LONGER-TERM PERSPECTIVE OF TESTING, ISOLATION AND QUARANTINE

RAG meeting 08/02/2022

This document served as a basis for discussions and recommendations at the RMG. The final RMG note, approved by the interministerial conference of 09/03/2022 is available here (Dutch version only).

CONTEXT

Almost two years ago, Belgium went into lockdown as the COVID-19 pandemic unfolded. Since then, periods of severe restrictions and intense viral circulation have been alternating with more favorable epidemiological circumstances. With increasing duration of the pandemic, other societal and health aspects (like mental health aspects) are becoming ever more important. Measures like quarantine severely disrupt people's lives and potentially their livelihoods. Moreover, it should be evaluated whether the costs (both direct and indirect) of extensive testing are still proportionate to the desired outcome. Finally, the increased immunity in the population (both through natural infection and repeated vaccination) and the Omicron variant have altered the equation between cases and burden on the healthcare system. On the other hand, extensive testing, isolation and quarantine have been important tools to slow down the spread of the virus this far. In contrast to 'blanket measures' like closing down entire parts of society, testing & tracing is a targeted intervention that impacts those proven to be infectious or at high risk of being infectious. It is still unclear what the further evolution of the epidemic will be. We need to bear in mind that immunity will wane over time or can be evaded by certain variants. Also, 'endemic' diseases, like tuberculosis and HIV, or Influenza can still cause a high burden of mortality and morbidity. In addition, thanks to remaining infection prevention measures in place, we have not yet encountered an overlap of a normal/severe influenza season together with a COVID peak, which would certainly cause additional strain on the healthcare capacity.
This document aims to set out broad lines for the future management of SARS-CoV-2 in Belgium, taking into account different possible scenarios and the management levels of the barometer.

RECOMMENDATIONS

A schematic overview of recommendations is presented in the table on the next page. More detailed recommendations are featured further on. **The table and recommendations aim to set a framework for future policy, however it will still remain necessary to evaluate the situation, taking into account all available information (e.g. immune escape and waning, transmissibility, performance of (self-) tests etc.).** Both viral and population characteristics (age structure, vaccination coverage, comorbidities…) determine what the ratio severe diseases/cases will be.

Of note, the impact of a variant with low severity and lower transmission will be limited (and unlikely to replace the current circulating strains) so this scenario is not featured in the table. In

case of a variant with high severity combined with very high transmission, very swift and drastic action will be necessary.

GENERAL GUIDING PRINCIPLES

		Characteristics circulating variant	
		Low ratio severe disease / cases (i.e. high circulation e.g. current Omicron)	High **or unknown** ratio severe disease / cases (e.g. introduction new VOC with immune escape)
Barometer level (~ number of severe infections)	Yellow	• *Relatively low levels of circulation* • Overall risk = low • Baseline surveillance to monitor situation • Focus on protecting populations at risk of severe disease	• *Low levels of circulation* • Future risk = high (or unknown) • Intense efforts to prevent VOC from becoming established: source investigation + rigorous contact tracing with compulsory quarantine
	Orange	• *High levels of circulation* → protect 1st line / test capacity from becoming overwhelmed • Empower individuals to manage risk: self-testing of symptomatic persons and HRCs within the household • Supervised testing for people with symptoms/HRCs in contact with population at risk of severe disease (LTCFs, healthcare staff and patients, closed communities…)	• *Still relatively low levels of viral circulation* • Increase of infections has high impact on healthcare and mortality → continue contact tracing, test all HRCs • Entry screening in healthcare facilities/LTCFs to protect residents and healthcare system
	Red	• *Very high levels of viral circulation* • Test capacity to be prioritized (e.g. for those eligible for prophylactic antiviral treatment) • Control spread by general NPIs rather than contact tracing • Reserve part of test capacity and human resources for outbreak management in healthcare settings or closed communities with persons at risk of severe disease, if required	• *High levels of viral circulation* • Increase of infections has high impact on healthcare and mortality → continue contact tracing if possible, at least for household contacts and persons at risk of severe disease AND strengthen NPIs • Entry screening in healthcare facilities/LTCFs to protect residents and healthcare system

