Consistency of carrier screening guidelines across seven populations and 408,000 individuals

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ESHG 2020

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Disclosure(s)

I am an employee and stockholder at Myriad Genetics

Purpose of carrier screening

"...the goal of preconception and prenatal carrier screening is to **provide couples with information to optimize outcomes** based on their personal values and preferences."

A Joint Statement of the American College of Medical Genetics and Genomics (ACMG), American College of Obstetricians and Gynecologists (ACOG), National Society of Genetic Counselors (NSGC), Perinatal Quality Foundation, and Society for Maternal-Fetal Medicine (SMFM).

-from Expanded Carrier Screening in Reproductive Medicine—Points to Consider

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 690 • March 2017

Carrier Screening in the Age of Genomic Medicine

"Ethnic-specific, panethnic, and expanded carrier screening are acceptable strategies for prepregnancy and prenatal screening"

The American College of Obstetricians and Gynecologists
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"Disorders selected for inclusion [in expanded carrier screening] should meet **several** of the following consensus-determined criteria":

1. **≥1-in-100 carrier frequency**
2. Well-defined phenotype
3. Detrimental to quality of life
4. Cause cognitive/physical impairment
5. Require surgical or medical intervention
6. Early onset in life
7. Have prenatal diagnosis available

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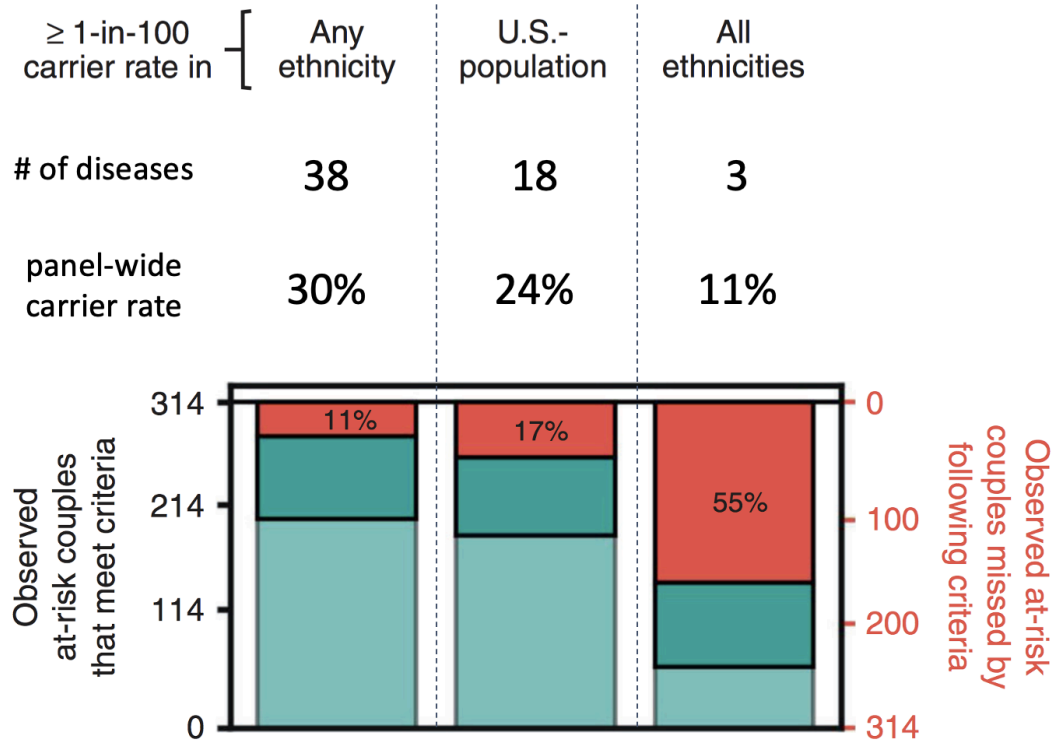
Open

A data-driven evaluation of the size and content of expanded carrier screening panels

Rotem Ben-Shachar, PhD[1], Ashley Svenson, MS CGC[1], James D. Goldberg, MD[1] and Dale Muzzey, PhD[1]



- Interpretation of 1-in-100 frequency cutoff has substantial impact on ECS panels

