

Attitude towards and factors affecting uptake of population based *BRCA* testing in the Ashkenazi Jewish population: a cohort study

*Ranjit Manchanda ^{1,2}, Matthew Burnell ³, Faiza Gaba^{1,2}, Saskia Sanderson ⁴, Kelly Loggenberg ⁵, Sue Gessler ³, **Jane Wardle ⁴, Lucy Side ⁶, Rakshit Desai³, Angela F Brady ⁷, Huw Dorkins ⁸, Yvonne Wallis ⁹, Cyril Chapman ¹⁰, Chris Jacobs ^{11,12}, Ian Tomlinson ¹³, Uziel Beller ¹⁴, Usha Menon ³, and Ian Jacobs ¹⁵.

¹Barts Cancer Institute, Queen Mary University of London, Old Anatomy Building, Charterhouse Square, London, EC1M 6BQ, UK

²Department of Gynaecological Oncology, St Bartholomew's Hospital, London, UK, EC1A 7BE

³Gynaecological Cancer Research Centre, Department of Women's Cancer, Institute for Women's Health, University College London, 149 Tottenham Court Road, London, UK, W1T 7DN.

⁴Behavioral Sciences Unit, Department of Epidemiology and Public Health, University College London

⁵Dept Clinical Genetics, North East Thames Regional Genetics Unit, Great Ormond Street Hospital, London, UK

⁶University Hospital Southampton NHS Foundation Trust

⁷Dept Clinical Genetics, North West Thames Regional Genetics Unit, Northwick Park Hospital, London, UK,

⁸St Peter's College, University of Oxford, Oxford, UK

⁹West Midlands Regional Genetics Laboratory, Birmingham Women's NHS Foundation Trust, Birmingham, UK,

¹⁰Dept Clinical Genetics, West Midlands Regional Genetics Service, Birmingham Women's NHS Foundation Trust, Birmingham, UK,

¹¹Dept Clinical Genetics, Guy's Hospital, London SE1 9RT, UK

¹²University of Technology Sydney, Australia, NSW 2007

¹³Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham, UK

¹⁴Department of Gynaecology, Shaare Zedek Medical Center, Jerusalem, Israel

¹⁵University of New South Wales, Australia, Level 1, Chancellery Building, UNSW Sydney NSW 2052

***Corresponding author:**

Dr Ranjit Manchanda

Clinical Senior Lecturer & Consultant Gynaecological Oncologist

Barts Cancer Institute, Queen Mary University of London

Room 4, Basement, Old Anatomy Building

Charterhouse Square, London EC1M 6BQ

Email: r.manchanda@qmul.ac.uk

****Deceased**

Running Title: Factors affecting uptake of BRCA testing in Ashkenazi Jews

Word count: 3504

Attitude towards and factors affecting uptake of population based *BRCA* testing in the Ashkenazi Jewish population: a cohort study

Objective

To evaluate factors affecting unselected-population-based-*BRCA*-testing in Ashkenazi-Jews (AJ).

Design

Cohort-study set within recruitment to the GCaPPS-trial (ISRCTN73338115)

Setting

North-London AJ-population

Population or Sample

AJ women/men >18-years, recruited through self-referral.

Methods

AJ-women/men underwent pre-test counselling for *BRCA*-testing through recruitment clinics (clusters). Consenting individuals provided blood-sample for *BRCA*-testing. Socio-demographic/family-history/knowledge/psychological well-being data along-with benefits/risks/cultural-influences (18-item-questionnaire measuring 'attitude') were collected. 4-item likert-scales analysed initial 'interest' and 'intention-to-test' pre-counselling. Uni-&-multivariable logistic-regression-models evaluated factors affecting uptake/interest/intention-to undergo *BRCA*-testing. Statistical inference was based on cluster robust standard-errors and joint Wald-tests for significance. Item-Response-Theory and graded-response-models modelled responses to 18-item questionnaire.

Main Outcome Measures:

Interest, intention, uptake, attitude towards *BRCA*-testing

Results

935 (women=67%/men=33%; mean-age=53.8(S.D=15.02) years) individuals underwent pre-test genetic-counselling. Pre-counselling 96% expressed interest but 60% indicated clear intention-to

undergo *BRCA*-testing. Subsequently 88% opted for *BRCA*-testing. *BRCA*-related knowledge ($p=0.013$) and degree-level education($p=0.01$) were positively and negatively (respectively) associated with intention-to-test. Being married/cohabiting had four-fold higher-odds for *BRCA*-testing uptake ($p=0.009$). Perceived benefits were associated with higher pre-counselling odds for interest and intention-to undergo *BRCA*-testing. Reduced uncertainty/reassurance were the most important factors contributing to decision-making. Increased importance/concern towards risks/limitations (confidentiality/insurance/emotional-impact/inability to prevent cancer/marriage-ability/ethnic-focus/stigmatization) were significantly associated with lower-odds of uptake-of *BRCA*-testing, and discriminated between acceptors and decliners. Male-gender/degree-level-education ($p=0.001$) had weaker, while having children had stronger ($p=0.005$) attitudes towards *BRCA*-testing.

Conclusions

BRCA-testing in the AJ-population has high acceptability. Pre-test counselling increases awareness of disadvantages/limitations of *BRCA*-testing, influencing final cost-benefit perception and decision-making on undergoing testing.

Funding

The Eve-Appeal Charity (Grant-GTCV)

Key Words

BRCA, genetic-testing, population-based, Ashkenazi-Jewish, attitude, uptake, interest, intention.

Tweetable Abstract

BRCA testing in Ashkenazi Jews has high acceptability and uptake. Pre-test counselling facilitates informed decision making.

Attitude towards and Factors affecting uptake of Population based *BRCA* testing in the Ashkenazi Jewish population: a cohort study

INTRODUCTION

Unselected population-based Founder Mutation *BRCA*-testing in the Ashkenazi-Jewish (AJ) population has been investigated in the UK Genetic Cancer-Prediction through Population-Screening (GCaPPS) randomised-controlled trial (RCT) (ISRCTN73338115),¹ as well as in Israeli² and Canadian³ single-arm cohort studies. The GCaPPS trial offered pre-test counselling outside a hospital in a high-street/community-based setting. Both traditional face-to-face and DVD-based approaches were compared and found to be equivalent.⁴ The Israeli/Canadian studies provided only post-test counselling to mutation carriers or those with a strong family-history (FH) of cancer. High satisfaction rates have been reported in all three studies.^{1, 4-6} A population-based approach identifies >50% additional *BRCA*-carriers than clinical-criteria/FH-based testing, does not detrimentally affect psychological well-being or quality-of-life on a population basis^{1, 5} and has been found to be extremely cost-effective.⁷ This has led to calls by a number of experts for changing the paradigm to population-based *BRCA*-testing in the AJ-population.^{8, 9}

Only limited data exist on attitude and factors affecting uptake of population-based *BRCA*-testing in the Jewish population, and these are largely restricted to women.^{5, 10} Differences have also been reported between those who are self-referred and those recruited through clinical services.⁵ The Jewish-population is the first population for whom population-based *BRCA*-testing is likely to become a reality. Understanding attitudes and factors affecting uptake are essential to help in the planning of clinical services, supportive care/interventions and future genetic testing programmes. In this paper we describe the attitudes towards and factors affecting uptake as well as interest, and intention-to-access population-based *BRCA*-testing amongst AJ women and men.

METHODS

GCaPPS participants were recruited from the North-London Jewish community. Recruitment was based on self-referral.¹ Study flyers were made available through community charities, a high-street pharmacy (Boots), select GP-practices and a web-site. Inclusion and exclusion criteria have been described earlier.¹ Individuals expressing an interest registered with the study team and were sent a detailed trial information booklet. Pre-test counselling was undertaken through six high-street/community-based centres in London.¹ Recruitment clinics (clusters) were randomised to traditional face-to-face and DVD-counselling approaches between 2009-2010, outcomes from which were reported earlier.⁴ We report on data from individuals who underwent pre-test counselling in recruitment clinic clusters. Genetic-counselling was undertaken by a qualified genetic-counsellor and a clinical-fellow experienced in cancer-genetics risk-assessment and management. It covered FH, cancer risk, genetic inheritance, risk management, psychosocial implications, and advantages/disadvantages to meet counselling goals¹¹⁻¹³ and enable informed choice and adaptation. Individuals opting for genetic-testing provided a blood sample for the three AJ *BRCA* founder-mutations: 185delAG(c.68_69delAG), 5382insC(c.5266dupC) and 6174delT(c.5946delT). A baseline questionnaire assessed socio-demographic characteristics and FH. Knowledge was assessed by a specially developed 10-item (True=1/False=0) questionnaire described earlier.⁴ Anxiety/depression were assessed by the Hospital anxiety-&-depression scale (HADS).¹⁴ Attitude towards *BRCA*-testing was assessed by an 18-item questionnaire (Appendix -S1) comprising: (a) 7-items assessing perceived benefits (to be reassured, enhance cancer prevention, learn about my children's risk, make decision about preventive surgery, make childbearing decisions, know if I need to get cancer screening, reduce uncertainty); (b) 7-items assessing perceived limitations/risks (worried about insurance, loss of confidentiality, stigmatization, don't trust modern medicine, nothing can be done to prevent cancer, concerned about impact on family, unable to handle it emotionally); and (c) 4-items assessing cultural/religious influences (too focused on Jewish community, marriage-ability, singling out individuals of a particular ethnic group, altruism). A likert-

scale assessed the level of importance participants attached to each of these items (1=not-at-all important, 2=somewhat important, 3=very important; or 1=definitely not, 2=somewhat and 3=definitely). The 14-items in sections (a) and (b) were taken from Lerman^{15, 16} and have been used by others^{17, 18}. Items in section-(c) were adapted from Phillips¹⁹ and Andrews²⁰.

