RECOMMANDATIONS CONCERNANT L'INTERPRÉTATION DES RÉSULTATS DU TEST AG RAPIDE DANS UN CONTEXTE D'AUTOTEST À DOMICILE

RAG sous Testing – 23 mars 2021

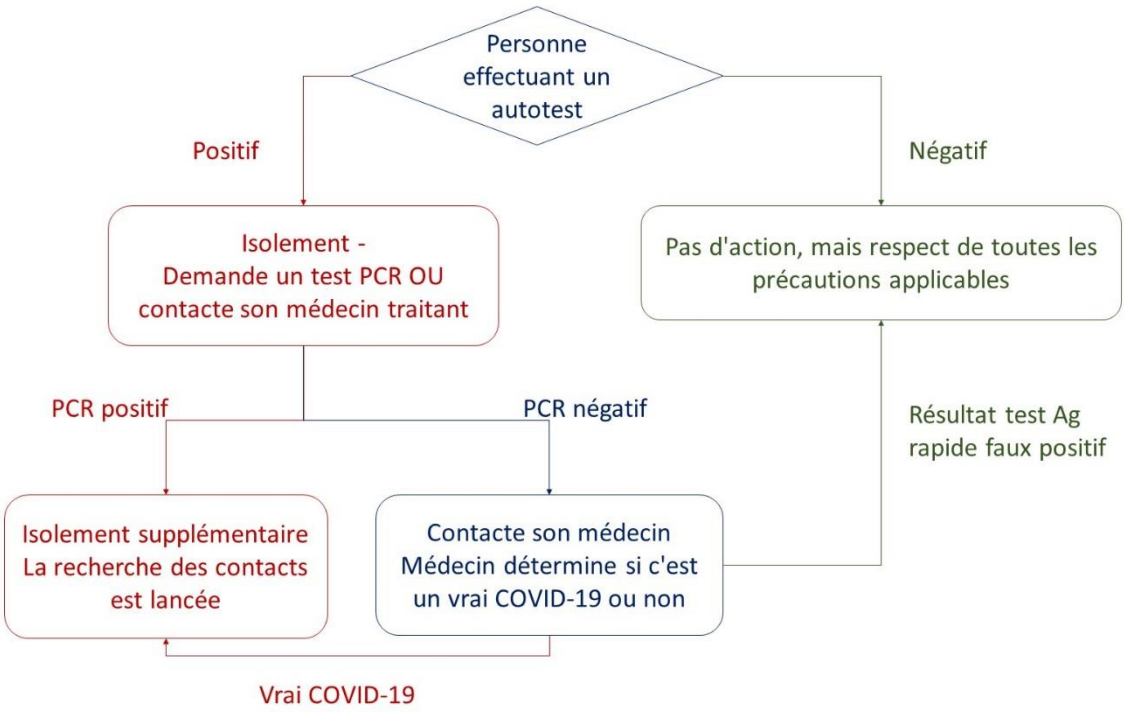
Cet avis a été validé par le RMG le 1er avril sous réserve de la modification de la mesure pour les contacts étroits d'une personne ayant un autotest positif. Le RMG a décidé que ces personnes ne devaient pas être mises en quarantaine en attendant le résultat du test PCR sur la personne index. L'algorithme a été modifié à la suite de cette décision.

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

Recommandations :

- Un résultat négatif d'un autotest ne dispense pas la personne d'observer toutes les mesures de précaution en application.
- Si le résultat d'un autotest est positif, la personne entre immédiatement en isolement.
- Un résultat positif d'un autotest à domicile est confirmé par un test RT-PCR. La personne demande un test RT-PCR dans un centre de test (via une application à développer) ou (si aucune application n'est disponible) demande à son médecin traitant de le faire. Si nécessaire, par exemple en cas de symptômes ou de besoin d'informations, la personne peut contacter son médecin traitant, qui décidera alors des prochaines étapes.
- Dans l'attente du résultat du test RT-PCR, la personne n'est pas encore enregistrée comme un cas confirmé, mas comme un cas suspect (tout comme une personne symptomatique qui attend son résultat).
    - Si le résultat du test RT-PCR est positif, la personne est enregistrée, la recherche des contacts est lancée et la personne reste isolée jusqu'à 10 jours après le résultat positif du test Ag rapide.
    - Si le résultat de la RT-PCR est négatif, la personne prend rendez-vous avec le médecin traitant, qui décide alors des prochaines étapes en fonction du contexte clinique et épidémiologique.
        - Si le médecin généraliste décide qu'il s'agit d'un cas confirmé de COVID-19, l'enregistrement (en tant que cas de test Ag rapide positif) et la recherche des contacts sont lancés et la personne reste isolée jusqu'à 10 jours après le résultat positif du test Ag rapide.
        - Si le médecin décide que le résultat du test Ag rapide était probablement un faux positif, la personne n'est pas considérée comme un cas de COVID-19.

