RECOMMANDATIONS SUR LE DÉPISTAGE PÉRIODIQUE DANS DES POPULATIONS SPÉCIFIQUES

RAG subgroep testing – 4 février 2021

Note : Les recommandations actuelles sont susceptibles d'être modifiées en fonction de nouvelles informations et/ou de l'évolution de l'épidémie

Principales recommandations :

Populations dont il faut envisager le dépistage périodique

- Le dépistage périodique chez les personnes susceptibles d'infecter de nombreuses autres personnes ou d'entrer en contact avec des personnes exposées à un risque d'infection grave ; et lorsque des mesures préventives efficaces ne sont pas ou sont difficiles à mettre en œuvre est toujours considéré comme utile (mais pas nécessaire). Il est facultatif et dépend de la situation épidémiologique.
- La principale priorité en matière de tests reste, entre autres, les personnes symptomatiques, les contacts à haut risque, les voyageurs de retour et l'investigation de clusters (cfr avis RAG Update 12/2020). Le dépistage périodique ne peut jamais se faire au détriment de ces priorités.
- Il existe plusieurs populations pour lesquels un dépistage périodique peut être utile. Toutefois, il n'est pas possible de réaliser le dépistage périodique chez toutes ces populations.
- Le RAG a évalué, pour trois groupes de population, dans quelle mesure le dépistage périodique est utile pour prévenir de nouvelles infections. Cette liste n'est pas exhaustive et l'évaluation peut s'appliquer à d'autres groupes. En outre, il existe d'autres facteurs de nature socio-économique et opérationnelle (telles que la faisabilité et l'acceptabilité) qui doivent être pris en compte dans la décision finale quant aux groupes qui doivent être sélectionnés en priorité.

Recommandations générales sur le dépistage périodique

- Une stratégie de dépistage périodique devrait toujours être holistique et inclure entre autres les mesures à prendre en cas de résultat positif et de résultat négatif, les conséquences de la participation ou non-participation au dépistage, les précautions à prendre en dehors du dépistage, les implications pour les contacts à risque, etc.
- Le test recommandé est une détection moléculaire sur un échantillon de salive ou de dérivés de salive. Une procédure décrivant un prélèvement correct doit être disponible (par exemple, une procédure pour obtenir du crachat ou de la salive gargarisée).
- Le pooling des échantillons peut réduire les coûts et les délais d'exécution, et est donc recommandé chaque fois que cela est possible. La taille effective du pool doit être déterminée dans une procédure.
- La fréquence recommandée de dépistage est au moins hebdomadaire.

- Un résultat négatif n'exclut pas la possibilité que la personne soit encore infectée/ contagieuse ou le devienne dans les prochains jours. Toutes les mesures de précaution en vigueur doivent donc être respectées.
- Tous les résultats, ou au moins les résultats positifs, doivent être communiqués aux centres de recherche de contact et Sciensano via health/data, pour permettre la recherche des contacts. Ainsi, le dépistage ne peut pas être anonyme.

Recommandations spécifiques concernant les trois populations

Enseignants et autres membres du personnel scolaire

- Il existe suffisamment de preuves pour conclure que le dépistage périodique du personnel des écoles peut être utile dans le contexte actuel.
- Il est conseillé d'élaborer une stratégie de mise en œuvre par étape, en vérifiant d'abord la faisabilité et l'acceptabilité dans un nombre limité d'écoles.
- S'il est faisable et acceptable, il est recommandé de l'étendre à l'échelle nationale dès que possible.
- Le critère de priorité pour ce domaine pourrait être les écoles situées dans des zones à haut risque de transmission (sur la base d'indicateurs épidémiologiques).

Professions de contact non médicales

- Le risque de transmission est élevé, et le dépistage périodique des professions de contact non médicales peut donc également être utile.
- Toutefois, ce contexte est moins étudié et des incertitudes subsistent, comme la mesure dans laquelle le résultat du test déterminera le comportement et le respect des mesures de précaution, d'autant plus que le dépistage peut avoir des implications financières dans ce groupe cible.
- Le développement et l'opérationnalisation du dépistage périodique dans ce groupe doivent partir de zéro et risquent de prendre beaucoup de temps.
- C'est pourquoi le dépistage périodique n'est recommandé dans ce groupe que si :
    - Il y a des raisons socio-économiques qui en font une priorité ;
    - Il est possible de rendre la stratégie opérationnelle dans un délai raisonnable (moins d'un mois) ;
    - Il est acceptable pour le groupe cible.
- Comme pour le personnel des écoles, il est conseillé de travailler par étapes : premièrement tester la faisabilité et l'acceptabilité dans quelques services, puis un déploiement à plus grande échelle.

Les étudiants de l'enseignement supérieur

- Il existe suffisamment de preuves indiquant que des tests plus fréquents réalisés chez des étudiants de l'enseignement supérieur contribuent à réduire la transmission, et ils sont donc considérés comme utiles.
- Le dépistage périodique est un moyen efficace de réduire la transmission, mais ce n'est pas le seul. La KULeuven mène actuellement un projet pilote dans le cadre duquel les étudiants sont motivés pour tester plus rapidement/fréquemment, et cette approche a également le potentiel d'être efficace.
- L'introduction d'un dépistage périodique dans l'enseignement supérieur peut être envisagé par ces associations d'universités et d'écoles supérieures qui le considèrent pertinent et faisable.
- Le RAG soutient le développement de projets alternatifs, tel que par KULeuven, et des conseils à ce sujet suivront ultérieurement.

Les personnes suivantes ont participé à cet avis :

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CONTEXT

The current test capacity offers opportunities for a broader testing as a means to control the spread of SARS-CoV-2. In addition, the increasing circulation of new variants, with a higher infectiousness, creates concerns about a possible surge in incidence. In this context, an advice was requested with regards to repetitive screening in specific populations. More specifically:

- Is repetitive screening in teachers/ school staff recommendable or useful?
- Is repetitive screening in practitioners of non-medical contact professions (hairdressers, beauty specialists…) recommendable or useful?
- Is repetitive screening a recommendable or useful strategy to control transmission between higher education students, and between students and their families?

A proposal for a pilot project of repetitive screening in teachers, developed by UAntwerpen in collaboration with the Commissariat and the Ministry of Health, was discussed in the Task Force Testing and presented to the RAG. Teachers and other adult school staff would be weekly screened on early morning saliva. Saliva will be collected by spitting, using the device developed by ULiège. Samples will be tested with RT-PCR, pooled by three. Results will be communicated trough a fast sample registration and reporting system. To address a possible negative effect on respecting protective measures, a behavior change and engagement campaign through online pledging will be implemented simultaneously. This approach has shown to be successful in tackling antimicrobial resistance. Reporting through the e-forms will be difficult, and an alternative software is being developed to report results to the call center and Sciensano.

PREVIOUS RECOMMENDATIONS

The current recommendations (December update) with regards to repetitive screening (using saliva samples) are:

- We recommend repetitive screening in populations that are in frequent contact with people vulnerable to severe COVID-19 disease (staff at nursing homes, home nurses attending to elderly clients).
- Repetitive screening of other populations is currently not recommended, but can be considered if it is justified from a public health point of view, i.e. in persons who have a high potential for infecting others (relatively high prevalence, and close contact with a high number of persons or risk of further spread within a collectivity) or who are in contact with persons at risk of serious infection; and where effective preventive measures are not available or are difficult to achieve. Repetitive screening should never have as its main goal the relaxation of measures. If the measures are relaxed for other, socio-economic reasons, repetitive screening can be a means of minimizing the negative impact of these relaxations.

