BRCA2 Germline Pathogenic Variant Carriers Management Guidelines for Healthcare Professionals

Female *BRCA2* Pathogenic Variant (GPV) carrier age-dependent cumulative cancer risks (95% confidence intervals) *		
Age (years)	**Breast cancer** (Note population risk to age 80 approx 10%*)	**Tubo-ovarian cancer** (Note population risk to age 80 approx 1.5%*)
21-30	4% (2-9%)	-
31-40	13% (9-19%)	<0.5%
41-50	35% (29-41%)	1-2%
51-60	53% (46-59%)	7% (4-11%)
61-70	61% (55-68%)	15% (10-23%)
71-80	69% (61-77%)	17% (11-25%)†

†Risk of OC >70 is likely underestimated by referenced study, see management below and FAQ

Other cancers	*BRCA2* GPV carrier risk (95% confidence interval)	Population risk*
Male breast cancer	4% (2-8%) by age 80	Rare
Prostate cancer † Adjusted risk for screening effect, please see FAQ for unadjusted figures	41% (22-54%) by age 85† (Nyberg et al, 2020)	Approx 12% by age 80
	27% (21-35%) by age 80 (Li et al, 2022)	
Pancreatic cancer*	**Male:** Approx 4-5% by age 80	Approx 1% by age 80
	Female: Approx 2% by age 80	Up to 1% by age 80
No significant association consistently found for other cancers.		

Cumulative risk for contralateral breast cancer by time since first breast cancer *	
≤5 years	8% (6-12%)
>5-10 years	16% (12-21%)
>10-15 years	21% (17-26%)
>15-20 years	26% (20-33%)
>20-43 years	65% (25-98%)

Patient resources

- A Beginner's Guide to *BRCA1* and *BRCA2* (patientinfolibrary.royalmarsden.nhs.uk)
- breastcancernow.org "Someone like me" https://breastcancernow.org/information-support/support-you/someone-me-telephone-support
- coppafeel.org
- https://www.macmillan.org.uk/cancer-information-and-support/worried-about-cancer/causes-and-risk-factors/brca-gene

Notes

It is important to manage patients in the context of their family history of cancer. Individualised risk estimates available from https://canrisk.org/ **should be used instead of the general risk estimates wherever possible.***See FAQ document for further information and references.

Management recommendations	
Screening	**Breast**: Annual MRI Breast from 30 years. Annual mammography from 40 years. Earlier commencement of annual breast MRI from age 25 may be considered for women with an individualised 10 year breast cancer risk of ≥ 8%*. For women with previous breast cancer, as above if residual breast tissue.
	Tubo-ovarian: Not currently recommended. No evidence based screening programme.
	Prostate: Annual PSA from 40 with onward referral if PSA >3.0ng/ml.
	Pancreatic: Not currently recommended outside of research. Consider the EUROPAC study.
Risk-reducing surgery	**Breast**: Discuss bilateral mastectomy. Individualised* assessment recommended.
	Tubo-ovarian: Discuss risk-reducing bilateral salpingo-oophorectomy (RRBSO), offer when childbearing is complete and no earlier than age 40 – 45. Due to continued risk of ovarian cancer at older ages, RRBSO should be discussed with all women, with consideration of general fitness/co-morbidities.
Hormone replacement	Women undergoing RRBSO with no previous history of breast cancer, should consider taking HRT until 50. For women with previous breast cancer, individualised discussion with Oncologist is advised.
Chemoprevention	Discuss the pros and cons of chemoprevention. Can be offered if no contraindications. No studies have been conducted to date on efficacy of chemoprevention in *BRCA2* GPV carriers.
Cancer management	*BRCA2* GPV carrier status may influence management of current cancers – ensure oncologist aware of carrier status and manage as part of a multidisciplinary team. Consider long term prognosis / competing risks prior to considering risk-reducing surgery.
Lifestyle information	-Provide information about regular self-breast examination and ovarian cancer symptom awareness. -Provide information on the benefits of smoking cessation, minimising alcohol intake and maintaining a healthy weight to lower the chance of getting cancer. -Contraception: use of oral contraceptive pill (OCP) is not contraindicated, but requires informed discussion and consideration of alternative forms of contraception*.
Family matters	-Refer to clinical genetics to facilitate genetic testing in at-risk family members. -Refer to clinical genetics for discussions on reproductive options.
Psychological	-Consider referral to clinical psychology support services if appropriate.