

GEBRUIK VAN ONDIEPE NEUSWISSERS VOOR DE DETECTIE VAN SARS-COV-2

RAG subgroep Testing – 17 mei 2021

Opmerking: De huidige aanbevelingen zijn onderhevig aan veranderingen afhankelijk van nieuwe wetenschappelijke gegevens en/of de evolutie van de epidemie.

Aanbevelingen:

- Een nasofaryngeale afname blijft de voorkeur genieten, maar een ondiepe neuswisser (anterieur nasaal of midden turbinaat) is een aanvaardbaar alternatief in bepaalde situaties, zoals indien een patiënt teveel pijn of ongemak ervaart tijdens een nasofaryngeale afname.
- Dit geldt enkel voor het testen van symptomatische patiënten met symptomen sinds ≤ 5 dagen (in huisartspraktijk, triage en afname centrum, of spoeddienst).
- Zelf-testen kan steeds met een ondiepe neusafname gebeuren, dit kan zowel een anterieur nasale of midden turbinaat afname zijn.
- Voor zelftesten kunnen ook wissers gebruikt worden die voor een nasofaryngeale afname bedoeld zijn. De nasofaryngeale wissers geleverd bij snelle Ag tests kunnen dus in principe ook gebruikt worden voor een ondiepe nasale afname, onder voorwaarde dat de fabrikant dit toelaat.

De volgende personen hebben deelgenomen aan dit advies:

Emmanuel André (KU Leuven); Emmanuel Bottieau (ITG/IMT) ; Olivier Denis (CHU-UCL Namur); Achille Djiena (AVIQ); Herman Goossens (UAntwerpen); Marie Pierre Hayette (CHU-Liège); Yves Lafort (Sciensano); Barbara Legiest (ZG); Tinne Lernout (Sciensano); Romain Mahieu (COCOM); Elizaveta Padalko (UZGent); Olivier Vandenberg (LHUB-ULB); Ann Van den Bruel (KU Leuven); Steven Van Gucht (Sciensano); Pieter Vermeersch (UZ-Leuven)

CONTEXT

Self-testing, using self-administered nasal swabs, has been approved and self-tests are now available to the general public at pharmacies, and being used in a context of repetitive testing of employees. However, no guidance exists on what type of swab to use, and what type of nasal specimen to collect. The RAG testing was therefore requested to advice on (1) if the nasal sample has to be a mid-turbinate nasal swab or if it can be an anterior nasal swab; (2) if the swab to use has to be a swab specific for nasal samples, such as a tapered swab or a full-sized tip swab, or if the nasopharyngeal swab provided with most rapid Ag test kits is acceptable for self-testing.

TYPE OF NASAL SPECIMENS

A difference is generally made between specimens taken in the front of the nasal cavity (anterior nasal) and a specimen deeper into the nasal cavity (mid-turbinate nasal). CDC uses the following definitions (1):

Anterior nasal specimen:

- Swab is inserted 1 to 1.5 cm inside the nostril and rotated in a circular path against the nasal wall at least 4 times.

Nasal mid-turbinate (NMT) specimen:

- Head is tilted back 70 degrees and swab is inserted about 2 cm into nostril parallel to the palate (not upwards) until resistance is met at turbinates.

TYPE OF NASAL SWABS

Swabs can differ in terms of materials used, size and flexibility. CDC and the FDA recommend the following type of swabs for different COVID-19 sample collection methods (1,2):

For nasopharyngeal specimens:

- Synthetic fiber swabs with thin plastic or wire shafts that have been designed for sampling the nasopharyngeal mucosa and have a specialized mini-tip. Calcium alginate swabs or swabs with wooden shafts can never be used. When available, a flocked swab¹ is preferred.

For mid-turbinate nasal specimens:

- A specialized, flocked tapered (cone-shaped) swab.

For anterior nasal specimens:

- A flocked swab, round foam swab, or spun fiber swab. A swab with a full-sized tip (oropharyngeal-type swab) is generally preferred over a swab with a mini-tip (NP-type swab).

Some pictures of different types of swabs are presented in Annex 1.

TYPE OF COLLECTED SAMPLE AND SWAB USED IN SELF-TEST KITS CURRENTLY AVAILABLE IN BELGIUM

The federal agency for medicines and medical products (FAGG/AFMPS) has approved three rapid Ag tests which may be sold as a self-test (4):

- The 'SARS-CoV-2 Rapid Antigen Test Nasal' of SD Biosensor (distributed by Roche);
- The 'BIOSYNEX COVID-19 Ag BSS self-test' of Biosynex Switzerland; and

¹ Flocked swabs utilize an exclusive spray-on nylon flocked fiber technology. The perpendicular nylon fibers act like a soft brush to allow the improved collection and release of patient samples (3)

- The 'COVID-19 Antigen Detection Kit' of New Gene (Hangzhou) Bioengineering (distributed by SUNGO Europe).

