

ERRATUM

A.A.S. 1, 319-343 (2007)

APPLICATION OF A POLYGENIC MODEL OF BREAST AND OVARIAN CANCER TO CRITICAL ILLNESS INSURANCE

A typographical error in Antoniou *et al.* (2002) was carried forward into Macdonald & McIvor (2007), in which paper it affected the numerical results, though not the overall conclusions. The error was in the displayed equation on page 77 of Antoniou *et al.* (2002); the term σ_p appeared in the numerator instead of in the denominator. Thus, equation (6) in Macdonald & McIvor (2007) (using their notation) should read:

$$R \approx \frac{P}{\sqrt{n/2}} \sigma_R. \quad (1)$$

As a result, the rates of onset of breast cancer given a value P of the polygene (equation (5) in Macdonald & McIvor (2007)) contain a term e^R in which R is understated by a factor $\sigma_r^2 = 1.291$. The range of breast cancer risk conferred by the polygene is therefore greater than was shown in Macdonald & McIvor (2007). It is evident that the corrected results shown here do not contradict their conclusions, in fact they lend them greater emphasis.

The results affected are those shown in Tables 3, 5, 6, 7 and 8, and in Figures 3 and 4 of Macdonald & McIvor (2007), corrected versions of which follow.

We understand that an erratum correcting the error in Antoniou *et al.* (2002) will appear in *British Journal of Cancer*.

REFERENCES

- ANTONIOU, A.C., PHAROAH, P.D.P., McMULLAN, G., DAY, N.E., STRATTON, M.R., PETO, J., PONDER, B.J. & EASTON, D.F. (2002). A comprehensive model for familial breast cancer incorporating BRCA1, BRCA2 and other genes. *British Journal of Cancer*, **86**, 76-83.
- MACDONALD, A.S. & MCIVOR, K.R. (2006). Application of a polygenic model of breast and ovarian cancer to critical illness insurance. *Annals of Actuarial Science*, **1**, 319-343.

Table 3. Level net premium for women, depending on polygenotype, as a percentage of the level net premium for a woman free of BRCA1/2 mutations and with the mean polygene $P = 0$

