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COST-EFFECTIVENESS OF POPULATION BASED BRCA TESTING WITH VARYING ASHKENAZI JEWISH ANCESTRY

Manchanda R1,2, Patel S1,3, Antoniou A4, Levy-Lahad E5, Turnbull C6, Evans G7, Hopper J8, MacInnis R9, Menon U10, Jacobs I11, Legood R3

1Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, United Kingdom, 2Department of Gynaecological Oncology, Bartshealth NHS Trust, Royal London Hospital, United Kingdom, 3Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, United Kingdom, 4Centre for Cancer Genetic Epidemiology, University of Cambridge, United Kingdom, 5Medical Genetics Institute, Shaare Zedek Hospital, Jerusalem, Israel, 6Barts Cancer Institute, Queen Mary University of London, United Kingdom, 7Centre for Genomic Medicine, Division of Evolution and Genomic Science, University of Manchester, United Kingdom, 8Centre for Epidemiology & Biostatistics, Melbourne School of Population & Global Health, University of Melbourne, Australia, 9Cancer Epidemiology & Intelligence Division, Cancer Council Victoria, Melbourne, Australia, 10Gynaecological Cancer Research Centre, Department of Women’s Cancer, Institute for Women’s Health, University College London, United Kingdom, 11University of New South Wales, Australia

Background
Population-based BRCA1/2 testing in Ashkenazi Jewish (AJ) women aged ≥30 years with four AJ grandparents, has found to be cost-effective in comparison to family history (FH) based testing. However, 25% UK and 44% USA Jewish marriages are to non-Jews. Hence, many women may have differing AJ ancestry consisting of one, two, three or four AJ grandparents. This study aims to model the cost-effectiveness of population-based BRCA1/BRCA2 testing compared to family-history based testing in women with differing AJ ancestry.

Method
A decision-analytical model developed to calculate cost-effectiveness for screening women with four AJ grandparents was adapted to model cost-effectiveness outcomes for women of differing AJ ancestry. The following model estimates were recalculated: population prevalence of BRCA1/2, the probability of having a positive family history and the BRCA1/2 prevalence in FH negative individuals. These probability parameters were adjusted for relative BRCA mutation frequency in AJ and general populations. BRCA prevalence with 3AJ grandparents= (0.75*AJprevalence) + (0.25*General-populationprevalence); for 2 AJ grandparents= (0.5*AJprevalence+0.5*General-populationprevalence) and for 1 AJ grandparent= (0.25*AJprevalence+0.75*General-populationprevalence). One-way and probabilistic sensitivity analysis (PSA) were conducted on all four scenarios to account for any uncertainty.

Results
Population-testing in women with two, three and four AJ grandparent ancestry was found to be cost-saving and cost-effective at -£235, -£569, -£767 per QALY (quality adjusted life year) respectively. A cost-effective ICER of £423/QALY was observed for women with one AJgrandparent. The PSA showed ≥95% of simulations for one, two, three and four AJ women were cost-effective at the £20,000/QALY threshold used by the National Institute for Health and Care Excellence.

Conclusion
This study demonstrates the cost-effectiveness of population-based BRCA1/2 testing in women with differing AJ ancestry. Our results support the move for changing the paradigm from FH to population-based testing across the entire AJ population. These results however cannot be extrapolated to the general non-Jewish population.