

Women's Health

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New ACMG Practice Resource recommends an ethnic-neutral screening approach and more equitable care for all patients

The evolution of carrier screening

In the 1970s, carrier screening programs for sickle cell and Tay-Sachs disease were initiated. Since DNA-based testing was still in the early discovery phase, these screens were performed via routine chemistry and biochemistry.^{1,2} Twenty to twenty five years passed before the genes associated with cystic fibrosis (CFTR) and spinal muscular atrophy (SMN) were identified; with hundreds of genes discovered thereafter.^{3,4} These discoveries, along with the association of higher disease prevalence for specific conditions in certain populations, prompted ethnicity-based carrier screening recommendations from the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG).^{5,6,7}

Impact of next-generation sequencing (NGS)

NGS transformed carrier screening offerings by allowing for a large number of genes to be analyzed simultaneously, and at a lower cost compared to single-gene testing.² In a Practice Bulletin published in 2017 ACOG identified large carrier screening panels, panethnic screening (CF and SMA), or ethnicity-based screening as acceptable carrier screening strategies “as long as a standard approach is consistently offered to and discussed with each patient.”⁸

A new approach to carrier screening

In July 2021, ACMG released a Practice Resource on carrier screening for autosomal recessive and X-linked conditions during pregnancy and preconception. In this document, ACMG outlined a tiered carrier screening approach (Figure 1) and recommended an ethnicity- and population-neutral approach to provide equitable care to all patients (Figure 2). This abandons the previously established ethnicity-based carrier screening guidelines ACMG published in the 2000s.² Ethnic-neutral carrier screening is more inclusive and representative of the current US population, which has seen a 276% increase in individuals identifying as multiethnic, compared to 2010.⁹

Figure 1. ACMG's tier-based approach to carrier screening

ACMG's 4 tier system ² :	
Tier 1:	CF + SMA + Risk based screening
Tier 2:	≥1/100 carrier frequency (includes conditions in Tier 1)
Tier 3:	≥1/200 carrier frequency (includes conditions in Tier 2) and includes X-linked conditions
Tier 4:	<1/200 carrier screening (includes conditions in Tier 3) genes/conditions will vary by lab

Figure 2. ACMG recommendations

ACMG recommends ² :	ACMG does not recommend ² :
<ul style="list-style-type: none"> • All pregnant patients and those planning a pregnancy should be offered Tier 3 carrier screening. • Tier 4 screening should be considered: <ul style="list-style-type: none"> • When a pregnancy stems from a known or possible consanguineous relationship (second cousins or closer) • When a family or personal medical history warrants 	<ul style="list-style-type: none"> • Offering Tier 1 and/or Tier 2 screening, because these do not provide equitable evaluation of all racial/ethnic groups • Routine offering of Tier 4 panels

Implementing a new carrier screening paradigm

ACMG acknowledges carrier screening is best performed in the preconception period to allow couples access to all reproductive options. When a patient is identified as a carrier, comprehensive gene-specific sequencing for the partner should be performed and the option of reporting variants of uncertain significance (VUS) discussed. Diagnostic testing should be offered when a pregnancy is known to be at 50% risk for X-linked disorders and at least 25% for autosomal recessive disorders, but also if the partner does not proceed with testing, or if results will not be back in time for reproductive decision making. Regardless of when carrier screening is performed, pre- and post-test education should be provided².

Labcorp is committed to offering comprehensive carrier screening options for preconception and pregnant patients. From multiple ethnic-neutral panels of various sizes, to comprehensive partner testing with or without VUS analysis and prenatal diagnosis, Labcorp is well-aligned with ACMG's Practice Resource. In addition, Labcorp offers a national network of board-certified genetic counselors to help support you and your patients.

Click [here](#) for more information on Labcorp's carrier screening options.

November Health Awareness Calendar

- Genetic Counselor Awareness Day (Nov 4)
- World Prematurity Day (Nov 17)
- National Family Health History Day (Nov 25)
- Epilepsy Awareness Month
- American Diabetes Month



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