Uptake of testing was calculated by the proportion of individuals who underwent *BRCA*- testing following pre-test counselling. Initial pre-counselling 'interest' to undergo testing was measured with: 'If it were available to you now, would you, in the next 6-months, have a *BRCA*-test to see if you are at risk of developing cancer in the future?' Response options: 'yes-definitely'/'yes-probably'/'no probably-not'/'no definitely-not'. This item was adapted from previous research (Sanderson)²¹⁻²³, and chosen on the basis that the 6-month time frame made the hypothetical question more concrete and is the period about as far into the future that most people plan a specific change in behaviour.²⁴ Pre-counselling 'intention-to' take the *BRCA*-test was assessed with an item adapted from Lerman¹⁵ and Schwartz¹⁸: At the present time, which of the following statements describes you best? Response options: Haven't thought about it/not considering *BRCA*-testing; Considering *BRCA*-testing; Probably-will have *BRCA*-testing; Definitely-will have *BRCA*-testing.

Statistical analysis:

Baseline characteristics were calculated using descriptive statistics.

Interest, Intention and Uptake of *BRCA*-testing:

Socio-demographic factors of interest and their relationship with 1) interest-in *BRCA*-testing, 2) intention-to undergo *BRCA*-testing and 3) uptake of *BRCA*-testing were explored in logistic-regression models in both univariable and multivariable settings. Specifically, 1) and 2) used an ordinal regression-model as the outcome variables contained 4 clearly ordered options (listed above), whereas the uptake model used binary logistic-regression ("Acceptor/Decliner"). All models

were regressed on the factors: gender (men versus women), marital-status (married/cohabiting versus widowed/divorced/single), income (£10,000-to-<£20,000, £20,000-to-<£30,000, £30,000-to-<£40,000, £40,000-to-<£50,000 and >£50,000 versus <£10,000), education (degree-level/above versus no formal qualification/GCSE/O-level/CSE/NVQ1/NVQ2/A-level education), family-history (low-risk versus high-risk), Having children (yes versus no), age, HADs score, cancer-risk perception scale and a *BRCA*-knowledge score. Statistical inference was based on cluster robust standard errors, with the cluster based on counselling clinics. Joint Wald tests were used to test the joint significance of more than one parameter.

Attitudes to *BRCA*-Testing- Item Response Theory:

The Item-Response Theory (IRT) was used to model responses of the 935 volunteers to the 18-items (covering positive-reasoning/negative-reasoning/cultural issues) regarding attitudes to *BRCA*-testing. IRT is a unified methodology for measuring of both individuals in terms of an unobserved latent trait ('ability') and the items themselves from the administered instrument on the same metric. Statistical models are used to relate the responses to the items in terms of item 'difficulty' and item 'discrimination'. Difficulty reflects the location of the item on the continuous trait, specifically the point where the item is successfully responded to with 50% probability. Discrimination reflects the steepness of the s-shaped (logistic) curve meaning how quickly the probability of 'success' changes with ability values near the item difficulty. A steeper item implies an item better able to discriminate between individuals closely placed on the continuum. Advantages of IRT over more common and simplistic methods of scoring include: the allowance for missing data– the latent value is estimated simply on the items that have been answered, and so is not generally test-dependent; the ability to compare item and individual simultaneously; and the characterisation of statistical uncertainty regarding parameters and scores.

In IRT the items are modelled by a collective set of logistic-regression type models. However, the items are 'regressed' on the latent trait which is unobserved. Hence, the trait is assumed to be

(standard) normally distributed and marginal maximum-likelihood estimation is used, with the assumed latent distribution integrated out. Because the items used in the (attitude to *BRCA*-testing) scale each have multiple responses in a naturally ordered manner (“Not-at-all important/Somewhat-important/Very-important”) we have used the graded response model (GRM) for each item, analogous to ordered logistic-regression. For each item category boundary there is a difficulty estimate (between “Not-at-all important/Somewhat important” and between “Somewhat-important/Very-important”) and a single discrimination parameter for each of the 18-items. Graphical methods used to display the GRM include: boundary characteristic curves (BCCs - where the next category becomes more likely), category characteristic curves (CCCs – the probability of response for each item category along the continuum), individual and overall item information functions (IIFs – showing the amount of statistical information reflected by the item or the scale as a whole, respectively), and the density plot of the scores. Attitudes to testing scores for each individual based on their response pattern were calculated marginally by integrating over the latent trait distribution and using the posterior-mean. The distribution of scores was investigated with a kernel density-plot. The association of socio-demographic factors with the GRM attitude to testing scores were also explored with multivariable linear regression.

Funding: The study underwent peer review and was funded by The Eve Appeal Charity (Grant award number- GTCV). The funding body (The Eve Appeal charity) had no role in the study design, data collection, analysis, interpretation or writing of the report or decision to submit for publication. The research team was independent of funders.

Core Outcome Sets (COS): There are no Core Outcome Sets for population or *BRCA* testing at present.

Patient & Public Involvement (PPI): The research team undertook an extensive community engagement exercise prior to commencement of the study. This included meetings with decision makers, Rabbis, Jewish Medical Association, numerous Jewish Charities and stakeholders across all sections of the Jewish community (e.g. Orthodox, Liberal, Reform, Masorti and Unaffiliated). This

was essential to understand the perspectives of all community stakeholders, address concerns, ensure stakeholder management, increase engagement and awareness as well as facilitate development and delivery of study. PPI stakeholders contributed to development and design of study materials, provided representation on the Trial Steering committee and also provided community based premises for conduct of the study. Supporting charities and organisations helped increase awareness of the study through organising workshops, meetings and newsletters. Feedback received highlighted the importance of having community based easily accessible centres for counselling (non-hospital settings) to promote anonymity and easy access. Charities- Jewish Care, Norwood, Agudas Israeli Housing Association provided premises for pre and post-test counselling. Input into patient facing document design helped highlight sensitive issues around testing and avoid anything the public may find insensitive or potentially offensive. The study title was also modified following feedback from the community. A cooling off period of 2 weeks was introduced to enable withdrawal in case people changed their minds. This PPI exercise was critical for the success of the study. *BRCA* testing is a sensitive issue and can lead to a range of opinions and emotions. It highlighted issues of concern in the community which were addressed by the study team prior to commencement of the study and also provided an opportunity of engagement to reassure stakeholders on the structure and governance around the study as well as the necessity and commitment to informed consent.

RESULTS

Overall 935 people underwent pre-test genetic-counselling in recruitment clinic clusters (256 Clusters, mean cluster size= 3.64) in the GCaPPS study. The mean age of participants was 53.8 (S.D=15.02) years. Table-1 describes the baseline characteristics of the cohort. Pre-counselling levels of 'interest' were much higher than levels of any clear 'intention' to undergo *BRCA*-testing (Table-1). While 96% expressed interest, only 60% indicated clear intention to undergo *BRCA*-testing pre-counselling. Overall 88% subsequently opted for *BRCA*-testing. Of these 67% were women (33% men), 59% had degree or higher level of education and 79% were married/cohabiting.

The association of socio-demographic variables with uptake, intention and interest in *BRCA*-testing observed on uni-variable and multi-variable logistic-regression analyses are described in Table-2. Increased cancer risk perception was significantly associated with higher levels of interest-in testing ($p=0.017$). Higher education level was associated with reduced intention-to test ($p=0.033$). However, higher levels of *BRCA*-related knowledge were associated with increased interest ($p=0.012$), intention-to test ($p=0.003$) as well as increased uptake of *BRCA*-testing ($p=0.002$). Increased anxiety (anxiety HADS $p= 0.009$; total HADS $p=0.016$) was associated with reduced uptake of *BRCA*-testing. Multivariable modelling confirmed that knowledge ($p=0.013$) and education ($p=0.01$) remained significantly associated with intention-to test, while being married/cohabiting was associated with four-fold higher odds of uptake of *BRCA*-testing ($p=0.009$) (Table-2). We did not find a statistically significant association of FH, gender, income or age with uptake/intention/interest in *BRCA*-testing.

