THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Using Genes to Guide Better Care: The Role of Genomic Medicine in Adult with IDD

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Financial Disclosure

- Nothing to disclose

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  - U01NS139216: Increasing Access, Diagnostic Yield, and Efficiency in Clinical Evaluations of Rare Disorders (Undiagnosed Disease Network)

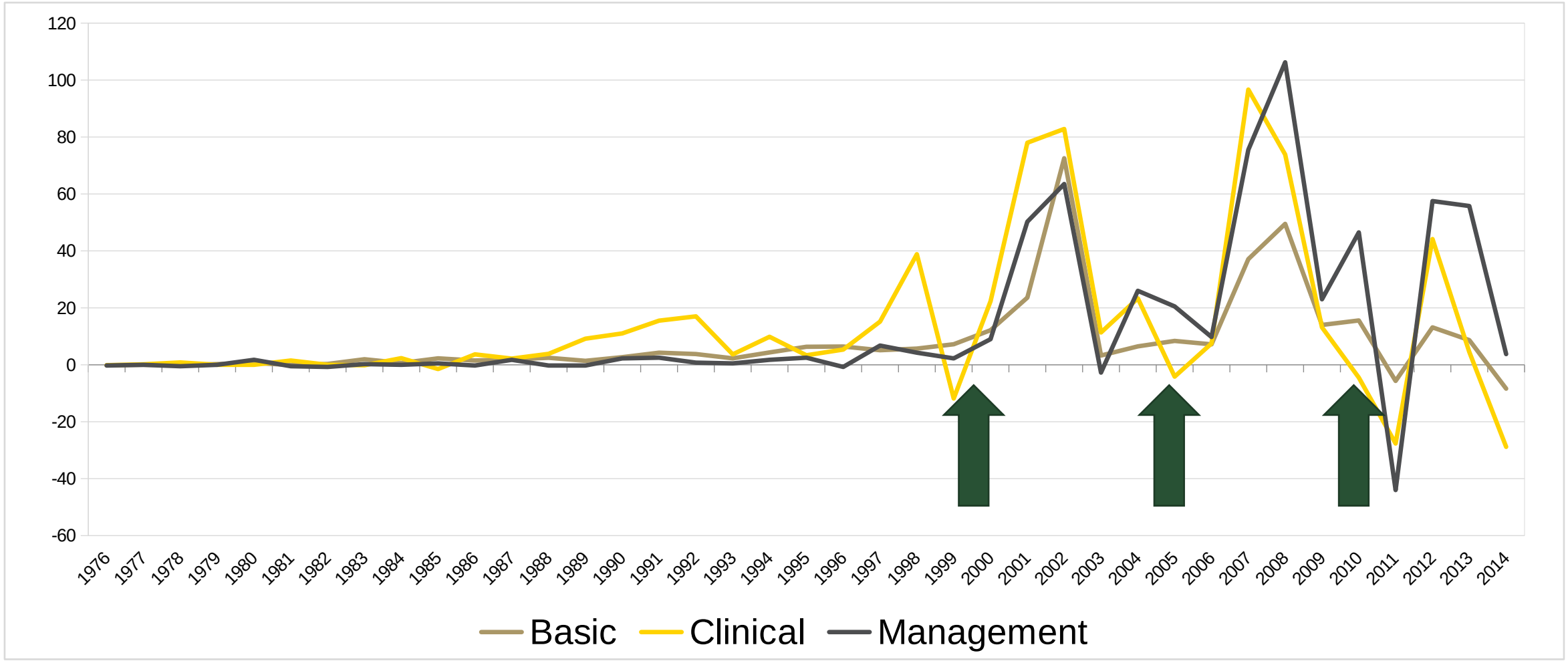
  - SBIR-219296: Leveraging Large Language Models to Enhance Regional Genomic Medicine eConsults

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Roadmaps

1. Footsteps in genetic and genomics
2. Current recommendations for genetic testing in Adults with IDD
3. Clinical pearls from UAB Adult Genetics clinic
4. Gaps in care for Adults with IDD and Resources

Footsteps in Genetics and Genomics



Bornstein et al., *Mol Genet Metab* 2016

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Footsteps in Genetics and Genomics

1865
Mendel's Pea

1953
Watson and Crick Double Helix DNA

1959
Down syndrome

1975
Sanger sequencing

1983
First gene mapped (*HTT*)

1990
FISH and Molecular Cytogenetics

1990-2003
Human Genome Project



2004
Molecular Karyotyping (Microarray)

2009
Next-Generation Sequencing

Long read sequencing

RNA-seq
ChIP-seq
CRISPR-seq

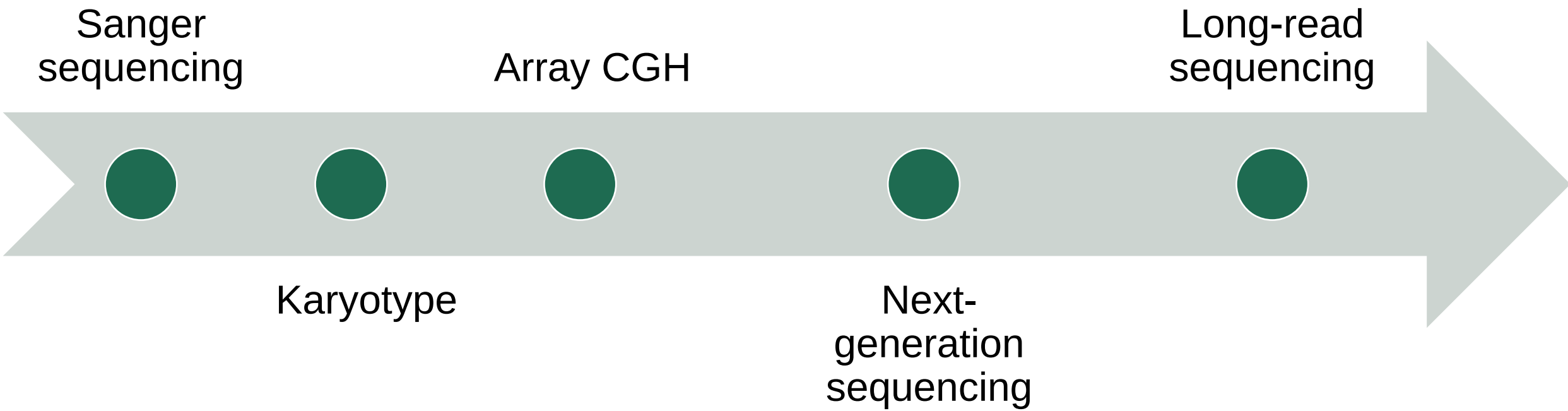
Ease of analysis

Amount of genomic data per run

Sanger | MLPA/CGH | Gene panels | Exome | Genome

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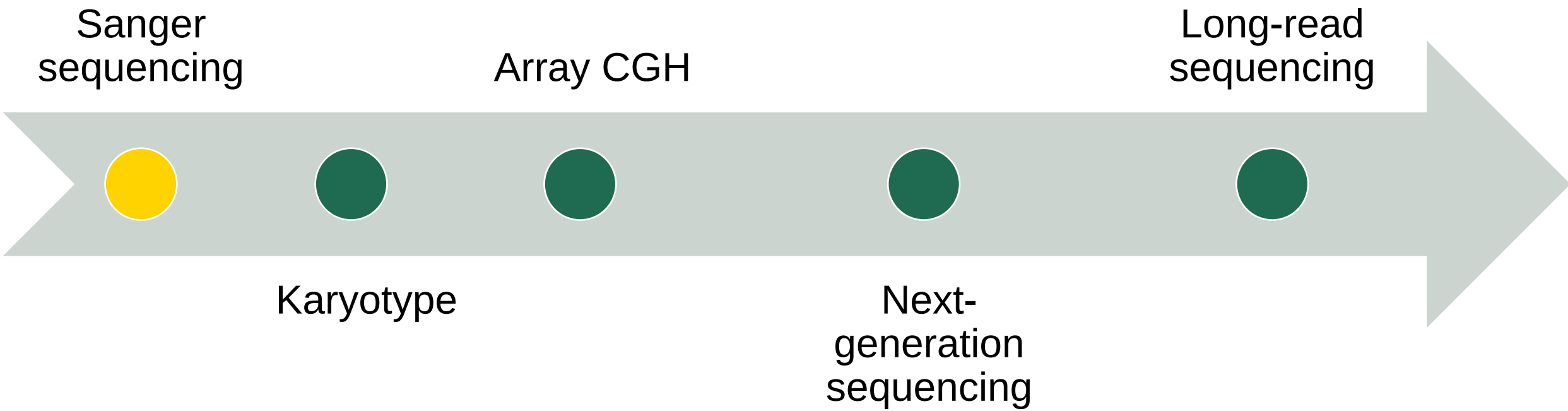
Availability of tools in the clinical genetics space



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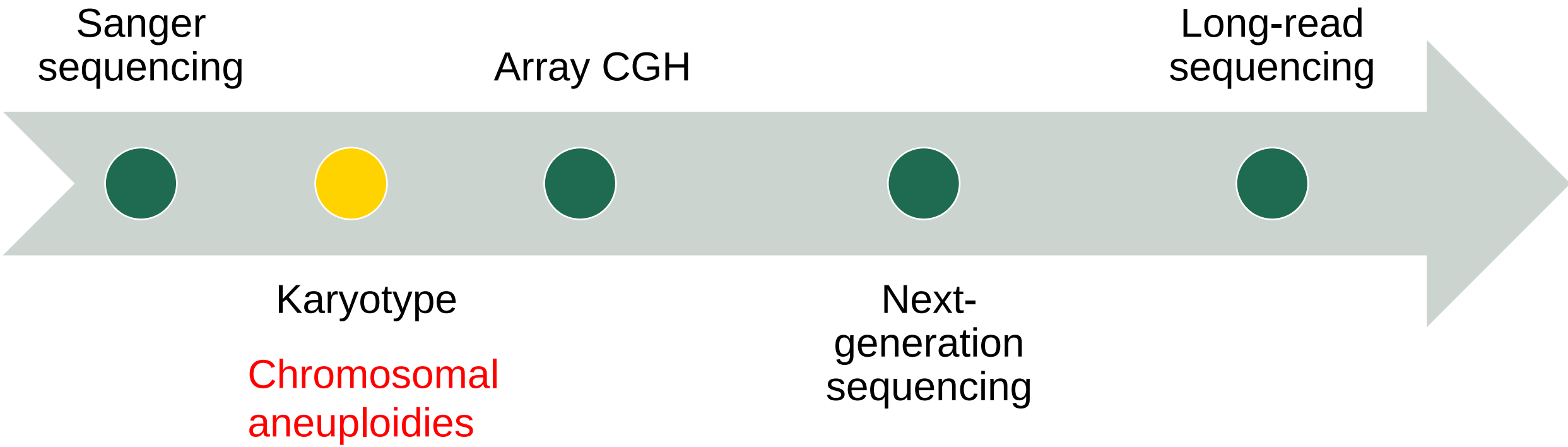
Availability of tools in the clinical genetics space

Single Gene testing



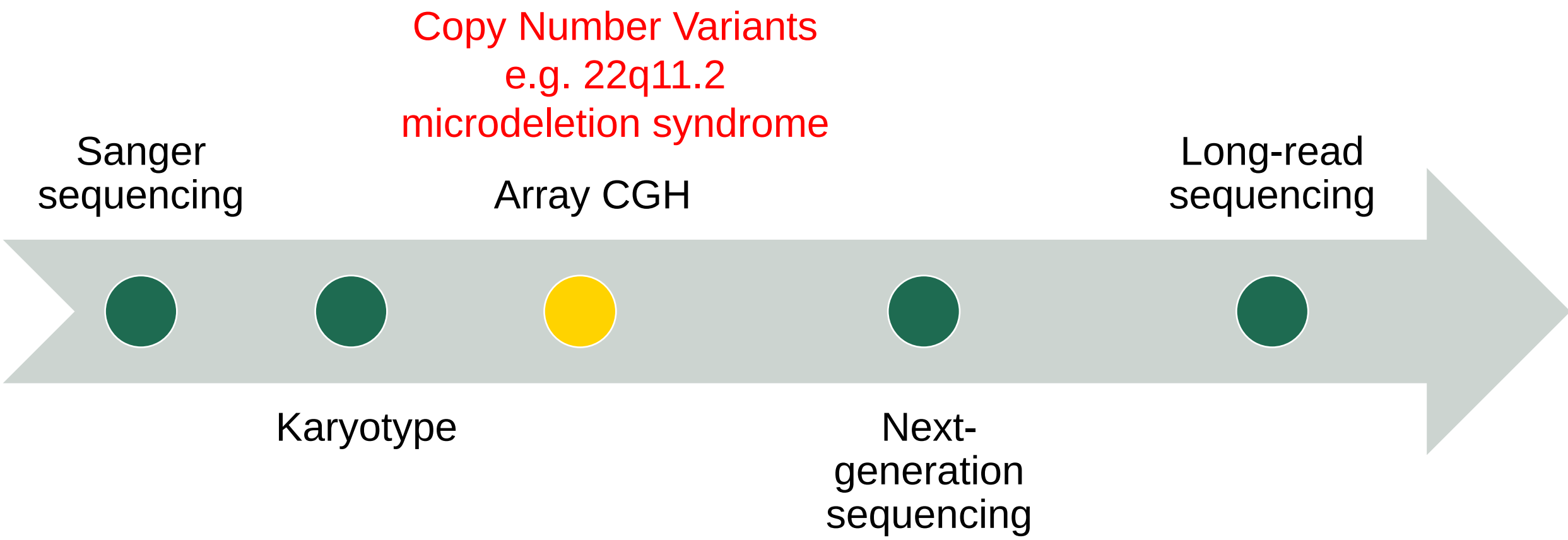
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Availability of tools in the clinical genetics space

