

An evidence-based evaluation of guidelines criteria for condition inclusion on ECS panels: identifying a guidelines-compliant panel

Katie Johansen Taber, PhD; Raul Torres, PhD; Rotem Ben-Shachar, PhD; Aishwarya Arjunan, MS, MPH, CGC; Jim Goldberg, MD

OBJECTIVE

- The American College of Obstetrics and Gynecology (ACOG) states that expanded carrier screening (ECS) is an acceptable strategy for carrier screening and that conditions selected for inclusion on ECS panels should meet several of the following criteria:
 - have a carrier frequency of 1 in 100 or greater,
 - have a well-defined phenotype,
 - have a detrimental effect on quality of life,
 - cause cognitive or physical impairment,
 - require surgical or medical intervention,
 - have an onset early in life, and
 - can be diagnosed prenatally.
- These criteria lack specificity, making them difficult to interpret.

DESIGN

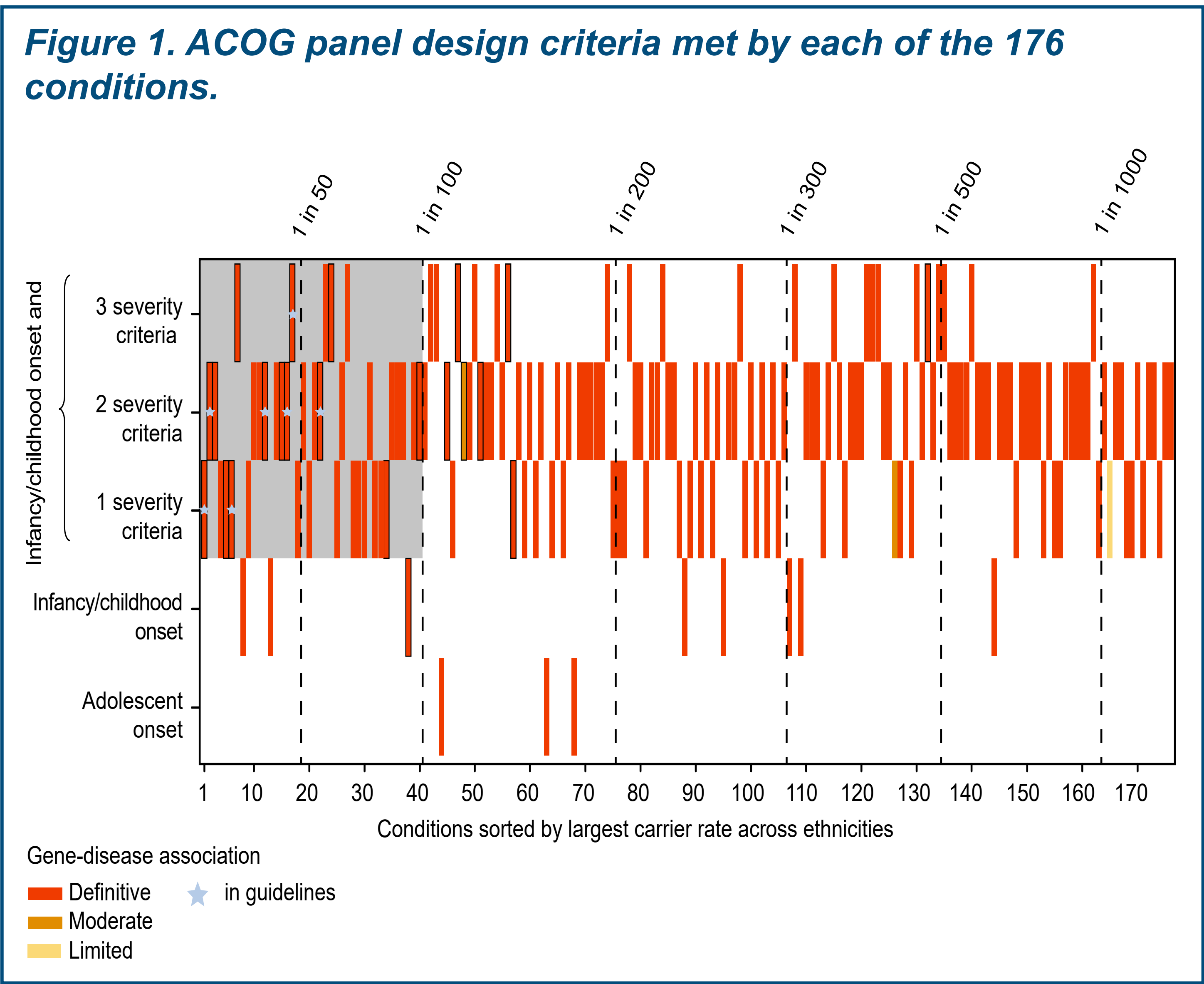
- We drew from published, quantitative frameworks to clarify and operationalize each criterion, and then identified conditions that unambiguously met the criteria.