The association of perceived benefits, risks and cultural factors with uptake of *BRCA*-testing as well as prior 'intention-to' test and 'interest' in *BRCA*-testing are given in Table-3. The various perceived benefits of *BRCA*-testing were significantly associated with higher pre-counselling odds of interest and intention to undergo *BRCA*-testing but not with actual uptake of testing (except to make childbearing decisions) (Table-3). The risks associated with insurance, confidentiality, emotional impact, inability to prevent cancer/lack of trust in modern medicine, were negatively associated with interest but not associated with intention-to undergo testing. However, increased importance attached to all the risks/limitations were significantly associated with lower-odds of uptake of *BRCA*-testing (Table-3). Increased levels of concern associated with focus on the Jewish ethnic community, singling out an ethnic group and marriage-ability were associated significantly lower interest/intention and lower odds of uptake of *BRCA*-testing. Altruism did not affect intention or uptake of *BRCA*-testing (Table-S1).

The individual item information functions (IIFs – showing the amount of statistical information reflected by each item of the scale) is given in Figure-S1. It suggests that reduction in uncertainty and reassurance were the most important of all factors associated with *BRCA*-testing. The category characteristic curves for the GRM are given in Figure-S2 and the boundary characteristic curves (BCCs) are given in Figure-S3. The density plot of the scores had a normal distribution and is given in Figure-S4. Table-4 provides the association of socio-demographic variables with the overall GRM attitude to testing (benefits/risks/cultural factors) scores. Men ($p=0.001$) and those with higher education ($p=0.001$) had lower attitude scores while those with children had higher scores ($p=0.005$) associated with *BRCA*-testing.

DISCUSSION

Main Findings

We found a high uptake of *BRCA*-testing (88%) reconfirming the broad acceptability/support for *BRCA*-testing in the AJ-population. The apparent benefits of cancer prevention, screening, reassurance, information about children's risk and reduction in uncertainty were major motivators for *BRCA*-testing. However, it was perceived disadvantages and cultural factors (not benefits) that were statistically significantly associated with final 'uptake' (lower odds) of *BRCA*-testing and differentiated 'acceptors' from 'decliners'. Marriage-ability, ethnic focus, stigmatization, confidentiality, insurance and emotional impact were concerns for some participants and associated with lower odds of undergoing *BRCA*-testing. Pre-test counselling enabled informed decision-making on uptake of testing. People with stronger attitudes towards *BRCA*-testing included women, those with less than degree level education and those with children. However, individuals with a PhD/Masters/Bachelors' degree had weaker attitude and lower levels of initial 'intention' than those with lower/no qualifications

Strengths and Limitations:

Strengths of our study include its population-based ascertainment, pre-test counselling for all, and presence of women and male participants. Our study population is likely to represent a good estimate and distribution of the characteristics of people who may come forward for population-based *BRCA*-testing should it be offered in the future. A limitation is lack of qualitative data on factors affecting attitude/uptake on *BRCA*-testing. Nevertheless, a number of our findings are consistent with qualitative data reported by others.¹⁰

Interpretation

Our findings of *BRCA*-testing acceptability are consistent with reports from Israel and Canada.^{3, 5, 10}

Our uptake was slightly higher than the 67% reported in the Israeli study.⁵ This could be due to population differences or recruitment location. Uptake rates appear to be higher when testing services are delivered in the community. Uptake rates reported in ambulatory clinics in the Israeli study were similar to ours. An extensive community engagement exercise undertaken during study development highlighted the importance of providing testing within the community outside a hospital environment and facilitated uptake. Additionally our study included standardised pre-test counselling.

Motivators for *BRCA*-testing observed by us have also been reported in the Israeli population-testing study,¹⁰ telephone surveys^{17, 25} and interviews with high-risk AJ women.¹⁹ While potential discrimination concerns some people, this is not widespread in the majority of the population. Unlike earlier reports¹⁹ we did not find altruism to be associated with uptake of *BRCA*-testing. Our findings in the low-risk AJ-population are consistent with some reports from high-risk clinics,^{15, 16} and indicate that people initially coming forward for *BRCA*-testing are better informed of its benefits, and rate these higher, while giving less consideration to limitations/risks. Our results suggest education and counselling in an unselected-Jewish-population leads to increased awareness of disadvantages

of *BRCA*-testing which does influence the final cost-benefit perception and choices people make.^{15, 16,}

18

The high level of initial ‘interest’ in *BRCA*-testing seen in our participants is consistent with self-referral. It has also been reflected in recruitment to the Israeli/Canadian studies and reported in earlier smaller studies of varying ascertainment.²⁵⁻²⁷ However, only 60% of participants indicated a clear ‘intention-to’ undergo testing before counselling. That 88% of attendees eventually consented to genetic-testing suggests that *BRCA*-testing may be acceptable to a large proportion of the AJ-population and reflects the impact of pre-test education/counselling on informed decision-making. Most of the 40% who had not thought about/would not consider/were still considering *BRCA1/2*-testing opted to proceed with testing.

The items used by us for evaluating benefits/risks/cultural influences (attitude) towards *BRCA*-testing have been adapted from items previously described and used by others in high-risk populations^{15, 16, 19, 20} and appear reliable and reproducible in a lower-risk population unselected for FH. The gender based differences in attitude is an interesting finding and explains why 30% more women came forward for testing compared to men. Limited data exist on differences between men and women towards *BRCA1/2*-testing. The main predictors reported for men include need to know about children’s risk and influence of women/other carriers in the family.²⁸⁻³⁰ Men have been stated to be less likely than women to alter screening practices, require support or experience a changed psychological state.³¹ Any population-screening programme will need to better understand and address the concerns of men. We found attitudinal factors were independent of FH of cancer. A positive correlation of attitude with knowledge¹⁵ and FH¹⁵ as well as an inverse¹⁸ correlation with FH has been previously reported. The mean age (53.8 years) of study participants was slightly older and probably reflects, the **age distribution of individuals proactively coming forward for testing in the study (self-referral based recruitment), greater awareness of these issues at older ages, the**

significantly older age of the Jewish population compared to the non-Jewish population in the UK (44 vs 38 years for women and 41 vs 36 years for men),³² as well as the likelihood that older individuals are more likely to be married (a factor significantly associated with uptake of testing). Nevertheless, study participants had a broad range of ages ranging from 18 years to 88 years, with 12% being <35 years and 21% <40 years. Our analyses are adjusted for age of participants and we did not find age to affect interest/intention/uptake or overall attitude towards *BRCA*-testing.

Our finding that individuals who were married/cohabiting were more likely to undergo *BRCA*-testing could partly reflect the importance of genetic-testing on marriage-ability in Jewish-communities and impact of our highlighting this issue at counselling prior to decision making. Baseline knowledge showed a significant association with final uptake as well as initial interest/intention for *BRCA*-testing. Baseline knowledge of volunteers in our study is higher than earlier reports.^{18, 33} This may reflect increasing public awareness and easier access to information on genes, cancer-risk and genetic-testing over the last decade. Higher levels of education are linked to increased concern regarding genetic-discrimination and may explain our findings of an inverse association with *BRCA*-testing.¹⁷ Our findings are consistent with earlier reports which found education²⁵ to be inversely correlated, knowledge¹⁵ positively correlated and FH or age to lack correlation^{19, 33} with intention-to-test. However, a positive correlation with FH^{15, 18} and none with education¹⁹ has also been reported.

The decision to undergo genetic-testing falls under the category of health decisions where there is no single paramount choice but the decision needs to be individualised depending on how the person values benefits/harms of the intervention. This can be complex, potentially difficult and dependent on numerous factors. Each factor has benefits and risks that people may value differently. It is important that individuals reflect on positive/negative consequences for informed decision making^{34, 35} based on their values/opinions. We found pre-test counselling in a low-risk population helped participants to weigh up the consequences of testing and enabled informed

decision making. Recent Canadian^{3, 6} and Israeli³⁶ single arm population-based studies provided post-test-counselling but not pre-test-counselling. Reports from the Canadian study suggest 58.5% women who tested positive and 19% overall would have preferred the opportunity to have had pre-test counselling.⁶ Nevertheless both 'pre-test' and 'post-test only' counselling approaches explored in all three population studies report similar and extremely high-levels of overall satisfaction of 91-95% with the testing process. Earlier randomised-trials found standard face-to-face pre-test counselling comparable with pre-test telephone, DVD-based and tele-genetic counselling.^{4, 37-40} The changing landscape, increasing awareness and expanding applicability enabling large scale high volume genetic-testing has resulted in exploration of novel approaches with a move away from traditional face-to-face counselling. A web-based decision-aid and telephone helpline approach for pre-test decision making is being piloted in a pilot population-based panel-testing study (PROMISE feasibility-study).⁴¹ However, there are currently no randomised data comparing pre-test counselling with 'no pre-test' or 'only post-test' counselling. This topic remains an important area for future research.

Conclusion

BRCA-testing is acceptable to a large proportion of AJ. Our findings show that a number of factors affecting *BRCA*-testing in a low-risk AJ population are similar to those previously reported from high-risk clinics. These data would be of interest to planners of genetic services and any population-based programme should this be instituted in the future. Pre-test counselling in the population-testing setting too facilitates informed-decision-making on *BRCA*-testing. Further research is needed to robustly compare pre-test counselling (current standard-of-care) with newer approaches such as pre-test decision-aids and/or helpline alone.

Acknowledgements:

The study is supported by researchers at the Barts Cancer Institute Cancer Research UK Centre for Excellence, Queen Mary University of London (C16420/A18066).

