UPDATE RECOMMENDATIONS WITH REGARDS TO TESTING, ISOLATION AND QUARANTINE

RAG 12/08/2021 – gevalideerd door RMG 15/08/2021

Opgepast: de uiteindelijke beslissingen (die op sommige punten afwijken van het advies dat hieronder wordt voorgesteld) werden genomen door het overlegcomité op 20/08/2021 en de IMC op 25/08/2021.

Aanbevelingen:

- Behoud van algemene maatregelen (testen, isolatie/quarantaine, contact opsporing) om de viruscirculatie op een laag niveau te houden en het risico van overdracht op kwetsbare bevolkingsgroepen te beperken.
- Prioriteiten voor testen blijven het testen van symptomatische personen, hoog-risico contacten, terugkerende reizigers en clusteronderzoek.
- Toegang tot testen makkelijker maken, bijvoorbeeld door meer gebruik te maken van speekselafname (update advies door RAG-testing).
- Voor volledig gevaccineerde personen: behoud van de bestaande procedures/maatregelen behalve :
  - Invoeren van een tweede test op dag 7 voor HRC;
  - Aanbeveling gebruik van een zelftest voor terugkerende reizigers uit een rode zone indien risicogedrag;
  - Terugkerende reizigers uit een VOC land binnen EU/Schengen : twee testen.
- Voor niet of onvolledig gevaccineerde personen: behoud van de bestaande procedures/maatregelen behalve :
  - Minder beperkingen voor laag-risicocontacten;
  - Herhaalde screening is niet nuttig in alarmfase 1;
  - Uitbreiden van de testen voor terugkerende reizigers uit een rode zone binnen EU/Schengen, waarbij dezelfde maatregelen gevolgd worden als voor rode zones in derde landen (twee testen en quarantaine).

CONTEXT

Belgium is successfully rolling out the COVID-19 vaccination program. At the beginning of August 2021, 59.3% of the Belgian population had received complete vaccination (73.4% among >=18 years old) and 69.8% had received partial vaccination (83.5% among >=18 years old). The high vaccination coverage has an important impact on the COVID-19 transmission dynamics and on how the epidemic is evolving. Therefore, questions are raised if the current measures with regards to testing, isolation and quarantine need to be adapted.

The current procedures with regards to testing, isolation and quarantine in different contexts are summarized in the table in Annex 1.

The recommendations in this advice consider the coming months, in a context of further virus circulation with still unclear impact on hospitalizations. If the epidemiological situation remains stable and under control (alarm level 1 in all provinces) for at least one month or depending on the evolution of the circulation of other respiratory viruses in autumn, a new update will be made.

This advice is complementary to an advice of the GEMS on maintaining (or not) other non-pharmaceutical measures, such as mask wearing.

ELEMENTS OF DISCUSSION

- Scientific evidence shows a similar vaccine effectiveness (VE) of full vaccination with Pfizer or AstraZeneca against hospitalisation, and a slightly lower protection against symptomatic disease caused by the Delta variant, which has become the predominant variant in Belgium (see Literature section below). The difference after only one dose is, however, larger, highlighting the importance of full vaccination.
- Evidence on vaccine effectiveness against infection with the Delta variant is still scarce. However, one study found a substantial lesser protective effect, even after complete vaccination. The lesser protection of vaccination against infections by the Delta variant is also shown by several studies investigating post-vaccination breakthrough infections.
- A high level of virus circulation can still lead to outbreaks among vulnerable people, as has been recently the case also in Belgium, with some outbreaks in nursing homes with a high lethality, despite high vaccination coverage. Also, even if the risk of severe disease is strongly reduced by vaccination, if the number of infected persons is very high, this can still lead to a high number of new hospitalizations. In addition, a high number of symptomatic cases with mild disease will put a high pressure on the first line health care. Therefore, virus circulation should remain under control.
- Guidelines in other countries indicate that some countries (like the US and France), where testing of fully vaccinated HRC was not recommended, reintroduced or expanded testing in response to the Delta variant.
- In the absence of other non-pharmaceutical measures (NPIs) such as mask wearing and keeping distance, the number of other respiratory infections will also be on the rise again (as opposed to the previous autumn and winter). Testing every person with respiratory symptoms might become very difficult in this context. Keeping certain NPIs is therefore essential the coming months. And alternative sampling and testing methods (such as multiplex testing) should be investigated.
- Studies investigating post-vaccination breakthrough infections found that the viral load in Delta infections in fully vaccinated people was similar to that in non-vaccinated people. Also, identification of the variant involved doesn't seem to be necessary/feasible for all breakthrough infections (of note: an advice of the RAG testing has been requested on this topic). Therefore, rapid Ag testing for symptomatic vaccinated patients could be used as an alternative to PCR testing in the first days of symptoms, and self-tests can also be used in vaccinated people.
- One publication (from Singapore) reports that viral loads decreased faster in vaccinated individuals, indicating that the isolation period for vaccinated people could possibly be

