Annex A: Population groups recommended for genetic testing to characterise breast cancer-related gene variants*

**ATM, BARD1, BRCA1, BRCA2, CDH1, CHEK2, NF1, PALB2, PTEN, RAD51C, RAD51D, STK11* or *TP53*

A. Individuals with a personal history of breast cancer, who have risk factors for hereditary breast cancer who meet **any** of the following**:**

A1. A pathogenic variant (PV) identified on tumour genomic testing that would have clinical implications if confirmed to be germline; or

A2. A personal history of breast cancer with specific features:

i. ≤50 years old; or
ii. Triple-negative breast cancer; or
iii. Multiple primary breast cancers (synchronous or metachronous); or
iv. Lobular breast cancer with personal or family history of diffuse gastric cancer; or
v. Male breast cancer; or

A3. Ancestry: Ashkenazi Jewish ancestry; or

A4. A family history of:

i. ≥1 close biological relative (includes first-, second-, and third-degree relatives on the same side of the family) with:
   - Breast cancer at age ≤50 years old; or
   - Male breast cancer; or
   - Ovarian cancer; or
   - Pancreatic cancer; or
   - Prostate cancer with metastasis, or high- or very-high-risk group; or

ii. ≥3 diagnoses of breast and/or prostate cancer (any grade) on the same side of the family including the patient with breast cancer

A5. An estimated ≥10% probability of a *BRCA1/2* PV based on prior probability models (e.g. Manchester Score, CanRisk) even if criteria A1-A4 are not met

B. Individuals with a significant family history of breast cancer, and unknown familial genetic status. These individuals should meet **both** of the following**:**

B1.

- The individual has a first-degree biological relative with breast cancer who is unavailable for genetic testing; or
- The individual has a second-degree relative with breast cancer (unavailable for genetic testing), if no first-degree relative is available^; and

B2. An estimated ≥10% probability of a *BRCA1/2* PV based on prior probability models (e.g. Manchester Score, CanRisk)

C. Biological relatives of a known pathogenic/likely pathogenic variant (P/LPV) carrier:

C1.

- First-degree biological relatives of an individual who carries a P/LPV in a breast cancer susceptibility gene; or
- Second-degree biological relatives may be considered if the first-degree relative is unavailable^

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^ *HBOC syndrome-related P/LPVs are typically inherited in an autosomal-dominant manner. As a result:*

- *First-degree relatives (i.e. biological parents, children, siblings) of an individual with a PV have an estimated 50% chance of inheriting the variant and are therefore prioritised for cascade genetic screening*
- *Second-degree relatives to index patients (i.e. biological grandparents, aunts/uncles, nieces/nephews, grandchildren) have an estimated 25% chance of inhering the variant.*

*- If a first-degree relative is **unavailable for genetic testing (e.g. deceased, declined genetic testing or uncontactable)** and his/her genetic result is unknown, a second-degree relative in the direct lineage of the first-degree relative (e.g. the child of the affected first degree relative) may be considered for genetic testing.*

- Where a first-degree relative is known to test negative for the familial PV, testing of second-degree relatives is not required.

- At present, subsidised HBOC genetic testing is available for eligible first-degree relatives only. Eligibility criteria should be checked against the prevailing funding guidance, which may be updated over time.