Economic Evaluation of the Familial Cancer Program, Genetic Services WA

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Predictive Genetic Tests for Colorectal (FAP, HNPCC), Breast and Ovarian Cancers (BRCA Mutations)

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Executive Summary

The availability of genetic testing for a range of familial cancers represents an important advance in targeted screening. Although the familial component of cancer is relatively small at present, it is growing rapidly as new genes are discovered and the role of genes and their interaction with the environment are better understood. In lieu of the continually expanding demands and future technological developments that will impact upon such a service, an economic evaluation of the Familial Cancer Program at Genetic Services of Western Australia (GSWA) is a timely project.

This study aimed to evaluate costs and outcomes of genetic testing for familial colorectal, breast and ovarian cancer through services provided by GSWA. Costs and outcomes of cancers suitable for predictive DNA based tests were assessed using a decision analytic model. Genetic tests for Familial Adenomatous Polyposis (FAP), Hereditary Non-Polyposis Colorectal Carcinoma (HNPCC), breast and ovarian cancer due to BRCA1/2 mutations were included. Costs were estimated according to standards of care in WA. Cancer risks and the efficacy of surveillance on long-term outcomes were derived from the published literature.

The cost-effectiveness of genetic testing was compared in first-degree relatives of known mutation-carriers who are at 50% risk of carrying the gene mutation (intervention group) to individuals with the same risk, but who did not undergo a genetic test (control subjects). The surveillance behaviour of the control subjects was modelled using two dichotomous scenarios for the period observed (age 25-70 except for FAP surveillance which begins at age 10). This was necessary because individuals who are unsure of their mutation status may or may not increase their surveillance based on family history alone (perceived cancer risk). Thus the intervention group (known mutation status) was compared with control subjects (unknown mutation status) having intensive surveillance and surgery, or population surveillance.

Projections from the models indicate that genetic screening for familial cancer in Western Australia is a cost-effective use of resources under a range of scenarios. Genetic testing enables the restriction of intensive surveillance to individuals with an identified gene mutation providing an efficient use of resources.

For example, compared with control subjects undergoing intensive surveillance and prophylaxis, the ovarian intervention group provided total net savings of $980-$1008 per woman. The breast intervention group provided total net savings of $1681-$1795 per woman and delayed the onset of breast cancer (6mths BRCA1, 3mths BRCA2). Similarly, FAP and HNPCC intervention groups provided total savings of $13,390 and $14,783-$15,460 per person (males-females). HPNCC mutation-carriers also gained 1 colorectal-cancer-free year.

Compared to control subjects undergoing only population surveillance, it was predicted the onset of cancer could be delayed in the genetic testing intervention group.

For example, breast cancer could be delayed at a total net cost of $3055 (5.1yrs) to $3389 (3.2yrs) for women with identified BRCA1 or 2 mutations. This is a cost of $601 or $1070 per cancer-free year gained. Since population surveillance is not currently recommended for ovarian cancer, control subjects undergoing no surveillance were compared with women in the intervention group who were expected to delay the onset of ovarian cancer at a net cost of $1630 (3.5yrs) to $2509 (1.2years) for women with BRCA1 or 2 mutations. This is a cost of $477 or $2150 per cancer-free year gained.

The onset of colorectal-cancer (CRC) could be delayed by 40 years for individuals in the FAP intervention group at a net cost of $9,042 which is $226 per CRC-free year gained. Similarly, individuals in the HNPCC intervention group were expected to delay the onset of CRC by 8 years at a net cost of cost of $12,141 for males and $12,596 for females, or $1,518 -$1,575 for each year that CRC is delayed.

Though improved outcomes (cancer-free years) are gained at a cost, these outlays are well within an acceptable threshold for cost-effectiveness.

Further studies are needed to verify the results of long-term gains and or costs from genetic testing. Additional research into compliance with clinical recommendations for surveillance, the disclosure of risk information to relatives and the degree of community support for such a program is also required, since the cost-effectiveness of genetic testing will depend on the value of this information to patients and society.

Method and Results

Literature Review

Internet based searches were conducted using PubMed, Medline and Ovid on the cost-effectiveness of genetic testing, cancer surveillance and surgical intervention to reduce cancer morbidity. A review of the published literature was also used to derive long-term risks of familial cancer associated with specific genetic mutations.

Generic Model

Economic tools provide a means of comparing the efficiency of competing scenarios. Cost-effectiveness studies compare net costs with net outcomes to calculate a cost-effectiveness ratio.

Genetic screening and intervention provides a unique model for cost-effectiveness because of the highly variable rates of penetrance, different surveillance options, age of disease onset and potential outcomes. A flexible model was needed that could incorporate data from multiple sources, project beyond the time horizon of the study and consider all available options simultaneously.

For these reasons purpose designed (TreeAge Data™ version 4.0) economic decision modelling software was used to develop a generic model in consultation with the Familial Cancer Committee. The generic model represents the course of testing and treatment for individuals entering the Familial Cancer Program at GSWA. The path of testing is mapped across various phases: triage, pre-test counselling, test eligibility, genetic testing, post-test counselling, intervention and outcome (die from cancer, die from other causes or survive).

The generic model represents the index case who has been diagnosed with cancer and may undergo a diagnostic genetic test, relatives who are not diagnosed with cancer but satisfy the family history criteria and may elect to have a predictive genetic test and relatives who are ineligible to test since their family history can not be validated or the index case mutation diagnosed. See Figure 1.

Cancer-Specific Models

Only first-degree relatives of known mutation-carriers (at 50% risk of inheriting the gene mutation) eligible for a predictive genetic test were simulated in the cancer-specific models. Full compliance with clinical recommendations was assumed. Complications from medical intervention were not incorporated, nor were intangible costs and benefits. See Figure 2.

Age-related cancer risks and intervention costs for carriers of a gene mutation compared with non-mutation carriers and control subjects were integrated using Markov models which are designed to represent recursive events. The Markov facility allows the same decision path for each cycle but the probability of an event occurring is dependent on both the cycle number and the health status.

Each Markov cycle represented one year. Associated with each cycle, the age and penetrance (or likelihood a person would develop cancer) determined how many within the group remained in the 'well' state or progressed into the 'cancer' state. Although the generic model simulated cancer mortality for mutation carriers, this study focus was confined to the incidence of disease and the number of cancer-free years gained measured.

Cancer Risks

The age-related population risks of colorectal, breast and ovarian cancers represent national rates in 2000 (AIHW 2003). Cumulative age-related cancer incidence in mutation carriers with, and without the recommended clinical intervention, were gathered from previous studies and factored for attrition, the gradual reduction in numbers as patients develop cancer (Bisgaard 1994; Hartmann 1999; Heiskanen 2000; Green 2002; Haber 2002; IARC 2002; Rebbeck 2002; Antoniou 2003; Lynch 2003). See Table 1 to Table 8.

Clinical Interventions and Costs

Clinical interventions for known mutation carriers were based on patterns of care in WA which are consistent with NHMRC clinical practice guidelines for the detection and treatment of familial cancer (NHMRC 1999; NHMRC 1999; NHMRC 2001) and corroborated by WA surgeons and oncologists working in the area. The models cover the period from age 25 to 70 except for the FAP model in which surveillance begins at age 10. See Table 9 and Table 10.

Cost estimates came from a range of sources. Counselling costs were calculated in co-operation with GSWA and based on a retrospective analysis of time allocated to Familial Cancer Program patients. Hourly costs were attributed based on staff salaries and office consumables. See Table 11 to Table 13.

Genetic test costs were estimated by the Molecular Genetic Laboratory at the Women's and Children's Health Service, WA. Though only predictive tests were modeled (test $65), since a family index case must be confirmed through a diagnostic test (test plus counselling $2000) before cascade testing is possible, a diagnostic component was added. It was estimated around five relatives would undergo cascade testing hence, the diagnostic component of $400.

Intervention costs were provided by costing centres in Perth's major teaching hospitals based on a breakdown (pathology, medical, nursing, allied health and other) of

surgical procedures in 2001-2002 and averaged to provide an estimate. Capital expenditure was not assessed though an examination of total WA health expenditure in 2000-2001 indicates this component would comprise less than 5% (AIHW 2003).

Lifetime cancer treatment costs were taken from the Australian Institute of Health and Welfare (AIHW 2004).

All costs were standardised at 2001-2002 prices using health index deflators (AIHW 2003). A discount rate of 5% per annum was applied to costs to be incurred in the future. Mean age was used to estimate the discounted cost of surgery, and cancer treatment (Meiser 2000; Friedl 2001; Haber 2002; Rebbeck 2002; GSWA 2003; Lynch 2003; Rebbeck 2004). See Table 14.

Sensitivity Analysis

Though the approach in these models has been to use conservative estimates, assumptions made reflect uncertainties in available data particularly the relative risks of disease, the effectiveness of intervention and effect of the discount rate. One-way sensitivity analysis was undertaken to check the robustness of the outcome given uncertainty in these variables. Sensitivity analysis results reported in Table 15 to Table 41 illustrate best and worse case scenarios such as a greater versus a smaller rate of discount.

Model Outcomes

Costs and outcomes for the intervention group compared to control group 1 and 2 are reported in Figure 3 to Figure 6. Despite their high-risk family history, the surveillance behaviour of control subjects was uncertain since their mutation status was unknown. Patients may or may not have increased their surveillance based on family history alone (perceived cancer risk) so dichotomous scenarios were reviewed corresponding to surveillance extremes. For example, the intervention group (known mutation status) was compared with control subjects (unknown mutation status) who adhered to clinical recommendations for increased surveillance based on their family history alone (control group 1). The intervention group was then compared with control subjects who have population or no surveillance, despite their high-risk family history (control group 2). The actual cost-effectiveness lies somewhere in-between.

