STRATÉGIE DE TEST – MISE À JOUR OCTOBRE 2021

réunion RAG 05/10/2021

CONTEXTE

À l'approche de la saison hivernale, d'autres virus respiratoires recommencent à circuler, ce qui rend plus difficile l'identification des cas possibles de COVID-19 sur la base des symptômes cliniques. De plus, avec l'augmentation de la couverture vaccinale, la pression limitée sur les unités de soins intensifs et la lassitude face à la pandémie, la conformité à la stratégie actuelle est remise en question. En outre, les médecins généralistes (GP) demandent à réduire le nombre de tests qu'ils doivent effectuer, afin de pouvoir se concentrer à nouveau sur leurs tâches principales, après presque 20 mois de pandémie. La stratégie de dépistage est un vaste sujet qui englobe plusieurs aspects et constitue la pierre angulaire de diverses autres mesures.

RECOMMANDATIONS

1. Recommandations générales

- **Les médecins généralistes doivent pouvoir se concentrer sur leurs tâches principales, à savoir s'occuper des personnes qui ont besoin de soins cliniques**. Il est de la plus haute importance que des structures soient mises en place ou maintenues pour réduire la charge des médecins généralistes en matière de dépistage/testing. Le testing doit être disponible près du domicile et sans barrière, sinon les gens n'utiliseront pas ces structures et appelleront de toute façon leur médecin généraliste.
    - La stratégie de dépistage dépendra du succès avec lequel ces structures seront effectivement mises en place et/ou maintenues. En cas d'échec, il faudra inévitablement modifier la stratégie de test, par exemple comme le propose Domus Medica (voir annexe 5).
    - La charge de travail des médecins généralistes (par le biais du baromètre des médecins généralistes) et les délais d'obtention des résultats de laboratoire devront continuer à être surveillés.
    - Maintenir les centres de dépistage ouverts tant que la stratégie consiste à contrôler la propagation du virus dans la société, avec identification/isolement des personnes infectées et recherche des contacts.
- Pour permettre à la société de rester ouverte, des interventions ciblées sont encore nécessaires pour les personnes infectées ou ayant été exposées à un risque plus élevé. Par conséquent, dans la situation actuelle**, le testing des personnes présentant des symptômes possibles de COVID-19 ne doit pas être abandonné mais doit être rendu possible d'un point de vue logistique**.
- L'utilisation de **masques dans les lieux public fortement fréquentés**, l'attention portée à **l'hygiène des mains et de la toux** et la **promotion du télétravail** resteront importantes pour réduire la circulation du SRAS-CoV-2 ainsi que d'autres maladies respiratoires**.**

2. Testing des personnes présentant des symptômes possibles du COVID-19

- **Le testing des personnes présentant des symptômes légers (qu'elles soient vaccinées ou non) reste important pour limiter la transmission virale.** En cas de test positif, la personne infectée doit être isolée et ses contacts testés.

- Comme beaucoup de ces personnes présentant des symptômes légers ne nécessitent pas de soins cliniques, le test ne doit PAS être effectué par les médecins généralistes.
    - Créer un outil d'auto-évaluation pour permettre aux personnes présentant des symptômes légers d'obtenir une ordonnance de test gratuite sans passer par un généraliste. Une prescription de test devrait compter comme une preuve d'absence du travail ce jour-là (ou de télétravail). Pour éviter les abus, on peut fixer un nombre maximal de tests pouvant être demandés par ce système (par exemple 2 par mois / 3 par 3 mois...)
    - Fournir aux contacts à haut risque symptomatiques un code de test immédiatement (comme c'est le cas pour les HRCs asymptomatiques), au lieu de les référer à un médecin généraliste (les scripts pour les centres d'appel doivent être modifiés).
    - Autoriser le dépistage des personnes présentant des symptômes légers par le biais de tests antigéniques rapides effectués en pharmacie (avec des mesures appropriées de contrôle de la prévention des infections et en plus des tests déjà en place pour les voyageurs en partance).

- Le COVID-19 ayant une présentation clinique aspécifique, une **définition de cas large restera nécessaire**.
    - Il est rappelé que les cliniciens peuvent (et doivent) utiliser leur jugement clinique et qu'aucun test n'est nécessaire si une autre cause claire est identifiée (par exemple, fièvre post-vaccination, angor pectoris...) ou en cas de symptômes légers avec une infection récente (<180 jours).
    - Il est également rappelé que la diarrhée aqueuse, la confusion aiguë et le collapsus soudain ne doivent être considérés comme des symptômes possibles de COVID-19 que dans des populations spécifiques telles que les personnes âgées.

3. Testing des contacts à haut risque

- La stratégie actuelle de dépistage des contacts à haut risque doit être maintenue, y compris pour les enfants de moins de 12 ans. Comme mentionné ci-dessus, ce dépistage ne doit PAS impliquer les médecins généralistes.

4. Testing des voyageurs

- **L'objectif principal de la stratégie de test pour les voyageurs doit être de retarder l'introduction d'un nouveau VOC en Belgique**, par l'identification et l'isolement des personnes infectées. Tant que les nouvelles propositions d'approche harmonisée au niveau européen sont compatibles avec cet objectif, elles sont acceptables.
    - Il n'est pas possible de créer une nouvelle catégorie de pays pour avoir une stratégie différente pour les pays non membres de l'UE/Schengen, à l'exception de la catégorie existante de la "white list". Par conséquent, tant que le Royaume-Uni ne fait pas partie

de la liste blanche européenne, les mêmes mesures devraient s'appliquer que pour les autres pays tiers.

- Les mesures destinées aux voyageurs doivent être aussi simples et harmonisées que possible. Pour réduire les risques, tous les voyageurs entrants pour lesquels il existe une obligation de dépistage devraient avoir la preuve d'un résultat négatif récent au test PCR avant le voyage plutôt qu'après l'arrivée (puisqu'un test positif après l'arrivée signifierait que les autres passagers ont déjà été exposés). Par conséquent, l'option d'effectuer un test uniquement au retour devrait être supprimée.

ELEMENTS OF DISCUSSION

- We are in an **intermittent phase**, where SARS-CoV-2 is evolving from an unknown virus with enormous epidemic potential to an endemic virus. However, at this stage, there are still a lot of unknowns on what can be expected the coming winter months.
    - For endemic respiratory viruses, testing is only done for clinical reasons. Surveillance of endemic respiratory viruses in Belgium is performed through a sentinel GP system.
    - To limit viral transmission during the pandemic, non-pharmaceutical interventions were done, including contact tracing. The advantage of **contact tracing is that it is a targeted intervention**: rather than imposing restrictive measures to the entire society, restrictions are only imposed to those with a direct exposure to the virus.
- In order to be able to perform contact tracing, infectious individuals need to be identified. The clinical presentation of COVID-19 is aspecific and overlaps with other respiratory illnesses. As the circulation of other respiratory viruses increases, this means that more tests will need to be performed to identify infectious individuals.
- There are clear signals from the field that the current burden for testing people with mild symptoms on the first line health system (GPs) cannot be sustained. The workload brought on by this has a tangible impact on access to health care for other patients (e.g. with chronic conditions or mental health issues).
- For most people with mild symptoms, testing offers little to no direct clinical benefit.
- Surveillance of the epidemic can be done through other routes (e.g. sentinel surveillance, surveillance of Severe Acute Respiratory Infection) than through testing of all symptomatic individuals, and is also based on other indicators (such as hospitalization). The purpose of testing is thus not surveillance.
- As there are currently many respiratory viruses circulating and barriers to testing are high, current testing guidelines are not being followed (neither by patients nor GPs).
- Currently, the average delay between symptom onset and seeking a test is about 2 days. Adding on to that are the delays to actually get the test and receive the result. On average, the call centre contacts an index case about 4 days after symptom onset. As the infectious period precedes symptom onset, the effectiveness of contact tracing (especially in a relatively open society) is questioned by some experts.
- On the other hand, especially because there are very few NPIs still in place, contact tracing might be even more important. It is recognized that the current strategy will never lead to full suppression of the virus and still allow for some transmission. However, even modest reductions in number of contacts (for infected people) can have great impacts on the increase in hospitalizations, as is shown by ECDC modelling in their most recent risk assessment.

