

FORMAL COMMENT

The importance of using public data to validate reported associations

Georgia Chenevix-Trench¹*, Jonathan Beesley¹, Paul D. P. Pharoah², Andrew Berchuck³

1 Queensland Institute of Medical Research Berghofer, Herston, Queensland, Australia, **2** Centre for Cancer Genetic Epidemiology, Department of Public Health and Primary Care, University of Cambridge, Strangeways Research Laboratory, Cambridge, United Kingdom, **3** Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina, United States of America

* georgiaT@qimr.edu.au



OPEN ACCESS

Citation: Chenevix-Trench G, Beesley J, Pharoah PDP, Berchuck A (2018) The importance of using public data to validate reported associations. PLoS Genet 14(6): e1007416. <https://doi.org/10.1371/journal.pgen.1007416>

Editor: Charis Eng, Cleveland Clinic Genomic Medicine Institute, UNITED STATES

Received: March 21, 2018

Accepted: April 24, 2018

Published: June 29, 2018

Copyright: © 2018 Chenevix-Trench et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The COGS project was funded through a European Commission's Seventh Framework Programme grant (agreement number 223175 - HEALTH-F2-2009-223175). The Ovarian Cancer Association Consortium is supported by a grant from the Ovarian Cancer Research Fund thanks to donations by the family and friends of Kathryn Sladek Smith (PPD/RPCI.07). The scientific development and funding for this project were in part supported by the US National Cancer Institute GAME-ON Post-GWAS Initiative (U19-CA148112). This study made use of data generated by the Wellcome Trust Case Control consortium. Funding

We were interested to read the paper by Eng and colleagues on paternal lineage early onset hereditary ovarian cancers [1]. They found by exome sequencing of 159 non-*BRCA1/2* ovarian cancer cases that one missense variant (rs176026 in *MAGEC3*) was associated with risk at “chromosome-wide significance” (Hazard ratio [HR] = 2.85, 95% CI 1.75–4.65) and with a 6.7-year-earlier age of onset. They also report some *in silico* analyses of rs176026 and *MAGEC3*. However, other publicly available data on ovarian cancer risk for this SNP do not support these findings. In an analysis by the Ovarian Cancer Association Consortium (OCAC) [2], in over 25,000 ovarian cancer cases and 40,000 controls, no significant association was found for overall ovarian cancer risk ($P = 0.24$) or for any histological subtypes examined ($P = 0.20$ for high-grade serous ovarian cancer). In this data set, rs176026 was imputed with an imputation r-squared of 0.79.

We believe that it ought to be standard practice in an era of widespread data sharing for authors to identify relevant data that are publicly available and report and discuss their own findings in the context of the findings from such data. Relevant data would include data on the same or closely related phenotypes and on the same or highly correlated genetic variants.

In this instance, such data are publicly available at <http://ocac.ccge.medschl.cam.ac.uk/data-projects/results-lookup-by-region/>, and the authors should have checked the findings in the OCAC data (to which they are contributors) and discussed its relevance to their own findings.

Author Contributions

Conceptualization: Georgia Chenevix-Trench.

Writing – original draft: Georgia Chenevix-Trench, Paul D. P. Pharoah.

Writing – review & editing: Jonathan Beesley, Andrew Berchuck.

for the project was provided by the Wellcome Trust under award 076113. The results published here are in part based upon data generated by The Cancer Genome Atlas Pilot Project established by the National Cancer Institute and National Human Genome Research Institute (dbGap accession number phs000178.v8.p7). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests.

References

1. Eng KH, Szender JB, Etter JL, Kaur J, Poblete S, Huang RY et al. (2018) Paternal lineage early onset hereditary ovarian cancers: A Familial Ovarian Cancer Registry study. *PLoS Genet.* 14(2): e1007194. <https://doi.org/10.1371/journal.pgen.1007194> PMID: 29447163
2. Phelan CM, Kuchenbaecker KB, Tyrer JP, Kar SP, Lawrence K, Winham SJ et al Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. *Nat Genet.* 2017; 49: 680–691. <https://doi.org/10.1038/ng.3826> PMID: 28346442