sciensano

IMPACT DE LA STRATÉGIE DE VACCINATION SUR LES MESURES EN PLACE POUR LES TESTS ET LA QUARANTAINE - 2ème MISE À JOUR.

Réunion du RAG 20/04/2021

Un premier avis avait été émis fin décembre concernant d'**éventuelles modifications des procédures actuellement en place pour la quarantaine et les tests des personnes vaccinées**. Une première mise à jour a été publiée à la fin du mois de février. En raison d'un taux de vaccination initial faible dans les groupes à risque et de données insuffisantes sur l'effet sur la transmission, seules des modifications très limitées des lignes directrices actuelles avaient été recommandées. Le document actuel contient une 2ème mise à jour. Dans ses avis précédents, le RAG a déjà mentionné d'éventuels problèmes d'équité tant que tout le monde n'a pas eu accès à la vaccination et tant qu'il n'y a pas de libre choix du type de vaccin. Actuellement, un groupe d'experts du GEMS, complété par des experts en droit, en éthique et en sociologie, se penche sur ces questions éthiques et sociales (par exemple, que peuvent faire les personnes vaccinées entre elles ?).

1. Recommandations :

- **Les premiers résultats obtenus dans d'autres pays confirment que la vaccination joue un rôle clé dans le retour à une vie normale. Il est donc extrêmement important de motiver la population à se faire vacciner. Une information correcte et une communication ciblée sont indispensables à cet égard, en soulignant à la fois les avantages pour l'individu (protection contre les maladies graves) et pour la société (protection du système de santé, réduction de la circulation du virus).**
- Toutefois, étant donné la disponibilité limitée des vaccins, le déploiement de la vacicnation est progressif. La couverture vaccinale a récemment fortement augmenté, mais elle reste toujours faible dans les groupes à haut risque. Dans ces circonstances, les interventions non pharmaceutiques (telles que le port du masque, les tests et la quarantaine) restent particulièrement importantes. Le rythme auquel un assouplissement des règles pour l'ensemble de la population peut avoir lieu fait l'objet de décisions politiques, et tient compte des avis scientifiques préparés par le GEMS.
- Les différents aspects influençant cet avis, à savoir la situation épidémiologique en Belgique (en particulier les hospitalisations), la couverture vaccinale, la circulation des variants de préoccupation (VOC), et les connaissances scientifiques liées à la vaccination (en particulier concernant le risque de transmission après vaccination) seront suivis de près. Une mise à jour de cet avis est donc prévue dans un délai d'un mois.
- Pour des raisons pratiques (vérifiabilité) et compte tenu des connaissances limitées sur l'effet de la vaccination sur la transmission, les mesures préventives générales telles que la distance physique et le port du masque dans les lieux publics continuent de s'appliquer aux personnes déjà vaccinées.

- Dans les recommandations formulées dans le présent document, le terme "vacciné" signifie que les personnes ont été entièrement vaccinées, c'est-à-dire qu'elles ont reçu un vaccin complet :
    - pour Comirnaty® (Pfizer-BioNTech) : ≥7 jours après la deuxième dose.
    - pour le vaccin COVID-19 Moderna : ≥14 jours après la deuxième dose
    - pour Vaxzevria® (AstraZeneca-Oxford) : ≥15 jours après la deuxième dose.
    - pour le vaccin COVID-19 Janssen: ≥14 jours après la première dose