Major genotype	Polygenotype	Age 20					Age 30					Age 40					Age 50		
		10 years %	20 years %	30 years %	40 years %	50 years %	10 years %	20 years %	30 years %	40 years %	50 years %	10 years %	20 years %	30 years %	40 years %	50 years %	10 years %	20 years %	
BRCA0	-3	94.0	86.0	82.4	84.0	81.6	79.9	82.5	78.6	82.4	85.3	85.3	82.4	85.3	85.3	82.4	85.3	85.3	85.3
	-2	94.5	87.2	83.8	85.3	83.1	81.5	84.0	80.4	83.9	86.5	86.5	83.9	86.5	86.5	83.9	86.5	86.5	86.5
	-1	96.0	90.5	88.0	89.1	87.5	86.3	88.1	85.4	88.0	90.0	90.0	88.0	90.0	90.0	88.0	90.0	90.0	90.0
	0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	+1	111.4	127.4	134.0	130.6	136.0	139.0	133.6	141.6	134.2	128.6	128.6	134.2	128.6	128.6	134.2	128.6	128.6	128.6
	+2	144.6	205.3	228.4	213.3	238.7	248.7	226.5	260.7	231.0	210.5	210.5	231.0	210.5	210.5	231.0	210.5	210.5	210.5
	+3	239.2	423.7	475.2	414.6	531.3	546.6	467.1	597.8	444.3	444.3	597.8	444.3	444.3	597.8	444.3	444.3	444.3	
BRCA1	-3	94.0	102.4	182.4	167.7	106.7	201.2	178.7	263.6	205.1	154.9	154.9	205.1	154.9	154.9	205.1	154.9	154.9	154.9
	-2	94.5	126.2	203.6	182.4	143.0	227.4	196.0	285.3	218.5	160.9	160.9	218.5	160.9	160.9	218.5	160.9	160.9	160.9
	-1	96.0	193.9	263.4	223.9	246.9	302.0	245.6	347.2	256.8	177.9	177.9	256.8	177.9	177.9	256.8	177.9	177.9	177.9
	0	100.0	383.3	425.6	336.1	542.5	511.7	386.2	523.8	367.8	226.7	226.7	367.8	226.7	226.7	367.8	226.7	226.7	226.7
	+1	111.4	887.4	823.8	609.1	1,372.0	1,080.2	774.2	1,020.8	691.5	366.1	366.1	691.5	366.1	366.1	691.5	366.1	366.1	366.1
	+2	144.6	2,057.4	1,575.5	1,112.2	3,605.9	2,490.6	1,760.2	2,376.6	1,642.8	762.6	762.6	1,642.8	762.6	762.6	1,642.8	762.6	762.6	762.6
	+3	239.2	3,944.7	2,464.5	1,705.7	9,068.7	5,610.6	3,958.7	5,908.8	4,271.7	1,875.7	1,875.7	4,271.7	1,875.7	1,875.7	4,271.7	1,875.7	1,875.7	
BRCA2	-3	94.0	99.4	95.2	107.5	102.2	95.4	109.1	91.2	111.1	129.2	129.2	111.1	129.2	129.2	111.1	129.2	129.2	129.2
	-2	94.5	116.9	113.2	123.4	128.8	117.1	127.2	110.3	127.4	143.9	143.9	127.4	143.9	143.9	127.4	143.9	143.9	143.9
	-1	96.0	166.9	164.1	167.6	205.1	179.0	178.3	164.9	173.8	185.8	185.8	173.8	185.8	185.8	173.8	185.8	185.8	185.8
	0	100.0	307.7	303.1	284.3	422.7	353.1	318.7	320.6	304.3	306.0	306.0	304.3	306.0	306.0	304.3	306.0	306.0	306.0
	+1	111.4	690.0	652.1	551.0	1,036.9	824.7	677.7	760.0	658.7	647.9	647.9	658.7	647.9	647.9	658.7	647.9	647.9	647.9
	+2	144.6	1,628.6	1,347.1	1,000.3	2,718.3	1,988.6	1,480.4	1,964.3	1,553.9	1,609.5	1,609.5	1,553.9	1,609.5	1,609.5	1,553.9	1,609.5	1,609.5	1,609.5
	+3	239.2	3,373.8	2,230.8	1,547.9	6,975.4	4,482.6	3,170.4	5,101.4	3,753.5	4,293.2	4,293.2	3,753.5	4,293.2	4,293.2	3,753.5	4,293.2	4,293.2	

Table 5. Numbers of daughters with no family history and given major genotype, in each state in the CI model (see Figure 2), at selected ages

Family	Genotype		Daughter's ages						
	Applicant	State	0	10	20	30	40	50	60
BRCA0	BRCA0	Healthy	15,944,331	15,888,102	15,828,825	15,686,533	15,265,549	14,140,830	12,290,717
BRCA1	BRCA0	Healthy	16,091	16,018	15,961	15,815	15,150	13,463	11,677
BRCA1	BRCA1	Healthy	16,045	15,859	15,799	15,655	12,815	8,857	6,817
BRCA2	BRCA0	Healthy	21,808	21,697	21,599	21,422	20,642	18,596	16,188
BRCA2	BRCA2	Healthy	21,559	21,380	21,273	21,046	18,014	13,879	9,850
BRCA0	BRCA0	BC	0	1,725	2,241	16,279	139,815	462,864	900,578
BRCA1	BRCA0	BC	0	25	25	43	122	323	742
BRCA1	BRCA1	BC	0	112	113	133	1,837	2,708	3,350
BRCA2	BRCA0	BC	0	33	34	51	161	440	989
BRCA2	BRCA2	BC	0	118	118	136	2,055	3,544	5,934
BRCA0	BRCA0	OC	0	262	1,287	4,195	11,900	37,058	86,850
BRCA1	BRCA0	OC	0	1	3	9	15	37	98
BRCA1	BRCA1	OC	0	23	24	25	34	779	1,396
BRCA2	BRCA0	OC	0	2	3	7	14	41	95
BRCA2	BRCA2	OC	0	3	7	12	44	72	586
BRCA0	BRCA0	Other	0	10,947	41,283	125,342	351,838	929,402	2,094,960
BRCA1	BRCA0	Other	0	17	52	136	367	926	2,065
BRCA1	BRCA1	Other	0	10	48	136	337	732	1,387
BRCA2	BRCA0	Other	0	11	57	162	496	1,238	2,800
BRCA2	BRCA2	Other	0	11	67	208	511	1,137	2,094
BRCA0	BRCA0	Dead	0	43,295	70,695	111,829	162,694	252,925	449,974
BRCA1	BRCA0	Dead	0	30	50	87	133	224	391
BRCA1	BRCA1	Dead	0	41	61	89	162	220	346
BRCA2	BRCA0	Dead	0	65	115	162	237	358	601
BRCA2	BRCA2	Dead	0	47	94	153	210	300	468