- Repetitive screening in other populations is only justifiable if the following conditions are fulfilled:
    - Risk of rapid spread of the infection to a large number of people; AND
    - No possibility to fully apply effective protective measures; AND
    - The number of people to test is feasible.
- Frequency of testing will be defined by the modelling exercise currently in development. Meanwhile, we recommend a frequency of at least weekly.
- We recommend the use of an RT-PCR test on saliva specimens. The use of Ag RDTs on nasal/oral swabs can be a valid alternative if the delay in getting the result is >24 hours because of reduced RT-PCR capacity.
- People testing negative are considered as not being infectious and/or not having COVID-19. Basic preventive measures need nevertheless to be maintained. People testing positive are considered as confirmed cases and the procedures with regards isolation and contact tracing is initiated.

DISCUSSION

Usefulness of repetitive screening of teachers/ adult school staff

Arguments pro:

- Considering the higher infectiousness of the newly circulating variants, an additional measure might be useful to prevent and control the spread through school populations.
- Mathematical models often indicate an added value of repetitive screening of schools staff on transmission reduction.
- The experience in the primary school in Liège showed a high acceptability.
- A behavior change and engagement campaign can reduce the risk of a false sense of security.
- Is already recommended in some areas (England, some US school counties). CDC states that it can be considered if risk of transmission is moderate or high, and Belgium fulfills currently these criteria.

Arguments contra:

- There is still a lack of scientific evidence on the effect of repetitive screening of school staff on transmission reduction (in addition to the effect obtained by the infection control measures in place), in a real life situation. The few documented experiences in the field are not always convincing, with sometimes very few additional cases detected. For example, in a study in Germany 10,836 repetitive rapid Ag tests were performed in 602 teachers, resulting in the detection of 5 true-positives (of which 4 had mild symptoms) and 16 false-positives.

- Previous data showed that most within-school transmission appears to be between school staff, and not from school staff to pupils or between pupils. However, recent experiences appear to indicate that this might no longer be the case.
- High number of school staff (>200.000), resulting in a high operational cost
- Risk of unnecessarily quarantining many people if a test with a lesser specificity is used, such as a rapid Ag test
- Risk of a false sense of security, considering that the sensitivity of the tests used is not 100%, leading to less respecting control measures

Weighing the pro's and the contra's, the RAG testing considers repetitive testing of school staff as a potential useful strategy in the current context. The planned pilot should provide more evidence on its feasibility and potential effectiveness.

When expanding the strategy to a national level, criteria could be established to identify schools where it is most relevant. Following the example of CDC, schools located in areas with a higher risk of transmission, based on criteria such as incidence, positivity rate and % change in new cases, could be prioritized.

Usefulness of repetitive screening of non-medical contact professions

Arguments pro:

- There is sufficient evidence of a high risk of transmission during non-medical contact professions, even with protective measures in place
- There is a high demand/need to reopen non-medical contact professions for socio-economic reasons
- Theoretically, repetitive screening is expected to have an effect on reducing transmission in this context (fulfills the criteria of close contact with a high number of persons)

Arguments contra:

- There is some limited evidence that the correct use of preventive measures (in particular correctly using masks) may prevent most transmission in the context of non-medical contact professions
- Risk of a false sense of security, leading to less respecting control measures

While there is convincing evidence that repetitive testing is potentially effective in high education students and teachers, there is less evidence with regard to non-medical contact professions. On the other hand, there is sufficient data to confirm that the risk of transmission is high and that therefore we can assume that repetitive testing can have a substantial effect.

An important unknown factor is the effect of repetitive testing on the professionals' behavior. There is a risk of hiding positive results, to avoid closure, and of relaxing protective measures when testing negative. Unlike for the pilot in school staff, pledging for behavior change is more difficult to achieve.

From an operational point of view, introducing repetitive testing in non-medical professions will require more preparation (in particular with regards to prescription and reporting) and it is doubtful that it can be implemented within a short time period. The procedures will also need to be piloted before implementing them on a nationwide scale.

Usefulness of repetitive screening of higher education students

Arguments pro:

- The relatively higher increase in incidence observed in the 20-29 years old during the period September-October 2020 is believed to be related to the reopening of higher education institutions, fueling the transmission in the other age groups.
- Because higher education students often have two bubbles (a bubble with their fellow students living in the same residence ('kot bubble'), and a bubble with their family household members), they form a large network through which the virus can rapidly spread.
- There is scientific evidence, both from mathematical models and real-life experiences, that strategies of screening university students can be effective in reducing transmission and prevent outbreaks.
- There is a high demand/need to relax measures for higher education students for psycho-social reasons

Arguments contra:

- There are currently (at least until the end of February) limited activities in universities and high schools. Distance learning is the norm and a maximum of 10% of the campus capacity may be utilized. Contact teaching is used very sparingly: only essentials are possible for the sake of the vulnerable students who really need it. However, universities are planning to start contact teaching (e.g. at least a day a week) as soon as possible.
- Most of the evidence on the effect of testing strategies among high education students comes from the US, that has a different type of residential student housing.

Increasing testing in higher education students is without doubt a useful intervention. There is sufficient evidence that it contributes to reducing the spread of the virus, the proportion of asymptomatic infections is higher in this age group, students are among those who will be vaccinated the latest, and there is a need to relax measures for psycho-social reasons.

It is less clear if repetitive testing is the most appropriate testing strategy. If not compulsory or anonymous, participation might be low. There exist alternative strategies. For example KULeuven encourages students through peers to go asap for testing when indicated (symptomatic, high-risk contact, returning traveler…) or based on their self-assessed infection risk; This approach has not yet demonstrated elsewhere to be effective, but is promising and worth exploring.

Usefulness of repetitive screening of other populations

While there has been no request to give an advice on repetitive screening in other populations, there are populations in a similar situation as some of the above. For example, medical and paramedical contact professions, examiners of practical driving exams and/or instructors of practical driving lessons, staff working in collectivities with mentally disabled people, among others.

Cross-cutting issues

- Test and sample to use.
    - The current consensus is to use an RT-PCR on saliva samples for repetitive screening. The arguments are its ease of use, even permitting self-collection, and the lesser need for having a high sensitivity test in repetitive screening.
    - The current device used in Belgium is the spitting device developed by ULiège. Gargling has, however, shown in the primary school study in Liège to be easy to perform and in studies to have a higher sensitivity than spitting and to be more acceptable. In the planned pilot in school staff, the collected sample is spitted saliva using the device developed by ULiège. While gargling might be a better option, changing the collection method will introduce additional delays. The spitting device has shown good results in Liège, and can therefore be used.
    - ULiège is applying a strategy of pooled testing of three samples, which reduces substantially the cost and gave good results. Therefore, a similar approach is recommended in other repetitive screening settings. However, at laboratories where pooling is difficult to realize, samples can be tested individually.
    - Rapid Ag tests can be a valid alternative, but care has to be taken with the interpretation of positive results because of the possibly low positive predictive value if prevalence is low.
- Periodicity and timing
    - Because of lack of accurate data, the current recommendation is to test weekly. The ideal periodicity depends however on several factors, such as sensitivity and specificity of the test, the positivity ratio in the tested population, the reproductive number, the compliance to measures taken for positive cases and the logistical capacity to collect the samples. In the case of non-medical contact professions, where the risk of transmission is high, testing twice a week might be a better frequency.
    - One modeling study found that testing teachers in the beginning of the workweek has the most effect.

- Alternative test strategies:
    - For higher education students there exist alternative strategies, such as one-time universal screening at the beginning of a term or 2-phased universal screening: pre-arrival testing paired with a follow-up test, typically about 1 week after arrival. Another possible strategy is to screen students before a high-risk exposure with a rapid Ag test. All these strategies are however less effective or less feasible than repetitive testing.

    - A possibility is to align screening with contact teaching: students alternate one-week contact teaching with one-week online teaching, and are tested <72 hours before the week contact teaching.

