POOLAGE D'ÉCHANTILLONS PROVENANT D'UN MÊME MENAGE POUR LE DÉPISTAGE DE SARS-COV-2

RAG sous-groupe Testing – 31 mai 2021

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

Recommandations :

- Explorer davantage le potentiel du poolage d'échantillons provenant d'un même ménage ou d'une même bulle (« household pooling ») avant de les envoyer au laboratoire.
- Piloter « household pooling » dans un contexte réel.
- « Household pooling » est considéré comme pertinent dans les cas suivants :
    - Dépistage de voyageurs de retour ou de voyageurs en partance qui appartiennent au même ménage/à la même bulle.
    - Dépistage de personnes appartenant à un même ménage/une même bulle dans le contexte d'événements (pré-événement ou post-événement).
- Actuellement, le « Household pooling » n'est pas recommandé pour le dépistage universel dans certaines populations ou zones où une recrudescence épidémique est observée.
- Les procédures recommandées pour le « Household pooling » sont les suivantes :
  Si un pool teste positif :
    - Effectuer une deuxième série de tests individuels.
    - Tous les membres du pool sont mis en isolement jusqu'à ce que les résultats du second tests soient connus.
    - Les membres dont le test individuel est négatif peuvent mettre fin à l'isolement et sont déclarés négatifs, mais doivent être mis en quarantaine en tant que contact à haut risque et être testés à nouveau après 7 jours.
    - Les membres dont le test est positif individuellement poursuivent leur isolement, sont déclarés comme des cas positifs et la recherche des contacts est lancée.
  Si un pool teste négatif :
    - Tous les membres sont déclarés comme négatifs.
- La taille proposée d'un pool de 6 échantillons maximum est considérée comme appropriée.

Les personnes suivantes ont participé à cet avis :

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CONTEXT

Pooling of samples for RT-PCR testing for SARS-CoV-2 can substantially reduce the cost when the positivity rate is low. A [RAG advice of February 16](#), 2021 states that pooling (at the laboratory) can be used for screening of large asymptomatic populations expected to have a low prevalence, such as in repetitive screenings. The prevalence threshold above which pooling is no longer considered useful is a positivity rate in the tested population of 10% or more. Household pooling, in which the whole household is put in quarantine without a second round of testing, as had been modelled by UHasselt, was considered an interesting approach, but not yet feasible because of a number of challenges at laboratory level.

Since then, KU Leuven has further explored the potential of household pooling. It developed a 'Social Pooling tube', that can contain up to 6 swabs, and conducted a laboratory validation study. While further validation is still needed, an advice was requested from the RAG Testing to provide guidance on circumstances in which household pooling, if proven to be efficient, could be applied.

KU LEUVEN LABORATORY VALIDATION STUDY RESULTS

Stability
- No decrease of PCR sensitivity after 2 weeks at room temperature
- No evidence of increased inhibition rate related to the fact that 6 swabs are inserted in the same tube (limited numbers)

Impact of pooling on sensitivity
- Limited impact (decrease of 1,5 Cq)
- No qualitative impact when $\frac{1}{6}$ sample positive with a Cq up to 30 (not yet tested for Cq above 30)
- Precision : OK

Automation
- Compatible with automated and non-automated molecular laboratories (decappers, tecan, fastfinder,...)
- Decrease of risk of cross-contamination (no carry-over of swabs during pipetting)
- Accelerated TAT
- Decrease of hands-on time.

DISCUSSION

- There is sufficient scientific evidence that pooling of samples in a low-prevalence setting (<10%) can substantially reduce the cost of conducting RT-PCR tests, at an acceptable loss of sensitivity. The findings of the KU Leuven laboratory validation study confirm this.

- According two studies (Deckert et al., Hermani et al.), household pooling reduces even more the cost than random pooling.

- For positive pools, two isolation strategies exist: isolating the entire pool or performing a second test on all individual members and only isolate the ones testing positive. According to the study by UHasselt, individual isolation is the most appropriate strategy when positivity rate is low (lower number of pools that needs to be retested, better adherence to isolation, less unnecessary contact tracing).

- Pooling in the laboratory comes at a higher management and organizational cost, but this is avoided when the samples are pooled before reaching the lab, such as in the KU Leuven approach.

- There exist several pooling strategies, but two rounds of testing appears to be the most adequate in a setting of household pooling (straightforward, not too much loss of time).

- The exact threshold of the positivity rate in the tested population under which pooling becomes relevant differs from study to study, but is generally high. In the advice of February 2021, a threshold of 10% was withheld. Deckert et al. and Hermani et al. modeled that household pooling is more cost-effective than random pooling (and thus becomes cost-effective at an even higher prevalence rate) and both found that it is very cost-effective at a prevalence rate of 5%.