We are particularly grateful to the women and men who participated in the trial. We are grateful to the entire medical, nursing, and administrative staff who work on the GCaPPS trial and to the independent members of independent members of the trial steering committee (chaired by Prof Michael Baum) and data monitoring committee (chaired by Prof Jack Cuzick). We are especially grateful to Prof Michael Baum for his advice and support. We are grateful to the numerous supporting Jewish charities, community and religious organisations as well as numerous members of the Jewish community for their time, advice and support. We are grateful to Robert Liston, Vijay Devineni and Andy Ryan for their help with designing the trial management system and for IT support. We are grateful to the various regional genetic units in London (Great Ormond Street Hospital, Kennedy Galton Center Northwick Park Hospital, Guys Hospital and Royal Marsden Hospital) and the West Midlands Regional Genetics Service for their support of the study. We are grateful to the teams at Boots Pharmacy, Norwood, Jewish Care, Ovacome, Agudas Israel Housing Association, Academic Study group on Israel and the Middle East, Liberal Judaism, Movement for Reform Judaism, Indian Jewish Association, Stamford Hill Group Practice and Lane End Medical Center for their support. We are grateful to Dr Rohan Taylor, Katriina Whitaker, Mahesh Parmar, Anthony Silverstone, Margaret Jacobi, Marlana Schmool, Elizabeth Bancroft, Imelda Udeh, Naila Balogun, Judith Soloway, Jennifer Wiggins, Adina Roth, Hannah Lyons, Jane Lyons, Sarah Chamberlain, Michelle Johnson, Helen Mitchell, Katherine Duerden, Gemma Byrne, Fiona MacDonald, Louise Bayne, Ruth Payne and Dr Michelle Ferris for their support of the study.

Disclosures of interest

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, a Director of Women's Health Specialists Ltd and received consultancy from Beckton Dickinson. RM declares research funding from The Eve Appeal and Cancer Research UK into population testing and from Barts & the London Charity outside this work, as well as an honorarium for grant review from Israel National Institute for Health Policy Research. The other authors declare no conflict of interest.

Contribution to authorship

Conception: RM, IJ. Design & Development: RM, IJ and UM.

Questionnaire development: RM, SS, JW, IJ, UM, SG

Data collection and extraction: RM, FG, RD, KL

Data analysis: MB, RM

Preparation of tables and figures: RM, FG, MB

Trial management: RM, IJ, UM, KL, RD, JW, SG, LS, HD, YW, CC, IT, UB, AB

Genetic Testing and data collection from genetic laboratories: YW, CJ (Guys Hospital)

Initial draft of manuscript: RM, FG, MB

Manuscript writing and approval: RM, MB, FG, SS, KL, SG, LS, RD, AB, HD, YW, CC, CJ, IT, UB, UM, IJ.

Ethical approval

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 Randomized Controlled Trial Number

Register - ISRCTN 73338115 (<http://www.controlled-trials.com/ISRCTN73338115>)

All trial volunteers provided written informed consent to participate in the study.

Funding

This study was partly funded by 'The Eve Appeal' charity (grant number GTCV).

The study is supported by researchers at the Barts Cancer Institute Cancer Research UK Centre for Excellence, Queen Mary University of London (C16420/A18066).

The funding body (The Eve Appeal charity) had no role in the study design, data collection, analysis, interpretation or writing of the report or decision to submit for publication. The research team was independent of funders.

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.

References

1. Manchanda R, Loggenberg K, Sanderson S, Burnell M, Wardle J, Gessler S, et al. Population testing for cancer predisposing BRCA1/BRCA2 mutations in the Ashkenazi-Jewish community: a randomized controlled trial. *J Natl Cancer Inst.* 2015 Jan;107(1):379.
2. Gabai-Kapara E, Lahad A, Kaufman B, Friedman E, Segev S, Renbaum P, et al. Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2. *Proc Natl Acad Sci U S A.* 2014 Sep 30;111(39):14205-10.
3. Metcalfe KA, Poll A, Royer R, Llacuachaqui M, Tulman A, Sun P, et al. Screening for founder mutations in BRCA1 and BRCA2 in unselected Jewish women. *J Clin Oncol.* 2010 Jan 20;28(3):387-91.
4. Manchanda R, Burnell M, Loggenberg K, Desai R, Wardle J, Sanderson SC, et al. Cluster-randomised non-inferiority trial comparing DVD-assisted and traditional genetic counselling in systematic population testing for BRCA1/2 mutations. *J Med Genet.* 2016 Jul;53(7):472-80.
5. Lieberman S, Tomer A, Ben-Chetrit A, Olsha O, Strano S, Beeri R, et al. Population screening for BRCA1/BRCA2 founder mutations in Ashkenazi Jews: proactive recruitment compared with self-referral. *Genet Med.* 2016 Dec 08;10.1038/gim.2016.182.
6. Metcalfe KA, Poll A, Llacuachaqui M, Nanda S, Tulman A, Mian N, et al. Patient satisfaction and cancer-related distress among unselected Jewish women undergoing genetic testing for BRCA1 and BRCA2. *Clin Genet.* 2010 Nov;78(5):411-7.
7. Manchanda R, Legood R, Burnell M, McGuire A, Raikou M, Loggenberg K, et al. Cost-effectiveness of population screening for BRCA mutations in Ashkenazi Jewish women compared with family history-based testing. *J Natl Cancer Inst.* 2015 Jan;107(1):380.
8. Levy-Lahad E, Lahad A, King MC. Precision medicine meets public health: population screening for BRCA1 and BRCA2. *J Natl Cancer Inst.* 2015 Jan;107(1):420.
9. Manchanda R, Jacobs I. Genetic screening for gynecological cancer: where are we heading? *Future Oncol.* 2015 Dec 7.

10. Lieberman S, Lahad A, Tomer A, Cohen C, Levy-Lahad E, Raz A. Population screening for BRCA1/BRCA2 mutations: lessons from qualitative analysis of the screening experience. *Genet Med*. 2016 Dec 01;10.1038/gim.2016.175.
11. Genetic counseling. *Am J Hum Genet*. 1975 Mar;27(2):240-2.
12. Resta R, Biesecker BB, Bennett RL, Blum S, Hahn SE, Strecker MN, et al. A new definition of Genetic Counseling: National Society of Genetic Counselors' Task Force report. *J Genet Couns*. 2006 Apr;15(2):77-83.
13. NCI. Genetic Counselling. Cancer Genetics Overview (PDQ) 2013 31/07/2013 [cited 2013; Available from:
<http://www.cancer.gov/cancertopics/pdq/genetics/overview/healthprofessional/page2>
14. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983 Jun;67(6):361-70.
15. Lerman C, Biesecker B, Benkendorf JL, Kerner J, Gomez-Caminero A, Hughes C, et al. Controlled trial of pretest education approaches to enhance informed decision-making for BRCA1 gene testing. *J Natl Cancer Inst*. 1997 Jan 15;89(2):148-57.
16. Lerman C, Narod S, Schulman K, Hughes C, Gomez-Caminero A, Bonney G, et al. BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. *JAMA : the journal of the American Medical Association*. 1996 Jun 26;275(24):1885-92.
17. Lehmann LS, Weeks JC, Klar N, Garber JE. A population-based study of Ashkenazi Jewish women's attitudes toward genetic discrimination and BRCA1/2 testing. *Genet Med*. 2002 Sep-Oct;4(5):346-52.
18. Schwartz MD, Benkendorf J, Lerman C, Isaacs C, Ryan-Robertson A, Johnson L. Impact of educational print materials on knowledge, attitudes, and interest in BRCA1/BRCA2: testing among Ashkenazi Jewish women. *Cancer*. 2001 Aug 15;92(4):932-40.

19. Phillips KA, Warner E, Meschino WS, Hunter J, Abdolell M, Glendon G, et al. Perceptions of Ashkenazi Jewish breast cancer patients on genetic testing for mutations in BRCA1 and BRCA2. *Clin Genet*. 2000 May;57(5):376-83.
20. Andrews L, Meiser B, Apicella C, Tucker K. Psychological impact of genetic testing for breast cancer susceptibility in women of Ashkenazi Jewish background: a prospective study. *Genet Test*. 2004 Fall;8(3):240-7.
21. Sanderson SC, Wardle J, Jarvis MJ, Humphries SE. Public interest in genetic testing for susceptibility to heart disease and cancer: a population-based survey in the UK. *Prev Med*. 2004 Sep;39(3):458-64.
22. Bosompra K, Flynn BS, Ashikaga T, Rairikar CJ, Worden JK, Solomon LJ. Likelihood of undergoing genetic testing for cancer risk: a population-based study. *Preventive medicine*. 2000 Feb;30(2):155-66.
23. Bunn JY, Bosompra K, Ashikaga T, Flynn BS, Worden JK. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. *Preventive medicine*. 2002 Jun;34(6):567-77.
24. Prochaska JO, Velicer WF, Rossi JS, Goldstein MG, Marcus BH, Rakowski W, et al. Stages of change and decisional balance for 12 problem behaviors. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association*. 1994 Jan;13(1):39-46.
25. Press NA, Yasui Y, Reynolds S, Durfy SJ, Burke W. Women's interest in genetic testing for breast cancer susceptibility may be based on unrealistic expectations. *Am J Med Genet*. 2001 Mar 1;99(2):99-110.
26. Chaliki H, Loader S, Levenkron JC, Logan-Young W, Hall WJ, Rowley PT. Women's receptivity to testing for a genetic susceptibility to breast cancer. *American journal of public health*. 1995 Aug;85(8 Pt 1):1133-5.

