

Online Resource

Article title: Cost-utility analysis of germline BRCA1/2 testing in women with high-grade epithelial ovarian cancer in Spain.

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Caption of the Online Resource: Estimating the relative efficiency a long term of the genetic test BRCA1/2 in germinal line in women with/without familiar antecedents of OC or BC in the Spanish Health System.

Table 1. Epithelial ovarian cancer and breast cancer risks, risk reduction after surgery and survival rates.

5-year risk of developing EOC among female gBRCA1/2m carriers		
Age range (years)	gBRCA1m	gBRCA2m
30 - 39	2%	0%
40 - 44	3%	0%
45 - 49	3%	0%
50 - 54	6%	3.5%
55 - 59	6%	3.5%
60 - 64	10.5%	4%
65 - 69	10.5%	4%
70 - 79	3%	2%
5-year risk of developing BC among female gBRCA1/2m carriers		
Age range (years)	gBRCA1m	gBRCA2m
20 - 25	2%	2%
26 - 30	2%	2%
31 - 35	10%	4.5%
36 - 40	10%	4.5%
41 - 45	9.5%	11%
46 - 50	9.5%	11%
51 - 55	6.5%	9%
56 - 60	6.5%	9%
61 - 65	5%	4%
66 - 70	5%	4%
EOC risk after uptake RRS among female gBRCA1/2m carriers		
	gBRCA1m HR (95% CI)	gBRCA2m HR (95% CI)
Bilateral mastectomy	-	-
Bilateral salpingo-oophorectomy	0.16 (0.09 – 0.26)	0.12 (0.06 – 0.23)
Bilateral mastectomy and bilateral salpingo-oophorectomy	-	-
BC risk after uptake RRS among female gBRCA1/2m carriers		

	gBRCA1m HR (95% CI)	gBRCA2m HR (95% CI)
Bilateral mastectomy	0.10 (0.03 – 0.31)	0.09 (0.03 – 0.31)
Bilateral salpingo-oophorectomy	0.51 (0.39 – 0.66)	0.39 (0.29 – 0.54)
Bilateral mastectomy and bilateral salpingo-oophorectomy	0.05 (0.01 – 0.22)	0.05 (0.01 – 0.22)
5-year survival rate		
Age range (years)	OC	BC
15-44	69.9%	81.0%
45-54	52.3%	86.7%
55-64	43.6%	85.2%
65-74	29.0%	78.7%
75-84	18.8%	73.6%
85-99	18.8%	73.6%

Abbreviations: BC: breast cancer; CI: confidence interval; gBRCA1/2m: germline mutation in *BRCA1* or *BRCA2* genes; HR: hazard ratio; EOC: Epithelial Ovarian Cancer; RRS: risk-reducing surgery.

References: Kuchenbaecker et al., 2017 [1]; Eccleston et al., 2017 [2]; Chirlaque et al., 2010 [3].

Table 2 Unit costs (€ 2017)

	Unit costs
Testing	
BRCA point mutation test (Initial population).	€469.50
BRCA large rearrangement test (Initial population).	€100.47
BRCA exon sequence analysis (Relatives).	€55.15
BRCA large rearrangement test (Relatives).	€76.47
Genetic counselling visit	€156.06
CA125 test	€1.85
Risk-reduction surgery	
Bilateral salpingo-oophorectomy	€4,053.9
Bilateral mastectomy*	€4,726.7
Surveillance	
Magnetic resonance imaging	€12
Mammography	€9.45
Transvaginal ultrasound	€7.41
Palliative care	
Home visit (primary care physician)	€5.76
Nursing (domiciliary)	€4.00
Hospitalization (EOC patients)*	€5,610.51
Hospitalization (BC patients)*	€5,581.46
Home services	€1,700.00

References: Official Bulletins of Autonomous Communities [4], *Ministry of Health, Social Services and Equality [5].

Table 3. Cost of cancer management (€ 2017).

