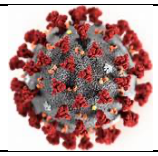
National COVID-19 Science Task Force (NCS-TF)



Type of document: Policy Brief	
Expert groups involved: Public health, diagnostics and testing, data and modelling	**Date of response:** 01/04/2021
Contact person: Nicola Low	
Comment on planned updates : As new evidence is published	

Considerations for intensified community testing for SARS-CoV-2 in Switzerland

Summary of request/problem

What are the key considerations for implementing SARS-CoV-2 testing that attempts to reach a substantial part of the mobile population repeatedly in community settings?

Executive summary

There is increasing optimism that intensified SARS-CoV-2 testing that reaches a large part of the community will improve control of transmission, so that societies can open up safely, in step with the roll-out of vaccination.

Intensified community testing involves repeated screening for asymptomatic SARS-CoV-2 infection in specific target groups, with the aim of reducing transmission in the population. Target groups are groups that are considered to be at high risk of SARS-CoV-2 infection and/or they attend places, such as schools and workplaces, where testing can be implemented on a large-scale. The paradigm for repeated testing prioritises coverage and frequency of testing, and speed of delivering results, over the sensitivity of the assay, which is the main consideration for diagnostic testing in symptomatic individuals.

The 'test' comprises both the assay type and the sample type. The two acceptable combinations are rapid antigen testing using nasopharyngeal or nasal+oropharyngeal samples, or laboratory-based RT-PCR testing using saliva samples.

Delivery of intensified community testing requires strong systems of organisation, management, information and monitoring to achieve and sustain high levels of coverage. In addition to testing of individuals, intensified testing should be extended to the contacts of infected people in households, schools and workplaces. Sustaining regular voluntary testing requires trust, endorsement and engagement by the community.

Effective communication and support are needed because most individuals do not benefit directly from participation but they experience the inconvenience of repeated testing, of isolation and quarantine, and the consequences of false positive and false negative tests. Preliminary findings from pilot studies in the canton of Graubünden suggest that moderate uptake was sustained and test positivity reduced within participating sites in the short-term (several weeks). Evidence of effectiveness in reducing transmission at the population level is still required.

Evaluation and monitoring plans should be introduced at cantonal and national level, in parallel with implementation. Recording the numbers and results of screening and diagnostic tests

separately is essential, so that increases in numbers of positive tests as a result of the programme can be distinguished from increases resulting from increased transmission. Research to find out about benefits and harms for participants is also needed. Compative evaluation studies of the outcomes of different ways to implement the programme and modelling studies will help to determine the most acceptable and effective approaches.

Main text

1 Definition and aim

Intensified testing for SARS-CoV-2 in the community involves repeated screening for asymptomatic SARS-CoV-2 infection in specific target groups. (Wilson and Jungner 1968, Raffle and Gray 2007). The aim is to reach large enough numbers of people regularly enough to break transmission chains by early detection and contact management of SARS-CoV-2 infections that would otherwise go undetected, either because there are no symptoms, or because of a lack of access to testing (European Centre for Disease Prevention and Control 2020).

Intensified testing should contribute to reducing the incidence of SARS-CoV-2 at the population level as part of a comprehensive package that includes mass social distancing measures, diagnostic testing, tracing isolation and quarantine (TTIQ), and individual mask, distancing and hygiene activities.

To reduce SARS-CoV-2 transmission, any intervention needs to interrupt a virus that is spread by respiratory droplets and aerosols, with transmission that starts before the onset of symptoms. Its effectiveness depends on having both appropriate tools that detect infectious individuals and strong organisation of services to deliver testing, contact tracing, isolation and quarantine, following a SARS-CoV-2 positive test result (Raffle et al. 2020).

Intensified SARS-CoV-2 testing in different settings can contribute to different goals: 'test-to-protect' susceptible people and settings (for example, care homes, schools, travellers); 'test-to-release' contacts of confirmed infected people sooner from quarantine than the stipulated period; and 'test-to-enable' careful return to activities to improve public health, social life and the economy (Buchan and University of Liverpool 2020).