  Pour les personnes qui ont été partiellement vaccinées, les mêmes règles que pour les personnes qui n'ont pas encore été vaccinées s'appliquent.
- La protection offerte par les vaccins est élevée, mais n'est pas à 100 %. Les **personnes vaccinées qui présentent des symptômes possibles de COVID-19 doivent donc contacter un médecin pour subir un test, tout comme les personnes non vaccinées**. Il est rappelé que l'autotest ne peut PAS être utilisé chez les personnes symptomatiques (vaccinées ou non).
- Les personnes qui sont infectées par le SARS-CoV-2 alors qu'elles ont été vaccinées doivent être isolées, tout comme les personnes non vaccinées, même si elles ne présentent aucun symptôme. Certains éléments indiquent que ces personnes sont généralement moins infectieuses, mais la contagiosité ne peut certainement pas être exclue. Cela s'applique également aux résidents de MRS où un taux de vaccination élevé a été atteint.
- Il y a de plus en plus de données montrant que la vaccination a également un effet sur la transmission. Cependant, la protection est partielle et peut dépendre du type de vaccin, de l'âge et des maladies pré-existantes de la personne vaccinée ainsi que des variants du virus en circulation. Tant que la **couverture vaccinale est faible dans les groupes à haut risque, des exceptions à la quarantaine ne peuvent être accordées** aux personnes qui ont déjà été vaccinées dans les situations décrites ci-dessous. La couverture vaccinale dans la population générale devrait augmenter de manière significative dans les semaines à venir, avec l'espoir que d'ici la mi-juin, chaque résident ≥45 ans aura reçu au moins sa première dose. Comme mentionné ci-dessus, cet avis sera réévalué dans un délai d'un mois, en tenant compte de toute nouvelle donnée sur la transmission après vaccination, de la situation épidémiologique générale et de l'augmentation de la couverture vaccinale.
    - Une couverture vaccinale élevée dans les groupes à haut risque est déjà atteinte dans de nombreuses maisons de soins et de repos. **Les membres du personnel vaccinés asymptomatiques des MRS peuvent continuer à travailler après un contact à haut risque si la couverture vaccinale est ≥90% chez les résidents et ≥70% chez les membres du personnel**. Ils doivent néanmoins être testés comme les autres HRC.
    - Les prestataires de soins de santé vaccinés qui ne relèvent pas de la situation susmentionnée doivent, en principe, être mis en quarantaine après un contact à haut risque. Une **exception à cette règle n'est autorisée que si elle est nécessaire à la continuité des soins**, dans les conditions déjà existantes (voir procédures).
- Le dépistage préventif a une probabilité pré-test plus faible que les autres indications. Chez les personnes vaccinées, le risque a priori d'infection est encore plus faible, de sorte que le dépistage préventif ne doit être effectué que si le risque en cas d'infection non détectée est particulièrement élevé. C'est par exemple le cas avant une transplantation (risque pour le récepteur) ou lors d'une admission à l'hôpital (risque pour les autres patients non vaccinés). Les décisions relatives au dépistage préventif dans les centres de soins résidentiels doivent toujours tenir compte de la couverture vaccinale du personnel et des résidents.
- Dans les centres de soins résidentiels ou autres collectivités résidentielles qui ont atteint une couverture vaccinale élevée, le risque d'une épidémie parmi les résidents est plus limité que dans la population générale. Cependant, les centres de soins résidentiels ne sont pas des îlots

isolés de la société: il existe toujours une interaction par le biais des visiteurs et du personnel. Certaines mesures, telles que le port du masque par le personnel, devraient donc continuer à s'appliquer.

- **Les recommandations sont résumées dans le tableau de la page suivante.**

sciensano

2. Aperçu des impacts possibles et des recommandations

Sujet	Principaux points de la procédure actuelle (lien)	Recommandation pour les personnes vaccinées
Cas possibles de COVID-19	Chaque cas possible est testé. Test antigène possible si les symptômes sont ≤5 jours.	Mêmes indications pour les tests **Préférence forte de PCR** Si positif : déclaration + séquençage
Isolement des personnes concernées	10 jours dont au moins 3 jours sans fièvre Règles spéciales dans les hôpitaux, les personnes immunodéprimées, les maladies graves.	Aucun changement.
Recherche des contacts		
Cas index	Identifier les HRCs à partir de 2d avant l'apparition des symptômes et les mettre en quarantaine	Aucun changement.
Contact à haut risque (HRC)	Test et quarantaine de 7 à 10 jours Travail exceptionnellement autorisé pour les soignants si nécessaire	Personnel de MRS: pas de quarantaine (mais test) si asymptomatique et couverture vaccinale ≥90% des résidents ET ≥70% du personnel. Aucun changement tant que la couverture vaccinale est faible dans les groupes à risque. Si le travail est exceptionnellement nécessaire pour la continuité des soins : priorité aux salariés vaccinés.
Cluster	Hors hôpital : tests plus poussés des contacts à faible risque avec des tests antigéniques- Hôpital: tests poussés du personnel/des résidents avec la PCR.	Aucun changement.
Voyageurs		
Voyageurs non-belges	Test négatif obligatoire et mise en quarantaine dans certaines circonstances	Aucun changement.
Résidents de retour	Quarantaine et test obligatoires dans certaines circonstances	Aucun changement.
Dépistage préventif		
Personnel MRS	Envisager un dépistage régulier par PCR sur un échantillon de salive	Pas de dépistage si couverture vaccinale résidents ≥90% et personnel ≥70%.
Visiteurs MRS	Envisager l'utilisation de tests rapides antingéniques avant les visites	Pas de dépistage si couverture vaccinale résidents ≥90% et personnel ≥70%.
Admission à l'hôpital	Dépistage systématique dans les unités à haute prévalence/risque	Dépistage si risque de transmission à d'autres patients non vaccinés.
Nouveau résident en collectivité (admission à partir du milieu familial)	Dépistage systématique et isolement en chambre en attendant les résultats	Tests systématiques. Aucun isolement dans la chambre n'est nécessaire dans l'attente des résultats, sauf si le taux de vaccination des résidents est <90 % ou <70% pour le personnel.
Autres professions (p.ex enseignants)	Médecin du travail peut décider d'un dépistage systématique	Aucun avantage du dépistage si vacciné sans contact groupes à risque.
Dépistage du donneur avant la transplantation	Examen systématique	Aucun changement (en raison du risque élevé pour l'accepteur)

