

Original Paper

Effectiveness of Self-Collected, Ambient Temperature–Preserved Nasal Swabs Compared to Samples Collected by Trained Staff for Genotyping of Respiratory Viruses by Shotgun RNA Sequencing: Comparative Study

Raymond Soto^{1*}, PhD; Litty Paul^{1*}, PhD; Christina A Porucznik^{1*}, PhD; Heng Xie^{2*}, PhD; Rita Czako Stinnett^{2*}, PhD; Benjamin Briggs^{2*}, PhD; Matthew Biggerstaff^{3*}, ScD; Joseph Stanford^{1*}, MD; Robert Schlaberg^{1,2*}, MD

¹Department of Family and Preventive Medicine, University of Utah, Salt Lake City, UT, United States

²IDbyDNA, Salt Lake City, UT, United States

³Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia

* all authors contributed equally

Corresponding Author:

Joseph Stanford, MD

Department of Family and Preventive Medicine

University of Utah

375 Chipeta Way #A

Salt Lake City, UT, 84108

United States

Phone: 1 801 581 7498

Email: joseph.stanford@utah.edu

Abstract

Background: The SARS-CoV-2 pandemic has underscored the need for field specimen collection and transport to diagnostic and public health laboratories. Self-collected nasal swabs transported without dependency on a cold chain have the potential to remove critical barriers to testing, expand testing capacity, and reduce opportunities for exposure of health professionals in the context of a pandemic.

Objective: We compared nasal swab collection by study participants from themselves and their children at home to collection by trained research staff.

Methods: Each adult participant collected 1 nasal swab, sampling both nares with the single swab, after which they collected 1 nasal swab from 1 child. After all the participant samples were collected for the household, the research staff member collected a separate single duplicate sample from each individual. Immediately after the sample collection, the adult participants completed a questionnaire about the acceptability of the sampling procedures. Swabs were placed in temperature-stable preservative and respiratory viruses were detected by shotgun RNA sequencing, enabling viral genome analysis.

Results: In total, 21 households participated in the study, each with 1 adult and 1 child, yielding 42 individuals with paired samples. Study participants reported that self-collection was acceptable. Agreement between identified respiratory viruses in both swabs by RNA sequencing demonstrated that adequate collection technique was achieved by brief instructions.

Conclusions: Our results support the feasibility of a scalable and convenient means for the identification of respiratory viruses and implementation in pandemic preparedness for novel respiratory pathogens.

(*JMIR Form Res* 2023;7:e32848) doi: [10.2196/32848](https://doi.org/10.2196/32848)

KEYWORDS

genotyping; self-collected nasal swabs; RNA sequencing; respiratory virus surveillance; surveillance; respiratory virus; influenza virus; pandemic; preparedness; testing capacity; self-test; viral genome analysis; swabs; barriers; early detection; nasal swab; temperature; public health; specimen; collection; diagnosis; laboratory; respiratory; virus; COVID-19

Introduction

Challenges to global control of SARS-CoV-2 have underscored the need for accurate, safe, and rapidly scalable laboratory testing to inform rapid diagnosis and implementation of appropriate clinical and public health measures. Furthermore, early detection of emerging infectious disease threats is critical to limit spread. Over the last 4 decades, 1-3 newly emerging pathogens have been identified annually [1]. The risk of emerging infections is increasing, in part due to closer proximity of humans to wildlife and expanding geographic ranges of insect and arthropod vectors [2,3]. Outbreaks of diseases caused by respiratory tract infections, such as COVID-19, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), pandemic H1N1 influenza, and avian influenza, have specifically illustrated the global health burden posed by respiratory viruses with RNA genomes, prompting the implementation of public health policies and efforts to monitor and contain outbreaks [4,5]. Due to the genetic diversity of respiratory viral pathogens and the overlap between syndromes associated with distinct viruses, contemporary disease control efforts generally rely on a combination of methods, including rapid identification of emerging viral strains through targeted polymerase chain reaction (PCR)-based methods coupled with sequencing-based methods to enable molecular epidemiologic tracking of transmission. These activities can be streamlined by new methods of viral detection, such as metagenomic next-generation sequencing (NGS), to simultaneously detect and sequence respiratory viruses from human specimens [6].

Lower per-sample sequencing costs, accessible results through user-friendly analysis tools, and rapid turnaround of sequencing data have led to a growing number of diagnostic and public health laboratories applying NGS-based pathogen detection and profiling, which has enhanced and accelerated the detection and surveillance of emerging viruses [7-9]. Reliable detection of respiratory viruses requires robust methods for sample collection and preservation of viral RNA during transport because poor sample quality can lead to missed identification of significant pathogenic viruses [10]. Traditionally, laboratory diagnosis of respiratory viral infections has relied on collection of nasopharyngeal swabs by health care providers and uninterrupted cold chain transport to testing laboratories. In a previous study, evaluation of nasopharyngeal swabs from individuals with a known respiratory infection by metagenomic RNA sequencing showed high diagnostic agreement with a commercially available reverse transcription-PCR (RT-PCR) viral respiratory panel in a clinical laboratory setting, generated partial or full-length sequences in 86% of known positive samples, and detected additional viruses compared to the commercial panel [11].

