ORIGINAL ARTICLE

Cluster-randomised non-inferiority trial comparing DVD-assisted and traditional genetic counselling in systematic population testing for BRCA1/2 mutations

Ranjit Manchanda,[1,2,3] Matthew Burnell,[1] Kelly Loggenberg,[1] Rakshit Desai,[1] Jane Wardle,[4] Saskia C Sanderson,[5] Sue Gessler,[1] Lucy Side,[1] Nyala Balogun,[1] Ajith Kumar,[6] Huw Dorkins,[7] Yvonne Wallis,[8] Cyril Chapman,[9] Ian Tomlinson,[10] Rohan Taylor,[11] Chris Jacobs,[12] Rosa Legood,[13] Maria Raikou,[14] Alistair McGuire,[14] Uziel Beller,[15] Usha Menon,[1] Ian Jacobs[1,16]

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For numbered affiliations see end of article.

Correspondence to
Dr Ranjit Manchanda, Consultant Gynaecological Oncologist, Clinical Senior Lecturer, Barts Cancer Institute, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, UK; r.manchanda@ucl.ac.uk

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ABSTRACT

Background Newer approaches to genetic counselling are required for population-based testing. We compare traditional face-to-face genetic counselling with a DVD-assisted approach for population-based BRCA1/2 testing.

Methods A cluster-randomised non-inferiority trial in the London Ashkenazi Jewish population.

Inclusion criteria Ashkenazi Jewish men/women >18 years; exclusion criteria: (a) known BRCA1/2 mutation, (b) previous BRCA1/2 testing and (c) first-degree relative of BRCA1/2 carrier. Ashkenazi Jewish men/women underwent pre-test genetic counselling prior to BRCA1/2 testing in the Genetic Cancer Prediction through Population Screening trial (ISRCTN73338115). Genetic counselling clinics (clusters) were randomised to traditional counselling (TC) and DVD-based counselling (DVD-C) approaches. DVD-C involved a DVD presentation followed by shorter face-to-face genetic counselling. Outcome measures included genetic testing uptake, cancer risk perception, increase in knowledge, counselling time and satisfaction (Genetic Counselling Satisfaction Scale). Random-effects models adjusted for covariates compared outcomes between TC and DVD-C groups. One-sided 97.5% CI was used to determine non-inferiority. Secondary outcomes: relevance, satisfaction, adequacy, emotional impact and improved understanding with the DVD; cost-minimisation analysis for TC and DVD-C approaches.

Results 936 individuals (clusters=256, mean-size=3.6) were randomised to TC (n=527, clusters=134) and DVD-C (n=409, clusters=122) approaches. Groups were similar at baseline, mean age=53.9 (SD=15) years, women=66.8%, men=33.2%. DVD-C was non-inferior to TC for increase in knowledge (d=−0.07; lower 97.5% CI=−0.41), counselling satisfaction (d=−0.38, 97.5% CI=1.2) and risk perception (d=0.08; upper 97.5% CI=3.1). Group differences and CIs did not cross non-inferiority margins. DVD-C was equivalent to TC for uptake of genetic testing (d=−3%; lower/upper 97.5% CI −7.9%/1.7%) and superior for counselling time (20.4 (CI 18.7 to 22.2) min reduction (p<0.005)). 98% people found the DVD length and information satisfactory. 85–89% felt it improved their understanding of risks/benefits/implications/purpose of genetic testing. 95% would recommend it to others. The cost of genetic counselling for DVD-C=£7787 and TC=£17 307. DVD-C resulted in cost savings=£9520 (£14/volunteer).

Conclusions DVD-C is an effective, acceptable, non-inferior, time-saving and cost-efficient alternative to TC.

Trial registration number ISRCTN 73338115.

INTRODUCTION

Genetic testing for high-penetrance BRCA1/2 mutations is usually available to individuals from high-risk families fulfilling stringent family history (FH) criteria following genetic counselling in specialised cancer genetic clinics. Recent studies show that a significant proportion of BRCA1/2 carriers lack a strong FH of cancer but can be identified through population-based approaches, not standard clinical care.[1–3] The Genetic Cancer Prediction through Population Screening (GCaPPS) randomised controlled trial (RCT) compared population screening (PS) with FH-based testing for BRCA1/2 mutations in Ashkenazi Jewish (AJ) individuals (ISRCTN73338115). We found that PS for BRCA1/2 mutations in AJ population does not harm quality of life/psychological well-being[3] and is extremely cost-effective, leading to 33 days gain in life expectancy and incremental cost-effectiveness ratio (ICER)='-£2079/quality-adjusted life-year (QALY)' well below the £20 000/QALY National Institute for Health and Care Excellence (NICE) threshold.[4]

Pre-test genetic counselling is a fundamental element of international guidelines[5] for informed decision-making prior to genetic testing. A range of decision aids varying from pamphlets, booklets, computer-based programmes, audiotapes, to web-based platforms have been used as adjuncts to counselling to facilitate decision-making in high-risk populations. Decision aids reduce decisional conflict and lead to an increase in knowledge, accuracy of perceived benefits/harms, participation in decision-making process and ability to make informed value-based choices.[6 7] In addition, group-based and telephone counselling approaches have been found to be beneficial and non-inferior in high-risk women.[8–12]

For large-scale, population-based genetic testing to become feasible and practical, it is necessary to

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move away from the 'traditional face-to-face genetic counselling' (TC)[13 14] approach, which is cost–intensive, requiring significant health professional time. At present, there is no established model for providing pre-test genetic counselling for genetic testing on a population basis.[15] We hypothesised that using a DVD (audio-visual tool) could significantly reduce the duration and increase cost-efficiency compared with traditional face-to-face counselling, while being non-inferior in terms of knowledge gained, counselling satisfaction, risk perception and equivalent in uptake of genetic testing. We report on outcomes from the only RCT that we are aware of comparing TC and DVD-based genetic counselling (DVD-C) approaches in an unselected population-based setting, undertaken during recruitment to the GCaPPS study.