Conclusion

Predictive DNA-based genetic testing allows targeted high-level surveillance for gene mutation carriers, which ensures efficient use of resources and reduces cancer-related morbidity if clinical recommendations for intervention are adopted.

Figure 1: Generic Model

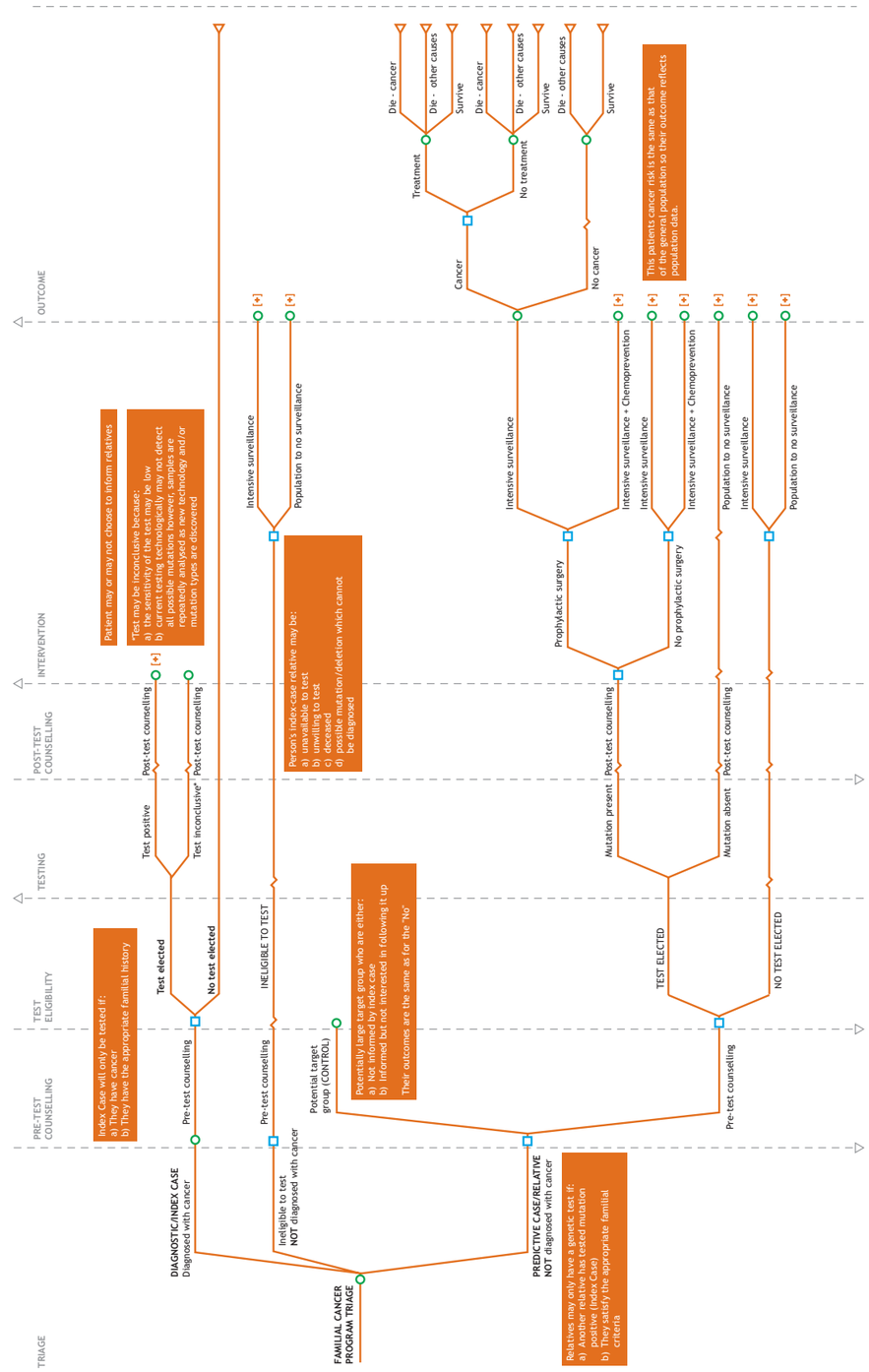

Figure 2: Example of a cancer-specific model

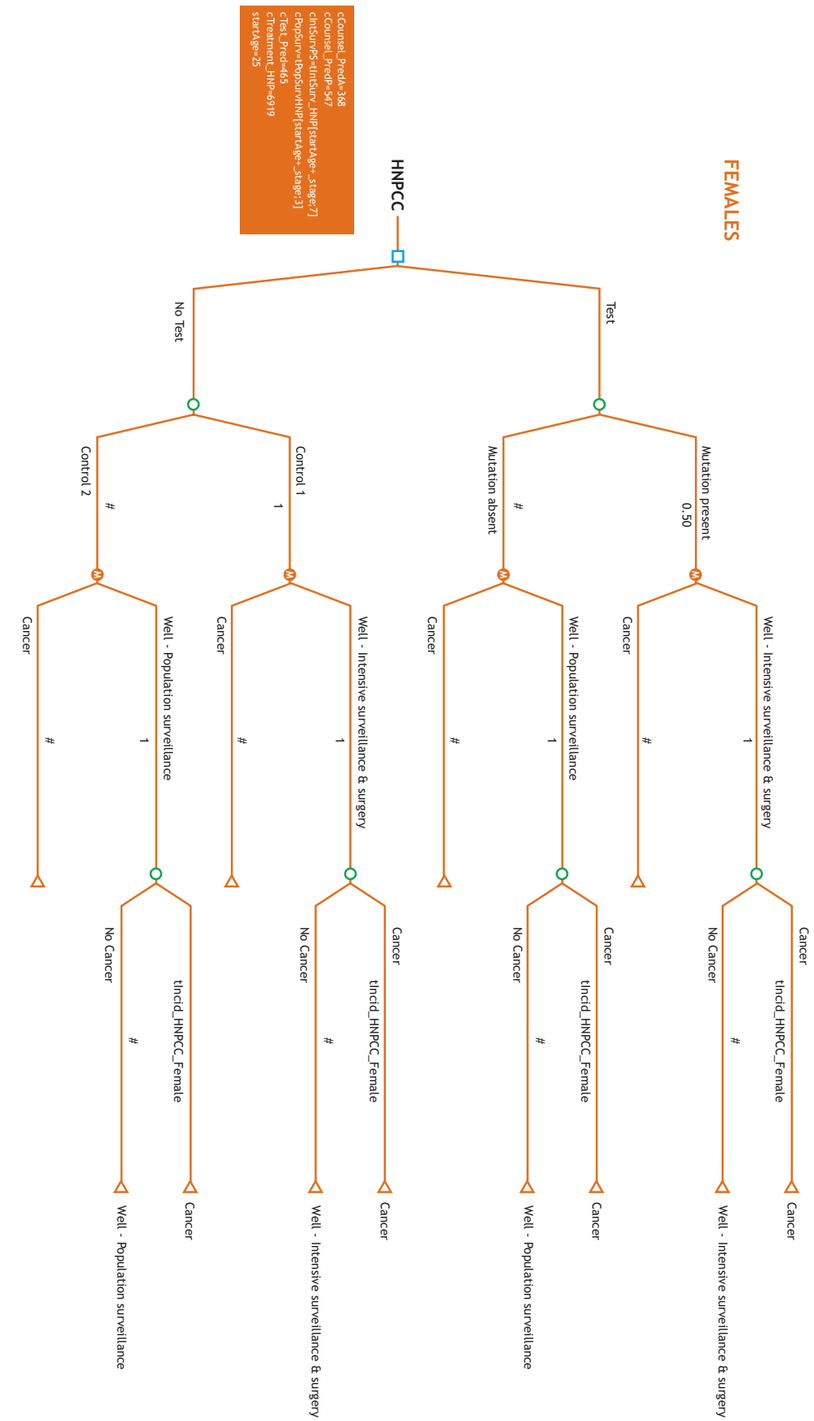

Table 1: Cumulative risks incorporating attrition for BRCA1

COHORT	AGE	ANNUAL CANCER INCIDENCE	ANNUAL CANCER CASES	CUMULATIVE CANCER CASES	CUMULATIVE INCIDENCE
100,000	25	0.001	85	85	
	26	0.001	129	214	
	27	0.002	173	387	
	28	0.002	216	603	
	29	0.003	259	862	
	30	0.003	302	1,164	
	31	0.004	372	1,536	
	32	0.004	440	1,976	
	33	0.005	508	2,485	
	34	0.006	575	3,060	
	35	0.007	641	3,701	
	36	0.008	765	4,465	
	37	0.009	885	5,351	
	38	0.011	1,003	6,353	
	39	0.012	1,116	7,470	
	40	0.013	1,226	8,696	
	41	0.015	1,363	10,059	
	42	0.017	1,494	11,553	
	43	0.018	1,618	13,172	
	44	0.020	1,735	14,907	
	45	0.022	1,844	16,750	
	46	0.023	1,923	18,673	
	47	0.025	1,995	20,669	
	48	0.026	2,060	22,728	
	49	0.027	2,117	24,845	
	50	0.029	2,167	27,012	
	51	0.030	2,191	29,203	
	52	0.031	2,209	31,413	
	53	0.032	2,222	33,635	
	54	0.034	2,229	35,864	
	55	0.035	2,230	38,094	
	56	0.036	2,202	40,297	
	57	0.036	2,172	42,468	
	58	0.037	2,139	44,607	
	59	0.038	2,104	46,711	
	60	0.039	2,066	48,777	
	61	0.038	1,971	50,748	
	62	0.038	1,880	52,628	
	63	0.038	1,794	54,422	
	64	0.038	1,712	56,134	
	65	0.037	1,634	57,768	
	66	0.037	1,579	59,348	
	67	0.038	1,525	60,873	
	68	0.038	1,473	62,346	
	69	0.038	1,423	63,769	
	70	0.038	1,374	65,143	65%