In addition, FAGG/AFMPS lists another rapid Ag test that received a CE-certificate for sales in pharmacies:

- The 'Rapid SARS-CoV-2 Antigen Test Card' of Xiamen Boson Biotech Co., Ltd. (distributed by Lotus NL).

The information provided by the manufacturer with regards to the sampling and the type of swab is summarized below. However, most manufacturers do not specify clearly the type of swab.

SD Biosensor

- Mid-turbinate sample (head tilted-back, swab is inserted horizontally until resistance is met)
- Not specified – regular swab (not tapered, normal tip – in between mini and full-sized, not flexible)

Biosynex

- In between mid-turbinate and nasal: head is not tilted back, swab is inserted vertically until resistance is met
- Nasopharyngeal swab, according to Biosynex website (5)

New gene

- In between mid-turbinate and nasal: head is not tilted back, swab is inserted vertically 2-3 cm
- Type of swab not specified

Xiamen Boson

- Anterior nasal? (No clear instructions available on the website)
- Nasopharyngeal swab (6)

DISCUSSION

Type of nasal specimen

Summary of studies comparing nasal swab vs. nasopharyngeal swabs

Self-administered nasal swabs² (PCR) and NPS (PCR):

- Several good quality studies in symptomatic patients showed comparable results of nasal and nasopharyngeal swabs. Only two (poor quality) studies in asymptomatic people were reported.

Self-administered nasal swabs² (Ag RDT) and NPS (Ag-RDT or PCR):

- Several very good quality studies, mostly in symptomatic patients, showed excellent agreement (although based on very small samples) between results of nasal and nasopharyngeal swabs using same detection method.

² Mainly under professional supervision

HCP provider-collected nasal swabs (PCR) and NPS (PCR):

- Low quality studies. Data suggest good agreement if medium-to-high viral load

HCP provider-collected swabs (Ag RDT) and NPS (Ag-RDT or PCR):

- Excellent agreement (although based on only one study with small sample size) if high medium-to-high viral load and/or during first 5 days of symptoms

Other conclusions:

- Many studies used flocked swabs for nasal swabbing and showed excellent results. Only problem: more tickling and sneezing.
- Most studies are among symptomatic patients and there is less data on the performance among asymptomatic people.
- Several studies are of low quality and/or had a small sample size.
- In most studies evaluating self-administered nasal samples, the sample was self-collected with instructions from, and under supervision/observation of, a health care provider. Only two studies assessed the performance of at-home, unsupervised self-collection.
- Only two studies compared anterior nasal swabs with mid-turbinate nasal swabs. One found that the MTN swab performed (slightly) better, but the other did not find a difference. We can conclude that there is no real difference.
- Most studies evaluating self-administered nasal samples compared specimens tested with an RT-PCR, only three compared specimens tested with a rapid Ag test.

International guidelines

- Most countries appear to accept anterior nasal sampling for at-home self-testing.

Type of swab

- There is little scientific information with regards to the performance of different types of swabs for testing with a rapid Ag test on nasal samples.
- The US was the only country identified providing guidance. They recommend a tapered swab for mid-turbinate nasal samples, and a full-sized tipped swab for anterior nasal samples.
- On the other hand, some approved self-test kits appear to use nasopharyngeal type of swabs for nasal sampling, and this type of swab was also used in several studies evaluating the performance of nasal samples.

CONCLUSIONS

- Several good quality studies showed consistently a good concordance between self-administered supervised nasal swabs and HCP-collected nasopharyngeal swabs among symptomatic outpatients, whether paired detection was based on Ag RDT or PCR.

- These studies also showed that flocked swabs can be used for nasal swabbing. However, flocked swabs caused more tickling and sneezing effect.
- The anterior nasal collection was associated with a significantly lower degree of coughs or sneezes, and severity of pain in comparison to nasopharyngeal collection.
- Only one (good) study evaluated at-home self-collection of nasal swabs and showed comparable results with HCP-collected nasopharyngeal swabs (both analyzed by PCR)
- Only one (good) study evaluated at-home Ag-RDT self-testing and found slightly lower sensitivity compared with PCR of HCP-collected nasopharyngeal swabs among patients with high viral load.
- We found no good studies on asymptomatic people.

RECOMMENDATIONS

- Among symptomatic outpatients, tested at a test center, emergency department or by a general practitioner, nasal swabs, either anterior nasal or mid-turbinate, can be an acceptable alternative to nasopharyngeal swabs during the first 5 days of symptoms. The nasopharyngeal swab remains the standard, but a nasal swab can be considered in situations where a patient experiences too much pain or discomfort during the nasopharyngeal swabbing. The test used can be either RT-PCR or a rapid Ag test.
- For self-testing, either anterior or mid-turbinate swabbing can be used
- For self-testing, also nasopharyngeal swabs (e.g. flocked swabs) can be used. The nasopharyngeal swab provided with the rapid Ag test kits intended for nasopharyngeal swabbing can thus also be used for nasal swabbing, if this would be allowed by the manufacturer.

