Advice about epidemiological parameters for the new app for contact tracing

RAG 31/07/2020

CONTEXT

To improve contact tracing, a contact tracing app will be deployed in Belgium in September 2020.

This app will follow the DP-3T Protocol (Distributed Privacy-Preserving Proximity Tracing), created in March 2020 by an international consortium of technologists, legal experts, engineers and epidemiologists. Since May 2020, a variant of the DP-3T protocol is supported in Android and iOS by the Exposure Notification Interface developed by Google and Apple. More than 15 countries have already deployed or plan to deploy this solution. In April 2020, the work has started on integrating this protocol into the Belgian healthcare context and a special task force was set up, under supervision of the Interfederal Committee for Tracking and Tracing.

The RAG has been requested to give epidemiological/scientific input on some specific questions.

QUESTIONS

1) *When taking the sample, the general practitioner determines the date on which the patient probably became contagious: is-it 2 or 3 days (or more) before the beginning of symptoms?*
   For example, for their app, the following countries choose:
   - *Switzerland: date of onset of symptoms -2 days*
   - *Estonia: date of onset of symptoms -3 days (but not less than -14)*
   - *Germany: data of onset of symptoms -3 days (more complex)*
   a) *Which formula to use to determine this date? (should we apply a margin of error)?*
   b) *If the patient is asymptomatic on the date of the test, how many days will we go back from the date of the test ? (currently 10 days in some countries; maximum of 14 imposed by Google / Apple API).*

It is important to remain consistent with previous advice of the RAG, i.e. that a person is contagious 48 hours before the onset of symptoms. This is also used for manual contact tracing (with call center), and it is important for communication to be consistent. The RAG therefore proposes to keep the period of 2 days.

However the most recent literature will be reviewed to see if this advice needs to be changed. It is then possible to change this parameter very quickly in the application.

a) It does not seem necessary to have margins of error because we don't use it neither in the manual contact tracing.

b) Currently, during manual tracing contact, the asymptomatic patient is considered contagious 2 days before the test date.

   The difficulty here is that it is not known how long the patient has been positive with the PCR. Although viral loads drop after the first week, prolonged shedding has been described (up to 37 days), and several studies report positive tests up to 82 days after initial negative results. Viral shedding does however not equate with contagiousness, and no infectious virus has been isolated after day 8 after symptom onset.

Especially for persons with a positive PCR result in the context of a screening (e.g pre hospitalization), it is very difficult to know if it is a recent or old infection. Information on viral load is generally not available and has its own limitations for the interpretation of the PCR result (see previous RAG advice).
In addition, we need also use the available testing capacity in the best possible way.

No consensus was reached on this by the experts.
The possible options are:

Time period	Pros	Contras
- 2 days	The most important is to focus on the presymptomatic people (= infectious one or two days before presenting symptoms). Contacts of those who would remain fully asymptomatic are less harmful to miss as they are likely much less infectious. This is what is currently used in the contact center (no need to adapt the scripts). This is the same criteria as for symptomatic persons (i.e. simple message, no change).	Might be too restrictive and we will miss persons that were recently infected and have been infectious (but staying asymptomatic) for several days.
- 7 days	This is in line with the 7days period of infectivity that is used in the procedures. It is the safest option (will include the most possible contacts).	This considers than the person was tested the last day that he/she was infectious. This will not often be the case, and we will include too many people in the contact tracing & testing procedure. This might have an important impact on physicians, testing capacities and number of people put in quarantine. It will need a change of the script for the contact center.
- 4 days	Same argument as for 2 days, but more cautious: takes into account that presymptomatic people might be infectious more than 1-2 days before the symptoms.	This would mean that the period for symptomatic persons would need to be longer too (see above, review of literature needed). It will need a change of the script for the contact center.

The different options will be presented at the RMG, who is in charge of taking the final decision, depending on their priorities (being more or less sensitive).
Depending on the period that will be chosen, the same criteria will have to be used for the contact center.

To be able to take an evidence-based decision, information would be needed on how many of the contacts are tested positive and the time period between the contact and the positive test of the index case. Currently this information is not available (and it is not foreseen to be collected through the app). Also, the data collected through the contact center is still of low quality, but Sciensano will continue to try and collect as much information as possible on the contacts. If more information will be available, the current decision could be revised.

It is also noted that the acceptance of the app is very important (so keep it simple), a high acceptance, with some residual transmission might be a better scenario than no acceptance and continued high transmission.

2) Should a degree of risk be indicated to the user (for example none, normal or high) or is the risk binary?

The app should be simple, based on a binary model. If there was a possible exposure (contact within 1.5m for at least 15 minutes), the person will receive a message: "You have been identified as a high risk contact. You have to contact your GP to be tested and stay in quarantine". If there was no risk: no message sent.

