

Jewish Cultural and Religious factors and uptake of Population based *BRCA* testing across denominations: a cohort study

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Running short Title: Jewish cultural-religious factors & population BRCA testing

Jewish cultural and religious factors and uptake of population-based *BRCA*-testing across denominations: a cohort study

Objective

To evaluate the association of Jewish cultural and religious identity and denominational affiliation with interest-in, intention-to undertake and uptake-of population-based *BRCA* (*Breast Cancer Gene*)-testing

Design

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

Setting

London Ashkenazi-Jewish(AJ) population

Population or Sample

AJ men and women, >18years

Methods

Participants were self-referred, and attended recruitment clinics(clusters) for pre-test counselling. Subsequently consenting individuals underwent *BRCA*-testing. Participants self-identified to one Jewish denomination: Conservative/Liberal/Reform/Traditional/Orthodox/Unaffiliated. Validated scales measured Jewish Cultural-Identity (JI) and Jewish Religious-identity (JR). 4-item Likert-scales analysed initial 'interest' and 'intention-to-test' pre-counselling. Item-Response-Theory and graded-response-models, modelled responses to JI and JR scales. Ordered/multinomial logistic regression modelling evaluated association of JI-scale, JR-scale and Jewish Denominational affiliation on interest, intention and uptake-of *BRCA*-testing.

Main Outcome Measures:

Interest, intention, uptake-of *BRCA*-testing

Results

935 AJ women/men of mean-age=53.8 (S.D=15.02) years, received pre-test education and counselling through 256 recruitment clinic clusters (median cluster size=3). Denominational

affiliations included Conservative/Masorti=91(10.2%); Liberal=82(9.2%), Reform=135(15.1%), Traditional=212(23.7%), Orthodox=239(26.7%); and Unaffiliated/Non-practising=135(15.1%). Overall *BRCA*-testing uptake was 88%. Pre-counselling 96% expressed interest and 60% intention-to test. JI and JR scores were highest for Orthodox, followed by Conservative/Masorti, Traditional, Reform, Liberal and Unaffiliated Jewish denominations. Regression modelling showed no significant association between overall Jewish Cultural or Religious Identity with either interest, intention or uptake-of *BRCA*-testing. Interest, intention and uptake of *BRCA*-testing was not significantly associated with denominational affiliation.

Conclusions

Jewish religious/cultural identity and denominational affiliation do not appear to influence interest, intention or uptake of population-based *BRCA*-testing. *BRCA*-testing was robust across all Jewish denominations.

Funding

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Key-words

BRCA, population-based, Ashkenazi-Jewish, denomination, cultural, religious.

Tweetable Abstract

Jewish cultural/religious factors don't affect *BRCA*-testing with robust uptake seen across all denominational affiliations.

INTRODUCTION

Around 1/40 Ashkenazi Jewish (AJ) individuals carry one of the three common Jewish *BRCA* pathogenic variants called founder mutations. Population *BRCA* prevalence is 5-8 times higher in AJ than the general non-Jewish population.¹⁻³ Women carrying *BRCA1/BRCA2* mutations have a 17-44% ovarian cancer risk and 69-72% breast cancer risk till 80-years,⁴ most of which are potentially preventable. *BRCA* founder mutations cause 10% of breast cancers and 40% ovarian cancers in the Jewish population (a 2.5-fold higher proportion than the non-Jewish population). Carrier identification enables unaffected individuals (including those further identified through cascade testing) to access and opt for screening and preventive interventions to minimise their cancer risk: risk-reducing salpingo-oophorectomy (RRSO) to reduce their ovarian cancer risk^{5,6}, MRI/mammography screening, risk reducing mastectomy (RRM)⁷, or chemoprevention with selective estrogen receptor modulators (SERM) to reduce their breast cancer risk.⁸ Population-based *BRCA* testing in the AJ population has been shown to be feasible, acceptable, and safe. There is no evidence of harm to quality-of-life or psychological well-being and there is a reduction in long-term anxiety.^{1,9} Additionally, population-testing identifies up to 2.5 times the number of *BRCA*-carriers compared to current clinical criteria or family history (FH) based testing.^{1,9,10} The chance of carrying a non founder *BRCA* pathogenic variant if an AJ individual tests negative is extremely small, and testing for founder mutations alone obviates the need to deal with variants of uncertain significance. *BRCA*-testing can be delivered in a community setting^{11,12} and has been shown to be extremely cost-effective.^{13,14} These conclusions have led to calls for changing public health policy and national/international guidelines.¹⁵ US-based National Comprehensive Cancer Network (NCCN) guidelines, now support testing in unaffected Jewish individuals provided 'there is access to pre-test education along with post-test counselling, additional genetic testing if indicated and high-risk management.' Israel has recently changed national policy to offer population based *BRCA*-testing through their health system and pilot implementation sites are being considered for the UK National

Health Service (NHS) (*personal communication Cancer Programme Director, NHS England and Improvement*).

Whether to undergo *BRCA* testing or not involves complex decision making on several levels. It is vital to understand the various factors affecting uptake of *BRCA* testing in the Jewish population. This is essential to help with planning of future genetic testing programmes, implementing the necessary supportive care/community services and establishing relevant clinical pathways. A number of epidemiological and demographic variables have been shown to be associated with attitudes towards *BRCA* testing and subsequently the uptake of *BRCA* testing. Being married/cohabiting, having children, ability to reduce uncertainty, reassurance, perceived benefits such as reducing cancer risk are positively associated with *BRCA* testing.¹¹ While, the risks/limitations such as concerns around insurance, confidentiality, emotional impact, marriage-ability, and ethnic focus, are associated with lower odds of undergoing testing.¹¹ The Jewish community has a distinct identity which is a combination of elements of both a 'religious identity' and 'cultural identity'.¹⁶ Both religious as well as cultural factors are known to affect cancer screening¹⁷ and may also affect uptake of *BRCA* testing. However, empirical data focusing specifically on the cultural-religious identity in the AJ population and its outlook towards population *BRCA* testing are lacking. Additionally the Jewish population has distinct branches or denominations which have number of religious and cultural differences. Commonly described denominations in the UK include Conservative, Liberal, Reform, Traditional, Orthodox and Unaffiliated/Non-practising. It is unknown whether interest, intention or uptake of *BRCA*-testing differs across these Jewish denominational affiliations. Successful implementation of any future population-wide testing programme will need to develop effective approaches that take into account cultural and religious sensitivities. In this paper we address the gaps described above by examining the effect of denominational affiliation and religious and cultural outlook on interest in, intention to undertake and actual uptake of population-based *BRCA*-testing in participants recruited to the Genetic Cancer-Prediction through Population-Screening (GCaPPS) trial (ISRCTN73338115).^{9, 12}

METHODS

AJ individuals over 18 years of age living in North London, who had not had prior genetic testing, irrespective of their FH of cancer, were offered *BRCA* testing for the three AJ founder mutations^{9,12}: 185delAG(c.68_69delAG), 5382insC(c.5266dupC) and 6174delT(c.5946delT). Awareness was established through an extensive cross-denominational community engagement process (see below). All participants received a pre-test education booklet and counselling by a qualified genetic-counsellor or a clinical-fellow experienced in cancer-genetics risk-assessment and management to enable informed decision making. Counselling was structured to meet the goals of genetic-counselling and covered cancer risk, genetic inheritance, FH, risk management, psychosocial implications, as well as advantages/disadvantages of testing.¹⁸⁻²⁰ Recruitment was undertaken through community based counselling clinics (clusters) in a randomised setting using traditional face-to-face and DVD-counselling approaches, which have been shown to be non-inferior/equivalent.¹² Demographic and FH data were collected at baseline. Participants self-identified to one of six Jewish denominations (mentioned above). Validated scales were used to measure cultural and religious identity. Jewish Cultural Identity (JI) was assessed using an adapted version of the Multigroup Ethnic Identity Measure (14-item scale) initially used by Phinney (1992)²¹ and subsequently adapted (the word 'ethnic' was replaced to 'Jewish) and validated by Bowen et al (2003).¹⁷ A Likert-scale (Strongly disagree, Disagree, Agree, Strongly agree) was used to assess each item of the questionnaire. Jewish 'Religious' identity (JR) was assessed with a 5-item scale from Bowen (2003).¹⁷ Four items are assessed by a 6-point Likert-scales and one item by a 4-point Likert-scale. The JI and JR scales are given in Supplementary Table-S1.