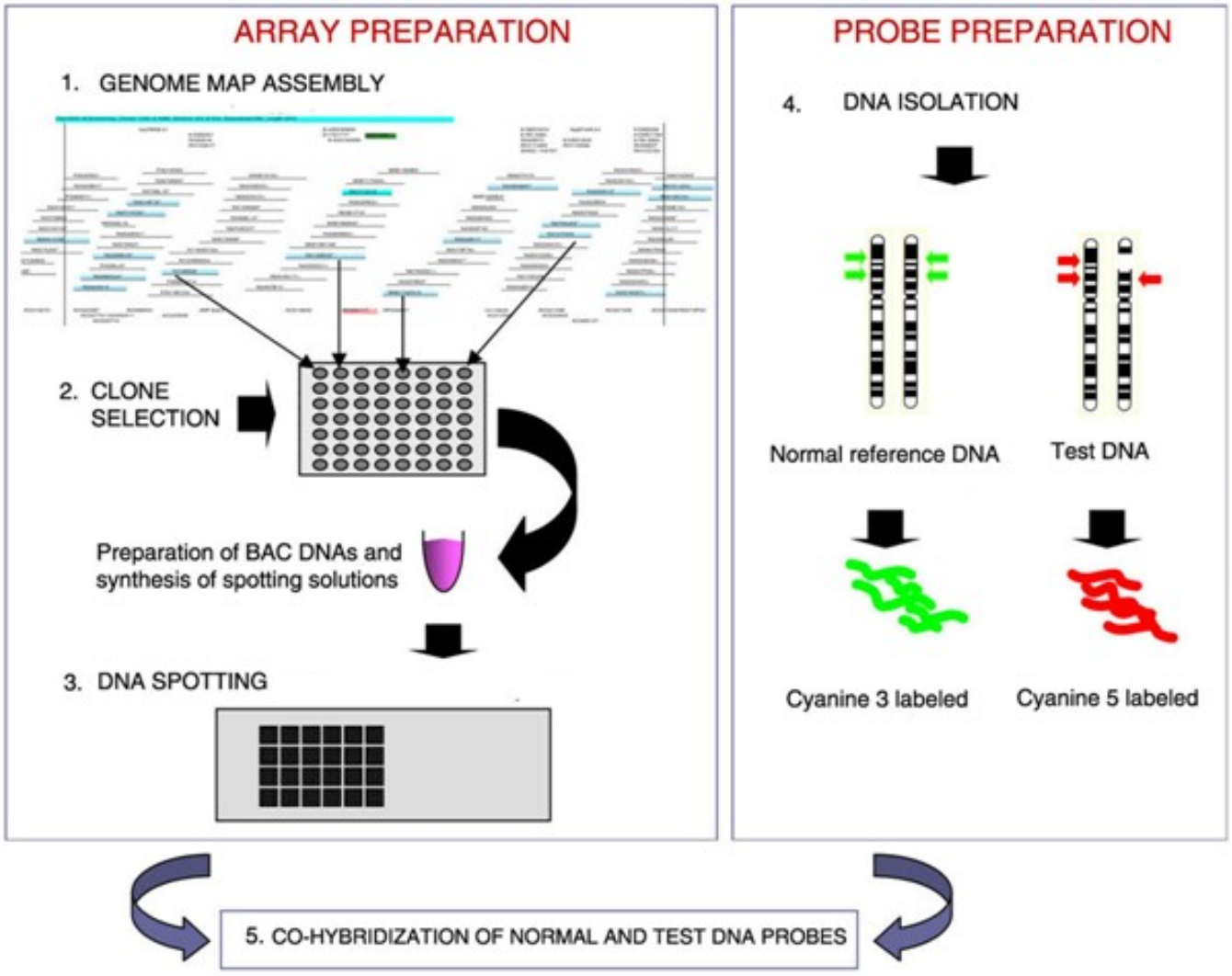


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Availability of tools in the clinical genetics space



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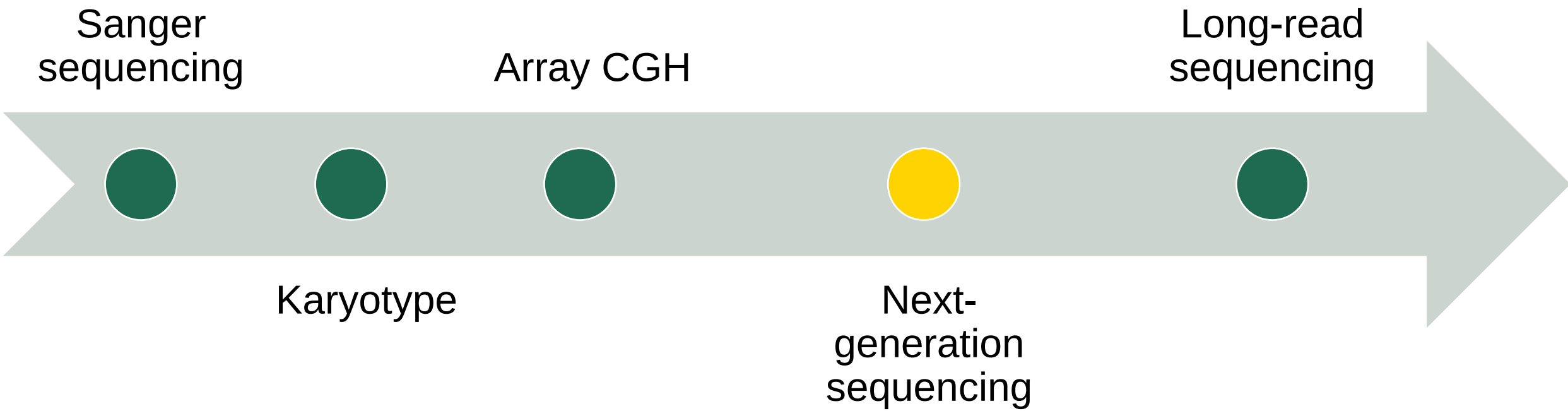


- Screen for copy gain/loss
- Detect Region of Homozygosity

https://embryology.med.unsw.edu.au/embryology/index.php?title=File:Steps_in_a_classic_array_CGH analysis_used_for_the_most_common_chromosomal_abnormalities.png

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Availability of tools in the clinical genetics space

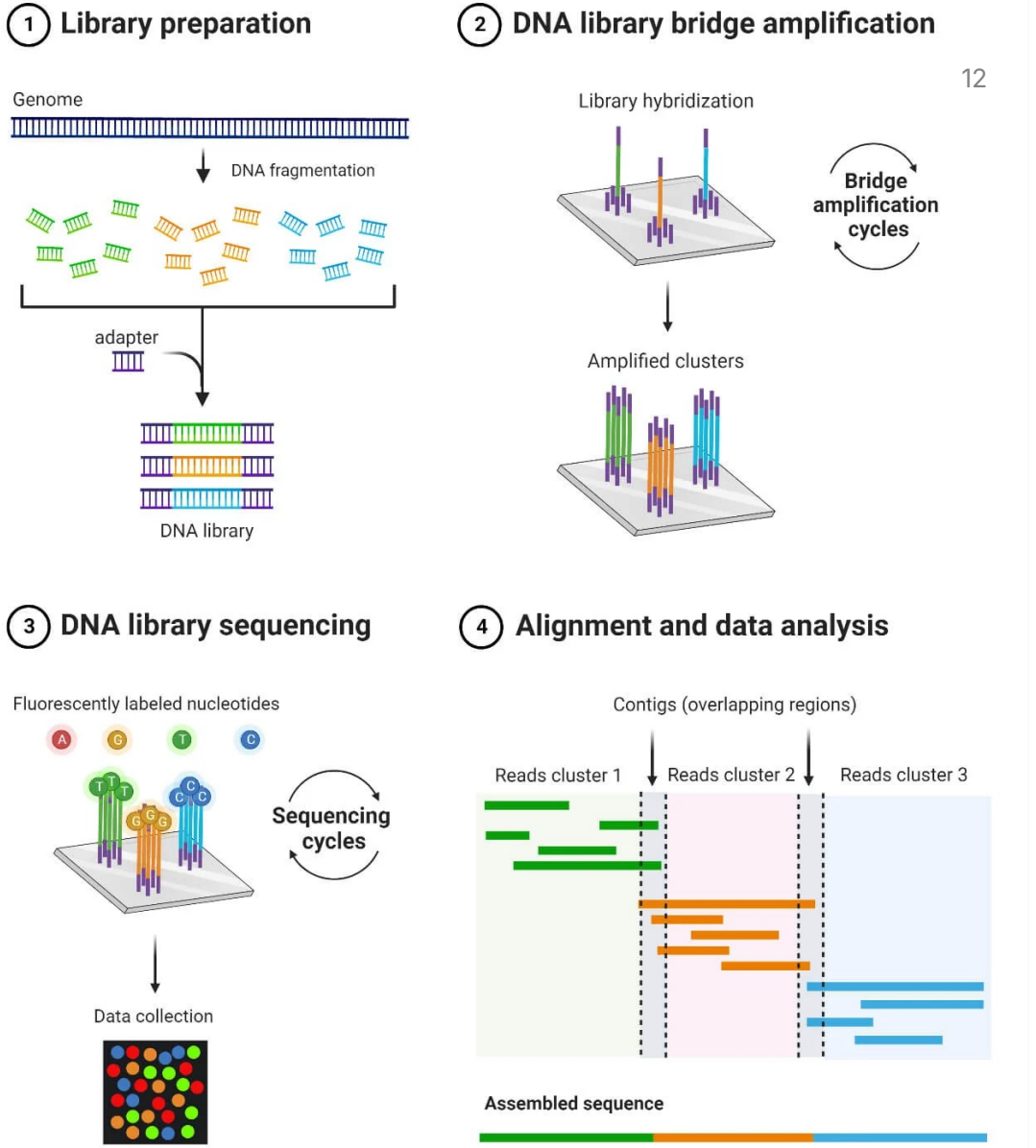


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Next-Generation Seq

- First generation (Sanger) sequencing read each DNA fragment on-by-one

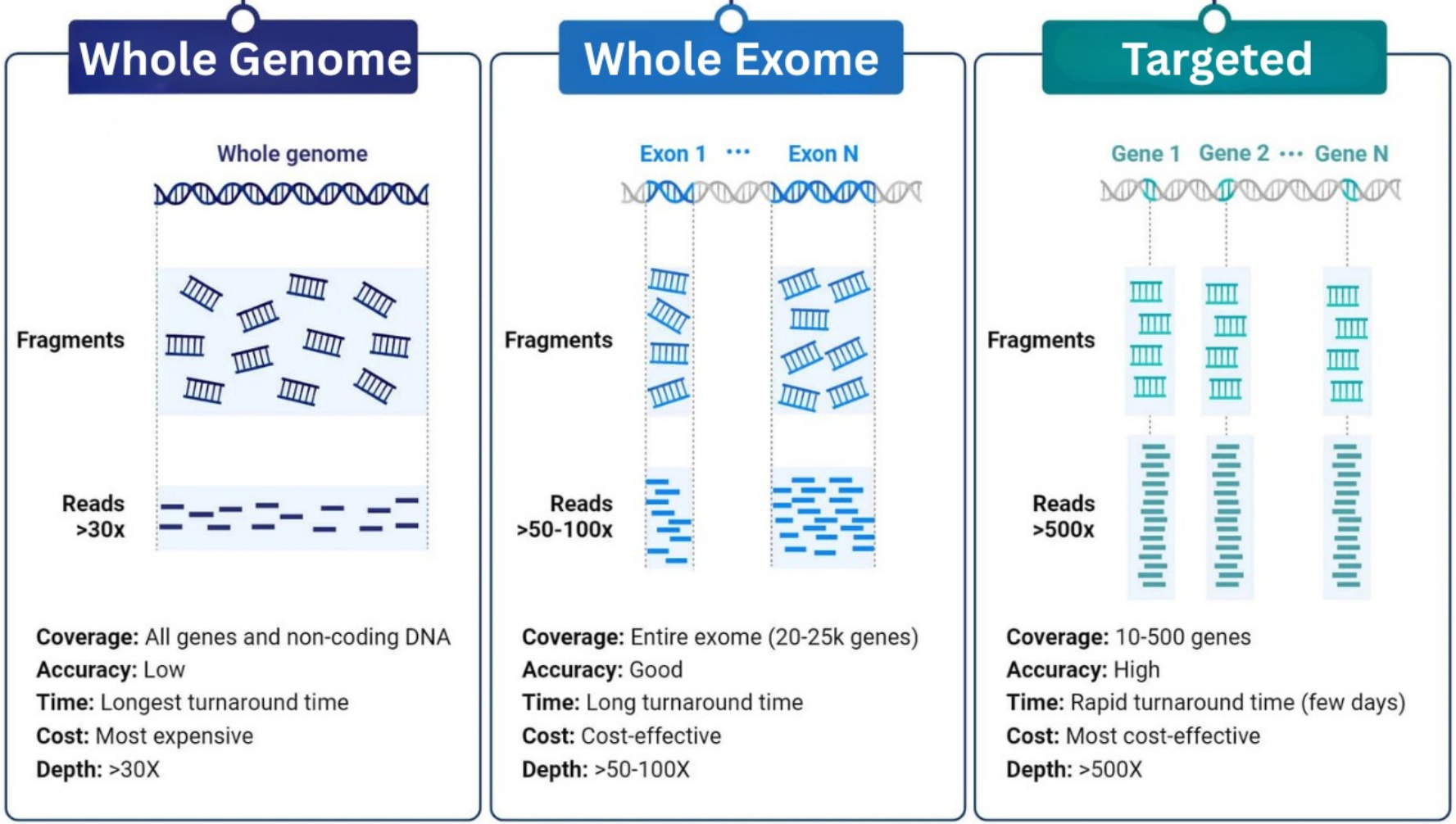
- Next-generation sequencing breaks down DNA into small pieces (50-300 base pairs) then reassemble