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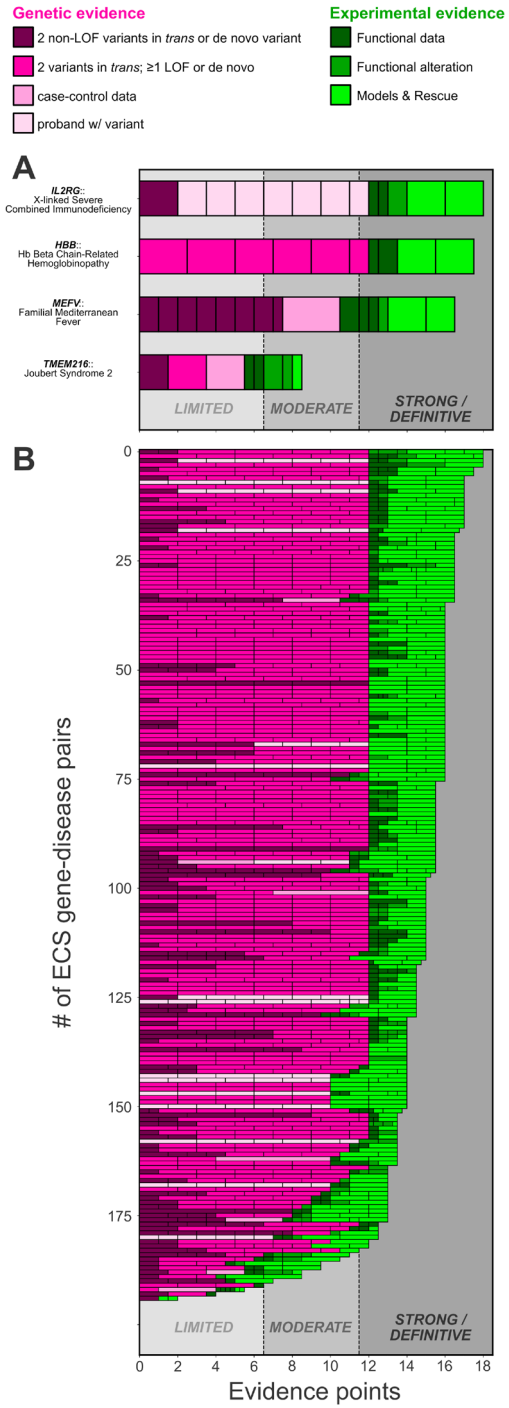

Clinical validity of expanded carrier screening: evaluating the gene-disease relationship in more than 200 conditions

Marie Balzotti, Linyan Meng, Dale Muzzey, Katherine Johansen Taber, Kyle Beauchamp, Myriad Genetics Curation Team, Baylor Genetics Curation Team, Rebecca Mar-Heyming ... See all authors

First published:07 May 2020 | https://doi.org/10.1002/humu.24033

- All 208 evaluated conditions met the evidence threshold for supporting a gene-disease association.
- 203 of 208 (98%) achieved the strongest (“Definitive”) level of gene-disease association.

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Evaluation and classification of severity for 176 genes on an expanded carrier screening panel

Aishwarya Arjunan, Holly Bellerose, Raul Torres, Rotem Ben-Shachar, Jodi D. Hoffman, Brad Angle, Robert Nathan Slotnik, Brittany N. Simpson, Andrea M. Lewis, Pilar L. Magoulas, Kelly Bontempo, Jeanine Schulze, Jennifer Tarpinian, Jessica A. Bucher, Richard Dineen, Allison Goetsch, Gabriel Lazarin, Katherine Johansen Taber