- Feasibility and cost
    - The number of hairdressers in Belgium is about 24,000 and the number of beauty specialist around 13,000. Other non-medical contact professions are e.g. personal physical coaches, tattoo artists… The weekly number of non-medical contact professionals to be tested each week is therefore expected to be around 50 thousand people.
    - The number of school staff and of higher education students is much higher (both estimated to be above 250.000).
    - The current capacity for prescription and sample collection is overstretched, and it is has to be decided who will prescribe the tests and how the (saliva) samples will be collected.
    - Weekly testing a large number of people comes at a substantial cost, including an ecological cost.
    - It will not be possible to repetitively test all populations where this is potentially useful and choices will need to be made. The potential effect on reducing transmission is one, important, criterion, but other criteria, such as operational feasibility, cost and the need to relax measures in a specific population for socio-economic reasons also play.

- Reporting
    - In the only experience with repetitive screening in Belgium so far, the testing of nursing home staff in Wallonia, it has not been possible to integrate the reporting of positive cases in the national system, resulting in no reporting to the call center or Sciensano and no initiation of contact tracing.
    - It is of uttermost importance that the repetitive testing result, or at least the positive results, are reported to the call center and Sciensano, to allow contact tracing. Repetitive testing can for that reason not be anonymous.

RECOMMENDATIONS

General

- It is not feasible to test all populations where repetitive screening can be useful and have a positive effect on reducing transmission. The current recommendation that repetitive screening *can be considered if it is justified from a public health point of view, i.e. in persons who have a high potential for infecting others or who are in contact with persons at risk of serious infection; and where effective preventive measures are not available or are difficult to achieve*, remains valid. However, which of these populations is prioritized depends on other criteria, such as feasibility, cost and the need to relax protective measures for socio-economic reasons of psychological well-being. The final decision is therefore a political one.

Repetitive screening of teachers/ adult school staff

Plans for piloting repetitive screening of school staff are already well advanced and can be implemented within a reasonable amount of time. In addition, there is sufficient evidence that repetitive screening of adult school staff can have a positive effect on reducing transmission, and thereby allowing schools to remain open. The RAG therefore recommends:

- To implement the pilot, as proposed, in a selected number of schools, and assess its feasibility and acceptability.
- To use the spitting device, but to evaluate on a longer term gargling as a possible alternative.
- To collect, as much as possible, the saliva sample in the beginning of the school week.
- When expanding to a larger number of schools, to prioritize schools in areas with the highest risk of transmission, based on a set of epidemiological criteria.

Repetitive screening of non-medical contact professions

Repetitive screening of non-medical contact professions, once reopened, has the potential to reduce transmission between the professionals and their clients. Compared to the two other populations considered in this advice, there is, however, less experience with this approach and more uncertainty about the effect of screening on protective behavior change. In addition, the operational challenges are more important. The RAG recommends:

- To introduce this approach only if:
    - It is politically, for example for socio-economic reason, a higher priority than repetitive screening in other populations;
    - It is feasible to develop and operationalize a system of repetitive screening, including correct reporting to the call center and Sciensano, within a reasonable period of time (less than one month);
    - It is acceptable to the targeted population.
- To first pilot it (during a couple of weeks) in a limited number of professionals and assess the effect on behavior, before expanding it nationwide.

Repetitive screening of higher education students

Increasing testing in students is definitely useful. Different approaches exist. Repetitive screening has shown to be effective in reducing transmission, assuming sufficient participation. Alternative strategies, such as the one currently piloted in KULeuven, are, however, also worth further exploring. The RAG advises:

- To let each higher education institution define its preferred strategy.
- Useful strategies are, among possibly others:
    - Repetitive weekly screening of all students on a voluntary basis, as currently implemented in ULiège.

    - Removing barriers to testing and expand indications for testing, as currently piloted in KULeuven.

- Whatever strategy is used, testing of higher education students should always be integrated in the national systems, and the results reported to the call center and Sciensano.

Repetitive screening of other populations

As mentioned above, repetitive screening can also be useful in other populations that fulfill the above described criteria (high potential for infecting others or who are in contact with persons at risk of serious infection; and where effective preventive measures are not available or are difficult to achieve). This has to be taken into consideration when defining the priority populations for repetitive testing.

Cross-cutting issues

- The recommended test is an RT-PCR on an oral fluid sample collected through either spitting or gargling. Rapid Ag tests can be a valid alternative, in situations where this is preferred (for example for operational or cost reasons). In that event, care has to be taken with the interpretation of positive results (increased risk of false positive results). If the positivity rate in the test population is low (<5%), it is recommended to confirm positive results with an RT-PCR.

- Pooling of a selected number of samples is a useful technique to reduce cost and reduce turn-around-time. It is therefore recommended, wherever possible. The recommended number to pool is three, unless there is evidence that another number is more efficient.

- The recommended periodicity continues to be 'at least weekly'. If more accurate information on the best periodicity becomes available, for example from modelling exercises, this can be adapted.

- People testing negative are considered as not being infectious and/or not having COVID-19. Nevertheless, some might become infectious in the next days and, because of the lower sensitivity of saliva samples, some infectious cases might have been missed. Therefore, basic preventive measures need to be maintained.

- People testing positive are considered as confirmed cases and the procedures with regards to isolation and contact tracing is initiated.

- All test results, or at least the positive results, need to be correctly reported to the call center and Sciensano.

BACKGROUND

Scientific literature

Repetitive screening

Several modelling studies have assessed the effectiveness of repetitive screening in controlling SARS-CoV-2 spread in specific populations. All these models showed that frequent testing with a less sensitive test (rapid antigen test) or a less sensitive sample (saliva) is more effective than one-time testing with the more sensitive RT-PCR on a naso-pharyngeal sample (1–3). The recommended periodicity varies across models and is dependent on various factors, such as the sensitivity and specificity of the test, the prevalence, the reproductive number and the compliance to measures taken for positive cases. Most studies recommend a periodicity of at least 2-3 times a week (4–7), but other state that relatively infrequent testing, such as every one or two weeks, is already sufficient to keep controlled outbreaks small (8). One study modelled the potential impact of different testing and isolation strategies on SARS-CoV-2 transmission, defined as the percentage reduction in R. Self-isolation of symptomatic individuals would result in a reduction in R of 47%, and weekly screening of health-care workers and other high-risk groups irrespective of symptoms by use of PCR testing by an additional 23%, assuming results are available at 24 h (9).

One study assessed the effect of regular universal testing and concluded that this strategy would require unrealistic high testing frequencies to reopen society while maintaining control of virus transmission (10). Another study modeling the effect of mass testing, using data from France, came to a similar conclusion that it might help to reduce infections but that campaigns need to be frequent and have to be combined with other interventions (11). A pre-print article presenting results of mass testing in Slovakia estimated the decrease in prevalence compared to a scenario of unmitigated growth to be 70% (67-73%). However, the mass campaign coincided with other infection control measures and it is not known to what extent the mass campaign is responsible for the decrease (12).

UHasselt investigated through modelling to what extent the use of universal testing, by pooling samples of individuals that belong to the same households, can be utilized to mitigate the epidemic. The model shows through simulation, that weekly universal testing is able to control the epidemic, even when many of the contact reductions are relieved (13).

Atkeson at al. assessed the economic benefits of repeated testing (with a rapid antigen test) and concluded that the fiscal, macroeconomic, and health benefits of rapid SARS-CoV-2 screening testing programs far exceed their costs (14). A weekly testing in a regime with high compliance comes close to suppressing the virus, and moving to a four-day cadence is highly effective. They point out however, that the screening testing program must have high specificity to be credible and to evoke high adherence. If specificity is not close to 100%, the positive predictive value is low in low-prevalence settings, putting many people unnecessary in isolation. They propose therefore confirmation of positive results with an RT-PCR test. The problem of low positive predictive value in low prevalence settings, and therefore a need to confirm positive results, is also addressed in another study (15).