https://microbenotes.com/next-generation-sequencing-ngs/

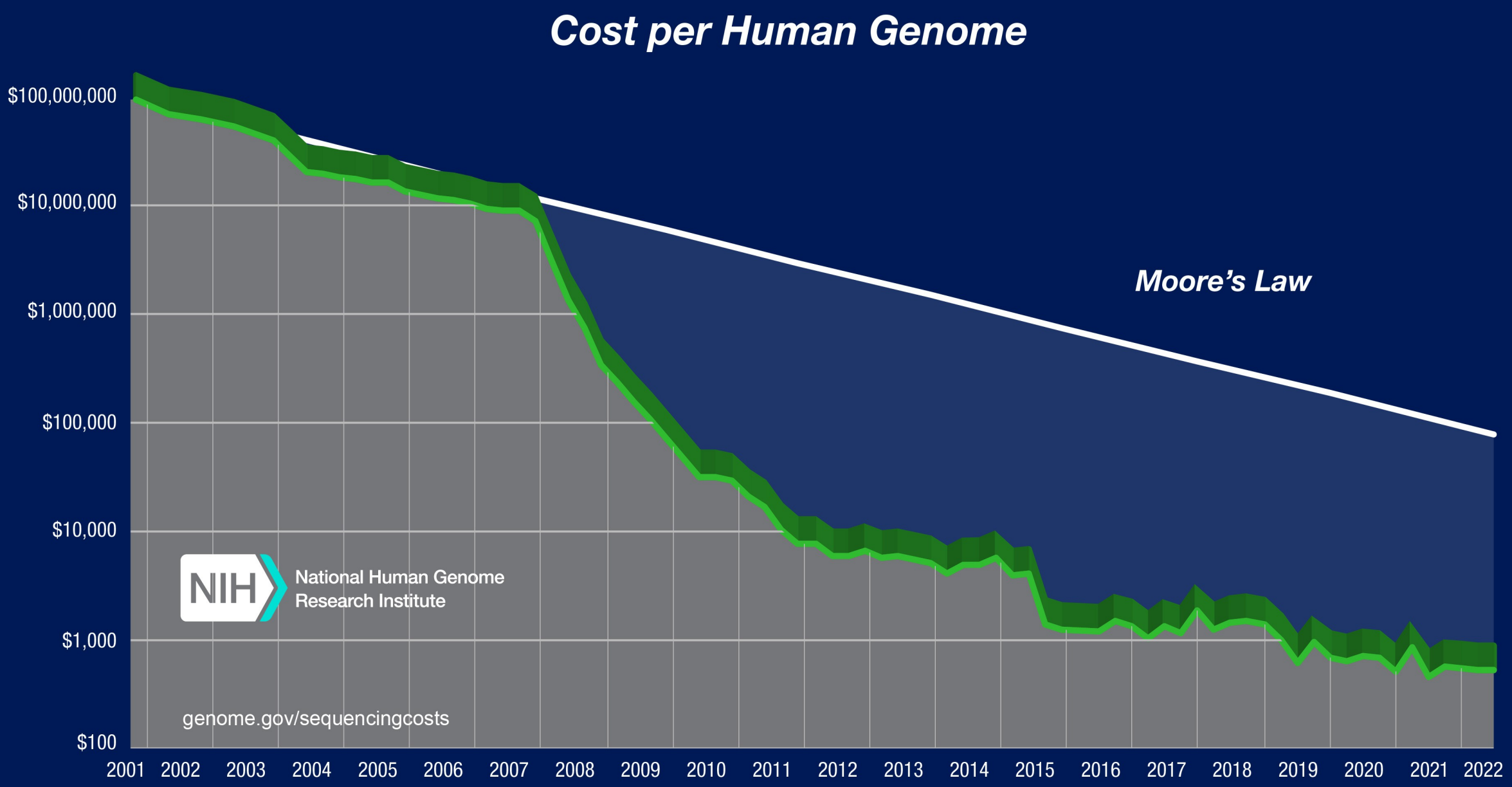
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DNA Sequencing

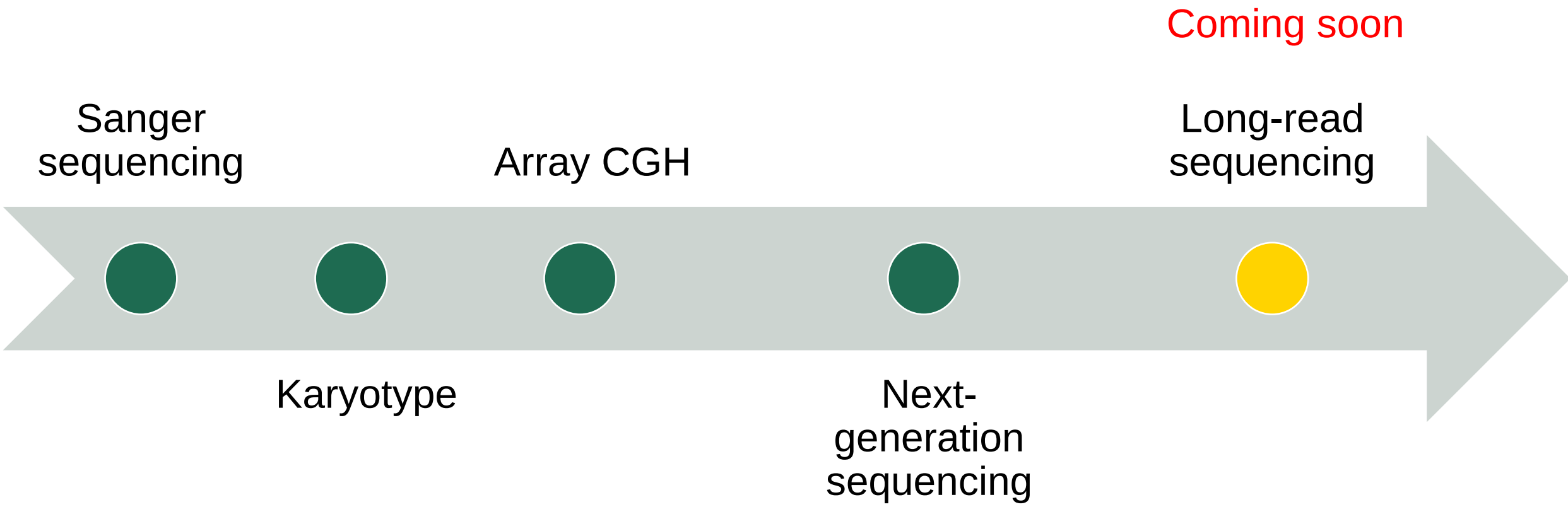


https://ngs101.com/how-to-analyze-whole-exome-sequencing-data-from-raw-reads-to-high-quality-variants-mutations-and-cnvs/

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Cost per Human Genome
$100,000,000
$10,000,000
$1,000,000
$100,000
$10,000
$1,000
$100
Moore's Law
NIH
National Human Genome
Research Institute
genome.gov/sequencingcosts
2001
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2022

Availability of tools in the clinical genetics space



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Roadmaps

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Current recommendations for undiagnosed IDD

ACMG
American College of Medical Genetics and Genomics

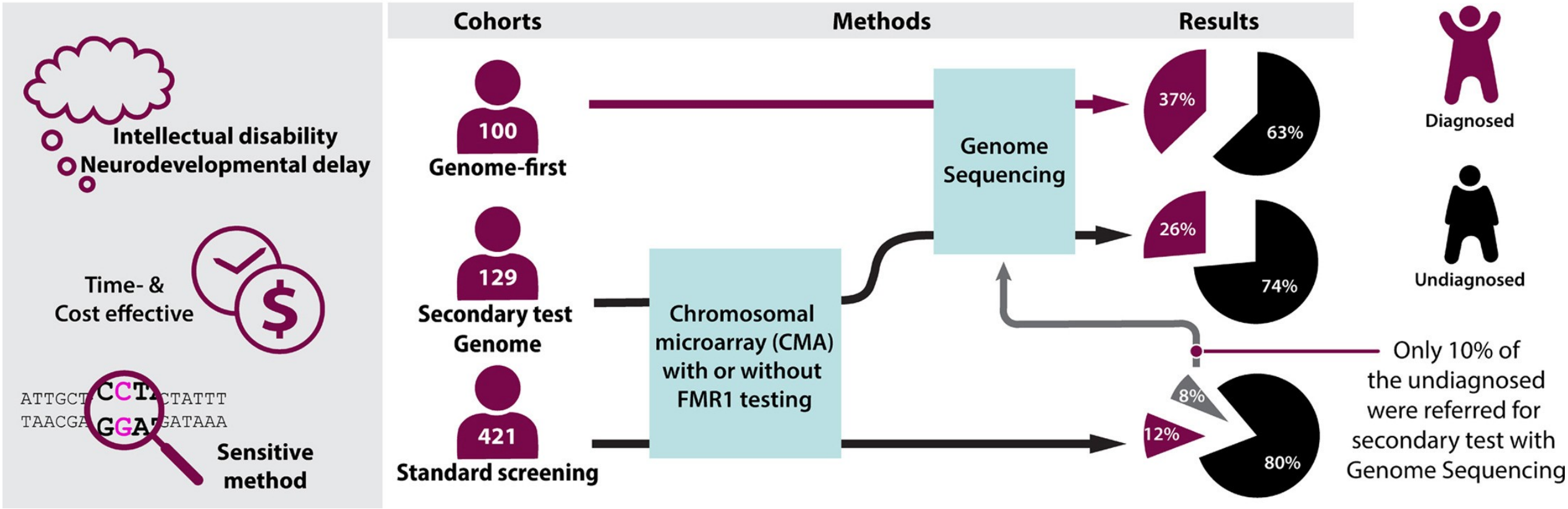
American Academy of Pediatrics
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American Academy of Neurology™

Canadian Paediatric Society

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Genome Sequencing is a sensitive first-line test to diagnose individuals with intellectual disability



Lindstrand A, Ek M, Kvarnung M, Anderlid BM, Björck E, Carlsten J, Eisfeldt J, Grigelioniene G, Gustavsson P, Hammarsjö A, Helgadóttir HT, Hellström-Pigg M, Kuchinskaya E, Lagerstedt-Robinson K, Levin LÅ, Lieden A, Lindelöf H, Malmgren H, Nilsson D, Svensson E, Paucar M, Sahlin E, Tesi B, Tham E, Winberg J, Winerdal M, Wincent J, Johansson Soller M, Pettersson M, Nordgren A. Genome sequencing is a sensitive first-line test to diagnose individuals with intellectual disability. Genet Med. 2022 Nov;24(11):2296-2307. doi: 10.1016/j.gim.2022.07.022. Epub 2022 Sep 6. PMID: 36066546.

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Array CGH in 2010

- Diagnostic yield of 15-20%

- Compared to 3% G-banded Karyotype

ARTICLE

Consensus Statement: Chromosomal Microarray Is a First-Tier Clinical Diagnostic Test for Individuals with Developmental Disabilities or Congenital Anomalies

David T. Miller,[1,*] Margaret P. Adam,[2,3] Swaroop Aradhya,[4] Leslie G. Biesecker,[5] Arthur R. Brothman,[6] Nigel P. Carter,[7] Deanna M. Church,[8] John A. Crolla,[9] Evan E. Eichler,[10] Charles J. Epstein,[11] W. Andrew Faucett,[2] Lars Feuk,[12] Jan M. Friedman,[13] Ada Hamosh,[14] Laird Jackson,[15] Erin B. Kaminsky,[2] Klaas Kok,[16] Ian D. Krantz,[17] Robert M. Kuhn,[18] Charles Lee,[19] James M. Ostell,[8] Carla Rosenberg,[20] Stephen W. Scherer,[21] Nancy B. Spinner,[17] Dimitri J. Stavropoulos,[22] James H. Tepperberg,[23] Erik C. Thorland,[24] Joris R. Vermeesch,[25] Darrel J. Waggoner,[26] Michael S. Watson,[27] Christa Lese Martin,[2] and David H. Ledbetter[2,*]

Chromosomal microarray (CMA) is increasingly utilized for genetic testing of individuals with unexplained developmental delay/intellectual disability (DD/ID), autism spectrum disorders (ASD), or multiple congenital anomalies (MCA). Performing CMA and G-banded karyotyping on every patient substantially increases the total cost of genetic testing. The International Standard Cytogenomic Array (ISCA) Consortium held two international workshops and conducted a literature review of 33 studies, including 21,698 patients tested by CMA. We provide an evidence-based summary of clinical cytogenetic testing comparing CMA to G-banded karyotyping with respect to technical advantages and limitations, diagnostic yield for various types of chromosomal aberrations, and issues that affect test interpretation. CMA offers a much higher diagnostic yield (15%–20%) for genetic testing of individuals with unexplained DD/ID, ASD, or MCA than a G-banded karyotype (~3%, excluding Down syndrome and other recognizable chromosomal syndromes), primarily because of its higher sensitivity for submicroscopic deletions and duplications. Truly balanced rearrangements and low-level mosaicism are generally not detectable by arrays, but these are relatively infrequent causes of abnormal phenotypes in this population (<1%). Available evidence strongly supports the use of CMA in place of G-banded karyotyping as the first-tier cytogenetic diagnostic test for patients with DD/ID, ASD, or MCA. G-banded karyotype analysis should be reserved for patients with obvious chromosomal syndromes (e.g., Down syndrome), a family history of chromosomal rearrangement, or a history of multiple miscarriages.

Introduction

Scope and Purpose

3%,[1] and ASD affects ~1:150 individuals.[2,3] Most patients lack sufficient specific history or features from physical examination to suggest a specific genetic (or non-genetic)

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Exome/Genome in 2021

- Estimated diagnostic yield of 34-43%
- Standard testing (Array CGH) was 21%

Genetics inMedicine

www.nature.com/gim

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ACMG PRACTICE GUIDELINE

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)

Kandamurugu Manickam[1,2], Monica R. McClain[3], Laurie A. Demmer[4], Sawona Biswas[5], Hutton M. Kearney[6], Jennifer Malinowski[7], Lauren J. Massingham[8,9], Danny Miller[10], Timothy W. Yu[11,12], Fuki M. Hisama[13] and ACMG Board of Directors[14]*

Disclaimer: The ACMG has recruited expert panels, chosen for their scientific and clinical expertise, to develop evidence-based guidelines (EBG) for clinical practice. An EBG focuses on a specific scientific question and then describes recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. ACMG EBGs are provided primarily as an educational resource for medical geneticists and other clinicians to help them provide quality medical services. They should not be considered inclusive of all relevant information on the topic reviewed.

