Clinical Utility and Diagnostic Yield of Multigene SNHL Panels in a Pediatric Cohort

Grace Anderson BS[1]; Karoline Kraechan, BSN[2]; Kristan Alfonso, MD[2,3]; Nathan R. Lindquist, MD[2,3]

1: Baylor College of Medicine, Houston, TX
2: Division of Otolaryngology—Head & Neck Surgery, Department of Surgery, Texas Children's Hospital, Houston, TX
3: Bobby R. Alford Department of Otolaryngology—Head & Neck Surgery, Baylor College of Medicine, Houston, TX

Introduction

Comprehensive genetic screening is increasingly utilized in the evaluation of pediatric sensorineural hearing loss (SNHL).[1] The GeneDx Hearing Loss Panel evaluates over 150 genes,[2] while the PreventionGenetics Resonate® panel evaluates 274 genes,[3] including a broad subset associated with syndromic hearing loss. Recently, eligibility for testing has expanded to include children with unilateral SNHL. We report the early institutional diagnostic yield and clinical impact of these screening tests following their introduction into routine pediatric otology practice.

Patient Characteristic	N = 50
Gender	
Male	29 (58%)
Female	21 (42%)
Ethnicity	
White Non-Hispanic	11 (22%)
Black	3 (6%)
Hispanic/Latino	15 (30%)
Unknown/Not Identified	21 (42%)
Laterality of SNHL	
Bilateral	30 (60%)
Unilateral	20 (40%)

