

Population-Based, Risk-Stratified Genetic Testing for Ovarian Cancer Risk: A Focus Group Study

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Key Words

Focus groups · Implementation · Ovarian cancer · Predictive genetic testing · Risk · Stratification

Abstract

Study Purpose: A population-based risk stratification programme for ovarian cancer (OC) may improve OC survival by identifying women at increased risk and implementing an appropriate risk management strategy. The present study explored attitudes towards an OC risk stratification programme incorporating predictive genetic testing and risk-stratified screening as part of a larger study investigating OC screening. **Methods:** Focus groups consisting of 56 members of the general public (mean age 45 years; 34% non-white) were conducted using a hypothetical scenario. The group sessions were recorded, transcribed verbatim and analysed using Framework Analysis. **Results:** There was strong support for the proposed programme. Genetic testing and risk-stratified screening was thought to raise awareness, offer reassurance and offer opportunities for early intervention. Anxiety was only mentioned in relation to receiving a diagnosis of OC and not with screening per se. Perhaps because lay models of cancer already embrace both environmental and genetic factors, a low-risk result was not antici-

pated to result in a false sense of immunity. Unexpectedly, participants also wanted to receive cancer prevention advice in conjunction with genetic testing; screening alone was not regarded as sufficient. **Conclusion:** The encouraging results from this small study warrant further large-scale research into risk-stratified OC screening.

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Introduction

Cancer survival depends strongly on stage at diagnosis, with earlier stage diagnoses resulting in more favourable outcomes [1]. Although progress has been made in improving early diagnosis for many cancers, timely detection of ovarian cancer (OC) remains a challenge [2]. The absence of a distinct 'pre-cancerous' stage, in combination with the relatively low population frequency of the disease, has meant that 'traditional' screening approaches are not feasible [3], leading to a quest for alternative strategies to identify OC early in both the general and the higher risk population [4–6].

Genetic testing for germline mutations associated with higher risk of OC is becoming increasingly affordable and offers an opportunity to identify higher risk women be-

fore OC develops, irrespective of known family history. This raises the possibility of more intense screening in those at higher risk, potentially improving treatment outcomes and survival [6]. Mutations in the *BRCA1* and *BRCA2* genes increase the lifetime risk of OC by age 70 by 39–65, and 11–37%, respectively, but these mutations are rare [7–9]. Mutations in other genes are more common, influencing OC development despite low penetrance [10]. Combined testing for several genes so far associated with increased OC risk, in conjunction with more ‘traditional’ risk factors (age, family history, parity, and oral contraceptive pill use), may lead to more accurate risk estimation than any approach in isolation [5].

Attitudes towards genetic testing for *BRCA1/2* mutations have been explored extensively, particularly in individuals with a family history of breast cancer. A review of the literature in 2006 found high levels of interest in genetic testing among women with a family history (80–90%), although actual test uptake tends to be lower (~60%). In general population samples, interest in testing is lower (50–70%), although test uptake is comparable [11]. Other factors that have been associated with uptake are older age [e.g. 12], Ashkenazi Jewish heritage [e.g. 13] and being unmarried [14], although studies have been heterogeneous in approach, sample size and statistical analyses. This makes it difficult to draw definite conclusions about who would be most likely to undergo testing.

One barrier to implementation of population-based genetic testing for OC risk is the concern about adverse psychological reactions [15, 16]. Evidence from studies using *BRCA1/2* testing shows that in the majority of studies, genetic test feedback was perceived as positive in carriers and non-carriers alike, and negative psychological outcomes tended to be short-lived [17–20]. However, these findings stem largely from studies of highly selected groups who were well aware of the possibility of increased risk prior to testing, so the results need to be viewed with caution.