Reliance on this EBG is completely voluntary and does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should consider the best available evidence, and apply his or her own professional judgment, taking into account the needs, preferences and specific clinical circumstances presented by the individual patient. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this EBG. Clinicians are also advised to take notice of the date this EBG was published, and to consider other medical and scientific information that becomes available after that date.

PURPOSE: To develop an evidence-based clinical practice guideline for the use of exome and genome sequencing (ES/GS) in the care of pediatric patients with one or more congenital anomalies (CA) with onset prior to age 1 year or developmental delay (DD) or intellectual disability (ID) with onset prior to age 18 years.

METHODS: The Pediatric Exome/Genome Sequencing Evidence-Based Guideline Work Group ($n = 10$) used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence to decision (EtD) framework based on the recent American College of Medical Genetics and Genomics (ACMG) systematic review, and an Ontario Health Technology Assessment to develop and present evidence summaries and health-care recommendations. The document underwent extensive internal and external peer review, and public comment, before approval by the ACMG Board of Directors.

RESULTS: The literature supports the clinical utility and desirable effects of ES/GS on active and long-term clinical management of patients with CA/DD/ID, and on family-focused and reproductive outcomes with relatively few harms. Compared with standard genetic testing, ES/GS has a higher diagnostic yield and may be more cost-effective when ordered early in the diagnostic evaluation.

CONCLUSION: We strongly recommend that ES/GS be considered as a first- or second-tier test for patients with CA/DD/ID.

Genetics in Medicine (2021) 23:2029–2037; https://doi.org/10.1038/s41436-021-01242-6

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Impact to active clinical management

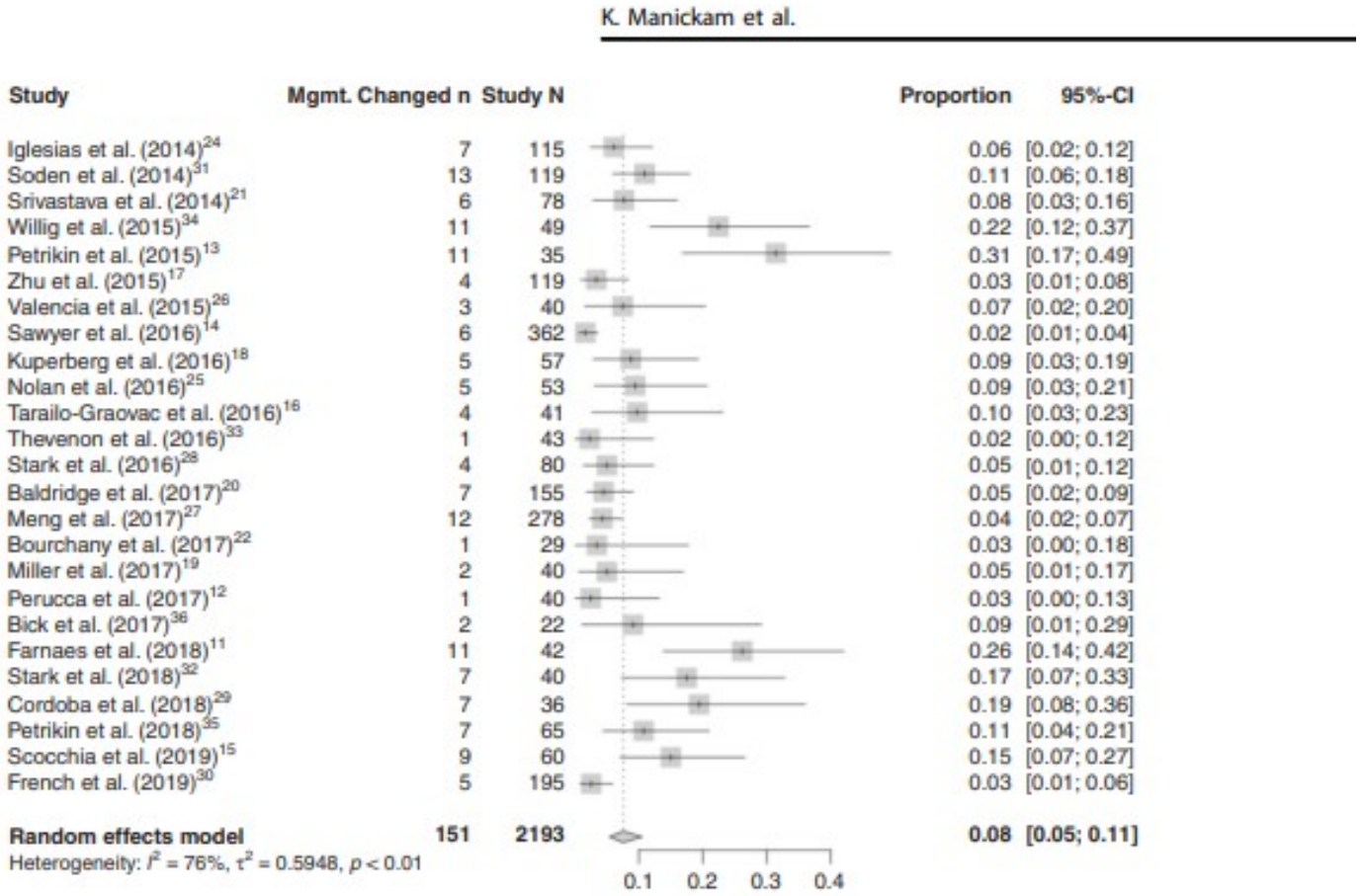


Fig. 1 Forest plot of included studies showing summation for active clinical management outcomes. *CI* confidence interval.

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Impact to monitoring/long-term outcomes

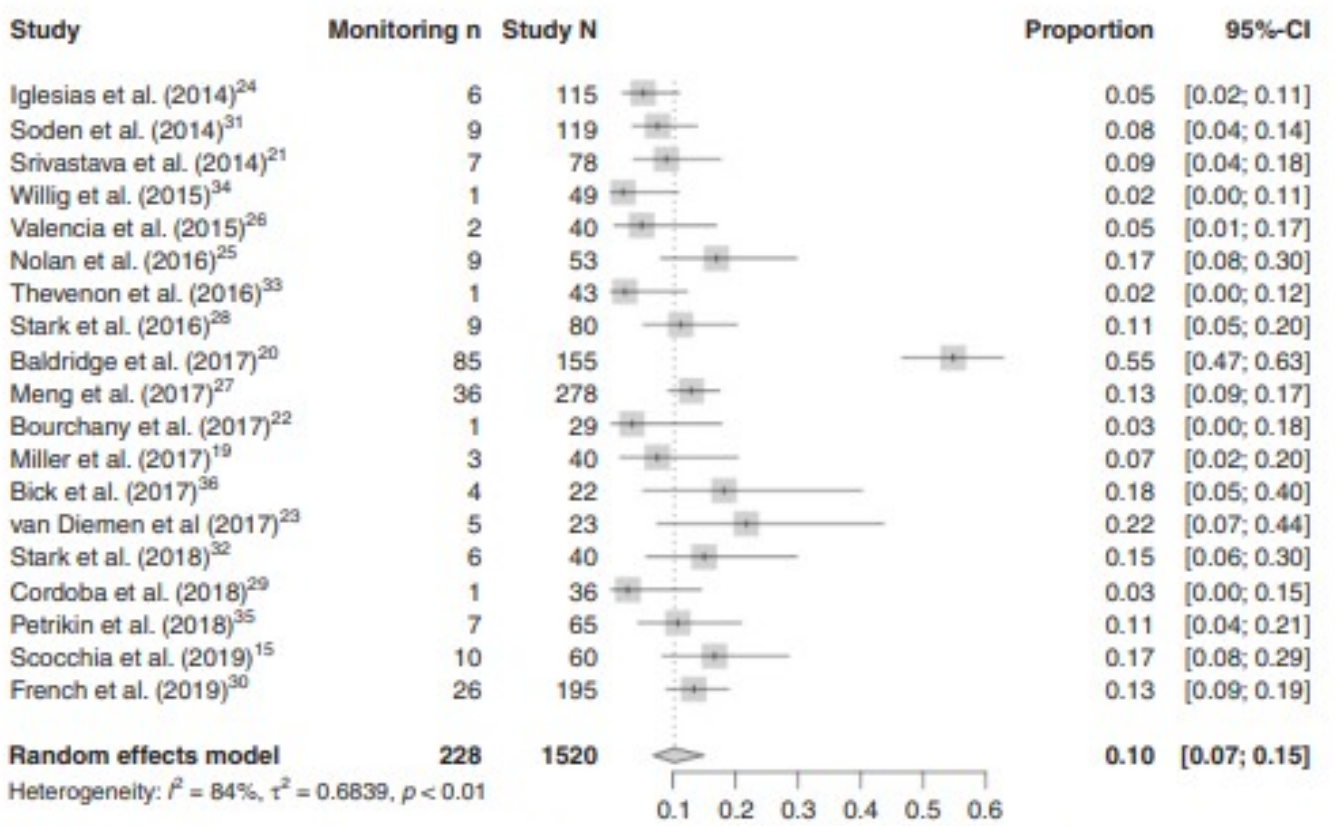


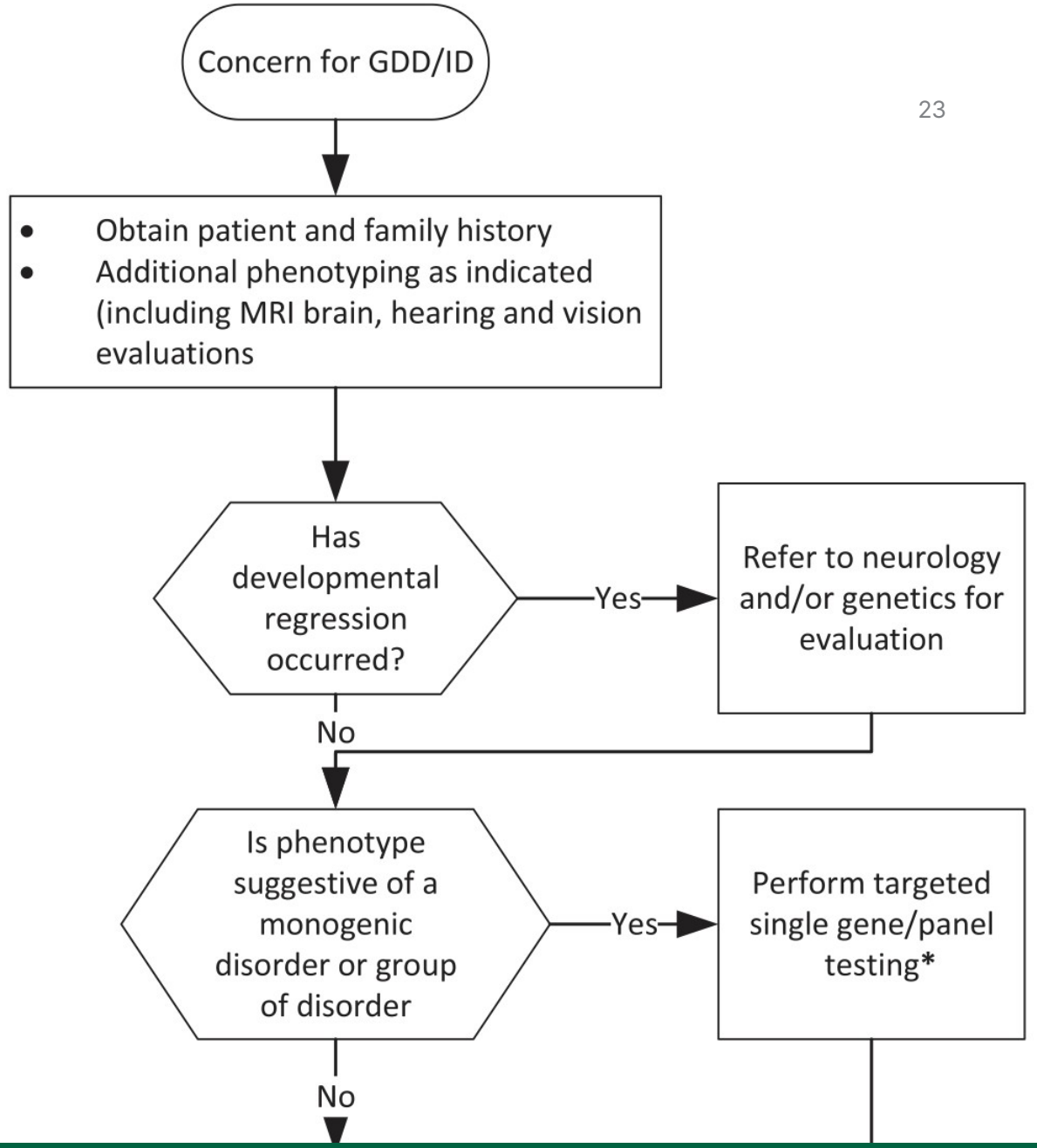
Fig. 2 Forest plot of included studies showing summation for monitoring and long-term clinical management outcomes. *CI* confidence interval.