'Interest' in undergoing *BRCA*-testing was assessed by the question: '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?' A 4-item Likert-scale (yes-definitely/yes-probably/no probably-not/no definitely-not) evaluated the responses. This scale was chosen because most people plan a specific behaviour

change up to six months into the future,²² and was adapted from earlier research.²³⁻²⁵ Intention-to-undergo *BRCA*-testing was evaluated by the question: “At the present time, which of the following statements describes you best?": Haven’t thought about/not considering *BRCA*-testing; Considering *BRCA*-testing; Probably-will have *BRCA*-testing; Definitely-will have *BRCA*-testing. This item was adapted from Lerman²⁶ and Schwartz.²⁷ Uptake of testing was calculated by the proportion of individuals who actually underwent *BRCA*-testing following counselling.

Statistical Analysis:

Baseline characteristics were calculated using descriptive statistics.

Scoring Jewish Cultural Identity and Religiousness - Item Response Theory

We used Item Response Theory (IRT) to estimate the value of the latent traits of Jewish Cultural Identity (JI) and Jewish Religiousness (JR) amongst the 935 trial volunteers. IRT is a unified methodology for the 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 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 both JI and JR scales each have multiple responses in a naturally ordered manner (for example strongly disagree, disagree, agree, strongly agree) 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 (e.g. between strongly disagree versus disagree, agree and strongly agree) and a single discrimination parameter for each item. 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).

Association of Jewish Cultural Identity and Jewish Religiousness with Interest, Intention and Uptake of *BRCA*-testing

The JI and JR scale scores derived by IRT were used as predictor variables in regression models for 1) interest in *BRCA*-testing; 2) intention of volunteers regarding undergoing *BRCA*-testing, and 3) uptake of *BRCA*-testing. For outcomes 1) and 2) the question had four possible answers and were modelled using ordered logistic regression. Uptake of *BRCA*-testing was a binary response so standard logistic regression was used. In all models in this paper, including the IRT models (above), cluster robust standard errors were calculated, with the cluster based on genetic counselling clinics. Joint Wald tests were used to test the joint significance of more than one parameter. In addition, the interest, intention and uptake outcomes were regressed on the individual JI and JR sub-scale items using ordered logistic regression.

Jewish Denomination Self-Description

Self described Jewish Denominational affiliation (Non-Practicing /Unaffiliated, Conservative, Liberal, Orthodox, Reform, Traditional) was also used to examine any associations with intention, interest and uptake as a predictor in (multinomial) logistic regression models. Finally, the JI and JR scale

scores were regressed on the given self-description denominational affiliation using linear regression. Additionally, all pair wise comparisons were undertaken between denominational affiliations with p-values adjusted for multiple comparisons (Bonferroni adjustment).

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

Patient & Public Involvement (PPI): the study was preceded by an extensive engagement exercise with all stakeholders and key decision makers from the UK Jewish community including community leaders, Rabbis, Jewish Charities and Jewish Medical Association. Representation was ensured across all Jewish denominations. Community stakeholders supported development and design of study materials, provided locations and equipment for conduct of the study, supported recruitment, as well as membership of trial oversight committees. This process helped underscore sensitivities around genetic testing and address the concerns raised by the community at the outset. It helped ensure close stakeholder engagement and reassure community representatives of the design, structure, governance and informed consent process associated with the study.

RESULTS

Pre-test education and counselling in the GCaPPS study was provided to 935 AJ individuals through 256 recruitment clinic clusters (mean cluster size=3.64). Of these 91 (10.2%) were Conservative/Masorti, 82 (9.2%) Liberal, 135 (15.1%) Reform, 212 (23.7%) Traditional, 239 (26.7%) Orthodox and 135 (15.1%) Unaffiliated/ Non-practising. The mean age of participants was 53.8 (S.D=15.02) years, of whom 310 (33%) were men, 625 (67%) women, 721 (79%) were married/cohabiting, and 744 (81%) had children. Gender distribution by denominational affiliation included:

Conservative/Masorti Men=29% and women=71%; Liberal Men=34% and women=66%; Reform

Men=33% and women=67%; Traditional Men=28% and women=72%; Orthodox Men=38% and women=62%; Unaffiliated/ Non-practising Men=39% and women=61%. Pre-counselling 96% had expressed interest but only 60% indicated clear intention to undergo (probably/definitely will undergo) *BRCA* testing at the outset. Overall 88% participants opted for *BRCA* testing. Uptake rates were 85.7% for Conservative/Masorti, 90.2% Liberal, 88.9% Reform, 89.1% Traditional, 87% Orthodox and 92% for Unaffiliated/Non-practising denominational affiliations. Gender did not affect uptake of testing ($p=0.536$).

The individual item information functions (IIFs – showing the amount of statistical information reflected by each item of the scale) for JI and JR scales are given in Figure-1. It suggests that feeling a strong attachment towards the Jewish community and feeling good about one's Jewish background were the two most important items for cultural identity, followed by having a strong sense of belonging to the Jewish community which together provided most information on the JI scale. Attending religious services regularly and the frequency of religious services attended were the two most important factors contributing to the religious identity followed by frequency of observation of religious holidays. These provided most information on the JR scale. The category characteristic curves (CCCs) for the JR scale GRM are given in Figure-S1 and the boundary characteristic curves (BCCs) are given in Figure-S2. The category characteristic curves (CCCs) for the JI scale GRM are given in Figure-S3 and the boundary characteristic curves (BCCs) are given in Figure-S4.

Evaluation of impact of each of the individual items within the construct of the JI and JR scales on interest, intention and uptake of *BRCA*-testing using graded response models (see supplementary table S2) suggested that those who had higher frequency of attendance of religious services had lower pre-counselling odds (OR ranging from 0.67 to 0.91) of intention to undergo *BRCA*-testing ($p=0.024$) and those who increasingly celebrated Jewish holidays ($p=0.042$) had lower pre-counselling odds (OR ranging from 0.70 to 0.88) of intention to undergo *BRCA*-testing. Additionally,

those who attached higher importance to attending religious services had lower odds of uptake of testing ($p=0.03$) and those for whom religious beliefs provided greater comfort & support had lower odds (OR ranging from 0.27 to 0.6) of undergoing *BRCA*-testing ($p=0.015$). Individuals who agreed (OR 2.9; CI 0.98, 8.55) or strongly-agreed (OR 3.7; CI 1.3, 10.8) with feeling good about their Jewish cultural background had 3-4 times higher odds of interest in *BRCA*-testing ($p=0.035$); and those who agreed (OR 4.96; CI 1.45, 16.99) or strongly-agreed (OR 3.9; CI 1.12, 13.7) with feeling good about their Jewish cultural background had 4-5 times higher odds of uptake of *BRCA*-testing ($p=0.05$). Those who had a clear sense of their Jewish heritage had greater intention to undergo testing pre-counselling ($p=0.036$). A number of these estimates have wide confidence intervals and some of the p values are borderline. Details are given in supplementary table-S2.

However, when the overall JI or JR questionnaire scale was considered, regression modelling showed no statistically significant association between overall Jewish Cultural Identity (JI scale score) or Jewish Religiousness (JR scale scores), with either interest or intention or uptake of *BRCA*-testing (Table-1).