27. Tambor ES, Rimer BK, Strigo TS. Genetic testing for breast cancer susceptibility: awareness and interest among women in the general population. *American journal of medical genetics*. 1997 Jan 10;68(1):43-9.
28. Hallowell N, Ardern-Jones A, Eeles R, Foster C, Lucassen A, Moynihan C, et al. Men's decision-making about predictive BRCA1/2 testing: the role of family. *Journal of genetic counseling*. 2005 Jun;14(3):207-17.
29. Lodder L, Frets PG, Trijsburg RW, Tibben A, Meijers-Heijboer EJ, Duivenvoorden HJ, et al. Men at risk of being a mutation carrier for hereditary breast/ovarian cancer: an exploration of attitudes and psychological functioning during genetic testing. *European journal of human genetics : EJHG*. 2001 Jul;9(7):492-500.
30. Shiloh S, Dagan E, Friedman I, Blank N, Friedman E. A follow-up study on men tested for BRCA1/BRCA2 mutations: impacts and coping processes. *Psycho-oncology*. 2011 Dec 2.
31. Liede A, Metcalfe K, Hanna D, Hoodfar E, Snyder C, Durham C, et al. Evaluation of the needs of male carriers of mutations in BRCA1 or BRCA2 who have undergone genetic counseling. *Am J Hum Genet*. 2000 Dec;67(6):1494-504.
32. JPR. JPR/ Report. Key trends in the British Jewish community. London, UK: Institute for Jewish Policy Research; 2011.
33. Durfy SJ, Bowen DJ, McTiernan A, Sporleder J, Burke W. Attitudes and interest in genetic testing for breast and ovarian cancer susceptibility in diverse groups of women in western Washington. *Cancer Epidemiol Biomarkers Prev*. 1999 Apr;8(4 Pt 2):369-75.
34. Briss P, Rimer B, Reilley B, Coates RC, Lee NC, Mullen P, et al. Promoting informed decisions about cancer screening in communities and healthcare systems. *Am J Prev Med*. 2004 Jan;26(1):67-80.
35. Sepucha KR, Fowler FJ, Jr., Mulley AG, Jr. Policy support for patient-centered care: the need for measurable improvements in decision quality. *Health Aff (Millwood)*. 2004;Suppl Variation:VAR54-62.

36. Levy-Lahad E, Gabai-Kapara E, Kaufman B, Catane R, Segev S, Renbaum P, et al. Identification of BRCA1/BRCA2 carriers by screening in the healthy population and its implications. American Society of Clinical Oncology, Annual meeting; 2011: J Clin Oncol 29: 2011 (suppl; abstr 1513); 2011.
37. Schwartz MD, Valdimarsdottir HB, Peshkin BN, Mandelblatt J, Nusbaum R, Huang AT, et al. Randomized noninferiority trial of telephone versus in-person genetic counseling for hereditary breast and ovarian cancer. J Clin Oncol. 2014 Mar 1;32(7):618-26.
38. Kinney AY, Butler KM, Schwartz MD, Mandelblatt JS, Boucher KM, Pappas LM, et al. Expanding access to BRCA1/2 genetic counseling with telephone delivery: a cluster randomized trial. J Natl Cancer Inst. 2014 Dec;106(12).
39. Kinney AY, Steffen LE, Brumbach BH, Kohlmann W, Du R, Lee JH, et al. Randomized Noninferiority Trial of Telephone Delivery of BRCA1/2 Genetic Counseling Compared With In-Person Counseling: 1-Year Follow-Up. J Clin Oncol. 2016 Aug 20;34(24):2914-24.
40. Buchanan AH, Datta SK, Skinner CS, Hollowell GP, Beresford HF, Freeland T, et al. Randomized Trial of Telegenetics vs. In-Person Cancer Genetic Counseling: Cost, Patient Satisfaction and Attendance. J Genet Couns. 2015 Apr 3.
41. Manchanda R. Predicting risk of ovarian malignancy improved screening and early detection feasibility study ISRCTN Registry: ISRCTN54246466. London, UK: BioMed Central; 2017.

Table-1: Baseline description of cohort

N=935		Mean	S.D
Age	Age in years	53.8	15.02
Number of Clusters		256	
Mean Cluster size		3.64	
HADS	HADS Anxiety	6.25	3.6
	HADS Depression	2.92	2.57
	HADS Total	9.18	5.36
Baseline Knowledge	Knowledge Score (S.D)	8.3	2.09
		n	%
Gender	Female	625	0.6684
	Male	310	0.3316
Children	yes	744	0.8185
	no	165	0.1815
Marital Status	Single/Divorced/Separated/ Widowed	196	0.2137
	Married/Cohabiting	721	0.7863
Education	Below degree Level (No-Formal- Qualification/ GCSE, O-level, CSE/ NVQ1,NVQ2/ A-level,NVQ-3/ NVQ-4)	361	0.4065
	Degree level or above (Bachelors/ Masters/ Phd)	527	0.5935
Income (£) (K=thousand)	<10K	42	0.0518
	10K-19.9K	64	0.0789
	20K-29.9K	82	0.1011
	30K-39.9K	99	0.1221
	40K-49.9K	92	0.1134
	≥50K	432	0.5327
Interest: Would you, in the next 6 months, have a BRCA1/2 genetic test	No Definitely Not	4	0.0046
	No Probably not	24	0.0278
	Yes Probably	293	0.3399
	Yes Definitely	541	0.6276
Intention: At the present time, what describes you best	Haven't thought about it/ Not considering BRCA1/2 testing	203	0.2358
	Considering BRCA1/2 testing	141	0.1638
	Probably will have BRCA1/2 testing	178	0.2067
	Definitely will have BRCA1/2 testing	339	0.3937
Uptake of genetic testing	Acceptors (Yes)	826	0.8834
	Decliners (No)	109	0.1166

FH- family history, HADS- hospital anxiety and depression scale, S.D – Standard Deviation

Table-2: Factors affecting Uptake, Intention and Interest in undergoing *BRCA*-testing