Table 6. Numbers of daughters with a family history and given major genotype, in each state in the CI model (see Figure 2), at selected ages

Genotype			Daughters' ages						
Family	Applicant	State	0	10	20	30	40	50	60
BRCA0	BRCA0	Healthy	0	0	0	80	5,936	48,761	35,837
BRCA1	BRCA0	Healthy	0	0	0	1	234	799	666
BRCA1	BRCA1	Healthy	0	0	0	6	148	427	288
BRCA2	BRCA0	Healthy	0	0	0	4	175	763	633
BRCA2	BRCA2	Healthy	0	0	0	3	134	497	244
BRCA0	BRCA0	BC	0	0	0	62	6,180	65,908	74,279
BRCA1	BRCA0	BC	0	0	0	0	58	233	284
BRCA1	BRCA1	BC	0	0	0	1	687	1,938	2,004
BRCA2	BRCA0	BC	0	0	0	0	70	287	357
BRCA2	BRCA2	BC	0	0	0	1	573	2,049	2,237
BRCA0	BRCA0	OC	0	0	0	11	278	2,869	3,342
BRCA1	BRCA0	OC	0	0	0	0	4	17	21
BRCA1	BRCA1	OC	0	0	0	0	13	322	364
BRCA2	BRCA0	OC	0	0	0	0	3	20	22
BRCA2	BRCA2	OC	0	0	0	0	9	37	63
BRCA0	BRCA0	Other	0	0	0	0	99	2,947	6,411
BRCA1	BRCA0	Other	0	0	0	0	5	55	124
BRCA1	BRCA1	Other	0	0	0	0	8	47	70
BRCA2	BRCA0	Other	0	0	0	0	5	49	101
BRCA2	BRCA2	Other	0	0	0	0	5	28	57
BRCA0	BRCA0	Dead	0	0	0	0	42	767	1,383
BRCA1	BRCA0	Dead	0	0	0	0	3	14	23
BRCA1	BRCA1	Dead	0	0	0	0	4	15	23
BRCA2	BRCA0	Dead	0	0	0	0	5	16	22
BRCA2	BRCA2	Dead	0	0	0	0	4	16	26