- The most efficient pool size depends on the expected positivity rate. When positivity rate (PR) is relatively high (10%), most studies find the highest efficiency using pools of 4, when PR is 3-4%, pools of 6, when PR is 2%, 8, and when PR is <2%, 10. However, the two studies evaluating household pooling at different prevalence rates found that at a prevalence rate of 1% the reduction in number of tests required already increases substantially from a pool of 2-3 samples onwards, and is highest around 5. The pilot project in the UK used a pool of up to 5.

- Pooling of respiratory samples from different people belonging to a same bubble (household or other bubble), before sending to the lab, appears thus a good strategy to reduce costs and increase test capacity in a low positivity rate population. Possible applications suggested by KU Leuven are:
    - Screening of returning travelers or departing travelers belonging to the same bubble
    - Screening of people belonging to the same bubble in the context of mass events (entry or follow-up screening)

o   Mass screening in targeted communities/areas where an epidemic resurgence is observed

- A possible limitation is that it is unclear if manufacturers of RT-PCR tests allow their tests to be used on pooled samples. However, pooled RT-PCR testing is already applied in many countries, including in Belgium (ULiège).

RECOMMENDATIONS

- The RAG Testing supports the further exploration of the potential of household pooling.

- The performance of household pooling should be piloted in a real-life setting.

- The RAG Testing approves household pooling in the following settings:
  o   Screening of returning travelers or departing travelers belonging to the same household/ bubble
  o   Screening of people belonging to the same household/ bubble in the context of mass events (entry or follow-up screening)
- The RAG Testing does not approve, at this stage, household pooling for mass screening in targeted communities/areas where an epidemic resurgence is observed

- The recommended procedures for household pooling are:
  If a pool test positive:
  o   Conduct a second round of individual testing
  o   All members go in isolation until the results of the second round are known
  o   Pool members individually testing negative can stop isolation and are reported as negative, but have to go into quarantine as high-risk contact and be re-tested after 7 days.
  o   Pool members individually testing positive continue isolation, are reported as positive cases and contact tracing is initiated
  If a pool test negative:
  o   All members are reported as negative

- The proposed pool size of up to 6 samples is appropriate.

SCIENTIFIC LITERATURE

An extensive literature review with regards to (laboratory) pooling of samples for SARS-CoV-2 RT-PCR testing is available in the RAG advices of February 2021 and August 2020.

The most important points are:

- Pooling is only efficient when the expected positivity rate in in the tested population is low (<10%)
- Several pooling strategies are possible (two rounds of testing; three or more rounds of testing; second round in multiple overlapping groups; matrix of overlapping groups)
- Optimal pooling size depends on the positivity rate (the lower the rate, the larger the pool size), the method used and the viral load of positive samples.
- Pooling comes with a loss of sensitivity. However, the loss is generally low and it are mostly cases with a low viral load that go undetected.

Literature specifically on social pooling or household pooling is still scarce, although that an increasing number of modeling studies is being published.

UHasselt (Libin et al.) modeled PCR test pooling of individuals that belong to the same households in a context of universal testing (1). They evaluated two isolation strategies: pool isolation, where all individuals that belong to a positive PCR test pool are isolated, and individual isolation, where an additional test is done on all individuals that belong to the positive pool. They concluded that weekly universal testing could prove a successful strategy to control SARS-CoV-2 outbreaks. When incidence is high pool isolation appears to be the most effective strategy, and when incidence is low individual isolation.

