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When Guidelines Outpace Capacity: A Systems Analysis of Genome-First Testing in Neurodevelopmental Disorders

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Abstract

Purpose

Clinical guidelines now recommend exome or genome sequencing as first-line testing for autism spectrum disorder (ASD), intellectual disability (ID), and global developmental delay (GDD). However, the systems-level capacity needed to implement genome-first testing at scale remains poorly characterized. We quantified institutional demand for genomic testing among neurodevelopmental patients and compared it with available genetics clinic capacity.

Methods

We conducted a retrospective EHR review of all patients scheduled within a large Division of Developmental and Behavioral Pediatrics (DDBP) over four weeks (January 26–February 20, 2026). Patients were eligible if they had ASD, ID, and/or GDD and had not previously undergone exome or genome sequencing. We extracted demographics, prior genetic testing, and Social Deprivation Index (SDI) scores, and quantified available general and neurodevelopmental genetics clinic appointment slots during the same interval to assess workforce capacity.

Results

Of 473 eligible individuals, 72% were test-naïve. Most were male (72%) and Medicaid-insured (62%), with a mean SDI score of 54 (SD 26). Only 240 genetics clinic slots were available institution-wide during the same period, roughly half the eligible volume, revealing a substantial gap between guideline-recommended eligibility and specialist capacity.

Conclusion

At our institution, genome-first testing guidelines have outpaced existing genetics workforce capacity. These findings motivate an ongoing systems-redesign effort; alternative consent and testing-initiation workflows embedded within DDBP clinics may help bridge the evidence-to-practice gap and support equitable access to genomic medicine.

Introduction

Clinical genetic testing using exome or genome sequencing is now recommended as a first-line diagnostic test for individuals with intellectual disability (ID) and global developmental delay (GDD) (Manickam et al., 2021; Rodan et al., 2025; Srivastava et al., 2024). Genome sequencing also represents an effective first-line test for individuals with isolated autism spectrum disorder (ASD), as it encompasses prior guideline-recommended testing, including chromosomal microarray and *FMR1*

analysis, while offering additional diagnostic yield through comprehensive single-gene interrogation (Lindstrand et al., 2022).

In response to these evolving guidelines and increased yield of broad test approach (Lowther et al., 2023), the Division of Developmental and Behavioral Pediatrics (DDBP) and the Division of Human Genetics (DHG) at our large pediatric academic hospital medical center have adopted a genome-first diagnostic approach for individuals diagnosed with ASD, ID, and/or GDD. While this approach aligns with best practices in precision medicine, it also introduces substantial logistical challenges. Identifying eligible patients, providing education and informed consent for advanced genomic testing, and ordering appropriate testing are time-intensive processes that have traditionally occurred within the scope of specialized genetics clinics (Wang et al., 2024). We focused on DDBP because it is the institutional point of entry for the genome-first policy described above: DDBP providers are the ones being asked, under current guidelines and institutional workflow, to identify individuals with a diagnosis of ASD/ID/GDD as candidates for first-line genomic testing, making DDBP referral volume the most direct measure of downstream demand on genetics clinic capacity. Other pediatric subspecialties may independently refer patients for genetic evaluation, but those referrals were outside the scope of this analysis, which was designed specifically around the new DDBP-genetics care pathway.

The widespread adoption of genome-first testing therefore raises a critical systems-level question: Can existing genetics clinic capacity meet the volume of patients now eligible for first-line genomic testing? This question is particularly salient in large neurodevelopmental referral centers, where demand for both developmental and genetic services continues to grow.

To address this question, we conducted an exploratory electronic health record (EHR) review, examining a one-month snapshot of patients scheduled in DDBP clinics. Our objectives were to (1) quantify the number of patients who would be eligible for genome sequencing under current guidelines and institutional practice, and (2) compare this need with the number of available general or neurodevelopmental genetics clinic appointment slots during the same time period. Rather than offering a comprehensive workforce assessment, this analysis is intended as a deliberately narrow, descriptive snapshot that establishes institutional rationale and motivates a subsequent, more comprehensive systems-level evaluation. This preliminary analysis was conducted as part of a larger, ongoing study evaluating a virtual genome consent video intervention, and is reported here as foundational background motivating that larger effort, with the present work focusing specifically on characterizing unmet institutional need for genetic testing within a defined neurodevelopmental population.

Methods

We conducted a retrospective review of EHR scheduling data for all DDBP providers at our institution over a four-week period (January 26, 2026-February 20, 2026). Patients were considered eligible for genome sequencing if they carried a diagnosis of ASD, GDD, and/or ID. This window was selected as a

convenience sample reflecting routine winter clinic operations; we did not independently verify that scheduling volume or genetics staffing during this period was representative of other months.