3) If the app indicates that there has been a risk contact, is the user always tested?

The same measures have to be adopted as for high-risk contacts (quarantine and test).
Note: the person will have to enter a date into the app to calculate the possible risk period. This should be the <u>date of start of the infectious period</u>. This date should be decided upon by the GP, during the consultation (based on start symptoms or date of the test if asymptomatic). It is important that this date is carefully registered into the app, so preferably during the consultation itself. Since the organization of sampling for asymptomatic persons will possibly change in the coming weeks/months, e.g. with sampling at drive in testing centers or in a laboratory and without consultation at GP, this should be taken into consideration by the developers of the app.

4) How should the tradeoff false positives/false negatives be set? (identify too many or too few people as risky). More specifically, this is translated into duration of exposure and estimated distance (see documents for explanation). Note that this can be adjusted while the app is in use, but initial parameters must be selected.

There are several proposals, from Switzerland and from Germany. This question is very technical and we leave it to the designers of the app, very well informed on the subject, to make the best proposal to the RAG.
The app will start with the following parameters: 55 dB and 63 dB.
These are the parameters used by the Swiss app, which considers two type of contacts: nearby contacts where the duration gets a weight of 1 and slightly farther contacts, where the duration gets a weight 0.5. The total risk is the weighted sum; if this sum is >= 15 minutes a risk is declared.
There are thus two thresholds: the threshold between nearby and farther contacts and the threshold above which everything is ignored.
These parameters can be changed later on if needed (e.g. based on experience of other countries).

5) The German risk assessment can be further refined if the app knows the date since onset of symptoms. Would it be useful and feasible to make simulations to improve the model?

Since the decision was taken to follow the Swiss model (more simple and easier to adapt) and not the German model, this question is not applicable anymore.

The following persons participated to this RAG advice:

Scientific input: Emmanuel André (KULeuven); Leïla Belkhir (UCL); Philippe Beutels (UA); Myriam Boreux (AViQ) ; Emmanuel Bottieau (ITG); Steven Callens (UZGent); Laura Cornelissen (Sciensano); Bénédicte Delaere (Mont Godinne); Mathias Dewatripont (ULB); Jean-Luc Gala (UCL); Michèle Gérard (CHU St Pierre); Stéphanie Jacquinet (Sciesano); Valeska Laisnez (AZG); Tinne Lernout (Sciensano); Romain Mahieu (COCOM); Dominique Ngoumtsa (AViQ); Stefan Teughels (Wachtposten Vlaanderen); Steven Van Gucht (Sciensano); Greet van Kersschaever (Domus Medica); Marc Van Ranst (UZLeuven).

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Observer : Patrick Waterbley (SPF Santé Publique).

BACKGROUND INFORMATION

1) Corona App Task Force. A Distributed Privacy-Friendly Contact Tracing App for Belgium. Version 1.1, 22 July 2020.
2) SwissCovid Exposure Score Calculation Version of 06 July 2020
3) CWA Team. Epidemiological Motivation of the Transmission Risk Level. 15 June 2020.
4) G. Cencetti, G. Santin, A. Longa, E. Pigani, A. Barrat, C. Cattuto, S. Lehmann, M. Salathé and B. Lepri. Digital Proximity Tracing in the COVID-19 Pandemic on Empirical Contact Networks.
5) R. Hinch, W. Probert, A. Nurtay, M. Kendall, C. Wymant, M. Hall, K. Lythgoe, A. Bulas Cruz, L Zhao, et al. Effective Configurations of a Digital Contact Tracing App: A report to NHSX. 16 April 2020.
6) Yuan J, Kou S, Liang Y, Zeng J, Pan Y, Liu L. PCR Assays Turned Positive in 25 Discharged COVID-19 Patients. Clin Infect Dis [Internet]. [cited 2020 Apr 8]; Available from: http://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa398/5817588 101.
7) Xiao AT, Tong YX, Zhang S. False-negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. Journal of Medical Virology [Internet]. [cited 2020 Apr 10];n/a(n/a). Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25855
8) Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA 2020 Mar 11. Available from: https://jamanetwork.com/journals/jama/fullarticle/2762997
9) Woelfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Mueller MA, et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in atravel-associated transmission cluster. medRxiv. 2020 Mar 8;2020.03.05.20030502
10) He X, Lau EHY, Wu P *et al.* Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 26, 672–675 (2020). Available from: https://www.nature.com/articles/s41591-020-0869-5
11) Lau EHY, Leung G. Author correction: temporal dynamics in viral shedding and transmissibility of COVID-19. Available from: https://covid19.sph.hku.hk/images/Correction_He_et_al_Nat_Med.pdf