Both the JI and JR scale scores were significantly different ($p<0.0001$) and appeared to discriminate between the various Jewish Denominations (Table-2, Figure-2). All possible pair wise comparisons undertaken between denominational affiliations, with p -values adjusted for multiple comparisons (Bonferroni adjustment) indicated most of these comparisons (12 of 15 JI and 13 of 15 JR scale comparisons) were highly significant. Both Cultural identity and Religious identity scores were highest for Orthodox Jews, followed by Conservative/Masorti, Traditional, Reform, Liberal and Unaffiliated Jewish denominations in descending order (Table-2, Figure-2). However, there was no significant difference in outcomes of interest in *BRCA*-testing, intention to undergo *BRCA*-testing or final uptake of *BRCA*-testing observed between any of these six Jewish groups. This indicates that

interest, intention and uptake of *BRCA*-testing is equally robust irrespective of denominational affiliation.

DISCUSSION

Main Findings:

For the first time we report on the impact of Jewish cultural and religious identity as it relates to population based *BRCA* testing. While a number of cultural and religious factors were important for decision making, the 'interest in' or 'intention to undergo' or 'uptake of' *BRCA* testing was not affected by overall Jewish identity and was also independent of the Jewish denominational affiliation, whether Orthodox, Reform, Liberal, Conservative, Traditional or Unaffiliated.

Strengths and limitations:

Our study has a number of strengths including, population based cohort design, pre-test counselling for all, good representation from all Jewish groups or denominations including the unaffiliated, inclusion of both men and women, its unselected ascertainment irrespective of cancer history, extensive community engagement and use of validated scales to assess outcomes. Our study is illustrative of attributes and characteristics of individuals who are likely to opt for unselected *BRCA*-testing from the UK Jewish population. Lack of corroborating qualitative data is a limitation of the study. Additionally, the study does not account for any possible regional variation in the UK, as it was based in London. However, two thirds of the UK Jewish population resides in London²⁸ and the study had broad representation from across different sections of the Jewish community. While all denominational affiliations are well represented and had high uptake, there remains some uncertainty around the degree to which the distribution of denominational affiliations in our study mirrors the true distribution of denominational affiliation in the UK, and this can be a limitation as it may not reflect the overall uptake that would occur if offered to all Jewry. An accurate estimate of

the true denominational affiliation in the wider UK Jewish population is difficult to come by. A 2011 Jewish Policy Research (JPR) report suggests 65% may be orthodox²⁹ and compared to this figure, the orthodox denomination is underrepresented in our study. However, this report ignores the 'unaffiliated' which are a substantial number, and denominational data are ascertained through household registration in synagogues unlike our study where participants are asked to report their affiliation. Hence, proportions for the various denominations in this report²⁹ are upwardly biased. Additionally a number of the 'Central Orthodox' category in this publication²⁹ are members of United Synagogue/Federation of Synagogues and may describe themselves as 'Traditional' if asked. We could not find separate statistics on the proportion of UK Jews who are 'unaffiliated' but a Pew Report suggests 30% of American Jews describe themselves as 'unaffiliated'.³⁰ A subsequent 2014 JPR publication²⁸ which directly surveyed 9895 Jewish individuals from 3736 households reports denominational statistics nearer to our findings, describing 26% Jews as traditional, 18% as reform or progressive and 16% as Orthodox.²⁸ A final limitation is that our study does not address the needs, attitudes and intentions of the small non-Ashkenazi, that is, Sephardi, Mizrahi and Dutch-Portuguese communities within the broad umbrella of Anglo-Jewry.

Interpretation:

Jewish identity is an amalgamation of several complex components refracted through both religious and cultural dimensions. Our finding that cultural-religious identity and communal affiliation does not overall appear to significantly affect interest, intention and uptake of *BRCA* testing, suggests that genetic (*BRCA*) testing related health behaviour could be less strongly linked to cultural-religious behaviour in the UK AJ population than in other ethno-religious groups. It is well-known that cultural values and religious stipulations, as well as ethnic practices and cultural taboos, play important roles in health behaviour.³¹ As a case in point, this has also been demonstrated in the high-risk AJ population with respect to breast cancer screening practices, wherein a stronger religious identity has been positively associated with intention to undergo breast screening.¹⁷ A smaller study in high

risk Jewish women in the USA, reported religious identity to be negatively associated and cultural identity positively associated with 'intention-to undergo' genetic testing.¹⁷ However, our data do not show this to be the case in an unselected UK AJ population with respect to *BRCA*-testing. These differences might reflect the intention behaviour gap (as the aforementioned study evaluated intention rather than actual behaviour), the impact of genetic counselling (as only 60% intended to undergo *BRCA*-testing at the outset) or population differences. It might also reflect the widespread Jewish principle of 'pikuach nefesh', the religious obligation to save a life in jeopardy (including ones own), which influences Jewish health-related thinking both for religiously affiliated and secular Jews.³² Nevertheless, similar to earlier reports, sub-scale analysis in this study showed that those who felt good about their Jewish cultural background were more likely to undergo *BRCA*-testing. Whereas those for whom attending religious services was important and where religious beliefs provided greater comfort & support were less likely to do so. Overall we had a high rate of uptake of genetic testing in an unaffected unselected population. Varying rates of uptake of genetic testing which are both similar and lower have been reported in individuals undergoing clinical-criteria based testing in high risk families through cancer genetics clinics.^{33, 34} Genetic testing uptake is also known to increase with time and has been found to be higher in women than men.³⁴ However, we did not find a gender based difference in uptake rates, though more women were recruited to our study than men.

The Jewish community is religiously and culturally diverse. Many British Jews do not identify as religious and synagogue membership is not necessarily an indicator of cultural identification or religious practice. The fact that our JI and JR scales discriminated between the six Jewish denominations/ groups adds to the robustness of the results that Jewish denomination does not affect *BRCA* testing behaviour. All these branches in the Jewish community have distinct though at times slightly overlapping identities. We too found a small overlap mainly between reform and liberal denominations; and between conservative/masorti and traditional denominations. The more

religious and orthodox sections of the community have previously been perceived to be less engaged with health behaviour related to cancer prevention or early diagnosis. Rabbinic consultation has been highlighted as an important factor in medical decision making particularly in the Orthodox community.³⁵ The fact that we found equally high uptake rates of *BRCA*-testing across the different Jewish groups is an extremely important finding and one that has not been reported before. This may also be reflective of the extensive community engagement including with Rabbis and religious leaders from all Jewish denominations that preceded our study, resulting in a large number of community and religious groups from all sections of the community supporting the study. A cross sectional survey in the US indicated higher uptake of *BRCA* testing in Modern Orthodox Jews compared to Ultra-Orthodox sub-groups.³⁵ However, this study did not include members of non-orthodox Jewish denominations or unaffiliated Jews. Other factors affecting decision making found in this study are similar to those reported before.¹¹

We have previously reported on perceived benefits, risks, epidemiological and socio-economic factors affecting uptake of population-based *BRCA*-testing in the AJ population.¹¹ Here we for the first time address the important issue of role of Jewish identity and denominational affiliation on population based *BRCA* testing. Our findings are important and reassuring given the ongoing implementation of population based *BRCA* testing in the Jewish population in Israel as well as the planned/potential implementation in the UK and other parts of the world in the near future. It is important that the offer of genetic testing is not withheld by clinicians on the basis of Jewish denomination. Our study also highlights the importance of broadest possible stakeholder engagement and management being necessary for successful implementation of population based testing.

Conclusion:

Jewish religious and cultural identity do not appear to influence attitudes towards population based *BRCA*-testing. Interest in, intention to undergo and actual uptake of *BRCA*-testing was similar across all Jewish denominations: Orthodox, Reform, Liberal, Conservative, Traditional or Unaffiliated.

Data availability

Relevant anonymised data can be obtained on reasonable request from the corresponding author on completion of secondary analyses which are ongoing.

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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. RM declares research funding from The Eve Appeal and Cancer Research UK into population testing and from Barts & the London Charity and Rose Trees Trust outside this work, an honorarium for grant review from Israel National Institute for Health Policy Research and honorarium for advisory board membership from Astrazeneca/MSD/GSK. RM is supported by an NHS Innovation Accelerator (NIA) Fellowship for population testing. The other authors declare no conflict of interest.

