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, on behalf of UKCGG

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, BRIPI, 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 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. 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 Lalloo, 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.

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ORCID iD  Helen Hanson http://orcid.org/0000-0002-3303-8713

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