Hermani et al. modeled the effectiveness of different asymptomatic testing strategies within a university setting (2). They found that when positive cases are clustered by known social structures, such as student households, the pooling of samples by these social structures can substantially reduce the total cost of conducting RT-PCR tests (see Figure below) with an acceptable loss of sensitivity. They argue that the results could extend to households in general. An adaptive strategy, whereby different pooling schemes are used depending on the estimated prevalence and R values, could be optimal.
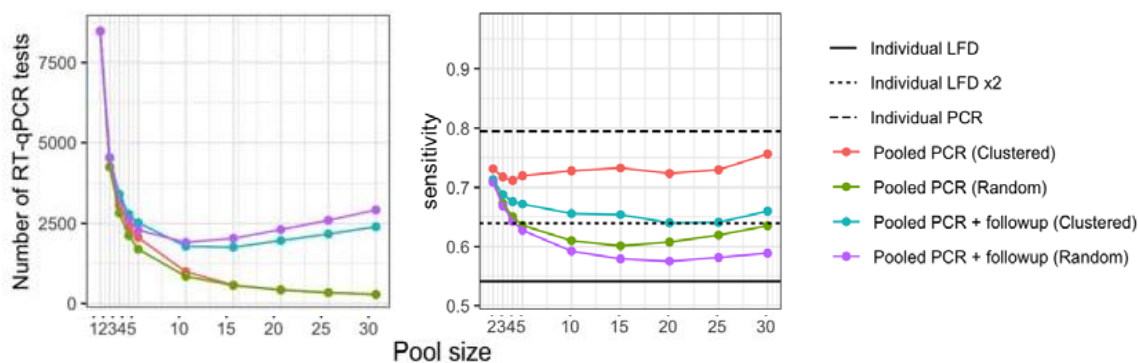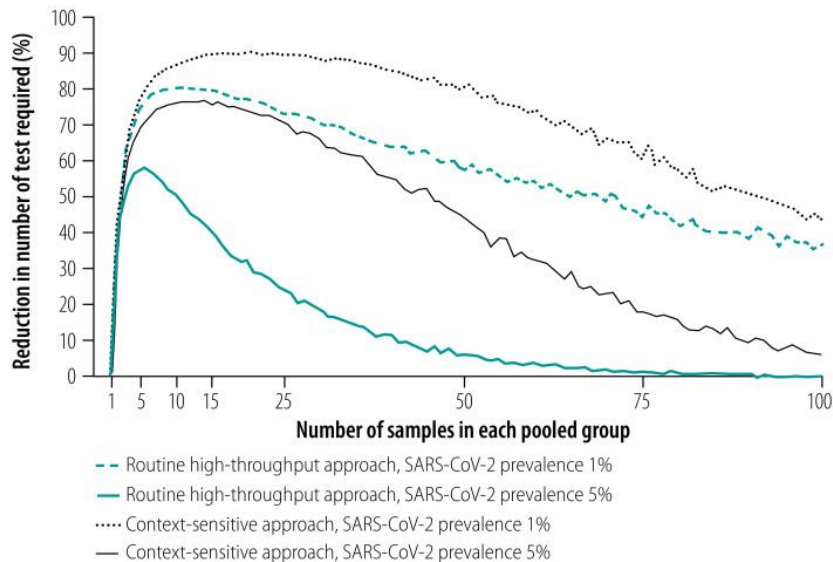

Figure: Comparison of number of tests required across different test strategies and loss of sensitivity with R=0.8 and a prevalence of 1%.

Deckert et al. modeled two different pooled-sample analysis strategies, a "routine high-throughput" heterogeneous group and a "door-to-door" homogeneous group strategy (3). In the routine high-throughput pooled-sample the sample pools are composed randomly, while in the

"door-to-door" pooled-sample groups of similar people are first formed[1]. The door-to-door approach required around 56% to 93% less tests in low to moderate prevalence settings and group sizes from 3 up to 25 in a population of 150 000, compared to individual testing, and was more efficient than the routine high-throughput (see Figure below). The authors conclude that pooled-sample PCR analysis strategies will save substantial resources for COVID-19 mass testing.

--- Routine high-throughput approach, SARS-CoV-2 prevalence 1%
— Routine high-throughput approach, SARS-CoV-2 prevalence 5%
····· Context-sensitive approach, SARS-CoV-2 prevalence 1%
— Context-sensitive approach, SARS-CoV-2 prevalence 5%

INTERNATIONAL GUIDELINES

International guidelines with regards to pooling of samples for SARS-CoV-2 testing in general are available in the advice of February 2021. No guidelines specifically with regards to household pooling were identified.

The only country identified where household-type pooling has been piloted is the UK. In November 2020 a pooled testing pilot was started among university students, in a context of testing before returning home (4). However, no results of this pilot were found.

REFERENCES

1. Libin PJK, 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. PLoS Comput Biol. 2021 Mar;17(3):e1008688.

2. Hemani G, Thomas AC, Walker JG, Trickey A, Nixon E, Ellis D, et al. Modelling pooling strategies for SARS-CoV-2 testing in a university setting. medRxiv. 2021 Jan 20;2021.01.19.20248560.

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[1] Groups of similar people are groups of which the within-group of positivity rate variation is smaller than the between-group variation. Examples are households, people in a same office, seat rows in an aircraft.

3. Deckert A, Bärnighausen T, Kyei NN. Simulation of pooled-sample analysis strategies for COVID-19 mass testing. Bull World Health Organ. 2020 Sep 1;98(9):590–8.

4. Pooled testing for coronavirus (COVID-19) pilot: guidance for university students [Internet]. GOV.UK. [cited 2021 May 28]. Available from: https://www.gov.uk/government/publications/cohort-pool-testing-for-coronavirus-covid-19/pooled-testing-for-coronavirus-covid-19-pilot-guidance-for-university-students