MATERIALS AND METHODS

- Carrier frequencies were calculated from an internal database of more than 450,000 carriers of condition(s) on a 176-condition panel.
 - “Well-defined phenotype” was defined by the ClinGen categorization of the strength of gene-disease association.
 - The four severity-related criteria (criteria 3-6) were defined by the mapping of disease traits to each criterion by 12 independent board-certified genetics providers (genetic counselors and medical geneticists).
 - The ability to be diagnosed prenatally was considered to be a feature of all monogenic conditions.
- Presented at NSGC from November 17-22, 2020.

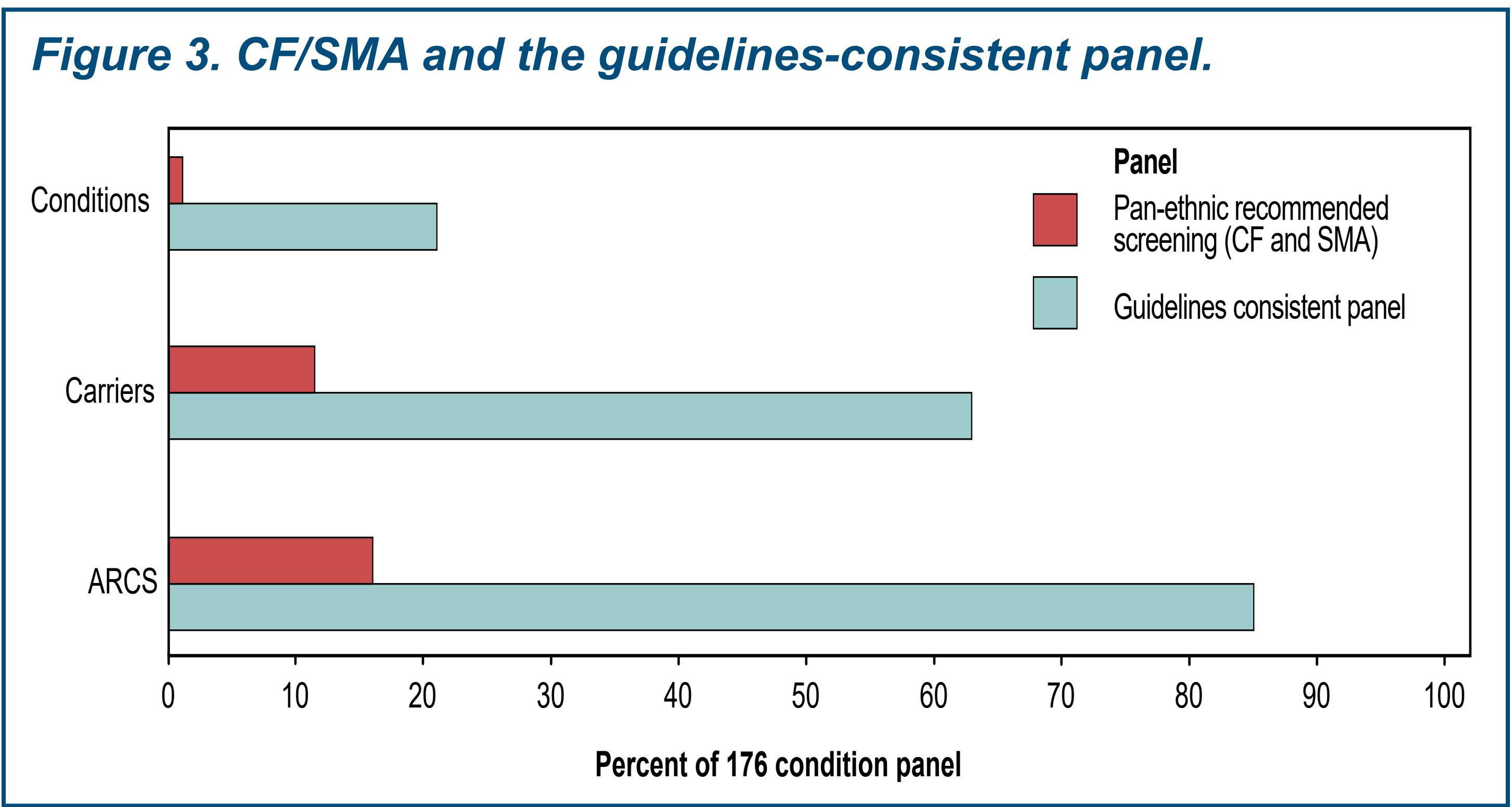
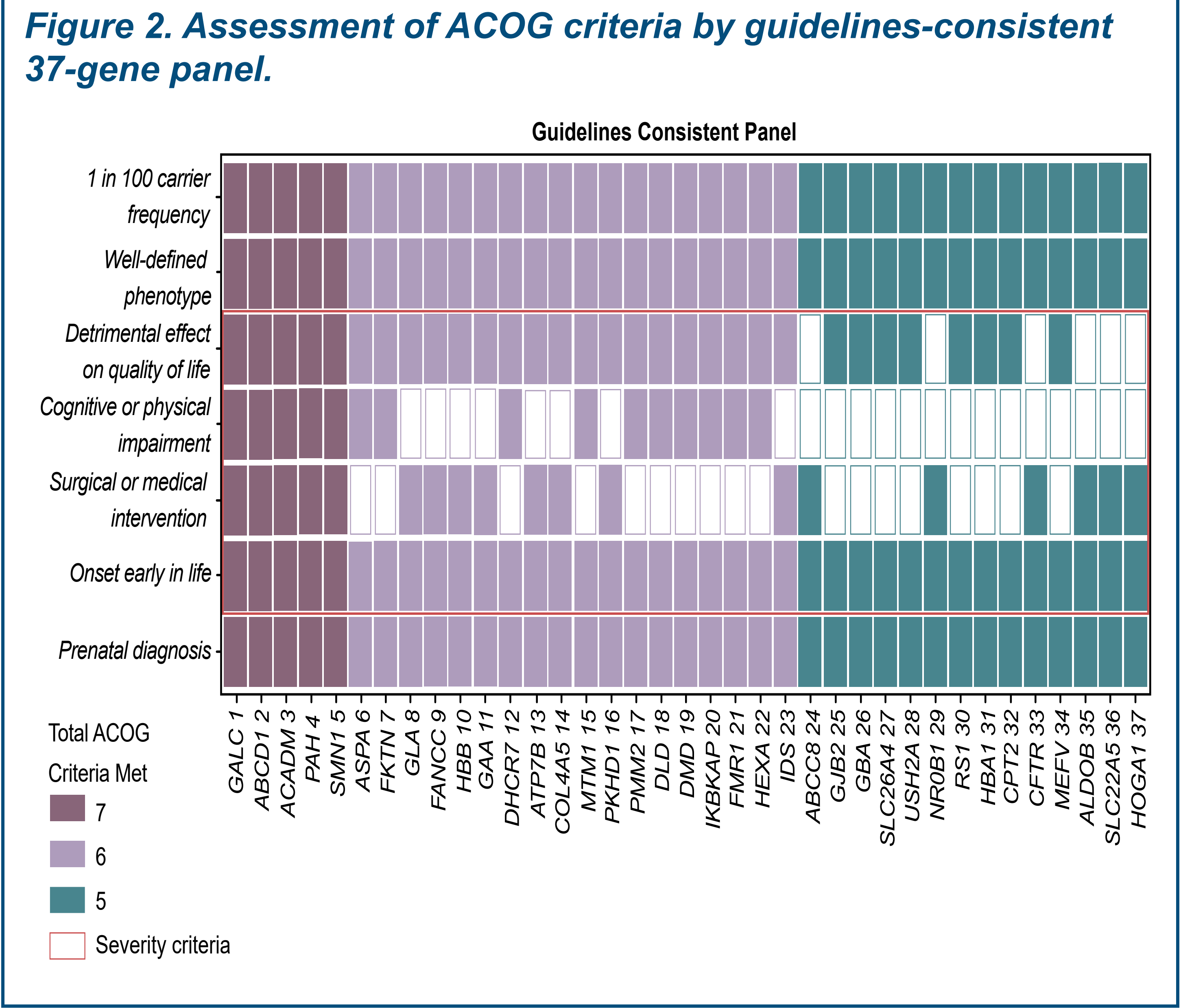
RESULTS

- It is unclear how many criteria ACOG deems acceptable to adhere to its statement that “several” criteria should be met. Therefore, the two conditions that ACOG currently recommends for panethnic carrier screening, cystic fibrosis (CF) and spinal muscular atrophy (SMA), were used to establish baseline thresholds.
- Both conditions have carrier frequencies greater than 1 in 100 in any ethnicity, have definitive gene-disease associations, meet at least one severity-related criterion (CF met one and SMA met four), and can be diagnosed prenatally.
- 176 conditions were then analyzed using these thresholds: 40 had carrier frequencies greater than 1 in 100 in any ethnicity, 173 had definitive gene-disease associations, 165 met at least one severity-related criterion, and all could be diagnosed prenatally (Figure 1). Combining these thresholds yields a guidelines-consistent panel of 37 conditions (Figure 1, gray box; Figure 2), with a combined carrier detection rate of 30.4% and an ARC detection rate of 1.0%.
- Relative to a 176-condition panel, the 37-condition panel would detect 84.6% of ARCs (Figure 3).



DISCLOSURE

All authors are current or former employees of Myriad Genetics, Inc.



CONCLUSION

- Evidence-based application of the ACOG severity criteria resulted in the identification of a guidelines-consistent panel consisting of 37 conditions.