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Table 2: Age-specific rates of cancer incidence in the FAP model

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
10	0.00000	0.00	0.0000	0.0000	0.0000
15	0.00000	0.05	0.0010	0.0005	0.0250
20	0.00001	0.10	0.0020	0.0010	0.0500
25	0.00002	0.15	0.0030	0.0015	0.0750
30	0.00004	0.20	0.0040	0.0020	0.1000
35	0.00008	0.25	0.0050	0.0025	0.1250
40	0.00017	0.30	0.0060	0.0031	0.1501
45	0.00034	0.30	0.0060	0.0032	0.1502
50	0.00062	0.30	0.0060	0.0033	0.1503
55	0.00111	0.30	0.0060	0.0036	0.1506
60	0.00181	0.30	0.0060	0.0039	0.1509
65	0.00246	0.30	0.0060	0.0042	0.1512
70	0.00339	0.30	0.0060	0.0047	0.1517
75	0.00403	0.30	0.0060	0.0050	0.1520

Note:

PPOPCRC is the proportion of persons (per 100,000) with cancer of the colon and rectum including anus (ICD-10 C18-C21) in Australia in 2000 (AIHW 2003)

PCARRIER_INCID is the risk of CRC for FAP mutation carriers. It is an estimate derived from the literature based on 100% penetrance by age 40 (Bisgaard 1994; Heiskanen 2000).

PCARRIER_INTSURVPS is the risk of CRC in FAP mutation carriers based on a lifetime CRC risk of 4% following intensive surveillance and surgery (Heiskanen 2000)

CONTROL_1 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having intensive surveillance and surgery (half the group)

CONTROL_2 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having only population surveillance (half the group)

Table 3: Age-specific rates of cancer incidence in the HNPCC model for males

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00002	0.00495	0.002	0.001	0.002
30	0.00005	0.01058	0.005	0.003	0.005
35	0.00008	0.01755	0.009	0.004	0.009
40	0.00019	0.04185	0.021	0.011	0.021
45	0.00036	0.07988	0.040	0.020	0.040
50	0.00068	0.15323	0.077	0.039	0.077
55	0.00131	0.00131	0.001	0.001	0.001
60	0.00221	0.00221	0.001	0.002	0.002
65	0.00302	0.00302	0.002	0.002	0.003
70	0.00422	0.00422	0.002	0.003	0.004
75	0.00495	0.00495	0.002	0.004	0.005

Table 4: Age-specific rates of cancer incidence in the HNPCC model for females

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00002	0.0044	0.002	0.001	0.002
30	0.00004	0.0101	0.005	0.003	0.005
35	0.00007	0.0190	0.009	0.005	0.010
40	0.00016	0.0411	0.021	0.010	0.021
45	0.00032	0.0832	0.042	0.021	0.042
50	0.00056	0.1456	0.073	0.037	0.073
55	0.00091	0.0009	0.000	0.001	0.001
60	0.00142	0.0014	0.001	0.001	0.001
65	0.00189	0.0019	0.001	0.001	0.002
70	0.00255	0.0026	0.001	0.002	0.003
75	0.00311	0.0031	0.002	0.002	0.003

Note:

PPOPCRC is the proportion of males or females with cancer of the colon and rectum including anus (ICD-10 C18-C21) in Australia in 2000 (AIHW 2003)

PCARRIER_INCID is the risk of CRC in HNPCC mutation carriers based on 72% incidence by age 50 (Green 2002)

PCARRIER_INTSURVPS is the risk of CRC in HNPCC mutation carriers based on an estimated 50% reduction of CRC following intensive surveillance and surgery (Lynch 2003)

CONTROL_1 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having intensive surveillance and surgery (half the group)

CONTROL_2 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having only population surveillance (half the group)

Table 5: Age-specific rates of cancer incidence in the breast model for BRCA1

AGE	PPOPINCID	PINCID_BRCA1	PINCID_INTSURVPS	PINCID_SURVONLY	CONTROL_1	CONTROL_2
25	0.00007	0.0009	0.0001	0.0009	0.0005	0.0005
30	0.00027	0.0030	0.0003	0.0009	0.0006	0.0017
35	0.00058	0.0066	0.0007	0.0006	0.0006	0.0036
40	0.00115	0.0132	0.0013	0.0020	0.0016	0.0072
45	0.00188	0.0217	0.0022	0.0043	0.0031	0.0118
50	0.00251	0.0288	0.0029	0.0086	0.0056	0.0157
55	0.00302	0.0348	0.0035	0.0141	0.0086	0.0189
60	0.00337	0.0388	0.0039	0.0187	0.0111	0.0211
65	0.00324	0.0373	0.0037	0.0226	0.0129	0.0203
70	0.00330	0.0379	0.0038	0.0252	0.0143	0.0206
75	0.00310	0.0356	0.0036	0.0242	0.0137	0.0194

Table 6: Age-specific rates of cancer incidence in the breast model for BRCA2

AGE	PPOPINCID	PINCID_BRCA2	PINCID_INTSURVPS	PINCID_SURVONLY	CONTROL_1	CONTROL_2
25	0.00007	0.0005	0.0000	0.0005	0.0003	0.0003
30	0.00027	0.0017	0.0002	0.0017	0.0010	0.0010
35	0.00058	0.0037	0.0004	0.0003	0.0004	0.0022
40	0.00115	0.0075	0.0007	0.0011	0.0011	0.0043
45	0.00188	0.0122	0.0012	0.0024	0.0022	0.0071
50	0.00251	0.0163	0.0016	0.0049	0.0037	0.0094
55	0.00302	0.0197	0.0020	0.0080	0.0055	0.0113
60	0.00337	0.0219	0.0022	0.0106	0.0070	0.0126
65	0.00324	0.0211	0.0021	0.0128	0.0080	0.0122
70	0.00330	0.0214	0.0021	0.0142	0.0088	0.0124
75	0.00310	0.0201	0.0020	0.0137	0.0084	0.0116

Note:

PPOPINCID is the proportion of females with cancer of the breast (ICD-10 C50) in Australia in 2000 [AIHW 2003]

PINCID_BRCA1/2 is the risk of breast cancer for mutation carriers based on cumulative risk estimates of 45% (BRCA1) or 65% (BRCA2) by age 70 [Antoniou 2003]

PINCIDINTSURVPS is the risk of breast cancer based on an estimated 90% risk reduction for mutation carriers following intensive surveillance and prophylactic surgery (Hartmann 1999)

PINCIDSURVONLY is the risk of breast cancer for mutation carriers following intensive surveillance only based on 35% risk reduction in women aged 50-69 (IARC 2002). This risk reduction was assumed to also occur in 35-49 year old women.

CONTROL_1 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having intensive surveillance but no surgery (half the group)

CONTROL_2 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having only population surveillance (half the group)

Table 7: Age-specific rates of cancer incidence in the ovarian model for BRCA1

AGE	PPOPINCID	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00003	0.0017	-	0.0000	0.0009
30	0.00003	0.0019	-	0.0001	0.0009
35	0.00005	0.0032	-	0.0001	0.0016
40	0.00008	0.0045	-	0.0001	0.0023
45	0.00013	0.0077	-	0.0002	0.0039
50	0.00022	0.0132	0.001	0.0004	0.0067
55	0.00022	0.0134	0.001	0.0004	0.0068
60	0.00033	0.0198	0.001	0.0006	0.0101
65	0.00032	0.0193	0.001	0.0005	0.0098
70	0.00041	0.0248	0.001	0.0007	0.0126
75	0.00054	0.0321	0.001	0.0009	0.0163

Table 8: Age-specific rates of cancer incidence in the ovarian model for BRCA2

AGE	PPOPINCID	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00003	0.0004	-	0.0000	0.0002
30	0.00003	0.0004	-	0.0000	0.0002
35	0.00005	0.0007	-	0.0000	0.0004
40	0.00008	0.0011	-	0.0001	0.0006
45	0.00013	0.0018	-	0.0001	0.0010
50	0.00022	0.0031	-	0.0002	0.0017
55	0.00022	0.0031	-	0.0002	0.0017
60	0.00033	0.0046	-	0.0003	0.0025
65	0.00032	0.0045	-	0.0003	0.0024
70	0.00041	0.0058	-	0.0003	0.0031
75	0.00054	0.0075	-	0.0004	0.0040

Note

PPOPINCID is the proportion of females (per 100,000) with cancer of the ovaries (ICD-10 C56) in Australia in 2000 (AIHW 2003)

PCARRIER_INCID is the risk of ovarian cancer for mutation carriers based on cumulative risk estimates of 39% (BRCA1) or 11% (BRCA2) by age 70 [Antoniou 2003]

PCARRIER_INTSURVPS is the risk of ovarian cancer for mutation carriers following intensive surveillance and prophylactic surgery based on a 96% risk reduction (Haber 2002; Rebbeck 2002)

CONTROL_1 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having intensive surveillance and surgery (half the group)

CONTROL_2 is a composite risk comprising the population risk of cancer (half the group) and the risk of cancer for mutation carriers having only population surveillance (half the group)

Table 9: Clinical intervention for familial colorectal cancer (FAP and HNPCC) at 2001-2002 prices