- Broad testing could have the advantage to allow mildly symptomatic persons with a negative test result to resume some of their activities.
- The proposal of Domus Medica to stop testing children <12y was discussed. The majority of participants however felt that the current situation (high PR in symptomatic children, few restrictions in place, intergenerational contact) does not allow to broaden the exceptions on testing for children <6y with mild symptoms.
- Even when test-positivity rate in symptomatic individuals is rather low (e.g. test-positivity rate of 10%, meaning 9 out of every 10 people will be tested in vain), abandoning testing of this group would quickly lead to high absolute cumulative numbers of infectious individuals in society.
- Using an online self-assessment tool for persons with mild symptoms to check if they fulfill the case definition and could get a code for a test was already recommended by the RAG about a year ago, but never implemented. It is however also used in other countries and would allow to limit the pressure on GPs.
- Despite the recommendation to test persons with recent symptoms with a rapid antigen tests (RATs), their actual use remains currently limited: only 7% of all RATs are performed for possible cases. It is important to also consider administrative aspects (certificate of illness) when designing test routes not involving the GP.
- The current case definition already incorporates clinical judgement (no testing required if clear other cause for symptoms, e.g. fever post-vaccination) and excludes testing of people with only a runny nose. Clear information (such as e.g. here) should be made available to the public.

Testing returning/arriving travelers

- The objectives of testing arriving international travelers are (1) to screen people who have potentially a high risk of being infected with SARS-CoV-2 and detect the positive cases before, or as soon as possible after, entering the country, and (2) to delay introduction of and rapidly detect newly emerging variants that are not yet widespread in Belgium. Available evidence and the relatively high PR among screened incoming travelers in Belgium justifies to continue screening. Travelers are a targeted population for extensive sequencing of positive test results, but not all positive tests are sequenced. However, as long as positive results are detected and those travelers isolated, the test strategy will delay introduction of new VOCs in society.

- Testing of arriving (non-vaccinated) travelers remains also important to avoid (massive) introduction of infected persons from countries with a widespread virus circulation, including from some EU countries with a low vaccine coverage (< 50%), currently experiencing a surge of infections and high incidences (Latvia, Estonia, Romania, ..).

- The number of tests conducted among returning/arriving travelers is determined by the extent of traveling, by the amount of areas considered as high-risk and by the vaccination status of the travelers. It is difficult to predict what this number will be in the coming months. It is expected that in the period before Christmas the number of travelers will remain quite stable, that the number of high-risk areas will not substantially increase and that the % of travelers who are fully vaccinated will only increase. During the month of September 2021 the weekly number of travelers requiring at least one test was on average 32,458. The Task Force Testing

estimates that the weekly number of tests among incoming travelers in the coming months (maintaining the current test indications) will be between 17,500 and 21,000.

- Different test strategies are possible and the evidence documenting what strategy is most effective is limited. The available evidence indicates that a test before or just after arrival detects most positive cases, but that a second test later after arrival still detects an important number of additional positive cases.

- The lack of precise evidence results in countries applying a big diversity of test strategies, in whom to test, how often to test and when to test. They are often a compromise between what is most effective and what is feasible/acceptable. Overall, **most countries are more strict than Belgium with regards to having proof of a negative test before embarking on the return, and some are less demanding with regards to testing after arrival**.

BACKGROUND

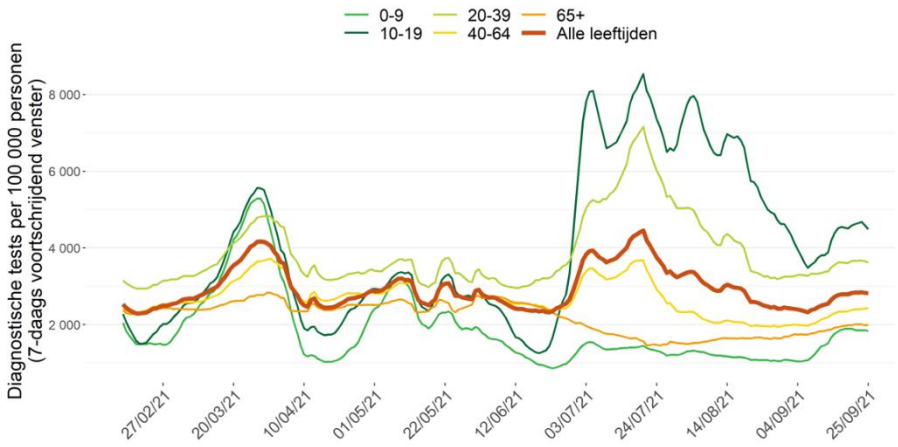
1. BELGIAN DATA

General

- An overview of the epidemiological situation can be found in the RAG epidemiology (NL/FR). Belgium is currently in alert phase 2, with a relatively limited pressure on the hospital system.
- Long-term predictions on the evolution of the epidemic have a high degree of uncertainty and highly depend on behavioral patterns. So far, it seems we are following the most favorable scenario of the prediction models (predictions available here).

- The total number of tests per age category is presented in Figure 1. For all age categories except <10y and 65+, the **total number of tests performed was much higher over summer than it currently is**. Since May 2021, younger children (0-9 years old) have always been the least tested age group.

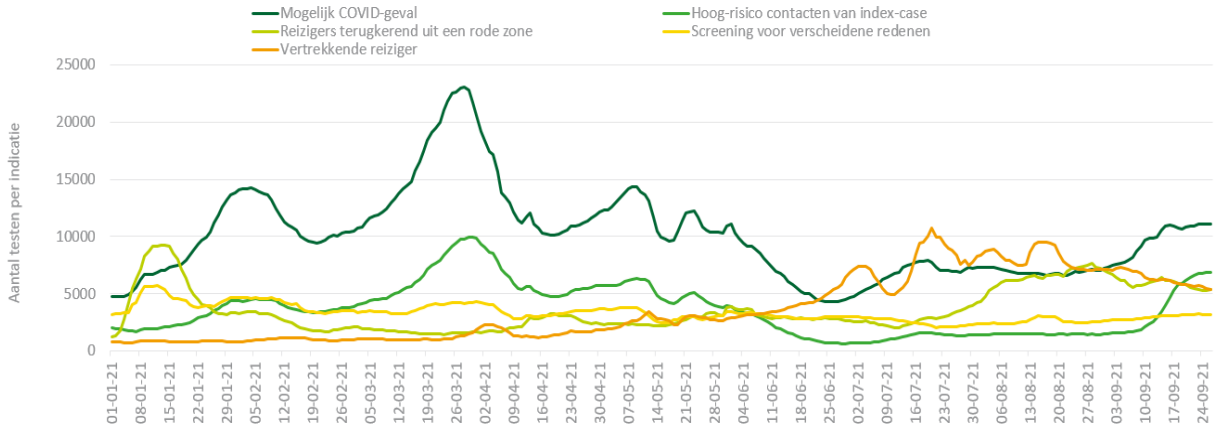
Figure 1: total number of tests performed by age category (per 100,000 persons) since 15/02/2021



Testing of symptomatic individuals

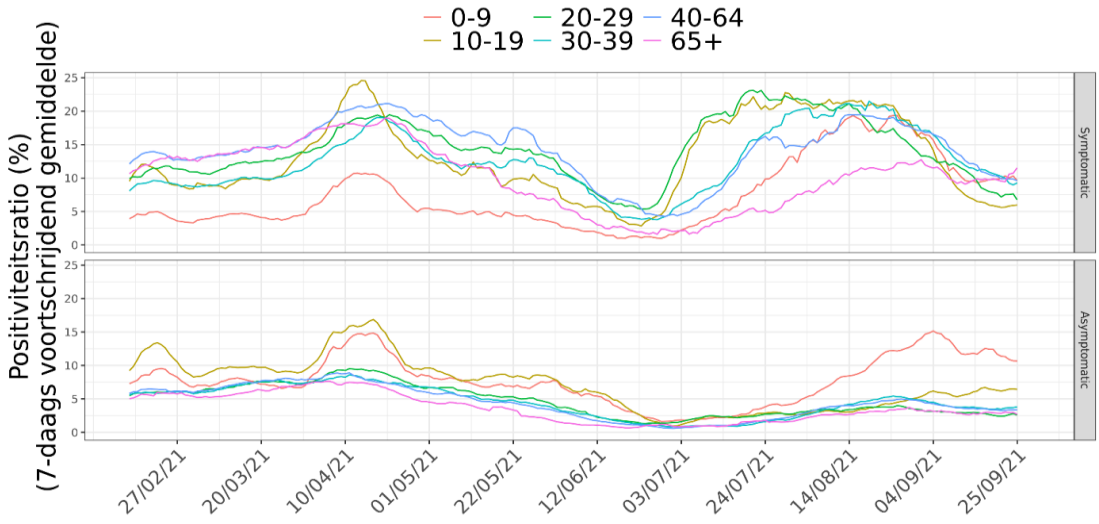
- Since the end of the summer, **testing for possible cases is the most frequent reason for testing** (for tests with eForm/CTPC code). The current level of tests being performed for possible cases is comparable to the number of tests performed for departing travelers over summer and much lower than the number of tests in spring 2021 (Figure 2).