However, community- and household-based sampling strategies offer potential advantages over sampling by health care workers in preparation for and during an outbreak. Specifically, anterior nasal swabs represent a noninvasive means for the detection and profiling of respiratory viruses via molecular diagnostic methods, provided appropriate measures to maintain sample integrity are taken [12-14]. Furthermore, nasal swabs can be collected at home by patients or their family members, limiting

opportunities for further transmission from exposed individuals within health care facilities. Recent work has demonstrated high percent positive agreement in the detection of SARS-CoV-2 by targeted RT-PCR from self-collected nasal swabs compared to health care provider-collected nasopharyngeal swabs [15-17]. The feasibility of self-collected nasal swabs for detection of pathogen carriage and infection has also been previously demonstrated in an outpatient clinic setting for PCR-based detection of influenza from symptomatic patients [12,14]. Studies to date have focused on PCR-based detection of specific pathogens, and relatively few studies have directly compared the yield from participants to trained researchers or clinical workers.

In this feasibility study, we assessed detection of respiratory viruses by shotgun RNA sequencing using a room temperature-stable at-home nasal swab sampling kit, comparing swabs collected by participants to swabs collected by trained research staff. We also determined the acceptability to participants of collecting nasal swabs from their children and potential barriers to collection at home.

Methods

Study Participants

The inclusion criteria were families with children younger than 7 years who lived in Salt Lake County (to facilitate the required home visits) and in which the parent was able to read English. Invitation letters were sent to 34 families that were currently part of an ongoing cohort study (the Utah Children's Project). In addition, a request for volunteers was posted on the Utah Children's Project Facebook page. In total, 32 families responded, of which 4 declined to participate, 4 were not eligible, and 3 were eligible but not able to schedule a visit in the time window of the study. Thus, 21 families were enrolled over a period of 7 weeks from February to April 2018. This number of families was based on logistical considerations, without any power calculations. Study surveys were collected by paper questionnaire during the scheduled home visit to collect participants' age, gender, ethnicity, race, household composition, and feedback on the sample collection process. The questionnaire was not pilot-tested or otherwise validated.

Ethical Considerations

All aspects of this study were approved and carried out in accordance with the University of Utah Institutional Review Board (IRB_00086963).

Nasal Swab Collection

After the enrollment questionnaire was completed, participants were given a packet containing the necessary instructions and materials to collect the nasal swab samples from 1 adult and 1 child in each home. Swab collection kits containing DNA/RNA Shield HydraFlock swabs and 1-mL collection vials with self-centering caps (Puritan) were used for collection of nasal swab samples. The research staff member also provided a link to an existing video demonstrating collection procedures and access to an iPad (Apple) to view the video immediately prior to sample collection. Participants were given the opportunity and time to independently review the instructions, collect the

nasal swab samples, and package them for mailing. Adult parents collected their own sample and separately collected the sample for their child. During this time, research staff were present but did not aid or guide in self-collection. Each participant collected 1 nasal swab and sampled both nares with the single swab. Once all the participant samples were collected for the household, the research staff member collected a separate single duplicate sample from each individual, again sampling both nares. Samples collected by research staff were transported at ambient temperature and transferred to a -80°C freezer on the same day. Samples were labeled with IDs corresponding to the following information: family ID (F01-F21), participant type (A: adult; C: child), and collection type (S: self-collected; R: research staff-collected).

Questionnaires

At the beginning of the home study visit, adult participants completed a pen and paper enrollment questionnaire about demographics and household characteristics. Questions were taken from the National Children's Study enrollment questionnaire [18]. At the end of the home study visit, adult participants completed a brief pen and paper experience questionnaire about the collection of the sample, which included questions previously used in the National Children's Study. Questions regarding nasal swab self-collection were generated specifically for this study and were not otherwise validated prior to this study.

RNA Extraction, Next-Generation Sequencing, and Data Analysis

RNA was extracted using the ZymoBIOMICS DNA/RNA Miniprep kit (Zymo Research). cDNA libraries were prepared using the Trio RNA-Seq kit (NuGEN Technologies), quantified

by quantitative-PCR using the KAPA library quantification kit (Roche), and sequenced on a NextSeq500 instrument (Illumina) to a depth of approximately 15 million 150-base-pair reads per sample. Sequencing data were demultiplexed allowing for no mismatches in the barcode sequences. Adapter sequences were trimmed, and the data were quality-filtered. Respiratory viruses were detected and viral genome sequences were assembled using the Explify Platform (v2, IDbyDNA). For phylogenetic analyses, complete human metapneumovirus (HMPV) genome sequences were obtained from GenBank. Multiple sequence alignments were performed with Geneious, and neighbor-joining trees were constructed with the Tamura-Nei method and bootstrapped using 500 replicates (Geneious v11.1.5).

Statistical Analysis

Proportions and 95% CIs were calculated. Agreement between self-collected and staff-collected samples was assessed by Cohen κ statistic, which was estimated using Prism version 8.3.0 (GraphPad).

Results

Description of Study Participants

The demographics of the study participants are presented in Table 1. Of the adult participants, 85.7% (18/21) were female, while 52.4% (11/21) of children were female. The mean age was 32 (SD 3) years for adults and 3 (SD 2) years for children. The majority of participants self-identified as White (38/42, 90.5%) and of non-Hispanic/Latino ethnicity (41/42, 97.6%). Most adult participants (17/21, 80.9%) indicated they had a bachelor's degree or higher. Of the 21 families, 10 (47.6%) reported a recent upper respiratory illness, but the exact time frame was not defined.

Table 1. Demographics of enrolled participants.

	Adults (n=21)	Children (n=21)
Sex, n		
Female	18	11
Male	3	10
Age (years), mean (SD)	32 (3)	3 (2)
Ethnicity, n		
Non-Hispanic/Latino	21	20
Hispanic/Latino	0	1
Race, n		
Asian	1	1
White	19	19
White and Asian	1	1
Education, n		
Some college	4	N/A ^a
Bachelor's degree	7	N/A
Graduate degree	10	N/A

^aN/A: not applicable.