INTERVENTION	AGE OF INTERVENTION (YRS)	FREQUENCY OF EVENT	COST PER EVENT (UNDISCOUNTED)
Genetic counselling + test, carrier		once only	$1,012
FAP Intensive Surveillance & Surgery			
Flexible sigmoidoscopy	10-20	18mths	$842
Colorectal surgery	21	once only	$16,759
Upper gastrointestinal endoscopy	22-70	18mths	$793
Flexible sigmoidoscopy	22-70	12mths	$842
HNPCC Intensive Surveillance & Surgery			
Colonoscopy	25-44	12mths	$943
Upper gastrointestinal endoscopy	25-44	24mths	$793
Urinanaylsis and cytology	25-44	12mths	$48
Colorectal surgery	45	once only	$16,759
Flexible sigmoidoscopy	46-70	12mths	$842
Upper gastrointestinal endoscopy	46-70	12mths	$793
Transvaginal ultrasound (females only)	35-70	12mths	$129
CA125 (females only)	50-70	12mths	$24
Population Surveillance			
Faecal Occult Blood Test	50-70	18mths	$26

Table 10: Clinical intervention for familial breast or ovarian cancer (BRCA1/2 mutations) at 2001-2002 prices

INTERVENTION	AGE OF INTERVENTION (YRS)	FREQUENCY OF EVENT	COST PER EVENT (UNDISCOUNTED)
Genetic counselling + test, carrier		once only	$1,012
Ovarian Cancer Intensive Surveillance & Prophylaxis			
Transvaginal ultrasound	35*-40	12mths	$129
CA125	35-40	12mths	$24
Prophylactic salpingo-oophorectomy	40	once only	$7,216
Breast Cancer Intensive Surveillance & Prophylaxis			
Clinical breast examination	25-37	4mths	$65
Mammogram	35*-37	12mths	$163
Prophylactic bilateral mastectomy	38	once only	$11,547
CT chest scan post surgery	39	once only	$175
Clinical ex. of chest wall and lymph nodes	39-70	6mths	$65
Breast Cancer Intensive Surveillance only			
Clinical breast examination	25-70	4mths	$65
Mammogram	35*-70	12mths	$163
Population Surveillance (breast cancer only)			
Mammogram	50-69	24mths	$163
Ovarian cancer treatment (life)		once only	$19,735
Breast cancer treatment (life)		once only	$11,616

**Or 5yrs before youngest affected family member*

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Table 11: Average counselling process for predictive testing, mutation detected

STEP	COUNSELLING PROCESS	PRE-TEST	POST-TEST	TOTAL
1	Patient contacts GSWA or written referral	0		
2	First phone consultation with genetic counsellor (includes preparation and follow-up)	75		
3	In-person interview with genetic counsellor (includes preparation and notes)	90		
4	Second phone consultation with genetic counsellor (includes follow-up)	30		
5	In-person testing interview with clinical geneticist (plus genetic counsellor if required)	75		
6	Third phone follow-up consultation - genetic counsellor		30	
7	In-person result consultation with clinical geneticist (plus genetic counsellor)		75	
8	Fourth phone follow-up consultation - genetic counsellor		30	
9	Coding by genetic counsellor		15	
10	Fifth phone consultation with genetic counsellor at 6-12 months		30	
TOTAL		**270**	**180**	**450**

Table 12: Average counselling process for predictive testing, mutation not detected

STEP	COUNSELLING PROCESS	PRE-TEST	POST-TEST	TOTAL
1	Patient contacts GSWA or written referral	0		
2	First phone consultation with genetic counsellor (includes preparation and follow-up)	75		
3	In-person interview with genetic counsellor (includes preparation and notes)	90		
4	Second phone consultation with genetic counsellor	30		
7	In-person result consultation with clinical geneticist (plus genetic counsellor)		45	
8	Fourth phone follow-up consultation with genetic counsellor		30	
9	Coding by genetic counsellor		15	
10	Fifth phone consultation with genetic counsellor at 6-12 months		30	
TOTAL		**195**	**120**	**315**

Table 13: Average duration and cost of familial cancer counselling by patient type

PATIENT	HOURS	COST
Diagnostic /Index Case - Positive	5.5	$486
Diagnostic /Index Case - Inconclusive	3.5	$347
High Risk - ineligible to test	3.0	$252
Predictive /Relative Case-Mutation Present	7.5	$547
Predictive /Relative Case-Mutation Absent	5.3	$368

Table 14: Mean age of surgery and cancer diagnosis used for discount

	COLORECTAL (FAP)	COLORECTAL (HNPCC)	BREAST	OVARIAN
Mean age of surgery	21	45	38	40
Cost of surgery - undiscounted	$16,759	$16,759	$11,547	$7,216
Cost of surgery – discounted (5% per annum)	$9,799	$6,316	$6,124	$3,471
Mean age of cancer diagnosis	33	45	41	50
Cost of cancer treatment - undiscounted	$18,358	$18,358	$11,616	$19,735
Cost of cancer treatment – discounted (5% p.a.)	$5,977	$6,919	$5,321	$5,828

Source: (Meiser 2000; Friedl 2001; Haber 2002; Rebbeck 2002; GSWA 2003; Lynch 2003; Rebbeck 2004)

Table 15: Impact of less effective surveillance (80%) in the FAP model

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
10	0.00000	0.0000	0.0000	0.0000	0.0000
15	0.00000	0.0500	0.0100	0.0050	0.0250
20	0.00001	0.1000	0.0200	0.0100	0.0500
25	0.00002	0.1500	0.0300	0.0150	0.0750
30	0.00004	0.2000	0.0400	0.0200	0.1000
35	0.00008	0.2500	0.0500	0.0250	0.1250
40	0.00017	0.3000	0.0600	0.0301	0.1501
45	0.00034	0.3000	0.0600	0.0302	0.1502
50	0.00062	0.3000	0.0600	0.0303	0.1503
55	0.00111	0.3000	0.0600	0.0306	0.1506
60	0.00181	0.3000	0.0600	0.0309	0.1509
65	0.00246	0.3000	0.0600	0.0312	0.1512
70	0.00339	0.3000	0.0600	0.0317	0.1517
75	0.00403	0.3000	0.0600	0.0320	0.1520

Table 16: Impact of more effective surveillance (100%) in the FAP model

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
10	0.00000	0.0000	0.0000	0.0000	0.0000
15	0.00000	0.0500	0.0000	0.0000	0.0250
20	0.00001	0.1000	0.0000	0.0000	0.0500
25	0.00002	0.1500	0.0000	0.0000	0.0750
30	0.00004	0.2000	0.0000	0.0000	0.1000
35	0.00008	0.2500	0.0000	0.0000	0.1250
40	0.00017	0.3000	0.0000	0.0001	0.1501
45	0.00034	0.3000	0.0000	0.0002	0.1502
50	0.00062	0.3000	0.0000	0.0003	0.1503
55	0.00111	0.3000	0.0000	0.0006	0.1506
60	0.00181	0.3000	0.0000	0.0009	0.1509
65	0.00246	0.3000	0.0000	0.0012	0.1512
70	0.00339	0.3000	0.0000	0.0017	0.1517
75	0.00403	0.3000	0.0000	0.0020	0.1520

Table 17: Impact of adjusting the efficacy of surveillance in the FAP model

EFFICACY OF SURVEILLANCE	ANNUAL CRC RISK REDUCTION	INTERVENTION GROUP	CONTROL GROUP 1	CONTROL GROUP 2
Less effective	80%	45yrs ($14,994)	39yrs ($29,286)	18yrs ($6,917)
Current	98%	58yrs ($15,959)	58yrs ($29,349)	18yrs ($6,917)
More effective	100%	61yrs ($15,732)	61yrs ($29,101)	18yrs ($6,917)

Table 18: Impact of less effective surveillance (30%) in the HNPCC model

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00002	0.004	0.003	0.002	0.002
30	0.00004	0.010	0.007	0.004	0.005
35	0.00007	0.019	0.013	0.007	0.010
40	0.00016	0.041	0.029	0.014	0.021
45	0.00032	0.083	0.058	0.029	0.042
50	0.00056	0.146	0.102	0.051	0.073
55	0.00091	0.001	0.001	0.001	0.001
60	0.00142	0.001	0.001	0.001	0.001
65	0.00189	0.002	0.001	0.002	0.002
70	0.00255	0.003	0.002	0.002	0.003
75	0.00311	0.003	0.002	0.003	0.003

Table 19: Impact of more effective surveillance (70%) in the HNPCC model

AGE	PPOPCRC	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00002	0.004	0.001	0.001	0.002
30	0.00004	0.010	0.003	0.002	0.005
35	0.00007	0.019	0.006	0.003	0.010
40	0.00016	0.041	0.012	0.006	0.021
45	0.00032	0.083	0.025	0.013	0.042
50	0.00056	0.146	0.044	0.022	0.073
55	0.00091	0.001	0.000	0.001	0.001
60	0.00142	0.001	0.000	0.001	0.001
65	0.00189	0.002	0.001	0.001	0.002
70	0.00255	0.003	0.001	0.002	0.003
75	0.00311	0.003	0.001	0.002	0.003

Table 20: Impact of adjusting the efficacy of surveillance in the HNPCC female model

EFFICACY OF SURVEILLANCE	ANNUAL CRC RISK REDUCTION	INTERVENTION GROUP	CONTROL GROUP 1	CONTROL GROUP 2
Less effective	30%	37yrs ($16,227)	35yrs ($31,590)	31yrs ($4,183)
Current	50%	39yrs ($16,779)	38yrs ($32,239)	31yrs ($4,183)
More effective	70%	41yrs ($17,379)	40yrs ($32,861)	31yrs ($4,183)