METHODOLOGY

Cluster-randomised non-inferiority trial set within GCaPPS (ISRCTN73338115). Inclusion criteria: (a) individuals >18 years, (b) AJ ethnicity; exclusion criteria: (a) known BRCA1/2 mutation, (b) previous BRCA1/2 testing and (c) first-degree relative of a BRCA1/2 carrier. All volunteers received non-directive pre-test genetic counselling regarding genetic testing for AJ BRCA1/2 founder mutations. Genetic counselling was undertaken by a qualified genetic counsellor with clinical/counselling supervision provided by a regional genetics centre and a clinical fellow experienced in cancer genetics risk assessment and management. It was structured to meet the goals of genetic counselling,[16–18] covering interpretation of FH, knowledge about risk, inheritance, management options, advantages, disadvantages and psychosocial implications to promote informed choice and adaptation.

Recruitment clinics (clusters) were randomised to TC and DVD-C approaches. Randomisation of clinics was essential for logistic, organisational and pragmatic reasons. There was an initial DVD development process from November 2008 to January 2009. This study reports on genetic counselling outcomes of clinics randomised from February 2009 until end of recruitment (July 2010) using the final DVD version. Randomisation was undertaken by a computer-generated random number algorithm. Participants were blinded to the type of genetic counselling when making an appointment. Appointments were made and randomisation implemented by the study administrator independent of the counsellors. DVD-C approach involved a DVD presentation (in the recruitment clinic) to small groups of volunteers (2–5) at a time. DVD-C volunteers subsequently saw a genetic counsellor for an individual genetic counselling session (post-DVD) at the same appointment. Participants in the TC group underwent face-to-face genetic counselling only. FH and baseline questionnaires were collected prior to the DVD presentation (DVD-C) or prior to seeing the genetic counsellor (TC group). Time taken for genetic counselling was documented. Postcounselling questionnaires were filled and collected after the genetic counselling session. Individuals deciding to undergo BRCA1/2 genetic testing were consented after genetic counselling.

Outcomes included uptake of genetic testing, change in cancer risk perception, increase in knowledge, counselling time and counselling satisfaction.

Secondary outcomes included relevance, satisfaction, adequacy, emotional impact and improvement of understanding with the DVD, and cost-minimisation analysis.

A baseline questionnaire assessed FH and socio-demographic characteristics. Knowledge was assessed by a specially developed 10-item (true=1/false=0) questionnaire (see online supplementary table S1) at baseline and postgenetic counselling. Satisfaction with genetic counselling was assessed postcounselling by the validated six-item Genetic Counselling Satisfaction

Table 1 Comparison of traditional face-to-face (TC) and DVD-based counselling (DVD-C) groups

	TC	DVD-C
n	527	409
Number of clusters	134	122
Mean cluster size (SD)	3.8 (2)	3.4 (2.1)
Age in years (SD)	53.9 (15.1)	53.9 (14.9)
Marital status		
Single	43/520 (8.3%)	46/398 (11.6%)
Married	400/520 (76.9%)	289/398 (72.6%)
Cohabiting (living with partner)	15/520 (2.9%)	18/398 (4.5%)
Divorced/separated	30/520 (5.8%)	27/398 (6.8%)
Widowed	32/520 (6.2%)	18/398 (4.5%)
Children		
Have children	79.7%	83%
Number of children (SD)	2.3 (1.29)	2.22 (1.27)
Gender		
Men	169 (32.1%)	142 (34.7%)
Women	358 (67.9%)	267 (65.3%)
Education		
No formal qualification	40/500 (8%)	25/389 (6.4%)
GCSE, O-level, CSE	101/500 (20.2%)	71/389 (18.3%)
NVQ-1, NVQ-2	5/500 (1%)	8/389 (2.1%)
A-level, NVQ-3	52/500 (10.4%)	44/389 (11.3%)
NVQ-4	7/500 (1.4%)	9/389 (2.3%)
Bachelor's	196/500 (39.2%)	136/389 (35%)
Master's	82/500 (16.4%)	75/389 (19.3%)
PhD	17 (3.4%)	21 (5.4%)
Income (£)		
<10K	21/456 (4.6%)	21/357 (5.9%)
10K–19.9K	32/456 (7%)	33/357 (9.2%)
20K–29.9K	46/456 (10.1%)	36/357 (10.1%)
30K–39.9K	50/456 (11%)	49/357 (13.7%)
40K–49.9K	59/456 (12.9%)	33/357 (9.2%)
≥50K	248/456 (54.4%)	185/357 (51.8%)
FH		
FH of cancer	64 (12.8%)	49 (12.9%)
Anxiety and depression		
HADS-anxiety (SD)	6.1 (3.5)	6.4 (3.7)
HADS-depression (SD)	2.9 (2.5)	3 (2.6)
HADS-total (SD)	9 (5.2)	9.4 (5.6)
Genetic testing uptake		
Consented to genetic testing	470 (89.2%)	357 (87.3%)
Declined genetic testing	57 (10.8%)	52 (12.7%)
Knowledge score		
Knowledge score (BL)	7.52 (3.16)	7.71 (3.02)
Knowledge score (PC)	9.41 (1.28)	9.35 (1.28)
Counselling satisfaction		
GCSS score	25.59 (4.45)	25.03 (5.27)
Counselling time		
Mean time in minutes (SD)	46 (49.7)	21.3 (8.4)
Perceived risk		
Baseline risk (SD)	50.6 (50.7)	49.6 (22.1)
PC risk (SD)	47.4 (23.4)	48.9 (22.7)

