ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

Clarifications to ACMG's recent statement on
The use of ACMG secondary findings recommendations for general population screening: a policy statement of the American College of Medical Genetics and Genomics (ACMG)

On April 25, 2019 the ACMG Board of Directors released, *The use of ACMG secondary findings recommendations for general population screening: a policy statement of the American College of Medical Genetics and Genomics (ACMG)*. This statement followed several major observations.

1. The term ACMG SF v2.0 and ACMG 59 appeared in marketing materials for commercial laboratories focused on population screening,
2. ACMG SF and ACMG 59 are trademarks of the ACMG that cannot be used for commercial purposes,
3. The ACMG did not intend the secondary findings list for use in general population screening, and
4. The penetrance for many of the genes listed on the ACMG SF v 2.0 is incomplete or unknown.

Given recent commentary, the ACMG Board of Directors would like to clarify its recent statement.

1. The secondary findings list (in aggregate) represents a list of genes for which variants are reportable when identified as a consequence of next generation sequencing (NGS) already being performed for an unrelated reason.
2. The risk benefit suggests that when these variants are present, they should be reported to care providers. This is analogous to what is done in other aspects of medicine such as imaging procedures.
3. When screening the general population for this aggregate of variants additional factors must be considered. This includes ensuring that adequate expertise and follow-up systems are in place for the conditions being screened.
4. The College is aware of examples where asymptomatic patients have received the same care as that of a person who expresses the phenotype (e.g., ventricular arrhythmia). For many of the genes on the secondary findings list, population penetrance is not known. Interventions (e.g., implantation of defibrillators) may not be the

7101 Wisconsin Avenue
Suite 1101, Bethesda, MD 20814
Telephone: 301-718-9603
Fax: 301-718-9604

www.acmg.net

correct response to these genomic observations. In short, a basic tenet of any population-based screening program is that the benefits should outweigh the harms.

5. The ACMG policy statement does not speak to the sequencing of specific genes for which penetrance of variants in those genes is widely known and population-based screening in some form is already occurring (e.g., many of the cancer predisposition genes).
6. ACMG does not sanction the use of this "package" of genes for population-based screening until penetrance is better understood in asymptomatic individuals and appropriate follow-up care approaches can be assured.
7. We respect that ongoing research studies are compiling genomic data on asymptomatic patients and that these studies incorporate all or many of the genes that are on the ACMG list of secondary findings. It should be emphasized that these research studies could establish how to respond when pathogenic and likely pathogenic variants are identified in asymptomatic patients.
8. We also understand that the issue of penetrance is equally relevant to the follow-up of patients who are identified to have variants in the ACMG list through opportunistic analysis of variants in the ACMG gene list, during sequencing for other indications. Indeed, these data may lead to updates to the existing list based on better understanding of penetrance.
9. The secondary findings of genes/variants are available to providers at only minimal added cost to the US health care system when NGS is already being performed for unrelated reasons. Cost effectiveness has not been established when testing is performed at a population level once again, emphasizing the importance of ongoing funded research studies that ACMG believes will add clarity on when and how NGS can be used to advance public health.

Therefore,

- The ACMG strongly discourages any reference to the term ACMG SF v2.0 (or ACMG 59) outside of the reporting of incidental findings after clinical sequencing.
- Further, ACMG SF™, ACMG 59™, ACMG 56™, and related words and designs incorporating ACMG™, are trademarks of the American College of Medical Genetics and Genomics. They may not be used for any commercial purpose.
- The ACMG encourages further ascertainment of genotype–phenotype correlation and research to establish the efficacy of interventions in asymptomatic patients with pathogenic and likely pathogenic variants in known associated genes.

The original ACMG statement, “The Use of ACMG Secondary Findings Recommendations for General Population Screening” may be found here.