IN SUPPORT OF NASAL SWABS & SELF COLLECTION FOR SARS-COV2 DETECTION

This summary reviews the evidence from recent studies that have compared the performance of healthcare worker (HCW) collected nasopharyngeal (NP) oropharyngeal (OP) or other respiratory specimens to both supervised and unsupervised self-collected mid turbinate nasal swabs for the detection of SARS-CoV-2.

The studies found that self-collected nasal swabs are a reliable alternative to standard of care NP or OP sample collection methods.

In turn the US Centers for Disease Control and Prevention (CDC) and the FDA have approved self-collected nasal sampling (supervised or at-home) as an acceptable specimen collection method for SARS-CoV-2 testing.[1]

In addition to reliability, nasal swabbing was supported[2] for the following reasons,

- **Nasal sampling is less invasive and results in less patient discomfort than sampling from other upper respiratory sites.**
- **Collection of nasal swab specimens is less technically complex, so can reduce the risk of the spread of infection to healthcare providers, by reducing the duration of the procedure, and allowing the patient to perform self-collection while under supervision.**
- **Nasal sampling also reduces PPE utilisation, given that the patient can perform self collection with and without supervision (versus the health care provider performing the collection).**

> *"Nasal swabs gave comparable and very good diagnostic performance and are clinically acceptable alternative specimen collection methods.[3]"*

PEER REVIEWED

Tsang, N. N. Y., So, H. C., Ng, K. Y., Cowling, B. J., Leung, G. M., & Ip, D. K. M. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. The Lancet Infectious Diseases. doi:10.1016/S1473-3099(21)00146-8

THE LANCET Infectious Diseases

DESIGN

A systematic review and meta-analysis to compare the diagnostic performance of different clinical specimen collection methods from 5577 studies.

METHOD

A search of PubMed, Embase, MEDLINE, Web of Science, *medRxiv*, *bioRxiv*, SSRN, and Research Square from Jan 1, 2000, to Nov 16, 2020 was conducted. Original clinical studies that examined the performance of nasopharyngeal swabs and any additional respiratory specimens for the diagnosis of SARS-CoV-2 infection among individuals presenting in ambulatory care were include in the review. Studies without data on paired samples, or those that only examined different samples from confirmed SARS-CoV-2 cases were excluded. Diagnostic performance, including sensitivity, specificity, positive predictive value, and negative predictive value, was examined using random effects models and double arcsine transformation.

RESULTS

- A comparably high positive predictive value was obtained by pooled nasal and throat (97%, 90–100) and nasal swabs (96%, 87–100).
- Self-collection for pooled nasal and throat swabs and nasal swabs was not associated with any significant impairment of diagnostic accuracy.

LIMITATIONS

Substantial heterogeneity was observed in several of the diagnostic performance indicators in studies on saliva and nasal swabs, which varied in terms of the disease prevalence, study location, symptom status of the study sample, and number of candidate genes tested. Also, geographical coverage was skewed, with most studies of saliva and nasal swabs done in the USA.

DISCUSSION

- Nasal swabs gave comparable and very good diagnostic performance and are clinically acceptable alternative specimen collection methods.
- The comparable diagnostic accuracy of alternative specimen collection methods, as shown in our findings, has practical benefits in clinical practice including,

- Reduced procedural discomfort might help to prevent the triggering of gag reflexes, coughing, and sneezing and reduce the associated exposure risk for the health-care workers.
- Reduced requirement for trained health-care workers and high-level PPE.
- Procedural simplicity could also allow for self-collection by patients or their relatives in different community settings.

The feasibility, accessibility, and acceptability of the self-collection for testing might help to facilitate the scaling up of SARS-CoV-2 testing in communities.

> *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.[4]"*

PEER REVIEWED

McCulloch, D. J., Kim, A. E., Wilcox, N. C., Logue, J. K., Greninger, A. L., Englund, J. A., & Chu, H. Y. (2020). Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. JAMA Network Open, 3(7), e2016382-e2016382. doi:10.1001/jamanetworkopen.2020.16382

DESIGN

A cross sectional study with 185 participants, of which 41 had positive results.