		Uptake Model				Intention Model				Interest Model			
		OR	SE	P> z	95% CI	OR	SE	P> z	95% CI	OR	SE	P> z	95% CI
MULTIVARIABLE MODELS FOR UPTAKE, INTENTION & INTEREST	Gender	0.73	0.283	0.473	0.31, 1.72	1.22	0.217	0.258	0.87, 1.71	1.05	0.229	0.819	0.69, 1.61
	Family History	0.66	0.473	0.565	0.16, 2.69	0.69	0.173	0.138	0.42, 1.13	0.8	0.229	0.432	0.45, 1.4
	Income (£)												
	10K-20K (£)	0.59	0.702	0.656	0.06, 6.12	0.73	0.399	0.56	0.25, 2.13	0.94	0.584	0.917	0.28, 3.18
	20K-30K (£)	0.32	0.381	0.339	0.03, 3.29	0.82	0.462	0.722	0.27, 2.48	1.31	0.788	0.647	0.41, 4.25
	30K-40K (£)	1.64	2.217	0.716	0.12, 23.27	0.69	0.375	0.494	0.24, 2.01	0.91	0.538	0.869	0.28, 2.9
	40K-50K (£)	1				0.65	0.319	0.381	0.25, 1.7	1.1	0.615	0.858	0.37, 3.29
	>50K (£)	0.46	0.48	0.457	0.06, 3.58	0.6	0.277	0.268	0.24, 1.48	1.05	0.553	0.92	0.38, 2.95
	Children	0.38	0.273	0.178	0.09, 1.56	0.76	0.218	0.343	0.43, 1.34	0.78	0.236	0.414	0.43, 1.41
	Education	1.79	0.925	0.261	0.65, 4.93	0.64	0.111	0.01	0.46, 0.09	0.8	0.172	0.306	0.53, 1.22
	Marital Status	4.03	2.159	0.009	1.41, 11.52	1.17	0.311	0.563	0.69, 1.97	1.47	0.417	0.17	0.85, 2.57
	Age	1.01	0.017	0.403	0.98, 1.05	1.01	0.007	0.137	0.99, 1.02	1.01	0.008	0.145	0.99, 1.03
	HADS Total	0.99	0.033	0.814	0.93, 1.06	0.97	0.016	0.07	0.94, 1.03	0.96	0.019	0.052	0.92, 1.0
	Knowledge	1.03	0.138	0.826	0.79, 1.34	1.17	0.049	0.013	1.02, 1.22	1.1	0.059	0.075	0.99, 1.22
	Cancer Risk Perception	0.999	0.002	0.658	0.99, 1.002	1.002	0.003	0.402	0.997, 1.008	1.01	0.004	0.079	0.999, 1.02
UNIVARIATE MODELS FOR UPTAKE, INTENTION & INTEREST		Uptake				Intention				Interest			
		OR	SE	P> z	95% CI	OR	SE	P> z	95% CI	OR	SE	P> z	95% CI
	Gender	0.871	0.164	0.463	0.601, 1.261	0.902	0.120	0.441	0.694, 1.172	0.890	0.134	0.446	0.663, 1.198
	Family History	0.62	0.296	0.316	0.243, 1.58	0.734	0.149	0.127	0.494, 1.091	0.750	0.170	0.202	0.478, 1.168
	Income (£)			0.621				0.569				0.893	
	10K-20K (£)	2.022	1.303	0.274	0.573, 7.146	1.220	0.447	0.588	0.595, 2.502	0.860	0.380	0.734	0.363, 2.045
	20K-30K (£)	0.986	0.558	0.980	0.325, 2.991	1.194	0.422	0.616	0.598, 2.386	0.860	0.358	0.711	0.377, 1.946
	30K-40K (£)	2.253	1.435	0.202	0.647, 7.851	1.410	0.509	0.342	0.694, 2.862	1.100	0.475	0.734	0.512, 2.585
	40K-50K (£)	1.580	0.938	0.440	0.494, 5.060	1.089	0.381	0.808	0.548, 2.161	0.930	0.369	0.861	0.430, 2.024
	>50K (£)	1.371	0.664	0.514	0.531, 3.544	0.966	0.290	0.909	0.536, 1.741	1.060	0.379	0.854	0.532, 2.142
	Children	0.972	0.262	0.917	0.572, 1.651	0.885	0.158	0.495	0.624, 1.256	0.910	0.175	0.613	0.621, 1.325
	Education	1.260	0.275	0.288	0.822, 1.936	0.774	0.093	0.033	0.612, 0.979	0.910	0.131	0.508	0.686, 1.206
	Marital Status	1.525	0.383	0.093	0.932, 2.496	1.136	0.173	0.403	0.842, 1.532	1.340	0.229	0.083	0.96, 1.87
	Age	0.987	0.008	0.112	0.970, 1.003	0.997	0.004	0.441	0.988, 1.005	0.990	0.005	0.244	0.984, 1.004
	HADS Total	0.960	0.017	0.016	0.925, 0.992	0.988	0.012	0.342	0.964, 1.013	0.980	0.013	0.115	0.953, 1.005
	HADS Anxiety	0.930	0.026	0.009	0.879, 0.982	0.991	0.018	0.597	0.957, 1.026	0.970	0.019	0.107	0.932, 1.007
	HADS Depression	0.950	0.037	0.233	0.883, 1.031	0.964	0.026	0.178	0.915, 1.017	0.970	0.029	0.289	0.92, 1.03
	Knowledge	1.180	0.063	0.002	1.062, 1.311	1.103	0.036	0.003	1.035, 1.175	1.090	0.039	0.012	1.02, 1.17
	Cancer Risk Perception	0.998	0.002	0.500	0.995, 1.002	1.003	0.003	0.352	0.997, 1.008	1.008	0.003	0.017	1.001, 1.015

OR- odds ratio; SE- standard error, K- thousand, HADS- hospital anxiety and depression scale, CI- confidence interval.

Table-3: Attitudes towards *BRCA*-testing

FACTORS		Uptake				Intention				Interest			
BENEFITS		OR	SE	P >Chisq	95% CI	OR	SE	P >Chisq	95% CI	OR	SE	P >Chisq	95% CI
To be reassured	Somewhat imp	0.188	-2.36	0.0618	0.047, 0.753	1.18	0.248	0.0001	0.779, 1.779	1.26	0.303	<0.0005	0.790, 2.021
	Very imp	0.188	-2.25		0.044, 0.805	2	0.425		1.319, 3.034	2.49	0.612		1.539, 4.031
To enhance cancer prevention	Somewhat imp	1.4	0.537	0.3772	0.662, 2.970	1.39	0.659	0.0062	0.555, 3.524	1.25	0.571	<0.0005	0.512, 3.061
	Very imp	*				2.19	0.999		0.900, 5.360	3.03	1.36		1.257, 7.303
To learn about my children's risk	Somewhat imp	1.03	0.327	0.935	0.550, 1.916	1.19	0.55	0.0019	0.480, 2.947	1.08	0.547	0.0009	0.401, 2.917
	Very imp	*				1.96	0.859		0.835, 4.630	2.08	1.01		0.798, 5.412
To make a decision about preventive surgery	Somewhat imp	1.02	0.373	0.597	0.499, 2.091	1.04	0.21	0.016	0.706, 1.553	0.93	0.212	0.0003	0.595, 1.457
	Very imp	1.43	0.54		0.682, 2.999	1.61	0.325		1.090, 2.399	2.24	0.567		1.362, 3.680
To make childbearing decisions	Somewhat imp	1.04	0.698	0.028	0.284, 3.869	0.66	0.169	0.189	0.397, 1.087	1.06	0.344	0.7734	0.561, 2.002
	Very imp	0.351	0.145		0.156, 0.789	1.02	0.299		0.580, 1.818	0.8	0.267		0.418, 1.542
To know if I need to get cancer screening	Somewhat imp	1.014	0.272	0.959	0.598, 1.718	1.21	0.554	0.0002	0.495, 2.973	0.83	0.367	<0.0005	0.353, 1.976
	Very imp	*				2.1	0.929		0.888, 5.002	2.27	0.993		0.965, 5.354
To reduce uncertainty	Somewhat imp	0.215	0.158	0.111	0.051, 0.908	1.16	0.275	0.0211	0.726, 1.847	1.02	0.258	<0.0005	0.624, 1.678
	Very imp	0.229	0.166		0.056, 0.951	1.59	0.38		0.997, 2.542	2.21	0.588		1.309, 3.720
RISKS / LIMITATIONS		OR	SE	P >Chisq	95% CI	OR	SE	P >Chisq	95% CI	OR	SE	P >Chisq	95% CI
Worried about losing my insurance	Somewhat imp	0.518	0.169	<0.0005	0.273, 0.985	0.88	0.144	0.743	0.640, 1.215	0.64	0.117	0.0009	0.450, 0.918
	Very imp	0.233	0.075		0.124, 0.440	0.97	0.176		0.675, 1.381	0.46	0.104		0.295, 0.715
Worried about loss of confidentiality	Somewhat imp	0.32	0.1	<0.0005	0.174, 0.591	0.77	0.134	0.311	0.543, 1.082	0.55	0.113	0.0026	0.369, 0.827
	Very imp	0.243	0.087		0.120, 0.493	0.9	0.2		0.583, 1.392	0.55	0.137		0.338, 0.899
Worried about stigmatization	Somewhat imp	0.275	0.094	<0.0005	0.142, 0.536	0.83	0.199	0.679	0.516, 1.329	0.72	0.222	0.476	0.395, 1.321
	Very imp	0.181	0.093		0.066, 0.494	1.13	0.405		0.556, 2.281	0.76	0.315		0.338, 1.715
Do not trust modern medicine	Somewhat imp	0.374	0.159		0.162, 0.863	0.71	0.147	0.22	0.476, 1.069	0.54	0.179	0.034	0.284, 1.036
	Very imp	0.097	0.058	0.0001	0.030, 0.312	0.78	0.257		0.409, 1.491	0.39	0.184		0.154, 0.984
Nothing that can be done to prevent getting cancer	Somewhat imp	0.64	0.189	0.011	0.272, 1.072	0.59	0.103	0.011	0.422, 0.835	0.44	0.091	0.0002	0.297, 0.664
	Very imp	0.396	0.131		0.207, 0.759	0.85	0.154		0.596, 1.212	0.97	0.216		0.630, 1.506
Concerned about the effect it would have on my family	Somewhat imp	0.373	0.132	<0.0005	0.187, 0.746	0.84	0.135	0.384	0.614, 1.151	0.66	0.123	0.059	0.457, 0.950
	Very imp	0.218	0.073		0.114, 0.419	0.82	0.127		0.602, 1.108	0.72	0.142		0.496, 1.067
Concerned that I could not handle it emotionally	Somewhat imp	0.556	0.184	<0.0005	0.291, 1.064	0.73	0.112	0.054	0.539, 0.985	0.79	0.141	0.0013	0.554, 1.120
	Very imp	0.129	0.045		0.066, 0.254	0.69	0.129		0.480, 0.995	0.43	0.101		0.273, 0.684

OR- odds ratio, SE- standard error, CI- confidence interval.

*omitted due to collinearity

'Not at all important' - Reference category for the first 14 items.