Table 21: Impact of lower penetrance (44%) in the breast BRCA1 model

AGE	PPOPINCID	PINCID_BRCA1	PINCID_INTSURVPS	PINCID_SURVONLY	CONTROL_1	CONTROL_2
25	0.00007	0.0005	0.0000	0.0005	0.0003	0.0003
30	0.00027	0.0017	0.0002	0.0005	0.0004	0.0010
35	0.00058	0.0037	0.0004	0.0003	0.0004	0.0021
40	0.00115	0.0074	0.0007	0.0011	0.0011	0.0043
45	0.00188	0.0121	0.0012	0.0024	0.0021	0.0070
50	0.00251	0.0160	0.0016	0.0048	0.0036	0.0093
55	0.00302	0.0194	0.0019	0.0078	0.0054	0.0112
60	0.00337	0.0216	0.0022	0.0104	0.0069	0.0125
65	0.00324	0.0207	0.0021	0.0126	0.0079	0.0120
70	0.00330	0.0211	0.0021	0.0140	0.0087	0.0122
75	0.00310	0.0198	0.0020	0.0135	0.0083	0.0115

Table 22: Impact of higher penetrance (78%) in the breast BRCA1 model

AGE	PPOPINCID	PINCID_BRCA1	PINCID_INTSURVPS	PINCID_SURVONLY	CONTROL_1	CONTROL_2
25	0.00007	0.0012	0.0001	0.0012	0.0006	0.0006
30	0.00027	0.0044	0.0004	0.0012	0.0007	0.0023
35	0.00058	0.0095	0.0009	0.0008	0.0007	0.0050
40	0.00115	0.0190	0.0019	0.0028	0.0020	0.0101
45	0.00188	0.0311	0.0031	0.0062	0.0040	0.0165
50	0.00251	0.0414	0.0041	0.0124	0.0074	0.0219
55	0.00302	0.0499	0.0050	0.0202	0.0116	0.0265
60	0.00337	0.0556	0.0056	0.0269	0.0151	0.0295
65	0.00324	0.0535	0.0053	0.0324	0.0178	0.0284
70	0.00330	0.0544	0.0054	0.0362	0.0197	0.0288
75	0.00310	0.0511	0.0051	0.0347	0.0189	0.0271

Table 23: Impact of lower penetrance (31%) in the breast BRCA2 model

AGE	PPOPINCID	PINCID_BRCA2	PINCID_INTSURVPS	PINCID_SURVONLY	CONTROL_1	CONTROL_2
25	0.00007	0.0003	0.0000	0.0003	0.0002	0.0002
30	0.00027	0.0011	0.0001	0.0003	0.0003	0.0007
35	0.00058	0.0024	0.0002	0.0002	0.0004	0.0015
40	0.00115	0.0047	0.0005	0.0007	0.0009	0.0029
45	0.00188	0.0077	0.0008	0.0015	0.0017	0.0048
50	0.00251	0.0103	0.0010	0.0031	0.0028	0.0064
55	0.00302	0.0124	0.0012	0.0050	0.0040	0.0077
60	0.00337	0.0138	0.0014	0.0067	0.0050	0.0086
65	0.00324	0.0133	0.0013	0.0081	0.0056	0.0083
70	0.00330	0.0135	0.0014	0.0090	0.0061	0.0084
75	0.00310	0.0127	0.0013	0.0086	0.0059	0.0079

Table 24: Impact of higher penetrance (56%) in the breast BRCA2 model

AGE	PPOPINCID	PINCID_BRCA2	PINCID_INTSURVPS	PINCID_SURVONLY	CONTROL_1	CONTROL_2
25	0.00007	0.0006	0.0001	0.0006	0.0003	0.0003
30	0.00027	0.0021	0.0002	0.0006	0.0004	0.0012
35	0.00058	0.0046	0.0005	0.0004	0.0005	0.0026
40	0.00115	0.0092	0.0009	0.0014	0.0013	0.0052
45	0.00188	0.0151	0.0015	0.0030	0.0024	0.0085
50	0.00251	0.0201	0.0020	0.0060	0.0042	0.0113
55	0.00302	0.0242	0.0024	0.0098	0.0064	0.0136
60	0.00337	0.0270	0.0027	0.0130	0.0082	0.0152
65	0.00324	0.0259	0.0026	0.0157	0.0095	0.0146
70	0.00330	0.0264	0.0026	0.0175	0.0104	0.0148
75	0.00310	0.0248	0.0025	0.0168	0.0100	0.0139

Table 25: Impact of adjusted mutation penetrance on cost-effectiveness in the breast model

	CUMULATIVE INCIDENCE	NET SAVING	NET COST
BRCA1 - Low	44%	$1687 (3mths)	$3581 (3.2yrs)
- High	78%	$1900 (7mths)	$2656 (6.6yrs)
BRCA2 - Low	31%	$1642 (2mths)	$3865 (2.3yrs)
- High	56%	$1719 (4mths)	$3403 (3.9yrs)

Table 26: Impact of lower penetrance (18%) in the ovarian BRCA1 model

AGE	PPOPINCID	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00003	0.0007	0.000	0.0000	0.0004
30	0.00003	0.0007	0.000	0.0000	0.0004
35	0.00005	0.0013	0.000	0.0001	0.0007
40	0.00008	0.0018	0.000	0.0001	0.0009
45	0.00013	0.0031	0.000	0.0001	0.0016
50	0.00022	0.0053	0.000	0.0002	0.0028
55	0.00022	0.0054	0.000	0.0002	0.0028
60	0.00033	0.0079	0.000	0.0003	0.0041
65	0.00032	0.0077	0.000	0.0003	0.0040
70	0.00041	0.0099	0.000	0.0004	0.0052
75	0.00054	0.0128	0.001	0.0005	0.0067

Table 27: Impact of higher penetrance (54%) in the ovarian BRCA1 model

AGE	PPOPINCID	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00003	0.0027	0.000	0.0001	0.0014
30	0.00003	0.0029	0.000	0.0001	0.0015
35	0.00005	0.0049	0.000	0.0001	0.0025
40	0.00008	0.0070	0.000	0.0002	0.0035
45	0.00013	0.0119	0.000	0.0003	0.0060
50	0.00022	0.0205	0.001	0.0005	0.0103
55	0.00022	0.0208	0.001	0.0005	0.0105
60	0.00033	0.0307	0.001	0.0008	0.0155
65	0.00032	0.0299	0.001	0.0008	0.0151
70	0.00041	0.0385	0.002	0.0010	0.0195
75	0.00054	0.0498	0.002	0.0013	0.0251

Table 28: Impact of lower penetrance (2.4%) in the ovarian BRCA2 model

AGE	PPOPINCID	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00003	0.0001	0.000	0.0000	0.0001
30	0.00003	0.0001	0.000	0.0000	0.0001
35	0.00005	0.0002	0.000	0.0000	0.0001
40	0.00008	0.0002	0.000	0.0000	0.0002
45	0.00013	0.0004	0.000	0.0001	0.0003
50	0.00022	0.0007	0.000	0.0001	0.0004
55	0.00022	0.0007	0.000	0.0001	0.0004
60	0.00033	0.0010	0.000	0.0002	0.0007
65	0.00032	0.0010	0.000	0.0002	0.0006
70	0.00041	0.0012	0.000	0.0002	0.0008
75	0.00054	0.0016	0.000	0.0003	0.0011

Table 29: Impact of higher penetrance (19%) in the ovarian BRCA2 model

AGE	PPOPINCID	PCARRIER_INCID	PCARRIER_INTSURVPS	CONTROL_1	CONTROL_2
25	0.00003	0.0007	0.000	0.0000	0.0004
30	0.00003	0.0008	0.000	0.0000	0.0004
35	0.00005	0.0013	0.000	0.0001	0.0007
40	0.00008	0.0019	0.000	0.0001	0.0010
45	0.00013	0.0032	0.000	0.0001	0.0017
50	0.00022	0.0055	0.000	0.0002	0.0029
55	0.00022	0.0056	0.000	0.0002	0.0029
60	0.00033	0.0083	0.000	0.0003	0.0043
65	0.00032	0.0081	0.000	0.0003	0.0042
70	0.00041	0.0104	0.000	0.0004	0.0054
75	0.00054	0.0134	0.001	0.0005	0.0070

Table 30: Impact of adjusted mutation penetrance on cost-effectiveness in the ovarian model

	CUMULATIVE INCIDENCE	NET SAVING	NET COST
BRCA1 - Low	18%	$1011 (0mths)	$2289 (1.8yrs)
- High	54%	$1002 (1mth)	$1056 (5.0yrs)
BRCA2 - Low	2.4%	$993 (1mth)	$2765 (6mths)
- High	19%	$1011 (0mths)	$2265 (1.8yrs)