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Ethics Declaration

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, and for publication of de-identified participant data.

Disclosure

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Table-1: Regression models for effect of Jewish Identity and Jewish Religious scales on overall interest, intention, uptake of *BRCA*-testing

Legend

OR- Odds Ratio, SE- Standard Error, CI- Confidence Interval, GRM- graded response model

Models depict the odds of 'interest in', 'intention to undergo' and 'uptake of' *BRCA* testing, for each Standard Deviation increase in score of 'Jewish Identity (JI) and Jewish Religious (JR) Scales respectively.

Table-2: Regression models for Jewish Cultural Identity and Religious Scores by Jewish

Denomination

Legend

SE- Standard Error, CI- Confidence Interval, GRM- graded response model

Reference Category- Unaffiliated / Non-practising

Figure-1: Item Information Functions Cultural Identity scale and Religious Identity scale

The **Right panel** of this figure shows the amount of statistical information reflected by Cultural Identity scale. **Right panel A**, reflects the amount of statistical information contained overall in the scale. **Right panel B** of this figure shows the amount of statistical information reflected by each of the different (n=14) items contributing to the Cultural Identity scale. The greater the area under each curve (for each item), the greater the contribution of the item to the overall construct of the scale.

'Attachment' and 'Background' were the two most important of all Cultural Identity factors associated with *BRCA*-testing

Identity_Search: I have spent time trying to find out more about my own Jewish heritage / identity, such as history, traditions and customs

Active_Participation: I am active in organizations or social groups that include mostly members of the Jewish community

Sense_Heritage: I have a clear sense of Jewish heritage and what it means to me

Affect_By_Heritage: I think a lot about my life will be affected by my Jewish heritage

Happy: I am happy that I am Jewish

Notclear_Heritage: I am not very clear about the role of Jewish heritage in my life

Time_Spent_History: I really have not spent much time trying to learn more about Jewish history

Strong_Sense: I have a strong sense of belonging to the Jewish community

Understanding_Jewish_Heritage: I Understand pretty well what Jewish heritage means to me in terms of relating Jews and non-Jews

Heritage_Learning: In order to learn more about my Jewish heritage, I have often talked about the Jewish community

Pride: I have a lot of pride in the Jewish community and its accomplishment

Culture_Participation: I participate in Jewish culture, such as Jewish food, music and customs.

Attachment: I feel a strong attachment towards the Jewish community

Background: I feel good about my Jewish Background

The **Left panel** of this figure shows the amount of statistical information reflected by Religious Identity scale. **Left panel A**, reflects the amount of statistical information contained overall in the scale. The **Left Panel B** of this figure shows the amount of statistical information reflected by each of the different (n=5) items contributing to the Religious Identity scale. The greater the area under each curve (for each item), the greater the contribution of the item to the overall construct of the scale. 'Religious_Service' and 'Religious_Service_Frequency' were the two most important of all Religious Identity factors associated with *BRCA*-testing

Religious_Service: How important is it to you to attend religious services regularly?

Religious_Celebration: How often do you observe / celebrate religious holidays at home?

Religious_Service_Frequency: How frequently do you attend religious services?

Religious_Strength: How strong would you say your religious or spiritual faith is?

Religious_Comfort: How much do religious or spiritual beliefs serve as a source of comfort & support?

Figure 2: Jewish Identity Scale and Jewish Religiousness Scale IRT model scores by Jewish

Denomination

X-axis: Jewish Denomination Categories: 1= Non-Practicing / Unaffiliated; 2= Conservative / Masorti; 3= Liberal; 4= Orthodox; 5= Reform; 6= Traditional

Y-axis Left Panel: Jewish Identity Scale Item Response Theory (IRT) model scores

Y-axis Right Panel: Jewish Religiousness Scale Item Response Theory (IRT) model scores

This figure depicts the distribution of JI and JR scale scores across the six different Jewish denominations

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VIDEO ABSTRACT

This article has a Video Abstract presented by Ranjit Manchanda

Table-1: Regression models for effect of Jewish Identity and Jewish Religious scales on overall interest, intention, uptake of BRCA-testing

	JEWISH IDENTITY SCALE					JEWISH RELIGIOUS SCALE			
	INTEREST					INTEREST			
	OR	SE	P> z	95% CI		OR	SE	P> z	95% CI
Theta JI GRM	1.073	0.082	0.354	0.92, 1.25	Theta J- REL GRM	1.014	0.08	0.866	0.86-1.19
	INTENTION					INTENTION			
	OR	SE	P> z	95% CI		OR	SE	P> z	95% CI
Theta JI GRM	0.965	0.057	0.551	0.86, 1.08	Theta J- REL GRM	0.90	0.058	0.114	0.80, 1.02
	UPTAKE OF TESTING					UPTAKE OF TESTING			
	OR	SE	P> z	95% CI		OR	SE	P> z	95% CI
Theta JI GRM	0.997	0.122	0.978	0.78, 1.27	Theta J- REL GRM	0.822	0.089	0.071	0.67, 1.02

OR- Odds Ratio, SE- Standard Error, CI- Confidence Interval, GRM- graded response model

Models depict the odds of 'interest in', 'intention to undergo' and 'uptake of' BRCA testing, for each Standard Deviation increase in score of 'Jewish Identity (JI) and Jewish Religious (JR) Scales respectively.

Table-2: Regression models for Jewish Cultural Identity and Religious Scores by Jewish

Denomination

Theta JI GRM	JEWISH IDENTITY SCORE				Theta J-REL GRM	JEWISH RELIGIOUS SCORE			
	Coeff	SE	P> t	95% CI		Coeff	SE	P> t	95% CI
Conservative / Masorti	1.126	0.11	<0.0001	0.91, 1.34	Conservative / Masorti	1.550	0.086	<0.0001	1.38, 1.72
Liberal	0.755	0.096	<0.0001	0.57, 0.95	Liberal	1.053	0.08	<0.0001	0.90, 1.21
Orthodox	1.6	0.084	<0.0001	1.44, 1.77	Orthodox	2.257	0.073	<0.0001	2.11, 2.40
Reform	0.866	0.082	<0.0001	0.071, 1.03	Reform	1.163	0.084	<0.0001	0.997, 1.33
Traditional	0.979	0.074	<0.0001	0.83, 1.13	Traditional	1.41	0.063	<0.0001	1.28, 1.53

SE- Standard Error, CI- Confidence Interval, GRM- graded response model

Reference Category- Unaffiliated / Non-practising

Figure-1: Item Information Functions Cultural Identity scale and Religious Identity scale

The **Right panel** of this figure shows the amount of statistical information reflected by Cultural Identity scale. **Right panel A**, reflects the amount of statistical information contained overall in the scale. **Right panel B** of this figure shows the amount of statistical information reflected by each of the different (n=14) items contributing to the Cultural Identity scale. The greater the area under each curve (for each item), the greater the contribution of the item to the overall construct of the scale.

'Attachment' and 'Background' were the two most important of all Cultural Identity factors associated with *BRCA*-testing

Identity_Search: I have spent time trying to find out more about my own Jewish heritage / identity, such as history, traditions and customs

Active_Participation: I am active in organizations or social groups that include mostly members of the Jewish community

Sense_Heritage: I have a clear sense of Jewish heritage and what it means to me

Affect_By_Heritage: I think a lot about my life will be affected by my Jewish heritage

Happy: I am happy that I am Jewish

Notclear_Heritage: I am not very clear about the role of Jewish heritage in my life

Time_Spent_History: I really have not spent much time trying to learn more about Jewish history

Strong_Sense: I have a strong sense of belonging to the Jewish community

Understanding_Jewish_Heritage: I Understand pretty well what Jewish heritage means to me in terms of relating Jews and non-Jews

Heritage_Learning: In order to learn more about my Jewish heritage, I have often talked about the Jewish community

Pride: I have a lot of pride in the Jewish community and its accomplishment

Culture_Participation: I participate in Jewish culture, such as Jewish food, music and customs.