Epithelial ovarian cancer	Stage	I		II	III	IV	Total
	Incident patients	37.00%		6.00%	35.00%	22.00%	100%
	HDC Without surgery*	€4,652.4		€7,553.8	€20,423.5	€37,936.9	€17,067
	HDC With surgery*	€5,446.7		€9,104.2	23.303,2 €	€41,147.6	€19,091.6
Breast cancer	Stage	0	I	II	III	IV	Total
	Incident patients	9.34%	47.40%	31.37%	9.55%	2.01%	100%
	CT Without surgery	€6,843.5	€13,266	€18,161.9	€24,825.6	€14,959.3	€15,355.7
	CT With surgery	€9,886.4	€17,358.0	€22,254.0	€28,917.7	€14,959.3	€19,267.6
	Hormone therapy	-					704,45€
	Other healthcare cost	-					€8,057.1
	HDC Without surgery	-					€23,412.8
	HDC With surgery	-					€27,324.7

Abbreviations: CT: cost of treatment; HDC: healthcare direct costs.

Notes: *Do not include the cost of the hormone therapy (anastrozol).

References: Arrospe et al., 2015 [6]; García-Gutiérrez et al., 2018 [7], Luengo et al., 2013 [8], and OvarCost study [9].

Table 4. Utility values.

Health states	Utilities				Duration of the effect (years) [§]
	General population [‡]	BRCA1/2 carriers	OC patients	BC patients	
General population: Perfect health	1.00	1.00	-	-	-
1 – 24 years	0.94	-	-	-	-
25 - 34 years	0.93	-	-	-	-
35 - 44 years	0.91	-	-	-	-
45 - 54 years	0.85	-	-	-	-
55 - 64 years	0.81	-	-	-	-
65 – 74 years	0.78	-	-	-	-
75 - 101 years	0.71	-	-	-	-
Risk-reducing surgery					
Bilateral salpingo-oophorectomy (\pm SD)	0.90 \pm 0.14	0.95 \pm 0.10	-	-	1.00
Bilateral mastectomy (\pm SD)	0.88 \pm 0.17	0.88 \pm 0.22	-	-	1.00
Bilateral mastectomy and bilateral salpingo-oophorectomy (\pm SD)	0.79 \pm 0.21	0.84 \pm 0.23	-	-	1.00
Psychological impact of a positive result in germline BRCA1/2 testing*	1.00	1.00	-	-	-
After diagnosis of cancer					
Year 1	-	-	0.50	0.71	-
Year 2	-	-	0.65	0.72	-
Year 3	-	-	0.67	0.73	-
Year 4	-	-	0.69	0.74	-
Year 5	-	-	0.70	0.76	-
Year 6 and following years	-	-	0.72	0.77	-
Death	0.00	0.00	-	-	-

Notes: *Assumption based on Halbert *et al.*, 2011 [10] and Sie *et al.*, 2015 [11]; §Assumption from the Institute of cancer research; ‡ Population with an unknown BRCA1/2 status.

References: Grann *et al.*, 2011 [12], Havrilesky *et al.*, 2009 [13], Kind *et al.*, 1999 [14], NICE, 2013 [15] and Peasgood *et al.*, 2010 [16]. Abbreviations: SD: standard deviation.

Table 5. Sensitivity analysis parameters.

Parameter	Base case	Standard error	Distribution
Base case			
Discount rate (cost)	3%	0.004	Beta
Discount rate (utility)	3%	0.004	Beta
Time horizon (years)	50	–	None
EOC risk in 5 years			
BRCA1 patients: age 30–39	2.0%	0.003	Beta
BRCA1 patients: age 40–44	3.0%	0.004	Beta
BRCA1 patients: age 45–49	3.0%	0.004	Beta
BRCA1 patients: age 50–54	6.0%	0.008	Beta
BRCA1 patients: age 55–59	6.0%	0.008	Beta
BRCA1 patients: age 60–64	10.5%	0.013	Beta
BRCA1 patients: age 65–69	10.5%	0.013	Beta
BRCA1 patients: age 70–79	3.0%	0.004	Beta
BRCA2 patients: age 30–39	0.0%	0.000	Beta
BRCA2 patients: age 40–44	0.0%	0.000	Beta
BRCA2 patients: age 45–49	0.0%	0.000	Beta
BRCA2 patients: age 50–54	3.5%	0.004	Beta
BRCA2 patients: age 55–59	3.5%	0.004	Beta
BRCA2 patients: age 60–64	4.0%	0.005	Beta
BRCA2 patients: age 65–69	4.0%	0.005	Beta
BRCA2 patients: age 70–79	2.0%	0.003	Beta
BC risk in 5 years			
BRCA1 patients: age 20–25	2.0%	0.003	Beta
BRCA1 patients: age 26–30	2.0%	0.003	Beta
BRCA1 patients: age 31–35	10.0%	0.013	Beta
BRCA1 patients: age 36–40	10.0%	0.013	Beta
BRCA1 patients: age 41–45	9.5%	0.012	Beta
BRCA1 patients: age 46–50	9.5%	0.012	Beta
BRCA1 patients: age 51–55	6.5%	0.008	Beta
BRCA1 patients: age 56–60	6.5%	0.008	Beta
BRCA1 patients: age 61–65	5.0%	0.006	Beta
BRCA1 patients: age 66–70	5.0%	0.006	Beta
BRCA2 patients: age 20–25	2.0%	0.003	Beta
BRCA2 patients: age 26–30	2.0%	0.003	Beta
BRCA2 patients: age 31–35	4.5%	0.006	Beta