Feedback on the Self-Collection Experience

Most adult participants (18/21, 85.5%) collected nasal swab samples with no (11/21, 52.4%) or little (7/21, 33.3%) self-reported difficulty (Table 2). All enrolled adult participants indicated that they would feel comfortable collecting nasal swab

samples based on the provided instructions, and 95.2% (20/21) reported that they felt they could mail the collected samples back without problems (Table 2). However, in this study, samples were transported by research staff. Most adult participants (18/21, 86%) preferred both video and written instructions.

Table 2. Adults' responses to the collection experience survey.

Question	Responses (n=21), n
Did you experience any difficulties in collecting the sample today?	
Not at all	11
A little	7
Some	3
A lot	0
Could you have collected this sample if there were no study staff present, using only the instruction materials provided?	
Yes	21
No	0
Could participant have followed instructions to mail samples back without problems:	
Yes	20
Unsure	1
If it were available, would participant have preferred:	
Video and written instructions	16
Written instructions only	3
Video instructions only	2
In your opinion, in a real pandemic influenza study that involved nasal swabs, which household members would be willing to participate?	
Myself	19
Other adults	20
Children	17

RNA-seq Data Quality and RNA Composition

A median of 9.05 (IQR 8.21-10.2) million sequencing reads were generated per sample. Respiratory viruses were detected in members of 52% (11/21) of families, including 6/10 (60%) families that had reported recent illness (Figure 1). Children tested positive in 10 families and adults tested positive in 6 families. In total, 9 different respiratory viruses were detected: human metapneumovirus type B (HMPV-B; detected in F02, F07, F09, and F21); respiratory syncytial virus type A (RSV-A; detected in F15); respiratory syncytial virus type B (RSV-B; detected in F13); human rhinovirus (HRV) types A40 (detected in F06), A80 (detected in F04), C42 (detected in F03 and F21), C45 (detected in F02 and F18), and C54 (detected in F06); and a diverse HRV-C most similar to HRV-C36 (detected in F19). In 2 children, 2 different respiratory viruses were detected (HRV-A40 and HRV-C54 in F06-C and HMPV-B and HRV-C56 in F21-C). Similarly, in 1 adult, 2 different respiratory viruses were detected (HMPV-B and HRV-C45 in F02-A). With 3 exceptions, the same viral status (including the status of absence of any virus) was identified in the staff- and self-collected swabs from the same participant (39/42, 93%

agreement; $\kappa=0.84$, 95% CI 0.66-1.00). In 2 participants (F13-C and F21-A), RSV-B and HRV-C42 were detected only in the staff-collected swabs (Figure 1). In both cases, low concentrations of virus were detected and attempts to detect the same virus in the matching self-collected swabs by RT-PCR failed, consistent with the absence of viral detection in those self-collected samples. In a third participant (F02-A), 2 viruses (HMPV-B and HRV-C45) were detected only in the self-collected swab.

Partial or full-length viral genome sequences with >80% coverage could be determined in 63% (22/35) of total detections. Among the samples for which depth of coverage could be calculated, the median depth of coverage was 89-fold (IQR 21-222; Figure 2). Concordance in viral subtype was evaluated in those cases where NGS detected the same viral pathogen with sufficient coverage of viral genomes from paired staff- and self-collected swabs. Results were consistent with the identification of the same strain in all cases with sufficient genome coverage. In sample pairs from 2 adult study participants (F09-A and F21-A), there was insufficient coverage to make a full comparison, despite agreement in virus detection between staff- and self-collected samples.

Figure 1. Detection of respiratory viruses by RNA sequencing. The color code indicates the number of normalized viral reads. Rows represent different samples and columns represent the viruses detected. Sample IDs convey the following information: family ID (F01-F21), participant type (A: adult; C: child), and collection type (S: self-collected; R: research staff–collected). HMPV: human metapneumovirus; HRV: human rhinovirus; RSV: respiratory syncytial virus.