Attachment: I feel a strong attachment towards the Jewish community

Background: I feel good about my Jewish Background

The **Left panel** of this figure shows the amount of statistical information reflected by Religious Identity scale. **Left panel A**, reflects the amount of statistical information contained overall in the scale. The **Left Panel B** of this figure shows the amount of statistical information reflected by each of the different (n=5) items contributing to the Religious Identity scale. The greater the area under each curve (for each item), the greater the contribution of the item to the overall construct of the scale. 'Religious_Service' and 'Religious_Service_Frequency' were the two most important of all Religious Identity factors associated with *BRCA*-testing

Religious_Service: How important is it to you to attend religious services regularly?

Religious_Celebration: How often do you observe / celebrate religious holidays at home?

Religious_Service_Frequency: How frequently do you attend religious services?

Religious_Strength: How strong would you say your religious or spiritual faith is?

Religious_Comfort: How much do religious or spiritual beliefs serve as a source of comfort & support?

Figure 2: Jewish Identity Scale and Jewish Religiousness Scale IRT model scores by Jewish

Denomination

X-axis: Jewish Denomination Categories: 1= Non-Practicing / Unaffiliated; 2= Conservative / Masorti;

3= Liberal; 4= Orthodox; 5= Reform; 6= Traditional

Y-axis Left Panel: Jewish Identity Scale Item Response Theory (IRT) model scores

Y-axis Right Panel: Jewish Religiousness Scale Item Response Theory (IRT) model scores

This figure depicts the distribution of JI and JR scale scores across the six different Jewish denominations