doi: https://doi.org/10.1101/2019.12.14.19014951

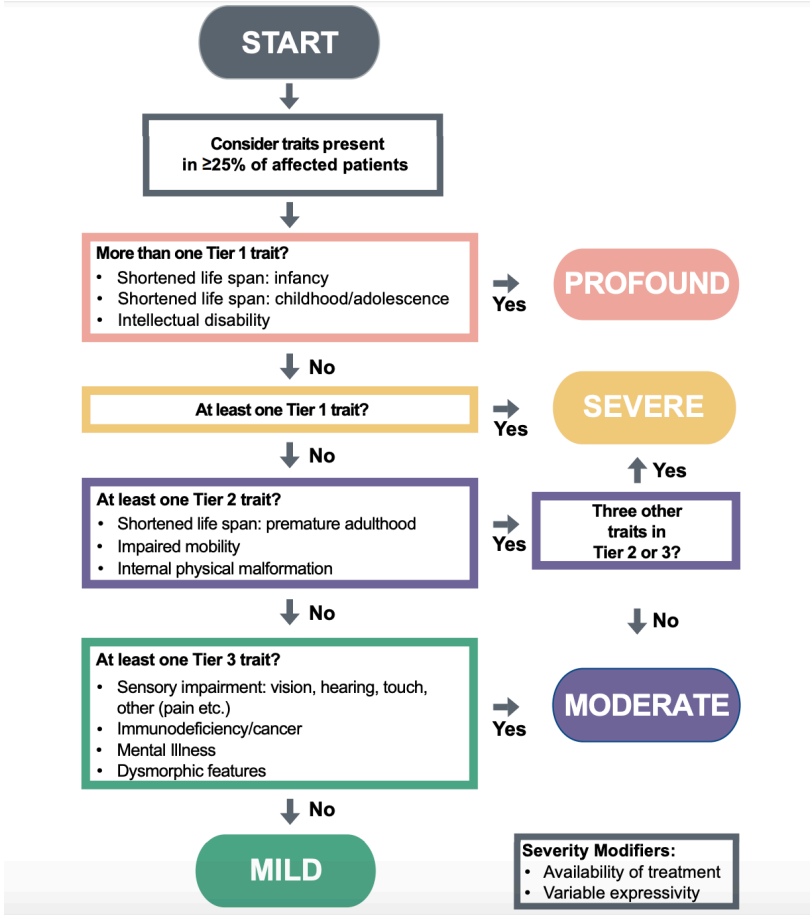

Table 2. Mapping of the algorithm's disease traits to ACOG severity criteria.

ACOG Severity Criteria	Have a detrimental effect on quality of life	Cause cognitive or physical impairment	Have an onset early in life	Require surgical or medical intervention
Algorithm Disease Traits	Intellectual disability Impaired mobility Internal physical malformation Sensory impairment Dysmorphic features Mental illness Immunodeficiency/ cancer	Intellectual disability Impaired mobility	Shortened lifespan: infancy/ childhood/adolescence	Availability of treatment