3. Situation

- Au 20/4/2021, l'incidence cumulée sur 14 jours des nouveaux cas était de 424/100 000 habitants et la moyenne hebdomadaire était de 233 nouvelles hospitalisations par jour.

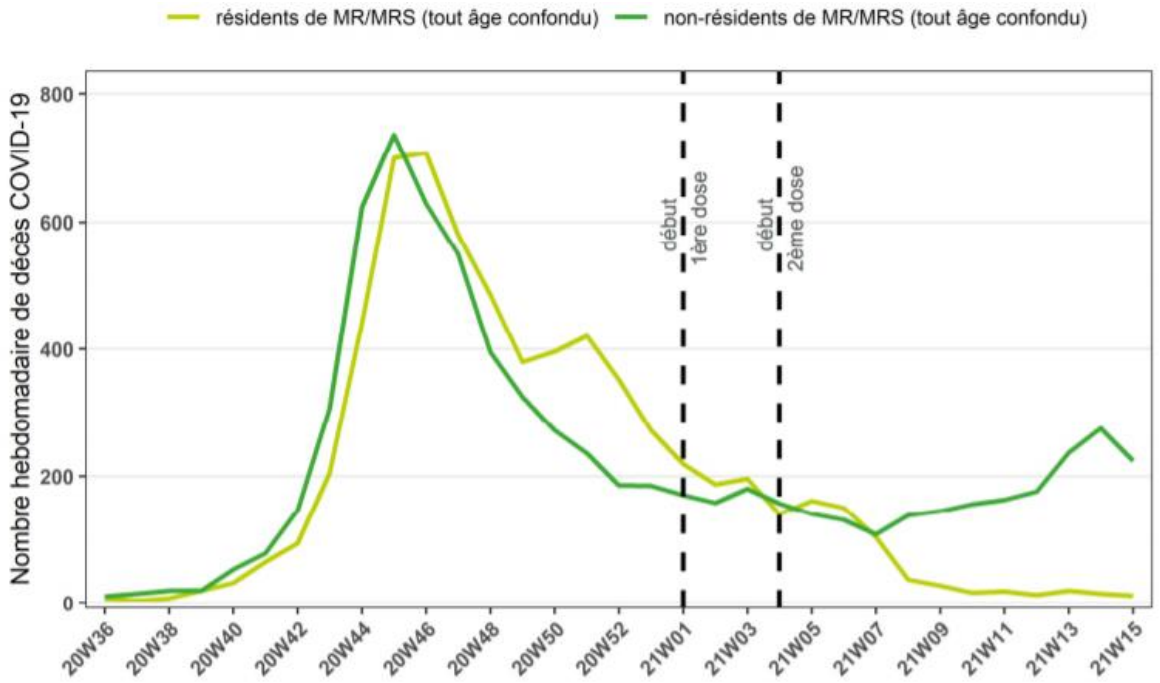
Tableau 1 : Nombre cumulé de personnes ayant reçu une première et une deuxième dose du vaccin COVID-19, par groupe d'âge, situation au 20/04/2021 *Source : Vaccinnet+, rapport épidémiologique quotidien Sciensano*