One study has assessed the effects of receiving genetic test feedback for a range of conditions, including breast cancer risk, in a large general population sample [21]. Interested individuals who accessed the Navigenics website without prompting could obtain the ‘Navigenics Health Compass’ (<http://www.navigenics.com>) at a reduced rate in return for responding to a survey 6 months after viewing their genetic test results. Intentions to screen for various cancers increased significantly in the whole sample, with no increase in negative affect at the 6-month follow-up. However, in this study, genetic feedback was given for over 23 conditions, which would likely generate raised risk

Table 1. Demographic characteristics of the sample (n = 56)

	% (n)
Mean age \pm SD, years	44.9 \pm 13.2
Ethnicity (white)	66.0 (37)
Education (higher degree)	55.3 (31)
Employment (full-time)	39.2 (22)
Marital status (married)	33.9 (19)
Living arrangement (homeowner)	51.7 (29)
Lifetime screening (mammogram/ Pap/FoBt/prostate men)	73.2 (41)
Cancer within social network	78.5 (44)

for some conditions and lowered risk for others, potentially leading to a null effect in overall risk perception and hence no increase in negative affect. Reactions to genetic test feedback for a single, serious condition, in a population largely unaware of their genetic risk, may be different.

The present study explored attitudes towards an OC risk stratification programme incorporating predictive genetic testing and risk-stratified screening for OC. As this is a relatively new area, a qualitative methodology was used, with focus groups from the general public who are asked to consider how they might respond to the opportunity of genetic testing and risk-stratified screening. Hypothetical scenarios are an important step when implementing novel technologies, both to ascertain any likely adverse reactions and to gain insight into facilitators and barriers to their use [22].

Materials and Methods

Participants

Participants were 56 members of the general public, recruited by Saros UK, a qualitative recruitment service with a participant database of over 250,000. Individuals from a range of ages, socioeconomic backgrounds and ethnicities from London and surrounding areas were invited. We specified ‘not currently affected by cancer’ as the only exclusion criterion because we were interested in views from a broad segment of the general public. Participants were selected on a first-come-first-serve basis based on availability. They were seen in 7 focus groups of 6–9 individuals each (mean n = 7). One group of 9 men was included because men can pass genetic mutations on to female offspring. Participants were reimbursed with 30 GBP for their time and effort. Participant characteristics are displayed in table 1.

Procedure

Ethical approval was obtained from the University College London Ethics Committee for non-NHS Research (project ID 3162/001). After participants had signed consent forms and pro-

vided brief demographic information, the focus group moderator (S.M.) introduced herself, the funding source (Cancer Research UK) and the topic of discussion. Participants were informed that the discussion would be recorded, but all answers were confidential and anonymity would be maintained. It was made clear that there were no right or wrong answers and that we were interested in each person's views. A focus group guide using some predefined questions was used to ensure all important topic areas were covered (table 2). Efforts were made to keep questions open by using a non-directive questioning style and to include participants who appeared to be less forthcoming by asking them directly about their thoughts. The focus group moderator moved on to the next topic only when it was felt that the discussion came to a natural conclusion or no new answers were forthcoming.

Table 2 displays the questions asked in each section. Questions were chosen after examining the literature pertaining genetic test feedback and cancer and discussions within the research team on the basis that they would best cover the area of interest. First, participants were asked about their awareness of OC. Then they were given a brief presentation (5 slides) about the contribution of genes to OC, the existence of a genetic test, and the idea of population-based, risk-stratified screening. The presentation was based on existing OC information leaflets widely available in the UK (e.g. <http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Ovary/Aboutovariancancer/Aboutovariancancer.aspx>), explaining all concepts in lay terms. We opted for a presentation over written information to ensure the information participants received was unaffected by their literacy. Participants were told that in the proposed stratified screening programme a number of risk factors would be combined to give an individual risk estimate and that genetic testing would be part of this assessment. It was explained that *BRCA1/2* mutations were rare but would confer high risk, whereas mutations in other genes were more common but would raise OC risk only marginally. This was reinforced by telling participants explicitly that they would be unlikely to have a rare *BRCA1* or *BRCA2* mutation, but more likely to have one or more of the more 'common' genetic mutations, which would raise OC risk to an intermediate level. They were asked about (i) their understanding of the issues covered in the slides, (ii) their opinions about undergoing genetic testing and risk-stratified screening, and (iii) their thoughts and opinions about risk management, including up to 4-monthly screening for those identified at 'higher risk'. Participants were not explicitly informed about risks of screening or what primary preventive options entailed because we wanted to explore whether they would request this kind of information, but they were discussed when the question arose. Before concluding the group, participants had the opportunity to express any issues not mentioned earlier and were directed to relevant sources of information about OC (Macmillan and Cancer Research UK websites).