Table 1. Patient Characteristics

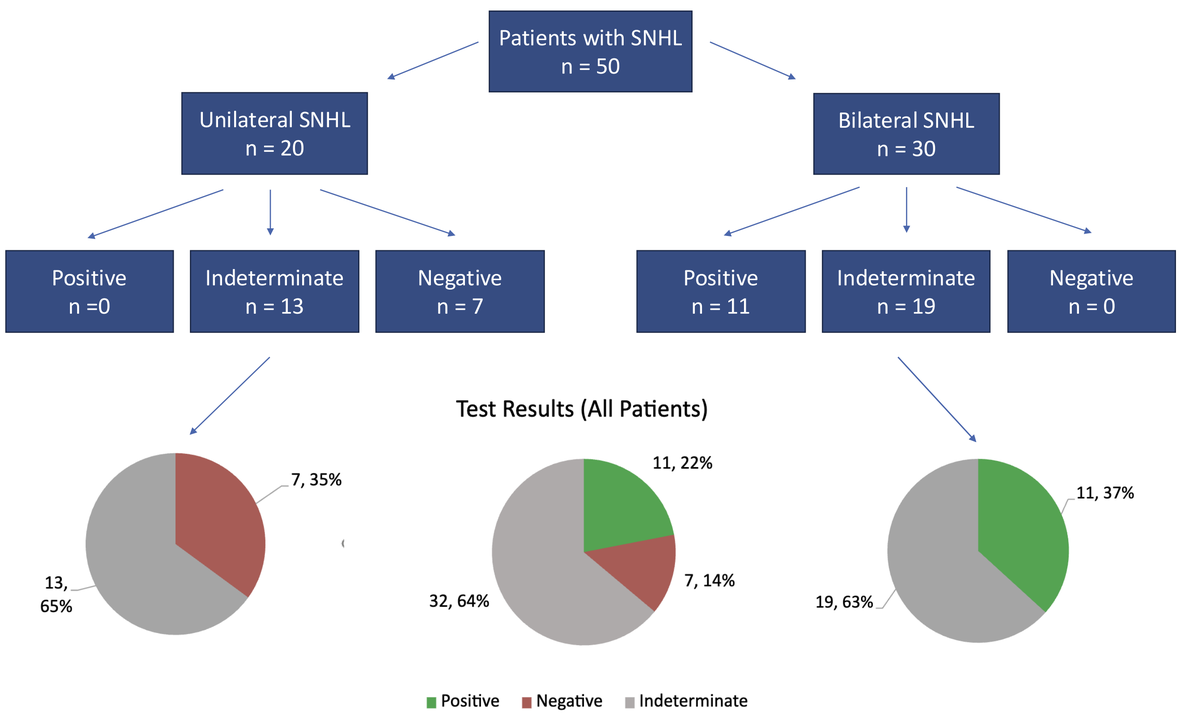


Figure 1. Diagnostic yield summary

Methods

50 pediatric patients were randomly selected from a cohort with both unilateral and bilateral SNHL who received genetic testing from both GeneDx and PreventionGenetics at Texas Children's Hospital, from 2022 to 2025. Ages ranged from 2 months to 18.2 years old. Average age was 6.5 years old. Test results were categorized by positive, indeterminate, or negative molecular diagnosis. Charts were individually reviewed for record of laterality of hearing loss (bilateral vs unilateral), family history, risk factors, and change in clinical management. Change in clinical management was defined by medical intervention or new diagnosis made by the ordering neurotologist. Referrals to genetic counseling were not included in this category. Test result and chart data were cross-referenced to assess diagnostic yield and overall clinical influence.

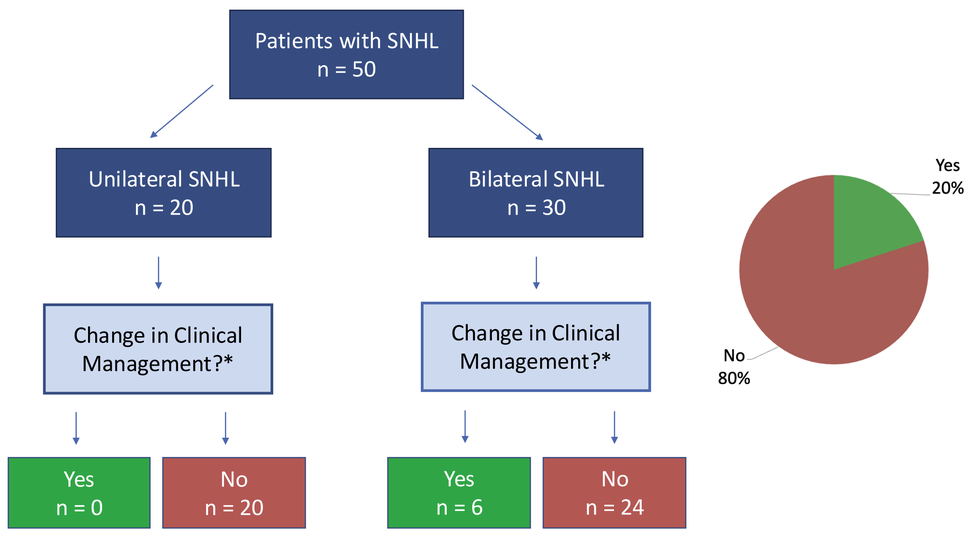


Figure 2. Clinical relevance flow chart
*Change in clinical management as defined in methods section

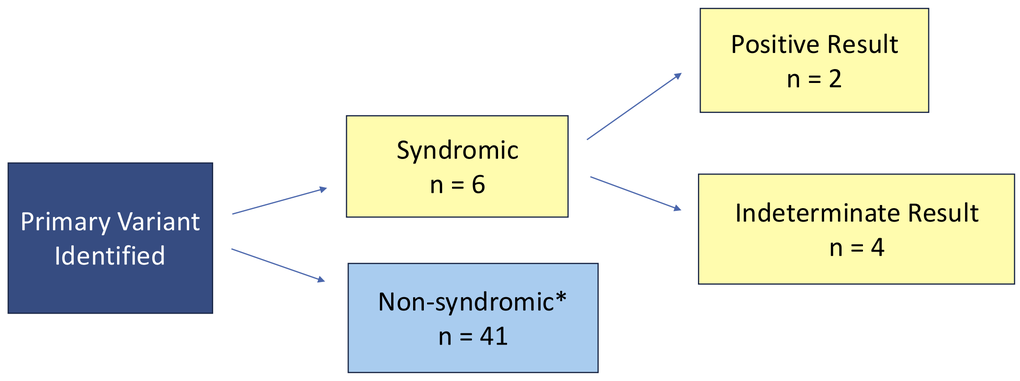


Figure 3. Variant status flow chart, per patient
*non-syndromic includes benign variants

