UKCGG-National Cancer Genetics MDT meeting: 17th July 2025

Challenges associated with calculating breast cancer risk - lead by Leeds

Meeting contact: Hannah Musgrave (Hannah.Musgrave@nhs.net)

Thank you to everyone who attended this session. Below is a summary of the presented cases and relevant publications and resources to refer to.

Presented Cases

Case 1	**Any further Ix for family with strong history of breast/thyroid and stomach cancer** Extensive gene testing done	Presented by: Emma O'Donoghue CHI Crumlin (Genetics) Emma.ODonoghue@childrenshealthireland.ie
	Actions/Outcome: No further gene testing (other than ???CTNNA1 due to lobular br ca and 1 x rel with gastric cancer type unknown) to consider but clinical review to see if clinical diagnosis of PTEN Tumour Predisposition Syndrome can be made/is likely.	
Case 2	**Risk assessment with CHEK2 and ATM high risk variant in the family** CanRisk assessment complicated as CanRisk weights CHEK2 above ATM in terms of cancer risk and cannot account for high risk variant. Patient in question was CHEK2+ ATM high risk variant – but CanRisk giving v high risk assessment. Clinical felt that most FHx likely to be ATM-related	Presented by: Max Cole Peninsular Genetics, RD&E max.cole@nhs.net
	Actions/Outcome: Clinical risk assessment sometimes more appropriate than CanRisk (important to acknowledge limits). Offering chemoprevention important given association with ER+ tumours. Caution around RRM – no consensus to offer given usual moderate risk attributed to CHEK2. Cascade testing in family may help to refine risk but max had tried CanRisk changing ATM variant to BRCA1 and proband still came out as high risk on canRisk.	
Case 3	**Difficulties in RAD51C** Case to illustrate the them today. Assessed as eligible for RRM on CanRisk BUT not able to access additional breast screening past 60. Ovarian cancer risk assessed below 5% but not able to calculate a LTR. Referred for annual screening to 59 and to gynae for BSO discussion.	Presented by: Dr Rupa Kumar Royal Marsden Hospital [presenter email address]
	Actions/Outcome: action plan agreed and complexities noted. CanRisk will hopefully capture LTR ovarian cancer in the future.	
Case 4	**Lack of access to VHR breast screening after age 50** Case illustration for patient with estimated CBC risk of >40% but over age 50 and not able to access VHR screening (ATM+) and does not want to consider further surgery.	Presented by: Aditi Valecha Nottingham Clinical Genetics aditi.valecha@nhs.net

	Actions/Outcome: Discussion around the awareness of this issue in UKCGG and Breast screening leads. Looking at trying to evidence the number of patients who would have a risk consider to be equivalent (Prof G Evans data suggests 10 year risk of 12% at each subsequent decade after 40-50 also applicable). Screening service concerned about screening "new" group of patients. Have tried to argue that many of us have referred at 40% LTR where we cannot evidence 10 year risk. Work ongoing.	
Case 5	**Ovarian cancer management for reduced penetrance BRCA2 variant carrier** Female carrier of red pen BRCA2 variant, ca Ovary in mum. Not able to use CanRisk but wondering about supporting BSO or PROTECTOR trial.	Presented by: Charlotte Jaggard All Wales Medical Genetics Service Charlotte.Jaggard2@wales.nhs.uk
	Actions/Outcome: MDT agreed reasonable course of action to support BSO given lack of effective screening. LTR likely to be >5% even with red pen BRCA2 variant. Probably delay until menopause. Protector may be an option.	
Case 6	**ATM not clearly truncating variants** **Drawing our attention to recent discussions and decision that CanVig cannot manage a possible exceptional variant list (too many submissions)**	Presented by: Terri McVeigh Royal Marsden Hopsital terri.mcveigh@nhs.net
	Actions/Outcome: Advice for lab teams re importance of clearly reporting uncertain cancer risk associated with reported ATM variant. Advice for clinical teams about deciding whether or not to offer cascade test – will it affect management? Caution around canRisk (not able to differentiate between truncating and non-truncating variants) and importance of considering cross-service consistency especially where testing IS offered.	
Case 7	**General question from East of England breast nurses -** **Do we make an assessment based on non-family history factors** Discussion around modifiable risk factors that can change over time. CanRisk consensus document recommended all available info be used but had a smaller list of required fields. Further discussion around when to use a CanRisk e.g. if NICE guidance for eligibility for a FHx assessment not met.	Presented by: H Musgrave on behalf of Dr Claire Searle Nottingham Clinical Genetics clairesearle@nhs.net
	Actions/Outcome: refer back to CanRisk consensus guidelines. Some variability in practice. Caution where modifiable lifestyle factors change a risk grouping – discussion with patient about this and consider appropriateness of the advice. NICE CG164 will be reviewed in the coming 12-18 months so more guidance to follow.	

Relevant publications/resources

Topic	Link
ATM variant reporting	https://www.ukcgg.org/information-education/exceptional-variantsgene-specific-variant-reporting/
CanRisk Consensus document	https://www.nature.com/articles/s41416-024-02733-4

Expert Speaker Talk

Hannah Musgrave presented in expert speaker slot – introduction and scene setting for topic, and shared some UKCGG survey results

Talk Summary:

Current CanRisk limitations (from Antonis Antoniou)

- The model uses the same genetic risk factor relative risks for the first breast cancer and CBC. This is for all genes.
- Does not incorporate yet the latest evidence showing that the effects of rare pathogenic variants may differ for CBC compared to first breast cancer (this applies to all genes, including ATM)
- Does not account for the treatment of the first breast cancer (which is a key determinant of CBC risk)
- Does not account for tumour characteristics of the first breast cancer.
- Predicts only CBC risk, and does not include ipsilateral risk

From survey:

- Variability in practice around how risk is assessed and who is offered risk reducing surgery in the context of an affected woman/person with breasts.
- Some mixed feelings about further defining thresholds (note wording of the question around guiding discussions). Appetite for guidance around how to assess risk.
- To share survey results back with UKCGG community

Next meeting details

Date	Thursday September 18th 2025
Time	12:30 pm-1:45 pm
Theme	Variant interpretation and complex cases
Leading centre	Leicester
Contact for cases	Julian Barwell Julian.barwell@nhs.net

Please send any questions or ideas for future meetings to
UKCGGNationalMDT@icr.ac.uk