2 Approaches for intensified community testing

Two main screening approaches are used to reach large fractions of a population that is asymptomatic: population-based mass testing; and testing of target populations in specific settings (referred to here as intensified community testing, and also known as focused testing or opportunistic testing). Population-based mass testing is not considered sustainable beyond one or two screening rounds. In countries that have used this approach over a short time period (e.g. Austria, England, Slovakia), the army provided logistical support during periods of high for SARS-CoV-2 transmission to install test sites and facilitate testing (Buchan and University of Liverpool 2020, Pavelka et al. 2021).[1]

Intensified community testing of target groups of asymptomatic people is proposed as a feasible and sustainable screening approach (Buchan and University of Liverpool 2020, Crozier et al. 2021). Target groups are defined groups that are either considered to be at high risk of SARS-CoV-2 infection, or they attend places where testing can be implemented on a large-scale, for example: staff and residents in institutions, such as long-term care facilities; staff and students in schools and universities, and employees in public or private sector workplaces. In Switzerland, intensified community testing has been piloted in the cantons of Graubünden and Basel Landschaft.

[1] Austria: Hödl P, personal communication

This document summarises the key considerations, adapted from criteria used in the United Kingdom to appraise the viability and appropriateness of screening (UK National Screening Committee 2011).

3 The test (= assay + sample)

There should be a simple, safe, precise and validated test (UK National Screening Committee 2011). To maximise early detection and isolation of the people without symptoms in the infectious period for SARS-CoV-2, it is argued that the frequency of testing and speed of delivering results are more important than the sensitivity of the assay (Mina et al. 2020, Larremore et al. 2021). This paradigm shifts the focus away from test sensitivity (high probability of detecting true cases), which is the main requirement for diagnostic testing to detect SARS-CoV-2 in people with symptoms and for classic screening tests. A simulation study, which used data about RT-PCR test results and cycle threshold values in pairs of diagnosed cases and contacts in the UK, together with assumptions about the limit of detection of antigen detection tests, suggested that lateral flow tests would detect more than 80% of infectious cases (Lee et al. 2021).

The 'test' comprises both the assay type and the sample type. Acceptability of the sample type, in terms of comfort, ease of use and convenience, is also critical to ensuring continued frequent use. The person taking the test (e.g. trained personnel or self-taken) also affects the performance of any test. Table 1 gives a qualitative summary of the most common classes of SARS-CoV-2 assay, sample types and acceptability. A separate policy brief will give detailed updated information about test performance soon.

Table 1. Acceptability for repeated sampling of different sample types and performance for SARS-CoV-2 detection of different assay types

Sample type	**Sample acceptability for repeat testing**	**Assay type**	**Assay sensitivity for infectious SARS-CoV-2**[a]	**Assay turnaround time**[b]
Nasopharyngeal swab	+	Laboratory RT-PCR[c]	+++	+
		Antigen detection test[d]	++	+++
		Rapid RT-PCR [e]	++(+)	++
Nasal + oropharyngeal swab	++	Laboratory RT-PCR[c]	+++	+
		Antigen detection test[d]	++	+++
		Rapid RT-PCR[e]	++	++
Saliva	+++	Laboratory RT-PCR[c]	+++	+
		Antigen detection test[d]	+	+++
		Rapid RT-PCR[e]	++	++

a. Infectiousness of SARS-CoV-2 assumed to correlate with RT-PCR cycle threshold values. The precise relationship between viral load and infectiousness remains unknown (Dahdouh et al. 2020, Deeks and Raffle 2020, Cevik et al. 2021);

b. Turnaround time is the time from start of taking sample to acting on a positive test result under routine field conditions (+++ <1 hour; ++ <12 hours; + ≥12 hours). For pooled samples, the turnaround time includes the time for repeat sampling and testing of individuals in a reactive pool;

c. RT-PCR detects SARS-CoV-2-specific RNA gene sequences; includes testing of individual samples and of pooled samples; sensitivity for detection of infectious SARS-CoV-2 (+++)

d. Lateral flow assays detect SARS-CoV-2 antigens, which need to be present in higher amounts than the nucleic acids detected by RT-PCR, so have lower sensitivity (+) (Bruemmer et al. 2021);
e. Rapid RT-PCR assays, e.g. RT-loop-mediated isothermal amplification also detect SARS-CoV-2-specific RNA sequences and their sensitivity should approach that of laboratory-based RT-PCR assays (++) (Schellenberg et al. 2021).

Saliva is the most acceptable sample type because it does not casue any discomfort, and RT-PCR assays in adults and children retain high sensitivity (Huber et al. 2020). Saliva is not a suitable sample type for antigen detection tests (such as lateral flow tests) for now. Rapid tests, including lateral flow tests, provide the quickest turnaround time. All assay types can give false negative results but these are most common with antigen detection tests. A negative result from an antigen detection test might not rule out infectiousness (Deeks and Raffle 2020). Results need to be carefully explained and people with a negative result should continue to use individual level preventive measures.