Analysis

Focus group recordings were transcribed verbatim and coded using framework analysis [23]. This method is appropriate because it allows data analysis by group and theme. It also provides a simple way of differentiating between common and rare themes. Transcripts were read and reread. A matrix (framework) contain-

Table 2. Focus group guide (themes, information and questions)

General attitudes towards ovarian cancer risk and their experience of it

Knowledge, how common is it?, symptoms
Do you feel at risk?, what are the risk factors?
Anything that you can do to reduce the risk of ovarian cancer?

Opinions on understanding genetic information

(Participants presented with slides on genetic risk)

Does the genetic risk information make sense?
Would you be interested in receiving genetic information?
How would you like to receive it?
(in what format?/from who?, etc.)

Opinions on a screening programme using risk stratification approach

Mod: Risk stratification means that women can be grouped based on their likelihood of getting ovarian cancer. Women can be described as having a low, intermediate or high risk. The level of risk is based on a woman's genetic risk and other risk factors. Identifying genetic risk involves having a blood test. Identifying other risk factors would involve filling in questionnaires about family history, background and health information. Scientists can then put all of this information together and estimate whether a woman is at low, intermediate or high risk. It is estimated that 50–60% of women will be at low risk, 30–45% at intermediate risk, and 4–7% at high risk.

What do you think about a risk stratified approach to screening? (pros, cons)
Would you like to have a screening test for ovarian cancer risk?
How would you feel if you were told that you were at low/intermediate/high risk?
Do you see risk stratification as a positive, neutral or negative development in screening provision?

Opinions on possible risk management options

Mod: Depending on a woman's risk level (low, intermediate or high), she would receive different levels of risk management for ovarian cancer. Women at low risk would receive information telling them that they are at low risk and that they do not need further monitoring. This information would also let low-risk individuals know about symptoms of ovarian cancer. Women at intermediate risk would receive screening every year (screening involves a blood test to check for levels of the biomarker CA-125 followed by transvaginal ultrasound). Those at high risk would be screened every 4 months. High-risk women may also be referred to a specialist to discuss risk-reducing surgery.

What do you think of the risk management options? (e.g. reassurance, annual, 4 monthly)
How would you feel if you were in the low/intermediate/high risk management group?
What are the pros and cons of this approach?

ing common emerging themes was developed by categorising statements loosely at first, then developing more detailed themes as statements within a category increased. As new themes emerged, they were added to the matrix. Analysis was both inductive and deductive because the semi-structured format of the focus groups ensured that predetermined areas were covered while allowing emergence of new concepts from the participants. All transcripts were independently coded by S.M. and a researcher not involved in the study to assess validity and inter-rater reliability. After coding, the raters discussed any differences. Agreement was high, but where minor discrepancies arose, transcripts were reread and discussed until agreement was reached. For example, in some quotes, it was unclear whether women spoke from their own experience or whether they spoke about other women's possible responses. Here, both raters discussed the context in which the statement was made to decide on its most likely meaning.

Results

Awareness of OC and Its Risk Factors

OC awareness was consistently low. Some women indicated that the general lack of awareness demonstrated that OC is 'not one of the cancers to worry about'. Many had never thought about OC, and consequently did not feel at risk of developing it. A few women who had thought about OC cited a news story about a UK celebrity who died of cervical cancer as primary reason. Several women believed that cervical screening would test for all 'women's cancers', and they were surprised to hear that this was not the case.