		Population totale [1]	Population âgée de 18 ans et plus [1,2]	Population âgée de 65 ans et plus [1,2]
Couverture vaccinale au moins 1 dose	Belgique	19,9%	24,9%	64,4%
	Bruxelles [3]	14,8%	19,2%	66,0%
	Flandre [3]	20,7%	25,6%	64,0%
	Wallonie [3,4]	20,0%	25,2%	64,1%
	Communauté germanophone [3]	20,8%	25,7%	78,1%
Couverture vaccinale entièrement vacciné	Belgique	6,2%	7,7%	12,7%
	Bruxelles [3]	4,1%	5,2%	14,5%
	Flandre [3]	6,4%	8,0%	11,8%
	Wallonie [3,4]	6,3%	7,9%	13,8%
	Communauté germanophone [3]	7,2%	9,0%	19,9%

Source de données registre Vaccinnet+. Un délai entre le moment de la vaccination et celui de l'enregistrement dans la base de

- Des informations détaillées sur la couverture vaccinale dans les MRS sont disponibles dans un rapport séparé. Sur base d'une surveillance à laquelle > 85 % des MR/MRS belges ont participé, la couverture vaccinale atteinte chez les résidents des MR/MRS était très élevée dans l'ensemble de ces établissements, avec une moyenne nationale de 89,4 %. Les premiers signaux de l'impact bénéfique de cette vaccination massive sur l'épidémie du COVID-19 apparaissent, avec une diminution du nombre de clusters de cas confirmés en MR/MRS mais également du nombre d'hospitalisations et de décès parmi les résidents des MR/MRS belges.

Figure 1 : Comparaison de la mortalité dans deux groupes ayant une couverture vaccinale significativement différente : les résidents des maisons de retraite et la population générale. *Source : Rapport thématique COVID-19 sur la vaccination dans les centres de soins résidentiels, Sciensano*



4. Considérations

- Il y a de plus en plus de données montrant que la vaccination a également un effet sur la transmission. Toutefois, la protection est partielle et peut dépendre du type de vaccin, de l'âge et des maladies pré-existantes de la personne vaccinée ainsi que des variants du virus en circulation.
- Toute modification des procédures existantes nécessite un temps suffisant pour sa mise en œuvre sur le terrain (information des parties prenantes, formation du personnel du centre d'appels, mise en œuvre technique...) et ne doit pas, de préférence, être trop complexe. Il existe aujourd'hui sur le marché plusieurs vaccins présentant des caractéristiques différentes. L'individu n'est pas libre de choisir le type de vaccin. Les directives traitant toutes les personnes vaccinées de la même manière (quel que soit le type de vaccin reçu) sont les plus simples en termes d'implications logistiques et de clarté de la communication à la population.
- Les membres du RAG ont déjà exprimé plus tôt leurs préoccupations quant à une éventuelle inégalité de traitement :
    - D'un point de vue motivationnel, le fait de lier certains avantages à la vaccination (par exemple l'absence de quarantaine ou une quarantaine réduite) pourrait accroître la volonté de se faire vacciner. D'autre part, la politique suivie jusqu'à présent a toujours été celle de la solidarité et de la limitation de la transmission en exigeant que les personnes présentant un faible risque personnel de maladie grave (par exemple les jeunes) respectent également les mesures.
    - Attacher certains avantages à la vaccination pose potentiellement un problème d'équité tant que l'accès aux vaccins n'est pas égal pour tous. De plus, l'intervalle entre la 1ère dose et l'obtention d'une protection vaccinatale complète est différent selon le vaccin (2 semaines après la 1ère dose pour Johnson&Johnson vs. 14 semaines après la

premiere dose pour AstraZeneca-Oxford vs. 8 semaines pour Pfizer-BioNTech) de sorte que même les personnes appartenant au même groupe, comme les prestataires de soins de santé en 1ère ligne, ne seront pas complètement vaccinées au même moment.

Le RAG note que ces préoccupations font actuellement l'objet d'un avis pluridisciplinaire préparé par un groupe de travail distinct et sur base duquel une décision politique devra être prise. Par conséquent, le RAG a abordé les questions présentées concernant les exceptions possibles à la quarantaine d'un point de vue scientifique : les données limitées de l'effet de la vaccination sur la transmission suggèrent un effet réel mais partiel, dans le contexte actuel de circulation élevée du virus et de forte pression sur le système de soins de santé, avec une couverture vaccinale croissante mais encore faible et des effets des VOC encore peu clairs.