shortened. There is however not enough evidence on the duration of infectivity of infected vaccinated patients to allow to apply this at this moment. The literature on this topic will be followed up closely, and if there is more evidence, the duration of isolation for vaccinated people will be discussed again.

- Since the end of June, fully vaccinated high-risk contacts are exempt of quarantine if they have a negative test result for a test performed as soon as possible after the (last) high risk exposure. This was a political decision, whereas the RAG advised to perform two tests. The purpose of the two tests is however different: the first test is to identify if the HRC was actually the source of infection for the case and see if further contact tracing is needed, and the second test is to exclude that the HRC became infected by the case. Just limiting the testing to a test as soon as possible will not prevent all possible further transmission by the vaccinated HRC, who can still become infected despite vaccination, and might remain asymptomatic. This is particularly relevant in the context of the lower vaccination effectiveness against infection for the Delta variant than for other variants, and that viral load and duration of shedding is higher in breakthrough cases by the Delta variant (see above). In this context, the decision on testing of vaccinated HRC needs to be reconsidered. Hereby, a distinction could be made between household contacts or other contacts with repeated exposure (at least 2 in the past week), and single/one-time contacts (eg people met for a meal in a restaurant a specific day, of whom someone is positive the following 1 or 2 days). For the latter, the first test is not useful, because the HRC cannot have been the source of infection. A single test at day 5 would be more useful in this situation. In practice however, different rules depending on the type of exposure might be very difficult to implement at the level of the call centers, and also confusing for the population.
- Quarantine in between the two tests for vaccinated HRC is not recommended, despite the low risk that fully vaccinated HRC get infected, especially with the dominance of the Delta variant, because measures need to be balanced.
- For non-vaccinated low-risk contacts, the current recommendation is that social contacts should be limited to a minimum, with respect of a distance of 1,5m. This implies that people can continue necessary activities, such as school and work, but not other social activities. In a context where a higher proportion of the population is vaccinated, more contacts can be accepted for the LRC, except with people at risk for severe disease. Extra attention for hygienic measures should be continued, as well as testing in case of symptoms.
- Returning travelers: similar to the summer of 2020, data from returning travelers this summer indicate importation of virus into the country. The PR in returning travelers that are tested (single test at arrival) is about 2-3 times higher than the PR of travelers at departure. In addition, data from the PLF for the first year after implementation, report an ~ equally high PR for a second test (that was performed one week after arrival) than for the first test (2.4% versus 2.8% respectively). This is not unexpected, since people might still be in the incubation period when the first test is performed, and thus become infectious after their return. Taking into account a total number of about 200,000 returning travelers from a red zone during one week (data for the first week of August), of which about 25% fulfill the criteria for testing, this would mean 1,200 missed infections, possibly leading to further transmission. Therefore, measures

for non-vaccinated returning travelers should be reinforced and no distinction should be made between red zones within the EU/Schengen and red third countries.

- Test results among incoming travelers during the past 2 weeks show that the positivity rate among vaccinated travelers is 2.8%, vs. 3.2% among non-vaccinated travelers. It is important to note that comparison is risky because only vaccinated travelers coming from non-EU/Schengen/white list countries red zones are tested, while the non-vaccinated comprise mostly people coming from red zones in EU/Schengen/white list countries. No information is available on the positivity rate among vaccinated people coming from EU/Schengen/white list countries. Despite this observation, it doesn't seem to be necessary to test all vaccinated travelers returning from a EU/Schengen/white list red zone, because the risk of infection during travel, although not zero, is lower than for non-vaccinated. Instead, the threshold for testing could be lowered in this group. If people think they might have had a risk, testing should be easily available. Easy travel has been promoted as an advantage of vaccination, so it might be contra productive to now ask fully vaccinated travelers within Europe to get tested.
- It is reminded that the RAG advice of 25 May on measures for vaccinated individuals recommended that the exception for quarantine for vaccinated travelers did not apply for subjects returning from an area of intense circulation of VOC/VOI with possible immune escape.
- Repetitive screening of asymptomatic staff and residents is not recommended in nursing homes with high vaccination coverage (see table in Annex) and there is no reason to change this at this stage, despite the occurrence of some outbreaks recently. However, the threshold for testing in case of symptoms should be kept very low, in order to rapidly detect a possible introduction of the virus and allow further contact tracing/screening.
- One-time screening for vaccinated persons is also not recommended, except for the current categories (see table).

