

EVIDENCE BASED GUIDELINES PROGRAM

SEMI-ANNUAL UPDATE¹ ON DEVELOPMENT and WORK GROUP ACTIONS FEBRUARY 2021

INTRODUCTION

The ACMG Foundation for Medical Genetics and Genomics published our first Semi-Annual Update on the Evidence Based Guidelines (EBG) Program in September of 2020, or about one year after the founding of this new ACMG initiative. While a few items from that report are repeated at the end of this document, that Update from [September of 2020](#) is also worth reading.

Successful 2020 Development Efforts

The ACMG Foundation is thrilled that our development efforts secured over \$500,000 in funding for the EBG Program in 2020. This very positive response to our new Program shows our work is providing both the medical genetics and larger health care community a highly sought-after product. As the ACMG's EBG Program ramps-up this year, we applaud our major 2020 donors: Illumina, BioMarin, Invitae, Horizon Pharmaceuticals, and Evan and Cindy Jones. We are particularly grateful to Illumina for their major donation in 2020 *and* for the seed funding in 2019 that helped launch the EBG Program.

The support that the Foundation received in 2020 will enable ACMG to build a team of highly technical individuals to staff this growing program. With these key staff positions in place, ACMG Members and volunteers will be able to review multiple issues simultaneously and produce evidence based guidelines at a faster pace than ever before.

The ACMG Foundation set a goal of securing \$700,000 in 2021. This program cannot exist without highly qualified staff. We must secure the resources needed to maintain a stable and predictable work environment to attract great candidates.

GUIDELINE DEVELOPEMNT: THREE TOPICS PROCEED

The N.I.P.S. Guideline

Since September of 2020, a team of ACMG member volunteers and the College's full time methodologist have continued to drive the Noninvasive Prenatal Screening (N.I.P.S.) Guideline through the formal Evidence Based Guidelines Program at ACMG. Since our last update, work has been focused within the

¹ The ACMG Foundation will work to publish an update to this document on a quarterly basis, or at other times when the work of the related committees or work groups warrants an update to our EBG constituency.

Systematic Evidence Review (SER) Work Group.² After the N.I.P.S. EBG Work Group³ sent their SER partners several “Key Questions” in June of 2020, ACMG’s methodologist and medical librarian performed database searches and reviewed all relevant medical literature. The SER Work Group, comprised of ACMG member volunteers, has completed the title and abstract screening, full-text article review, and data abstraction and quality assessment training. They are now in the process of abstracting the data and assessing the quality of the included articles using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) method.

The SER Work Group will meet in late February 2021 to summarize the results of this research and will develop a summary document for the EBG Work Group’s use to inform their recommendations and develop guidelines. The systematic evidence review will be submitted for peer review and publication in ACMG’s *Genetics in Medicine* Journal in the second quarter of 2021.

Before a new or revised guideline is published, the final document is circulated to ACMG members for comment.

The “Peds ES/GS (CA, DD, ID)” Guideline

Yes, we use the acronym above because nobody can say “**Pediatric Exome-/Genome-Sequencing for Congenital Anomalies, Developmental Delay or Intellectual Disability Guideline**” quickly. Since September, the “Peds EBG Work Group” has continued to meet bi-monthly. All background work necessary to inform the writing of the guidelines and recommendations is complete, including a detailed *Summary of Findings* table covering 1) each of the included outcomes and 2) the quality of evidence rating for each one. This format provides reviewers key decision-relevant information in summary form to aid them in making recommendations. Also included was the evidence-to-decision framework that presents key information in a visual format.

The Work Group met in January 2021 to draft the Guidelines and is now putting those guidelines into a manuscript. This manuscript will be reviewed by the Board of Directors and then sent to ACMG membership for comment.

Phenylalanine hydroxylase deficiency (PKU) Guideline

During the third quarter of 2020, the PKU SER Work Group completed the title and abstract screening, full-text article review, and data abstraction and quality assessment training. The team is currently abstracting the data and assessing the quality of the included articles – again, using the ROBINS-I method. Once this step is complete in February of 2021, summary analyses will be written, and the systematic evidence review will be submitted for peer review and publication in ACMG’s *Genetics in Medicine* Journal. The PKU EBG Work Group will then revise ACMG’s PKU Guideline as needed.

