# COST-EFFECTIVENESS ANALYSIS (CEA) OF SURVEILLANCE AND PREVENTIVE STRATEGIES OF OVARIAN CANCER IN WOMEN WITH BRCA1/2 PATHOGENIC VARIANTS.

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## BACKGROUND

✔ Pathogenic Variants (PVs) in BRCA1 and BRCA2 genes are associated with elevated risk of breast (BC) and ovarian cancer (OC) with significant clinical and socioeconomic burden. Prevention of cancer risk in BRCA1 and BRCA2 PV carriers varies among countries with different combinations of preventive and surveillance strategies. Preventive strategies includes risk-reducing surgical interventions, while standardized surveillance strategies are still not defined.

✔ The main aim of this study was to assess **cost-effectiveness** of a combined **OC surveillance and prevention** strategy in BRCA1 and BRCA2 PV carriers.

## METHODS

✔ A Markov decision model was developed to simulate progression of BC and OC in BRCA1 and BRCA2 PV carriers separately. The model estimated benefits and costs associated with three OC surveillance and/or preventive strategies.

| Strategy | Description |
|---|---|
| **Surveillance-Surgery - SS** | Annual surveillance with two gynecological visits, two transvaginal ultrasounds, and two CA125 measurements, up to the proposal of salpingo-oophorectomy (SO), in addition to bilateral mastectomy (RM) at appropriate age. |
| **Only-Surgery - OS** | Proposal of SO and RM at appropriate age without surveillance programs. |
| **No-Intervention - NI** | No prevention or surveillance programs. |

✔ The Markov model simulated disease progression separately in women with BRCA1 and BRCA2 mutations. The initial cohort consisted of 30-year-old women carrying a BRCA mutation with no history of BC or OC. The model duration was 80 cycles, each lasting 1 year (i.e., up to the age of 110 or death). The model simulating the SS and OS strategies included 15 health states as illustrated in **Figure 1**. The model simulating the NI strategy didn't include health states related to interventions or post-intervention and therefore it had 9 health states.

**Figure 1**. Markov Model Structure



SO = salpingo-oophorectomy
RM = reducing mastectomy
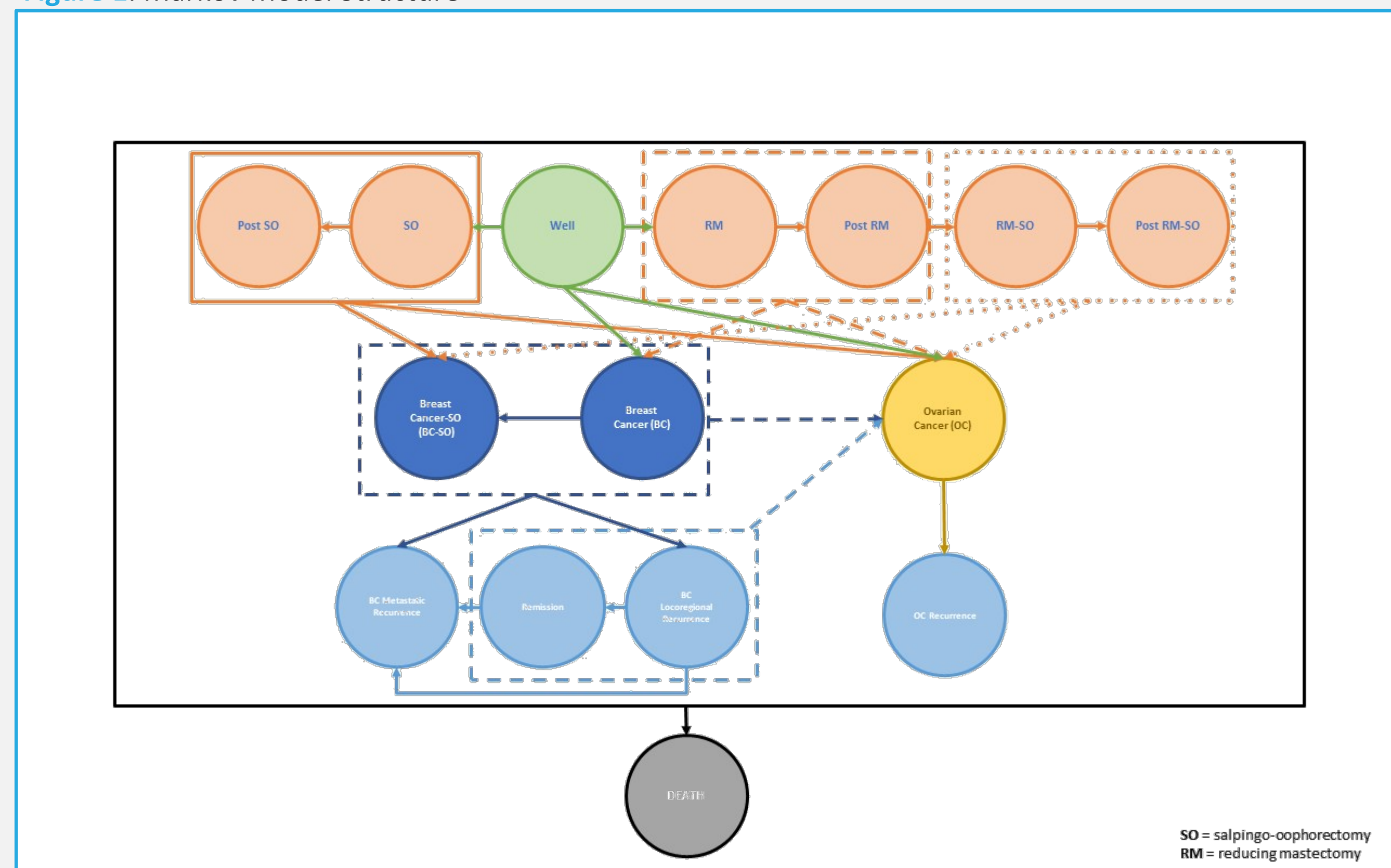
✔ The simulation model was designed to reflect a cohort of Italian women with BRCA1 or BRCA2 PVs and it was populated using data related to the Italian context, as much as possible taken from literature or clinical practice.