Figure-1

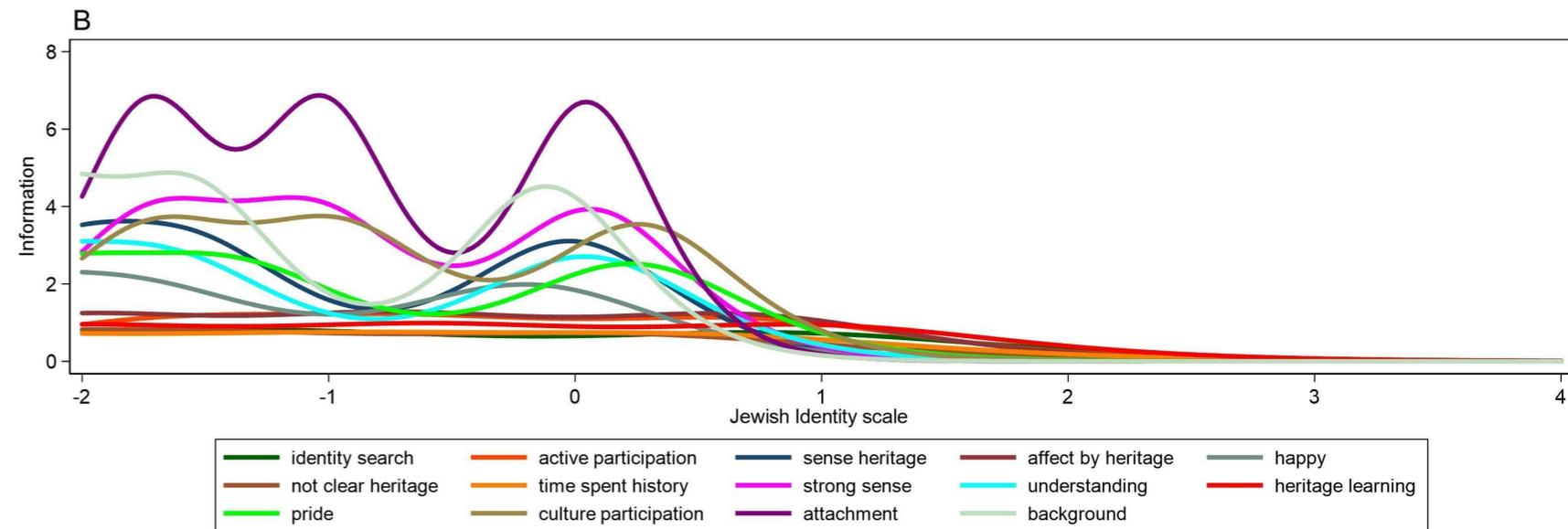
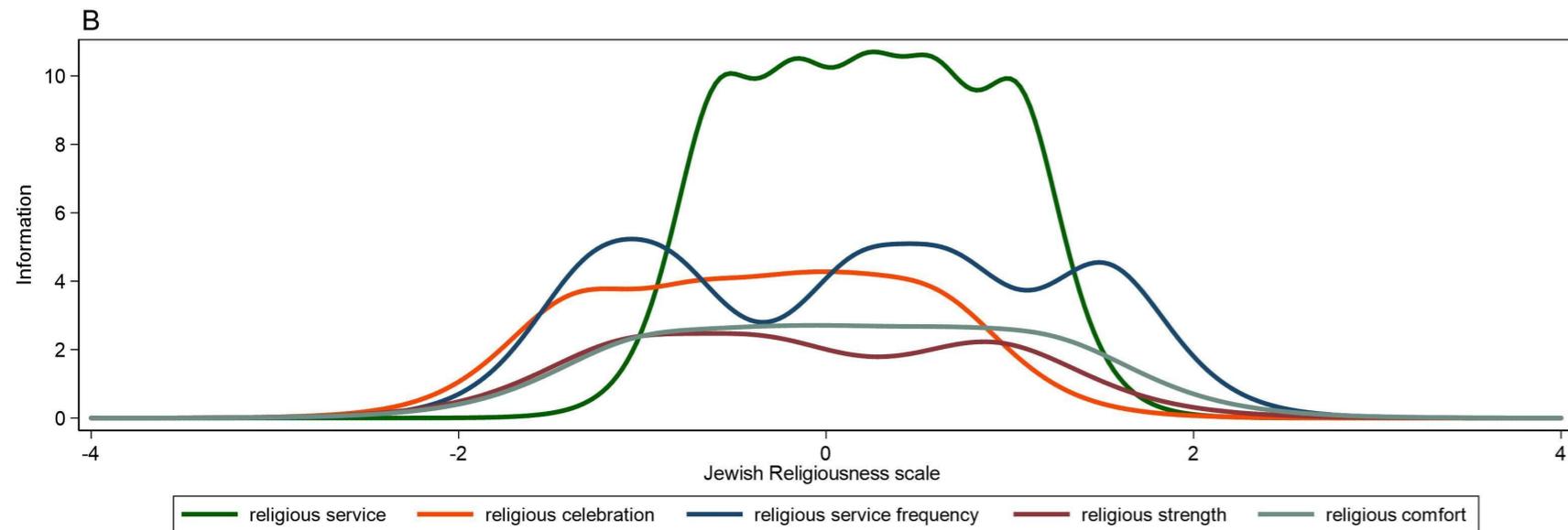
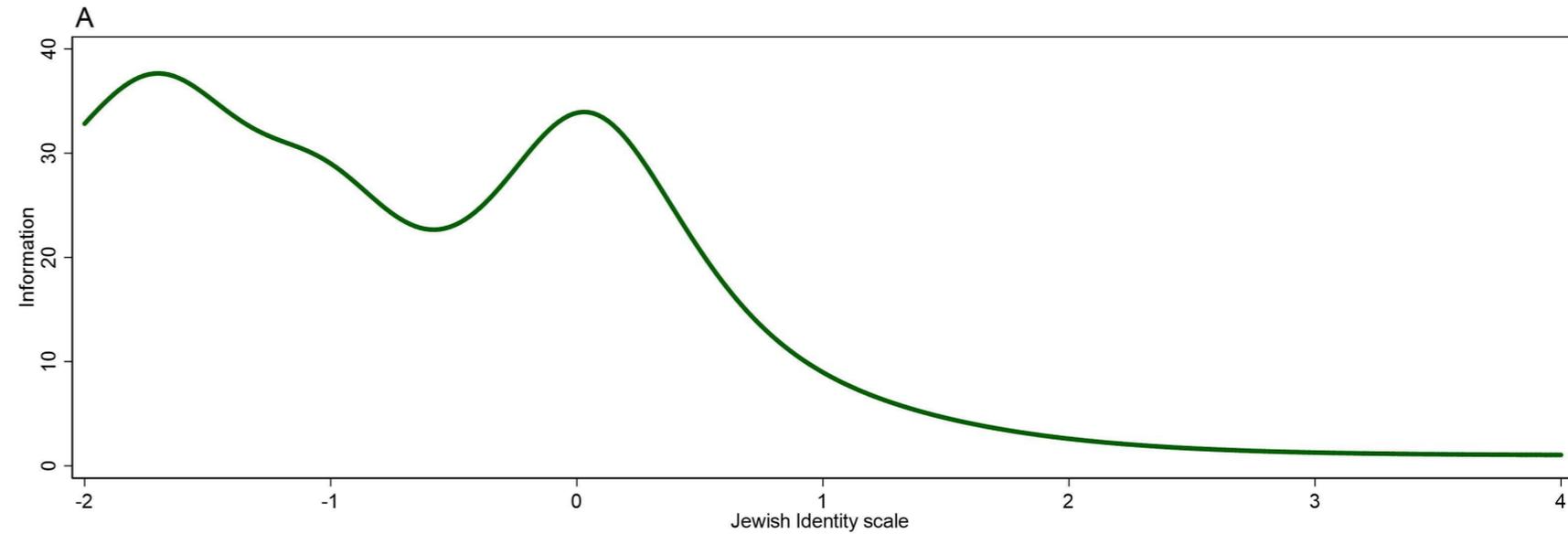
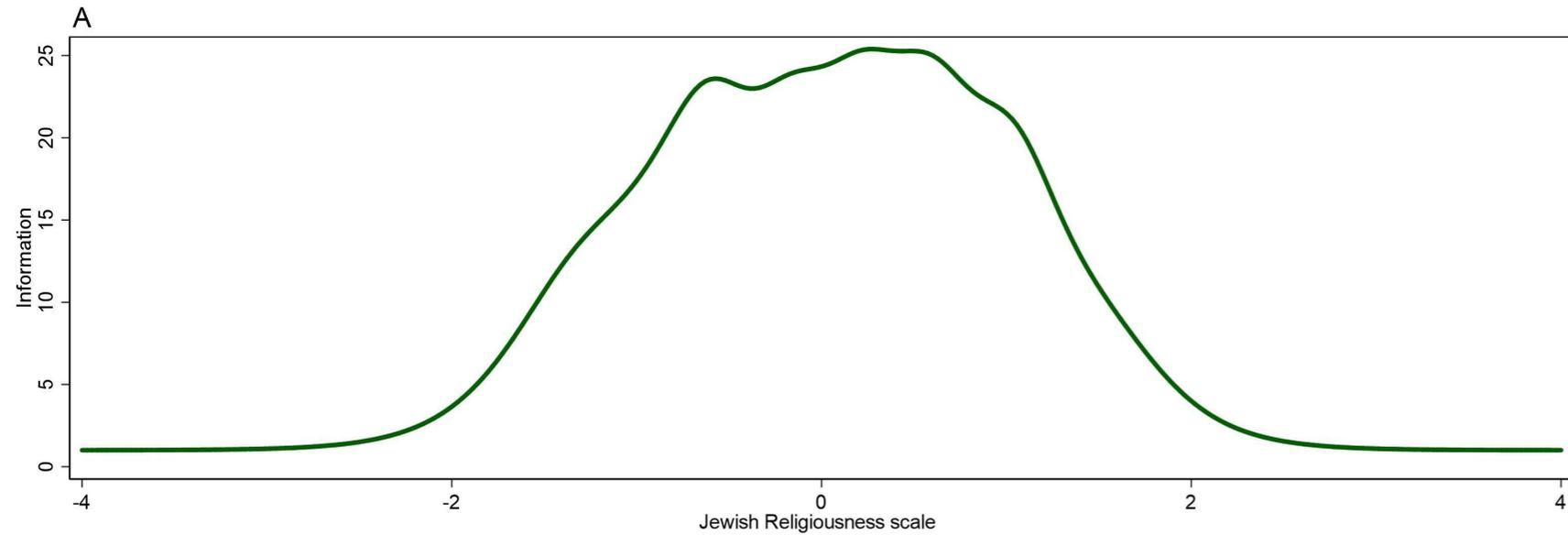
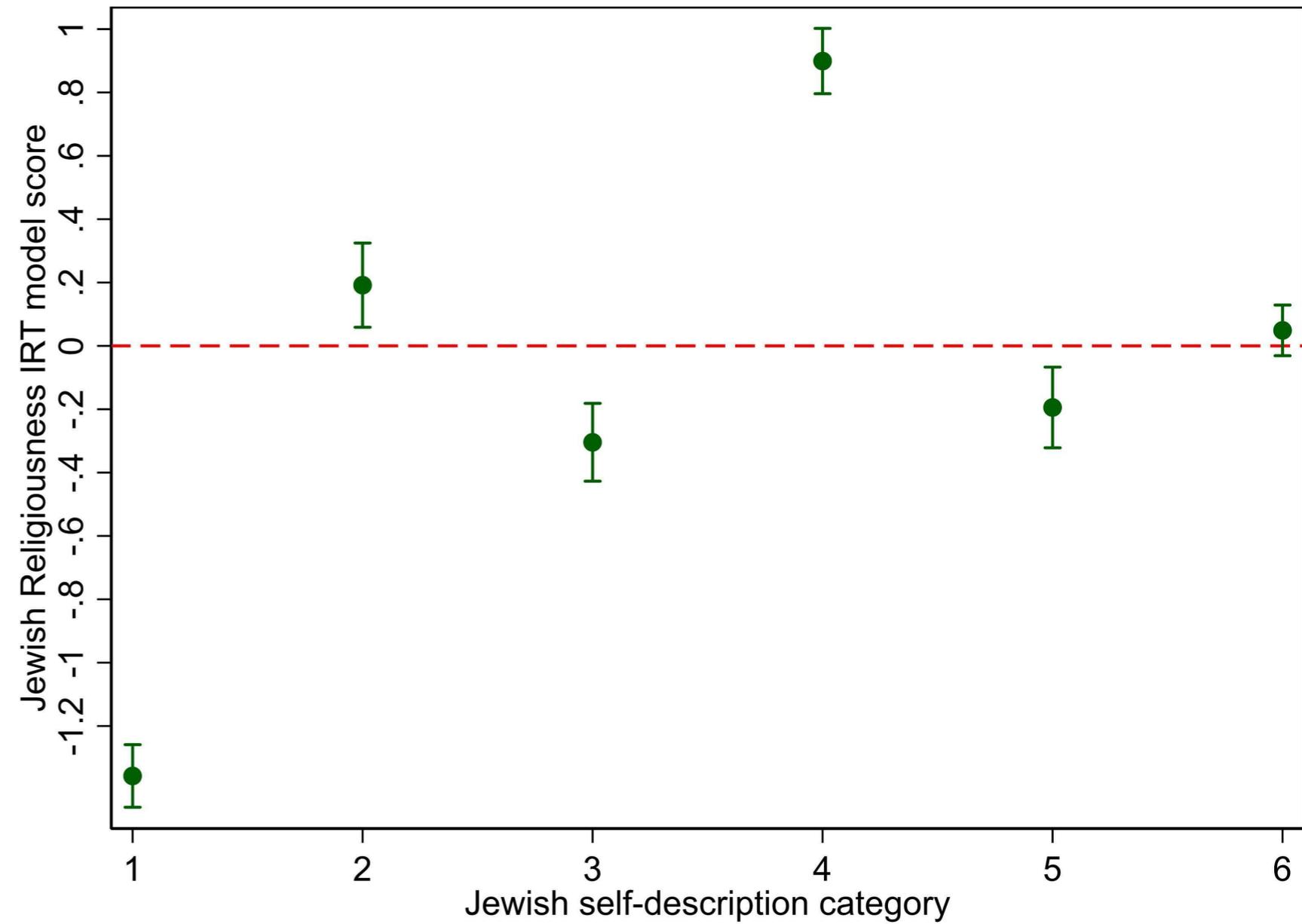
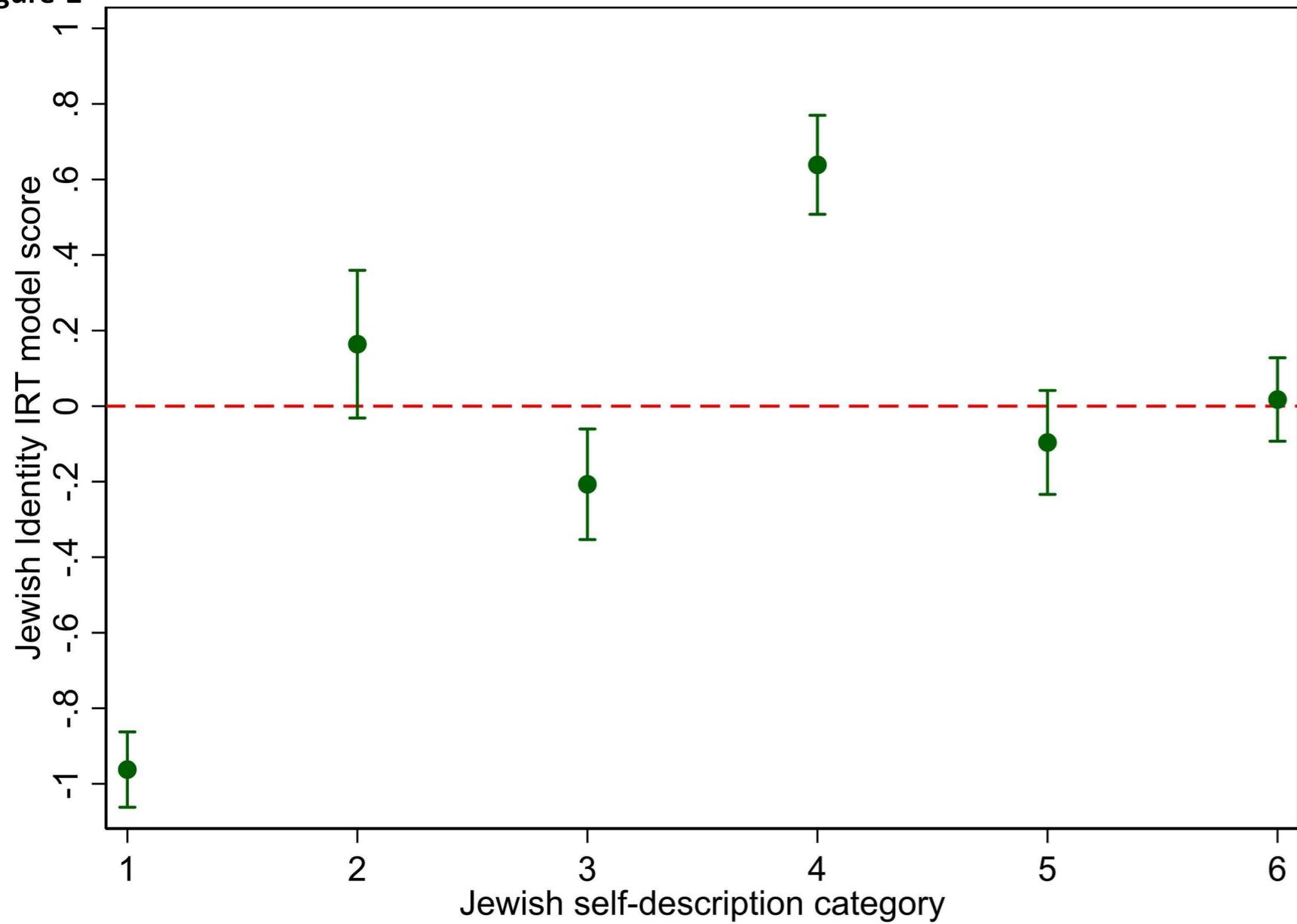