Figure 2: Number of tests performed by indication and per day from 01/01/2021
Source: eForms/CTPC codes, available for ~60% of tests



- In a context of increased testing of symptomatic people and probably increased co-circulation of other respiratory viruses, the test-positivity rate (PR) for symptomatic persons decreased at the end of the summer, and is currently stabilizing (Figure 3). The trend is comparable in all age groups, except a recent small increase in 65+. Overall, , the PR for symptomatic individuals is around 10% (ranging between 5% n Flanders and 15% in Brussels) and remains about twice as high as the overall PR.

Figure 3: Test-positivity rate split by symptom status at time of test and by age group

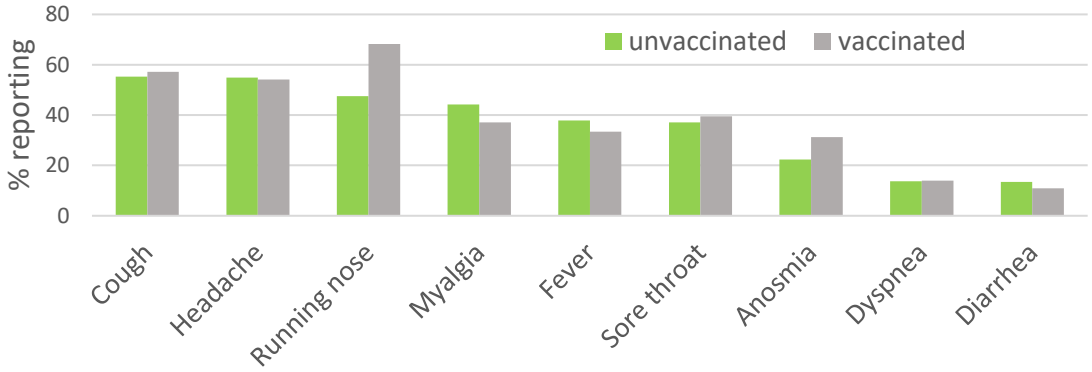


- Since the 1st of August 2021, 81% of all rapid antigen tests (RAT) were performed in pharmacies (230,750 out of a total of 285,053 tests). The use of RATs in symptomatic persons

is very limited: **only 7% of all RATs were performed for symptomatic persons.** Similar to the global results, PR for RATs in symptomatic persons have gone down in the recent weeks (currently about 5%), but remain much higher than in asymptomatic persons (Figure in Annex 3).

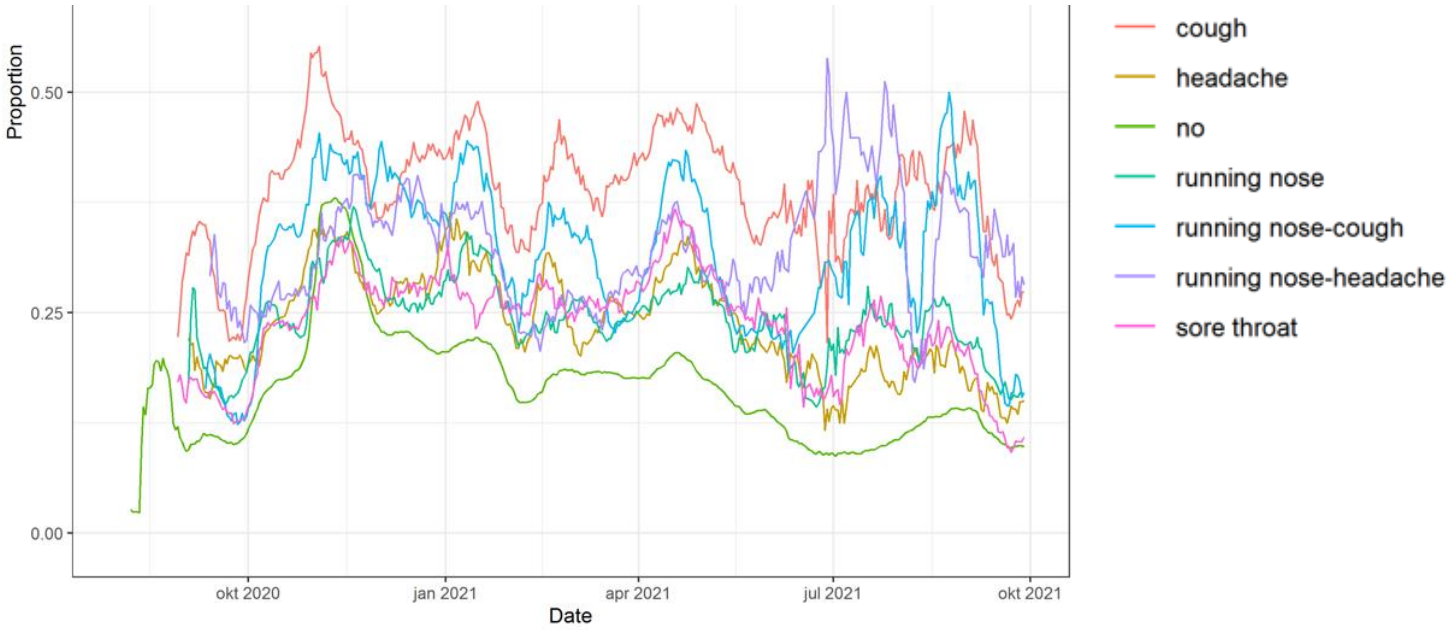
- Upon contact by the call centre, all index cases are asked about possible symptoms. Figure 4 below presents the most frequent symptoms as reported by the symptomatic index cases since 01/01/2021. Reported symptoms have not importantly changed over time (data not shown).

Figure 4: Most frequent symptoms reported by symptomatic index cases (n= 313,041 unvaccinated / 24,802 vaccinated) since 01/01/2021 *Source: Belgian contact tracing data*



- Some symptoms from the figure above (like headache and runny nose) might just be very prevalent in the population, including in those testing negative for SARS-CoV-2. Linking symptoms reported by high-risk contacts with their test results, allows to identify those symptoms most predictive (specific) for COVID-19. Anosmia and fever have the highest positive predictive value (64% and 61%) but lack sensitivity, as <40% of cases are presenting with this symptom. As is shown in Figure 5, high-risk contacts with a cough (alone or in combination with a runny nose) or a combination of runny nose and headache at the time of contact with the call center are those most likely to test positive.

Figure 5: test-positivity rate for high-risk contacts by most frequently reported symptom(s) at time of contact with call centre *Souce: Belgian contact tracing data, 1/10/2020-30/09/2021*



- Pre-COVID-19, the highest incidence of consultations for influenza-like-illnesses was in the period January-March. At the height of the peak, up to 800/100.000 inhabitants per week would contact their GP, corresponding with approximately 90.000 cases/week or an average of 13.000/day (graph presented in Annex 5). In comparison, during previous COVID-waves, a maximum of 80,000 tests/day were done (including other indications than symptomatic testing).

Testing of (vaccinated) contacts

- With the current high vaccination coverage, vaccinated individuals will make up a larger part of index cases and high-risk contacts. Between 25/06/2021-25/09/2021, fully vaccinated individuals made up 23% of index cases and 40% of high-risk contacts.

