

New paradigms for *BRCA1/BRCA2* testing in women with ovarian cancer – results of the Genetic Testing in Epithelial Ovarian Cancer (GTEOC) Study

Supplementary Files

Resource - activity	Unit cost (£)	Unit description	Source of data
Existing pathway			
Basic family history check in Oncology	19.28	This activity involves discussing family history with the patient in order to determine whether the patient is potentially eligible for genetic testing and therefore referral to the cancer genetics service	Primary data collection at CUH NHS Foundation Trust
Referred to cancer genetic service (+ve FH)	65.03	Patient is sent a letter with FH form to return to cancer genetics service. FH form is received and checked and includes letter sent for appointment or for ineligibility regarding testing	Primary data collection at CUH NHS Foundation Trust
Eligible for test, offered appointment and attends cancer genetics service	434.47	Patient attends 45 minute appointment with genetic counsellor (70% led) and clinical geneticist (30% led) to provide counselling and offer genetic test	NHS reference costs: financial year 2014-2015
Offered and accepts <i>BRCA1/BRCA2</i> genetic test	850.00	NHS test price at Addenbrooke's Hospital. Test involves sequencing of the entire coding region of genes plus copy number analysis.	UKGTN website
<i>BRCA1/BRCA2</i> negative	81.36	Patient receives result as agreed during appointment either by letter (45%), phone call (45%) or face-to-face appointment (10%)	Primary data collection at CUH NHS Foundation Trust
<i>BRCA1/BRCA2</i> VUS	81.36	Patient receives result as agreed during appointment either by letter (45%), phone call (45%) or face-to-face appointment (10%) – same as <i>BRCA1/BRCA2</i> negative	Primary data collection at CUH NHS Foundation Trust
<i>BRCA1/BRCA2</i> positive	95.09	Patient receives result as agreed during appointment either by letter or phone call (85%) or by face-to-face appointment (15%)	Primary data collection at CUH NHS Foundation Trust
New proposed pathway			
Referred to cancer genetic service	47.28	Patient details collected by genetic counsellor and processes eligibility for genetic testing over the phone via family history	Primary data collection at CUH NHS Foundation Trust
Eligible for test, offered appointment and attends cancer genetics service	144.82	Patient attends 15 minute appointment with genetic counsellor (70% led) and clinical geneticist (30% led) to provide counselling and offer genetic	NHS reference costs: financial year 2014-2015

		test	
Offered and accepts <i>BRCA1/BRCA2</i> genetic test	850.00	NHS test price at Addenbrooke's Hospital. Test involves sequencing of the entire coding region of genes plus copy number analysis.	UKGTN website
<i>BRCA1/BRCA2</i> negative	57.68	Patient receives result by letter	Primary data collection at CUH NHS Foundation Trust
<i>BRCA1/BRCA2</i> VUS	23.19	Patient receives result by letter with 20% of patients also receiving a phone call from genetic counsellor	Primary data collection at CUH NHS Foundation Trust
<i>BRCA1/BRCA2</i> positive	385.82	Patient received result by letter and an appointment is made for patients to attend and discuss results with clinical geneticist	Primary data collection at CUH NHS Foundation Trust

Table S1: Estimated resources, test unit costs and assumptions (2015)