Patients were excluded if they had previously undergone exome or genome sequencing. Additional exclusions included patients without an identified legal guardian able to provide informed consent (e.g., children in foster care) and patients requiring an interpreter, as the larger parent study intervention is currently available only in English (Conrad & Shillington, 2025). Eligibility, as defined here, reflects diagnostic candidacy for genome-first testing rather than confirmed intent to pursue testing; we did not track whether eligible patients or families would accept a genetics referral if offered one, so eligible volume represents an upper-bound estimate of referral demand rather than a prediction of completed testing encounters.

Extracted demographic variables included age, sex, race and ethnicity, Social Deprivation Index (SDI) score (Limburg et al., 2025), insurance type, and prior genetic testing history (e.g., chromosomal microarray, *FMR1* testing, karyotype, or targeted/broad gene panels). Individuals were categorized as either test-naïve or previously tested under earlier guideline recommendations (Schaefer & Mendelsohn, 2013). Demographic and socioeconomic variables (race/ethnicity, insurance type, and SDI) were collected because equitable access is a central concern in genome-first implementation: genetic services have historically been less accessible to publicly insured, racially/ethnically minoritized, and socioeconomically disadvantaged populations, and we wanted to describe whether the population newly designated as eligible for first-line testing under this policy reflected that same risk profile. Race and ethnicity were dichotomized as White/non-Hispanic versus all other categories combined because our institution's structured EHR race/ethnicity field is not consistently granular below this level for scheduling-data extraction and because our primary comparison of interest was eligibility relative to a historically well-served reference group; we recognize this collapses heterogeneous populations into a single category and address this further in the Limitations.

To assess institutional capacity for genetics services, we also reviewed the number of available general and neurodevelopmental genetics clinic appointment slots during the same four-week period. Available appointments were categorized by provider type, including physician, advanced practice registered nurse (APRN), and genetic counselor-only visits. This analysis was limited to scheduled appointment slot counts; we did not extract clinical full-time equivalent (FTE) staffing for either DDBP or genetics providers, nor did we capture next-available new-patient or established-patient visit wait times for either division, prior authorization processing time, or the proportion of ordered ES/GS tests subsequently denied or unreimbursed by insurance. These additional operational metrics, while important to a full capacity analysis, were beyond the scope of this descriptive snapshot and are discussed further below.

Results

Demographics

A total of 473 individuals met inclusion criteria. The mean age was 7.23 years (SD = 4.04), and 341 of 473 individuals (72%) were male. The majority of individuals (192/473; 63%) identified as White and non-Hispanic. The mean Social Deprivation Index score was 54 (SD = 26). Most patients (202/473; 62%) were insured through state Medicaid programs.

Diagnostic Characteristics and Prior Testing

Among included patients, 103 of 473 (22%) had a diagnosis of ASD without co-occurring ID or GDD, 48 of 473 (10%) had ID or GDD without ASD, and 322 of 473 (68%) carried diagnoses of both ASD and ID or GDD. We report these three diagnostic subgroups separately because the underlying genome-first guidelines were established along different evidence tracks for ASD versus ID/GDD, and because patients with comorbid ASD and ID/GDD may already be more likely to have been referred to genetics under prior, narrower testing criteria; distinguishing the groups allows readers to see how much of the eligible population is newly captured by the expanded, ASD-inclusive guideline rather than already being addressed under legacy referral patterns.

The majority of patients (339/473; 72%) were test-naïve with respect to genetic evaluation. The remaining 134 patients (28%) had undergone prior genetic testing, including chromosomal microarray, *FMR1* testing, karyotype, or targeted or broad gene panel testing.

Genetics Clinic Capacity

During the same four-week interval, 240 general or neurodevelopmental genetics clinic appointment slots were available across the institution. These included 48 genetic counselor-only appointments, 56 genetics APRN appointments, and 136 genetics physician appointments.

Discussion

The growing demand for genetic services in the context of a limited workforce represents one of the most significant challenges facing the field of medical genetics (Raspa et al., 2021). In the United States, there is approximately one genetics medical provider per 300,000 individuals, and approximately 2,500 certified genetic counselors, equating to 8.1 genetic counselors per million population (Raspa et al., 2021). A large scoping review of genetic service delivery models identified time-intensive counseling requirements and prolonged wait times as two of the most substantial barriers to care (Raspa et al., 2021). These workforce shortages and the resulting wait times across genetics subspecialties have been documented in detail elsewhere, including a national clinical genetics workforce analysis and a recent multi-institutional comparison of wait times across genetics subspecialties (Dulchavsky et al., 2026; Jenkins et al., 2021). Rather than re-establishing that a national genetics workforce shortage exists, our contribution is institution-specific: we quantify how that shortage manifests as a concrete, current mismatch between guideline-driven referral volume from a single large neurodevelopmental

program and the genetics appointment capacity available to absorb it, providing the local motivating data for a subsequent systems-redesign intervention at our center.

