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

FOR IMMEDIATE RELEASE

Judy Froehlich, MBA
jfroehlich@acmg.net

American College of Medical Genetics and Genomics Releases New Clinical Practice Resource on Managing *RAD51C, RAD51D*, and *BRIP1* Variants

BETHESDA, MD – November 10, 2025 | The American College of Medical Genetics and Genomics (ACMG) has published a new clinical practice resource, "Management of Individuals with Heterozygous Germline Pathogenic Variants in *RAD51C, RAD51D*, and *BRIP1*: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG)," in its official journal, *Genetics in Medicine*. The publication provides evidence-based guidance for clinicians managing individuals with heterozygous germline pathogenic variants (GPVs) in *RAD51C*, *RAD51D*, and *BRIP1*, genes associated with increased cancer risks, particularly ovarian and breast cancers.

This practice resource provides guidance for clinicians caring for individuals with these moderate-penetrance cancer susceptibility variants, offering evidence-based recommendations on personalized risk assessment, surveillance, and risk-reducing interventions.

"Variants in *RAD51C*, *RAD51D*, and *BRIP1* are increasingly being identified through multi-gene panel testing," said Joanne Ngeow, MBBS, MPH, Senior Consultant and Head of Cancer Genetics Service, National Cancer Centre Singapore, Associate Professor, Nanyang Technological University, Singapore's Lee Kong Chian School of Medicine, and lead author of the practice resource. "Our guidance helps clinicians interpret these findings, communicate cancer risks to patients, and make informed decisions on interventions such as risk-reducing surgery and enhanced surveillance strategies."

Key recommendations include:

- **Ovarian cancer risk management:** Risk-reducing salpingo-oophorectomy is recommended close to menopause based on individualized, age-specific risk estimates.
- **Breast cancer surveillance:** Enhanced breast surveillance may be considered for *RAD51C* and *RAD51D* heterozygotes; routine risk-reducing mastectomy is generally not indicated.
- **Variant interpretation:** Variants of uncertain significance (VUS) should not guide clinical management, and clinicians should communicate the potential for reclassification to patients.

-more-

- **Research and therapeutic implications:** Evidence for targeted treatment in heterozygotes of these GPVs is currently limited; ongoing studies are exploring targeted therapies such as PARP inhibitors.

The practice resource also highlights the importance of personalized risk assessments that integrate family history, polygenic risk scores, and other clinical factors, as well as the need for genetic counseling to guide patients and families through testing, risk management, and reproductive planning. It represents an important step in translating emerging research into clinical practice, ensuring that new genetic insights lead to actionable care for patients today, even as the science continues to evolve.

"This resource reflects ACMG's commitment to providing clinicians with actionable, evidence-based guidance. By developing this clinical resource through an international workgroup, we can better support individuals with *RAD51C*, *RAD51D*, and *BRIP1* variants in understanding their cancer risks and taking proactive steps to manage their health. Resources like this are essential for helping clinicians apply rapidly advancing research in real-world care and for ensuring we continue to move forward, even as new data emerge," said Helen Hanson, MD, Consultant and Associate Professor Clinical Cancer Genetics, Royal Devon University NHS Foundation Trust and University of Exeter Medical School, and senior author of the practice resource.

The full journal publication can be found here: https://www.gimjournal.org/article/S1098-3600(25)00204-7/fulltext.

About the American College of Medical Genetics and Genomics (ACMG) and ACMG Foundation

Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is a prominent authority in the field of medical genetics and genomics and the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics. The only medical specialty society in the US that represents the full spectrum of medical genetics disciplines in a single organization, the ACMG provides education, resources and a voice for more than 2,500 clinical and laboratory practice of medical genetics as well as through advocacy, education and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health. *Genetics in Medicine* and *Genetics in Medicine Open*, a gold open access journal, are the official ACMG journals. ACMG's website, acmg.net, offers resources including policy statements, practice guidelines, and educational programs. The ACMG Foundation for Genetic and Genomic Medicine works to advance ACMG educational and public health programs through philanthropic gifts from corporations, foundations, and individuals.

-end-