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AAP recommended ES/GS + Array CGH in 2025

- Previous version was 2014

- Exome/Genome sequencing as first-tier testing (+ Array CGH)

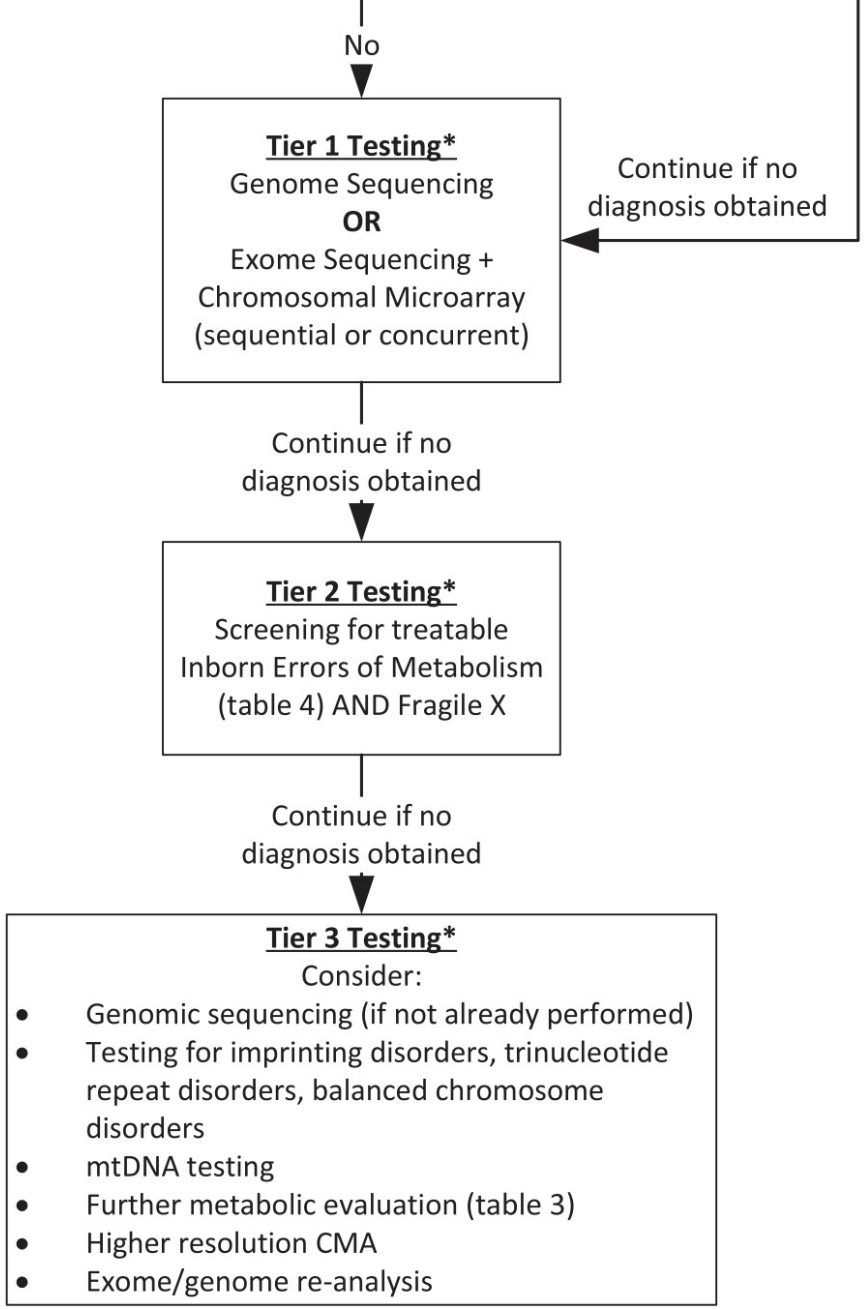


https://publications.aap.org/pediatrics/article/156/1/e2025072219/202230/Genetic-Evaluation-of-the-Child-With-Intellectual?autologincheck=redirected

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AAP recommended ES/GS + Array CGH in 2025

- Exome yielded 28-43%
- Genome with additional 10-20% yield



https://publications.aap.org/pediatrics/article/156/1/e2025072219/202230/Genetic-Evaluation-of-the-Child-With-Intellectual?autologincheck=redirected

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Diagnostic Dilemma…

ACMG Practice Guideline

October 2005 · Vol. 7 · No. 8

Fragile X syndrome: Diagnostic and carrier testing

Stephanie Sherman, PhD[1,2], Beth A. Pletcher, MD[1,3], and Deborah A. Driscoll, MD[1,4]

Key Words: *fragile X syndrome, genetic testing, FMR1, X-linked mental retardation*

Disclaimer: *This guideline is designed primarily as an educational resource for medical geneticists and other health care providers to help them provide quality medical genetic services. Adherence to this guideline does not necessarily assure a successful medical outcome. This guideline should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the geneticist should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from this guideline.*

RECOMMENDATIONS FOR DIAGNOSTIC TESTING

The purpose of these recommendations is to provide general guidelines to aid clinicians in making referrals for testing the repeat region of the FMR1 gene.

Individuals for Whom Testing Should Be Considered

Fragile X syndrome:

- Individuals of either sex with mental retardation, developmental delay, or autism, especially if they have (a) any physical or behavioral characteristics of fragile X syndrome, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.
- Individuals seeking reproductive counseling who have (a) a family history of fragile X syndrome or (b) a family history of undiagnosed mental retardation.
- Fetuses of known carrier mothers.
- Affected individuals or their relatives in the context of a positive cytogenetic fragile X test result who are seeking further counseling related to the risk of carrier status among themselves or their relatives. The cytogenetic test was used prior to the identification of the FMR1 gene and is significantly less accurate than the current DNA test. DNA testing on such individuals is warranted to accurately identify premutation carriers and to distinguish premutation from full mutation carrier women.

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EDITORIAL

CURRENT OPINION

Sometimes we should think of adults as big children

Pongtawat Lertwilaiwittaya[a,b] *and Nathaniel H. Robin*[a]

It is common saying in both internal medicine and pediatrics that children are not small adults, and adults are not large children. It is true considering that weight-based medication dosing calculation is more stringent in the pediatrics than internal medicine practice. But perhaps in one instance, adults should be considered just big children.

In the fast-paced adult primary care setting, past medical issues often take a back seat to the more immediate medical concerns such as hyper-

new adult with intellectual developmental disorder patients in our clinic was around 58% which was higher than what we have observed in the pediatric cohort which was estimated to be around 34–43% [2]. Iterative phenotyping at the result disclosure visit has also taught us that it is challenging to rely on dysmorphological examination in these adult patients as a tool to narrow down a potential differential diagnosis, as significant weight loss/gain, orthodontic surgery, and the effects of aging

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Existing literature in Adults with NDDE

www.nature.com/gim

Genetics inMedicine

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ARTICLE

The genetic landscape of intellectual disability and epilepsy in adults and the elderly: a systematic genetic work-up of 150 individuals

Pia Zacher[1,2✉], Thomas Mayer[1], Frank Brandhoff[1], Tobias Bartolomaeus[2,3], Diana Le Duc[2], Martin Finzel[1], Anja Heinze[2], Susanne Horn[2], Chiara Klöckner[2], Gudrun Körber[1], Julia Hentschel[2], Malgorzata Kalita[1], Ilona Krey[2], Marina Nastainczyk-Wulf[2,4], Konrad Platzer[2], Johannes Rebstock[1], Bernt Popp[2], Mathias Stiller[2], Anne-Christin Teichmann[2], Rami Abou Jamra[2] and Johannes R. Lemke[2,5✉]

PURPOSE: Genetic diagnostics of neurodevelopmental disorders with epilepsy (NDDE) are predominantly applied in children, thus limited information is available regarding adults or elderly.
METHODS: We investigated 150 adult/elderly individuals with NDDE by conventional karyotyping, *FMR1* testing, chromosomal microarray, panel sequencing, and for unresolved cases, also by exome sequencing ($n_{single} = 71$, $n_{trios} = 24$).
RESULTS: We identified (likely) pathogenic variants in 71 cases (47.3%) comprising fragile X syndrome ($n = 1$), disease-causing copy number ($n = 23$), and single-nucleotide variants ($n = 49$). Seven individuals displayed multiple independent genetic diagnoses. The diagnostic yield correlated with the severity of intellectual disability. Individuals with anecdotal evidence of exogenic early-life events (e.g., nuchal cord, complications at delivery) with alleged/unproven association to the disorder had a particularly high yield of 58.3%. Screening for disease-specific comorbidities was indicated in 45.1% and direct treatment consequences arose in 11.8% of diagnosed individuals.
CONCLUSION: Panel/exome sequencing displayed the highest yield and should be considered as first-tier diagnostics in NDDE. This high yield and the numerous indications for additional screening or treatment modifications arising from genetic diagnoses indicate a current medical undersupply of genetically undiagnosed adult/elderly individuals with NDDE. Moreover, knowledge of the course of elderly individuals will ultimately help in counseling newly diagnosed individuals with NDDE.

Genetics in Medicine (2021) 23:1492–1497; https://doi.org/10.1038/s41436-021-01153-6

INTRODUCTION

MATERIALS AND METHODS

- Average age 41 years
- Include Karyotype, Array CGH, FMR1, Exome, Genome

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Prior review of Adult NDDE

Diagnostic Yield of 47.3%

Diagnosis included:

- One *FMR1* at >280 CGG repeats (61 yo male)
- 24 individuals with disease-causing CNVs (16%)
- Coffin-Siris syndrome, *SCN1A*, *PTEN*
- 80 yo with *GLUT1* deficiency

Higher yield in a more severe level of IDD

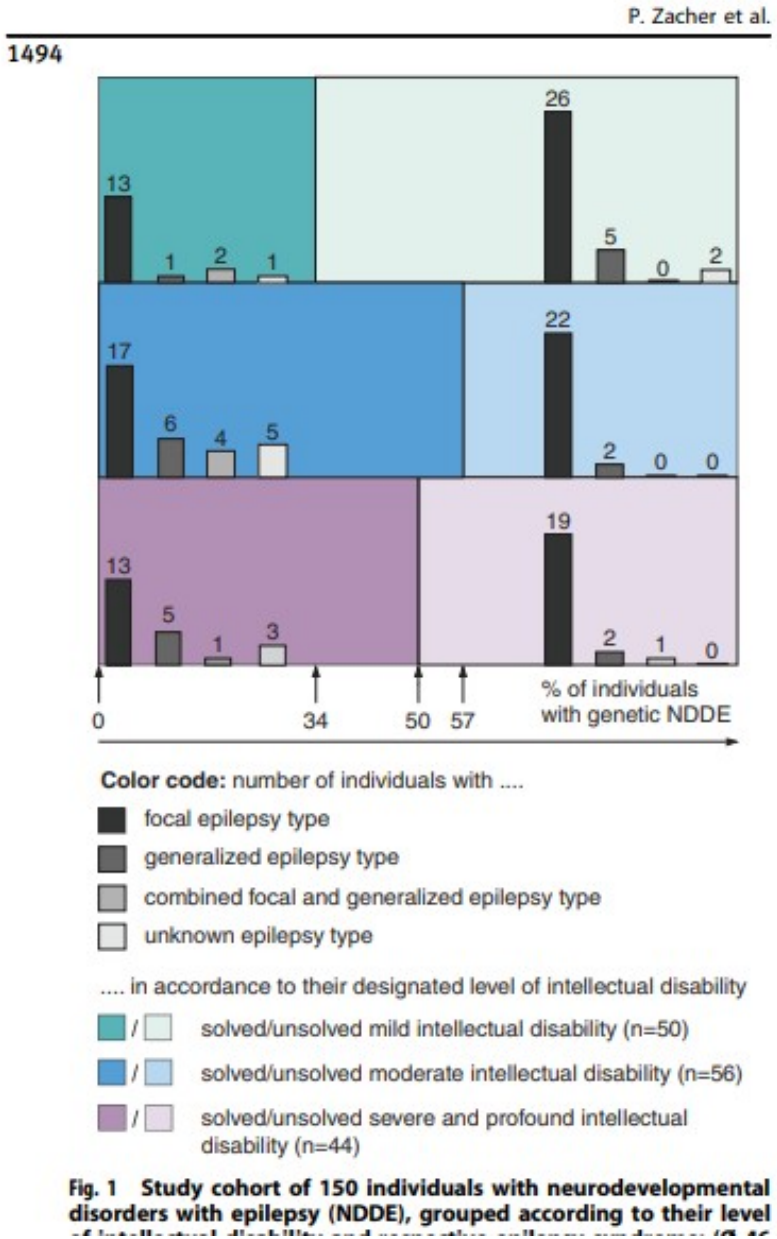


Fig. 1 Study cohort of 150 individuals with neurodevelopmental disorders with epilepsy (NDDE), grouped according to their level

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Roadmaps

1. Footsteps in genetic and genomics
2. Current recommendations for genetic testing in Adults with IDD
3. Clinical pearls from UAB Adult Genetics clinic
4. Gaps in care for Adults with IDD and Resources