RECOMMENDATIONS

- Despite the overall high vaccination coverage, continued measures are still needed to maintain virus circulation at a low level and reduce risk of transmission to vulnerable populations, at least until the vaccination campaign is completed and that the impact of it on hospitalizations in the upcoming flu season will be more clear. These measures include early identification of cases by testing people with symptoms, isolation of infected people, contact

tracing with testing and possibly quarantine of HRC and limiting the introduction of virus/variants by travelers.

- The priorities for testing remain testing of symptomatic people, high-risk contacts, returning travelers and cluster investigation, and tests for these categories specifically should remain free of charge and easily accessible.
- Overall, access to testing should be made more easy, for example through more use of saliva sampling. The RAG testing could be requested to give an advice on alternative sampling and testing methods to be explored.
- The recommendations are the same for all the alarm levels, except for repetitive screening of asymptomatic persons.

Current testing and quarantine procedures for fully vaccinated people

- No change of procedures for isolation and quarantine.
- Revise the testing procedure for fully vaccinated HRCs: the RAG strongly recommends to apply the same procedure for testing as for non-fully vaccinated HRC, with a second test on day 7, since both tests are performed for a different reason (see above). No quarantine should be observed between the two tests. The second test is especially important in case of continued or repetitive exposure, such as in households. If distinction between repeated/multiple and single exposure is feasible at the level of the call centers, only one test at day 5 could be considered for the latter.
- No change for fully vaccinated HRCs/travelers from red zones. However, the use of a self-test could be recommended if people are worried about a possible exposure during the travel or had risk behavior. An assessment tool to help people evaluate the risk could be useful, but not as a mandatory questionnaire (as it was the case for the SAT). In addition, returning travelers coming from a VOC country within the EU/Schengen should be tested twice.
- Self-tests can also be used by fully vaccinated people, for the same indications as for non-vaccinated (see RAG advice), bearing in mind the limitations of these tests (lower sensibility).
- Maintain current guideline for repetitive and one-time screening.

Current testing and quarantine procedures for non- or partially-vaccinated people

- Maintain all the current measures, except for:
    - LRC, for which there is no restriction any more of activities for two weeks, except for contact with persons at risk of severe disease (such as grandparents for a child LRC);
    - repetitive screening: not recommended in alarm level 1 (national level).
- Increase testing of non-vaccinated travelers without recovery certificate arriving/returning from a red zone and apply the same procedure for travelers coming from a red zone in an EU/Schengen/white list country as for travelers coming from another red country, i.e. two tests and quarantine.

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INTERNATIONAL RECOMMENDATIONS

CDC

In its Interim Public Health Recommendations for Fully Vaccinated People, CDC added a recommendation for fully vaccinated people who have come into close contact with someone with suspected or confirmed COVID-19 **to be tested 3-5 days after exposure**, and to wear a mask in public indoor settings for 14 days or until they receive a negative test result.

Fully vaccinated domestic travelers do not need to get a test before or after travel, or self-quarantine after travel, but fully vaccinated air travelers coming to the United States from abroad, including U.S. citizens, are still required to have a negative test result or documentation of recovery from COVID-19 before they board a flight to the United States. International travelers arriving in the United States are recommended to get a test 3-5 days after travel regardless of vaccination status, but do not need to self-quarantine.

France

Also France has slightly adopted its recommendations for fully vaccinated people in response to the Delta variant. The High Counsel for Public Health recommends to test fully vaccinated people with a proven risk contact with a COVID-19 case at day 0 and day 7. Quarantine is not necessary, but if there are repeated contacts in a household settings adherence to barrier measures is recommended.

The High Counsel also states that self-surveillance with self-tests is not recommended for fully vaccinated people.

United Kingdom

Public Health England informs that from 16 August fully vaccinated contacts do no longer have to self-isolate. They are, however, still advised to have a PCR test as soon as possible, just as non-vaccinated contacts.

British Academy of Medical Sciences

The British Academy of Medical Sciences recently published a rapid review into 'COVID-19: Preparing for the future'. The document focusses on the winter 2021/2022 and makes recommendations for the transition towards lower levels of virus circulation.