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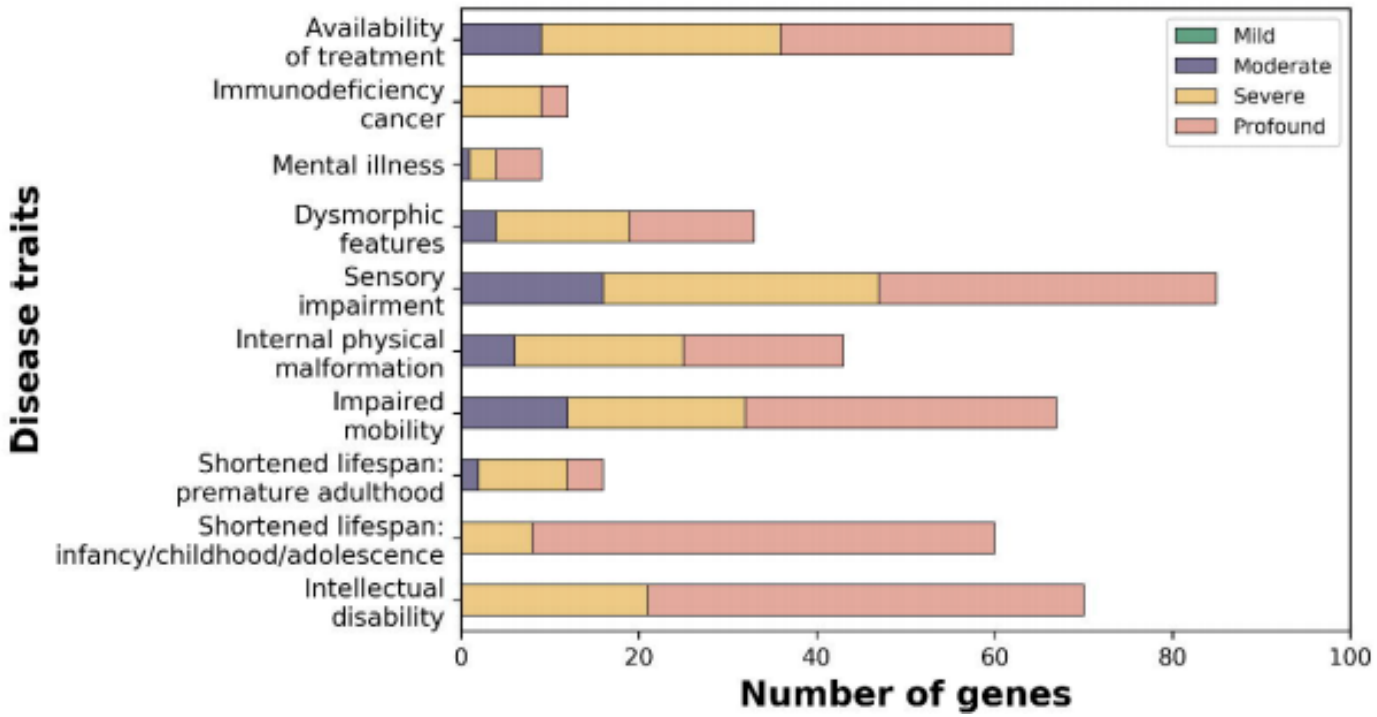
