Comirnaty®. Data was insufficient to assess the effect after the second dose (26). These results are in line with data from the VIVALDI study in the UK, reporting on over 10,000 LTCF residents (median age 86 years) who undergo monthly PCR screening. VE was found to be 62% [23-81%] 28-34 days after the first dose of either Comirnaty® (33% of vaccinated) or Vaxzevria® (67%) (27). Interestingly, in a sensitivity analysis excluding unvaccinated individuals from LTCFs where vaccination had been offered, in order to eliminate bias due to possible herd immunity effect, VE increased to 76% [37-91%]. At ≥49 days after the first dose, the point estimate of VE was only a little lower than at 35-48 days, but the confidence intervals were wide and crossing the null (VE 51% [-17 – 80%]). In a comparable population of LTCF residents in Denmark, a similar vaccine effectiveness of 64% [14-84%] was found after full vaccination with the 2 doses of Comirnaty® (9) (pre-print). Notably, the same Danish study found high effectiveness (90% [82-95%]) against infection for staff members that were offered weekly screening.

In the original Moderna COVID-19 vaccine randomized controlled trial (1), a subgroup of asymptomatic participants underwent PCR-testing at the time of administering the second dose. Using these results, another pre-print study estimated that one dose of vaccination reduced the potential for viral transmission with at least 61% (28).

It is possible that effects differ according to vaccine type. Currently, most data is available for mRNA vaccines (Comirnaty® and the COVID-19 Moderna vaccine). Reassuringly though, the abovementioned VIVALDI trial found similar results for both Comirnaty and Vaxzevria (27). For the **Vaxzevria®** vaccine, we can also draw on results of a subgroup of participants of the initial RCT which was tested weekly (regardless of symptoms) with self-administered throat and nose swabs. Overall, no protective effect on asymptomatic infections was noted in this subgroup. However, when limiting the analysis to those who received the two doses with an interval of at least 12 weeks (the current dosing regimen in Belgium), there was **a vaccine efficacy of 47.2% [5.0-70.7%].** Data on overall reduction of infection (i.e. symptomatic + asymptomatic) is not reported separately for this subgroup (29).

5.3 PROTECTION AGAINST VARIANTS OF CONCERN (VOC)

Most studies have been conducted in the absence of circulating VOCs. Concerns have been raised about the efficacy of the vaccines against currently circulating variants of concern, **especially those bearing the E484K-mutation, a mutation improving the ability of the virus to evade the host's immune system**, namely the P1-strain first detected in Brazil and B1.351 first detected in South Africa.

Real life effectiveness data from the UK are reassuring in terms of the effectiveness of both Comirnaty® (Pfizer-BioNTech) and Vaxzevria® (AstraZeneca-Oxford) against the UK variant (4,5,12).

A **South African** study, held at a time of high circulation of the B1.351 variant, found a very low effectiveness 10.6% (95% CI:-66.4 to 52.2) of two doses of Vaxzevria® against mild to moderate laboratory confirmed COVID-19 (30). It should be noted however that **no data was available on protection against severe disease or death** and that the dosing interval was only 21-35 days, which is substantially lower than the 12 weeks interval used in Belgium. Longer dosing intervals have been shown to yield higher protection. A recent pre-print study from Israël also found a higher than expected proportion of B1.351 breakthrough infections after vaccination with the Comirnaty® vaccine, compared to non-vaccinated individuals (31). The study used a case-control design whereby breakthrough infections were matched to infections in unvaccinated control subjects with similar demographic characteristics (date of PCR, age, sex, ethnic sector, and geographic location). Importantly though, among the 400 case-control pairs (i.e. 800 infections), only 11 infections were caused by the B1.351 variant (8 in fully vaccinated individuals, 1 after the 1st dose and 2 in unvaccinated). The authors therefore note that "there may be higher rates of vaccine breakthrough with B.1.351, but it is possible that (a) vaccine effectiveness coupled with enacted nonpharmaceutical interventions remain sufficient to prevent its spread, and/or (b) B.1.1.7
outcompetes B.1.351, possibly due to its high transmission rate." In addition, several studies suggest a reduction in neutralizing capacity of vaccine elicited antibodies (32–35). The extent of this reduction and the impact on effectiveness remains to be determined, since correlates of protection have not been determined yet.