Table 1: Number of tests and test-positivity rates by vaccination status, 01/09/2021 – 02/10/2021, Belgium

HRC		Total	T1 tested	T1 positive	T2 tested*	T2 positive
Vaccinated	N	21,749	19,409	1,505	10,307	696
	%	100%	89%	8%	58% *	7%
Unvaccinated	N	12,544	9,795	2,473	4,741	780
	%	100%	78%	25%	65% *	16%

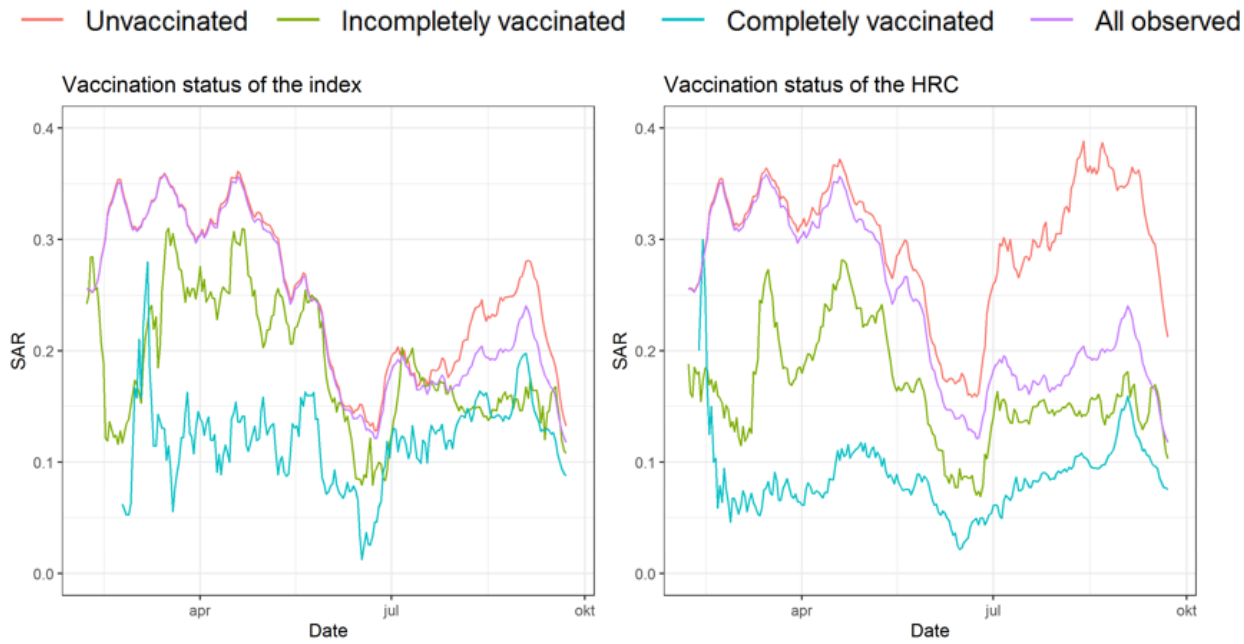
*% of those with first negative test

- Comparing compliance to the test-strategy and test-positivity rates in vaccinated vs. unvaccinated high-risk contacts for the past month, we can note the following (table 1):
  - Vaccinated HRC are **more** likely to get a first test (to be released from quarantine) but **les**s likely to get a second test compared to unvaccinated HRCs
  - Test-positivity rates are >2x as high in unvaccinated HRCs

- Test-positivity rates for vaccinated HRCs are similar for first test than for second test (cave: there might be some bias since loss of follow-up for 2nd test)

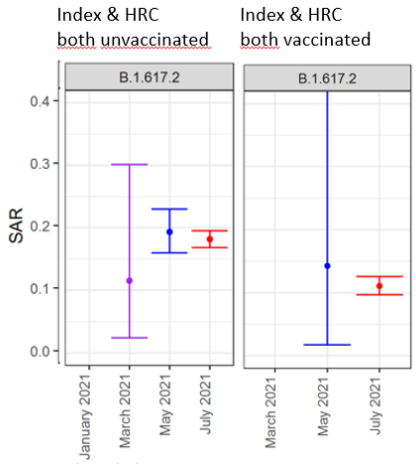
- Both the vaccination status of the index patient and his/her HRC influence risk of infection, but the most important factor is the vaccination status of the HRC. This can be seen from Figure 6 below: there is a wider gap between the red and blue line for HRCs for the most recent period.

Figure 6: Secondary attack rates by vaccination status of index case (left) or high-risk contact (right) *Source: Belgian contact tracing data*



- Even with the delta variant (dominant in Belgium since early July), it seems that spread between fully vaccinated individuals remains more limited than between unvaccinated individuals. Of note though is that there is still non-negligible spread between fully vaccinated index cases and HRC. The secondary attack rates presented in Figure 7 might be an underestimation since fully vaccinated HRC only required a first test in the period 25/06-31/08.

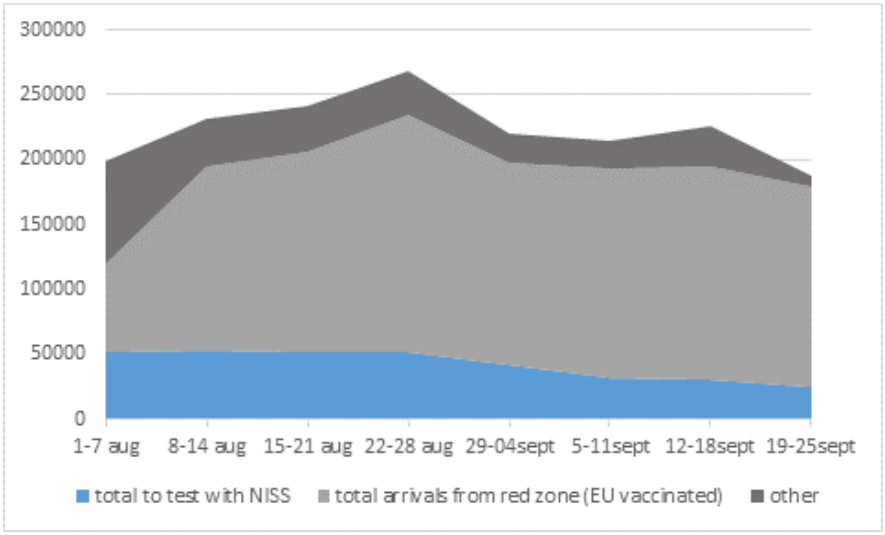
Figure 7: Secondary attack rates for confirmed infections with delta variant by vaccination status of both index case and high-risk contact *Source: Belgian contact tracing data & genomic surveillance*



Testing of incoming travelers

- Figure 8 shows the total number of weekly arrivals in Belgium from red zones (both EU and non-EU). In blue is the total of travelers that provided a NISS code and required testing according to the regulations. In light grey are fully vaccinated travelers coming from EU red zones who were exempt from testing and dark grey is travelers from red zones who required testing but for which no test result is available (either not tested or result not linked since NISS lacking, e.g. for foreign residents). **In September, the average weekly arrivals from red zones was 209,224 travelers, of which 38,549 were identified as needed to be tested**.

Figure 8: Number of arrivals in Belgium from Red zones, August-September 2021 *(Source: Paloma platform)*



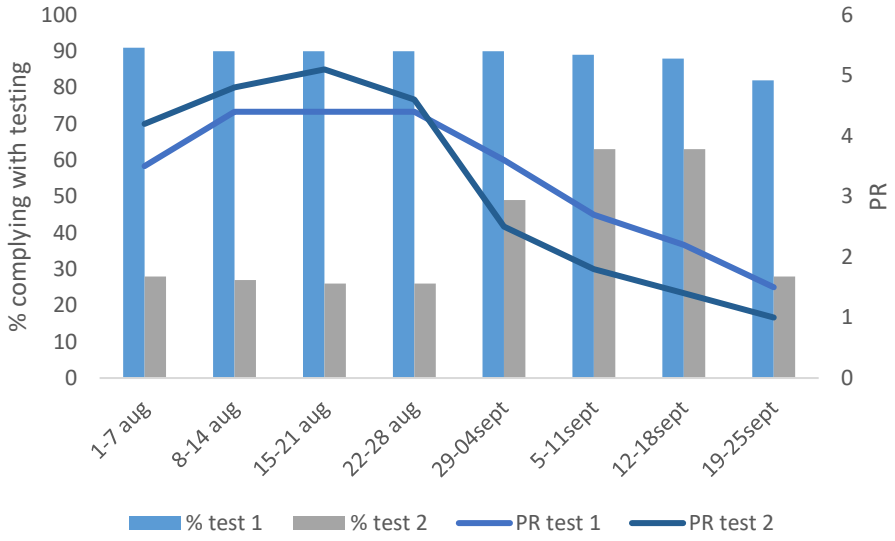
- Among the travelers who received a code for a test in August and September 2021, **on average 89% performed a first test**. This is usually the test on day 0, but is in some cases (when having proof of a negative test before returning, and no test on day 0 is needed) the test on day 7. On August 31st the regulations changed and a second test on day 7 was required for unvaccinated travelers arriving from red EU/Schengen countries and vaccinated travelers arriving from other red countries. **The number of travelers having a 2nd test on day 7 increased in September to 60%.** The average number of weekly tests performed among travelers was in September 45,216, of which 28,471 1st tests and 16,745 2nd tests.