BACKGROUND LITERATURE

Type of nasal specimen

Several studies compared the performance of COVID-19 tests on different types of nasal specimens, either self-collected or collected by a professional, to the same test on a nasopharyngeal specimen collected by a health care provider. Most used RT-PCR testing, although that some compared the performance using rapid Ag tests. A summary table of the results is presented in Annex 2.

Self-administered nasal swabs tested with RT-PCR

Teo et al. recruited participants from a large cohort of migrant workers in Singapore (7). Participants included cases already confirmed to have COVID-19, roommates of confirmed cases and people with respiratory symptoms. After the routine NPS was obtained by a health care worker at a medical post, participants were requested to self-collect a nasal swab and to provide a spitted saliva sample, under supervision of the health care provider. Samples were tested with two different RT-PCR tests. The denominator is samples that tested positive on any specimen.

The nasal swab detected markedly less infections among the symptomatic cases, but more among the asymptomatic cases than the NPS. In the latter, the saliva sample detected many cases not detected by either the nasal swab or NPS. It is not specified if the nasal swab was anterior or mid-turbinate.

Tu et al. obtained NPS and at least one other specimen from 530 patients with respiratory symptoms seen in ambulatory clinics in the US (8). Patients were provided with instructions and asked to collect tongue, nasal, and mid-turbinate samples at the clinic. When a nasopharyngeal sample collected by a healthcare provider was used as the comparator, the mid-turbinate swab was slightly less sensitive than the NPS (96.2%), and the anterior nasal swab (<2 cm) still slightly lesser (94%). The correlation coefficient between Ct values of the positive NPS results and the positive anterior nasal and mid-turbinate nasal swabs results were 0.78, and 0.86, respectively, indicating that the viral load may be higher in the nasal swabs than in the NPS swabs.

Hanson et al. recruited symptomatic patients at a drive-thru test center in the US (9). Participants were instructed to swab both nostrils with a foam swab and to spit saliva into a sterile tube, in the presence of a healthcare worker, and were then taken a NPS. Sensitivity of PCR on the self-administered nasal swab was 81.4% (using PCR+ on either NPS or saliva as reference) and of PCR on NPS 93.0%. No data were available on Ct values of NPS positive vs. nasal swab positive specimen. The authors concluded that NPS and saliva were superior to ANS alone for the detection of SARS-CoV-2 in symptomatic patients.

Also McCulloch et al. recruited symptomatic patients at a drive-thru test center in the US (10). Participants were provided test kits for unsupervised home self-collection of a mid-nasal swab. Home swab performance was compared with clinician-collected nasopharyngeal swabs. Sensitivity of the self-administered nasal swab was substantially lower than that of the NPS. Home self-collected mid-nasal swab Ct values were positively associated with the clinician collected NPS Ct values (correlation coefficient, 0.81). The correlation coefficient between Ct values of home swabs and clinician swabs was 0.81, indicating a higher viral load in the nasal swabs than in the NPS swabs. The authors concluded that unsupervised home mid-nasal swab collection was comparable to clinician-collected nasopharyngeal swab collection for detection of SARS-CoV-2 in symptomatic patients, particularly those with higher viral loads.

Kojima et al. recruited people who recently tested for COVID-19 at a drive-thru test center in the US (both symptomatic and asymptomatic) (11). They obtained unsupervised self-collected oral fluid swab specimens, clinician-supervised self-collected oral fluid swab specimens, clinician-supervised self-collected mid-turbinate nasal swab specimens, and clinician-collected posterior nasopharyngeal swab specimens. Participants were verbally instructed to insert the swab into one nostril to the depth of 3-4 cm and rotate it for 5 to 10 seconds. Sensitivity was identical between the mid-turbinate swab and the NPS, although that the sample size was small.

Self-administered nasal swabs tested with rapid Ag test

Lindner et al. compared the performance of testing with a health care provider-administered (HCP) rapid Ag test (SD Biosensor) on a supervised, self-collected nasal swab and testing with a HCP-administered rapid Ag test on a HCP-collected NPS in Germany (12). Participants were symptomatic patients at a hospital OPD. Verbal instruction was given to insert the swab horizontally 2-3 cm into the nostril and rotate it for 15 seconds against the nasal walls on each side. Sensitivity of the rapid Ag test, compared to an RT-PCR on a NPS/OPS, was 79.5% with the HCP-collected NPS and 74.4% with the self-collected nasal swab. Of the two patients

detected by NPS but not by nasal sampling, one patient collected the swab only with gentle rotation, and the second presented 10 days post symptom onset with a low viral load. Among 23 patients with high viral load ($>7.0 \log_{10}/\text{swab}$), all were detected with the NPS and one was missed with the nasal swab. The authors concluded that supervised self-sampling from the anterior nose is a reliable alternative to professional nasopharyngeal sampling.