MORE DETAILED BREAKDOWN: see next page

		Characteristics circulating variant	
		Low ratio severe disease / cases (i.e. high circulation e.g. current Omicron)	**High or unknown** ratio severe disease / cases (e.g. introduction new VOC with immune escape)
Barometer level (~ number of severe infections)	Yellow	**Symptomatic:** -test only for clinical reasons or persons at risk of severe disease -at least self-test if in contact with persons at risk of severe disease -encourage to stay at home when symptomatic **Contact tracing:** - only in case of large outbreak in a population at risk of severe disease **Screening:** - not generally recommended for new residents in collectivities, hospital admissions or travelers (except for VOC countries) - can be considered for healthcare settings with clinically extremely vulnerable patients	**Symptomatic:** - test all with compatible symptoms by PCR or RAT **Contact tracing:** - for all cases + source investigation - test LRCs in case of outbreak - quarantine and test all HRCs (both household and other) **Screening:** - screen admissions in healthcare settings with persons at risk of severe disease (not all hospital admissions), including LTCFs - screen incoming travelers from high-risk areas and VOC countries
	65 daily new hospitalizations for COVID / 300 patients in COVID-19+ patients in ICU *(+ trend new infections)*		
	Orange	**Symptomatic:** - test and isolate all - if no (contact with) vulnerable groups: self-test ok (no confirmation required), or RAT at pharmacy **Contact tracing:** - ensure access to PCR-testing for HRCs with immunosuppression (eligible for prophylactic antiviral treatment) - household contacts: no Q but for ≥6y 7d mask-wearing for all contacts outside of household, or daily self-test if mask-wearing is not possible - focus on healthcare settings / LTCFs / closed communities like homeless shelters and prisons: repeated PCR-testing for HRCs **Screening:** **-** screen admissions in healthcare settings with clinically vulnerable patients (not all hospital admissions), including LTCFs - only test + quarantine incoming travelers from VOC-countries	**Symptomatic:** **-** test and isolate all with RAT or PCR **Contact tracing:** - for all cases - test all HRCs with PCR as soon as possible and D7 - consider exceptions for quarantine after first negative test, except if outbreak in residential collectivity >18y **Screening:** **-** screen all hospital admissions and new residents in LTCFs - only test + quarantine incoming travelers from VOC-countries

	150 daily new hospitalizations for COVID / 500 patients in COVID-19+ patients in ICU *(+ trend new infections)*		
	Red	**Symptomatic:** - test and isolate all, allow self-tests (no confirmation needed) **Contact tracing:** - ensure possibilities of outbreak management in healthcare settings / LTCFs / closed communities like homeless shelters and prisons, e.g. PCR-testing +- quarantine (tailor to situation) - ensure access to PCR-testing for HRCs with immunosuppression (eligible for prophylactic antiviral treatment) - strengthen general NPIs in society to reduce number of non-household contacts **Screening:** - screen all hospital admissions and all new residents in LTFCs - only test + quarantine incoming travelers from VOC-countries	**Symptomatic:** - test and isolate all, allow self-tests **Contact tracing:** - preferably continue exhaustive CT. If not possible: focus on household contacts and healthcare settings / LTCFs / closed communities like homeless shelters and prisons - strengthen general NPIs in society to reduce number of non-household contacts **Screening:** - screen all hospital admissions and all new residents in LTFCs - do not test incoming travelers (as already high circulation)

1. General recommendations

- **Different epidemiological situations will require different strategies** and hence some flexibility and scalability will need to be foreseen within the systems. However, to increase compliance, **the aim should be to keep procedures as stable as possible** as long as there are no important changes in the epidemiological situation.
- The **categories of the barometer should be used** both for rules in society (as already approved by the OCC) and for testing, isolation and quarantine procedures.
- Additional NPIs like reduction of contacts, use of face masks in crowded public areas, attention to hand- and cough hygiene and promoting telework can also importantly reduce the circulation of SARS-CoV-2 as well as other respiratory illnesses. **Isolation and quarantine rules for all age groups (including unvaccinated children) should be proportionate to overall measures in society**.
- If the barometer is no longer used, or we would be in a "green situation", the measures as outlined in yellow/new VOC should initially be followed if a new VOC would be detected.

2. Testing of people with possible symptoms of COVID-19

- **Testing of persons with symptoms compatible with COVID-19 should always be possible for clinical reasons** such as ruling out alternative diagnoses or initiating antiviral treatments.
- Depending on the epidemiological situation (see grid), testing of people with mild symptoms that are not at risk for severe disease, might not always be necessary.
    - As general good practice, people who are ill should always be encouraged to stay home until symptoms have resolved.
    - Special attention is needed for people either living in collectivities with residents at risk of severe disease (e.g. homeless shelters, prisons, LTCFs) or associated with healthcare (including both staff and patients/residents).
- People tested positive for SARS-CoV-2 should always be isolated, regardless of symptoms. For the Omicron variant, the duration of isolation should be maintained at 7 days (+3 additional days of precautions). In case of a new variant, the duration of the isolation period might need to be re-evaluated.

3. Contact tracing and testing of high-risk contacts

- Contact tracing without adequate testing or quarantine for identified contacts should be avoided, because the impact will be limited.
- There should **always be the possibility to trace, test and quarantine high-risk contacts in case of outbreaks**, especially in collectivities with residents at risk of severe disease or in a healthcare-setting.
- A first option to scale down contact tracing, could be to focus on household contacts only.
- Testing of high-risk contacts by a healthcare provider should be prioritized over quarantine without testing, if testing capacity is sufficient.

