II UPDATE SWISS GUIDELINES FOR GENETIC COUNSELLING AND TESTING FOR PREDISPOSITION TO BREAST, OVARIAN, PROSTATE AND PANCREATIC CANCER 2024

WOMEN WITH A PERSONAL HISTORY OF BREAST CANCER OR DCIS AND ONE OF THE FOLLOWING	
Age at diagnosis ≤ 40 y (any case) or ≤ 50 y at oncogeneticist's discretion	
Triple negative (ER, PR and HER2 negative) BC ≤ 60 y or older at oncogeneticist's discretion	
Bilateral BC or second separate primary	• if the first cancer was diagnosed ≤ 50 y • with ≥ 1 close relative with BC (if only one relative affected, then age at diagnosis ≤ 50 y)
Age at diagnosis ≤ 50 y	• with 1 close relative with BC ≤ 50 y • limited family history
Diagnosed at any age	• with ≥ 2 close relatives with BC or Prostate CA • a close male relative with BC • with ≥ 1 close relative with epithelial OC, Pancreatic CA or metastatic or high-risk Prostate CA (see section Prostate CA below) • Ashkenazi Jewish ancestry (see section Ashkenazi Jewish ancestry below)
MEN WITH A PERSONAL HISTORY OF BREAST CANCER	
HEREDITARY PREDISPOSITION TO OVARIAN CANCER (including fallopian tube or peritoneal CA)	
• Personal history of epithelial OC (including fallopian tube or peritoneal CA) at any age • Personal history of STIC (serous tubal intraepithelial CA): Consider genetic counselling/testing • Unaffected with OC with a first- or second-degree relative with epithelial OC (including fallopian tube or peritoneal CA) at any age	
ASHKENAZI JEWISH HERITAGE	
Search for the 3 founder BRCA1 and BRCA2 P/LP variants may be considered regardless of personal or family history	
RISK ACCORDING TO CALCULATIONS OF RISK MODELS	
Individuals affected or unaffected with BC or OC not meeting the criteria above with a probability > 5% of a BRCA1/2 P/LP variant based on prior probability models (eg, Tyrer-Cuzick, CanRisk)	
PANCREATIC CANCER	
Exocrine Pancreatic CA (adenocarcinoma) at any age	
Unaffected individuals with	• 1 first-degree relative with ≥ 1 or more first- or second-degree relatives with Pancreatic CA • ≥ 3 individuals with Pancreatic CA (same side of the family)
PROSTATE CANCER	
• Metastatic Prostate CA at any age • High-risk localised or locally advanced Prostate CA (PSA >20ng/mL or ISUP Grade Group 4 or 5 or ≥ cT2c or cN1) irrespective of the family history • Localised Prostate CA (any grade) with ≥ 3 close relatives with BC, OC, Pancreatic or Prostate CA	
TREATMENT INDICATIONS	
• PARP inhibitors for BC and OC in the early and metastatic setting • PARP inhibitors in Prostate CA and Pancreatic CA in the metastatic setting	

FAMILY HISTORY ONLY
Testing of individuals (affected or unaffected by CA themselves) with ≥ 1 close relative with BC, OC, Pancreatic CA and/or Prostate CA fulfilling one of the above criteria
CARRIER TESTING
Testing of an individual from a family with a known P/LP variant in a gene conferring high or moderate risk for CA
TUMOR PATHOGENIC VARIANT
Germline confirmation of a P/LP variant of a gene conferring a high or moderate CA risk detected by tumor profiling
FURTHER RECOMMENDATIONS
• **Hereditary Colorectal CA (Lynch syndrome, polyposis syndromes), Renal cell CA, Urothelial CA, Paraganglioma, Pheochromocytoma and Neuroendocrine tumors: See current version of the NCCN Guidelines** • **Patients with hereditary Renal cell CA, Urothelial CA, Paraganglioma, Pheochromocytoma and Neuroendocrine tumors should preferably be referred to experts/centers with solid experience in these issues**
Abbreviations: **BC, breast cancer; CA, cancer; DCIS, ductal carcinoma in situ; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LP, likely pathogenic; P, pathogenic; PR, progesterone receptor; OC, ovarian cancer; y, years**
Definitions: • **Ashkenazi Jewish founder P/LP variants: BRCA1: c.68_69delAG, c.5266dupC; BRCA2: c.5946delT** • **Ashkenazi Jewish heritage: At least one parent or grandparent of Ashkenazi Jewish ancestry** • **Close relative: First- or second-degree relative on the same side of the family. First-degree relatives: Mother/father, sister/brother, daughter/son. Second-degree relatives: Grandparents, aunt/uncle, niece/nephew, grandchildren** • **Limited family history: ≤ 2 female close relatives having lived beyond age 45 y in either lineage**

References:
- Chappuis P. et al. Genetic predisposition to breast and ovarian cancer. Schw. Ärztezeitung 2017
- Stoll S. et al. Update Swiss guideline for counselling and testing for predisposition to breast, ovarian, pancreatic and prostate cancer. Swiss Med Wkly. 2021;151:w30038