ALGORITHME



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CONTEXT

The increased availability of rapid Ag tests and the current RT-PCR capacity offer opportunities to expand test indications for SARS-CoV-2. A possible strategy to enhance accessibility to testing is self-testing. A RAG advice of 3 March 2021 has recommended to lift the legal ban on self-swabbing and self-testing for COVID-19, and to identify settings in which self-testing might be useful. One possible use is at-home self-testing for self-control, as is currently piloted/ implemented in some other countries, and the Belgian government is considering to make rapid Ag tests available to a broader public for self-testing from mid-April onwards. The RAG testing was requested to provide an advice on the interpretation of the result of a rapid Ag test that was self-administered on a self-sampled swab.

DISCUSSION

- Several studies have shown that when using rapid Ag tests in screening settings, a large proportion of the positive results is not confirmed with an RT-PCR (PPV ranging between 10% to 33%).
- As a result, ECDC, WHO and CDC all recommend confirming positive rapid Ag test results with an RT-PCR in low-prevalence settings.
- Self-testing by asymptomatic people who had no close contact with a COVID-19 case, in a context of self-control or in a context of repetitive screening, is a low-prevalence setting. This is confirmed with the available positivity rate data in such settings (for example students tested after a self-risk assessment: 0.3%).
- On the other hand, the RT-PCR may also be negative if there is insufficient virus present (the amount of virus in an infected person is not constant and the discordance between the rapid Ag test and the RT-PCR may be due to this) or the result may be negative due to poor collection.
- Current guidelines on confirming positive rapid Ag test results in a context of self-testing from neighboring countries are inconsistent. Some countries do not recommend to confirm positive results (e.g. the UK). Germany recommends to confirm positive rapid Ag test results with an RT-PCR.
- A difference need to be made between self-testing under supervision, in which the result is interpreted by a trained health worker, and self-testing without supervision, in which it is the person itself who interprets the results (for example at home). The current advice relates to unsupervised self-testing.
- The risk of a false-positive or a false-negative result is expected to be greater in unsupervised self-testing than in self-testing under supervision, or than in testing by a health care provider.
- A negative result in unsupervised self-testing has always to be interpreted with caution, and can never be an excuse for no longer respecting the precautionary measures in place.
- Also a positive result in unsupervised self-testing has to be interpreted with caution and is best confirmed with an RT-PCR. Systematically contacting a GP in the event of a positive self-test risks to overburden the GPs. The possibility should therefore exist to directly request an RT-PCR test, without passing by a GP. This implies developing an electronic platform through which a test can be requested. Directly calling the call center will overburden it.
- Another possibility is to contact the GP and let the GP decide if confirmation is needed. This has, however, the disadvantage of (1) overburdening GPs; (2) making it confusing for the public (sometimes confirmation, sometimes not).
- A possibility is not to await the confirmatory PCR result and initiate the testing of the household contacts immediately. This could by RT-PCR, although that it will complicates

registration since the index case is not yet a confirmed COVID-19 case and the household members are therefore not yet officially close contacts. Or they could self-test with a rapid Ag test. But also this will make it complicated because if the index case is confirmed with an RT-PCR the household members will still be requested to have an RT-PCR as close contacts.

RECOMMENDATIONS

- A negative at-home self-test result does not exempt a person from respecting all precautionary measures in place.
- A person who has a positive at-home self-test result goes immediately in isolation.
- A positive at-home self-test result is confirmed with an RT-PCR test. The person requests an RT-PCR test in a testing center (through an application still to be developed) or (if no application is yet available) asks his/her GP to do so. If needed, for example if symptoms or need for information, the person can contact his/her GP, who then decides what the next steps are.

  While awaiting the RT-PCR result, the person is not yet registered as a confirmed case. He/she is considered a suspected case, similar to a symptomatic person awaiting his/her PCR test result.

  - If the RT-PCR result is positive, the person is registered, contact tracing is initiated and the person continues the isolation until 10 days after the positive rapid Ag test results.
  - If the RT-PCR result is negative, the person makes an appointment with the GP, who then decides what the next steps are based on the clinical and epidemiological context. If the GP decides that the person has to be considered as a confirmed COVID-19 case, registration (as a positive rapid Ag test case) and contact tracing is initiated and the person continues the isolation until 10 days after the positive rapid Ag test results. If the GP decides that the rapid Ag test result was probably a false positive, the person is not considered as a COVID-19 case.

BACKGROUND

Background literature

Hoehl et al. piloted at-home self-testing of teachers with a rapid Ag test on a self-collected anterior nasal swab (1). On a total of 10,836 tests among 602 teachers, 21 tested positive, but **only 5 of these were confirmed by the RT-PCR performed on the same sample (resulting in a positive predictive value of only 23.8%)**.

A study in Switzerland by Kriemler et al. 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 (2). **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 (corresponding with a PPV of 10%)**.

The validity of a rapid Ag test in the context of screening university students was assessed in a study in Wisconsin (3). 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%.**

Sudlow et al. calculated that with a sensitivity of 80%, infection **prevalence of 1 in 2,000**, and **specificity of 99.9%** on all tests, **PPV** in the tested population of 100,000 **will be only 29%** with one test, increasing to >99.5% (100% when rounded to the nearest %) with repeat testing of positive results (4). More realistically, if specificity is 95% for the first and 99.9% for subsequent tests, single test PPV will be only 1%, increasing to 86% with repeat testing of positive results. They conclude that PPV falls to unacceptably low levels with lower test specificity.