4. Entry screening

- For **events**: the circumstances (barometer level orange and red) and type of events for which a negative test can be required have been previously decided by the OCC.
- Screening before **admission in hospital** can be restricted to high-risk services (oncology, geriatrics, hematology, dialysis, intensive care unit…) in case of more favorable epidemiological circumstances.
- **New residents of collectivities**: in favorable epidemiological circumstances, screening can be omitted.
- Other types of screening (e.g. in the workplace) are optional and should never jeopardize the testing capacity for the priorities as identified in the table.
- **For travelers:**
    - if a **VOC country** can be clearly identified, it is important to screen incoming travelers to prevent / delay introduction. However, if many countries switch to lower levels of testing / sentinel surveillance, it might be a challenge to pick-up VOCs in an early stage;
    - screening of incoming **travelers from areas with high incidences (non-VOC)** is only useful if Belgium itself has relatively low incidences, so only to be considered in code yellow. Residents without vaccination or recovery certificate can then be asked for a test upon arrival;
    - for non-EU third countries, at least the same measures should apply as for the dark-red areas

ELEMENTS OF DISCUSSION

- The **aim should be to reduce the burden on the healthcare system as much as possible and to return to 'code yellow'** (before being in a situation of complete predictability). Letting go of measures too soon, might mean we end up in an equilibrium with high viral transmission and continued high pressure on the healthcare system and necessity to continue NPIs in society.
- Whilst the barometer levels offer the advantage of clarity and uniformity with overall measures in society, it is important to realize that they are mostly based on late indicators (hospital admissions, ICU) and will not capture rapid changes. There needs to be willingness to quickly change levels if required based on the evolution of the number of infections.
- High levels of viral circulation, even when not leading to many cases of severe disease, should still be avoided as **high levels of absenteeism can still severely disrupt** essential parts of society.
- Alternative surveillance system (e.g. sentinel surveillance) should be developed or expanded to continue monitoring of the epidemic, regardless of the testing strategy.
- The current system of contact tracing, where all HR contacts are traced, but the advised measures are very limited and there is no systematic testing of asymptomatic individuals, probably has very limited impact on the evolution of the epidemic.
- **At very high levels of viral circulation, contact tracing is not feasible and insufficient** to bring the epidemic under control. For variants with lower severity, high levels of viral transmission can already be reached in the orange level.
- Moreover, at higher levels of viral circulation, contact tracing might be less cost-effective and the focus should shift towards protecting people at risk of severe disease.

- There is an impression that many persons are already relying on self-tests and not confirming positive results, hence not being part of the official system. When self-tests do not require confirmatory testing, it needs to be considered how these tests can be registered. People requiring proof of COVID-infection (e.g. for their employer, if telework is not possible), should rather be tested by RAT at the pharmacy then by a self-test.
- **Sufficient attention should be paid to administrative implications**: restricting access to PCR-testing for HRC's might lead to increase demands of patients to their GPs, either for test prescriptions or for sick leave certificates.
- At high levels of circulation, it might be preferable to reduce testing in healthcare staff and rather **rely on universal precautions** (FFP2-masks, strict distancing, separate lunch breaks…) On the other hand, knowing someone's COVID-status will allow for some better differentiation of preventive measures and e.g. restricting access of COVID+ healthcare workers to non-COVID wards or wards very high risk patients.
- If self-testing is recommended, there should not be a financial threshold. It could be considered to e.g. provide a code to the index case that would allow the household contacts to collect free self-tests at the pharmacy.
- There is currently no systematic testing of asymptomatic high-risk contacts (only self-testing recommended) and we are still seeing a downward trend.

