# Ethnicity-Based Carrier Screening

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**KEYWORDS**

• Ethnicity • Carrier screening • Autosomal recessive • Preconception

**KEY POINTS**

- Ethnicity-based carrier screening is an important component of preconception and prenatal care.
- Pretest and posttest counseling are essential to ensure patient understanding.
- Providers should understand the benefits and limitations of the screening tests they offer.
- Expanded carrier screening may replace ethnicity-based carrier screening in the near future.

## INTRODUCTION

Ethnicity-based carrier screening for single-gene disorders has been in clinical practice since the 1960s and has expanded over the decades with advancing technology. It has been almost 50 years since Wilson and Jungner[1] published their classic report on the principles and practice of screening for disease. The original criteria established by Wilson and Jungner[1] (**Box 1**) were updated by the World Health Organization in 2008.[2] Important consideration has also been given to applying the modern criteria to the prenatal setting[3,4] (**Box 2**). Understanding the basis for these criteria has become particularly valuable as technology such as whole-exome sequencing and whole-genome sequencing become more common in Western medicine.

Historically, the need for ethnicity-based carrier screening was a result of the recognition of the founder effect, which was first described by Ernst Mayr[5,6] in 1942. A founder effect accounts for the presence of a disease-associated allele at an unusually high frequency in an isolated population. A founder effect can result from the establishment of a new population from a few individuals derived from a

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**Box 1**
**Wilson and Jungner[1] carrier screening criteria**

1. The condition sought should be an important health problem.
2. There should be an accepted treatment of patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed-on policy on whom to treat as patients.
9. The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case finding should be a continuing process and not a once-and-for-all project.

*From* Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva (Switzerland): World Health Organization (WHO); 1968; with permission.

larger population or from a dramatic reduction in population size followed by rapid expansion, also described as a genetic bottleneck.[7] For example, complete genome sequencing data from 128 Ashkenazi Jewish controls support a narrow population bottleneck of just a few hundred individuals.[8] This narrow bottleneck explains the highly specific genetic variation within the Ashkenazi Jews, despite the current large size of the population. Another term used to account for specific disease-associated alleles found in certain populations is called heterozygote advantage.[9,10] Heterozygote advantage is the favored explanation for descendants from the Mediterranean, southeast Asia (including the Indian subcontinent), the Middle East, and Africa being carriers for hemoglobinopathies. In the past, hemoglobinopathies were found in the geographic regions of malaria endemicity because carriers have some degree of protection against infection.[11,12] Despite this explanation, the net result is a population at increased risk for autosomal recessive diseases.

**Box 2**
**Modern criteria for prenatal carrier screening**

1. The natural history of the disorder should be well understood and should severely impair the health of an affected offspring.
2. There should be a high frequency of carriers in the screened population.
3. Technically valid screening methods should be available.
4. The genotypic and phenotypic correlations should be predictable and strong.
5. Prenatal diagnosis and intervention should be valid reproductive options.

*Data from* Ram KT, Klugman SD. Best practices: antenatal screening for common genetic conditions other than aneuploidy. Curr Opin Obstet Gynecol 2010;22(2):139–45.

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