These national challenges are reflected locally at our institution, where genetics clinics experience some of the longest wait times across all clinical divisions, compounded by a limited number of practicing geneticists. Our findings demonstrate a clear mismatch between the number of patients eligible for genome sequencing under current guidelines and institutional practices and the available genetics clinic capacity to initiate such testing. We note that our eligibility count assumes that every eligible patient would accept a genetics referral and proceed to testing; in practice, some families decline referral or do not complete scheduling, so the true gap in realized demand is likely smaller than the gap in diagnostic eligibility we report here.

We also observed a marked male predominance in our eligible sample (72% male), a ratio more skewed than the roughly 3:1 to 4:1 male-to-female ratio typically reported for ASD and the closer-to-even ratio reported for ID/GDD. This likely reflects the composition of DDBP referrals during the study period rather than a sex-specific difference in genome-first eligibility itself, since eligibility was defined solely by diagnosis. We did not formally test this sex distribution against institutional or population referral norms, and we did not collect data that would allow us to determine whether male and female patients were referred to or evaluated in DDBP at different rates; we flag this as an area for further study rather than a finding we can fully explain with the present data.

At present, patients with neurodevelopmental disorders who pursue genetic testing typically require at least two genetics clinic visits: an initial visit for pre-test counseling and consent, followed by a return visit for results disclosure and medical management. Transitioning pre-test counseling and test initiation outside of the traditional genetics clinic setting has the potential to reduce genetics clinic utilization by up to 50% for this patient population. This shift could preserve limited genetics clinic appointments for higher-acuity post-test counseling, complex medical management, and diagnostic clarification.

Importantly, some individuals, particularly those with negative or non-diagnostic results, may not require a formal genetics clinic visit at all. Streamlining test initiation could therefore significantly increase system efficiency while maintaining quality of care.

The benefits of identifying a genetic diagnosis in individuals with neurodevelopmental disorders are well established. A molecular diagnosis can inform medical surveillance and management, enable syndrome-specific interventions, refine prognostic counseling, improve reproductive risk assessment, facilitate access to disorder-specific community resources, and support participation in gene-specific research and clinical trials (Besterman et al., 2020). Clinical exome and genome sequencing yield diagnostic results in approximately 25–35% of individuals with neurodevelopmental disorders (Meienberg et al., 2016), and such diagnoses result in changes to medical management in up to 70% of cases (Harris et al., 2020; Shillington et al., 2022). Precision genotyping is also a prerequisite for clinical trial readiness and equitable access to emerging gene-targeted therapies (Peña et al., 2023).

Our data indicate that, at the upper bound, fully meeting the genetic testing needs of all DDBP patients eligible under current guidelines and practices could require scheduling on the order of 473 genetics-related encounters per month against an existing capacity of 240. Even allowing that not every eligible patient would ultimately pursue or accept testing, this gap is large enough that incremental expansion of genetics clinic volume alone is unlikely to close it given workforce constraints. Instead, innovative care delivery models that integrate genetic test initiation directly into DDBP encounters may represent a more sustainable and equitable solution.

By empowering non-genetics providers to initiate genome sequencing through structured consent workflows and decision support, institutions may reduce wait times, shorten diagnostic odysseys by six months or more (Maiese et al., 2019; Shillington et al., 2022), and improve access to medically indicated testing for historically underserved populations (Lindly et al., 2019). Redesigning care pathways to initiate testing earlier has the potential to substantially improve both patient experience and clinical outcomes.

This study provides systems-level evidence that current care pathways for genomic test initiation are misaligned with contemporary testing guidelines. Within implementation science frameworks, this represents a classic “evidence-to-practice gap”: the clinical evidence supporting genome-first testing is established, yet structural and workflow barriers impede consistent delivery.

Our findings suggest that the traditional model, requiring a genetics provider to complete pre-test counseling and consent, functions as a limiting implementation bottleneck. Pre-test consent, while ethically essential, is time-intensive and often duplicative across similar patient populations. When scaled across large NDD clinics engaging and supporting non-genetics neurodevelopmental providers, this model becomes operationally unsustainable.