BACKGROUND

1. BELGIAN DATA

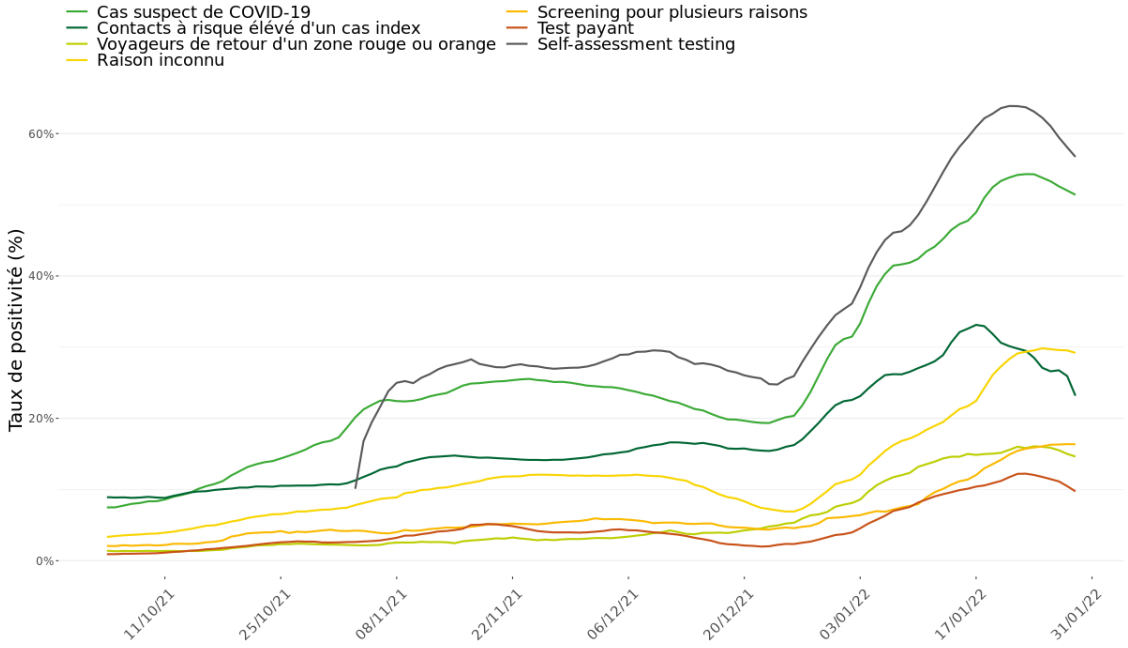
General

- An overview of the epidemiological situation can be found in the RAG epidemiology (NL/FR). Belgium is currently in the highest level of the barometer based on pressure on the healthcare system (hospitalizations + ICU occupancy), but a downward trend is expected.
- Important changes to the testing strategy, with only self-testing for asymptomatic HRCs, have already been implemented on 10/01/2022. These changes were announced to be temporary.
- The overall test-positivity rate has varied over time, parallel with the evolution of the pandemic, but is currently very high, at 45.3%, indicating important levels of underdetection.

Testing of symptomatic individuals

- The test-positivity rate (PR) in symptomatic individuals has equally varied over time, but has always been highest in symptomatic individuals, including during summer.
- According to the last Health Information Survey of Sciensano (end of December, 22 354 respondents, representative sample of the population), **>95% of respondents believed that staying home when being sick was an effective measure** to control spread of SARS-CoV-2 and 84% of respondents reported to comply with the measure.
- However, according to the same survey, **only 35% of respondents that presented possible symptoms of COVID intended to get tested**. Most important reasons for non-compliance were:
    - not being aware the symptoms are a reason for testing (55%)
    - having a negative self-test (22%)
    - believing an alternative diagnosis is causing the symptoms (14%)

Figure 1 : Positivity rate by testing indication since 04/10/2021 (Belgium) *Source: eForms/CTPC, available for 77% of tests*



Testing of (vaccinated) contacts

- Before stopping the systematic testing of high risk contacts, high PRs were observed among close contacts. **PRs are higher in household contacts than other contacts** (table 1) and in unvaccinated contacts (39%) than in vaccinated contacts (26%).

Table 1: test-positivity rates for high-risk contacts between 27/12/2021-02/01/2022

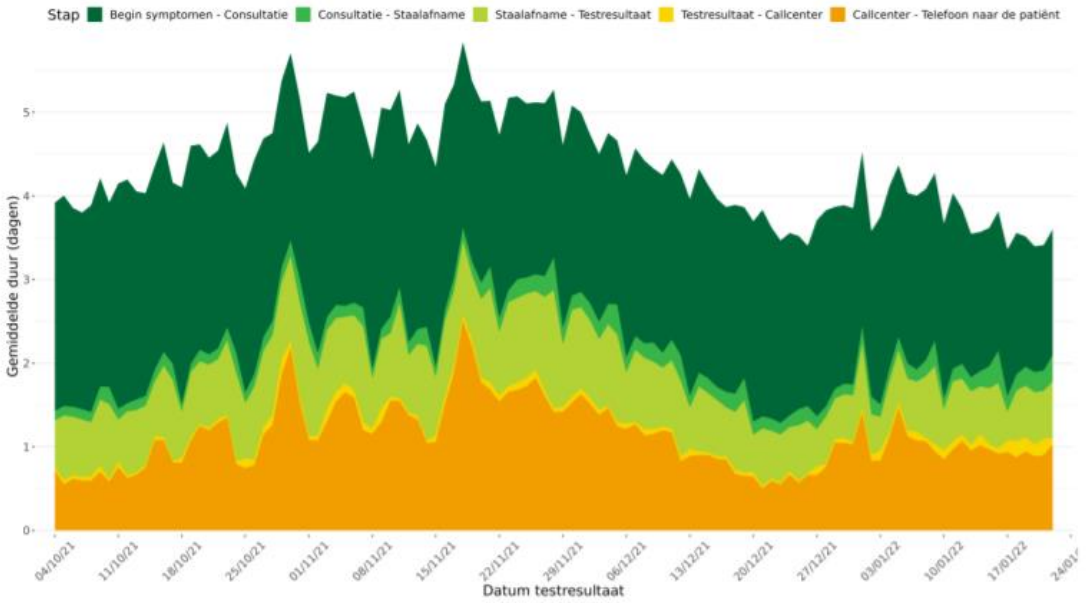
	1st test	2nd test
Household contact	35.2%%	32.1%
Other contacts	20.5%	26.1%

Contact tracing

- Since 04/10/2021, 734 046 confirmed COVID-19 cases were contacted of which 82.4 % reported contacts. However, in the period from 17-23/01/2022, **with very high daily numbers of index cases, only 26.5 % of confirmed COVID-19 cases were successfully called**. The remaining index cases received an sms only and could report contacts through on online tool.
- 84% of contacted index cases reported contacts. The **average number of reported contacts is 2.3.** This number has been surprisingly stable throughout the pandemic, despite relaxations in society. Although not all contacts are traced by the call centre (e.g. work-related contacts by occupational health services), this number probably represents an underreporting of contacts.
- Overall, the **time between symptom onset in index case until contact of the high-risk contacts by the call centre is about 3-5 days**. The biggest delay is between onset of symptoms and request of test (~2 days), with an additional 24h to get the test result. Recently

this delay has been shortened, potentially because symptomatic people can request access to testing themselves through a self-assessment tool and rapid results from antigen-testing at pharmacies.