The choice of test therefore depends on the relative priorities given to frequency, speed and sensitivity, together with considerations about cost and logistical requirements. The operational considerations of repeated testing are outlined in section 5.1 of this brief. The long-term acceptability of repeated testing by these approaches is not known.

4 The testing programme

There should be evidence that a mass testing programme reduces morbidity or mortality and the complete intensified testing programme should be clinically, socially and ethically acceptable to health professionals and the public (UK National Screening Committee 2011).

Given the urgency of the SARS-CoV-2 pandemic situation and the need for rapid implementation, the evidence available is limited to a small number of process evaluations of ongoing projects and results of mathematical modelling studies. In Liverpool, England, local authorities introduced 'systematic, meaningful, asymptomatic, repeated testing' (SMART), which can be seen as intensified community testing. The goal was to achieve twice weekly testing using lateral flow tests with self-taken nasal and oropharyngeal swabs, taken under supervision across a range of settings. Available data are not disaggregated by setting, but from 08.12.2020-04.03.2021, there were 333,835 tests in 161,184 people; an average of two tests per person over 12 weeks. Higher uptake, sustained over a few months, was reported in secondary schools.[2] In Austria, lateral flow testing three times weekly, using anterior nasal swabs, has been implemented as a requirement for in-person teaching in schools, with reportedly high uptake in that setting. In the canton of Graubünden, Switzerland, intensified community testing has been piloted. A newspaper article has reported 35% participation in regular testing in workplaces and schools, using weekly RT-PCR testing of saliva samples from February-March 2021 (Hardegger 2021). A full publication of the results, including evidence about is awaited.

The alternative screening approach, population-based mass testing was evaluated in the whole of Slovakia in October-November 2020 (Pavelka et al. 2021). Two rounds of population-wide rapid antigen detection testing for SARS-CoV-2 one week apart reached more than 80% of 10-65 year olds, with more than 5 million tests nationally. Test positivity nationally fell from 1% to 0.6% (estimated decline 56%, 95% CI 52-59%). It was impossible to disentangle the contribution of testing from the strict control measures in place at the time, but a modelling study found that the observed reduction could not have been achieved without a substantial contribution from the screening. Incidence rebounded when measures were lifted.

[2] Iain Buchan, University of Liverpool, personal communication

Modelling studies have provided the theoretical evidence for the presumed effectiveness of intensified testing for SARS-CoV-2.

In the USA, Larremore et al. compared population-wide testing using tests with characteristics of a lateral flow test. They found the highest impact with frequent testing (daily or twice weekly) and same day results when testing the whole population (Larremore et al. 2021). These factors were more important than the sensitivity of the test.

In Switzerland, Gorji et al. have used a mathematical model to investigate the test requirements and expected impact of repeated testing in a Swiss population (Gorji et al. 2020). The model outputs show that the coverage of testing has more influence on the impact than the frequency of testing. The model outputs predict that if the starting reproduction number is 1.4, weekly testing of 40% of the population with a test that has a sensitivity of 95% and 0.5 to 1 day delay until results would keep the effective reproduction number at around one.[3] These assumptions can be varied using an online application

4.1 Acceptability, benefits and harms to the target population

Sustained uptake of repeated SARS-CoV-2 testing on a voluntary basis relies on trust, endorsement and engagement of all target groups in the community (Buchan and University of Liverpool 2020, Raffle et al. 2020). Most individuals do not benefit directly because they have no symptoms and the expected proportion of positive tests is below 1%. It is individuals, however, who experience the inconvenience of repeated testing, isolation and quarantine.

Participation needs to be equitable; people living in deprived communities and from minority ethnic groups were found to have poor uptake in the Liverpool SMART programme, but had high levels of test positivity (Green et al. 2021). Support and incentives for participation may be needed for employers to participate in the programme, for working adults to compensate for time off work, and for disruption to education for school students. In the Liverpool SMART programme, local authorities developed the programme with stakeholders and used a multimedia strategy to communicate the purpose and consequences of testing with the population (Buchan and University of Liverpool 2020).

There are also harms of inaccurate test results. False positive results mean that people who are uninfected need to isolate unnecessarily and their close contacts need to quarantine. False negative test results, which are more likely with antigen detection tests than RT-PCR tests, can result in onward SARS-CoV-2 transmission if people are falsely reassured and reduce their usual level of preventive behaviours.

4.2 Cost-effectiveness and opportunity costs

The costs of intensified community testing include not only the diagnostic tests, but additional clinical, laboratory and administrative staff, transport, information systems and evaluation. We did not find any economic evaluation of intensified testing programmes. The opportunity costs include investments in existing TTIQ systems or preventive measures and in delivering SARS-CoV-2 vaccination.