Nikolai et al. compared a self-administered mid-turbinate nasal swab with a health care provider-collected NPS, for testing with a rapid Ag test (SD Biosensor), among symptomatic patients at a testing facility in Germany (13). While tilting the head back (70°) the swab was inserted horizontally (parallel to the palate) into both nostrils for about 2 cm until resistance occurred, and then rotated 4 times against the nasal walls. Procedures were observed without answering questions or providing corrections. The self-collected mid-turbinate nasal swab had the same sensitivity as the health care provider-collected NPS. Both detected all cases with a high viral load.

Klein et al. compared, among people attending a test center in Germany (symptomatic or high-risk contact), the accuracy of a rapid Ag test (Panbio) performed on a supervised, self-collected nasal mid-turbinate swab versus a professionally collected NP swab (14). Overall the sensitivity was higher with the NPS (89% vs. 84%), but equal between the NPS and the MTN swab in cases with a high viral load. It is noteworthy that of 45 cases, 4 tested positive on the NPS and negative on the MTN swab, but also 2 tested positive on the MTN swab and negative on the NPS.

Stohr et al. compared self-testing at home with a rapid Ag test (BD Veritor and Roche) on a mid-turbinate nasal swab with RT-PCR on a provider-collected combined oro-nasopharyngeal swab, among people attending a test center in the Netherlands (15). They did, however, not compare it to a rapid Ag test on a provider-collected NPS. Thus, the lesser sensitivity is a combination of the loss due to the use of a rapid antigen test and the use of a nasal swab.

Health care provider-collected nasal swabs tested with RT-PCR

Pinninti et al. compared health care provider-collected mid-turbinate nasal and nasopharyngeal swabs from hospitalized patients with confirmed COVID-19 infection in the US (16). Mid-turbinate nasal swabs were less sensitive than NPS, in particular one week after admission and when Ct value was low.

Péré et al. compared nasal specimens (inserted until hitting the inferior concha) with nasopharyngeal specimens of patients attending a hospital OPD in France (17). Out of 37 patients that were positive for SARS-CoV-2 by nasopharyngeal swab testing, 33 (89%) also tested positive by nasal sampling, and 4 tested negative. All 7 SARS-CoV-2-negative patients with nasopharyngeal swabs tested also negative using nasal swabs. Positive nasal and positive nasopharyngeal specimens had a similar Ct value.

Tsujimoto et al. compared nasal (inserted approximately 1–2 cm into each nostril and rotated for 5 seconds) and saliva swabs to NPS in several samples at different time periods after admission among 10 hospitalized patients in Japan (18). Overall, nasal specimens had a sensitivity of 67.5% compared to NPS, and among people with recent onset of symptoms 86.4%. The Ct values were on average lower in the nasal specimens. Saliva swabs had still a much lower overall sensitivity (33.3%) and the authors concluded that NS samples are more reliable than SS samples and can be an alternative to NPS samples.

Griesemer et al. recruited participants at two testing centers (symptomatic and high-risk contacts) in the US and compared nasal swabs and saliva to NPS (19). Collection of NS was by bilateral swabbing on flocked swabs with insertion to approximately one inch (2.5cm) and gentle rotation for several seconds. Nasal swabs had a lower sensitivity than NPS (87% vs. 98%). The mean Ct values for NPS and NS were not significantly different from one another.

Berenger et al. contacted 30 people who had previously tested positive in Canada, and compared nasal and throat swabs with NPS (20). The mean number of days since the previous test was 4 days and since onset of symptoms 10 days. For nasal collection, both nares were swabbed to a depth of at least 3 cm (or until resistance felt) and rotated three times. NPS had a better sensitivity than NS (90% vs. 80%), and the mean Ct value was higher in nasal samples than in NPS.

Callahan et al. compared health care provider-collected nasal swabs with NPS among patients attending an OPD in the US, either because of symptoms or for a follow-up visit (21). Nasal swabs were compared under three different specimen-transport conditions and two different collection procedures were applied. In procedure 1, for each naris, the swab tip was inserted into the nostril, the patient was told to press a finger against the exterior of that naris, and the swab was rotated against this external pressure for 10 seconds; in procedure 2, the swab was inserted into the naris until resistance was felt, and the swab was then rotated for 15 seconds without external pressure. Comparison of Ct values between nasal and NP swabs showed higher Cts for nasal swabs than for NP swabs. Overall sensitivity was low (result not shown), but there was a marked decrease in false negatives for NP-swabs with lower Ct values. There were no obvious differences between the two swab procedures or among the collection methods.