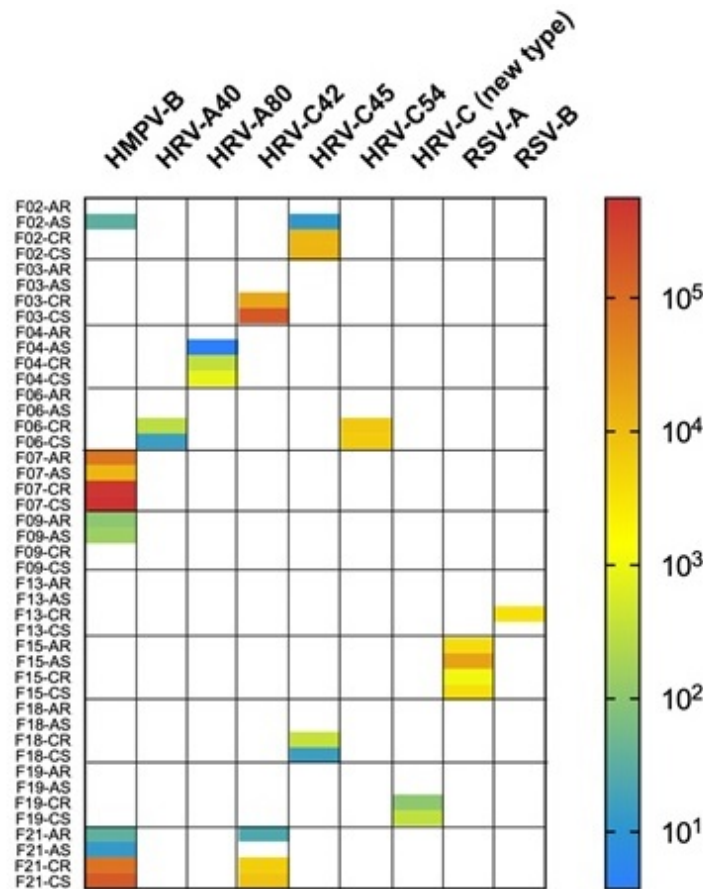
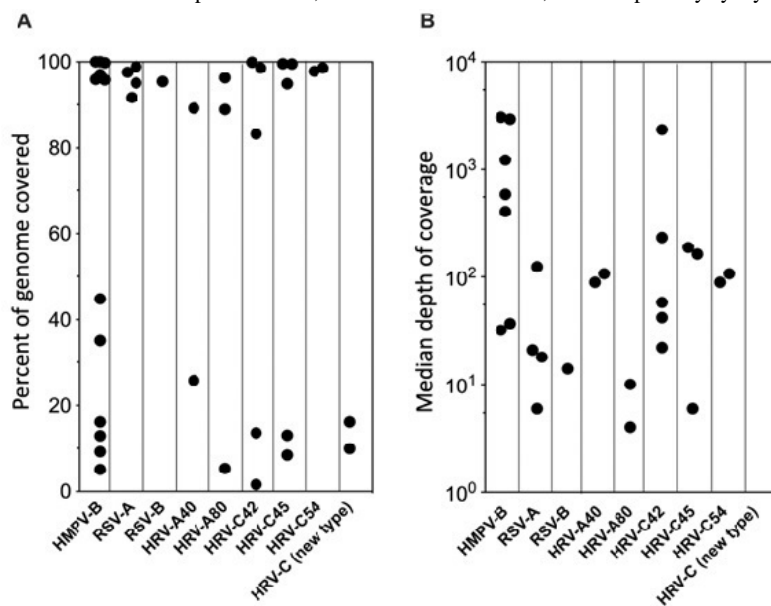


Figure 2. Summary of RNA sequencing depth of coverage. (A) Percentage of full-length assembly achieved for viral genomes. (B) Depth of coverage for each detected viral sample. HMPV: human metapneumovirus; HRV: human rhinovirus; RSV: respiratory syncytial virus.



In one family (F14), the putative detection of an additional virus (human parainfluenza virus 4b) was suggested by sequencing reads that mapped to an identical reference genome in the self-collected adult swab (F14-AS) and in the staff-collected child swab (F14-CR); however, in both cases, genome coverage

did not meet previously established criteria for positive diagnostic identification.

Discussion

In this pilot, proof-of-concept study, we found that respiratory samples (anterior nasal swabs) self-collected from adults and children who were trained via online video and written instructions had comparable detection of respiratory viruses to samples concurrently collected by trained research personnel, with transport at ambient temperatures, as assessed by unbiased detection of respiratory viruses by NGS. All participants found the home collection procedures acceptable, and 85% reported minimal or no difficulty collecting the samples.

Our findings are consistent with prior studies that have found home collection of anterior nasal swabs to be acceptable in general populations, with high levels of good-quality samples [13,19-24]. Our results are also consistent with a growing body of studies indicating high agreement between self-collected swabs in adults and children (by parents) and swabs collected by health care workers or research personnel; $\kappa \geq 0.85$ has been reported for the detection of several respiratory viruses, including influenza viruses, SARS-CoV-2, and metapneumovirus [12,13,17,25-30]. To our knowledge, this study is the first to evaluate agreement in self-collected versus researcher-collected nasal swabs specifically for shotgun RNA sequencing.

We considered any risk of nasal injury by self-collection to be minimal and outweighed by the potential benefit of understanding the feasibility and acceptability of self-collection of nasal samples for future research and public health surveillance. In one large, community-based study of over 4000 individuals given home collection kits with nasal swabs to be used on themselves or family members, there was one mild adverse event that did not require any medical attention and had no long-term impacts [31].

This method could be applied to test exposed or symptomatic individuals without the need for visits to a health care facility during outbreaks of emerging respiratory viruses [24,30,32]. In addition, it could streamline surveillance for known or emerging infectious disease threats by application to sentinels. Prior studies have supported the contributions of self-collected swab submission for molecular testing as a supplement to passive and syndromic surveillance for acute respiratory infections [11,14,19,20,32,33]. Guidance from the United States Food and Drug Administration (FDA) to permit the submission of self-collected swabs for SARS-CoV-2 testing illustrates the

advantages of this strategy to reduce opportunities for transmission from infected individuals to health care workers and vulnerable populations and to mitigate bottlenecks associated with sample collection by providers [34]. The nasal swab collection kits used in this study have a shelf life of 3 years and stabilize samples at ambient temperature for up to 30 days. This allows for economical stocking and transport of collection kits during an outbreak or in support of surveillance efforts.

This study had several limitations. The sample size was small in this pilot study. Recent respiratory illness was self-reported and no information was collected about the duration of symptoms or the time between onset of symptoms and sample collection. It is therefore possible that individuals may no longer have been shedding virus at the time of sampling. Diagnostic performance of metagenomic sequencing was not compared to a reference method (eg, FDA-cleared PCR panels for the detection of respiratory pathogens), although high agreement has been previously reported [11].