6. International recommendations

6.1. ECDC

On the 29th of March, the agency published a Technical Report on Risk of SARS-CoV-2 transmission from newly-infected individuals with documented previous infection or vaccination. The key points regarding vaccination are:

> *"The review of evidence on immunity and possibilities for transmission from infected, previously-vaccinated individuals to susceptible contacts found that:*
>
> - *Direct evidence of the impact of vaccination on the risk of transmission is only available from one study, a large register-based household transmission study from Scotland. This study suggests that vaccination of a household member reduces the risk of infection in susceptible household members by at least 30%.*
> - *There is evidence that vaccination significantly reduces viral load and symptomatic/asymptomatic infections in vaccinated individuals, which could translate into reduced transmission, although the vaccine efficacy varies by vaccine product and target*

group. In light of this fact, the total number of infections is expected to decrease significantly as vaccination coverage increases, provided that there is a match between the vaccine strains and the circulating virus strains. This will lead to decreased transmission overall.

- *Follow-up periods for vaccinated persons are not yet sufficiently long enough to draw conclusions on the duration of protection against infection long-term. Antibody titres in vaccinated individuals peak at 3−4 weeks following vaccination.*
- *Many of the vaccine efficacy studies were carried out before the emergence of SARS-CoV-2 VOCs. In studies that address the variants, there is limited preliminary evidence of reduced vaccine efficacy, in particular for B.1.351 and possibly also for P.1.*

Follow-up of cohorts with previous SARS-CoV-2 infection and vaccination is needed to better assess the magnitude and duration of protection from reinfection leading to asymptomatic/symptomatic disease, and the effect of protection against further transmission to contacts."

On the 21st of April, "Interim guidance on the benefits of full vaccination against COVID-19 for transmission and implications for non-pharmaceutical interventions" was published.

On the topic of quarantine and testing of fully vaccinated individuals, it is mentioned that:

- *"When contact tracing, **vaccinated contacts who have been exposed to a confirmed case should continue to be managed according to existing ECDC guidance**. However, health authorities may consider undertaking a risk assessment on a case-by-case basis and subsequently classify some fully vaccinated contacts as low-risk contacts. Factors that need to be taken into consideration in such assessments include, for example, the local epidemiological situation in terms of circulating variants, the type of vaccine received, and the age of the contact. The risk of onward transmission to vulnerable persons by the contact should also be considered.*

- *Requirements for **testing and quarantine of travellers (if implemented) and regular testing at workplaces can be waived** or modified for fully vaccinated individuals as long as there is no or very low level circulation of immune escape variants (in the community in the country of origin, in the case of travellers)."*

6.2. CDC:

CDC updated their Science Brief "Background Rationale and Evidence for Public Health Recommendations for Fully Vaccinated People" on the 2nd of April. Key points are:

- *COVID-19 vaccines currently authorized in the United States are effective against COVID-19, including severe disease.*
- *Preliminary evidence suggests that the currently authorized COVID-19 vaccines may provide some protection against a variety of strains, including B.1.1.7 (originally identified in the United Kingdom). Reduced antibody neutralization and efficacy have been observed for the B.1.351 strain (originally identified in South Africa). However, across studies, antibody neutralizing activity of sera from vaccinated people was still generally higher than that observed for convalescent sera from people who have recovered from COVID-19.*
- *A growing body of evidence suggests that fully vaccinated people are less likely to have asymptomatic infection and potentially less likely to transmit SARS-CoV-2 to others. However, further investigation is ongoing.*
- *Modeling studies suggest that preventive measures such as mask use and social distancing will continue to be important during vaccine implementation. However, there are ways to take a balanced approach by allowing vaccinated people to resume some lower-risk activities.*
- *Taking steps towards relaxing certain measures for vaccinated people may help improve COVID-19 vaccine acceptance and uptake.*

