Cost-effectiveness Analysis of Cancer Susceptibility Gene-Specific Prevention Strategies for Ovarian and Breast Cancer

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Introduction

- Around 15–20% ovarian cancer (OC) and 5% of breast cancer (BC) are caused by known pathogenic variants (PVs) in cancer susceptibility genes (CSGs).
- PVs in *BRCA1, BRCA2, PALB2, RAD51C, RAD51D, BRIP1* confer varying lifetime OC risks of 44–48%, 17–20%, 5%, 11%, 13%, and 5.8%, respectively; *BRCA1, BRCA2, PALB2, RAD51C, RAD51D* PVs also confer elevated lifetime BC risks of 65–72%, 61–69%, 53%, 21%, and 20%, respectively.
- Individuals with PV in these CSGs have options to prevent OC or BC, including risk-reducing surgery, medical prevention, and breast cancer surveillance. Risk-reducing salpingo-oophorectomy (RRSO) and risk-reducing mastectomy (RRM) remain the most clinically effective preventive strategies.
- Existing guidelines mainly focus on *BRCA1* and *BRCA2* and the optimal timing of management for all CSGs is not well addressed.
- No cost-effectiveness studies for risk-reducing surgeries for non-*BRCA* CSG carriers (*PALB2, RAD51C, RAD51D, BRIP1*) have been undertaken, and UK health system specific cost-effectiveness evidence for *BRCA1/BRCA2* is lacking.

Objectives

This study aimed to evaluate the cost-effectiveness of eligible prevention and surveillance strategies and the optimal timing of management in *BRCA1, BRCA2, PALB2, RAD51C, RAD51D,* and *BRIP1* PV carriers. This analysis was used to inform the UK NICE guideline on identifying and managing familial and genetic OC risk and has been presented in the closed Guideline Committee Meeting.

Methods

- Study design: decision-analytic Markov model.
- Target population: UK unaffected women with PVs in *BRCA1, BRCA2, PLAB2, RAD51C, RAD51D, BRIP1.*
- Time horizon: lifetime (age 30-100 years).
- Research perspective: Payer/UK NHS.
- Discount rate: 3.5% as recommended by NICE.
- Willingness-to-pay threshold: £20,000-30,000 per quality-adjusted life-year (QALY).