We detected a diverse range of respiratory viruses, determined viral genome sequences in the majority of cases, and showed that viral genomes were identical in staff- and self-collected swabs. Our identification of a divergent strain of HRV-C with only 74% nucleotide sequence identity with the most similar known strain demonstrates the power of unbiased pathogen detection by metagenomics in the context of the well-described diversity of rhinoviruses [35,36]. This suggests an advantage of sequencing-based surveillance for generating viral genomes for high-resolution molecular typing. Studies in hospitalized patients have shown that this genotypic information can assist in efforts to contain transmission [37-39].

In summary, our findings support a growing body of evidence that at-home nasal swab kits for viral detection can be reliably used, are well-tolerated, and provide a scalable solution for the detection and profiling of respiratory viruses. In addition to prior work showing the reliability of self-collected nasal swabs with PCR-based diagnostic tests, our findings suggest that self-collected nasal swabs can be reliable for shotgun RNA sequencing. As metagenomics is integrated into routine diagnostic workflows in a rapidly growing number of laboratories, pathogen genotypic information generated as part of diagnostic testing can be more easily shared and is likely to prove valuable in support of surveillance research and public health applications.

Acknowledgments

Funding for this study was provided by the Centers for Disease Control and Prevention (grant HHSD20002013M53890B/200-2013-F-57544); the Environmental Influences on Child Health Outcomes program by the National Institutes of Health (grant 1UG3OD023249-01); and the Department of Pediatrics, University of Utah.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. At the time that the study was conducted, R Schlager, BB, RCS, and HX were employees of IDbyDNA Inc.

Conflicts of Interest

R Schlaberg was co-founder, director, and employee of IDbyDNA; a co-inventor of Taxonomer, which has been licensed by IDbyDNA; and held equity in IDbyDNA prior to its acquisition by Illumina in July 2022. BB is the Chief Medical Officer at CosmosID. RCS receives salary from Illumina Medical Affairs.