Studies evaluating the effect of repetitive screening in a real-life situation are rare. One study evaluated a longitudinal screening program for critical on-site employees within a research institute, and concluded that it was accepted by employees and can be used to maintain the health of the workforce, potentially keeping positivity rates below community levels (16). Another study screened asymptomatic HCWs in a large hospital over a 3-week period and concluded that such an approach is critical for protecting patients and hospital staff (17). Both these studies used RT-PCR tests.

Repetitive screening in a school environment

Scientific literature on testing strategies in students is mostly limited to university students (in particular on or before arrival on campus). Little literature is available with regards to primary or secondary schools.

Evidence on the potential effectiveness of repetitive screening in schools comes mostly from mathematical modelling studies. One study concluded that high frequency testing with a moderate or high sensitivity test and minimal results delay can have a positive effect on cases averted in schools and businesses (18). Sample pooling allows for operational efficiency and cost savings with minimal loss of model performance. Pooling of samples from multiple individuals into a single test has also been proposed as a way to circumvent the high cost, which is an important barrier, of routine screening in another article (19).

Some reports of experiences with screening programs in schools are available in the general media. For example, schools in some districts of suburban Chicago, Illinois run a voluntary screening program deploying saliva tests aimed at catching asymptomatic children (20). Once a week, twice after holiday weekends, students are tested for COVID-19 on their way out of class. School officials believe this program has helped contain potential outbreaks, but no specific numbers are reported.

An article in the New England Journal of Medicine, mentions a routine screening program in the Los Angeles Unified School District and that testing strategies are conspicuously absent in schools in most other districts in the US (21). The authors recommend instituting screening testing in schools, in places where adequate testing capacity exists, despite the lack of evidence on the effectiveness of such testing in real-life.

An assessment of which policies most effectively reduce SARS-CoV-2 transmission in schools in New-York City, found that the greatest (theoretical) transmission reduction is associated with the infection control measures, followed by small class cohorts with an option for all-remote instruction, symptom screening, and finally randomly testing 10-20% of school attendees (22). Assuming adult staff are the primary source of within-school SARS-CoV-2 transmission, weekly testing of staff could be at least as effective as symptom screening, and potentially more so if testing days occur in the beginning of the workweek with results available by the following day. A combination of daily symptom screening and testing on the first workday of each week could reduce transmission by 70%. The authors concluded that randomly testing 10-20% of attendees weekly or monthly does not meaningfully curtail transmission and may not detect outbreaks before they have spread beyond a handful of individuals.

In a pilot study in Germany, school teachers tested themselves every 48 hours at home with a rapid antigen test in a self-collected anterior nasal swab (23). Positive results in the antigen test were confirmed via RT-PCR from the same sample. 10 836 tests from 602 teachers were analyzed, resulting in the detection of 5 true-positives (of which 4 had mild symptoms) and 16 false-positives. For four teachers, a false negative result was assumed, as they reported to have received a positive PCR test result during the self-testing period. Although that the authors concluded that high-frequency, self-performed rapid antigen tests can potentially reduce transmissions, and that testing may be most beneficial when applied during high local incidence and when mild or atypical symptoms are present, the study provides little evidence for the claimed additional value. It rather suggests that intensifying symptom screening might be as effective.

A study in Switzerland prospectively tested 641 6-16-year-old school children and 66 teachers twice 1 week apart with both a rapid Ag test and a PCR (24). 1 child had a positive PCR at T1, corresponding to a point-prevalence in children of 0.2% (95% CI 0.0% to 1.1%), and no positive PCR was detected at T2. The child with a positive PCR was negative on the rapid Ag test, and there were 9 false positive rapid Ag test results. The authors concluded that given the low point prevalence even in a setting of very high incidence, a targeted test, track, isolate and quarantine strategy for symptomatic children and school personnel adapted to school settings is likely more suitable approach than surveillance on entire classes and schools.

Repetitive screening in contact professions

No scientific literature was identified with regard to the effectiveness of repetitive screening in non-medical contact professions. Also scientific literature on the risk of transmission through non-medical contact professions is rare.

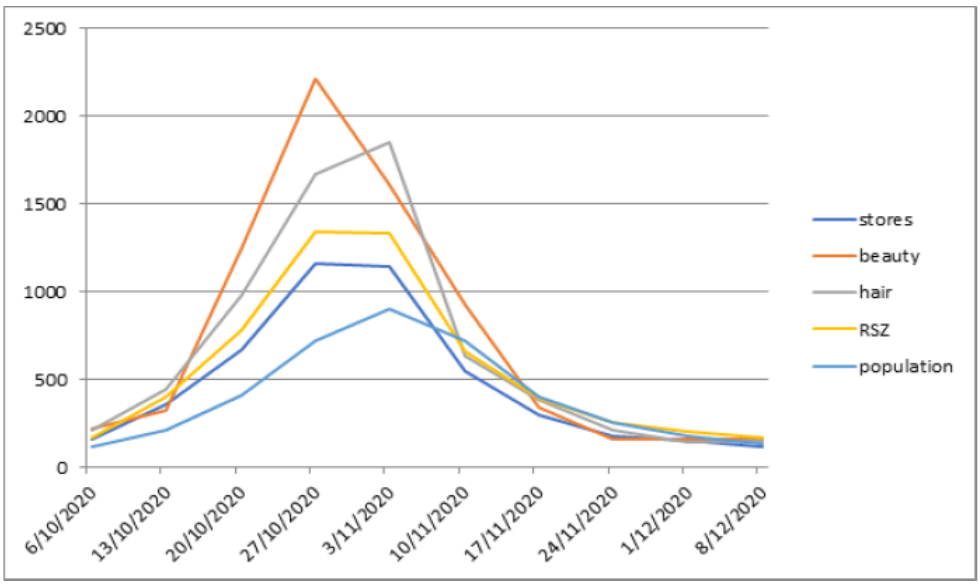
In a retrospective case-control study in the UK, using data from three periods (late August, late September, and late October 2020), employees in close contact services (barbers, hairdressers, nail salons, tattoo studios and tanning salons and any other services which require close contact) had increased odds of infection in all three periods. After adjustment for possible confounding factors, the odds ratio was 2.9 (95%CI 1.1-7.7), 1.1 (95%CI 0.4-3.0) and 1.2 (95%CI 1.8-1.9) in the three periods, respectively (25).

A study in the Netherlands, analyzing weekly test positivity in public test locations by population subgroup between 1 June and 17 October 2020, found that hairdressers and aestheticians had higher test positivity compared with a reference group of individuals without a close-contact occupation (26).

A case report of two hair stylists in the US who continued working with clients while positive and with symptoms of COVID-19, and of which none of the 67 of the 139 clients they had serviced and who had agreed to be tested, tested positive, received a lot of media attention. This lack of apparent transmission was explained by the correct use of preventive measures (correctly using masks) in this particular case (27).

