Accuracy and Discomfort of Different Types of Intranasal Specimen Collection Methods for Molecular Influenza Testing in Emergency Department Patients

Bradley W. Frazee, MD*; Amparo Rodríguez-Hoces de la Guardia, PhD; Harrison Alter, MD, MS; Carol G. Chen, PhD; Eugenia L. Fuentes, MSc; Alison K. Holzer, PhD; Macarena Lolas, MD, PhD; Debkishore Mitra, PhD; Jaspreet Vohra, MD; Cornelia L. Dekker, MD

*Corresponding Author. E-mail: bradf_98@yahoo.com.

Study objective: While development is under way of accurate, point-of-care molecular tests for influenza infection, the optimal specimen type for molecular tests remains unclear. Compared with standard nasopharyngeal swab specimens, less invasive nasal swab and midturbinate swab specimens may cause less patient discomfort and be more suitable for routine emergency department (ED) testing, although possibly at the expense of diagnostic accuracy. We compare both the accuracy of a polymerase chain reaction molecular influenza test and discomfort between these 3 intranasal specimen types.

Methods: A convenience sample of adult and pediatric patients with influenza-like illness and presenting to 2 Northern California EDs and 2 EDs in Santiago, Chile, was prospectively enrolled during the 2015 to 2016 influenza season. Research nurses collected nasopharyngeal swab, midturbinate swab, and nasal swab specimens from each subject and assessed discomfort on a validated 6-point scale. Specimens were tested for influenza A and B by real-time polymerase chain reaction at reference laboratories. Outcome measures were comparison of test performance between nasal swab and midturbinate swab, when compared with a reference standard nasopharyngeal swab; and comparison of discomfort between all 3 specimen types.

Results: Four hundred eighty-four subjects were enrolled, and all 3 swabs were obtained for each subject; 14% were children. The prevalence of influenza (A or B) was 30.0% (95% confidence interval [CI] 26.0% to 34.8%). The sensitivity for detecting influenza was 98% (95% CI 94.25% to 99.65%) with the midturbinate swab versus 84.4% (95% CI 77.5% to 89.8%) with the nasal swab, difference 13.6% (95% CI 8.2% to 19.3%). Specificity was 98.5% (95% CI 96.6% to 99.5%) with the midturbinate swab versus 99.1% (95% CI 97.4% to 99.8%) with the nasal swab, difference −0.6% (95% CI −1.8% to 0.6%). Swab discomfort levels correlated with the depth of the swab type. Median discomfort scores for the nasal swab, midturbinate swab, and nasopharyngeal swab were 0, 1, and 3, respectively; the median differences were nasopharyngeal swab–midturbinate swab 2 (95% CI 1 to 2), nasopharyngeal swab–nasal swab 3 (95% CI 2 to 3), and midturbinate swab–nasal swab 1 (95% CI 1 to 2).

Conclusion: Compared with the reference standard nasopharyngeal swab specimen, midturbinate swab specimens provided a significantly more comfortable sampling experience, with only a small sacrifice in sensitivity for influenza detection. Nasal swab specimens were significantly less sensitive than midturbinate swab. Our results suggest the midturbinate swab is the sampling method of choice for molecular influenza testing in ED patients. [Ann Emerg Med. 2017;■:1-9.]

Please see page XX for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Influenza virus infects 5% to 20% of the US population annually, resulting in more than 120,000 hospitalizations and 20,000 deaths.[1-4] In the United States, Canada, and Chile, emergency departments (EDs) serve as a major source of care for patients with acute influenza-like illness in the winter months, although only 5% to 70% of such patients actually have influenza, depending on the year and relation to peak community influenza activity.[5-8] Rapid, accurate diagnosis of influenza infection is important, in part because currently approved influenza antiviral drugs

Editor's Capsule Summary

What is already known on this topic

The recommended specimen type for influenza testing is a nasopharyngeal swab, but it can be uncomfortable.

What question this study addressed

Swabs taken from the anterior nares and midtubinate region were compared to a nasopharyngeal swab for accuracy of influenza polymerase chain reaction testing and for patient discomfort.

What this study adds to our knowledge

Among 484 patients with flu-like illness during flu season, sensitivity of the anterior nares swab and midturbinate swab were 84.4% and 98%, respectively, compared with the nasopharyngeal swab. Median discomfort scores on a 10-point scale for each specimen type were 0 for anterior nasal, 1 for midturbinate, and 3 for nasopharyngeal.

