INTRODUCTION
Breast and ovarian cancers are malignant tumours of the breast tissue and of the ovaries, respectively. Breast cancer is common in women, with a lifetime risk of up to 1 in 8 in the general population (depending on ethnic origin). Approximately 5-10% of these cancer cases may be due to an inherited genetic defect in either the \textit{BRCA1} or \textit{BRCA2} genes which predispose to breast, ovarian and other cancers. Male pathogenic mutation carriers may have an increased risk of developing breast cancer (primarily \textit{BRCA2} carriers), prostate cancer and other cancers. The likelihood of there being a hereditary predisposition to breast cancer in a patient is increased by a patient having early-onset breast cancer, bilateral breast cancer, or the fact that they have Ashkenazi Jewish ancestry.

TESTING AND REFERRALS
All referrals are through clinical genetics or through one of the following: Consultant Oncologists, Consultant Gynaecologists, Consultant Breast Surgeons.

Diagnostic tests: Patients may qualify for \textit{BRCA1} and \textit{BRCA2} screening if they meet the UKGTN criteria (http://ukgtn.nhs.uk/uploads/tx_ukgtn/UKGTN_breast_cancer_testing_criteria_Final_161014.pdf).

Patients may be screened if they:
- have breast cancer and a family history of relevant cancers
- have early-onset and/or bilateral breast cancer
- have a triple negative breast cancer
- have breast cancer and non-mucinous epithelial ovarian cancer
- have high-grade serous epithelial carcinoma of the ovaries
- are unaffected, but have a significant family history of relevant cancers

Presymptomatic/Confirmatory tests for a pathogenic familial variant:
- Individuals qualify for testing if they are at risk of inheriting a cancer-predisposing variant from a family member. Testing of family members (presymptomatic or diagnostic confirmation) is for the familial variant only.

STRATEGY & TECHNICAL INFORMATION
- Diagnostic screening tests: \textit{BRCA1} and \textit{BRCA2} are analysed by Multiplicom’s MASTR™ Dx by the use of Illumina MiSeq sequence technology for small mutations and multiplex ligation-dependant probe amplification (MLPA) to screen for large-scale gene copy number changes.
- Ashkenazi Jewish population testing: patients can be screened for the 3 pathogenic founder variants in this population by fluorescent sequencing. These variants are: \textit{BRCA1} c.68_69delAG, \textit{BRCA1} c.5266dupC, and \textit{BRCA2} c.5946delT. Individuals referred for Ashkenazi Jewish testing who have one of the variants previously identified in their family are tested for all three variants.
- Polish population testing: patients can be screened for the 3 pathogenic founder variants in this population by fluorescent sequencing. These variants are: \textit{BRCA1} c.181T>G, \textit{BRCA1} c.4035delA, \textit{BRCA1} c.5266dupC
- Presymptomatic/Confirmatory testing: testing for pathogenic familial \textit{BRCA1} and \textit{BRCA2} variants is undertaken by Sanger sequencing and/or MLPA as appropriate. If a family has not been previously analysed in-house, the familial test should ideally be discussed with the laboratory in advance so a control can be obtained.

TARGET REPORTING TIMES
Diagnostic test: 40 working days
Presymptomatic/Familial Mutation test: 10 working days

CLINICAL SENSITIVITY
Germline pathogenic \textit{BRCA1} and \textit{BRCA2} variants may account for 5 - 10% of breast cancers and 10 - 15% of ovarian cancers among white women (United States). Campeau et al, Human Genetics 2008; 124(1):31–42. These figures increase in pre-selected cohorts, but vary with the selection criteria applied.

N.B. Details are correct for the date of printing only – last updated 16/06/2015