An analysis of the 7-day incidences for the general Belgian population, for all employees recorded in the RSZ database, and for the employees in stores, the hairdresser sector, and

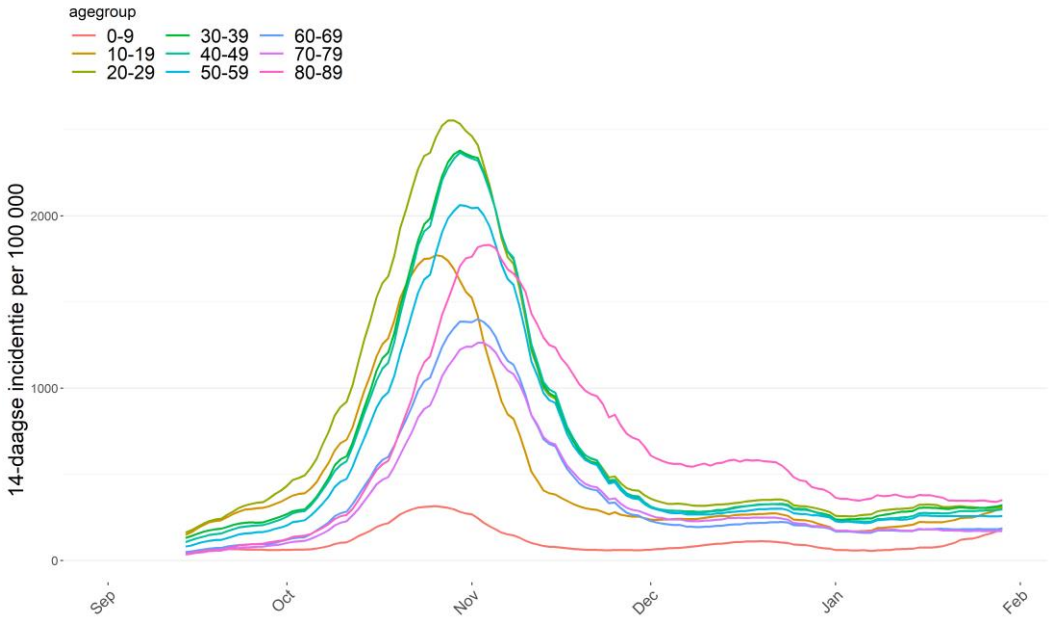
the beauty sector showed that the incidence during the second wave in hair and especially the beauty sector rose well above the average RSZ population (Figure below).



A simple thought experiment concluded that with this high incidence (of more than 1,000/100,000/week) hair dressers and beauty specialists could in Belgium potentially have up to 30,000 infectious close contacts over a three week period. Assuming a 20% infection rate, this would result in 6,000 new infections over three weeks, or 286 a day (28).

Repetitive screening in higher education students

The 14-day cumulative incidence per age group in Belgium during the second wave provide some evidence that reopening higher education institutions can affect the spread of the virus. From mid-September onwards, incidence increased most rapidly in the 20-29 years old age group and attained a higher level than in the other age groups (Figure below).



Most literature on test strategies in higher-education students comes from the United States.

A prevention strategy including risk reduction behaviors, frequent testing using pooled SARS-CoV-2 PCR testing, and contact tracing in an American university was successful in limiting SARS-CoV-2 transmission (29). Entry testing of 8,873 students detected 17 positive cases and repetitive pooled testing (residential undergraduates twice weekly, off-campus undergraduates one to two times per week, and graduate students approximately once weekly) 29 positive cases. One half of infections were asymptomatic, and some had high viral loads. Pooled testing reduced the need for resources while allowing high throughput with high sensitivity and rapid turnaround of results.

A study assessing the most efficient strategy to detect among university students as many as possible true positives with as less as possible tests, concluded that a single RT-PCR strategy is never preferred (30,31). If the cost of RT-PCR is not of concern, RT-PCR testing for all students and retesting all students with a negative first test, is the strategy detecting most true positives (87%). If the cost of RT-PCR testing is of concern, a staged approach involving initial testing of all returning students followed by a repeat testing decision based on the measured prevalence of infection might be considered.

The potential effectiveness in reducing SARS-CoV-2 transmission through repetitive screening (every 2 days) of university students using a rapid, inexpensive, and even poorly sensitive (>70%) test, coupled with strict behavioral interventions, has also been demonstrated by analytic modeling studies (32).

The validity of a rapid Ag test in the context of screening university students was assessed in a study in Wisconsin (33). 1,098 paired nasal swabs were tested with the rapid Ag test and an RT-PCR. Sensitivity among asymptomatic students was only 41.2%. Specificity was 98.4%, but with a prevalence of only 2.0%, the positive predictive value was only 33.3%.

Use of saliva specimens for repetitive screening

Several systematic reviews and meta-analyses of saliva as a possible tool for COVID-19 detection have been published or are in pre-print (34–38). Most of these show a large heterogeneity between studies, due to factors such as type of saliva specimen used, study design, type of analysis done, among others. They often conclude that there is a need for more research.

Nevertheless, the overall conclusion is that saliva specimens have a role in the detection of the SARS-CoV-2 virus. One article reviewed 39 studies and concluded that detection was as consistent and sensitive as the nasopharyngeal swabs (NPS) in most studies, although that a faster decrease in viral load was a limitation (35). A meta-analysis of 25 studies calculated that 88% (95%CI 81% – 93%) of all positives for at least one sample type, tested positive with a saliva sample (37). % positive saliva was higher for studies that specified cough or deep throat saliva specimen vs studies that did not specifically ask for this. Important was that saliva specimens were often effective in detecting asymptomatic infections previously tested

negative in nasopharyngeal samples. A possible explanation was that this was because of viral nucleic acids from the duct of the salivary gland.

Two recent preprint studies assessing the use of saliva samples for detection of SARS-CoV-2 obtained comparable results. One prospective study in three primary care centers, found a sensitivity of 86% for saliva specimens collected under supervision and 66.7% for self-collected samples (39). The sensitivity was highest in samples collected under supervision with lower Ct values: 97% in symptomatic and 88.9% in asymptomatic individuals. Another study in out-patient test centers and an emergency unit measured a sensitivity of 99.7% in patients with a Ct value<=33 and 55.9% in patients with a Ct value>33 (40).

A recent systematic review and meta-analysis, published in January 2021, of 37 studies with 7332 paired nasopharyngeal swab and saliva samples, found that the sensitivity of saliva was 3.4 percentage points lower than the sensitivity of NPS (41). Pooled sensitivity of saliva was 86.9% of all samples positive on either saliva or NPS. There was, however, a marked difference between studies with data on persons presenting for testing (7.9 % points lower) and studies retrospectively assessing data of persons with previously confirmed infection. In the latter, saliva's sensitivity was 1.5 % points higher. Performance of saliva was also better in asymptomatic people (1.6 % points less) than in symptomatic (4.9 % points less).

Another recent systematic review and meta-analysis of 8 peer-reviewed studies and 8 preprints (5922 unique patients) – of which most were also include in the review above - calculated a pooled sensitivity of 83.2% (95%CI 74.7-91.4) and a pooled specificity of 99.2% (95%CI 98.2-99.8) of PCR on saliva specimens (42). The nasopharyngeal swab had a sensitivity of 84.8% (95%CI 76.8-92.4) and a specificity of 98.9% (95%CI 97.4-99.8). The authors concluded that saliva PCR diagnostic accuracy is similar to that of nasopharyngeal swab PCR, especially in the ambulatory setting.

A study assessing the validity and accessibility of self-collected saliva and saline mouth rinse/gargle samples among 50 participants, of which 40 were confirmed with COVID-19, found that gargling was more sensitive, detecting 39 (98%) of the cases, than saliva (26/33 – 79%) and more acceptable (score of 4.9, versus 4.4 for saliva) (43).

Relevant experiences in Belgium

- ULiège invited during the first trimester of the current academic year all its 30.000 students to submit weekly a saliva sample that is then tested and its results made available on a website. The project went on during the whole first trimester, was put on hold during the Christmas period and will now restart. Participation fluctuated around 50% of students. Most consulted their results. Positivity rate was high during the second wave, but is now expected to be lower. There are no data what the effect was on students behavior, but ULiège is convinced that positive testing students adhered to their isolation. Anonymity was obligatory, because in a study context, and therefore positive students could not be reported and tracing of their high-risk contacts not initiated.
- KU Leuven is implementing convenient and free testing, comprehensive contact tracing, preventive measures in student residences and proactive communications to encourage

students at risk to go asap for testing when indicated (symptomatic, high-risk contact, returning traveler…) and adhere to isolation and quarantine rules. Building on this, a pilot is proposed in which testing criteria are expanded in the local student population to allow an individual student to book a test based on their self-assessed infection in addition to the current criteria. This combined with education and communications on temporal patterns of infectiousness, diagnostic accuracy of PCR tests and on risk mitigation strategies could improve transmission control while edging towards mitigation instead of pure restriction. The pilot will be strictly and continuously monitored by the existing test & trace operations.