Figure 2 : Time intervals in the process of testing and tracing



- Between 01/01-30/09/2021, 24% of all index cases had already been identified and quarantined as a high-risk contact.

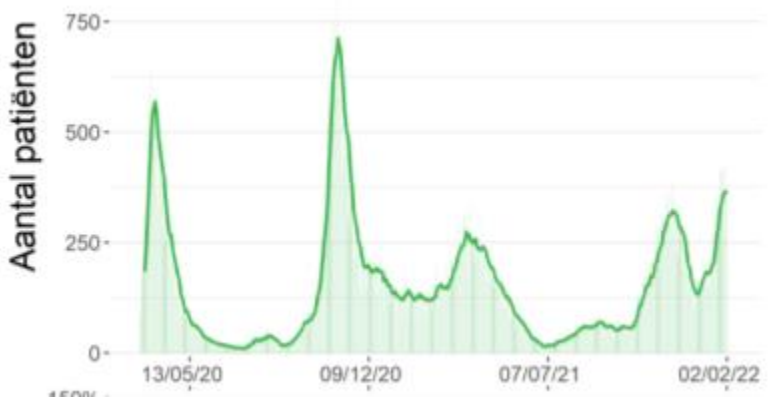
Pressure healthcare system

- As in other countries, over the course of the epidemic, the relation between cases and hospitalizations for COVID has changed over time. Currently, less patients are admitted for every 100 cases than early last year.

Figure 3: Number of COVID-19 hospital admissions per 100 infections, Belgium

- However, even despite lower relative severity, the absolute number of patients admitted to hospital because of COVID-19 remain high because of very high viral circulation.

Figure 4: 7-day average of new hospital admissions because of COVID-19 since 03/2020



Screening

- As can be seen from Figure 1, in times of high viral circulation (= high PR in symptomatics), screening also yields (very) high number of positive cases.

2. INTERNATIONAL RECOMMENDATIONS

WHO

The World Health Organization is preparing new guidance on testing and tracing. On 02/02/2022 the WHO director general stressed that it is premature to declare victory over SARS-CoV-2 and that "**countries should continue to use every tool in their toolbox, rather than relying on vaccines alone**". Dr Tedros further stated that *"We're concerned that a narrative has taken hold in some countries that because of vaccines and because of Omicron's high transmissibility and lower severity, preventing transmission is no longer possible, and no longer necessary. Nothing could be further from the truth. More COVID-19 transmission means more deaths.*"

ECDC

In its latest risk assessment of the Omicron spread in Europe**, ECDC also warns for unfounded optimism**: "*The inevitable information voids that accompany a new VOC facilitate the emergence and spread of misinformation, which can include unfounded assumptions (as per current scientific understanding) that may or may not end up being correct. One of these assumptions is the speculation that Omicron represents the last major wave of the pandemic, after which we will be able to return to a life that includes 'living with COVID-19' as an endemic virus and an accepted risk.*"

Regarding duration of isolation and quarantine, ECDC issued guidance on the 7th of January, on options for a shortened quarantine and isolation in case of high or extreme pressure on healthcare systems and society. They explicitly state these recommendations to shorten isolation are not scientifically based but rather a pragmatic approach.

	Standard	High pressure	Extreme pressure
Vaccinated* cases	**6**d after symptom onset + 24 without fever OR 2 neg RAT/PCR (24h interval) + 24h without fever	**3**d after symptom onset + 24h without fever + negative RAT/PCR D3 + 3d FFP2	**3**d after symptom onset + 24h without fever (+ negative RAT/PCR) +5d FFP2
Unvaccinated cases	**10**d after symptom onset + 24 without fever OR 2 neg RAT/PCR (24h interval)l + 24h without fever	**5**d after symptom onset + negative RAT/PCR D5 + 24h without fever + 5d FFP2	**5**d after symptom onset + 24h without fever (+ negative RAT/PCR) +5d FFP2

*boosted or <6 months after primary vaccination. For regions with Omicron dominance <3m after primary vax

The latest ECDC guidance on contact tracing features a paragraph on when to perform contact tracing:

"*Each country should adapt their response to the local epidemiological situation and available resources. The rigorous and timely application of contact tracing measures in areas where there are a limited number of cases can play a key role in limiting further spread of the outbreak. However, if resources allow, contact tracing should also be undertaken in geographical locations with more widespread transmission. Even if not all contacts of each case are identified and traced, contact tracing is still thought to contribute to reducing transmission in combination with other non-pharmaceutical interventions [43,44]. Contact tracing efforts should always aim to cover at least cases occurring in high-risk settings such as long-term care facilities, hospitals, prisons and refugee camps to reduce transmission and mitigate the impact on population at risk of severe diseases. Contact tracing can also help prevent emerging VOCs from becoming established.*"

ECDC also recently audited Belgium's testing strategy. Whilst the final report is not available yet, first feedback pointed towards the need to prioritize testing indications if there is a high cumulative incidence (e.g. from 500/100,000) and to start the transition towards a sustainable sentinel surveillance, as is used for Influenza.