BL, baseline; FH, family history; GCSS, Genetic Counselling Satisfaction Scale; HADS, Hospital Anxiety and Depression Scale; NVQ, National Vocational Qualification; PC, postcounselling.

Scale (GCSS): five-point Likert scale (strongly disagree=1, strongly agree=5) for each item, maximum score=30.[19 20] Cancer risk perception was measured on a previously used 0–100 scale at baseline and postcounselling.[21] A DVD evaluation questionnaire (see online supplementary table S2) assessed DVD impact (secondary outcomes) from May 2009 till July 2010. This was completed by DVD-C volunteers after watching the DVD and before meeting the genetic counsellor. Development of the knowledge questionnaire and DVD is described in online supplementary tables S3 and S4, respectively.

Participants were recruited from the North London Jewish community. Recruitment was based on self-referral. Study flyers were made available through community charities, a high-street pharmacy (Boots) and website (http://www.gcapps.org). Eligible individuals who registered with the study team were sent a detailed trial information booklet. Genetic counselling was undertaken at high-street/community-based centres outside a hospital setting.

Statistical analysis

Statistical analyses were undertaken in 'Stata-13.0' (Stata, Texas, USA).

Baseline characteristics were calculated using descriptive statistics. χ^2 tests compared categorical variables and t test (parametric) and Mann–Whitney (non-parametric) tests compared continuous outcome variables between two independent samples.

Random-effects models that included a random intercept term for each cluster (clinic) compared outcomes between TC and DVD-C groups, and were adjusted for potential confounders: FH (high/low risk), age, gender, parity, income, education and marital status. The total knowledge score was calculated as a sum of true=1 and false=0 for all 10 questions. Sensitivity analysis for knowledge scores was undertaken by (a) correcting final score to reflect proportion of valid questions answered and (b) assigning a score='0' for missing answers. As the GCSS scores were highly skewed with a significant peak at 30, the transformation |GCSS score − 30| was considered. The resulting data distribution was approximated by a zero-inflated negative binomial regression model, adjusted with the same confounders. Per-protocol and intention-to-treat analysis were evaluated for outcomes of DVD-C and TC groups. A sensitivity analysis with multivariate imputation using chained equations (MICE)[22] for missing data was undertaken for all outcomes. MICE iteratively simulates from suitable univariate imputation models that are fully conditional on all selected predictor variables until convergence is reached. Fifty fully imputed data sets were created to generate valid estimates and SEs, and produce correct statistical inference.

Non-inferiority analysis is needed to determine whether DVD-C is not worse than the current standard (TC) by an acceptable amount. A one-sided 97.5% CI was used to determine non-inferiority for cancer risk perception, increase in knowledge and counselling satisfaction. Non-inferiority was established when the 97.5% CI did not cross the non-inferiority margin. A two-sided 95% CI was used to test equivalency of genetic testing uptake as the aim of genetic counselling is informed decision-making rather than to increase/decrease testing. A superiority analysis was undertaken for counselling time.

The non-inferiority margins were based on clinically meaningful changes where available or set at no more than 0.5 SD worse than that for TC from prior studies[19 23] or data collected during initial counselling undertaken from November 2008 to January 2009. The non-inferiority margin for knowledge gain=1 unit (minimum possible change on the scale, SD=3);