How this is relevant to clinical practice

A midturbinate nasal swab causes less discomfort than a nasopharyngeal swab, with similar sensitivity for influenza polymerase chain reaction, and should be the preferred method.

are effective only within 48 hours of infection.[9] Unfortunately, clinical diagnosis of influenza by ED providers is not accurate enough to guide treatment decisions, except during the peak of community influenza activity.[5,10] The Centers for Disease Control and Prevention (CDC) and Infectious Disease Society of America therefore recommend the routine use of rapid influenza diagnostic tests to assist with management decisions in high-risk patients with influenza-like illness.[11,12]

Reference standard diagnostic tests for influenza infection include viral culture and reverse transcriptase–polymerase chain reaction (RT-PCR).[13] Compared with these tests, current, widely available rapid influenza antigen detection tests have sensitivities of only 40% to 70%.[13] The CDC and others therefore recommend that a negative rapid antigen test result not be used for clinical decisionmaking and should be followed up with confirmatory RT-PCR or culture.[9,11] These poor diagnostic test characteristics and the need for follow-up testing severely limit the utility of rapid antigen detection tests in the ED. Point-of-care molecular influenza tests, which are both rapid and sensitive, have recently been approved by the Food and Drug Administration.[14,15] Combined with real-time estimates of disease prevalence, such rapidly available molecular test results could significantly improve bedside influenza diagnosis in the ED and other outpatient settings.[16]

Influenza testing can be performed on several types of upper respiratory specimens, including swabs, washes, and aspirates, sampled from the nasal, nasopharyngeal, or oropharyngeal regions. The CDC recommends nasopharyngeal sampling for detecting viral ribonucleic acid by RT-PCR because of better sensitivity compared with nasal or oropharynx samples.[11,17] However, nasal sampling is less invasive and assumed to cause less discomfort, and some studies have reported similar accuracy between nasal and nasopharyngeal specimens.[18-21] Many authors suggest that swabs are preferred to cumbersome liquid aspirates or washes, particularly in the outpatient setting.[22-25] Flocked intranasal swabs, which are designed to sample from the midturbinate region and maximize mucosal contact, have recently been developed and evaluated in pediatric and adult studies.[24,26,27]

Importance

To our knowledge, there have been no studies to determine what is the best specimen type for routine molecular influenza testing in the ED setting.[11] Considerations include not only demonstrated accuracy in a research setting but also patient comfort and ease with which the specimen can be obtained, which, in turn, will likely affect uptake and accuracy in the day-to-day setting.

Goals of This Investigation

We sought to determine which specimen collection method for molecular influenza testing in the ED optimally balances accuracy and discomfort. In a cohort of symptomatic adult and pediatric ED patients, we compared RT-PCR test performance between nasal swab and midturbinate swab, with nasopharyngeal swab serving as the reference standard, and compared discomfort between all 3 specimen types. Our a priori hypothesis was that midturbinate swab and nasal swab specimens would show similar test performance characteristics but be associated with significantly less discomfort than a nasopharyngeal swab.

MATERIALS AND METHODS

Study Design

We performed a multicenter, prospective cohort study comparing test accuracy and discomfort between different

specimen collection types for molecular influenza testing.[28] The study methods and reporting conform to the Standards for Reporting Diagnostic Accuracy Studies.[28] The data were collected in tandem with a separate pilot study assessing optimal swab sampling location for a new point-of-care molecular influenza assay.

Setting

The study was carried out in 4 EDs. Two are located in the San Francisco Bay Area (one an urban public hospital [90,000 annual ED visits] and one a suburban academic medical center [55,000 annual ED visits]), and 2 are located in Santiago, Chile (one a large military hospital [120,000 annual ED visits] and one a freestanding community ED [100,000 annual visits]). The study was approved by the human subjects research committees at all participating sites.

Enrollment occurred during the 2015 to 2016 North American and South American influenza seasons, between February 1 and May 10, 2016, in California and between July 28 and October 14, 2016, in Chile. Convenience sampling was used when research nurses were on duty. According to the CDC and World Health Organization, the overall predominant influenza strain in 2016 in both North and South America was H1N1, although influenza B predominated in North America in April and May and influenza H3 predominated in South America from mid-September to November.

Selection of Participants

Patients aged 2 years and older presenting to the ED with influenzalike illness were approached for enrollment. Patients were eligible for participation if they had a documented fever (temperature >100°F [37.8°C]) at triage or self-reported fever within the last 72 hours and at least one additional influenza-like symptom, including headache, extreme tiredness, dry cough, sore throat, runny or stuffy nose, or muscle aches. Patients were ineligible if they had received a nasal flu vaccine within the past 10 days or had received influenza antiviral therapy within the previous 30 days.