CDC

The US CDC continues to recommend testing of all possible cases. They issued recommendations in the context of Omicron to shorten the isolation period to 5 days after symptom onset + 5 additional days of mask-wearing for the general population. They also advised to shorten the quarantine period to 5 days (followed by 5 days of strict mask-wearing). Quarantine can be waived for fully vaccinated individuals, but they should be tested on D5 after exposure.

Other European countries

As the situation is rapidly changing in terms of case load, pressure on the healthcare system and societal evolutions, many countries are changing their guidelines and it is challenging to provide an overview.

Several countries that have let go of COVID-19 restrictions in general society, such as UK and Denmark, continue to provide recommendations on testing and isolation of all persons with possible symptoms of COVID-19. The exception is Sweden, where from 9th of February, only people with possible symptoms who are related to healthcare (i.e. staff and residents) still need to be tested. Other countries continue to isolate confirmed cases and to have a system of contact tracing in place although they allow for exceptions on quarantine for fully vaccinated individuals or children, provided they do daily self-testing (UK) or a single PCR-test 3 days after the contact or after symptom onset of the index case (Denmark).

The following tables provide an overview of the isolation and quarantine requirements in EU-member states mid-January.

Table 3: Overview of duration of quarantine for HRC in EU-member states (mid-January)

Vaccinated contacts					Unvaccinated contacts				
Number of days					Number of days				
0		5	7	10	5	7	10		14
BE	SE	CZ	CY	AT	CZ	CY	AT	LT	MT
DE	SI	EL	HR	BG	DK	EE	**BE**	LV	
DK	SK	FI	IE	LT	EL	ES	BG	NL	
EE	LIE		LU	LV	FI	HU	DE	RO	
ES	CH		PL	MT	IT	IE	FR	IS	
FR			PT	NL	SE	LU	HR	NO	
HU				RO	SK	PL			
IT				IS	LIE	PT			
					CH	SI			

Table 4: Overview of duration of isolation in EU-member states (mid-January)

Vaccinated cases						Unvaccinated cases						
Number of days						Number of days						
4	5	6	7	10	14	4	5	6	7	10		14
NO	CZ	LU	**BE**	AT	BG	NO	CZ	LU	**BE**	AT	IE	BG
	EL	NO	DK	CY	LV		EL		DK	CY	LT	LV
	FR		ES	DE			SE		ES	DE	PL	MT
	SE		HR	EE			SK		HU	EE	PT	
	SK		HU	LT			LIE		IE	FI	RO	
	LIE			MT			CH		NL	FR	SI	

