Title Page

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

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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 >18years; Exclusion-criteria: (a)known BRCA1/2 mutation, (b)previous BRCA1/2 testing, (c)first-degree-relative of BRCA1/2 carrier. Ashkenazi-Jewish men/women underwent pre-test genetic-counselling prior to BRCA1/2 testing in the GCaPPS 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(GCSS-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 & 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) & DVD-C (n=409,clusters=122) approaches. Groups were similar at baseline, mean-age=53.9(S.D=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), risk perception (d=0.08;upper-97.5%CI=3.1). Group differences and CIs didn't 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=18.7,22.2) minutes reduction(p<0.005)). 98% people found the DVD length-&-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=£7,787 and TC=£17,307. DVD-C resulted in cost-savings=£9,520(£14/volunteer).

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

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 specialized 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, 2, 3] The GCaPPS (Genetic-Cancer-Prediction through Population-Screening) 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 33days gain in life-expectancy and incremental cost-effectiveness ratio(ICER)='-£2079/quality-adjusted-life-year(QALY)' well below the £20,000/QALY 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, 9, 10, 11, 12]

For large-scale, population-based genetic testing to become feasible and practical it is necessary to 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 >18years, (b)AJ ethnicity Exclusion criteria: (a)known BRCA1/2 mutation, (b)previous BRCA1/2 testing, (c)first-degree relative(FDR) 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, 17, 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 Nov-2008 to Jan-2009. This study reports on genetic-counselling outcomes of clinics randomised from Feb-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. Post-counselling 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: 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 (supplementary table-S1) at baseline and post genetic-counselling. Satisfaction with genetic-counselling was assessed post-counselling by the validated 6-item Genetic-Counselling-Satisfaction-Scale (GCSS): 5-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 post-counselling.[21] A DVD-evaluation questionnaire (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 are descried in 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 web-site (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-Corp-LP, Texas, USA). Baseline characteristics were calculated using descriptive statistics. Chi-square 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. 50 fully imputed datasets were created to generate valid estimates and standard errors, and produce correct statistical inference.

Non-inferiority analysis is needed to determine if 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.

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The non-inferiority margins were based on clinically meaningful changes where available or set at no more than 0.5S.D worse than that for TC from prior studies[19, 23] or data collected during initial counselling undertaken from Nov-2008 to Jan-2009. The non-inferiority margin for knowledge gain=1 unit (minimum possible change on the scale, S.D=3); GCSS= 2 units(S.D=5.6); risk perception= 7(S.D=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 intra-class correlation(ICC) from clustering. Sample size= K*n/[1+(n-1)*ICC]; where K=number of clusters, n=cluster-size, ICC=intra-class 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)x1.54.
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, risk perception=554. Sample size for 15min reduction in counselling time (S.D=9.9)=37 and for non-inferiority margin of 0.5SD 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/hour of client contact and the cost assumed for a psychologist appointment (if needed)=£73/hour face-to-face contact (from PSSRU Unit costs of Health-&-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 (Supplementary table-S5).

RESULTS

Between Feb-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(S.D15) 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 participants opted for genetic-testing following counselling. The uptake of testing rates and means(S.D) for knowledge, GCSS, counselling time and risk perception are 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=18.7,22.2) minutes reduction in counselling time ($p<0.005$)(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. 98% people were satisfied with the overall information, amount of information and DVD length. 13% felt certain parts required more detailed explanation. Only 2% felt some parts could be left out (supplementary table-S5). 95% would recommend the DVD to others and 85-89% indicated it improved their understanding of risks/benefits/implications and 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=£7,786.65(£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=£9,520.03. 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 health care 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, GP 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 to 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 to 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 to TC in a RCT and reported to cost less 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 in clinical practice, but have not yet been directly compared to TC or other approaches in a 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 is 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 generalizability to other populations. We were also unable to analyse long term outcomes post-disclosure of the test result and this may be a limitation of the analysis. We did not include the 15 minute patient time taken to watch the DVD in the

cost-minimisation analysis because our analysis covers a health care 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 for 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 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 to 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-rho=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 suggests our 15minute 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 Ashkenazi Jews. This can generate cost savings which 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, 44, 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, personalized, and participatory(P4) medicine for cancer prevention.

Ethics approval and trial registration

The GCaPPS study received full ethics approval from the Institute of Child Health/ Great Ormond Street Hospital Research Ethics Committee on 8th June 2008 (REC Reference number 08/H0713/44). The study was registered with the International Standard Randomised Controlled Trial Number Register - ISRCTN 73338115 (http://www.controlled-trials.com/ISRCTN73338115)

Contribution to authorship

RM, IJ and UM were responsible for literature search and design of the study. RM, IJ, UM, JW, KL, SG, SS, AK were involved in developing interventional questionnaires. RM, KL, MB, AMG, MR were involved in data collection and analysis. RM, MB did the statistical analysis. RM, MR, AMG, RL did the cost minimisation analysis. RM, MB prepared the tables and figures. RT, CJ were collaborators and helped with study development and data collection from genetic laboratories. RM, IJ prepared the first draft of the manuscript. RM, IJ, UM, KL, JW, SG, LS, NB, RD, AK, HD, YW, CC, IT, AMG, UB were involved in running the study. YW did the genetic testing. All authors critically contributed to and revised the manuscript and approved the final version.