Table 31: Impact on costs when the discount rate is varied in the FAP model

	POPULATION SURVEILLANCE				INTENSIVE SURVEILLANCE			
AGE	NODISC	DISC3%	DISC5%	DISC7%	NODISC	DISC3%	DISC5%	DISC7%
10	0.00	0.00	0.00	0.00	561.33	561.33	561.33	561.33
11	0.00	0.00	0.00	0.00	561.33	544.98	534.60	524.61
12	0.00	0.00	0.00	0.00	561.33	529.11	509.15	490.29
13	0.00	0.00	0.00	0.00	561.33	513.70	484.90	458.22
14	0.00	0.00	0.00	0.00	561.33	498.74	461.81	428.24
15	0.00	0.00	0.00	0.00	561.33	484.21	439.82	400.22
16	0.00	0.00	0.00	0.00	561.33	470.11	418.88	374.04
17	0.00	0.00	0.00	0.00	561.33	456.42	398.93	349.57
18	0.00	0.00	0.00	0.00	561.33	443.12	379.93	326.70
19	0.00	0.00	0.00	0.00	561.33	430.22	361.84	305.33
20	0.00	0.00	0.00	0.00	561.33	417.68	344.61	285.35
21	0.00	0.00	0.00	0.00	16759.00	12107.06	9798.64	7962.08
22	0.00	0.00	0.00	0.00	1370.67	961.36	763.24	608.59
23	0.00	0.00	0.00	0.00	1370.67	933.36	726.89	568.78
24	0.00	0.00	0.00	0.00	1370.67	906.17	692.28	531.57
25	0.00	0.00	0.00	0.00	1370.67	879.78	659.31	496.79
26	0.00	0.00	0.00	0.00	1370.67	854.15	627.92	464.29
27	0.00	0.00	0.00	0.00	1370.67	829.28	598.02	433.92
28	0.00	0.00	0.00	0.00	1370.67	805.12	569.54	405.53
29	0.00	0.00	0.00	0.00	1370.67	781.67	542.42	379.00
30	0.00	0.00	0.00	0.00	1370.67	758.90	516.59	354.21
31	0.00	0.00	0.00	0.00	1370.67	736.80	491.99	331.03
32	0.00	0.00	0.00	0.00	1370.67	715.34	468.56	309.38
33	0.00	0.00	0.00	0.00	1370.67	694.51	446.25	289.14
34	0.00	0.00	0.00	0.00	1370.67	674.28	425.00	270.22
35	0.00	0.00	0.00	0.00	1370.67	654.64	404.76	252.54
36	0.00	0.00	0.00	0.00	1370.67	635.57	385.49	236.02
37	0.00	0.00	0.00	0.00	1370.67	617.06	367.13	220.58
38	0.00	0.00	0.00	0.00	1370.67	599.09	349.65	206.15
39	0.00	0.00	0.00	0.00	1370.67	581.64	333.00	192.66
40	0.00	0.00	0.00	0.00	1370.67	564.70	317.14	180.06
41	0.00	0.00	0.00	0.00	1370.67	548.25	302.04	168.28
42	0.00	0.00	0.00	0.00	1370.67	532.28	287.66	157.27
43	0.00	0.00	0.00	0.00	1370.67	516.78	273.96	146.98
44	0.00	0.00	0.00	0.00	1370.67	501.73	260.91	137.37
45	0.00	0.00	0.00	0.00	1370.67	487.11	248.49	128.38
46	0.00	0.00	0.00	0.00	1370.67	472.92	236.66	119.98
47	0.00	0.00	0.00	0.00	1370.67	459.15	225.39	112.13
48	0.00	0.00	0.00	0.00	1370.67	445.78	214.65	104.80
49	0.00	0.00	0.00	0.00	1370.67	432.79	204.43	97.94
50	185.73	56.94	26.38	12.40	1370.67	420.19	194.70	91.53
51	185.73	55.28	25.13	11.59	1370.67	407.95	185.43	85.55
52	185.73	53.67	23.93	10.83	1370.67	396.07	176.60	79.95
53	185.73	52.11	22.79	10.12	1370.67	384.53	168.19	74.72
54	185.73	50.59	21.71	9.46	1370.67	373.33	160.18	69.83
55	185.73	49.12	20.67	8.84	1370.67	362.46	152.55	65.26
56	185.73	47.68	19.69	8.26	1370.67	351.90	145.29	60.99
57	185.73	46.30	18.75	7.72	1370.67	341.65	138.37	57.00
58	185.73	44.95	17.86	7.22	1370.67	331.70	131.78	53.27
59	185.73	43.64	17.01	6.75	1370.67	322.04	125.50	49.79
60	185.73	42.37	16.20	6.31	1370.67	312.66	119.53	46.53
61	185.73	41.13	15.43	5.89	1370.67	303.55	113.84	43.49
62	185.73	39.94	14.69	5.51	1370.67	294.71	108.41	40.64
63	185.73	38.77	13.99	5.15	1370.67	286.13	103.25	37.98
64	185.73	37.64	13.33	4.81	1370.67	277.79	98.34	35.50
65	185.73	36.55	12.69	4.50	1370.67	269.70	93.65	33.18
66	185.73	35.48	12.09	4.20	1370.67	261.85	89.19	31.01
67	185.73	34.45	11.51	3.93	1370.67	254.22	84.95	28.98
68	185.73	33.44	10.96	3.67	1370.67	246.82	80.90	27.08
69	185.73	32.47	10.44	3.43	1370.67	239.63	77.05	25.31
70	185.73	31.53	9.94	3.21	1370.67	232.65	73.38	23.65
71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
72	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
73	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
74	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL	$3,900	$904	$355	$144	$90,096	$42,708	$29,255	$21,431

Table 32: Summary of results when the discount rate is varied in the FAP model

DISCOUNT RATE	NET SAVING	NET COST
No discount	$41,762	$27,922
Discount 3%	$19,809	$12,644
Discount 5%	$13,390	$9,042
Discount 7%	$9,592	$7,168

Table 33: Impact on population surveillance costs when the discount rate is varied in the HNPCC model

AGE	NODISC	DISC3%	DISC5%	DISC7%
25	0.00	0.00	0.00	0.00
26	0.00	0.00	0.00	0.00
27	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00
29	0.00	0.00	0.00	0.00
30	0.00	0.00	0.00	0.00
31	0.00	0.00	0.00	0.00
32	0.00	0.00	0.00	0.00
33	0.00	0.00	0.00	0.00
34	0.00	0.00	0.00	0.00
35	0.00	0.00	0.00	0.00
36	0.00	0.00	0.00	0.00
37	0.00	0.00	0.00	0.00
38	0.00	0.00	0.00	0.00
39	0.00	0.00	0.00	0.00
40	0.00	0.00	0.00	0.00
41	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00
43	0.00	0.00	0.00	0.00
44	0.00	0.00	0.00	0.00
45	0.00	0.00	0.00	0.00
46	0.00	0.00	0.00	0.00
47	0.00	0.00	0.00	0.00
48	0.00	0.00	0.00	0.00
49	0.00	0.00	0.00	0.00
50	185.73	88.71	54.85	34.22
51	185.73	86.12	52.24	31.98
52	185.73	83.62	49.75	29.89
53	185.73	81.18	47.38	27.93
54	185.73	78.82	45.12	26.11
55	185.73	76.52	42.97	24.40
56	185.73	74.29	40.93	22.80
57	185.73	72.13	38.98	21.31
58	185.73	70.03	37.12	19.92
59	185.73	67.99	35.36	18.61
60	185.73	66.01	33.67	17.40
61	185.73	64.08	32.07	16.26
62	185.73	62.22	30.54	15.19
63	185.73	60.41	29.09	14.20
64	185.73	58.65	27.70	13.27
65	185.73	56.94	26.38	12.40
66	185.73	55.28	25.13	11.59
67	185.73	53.67	23.93	10.83
68	185.73	52.11	22.79	10.12
69	185.73	50.59	21.71	9.46
70	185.73	49.12	20.67	8.84
71	0.00	0.00	0.00	0.00
72	0.00	0.00	0.00	0.00
73	0.00	0.00	0.00	0.00
74	0.00	0.00	0.00	0.00
75	0.00	0.00	0.00	0.00
TOTAL	**$3,900**	**$,408**	**$ 738**	**$ 397**

Table 34: Impact on intensive surveillance costs when the discount rate is varied in the HNPCC model

AGE	M_NODISC	M_DISC3%	M_DISC5%	M_DISC7%	F_NODISC	F_DISC3%	F_DISC5%	F_DISC7%
25	1387.50	1387.50	1387.50	1387.50	1387.50	1387.50	1387.50	1387.50
26	1387.50	1347.09	1321.43	1296.73	1387.50	1347.09	1321.43	1296.73
27	1387.50	1307.85	1258.50	1211.90	1387.50	1307.85	1258.50	1211.90
28	1387.50	1269.76	1198.57	1132.61	1387.50	1269.76	1198.57	1132.61
29	1387.50	1232.78	1141.50	1058.52	1387.50	1232.78	1141.50	1058.52
30	1387.50	1196.87	1087.14	989.27	1387.50	1196.87	1087.14	989.27
31	1387.50	1162.01	1035.37	924.55	1387.50	1162.01	1035.37	924.55
32	1387.50	1128.16	986.07	864.07	1387.50	1128.16	986.07	864.07
33	1387.50	1095.31	939.11	807.54	1387.50	1095.31	939.11	807.54
34	1387.50	1063.40	894.39	754.71	1387.50	1063.40	894.39	754.71
35	1387.50	1032.43	851.80	705.33	1516.50	1128.42	931.00	770.91
36	1387.50	1002.36	811.24	659.19	1516.50	1095.55	886.67	720.48
37	1387.50	973.16	772.61	616.07	1516.50	1063.64	844.44	673.34
38	1387.50	944.82	735.82	575.76	1516.50	1032.66	804.23	629.29
39	1387.50	917.30	700.78	538.10	1516.50	1002.59	765.94	588.12
40	1387.50	890.58	667.41	502.89	1516.50	973.38	729.46	549.65
41	1387.50	864.64	635.63	469.99	1516.50	945.03	694.73	513.69
42	1387.50	839.46	605.36	439.25	1516.50	917.51	661.64	480.09
43	1387.50	815.01	576.53	410.51	1516.50	890.78	630.14	448.68
44	1387.50	791.27	549.08	383.66	1516.50	864.84	600.13	419.32
45	16759.00	9279.05	6316.29	4330.84	16759.00	9279.05	6316.29	4330.84
46	1635.00	878.89	586.87	394.87	1764.00	948.24	633.17	426.03
47	1635.00	853.29	558.92	369.04	1764.00	920.62	603.02	398.16
48	1635.00	828.44	532.31	344.90	1764.00	893.80	574.31	372.11
49	1635.00	804.31	506.96	322.33	1764.00	867.77	546.96	347.77
50	1635.00	780.89	482.82	301.25	1788.00	853.96	528.00	329.44
51	1635.00	758.14	459.83	281.54	1788.00	829.09	502.86	307.89
52	1635.00	736.06	437.93	263.12	1788.00	804.94	478.91	287.74
53	1635.00	714.62	417.08	245.91	1788.00	781.49	456.11	268.92
54	1635.00	693.81	397.22	229.82	1788.00	758.73	434.39	251.33
55	1635.00	673.60	378.30	214.79	1788.00	736.63	413.70	234.88
56	1635.00	653.98	360.29	200.73	1788.00	715.18	394.00	219.52
57	1635.00	634.93	343.13	187.60	1788.00	694.35	375.24	205.16
58	1635.00	616.44	326.79	175.33	1788.00	674.12	357.37	191.74
59	1635.00	598.48	311.23	163.86	1788.00	654.49	340.35	179.19
60	1635.00	581.05	296.41	153.14	1788.00	635.43	324.15	167.47
61	1635.00	564.13	282.29	143.12	1788.00	616.92	308.71	156.51
62	1635.00	547.70	268.85	133.76	1788.00	598.95	294.01	146.27
63	1635.00	531.74	256.05	125.01	1788.00	581.50	280.01	136.70
64	1635.00	516.26	243.86	116.83	1788.00	564.57	266.68	127.76
65	1635.00	501.22	232.24	109.19	1788.00	548.12	253.98	119.40
66	1635.00	486.62	221.19	102.04	1788.00	532.16	241.88	111.59
67	1635.00	472.45	210.65	95.37	1788.00	516.66	230.37	104.29
68	1635.00	458.69	200.62	89.13	1788.00	501.61	219.40	97.47
69	1635.00	445.33	191.07	83.30	1788.00	487.00	208.95	91.09
70	1635.00	432.36	181.97	77.85	1788.00	472.82	199.00	85.13
71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
72	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
73	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
74	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL	**$85,384**	**$46,304**	**$33,157**	**$24,983**	**$90,403**	**$48,573**	**$34,580**	**$25,915**