METHOD

Study participants were recruited from symptomatic outpatients testing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive and symptomatic health care workers presenting to drive-through clinics. 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, which were collected by medical assistants and nurses.

RESULTS

Compared with clinician swabs,

- The sensitivity of home swabs was 80.0% (95% CI, 63%-91%) and respectively (Table). Cohen κ statistic was 0.81 (95% CI, 0.70-0.93).
- The specificity of home swabs was 97.9% (95% CI, 94%-99.5%).
- Cohen κ statistic was 0.81 (95% CI, 0.70-0.93), suggesting substantial agreement.

LIMITATIONS

Shipping at ambient temperature may have led to sample degradation, however stability was demonstrated at ambient temperatures up to 9 days. Home self-collection often occurred one day after clinician collection, likely leading to samples with lower viral load. In addition, many participants were health care workers, potentially limiting generalizability to the general population.

DISCUSSION

- Unsupervised home self-swab collection presents several advantages, including accessibility outside of the health care system and minimizing personal protective equipment use.
- This approach is safe and scalable in the pandemic setting.

> *These findings contribute to the recently released US Food and Drug Administration guidance that lists patient-collected lower nasal swab as an acceptable specimen collection method for SARS-CoV-2 testing.[5]"*

PEER REVIEWED

Altamirano, J., Govindarajan, P., Blomkalns, A. L., Kushner, L. E., Stevens, B. A., Pinsky, B. A., & Maldonado, Y. (2020). Assessment of Sensitivity and Specificity of Patient-Collected Lower Nasal Specimens for Severe Acute Respiratory Syndrome Coronavirus 2Testing. JAMA Network Open, 3(6), e2012005-e2012005. doi:10.1001/jamanetworkopen.2020.12005

DESIGN

This was a prognostic study, approved by the Stanford University institutional review board with 30 participants infected with SARS-CoV-2.

METHOD

Patients were recruited remotely and attended Stanford Health Care for drive-through collection of three specimens using a patient-collected lower nasal swab, a physician-collected lower nasal swab and a physician-collected oropharyngeal swab. Specimens were tested for SARS-CoV-2 using reverse transcriptase–polymerase chain reaction targeting the envelope or open reading frame 1 ab genes.

RESULTS

- Diagnostic equivalence was seen across the three methods of specimen collection.
- Eleven participants (37%) had test results that were positive for SARS-CoV-2 across patient- and physician-collected specimens,
- Eighteen participants (60%) had results that were negative for SARS-CoV-2 across patient- and physician-collected specimens.

LIMITATIONS

Small sample size limits generalizability, however, further validation efforts are currently under way.

DISCUSSION

- Self-collected lower nasal swabs could also be used for home or office-based testing of asymptomatic patients.

"Self-collection of nasal and throat swabs offers a reliable alternative to health worker collection for the diagnosis of SARS-CoV-2 and other respiratory viruses.[6]"

PEER REVIEWED

Wehrhahn, M. C., Robson, J., Brown, S., Bursle, E., Byrne, S., New, D., Hadlow, N. (2020). Self-collection: An appropriate alternative during the SARS-CoV-2 pandemic. Journal of Clinical Virology, 128, 104417. doi:https://doi.org/10.1016/j.jcv.2020.104417

Journal of Clinical Virology

DESIGN

A prospective study of 236 patients.

METHOD

Patients from two states in Australia attending dedicated COVID-19 collection clinics were offered the option to first self-collect (SC) nasal and throat swabs (SCNT) prior to health worker collect (HCW) using throat and nasal swabs (Site 1) or throat and nasopharyngeal swabs (Site 2). Samples were analysed for SARS-CoV-2 as well as common respiratory viruses. Concordance of results between methods was assessed using Cohen's kappa (κ) and Cycle threshold (Ct) values were recorded for all positive results as a surrogate measure for viral load.