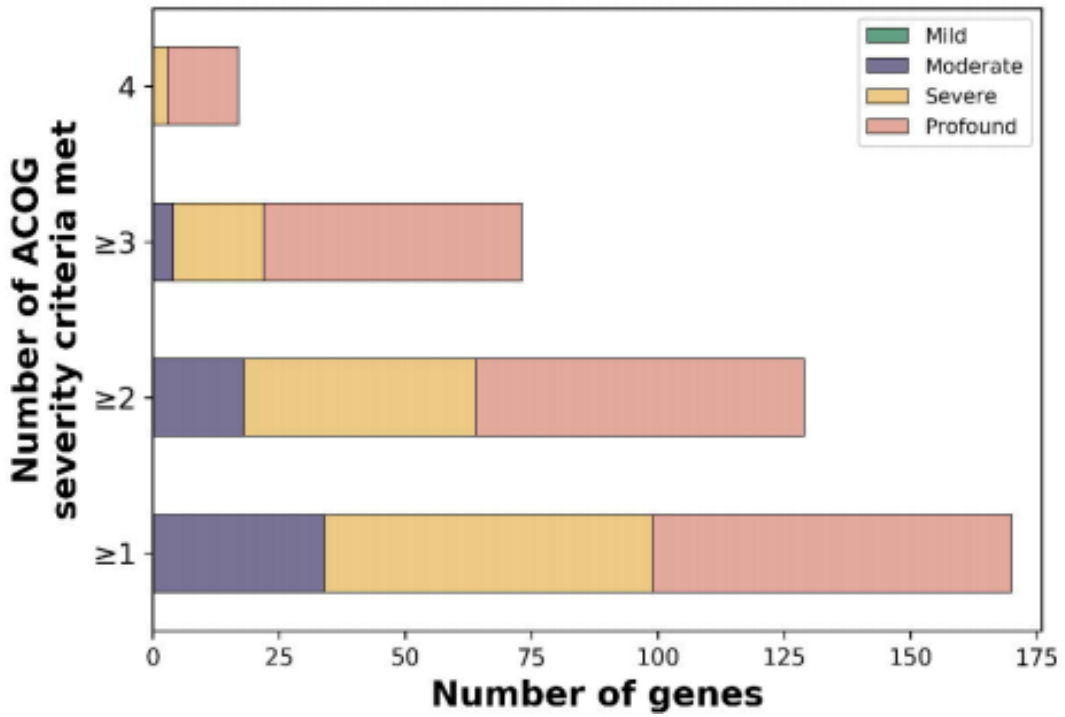
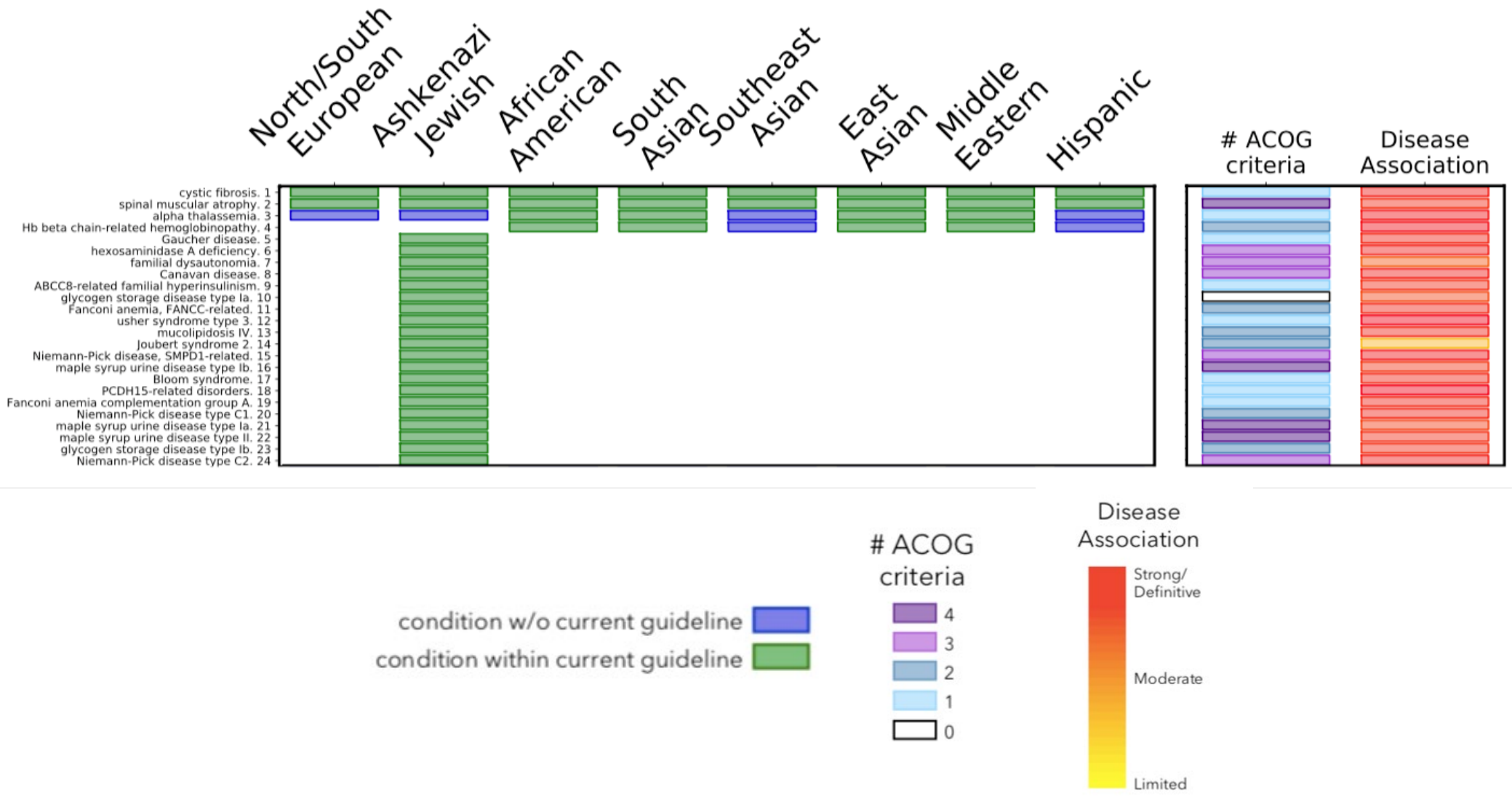




