National Institute for Health and Care Excellence

Final

# Ovarian cancer: identifying and managing familial and genetic risk

## [B] Support interventions

*NICE guideline NG241*

*Evidence reviews underpinning recommendations 1.2.7 to 1.2.11, 1.3.2, as well as bullet 8 in table 1, bullet 6 in table 2 and research recommendation 1 in the NICE guideline*

*March 2024*

*Final*

*These evidence reviews were developed by NICE*

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## Contents

# Interventions to support decision making about management options for women at increased risk of ovarian cancer

## Review question

Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

### Introduction

Preventing inheritable ovarian cancer is a clinical priority. This can be achieved by identifying those at risk and offering them interventions that support them to make decisions that can reduce their chance of getting ovarian cancer. This is important as risk is not a straightforward concept and many ways by which we reduce an individual's risk of ovarian cancer are not without potential harms. Therefore, those at familial risk of ovarian cancer need to be informed in a way that is meaningful to them. Healthcare systems also have to find interventions that they can deliver consistently. The aim of this review is to assess which interventions are most effective in supporting women to make decisions around their familial risk of cancer and enable them to make robust decisions as to how to best mitigate their risk.

### Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

**Table 1: Summary of the protocol (PICO table)**

| | |
|---|---|
| **Population** | Women with familial ovarian cancer or at increased risk of ovarian cancer preparing to make a healthcare decision |
| **Intervention** | • Decision coaching for decision making such as:<br>  ○ Health counselling (including genetic counselling)<br>  ○ Psychological support<br>• Evidence based information (including online tools) such as:<br>  ○ Decision aids<br>• Combination of decision coaching and evidence-based information |
| **Comparison** | • Interventions compared with each other<br>• Usual care (no formal method used to help with decision making) |
| **Outcomes** | **Critical**<br>• Preparation for active participation in making an informed health decision<br>• Resolution of decisional needs<br>• Adverse effects (during or after decision making) such as:<br>  ○ Decision regret<br>  ○ Anxiety<br>  ○ Depression<br>  ○ Distress<br>  ○ Grief or loss<br>  ○ Cancer worry<br>**Important**<br>• Satisfaction with decision support intervention<br>• Uptake of the management option being considered |

| | |
|---|---|
| | • Decision quality<br>• Quality of life |

For further details see the review protocol in appendix A.

## Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

## Effectiveness evidence

### Included studies

Overall 16 studies were included for this review: 10 randomised controlled trials (RCTs; Armstrong 2005, Calzone 2005, Drescher 2016, Green 2004, Lerman 1997, Roussi 2010, Schwartz 2014, Tiller 2006, Vogel 2019, Wang 2005) and 6 cluster RCTs (Kinney 2014, Manchanda 2016, van Roosmalen 2004a, van Roosmalen 2004b, Wakefield 2008a, Wakefield 2008b).

In 5 of the cluster randomised trials the unit of clustering was the family and the cluster-size was small ranging from 1.02 to 1.16 (Kinney 2014, van Roosmalen 2004a, van Roosmalen 2004b, Wakefield 2008a, Wakefield 2008b). In Manchanda 2016 clustering was by clinic with an average cluster size of 3.8.

Two studies compared genetic counselling with usual care (Lerman 1997, Drescher 2016).

Seven studies looked at augmenting genetic counselling with some form of decision support intervention (Green 2004, Tiller 2006, van Roosmalen 2004a, Roussi 2010, Wakefield 2004a, Wakefield 2004b, Wang 2005).

Two studies compared telephone with in-person genetic counselling (Kinney 2014, Schwartz 2014).

Two studies examined whether a group education session before individual genetic counselling could reduce the time needed for the individual session (Calzone 2005, Manchanda 2016).

Two studies compared decision support interventions with usual care in women who were *BRCA1/2* mutation carriers (Armstrong 2005, van Roosmalen 2004b).

One study looked at an educational mobile app about genetic counselling for women with ovarian cancer (Vogel 2019).

Some of the studies included not only women but also men (Calzone 2005 5.6% in the group counselling and 4.2% in the individual counselling; Manchanda 2016: 35% men in the DVD + group counselling and 32% men in the group counselling). Whilst the population in the protocol is women, the committee agreed that these percentages of men are acceptable.