Health care provider-collected nasal swabs tested with rapid Ag test

Nikolai et al. compared two different provider-collected nasal sampling methods, anterior nasal and mid-turbinate nasal, with a health care provider-collected NPS, for testing with a rapid Ag test (SD Biosensor), among symptomatic patients at a testing facility in Germany (13). For AN-sampling, the tip of a swab was inserted into the nose vertically 1 to 1.5 cm and rotated against the nasal walls for 15 seconds in both nostrils. For NMT-sampling, while tilting the head back (70°) the swab was inserted horizontally (parallel to the palate) into both nostrils for about 2 cm until resistance occurred, and then rotated 4 times against the nasal walls. The sensitivity of the rapid Ag test on nasal swabs was 86.1% for both sampling methods, against 100% for the rapid Ag test on a NPS. In cases with high viral load, the sensitivity with NS was 96.6%, against 100% with NPS. The authors concluded that AN-sampling is a suitable alternative to NMT- or NPS-sampling.

Takeuchi et al. compared a rapid Ag test (QuickNavi-COVID19 Ag kit) on a health care provider-collected anterior nasal sample to an RT-PCR on a NPS, among symptomatic people attending a testing center in Japan (22). A nasopharyngeal-type flocked swab was inserted to 2 cm depth in one nasal cavity, rotated five times, and held in place for five seconds. Sensitivity was 72.5% but the rapid Ag test could detect SARS-CoV-2 in almost all samples with Ct values < 30 (exact figures not provided). They did not assess the performance of the rapid Ag test on NPS, and it is therefore not known to what extent the lesser sensitivity is due to the rapid antigen test or to the use of a nasal swab. The anterior nasal collection was associated with a significantly lower degree of coughs or sneezes, and severity of pain in comparison to nasopharyngeal collection.

Abdulrahman et al. assessed the performance of a rapid Ag test (Panbio) on a nasal sample among mildly symptomatic patients in Bahrein (23), although without comparing it to other

samples. The patient's head was tilted laid back by 70°, then the swab was inserted by approximately 2cm into the nostril while gently rotating it, rolled it several times then removed it. Sensitivity was 82%, and higher among patients with high viral load (88% in cases with Ct value<25).

Systematic review and meta-analysis

One systematic review and meta-analysis was identified, by Tsang et al. (24). The review included studies examining the performance of any additional respiratory specimens to NPS. It identified 6 studies evaluating nasal swabs (all included in the list above). Using nasopharyngeal swabs as the gold standard, pooled nasal and throat swabs gave the highest sensitivity of (97%), whereas lower sensitivities were achieved by saliva (85%) and nasal swabs (86%) and a much lower sensitivity by throat swabs (68%). Comparison between health-care-worker collection and self-collection for pooled nasal and throat swabs and nasal swabs showed comparable diagnostic performance. The authors concluded that nasal swabs are a clinically acceptable alternative specimen collection method.

Type of swab

No scientific literature was identified comparing different types of swabs for the collection of nasal samples. Most of the above studies did not specify what type of swab was used. The information of those studies that did provide some is summarized in the table below. Two studies used the same type of swab for the collection of the nasopharyngeal sample and the nasal sample.

Study	Type of swab used
Hanson et al.	Foam swab
Kojima et al.	Flocked swab (Copan Diagnostics, Murrieta, CA)
Klein et al.	Non-flocked swab (Jiangsu Changfeng Medical Industry Co., Ltd., Jiangsu, China)
Péré et al.	Nasal swab (Copan Transystem; Copan, Brescia, Italy)
Tsujimoto et al.	Dry swabs from the Cobas PCR media (CPM) kit (Roche Molecular Systems, South Branchburg, NJ)
Griesemer et al.	Flocked swab
Berenger et al.	Nasal swabs using APTIMA Unisex Collection Kit (Hologic Inc., Marlborough, Mass)
Takeuchi et al.	All samples (NS and NPS) were obtained with nasopharyngeal-type flocced swabs (FLOQSwabs - Copan Italia S.p.A., Brescia, Italy)
Abdulrahman et al.	Nasal samples were collected, using the nasopharyngeal swab provided with the Panbio rapid Ag test kit

INTERNATIONAL GUIDELINES

Few countries provide guidance on what type of nasal specimen to collect, or what type of swab to use.