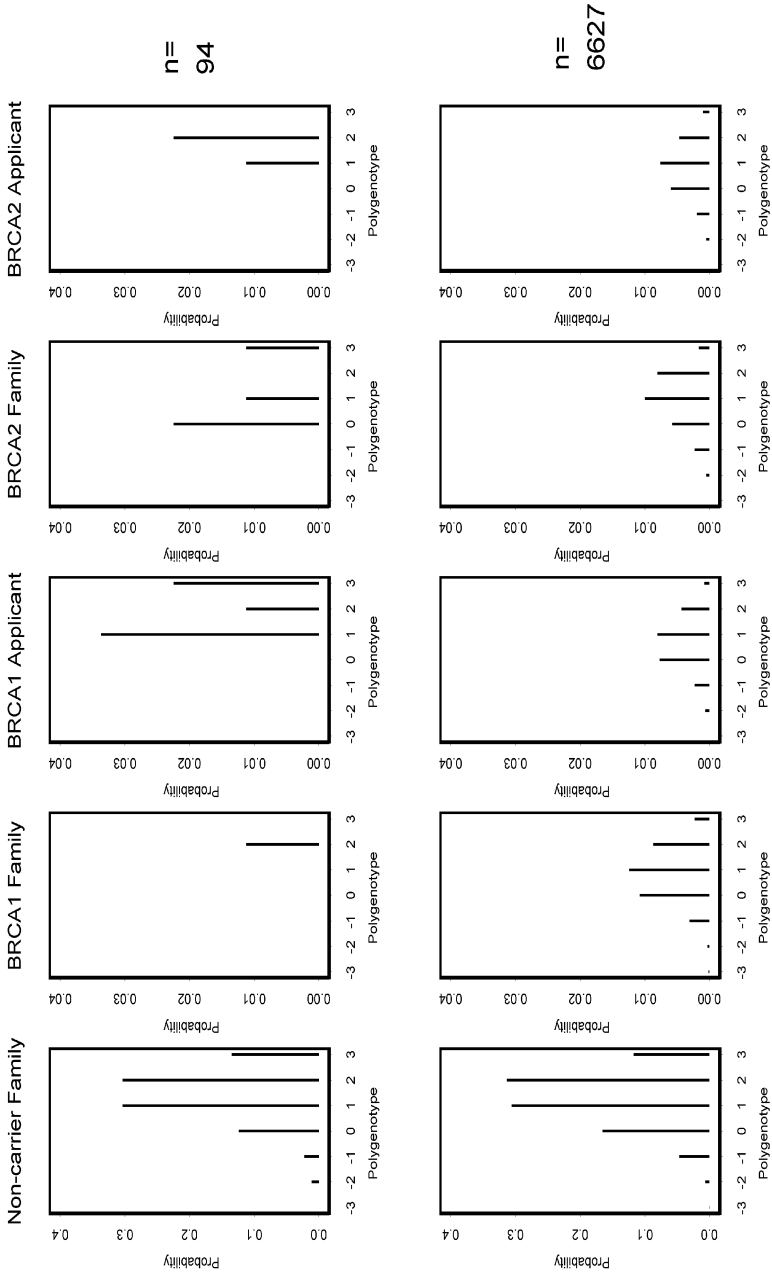


Figure 3. Distribution of polygenotypes by major genotype among healthy daughters aged 30 and 40, with a family history; based on 10,000,000 simulated families; the total number of individuals is shown on the right — note different vertical scale for non-carrier families