Figure-2



I feel a strong attachment towards the Jewish community.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
I feel good about my Jewish background.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
How important is it to you to attend religious services regularly? (cross one box)					
1	2	3	4	5	6
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Not at all important					Very important
How often do you observe / celebrate religious holidays at home? (cross one box)					
1	2	3	4	5	6
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Not at all					Very much
How frequently do you attend religious services? (cross one box)					
1	2	3	4	5	6
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Not at all	Once every few years	A few times per year	About once per month	About once per week	More than once per week
How strong would you say your religious or spiritual faith is? (cross one box)					
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Not at all strong	Not very strong	Moderately strong	Very strong	
How much do religious or spiritual beliefs serve as a source of comfort and support? (cross one box)					
1	2	3	4	5	6
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Not at all					Very much

Supplementary table S2: Regression models for Jewish Identity and Jewish Religious Subscales on interest, intention and uptake of genetic testing

INTEREST and Jewish Identity Scale	OR	SE	P> z 	95% CI
Jl_Background Subscale*			0.0349	
Disagree	2.22	1.41	0.209	0.64, 7.68
Agree	2.90	1.60	0.054	0.98, 8.55
Strongly agree	3.71	2.02	0.016	1.28, 10.80
INTENTION and Jewish Identity Scale	OR	SE	P> z 	95% CI
Jl_Sense_Heritage Subscale*			0.0358	
Disagree	2.32	1.08	0.07	0.93, 5.78
Agree	1.94	0.65	0.05	1.00, 3.76
Strongly agree	1.42	0.46	0.28	0.31, 1.56
UPTAKE and Jewish Identity Scale	OR	SE	P> z 	95% CI
Jl_Background Subscale*			0.0534	
Disagree	2.7	2.17	0.217	0.56, 13.07
Agree	4.96	3.12	0.011	1.45, 16.99
Strongly agree	3.92	2.50	0.032	1.12, 13.69
<i>*Reference Category= Strongly disagree</i>				
INTENTION and Jewish Religious Scale	OR	SE	P> z 	95% CI
Jl_Religious_Celebration Subscale**			0.042	
2	1.17	0.30	0.547	0.71, 1.93
3	1.11	0.26	0.652	0.70, 1.75
4	0.88	0.19	0.556	0.57, 1.36
5	0.84	0.21	0.501	0.52, 1.38
6	0.70	0.15	0.106	0.46, 1.08
Likert scale 1 to 6, 1= Not at all, 6= Very much; **Reference Category=1 (Not at all)				
INTENTION and Jewish Religious Scale	OR	SE	P> z 	95% CI
Jl_Religious_Service_Frequency Subscale***			0.0239	
Once every few years	1.07	0.33	0.820	0.59, 1.94
A few times per year	1.00	0.23	0.988	0.64, 1.57
About once per month	0.67	0.16	0.095	0.41, 1.07
About once per week	0.63	0.15	0.049	0.40, 0.99
More than once per week	0.91	0.27	0.748	0.51, 1.62
***Reference Category = Not at all				
UPTAKE and Jewish Religious Scale	OR	SE	P> z 	95% CI
Jl_Religious_Service Subscale**			0.0298	
2	0.47	0.15	0.015	0.25, 0.86
3	0.63	0.22	0.189	0.32, 1.26
4	1.52	0.71	0.368	0.61, 3.80
5	0.80	0.31	0.565	0.37, 1.72
6	0.49	0.16	0.024	0.26, 0.91

Likert scale 1 to 6, 1= Not at all important 6= Very Important;
 **Reference Category=1 (Not at all important)

UPTAKE and Jewish Religious Scale	OR	SE	P> z 	95% CI
Jl_Religious_Comfort Subscale**			0.0154	
2	0.43	0.19	0.062	0.18, 1.04
3	0.30	0.13	0.005	0.13, 0.70
4	0.47	0.21	0.085	0.19, 1.11
5	0.60	0.28	0.265	0.24, 1.47
6	0.27	0.11	0.001	0.19, 0.59

Likert scale 1 to 6, 1= Not at all, 6= Very much; **Reference Category=1 (Not at all)

OR- Odds Ratio, SE- Standard Error, CI- Confidence Interval

Jewish Cultural identity subscales:

Jl_Background: I feel good about my Jewish Background

Jl_Sense_Heritage: I have a clear sense of Jewish heritage and what it means to me

Jewish Religious identity subscales:

Jl_Religious_Celebration: How often do you observe / celebrate religious holidays at home?