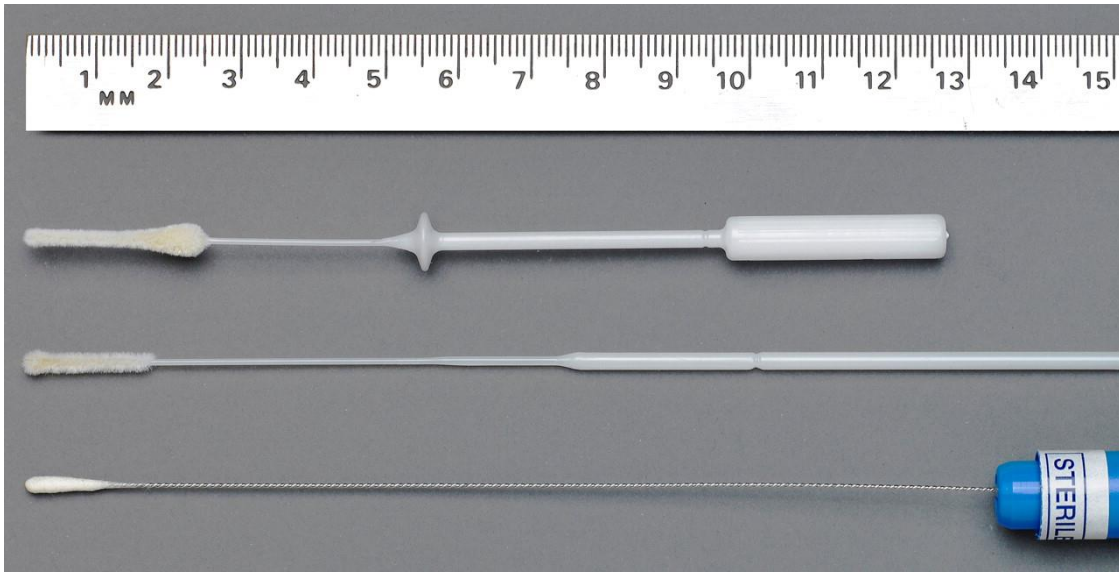
CDC approves both mid-turbinate and anterior nasal samples for at home self-testing for COVID-19, and provided guidance on what type of swab to use (see above). No other countries were identified that specify what type of nasal specimen needs to be collected, or what type of swab used. Some countries refer to the manufacturer's instructions, others have purchased self-tests using anterior nasal sampling (Austria).

REFERENCES

1. CDC. Labs [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2021 May 1]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html>
2. Health C for D and R. COVID-19 Testing Supplies: FAQs on Testing for SARS-CoV-2. FDA [Internet]. 2021 Apr 30 [cited 2021 May 7]; Available from: <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/covid-19-testing-supplies-faqs-testing-sars-cov-2>
3. Daley P, Castriciano S, Chernesky M, Smieja M. Comparison of flocked and rayon swabs for collection of respiratory epithelial cells from uninfected volunteers and symptomatic patients. *J Clin Microbiol*. 2006 Jun;44(6):2265–7.
4. Tests | FAGG [Internet]. [cited 2021 May 4]. Available from: https://www.fagg-afmps.be/nl/MENSELIJK_gebruik/gezondheidsproducten/medische_hulpmiddelen_hulpstukken/covid_19/tests
5. supportweb. TEST COVID-19 [Internet]. Biosynex. [cited 2021 May 7]. Available from: <https://www.biosynex.com/en/pharmacie-para-test-covid-19/>
6. Boson SARS-CoV-2 Antigen Rapid Test [Internet]. [cited 2021 May 7]. Available from: <https://www.bps-health.com/product/boson-rapid-test>
7. Teo AKJ, Choudhury Y, Tan IB, Cher CY, Chew SH, Wan ZY, et al. Validation of Saliva and Self-Administered Nasal Swabs for COVID-19 Testing. *medRxiv*. 2020 Aug 14;2020.08.13.20173807.
8. Tu Y-P, Jennings R, Hart B, Cangelosi GA, Wood RC, Wehber K, et al. Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. *N Engl J Med*. 2020 Jul 30;383(5):494–6.
9. Hanson KE, Barker AP, Hillyard DR, Gilmore N, Barrett JW, Orlandi RR, et al. Self-Collected Anterior Nasal and Saliva Specimens versus Healthcare Worker-Collected Nasopharyngeal Swabs for the Molecular Detection of SARS-CoV-2. *medRxiv*. 2020 Jul 19;2020.07.17.20155754.
10. McCulloch DJ, Kim AE, Wilcox NC, Logue JK, Greninger AL, Englund JA, et al. Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. *JAMA Netw Open*. 2020 Jul 1;3(7):e2016382.
11. Kojima N, Turner F, Slepnev V, Bacelar A, Deming L, Kodeboyina S, et al. Self-Collected Oral Fluid and Nasal Swabs Demonstrate Comparable Sensitivity to Clinician Collected Nasopharyngeal Swabs for Covid-19 Detection. *medRxiv*. 2020 Apr 15;2020.04.11.20062372.
12. Lindner AK, Nikolai O, Kausch F, Wintel M, Hommes F, Gertler M, et al. Head-to-head comparison of SARS-CoV-2 antigen-detecting rapid test with self-collected anterior nasal swab versus professional-collected nasopharyngeal swab. *Eur Respir J*. 2020 Dec 10;