Table-4: Factors affecting overall attitude (risks, limitations and cultural factors) towards testing

Theta_GRM	Coeff	SE	P> t	95% CI
Gender	-0.252	0.077	0.001	-0.404, -0.100
Family History	-0.038	0.115	0.738	-0.264, 0.188
Income (£)				
10K-20K (£)	-0.006	0.239	0.98	-0.476, 0.464
20K-30K (£)	-0.016	0.253	0.95	-0.515, 0.483
30K-40K (£)	-0.027	0.24	0.911	-0.500, 0.447
40K-50K (£)	0.036	0.23	0.876	-0.417, 0.489
>50K (£)	-0.164	0.22	0.456	-0.597, 0.269
Children	0.335	0.117	0.005	0.103, 0.506
Education	-0.3	0.087	0.001	-0.472, -0.129
Marital Status	0.057	0.107	0.593	-0.153, 0.268
Age	-0.002	0.003	0.496	-0.007, 0.003
HADS Total	0.017	0.007	0.018	0.003, 0.03
Knowledge	0.002	0.018	0.914	-0.034, 0.038
Cancer Risk Perception	0.0002	0.0006	0.783	-0.001, 0.001

Coeff- coefficient, SE- standard error, CI- confidence interval, K- thousand, HADS- hospital anxiety and depression scale

Table S1- Cultural/Religious factors affecting Attitudes towards *BRCA*-testing

CULTURAL / RELIGIOUS		OR	SE	P >Chisq	95% CI	OR	SE	P >Chisq	95% CI	OR	SE	P >Chisq	95% CI
Worried that the study is too focused on Jewish community	Somewhat	0.417	0.134	0.0067	0.222, 0.784	0.5	0.092	0.0005	0.347, 0.716	0.33	0.074	<0.0005	0.22, 0.51
	Yes, definitely	0.293	0.293		0.076, 1.127	1.37	0.615		0.571, 3.306	0.57	0.435	0.13	0.13, 2.5
Concerned that being a gene carrier might alter marriage prospects for myself or my family members	Somewhat	0.357	0.12	0.0024	0.185, 0.690	0.6	0.135	0.07	0.382, 0.932	0.44	0.101	0.0017	0.28, 0.69
	Yes, definitely	0.38	0.212		0.127, 1.138	0.77	0.285		0.373, 1.592	1.1	0.614		0.37, 3.28
Concerned genetic information might be used to single out individuals of a particular ethnic group	Somewhat	0.462	0.135	0.0059	0.260, 0.822	0.55	0.116	0.018	0.363, 0.832	0.45	0.093	0.0004	0.30, 0.68
	Yes, definitely	0.307	0.164		0.108, 0.876	0.87	0.352		0.392, 1.922	0.52	0.233		0.22, 1.25
Potential to improve the health of the Jewish Community will influence my decision to be tested	Somewhat	0.936	0.284	0.564	0.517, 1.696	0.65	0.116	0.055	0.460, 0.924	0.46	0.103	0.0007	0.30, 0.71
	Yes, definitely	1.27	0.38		0.707, 2.284	0.79	0.126		0.582, 1.085	0.72	0.144		0.49, 1.07

OR- odds ratio, SE- standard error, CI- confidence interval.

‘Definitely not’ - Reference category for the last 4 items.