Women either had no knowledge about risk factors, or named risk and protective factors very tentatively after direct probing. This appeared to be partly due to a widespread assumption that risk reduction would be cancer-specific: 'If you smoke you are increasing your chances of lung cancer. You know if you smoke and drink heavily, you are increasing your risk of throat cancer [...]', and therefore, there was a perception that many common risk factors would not be relevant for developing OC. Confusion with cervical cancer was also frequent and hysterectomy was often mentioned as reducing or abolishing risk.

Awareness of Genes Affecting Cancer

All participants were aware that cancer 'runs in families', and that genes play a role. Non-white participants frequently mentioned family ties and inheritance patterns and gave relatively accurate descriptions about the role of genes in cancer development, for example: 'Generally, the genes that are prevalent to cancerous symptoms lie dormant until there is some trigger, like stress, and then the gene can kind of switch on, if you like, and you end up with cancer'. When asked directly, men acknowl-

edged that they could pass on genes for OC to their offspring, but it was apparent in the discussion that it was not on their minds. Women often spontaneously cited a responsibility to be tested in order 'not to pass anything bad on to [their] children'.

Reactions to the Idea of Genetic Testing for OC Risk Genetic Testing is Generally Embraced

Perhaps because participants were already aware of the genetic component to cancer, genetic testing for OC risk was seen as indisputably beneficial and no apprehensions were expressed. Many women drew on their experience with existing cancer screening programmes to note the importance of surveillance. The common view was that knowledge about OC risk would be empowering, especially because 'being aware of this now, actually reading up on it and getting as much information as possible, finding out what new technologies they are coming out with, and preventative measures [...]' would allow women to prepare for the future. Having genetic information on file was seen as aid to receiving better and more targeted care because 'doctors would then have something to go on, it wouldn't be sort of... Oh, it's just indigestion'. The option of not necessarily having to know the test result, but it being 'on file' for the healthcare provider, was introduced by those anticipating anxiety in response to their result as a hypothetical option of deriving the benefits from screening without inducing negative affect. Concerns about ethics, privacy, insurance issues, or the potential of using DNA unlawfully were not mentioned at all in the discussion, neither was the idea of DNA being in any way 'special'.

Anticipated Reactions to Risk-Stratified Screening Discussion in the Focus Groups Gravitated towards the Consequences of the Test Result, rather than the Idea of Risk-Stratified Screening per se

Risk-stratified screening after risk assessment incorporating genetic testing was received with enthusiasm throughout. In fact, in some groups the idea was brought up before the moderator introduced it: 'Why not just have an umbrella genetic screening to show prevalence and maybe initially to start with one particular age group that has propensity to acquire cancer of some description at a certain stage in life?' All participants took follow-up screening after genetic testing for granted and even expected it, especially for those at higher risk. However, screening was seen as a way to eventually detect cancer. It was not seen as protective or as a risk management strategy.

Worry was predominantly expressed in the context of coping with a diagnosis of OC, not with the screening: 'If I did have it [the gene] I think I wouldn't want to go for the treatment [screening], I'd just say, take my ovaries away, take them away'. Most women felt that their reaction would depend on their knowledge of OC, including symptoms, life expectancy after diagnosis, potential for metastasis, and cancer treatment options because 'if somebody says, yes, if it's caught early it's totally curable, right, ok, high risk, well, no big deal'. The likely frequency of OC screening required for 'higher risk' women was seen as potentially anxiety-inducing, but providing information on OC was viewed as helping to keep anxiety to a minimum. The predominant view by far was that screening would become increasingly 'normal' or 'routine' over time. Furthermore, the idea of being able to get advice and be 'fast-tracked' when classified at 'higher risk', if there were any worries about symptoms, mitigated potential anxieties for many participants.