✔ The analysis adopted the Italian National Health Service (NHS) perspective and a life-time horizon. It included direct healthcare costs and quality-adjusted life years (QALYs) as outcome measure. The model estimated both incremental cost-effectiveness ratio (ICER) and the net monetary benefit (NMB) with a willingness to pay (WTP) threshold of €30,000, using the SS strategy as reference. The model performed a base-case analysis and both deterministic and probabilistic sensitivity analyses.

## RESULTS

**Table 1.** Cost-effectiveness of surveillance and prevention strategies in women with BRCA1 and BRCA2 PVs.

| | BRCA1 | | | BRCA2 | | |
|---|---|---|---|---|---|---|
| | SS | OS | NI | SS | OS | NI |
| Cost (€) | 17,893 | 19,902 | 26,276 | 13,644 | 13,993 | 17,372 |
| QALY | 22.25 | 21.80 | 19.60 | 23.15 | 22.98 | 21.49 |
| | | | Reference – SS Strategy | | | |
| Δ Cost (€) | - | 2,008 | 8,382 | - | 349 | 3,729 |
| Δ QALY | - | -0.45 | -2.65 | - | -0.16 | -1.65 |
| ICER[1] | - | -4,428 | -3,161 | - | -2,118 | -2,255 |
| NMB[2] (€) | - | -16,974 | -95,894 | - | -5,785 | -58,302 |

SS=Surveillance-Surgery. OS=Only-Surgery. NI=No-Intervention. Values are reported per patient.
[1]Incremental cost-effectiveness ratio ICER = Δ Costi/ Δ QALY per patient.
[2]Net monetary benefit NMB =ΔΔ QALY - ΔCosti, con λ = willingness-to-pay €33.000 per QALY.

✔ Direct healthcare cost for lifetime management of a women with BRCA1 or BRCA2 PVs, implementing the SS strategy, amounts to €17,893 and €13,644, respectively (**Table 1**). The SS strategy dominates the others in both women with BRCA1 and BRCA2 PVs.

