

Table S1. Gene lists included in next-generation sequencing (NGS) hereditary cancer panel

Panel	Updated date	Genes
Hereditary NGS panel (23 genes)	2018.02	APC, ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD50, RAD51C, RET, STK11, TP53
Hereditary NGS panel (25 genes)	2018.10	APC, ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD50, RAD51C, RET, STK11, TP53, NF1, RAD51D
Hereditary NGS panel (28 genes)	2019.11	APC, ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD50, RAD51C, RET, STK11, TP53, NF1, RAD51D, POLD1, POLE, SMAD4
Hereditary NGS panel (73 genes)	2022.02	APC, ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD50, RAD51C, RET, STK11, TP53, NF1, RAD51D, POLD1, POLE, SMAD4, BMPR1A, CDKN2A, FH, HRAS, MAX, MET, MRE11, NF2, RB1, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, TSC1, TSC2, VHL, WT1, AIP, AXIN2, BAP1, CDC73, CDK12, CDK4, CDKN1B, CHEK1, CTNNA1, DICER1, EXT1, EXT2, FANCL, FLCN, GREM1, HOXB13, KIT, MSH3, NTHL1, PPP2R2A, PTCH1, RAD51B, RAD54L, SMARCA4, SMARCB1, SUFU

*Abbreviation: NGS, next-generation sequencing

Table S2. Comparative Guidelines for Screening and Managing BRCA Gene Mutations: Korea, US, and UK

Guidelines	Country	Breast cancer	Ovarian cancer	Other cancers	Ref
10th Korean Breast Cancer Treatment Guidelines (2023)	Korea	<p><u>Female carriers</u></p> <ul style="list-style-type: none">-Self-examination education from age 18.-Clinical breast examination every 6 months starting at age 25.-Annual MRI screening from age 25-29.-Annual MMG and MRI from age 30-75. <p><u>Male carriers</u></p> <ul style="list-style-type: none">-Monthly self-examination and clinical breast examination every 12 months starting at age 35-Annual MMG from age 50 for men with gynecomastia. <p><u>Management</u></p> <ul style="list-style-type: none">-Bilateral RRM may be considered for BRCA1/2 carriers.-Contralateral mastectomy may be considered in carriers diagnosed with breast cancer.	<p><u>Screening</u></p> <ul style="list-style-type: none">-Transvaginal ultrasound and CA125 blood test every 6 months starting at age 30.-Ultrasound is recommended between days 1-10 of the menstrual cycle; CA125 after day 5. <p><u>Management</u></p> <ul style="list-style-type: none">-RRSO is recommended for BRCA1/2 carriers to lower ovarian and breast cancer risk.-RRSO is recommended at age 35-40 after family planning is complete.-Timing of RRSO should be individualized based on patient discussions.	<p>Prostate Cancer</p> <ul style="list-style-type: none">-DRE and PSA blood test for early detection of prostate cancer from age 18.-Follow-up prostate cancer screening is recommended for <i>BRCA2</i> carriers. <p>Pancreatic Cancer</p> <ul style="list-style-type: none">-Initial screening with EUS, followed by alternating EUS and contrast-enhanced pancreatic MRI/MRCP, or annual MRI. <p>Gastric Cancer</p> <ul style="list-style-type: none">-Endoscopy every 2 years starting at age 40, or 10 years earlier than the earliest age of onset in the family if there is a family history. <p>Colorectal Cancer</p> <ul style="list-style-type: none">-Colonoscopy every 5 years starting at age 40, or 10 years earlier than the earliest age of onset in the family if there is a family history.	[40]
NCCN (2024)	US	<p><u>Female carriers</u></p> <ul style="list-style-type: none">-Breast awareness from age 18.-Clinical breast examination every 6-12 months starting at age 25.-Annual MRI screening from age 25-29 (MMG if MRI unavailable).-Annual MMG and MRI from age 30-75.-Individualized management after age 75. <p><u>Male carriers</u></p> <ul style="list-style-type: none">-Breast self-exam training and annual clinical breast examination starting at age 35- Annual MMG from age 50 or earlier depending on family history. <p><u>Management</u></p> <ul style="list-style-type: none">- RRM may be considered based on age, life expectancy, and residual breast cancer risk.	<p><u>Screening</u></p> <ul style="list-style-type: none">-Undescribed <p><u>Management</u></p> <ul style="list-style-type: none">-BRCA1 carriers: RRSO recommended at age 35-40.-BRCA2 carriers: RRSO can be delayed to age 40-45 unless family history suggests earlier intervention.-Pre-surgical CA125 testing and pelvic ultrasound recommended.-Combined OCP or hormonal IUDs can be considered to reduce ovarian cancer risk for women retaining their ovaries.-HRT may be considered post-RRSO, tailored to the presence or absence of the uterus.	<p>Prostate Cancer</p> <ul style="list-style-type: none">-Screening should begin at age 40.-Screening may be considered for <i>BRCA1</i> PV/LPV carriers.-Screening is recommended for <i>BRCA2</i> PV/LPV carriers. <p>Pancreatic Cancer</p> <ul style="list-style-type: none">-Screening for pancreatic cancer should be considered starting at age 50, or 10 years earlier than the earliest diagnosis of exocrine pancreatic cancer in a first- or second-degree relative with a germline PV/LPV, whichever comes first.-For individuals without a family history of exocrine pancreatic cancer, pancreatic cancer screening is not recommended for PV/LPV carriers in genes other than <i>ATM</i>, <i>BRCA2</i>, <i>STK11</i>, and <i>CDKN2A</i>.	[41]

				Melanoma - There are no specific guidelines for melanoma; however, annual full-body skin examinations are recommended. - General melanoma risk management, such as minimizing UV exposure, is appropriate.	
NICE (updated 2023)	UK	<u>Female carriers</u> -MRI and MMG not recommended from age 20-29. -Annual MRI and consider annual MMG from age 30-39. -Annual MRI and MMG from age 40-49. -Annual MMG from age 50-59 (MRI only for dense breasts). -Annual MMG from age 60-69 (MRI only for dense breasts). -MMG as part of the population screening program after 70. <u>Male carriers</u> -Undescribed <u>Management</u> -RRM available for <i>BRCA1</i> carriers, with detailed counseling on benefits and risks. Immediate or delayed breast reconstruction should be offered by specialized teams.	<u>Screening</u> - Serial CA125 testing every 4 months using validated algorithms - Annual consultations to discuss results and risk-reducing surgery. <u>Management</u> - <i>BRCA1</i> carriers: RRSO recommended after age 35. - <i>BRCA2</i> carriers: RRSO recommended after age 40. - Surgery should occur after family planning is complete. - Comprehensive discussion of benefits and risks is required. Surgery is not recommended for patients with significant comorbidities or limited life expectancy.	Not Applicable	[42]

* CA125: Cancer Antigen 125; DRE: Digital Rectal Examination; EUS: Endoscopic Ultrasound; LPV: Likely Pathogenic Variant; MMG: Mammogram; MRCP: Magnetic Resonance Cholangiopancreatography; MRI: Magnetic Resonance Imaging; NCCN: National Comprehensive Cancer Network; NICE: National Institute for Health and Care Excellence; OCP: Oral Contraceptives PV: Pathogenic Variant; RRM: Risk-Reducing Mastectomy; RRSO: Risk-Reducing Salpingo-Oophorectomy; UV: Ultraviolet