5 Implementation and evaluation

There should be a plan for managing and monitoring the testing programme and an agreed set of quality standards (UK National Screening Committee 2011). Individual and population level preventive measures, including core activities of surveillance and TTIQ need to be fully implemented and optimised to support an intensified testing intervention.

Evaluation and monitoring

Given the scarcity of information about the effectiveness of intensified SARS-CoV-2 testing, evaluation and monitoring plans are essential at cantonal and national level in parallel to implementation. Evaluation of the impact of mass testing requires recording the screening and

diagnostic tests separately and documentation of the denominator populations, so that increases in numbers of positive tests as a result of the programme can be distinguished from increases resulting from increased transmission. Relevant measures of structure and process include: coverage of the mobile population, which includes temporary as well as permanent residents; frequency of testing; uptake over time; test positivity; time to test results; and numbers of people in isolation and quarantine, according to sex, age, nationality and socioeconomic position.

Comparative evaluation studies between groups that receive intensified testing and standard practice, and between different models of implementation are required. In practice, implementation often occurs in stages. An unbiased comparison of outcomes can be made if the order of implementation can be randomised (step-wedge implementation) (Hussey and Hughes 2007). The findings between setting where testing is being done and those that are waiting to start testing can then be compared. This measure can reduce overestimation of impact that occurs when the most enthusiastic early implementers are evaluated first. When data are available from a testing programme, but there are no empirical data about the situation in which no testing was done, modelling studies involving simulated comparison communities can provide an indication of the effectiveness of intensified community testing (Buchan and University of Liverpool 2020, Pavelka et al. 2021).

5.1 Staffing levels for testing, management and evaluation

The need for additional staff resources should be anticipated (UK National Screening Committee 2011). Intensified community testing requires strong organisational, logistics, information and monitoring systems. For lateral flow testing, staff are needed on-site to distribute tests, supervise sampling and record and act on positive results. For laboratory-based RT-PCR testing, transport of samples from multiple sites is required. Pooling of samples reduces the costs of RT-PCR reagents but requires additional staff to manage pooling, communicate positive results and organise re-testing of individuals.

References

Bruemmer LE, Katzenschlager S, Gaeddert M, Erdmann C, Schmitz S, Bota M, Grilli M, Larmann J, Weigand MA, Pollock N, Carmona S, Ongarello S, Sacks J and Denkinger CM. The accuracy of novel antigen rapid diagnostics for SARS-CoV-2: a living systematic review and meta-analysis. MedRxiv 2021. https://www.medrxiv.org/content/10.1101/2021.02.26.21252546v1?rss=1'
https://www.medrxiv.org/content/medrxiv/early/2021/03/01/2021.02.26.21252546.full.pdf.

Buchan I and University of Liverpool. Liverpool Covid-19 Community Testing Pilot. Interim Evaluation Report, 23 December 2020. 2020.

Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J and Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. Lancet Microbe 2021;**2**(1): e13-e22. https://www.ncbi.nlm.nih.gov/pubmed/33521734
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7837230/pdf/main.pdf.

Crozier A, Rajan S, Buchan I and Mckee M. Put to the test: use of rapid testing technologies for covid-19. BMJ 2021;**372**: n208. https://www.ncbi.nlm.nih.gov/pubmed/33536228
https://www.bmj.com/content/bmj/372/bmj.n208.full.pdf.

Dahdouh E, Lazaro-Perona F, Romero-Gomez MP, Mingorance J and Garcia-Rodriguez J. Ct values from SARS-CoV-2 diagnostic PCR assays should not be used as direct estimates of viral load. J Infect 2020. https://www.ncbi.nlm.nih.gov/pubmed/33131699
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7585367/pdf/main.pdf.

Deeks JJ and Raffle AE. Lateral flow tests cannot rule out SARS-CoV-2 infection. BMJ 2020;**371**: m4787. https://www.ncbi.nlm.nih.gov/pubmed/33310701
https://www.bmj.com/content/bmj/371/bmj.m4787.full.pdf.

[3] Jenny P, Hardt W-D, Gorji H, Arnoldini M, Jenny D, Rudolf F. Mass testing zur Covid Mitigation.xlsx (personal communication)

European Centre for Disease Prevention and Control. Population-wide testing of SARS-CoV-2: country experiences and potential approaches in the EU/EEA and the United Kingdom. 19August 2020. 2020 Stockholm, European Centre for Disease Prevention and Control.