**Figure 2**. Tornado diagrams. Net Monetary Benefit (NMB) of OS and NI strategies with SS strategy as reference in women with PV BRCA1(a, b) and BRCA2(c,d).
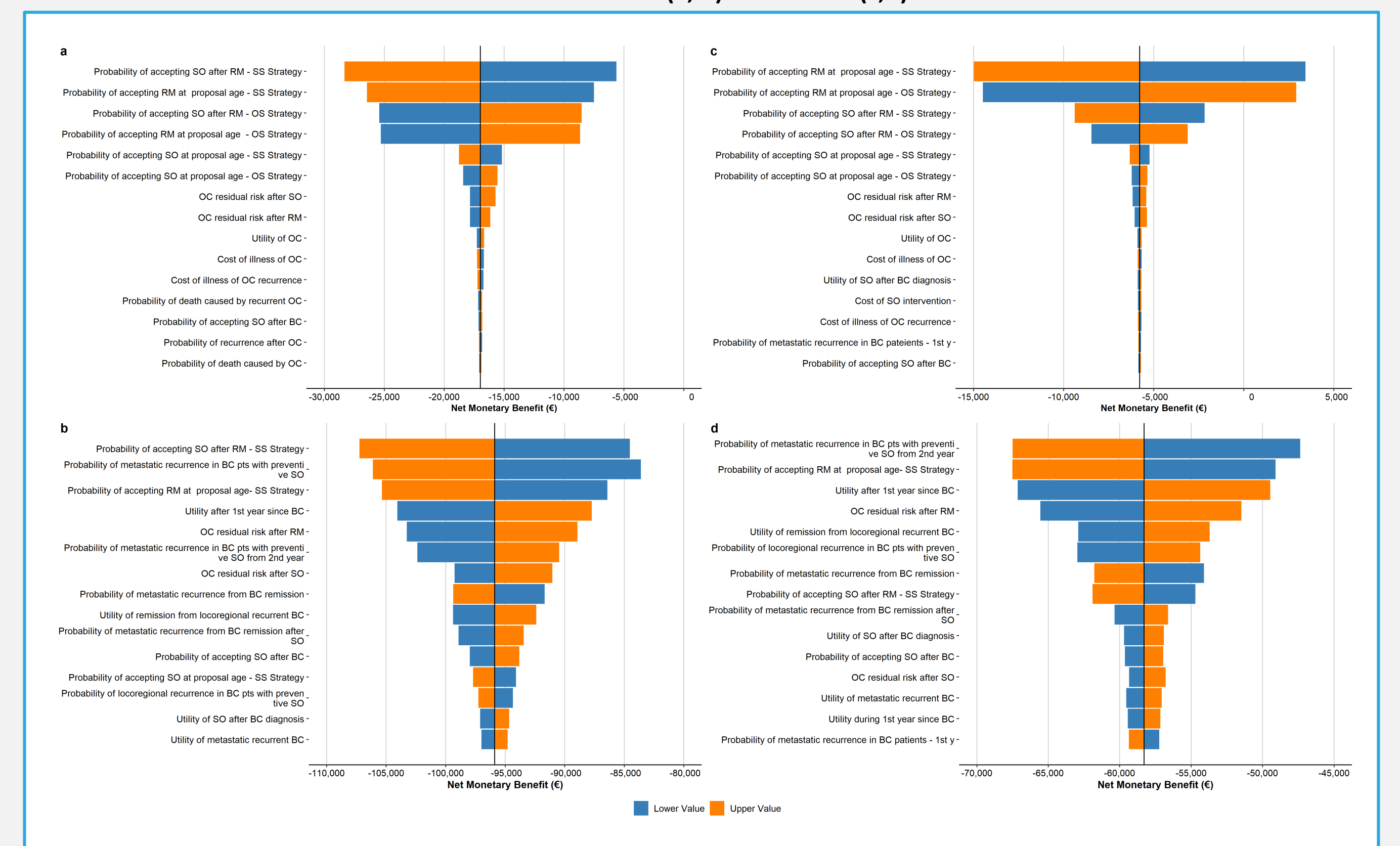


Diagrams show the top 15 parameters in descending order of NMB variation (WTP=€30,000)

✔ In the deterministic sensitivity analysis, the SS strategy is dominant over the NI strategy, and it is dominant or cost-effective compared to the OS strategy. The acceptance probability of risk reducing surgeries is one of the parameters with the greatest impact on cost-effectiveness measures (**Figure 2**).