Table 35: Summary of results when the discount rate is varied in the female HNPCC model

DISCOUNT RATE	NET SAVING	NET COST
No discount	$40,472	$3,380
Discount 3%	$21,869	$2,044
Discount 5%	$15,460	$1,575
Discount 7%	$11,411	$1,271

Table 36: Impact on population surveillance costs when the discount rate is varied in the breast model

AGE	NODISC	DISC3%	DISC5%	DISC7%
25	0.00	0.00	0.00	0.00
26	0.00	0.00	0.00	0.00
27	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00
29	0.00	0.00	0.00	0.00
30	0.00	0.00	0.00	0.00
31	0.00	0.00	0.00	0.00
32	0.00	0.00	0.00	0.00
33	0.00	0.00	0.00	0.00
34	0.00	0.00	0.00	0.00
35	0.00	0.00	0.00	0.00
36	0.00	0.00	0.00	0.00
37	0.00	0.00	0.00	0.00
38	0.00	0.00	0.00	0.00
39	0.00	0.00	0.00	0.00
40	0.00	0.00	0.00	0.00
41	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00
43	0.00	0.00	0.00	0.00
44	0.00	0.00	0.00	0.00
45	0.00	0.00	0.00	0.00
46	0.00	0.00	0.00	0.00
47	0.00	0.00	0.00	0.00
48	0.00	0.00	0.00	0.00
49	0.00	0.00	0.00	0.00
50	81.50	38.92	24.07	15.02
51	81.50	37.79	22.92	14.03
52	81.50	36.69	21.83	13.12
53	81.50	35.62	20.79	12.26
54	81.50	34.58	19.80	11.46
55	81.50	33.58	18.86	10.71
56	81.50	32.60	17.96	10.01
57	81.50	31.65	17.10	9.35
58	81.50	30.73	16.29	8.74
59	81.50	29.83	15.51	8.17
60	81.50	28.96	14.78	7.63
61	81.50	28.12	14.07	7.13
62	81.50	27.30	13.40	6.67
63	81.50	26.51	12.76	6.23
64	81.50	25.73	12.16	5.82
65	81.50	24.98	11.58	5.44
66	81.50	24.26	11.03	5.09
67	81.50	23.55	10.50	4.75
68	81.50	22.86	10.00	4.44
69	81.50	22.20	9.52	4.15
70	0.00	0.00	0.00	0.00
71	0.00	0.00	0.00	0.00
72	0.00	0.00	0.00	0.00
73	0.00	0.00	0.00	0.00
74	0.00	0.00	0.00	0.00
75	0.00	0.00	0.00	0.00
TOTAL	**$1,630**	**$596**	**$315**	**$170**

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Table 37: Impact on intensive surveillance costs when the discount rate is varied in the breast model

AGE	NODISC	DISC3%	DISC5%	DISC7%	NODISC	DISC3%	DISC5%	DISC7%
25	195.00	195.00	195.00	195.00	195.00	195.00	195.00	195.00
26	195.00	189.32	185.71	182.24	195.00	189.32	185.71	182.24
27	195.00	183.81	176.87	170.32	195.00	183.81	176.87	170.32
28	195.00	178.45	168.45	159.18	195.00	178.45	168.45	159.18
29	195.00	173.25	160.43	148.76	195.00	173.25	160.43	148.76
30	195.00	168.21	152.79	139.03	195.00	168.21	152.79	139.03
31	195.00	163.31	145.51	129.94	195.00	163.31	145.51	129.94
32	195.00	158.55	138.58	121.44	195.00	158.55	138.58	121.44
33	195.00	153.93	131.98	113.49	195.00	153.93	131.98	113.49
34	195.00	149.45	125.70	106.07	195.00	149.45	125.70	106.07
35	358.00	308.10	315.79	302.03	358.00	308.10	282.71	262.13
36	358.00	299.12	300.75	282.27	358.00	299.12	269.25	244.98
37	358.00	290.41	286.43	263.81	358.00	290.41	256.43	228.95
38	11,547.00	7,862.95	6,123.62	4,791.59	358.00	281.95	244.22	213.97
39	305.00	201.64	154.05	118.28	358.00	273.74	232.59	199.98
40	130.00	83.44	62.53	47.12	358.00	265.77	221.51	186.89
41	130.00	81.01	59.55	44.04	358.00	258.03	210.96	174.67
42	130.00	78.65	56.72	41.15	358.00	250.51	200.92	163.24
43	130.00	76.36	54.02	38.46	358.00	243.22	191.35	152.56
44	130.00	74.14	51.45	35.95	358.00	236.13	182.24	142.58
45	130.00	71.98	49.00	33.59	358.00	229.25	173.56	133.25
46	130.00	69.88	46.66	31.40	358.00	222.58	165.30	124.54
47	130.00	67.85	44.44	29.34	358.00	216.09	157.43	116.39
48	130.00	65.87	42.32	27.42	358.00	209.80	149.93	108.77
49	130.00	63.95	40.31	25.63	358.00	203.69	142.79	101.66
50	130.00	62.09	38.39	23.95	358.00	197.76	135.99	95.01
51	130.00	60.28	36.56	22.39	358.00	192.00	129.51	88.79
52	130.00	58.52	34.82	20.92	358.00	186.40	123.35	82.98
53	130.00	56.82	33.16	19.55	358.00	180.98	117.47	77.55
54	130.00	55.17	31.58	18.27	358.00	175.70	111.88	72.48
55	130.00	53.56	30.08	17.08	358.00	170.59	106.55	67.74
56	130.00	52.00	28.65	15.96	358.00	165.62	101.48	63.31
57	130.00	50.48	27.28	14.92	358.00	160.79	96.65	59.17
58	130.00	49.01	25.98	13.94	358.00	156.11	92.04	55.30
59	130.00	47.59	24.75	13.03	358.00	151.56	87.66	51.68
60	130.00	46.20	23.57	12.18	358.00	147.15	83.49	48.30
61	130.00	44.85	22.45	11.38	358.00	142.86	79.51	45.14
62	130.00	43.55	21.38	10.64	358.00	138.70	75.72	42.18
63	130.00	42.28	20.36	9.94	358.00	134.66	72.12	39.42
64	130.00	41.05	19.39	9.29	358.00	130.74	68.68	36.85
65	130.00	39.85	18.47	8.68	358.00	126.93	65.41	34.44
66	130.00	38.69	17.59	8.11	358.00	123.24	62.30	32.18
67	130.00	37.56	16.75	7.58	358.00	119.65	59.33	30.08
68	130.00	36.47	15.95	7.09	358.00	116.16	56.51	28.11
69	130.00	35.41	15.19	6.62	358.00	112.78	53.82	26.27
70	130.00	34.38	14.47	6.19	358.00	109.49	51.25	24.55
71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
72	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
73	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
74	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL	**$18,906**	**$12,394**	**$9,785**	**$7,855**	**$14,838**	**$8,642**	**$6,493**	**$5,122**

Table 38: Summary of results when the dicount rate is varied in the BRCA1 breast model

DISCOUNT RATE	NET SAVING	NET COST
No discount	$5028	$5012
Discount 3%	$2687	$3550
Discount 5%	$1795	$3055
Discount 7%	$1232	$2724

Table 39: Impact of prophylactic bilateral mastectomy uptake on cost-effectiveness

	UPTAKE OF PROPHYLAXIS	NET SAVING	NET COST
BRCA1	0%	$2125 (1mth)	$2725 (4.6yrs)
	30%	$1795 (6mths)	$3055 (5.1yrs)
	50%	$1574 (9mths)	$3276 (5.4yrs)
BRCA2	0%	$2081 (0mths)	$3179 (2.9yrs)
	30%	$1691 (3mths)	$3569 (3.2yrs)
	50%	$1432 (5mths)	$3828 (3.4yrs)

