



OPEN ACCESS

Brief communication

Update: variable implementation of the 2018 UKCGG/UKGTN guidelines for breast cancer gene panel tests offered by UK genetics services

Sarah Wedderburn,¹ Stephanie Archer,² Marc Tischkowitz,³ Helen Hanson ,⁴ on behalf of UKCGG

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/jmedgenet-2020-107529>).

¹Clinical Genetics, NHS Greater Glasgow and Clyde, Glasgow, UK

²Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK

³Academic Department of Medical Genetics, University of Cambridge, Cambridge, UK

⁴South West Thames Regional Genetic Services, St George's University Hospitals NHS Foundation Trust, London, UK

Correspondence to

Dr Helen Hanson, South West Thames Regional Genetics Service, London SW17 0QT, UK; helen.hanson@stgeorges.nhs.uk

Received 19 October 2020

Revised 2 December 2020

Accepted 5 December 2020

Published Online First 10 February 2021



© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY. Published by BMJ.

To cite: Wedderburn S, Archer S, Tischkowitz M, et al. *J Med Genet* 2021;**58**:579–580.

In 2017, the UK Cancer Genetics Group (UKCGG) and UK Genetic Testing Network (UKGTN) held a workshop which led to a consensus for UK cancer gene panel testing.¹ The agreed breast cancer panel included *BRCA1*, *BRCA2*, *PALB2*, *ATM*, *CHEK2*, *PTEN*, *STK11* and *TP53*. The genes *NBN*, *BRIP1*, *BARD1* and *CDH1* were discussed, but excluded from the panel. The agreed ovarian cancer panel included *BRCA1*, *BRCA2*, *BRIP1*, *MLH1*, *MSH2*, *MSH6*, *RAD51C* and *RAD51D*. The agreed genes were included as there is sufficient evidence of a clear association with breast or ovarian cancer predisposition and identifying a pathogenic variant in one of these genes would have clinical implications for cancer management, surveillance or risk reducing surgery. Of note, eligibility criteria for these panels were not addressed at the workshop. During March–May 2020, UKCGG conducted a review of breast cancer panel testing offered in the UK; each UK genetics centre was asked to complete a survey about testing (online supplemental information).

There was a 100% response rate from the 24 centres. **Figure 1** shows a comparison of testing pre-2018 versus post-2018 workshop. While some inconsistency remains on testing offered, there is a continued trend towards gene panel testing as agreed in 2018. Centres were additionally asked what testing they planned to offer following the introduction of the National Genomic Test Directory, which sets out the genomic tests commissioned by the National Health Service England and corresponding eligibility criteria.² While the first draft of the Test Directory (TD) was published in October 2018 and the current version in August 2020, genomic laboratory hubs are still transitioning to full implementation. The TD recommended a smaller panel consisting of *BRCA1*, *BRCA2* and *PALB2* for inherited breast cancer and isolated non-mucinous epithelial ovarian cancer (Criteria R208) with exclusion of *ATM* and *CHEK2*. *PTEN*, *STK11*, *TP53* and *CDH1* are recommended in specific situations where there are either additional syndromic features, specific pathology or young age of onset (Criteria R212, R213, R215, R216). An ovarian cancer panel as per UKCGG/UKGTN is recommended only where there are two or more cases of ovarian cancer in a family (Criteria R207).² With implementation of the TD, 33% of centres will

offer *BRCA1/BRCA2/PALB2*, and any combination of *TP53*, *CHEK2*, *ATM*, *STK11* or *PTEN*, 38% will offer only *BRCA1/BRCA2/PALB2*, and 29% planned to offer an alternative option for inherited breast cancer.

In reality, testing is not proscriptive, as seen in **figure 2** which summarises the responses to a variety of case scenarios. Centres are currently using a combination of TD criteria, national and/or local guidance, and the Manchester scoring system³ to direct testing decisions. The reasons for these differences are multifaceted and may reflect the recent reconfiguration of genetic laboratory services and the creation of the TD for centres in England which occurred after the 2018 guidelines were published, but has not yet been fully implemented in all centres. There is not a specific directory for the devolved nations, although some centres have chosen to follow the TD.

In summary, it appears that there is a willingness to move towards the 2018 consensus, but the ongoing differences in gene testing offered between centres continues to raise concerns about the current equity of service for patients and their families across the UK. Additionally, the difference in the recommendations from the UKCGG/UKGTN meeting and the TD have resulted in further variation in practice, particularly for the moderate risk breast cancer predisposition genes *ATM* and *CHEK2*. This is largely due to the UKCGG/UKGTN assessing only the appropriate inclusion of genes on a specific

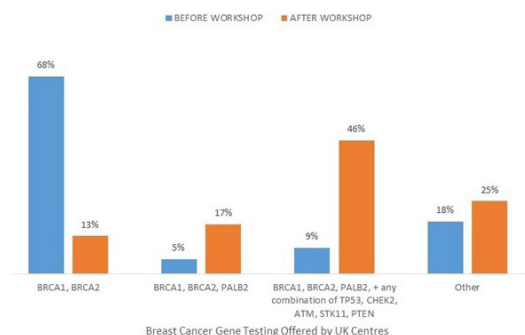


Figure 1 Comparison of what breast cancer gene testing was offered to non-syndromic breast cancer families in 24 UK Genetics Centres, before and after the UKCGG/UKGTN Inherited Cancer Panel workshop (n=24 responses).