Dedicated ED research nurses obtained consent, assessed eligibility, collected symptom data and swab specimens, and recorded discomfort data. Patient characteristics, symptom inventory, and discomfort scores were recorded on paper case report forms and then transcribed into an electronic data capture system or directly input into the system with dedicated research tablets. Samples for the point-of-care assay (nasal and midturbinate) were first obtained from one side of the nose; then the 3 samples for this study were taken from the opposite side. A randomly assigned study number was used to determine from which side of the nose specimens for this study were collected. Swabs were collected from shallow to deep, starting with the nasal swab, then the midturbinate swab, and finally the nasopharyngeal swab. Nasal swabs were collected from the nasal vestibule; midturbinate swabs were collected 2 to 3 cm inside the nasal passage, as controlled by the swab design; and nasopharyngeal swabs were collected from the posterior nasopharynx. Figure 1 describes the sampling and swab types. Per the manufacturer recommendations, one size midturbinate swab is used for adults and children older than 2 years. (There is a separate infant-size midturbinate swab.) We switched to a foam-tipped nasal swab in Chile because interim analysis of test performance data from California showed low sensitivity with the flocked nylon nasal swab, and other studies had shown good test performance with a foam nasal swab.[29-31]

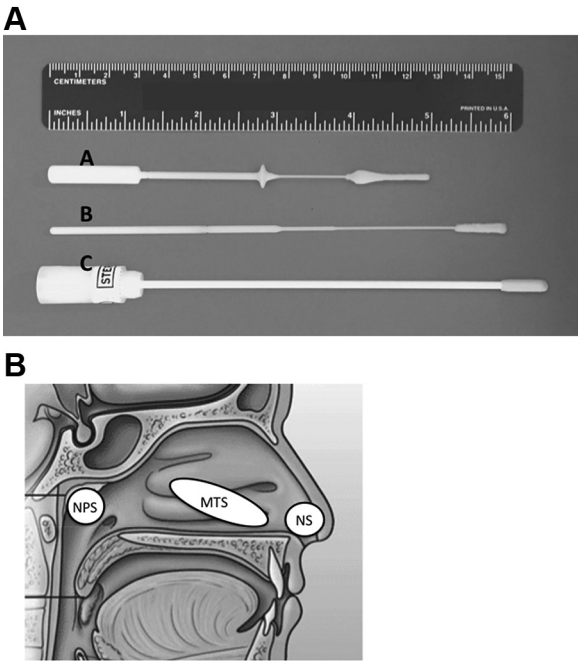

Figure 1. Specimen collection methods. *A*, Specimen collection swabs. Copan midturbinate adult flocked swab (A). Copan flexible nasopharyngeal flocked swab (B). Puritan sterile foam swab (C). Swab type B was used for both nasopharyngeal and nasal collection in California; swab type C was used for nasal collection in Chile. *B*, Sampling locations. *NPS*, Nasopharyngeal swab; *MTS*, midturbinate swab; *NS*, nasal swab.

Discomfort associated with each swab collection was measured with the 6-point Faces Pain Scale–Revised, which has been validated in children and adults.[32-34] Patients chose a discomfort level indicated by a drawing of a face and labeled with even numbers from 0 to 10, with zero being "no discomfort" and 10 being "worst imaginable