Gorji H, Arnoldini M, Jenny DF, Hardt WD and Jenny P. Smart Investment of Virus RNA Testing Resources to Enhance Covid-19 Mitigation. MedRxiv 2020. https://www.medrxiv.org/content/10.1101/2020.11.30.20239566v1?rss=1' https://www.medrxiv.org/content/medrxiv/early/2020/12/02/2020.11.30.20239566.full.pdf.

Green MA, García-Fiñana M, Barr B, Burnside G, Cheyne CP, Hughes D, Ashton M, Sheard S, Geddes A, Rankin J and Buchan IE. Evaluating social and spatial inequalities of large scale rapid lateral flow SARS-CoV-2 antigen testing in COVID-19 management: An observational study of Liverpool, UK (November 2020 to January 2021). medRxiv 2021: 2021.2002.2010.21251256. https://www.medrxiv.org/content/medrxiv/early/2021/02/19/2021.02.10.21251256.full.pdf.

Hardegger A (2021). Der grosse Test in Graubünden funktioniert. Neue Zürcher Zeitung. Zürich.

Huber M, Schreiber PW, Scheier T, Audige A, Buonomano R, Rudiger A, Braun DL, Eich G, Keller D, Hasse B, Berger C, Manrique A, Guenthard HF, Boeni J and Trkola A. 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. https://www.medrxiv.org/content/10.1101/2020.12.01.20241778v1?rss=1'.

Hussey MA and Hughes JP. Design and analysis of stepped wedge cluster randomized trials. Contemp.Clin.Trials 2007;**28**(2): 182-191. PM:16829207.

Larremore DB, Wilder B, Lester E, Shehata S, Burke JM, Hay JA, Tambe M, Mina MJ and Parker R. Test sensitivity is secondary to frequency and turnaround time for COVID-19 screening. Sci Adv 2021;**7**(1). https://www.ncbi.nlm.nih.gov/pubmed/33219112 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7775777/pdf/abd5393.pdf.

Lee LY, Rozmanowski S, Pang M, Charlett A, Anderson C, Hughes GJ, Barnard M, Peto L, Vipond R, Sienkiewicz A, Hopkins S, Bell J, Crook DW, Gent N, Walker AS, Peto TE and Eyre DW. SARS-CoV-2 infectivity by viral load, S gene variants and demographic factors and the utility of lateral flow devices to prevent transmission. medRxiv 2021: 2021.2003.2031.21254687. https://www.medrxiv.org/content/medrxiv/early/2021/04/05/2021.03.31.21254687.full.pdf.

Mina MJ, Parker R and Larremore DB. Rethinking Covid-19 Test Sensitivity - A Strategy for Containment. N Engl J Med 2020;**383**(22): e120. https://www.ncbi.nlm.nih.gov/pubmed/32997903 https://www.nejm.org/doi/pdf/10.1056/NEJMp2025631?articleTools=true.

Pavelka M, Van-Zandvoort K, Abbott S, Sherratt K, Majdan M, Group CC-W, Analyz IZ, Jarcuska P, Krajci M, Flasche S and Funk S. The impact of population-wide rapid antigen testing on SARS-CoV-2 prevalence in Slovakia. Science 2021. https://www.ncbi.nlm.nih.gov/pubmed/33758017 https://science.sciencemag.org/content/sci/early/2021/03/26/science.abf9648.full.pdf.

Raffle A and Gray M (2007). Screening: Evidence and practice. Oxford, Oxford University Press.

Raffle AE, Pollock AM and Harding-Edgar L. Covid-19 mass testing programmes. BMJ 2020;**370**: m3262. https://www.ncbi.nlm.nih.gov/pubmed/32819920 https://www.bmj.com/content/bmj/370/bmj.m3262.full.pdf.

Schellenberg JJ, Ormond M and Keynan Y. Extraction-free RT-LAMP to detect SARS-CoV-2 is less sensitive but highly specific compared to standard RT-PCR in 101 samples. J Clin Virol 2021;**136**: 104764. https://www.ncbi.nlm.nih.gov/pubmed/33636553 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7885624/pdf/main.pdf.

Uk National Screening Committee. (2011, 2015/10/23/). "Programme appraisal criteria. Criteria for appraising the viability, effectiveness and appropriateness of a screening programme. Retrieved 01.04.2021, from https://www.gov.uk/topic/population-screening-programmes/population-screening-evidence-guidance

Wilson JMG and Jungner G (1968). Principles and Practice of Screening for Disease. Geneva, World Health Organisation.