Mutations									
<i>ID</i>	<i>Gene</i>	<i>DNA level</i>	<i>Protein level</i>	<i>Age</i>	<i>Cancer</i>				
					<i>Pathology</i>	<i>Grade</i>	<i>Stage</i>	<i>MS</i>	<i>BOADICEA</i>
100	BRCA1	c.325_325dupGA	Leu1086fs	54	SP	3	4	13	3.2
126	BRCA1	c.2475delC	Asp825fs	75	SP	3	3c	14	1.4
63	BRCA1	c.4868C>G	Ala1623Gly	67	SP	3	3c	20	4.5
185	BRCA1	c.3307_3308insC	Cys1103Serfs*2	40	SP	3	3c	25	46.1
8	BRCA2	c.4154C>G	Ser1385Ter	65	SP	3	3	24	41.6
218	BRCA1	c.3193dupG	Asp1065fs	55	SP	3	3c	25	70.4
134	BRCA1	c.1961delA	Lys654fs	52	SP	3	3c	23	27.3
17	BRCA2	c.517-2A>G		67	SP	3	3	22	13.2
40	BRCA2	c.5247T>G	Tyr1749Ter	65	EC [†]	3	1c	21	7.1
59	BRCA1	c.3756-59delGTCT	Ser1253fs	54	SP	3	3b	21	16.4
14	BRCA1	c.122A>G	His41Arg	52	SP	3	3c	26	2.1
191	BRCA2	c.6275_6276delTT	Leu2092fs	68	SP	3	3c	11	1.4
137	BRCA2	c.4154C>G	Ser1385Ter	66	SP	3	4	11	0.7
90	BRCA1	c.1360_1361delAG	Ser 454Ter	59	SP	3	1b	26	60.2
168	BRCA2	Het del ex14-16		52	SP	3	1c	44	89.1
140	BRCA1	c.2641G>T	Glu881Ter	49	SP	3	3c	21	6.3
214	BRCA1	c.5153-26A>G		53	SP	3	3c	13	5.5
232	BRCA1	c.4524G>A	Trp1508Ter	45	SP	1	1c	13	3.8
VUS									
<i>ID</i>	<i>Gene</i>	<i>DNA level</i>	<i>Protein level</i>	<i>Age</i>	<i>Cancer</i>				
					<i>Pathology</i>	<i>Grade</i>	<i>Stage</i>	<i>MS</i>	<i>BOADICEA</i>
19	BRCA2	c.5278T>G	Ser1760Ala	76	SP	3	3c	14	4.4
31	BRCA2	c.4068G>A	Leu1356Leu	70	SP	3	4	10	0.3
102	BRCA2	c.8072C>T	Ser2691Phe	51	SP	3	3c	15	1.8
101	BRCA2	c.8111C>T	Ser2704Phe	67	SP	3	3c	18	11.8
162	BRCA2	c.6403A>C	Asn2135His	68	SP	3	3b	10	0.9
215	BRCA1	c.1534C>T	Leu512Phe	52	EC	1	1a	13	6.8
54	BRCA2	c.1798T>C	Tyr600His	72	SP	3	3c	11	0.8
	BRCA2	c.1909+8_1909+9delTG at the exon10/intron10 boundary							
	BRCA2	c.7504C>T	Arg2502Cys						
166	BRCA2	c.506A>G	Lys169Arg	72	SP	3	1c	10	0.5
176	BRCA2	c.1460C>A	Ala487Glu	41	SP	3	3c	21	28.4
111	BRCA2	c.8905G>A	Val2969Met	83	SP	3	3c	10	0.1
150	BRCA1	c.1534C>T	Leu512Phe	72	SP	3	3c	10	0.6
20	BRCA2	c.68-7T>A		74	SP	3	3c	10	0.7
1	BRCA1	c.1563A>G	Ala521Ala	55	EC	1	1a	14	4.1
28	BRCA2	c.223G>C	Ala75Pro	70	EC	3	1c	30	4.4
223	BRCA2	c.967G>T	Val323Leu	64	EC	2	1c	10	2.5

Table S2. BRCA1/BRCA2 Mutations and VUS identified in the study

[†]= High grade adenocarcinoma with features in favour of a grade 3 endometrioid adenocarcinoma

	Current patient testing pathway (£)			GTEOC patient testing pathway (£)		
	Budget	Average cost per BRCA positive	Average cost per test offered	Budget	Average cost per BRCA positive	Average cost per test offered
Base case, £850, 50%	142,702	11,892	2,265	253,617	14,919	1,093
Cost of test						
£650	130,102	10,842	2,065	207,217	12,189	893
£499	120,589	10,049	1,914	172,185	10,129	742
£350	111,202	9,267	1,765	137,617	8,095	593
£190	101,122	8,427	1,605	100,497	5,912	433
Percentage referral						
0%	105,772	8,814	1,679	253,617	14,919	1,093
25%	124,454	10,371	1,975	253,617	14,853	1,093
75%	160,950	13,412	2,554	253,617	14,853	1,093
100%	179,197	14,933	2,844	253,617	14,853	1,093
GTEOC age cut-off <70						
£850, 50%	142,702	11,892	2,265	148,429	9,895	1,091
Scenario						
£650, 50%, <70 age	130,102	10,842	2,065	121,229	8,082	891