- *The risks of SARS-CoV-2 infection in fully vaccinated people cannot be completely eliminated as long as there is continued community transmission of the virus. Vaccinated people could potentially still get COVID-19 and spread it to others. However, the benefits of relaxing some measures such as testing and self-quarantine requirements for travelers, post-exposure quarantine requirements and reducing social isolation may outweigh the residual risk of fully vaccinated people becoming ill with COVID-19 or transmitting the virus to others.*
- *At this time, there are limited data on vaccine protection in people who are immunocompromised. People with immunocompromising conditions, including those taking immunosuppressive medications, should discuss the need for personal protective measures after vaccination with their healthcare provider.*

Based on these data, CDC suggests that fully vaccinated people can:

- ***Visit with other fully vaccinated people indoors without wearing masks or physical distancing***
- *Visit with unvaccinated people from a single household who are at low risk for severe COVID-19 disease indoors without wearing masks or physical distancing*
- ***Refrain from quarantine and testing following a known exposure if asymptomatic***
- *Resume travel and refrain from testing before **or after travel** or self-quarantine after travel.*

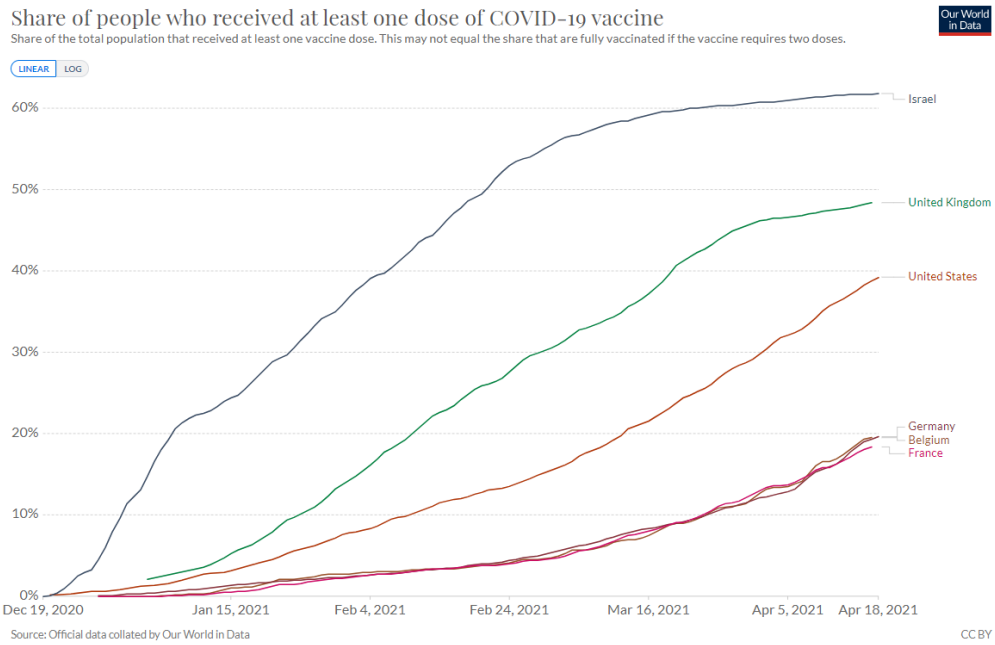
Specific measures are detailed for residents and staff of healthcare structures:

- ***Fully vaccinated healthcare personnel (HCP) with higher-risk exposures who are asymptomatic do not need to be restricted from work for 14 days following their exposure**.*
  - *Work restrictions for the following fully vaccinated HCP populations with higher-risk exposures should still be considered for HCP who have underlying immunocompromising conditions (e.g., organ transplantation, cancer treatment), which might impact level of protection provided by the COVID-19 vaccine. However, data on which immunocompromising conditions might affect response to the COVID-19 vaccine and the magnitude of risk are not available.*
- *HCP who have traveled should continue to follow CDC travel recommendations and requirements, including restriction from work, when recommended for any traveler.*
- *Recommendations for SARS-CoV-2 testing and use of PPE for HCP remain unchanged.*
- ***Fully vaccinated inpatients and residents in healthcare settings should continue to quarantine following prolonged close contact** (within 6 feet for a cumulative total of 15 minutes or more over a 24-hour period) with someone with SARS-CoV-2 infection; outpatients should be cared for using recommended Transmission-Based Precautions. This is due to limited information about vaccine effectiveness in this population, the higher risk of severe disease and death, and challenges with physical distancing in healthcare settings.*

When evaluating the recommendations of the CDC (or other international organizations), it is important to note that:

- Vaccine coverage in the US is significantly higher than in Belgium

Figure 2: Comparison in vaccine coverage between Belgium and selected other countries (*Source: Our World in Data)*



- As of April 13 2021, only mRNA vaccines have been deployed in the US

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7. Annex 1: overview of high-quality studies reporting effect of vaccination all SARS-CoV-2 infection (including asymptomatic)

Source	Study type	Population	N	Vaccine	Testing strategy	Outcome
Tande et al.	Retrospective cohort	asymptomatic undergoing pre-procedural screening USA	Total = 39,156 Vaccinated = 2,069 (min. 10d after 1st dose)	mRNA (94% Pfizer)	All pre-procedural	Vacc PCR+ 42/3,006 vs. 1,436/45,327 aRR >10d after D1 = 0.21 [0.12-0.37] aRR >0d after D2 = 0.20 [0.09-0.44]
Thompson et. al	Prospective cohort	HCW (1st line workers) USA	Total = 3,950 Unvaccinated = 989 Infections = 205	mRNA (63% Pfizer)	Weekly self-swab & at onset symptoms	VE ≥14d after D1 = 80% [59-90%] VE ≥14d after D2 = 90% [68-97%] only 10% infections truly asymptomatic
Hall et al (pre-print)	Prospective cohort (SIREN)	HCW UK	Total = 23,324 Unvaccinated = 2,683 Infections = 1,057	mRNA (100% Pfizer)	PCR 1x/2 weeks RDT 2x/week	VE ≥21d after D1= 72% [58-86%] VE ≥7d after D2 = 86% [76-97%]
Britton et al.	Retrospective cohort	Residents of LTCF USA	Total = 463 (50% ≥85y) Unvaccinated = 87 Infections = 97	mRNA (100% Pfizer)	Weekly PCR & at symptoms	VE ≥14d after D1 = 63% [33-79%] insufficient data after D2
Moustsen-Helms et al (pre-print)	Retrospective cohort	Residents and staff of LTCF Denmark	Residents = 39,040 (median age 84y) Infections = 572 Staff = 331,039 Infections = 5,725	mRNA (100% Pfizer)	Weekly screening offered in staff "increased testing" in LTCF (=?)	VE 14-25d after D1 (short window!) residents = 21% [-11-44%] staff = 17% [4-28%] VE >7d after D2 residents = 64% [14-84%] staff = 90% [82-95%]
Shrotri et al (pre-print)	Retrospective cohort	LTCF residents	Total = 10,412 Vaccinated = 1,252 Previous infection= 1,155 (11.1%) Infections = 1,334	33% Pfizer 66% Oxford-AZ	PCR 1x/month + outbreak	VE 28-34d after D1= 53% [0.19-76%] 35-48d after D1= 62% [23-81%]
Voysey et al	RCT (vaccine *efficacy*)	UK – trial particpants	Total = 8,207 Vaccinated = 4,071 Infections = 130	Oxford-AstraZeneca	Weekly self-swab	VE 14d after D2 for asymptomatic infection ONLY overall = 2.0% [-50.7-36.2%] if dosing interval ≥12w = 47.2% [5.0-70.7%]