Figure S1

Item Information Functions

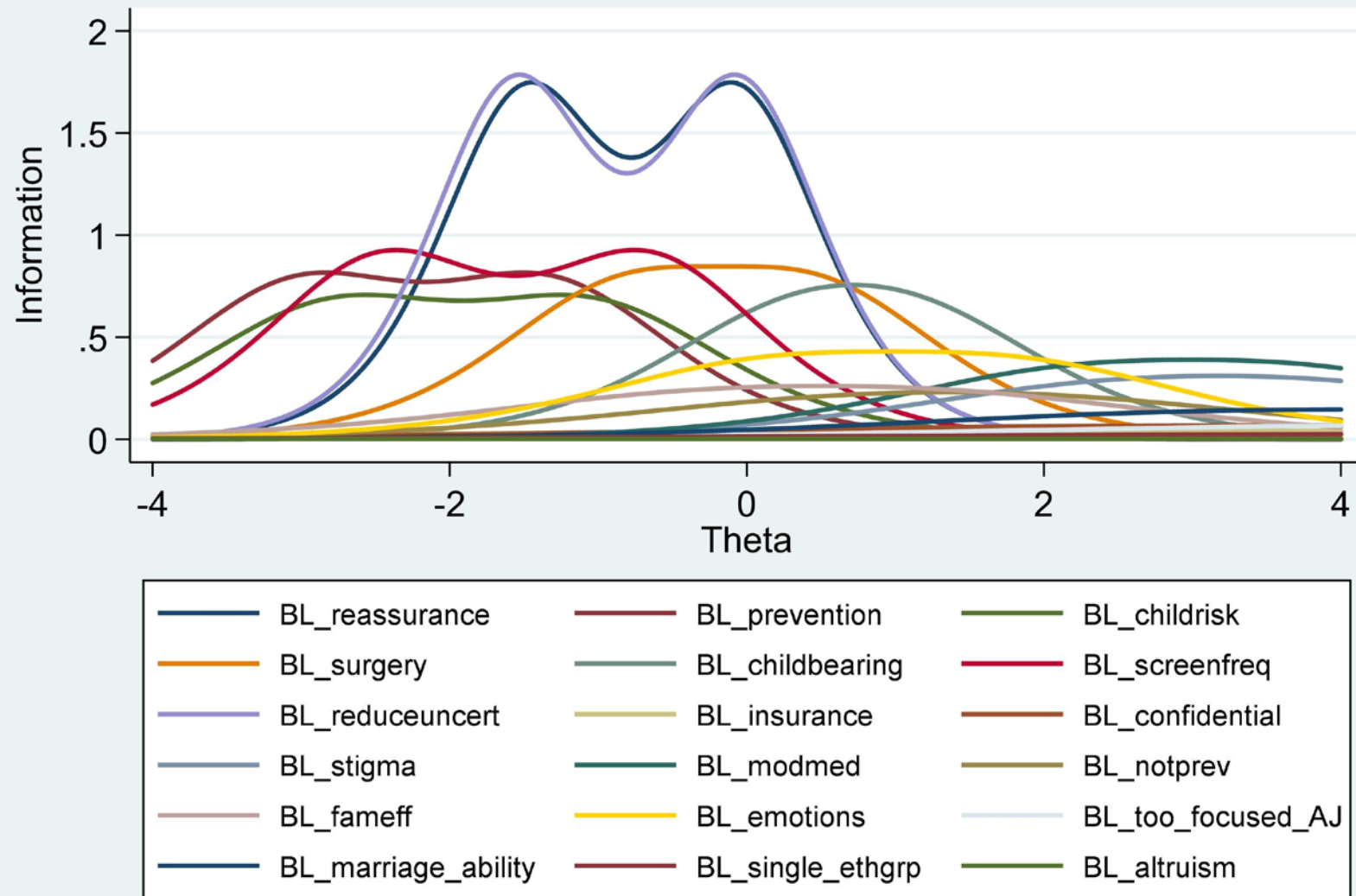


Figure S2: Category Characteristic Curves

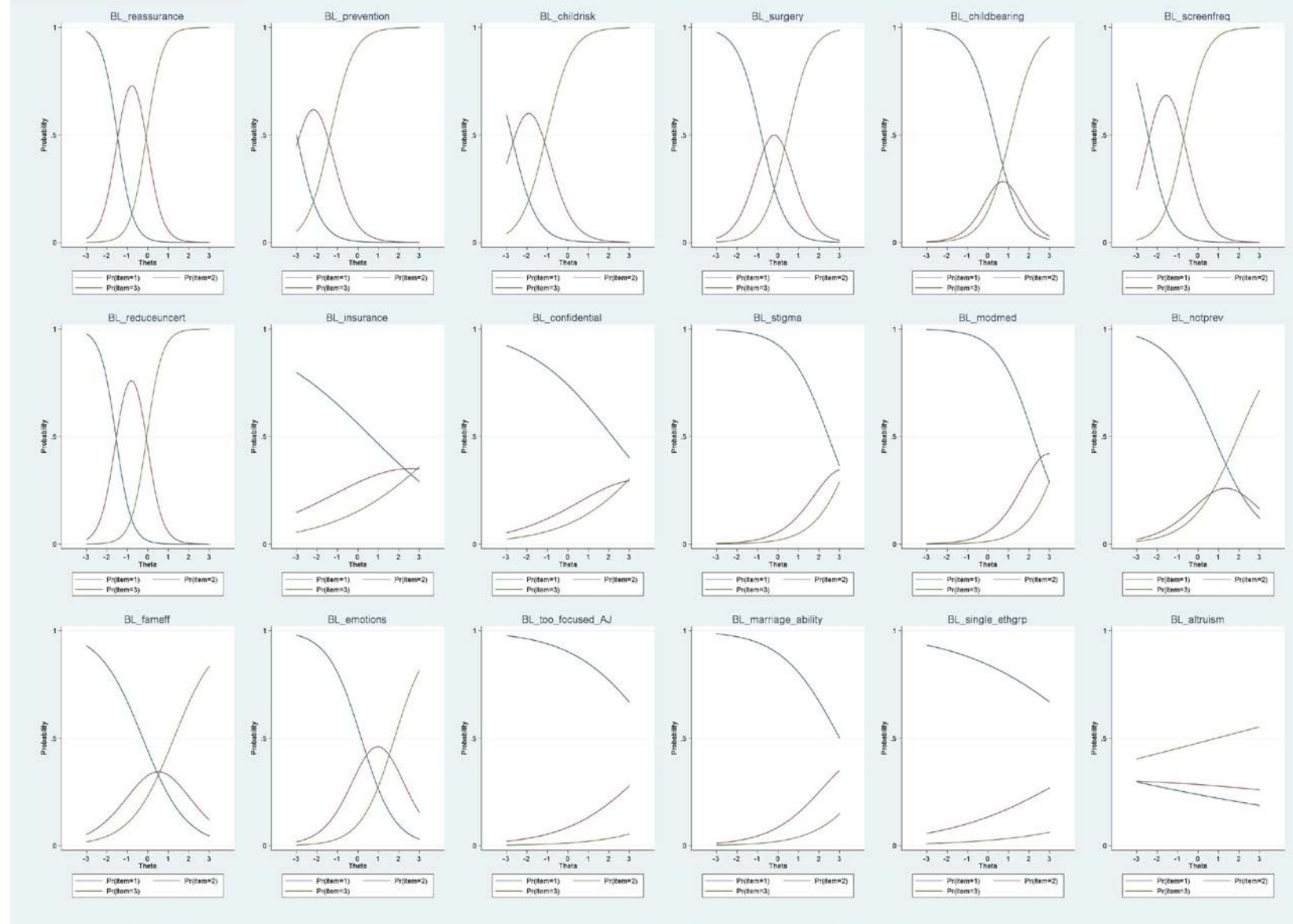


Figure S3: Boundary Characteristic Curves

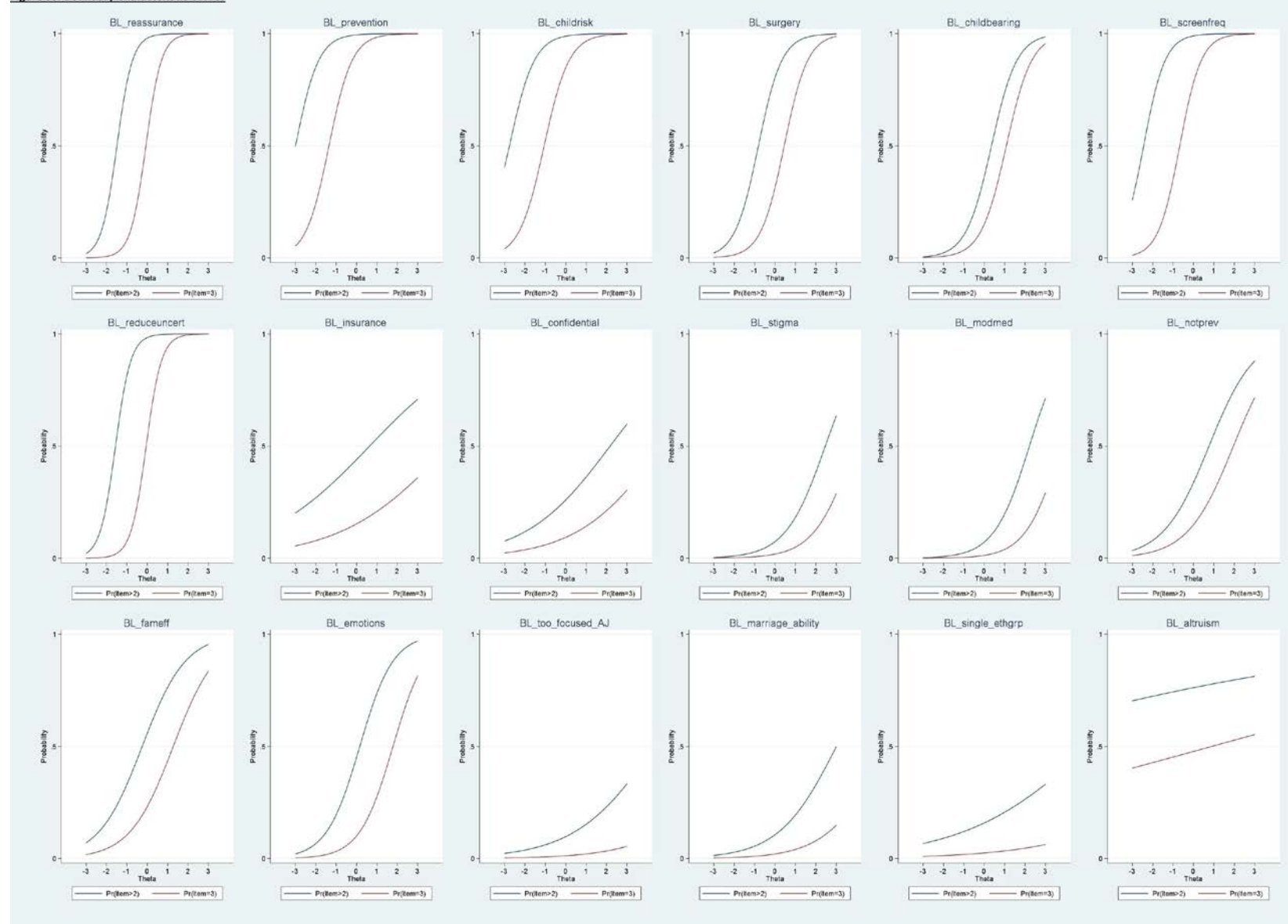
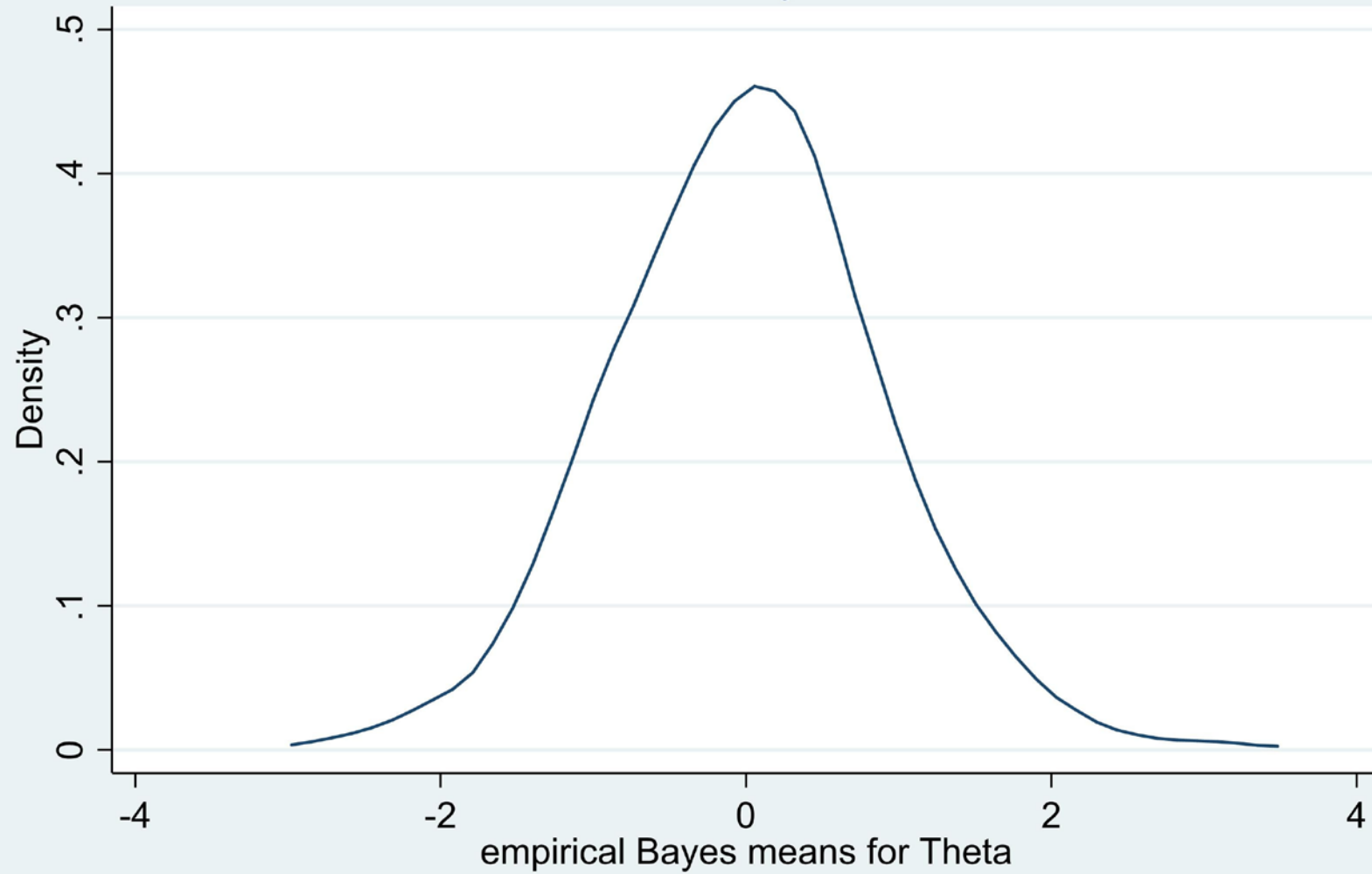


Figure S4: Density Plot of Attitude Scores

Kernel density estimate



kernel = epanechnikov, bandwidth = 0.3000