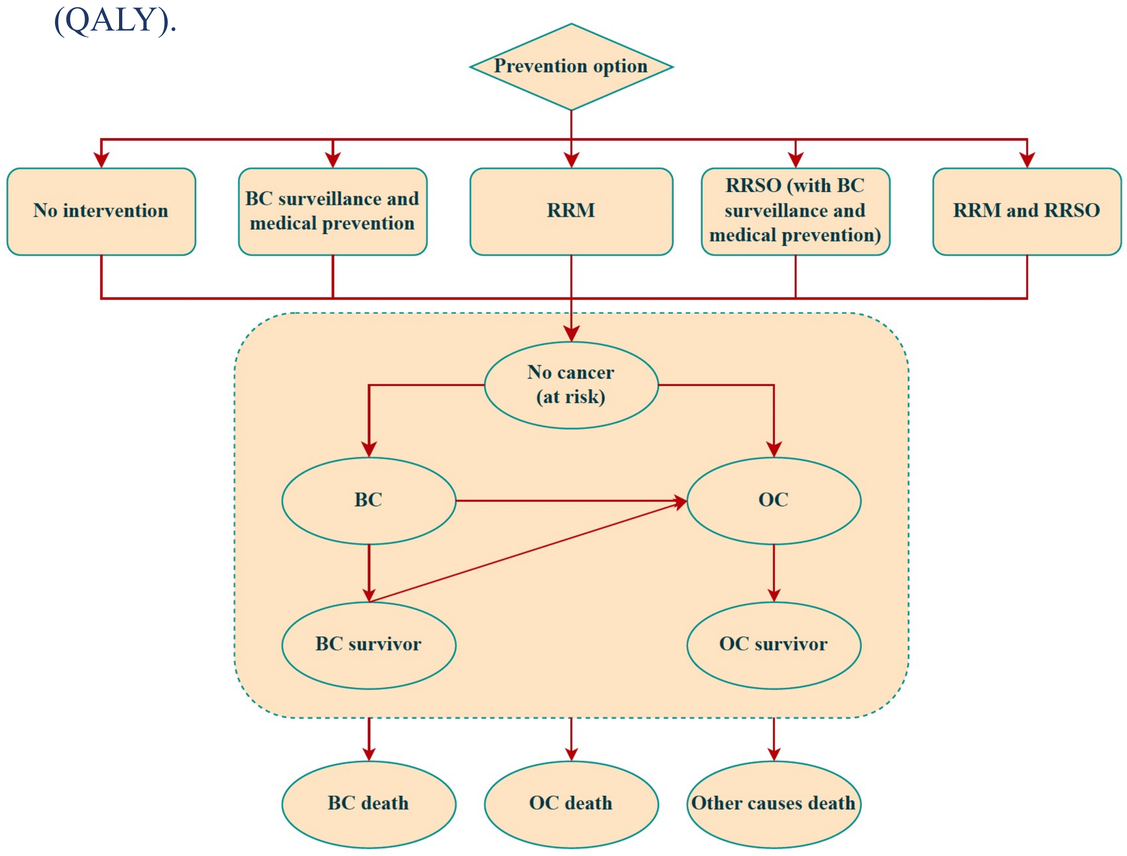


Figure 1. Markov model overview

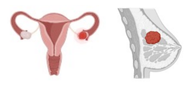
Results

- Undergoing both RRSO and RRM was most cost-effective for *BRCA1* (RRM: 30-years; RRSO: 35-years), *BRCA2* (RRM: 35-years; RRSO: 40-years), *PALB2* (RRM: 40-years; RRSO: 45-years) PV carriers.
- RRSO at age 45-years was cost-effective for *RAD51C, RAD51D,* and *BRIP1* PV carriers compared with non-surgical strategies.

Table 1. Base case analysis results

Strategy	Costs (£)	Life year	QALYs	Net monetary benefit (£)	Incremental cost-effectiveness ratio (ICER, £/QALY)
BRCA1					
High-risk BC surveillance and tamoxifen from age 30	24,767	22.40	17.45	324,295	Reference
RRM at age 30	25,368	22.67	18.82	350,956	441
RRSO at age 35 with high-risk BC surveillance and tamoxifen from age 30	18,042	24.33	19.11	364,086	-4,067
RRM at age 30 and RRSO at age 35	18,190	25.05	20.84	398,614	-1,942
BRCA2					
High-risk BC surveillance and tamoxifen from age 30	16,461	23.43	18.43	352,188	Reference
RRM at age 35	17,013	23.52	19.42	371,423	558
RRSO at age 40 with high-risk BC surveillance and tamoxifen from age 30	14,214	24.66	19.45	374,842	-2,202
RRM at age 35 and RRSO at age 40	16,272	25.00	20.56	394,892	-89
PALB2					
High-risk BC surveillance and tamoxifen from age 30	10,376	23.64	18.77	365,059	Reference
RRSO at age 45 with high-risk BC surveillance and tamoxifen from age 30	11,182	24.75	19.60	380,866	970
RRM at age 40	12,260	23.82	19.62	380,160	2,219
RRM at age 40 and RRSO at age 45	14,337	24.99	20.44	394,369	2,381
RAD51C					
Moderate-risk BC surveillance and tamoxifen from age 40	4,947	23.68	19.59	386,873	Reference
RRSO at age 45 with moderate-risk BC surveillance and tamoxifen from age 40	5,812	24.92	20.49	403,978	962
RAD51D					
Moderate-risk BC surveillance and tamoxifen from age 40	4,964	23.69	19.61	387,156	Reference
RRSO at age 45 with moderate-risk BC surveillance and tamoxifen from age 40	5,661	24.94	20.51	404,527	771
BRIP1					
No surgery	1,520	23.82	20.17	401,958	Reference
RRSO at age 45	3,525	25.05	21.03	416,975	2,355

- The most cost-effective strategy could prevent 923 OC/BC cases and 302 deaths for *BRCA1*; 686 OC/BC cases and 170 deaths for *BRCA2*, 464 OC/BC cases and 130 deaths for *PALB2*; 102 OC cases and 64 deaths for *RAD51C*; 118 OC cases and 76 deaths for *RAD51D*; 55 OC cases and 37 deaths for *BRIP1* per 1000 PV-carriers.