RESULTS

Of 236 patients sampled by health care worker and self-collection methods,

- 25 had SARS-CoV-2 (24 by HC and 25 by SC).
- 63 had other respiratory viruses (56 by HC and 58 by SC).
- Self-collection was highly concordant with HCW collected (κ = 0.890) for all viruses including SARS-CoV-2 and more concordant than HCW to positive results by any method (κ = 0.959 vs 0.933).
- Mean SARS-CoV-2 E-gene and N-gene, rhinovirus and parainfluenza Ct values did not differ between HC and SCNT.

DISCUSSION

- This study was the first to provide evidence of equivalence of self-collection for SARS-CoV-2. Self- collection has the potential to,
    - Increase accessibility and detection of SARS-CoV-2.
    - Preserve PPE supplies.
    - Reduce exposure to others.

Self-collection was also easy to perform and preferred by 74% participants (survey n=70).

"Patient collection of samples for SARS-CoV-2 testing from sites other than the nasopharynx is a useful approach during the COVID-19 pandemic.[7]"

PEER REVIEWED

Tu, Y.-P., Jennings, R., Hart, B., Cangelosi, G. A., Wood, R. C., Wehber, K., Berke, E. M. (2020). Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. New England Journal of Medicine, 383(5), 494-496. doi:10.1056/NEJMc2016321

The NEW ENGLAND JOURNAL of MEDICINE

DESIGN

A cross sectional study with 530 participants from five ambulatory clinics in the Puget Sound region of Washington, USA.

METHOD

Patients were provided with instructions and asked to collect tongue, nasal, and mid-turbinate samples, in that order. A nasopharyngeal sample was then collected from the patient by a health care worker. All samples were submitted to a reference laboratory for reverse-transcriptase–polymerase-chain-reaction (RT-PCR) testing that yielded qualitative results (positive or negative) and cycle threshold (Ct) values for positive samples only.

RESULTS

When compared to nasopharyngeal sample collected by a healthcare worker,

- The estimated sensitivity of the nasal sample collected by patients was 94.0% (97.5% CI, 83.8 to 100.0)
- The estimated sensitivity of the mid mid-turbinate sample collected by patients was 96.2% (97.5% CI, 87.0 to 100.0).
- Both the nasal and mid-turbinate samples may be clinically acceptable on the basis of estimated sensitivities above 90% and the 87% lower bound of the confidence interval for the sensitivity of the mid-turbinate sample being close to 90%.

LIMITATIONS

The study was performed in a single geographic region and limited to single comparisons with the results of nasopharyngeal sampling, which the authors described as "not a perfect standard test".

DISCUSSION

- Adoption of techniques for sampling by patients can reduce PPE use and provide a more comfortable patient experience.
- The authors stated that patient collection of samples for SARS-CoV-2 testing from sites other than the nasopharynx is a useful approach during the Covid-19 pandemic.

> *"Results support the superiority of nasal over oropharyngeal swab collection in pediatric populations.[8]"*

PEER REVIEWED

Palmas G., Moriondo M., Trapani S., Ricci S. , Calistri E., Pisano L., Perferi G., Galli L., Elisabetta Venturini E., Indolfi G., Azzari C. Nasal swab as preferred clinical specimen for Vovid-19 testing in children. The Pediatric Infectious Disease Journal • Volume 39, Number 9, September 2020

DESIGN

A prospective study of children (age 0–18) tested for detection of SARS-CoV-2 on both nasal and oropharyngeal specimens on admission to the Meyer Children's University Hospital in Florence, Italy between March 12 and March 31, 2020.

METHOD

After initial screening, 11 patients who tested positive, had a simultaneous collection of nasal and oropharyngeal specimen performed on admission and every 1–3 days during hospitalization. A total of 52 paired clinical specimens (26 nasal swabs and 26 oropharyngeal swabs) were collected. Paired results were considered in the statistical analysis, to compare the positivity rate of the 2 sampling techniques and to describe changes in the viral load.