Table S3: Base case analysis results plus sensitivity analysis of patient testing pathway budget, average patient pathway cost of BRCA positive, and average patient pathway cost per genetic test offered for the 232 women eligible for the GTEOC study. In the GTEOC testing pathway all the patients were given the genetic test. The budget is the overall cost of all patients receiving eligibility checks, counselling and genetic testing plus post-test work-up i.e., the average cost per test offered is the total budget divided by the number of tests offered which is 232. For the current testing pathway, we calculated the Manchester score for all patients and based on this, 63 patients would have been eligible for genetic testing and offered the test. For these patients the full work-up cost was calculated from eligibility check to test and post-test work-up. For the base case we then assumed that 50% of the remaining 169 patients would have still been referred for genetic test counselling and so would incur those costs. We calculated for these 84 patients the cost of eligibility and genetic counselling but did not include test costs as these patients did not meet test criteria. For

the remaining 85 patients we only included the cost of checking eligibility for the referral. The sum of these three sets of costs for the 232 patients equal the budget and the average cost per test offered is that budget divided by the number of tests offered (i.e., total budget divided by 63).

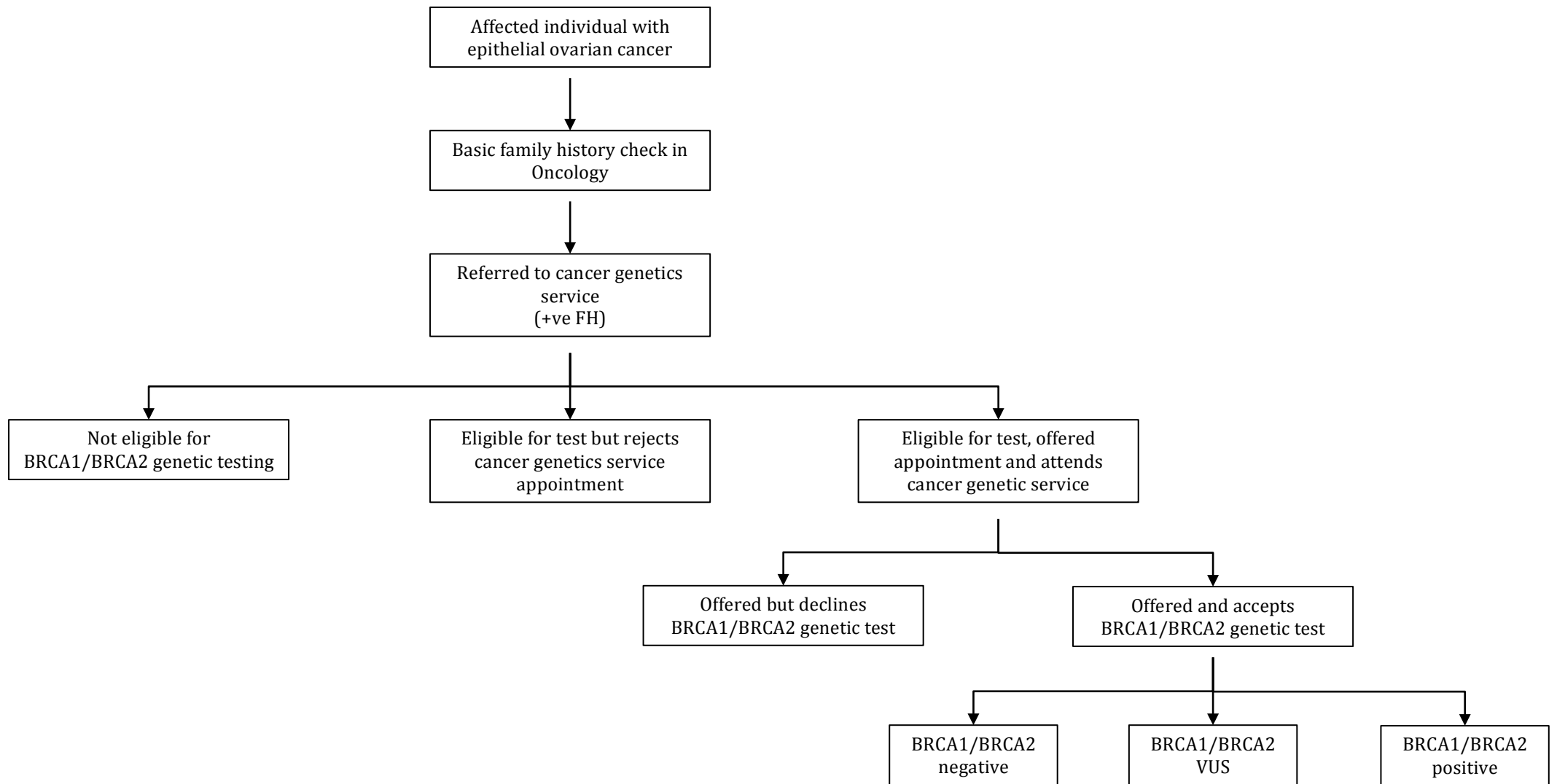


Figure S1: Patient pathway for the current provision of *BRCA1/BRCA2* testing in epithelial ovarian cancer patients

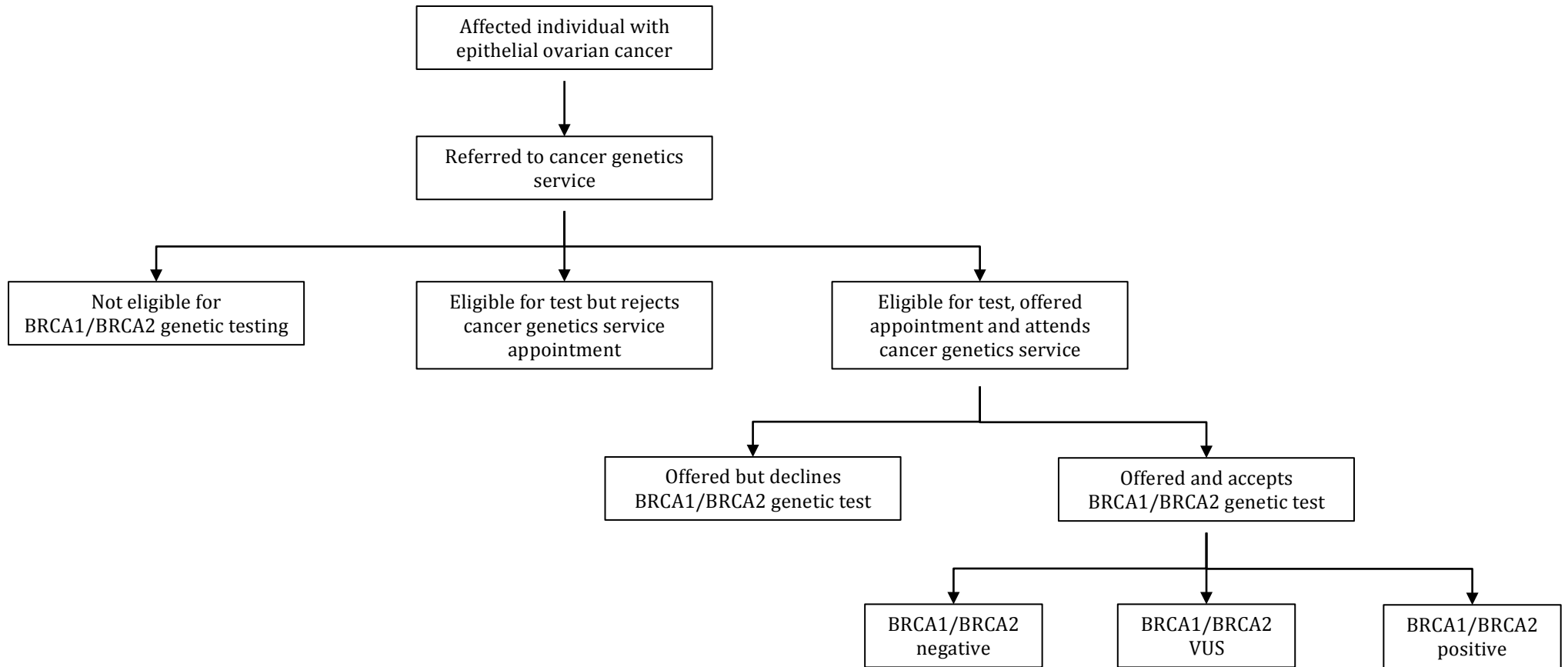


Figure S2: Proposed patient pathway for the provision of *BRCA1/BRCA2* testing in epithelial ovarian cancer patients from the GTEOC study.