- Positivity rates are different in vaccinated and unvaccinated travelers and according to the region of origin. For the period July-August, test-positivity rates for vaccinated travelers returning from third countries were 7% for Morocco (vs. 16% in unvaccinated), 2.7% for Turkey (vs. 8%) and 2% for UK (vs. 3%). As the example of Morocco shows, in case of very high viral transmission and many social contacts, high positivity rates are possible even in vaccinated returning travelers

- **The PR of the 1st test was 4.1% in August and decreased to 1.5% at the end of September. The PR of the 2nd test is similar to the PR of the 1st test and follows the same trend.** It has to be observed though that the denominator is not the same, because some travelers only have one test.

- Of the 103,243 incoming tested travelers in the month of September, of whom the test results was reported, the large majority were Belgian residents (97%), of which slightly more than half (58%) were fully-vaccinated (and thus returning from a red non-EU/Schengen/white list country). The low percentage of foreign travelers is probably due to underreporting in the Paloma platform (see above).

Figure 9: Percentage of travelers tested according to guidelines and PR, August-September 2021 *(Source: Paloma platform)*



2. INTERNATIONAL RECOMMENDATIONS

Testing of people with symptoms suggestive of COVID-19

	Strategy for possible cases	Criteria for testing
BE	Test all – RDT or PCR - except if clear other cause identified - except previous infection <180d	- **1** of cough, shortness of breath, thoracic pain, anosmia/dysgeusia OR - **2** of fever, myalgia, fatigue, coryza, sore throat, anorexia/watery diarrhea, altered mental state, sudden collapse
ECDC	Test all – preferably PCR	**1** of cough, fever, shortness of breath or sudden onset of anosmia, ageusia or dysgeusia
WHO	Test all if feasible	- **1**: sudden onset anosmia or ageusia without other identified cause (= probable case) OR - **2** fever + cough OR - at least **3** of fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental state
CDC	Test all RDT (confirm if negative) or PCR - except previous COVID <3m	**1** of fever or chills, cough, shortness of breath or difficulty breathing, new loss of taste or smell, fatigue, muscle or body aches, headache, sore throat, congestion or runny nose, nausea or vomiting, diarrhea
PHE	PCR asap	**1** of fever, new onset cough, ansomia/dysgeusia
NL	Test all	**1** of having a cold (coryza, sneezing, sore throat), cough, fever and chills, sudden anosmia/dysgeusia, dyspnea
DE	Test mild symptoms if in contact with risk group or high risk of infection (e.g. after event with >10 persons)	- **1** of acute bronchitis, pneumonia, fever, shortness of breath, anosmia or dysgeusia - acute respiratory symptoms in combination with being exposed to risk groups, large groups of people (e.g. teachers), several cases in the household or having participated to an event with >10 people
FR	Test all PCR or RDT	**1** of fever, cough, anosmia/dysgeusia, myalgia, fatigue, diarrhea, shortness of breath, anorexia

Testing of contacts of confirmed cases

	Definition of (high) risk contacts	Testing for vaccinated	Testing for non-vaccinated	Type of test
Belgium	Physical contact ***OR*** close contact for more than 15 minutes at <1,5m with an infected person	1st test as soon as possible + 2nd test at D7		PCR
CDC	Close contact for more than 15 minutes at <1,5m (6 feet) with an infected person	Test at D3-D5	1st test as soon as possible and 2nd test at D5-D7	NAAT or Antigen test
WHO	Close contact for more than 15 minutes at <1m with a probable or confirmed infected person	*Risk-based approach by country*	*Risk-based approach by country*	NAAT or Ag-RDTs
France	Close contact at <2m	asap + D7		PCR or Antigen test
UK	Face to face contact at <1m ***OR*** non-face to face contact at <1m for more than 1 minute ***OR*** contact for more than 15 minutes at <2m	asap		PCR
Netherlands	Close contact for more than 15 minutes at <1,5m on a 24h period	No test (unless you have symptoms)	asap + D5	PCR-, (TNO-)LAMP- or rapid antigen test
Denmark	Direct physical contact ***OR*** contact at <2m for more than 15 minutes ***OR*** contact at <2m during activities with heavy exhalation/physical exercise/enclosed space	D4 + D6		PCR

Testing of international travelers

The indications for testing returning or arriving travellers in selected countries are summarized in the table below and further described in the text. In short, test strategies differ substantially among countries. Some countries, such as the UK and the US, have stringent test requirements, while others are much more lenient. Except for the US, all countries distinguish between vaccinated and unvaccinated travellers.

Comparing the current Belgian strategy to some other countries, we observe that

- Belgium often makes a difference between Belgian residents and non-Belgian residents, while most countries don't.
- Belgium requires less pre-travel proof of a negative test and more often a test ASAP after arrival.
- With regards to differences between fully vaccinated and non-fully vaccinated, some countries are less distinctive (US) and some more (France, Germany).

- Most countries use a two-test strategy (a first test before or ASAP after arrival, and a second test later on), but some apply a one-test approach in certain circumstances. The Netherlands often recommends non-compulsory self-testing.

Summary test indications for returning/arriving travelers (>=12 years) in selected countries:

Country	Vaccinated		Unvaccinated	
	Before travel	After arrival	Before travel	After arrival
	Travelers coming from:			
Belgium	None	*Test on day 0 and 7:* • Other red countries • High-risk VOC countries	• Red countries (non-Belgian residents) *Optionally (in replacement of test on day 0):* • Red EU/Schengen countries (Belgian residents) • VOC EU/Schengen countries	*Test on day 0 and 7 (Belgian residents):* • Red countries • VOC countries *Test on day 7 (non-Belgian residents):* • Red countries • VOC countries
Netherlands	High-risk countries	• High-risk countries (day 5) *Not compulsory self-testing:* • All other countries	• Non-EU/Schengen countries • Non-green EU/Schengen countries	*Not compulsory self-testing:* • Green countries *Not compulsory test on day 2 and 5:* • Non-green countries
France	None	None	• All countries	*Randomly tested upon arrival:* • Orange countries *Systematically tested ASAP after arrival:* • Red countries
Germany	VOC areas	None	• All countries	• High-risk countries (day 5)
UK (currently)	All countries	*Test on day 2:* • Amber list countries *Test on day 2 and 8:* • Red list countries	• All countries	*Test on day 2:* • Green list countries *Test on day 2 and 8:* • Amber list countries • Red list countries
UK (from October onwards)	None	*Test on day 2:* • Non-red list countries *Test on day 2 and 8:* • Red list countries	• All countries	• All countries (day 2 and day 8)
USA	All countries	• All countries (day 3-5)	• All countries	• All countries (day 3-5)

ECDC

The latest ECDC guidelines for COVID-19 testing of travellers dates March 12, 2021. The guidelines were developed in a context of rapidly spreading VOC's and a still low vaccination coverage, and caution is therefore needed when translating them to the current context of no newly arising VOCs, high vaccination coverage and the predominance of the more transmissible Delta variant.

The recommendation was to apply, for travellers coming from areas with one or more VOCs or areas with a high level of SARS-CoV-2 community circulation, a combined approach of quarantine and testing travellers:

1. A pre-departure test, at the earliest 48 hours before departure or at the point of departure. If this is difficult or not feasible (e.g. for short business or personal trips or for any non-residents at the place of departure), this could be replaced by a test performed

immediately upon arrival at the destination, followed by contact tracing in the event of a positive test.
2. Testing five to seven days after arrival.

They point out that countries should carefully weigh the expected public health benefit against the public health resources required to implement such measures and the socially and economically disruptive effects they may cause.