LIMITATIONS

- Small sample size due to the low number of pediatric patients with known infection.
- Single swab-based screening of patients, due to shortages of specific materials in the first phase of the outbreak.

RESULTS

- Overall, 24 of 26 nasal specimens resulted positive, whereas 20 of 26 oropharyngeal specimens resulted positive.
- CT values of the first simultaneous collected materials were always lower in nasal specimens than in the paired oropharyngeal ones.
- The mean difference in CT values (delta CT) was 7, which corresponds approximately to a 100-fold difference in the viral load.

DISCUSSION

- Results support the superiority of nasal over oropharyngeal swab collection, determined by a significantly higher positivity rate and a significantly higher mean viral load on nasal samples.
- The difference in CT suggests a 100-fold higher viral load in nasal specimens when compared with the oropharyngeal ones. This finding was consistent on all the repeated testing during hospitalization.
- The results are consistent with those on adult SARS-CoV-2 infection.
- Nasal specimens tested positive for a longer time span. The virus was still detectable on nasal samples collected during the recovery phase of 2 patients, when the simultaneous oropharyngeal swab tested negative for the presence of the virus.

REFERENCES

[1]*Office of the Assistant Secretary for Health, US Public Health Service. Nasal (Anterior nasal) specimen collection for SARS-CoV-2 diagnostic testing. Fact sheet. 11 Nov 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/downloads/lab/OASH-nasal-specimen-collection-factsheet_updates_2020_11_11_508.pdf (last accessed February 2021).* [2]*Office of the Assistant Secretary for Health, US Public Health Service. Nasal (Anterior nasal) specimen collection for SARS-CoV-2 diagnostic testing. Fact sheet. 11 Nov 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/downloads/lab/OASH-nasal-specimen-collection-factsheet_updates_2020_11_11_508.pdf (last accessed February 2021).* [3]*Tsang, N. N. Y., So, H. C., Ng, K. Y., Cowling, B. J., Leung, G. M., & Ip, D. K. M. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. The Lancet Infectious Diseases. doi:10.1016/S1473-3099(21)00146-8* [4]*McCulloch, D. J., Kim, A. E., Wilcox, N. C., Logue, J. K., Greninger, A. L., Englund, J. A., & Chu, H. Y. (2020). Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. JAMA Network Open, 3(7), e2016382-e2016382. doi:10.1001/jamanetworkopen.2020.16382.* [5]*Altamirano, J., Govindarajan, P., Blomkalns, A. L., Kushner, L. E., Stevens, B. A., Pinsky, B. A., & Maldonado, Y. (2020). Assessment of Sensitivity and Specificity of Patient-Collected Lower Nasal Specimens for Severe Acute Respiratory Syndrome Coronavirus 2Testing. JAMA Network Open, 3(6), e2012005-e2012005. doi:10.1001/jamanetworkopen.2020.12005.* [6]*Wehrhahn, M. C., Robson, J., Brown, S., Bursle, E., Byrne, S., New, D., Hadlow, N. (2020). Self-collection: An appropriate alternative during the SARS-CoV-2 pandemic. Journal of Clinical Virology, 128, 104417. doi:https://doi.org/10.1016/j.jcv.2020.104417.* [7]*Tu, Y.-P., Jennings, R., Hart, B., Cangelosi, G. A., Wood, R. C., Wehber, K., Berke, E. M. (2020). Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. New England Journal of Medicine, 383(5), 494-496. doi:10.1056/NEJMc2016321.* [8]*Palmas G., Moriondo M., Trapani S., Ricci S. , Calistri E., Pisano L., Perferi G., Galli L., Elisabetta Venturini E., Indolfi G., Azzari C. Nasal swab as preferred clinical specimen for Vovid-19 testing in children. The Pediatric Infectious Disease Journal • Volume 39, Number 9, September 2020.*