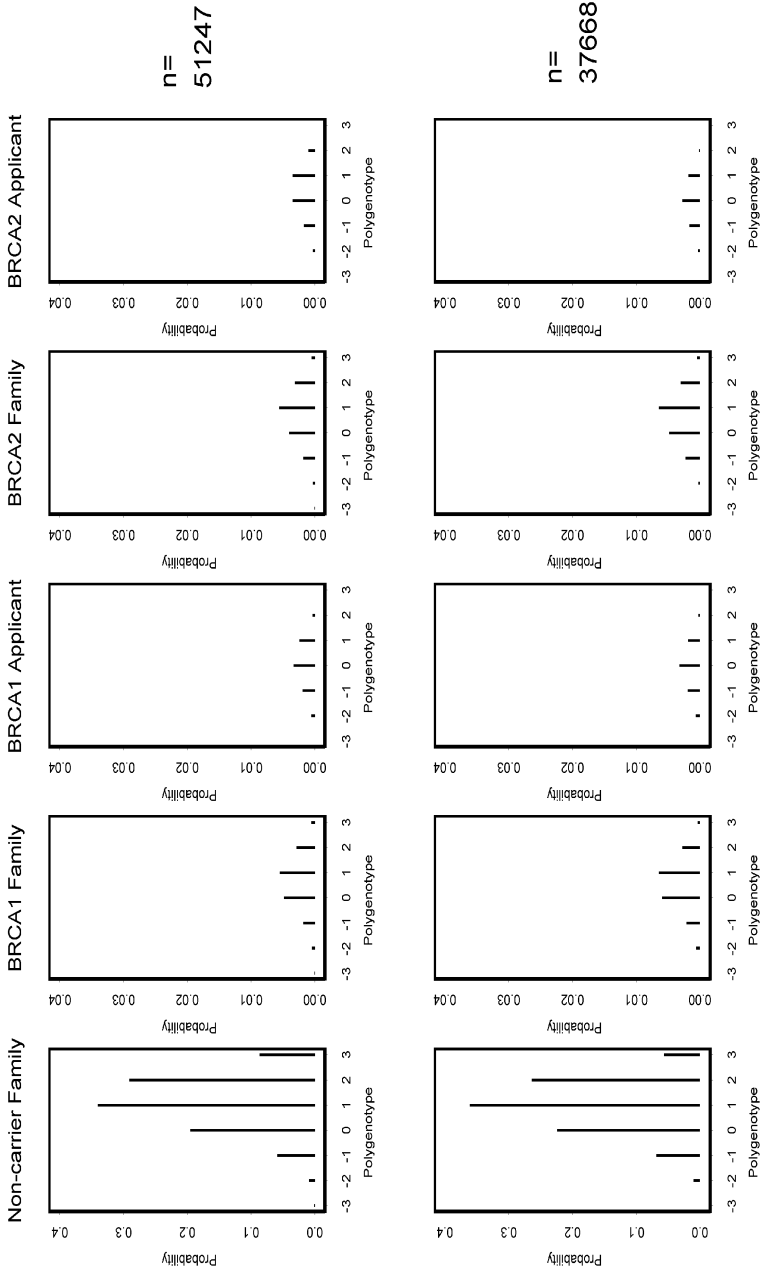


Figure 4. Distribution of polygenotypes by major genotype among healthy daughters aged 50 and 60, with a family history; based on 10,000,000 simulated families; the total number of individuals is shown on the right — note different vertical scale for non-carrier families

Table 7. Level net premium for females with a family history of BC or OC, as a percentage of the level net premium for a woman free of BRCA1/2 mutations and with polygenotype $P = 0$; the P + MG model uses both major gene and polygene probabilities in the weighted average EPVs, while the MG model uses only the major gene probabilities

Definition of family history	Genetic model	Age 30			Age 40		Age 50
		10 years %	20 years %	30 years %	10 years %	20 years %	10 years %
2 affected FDRs	P + MG	444.0	341.0	274.7	244.2	207.4	170.6
	MG	137.5	132.0	122.7	112.9	108.9	102.8
3 affected FDRs	P + MG	100.0	100.0	100.0	410.7	314.1	215.6
	MG	100.0	100.0	100.0	148.2	134.3	106.8
4 affected FDRs	P + MG	100.0	100.0	100.0	934.3	637.1	260.8
	MG	100.0	100.0	100.0	207.9	173.2	112.1

Table 8. Level net premium for females with a family history of BC or OC, as a percentage of the standard premium; the polygenic model is compared with the major-gene-only model of Gui *et al.* (2006); the latter assumed that onset rates of BC and OC among BRCA1/2 mutation carriers were either 100% or 50% of those estimated, as a rough allowance for ascertainment bias

Definition of family history	Genetic model	Age 30			Age 40		Age 50
		10 years %	20 years %	30 years %	10 years %	20 years %	10 years %
2 affected FDRs	P + MG	444.0	341.0	274.7	244.2	207.4	170.6
	MG	137.5	132.0	122.7	112.9	108.9	102.8
Gui <i>et al.</i> (2006)	100%	330	251	204	208	174	142
	50%	217	179	156	154	139	120