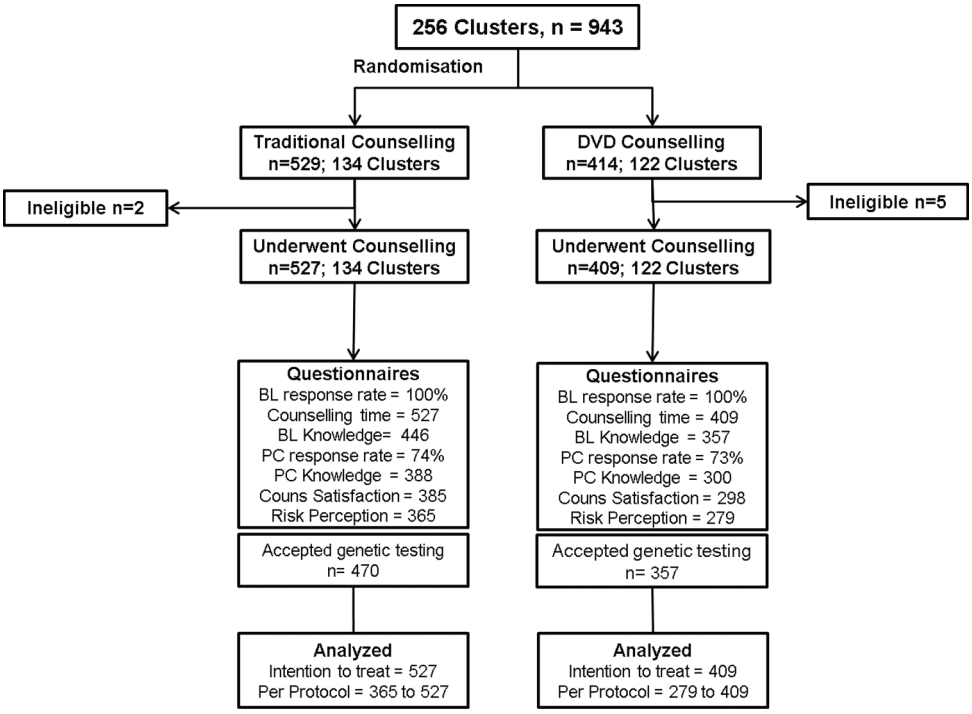

Figure 1 Consort flow chart for recruitment to Genetic Cancer Prediction through Population Screening. . Reasons for exclusion (ineligible volunteers): first-degree relative of BRCA1/2 carrier (n=4), did not have four Ashkenazi Jewish grandparents (n=2) and already had BRCA1/2 testing (n=1). The baseline questionnaire response rate was 100%. The postcounselling (PC) questionnaire response rate was 74% for traditional counselling and 73% for DVD counselling groups. The number of responses received for different outcomes is given in the questionnaire box. BL, baseline; Couns, counselling.

GCSS=2 units (SD=5.6); risk perception=7 (SD=23.7). A ±10% equivalence margin was used for uptake of testing.

The sample size was adjusted by a variance inflation factor calculated for the intraclass correlation (ICC) from clustering. Sample size=K×n/[1+(n−1)×ICC], where K is the number of clusters, n is the cluster size and ICC is the intraclass correlation coefficient. This was further increased by 10% to adjust for relative efficiency between varying and equal cluster sizes.[24] Assuming a mean cluster size=5, ICC=0.1, the adjusted sample size=(original sample)×1.54.

The total sample sizes needed for 80% power to detect 'equivalence' of uptake of testing=830 and 'non-inferiority' for knowledge=437, counselling satisfaction=382 and risk perception=554. Sample size for 15 min reduction in counselling time (SD=9.9)=37 and for non-inferiority margin of 0.5 SD of counselling time=265. Based on the final sample size of 936, cluster size=3.6, uptake of testing=89%, the study has >90% power for determining equivalence of uptake (ICC=0.21) and >95% power for establishing non-inferiority of knowledge gain (ICC=0.007), counselling satisfaction (ICC=0.0005), risk perception (ICC=0.053), and superiority for counselling time (ICC=0.15).

Cost-minimisation analysis was undertaken for TC and DVD-C approaches. The costs of filming the DVD=£300/- and burning a blank DVD=£0.60. The per-person cost=[DVD cost (unit cost=£((300/409)+0.60) per-volunteer)+genetic counselling cost]. The unit cost assumed for genetic counselling=£44/h of client contact, and the cost assumed for a psychologist appointment (if needed)=£73/h face-to-face contact (from Personal Social Services Research Unit's unit costs of health and social care 2010[25]).

Patient/community involvement

The study was preceded by an extensive broad-based consultation/engagement with all sections of the Jewish community, which lasted almost a year (see online supplementary table S5).

RESULTS

Between February 2009 and July 2010, 936 people underwent genetic counselling in GCaPPS and were cluster randomised by recruitment clinics (256 clusters) to TC (134 clusters, n=527) and DVD-C (122 clusters, n=409) groups. The mean cluster size=3.6 (TC=3.8, DVD-C=3.4). Baseline characteristics of participants were not significantly different between these groups (table 1). The mean age of participants was 53.9 (SD 15) years; 66.8% were women and 33.2% men. Our findings suggest a significant proportion of the AJ population are interested in BRCA1/2 testing and find it acceptable. Most (89%) of the participants opted for genetic testing following counselling. The uptake of testing rates and means (SD) for knowledge, GCSS, counselling time and risk perception is given in table 1. The consort flow chart is given in figure 1.

We found DVD-C was non-inferior to TC for increase in knowledge (d=−0.07; lower 97.5% CI=−0.41), counselling satisfaction (d=−0.38, 97.5% CI=1.2) and change in risk perception (d=0.08, upper 97.5% CI=3.1) (figure 2, table 2). Group differences and 97.5% CIs did not cross non-inferiority margins. Sensitivity analysis for knowledge scores and use of zero-inflated negative binomial regression for GCSS scores gave the same results of DVD-C being non-inferior to TC. DVD-C was equivalent to TC for uptake of genetic testing (d=−3%, lower/upper 97.5% CI −7.9%/1.7%) (figure 3, table 2). DVD-C was superior to TC in terms of counselling time leading to 20.5 (95% CI 18.7 to 22.2) min reduction in counselling time