References

1. Woolhouse M, Gaunt E. Ecological origins of novel human pathogens. *Crit Rev Microbiol* 2007;33(4):231-242 [doi: [10.1080/10408410701647560](https://doi.org/10.1080/10408410701647560)] [Medline: [18033594](https://pubmed.ncbi.nlm.nih.gov/18033594/)]
2. The U.S. government and global emerging infectious disease preparedness and response. The Henry J Kaiser Family Foundation. 2014. URL: <https://files.kff.org/attachment/the-u-s-government-global-emerging-infectious-disease-preparedness-and-response-fact-sheet> [accessed 2023-09-27]
3. Plowright RK, Parrish CR, McCallum H, Hudson PJ, Ko AI, Graham AL, et al. Pathways to zoonotic spillover. *Nat Rev Microbiol* 2017 Aug;15(8):502-510 [FREE Full text] [doi: [10.1038/nrmicro.2017.45](https://doi.org/10.1038/nrmicro.2017.45)] [Medline: [28555073](https://pubmed.ncbi.nlm.nih.gov/28555073/)]
4. Saunders-Hastings PR, Krewski D. Reviewing the history of pandemic influenza: understanding patterns of emergence and transmission. *Pathogens* 2016 Dec 06;5(4):66 [FREE Full text] [doi: [10.3390/pathogens5040066](https://doi.org/10.3390/pathogens5040066)] [Medline: [27929449](https://pubmed.ncbi.nlm.nih.gov/27929449/)]
5. Tang JW, Lam TT, Zaraket H, Lipkin WI, Drews SJ, Hatchette TF, et al. INSPIRE investigators. Global epidemiology of non-influenza RNA respiratory viruses: data gaps and a growing need for surveillance. *Lancet Infect Dis* 2017 Oct;17(10):e320-e326 [FREE Full text] [doi: [10.1016/S1473-3099\(17\)30238-4](https://doi.org/10.1016/S1473-3099(17)30238-4)] [Medline: [28457597](https://pubmed.ncbi.nlm.nih.gov/28457597/)]
6. Schlaberg R, Chiu CY, Miller S, Procop GW, Weinstock G, Professional Practice Committee and Committee on Laboratory Practices of the American Society for Microbiology; et al. Microbiology Resource Committee of the College of American Pathologists. Validation of metagenomic next-generation sequencing tests for universal pathogen detection. *Arch Pathol Lab Med* 2017 Jun;141(6):776-786 [FREE Full text] [doi: [10.5858/arpa.2016-0539-RA](https://doi.org/10.5858/arpa.2016-0539-RA)] [Medline: [28169558](https://pubmed.ncbi.nlm.nih.gov/28169558/)]
7. Besser J, Carleton HA, Gerner-Smidt P, Lindsey RL, Trees E. Next-generation sequencing technologies and their application to the study and control of bacterial infections. *Clin Microbiol Infect* 2018 Apr;24(4):335-341 [FREE Full text] [doi: [10.1016/j.cmi.2017.10.013](https://doi.org/10.1016/j.cmi.2017.10.013)] [Medline: [29074157](https://pubmed.ncbi.nlm.nih.gov/29074157/)]
8. Motro Y, Moran-Gilad J. Next-generation sequencing applications in clinical bacteriology. *Biomol Detect Quantif* 2017 Dec;14:1-6 [FREE Full text] [doi: [10.1016/j.bdq.2017.10.002](https://doi.org/10.1016/j.bdq.2017.10.002)] [Medline: [29255684](https://pubmed.ncbi.nlm.nih.gov/29255684/)]
9. Deurenberg RH, Bathoorn E, Chlebowicz MA, Couto N, Ferdous M, García-Cobos S, et al. Application of next generation sequencing in clinical microbiology and infection prevention. *J Biotechnol* 2017 Feb 10;243:16-24 [FREE Full text] [doi: [10.1016/j.jbiotec.2016.12.022](https://doi.org/10.1016/j.jbiotec.2016.12.022)] [Medline: [28042011](https://pubmed.ncbi.nlm.nih.gov/28042011/)]
10. Goldberg B, Sichtig H, Geyer C, Ledeboer N, Weinstock GM. Making the leap from research laboratory to clinic: challenges and opportunities for next-generation sequencing in infectious disease diagnostics. *mBio* 2015 Dec 08;6(6):e01888-e01815 [FREE Full text] [doi: [10.1128/mBio.01888-15](https://doi.org/10.1128/mBio.01888-15)] [Medline: [26646014](https://pubmed.ncbi.nlm.nih.gov/26646014/)]
11. Graf EH, Simmon KE, Tardif KD, Hymas W, Flygare S, Eilbeck K, et al. Unbiased detection of respiratory viruses by use of RNA sequencing-based metagenomics: a systematic comparison to a commercial PCR panel. *J Clin Microbiol* 2016 Apr;54(4):1000-1007 [FREE Full text] [doi: [10.1128/JCM.03060-15](https://doi.org/10.1128/JCM.03060-15)] [Medline: [26818672](https://pubmed.ncbi.nlm.nih.gov/26818672/)]
12. Akmatov MK, Gatzemeier A, Schughart K, Pessler F. Equivalence of self- and staff-collected nasal swabs for the detection of viral respiratory pathogens. *PLoS One* 2012;7(11):e48508 [FREE Full text] [doi: [10.1371/journal.pone.0048508](https://doi.org/10.1371/journal.pone.0048508)] [Medline: [23155387](https://pubmed.ncbi.nlm.nih.gov/23155387/)]
13. Dhiman N, Miller RM, Finley JL, Sztajnkrzyer MD, Nestler DM, Boggust AJ, et al. Effectiveness of patient-collected swabs for influenza testing. *Mayo Clin Proc* 2012 Jun;87(6):548-554 [FREE Full text] [doi: [10.1016/j.mayocp.2012.02.011](https://doi.org/10.1016/j.mayocp.2012.02.011)] [Medline: [22551906](https://pubmed.ncbi.nlm.nih.gov/22551906/)]
14. Elliot AJ, Powers C, Thornton A, Obi C, Hill C, Simms I, et al. Monitoring the emergence of community transmission of influenza A/H1N1 2009 in England: a cross sectional opportunistic survey of self sampled telephone callers to NHS Direct. *BMJ* 2009 Aug 27;339:b3403 [FREE Full text] [doi: [10.1136/bmj.b3403](https://doi.org/10.1136/bmj.b3403)] [Medline: [19713236](https://pubmed.ncbi.nlm.nih.gov/19713236/)]
15. Hanson K, Barker A, Hillyard D, Gilmore N, Barrett J, Orlandi R, et al. Self-collected anterior nasal and saliva specimens versus health care worker-collected nasopharyngeal swabs for the molecular detection of SARS-CoV-2. *J Clin Microbiol* 2020 Oct 21;58(11):e01824-e01820 [FREE Full text] [doi: [10.1128/JCM.01824-20](https://doi.org/10.1128/JCM.01824-20)] [Medline: [32817233](https://pubmed.ncbi.nlm.nih.gov/32817233/)]
16. Tu Y, 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):494-496 [FREE Full text] [doi: [10.1056/NEJMc2016321](https://doi.org/10.1056/NEJMc2016321)] [Medline: [32492294](https://pubmed.ncbi.nlm.nih.gov/32492294/)]
17. 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 01;3(7):e2016382 [FREE Full text] [doi: [10.1001/jamanetworkopen.2020.16382](https://doi.org/10.1001/jamanetworkopen.2020.16382)] [Medline: [32697321](https://pubmed.ncbi.nlm.nih.gov/32697321/)]
18. Landrigan PJ, Trasande L, Thorpe LE, Gwynn C, Liroy PJ, D'Alton ME, et al. The national children's study: a 21-year prospective study of 100,000 American children. *Pediatrics* 2006 Nov;118(5):2173-2186 [doi: [10.1542/peds.2006-0360](https://doi.org/10.1542/peds.2006-0360)] [Medline: [17079592](https://pubmed.ncbi.nlm.nih.gov/17079592/)]