- Uliège is since November 2020 inviting all staff of all nursing homes in Wallonia to weekly collect a morning saliva sample, which is then tested with an RT-PCR. Overall, 85% of the nursing homes participated each week, and it is believed at least 58% of the staff. 1158 people tested positive, corresponding with 0.92%. 96% of the positive tested people consulted their result. 115 clusters were detected. Sensitivity was good in samples with a high viral load (Ct value <25), comparable to what was found in the literature. A strategy of pooled testing of three samples was applied, with good results, only 0.3% of the positive samples was missed. Initially, a quite large proportion of the collected samples was unanalyzable, but the technique was gradually improved and at the end only 0.25% was unanalyzable. A downside of the set-up was that positive results were not reported to the Sciensano database/call centers, and therefore contact tracing could not automatically be launched.

- Also in Liège, 185 students, staff and parents of a primary school are since mid-September 2020 weekly tested on saliva samples obtained through gargling. 24.9% have tested positive during this period, 20.6% of the children and 27.1% of the adults. Infections among children were a combination of outside-school infections and one cluster of within-school infections (of 6/13 children the origin of the infection was unknown, family members negative at diagnosis, but 5 of them were positive as part of other positive samples within two different class rooms; 5/13 were detected positive at the same time than at least one parent). The experience of collecting samples through gargling was positive. The high positivity rate appears to indicate good sensitivity.

- Uhasselt is developing, jointly with INSERM, a model for modelling infections in a primary school environment. The model explores different scenarios, one with testing based on symptoms and one with repetitive screening. For symptomatic cases, an Ag RDT is used, for asymptomatic, a RT-PCR. The parameters can be changed and adapted to other environments, such as secondary schools. Preliminary results point towards a combination of testing all symptomatic and high-risk contacts with repetitive screening of teachers, as the probably best strategy in schools. More modelling is however needed, for example incorporating a presumed higher infectiousness of the UK strain.

- Another study by ULiège, still to be published[1], showed a higher sensitivity among symptomatic patients in samples collected through gargling (74.0%) than through spitting (68.2%).

- A study by UAntwerpen is ongoing in secondary schools. Paired saliva/naso-pharyngeal swab specimens were, as of mid-January, collected from 112 pupils (12-14 years), 263 health care personnel and 33 teachers. Saliva was collected using the spitting device developed by ULiège. Overall sensitivity of the saliva samples among adults is low (60%) and among pupils very low (33%), probably because viral load was low. A lower sensitivity in children than in adults has also been demonstrated in other studies. The percentage non-interpretable samples is high (around 10%). Collection in children was often difficult and required direct supervision.

International recommendations

Repetitive screening in general

Very few countries have issued guidelines on repetitive screening.

ECDC mentions in their Population-wide testing of SARS-CoV-2: country experiences and potential approaches in the EU/EEA and the United Kingdom report (19 August 2020) that most EU/EEA countries and the UK regularly test individuals in high-risk settings such as at healthcare facilities. Of the eight countries that responded to the ECDC enquiry that are not currently planning population-wide testing of individuals without symptoms, at least five regularly test individuals without any symptoms in high-risk settings e.g. healthcare workers, individuals working in long-term care facilities, and people in various other settings, such as patients admitted to hospitals, individuals in specific occupational settings, prisons, etc. Testing in these settings was sometimes occurring in response to a cluster of cases reported in that group or setting, or carried out to protect vulnerable populations (i.e. patient groups, health workers, patients or long-term care facility residents).

WHO
Apart from criteria for repetitive screening of health workers, no guidelines with regard to repetitive screening were identified.

Repetitive screening in a school environment

In their latest update (23 December), ECDC continues to recommend testing at schools and other educational settings only in the following circumstances: (1) symptomatic cases; (2) asymptomatic high-risk exposure (close) contacts of cases; and (3) possibly school-wide testing when clusters of confirmed cases. RT-PCR remains the gold standard, but rapid Ag tests can be considered as well.

[1] Defêche et al. (2020). In-depth comparison of clinical specimens to detect SARS-CoV-2. The New England Journal of Medicine [Submitted for publication]

USA-CDC

The latest recommendation from CDC with regard to testing in K-12 schools (elementary, middle and high-schools) dates from December 4 (44). The first priorities are (1) persons with symptoms of COVID-19; (2) persons who have had contact with someone with COVID-19; and (3) all students, faculty, and staff with possible exposure in the context of outbreak settings.

'Repeat testing and/or expanded testing of teachers, staff, and students can be considered in schools where the risk of transmission is moderate to high. Public health officials can determine, in collaboration with school administrators, the appropriateness of offering repeat testing to randomly-selected asymptomatic teachers, staff, and students at the school. Testing teachers and staff should be prioritized over students in any sampling strategy, and older students prioritized over younger students. Persons who have recovered from COVID-19 in the past 3 months should be excluded.'

CDC indicators to consider the risk of transmission moderate or high are (45):

Indicators	Moderate	Higher	Highest
Core			
14d incidence/100,000	20-50	50-200	>200
Positivity rate	5-8%	8-10%	>10%
Ability to correctly and consistently implement 5 key mitigation strategies	3-4 implemented	1-2 implemented	0 implemented
Secondary			
% change in new cases/7d	-5%-0	0-10%	>10%
% hospital beds occupied	80-90%	>90%	>90%
% IUC beds occupied	80-90%	>90%	>90%
% hospital beds occupied by COVID-19 patients	10-15%	>15%	>15%
Local outbreaks	Yes	Yes	Yes

'Entry testing or universal one-time testing is not specifically recommended because it is not known if testing of all staff, teachers, and students at one point in time provides any additional reduction in virus transmission above the key mitigation strategies recommended for schools. However, if infrastructure is in place, and resources are available, schools can serve as a venue for health departments to offer community-based testing to teachers, staff, students and potentially their family members.'

USA-Others

In a recent report, the Rockefeller Foundation recommends, building on positive experiences in some universities and schools in the US, to repetitively test students and staff (46). Students should be tested at least once a week — every week. Adults, including teachers and all in-classroom personnel as well as outside of classroom staff, should be tested at least twice a

week — every week. The authors recommend it in all schools (elementary, middle and high schools), starting with elementary schools as the first priority. The preferred test is an RT-PCR, although that a rapid Ag RDT is considered a good alternative.

UK (England)

From January 2021 onwards, all staff and students of all schools and colleges with secondary-age students were to be repeatedly tested (47). Students would be offered two rapid Ag tests a week, spaced three to five days apart and staff once weekly. Anyone with a positive result would need to leave school/college, and take a confirmatory RT-PCR. In a later phase, the strategy was to be expanded to primary schools. The test would be done on a (combined nasal/oral?) swab, possibly self-administered by the student/staff.

On 4 January 2021, a national lockdown was announced and schools and colleges could only allow vulnerable children and young people and the children of critical workers to attend (48). All other school and college children and young people will learn remotely until at least the February half term. The repeat test strategy will continue to be used for the support staff and children that still attend secondary schools.

No other country was identified that yet initiated a similar test strategy in schools.

Repetitive screening in contact professions

No country or agency was identified currently recommending repetitive screening in non-medical contact professions. In most neighboring countries (The Netherlands, Germany, most of the UK) non-medical contact services are currently closed. In France they continue open, but without testing strategy.

Repetitive screening in higher education students

Few countries have developed guidelines on testing strategies in higher education students.