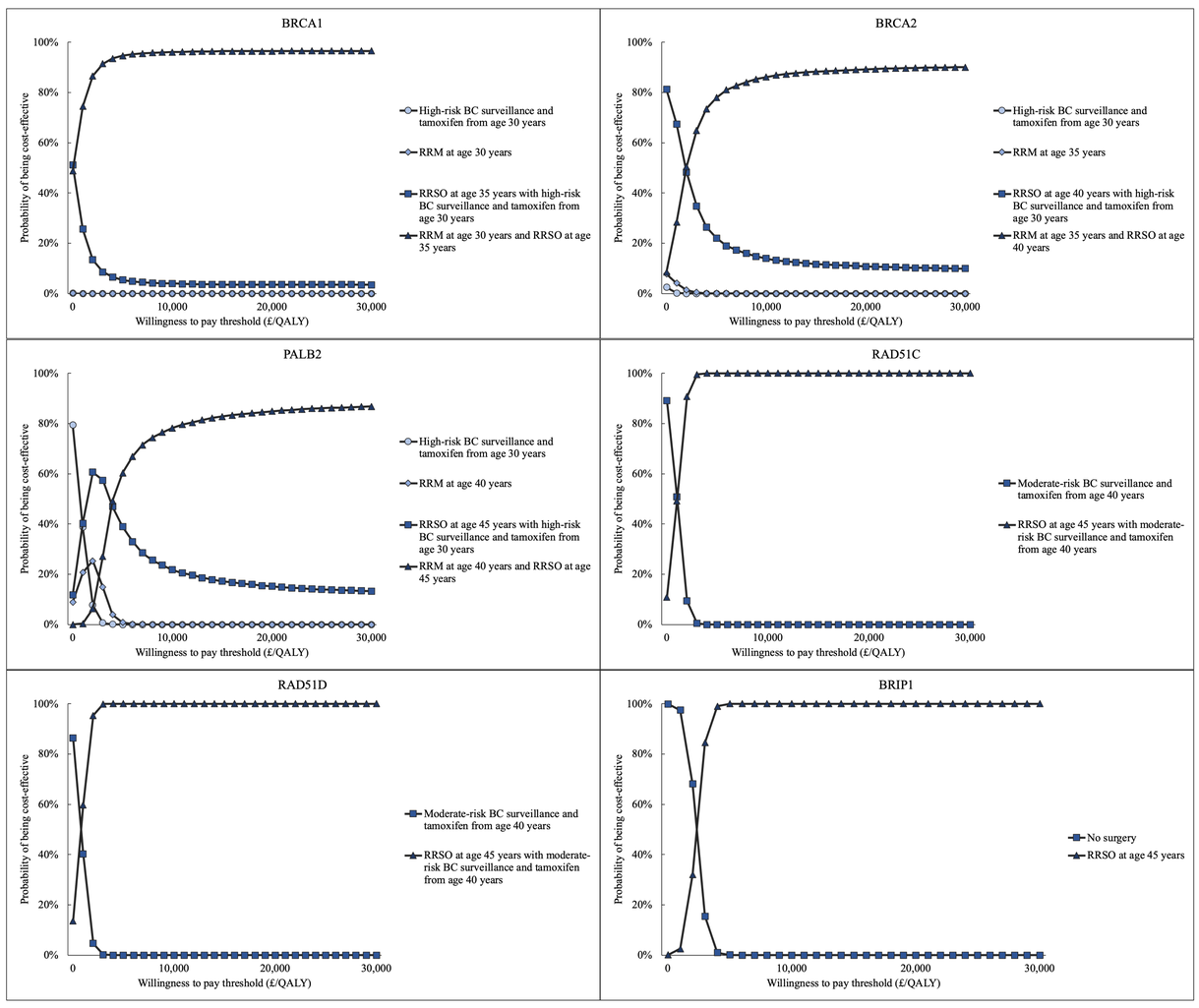


Figure 2. Probabilistic sensitivity analysis

RRM and RRSO was cost-effective in 96.5%, 89.2%, 84.8% simulations for *BRCA1, BRCA2, PALB2*, while RRSO was cost-effective in >99%% simulations for *RAD51C, RAD51D, BRIP1.*

Conclusions

- A one-size fits all approach is not the best for individual CSG PV carriers.
- This supports personalised surgical recommendations to prevent OC and BC specific to each CSG.
- These data have informed current NICE guideline on women at high risk of OC (expected publication March 2024).

Disclosure

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