European Commission

ECDC publishes every week a COVID-19 travel risk map, using color codes - green, orange, red and dark red - that represent the COVID-19 risk levels in EU zones. EU countries agreed on a common framework for possible measures for travelers from these zones.

Member states should:

- strongly discourage all non-essential travel to and from dark red areas
- require persons travelling from dark red areas to be in possession of a negative test certificate and to quarantine/self-isolate
- apply the same measures as dark red areas to areas with a high prevalence of COVID-19 variants of concern or interest
- require persons travelling from orange or red areas to be in possession of a negative test certificate
- exempt children under 12 from the requirement to undergo tests
- exempt children and young people under 18 from the requirement to undergo quarantine/self-isolation where there is no such requirement on the person accompanying them

However, fully vaccinated or travelers recovered from COVID-19 are exempted for testing or quarantine/self-isolation.

In June 2020, the European Council adopted a recommendation on temporary restrictions on non-essential travel into the EU and the possible lifting of such restrictions, that was last updated in May 2021. According to the recommendation, vaccinated persons, essential travelers and non-essential travelers from countries on the EU's list should be allowed to travel into the EU under certain conditions. The EU's list was last updated on 23 September 2021 and includes 14 non-EU countries fulfilling certain criteria relating to the epidemiological situation. It recommends that persons travelling from any country for an essential or non-essential reason should have tested negative for COVID-19 in a PCR test taken no more than 72 hours before. In addition, member states may require self-isolation or quarantine for a period of up to 14 days, as well as further COVID-19 testing as needed during the same period.

WHO

WHO issued guidance with regard to testing in the context of international travel on 16 December 2020, and published an update on 2 July 2021. It recommends to implement testing and/or quarantine measures to international travellers on a risk-based manner, taking into account the vaccination status and the probability of individuals from the country of departure being infected, in particular with a VOC. WHO does not recommend specific test schedules, but discourages the use of rapid Ag tests for screening travellers.

CDC

CDC has updated its guidance on international travel during COVID-19 on August 25, 2021, taking into account the higher transmissibility and viral load of Delta infections.

All air passengers coming to the United States, **including U.S. citizens and fully vaccinated people**, are required to have a negative COVID-19 test result no more than 3 days before travel or documentation of recovery from COVID-19 in the past 3 months. Both PCR and approved rapid Ag tests are accepted.

In addition, all air passengers must get tested 3-5 days after travel. Non-fully vaccinated travelers have to stay in quarantine for 7 days (independent of the test result). Fully vaccinated travelers only have to self-monitor possible symptoms.

Non-fully vaccinated travelers are also advised to get tested 1-3 days before their trip.

The Netherlands

The Netherlands require a negative COVID-19 test **pre-travel** for travelers >=12 years returning or arriving from non-green countries within EU/Schengen or from non-EU/Schengen countries. Fully vaccinated people and people with a recovery certificate are exempted, but depending on the country arriving from. Travelers from high-risk countries always need to have a negative test result. This list comprises currently no countries.

After arrival, testing is advised, including for fully-vaccinated people, but not compulsory. The advised test schedule depends on the country travelling from and the vaccination/recovery status:

- Green countries, regardless of vaccination or recovery status: self-test
- Non-green countries and vaccination or recovery certificate: self-test
- Non-green countries and no vaccination or recovery certificate: test with either a self-test or at a testing center (with a self-appointment) on day 2 and 5 after arrival
- High-risk countries, regardless of vaccination or recovery status: compulsory quarantine of 10 days, that can be shortened if negative test on day 5

France

France has developed guidelines per type of country arriving from (green, orange or red) and vaccination status.

Pre-travel, fully-vaccinated returning/arriving travelers (>=12 years) do not require a negative test, regardless of the type of country travelling from. Non-fully vaccinated people do require a negative test (PCR or rapid Ag test):

- <72 hours when arriving from a green country (comprises all EU/Schengen countries and non-EU/Schengen countries with low virus circulation)
- <72 hours if PCR, <48 hours if rapid Ag test, when arriving from an orange country
- <48 hours when arriving from a red country

After arrival, all travelers with vaccination/recovery certificate and travelers arriving from a green country, regardless of vaccination/recovery status, do not need to be tested. Travelers arriving from an orange country and without vaccination/recovery certificate can be randomly requested to be tested with a rapid Ag test, and are advised to self-isolate during 7 days. Travelers without

vaccination/recovery certificate arriving from a red country are obligatory tested with a rapid Ag test, as soon as possible after arrival, and have to stay in quarantine for 10 days.

United Kingdom

All travelers to England, Scotland, Wales or Northern Ireland from abroad, including UK citizens, need to have proof of a negative COVID-19 test (PCR, LAMP or Ag test) performed in the 3 days **before departure**, even if they are fully vaccinated or travelling from a country or territory on the green list.

After arrival, travelers from a green country or territory and fully vaccinated travelers from a country or territory on the amber list do not need to quarantine but must take a COVID-19 test on or before day 2 (paid for by the traveler). Non-fully vaccinated travelers who were in an amber country/territory in the 10 days before must quarantine for 10 days and take a test on or before day 2 test and on day 8. Travelers from a red country/territory must quarantine in a managed hotel and follow the same test procedures as non-fully vaccinated travelers from an amber country/territory, regardless of their vaccination status.

From October 4, 2021, onwards new rules will apply. The red, amber, green traffic light system will be changed to a single red list of countries and simplified travel measures for arrivals from the rest of the world.

Fully-vaccinated travelers from non-red list countries will no longer require a pre-departure test, but must still test after arrival on or before day 2. Fully-vaccinated travelers from red list countries (mostly African and Latin American countries) must still quarantine and test on or before day 2 and on day 8. The rules for fully vaccinated people will also apply to (non-fully vaccinated) under 18 years old residents in the UK or one of the countries or territories with approved vaccination programs.

Non-fully vaccinated travelers from any country outside the UK will need to have a pre-departure test, stay in quarantine and have an additional test on or before day 2 and on day 8.

Germany

Germany requires **pre-travel** proof of a negative COVID-19 test result from all non-fully vaccinated travelers (>=12 years) and from all travelers (regardless of vaccination status) coming from an area with a VOC. The test can either be a rapid Ag test (<48 hours; <24 hours if coming from a VOC area) or a PCR test (<72 hours).

After arrival, travelers entering Germany following a stay in a high-risk area must stay in quarantine (10 days), unless they can provide proof of vaccination or recovery. The quarantine period may be ended on the basis of a negative test carried out no earlier than five days after entry. For children under the age of twelve quarantine ends automatically after 5 instead of 10 days. Travelers from an area of variant of concern always have to quarantine for 14 days.

3. LITERATURE

Broad strategies for the winter season as outlined by other international organizations

Robert Koch Institute

Mid-September, the German RKI published a strategy outline for the coming fall and winter season. They insist that we are currently in a **transit phase** until spring 2022 and need to maintain basic measures, including for people who have been fully vaccinated. The main goal should still be to keep viral transmission at low levels, as RKI judges herd immunity to be impossible.

According to RKI, **contact tracing is an essential intervention, as it offers the advantage to be highly targeted**. The testing of symptomatic individuals therefore remains key, in order to kick-off the process of contact tracing and break the chains of transmission. **Testing of children with respiratory symptoms is explicitly mentioned as one of the strategies that need to be maintained.**

Other basic measures that need to be maintained are physical distancing where possible, hand hygiene, face masks, the corona-alert application and good ventilation.

British Academy of Medical Sciences (as mentioned in previous RAG advice)

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.

Symptoms caused by Delta variant infections

Research from the UK, relying on the widespread use of a symptom tracking app and link with testing data, shows that the most common symptoms for people testing positive as of 21/09/2021 were (1):

Vaccinated	**Unvaccinated**
Runny nose	Headache
Headache	Runny nose
Sneezing	Sore throat
Sore throat	Fever
Anosmia	Persistent cough

The same researchers previously showed that testing everybody experiencing any of seven key symptoms - cough, fever, loss of smell, fatigue, sore throat, headache or diarrhoea – would identify 96% of symptomatic cases. A study published in the Lancet Child and Adolescent Health identified headache and fatigue as the most common symptoms in both younger (5-11y) and older children (12-17y) (2). Only 1 in 3 presented with fever (38%) and 1 in 4 with cough (25%). The study period ran from September 2020 to January 2021 (before widespread circulation of Delta). No scientific literature was identified regarding a possible change in presenting symptoms for the delta variant. .