CDC

CDC states (49): Institutes of higher education might test students, faculty, or staff for purposes of surveillance, diagnosis, screening, or in the context of an outbreak. Individuals should be considered for and offered testing if they:

- Show signs or symptoms consistent with COVID-19 (diagnostic)
- Have a recent known or suspected exposure to a person with laboratory-confirmed COVID-19 (diagnostic)
- Have been asked or referred to get testing by their healthcare provider or health department (diagnostic)
- Are part of a cohort for whom testing is recommended (in the context of an outbreak)
- Are attending an institute that requires entry screening (entry testing as part of screening)
- Are in a community where public health officials are recommending expanded testing on a voluntary basis including testing of a sample of asymptomatic

individuals, especially in areas of moderate to high community transmission (screening)
- Volunteer to be tested in order to monitor occurrence of cases and positivity rate (surveillance)

With regard to testing asymptomatic individuals without known exposure, some institutes implement policies requiring testing of all students, faculty, and staff for COVID-19 before allowing campus entry (entry testing or universal one-time testing or two-phase entry testing) or testing repeatedly throughout the semester or at specific intervals. Testing a random sample of asymptomatic students, faculty, and staff could increase the timeliness of outbreak detection and response by rapidly identifying and isolating COVID-19 cases that would have otherwise gone undetected without testing; the number of students tested should take into consideration the population size. In a setting, with frequent movement of faculty, staff and students between the institute and the community, a strategy of entry screening combined with regular serial testing might prevent or reduce SARS-CoV-2 transmission. Implementation of mitigation strategies (e.g., social distancing, masks, hand hygiene, enhanced cleaning and disinfection) should go along with any of the various testing strategies.

Possible test strategies include:
- Testing a campus population at one point in time, such as at the beginning of the semester
- Universal testing, and repeat universal testing one week later as a requirement for some situations such as moving into on-campus residential halls
- Testing a random sub-sample of a campus population multiple times during a semester at specific intervals

In an opinion paper by CDC, the following possible strategies are listed (50):
- Universal entry screening: testing all students before arrival on campus;
- 2-phased universal screening: pre-arrival testing paired with a follow-up test, typically about 1 week after arrival;
- scheduled screening, with repeated testing of the entire campus population (eg,weekly);
- random screening, with testing a random sample of the campus population;
- testing on-demand, by making tests available to students on campus on demand but not requiring testing; and
- wastewater testing to detect virus in the sewage overall or for specific facilities (eg, residence halls).

UK

In December 2020, the government of the UK announced that all students should be offered Covid tests when they return to university to help identify and isolate those who are asymptomatic but could spread the virus (51). All universities would be offered testing facilities to give students two lateral flow tests, three days apart, with results turned around within an hour to help control the spread of the virus.

REFERENCES

1. Mina MJ, Parker R, Larremore DB. Rethinking Covid-19 Test Sensitivity — A Strategy for Containment. N Engl J Med [Internet]. 2020 Sep 30 [cited 2020 Oct 15]; Available from: https://www.nejm.org/doi/10.1056/NEJMp2025631

2. Larremore DB, Wilder B, Lester E, Shehata S, Burke JM, Hay JA, et al. Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance. medRxiv. 2020 Sep 8;2020.06.22.20136309.

3. Plebani M, Aita A, Cattelan AM, Bonfante F, Padoan A, Giaquinto C, et al. Frequent testing regimen based on salivary samples for an effective COVID-19 containment strategy. medRxiv. 2020 Oct 14;2020.10.13.20210013.

4. Hellewell J, Russell TW, Team TSI and FS, Consortium TCC-19, Group CC-19 working, Beale R, et al. Estimating the effectiveness of routine asymptomatic PCR testing at different frequencies for the detection of SARS-CoV-2 infections. medRxiv. 2020 Nov 24;2020.11.24.20229948.

5. Holmdahl I, Kahn R, Hay J, Buckee CO, Mina M. Frequent testing and immunity-based staffing will help mitigate outbreaks in nursing home settings. medRxiv. 2020 Nov 23;2020.11.04.20224758.

6. Chin ET, Lo NC, Huynh BQ, Murrill M, Basu S. Frequency of routine testing for SARS-CoV-2 to reduce transmission among workers. MedRxiv Prepr Serv Health Sci. 2020 May 6;

7. Chang JT, Crawford FW, Kaplan EH. Repeat SARS-CoV-2 Testing Models for Residential College Populations. medRxiv. 2020 Jul 16;2020.07.09.20149351.

8. Nash B, Badea A, Reddy A, Bosch M, Salcedo N, Gomez AR, et al. The impact of high frequency rapid viral antigen screening on COVID-19 spread and outcomes: a validation and modeling study. medRxiv. 2020 Nov 4;2020.09.01.20184713.

9. Grassly NC, Pons-Salort M, Parker EPK, White PJ, Ferguson NM, Imperial College COVID-19 Response Team. Comparison of molecular testing strategies for COVID-19 control: a mathematical modelling study. Lancet Infect Dis. 2020;20(12):1381–9.

10. Bootsma MCJ, Kretzschmar ME, Rozhnova G, Heesterbeek J a. P, Kluytmans J, Bonten MJM. Regular universal screening for SARS-CoV-2 infection may not allow reopening of society after controlling a pandemic wave. medRxiv. 2020 Nov 18;2020.11.18.20233122.

11. Bosetti P, Kiem CT, Yazdanpanah Y, Fontanet A, Lina B, Colizza V, et al. Impact of mass testing during an epidemic rebound of SARS-CoV-2: a modelling study using the example of France. Eurosurveillance. 2021 Jan 7;26(1):2001978.

12. Pavelka M, Van-Zandvoort K, Abbott S, Sherratt K, Majdan M, Group CC-19 working, et al. The effectiveness of population-wide, rapid antigen test based screening in reducing SARS-CoV-2 infection prevalence in Slovakia. medRxiv. 2020 Dec 4;2020.12.02.20240648.

13. Libin P, Willem L, Verstraeten T, Torneri A, Vanderlocht J, Hens N. Assessing the feasibility and effectiveness of household-pooled universal testing to control COVID-19 epidemics. medRxiv. 2020 Oct 6;2020.10.03.20205765.

14. Atkeson A, Droste M, Mina MJ, Stock JH. Economic Benefits of COVID-19 Screening Tests. medRxiv. 2020 Nov 1;2020.10.22.20217984.

15. Sudlow C, Diggle P, Warlow O, Seymour D, Gordon B, Walker R, et al. Testing for coronavirus (SARS-CoV-2) infection in populations with low infection prevalence: the largely ignored problem of false positives and the value of repeat testing. medRxiv. 2020 Aug 22;2020.08.19.20178137.

16. Goetz LH, DeLaughder TL, Kennedy KL, Schork NJ, McDaniel TK, Trent JM, et al. Asymptomatic Employee Screening for SARS-CoV-2: Implementation of and Reactions to an Employer-Based Testing Program. medRxiv. 2020 Nov 10;2020.11.06.20227314.

17. Rivett L, Sridhar S, Sparkes D, Routledge M, Jones NK, Forrest S, et al. Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission. medRxiv. 2020 May 15;2020.05.09.20082909.

18. Lyng GD, Sheils NE, Kennedy CJ, Griffin D, Berke EM. Identifying Optimal COVID-19 Testing Strategies for Schools and Businesses: Balancing Testing Frequency, Individual Test Technology, and Cost. medRxiv. 2020 Oct 12;2020.10.11.20211011.

19. Simas AM, Crott JW, Sedore C, Rohrbach A, Monaco AP, Gabriel SB, et al. Pooling for SARS-CoV2 Surveillance: Validation and Strategy for Implementation in K-12 Schools. medRxiv. 2020 Dec 16;2020.12.16.20248353.

20. Coronavirus Saliva Screening Program Expands at Suburban Schools [Internet]. NBC Chicago. [cited 2021 Jan 8]. Available from: https://www.nbcchicago.com/news/local/coronavirus-saliva-screening-program-expands-at-suburban-schools/2374812/

21. Rafiei Y, Mello MM. The Missing Piece — SARS-CoV-2 Testing and School Reopening. N Engl J Med. 2020 Dec 3;383(23):e126.