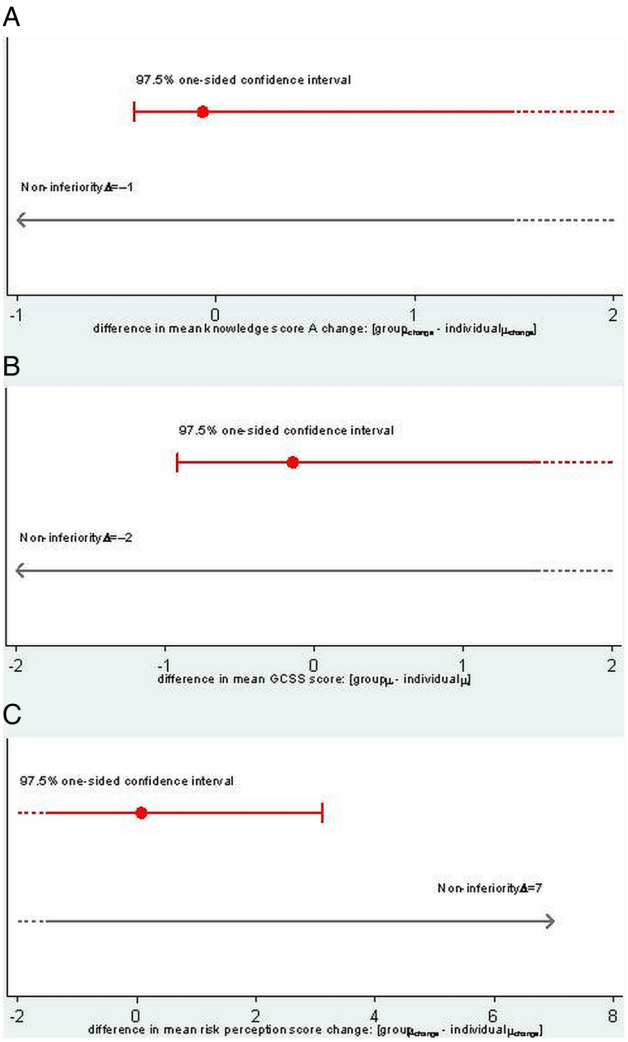

Figure 2 Non-inferiority outcomes for increase in knowledge, counselling satisfaction and risk perception. This figure shows outcomes and non-inferiority margins for difference between DVD-based counselling (DVD-C) and traditional face-to-face genetic counselling (TC) groups for increase in knowledge (A), counselling satisfaction (B) and cancer risk perception (C). Random-effects models adjusted for covariates of family history (high/low risk), age, gender, parity, income, education and marital status were used to compare outcomes between TC and DVD-C groups. A one-sided 97.5% CI was used to determine non-inferiority for increase in knowledge (A), counselling satisfaction (B) and cancer risk perception (C). The x-axis shows the adjusted mean difference (DVD-C–TC) and 97.5% confidence limit. Non-inferiority is established when the 97.5% CI (red line in the figure) does not cross the non-inferiority margin (black line in the figure). GCSS, Genetic Counselling Satisfaction Scale.

(p<0.005) (figure 3, table 2). Sensitivity analysis following multiple imputation of missing data also showed similar results (table 2).

Baseline knowledge level was significantly associated with decreasing age, and increasing levels of income and education, but independent of FH, gender, marital status and having children (table 3). Overall genetic counselling led to a significant increase in knowledge scores (p<0.0005).

Responses (n=316) to the DVD evaluation questionnaire are given in table 4. Ninety-eight per cent people were satisfied with the overall information, amount of information and DVD length. Thirteen per cent felt certain parts required more

Table 2 Difference in gain in knowledge, counselling satisfaction, uptake of testing, risk perception and counselling time between traditional face-to-face (TC) and DVD-based counselling (DVD-C) groups

Outcome	Difference between DVD-C and TC	Lower 97.5% CI	Upper 97.5% CI	SE	Non-inferiority margin	ICC
Outcomes from random-effects models						
Gain in knowledge	−0.07	−0.41	0.27	0.18	1	0.007
Counselling satisfaction	−0.38	−1.2	0.38	0.43	2	0.0005
Uptake of testing	−3%	−7.9%	1.7	0.0244	±10%	0.21
Risk perception	0.08	−2.9	3.1	1.55	7	0.053
Counselling time (min)	−20.4	−22.2	−18.7	0.87	15*	0.15
Multiple imputation analysis						
Gain in knowledge	−0.10	−0.40	0.19	0.15	1	0.00005
Counselling satisfaction	−0.47	−1.27	0.33	0.41	2	0.00003
Uptake of testing	−2.5%	−6.9%	2.04%	2.30%	±10%	0.26
Risk perception	−0.04	−2.5	2.4	1.3	7	0.001
Counselling time (min)	−20.6	−26.5	−14.6	3.03	15*	0.00005

*Superiority margin.ICC, intraclass correlation coefficient

detailed explanation. Only 2% felt some parts could be left out (see online supplementary table S5). Ninety-five per cent would recommend the DVD to others, and 85–89% indicated it improved their understanding of risks/benefits/implications and