**Figure 3**. Cost-Effectiveness Acceptability Curve for BRCA1 (a) and BRCA2 (b) PV carriers.
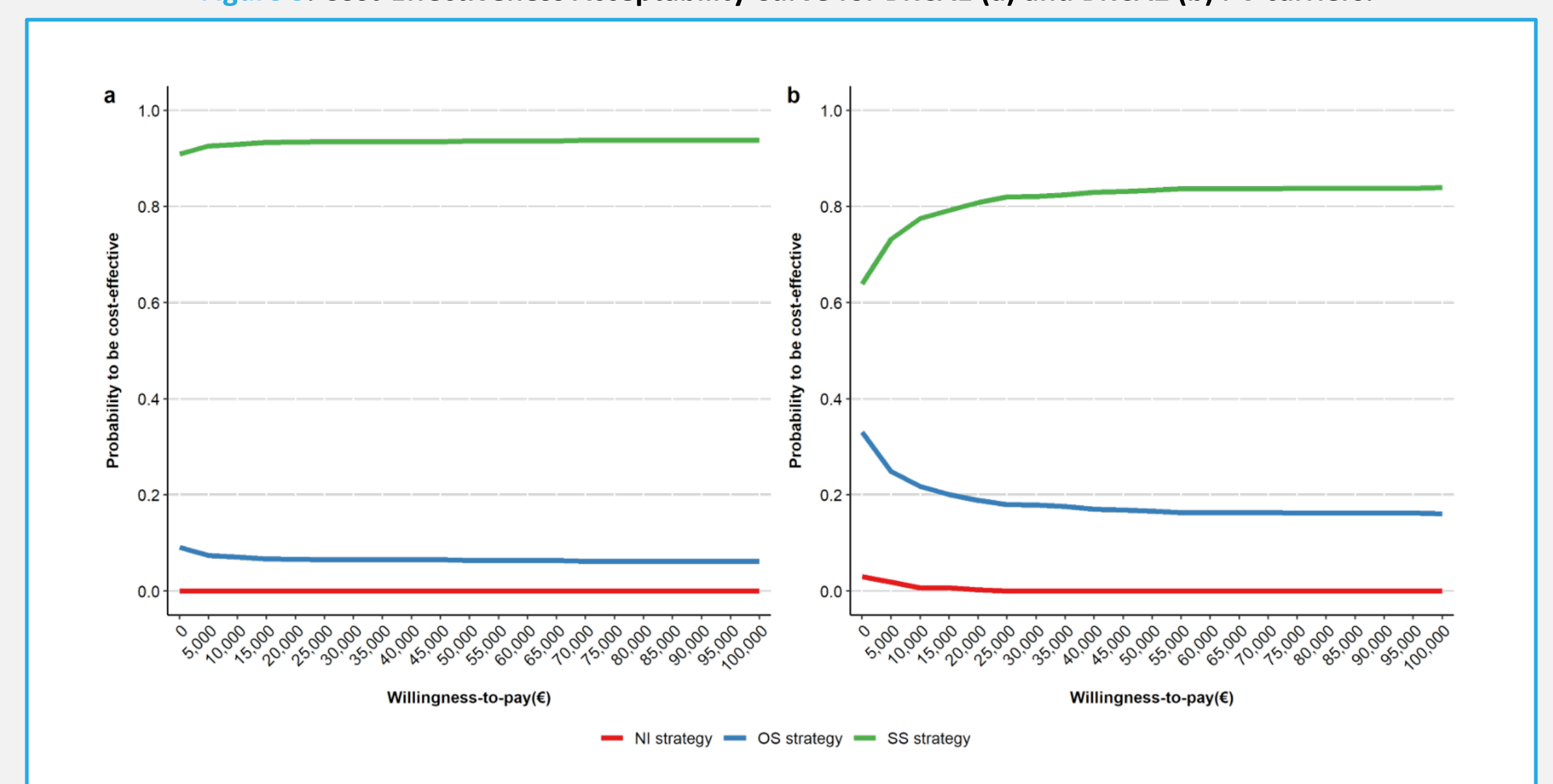


✔ The probabilistic sensitivity analysis confirms the SS strategy as the dominant strategy across all scenarios, with a probability of being cost-effective greater than 90% and 80% at a WTP threshold of €30,000 per QALY in women with BRCA1 and BRCA2 PV, respectively (**Figure 3**).

## CONCLUSIONS

✔ A combined OC surveillance and prevention strategy for BRCA1 and BRCA2 2 PV carriers at an appropriate age represents a highly cost-effective approach compared to surgical prophylaxis alone or no intervention.

✔ High surgical acceptance rates are crucial for maximizing the effectiveness of prevention strategies and surveillance programs can contribute to increase acceptance rates.

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