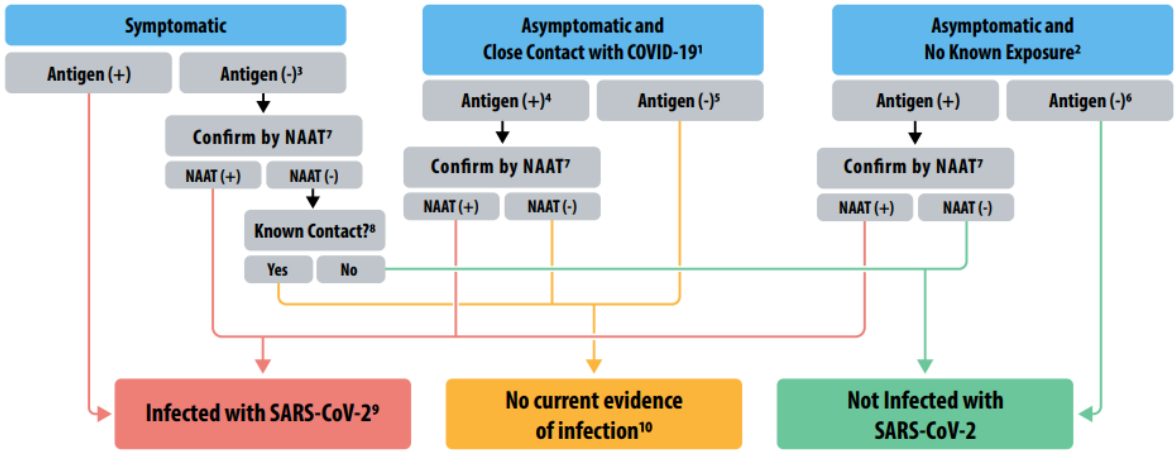
Atkeson at al. assessed the economic benefits of repeated testing with a rapid antigen test and concluded that the fiscal, macroeconomic, and health benefits of rapid SARS-CoV-2 screening testing programs far exceed their costs (5). A weekly testing in a regime with high compliance comes close to suppressing 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**.

International and national guidelines

ECDC states in its recent guidance on self-tests (17 March): 'The positive predictive value (PPV) of a test decreases with decreasing prevalence in the population where the test is being used. A test with 80% sensitivity and 99% specificity has a PPV of 44.7% and 7.4% respectively in populations with a 1% and 0.1% true point prevalence of SARS-CoV-2. This suggests that only a minority of cases testing positive in a self-test (and other rapid Ag tests) in a low prevalence setting would be positive if tested with RT-PCR. **Therefore, a confirmatory test with RT-PCR is recommended in such low-prevalence settings**.

WHO states in its SARS-CoV-2 antigen-detecting rapid diagnostic tests - AN IMPLEMENTATION GUIDE: 'An important point is that as prevalence decreases, so does PPV, meaning that the probability that a positive result is a true positive is reduced in low-prevalence settings; **therefore, confirmatory testing is strongly recommended.'**

CDC states in its recent overview of testing for SARS-CoV-2 (17 March): 'In screening settings where antigen tests are used on asymptomatic people, **laboratory-based confirmatory NAAT testing is recommended for individuals who test positive** (see algorithm below).



The Netherlands do not provide guidance on the interpretation of positive rapid Ag test results in a low-prevalence setting.

France, in its leaflet with instructions, does not advice to have a confirmatory test if testing positive with a rapid Ag test.

Germany: The Robert Koch institute states (translated from German): 'an antigen quick test is not as specific as a PCR test, which means that unlike PCR, a positive result is displayed if the person is not infected at all. **Therefore, a positive result in the antigen test should be confirmed by PCR**. The same advice applies in the context of self-testing.

The united Kingdom: In its advice on self-tests, the UK does not recommend to confirm positive self-test.

Data on prevalence in screening settings in Belgium

- Nursing home staff in Wallonia: **0.9%**
- Teachers and school staff: **0.4%**
- Students screened based on a self-risk assessment: **0.3%**

Relation between prevalence, test specificity and positive predictive value

The table below demonstrates how the positive predictive value rapidly decreases with decreasing prevalence.

Table: Positive predictive value by prevalence rate and test specificity, in a test with a sensitivity of 85%

Prevalence rate	Test specificity				
	97.0%	**98.0%**	**99.0%**	**99.5%**	**99.9%**
0.1%	2.8%	4.1%	7.8%	14.5%	46.0%
0.5%	12.5%	17.6%	29.9%	46.1%	81.0%
1.0%	22.3%	30.0%	46.2%	63.2%	89.6%
2.0%	36.6%	46.4%	63.4%	77.6%	94.5%
5.0%	59.9%	69.1%	81.7%	89.9%	97.8%

References

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3. 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.

4. 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.

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