Alternative delivery models, such as standardized video-based consent modules, decision aids, embedded order sets to support provider-initiated testing within developmental pediatric clinics, represent implementation strategies designed to increase reach, reduce time-to-testing, and preserve limited genetics specialist capacity for post-test management and complex cases.

Limitations

This study has several important limitations. First, our eligible-patient count assumes that every diagnostically eligible patient would accept a genetics referral and proceed to pre-test counseling and testing; this is unlikely to hold in practice, and the true number of patients who would actually present for genetics services is almost certainly lower than the 473 reported here. As such, our eligibility figure should be interpreted as an upper-bound estimate of potential demand rather than a literal projection of required clinic encounters. Second, this analysis captured only the volume of scheduled appointment slots and did not assess clinical FTE for either DDBP or genetics providers, nor did we measure next-available new-patient or established-patient visit wait times for either division; a true capacity comparison would benefit from incorporating these workforce and access metrics directly. Third, we did

not capture the time burden of prior authorization or the proportion of ordered ES/GS tests that were ultimately denied or not reimbursed by insurance, both of which represent additional, clinically meaningful capacity constraints on genome-first implementation that were beyond the scope of this descriptive snapshot. Fourth, our data reflect a single four-week period during winter months; clinic scheduling volume, patient mix, and genetics staffing availability may vary seasonally, and a full year of data would better characterize average institutional demand and capacity. Fifth, our binary categorization of race and ethnicity (White/non-Hispanic versus all other categories combined) does not capture the diversity of the non-White/non-Hispanic population in our sample; more granular categorization, where EHR data quality permits, would allow for a more nuanced equity analysis in future work. Finally, this analysis was restricted to referrals originating from DDBP and does not capture genetics referral volume from other pediatric subspecialties at our institution, so the total demand on genetics clinic capacity from all sources is likely larger than what we report here. Despite these limitations, we believe this descriptive snapshot provides useful, institution-specific motivating data for the larger systems-redesign effort described above, and we have framed our conclusions accordingly.

Declarations

Ethics Declaration: This study was reviewed and approved by the Cincinnati Children's Hospital Medical Center Institutional Review Board (IRB#2025-0641). The requirement for informed consent was waived for this retrospective review of de-identified electronic health record data. All procedures were conducted in accordance with institutional guidelines and the ethical standards of the Declaration of Helsinki.

IRB Statement: This study was approved by the Cincinnati Children's Hospital Medical Center Institutional Review Board (IRB#2025-0641).

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Data Availability:The data that support the findings of this study are not publicly available due to institutional privacy regulations and the inclusion of protected health information but are available from the corresponding author upon reasonable request and with appropriate institutional approvals.

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References

1. Besterman, A. D., Sadik, J., Enenbach, M. J., Quintero-Rivera, F., DeAntonio, M., & Martinez-Agosto, J. A. (2020). The feasibility and outcomes of genetic testing for autism and neurodevelopmental disorders on an inpatient child and adolescent psychiatry service. *Autism Research*, *13*(9), 1450–1464. https://doi.org/10.1002/aur.2338
2. Conrad, C., & Shillington, A. (2025). Consent for exome or genome sequencing: Cincinnati Children's [Video]. *YouTube*. https://www.youtube.com/watch?v=uvCrZI0FGXY
3. Dulchavsky, M., et al. (2026). Wait times for genetic services across subspecialties: A multi-institutional analysis. *Genetics in Medicine Open*.
4. Harris, H. K., Sideridis, G. D., Barbaresi, W. J., & Harstad, E. (2020). Pathogenic yield of genetic testing in autism spectrum disorder. *Pediatrics*, *146*(4).
5. Jenkins, B. D., Fischer, C. G., Polito, C. L., Maiese, D. R., Keehn, A. S., Lyon, M., Edick, M. J., Taylor, A. K., Andersson, H. C., Bodurtha, J. N., & Bristow, S. L. (2021). The 2019 US medical genetics workforce: A focus on clinical genetics. *Genetics in Medicine*, *23*(8), 1458–1464.
6. Limburg, A., Rehkopf, D. H., Gladish, N., Phillips, R. L., & Udalova, V. (2025). Validating 8 area-based measures of social risk for predicting health and mortality. *JAMA Health Forum*, *6*(8), Article e252669.
7. Lindly, O. J., Zuckerman, K. E., & Kuhlthau, K. A. (2019). Healthcare access and services use among US children with autism spectrum disorder. *Autism*, *23*(6), 1419–1430. https://doi.org/10.1177/1362361318815237
8. Lindstrand, A., Ek, M., Kvarnung, M., Anderlid, B. M., Björck, E., Carlsten, J., Eisfeldt, J., Grigelioniene, G., Gustavsson, P., Hammarsjoe, A., & Helgadottir, H. T. (2022). Genome sequencing is a sensitive first-line test to diagnose individuals with intellectual disability. *Genetics in Medicine*, *24*(11), 2296–2307.
9. Lowther, C., Valkanas, E., Giordano, J. L., Wang, H. Z., Currall, B. B., O'Keefe, K., Pierce-Hoffman, E., Kurtas, N. E., Whelan, C. W., Hao, S. P., & Weisburd, B. (2023). Systematic evaluation of genome sequencing for the diagnostic assessment of autism spectrum disorder and fetal structural anomalies. *The American Journal of Human Genetics*, *110*(9), 1454–1469.