- Le port du masque et d'autres mesures renforcées de prévention des infections ont également eu un effet bénéfique démontrable sur d'autres maladies respiratoires, comme la grippe, ce qui constitue un argument supplémentaire pour continuer à recommander le port de masques pour les membres du personnel, même dans les MRS où la couverture vaccinale est élevée.

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.**

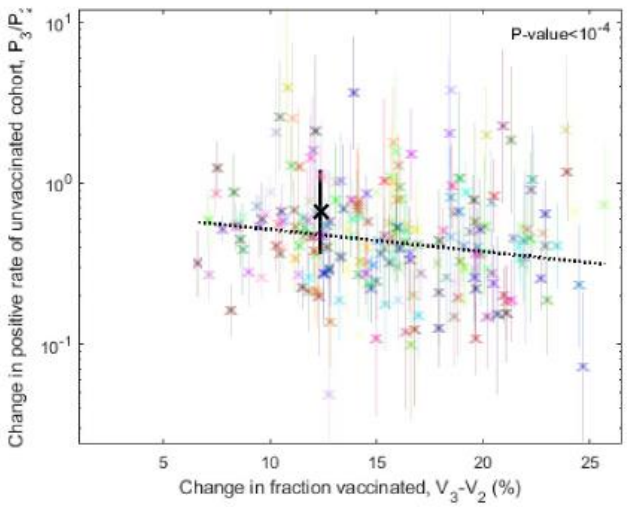
5.2. EFFECT ON TRANSMISSION

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

ECDC's latest guidance on infection prevention and control dates from February 9th 2021 and states:

> *"As long as there is community transmission of COVID-19, it is prudent for the current guidance on self-isolation in the event of COVID-19 symptoms or proven COVID-19 and on quarantine in the event of contact with a COVID-19 case without recommended PPE to also apply to vaccinated healthcare workers."*

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."

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.*

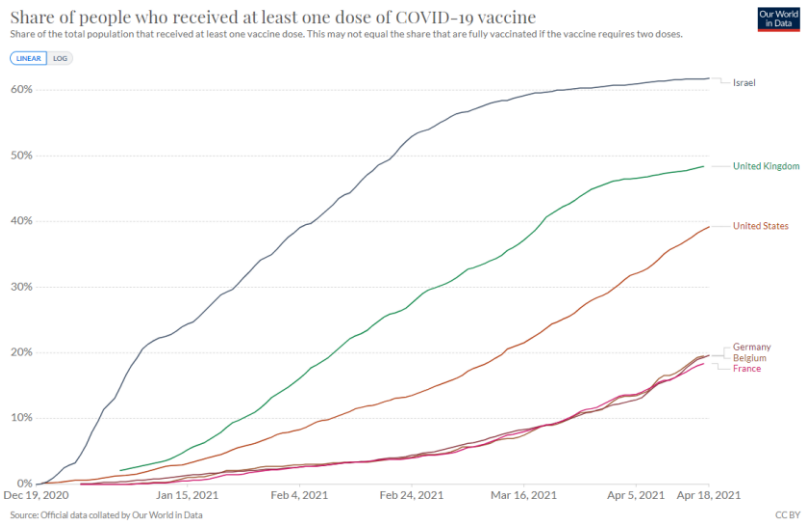
Specific measures are detailed for residents and staff of healthcare structures:

- ***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

Les experts suivants ont contribué à cet avis:

Emmanuel André (KUL-UZLeuven), Steven Callens (UZ Gent), Lucy Catteau (Sciensano), Bénédicte Delaere (CHU-UCL Namur), Olivier Denis (CHU-UCL Namur), Pierre-Louis Deudon (COCOM), Michèle Gérard (CHU St Pierre), Herman Goossens (UAntwerpen), Naïma Hammami (AZG), Valeska Laisnez (Sciensano), Barbara Legiest (AZG), Tinne Lernout (Sciensano), Geert Molenberghs (KU Leuven), Sophie Quoilin (Sciensano), Stefan Teughels (Domus Medica), Pierre Van Damme (UAntwerpen), Steven Van Gucht (Sciensano), Yves Van Laethem (CHU St Pierre), Xavier Holemans (Grand Hôpital de Charleroi), Pierrette Melin (CHU de Liège), Corinne Vandermeulen (KU Leuven), Laura Cornelissen (Sciensano).