Results

There was a significant difference between diagnostic yield, or probability of positive molecular diagnosis, between the BL and UL SNHL groups (p = 0.002 by Fisher's exact test). Notably, the BL SNHL group had no negative test results, and the UL SNHL group had no positive test results (Figure 1). 6 patients had a change in clinical management based on genetic testing results (Figure 2). Of these 6, 2 had positive results and 4 had indeterminate results (Figure 3). Those with indeterminate results had "likely pathogenic variants" that correlated with their clinical presentation. For example, a patient with suspected auditory sensory neuropathy tested positive for a likely pathogenic variant in the OPA1 gene,[4] which prompted close follow up with ophthalmology because of its association with optic atrophy. Intervention for other patients included direct referrals for new diagnoses that originated from these genetic tests, including Van Waardenburg and Branchial-Oto-Renal syndrome, as well as EKG and RUS to evaluate for syndromic sequelae (in the case of likely Axenfeld-Rieger syndrome). No patients with unilateral hearing loss had a change in clinical management. Among the 11 patients with positive test results, 4 were positive in GJB2.[5]

Discussion and Conclusions

Early institutional experience with commercially available in-office genetic screening tests demonstrates a substantial diagnostic yield in pediatric SNHL. Compared to bilateral SNHL, unilateral SNHL has a lower diagnostic yield with these in-office screening tools. Given the findings of this pilot study, further evaluation of the diagnostic yield of these screening tests should better inform clinicians as to the relative utility of genetic testing in unilateral and bilateral SNHL. For unilateral pediatric SNHL, imaging and CMV testing may be relatively more useful[6], though there are still a high proportion of indeterminate results in both cohorts that may ultimately become clinically relevant as our understanding and reporting of these indeterminate or "likely pathogenic variants" continues to improve. Clinicians should be facile in counseling patients, especially with regards to the likelihood of a variant of unknown significance (VUS) versus definitive result for patients of both cohorts.[7] Ongoing data collection will refine yield estimates and impact, supporting informed patient counseling as molecular therapies and eligibility continue to evolve.

Contact

Nathan Lindquist, MD
nathan.lindquist@bcm.edu
713-798-5900

Kristan Alfonso, MD
kristan.alfonso@bcm.edu

Grace E. Anderson, BS
Grace.Anderson@bcm.edu
281-685-5105

References

1. Sloan-Heggen CM, Bierer AO, Shearer AE, et al. Comprehensive genetic testing in the clinical evaluation of 1119 patients with hearing loss. Hum Genet. 2016;135(4):441-450. doi: 10.1007/s00439-016-1648-8. PMID: 26969326.

2. GeneDx, LLC. Hearing Loss Panel (test code J806). GeneDx Provider Portal. Accessed September 2026. providers.genedx.com/tests/detail/hearing-loss-panel-925

3. PreventionGenetics. Resonate® Hearing Loss Genetic Testing and Counseling Program. Accessed September 2026. preventiongenetics.com/sponsoredTesting/akouos-resonate

4. Kawakita M, Moteki H, Nishio SY, et al. Frequency and hearing loss phenotypes of OPA1 variants in a cohort of 18,475 patients with hearing impairment. Genes (Basel). 2026;17(3):341. doi: 10.3390/genes17030341.

5. Sun Q, Tan F, Zhang L, et al. Combined AAV-mediated specific Gjb2 expression restores hearing in DFNB1 mouse models. Mol Ther. 2025;33(7):3006-3021. doi: 10.1016/j.ymthe.2025.03.029. PMID: 40121530.

6. Preciado DA, Lim LHY, Cohen AP, et al. A diagnostic paradigm for childhood idiopathic sensorineural hearing loss. Otolaryngol Head Neck Surg. 2004;131(6):804-809. doi: 10.1016/j.otohns.2004.06.707. PMID: 15577772.

7. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of ACMG and AMP. Genet Med. 2015;17(5):405-423. doi: 10.1038/gim.2015.30.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com