Outbreaks in a highly vaccinated population

As shown above based on Belgian contact tracing data, spread of the virus is importantly reduced among vaccinated individuals(3). A recent case report from Israel highlights however the potential of continued transmission even in a highly vaccinated population. An undiagnosed COVID-19 infection in a fully vaccinated hemodialysis patient (whose symptoms were mistaken for a bloodstream infection) lead to a total of 42 cases, of which 39 were fully vaccinated. Most of the cases were in other patients (n=23), but also 16 staff members and 3 family members were involved, despite universal masking both by patients and staff still being the rule in the hospital (4).

Testing of international travelers

Several mathematical modeling and some observational studies have been published with regards to effectiveness of strategies of testing international travelers in reducing the spread of COVID-19. However, **almost all of these date from the era before vaccination roll-out and Delta predominance, and extrapolation to the current context is risky**. In addition, the few 'real-world' experiences are each in a particular context. A Cochrane review of 13 modelling

studies and 13 observational studies therefore concluded that these studies only provide 'low-certainty evidence' (5). Nevertheless, there is consensus that testing international travellers will likely reduce viral spread.

Observational studies generally show that **most positive cases are detected by testing upon arrival, although that still an important number are additionally detected by a second test later on**. For example, a study among 16,361 arriving international travelers at Toronto airport who were tested on day 0, day 7 and day 14 found that, of the 248 detected cases, 67% had tested positive on day 0, 27% on day 7 and 6% on day 14 (6). In a similar study among 2714 arriving international travelers at Bahrain International Airport, who were tested upon arrival and at the end of a 14-day quarantine period, unless they presented symptoms before, 188 tested positive of which 136 upon arrival (72%) and the remaining during or at the end of the quarantine period (7).

Some modelling studies have compared different test strategies. Kiang et al. estimated **that pre-travel PCR testing** reduces the number of infectious days (the number of days that travelers are infectious after arrival) with 36% (29–41) compared with no testing and identifies 88% (76–92) of actively infectious travelers on the day of flight (8). Adding post-travel quarantine and PCR reduces the number of infectious days further to 82% (80–84). If the pre-travel screening is done with a rapid Ag test, the reductions are 32% (26–38) and 70% (67-72), without and with post-travel quarantine and PCR respectively, and the % identified 86% (83–89). **Dickens et al. estimated that testing travelers upon arrival, followed by quarantine and a test on day 7, reduces case importation on average by 90.2%** (9). This was similar to testing upon arrival, followed by quarantine and a test on day 14 (91.7%) and to a 14-day quarantine without testing (91.2%), but much higher than a 7-day quarantine without testing (55.4%) and higher than testing upon arrival without quarantine and second test (77.2%). Johansson et al. found that a quarantine of 7 days combined with symptom monitoring and a test on day 3-4 after arrival is highly effective (95-99%). With effective quarantine after arrival, testing a few days later optimizes sensitivity to detect those infected immediately before or while traveling (10). Taylor et al. found that, without quarantine, a single RT-PCR taken upon arrival at the airport is only 39.6% effective (11). Alternatively, testing four days after arrival is 64.3% effective whereas a test at the airport plus additional test four days later is 68.9% effective. Clifford et al. observed that a quarantine period of 8 days on arrival with a PCR test on day 7 can reduce the number of infectious arrivals released into the community by a median 94% compared to a no quarantine, no test scenario (12).

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ANNEX 1: SUMMARY CURRENT TEST STRATEGY

Test indications are currently ordered by priority.

Level 1a indications are considered as necessary and include (in order of priority):

- Persons with suggestive symptoms
- High-risk contacts*
- Returning/arriving travelers from a risk zone
- Low-risk contacts during a cluster investigation

Level 1b indications are recommended in function of the epidemiological situation and if testing capacity allows it:

- Non-COVID patients upon admission to a high-risk ward of a hospital
- New residents of residential care centers
- Repeated screening of asymptomatic staff of residential care centers and home care nurses, if vaccination coverage of residents <90% or staff <70%.
- Visitors to residential care centers, if vaccination coverage of residents <90%.
- Low-risk contacts outside the context of a cluster study

Level 2 indications are considered useful but not necessary, and are therefore optional and depending on the epidemiological situation and other conditions to be met:

- One-time screening of asymptomatic persons who have the potential to infect many others and for whom effective preventive measures are not or are difficult to implement
- Repeated screening of asymptomatic populations who have the potential to infect many others and where effective preventive measures are not readily available or are difficult to achieve
- Testing based on self-risk assessment, including self-testing

*Source investigation (backward tracing and testing of high-risk contacts till 10 days before start of symptoms/positive test) can be done ad-hoc in specific situations, for example if a spreading event was identified or a new VOC is suspected, and once virus circulation has diminished (alarm level 1).

A more detailed description of when and whom to test, by vaccination status, and the type of sample and test to use is summarized below.

<table>
<tr><th>Vaccination status</th><th>Test procedure</th><th>Sample and test to use</th></tr>
<tr><td colspan="3">Symptomatic patients fulfilling case definition</td></tr>
<tr><td>Non-fully vaccinated</td><td rowspan="2">Systematically test if >= 6 years
Test <6 years only if there was a recent risk contact</td><td rowspan="2">If symptoms <=5 days and no severe disease, preferentially rapid Ag test on respiratory sample (NPS, COTS, ANS); otherwise PCR on respiratory sample or saliva</td></tr>
<tr><td>Fully vaccinated</td></tr>
</table>

Vaccination status	Test procedure	Sample and test to use
Asymptomatic high risk contacts		
Non-fully vaccinated	• 1st test ASAP after identification • Second test the earliest on day 7	PCR on nasopharyngeal swab (NPS) or combined oral-throat swab (COTS)
Fully vaccinated		
Returning/arriving travellers		

Non-fully vaccinated	• 1st test ASAP after arrival: Belgian residents returning from risk zone (if not tested before arrival)
	• Second test the earliest on day 7:
	  ○ Belgian residents returning from risk zone
	  ○ Non-Belgian residents arriving from a risk zone within EU
		PCR on nasopharyngeal swab (NPS) or combined oral-throat swab (COTS)

Fully vaccinated	• 1st test ASAP after arrival: Belgian residents returning from risk zone outside EU
	• Second test the earliest on day 7:
	  ○ Belgian residents returning from risk zone outside EU
	  ○ Non-Belgian residents arriving from a risk zone outside EU
		PCR on nasopharyngeal swab (NPS) or combined oral-throat swab (COTS)

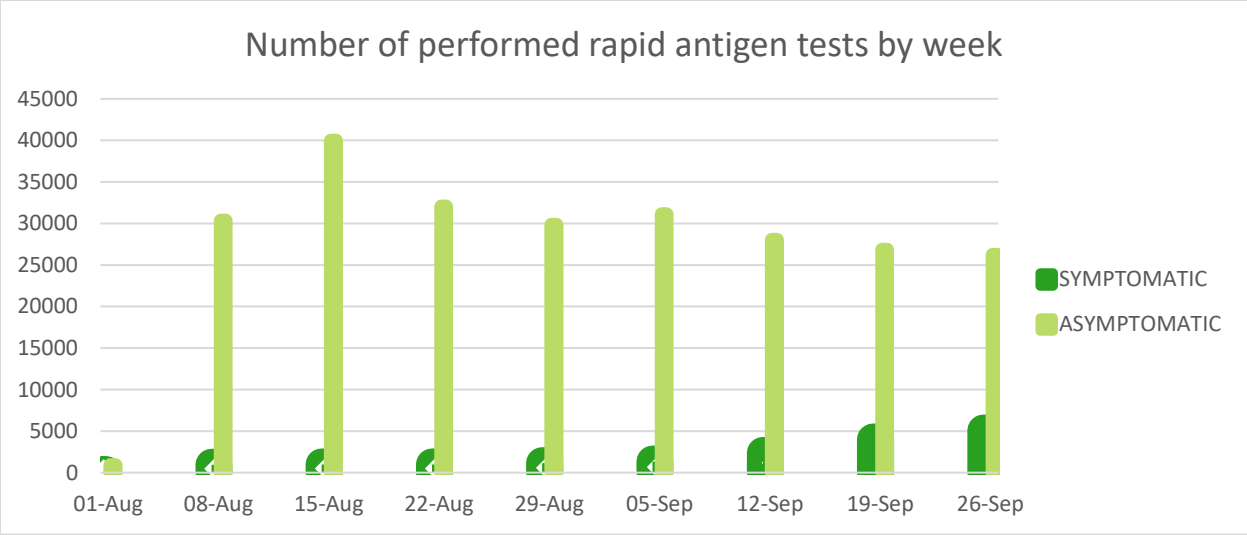
Asymptomatic low-risk contacts in cluster investigations		
Non-fully vaccinated	• Only if deemed useful by health inspector	PCR on NPS/COTS
Fully vaccinated		
Other asymptomatic low risk contacts		
Non-fully vaccinated	• Only if test capacity allows it	PCR on NPS/COTS
Fully vaccinated	• No testing	N/A
Recommended one-time screenings		
Non-fully vaccinated	• Non-COVID patients pre-hospitalization, according hospital guidelines • New residents nursing homes	PCR on NPS/COTS
Fully vaccinated	• Non-COVID patients pre-hospitalization, if at great risk (e.g. pre-transplant) • New residents nursing homes	PCR on NPS/COTS