Establishing a guidelines consistent panel



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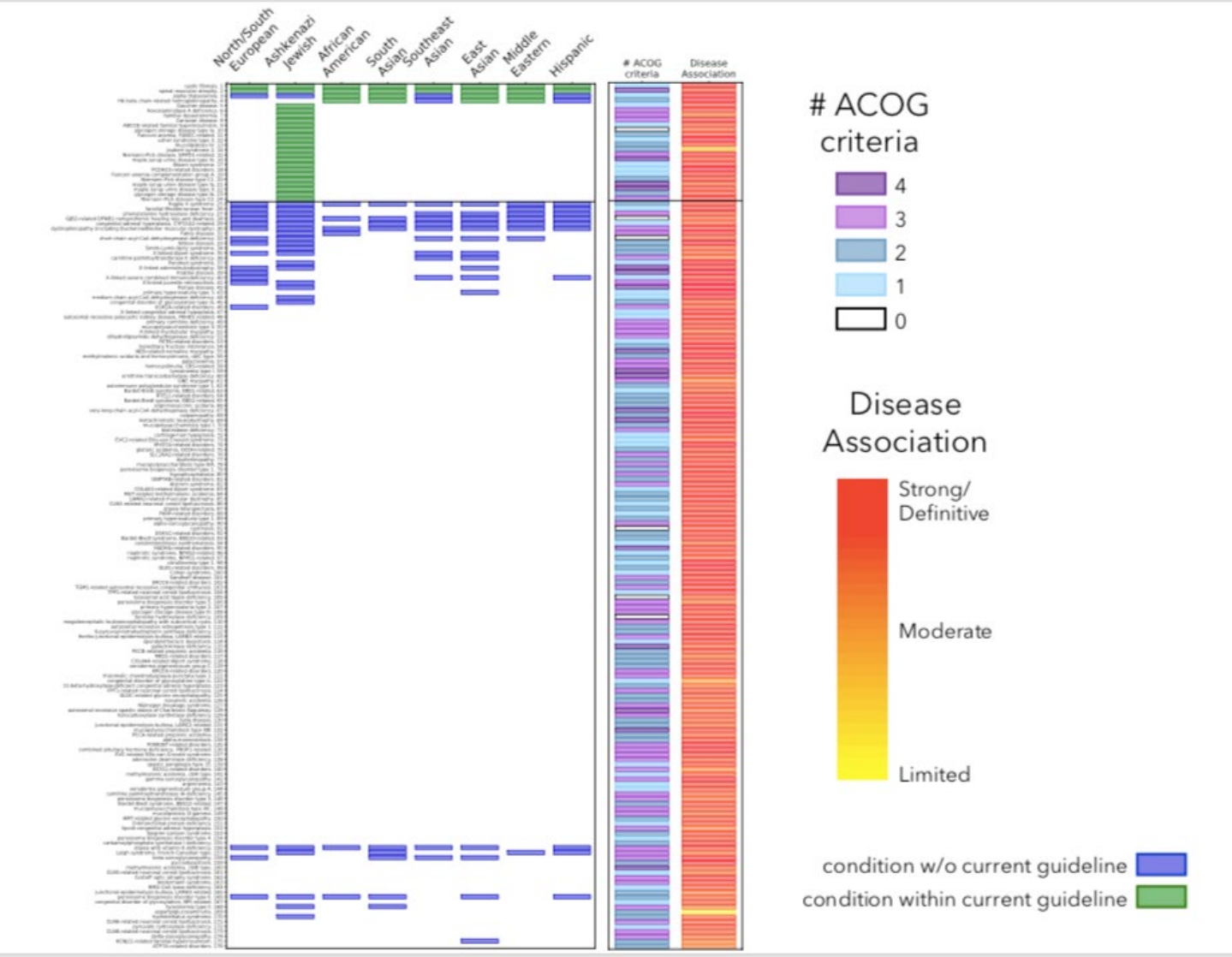

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1. ≥1-in-100 carrier frequency

   40 genes
2. Well-defined phenotype

   173 genes
3. Severity
   a) Detrimental to quality of life
   b) Cause cognitive/physical impairment
   c) Require surgical or medical intervention
   d) Early onset in life

   170 genes
4. Have prenatal diagnosis available

   All genes

Conclusions

- Using evidence-based analyses, we clarified and operationalized ECS panel design criteria.
- Stringent application of the criteria resulted in the identification of a guidelines-compliant panel consisting of **~40 conditions**
- Additional clarity of guidelines is needed to ensure standardization and equity of care.

Thank you!

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- Katie Johansen Taber
- Rotem Ben-Shachar
- Raul Torres

Contact

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Studies

- Research.myriadwomenshealth.com