² Members: Monica McClain as Chair, Danielle LaGrave, Elizabeth Barrie, Marco Leung, and Nancy Rose.

³ Members: Jeff Dungan as Chair, Kristin Monaghan, Susan Klugman, Bob Best, Mike Bashford, Yasmine Akkari, Angelika Erwin, Sandra Darilek, and Monica McClain.

The PKU SER Work Group members include, Monica McClain (Chair), Moises Fiesco-Roa, Judith Hobert, Pamela Arn, Jinglan Liu, April Dione Adams, Paul Rothberg, Melissa Murfin, and Lawrence Wong.

The EBG team, which will soon receive the final work product of their PKU team counterparts, is comprised of Jerry Vockley (Chair), Wendy Smith (co-chair), Kim McBride, Susan Berry, Barbara Burton, John Mitchell, Henry Mroczkowski, and Monica McClain.

NEXT STEPS

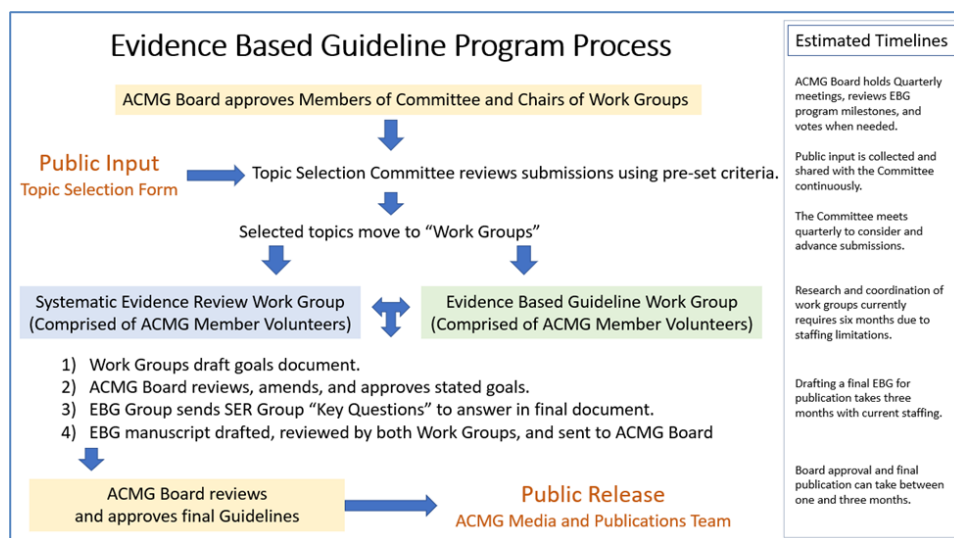
ACMG and the ACMG Foundation are committed to keeping our members, volunteers, donors, and partners updated on the EBG Program’s ongoing work. We will continue to update the Foundation’s webpage dedicated to the EBG Program. With some staffing adjustments and new team members on the horizon, we intend to make 2021 a banner year for the EBG Program.

Again, and thanks to successful fundraising campaigns in 2019 and 2020, ACMG can move forward with our plans to add a Chief Medical Officer and a second methodologist to the team (as early in 2021 as possible). We look forward to expanding our team and bolstering the work of our dedicated ACMG Members and volunteer experts. The Board, staff, and our volunteers are confident that 2021 guideline work will drive genetic and genomic medicine – and patent care – forward.

LINKS AND HELPFUL BACKGROUND INFORMATION

The ACMG Foundation is encouraging interested parties to visit [the EBG Program website](#) and, if interested, to follow the link to the online [Topic Submission Form](#). The EBG Program site will be updated as guidelines progress, as the selection committee makes further determinations, and as new donors help to expand the program.

The Process: This chart below is republished again in this EBG Update and seeks to answer the question, “How long does it take for an idea to become a published guideline?”



Please direct any questions to Karl Moeller via email at kmoeller@acmgfoundation.org.