BRCA2 patients: age 36–40	4.5%	0.006	Beta
BRCA2 patients: age 41–45	11.0%	0.014	Beta
BRCA2 patients: age 46–50	11.0%	0.014	Beta
BRCA2 patients: age 51–55	9.0%	0.011	Beta
BRCA2 patients: age 56–60	9.0%	0.011	Beta
BRCA2 patients: age 61–65	4.0%	0.005	Beta
BRCA2 patients: age 66–70	4.0%	0.005	Beta
Bilateral salpingo-oophorectomy			
BRCA1: Estimated age of surgery	35	4.46	Normal
BRCA1: Uptake rate	65%	0.08	Beta
BRCA2: Estimated age of surgery	35	4.46	Normal
BRCA2: Uptake rate	65%	0.08	Beta
BRCA1: EOC risk (HR)	0.16	0.27	Log-normal
BRCA1: BC risk (HR)	0.51	0.13	Log-normal
BRCA2: EOC risk (HR)	0.12	0.34	Log-normal
BRCA2: BC risk (HR)	0.39	0.16	Log-normal
Bilateral mastectomy			
BRCA1: Estimated age of surgery	40	5.10	Normal
BRCA1: Uptake rate	20%	0.03	Beta
BRCA2: Estimated age of surgery	40	5.10	Normal
BRCA2: Uptake rate	20%	0.03	Beta
BRCA1: BC risk (HR)	0.10	0.60	Log-normal
BRCA2: BC risk (HR)	0.09	0.60	Log-normal
Bilateral mastectomy and bilateral salpingo-oophorectomy			
BRCA1: Riesgo de sufrir COE (HR)	0.16	0.27	Log-normal
BRCA1: Riesgo de sufrir CM (HR)	0.05	0.79	Log-normal
BRCA2: Riesgo de sufrir COE (HR)	0.12	0.34	Log-normal
BRCA2: Riesgo de sufrir CM (HR)	0.05	0.79	Log-normal
Accumulated survival rate			
Male: age 0–101	–	–	Beta
Female: age 0–101	–	–	Beta
EOC survival rate in 5 years			
Age: 15–39	69.9%	0.09	Beta
Age: 40–49	52.3%	0.07	Beta
Age: 50–59	43.6%	0.06	Beta
Age: 60–69	29.0%	0.04	Beta
Age: 70–79	18.8%	0.02	Beta