13. Nikolai O, Rohardt C, Tobian F, Junge A, Corman VM, Jones TC, et al. Anterior nasal versus nasal mid-turbinate sampling for a SARS-CoV-2 antigen-detecting rapid test: does localisation or professional collection matter? medRxiv. 2021 Feb 16;2021.02.09.21251274.
14. Klein JAF, Krüger LJ, Tobian F, Gaeddert M, Lainati F, Schnitzler P, et al. Head-to-head performance comparison of self-collected nasal versus professional-collected nasopharyngeal swab for a WHO-listed SARS-CoV-2 antigen-detecting rapid diagnostic test. medRxiv. 2021 Mar 24;2021.03.17.21253076.
15. Stohr JJM, Zwart VF, Goderski G, Meijer A, Nagel-Imming CRS, Bergh MFQK den, et al. Self-testing for the detection of SARS-CoV-2 infection with rapid antigen tests. medRxiv. 2021 Feb 23;2021.02.21.21252153.
16. Pinninti S, Trieu C, Pati SK, Latting M, Cooper J, Seleme MC, et al. Comparing Nasopharyngeal and Midturbinate Nasal Swab Testing for the Identification of Severe Acute Respiratory Syndrome Coronavirus 2. *Clinical Infectious Diseases*. 2021 Apr 1;72(7):1253–5.
17. Péré H, Podglajen I, Wack M, Flamarion E, Mirault T, Goudot G, et al. Nasal Swab Sampling for SARS-CoV-2: a Convenient Alternative in Times of Nasopharyngeal Swab Shortage. *J Clin Microbiol*. 2020 May 26;58(6).
18. Tsujimoto Y, Terada J, Kimura M, Moriya A, Motohashi A, Izumi S, et al. Diagnostic accuracy of nasopharyngeal swab, nasal swab and saliva swab samples for the detection of SARS-CoV-2 using RT-PCR. *Infect Dis (Lond)*. 2021 Mar 24;1–9.
19. Griesemer SB, Van Slyke G, Ehrbar D, Strle K, Yildirim T, Centurioni DA, et al. Evaluation of Specimen Types and Saliva Stabilization Solutions for SARS-CoV-2 Testing. *J Clin Microbiol*. 2021 Apr 20;59(5).
20. Berenger BM, Fonseca K, Schneider AR, Hu J, Zelyas N. Sensitivity of Nasopharyngeal, Nasal and Throat Swab for the Detection of SARS-CoV-2. medRxiv. 2020 May 8;2020.05.05.20084889.
21. Callahan C, Lee R, Lee G, Zulauf KE, Kirby JE, Arnaout R. Nasal-Swab Testing Misses Patients with Low SARS-CoV-2 Viral Loads. medRxiv. 2020 Jun 14;
22. Takeuchi Y, Akashi Y, Kato D, Kuwahara M, Muramatsu S, Ueda A, et al. Diagnostic Performance and Characteristics of Anterior Nasal Collection for the SARS-CoV-2 Antigen Test: A Prospective Study in Japan. medRxiv. 2021 Mar 5;2021.03.03.21252425.
23. Abdulrahman A, Mustafa F, AlAwadhi AI, Alansari Q, AlAlawi B, AlQahtani M. Comparison of SARS-CoV-2 nasal antigen test to nasopharyngeal RT-PCR in mildly symptomatic patients. medRxiv. 2020 Dec 8;2020.11.10.20228973.
24. Tsang NNY, So HC, Ng KY, Cowling BJ, Leung GM, Ip DKM. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. *Lancet Infect Dis*. 2021 Apr 12;

ANNEX 1: PICTURES OF DIFFERENT TYPE OF SWABS



Flocced nasal mid-turbinate swab (top) compared to flocced nasopharyngeal (middle) and rayon nasopharyngeal (bottom) swabs, used for both nasal and nasopharyngeal sampling³.



Swab types used in the study: A—dacron swab, B—polyurethane foam, C—rayon swab, D—flocced nylon swab

4

³ Copied from: [Development and Evaluation of a Flocced Nasal Midturbinate Swab for Self-Collection in Respiratory Virus Infection Diagnostic Testing | Journal of Clinical Microbiology \(asm.org\)](#)

⁴ Copied from: [The influence of a swab type on the results of point-of-care tests | AMB Express | Full Text \(springeropen.com\)](#)