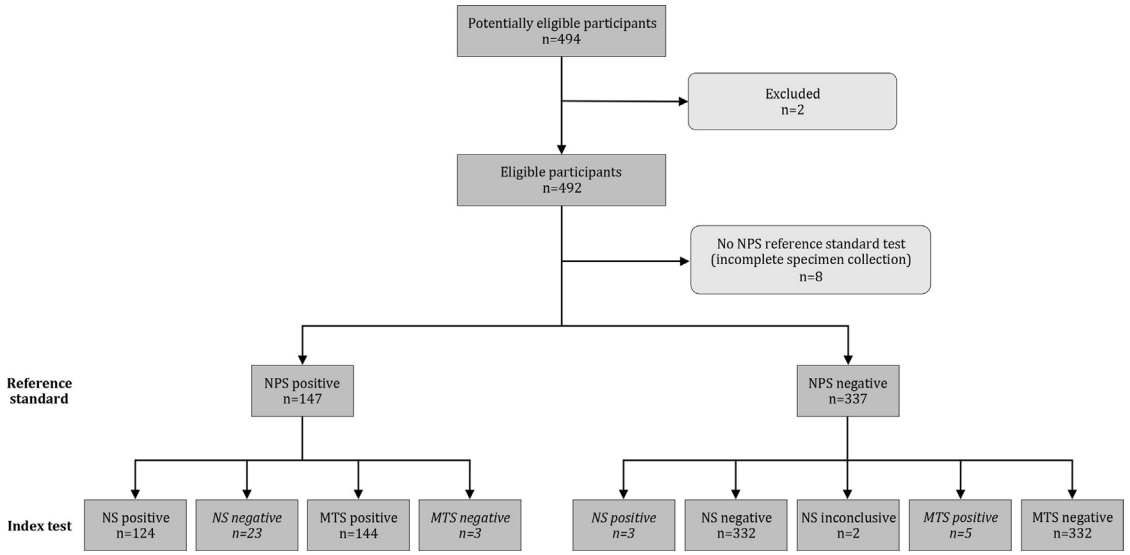

Figure 2. Study flow diagram.

discomfort." Parents assisted young children in assigning the discomfort level.

The nasopharyngeal swab, midturbinate swab, and nasal swab specimens were placed immediately in viral transport media and sent to a regional laboratory for RT-PCR testing. In California, specimens were sent to the Alameda Department of County Public Health Laboratory, which performed the CDC Human Influenza Virus Real-Time PCR Diagnostic Panel (Influenza A/B Typing Kit), and in Chile, specimens were sent to Bioscan Medical Molecular Biology Laboratory (a commercial laboratory), which performed the Argene Influenza A/B R-GENE (a RT-PCR kit). Thresholds for positivity are less than 38 and 40 cycles for the CDC and Argene assays, respectively.

Outcome Measures

The primary outcome measures were test performance of nasal swab versus midturbinate swab compared with the reference standard nasopharyngeal swab specimen for detection of influenza A or B, and comparison of swab discomfort between the 3 specimen types. In a post hoc analysis, we stratified the sample by age to explore whether the results differed significantly among adults and children. We also stratified the test performance results by hospital and by region to assess for clustering by study site.

Primary Data Analysis

To estimate sample size, we sought a large enough sample to detect a sensitivity of 95%, with a lower 95% confidence bound of 89%, derived from the Food and Drug Administration–recommended performance for Clinical Laboratory Improvement Amendments-waived in vitro diagnostic tests. A sample size of 153 positive results and 153 negative results achieves 80% power to detect a difference of –0.0600, using a one-sided binomial test. The target significance level was .03.

Analysis was restricted to subjects for whom a complete set of swab specimens was collected. For nasal swab and midturbinate swab test performance, we report sensitivities, specificities, and positive and negative likelihood ratios and receiver operator characteristics analysis compared with the nasopharyngeal swab reference standard. To compare test characteristics between midturbinate and nasal swabs to the reference standard, we used the method by Newcombe[35] to account for clustering by subject. This method requires paired data; in this case, that the 2 groups (midturbinate swab and nasal swab) consist of the same set of subjects. To comply, we removed data for 2 subjects for whom there was a midturbinate swab result but an indeterminate nasal swab result. To test for a statistical difference in median discomfort scores, we performed a clustered bootstrap analysis. Four hundred ninety-five individuals were randomly sampled (with replacement) and the differences in the medians of the discomfort scores of the respective tests were calculated. This was repeated 1,000 times to create a distribution from which we could gather the 2.5% and 97.5% percentiles for our confidence intervals (CIs).[35,36]

RESULTS

We enrolled 494 subjects; 2 were subsequently found to be ineligible and 8 withdrew before complete specimen collection, for a total of 484 evaluable participants

Table 1. Subject characteristics (N=484).

Subject and Clinical Characteristics	No. (%) or Median (IQR)
Median age, y	34 (23–49)
Adult (≥18 y)	417 (86.2)
Pediatric (<18 y)	67 (13.8)
Female subject	285 (58.9)
Enrolled in Chile	337 (69.6)
Enrolled in California	147 (30.4)
Symptom	
Fever (temperature ≥100°F [37.8°C])	
History of fever within past 3 days	480 (99.0)
Median duration of fever (N=480), h	24 (20–48)
Median measured temperature	99.7 (98.4–100.6)
Measured fever (temperature ≥100°F) at enrollment	228 (47.0)
Cough	388 (80.0)
Sore throat	359 (74.0)
Runny nose	352 (72.6)
Muscle aches	418 (86.2)
Headache	406 (83.7)
Fatigue	232 (47.8)
Influenza prevalence according to NPS result	
Influenza A	100 (20.6)
Influenza B	47 (9.7)
Influenza A or B*	147 (30.3)

IQR, Interquartile range.
*No cases of simultaneous influenza A and B.