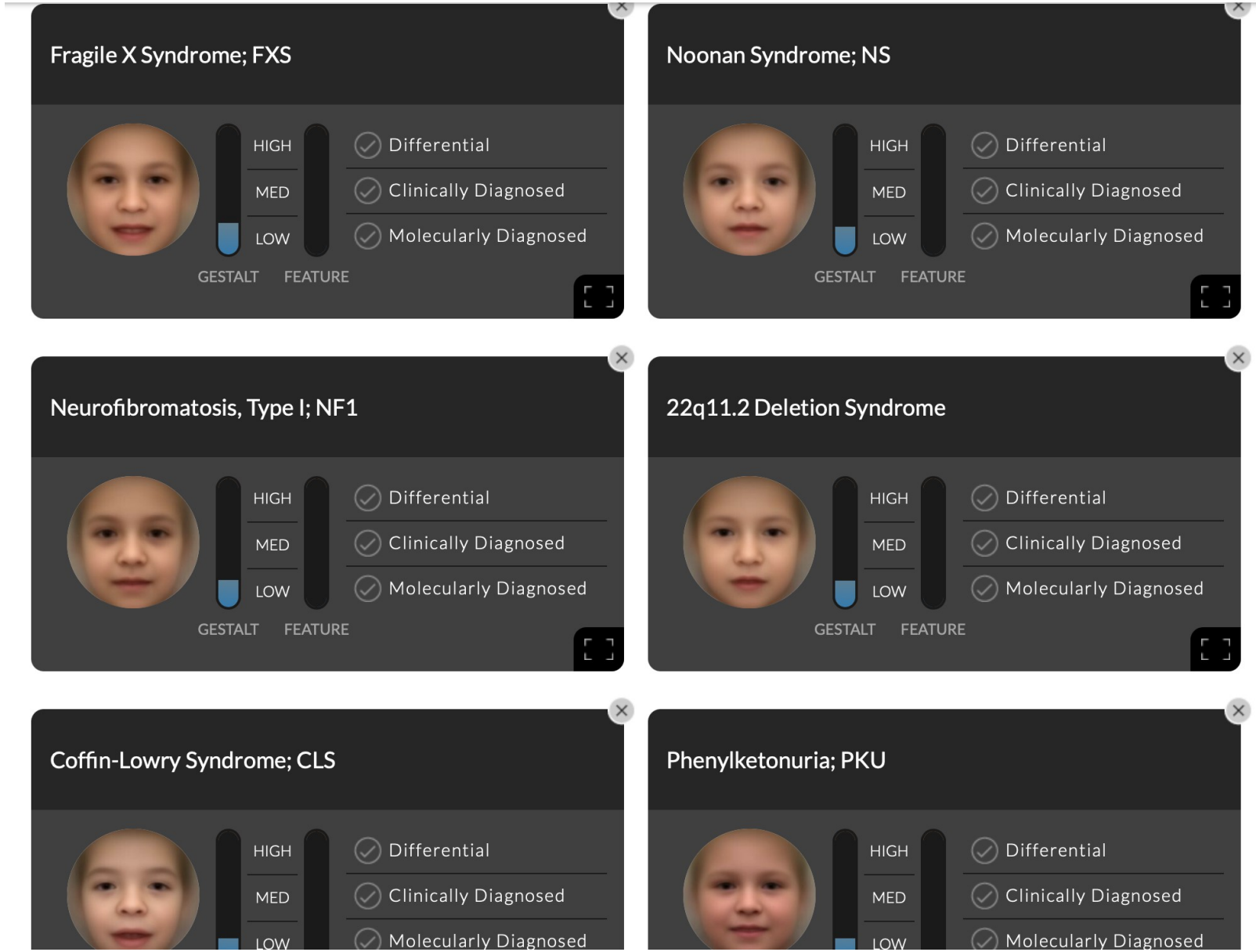
Case 1: 22 yo Female

- History/Physical Examination not in the learner slide

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Dysmorphology

- Important skills for clinical geneticist
- Knowledge base on pediatric population, with limited diversity in literature



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Why targeted approach is challenging

OMIM Gene Map Statistics

OMIM Morbid Map Scorecard (Updated October 30th, 2026) :

Total number of phenotypes* for which the molecular basis is known	7,771
Total number of genes with phenotype-causing mutation	5,099
* Phenotypes include (1) single-gene mendelian disorders and traits; (2) susceptibilities to cancer and complex disease (e.g., BRCA1 and familial breast-ovarian cancer susceptibility, 113705.0001, and CFH and macular degeneration, 134370.0008); (3) variations that lead to abnormal but benign laboratory test values ("nondiseases") and blood groups (e.g., lactate dehydrogenase B deficiency, 150100.0001 and ABO blood group system, 110300.0001); and (4) select somatic cell genetic disease (e.g., GNAS and McCune-Albright syndrome, 139320.0008 and IDH1 and glioblastoma multiforme, 147700.0001.)	

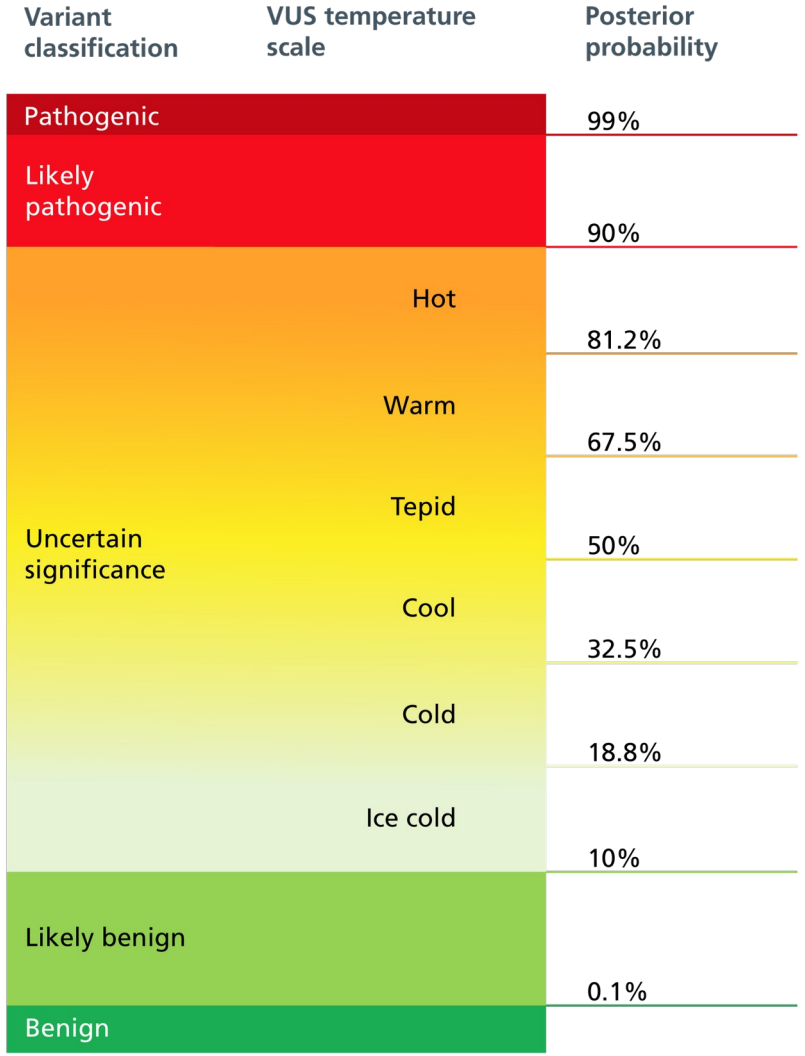
Distribution of Phenotypes across Genes (Updated October 30th, 2026) :

Number of genes with 1 phenotype	3,586
Number of genes with 2 phenotypes	918
Number of genes with 3 phenotypes	340
Number of genes with 4+ phenotypes	255

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Interpreting Genetics testing – ACMG variants

- In 2015, ACMG issued standard guidelines for variant interpretation
- Complex scoring system (prior report, functional data, epidemiology, computational…)



Richards S. et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-24. doi: 10.1038/gim.2015.30.

https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/variant-of-uncertain-significance-vus/

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OMIM®

An Online Catalog of Human Genes and Genetic Disorders

Updated November 2nd, 2026

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Need help? : Example Searches, OMIM Search Help, OMIM Video Tutorials

Mirror site : https://mirror.omim.org

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McKUSICK-NATHANS Department of Genetic Medicine

JOHNS HOPKINS MEDICINE

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Case 1: Revisit



GeneReviews® [Internet].

Show details

GeneReviews by Title

Search GeneReviews

GeneReviews Advanced Search Help

Okur-Chung Neurodevelopmental Syndrome

Synonym: *CSNK2A1*-Related Neurodevelopmental Syndrome

Wendy Chung, MD, PhD, FACMG and Volkan Okur, MD, FACMG.

Author Information and Affiliations

Initial Posting: June 9, 2022.

Estimated reading time: 21 minutes

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Case 1: Revisit

CSNK2A1 FOUNDATION

Understanding Okur-Chung Neurodevelopmental Syndrome



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Clinical pearls

- Targeted testing base on clinical dysmorphology is challenging in Adult with ID
- Be careful of pathogenic/likely pathogenic and VUS report
- There may be more than 1 diagnosis in a patient, avoid premature closure

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Case 2: 36 yo male with DD/IDD/CP/Epilepsy

- History/Physical Examination not in the learner slide

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Case 2:



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Case 2:

GeneReviews® [Internet].

Show details

GeneReviews by Title

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Creatine Deficiency Disorders

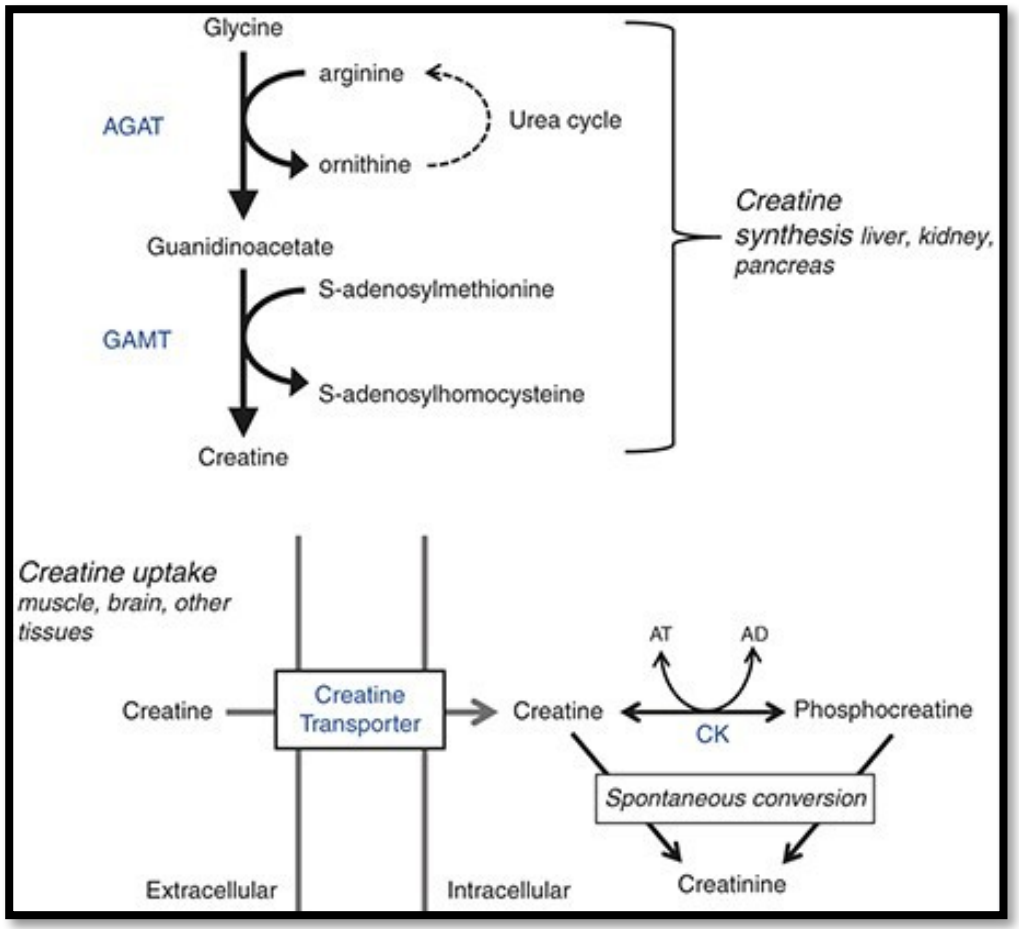
Synonym: Cerebral Creatine Deficiency Disorders

Saadet Mercimek-Andrews, MD, PhD, FCCMG, FRCPC and Gajja S Salomons, PhD.

Author Information and Affiliations

Initial Posting: January 15, 2009; Last Revision: August 7, 2025.

Estimated reading time: 38 minutes



CRTR deficiency. CRTR deficiency has been studied in many cohorts ranging from 49 to 4,426 individuals with familial or nonfamilial ID. These studies were summarized by van de Kamp et al [2014]; the prevalence in males with ID was estimated between 0.4% and 1.4%. In a recent study, the prevalence of creatine transporter deficiency was 2.64% in individuals with neurodevelopmental disorders [Bahl et al 2020].

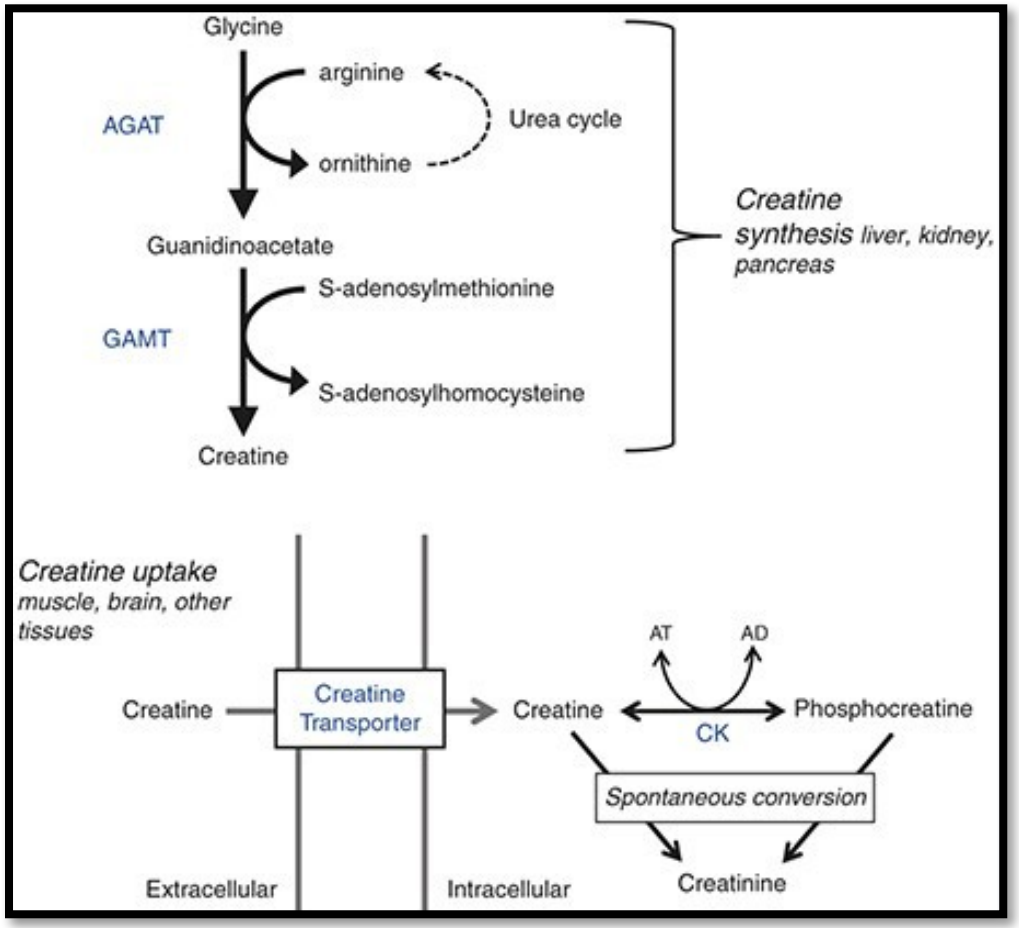
https://www.ncbi.nlm.nih.gov/books/NBK3794/