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

### Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

## Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

**Table 2: Summary of included studies**

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| Armstrong 2005<br><br>RCT<br><br>USA | N=27 women who underwent *BRCA1/2* testing<br><br>Age (mean [range], years): intervention 45 [30-59]; control 42 [26-54] | Decision support intervention (personalised survival and cancer incidence data associated with cancer management options) | Usual care (educational booklet) | • Decision satisfaction score |
| Calzone 2005<br><br>RCT<br><br>USA | N=142 individuals with known *BRCA1/2* mutation<br><br>Age, years: intervention 40; control 41 | Group education + brief individual counselling | Individual education + counselling | • Adverse effects: cancer worry<br>• Decision quality: objective knowledge<br>• Uptake of the option being considered: rate of genetic testing |
| Drescher 2016<br><br>RCT<br><br>USA | N=458 women identified from a mammography database; they had to meet the NCCN 2013 pedigree criteria for referral to a genetic counsellor<br><br>Age, mean (SD), years: intervention 54 (10) years; control 53 (10) | Genetic counselling | Usual care | • Uptake of the option being considered: rate of genetic testing and bilateral salpingo-oophorectomy |
| Green 2004<br><br>RCT<br><br>USA | N=211 women referred for genetic counselling for evaluation of personal or family history of breast cancer<br><br>Age, mean (SD not reported), | Computer education followed by genetic counselling | Genetic counselling | • Decision quality: objective knowledge test<br>• Adverse effects: anxiety<br>• Uptake of the option being considered: genetic testing |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| | years: intervention 45; control 44 | | | |
| Kinney 2014<br><br>Cluster RCT<br><br>USA | N=998 family clusters (1012 women with personal or family histories of breast or ovarian cancer<br><br>Age, mean years: 56.1 (SD 8.2) | Telephone genetic counselling | In person genetic counselling | • Adverse effects: anxiety<br>• Adverse effects: cancer worry<br>• Adverse effects: decision regret<br>• Decision quality: objective knowledge test<br>• Resolution of decisional needs: decisional conflict scale, range<br>• Uptake of the option being considered: genetic testing rate |
| Lerman 1997<br><br>RCT<br><br>USA | N=400 women who had at least one first-degree relative with breast and/or ovarian cancer<br><br>Age, years: >50: education 30%; education + counselling 25%, control 30% | Education<br><br>Education + counselling | Waiting list control | • Uptake of the option being considered: intention to get *BRCA1* test<br>• Decision quality: objective knowledge scale |
| Manchanda 2016<br><br>Cluster RCT<br><br>UK | N=256 clusters (936 Ashkenazi Jewish ethnicity individuals)<br><br>Age, mean (SD), years: intervention 53.9 (14.9), control 53.9 (15.1) | Group DVD + genetic counselling | Genetic counselling | • Uptake of the option being considered: genetic testing<br>• Satisfaction with intervention: counselling<br>• Decision quality: objective knowledge |
| Roussi 2010<br><br>RCT<br><br>USA | N=134 women who contacted a family risk assessment program and had a family history consistent with possible hereditary breast and/or ovarian cancer | Enhanced genetic counselling | Standard genetic counselling | • Decision quality: objective knowledge |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| | Age, years: 47% aged over 50 | | | |
| Schwartz 2014<br><br>RCT<br><br>USA | N=669 women with a minimum 10% risk for a *BRCA1/2* mutation<br><br>Age, mean (SD), years: intervention 47.7 (13.1); control 48.4 (14.2) | Telephone genetic counselling | In person genetic counselling | • Resolution of decisional needs: decisional conflict scale<br>• Adverse effects: cancer worry<br>• Uptake of the option being considered: rate of genetic testing<br>• Satisfaction with decision support intervention |
| Tiller 2006<br><br>RCT<br><br>Australia | N=131 women from high-risk families<br><br>Age, mean, years: intervention 45.8; control 46.3 | Decision aid + genetic counselling | genetic counselling | • Decision quality: objective knowledge<br>• Adverse effects: anxiety<br>• Adverse effects: depression<br>• Resolution of decisional needs: decisional conflict scale<br>• Uptake of the option being considered: rates of risk reducing surgery |
| van Roosmalen 2004a<br><br>Cluster RCT<br><br>the Netherlands | N=368 women at increased risk of carrying a pathogenic variant<br><br>Age mean (SD), years: intervention 43.7 (11.3); control43.5 (10.4) | Decision aid + genetic counselling | genetic counselling | • Adverse effects: anxiety<br>• Adverse effects: depression<br>• Adverse effects: cancer worry<br>• Resolution of decisional needs: decision conflict scale<br>• Satisfaction with decision support intervention<br>• Uptake of the option being considered: treatment choice prophylactic oophorectomy<br>• Uptake of the option being considered: treatment choice ovarian cancer screening<br>• Uptake of the option being considered: treatment choice undecided |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| van Roosmalen 2004b<br><br>Cluster RCT<br><br>The Netherlands | N=88 women affected and unaffected with breast/ovarian cancer who had chosen to undergo DNA testing<br><br>Age mean (SD), years: intervention 39.1 (9.7): control 39.9 (10.4) | Decision support intervention | Usual care | • Adverse effects: anxiety<br>• Adverse effects: depression<br>• Adverse effects: cancer worry |
| Vogel 2019<br><br>RCT<br><br>USA | N=104 women with a diagnosis of epithelial ovarian, primary peritoneal or fallopian tube cancer who had not previously received or scheduled genetic counselling or testing related to cancer<br><br>Age, mean (SD), years: intervention 60.9 (10.7); control 62 (12.0) | Mobile educational app for genetic information on cancer (mAGIC) | Usual care | • Uptake of the option being considered: rate of genetic counselling<br>• Decision quality: objective knowledge test |
| Wakefield 2008a<br><br>Cluster RCT<br><br>Australia | N=145 women with a family history consistent with a dominantly inherited hereditary breast/ovarian cancer syndrome who have an affected, living relative willing to provide a blood sample<br><br>Age, mean, years: intervention 45.8; control 49.6 | Decision aid + genetic counselling | Genetic counselling | • Resolution of decisional needs: decisional conflict scale<br>• Decision quality: objective knowledge<br>• Uptake of the option being considered: rate of genetic tests |