Jl_Religious_Service_Frequency: How frequently do you attend religious services?

Jl_Religious_Service: How important is it to you to attend religious services regularly?

Jl_Religious_Comfort: How much do religious or spiritual beliefs serve as a source of comfort & support?

Figure-S1: Category Characteristic Curves Jewish Religious Identity questionnaire

The curves show the probability of response for each item category in the Jewish Cultural Identity questionnaire along the continuum.

The curves reflect item 'difficulty': location of the item on the continuous trait, specifically the point where item is successfully responded to with 50% probability.

Y axis – probability of answering the item/question (1= yes, 0= No)

X axis- theta =0 is the theoretical mean of the population. 1= 1SD, 2= 2SD, 3= 3SD, -1=-1SD, -2=-2SD, -3= -3SD

The first three items and the fifth item in the questionnaire have 6 response items, while the fourth item in the questionnaire has 4 response items.

Religious_Service: How important is it to you to attend religious services regularly

Religious_Celebration: How often do you observe / celebrate religious holidays at home?

Religious_Service_Frequency: How frequently do you attend religious services

Religious_Strength: How strong would you say your religious or spiritual faith is

Religious_Comfort: How much do religious or spiritual beliefs serve as a source of comfort & support?

For item-1 (Religious_Service)

Pr (item=1) - 1 - Not at all important

Pr (item=2) - 2

Pr (item=3) - 3

Pr (item=4) - 4

Pr (item=5) - 5

Pr (item=6) - 6 - Very important

For item-2 (Religious_Celebration) & Item-5 (Religious_Comfort)

Pr (item=1) - 1 - Not at all

Pr (item=2) - 2

Pr (item=3) - 3

Pr (item=4) - 4

Pr (item=5) - 5

Pr (item=6) - 6 - Very much

For item-3 (Religious_Service_Frequency)

Pr (item=1) - 1 - Not at all

Pr (item=2) - 2 - Once every few years

Pr (item=3) - 3 - A few times per year

Pr (item=4) - 4 - About once per month

Pr (item=5) - 5 - About once per week

Pr (item=6) - 6 - More than once per week

For item-4 (Religious_Strength)

Pr (item=1) - Not at all strong

Pr (item=2) - Not very strong

Pr (item=3) - Moderately strong

Pr (item=4) - Very strong

Figure-S2: Boundary Characteristic curves Jewish Religious Identity questionnaire

This indicates discrimination for different items on the scale (where the next category becomes more likely).

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.

Religious_Service: How important is it to you to attend religious services regularly?

Religious_Celebration: How often do you observe / celebrate religious holidays at home?

Religious_Service_Frequency: How frequently do you attend religious services?

Religious_Strength: How strong would you say your religious or spiritual faith is?

Religious_Comfort: How much do religious or spiritual beliefs serve as a source of comfort & support?

For item-1 (Religious_Service)

Pr (item=1) - 1 - Not at all important

Pr (item=2) - 2

Pr (item=3) - 3

Pr (item=4) - 4

Pr (item=5) - 5

Pr (item=6) - 6 - Very important

For item-2 (Religious_Celebration) & Item-5 (Religious_Comfort)

Pr (item=1) - 1 - Not at all

Pr (item=2) - 2

Pr (item=3) - 3

Pr (item=4) - 4

Pr (item=5) - 5

Pr (item=6) - 6 - Very much

For item-3 (Religious_Service_Frequency)

Pr (item=1) - 1 - Not at all

Pr (item=2) - 2 - Once every few years

Pr (item=3) - 3 - A few times per year

Pr (item=4) - 4 - About once per month

Pr (item=5) - 5 - About once per week

Pr (item=6) - 6 - More than once per week

For item-4 (Religious_Strength)

Pr (item=1) - Not at all strong

Pr (item=2) - Not very strong

Pr (item=3) - Moderately strong

Pr (item=4) - Very strong

Figure-S3: Category Characteristic Curves Jewish Cultural Identity questionnaire

The curves show the probability of response for each item category in the Jewish Cultural Identity questionnaire along the continuum.

The curves reflect item 'difficulty': location of the item on the continuous trait, specifically the point where item is successfully responded to with 50% probability.

Y axis – probability of answering the item/question (1= yes, 0= No)

X axis- theta =0 is the theoretical mean of the population. 1= 1SD, 2= 2SD, 3= 3SD, -1=-1SD, -2=-2SD, -3= -3SD

Each of the 14-items in the questionnaire has 4 response items.

Identity_Search: I have spent time trying to find out more about my own Jewish heritage / identity, such as history, traditions and customs

Active_Participation: I am active in organizations or social groups that include mostly members of the Jewish community

Sense_Heritage: I have a clear sense of Jewish heritage and what it means to me

Affect_By_Heritage: I think a lot about my life will be affected by my Jewish heritage

Happy: I am happy that I am Jewish

Notclear_Heritage: I am not very clear about the role of Jewish heritage in my life

Time_Spent_History: I really have not spent much time trying to learn more about Jewish history

Strong_Sense: I have a strong sense of belonging to the Jewish community

Understanding_Jewish_Heritage: I Understand pretty well what Jewish heritage means to me in terms of relating Jews and non-Jews

Heritage_Learning: In order to learn more about my Jewish heritage, I have often talked about the Jewish community

Pride: I have a lot of pride in the Jewish community and its accomplishment

Culture_Participation: I participate in Jewish culture, such as Jewish food, music and customs.

Attachment: I feel a strong attachment towards the Jewish community

Background: I feel good about my Jewish Background

For the 14 items

Pr (item=1) – strongly disagree

Pr (item=2) - disagree

Pr (item=3) – agree

Pr (item=4) – strongly agree

Figure-S4: Boundary Characteristic curves Jewish Cultural Identity questionnaire

This indicates discrimination for different items on the scale (where the next category becomes more likely).

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.

Identity_Search: I have spent time trying to find out more about my own Jewish heritage / identity, such as history, traditions and customs

Active_Participation: I am active in organizations or social groups that include mostly members of the Jewish community

Sense_Heritage: I have a clear sense of Jewish heritage and what it means to me

Affect_By_Heritage: I think a lot about my life will be affected by my Jewish heritage

Happy: I am happy that I am Jewish

Notclear_Heritage: I am not very clear about the role of Jewish heritage in my life

Time_Spent_History: I really have not spent much time trying to learn more about Jewish history

Strong_Sense: I have a strong sense of belonging to the Jewish community

Understanding_Jewish_Heritage: I Understand pretty well what Jewish heritage means to me in terms of relating Jews and non-Jews

Heritage_Learning: In order to learn more about my Jewish heritage, I have often talked about the Jewish community

Pride: I have a lot of pride in the Jewish community and its accomplishment

Culture_Participation: I participate in Jewish culture, such as Jewish food, music and customs.

Attachment: I feel a strong attachment towards the Jewish community

Background: I feel good about my Jewish Background

For the 14 items

Pr (item=1) – strongly disagree

Pr (item=2) - disagree

Pr (item=3) – agree

Pr (item=4) – strongly agree