(Figure 2). Subject characteristics are presented in Table 1. Sixty-seven subjects (14%) were children and 337 (70%) were enrolled in Chile. Subjects reported being febrile for a median of 24 hours before enrollment and 47% had a documented fever at enrollment. Muscle aches were the most common symptom, reported in 86% of cases; cough was reported in 80%; most influenzalike illness symptoms were reported to be present in more than half of cases. No subjects were admitted on the day of enrollment. Based on results of RT-PCR from the nasopharyngeal swab specimen, the prevalence of influenza in our study population was 30.3%, of which 68% was influenza A and 32% influenza B. The prevalence in North and South America did not differ significantly, but there were large differences between hospital sites (Table 2).

In regard to swab test performance, the midturbinate swab had a significantly higher sensitivity for detecting influenza than nasal swab (98.0% [95% CI 94.2% to 99.6%] versus 84% [95% CI 77.5% to 89.8%], respectively) and a better negative likelihood ratio (0.02 [95% CI 0.01 to 0.06] versus 0.16 [95% CI 0.11 to 0.23]) (Table 2). The area under the curve was also significantly greater with midturbinate swab testing than nasal swab testing (0.982 [95% CI 0.969 to 0.996] versus 0.917 [95% CI 0.887 to 0.947], respectively). However, there was no statistically significant difference in specificity or positive likelihood ratios between the 2 specimen types.

Swab discomfort levels correlated with depth of specimen collection (Figure 3). Median discomfort scores for the nasal swab, midturbinate swab, and nasopharyngeal swab were 0, 1, and 3, respectively. The differences in median discomforts between swab types were found to be statistically significant by clustered bootstrap analysis. The differences were nasopharyngeal swab–midturbinate swab 2 (95% CI 1 to 2), nasopharyngeal swab–nasal swab 3 (95% CI 2 to 3), and midturbinate swab–nasal swab 1 (95% CI 1 to 2).

We found some evidence of better nasal swab and midturbinate swab test performance in children than adults, although the study was not powered to show this (Table 2). Although the 95% CIs for both sensitivity and specificity overlapped between pediatric and adult subjects, indicating no difference, the areas under the curve for the pediatric population were statistically higher than for adults, and the better performance was most marked for nasal swab specimens. Median discomfort scores did not differ between adult and pediatric subjects. We found some evidence of clustering by study site, indicated by differences in the areas under the curve of hospitals A and B compared with that of the overall cohort (Table 2 and Figure E1, available online at http://www.annemergmed.com).

LIMITATIONS

This study has the following limitations. Although it was undertaken in anticipation of wider availability of point-of-care molecular influenza tests, it did not actually use a point-of-care test. Moreover, many EDs continue to use influenza antigen detection tests; the differences in test performance between nasal swab and midturbinate swab specimens that we found with a molecular test may not apply to antigen tests. Our results are based only on the influenza strains that were prevalent in North and South America during the 2016 influenza season; different strains may produce more or less viral shedding that could affect test performance. Although this was a multicenter study, one hospital site in Chile contributed more subjects than the other 3 sites combined. Our cohort included many nonhigh-risk subjects who did not satisfy current recommended criteria for influenza testing and treatment. It also included only a small number of children and none younger than 6 years. Both test performance and discomfort results might skew differently in younger children; in particular, sensitivity of nasal swab specimens might have been higher if our cohort had included infants.[19,20] Generalizability of our findings to actual ED

Table 2. Swab performance compared with nasopharyngeal swab reference standard, N=482.*