REFERENTIES

1. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. New England Journal of Medicine. 2021 Feb 4;384(5):403–16.

2. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. New England Journal of Medicine [Internet]. 2020 Dec 10 [cited 2021 Feb 8]; Available from: https://www.nejm.org/doi/10.1056/NEJMoa2034577

3. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet [Internet]. 2020 Dec 8 [cited 2020 Dec 14];0(0). Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/abstract

4. Hall VJ, Foulkes S, Saei A, Andrews N, Oguti B, Charlett A, et al. Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study) [Internet]. Rochester, NY: Social Science Research Network; 2021 Feb [cited 2021 Feb 24]. Report No.: ID 3790399. Available from: https://papers.ssrn.com/abstract=3790399

5. Bernal JL, Andrews N, Gower C, Stowe J, Robertson C, Tessier E, et al. Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in England. medRxiv. 2021 Mar 2;2021.03.01.21252652.

6. Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. New England Journal of Medicine [Internet]. 2021 Feb 24 [cited 2021 Mar 1]; Available from: https://www.nejm.org/doi/10.1056/NEJMoa2101765

7. Amit S, Regev-Yochay G, Afek A, Kreiss Y, Leshem E. Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients. The Lancet. 2021 Mar 6;397(10277):875–7.

8. Thompson MG. Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021. MMWR Morb Mortal Wkly Rep [Internet]. 2021 [cited 2021 Mar 30];70. Available from: https://www.cdc.gov/mmwr/volumes/70/wr/mm7013e3.htm

9. Moustsen-Helms IR, Emborg H-D, Nielsen J, Nielsen KF, Krause TG, Molbak K, et al. Vaccine effectiveness after 1st and 2nd dose of the BNT162b2 mRNA Covid-19 Vaccine in long-term care

facility residents and healthcare workers – a Danish cohort study. medRxiv. 2021 Mar 9;2021.03.08.21252200.

10. Yelin I, Katz R, Herzel E, Berman-Zilberstein T, Ben-Tov A, Kuint J, et al. Associations of the BNT162b2 COVID-19 vaccine effectiveness with patient age and comorbidities. medRxiv. 2021 Mar 17;2021.03.16.21253686.

11. Shah ASV, Gribben C, Bishop J, Hanlon P, Caldwell D, Wood R, et al. Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households. medRxiv. 2021 Mar 21;2021.03.11.21253275.

12. Vasileiou E, Simpson C, Robertson C. Effectiveness of first dose of COVID-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people. Pre-print [Internet]. 2021 Feb 22 [cited 2021 Feb 23]; Available from: https://www.ed.ac.uk/files/atoms/files/scotland_firstvaccinedata_preprint.pdf

13. Qiu X, Nergiz AI, Maraolo AE, Bogoch II, Low N, Cevik M. Defining the role of asymptomatic and pre-symptomatic SARS-CoV-2 transmission – a living systematic review. Clinical Microbiology and Infection [Internet]. 2021 Jan 21 [cited 2021 Jan 28]; Available from: http://www.sciencedirect.com/science/article/pii/S1198743X21000380

14. Li F, Li Y-Y, Liu M-J, Fang L-Q, Dean NE, Wong GWK, et al. Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study. The Lancet Infectious Diseases [Internet]. 2021 Jan 18 [cited 2021 Jan 25];0(0). Available from: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30981-6/abstract

15. Byambasuren O, Cardona M, Bell K, Clark J, McLaws M-L, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: Systematic review and meta-analysis. Official Journal of the Association of Medical Microbiology and Infectious Disease Canada. 2020 Dec 11;e20200030.

16. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. PLOS Medicine. 2020 Sep 22;17(9):e1003346.

17. Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, et al. Decreased SARS-CoV-2 viral load following vaccination. medRxiv. 2021 Feb 8;2021.02.06.21251283.

18. Petter E, Mor O, Zuckerman N, Oz-Levi D, Younger A, Aran D, et al. Initial real world evidence for lower viral load of individuals who have been vaccinated by BNT162b2. medRxiv. 2021 Feb 8;2021.02.08.21251329.

19. Kawasuji H, Takegoshi Y, Kaneda M, Ueno A, Miyajima Y, Kawago K, et al. Transmissibility of COVID-19 depends on the viral load around onset in adult and symptomatic patients. PLOS ONE. 2020 Dec 9;15(12):e0243597.