The report stresses the importance of continued access to **fast and accurate testing of people with suspicious symptoms** and **self-isolation** of confirmed cases. It recommends to consider how to incorporate multiplex testing with the expected increase in other respiratory infections in autumn and winter.

Routine asymptomatic testing should be considered **where either the rate of susceptible individuals becoming infected or the potential for poor outcomes is particularly high** (e.g. health and social care settings). Wider routine asymptomatic testing may **not** be either **cost-effective**, or worth the testing fatigue that may be induced **where low prevalence rates lead to more false than true positive results**. The academy advises to first pilot and evaluate the 'novel' use of rapid Ag tests (e.g. testing to access travel or sports events) to demonstrate their utility for

either diagnosis or prevention, including understanding how it will affect wider test, trace and isolate compliance.

Surprisingly, the Academy has doubts about the usefulness of **onward contact tracing as currently performed in the UK.** It considers it as **unlikely to substantially reduce transmission**, and finds that **locally led outbreak investigations and surge testing** in outbreak areas **are likely to be more efficient** ways to control the epidemic – especially if case numbers are low. They see more benefit in providing the infected person and members of their household with clear advice on minimizing transmission risk to other household members by physical distancing within or outside the home. **Backward contact tracing** (i.e. identifying who infected symptomatic cases), on the other hand, is considered as a potentially powerful tool, in particular because a minority of individuals cause the majority of onward infections. It is likely to be most effective in the context of sporadic outbreaks rather than generalized epidemics. They recommend that future efforts be focused on evaluating and considering further use of tracing apps and backwards tracing.

They further recommend that **requirements for contacts to self-isolate may also be relaxed** once high levels of immunity are achieved through vaccination or natural infection, to significantly reduce societal impacts. Waste water surveillance is considered a useful tool to identify where outbreaks are occurring and rapidly manage them to limit onward transmission.

LITERATURE BACKGROUND

Vaccine effectiveness against and breakthrough infections by the Delta variant

Lopez-Bernal et al. used a test-negative case–control design to estimate VE (Pfizer and AstraZeneca) against symptomatic disease caused by the Delta variant compared to the Alpha variant. After 2 doses there were modest reductions in VE against the Delta variant as compared to the Alpha variant (88% vs. 94% for Pfizer; 67% vs. 75% for AstraZeneca; 80% vs. 88% for either vaccine). Absolute differences were bigger after only 1 dose (36% vs. 48% for Pfizer; 30% vs. 49% for AstraZeneca; 31% vs. 49% for either vaccine) (1). The same study group estimated VE against hospitalization and found no difference between Alpha and Delta infections. After 2 doses of either vaccine, VE for Alpha was 92% vs. 94% for Delta, and after one dose 78% vs. 75%. For the Pfizer vaccine VE after 2 doses was 95% and 96% for Alpha and Delta, respectively, and for 2 doses AstraZeneca 86% and 92%, respectively (2).

A Canadian pre-print shows similar results. In another test-negative design study, protection of 2 doses Pfizer against symptomatic infection was similar to that of the Alpha variant (89% and 87% for the Alpha and Delta variant, respectively). Protection of 1 dose was however lower than that for the Alpha variant (66% and 56% for the Alpha and Delta variant, respectively). Protection against hospitalization or death was similar to that of the Alpha variant (80% and 78% for the Alpha and Delta variant, respectively) (3).

In a correspondence in the Lancet, Sheikh reported the results of yet another test-negative case–control study looking at VE against infection 14 days after the second dose, using S gene positivity as a proxy for the Delta variant and S gene negativity as a proxy for the Alpha variant. The VE of the Pfizer vaccine was estimated at 92% for S gene-negative and 79% for those S gene-positive

infections. AstraZeneca showed a VE of 73% and 60% respectively (4). VE, by either vaccine, against hospitalization, 28 days after the first vaccine dose, was also lower in S gene positive infections than in S gene negative (62% vs. 72%), but the level of precision was too low (p=0.19) to conclude that it represents a real difference.