The Need for Prevention Advice as an Adjunct to the Test Result

All participants expressed a strong desire to receive lifestyle advice about how to lower OC risk. Although there was some sense of the inevitability of cancer development (sometimes healthy people can be 'struck by cancer'), many participants appeared to believe that behaviour change 'must' be effective in OC prevention. Screening attendance was not seen as a preventive action, but merely a means of early detection: 'Being told that you are high risk and all we are going to do is do a blood test every three months but there's no advice we can give you about changing your lifestyle, I think that's downright cruel'. In particular, a higher risk result was anticipated to be a 'wake-up call' to engage with behaviour change. The need to feel 'in control' over cancer development was a central theme in the discussion. Despite some understanding of genetic risk, there was an assumption that individuals could move between risk categories, with OC being perceived as both a 'given' and something that could be prevented, and participants regularly switching between the 2 perspectives within the course of the discussion.

No Evidence for Complacency with a Lower-Risk Result

Because participants were aware that genes are not fully indicative of cancer risk, a lower risk result was not seen as reason to be complacent: 'You would be relieved but you wouldn't be complacent because even if it's a low risk, you could still get it; it's not inevitable that you wouldn't'.

However, few women expressed concerns about further routine screening being unavailable following a lower risk result, although some wanted screening to be available on request. Without direct probing, there was little focus on reactions to an intermediate genetic risk result, but those who thought about it mentioned that it would increase their symptom awareness and prompt them to seek out information.

Discussion

Although practical barriers to implementation would have to be overcome [16], the findings of this qualitative study suggest that women would welcome the opportunity of genetic testing and subsequent risk-stratified screening for OC. They did not anticipate adverse psychological effects in response to the personal genetic test result, although a 'higher risk' result was often described as a 'wake-up call' for taking preventive action. On the contrary, the idea of a genetic test result being available to their healthcare provider was received with enthusiasm, even by individuals who anticipated some emotional discomfort because it was seen as a means of receiving more targeted, rapid and better care. Although these findings differ somewhat from earlier studies involving *BRCA1/2* testing for risk of breast cancer, which have shown increased, albeit short-lasting, distress and anxiety after testing [e.g. 24, 25], this may be because the current study used a hypothetical scenario. One limitation of this methodology is that people may have difficulty imagining themselves being negatively affected [26]. Alternatively, results may differ because participants in previous *BRCA* studies were from families highly affected by cancer where the gene penetrance is much higher and not from the general population; experience of cancer in the family, and not the genetic test result per se, may have been responsible for some of the negative emotional reactions. It is also possible that the general public's growing familiarity with genetics and awareness of the genetic contribution to cancer [27] are contributing to reduced concerns about ethics, privacy, or a 'special' status of DNA and an inherited susceptibility to cancer.

Despite the information that it would be unlikely to be found to have mutations in the *BRCA1/2* genes, and that 'common' OC genetic mutations would raise risk only modestly, a 'higher risk' result was frequently discussed as if it denoted being highly likely to develop OC. It is possible that participants retained only the 'gist' of the risk

information, including a binary (high vs. low) understanding as described in the Fuzzy Trace model [28], leading to misperceptions about the likelihood of cancer development. Alternatively, talking about 'higher risk' in the cancer context may have activated neural networks associated with cancer development and diagnosis, which in turn elicited networks associated with coping and treatment, as suggested by the Spreading Activation theory [29]. This could explain why the discussion about reactions to test feedback immediately focused on scenarios surrounding OC diagnosis and potential coping strategies, and why most participants ignored the 'lower risk' and 'intermediate risk' scenarios in discussion unless probed directly. Either way, the findings suggest that a better understanding of the cognitive processes that influence risk perception is important, and they highlight the need to provide information on the likelihood of cancer development in a format that is easy to understand and remember, both before testing and alongside the genetic test result.