20. Marks M, Millat-Martinez P, Ouchi D, Roberts C h, Alemany A, Corbacho-Monné M, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. The Lancet Infectious Diseases [Internet]. 2021 Feb 2 [cited 2021 Feb 18];0(0). Available from: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30985-3/abstract

21. Milman O, Yelin I, Aharony N, Katz R, Herzel E, Ben-Tov A, et al. SARS-CoV-2 infection risk among unvaccinated is negatively associated with community-level vaccination rates. medRxiv. 2021 Mar 31;2021.03.26.21254394.

22. Monge S, Olmedo C, Alejos B, Lapeña MF, Sierra MJ, Limia A, et al. Direct and indirect effectiveness of mRNA vaccination against SARS-CoV-2 infection in long-term care facilities in Spain. medRxiv. 2021 Apr 10;2021.04.08.21255055.

23. Jones NK, Rivett L, Seaman S, Samworth RJ, Warne B, Workman C, et al. Single-dose BNT162b2 vaccine protects against asymptomatic SARS-CoV-2 infection. van der Meer JW, editor. eLife. 2021 Apr 8;10:e68808.

24. Keehner J, Horton LE, Pfeffer MA, Longhurst CA, Schooley RT, Currier JS, et al. SARS-CoV-2 Infection after Vaccination in Health Care Workers in California. New England Journal of Medicine. 2021 Mar 23;0(0):null.

25. Tande AJ, Pollock BD, Shah ND, Farrugia G, Virk A, Swift M, et al. Impact of the COVID-19 Vaccine on Asymptomatic Infection Among Patients Undergoing Pre-Procedural COVID-19 Molecular Screening. Clin Infect Dis. 2021 Mar 10;

26. Britton A. Effectiveness of the Pfizer-BioNTech COVID-19 Vaccine Among Residents of Two Skilled Nursing Facilities Experiencing COVID-19 Outbreaks — Connecticut, December 2020–February 2021. MMWR Morb Mortal Wkly Rep [Internet]. 2021 [cited 2021 Apr 8];70. Available from: https://www.cdc.gov/mmwr/volumes/70/wr/mm7011e3.htm

27. Shrotri M, Krutikov M, Palmer T, Giddings R, Azmi B, Subbarao S, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of Long-Term Care Facilities (VIVALDI study). medRxiv. 2021 Mar 26;2021.03.26.21254391.

28. Lipsitch M, Kahn R. Interpreting vaccine efficacy trial results for infection and transmission. medRxiv. 2021 Feb 28;2021.02.25.21252415.

29. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. The Lancet. 2021 Mar 6;397(10277):881–91.

30. Madhi SA, Baillie V, Cutland CL, Voysey M, Koen AL, Fairlie L, et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. New England Journal of Medicine [Internet]. 2021 Mar 16 [cited 2021 Mar 23]; Available from: https://www.nejm.org/doi/10.1056/NEJMoa2102214

31. Kustin T, Harel N, Finkel U, Perchik S, Harari S, Tahor M, et al. Evidence for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2 mRNA vaccinated individuals. medRxiv. 2021 Apr 9;2021.04.06.21254882.

32. Kuzmina A, Khalaila Y, Voloshin O, Keren-Naus A, Bohehm L, Raviv Y, et al. SARS CoV-2 spike variants exhibit differential infectivity and neutralization resistance to convalescent or post-vaccination sera. Cell Host & Microbe [Internet]. 2021 Mar 20 [cited 2021 Mar 30]; Available from: https://www.sciencedirect.com/science/article/pii/S1931312821001360

33. Zhou D, Dejnirattisai W, Supasa P, Liu C, Mentzer AJ, Ginn HM, et al. Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine induced sera. Cell [Internet]. 2021 Feb 23 [cited 2021 Mar 8]; Available from: https://www.sciencedirect.com/science/article/pii/S0092867421002269

34. Wang Z, Schmidt F, Weisblum Y, Muecksch F, Barnes CO, Finkin S, et al. mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants. Nature. 2021 Feb 10;

35. Wu K, Werner AP, Koch M, Choi A, Narayanan E, Stewart-Jones GBE, et al. Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine. New England Journal of Medicine. 2021 Feb 17;0(0):null

sciensano

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%]