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Case 2: Follow up in the STEP/Genetics clinic

- Blood for Plasma Amino acid level was obtained

- Creatine supplementation was started at 5 g daily, referring to Metabolic clinic for Glycine/Arginine supplementation



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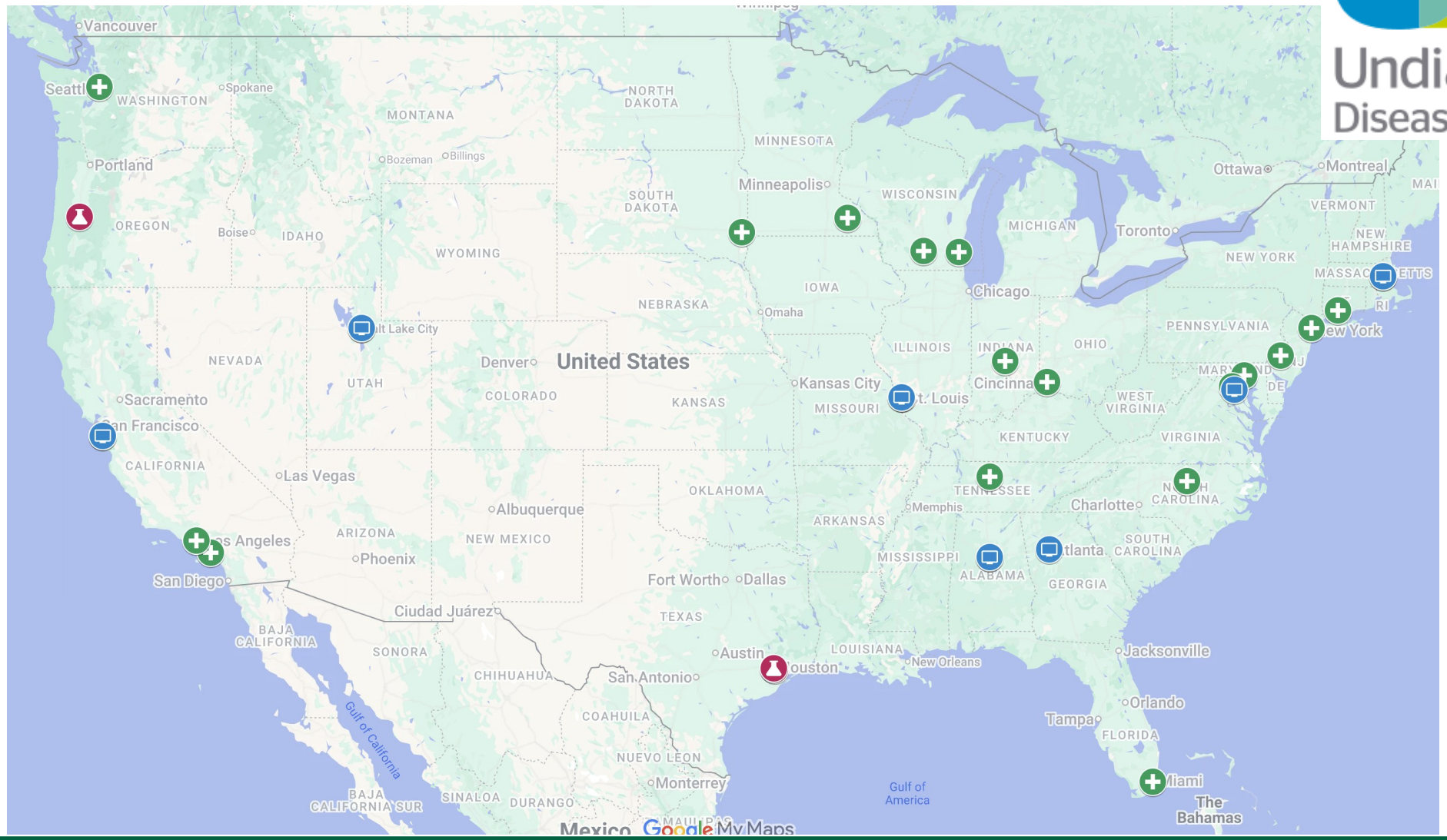
Clinical pearls

- Inherited disorder may run in the family with intrafamilial variability. Be careful during pretest genetic counseling
- Do not stop at an unconvincing molecular diagnosis
- Certain disorders are treatable, and genetic referral is highly encouraged

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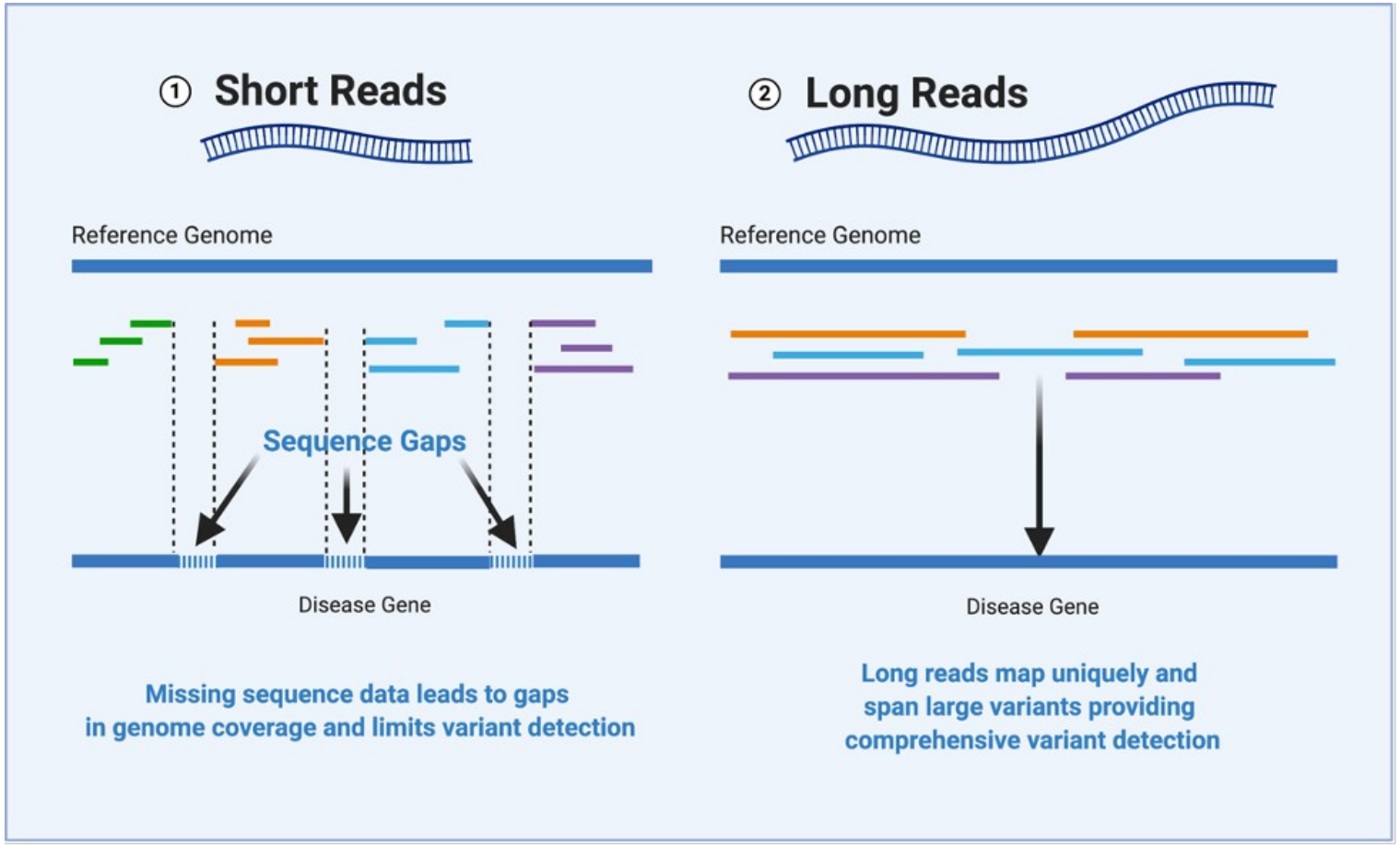
Case 3 (Undiagnosed Disease Network)

Undiagnosed Diseases Network



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Long read Genome sequencing (AGHI)



HUDSONALPHA
INSTITUTE FOR BIOTECHNOLOGY

Alabama Genomic
HEALTH INITIATIVE

https://www.hudsonalpha.org/hudsonalpha-researchers-use-highly-accurate-long-read-sequencing-technology-to-help-diagnose-rare-disease/

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Diagnostic Dilemma…

ACMG Practice Guideline

October 2005 · Vol. 7 · No. 8

Fragile X syndrome: Diagnostic and carrier testing

Stephanie Sherman, PhD[1,2], Beth A. Pletcher, MD[1,3], and Deborah A. Driscoll, MD[1,4]

Key Words: *fragile X syndrome, genetic testing, FMR1, X-linked mental retardation*

Disclaimer: *This guideline is designed primarily as an educational resource for medical geneticists and other health care providers to help them provide quality medical genetic services. Adherence to this guideline does not necessarily assure a successful medical outcome. This guideline should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the geneticist should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from this guideline.*

RECOMMENDATIONS FOR DIAGNOSTIC TESTING

The purpose of these recommendations is to provide general guidelines to aid clinicians in making referrals for testing the repeat region of the FMR1 gene.

Individuals for Whom Testing Should Be Considered

Fragile X syndrome:

- Individuals of either sex with mental retardation, developmental delay, or autism, especially if they have (a) any physical or behavioral characteristics of fragile X syndrome, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.
- Individuals seeking reproductive counseling who have (a) a family history of fragile X syndrome or (b) a family history of undiagnosed mental retardation.
- Fetuses of known carrier mothers.
- Affected individuals or their relatives in the context of a positive cytogenetic fragile X test result who are seeking further counseling related to the risk of carrier status among themselves or their relatives. The cytogenetic test was used prior to the identification of the FMR1 gene and is significantly less accurate than the current DNA test. DNA testing on such individuals is warranted to accurately identify premutation carriers and to distinguish premutation from full mutation carrier women.

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What are being missed in clinical short read ES

Repeat expansion disorders

- Huntington disease
- Huntington disease phenocopy
- C9orf72 repeat expansion disorder (Frontotemporal dementia – ALS)

Complex rearrangement

Deep intronic variant, Epigenetic modification…

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Clinical pearls

- Newer sequencing techniques are coming, patient with previous negative genetic diagnosis should be referred/followed by genetic team

- We miss 100% of what we don’t test for… Fragile X syndrome?

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Table 1. Potential benefits in making a genetic diagnosis

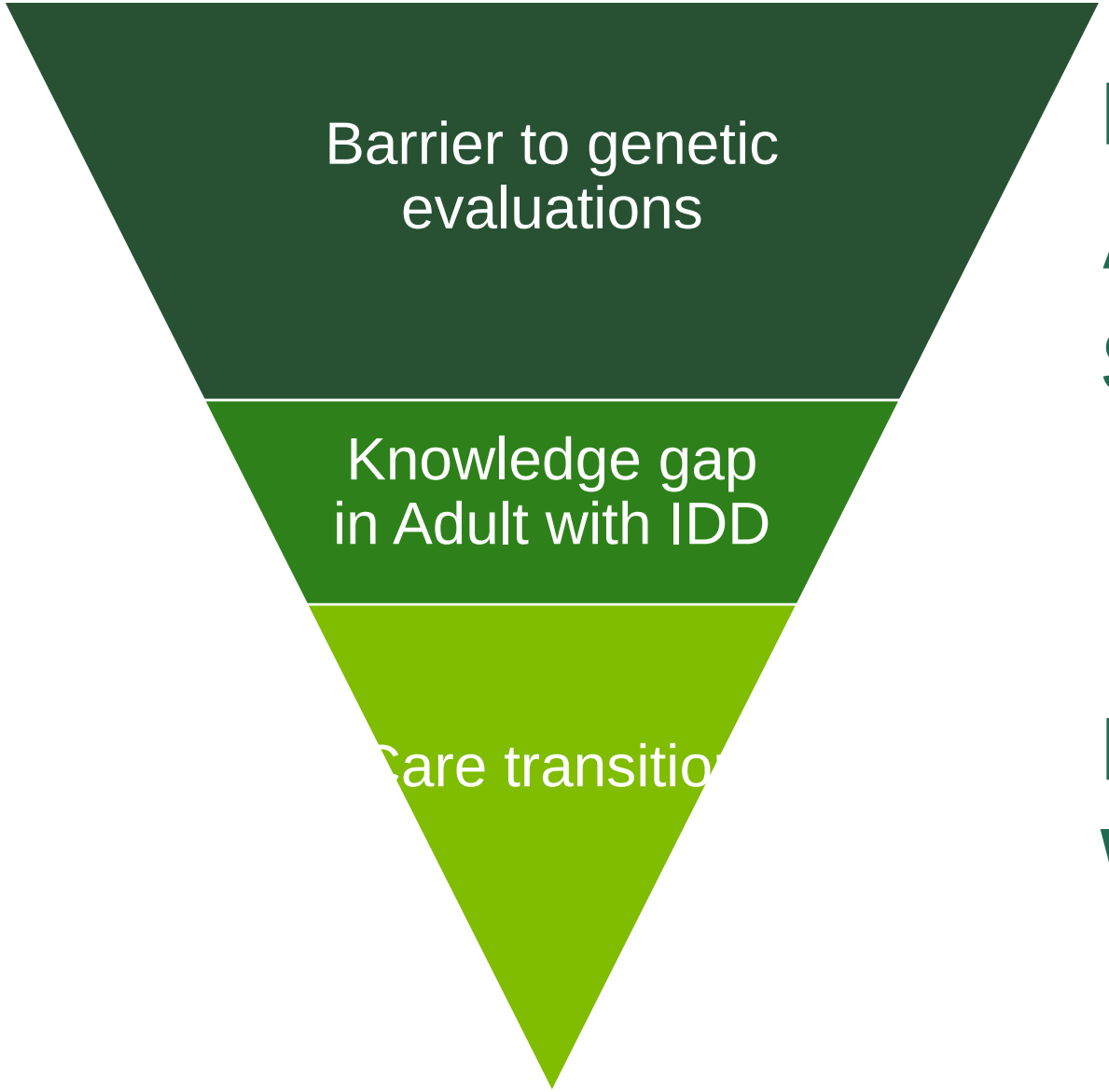
Potential benefits	Examples from our experience
Improved prognosis through targeted treatment	Identification of the *SCN1A* seizure disorder guided epileptologist in choice of antiepileptic drugs and dietary management (ketogenic diet). Identification of cerebral creatine deficiency disorders in a separate patient allowed for specific nutritional management
Improved targeted screening/long term management	Diagnosis of Phelan-McDermid syndrome with ring chromosome 22 allowed for targeted cancer screening of NF2-related brain tumor
Recurrence risk counseling/reproductive-focused outcomes	Diagnosis of Angelman syndrome allowed for more accurate recurrence risk for the patient's unaffected sibling
Access correct support groups	Diagnosis of Okur-Chung neurodevelopmental syndrome allowed parent to connect to a specific patient resource (https://www.csnk2a1foundation.org)
Answer the question "Why"	Diagnosis of Williams syndrome in a 58-year-old man. His NDD had been attributed to maternal alcohol use, a burden his 83-year-old mother had carried