ANNEX 2: SUMMARY OF STUDIES COMPARING PERFORMANCE BETWEEN TESTS ON NASAL SPECIMENS AND ON NASOPHARYNGEAL SPECIMENS

Author	Study quality	Study population	N (positive)	Specimen	Compared to	Sensitivity*	
						NS	NPS
<i>Self-administered, tested with RT-PCR</i>							
Teo et al.	Low	Symptomatic cases	155	Supervised self-administered nasal swab	HCP-collected nasopharyngeal swab	61.9%	79.4%
		Asymptomatic cases	75			41.3%	36.0%
		Ct value<30	63			90.5% 95.2% ¹	(100%)
Tu et al.	Good	Symptomatic out-patients	51	At-clinic self-administered anterior nasal swab	HCP-collected nasopharyngeal swab	94.1%	98.1%
			52	At-clinic self-administered mid-turbinate nasal swab		96.2%	
Hanson et al.	Average	Symptomatic test center attendees	86	Supervised self-administered anterior nasal swab	HCP-collected nasopharyngeal swab	81.4%	93.0%
McCulloch et al.	Good	Symptomatic test center attendees	41	At-home self-administered mid-nasal swab	HCP-collected nasopharyngeal swab	75.6%	92.7%
Kojima et al.	Low	Symptomatic and asymptomatic test center attendees	29	Supervised self-administered mid-turbinate nasal swab	HCP-collected nasopharyngeal swab	79.3%	79.3%
<i>Self-administered, tested with rapid Ag test (Sensitivity is compared to RT-PCR test on a NPS)</i>							
Lindner et al.	Very good	Symptomatic patients at hospital OPD	39	Supervised self-administered nasal swab (2-3 cm)	HCP-collected nasopharyngeal swab	74.4%	79.5%
		Viral load >7.0 log ₁₀ /swab	23			95.7%	100%
Nicolai et al.	Very good	Symptomatic test center attendees	34	Observed self-administered mid-turbinate nasal swab	HCP-collected nasopharyngeal swab	91.2%	91.2
		Viral load >7.0 log ₁₀ /swab	25	Observed self-administered mid-turbinate nasal swab		100%	100%
Klein et al.	Very good	Test center attendees (symptomatic or high-risk contact)	45	Supervised self-administered mid-turbinate nasal swab	HCP-collected nasopharyngeal swab	84.4%	88.9%
		Viral load >7.0 log ₁₀ /swab				96.3%	96.3%
Stohr et al. – BD Veritor	Very good	Symptomatic and asymptomatic test center attendees	88	At-home self-administered mid-turbinate nasal swab	-	48.9%	-
		Ct value below cutoff for positive viral culture	-			75.5%	-
Stohr et al. – Roche		Symptomatic and asymptomatic test center attendees	122	At-home self-administered mid-turbinate nasal swab	-	61.5%	-
		Ct value below cutoff for positive viral culture	-			80.1%	-

Author	Study quality	Study population	N (positive)	Specimen	Compared to	Sensitivity*	
						NS	NPS
<i>HCP-collected, tested with RT-PCR</i>							
Pinninti et al.	Low	Hospitalized patients upon admission	34	HCP-collected mid-turbinate swab	HCP-collected nasopharyngeal swab	85.3%	100%
		Hospitalized patients one week after admission	24			51.2%	100%
		Ct value ≤ 30	54			92.6%	100%
Péré et al.	Low	Symptomatic patients at hospital OPD	37	HCP-collected nasal swab	HCP-collected nasopharyngeal swab	89.2%	100%
Tsujiimoto et al.	Low	Several samples from 10 hospitalized patients	48	HCP-collected nasal swab (1-2cm)	HCP-collected nasopharyngeal swab	67.5%	100%
		Within 9 d after onset	22			86.4%	100%
		Upon admission	10			100%	100%
Griesemer et al.	Good	Symptomatic and asymptomatic test center attendees	105	HCP-collected nasal swab	HCP-collected nasopharyngeal swab	87.1%	97.9%
Berenger et al.	Low	People who had tested positive at testing centers	30	HCP-collected nasal swab	HCP-collected nasopharyngeal swab	80%	90%
<i>HCP-collected, tested with rapid Ag test (Sensitivity is compared to RT-PCR test on a NPS)</i>							
Nicolai et al.	Very good	Symptomatic test center attendees	36	HCP collected anterior nasal swab	HCP-collected nasopharyngeal swab	86.1%	100%
				HCP collected mid-turbinate nasal swab		86.1%	100%
		Viral load >7.0 log ₁₀ /swab	29	HCP collected anterior nasal swab		96.6%	100%
				HCP collected mid-turbinate nasal swab		96.6%	100%
Takeuchi et al.	Good	Symptomatic test center attendees	51	HCP-collected anterior nasal swab	HCP-collected nasopharyngeal swab	72.5%	-
Abdulrahman et al.	Very good	Mildly symptomatic patients	733	HCP-collected nasal swab (2cm)	-	82.1%	-
		Ct value <25	195			87.9%	-

*Denominator is 'being positive with any sample' (can sometimes include additional samples, such as saliva, hence explaining the sometimes low sensitivity of the NSP)

¹Depending on the RT-PCR test used