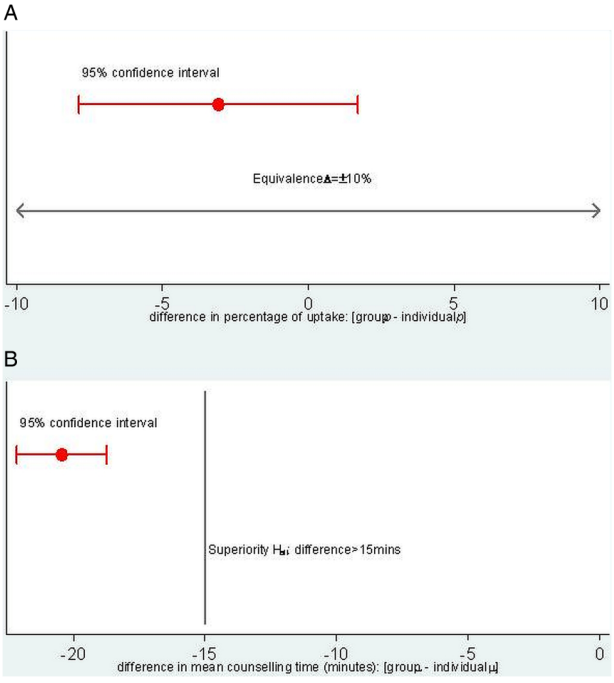

Figure 3 Equivalence analysis for uptake of testing and superiority analysis for counselling time. This figure shows outcomes of difference in uptake of testing with equivalence margins (A) and counselling time with superiority analysis (B) between DVD-based counselling (DVD-C) and traditional face-to-face genetic counselling (TC) groups. Random-effects models adjusted for covariates of family history (high/low risk), age, gender, parity, income, education and marital status were used to compare outcomes between TC and DVD-C groups. (A) A two-sided 97.5% CI was used to determine equivalence for uptake of testing. Equivalence was established when the 97.5% CI on either side (red line in the figure) did not cross the non-inferiority margin on either side (black line in the figure). (B) The CIs for difference in counselling time (horizontal red line) lie well to the left of the superiority margin (vertical black line), indicating DVD-C is superior to TC.

Table 3 Association of baseline variables with levels of knowledge

Variable	Mean knowledge score (SD)	p Value
Marital status		
Single	8.11 (2.39)	0.058
Married	7.6 (3.09)	
Cohabiting (living with partner)	8.13 (2.69)	
Divorced/separated	7.62 (2.92)	
Widowed	6.69 (3.11)	
Children		
Yes	7.64 (2.96)	0.794
No	7.73 (3.05)	
Gender		
Men	7.39 (3.38)	0.883
Women	7.7 (2.26)	
Education		
No-formal- qualification	5.68 (3.75)	p<0.005
GCSE, O-level, CSE	7.17 (3.22)	
NVQ-1, NVQ-2	8 (2.54)	
A-level, NVQ-3	7.38 (3.18)	
NVQ-4	7.06 (3.35)	
Bachelor's	7.94 (2.78)	
Master's	8.26 (2.40)	
PhD	8.67 (2.29)	
Income (£)		
<10K	6.98 (2.96)	0.007
10K–19.9K	7.73 (2.96)	
20K–29.9K	6.89 (3.68)	
30K–39.9K	7.31 (3.27)	
40K–49.9K	7.7 (2.96)	
≥50K	8.13 (2.59)	
FH positive		
Yes	8.19 (2.33)	0.121
No	7.52 (3.13)	
Age group (years)		
<30	8.6 (1.74)	p<0.005
30–50	8.68 (1.65)	
50–70	8.12 (2.16)	
>70	7.55 (2.77)	

FH, family history, NVQ, National Vocational Qualification.

Table 4 DVD evaluation questionnaire

n=316	Very satisfied	Satisfied	Neither satisfied/ dissatisfied	Dissatisfied	Very dissatisfied
Satisfaction with information provided (n=316), %	74.1	24.7	1.30	0	0
	Too little		**About right**		**Too much**
Amount of information provided (n=316), %	0.3		98.7		0.9
	Too short		**About right**		**Too long**
Time taken to watch the presentation (n=315), %	0		98.4		1.6
Any parts of the presentation need to be explained in more detail (n=315)	Yes	13.3%		No	86.7%
Any parts of the presentation that could be left out (n=313)	Yes	1.9%		No	97.2%
How much did the presentation improve your understanding of	**Not at all**	**Not very much**	**Somewhat**	**Quite a bit**	**A lot**
Purpose of genetic testing (n=316), %	5.4	8.9	24.1	43.7	18.0
Risks of genetic testing in your situation (n=316), %	3.5	7.6	30.7	39.2	19.0
Benefits of genetic testing in your situation (n=315), %	3.5	7.6	25.9	41.1	21.5
Implications of a positive result (n=314), %	3.5	6.6	23.1	39.6	26.6
How much did the presentation make you feel	**Not at all**	**Not very much**	**Somewhat**	**Quite a bit**	**A lot**
Worried or concerned (n=314), %	52.2	34.8	11.1	1.3	0
Reassured (n=308), %	9.2	10.8	46.8	21.5	9.2
Upset (n=312), %	82.6	13.0	3.2	0	0
	Yes, I would		**I'm not sure**		**No, I would not**
Would you recommend the presentation to others (n=315), %	94.9		4.4		0.3

purpose of genetic testing. Emotionally, 77% felt reassured; 87–95% felt no significant degree of worry/concern/upset; 11% felt somewhat worried/concerned, 3% somewhat upset and 1.3% 'quite a lot' worried/concerned after watching the DVD. Table 5 summarises responses on parts making people feel worried/concerned/upset/reassured.