NDD, neurodevelopmental disability.

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Roadmaps

1. Footsteps in genetic and genomics
2. Current recommendations for genetic testing in Adults with IDD
3. Clinical pearls from UAB Adult Genetics clinic
4. **Gaps in care for Adults with IDD and Resources**



Lack of awareness

Availability of geneticists

Socioeconomics

Lack of providers familiar with rare diseases

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In-press

EDITORIAL

All undiagnosed Adults with IDD should have genetics evaluation

CURRENT OPINION

Sometimes we should think of adults as big children

Pongtawat Lertwilaiwittaya[a,b] *and Nathaniel H. Robin*[a]

It is common saying in both internal medicine and pediatrics that children are not small adults, and adults are not large children. It is true considering that weight-based medication dosing calculation is more stringent in the pediatrics than internal medicine practice. But perhaps in one instance, adults should be considered just big children.

In the fast-paced adult primary care setting, past medical issues often take a back seat to the more immediate medical concerns such as hyper-

new adult with intellectual developmental disorder patients in our clinic was around 58% which was higher than what we have observed in the pediatric cohort which was estimated to be around 34–43% [2]. Iterative phenotyping at the result disclosure visit has also taught us that it is challenging to rely on dysmorphological examination in these adult patients as a tool to narrow down a potential differential diagnosis, as significant weight loss/ gain, orthodontic surgery, and the effects of aging

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Clinical Genetics service in Alabama

UAB Genetics, Birmingham, AL

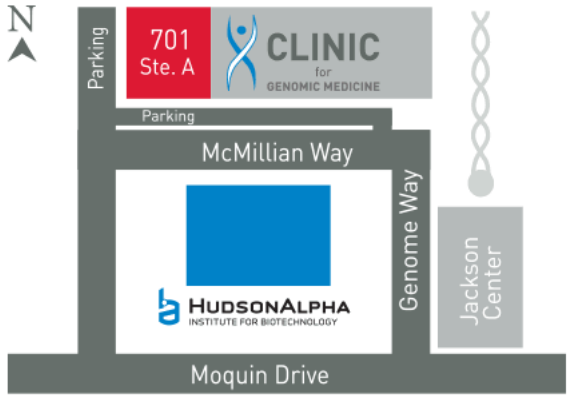
- Telephone 205-934-4983



STEP clinic (Genetics every 4th Wednesday)

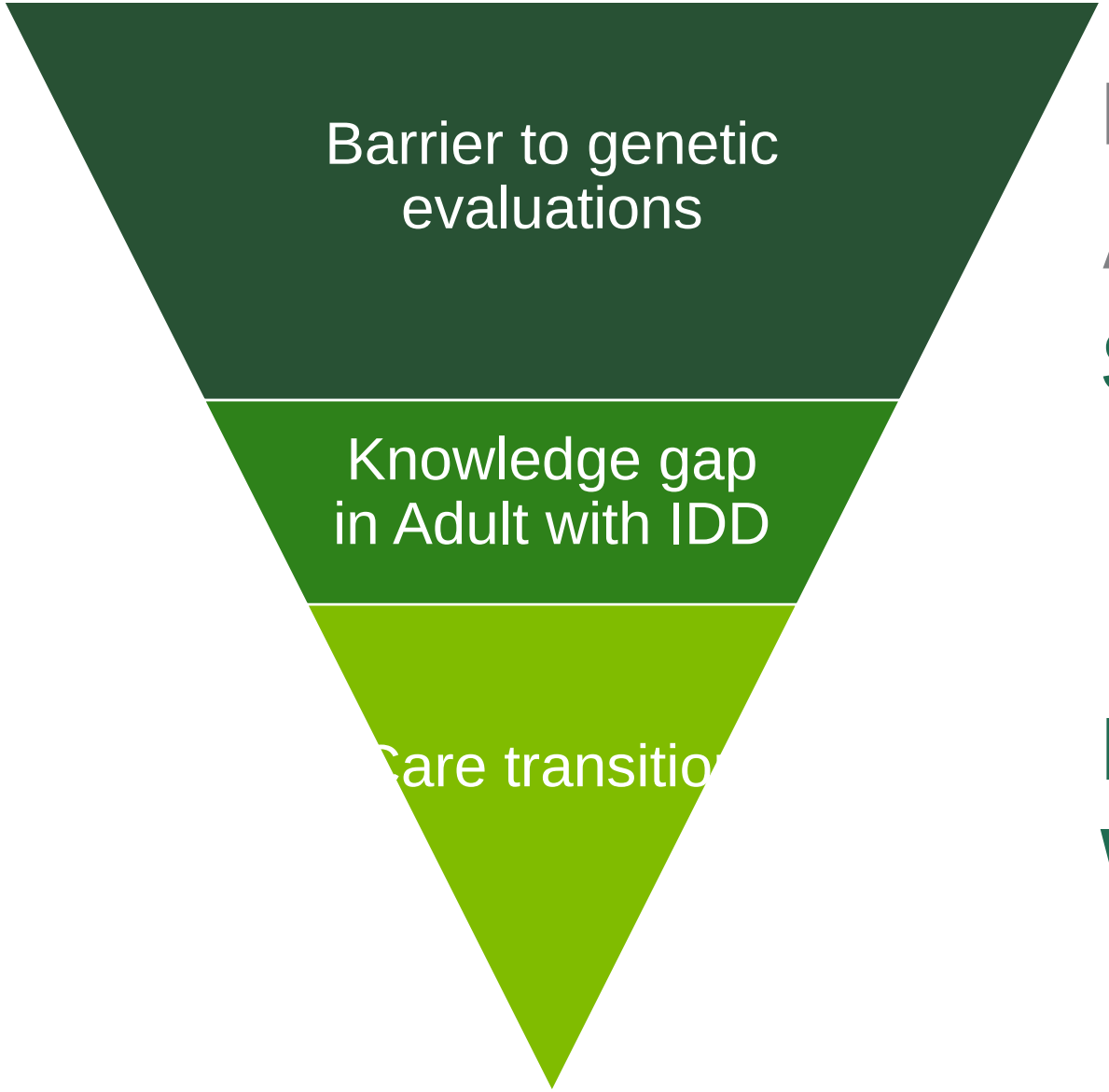
Smith Family Clinic, Huntsville, AL

- Telephone 256-327-9640



www.smithfamilyclinic.org

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Lack of awareness

Availability of geneticists

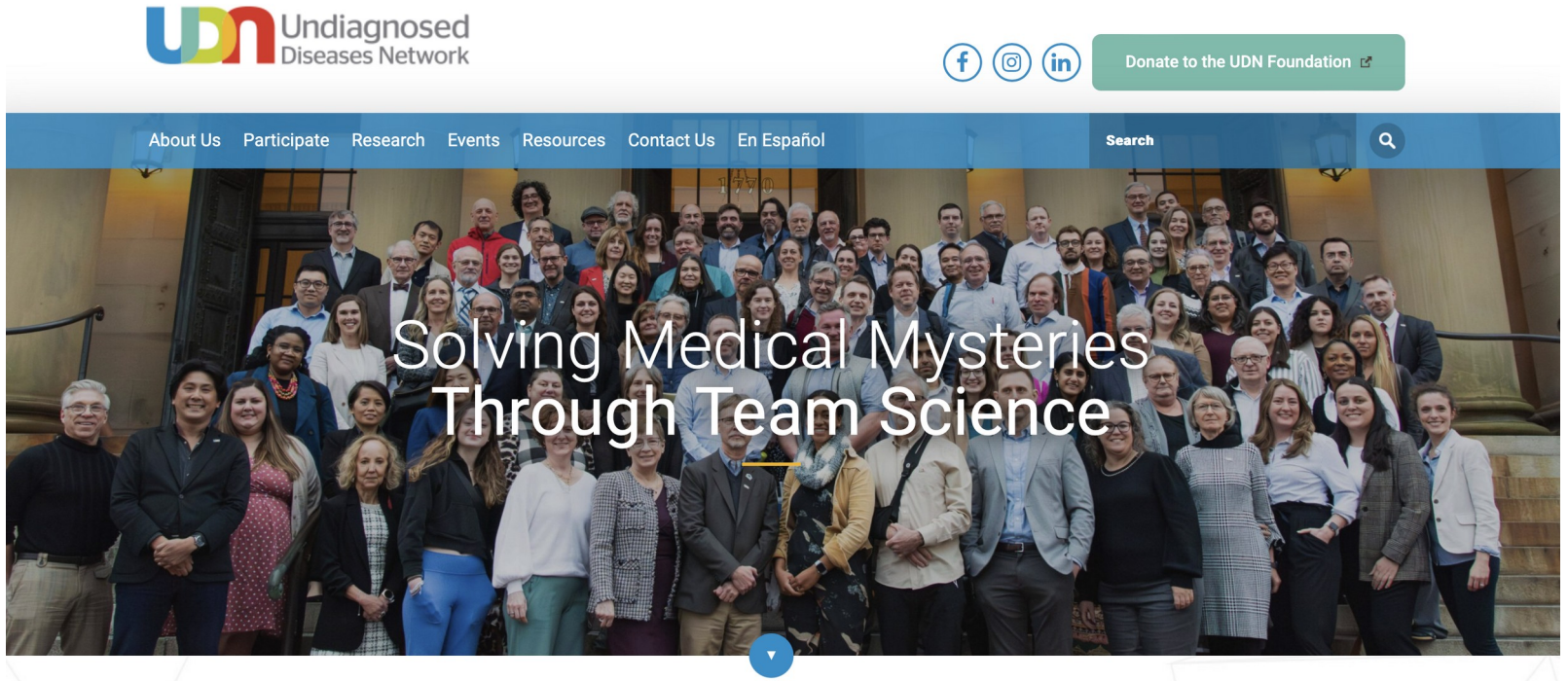
Socioeconomics

Lack of providers familiar with rare diseases

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Undiagnosed Disease Network

- Undiagnosed ID with strong family history/dysmorphic features
- https://undiagnosed.hms.harvard.edu

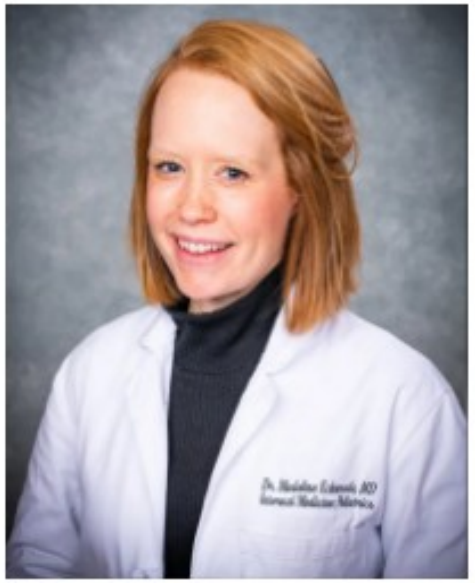


About The Undiagnosed Diseases Network

The Undiagnosed Diseases Network (UDN) is a research study that is funded by

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Staging Transition for Every Patient (STEP) clinic



Madeline Eckenrode, MD

Internal Medicine, Pediatrics



Carlie Somerville, MD

Internal Medicine, Pediatrics

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Clinic Inclusion Criteria

- Clinic Inclusion criteria for adults 18 and older:
  - **Intellectual disability** or Autism Spectrum Disorder requiring caregiver assistance and/or
  - 3 or more organ systems with chronic issues needing specialty co-management and/or
  - Technology Dependence (Ventilator, BIPAP, Trach, GT/JT/ wheelchair, Shunt)

SLIDE Courtesy of Dr. Somerville
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Take home points

- All Adults with IDD should be referred for genetic evaluation
- There are multiple emerging tests that have become clinically available, and providers should be familiar with genetic testing results and reports
- Utilize available resources in Alabama (clinical genetics, STEP clinic, UDN)

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THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Thank you!

Pongtawat Lertwilaiwittaya, MD, FACMG, FSSCI

Assistant Professor, Department of Genetics
University of Alabama at Birmingham