22. Bershteyn A, Kim H-Y, McGillen J, Braithwaite RS. Which policies most effectively reduce SARS-CoV-2 transmission in schools? medRxiv. 2020 Nov 27;2020.11.24.20237305.

23. Hoehl S, Schenk B, Rudych O, Göttig S, Foppa I, Kohmer N, et al. At-home self-testing of teachers with a SARS-CoV-2 rapid antigen test to reduce potential transmissions in schools: Results of the SAFE School Hesse Study. medRxiv. 2020 Dec 7;2020.12.04.20243410.

24. Kriemler S, Ulyte A, Ammann P, Peralta GP, Berger C, Puhan MA, et al. Surveillance of acute SARS-CoV-2 infections in school children and point-prevalence during a time of high community transmission in Switzerland. medRxiv. 2020 Dec 26;2020.12.24.20248558.

25. Hiironen I, Saavedra-Campos M, Panitz J, Ma T, Nsonwu O, Charlett A, et al. Occupational exposures associated with being a COVID-19 case; evidence from three case-controls studies. medRxiv. 2020 Dec 22;2020.12.21.20248161.

26. de Gier B, de Oliveira Bressane Lima P, van Gaalen RD, de Boer PT, Alblas J, Ruijten M, et al. Occupation- and age-associated risk of SARS-CoV-2 test positivity, the Netherlands, June to October 2020. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2020 Dec;25(50).

27. Hendrix MJ. Absence of Apparent Transmission of SARS-CoV-2 from Two Stylists After Exposure at a Hair Salon with a Universal Face Covering Policy — Springfield, Missouri, May 2020. MMWR Morb Mortal Wkly Rep [Internet]. 2020 [cited 2021 Jan 27];69. Available from: https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e2.htm

28. GEMS_Update_management_strategy_20210119.pdf [Internet]. [cited 2021 Jan 29]. Available from: https://d34j62pglfm3rr.cloudfront.net/celeval/GEMS_Update_management_strategy_20210119.pdf

29. Denny TN, Andrews L, Bonsignori M, Cavanaugh K, Datto MB, Deckard A, et al. Implementation of a Pooled Surveillance Testing Program for Asymptomatic SARS-CoV-2 Infections on a College Campus - Duke University, Durham, North Carolina, August 2-October 11, 2020. MMWR Morb Mortal Wkly Rep. 2020 Nov 20;69(46):1743–7.

30. Van Pelt A, Glick HA, Yang W, Rubin D, Feldman M, Kimmel SE. Evaluation of COVID-19 Testing Strategies for Repopulating College and University Campuses: A Decision Tree Analysis. J Adolesc Health Off Publ Soc Adolesc Med. 2021 Jan;68(1):28–34.

31. Barrios LC, Green RF, Honein MA. The Role of Testing in Reducing SARS-CoV-2 Transmission on College Campuses. J Adolesc Health Off Publ Soc Adolesc Med. 2021 Jan;68(1):1–2.

32. Paltiel AD, Zheng A, Walensky RP. Assessment of SARS-CoV-2 Screening Strategies to Permit the Safe Reopening of College Campuses in the United States. JAMA Netw Open. 2020 Jul 1;3(7):e2016818.

33. Pray IW, Ford L, Cole D, Lee C, Bigouette JP, Abedi GR, et al. Performance of an Antigen-Based Test for Asymptomatic and Symptomatic SARS-CoV-2 Testing at Two University Campuses - Wisconsin, September-October 2020. MMWR Morb Mortal Wkly Rep. 2021 Jan 1;69(5152):1642–7.

34. Azzi L, Maurino V, Baj A, Dani M, d'Aiuto A, Fasano M, et al. Diagnostic Salivary Tests for SARS-CoV-2. J Dent Res. 2020 Oct 31;22034520969670.

35. Medeiros da Silva RC, Nogueira Marinho LC, Neto de Araújo Silva D, Costa de Lima K, Pirih FQ, Luz de Aquino Martins AR. Saliva as a possible tool for the SARS-CoV-2 detection: a review. Travel Med Infect Dis [Internet]. 2020 Nov 19 [cited 2020 Nov 24]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7674016/

36. Michailidou E, Poulopoulos A, Tzimagiorgis G. Salivary diagnostics of the novel coronavirus SARS-CoV-2 (COVID-19). Oral Dis. 2020 Nov 19;

37. Lee RA, Herigon JC, Benedetti A, Pollock NR, Denkinger CM. Performance of Saliva, Oropharyngeal Swabs, and Nasal Swabs for SARS-CoV-2 Molecular Detection: A Systematic Review and Meta-analysis. medRxiv. 2020 Nov 13;2020.11.12.20230748.

38. Peeters E, Kaur Dhillon Ajit Singh S, Vandesompele J, Mestdagh P, Hutse V, Arbyn M. Rapid systematic review of the sensitivity of SARS-CoV-2 molecular testing on saliva compared to nasopharyngeal swabs. medRxiv. 2020 Jan 1;2020.08.05.20168716.

39. Fernández-González M, Agulló V, Rica A de la, Infante A, Carvajal M, García JA, et al. Performance of saliva specimens for the molecular detection of SARS-CoV-2 in the

community setting: does sample collection method matter? medRxiv. 2020 Dec 2;2020.12.01.20241349.

40. Huber M, Schreiber PW, Scheier T, Audigé A, Buonomano R, Rudiger A, et al. Large parallel screen of saliva and nasopharyngeal swabs in a test center setting proofs utility of saliva as alternate specimen for SARS-CoV-2 detection by RT-PCR. medRxiv. 2020 Dec 3;2020.12.01.20241778.

41. Bastos ML, Perlman-Arrow S, Menzies D, Campbell JR. The Sensitivity and Costs of Testing for SARS-CoV-2 Infection With Saliva Versus Nasopharyngeal Swabs : A Systematic Review and Meta-analysis. Ann Intern Med. 2021 Jan 12;

42. Butler-Laporte G, Lawandi A, Schiller I, Yao MC, Dendukuri N, McDonald EG, et al. Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2: A Systematic Review and Meta-analysis. JAMA Intern Med. 2021 Jan 15;

43. Goldfarb DM, Tilley P, Al-Rawahi GN, Srigley JA, Ford G, Pedersen H, et al. Self-collected Saline Gargle Samples as an Alternative to Healthcare Worker Collected Nasopharyngeal Swabs for COVID-19 Diagnosis in Outpatients. J Clin Microbiol. 2021 Jan 29;

44. CDC. Communities, Schools, Workplaces, & Events [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2021 Jan 8]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/k-12-testing.html

45. CDC. Community, Work, and School [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2021 Feb 1]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/indicators.html

46. Taking-Back-Control-a-Resetting-of-Americas-Response-to-Covid-19.pdf [Internet]. [cited 2021 Jan 8]. Available from: https://www.rockefellerfoundation.org/wp-content/uploads/2020/12/Taking-Back-Control-a-Resetting-of-Americas-Response-to-Covid-19.pdf

47. COVID-19 National Testing Programme: Schools & Colleges Handbook. NHS - Test and Trace; 2020.

48. What parents and carers need to know about early years providers, schools and colleges [Internet]. GOV.UK. [cited 2021 Jan 12]. Available from: https://www.gov.uk/government/publications/what-parents-and-carers-need-to-know-about-early-years-providers-schools-and-colleges-during-the-coronavirus-covid-19-outbreak

49. CDC. Community, Work, and School [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2021 Jan 25]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/community/colleges-universities/ihe-testing.html

50. Walke HT, Honein MA, Redfield RR. Preventing and Responding to COVID-19 on College Campuses. JAMA. 2020 Sep 29;

51. public 0370 000 2288 C newsdesk-for journalists 020 7783 8300 G enquiries- for members of the. All students offered testing on return to university [Internet]. GOV.UK. [cited 2021 Jan 25]. Available from: https://www.gov.uk/government/news/all-students-offered-testing-on-return-to-university