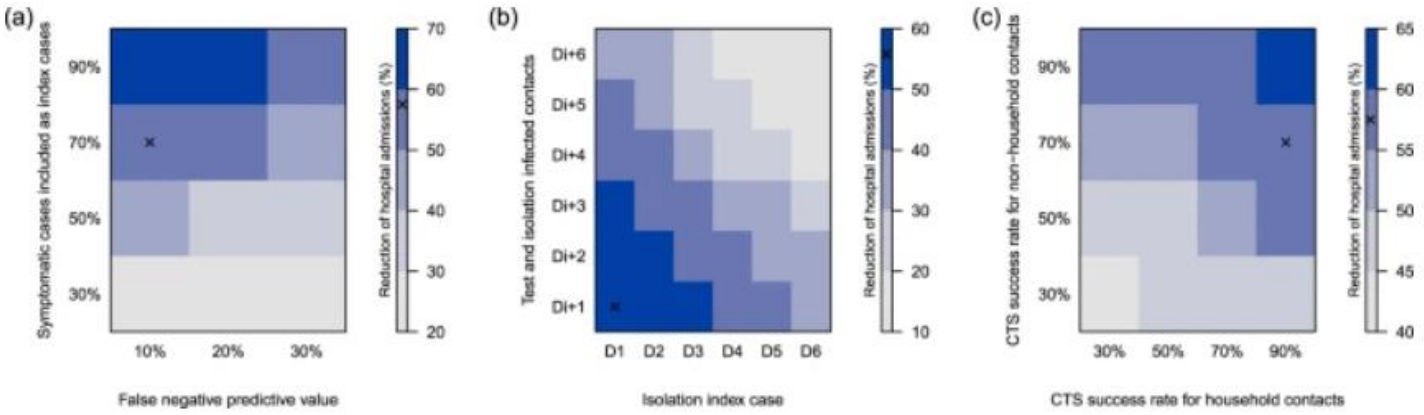
3. SCIENTIFIC LITERATURE

Effectiveness of contact tracing

Several modelling studies have shown that contact tracing can importantly reduce the spread of SARS-CoV-2 (1–5). The **biggest contribution to reduction of spread is made by testing and isolation of infectious individuals** (1,2). Hu et al estimate that, focusing only on testing and isolation of symptomatic individuals, reducing the infectious time in the community from 12 days (i.e. 2 days before and 10 days after symptom onset) to 4 days (2 days before, and 2 days after symptom onset), would reduce the number of infections by 85.2% (1). Piasecki et al. insist on the importance of **identifying a high enough proportion of cases**: if only 20% of cases would be detected, then isolation of these cases and contact tracing (even the most efficient system), would have limited impact on the evolution of the epidemic (3). On the other hand, it is not necessary to get a coverage of 100%: even reaching only 50% of cases can result in large impacts on the course of the epidemic. These conclusions are supported by modelling work from the team at the University of Hasselt (5), as shown in figure 5. Of note though, is that contact tracing is most effective in combination with other NPIs which will reduce the number of contacts. Another important conclusion of their work is that the overall turn-around time of contact tracing (from symptom onset index to quarantine of contacts) should preferably not be longer than 4 days (see Figure 5).

Modelling of Kretzschmar et al (4) support the conclusion that **minimizing testing delays** is of paramount importance to improve effectiveness of contact tracing. Although isolation of symptomatic individuals seems to have the highest impact, additional testing and tracing of high-risk contacts helps to bring down the number of infections: Kucharski et al note that self-isolation of symptomatic cases within the household would reduce transmission by 29%, whilst adding household quarantine would reduce transmission by 37% (so an additional 8%) and manually tracing known high-risk contacts would reduce transmission with 57% (so an additional 28%) (2). Piasecki et al point out that **the number of quarantined individuals and the infection rate among the quarantined contribute equally** to the reduction in transmission (3). That would mean that quarantining a lower number of infectious individuals but that are at very high risk of infection (e.g. only household contacts), is equally effective as quarantining a high number of people at lower risk of infection. On the other hand, and in line with the emphasis Piasecki et al. placed on detecting a high enough percentage of cases, **contact tracing strategies without testing of asymptomatic high-risk contacts might have only a very limited impact**. Modelling from the UK showed that the contact tracing system as applied in October 2020, detecting 40% of all cases (estimated by comparing with incidence estimates of random sampling as performed by the Office of National Statistics) and with a median 5 days from symptom onset in index to quarantine of contacts would only reduce the reproductive number with 1.7-4.6%, compared to a 16-28% reduction from isolation of symptomatic individuals (6). Even with reduced delays to quarantine, the additional reduction made by contact tracing would only be 7-10%. It is also clear that, especially with a high effective reproductive number, contact tracing alone will be insufficient to bring the epidemic under control (3,5).

Figure 5: Reduction of hospital admissions due to contact tracing according to the symptomatic cases included as an index case and the false-negative predictive value of testing (a) , delays (b) and the success rate of tracing, testing and isolating household and (non-)household contacts (c). *Source: Willem et al (5)*



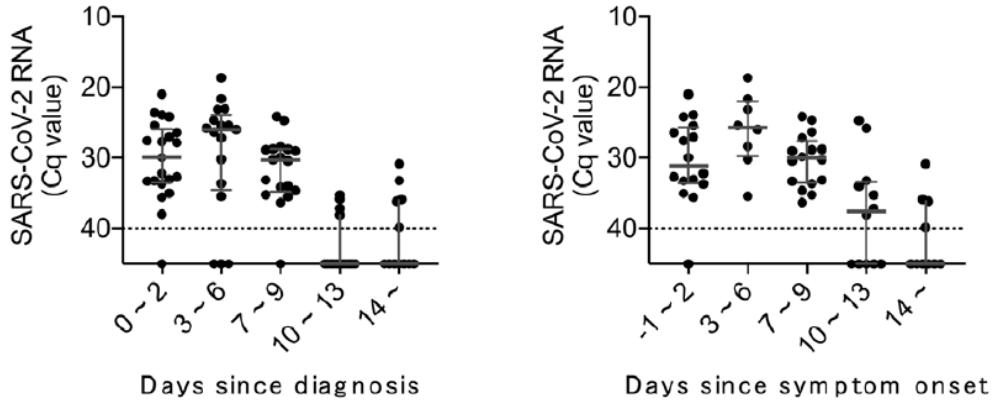
A very important limitation to the abovementioned evidence is that the models used parameters that were fitted to the observed reproductive number and generation interval of the Wuhan strain, and did not account for potential protection against infection/transmission offered by vaccines. With a high infectiousness early after exposure, contact tracing delays might need to be even shorter in order to be effective.

Infectious period of the Omicron variant and influence of vaccination

Regarding the influence on vaccination status on the infectious period in case of post-vaccination infection, we refer to the RAG advice of 04/01/2022. In general, it seems the infectious period is slightly shortened for breakthrough infections.