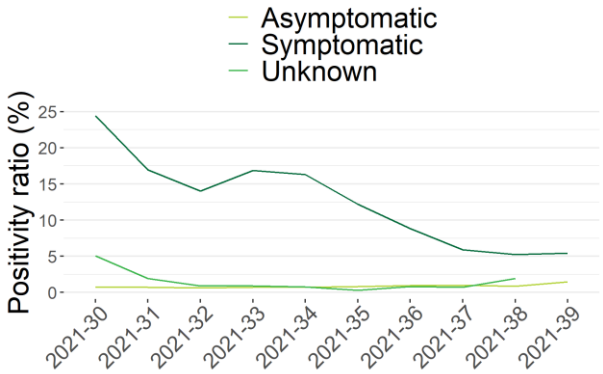
Vaccination status	Test procedure	Sample and test to use
Required one-time screenings, at the cost of the screened person		
Non-fully vaccinated	• Pre-event screening or other settings requiring CST	PCR<48h on NPS/COTS or saliva (under supervision) OR rapid Ag test<24h on NPS/COTS
	• Departing travellers, if required by country of destination	Per requirements of country of destination
Fully vaccinated	• Departing travellers, if required by country of destination	
Recommended repetitive screenings		
Non-fully vaccinated	• Staff nursing homes if low vaccination coverage (residents <90% or staff<70%)	1x/week PCR on saliva or 2x/week Rapid Ag Test test on NPS/COTS
Fully vaccinated	• No testing	N/A
Optional one-time screenings		
Non-fully vaccinated	• Visitors nursing homes with low vaccination coverage (residents <90%)	Rapid Ag test on NPS/COTS
	• Other settings fulfilling certain conditions	
Fully vaccinated	• No testing	N/A
Optional repetitive screenings		
Non-fully vaccinated	• In a workplace setting	1x/week PCR on saliva or 2x/week Rapid Ag Test test on NPS/COTS
	• In a school setting (if alarm level 2 or higher)	
Fully vaccinated	• No testing	N/A
Optional testing based on self-risk assessment		
Non-fully vaccinated	• In certain settings fulfilling certain conditions (for example university students)	PCR or Rapid Ag test on NPS/COTS
	• Self-testing at home preventive out of courtesy or after suspected contact	Rapid Ag test on anterior nasal swab (ANS)
Fully vaccinated	• No testing	N/A

ANNEX 2: ROUGH ESTIMATES OF NUMBER OF TESTS TO BE PERFORMED BY TEST INDICATION IN THE COMING MONTHS (TASK FORCE TESTING)

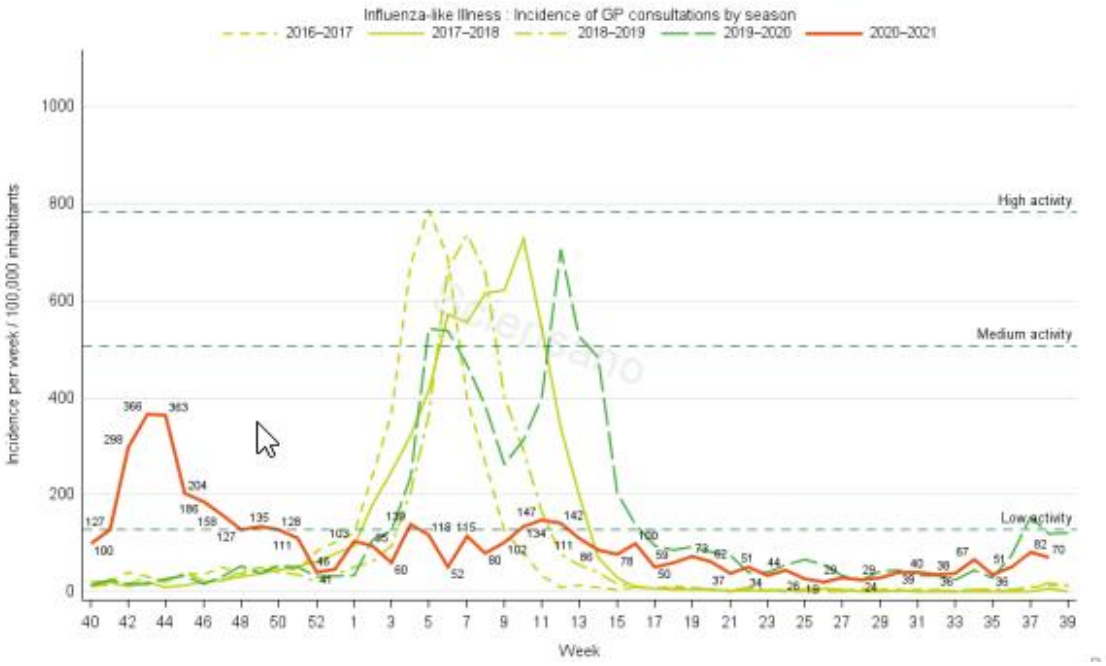
Indication	Assumption	Number of tests/ day
Symptomatic patients – primary care	Important number of flue and other respiratory infections	Up to 50.000
Symptomatic patients – secondary care		5000
Contacts	5-10 contacts per index case	15-20.000
New residents nursing homes		1000
Pre-event screening (CST)		2000
Departing travelers	Between 25.000 and 30.000 travelers, of which 85% with vaccination/recovery certificate	4000-5000
Returning/arriving travelers	Between 25.000 and 30.000 travelers, of which 90% with vaccination/recovery certificate	2500-3000

ANNEX 3: NUMBER OF RAPID ANTIGEN TESTS AND POSITIVITY RATES





ANNEX 4: NUMBER OF GP CONSULTATIONS FOR INLUENZA-LIKE ILLNESSES IN PREVIOUS SEASONS



ANNEX 5: PROPOSAL DOMUS MEDICA FOR TEST STRATEGY IF NO ADDITIONAL TEST CAPACITY OUTSIDE OF GP PRACTICES

- Forse aanpassing teststrategie
  - Gevaccineerden In HAP enkel nog klinische indicatie (ernstig zieke personen) -> als je als arts het nodig vindt om te testen moeten artsen die mogelijkheid hebben.
  - Niet gevaccineerden : testen volgens gevalsdefinitie (Niet-gevaccineerde volwassenen hebben hogere kans op ernstige ziekte en ziekteverspreiding)
  - -12 jarigen niet meer testen en geen quarantaine (groepsimmuniteit) tenzij klinische indicatie (ernstig ziek)
  - Personen boven 12 jaar met symptomen die nauwe contacten hebben met mensen uit een risicogroep (bv : zorgverleners, verschillende generaties onder hetzelfde dak, ..)
  - Personen die terugkeren uit risicogebieden waar een nieuwe variant opgedoken is (Om transmissie van nieuwe varianten snel op te sporen en in quarantaine te plaatsen)
  - Stimuleren zelftesten/Gevaccineerden zelf een CTPC-code kunnen aanmaken voor test in testcentrum (geruststelling)
  - Thuiswerk/mondmaskerplicht bij mild infectieuze klachten