The total genetic counselling cost estimate=£7786.65 (£19/volunteer) for DVD-C and £17 306.68 (£33/volunteer) for TC groups. The reduction in face-to-face health professional consultation time with the DVD translated into a total cost difference=£9520.03. DVD-based counselling led to a cost saving=£14/volunteer counselled. Although the cost minimisation of £14/volunteer may seem to be small in individual terms, when extrapolated across a whole population it actually amounts to quite a substantial saving for the healthcare system.

DISCUSSION

To the best of our knowledge, this is the first RCT to report on systematic pre-test genetic counselling in a low-risk population (unselected for FH) of men and women undergoing BRCA1/2 mutation testing. The finding that DVD-C is not inferior to TC with respect to increase in knowledge, risk perception or counselling satisfaction, equivalent in uptake of testing and more cost-efficient (cost saving=£14/volunteer) is of great importance and suggests that DVD-C can be used as an effective and efficient alternative to traditional pre-test genetic counselling.

Group genetic counselling is reported to reduce the duration of counselling in high-risk populations,[8] but this is the first report of using a DVD in this situation. DVD is an audio-visual tool with several advantages. It can be distributed/accessed by post, the web, general practitioner surgeries, community centres or other high-street sources and watched by people prior to their genetics appointment. Unlike group/telephone counselling, it does not require a health professional to deliver the educational material. Printed educational material is also effective in increasing knowledge and facilitating decision-making.[26 27] We did not directly compare a printed decision aid with a DVD in this study. Pre-test genetic counselling reduces distress, improves patients' risk perception[28] and currently remains part of international guidelines for genetic testing.[5] Although no pre-test genetic counselling was undertaken in two single-arm contemporaneous Canadian[2] and Israeli[29] population studies, post-test counselling was provided, and good satisfaction reported by participants with the testing process. Such an approach of 'no pre-test counselling' or only 'post-test counselling' has not yet been directly compared with TC in a randomised trial.

For population-based testing to be feasible, newer models for providing information for informed decision-making prior to genetic testing are necessary, which need to be properly evaluated in well-designed trials and ideally compared with the gold standard of TC. While we have demonstrated a viable DVD-based model, other models are also being explored/developed. Telephone genetic counselling has been successfully used for triaging women from high-risk families for TC[10] and disclosure of test result.[9 30 31] Three RCTs compared telephone counselling to TC in high-risk women attending genetics clinics. No difference in satisfaction[32] was reported in one. Two were non-inferiority trials and found telephone counselling was non-inferior to TC,[11 12] though lower testing uptake was reported in one.[11] Telegenetics has been compared with TC in an RCT and reported to costless with no difference in satisfaction, though it was associated with 10% lower attendance.[33] Telephone counselling/telegenetics have not yet been evaluated in a low-risk population unselected for FH. Newer models like mainstreaming counselling by the non-cancer genetics professional community[34] or trained nurse specialists[35] are currently being explored

Table 5 Parts of the DVD making people feel worried, upset or reassured

Parts leading to feeling worried, upset or reassured	n (%)
Nothing	
Nothing	6 (1.9%)
Worried	
3 months to result	1 (0.3%)
May not be tested	2 (0.6%)
General concern	2 (0.6%)
Insurance	3 (1%)
High probability of cancer	3 (1%)
Impact on children/family	3 (1%)
Implications	1 (0.3%)
Concentration not 100%	1 (0.3%)
Upset	
Increased gene frequency in Ashkenazi Jewish	2 (0.6%)
Reassured	
Clear presentation	8 (2.5%)
Logical balanced view	2 (0.6%)
Presenter has excellent skills	1 (0.3%)
Positive video	2 (0.6%)
Factual	2 (0.6%)
Statistics	2 (0.6%)
Insurance information	1 (0.3%)
Ability to participate	1 (0.3%)
Implications	2 (0.6%)
General reassurance	4 (1.3%)
Available help, options	4 (1.3%)
Follow-up available	2 (0.6%)
Other comments	
Difficult decision	1 (0.3%)
Unemotional	1 (0.3%)
Statistical	1 (0.3%)
Presenter needs better eye contact, body language	1 (0.3%)
Surprised not worried about risks	1 (0.3%)
Need time to absorb facts	1 (0.3%)

in clinical practice, but have not yet been directly compared with TC or other approaches in an RCT. It is likely that different models/pathways may be needed for different populations and different countries or healthcare systems. Further well-designed high-quality research is needed in this area.

The strengths of this report include the cluster-randomised design, non-inferiority analysis, community-based model for undergoing genetic testing and a high questionnaire response rate (73–100%). The differences in number of volunteers between the two study arms are explained by the randomisation of clinics (not volunteers), varying clinic times and differences in clinic sizes. But as expected, the baseline characteristics of the groups were in balance (table 1). Lack of qualitative data may be considered a weakness, and restriction to AJ participants may limit generalisability to other populations. We were also unable to analyse long-term outcomes postdisclosure of the test result, and this may be a limitation of the analysis. We did not include the 15 min patient time taken to watch the DVD in the cost-minimisation analysis because our analysis covers a healthcare perspective in line with NICE methods guidance, and therefore as per NICE guidance, patient costs are excluded. Besides, in practice, we would expect patients to have watched the DVD before attending a genetic counselling session. We guaranteed compliance and maximised questionnaire response by making people watch the DVD prior to counselling. Hence, in the future, when the DVD is delivered at home, it is important to ensure that people do watch the DVD at home prior to attending the genetic counselling session to ensure generalisability of results.