			Nasal Swab				Midturbinate Swab				
Cohort	N	Prev, % (95% CI)	Sens, % (95% CI)	Spec, % (95% CI)	LR+ (95% CI)	LR– (95% CI)	AUC (95% CI)	Sens, % (95% CI)	Spec, % (95% CI)	LR+ (95% CI)	LR– (95% CI)	AUC (95% CI)
Overall	482	30 (26–34.8)	84.4 (77.5–89.8)	99.1 (97.4–99.8)	94 (31–291)	0.16 (0.11–0.23)	0.917 (0.887–0.947)	98.0 (94.2–99.6)	98.5 (96.6–99.5)	65 (28–157)	0.02 (0.01–0.06)	0.982 (0.969–0.996)
Adult	415	30 (26–34.8)	83.2 (75.5–97)	99 (97–99.8)			0.911 (0.877–0.944)	97.6 (93.1–99.5)	98.3 (96.0–99.4)			0.979 (0.964–0.995)
Child	67	33 (22–45.4)	90.9 (70.8–98.9)	100 (92.1–100)			0.955 (0.893–1)	100 (84.6–100)	100 (92.1–100)			1 (1–1)
US	145	37 (29–44.9)	83 (70.2–91.9)	98.9 (94.1–100)			0.91 (0.858–0.962)	94.3 (84.3–98.8)	97.8 (92.4–99.7)			0.961 (0.926–0.996)
Chile	337	28 (23–33)	85.1 (76.3–91.6)	99.2 (97.1–99.9)			0.921 (0.885–0.958)	100 (96.2–100)	98.8 (96.4–99.7)			0.994 (0.987–1)
Hosp A	49	55 (40–69)	74.1 (53.7–88.9)	100 (84.6–100)			0.87† (0.786–0.955)	88.9 (70.8–97.6)	100 (84.6–100)			0.944† (0.884–1)
Hosp B	95	27 (19–37.5)	92.3 (74.9–99.1)	98.6 (92.2–100)			0.954† (0.9–1)	100 (86.8–100)	97.1 (89.9–99.6)			0.986 (0.966–1)
Hosp C	279	25 (20–30.2)	82.6 (71.6–90.7)	100 (98.3–100)			0.913 (0.868–0.958)	100 (94.8–100)	99.5 (97.4–100)			0.998 (0.993–1)
Hosp D	59	42 (40–55.9)	92 (74–99)	94.1 (80.3–99.3)			0.931 (0.863–0.998)	100 (86.3–100)	94.1 (80.3–99.3)			0.971 (0.93–1)

LR+, Positive likelihood ratio; *LR–*, negative likelihood ratio; *AUC*, area under the curve.

*Two nasal swab results were reported as inconclusive, which typically occurs because of insufficient sampling. Newcombe's method of comparing 2 tests to a reference standard required that these subjects' data be removed from both the nasal and midturbinate swab performance analyses.

†These AUC point estimates lie outside the 95% CI for the overall population, indicating clustering of test performance results according to hospital site.

practice is limited by convenience sampling and use of dedicated study nurses. Specimen collection is operator dependent, and experienced nurses likely obtain high-quality specimens more consistently than would be expected in routine ED practice. In Chile, a foam rather than flocked nasal swab was used. We did not assess nasal or nasopharyngeal washes or aspirates, or self-administered midturbinate swab specimens. We did not randomly vary the order in which swabs were obtained; the nasopharyngeal swab was always the third swab obtained, which might tend to be rated as more uncomfortable. We did not assess nurse satisfaction with the 3 specimen types.

DISCUSSION

To our knowledge, this is the first study to compare both discomfort on a validated scale and accuracy of a molecular influenza assay between 3 different types of intranasal swab specimens. We found that although discomfort increased significantly with depth of swab sampling, the discomfort associated with the midturbinate swab was more similar to that of the superficial nasal swab than to the deep nasopharyngeal swab. The sensitivity of the RT-PCR assay for detection of influenza infection was significantly higher with midturbinate swab specimens than nasal swab specimens. Clinically, this difference in test performance means, given our disease prevalence of 30%, the posttest probability of influenza after a negative result from a midturbinate swab would be 1% compared with 6% with a nasal swab. Strengths of our study include its large size; the multicenter design, which expands the influenza strains involved and the study's external validity; the high proportion of fever and acute influenza-like illness symptoms; and the careful and validated discomfort assessment.

The literature comparing the accuracy of various specimen types for respiratory virus testing is vast and the methodology is heterogeneous. Test performance among specimen types has been compared by using a variety of rapid antigen and PCR assays, as well as viral culture.[18-20,23,24,37,38] For reference standard testing, nasopharyngeal swabs and aspirates perform similarly well, and either can be used; however, swabs are preferred in the ambulatory setting because liquid aspirates are cumbersome, require a suction device, and may present more infectious risk to health care workers.[22-25] The superiority of a flocked swab design, in which nylon fibers are arranged radially from the shaft, compared with rayon or cotton swabs is well established, at least for nasopharyngeal sampling.[23]