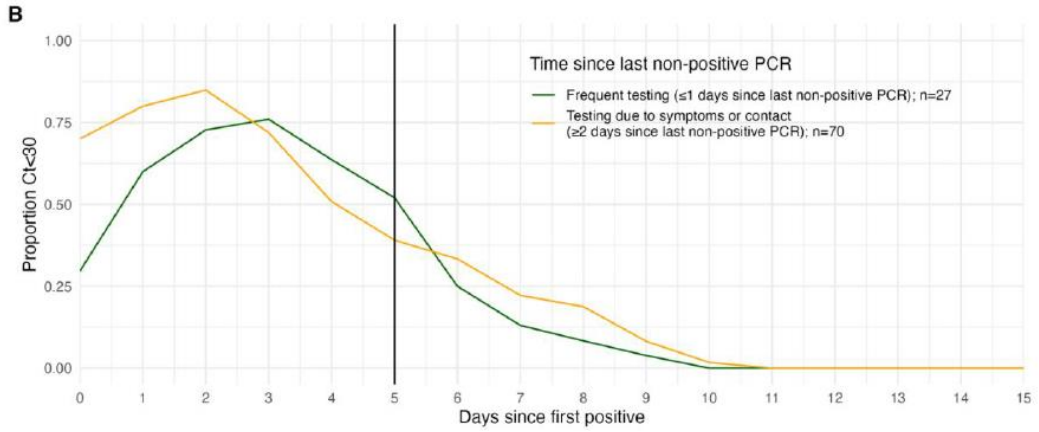
The RAG advice of 20/01/2022 summarizes evidence on duration of infectious period for Omicron infections and is repeated below:
Two pre-print studies, both with relative small sample sizes, have been identified that evaluate the duration of infectiousness for the Omicron variant.
In Japan, 21 individuals infected with the Omicron variant underwent daily PCR-testing (7). All cases were either mild (n=17) or asymptomatic (n=4) and almost all cases were vaccinated (19/21 = 90%). Peak viral load was around day 3-6, with still relatively high viral loads day 7-9 and a marked decrease after 10 days. As it is difficult to translate Ct-values to infectiousness, the authors also attempted viral culture. Importantly, **virus cultures were still positive for 3 out of 16 symptomatic cases (19%) day 7-9 after symptom onset**. As a positive viral culture is thought to equate infectiousness, this raises questions about the safety of ending isolation early. For all 4 asymptomatic cases, viral culture was negative from at least 6 days after initial positive test.

Fig 6. Evolution of viral load in Omicron-infections. *Source: NIIDDC (7)*



The second pre-print study evaluates testing data from the National Basketball Association in the US (8). Of note is that the tested population includes mostly healthy young men. When comparing 97 Omicron infected-individuals with 107 Delta-infections, overall time to PCR-negativity was slightly shorter for Omicron (9.87 days [95% CI 8.83-10.9]) than for Delta (10.9 days [9.41-12.41]), although confidence intervals overlap. The authors also note that the observed difference might be related to other factors than the variant in itself, as they did not account for prior immunity or vaccination status. **As in the Japanese study, a high proportion of cases still had Ct-values of <30 (used as a proxy for infectiousness) >5 days after the initial positive test (see Figure 6).** After day 10, virtually all samples had a Ct-value of >=30. Of note is that days are counted from the first positive test (and hence, for the orange curve, day 1 could e.g. represent day 3 after symptom onset if there was a delay in testing) and that not all participants were followed up until a negative test result was obtained. Hence the true proportion of individuals with Ct-values >30 might be higher than depicted in Figure 7.

Fig 7. Evolution of the proportion of potentially infectious individuals (as represented by Ct-value <30) per day post first positive test for Omicron-infections. *Source: Hay et al (8)*



Another pre-print, posted on 02/02/2022, adds to the evidence that the infectious period might be longer than 5-7 days (9). Following updated recommendations by the CDC, HCWs in the US could present to work 5 days after symptom onset if they were without fever and symptoms had

improved. During a time period where Omicron was dominant, 309 RATs were performed on 260 HCWs , day 5-10 after symptom onset. Overall, 43% of tests were still positive after 5 days. Interestingly, boosted HCWs were more likely to still test positive (Table 5after symptom onset. Overall, 43% of tests were still positive after 5 days. Interestingly, boosted HCWs were more likely to still test positive (Table 5).

Table 5: proportion of RATs still positive X days after symptom onset. *Source: Landon et al* (9)

Day of Illness		Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Total
Total 1st Tests	**n**	**52**	**53**	**68**	**46**	**28**	**13**	**260**
	% Positive	**46%**	**58%**	**38%**	**26%**	**25%**	**54%**	**41%**
Not Boosted	n	19	21	33	23	15	8	119
	% Positive	21%	38%	24%	22%	20%	50%	27%
Boosted	n	33	32	35	23	13	5	141
	% Positive	61%	72%	51%	30%	31%	60%	53%

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