Age: 80–99	18.8%	0.02	Beta
BC survival rate in 5 years			
Age: 15–39	81.0%	0.10	Beta
Age: 40–49	86.7%	0.09	Beta
Age: 50–59	85.2%	0.09	Beta
Age: 60–69	78.7%	0.10	Beta
Age: 70–79	73.6%	0.09	Beta
Age: 80–99	73.6%	0.09	Beta
Unit costs			
BRCA test (Initial population)	€479.55	€1.17	Gamma
Genetic counselling visit (Initial population)	€156.06	€19.91	Gamma
BRCA test (Relatives)	€2.80	€8.01	Gamma
Genetic counselling visit (Relatives)	€156.06	€19.91	Gamma
Bilateral salpingo-oophorectomy	€4,053.93	€17.09	Gamma
Bilateral mastectomy	€4,726.72	€602.91	Gamma
EOC (with surgery)	€17,067.00	€2,176.95	Gamma
BC (with surgery)	€7,249.51	€3,475.77	Gamma
EOC (without surgery)	€15,042.44	€1,918.71	Gamma
BC (without surgery)	€23,337.60	€2,976.79	Gamma
Palliative care (EOC)	€3,648	€465.36	Gamma
Palliative care (BC)	€3,522	€449.26	Gamma
Palliative care (all-cause mortality)	€74	€35.00	Gamma
Hormone therapy (per day)	€1.9	€0.25	Gamma
Magnetic resonance imaging	€12.0	€39.80	Gamma
Mammography, transvaginal ultrasound and CA125 test (annual screening)	€208.0	€26.53	Gamma
Utilities			
Perfect health (controls)	1.00	–	None
Bilateral salpingo-oophorectomy (controls)	0.90	0.08	Beta
Bilateral mastectomy (controls)	0.88	0.09	Beta
Bilateral mastectomy and bilateral salpingo-oophorectomy (controls)	0.79	0.10	Beta
Psychological impact of a positive result in germline BRCA1/2 testing (controls)	1.00	0.06	Beta
Death (controls)	0.00	–	None
Perfect health (patients)	1.00	–	None
Bilateral salpingo-oophorectomy (patients)	0.95	0.07	Beta
Bilateral mastectomy (patients)	0.88	0.09	Beta
Bilateral mastectomy and bilateral salpingo-oophorectomy (patients)	0.84	0.09	Beta

Psychological impact of a positive result in germline BRCA1/2 testing (patients)	1.00	0.06	Beta
Death (patients)	0.00	–	None
Utilities related to age 1–101 (males)	–	–	Beta
Utilities related to age 1–101 (females)	–	–	Beta
Year 1 (OC)	0.50	0.06	Beta
Year 2 (OC)	0.65	0.08	Beta
Year 3 (OC)	0.67	0.09	Beta
Year 4 (OC)	0.69	0.09	Beta
Year 5 (OC)	0.70	0.09	Beta
Year 6 and following years (OC)	0.72	0.09	Beta
Year 1 (BC)	0.71	0.09	Beta
Year 2 (BC)	0.72	0.09	Beta
Year 3 (BC)	0.73	0.09	Beta
Year 4 (BC)	0.74	0.09	Beta
Year 5 (BC)	0.76	0.10	Beta
Year 6 and following years (BC)	0.77	0.10	Beta
Duration of the effect (years)			
Perfect health	–	–	None
Bilateral salpingo-oophorectomy	1.00	0.06	Log-normal
Bilateral mastectomy	1.00	0.06	Log-normal
Bilateral mastectomy and bilateral salpingo-oophorectomy	1.00	0.06	Log-normal
Psychological impact of a positive result in germline BRCA1/2 testing	1.00	0.06	Log-normal
Death	–	–	None
Population			
Initial population	1,588	–	None
Age of the initial population (years), average	51	6.51	Normal
Age of the initial population (years), SD	5	–	None
Probability of gBRCA1/2m (initial population)	7.3%	0.01	Beta
Probability of mutation in <i>BRCA1</i> gene (initial population)	66.83%	0.09	Beta
Probability of gBRCA1/2m (first-degree relatives)	50%	0.06	Beta
Age of the mother (years), average	28	3.57	Normal
Age of the mother (years), SD	2	–	None
Age of the father (years), average	30	3.83	Normal
Age of the father (years), SD	2	–	None
Number of siblings, average	0.69	0.13	Log-normal
Number of siblings, SD	0.26	–	None

Age of siblings (relative to index population), average	2	–	None
Age of siblings (relative to index population), SD	0	–	None
Gender, probability female (among siblings)	48.34%	0.06	Beta
Number of children, average	1.55	–	None
Number of children, SD	0	-	None
Age of the siblings, average	-28	3.57	Normal
Age of the siblings, SD	2	–	None
Gender, probability female (among children)	48.34%	0.06	Beta
Probability of gBRCA1/2m (second-degree relatives)	25%	0.03	Beta
Surveillance			
Magnetic resonance imaging (years), minimum age	25	3.19	Normal
Magnetic resonance imaging (years), maximum age	70	8.93	Normal
Mammography, transvaginal ultrasound and CA125 tests [annual screening] (years), minimum age	30	–	–
Mammography, transvaginal ultrasound and CA125 tests [annual screening] (years), maximum age	75	9.57	Normal

Abbreviations: HR: hazard ratio; SD: standard deviation; gBRCA1/2m: germline mutations in *BRCA1* and *BRCA2* genes.

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