Conflict of interest statement

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author)
All authors declare support from the Eve Appeal charity for research funding of this work. RM, MB, KL, RD, JW, SS, SG, LS, NB, AK, HD, YW, CC, IT, RT, CJ, RL, MR, AMG, UB, declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years and no other relationships or activities that could appear to have influenced the submitted work. IJ declares consultancy arrangements with Becton Dickinson, in the field of molecular markers for ovarian cancer. IJ and UM have a financial interest in Abcodia, Ltd., a company formed to develop academic and commercial

development of biomarkers for screening and risk prediction. IJ is a member of the board of Abcodia Ltd and a Director of Women's Health Specialists Ltd.

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The study was funded by 'The Eve Appeal' charity. The funding body (The Eve Appeal charity) had no role in the study design, data collection, analysis, interpretation or writing of the report. The corresponding author had full access to all data in the study. The GCaPPS investigators had final responsibility for the decision to submit the report for publication.

Authors Statement

All authors' had full access to all of the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The GCaPPS investigators had final responsibility for the decision to submit the report for publication.

Data Sharing

Participants gave informed consent for use of data for publication. Separate consent for data sharing of non-identifiable data was sought and provided by a number of participants. Relevant anonymised patient level data can be obtained on reasonable request from the authors.

Transparency declaration

The corresponding author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Figure 1: Consort Flow Chart for Recruitment to GCaPPS

BL- Baseline, PC- Post Counselling, Couns- counselling

Reasons for exclusion (ineligible volunteers): first degree relative of BRCA1/2 carrier (n=4), did not have 4 Ashkenazi Jewish grandparents (n=2), already had BRCA1/2 testing (n=1). The baseline questionnaire response rate was 100%. The post-counselling questionnaire response rate was 74% for traditional counselling) and 73% for DVD-counselling groups. The number of responses received for different outcomes are given in the questionnaire box.

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 (Fig 2a), counselling satisfaction (Fig 2b) and cancer risk perception (Fig 2c). Random-effects models adjusted for covariates of FH (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 (Fig 2a), counselling satisfaction (Fig 2b) and cancer risk perception (Fig 2c). 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).

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 (Figure 3a) and counselling time with superiority analysis (Figure 3b) between DVD-based counselling (DVD-C) and traditional face-to-face genetic counselling (TC) groups. Random-effects models adjusted for covariates of FH (high/low risk), age, gender, parity, income, education and marital status were used to compare outcomes between TC and DVD-C groups. Figure 3a: 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). Figure 3b: 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.

Supplementary Table S1- Knowledge Questionnaire

Supplementary Table S2- DVD Evaluation Questionnaire

Supplementary Table S3- Development of Knowledge Questionnaire

Supplementary Table S4- Development of DVD

Supplementary table-S5- Parts of the DVD requiring more details or which could be left out

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

		Traditional face-to-face (TC)	DVD-based (DVD-C)
	n	527	409
	Number of Clusters	134	122
	Mean Cluster Size (S.D)	3.8 (2)	3.4 (2.1)
Age	Age in years (S.D)	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 (S.D)	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%)
	NVQ1,NVQ2	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%)
	Bachelors	196/500 (39.2%)	136/389 (35%)
	Masters	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 & Depression	HADS-Anxiety (S.D)	6.1 (3.5)	6.4 (3.7)
	HADS-Depresson (S.D)	2.9 (2.5)	3 (2.6)
	HADS-Total (S.D)	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	**MeanTime in minutes (S.D)**	**46 (49.7)**	**21.3 (8.4)**
Perceived risk	**Baseline Risk (S.D)**	**50.6 (50.7)**	**49.6 (22.1)**
	Post Counselling Risk (S.D)	**47.4 (23.4)**	**48.9 (22.7)**

FH- Family History, HADS- Hospital Anxiety and Depression Scale, S.D- standard deviation

Table-2: Difference in gain in knowledge, counselling satisfaction, uptake of testing, risk perception and counselling time between TC and DVD-C groups

OUTCOMES FROM RANDOM EFFECTS MODELS						
Outcome	**Difference between DVD-C & TC**	**Lower 97.5% CI**	**Upper 97.5% CI**	**Std. error**	**Non-inferiority Margin**	**ICC**
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						
Outcome	**Difference between DVD-C & TC**	**Lower 97.5% CI**	**Upper 97.5% CI**	**Std. error**	**Non-inferiority Margin**	**ICC**
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**

TC - Traditional face-to-face counselling, DVD-C - DVD-based counselling, ICC- intra-class correlation coefficient, std- standard, CI- confidence interval, min- minutes

*Superiority Margin

Table 3- Association of baseline variables with levels of Knowledge

Variable		Mean Knowledge Score (S.D)	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)	
	NVQ1,NVQ2	8 (2.54)	
	A-level,NVQ-3	7.38 (3.18)	
	NVQ-4	7.06 (3.35)	
	Bachelors	7.94 (2.78)	
	Masters	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	Age < 30 years	8.6 (1.74)	p<0.005
	Age 30-50 years	8.68 (1.65)	
	Age 50 - 70 years	8.12 (2.16)	
	Age >70 years	7.55 (2.77)	

FH- family history, S.D- standard deviation, 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%

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 AJ	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%)

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