**Efficient prevalence measurement and population screening for SARS-CoV-2**

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The most common testing method for SARS-CoV-2 is RT-PCR analysis of nasopharyngeal and/or throat swab samples. In most countries, testing capacity is highly limited due to lack of equipment and necessary testing reagents. Consequently, some laboratories have explored pooling techniques to increase the number of individuals tested with the available number of tests [1,2]. At Stavanger University Hospital we have operationally verified the possibility of pooling eight samples with maintained diagnostic sensitivity. We would like to draw the attention to two, maybe less obvious, opportunities enabled by pooling of up to 32 or even more samples that appear to be possible within the PCR protocol recommended by WHO for SARS-CoV-2 detection.

SARS-CoV-2 **prevalence measurement with minimal number of PCR tests**

Determination of the prevalence of SARS-CoV-2 in the population is of high importance for a number of reasons. For instance, the “true” prevalence is a crucial input to epidemiologic modelling, and for monitoring the effect of social distancing and other measures to suppress spread of SARS-CoV-2 [3]. By single-step pooled analysis, the number of PCR analyses necessary is reduced by a factor equal to the number of samples in each pool. An estimate of the prevalence can be calculated from the proportion of positive pools; it is not necessary to identify the exact number of positive samples in each pool. The technique is well described in the literature [4] and corrects for the possibility that there is more than one positive sample in each positive pool. To further reduce the number of required PCR analyses, a higher degree of pooling can be employed, even if the corresponding reduction in sensitivity would be considered unacceptable for diagnostic purposes. For prevalence estimation the reduced sensitivity is, however, straightforward to correct for, as long as it is known. Yelin et al. [1] have indicated that with pooling of 32 samples the sensitivity is 90% (10% false negative rate), relative to that of single sample analysis. With this degree of pooling it would take 200 PCR tests to estimate the prevalence from a dataset of 6400 individual samples. Figure x an y indicate the 90% confidence intervals for the prevalence for sample sizes 1000-5000(?) and for prevalences of 0.00x and 0.001.

*Ett par figurer fra simuleringane*

**Screening for SARS-CoV-2 in a low prevalence population**

The most common purpose of pooled testing is to analyze as many samples as possible with a given laboratory capacity and maintain a diagnostic level of sensitivity. Further, to combat the current covid-19 epidemic many countries are adapting a “suppression” strategy as recommended by Ferguson et al.[3]. The basic idea of this strategy is, after a period of aggressive social distancing measures, to do extensive testing, case tracing and isolation to keep the prevalence at a low level until a vaccine becomes available. In this context it would be of interest to maximize/increase the number of infected people detected with the available testing resources, rather than to insist on that all tests from the community setting are being performed with the highest possible level of sensitivity. Currently, the limited published literature indicates that with a pool size of 32 the sensitivity drops to around 90% [1]. When used for population screening pooling of 32 samples will nevertheless allow for detection of far more infected people than for the same number of PCR tests if using one test per person. If screening a population with a prevalence of 0.005 and using pooling of eight samples a mean of ~6000 people can be screened and a mean of 30 cases detected using 1000 PCR tests. By pooling 32 samples, however, ~11300 people can be screened and ~51 cases detected with the same 1000 PCR tests. This is even though the sensitivity of the analysis is reduced. Figure 3 and 4 show the corresponding numbers for a range of prevalence values in the screened population. It appears that if using this approach many high-income countries already would have the PCR capacity needed to perform extensive screening of the public, if the prevalence is first suppressed to a low level with strong social distancing measures.

 

Limitations of both of the above suggested applications of extended pooling is that while the required number of PCR analysis is reduced, the number of samples to be collected is unchanged. Further, the relationship between pool size and test sensitivity is not yet fully established and might also vary between individual laboratories and various PCR protocols, and therefore have to be verified locally.

**References**

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