10. Maiese, D. R., Keehn, A., Lyon, M., Flannery, D., Watson, M., & Working Groups of the National Coordinating Center for Seven Regional Genetics Service Collaboratives. (2019). Current conditions in medical genetics practice. *Genetics in Medicine*, *21*(8), 1874–1877.
11. Manickam, K., McClain, M. R., Demmer, L. A., Biswas, S., Kearney, H. M., Malinowski, J., Massingham, L. J., Miller, D., Yu, T. W., Hisama, F. M., & ACMG Board of Directors. (2021). Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine*, *23*(11), 2029–2037.
12. Meienberg, J., Bruggmann, R., Oexle, K., & Matyas, G. (2016). Clinical sequencing: Is WGS the better WES? *Human Genetics*, *135*, 359–362.
13. Peña, L. D., Burrage, L. C., Enns, G. M., Esplin, E. D., Harding, C., Mendell, J. R., Niu, Z. N., Scharfe, C., Yu, T., Koeberl, D. D., & ACMG Therapeutics Committee. (2023). Contributions from medical geneticists in clinical trials of genetic therapies: A points to consider statement of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine*, *25*(6), Article 100831.
14. Raspa, M., et al. (2021). Barriers and facilitators to genetic service delivery models: Scoping review. *Interactive Journal of Medical Research*, *10*(1), Article e23523.
15. Rodan, L. H., et al. (2025). Genetic evaluation of the child with intellectual disability or global developmental delay: Clinical report. *Pediatrics*, *156*(1), Article e2025072219.
16. Schaefer, G. B., & Mendelsohn, N. J. (2013). Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. *Genetics in Medicine*, *15*(5), 399–407.
17. Shillington, A., et al. (2022). A collaborative psychiatric-genetics inpatient care delivery model improves access to clinical genetic evaluation, testing, and diagnosis for patients with neurodevelopmental disorders. *Frontiers in Genetics*, *13*.
18. Srivastava, S., et al. (2024). Survey of the landscape of society practice guidelines for genetic testing of neurodevelopmental disorders. *Annals of Neurology*, *96*(5), 900–913.
19. Wang, A., Little, I. D., Carter, D., Pham, S., Piper, M., Ramírez-Renta, G. M., Telaak, S., & Gunter, C. (2024). Provider-reported experiences, barriers, and perspectives on genetic testing as part of autism diagnosis. *PLoS ONE*, *19*(2), Article e0296942.

Tables

Table 1: Demographic Characteristics of the Study Population (N=473)

This table summarizes the baseline characteristics of the patients identified in the one-month EHR review.

Characteristic	n (%) or Mean (SD)
Age (years)	7.23 (4.04)
Sex	
Male	341 (72%)
Female	132 (28%)
Race/Ethnicity	
White, non-Hispanic	192 (63%)
Other / Not Specified	112 (37%)
Insurance Type	
Public (Medicaid)	202 (62%)
Private / Other	124 (38%)
Social Deprivation Index (SDI)	54 (26)

Table 2: Clinical Indications and Genetics Workforce Capacity

This table highlights the "Capacity Gap" by comparing the number of eligible patients to the available institutional resources.

Clinical Category	Count (n)	Percentage (%)
Primary Diagnosis		
ASD only	103	22%
ID/GDD only	48	10%
Comorbid ASD and ID/GDD	322	68%
Prior Testing Status		
Test Naive	339	72%
Prior Testing (CMA, Karyotype, Gene Panel)	134	28%
Total Eligible for Genome Sequencing	473	100%
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Available Genetics Appointments (Monthly)	**Count**	**Professional Type**
Physician	136	MD / DO
Advanced Practice Registered Nurse	56	APRN
Genetic Counselor (Independent)	48	MS, CGC
Total Monthly Capacity	240	—