The high genetic testing uptake rate found in our study has also been reported by others.[2 36 37] This may also be a function of a self-selected population and/or non-directive informative pre-test counselling received by participants. Our knowledge questionnaire was able to detect changes in knowledge (sensitivity to change). The increase in knowledge following pre-test counselling found in a low-risk population is similar to previous reports from high-risk populations.[26 38 39] Older studies reported lower levels of knowledge about genetic testing and understanding of cancer risk.[26 39] However, our relatively higher mean baseline score (>7) suggests that the average person coming forward for BRCA1/2 testing today may have greater levels of awareness/knowledge, which is reassuring. The lack of difference in knowledge scores between those with and without a strong FH of cancer re-emphasises this point and is contrary to previous findings of an association between knowledge and FH of cancer.[38] The high baseline levels of knowledge may be a reflection of number of factors such as (a) self-selected trial participants, (b) the higher education and income levels known to be prevalent in the UK Jewish community compared with the rest of the non-Jewish general population and (c) ever-increasing public information and awareness on this issue. Our finding that level of knowledge is associated with education and income is consistent with earlier reports,[38 40] and with the positive correlation (Spearman's $r=0.3$, $p<0.005$) between income and education levels, expected in a general population. Younger people had greater knowledge about genetic testing than older people. To the best of our knowledge, this has not been reported before. Factors that could have contributed to this include greater awareness of genetics, its recent incorporation into school curriculums, proactive behaviour and better access to sources of information in younger age groups.

Decision-making where each option has benefits/risks that people may value differently can be a difficult process. Overall, our DVD was well received with high satisfaction levels and enabled people to make specific, deliberated choices appropriate for them. The increase in knowledge is consistent with the effectiveness of the DVD in providing relevant information and improving the understanding of purpose/benefits/risks/implications related to genetic testing. Getting the right balance between DVD length and amount of information provided is challenging. The 98% satisfaction with length/information, 88% feeling no need for further explanation and 95% willingness to recommend it suggest our 15 min DVD struck the right balance for most people. A longer/more detailed DVD would yield small improvements, while greatly increasing the proportion of disaffected people.[7] That the same information/content on a topic generated different reactions (reassurance/worry) suggests the DVD helped facilitate variable responses consistent with individual personal values. Need for more information on insurance/risks/inheritance highlighted by a small proportion represent areas for further development. The DVD quality can also be improved by incorporating qualitative data and using better production, film making and editing facilities.

The ability to identify 50% additional carriers, lack of psychological harm and cost-effectiveness of population testing for BRCA1/2 mutations in AJ individuals[3 4 29] calls for changing the clinical paradigm to population testing for BRCA1/2 founder mutations in this population. DVD-based counselling

approach is an effective, acceptable, non-inferior and cost-efficient alternative to TC and could be implemented for population testing in AJ. This can generate cost savings that is relevant for health authorities and commissioners of genetic counselling services and could enable more resources being directed to individuals who have difficulty coping with the genetic test result and/or needing greater support from genetics services following genetic testing.

Advances in high-throughput genetic testing technology, computational analytics and falling costs have made non-AJ general population testing technically feasible.[41 42] The identification of newer moderate penetrance genes (RAD51C/RAD51D/BRIP1)[43–45] and availability of panel testing will lead to an ever-increasing demand for genetic services with newer challenges for pre-test education and genetic counselling. Future research needs to compare telegenetics, telephone counselling, use of dial-in/web-based helplines, web apps along with DVD/other decision tools to identify/develop cost-efficient mass-based strategies to optimise education and facilitate informed decision-making without negatively affecting satisfaction, knowledge or psychological well-being in the general non-AJ population. A move away from TC is necessary to achieve the full benefit of genomic advances to deliver predictive, preventive, personalised and participatory (P4) medicine for cancer prevention.

Author affiliations
[1]Department of Women's Cancer, EGA Institute for Women's Health, University College London, London, UK
[2]Department of Gynaecological Oncology, Bartshealth NHS Trust, Royal London Hospital, London, UK
[3]Barts Cancer Institute, Queen Mary University of London, London, UK
[4]Behavioural Sciences Unit, Department of Epidemiology and Public Health, University College London, London, UK
[5]Mt Sinai University, New York, USA
[6]Department of Clinical Genetics, North East Thames Regional Genetics Unit, Great Ormond Street Hospital, London, UK
[7]Department of Clinical Genetics, North West Thames Regional Genetics Unit, Northwick Park Hospital, London, UK
[8]West Midlands Regional Genetics Laboratory, Birmingham Women's NHS Foundation Trust, Birmingham, UK
[9]Depatment of Clinical Genetics, West Midlands Regional Genetics, Birmingham Women's NHS Foundation Trust, Birmingham, UK
[10]London Research Institute, Cancer Research UK,
[11]South West Thames Molecular Genetics Diagnostic Laboratory, St George's Hospital, London, UK
[12]Department of Clinical Genetics, Guy's Hospital, London, UK
[13]Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London, UK
[14]Department of Health Economics, London School of Economics, London, UK
[15]Department of Gynaecology, Shaare Zedek Medical Centre, Jerusalem, Israel
[16]University of New South Wales, Sydney, Australia

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