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

** BRCA1, BRCA2, BRIP1, PALB2, RAD51C and RAD51D. EPCAM, MLH1, MSH2, MSH6 and PMS2, which are associated with an increased risk of ovarian cancers, are excluded from this annex because guidance on downstream management strategies will be addressed in upcoming Lynch Syndrome ACRs.*

A. Individuals with a personal history of ovarian cancer, which includes those with epithelial ovarian, fallopian tube or peritoneal 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 epithelial ovarian, fallopian tube or peritoneal cancer at any age; or

A3. An estimated ≥10% probability of a *BRCA1/2* PV based on prior probability models (e.g. Manchester Score, CanRisk), even if criteria A1- A2 are not met

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

B1.

- The individual has a first-degree biological relative with ovarian cancer who is unavailable for genetic testing; or
- The individual has a second-degree relative with ovarian 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 an ovarian 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.