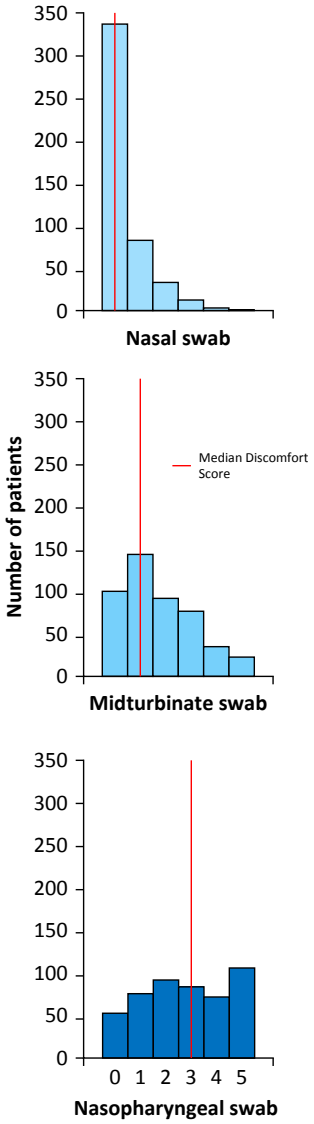

Figure 3. Discomfort scores (N=483*). Discomfort was assessed on a 6-point Faces Pain Scale, from 0 to 5. *There were 483 subjects in this analysis because one subject missing a discomfort score was excluded.

There is limited literature rigorously comparing the discomfort between different specimen collection types. Many studies have simply rated discomfort of a particular specimen type without a comparison. One study found that adults prefer a nasal wash to nasopharyngeal swab, but another found no difference, whereas another found that young children prefer a midturbinate swab to nasal wash.[25,39,40]

In our study, for nasal swab sampling, we chose the technique that is recommended for testing for *Staphylococcus aureus* nasal colonization, in which the swab is rotated in the nasal vestibule. Swab sampling in this anterior pocket, just within the nostril and distal to the cartilaginous septum, is assumed to cause very little discomfort. We chose to assess this relatively superficial swab location because previous pediatric studies have reported sensitivities up to 92% for detecting influenza by various assays using nasal swabs, and we hypothesized that the sensitivity might be even higher with a flocked swab and molecular testing.[18-21,41] It seemed possible that a comfortable swab and easy-to-obtain specimen might provide sufficient clinical sensitivity for routine use in the ED. Because to our knowledge previous studies have not explicitly specified such a distal site for sampling—nasal swabs in previous studies may actually have been taken closer to the midturbinate swab location—it is not possible to directly compare those results with ours. Although our study confirms that nasal swab specimens collected in the nasal vestibule cause little discomfort, we found that with this specimen type the sensitivity for influenza detection was too low to reliably rule out infection, even with a PCR test. We did not find that nasal swab test performance was statistically better in children, as we hypothesized we might, although our study had relatively few children and none younger than 7 years.

The flocked midturbinate swab used in this study was first described in 2010; the conical shape is designed to sample at a midturbinate depth, maximize mucosal contact, and improve collection and release of biological material; in the initial study involving volunteers, it caused mostly "mild discomfort."[26] In a subsequent study of 153 infants, midturbinate swab specimens (using a similar, but much smaller, midturbinate swab) were 93% sensitive for influenza detection with an antibody test compared with nasopharyngeal aspirates.[24] In a study of 38 adults, self-administered midturbinate swab specimens were 100% sensitive for influenza detection with RT-PCR compared with nasopharyngeal swab specimens.[27] Our results confirm the high accuracy of RT-PCR with midturbinate swab specimens in a much larger group of adults and children older than 2 years (for whom an adult-sized swab is used). To our knowledge, there are no other studies like ours comparing discomfort and accuracy between a health care provider–obtained midturbinate swab and another specimen type.

In 2 studies, however, self-collected midturbinate swab specimens have been compared with health care provider–collected midturbinate swab specimens, using RT-PCR. In a study of 203 children, half younger than 2 years, parent-collected midturbinate swab specimens were 89% sensitive for influenza detection compared with pediatrician-collected specimens, and satisfaction was higher with parent collection.[42] In a study of 58 adults, self-collected specimens had 90% sensitivity and 95% overall concordance compared with health care worker–collected specimens; 53% preferred self-collection and 21% preferred health care worker collection.[43] Taken

together with our results, these studies suggest that using midturbinate swab specimens for molecular testing, and providing the option of patient or parent self-collection, may represent the near-future state of the art for influenza testing in the ED setting. Self-collection may also reduce the risk of spread of infection to health care providers.

Although we believe that higher patient discomfort leads to poorer sample quality (because patients recoil before an adequate specimen can be obtained) and that this likely leads to lower nurse satisfaction and less test uptake in the clinical ED environment, these hypotheses were not tested. A link between patient comfort, satisfaction, and test uptake has been difficult to show for other tests.[44] The study we would like to see is one that evaluates a point-of-care molecular test; compares various specimen types, including self-collected midturbinate swab specimens; and assesses both patient and nurse satisfaction and test uptake in a day-to-day ED environment.