Fears that a 'lower risk' result would induce complacency did not receive much support. This may be because lay models of cancer development already incorporate the idea of genetic and environmental causal factors operating in parallel [30], so most people are aware that lower genetic risk does not mean immunity to OC. However, individuals trusted the genetic test to accurately identify risk, and there was no suggestion that those at lower risk would seek unnecessary screening. There was a notion that more frequent screening should be available to individuals who were worried after risk assessment regardless of risk category, but this was less pronounced than in a similar study about genetic testing and stratified screening for breast cancer [31]. This could be because breast screening is an established programme and has, therefore, become an 'acquired right' or because OC awareness is lower than breast cancer awareness and OC is, therefore, seen as less of a threat. The accuracy of either theory could be explored in further research.

Although participants viewed risk-stratified screening favourably, they were also adamant about the need for information on preventive action against OC development. Screening was *expected* after genetic testing and was even suggested before introduction by the moderator in some focus groups. However, while it was seen as helpful for 'catching OC early', it was perceived to be lamentably inadequate for cancer control. Misperceptions about the purpose of screening in the general public may perhaps be at the heart of this finding. Among the medical profession, screening is regarded as a 'secondary pre-

vention' strategy, aimed at reductions in morbidity and mortality; whereas the general public may only see 'primary prevention' (avoiding disease development altogether) as 'effective' prevention, while screening is 'early detection' which means they would still receive a cancer diagnosis. Further research may be warranted to investigate this issue in more detail. Participants saw tangible advice on taking preventive action as integral to any risk assessment programme, and the suggestion of omitting it (because there is no solid evidence on prevention) was met with disbelief. These attitudes seem to reflect the assumption that a key role of genetic test feedback is to motivate disease prevention, a perspective that appears to be widely held in the general public and is promoted by companies marketing genetic testing directly to consumers (www.23andme.com; www.decodeme.com), despite limited supportive evidence [32]. Regardless of the behavioural impact of preventive advice, the results of the present study suggest that the acceptability of any genetic testing programme depends in part on cancer prevention advice being made available.

The call for cancer prevention advice is also reflective of beliefs about individual control over cancer that are prevalent in Western society [33]. However, at the same time as believing that there must be strategies for disease prevention, many participants also characterised cancer as unpredictable or inevitable, and the 2 perspectives often existed in parallel. 'Switching' between perspectives occurred without hesitation, suggesting that people are unaware of any inconsistency. It would be useful to investigate the cognitive processes underlying beliefs about cancer to try to understand how contradictory views are formed and maintained.

The present study has limitations. It was based on a hypothetical scenario and, therefore, is only indicative of possible reactions to an actual opportunity for genetic testing for OC. Although the focus group participants were enthusiastic about the prospect of a genetic test, actual uptake is difficult to predict because intentions and behaviour correlate only weakly in this area [34, 35]. The qualitative format of the study means that the sample was small, and the results cannot be assumed to be representative of the UK population. Despite inclusion of individuals from a variety of ages, social strata and ethnicities, they were members of a recruitment agency and had self-selected into the study, and may be different from the general population. A larger, quantitative study is needed to draw conclusions about the range and frequency of the views presented here for the wider population. Furthermore, as with any qualitative study, analysis and interpretation are always coloured by

the researchers' culture and preconceived notions. We attempted to minimise bias by working as a team on the study, meeting frequently and discussing methods and procedure in detail. Lastly, focus groups always carry the risk of more outspoken participants overshadowing those who are more introverted, distorting the picture of true opinions presented [36]. To minimise this, we moderated the groups to reduce the chance of any one person dominating the conversation, and specifically addressed individuals who were less outspoken, to ensure that everyone had the opportunity to express their views; however, some variation in participation levels remained. The focus group format is also a strength because it allows an in-depth analysis of responses to a novel healthcare technology and makes it cost-effective to include a larger number of participants than in one-on-one interviews.

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Conclusion

These results provide a first indication that the public may be broadly positive about the offer of population-based genetic testing for OC risk and would support risk-stratified screening as long as cancer preventive advice was offered alongside the programme.

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