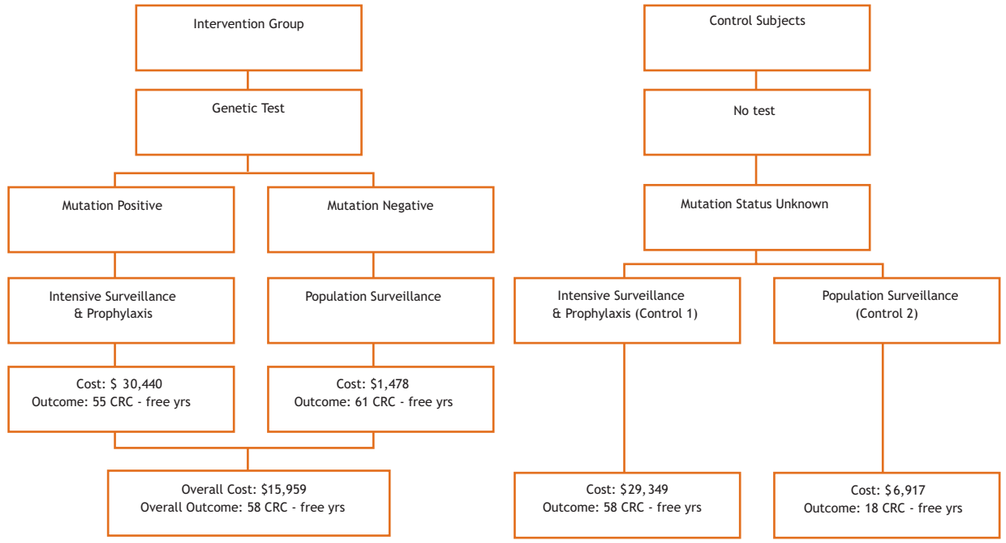
Table 40: Impact on intensive surveillance costs when the discount rate is varied in the ovarian model

AGE	NODISC	3% DISC	5% DISC	7% DISC
25	0.00	0.00	0.00	0.00
26	0.00	0.00	0.00	0.00
27	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00
29	0.00	0.00	0.00	0.00
30	0.00	0.00	0.00	0.00
31	0.00	0.00	0.00	0.00
32	0.00	0.00	0.00	0.00
33	0.00	0.00	0.00	0.00
34	0.00	0.00	0.00	0.00
35	153.00	95.99	79.19	65.58
36	153.00	93.19	75.42	61.29
37	153.00	90.48	71.83	57.28
38	153.00	87.84	68.41	53.53
39	153.00	85.28	65.15	50.03
40	7215.50	4631.35	3470.78	2615.23
41	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00
43	0.00	0.00	0.00	0.00
44	0.00	0.00	0.00	0.00
45	0.00	0.00	0.00	0.00
46	0.00	0.00	0.00	0.00
47	0.00	0.00	0.00	0.00
48	0.00	0.00	0.00	0.00
49	0.00	0.00	0.00	0.00
50	0.00	0.00	0.00	0.00
51	0.00	0.00	0.00	0.00
52	0.00	0.00	0.00	0.00
53	0.00	0.00	0.00	0.00
54	0.00	0.00	0.00	0.00
55	0.00	0.00	0.00	0.00
56	0.00	0.00	0.00	0.00
57	0.00	0.00	0.00	0.00
58	0.00	0.00	0.00	0.00
59	0.00	0.00	0.00	0.00
60	0.00	0.00	0.00	0.00
61	0.00	0.00	0.00	0.00
62	0.00	0.00	0.00	0.00
63	0.00	0.00	0.00	0.00
64	0.00	0.00	0.00	0.00
65	0.00	0.00	0.00	0.00
66	0.00	0.00	0.00	0.00
67	0.00	0.00	0.00	0.00
68	0.00	0.00	0.00	0.00
69	0.00	0.00	0.00	0.00
70	0.00	0.00	0.00	0.00
71	0.00	0.00	0.00	0.00
72	0.00	0.00	0.00	0.00
73	0.00	0.00	0.00	0.00
74	0.00	0.00	0.00	0.00
75	0.00	0.00	0.00	0.00
TOTAL	**$7,981**	**$5,084**	**$3,831**	**$2,903**

Table 41: Summary of results when the discount rate is varied in the BRCA1 ovarian model

DISCOUNT RATE	NET SAVING	NET COST
No discount	$5028	$5012
Discount 3%	$2687	$3550
Discount 5%	$1795	$3055
Discount 7%	$1232	$2724

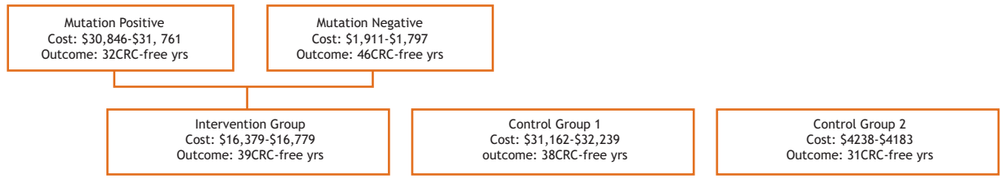
Figure 3: Cost-effectiveness of genetic testing for FAP



Thus genetic testing for FAP in the intervention group:

- Provide net savings of $13,390 per person, though effectiveness was unchanged to Control Group 1; or
- Incurred net costs of $9,042 per person for a gain of 40 CRC-free years, which is $226 for each year that CRC is delayed compared to Control Group 2.

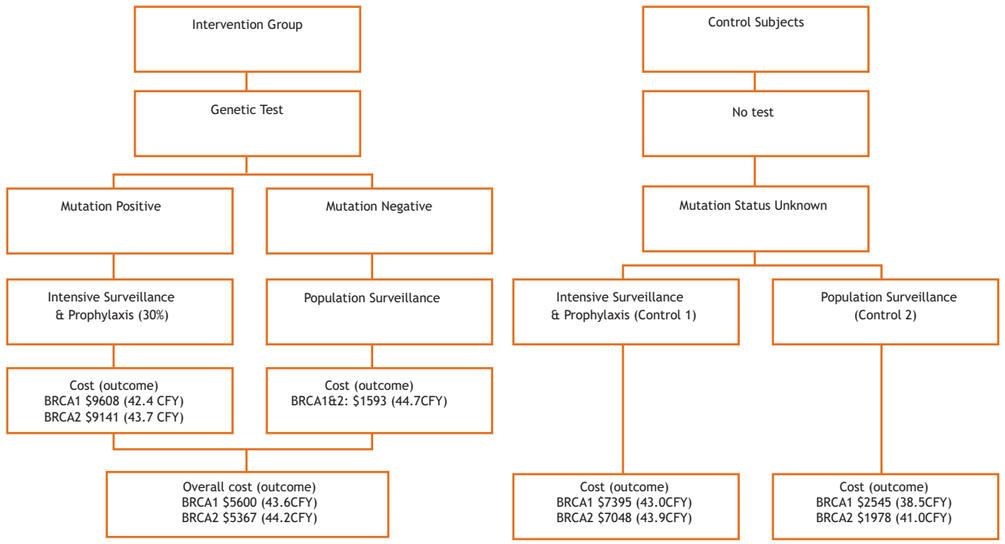
Figure 4: Cost-effectiveness of genetic testing for HNPCC (males-females)



Thus genetic testing for HNPC in the intervention group:

- Provide net savings of $14,783-$15,460 per male and female, and 1 CRCfree-year compared to Control Group 1; or
- Incurred net costs of $12,141-$12,596 per male and female for a gain of 8 CRC-free years, which is $1,518-1,575 for each year that CRC is delayed compared to Control Group 2.

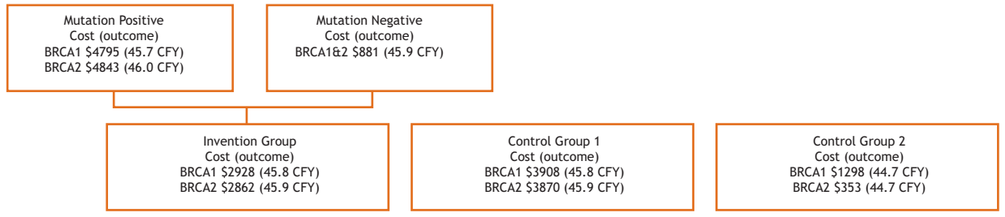
Figure 5: Cost-effectiveness of genetic testing for familial breast cancer (BRCA1/2)



For each woman that undertook genetic testing for breast cancer:

- Compared to Control Group 1, BRCA 1 intervention provided total savings of $1795 and delayed the onset of breast cancer by 6 months; BRCA2 intervention provided total net savings of $1681 and the cancer onset was de;ay by 3 months;
- Compared to Control Group 2, BRCA 1 intervention incurred a $3055 total net cost but delayed the onset of breast cancer by 5.1 years ($601 per cancer free year gained); BRCA2 intervention incurred $3389 net cost for gain of 3.2 cancer-free years, ($1070 per cancer-free year gained).

Figure 6: Cost-effectiveness of genetic testing for familial ovarian cancer (BRCA1/2)



Thus each woman that undertook genetic testing for ovarian cancer:

- Compared to Control Group 1, provided total net savings of $980-$1008 for BRCA 1 and 2 intervention with no change in effectiveness;
- Compared to Control Group 2, BRCA1 intervention incurred a $1630 total net cost but delayed the onset of ovarian cancer by 3.5 years ($477 per cancer -free years gained); BRCA2 intervention incurred $2509 total net cost for a gain of 1.2 cancer-free years, ($2159 per cancer-free year gained).

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