19. Haussig JM, Targosz A, Engelhart S, Herzhoff M, Prahm K, Buda S, et al. Feasibility study for the use of self-collected nasal swabs to identify pathogens among participants of a population-based surveillance system for acute respiratory infections (GrippeWeb-Plus)-Germany, 2016. *Influenza Other Respir Viruses* 2019 Jul;13(4):319-330 [FREE Full text] [doi: [10.1111/irv.12644](https://doi.org/10.1111/irv.12644)] [Medline: [30925029](https://pubmed.ncbi.nlm.nih.gov/30925029/)]
20. Jackson ML, Nguyen M, Kirlin B, Madziwa L. Self-collected nasal swabs for respiratory virus surveillance. *Open Forum Infect Dis* 2015 Dec;2(4):ofv152 [FREE Full text] [doi: [10.1093/ofid/ofv152](https://doi.org/10.1093/ofid/ofv152)] [Medline: [26613095](https://pubmed.ncbi.nlm.nih.gov/26613095/)]
21. Ricci S, Lodi L, Citera F, Nieddu F, Moriondo M, Guarnieri V, et al. How home anterior self-collected nasal swab simplifies SARS-CoV-2 testing: new surveillance horizons in public health and beyond. *Viol J* 2021 Mar 20;18(1):59 [FREE Full text] [doi: [10.1186/s12985-021-01533-z](https://doi.org/10.1186/s12985-021-01533-z)] [Medline: [33743711](https://pubmed.ncbi.nlm.nih.gov/33743711/)]
22. Zoch-Lesniak B, Ware RS, Grimwood K, Lambert SB. *J Pediatric Infect Dis Soc* 2020 Apr 30;9(2):134-141 [FREE Full text] [doi: [10.1093/jpids/piy136](https://doi.org/10.1093/jpids/piy136)] [Medline: [30657971](https://pubmed.ncbi.nlm.nih.gov/30657971/)]
23. Muñoz-Ramírez S, Escribano-López B, Rodrigo-Casares V, Vergara-Hernández C, Gil-Mary D, Sorribes-Monrabal I, et al. Feasibility of a hybrid clinical trial for respiratory virus detection in toddlers during the influenza season. *BMC Med Res Methodol* 2021 Dec 05;21(1):273 [FREE Full text] [doi: [10.1186/s12874-021-01474-9](https://doi.org/10.1186/s12874-021-01474-9)] [Medline: [34865624](https://pubmed.ncbi.nlm.nih.gov/34865624/)]
24. Heimonen J, McCulloch DJ, O'Hanlon J, Kim AE, Emanuels A, Wilcox N, et al. A remote household-based approach to influenza self-testing and antiviral treatment. *Influenza Other Respir Viruses* 2021 Jul;15(4):469-477 [FREE Full text] [doi: [10.1111/irv.12859](https://doi.org/10.1111/irv.12859)] [Medline: [33939275](https://pubmed.ncbi.nlm.nih.gov/33939275/)]
25. Murray MA, Schulz LA, Furst JW, Homme JH, Jenkins SM, Uhl JR, et al. Equal performance of self-collected and health care worker-collected pharyngeal swabs for group A streptococcus testing by PCR. *J Clin Microbiol* 2015 Feb;53(2):573-578 [FREE Full text] [doi: [10.1128/JCM.02500-14](https://doi.org/10.1128/JCM.02500-14)] [Medline: [25502528](https://pubmed.ncbi.nlm.nih.gov/25502528/)]
26. Emerson J, Cochrane E, McNamara S, Kuypers J, Gibson RL, Campbell AP. Home self-collection of nasal swabs for diagnosis of acute respiratory virus infections in children with cystic fibrosis. *J Pediatric Infect Dis Soc* 2013 Dec;2(4):345-351 [FREE Full text] [doi: [10.1093/jpids/pit039](https://doi.org/10.1093/jpids/pit039)] [Medline: [24363931](https://pubmed.ncbi.nlm.nih.gov/24363931/)]
27. Seaman CP, Tran LTT, Cowling BJ, Sullivan SG. Self-collected compared with professional-collected swabbing in the diagnosis of influenza in symptomatic individuals: A meta-analysis and assessment of validity. *J Clin Virol* 2019 Sep;118:28-35 [doi: [10.1016/j.jcv.2019.07.010](https://doi.org/10.1016/j.jcv.2019.07.010)] [Medline: [31400670](https://pubmed.ncbi.nlm.nih.gov/31400670/)]
28. Malosh RE, Petrie JG, Callear AP, Monto AS, Martin ET. Home collection of nasal swabs for detection of influenza in the Household Influenza Vaccine Evaluation Study. *Influenza Other Respir Viruses* 2021 Mar;15(2):227-234 [FREE Full text] [doi: [10.1111/irv.12822](https://doi.org/10.1111/irv.12822)] [Medline: [33107200](https://pubmed.ncbi.nlm.nih.gov/33107200/)]
29. Suntarattiwong P, Mott JA, Mohanty S, Sinthuwattanawibool C, Srisantiroj N, Patamasingh Na Ayudhaya O, et al. PRIME Study Group. Feasibility and performance of self-collected nasal swabs for detection of influenza virus, respiratory syncytial virus, and human metapneumovirus. *J Infect Dis* 2021 Sep 01;224(5):831-838 [doi: [10.1093/infdis/jiab023](https://doi.org/10.1093/infdis/jiab023)] [Medline: [34467984](https://pubmed.ncbi.nlm.nih.gov/34467984/)]
30. Woodall CA, Thornton HV, Anderson EC, Ingle SM, Muir P, Vipond B, et al. Prospective study of the performance of parent-collected nasal and saliva swab samples, compared with nurse-collected swab samples, for the molecular detection of respiratory microorganisms. *Microbiol Spectr* 2021 Dec 22;9(3):e0016421 [doi: [10.1128/spectrum.00164-21](https://doi.org/10.1128/spectrum.00164-21)]
31. Kim A, Brandstetter E, Wilcox N, Heimonen J, Graham C, Han P, et al. Evaluating specimen quality and results from a community-wide, home-based respiratory surveillance study. *J Clin Microbiol* 2021 Apr 20;59(5):e02934-e02920 [FREE Full text] [doi: [10.1128/JCM.02934-20](https://doi.org/10.1128/JCM.02934-20)] [Medline: [33563599](https://pubmed.ncbi.nlm.nih.gov/33563599/)]
32. Uyeki TM, Bernstein HH, Bradley JS, Englund JA, File TM, Fry AM, et al. Clinical practice guidelines by the infectious diseases society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clin Infect Dis* 2019 Mar 05;68(6):e1-e47 [FREE Full text] [doi: [10.1093/cid/ciy866](https://doi.org/10.1093/cid/ciy866)] [Medline: [30566567](https://pubmed.ncbi.nlm.nih.gov/30566567/)]
33. Brendish NJ, Malachira AK, Armstrong L, Houghton R, Aitken S, Nyimbili E, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *Lancet Respir Med* 2017 May;5(5):401-411 [FREE Full text] [doi: [10.1016/S2213-2600\(17\)30120-0](https://doi.org/10.1016/S2213-2600(17)30120-0)] [Medline: [28392237](https://pubmed.ncbi.nlm.nih.gov/28392237/)]
34. Coronavirus (COVID-19) Update: FDA, Gates Foundation, UnitedHealth Group, Quantigen, and U.S. Cotton Collaborate to Address Testing Supply Needs. U.S. Food & Drug Administration. 2020. URL: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-gates-foundation-unitedhealth-group-quantigen-and-us-cotton> [accessed 2023-09-27]
35. Lamson D, Renwick N, Kapoor V, Liu Z, Palacios G, Ju J, et al. MassTag polymerase-chain-reaction detection of respiratory pathogens, including a new rhinovirus genotype, that caused influenza-like illness in New York State during 2004-2005. *J Infect Dis* 2006 Nov 15;194(10):1398-1402 [FREE Full text] [doi: [10.1086/508551](https://doi.org/10.1086/508551)] [Medline: [17054069](https://pubmed.ncbi.nlm.nih.gov/17054069/)]
36. Lau SKP, Yip CCY, Tsoi H, Lee RA, So L, Lau Y, et al. Clinical features and complete genome characterization of a distinct human rhinovirus (HRV) genetic cluster, probably representing a previously undetected HRV species, HRV-C, associated with acute respiratory illness in children. *J Clin Microbiol* 2007 Nov;45(11):3655-3664 [FREE Full text] [doi: [10.1128/JCM.01254-07](https://doi.org/10.1128/JCM.01254-07)] [Medline: [17804649](https://pubmed.ncbi.nlm.nih.gov/17804649/)]