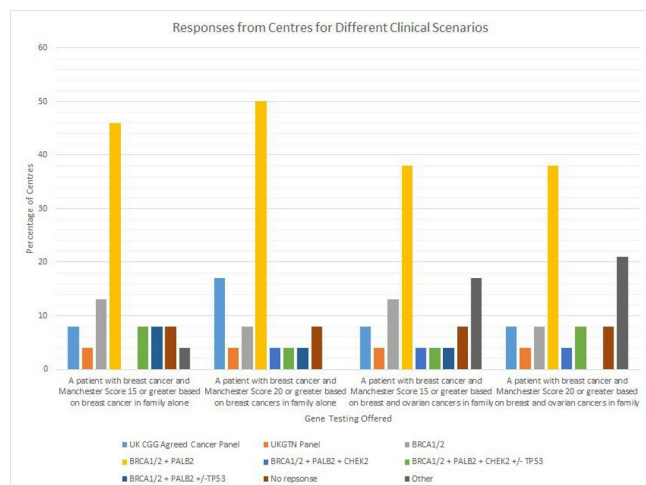


Figure 2 Responses from the 24 UK Genetics centres for different clinical scenarios.

panel and not the entry point for testing, which has been specified through the TD. Since the consensus meeting and first draft of the TD, there have been considerable advances in risk estimation for carriers of a pathogenic variant in *ATM* and *CHEK2* through the CanRisk model.⁴ This demonstrates the importance of a responsive TD that can adapt to new information that will impact both inclusion of genes on a specific panel and eligibility for testing. It is hoped that variation will be reduced once full implementation of the National TD takes place and the process for timely amendments to the TD is finalised.

Collaborators Dr Kai Ren Ong, Cancer Genetics Lead, West Midlands Genetics Service; Dr Alan Donaldson, Cancer Genetics Lead, Bristol Genetics Service; Dr Carole Brewer, Cancer Genetics Lead, Peninsula Genetics Service; Dr Julian Adlard, Cancer Genetics Lead, Yorkshire Genetics Service; Dr Julian Barwell, Cancer Genetics Lead, Leicester Genetics Service; Dr Lynn Greenhalgh, Cancer Genetics Lead, Liverpool Genetics Service; Dr Fiona Laloo, Cancer Genetics Lead, Manchester Genetics Service; Dr Rachel Harrison, Cancer Genetics Lead, Nottingham Genetics Service; Dr Dorothy Halliday, Cancer Genetics Lead, Oxford Genetics Service; Dr Zoe Kemp, Cancer Genetics Lead, Royal Marsden Genetics Service; Prof Zofia Miedzybrodzka, Cancer Genetics Lead, Aberdeen Genetics Service; Dr Mary Porteous, Cancer Genetics Lead, Edinburgh Genetics Service; Dr Rosemarie Davidson, Cancer Genetics Lead, Glasgow Genetics Service; Dr Jackie Cook, Cancer Genetics Lead, Sheffield Genetics

Service; Dr Lucy Side, Cancer Genetics Lead, Wessex Genetics Service; Dr Munaza Ahmed, Cancer Genetics Lead, NE Thames Genetics Service; Dr Anju Kulkarni, Cancer Genetics Lead, SE Thames Genetics Service; Dr Katie Snape and Dr Helen Hanson, Joint Cancer Genetics Leads, SW Thames Genetics Service; Dr Alex Murray, Cancer Genetics Lead, All Wales Genetics Service; Dr David Goudie, Cancer Genetics Lead, Dundee Genetics Service; Dr Richard Martin, Cancer Genetics Lead, Newcastle Upon Tyne Genetics Service; Dr Marc Tischkowitz, Cancer Genetics Lead, Cambridge Genetics Service; Dr Tabib Dabir, Cancer Genetics Lead, Belfast Genetics Service; Dr Angela Brady, Cancer Genetics Lead, NW Thames Genetics Service.

Contributors SW, HH, SA and MT designed the survey. All collaborators completed the survey. SW and SA collated the results. All authors contributed to the manuscript which was reviewed by collaborators.

Funding HH is supported by Cancer Research CRUK Catalyst Award, CanGene-CanVar (C61296/A27223).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: <https://creativecommons.org/licenses/by/4.0/>.

ORCID iD

Helen Hanson <http://orcid.org/0000-0002-3303-8713>

REFERENCES

- 1 Taylor A, Brady AF, Frayling IM, Hanson H, Tischkowitz M, Turnbull C, Side L, UK Cancer Genetics Group (UK-CGG). Consensus for genes to be included on cancer panel tests offered by UK genetics services: guidelines of the UK cancer genetics group. *J Med Genet* 2018;55:372–7.
- 2 NHSE. National genomic test directory. Available: <https://www.england.nhs.uk/publication/national-genomic-test-directories/>
- 3 Evans DGR, Eccles DM, Rahman N, Young K, Bulman M, Amir E, Shenton A, Howell A, Laloo F. A new scoring system for the chances of identifying a BRCA1/2 mutation outperforms existing models including BRCAPRO. *J Med Genet* 2004;41:474–80.
- 4 CanRisk. Available: <https://canrisk.org/>