In a mostly adult ED population with influenzalike illness, RT-PCR performed on midturbinate swab specimens was 98% sensitive for detecting influenza infection compared with standard nasopharyngeal swab specimens, yet midturbinate swab caused significantly less discomfort than nasopharyngeal swab. A superficial nasal swab caused the least discomfort, but nasal swab specimens were only 84% sensitive, which is too low to effectively rule out infection. Our results suggest that a flocked midturbinate swab is the preferred specimen type for molecular influenza testing in the ED.

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Author affiliations: From the Department of Emergency Medicine, Alameda Health System–Highland Hospital, Oakland, CA (Frazee, Alter, Vohra); Diassess Inc., Fundación Ciencia & Vida, Santiago, Chile (Rodríguez-Hoces de la Guardia, Fuentes, Lolas); Diassess Inc, Emeryville, CA (Chen, Mitra); and the Department of Pediatrics, Stanford University, Palo Alto, CA (Holzer, Dekker).

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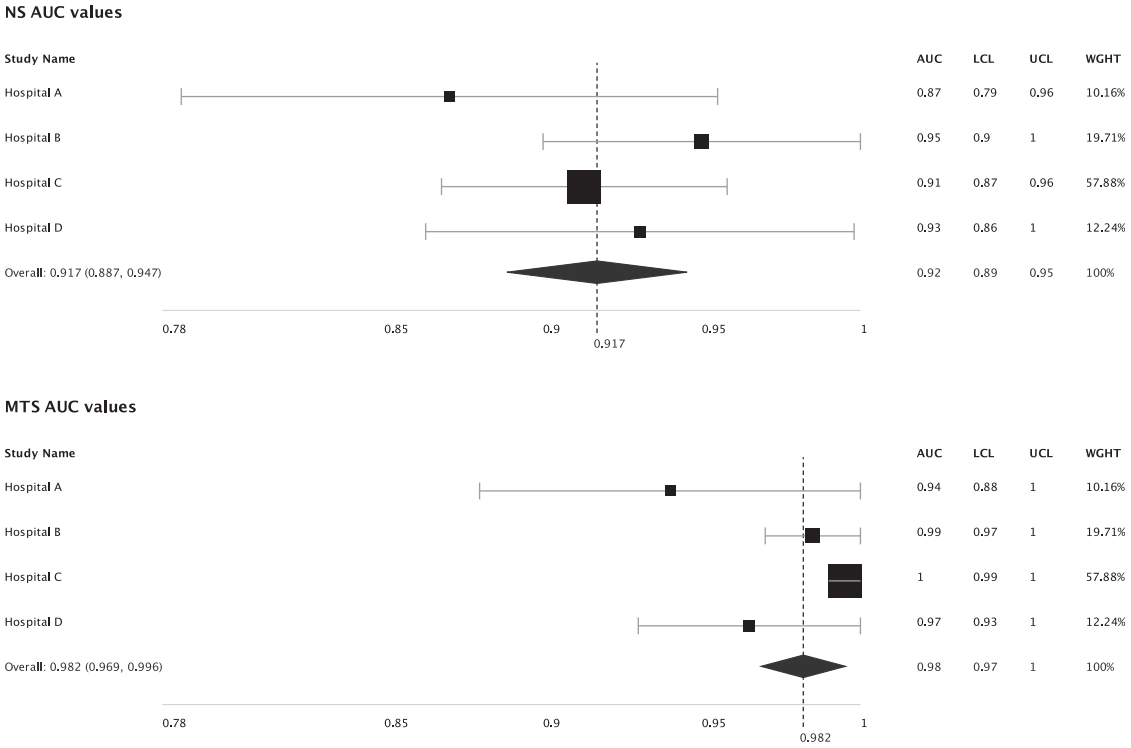

Figure E1. Analysis of clustering by hospital site. Forest plots showing results of the ROC analysis that assessed for clustering of test performance by hospital site. The AUC value for each site (boxes) is compared with that of the overall cohort (diamonds). Sizes of the boxes are proportional to the number of subjects enrolled at the site, or weight. The number of subjects at each hospital site was A=49, B=95, C=279, and D=59. The point estimates for hospital A lie outside the 95% CI of the overall cohort value, indicating that there was clustering. *LCL*, Lower confidence limit; *UCL*, upper confidence limit; *WGHT*, weight.