A study in Houston, Texas, found that Delta variants caused a significantly higher rate of vaccine breakthrough cases (17.4% compared to 5.8% for all other variants). Individuals with vaccine breakthrough cases caused by Delta variants had a low Ct value that was not significantly different than the Ct value observed in unvaccinated patients with COVID-19 caused by Delta variants (5). Also in an outbreak investigation in Barnstable County, Massachusetts, Ct values among Delta infections were similar among specimens from patients who were fully vaccinated and those who were not (6), and also a study in Wisconsin came to the same conclusions (7). A study in Singapore observed the same among hospitalized patients (8), but found that viral loads decreased faster in vaccinated individuals. In its update on what is known about the Delta variant, CDC concludes that fully vaccinated people with Delta variant breakthrough infections can spread the virus to others, but that vaccinated people appear to be infectious for a shorter period (9). However, CDC still advises that fully vaccinated people remain in isolation for a period of 10 days (10).

A study using data from India also found lower Ct values in Delta breakthrough cases in health care workers (mean Ct 16.5), fully vaccinated with the Covishield vaccine, compared to non-Delta breakthrough cases (mean Ct 19) and a larger cluster size with Delta breakthrough (11).

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Annex 1. Current procedures and measures

Procedure	Non-fully vaccinated	Fully vaccinated
Testing		
Symptomatic patients fulfilling case definition (>=6 years old)	Testing with PCR or rapid Ag test (if <= 5 days symptoms)	Testing with PCR
Risk contacts (>=6 years old)		
- High-risk contacts	PCR as soon as possible after identification and second test on day 7	PCR as soon as possible after identification, no second test
	No test if <180 days after previous infection	
- Low-risk contacts	Only if sufficient PCR capacity	No testing
- Low-risk contacts during cluster investigation	If deemed useful by health inspector	
Arriving/ returning travellers (>=12 years old)		
- From non-red EU/Schengen/white list countries	No testing	
- From red EU/Schengen/white list countries	PCR test <72h before or as soon as possible after arrival (if Belgian resident)	No testing*
- From other red countries	PCR test <72h before or soon as possible as possible after arrival (if Belgian resident) and second test on day 7	PCR as soon as possible after arrival*
- From EU/Schengen VOC countries	PCR test <72h before or as soon as possible after arrival (if Belgian resident) and second test on day 7	No testing*
- From other VOC countries	PCR test <72h before or as soon as possible after arrival (if Belgian resident) and second test on day 7	
Repetitive screenings (weekly with PCR or bi-weekly with rapid Ag test)		
- Nursing home staff	Only if low vaccination coverage (residents <90% or staff<70%)	No testing
- School staff and students	*See advice covid-19 management in the educational system*	No testing
- Other workplaces	Optional	No testing
One-time screenings		
- Pre-hospital admission	According hospital guidelines	Only when very high risk (e.g. pre-transplant)
- New residents nursing homes	Systematic testing	Systematic testing

Procedure	Non-fully vaccinated	Fully vaccinated
- Nursing home visitors	Optional and only when vaccination coverage residents <90%	No testing
- Pre-event screening	For events with >=1500 participants (PCR<48h or rapid Ag test<24h)	No testing*
- Self-testing	Optional and only when no other test indication applies	No testing
- Other one-time screenings	Optional and only when high risk of transmission	No testing
Isolation		
Confirmed ambulatory COVID-19 cases	Isolation until 10 days after onset of symptoms/positive test result and 3 days without fever	
Confirmed hospitalized/ nursing home resident COVID-19 cases	Isolation until 14 days after onset of symptoms and 3 days without fever	
Confirmed COVID-19 cases in ICU	Isolation until 21 days after onset of symptoms and 3 days without fever and clinical improvement OR 14d after onset of symptoms and PCR 2x $<10^5$ copies/mL with minimum 24h interval	
Confirmed immunocompromised COVID-19 cases	Isolation until 21 days after onset of symptoms and 3 days without fever and clinical improvement	
Quarantine		
High-risk contacts	7 days if day 7 test negative; 10 days if no day 7 test	Till negative test result received
	No quarantine if <180 days after previous infection	
Low-risk contacts	No quarantine; reinforcement of protective measures	No additional measures
Arriving/ returning travellers (>=12 years old)		
- From non-red EU/Schengen/white list countries	No quarantine	
- From red EU/Schengen/white list countries	No quarantine if negative PCR result <72h before arrival OR quarantine until negative result received after arrival (Belgian resident)	No quarantine*
- From other red countries	7 days if day 7 test negative; 10 days if no day 7 test	Till negative test result received*
- From EU/Schengen VOC countries	7 days if day 7 test negative; 10 days if no day 7 test	No quarantine*
- From other VOC countries	10 days, even if day 7 test negative	

*Also applies to people with a recovery certificate