37. Payne DC, Biggs HM, Al-Abdallat MM, Alqasrawi S, Lu X, Abedi GR, et al. Multihospital outbreak of a Middle East respiratory syndrome coronavirus deletion variant, Jordan: a molecular, serologic, and epidemiologic investigation. *Open Forum Infect Dis* 2018 May;5(5):ofy095 [FREE Full text] [doi: [10.1093/ofid/ofy095](https://doi.org/10.1093/ofid/ofy095)] [Medline: [30294616](https://pubmed.ncbi.nlm.nih.gov/30294616/)]
38. Houlihan CF, Frampton D, Ferns RB, Raffle J, Grant P, Reidy M, et al. Use of whole-genome sequencing in the investigation of a nosocomial influenza virus outbreak. *J Infect Dis* 2018 Sep 22;218(9):1485-1489 [FREE Full text] [doi: [10.1093/infdis/jiy335](https://doi.org/10.1093/infdis/jiy335)] [Medline: [29873767](https://pubmed.ncbi.nlm.nih.gov/29873767/)]
39. Li C, Li W, Zhou J, Zhang B, Feng Y, Xu C, et al. High resolution metagenomic characterization of complex infectomes in paediatric acute respiratory infection. *Sci Rep* 2020 Mar 03;10(1):3963 [FREE Full text] [doi: [10.1038/s41598-020-60992-6](https://doi.org/10.1038/s41598-020-60992-6)] [Medline: [32127629](https://pubmed.ncbi.nlm.nih.gov/32127629/)]

Abbreviations

FDA: Food and Drug Administration
HMPV: human metapneumovirus
HRV: human rhinovirus
MERS: Middle East respiratory syndrome
NGS: next-generation sequencing
PCR: polymerase chain reaction
RSV: respiratory syncytial virus
RT-PCR: reverse transcription–polymerase chain reaction
SARS: severe acute respiratory syndrome

Edited by A Mavragani; submitted 19.03.22; peer-reviewed by A Banerjee, MM Patwary; comments to author 08.07.22; revised version received 16.02.23; accepted 09.08.23; published 24.11.23

Please cite as:

Soto R, Paul L, Porucznik CA, Xie H, Stinnett RC, Briggs B, Biggerstaff M, Stanford J, Schlaberg R
Effectiveness of Self-Collected, Ambient Temperature–Preserved Nasal Swabs Compared to Samples Collected by Trained Staff for Genotyping of Respiratory Viruses by Shotgun RNA Sequencing: Comparative Study
JMIR Form Res 2023;7:e32848
URL: <https://formative.jmir.org/2023/1/e32848>
doi: [10.2196/32848](https://doi.org/10.2196/32848)
PMID: [37999952](https://pubmed.ncbi.nlm.nih.gov/37999952/)

©Raymond Soto, Litty Paul, Christina A Porucznik, Heng Xie, Rita Czako Stinnett, Benjamin Briggs, Matthew Biggerstaff, Joseph Stanford, Robert Schlaberg. Originally published in *JMIR Formative Research* (<https://formative.jmir.org>), 24.11.2023. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Formative Research*, is properly cited. The complete bibliographic information, a link to the original publication on <https://formative.jmir.org>, as well as this copyright and license information must be included.