Expanding BRCA1/2 testing criteria to include other confirmed breast and ovarian cancer susceptibility genes.

Fergus Couch, Hermela Shimelis, Jill S. Dolinsky, Eric Polley, Carolyn Horton, Anal Yussuf, Lily Hoang, Jenna Lileyquist, Virginia Speare, Chunling Hu, Steven Hart, Holly LaDuca; Mayo Clinic, Department of Laboratory Medicine and Pathology, Rochester, MN; Ambry Genetics, Aliso Viejo, CA; Mayo Clinic, Rochester, MN

**Note: The appearance of your abstract here is an approximation of how the abstract would appear in print, if accepted.**

**Background:** The National Comprehensive Cancer Network (NCCN) has expanded its breast and ovarian cancer (BC and OC) genetic testing and management recommendations to address the broader spectrum of cancer predisposition genes. However, management recommendations are pending for some candidate BC genes (e.g. **BARD1**, **RAD51D**) and OC genes (e.g. **ATM**, **NBN**) due to insufficient evidence of increased cancer risk, and indications for multi-gene panel testing (MGPT) remain vague overall. We aimed to further characterize BC and OC risks for 21 candidate susceptibility genes and explore the potential utility of BRCA1/2 testing criteria as an indication for MGPT. **Methods:** Gene-specific pathogenic variant (PV) frequencies among Caucasian BC and OC patients (unadjusted for other personal/family cancer history) ascertained from a cohort of > 175,000 patients referred for MGPT were compared to non-Finnish European reference controls from the genome aggregate database (gnomAD). Clinical histories of BC and OC patients were also reviewed to assess whether NCCN BRCA1/2 testing criteria were met (version 2.2017). **Results:** We confirmed the association of 15 genes with increased risk ( > 2.0-fold) of BC (**ATM**, **BARD1**, **BRCA1/2**, **CDH1**, **CDKN2A**, **CHEK2** (excluding **p.I157T**), **MLH1**, **MSH2**, **MSH6**, **NF1**, **PALB2**, **PTEN**, **RAD51D**, **TP53**). The pooled frequency of PVs in these genes was 9.2% among BC patients of all ethnicities (3.5% in BRCA1/2 and 5.7% in other genes) and 8.6% among BC patients meeting BRCA1/2 testing criteria (3.4% in BRCA1/2 and 5.2% in other genes). Eleven genes were associated with increased risk of OC ( > 2.0-fold, **ATM**, **BRCA1/2**, **BRIP1**, **MSH2**, **MSH6**, **NBN**, **PMS2**, **RAD51C**, **RAD51D**, **TP53**). PVs in these genes were detected among 13.0% of OC patients of all ethnicities (8.0% for BRCA1/2 and 5.0% for other genes combined). Therefore, inclusion of additional risk genes increases detection rate for BC and OC patients meeting BRCA1/2 testing criteria by 152.9% and 62.5%, respectively. **Conclusions:** These results further characterize gene-specific BC and OC risks, which can be used to refine management recommendations for at-risk patients. Current testing criteria fail to capture a substantial proportion of women with increased risk of BC and OC.

**Title:**
Expanding BRCA1/2 testing criteria to include other confirmed breast and ovarian cancer susceptibility genes.

**Submitter’s E-mail Address:**
couch.fergus@ mayo.edu

**Is this a late-breaking data submission?**
No

**Is this abstract a clinical trial?**
No

**Would like to be considered for a Merit Award:**
No

Have the data in this abstract been presented at another major medical meeting?
No

Has this research been submitted for publication in a medical journal?
No

Type of Research:
Prevention
Research Category:
Translational
Continued Trial Accrual:
No
Received Grant funding:
No
Sponsor:
Fergus Couch, PhD

First Author

Presenting Author
Corresponding Author
Fergus Couch, PhD
Mayo Clinic, Department of Laboratory Medicine and Pathology
Rochester, MN 55905
Phone Number: 507-284-2511
Email: couch.fergus@mayo.edu

Click to view Conflict of Interest Disclosure

Second Author

Hermela Shimelis
Mayo Clinic, Department of Laboratory Medicine and Pathology
Rochester, MN 55905
Email: shimelis.hermela@mayo.edu

Click to view Conflict of Interest Disclosure

Third Author

Jill S. Dolinsky, MS
Ambry Genetics
15 Argonaut
Aliso Viejo, CA 92656
Email: jdolinsky@ambrygen.com

Click to view Conflict of Interest Disclosure

Fourth Author

Eric Polley
Mayo Clinic
200 First Street SW
Rochester, MN 55905
Phone Number: 507-284-5679
Email: polley.eric@mayo.edu

Click to view Conflict of Interest Disclosure

Fifth Author

Carolyn Horton
Ambry Genetics
Sixth Author

Amal Yussuf
Amry Genetics
Aliso Viejo, CA
Email: ayussuf@amrygen.com

Click to view Conflict of Interest Disclosure

Seventh Author

Lily Hoang
Amry Genetics
Aliso Viejo, CA 92656
Email: lhoang@amrygen.com

Click to view Conflict of Interest Disclosure

Eighth Author

Jenna Lilyquist
Mayo Clinic
Rochester, MN 55905
Email: Lilyquist.Jenna@mayo.edu

Click to view Conflict of Interest Disclosure

Ninth Author

Virginia Speare, PhD
Amry Genetics
15 Argonaut
Aliso Viejo, CA 92656
Email: vspeare@amrygen.com

Click to view Conflict of Interest Disclosure

Tenth Author

Chunling Hu
Mayo Clinic
Rochester, MN 55905
Email: hu.chunling@mayo.edu

Click to view Conflict of Interest Disclosure

Eleventh Author

Steven Hart
Mayo Clinic
Rochester, MN
Email: hart.steven@mayo.edu

Click to view Conflict of Interest Disclosure

Twelfth Author

Holly LaDuca
Amry Genetics
Aliso Viejo, CA
Email: hduca@amrygen.com

Click to view Conflict of Interest Disclosure
If necessary, you can make changes to your abstract between now and the deadline of Tuesday, February 13, 2018

- To access your submission in the future, use the direct link to your abstract submission from one of the automatic confirmation emails that were sent to you during the submission.
- Or point your browser to /asco/reminder.cgi to have that URL mailed to you again. Your username/password are 228857/436881.

Any changes that you make will be reflected instantly in what is seen by the reviewers. You DO NOT need to go through all of the submission steps in order to change one thing. If you want to change the title, for example, just click "Title" in the abstract control panel and submit the new title.

When you have completed your submission, you may close this browser window.

Tell us what you think of the abstract submission process

Home Page