| Study | Population | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| Wakefield 2008b<br><br>Cluster RCT<br><br>Australia | N=123 women who contacted a familial cancer clinic and were eligible for genetic testing<br><br>Age, mean, years: intervention 49.2; control 48.2 | Decision aid + genetic counselling | Genetic counselling | • Resolution of decisional needs: decisional conflict scale<br>• Decision quality: objective knowledge<br>• Uptake of the option being considered: rate of genetic tests |
| Wang 2005<br><br>RCT<br><br>USA | N=198 women attending the Breast and Ovarian Cancer Risk Evaluation Program<br><br>Age, mean, years: 44-45 | 4 trial arms<br>CD-ROM + Genetic counselling<br><br>Feedback + Genetic counselling<br><br>CD-ROM+ Feedback + Genetic counselling | Genetic counselling | • Uptake of the option being considered: rate of genetic testing |

*CD-ROM: compact disc read only memory; NCCN: National Comprehensive Cancer Network; SD: standard deviation: RCT: randomised controlled trial*

See the full evidence tables in appendix D and the forest plots in appendix E.

## Summary of the evidence

Studies reported a variety of approaches to providing information and support for individuals to make decisions regarding genetic testing uptake and management options to reduce their risk of ovarian cancer.

### *Genetic counselling versus usual care*

Moderate quality evidence showed an important benefit of genetic counselling in terms of the uptake of genetic testing in those who were at potentially high risk of familial ovarian cancer. However, very low quality evidence showed no important difference for the same outcome between genetic counselling and usual care in those with low to moderate risk of cancer.

Low quality evidence showed an important benefit of genetic counselling in terms of the uptake of risk reducing surgery and better decision quality with genetic counselling as compared to usual care.

### *Genetic counselling plus decision support intervention versus genetic counselling alone*

In terms of decision quality, low quality evidence indicated an important benefit of decision support interventions used as an adjunct to genetic counselling when compared to genetic counselling alone. Moderate to high quality evidence showed an important benefit of decision support interventions used as an adjunct to genetic counselling in terms of increased satisfaction with the decision aid as well as a lowered likelihood of women choosing ovarian cancer screening as their treatment. However, moderate to high evidence also showed no

important difference in terms of other outcomes (for example, resolution of decision needs, adverse effects) between the 2 groups.

***Telephone genetic counselling versus in-person genetic counselling***

Very low to high quality evidence showed no important difference between telephone genetic counselling and in-person genetic counselling for outcomes such as resolution of decision needs, adverse effects, the uptake of genetic testing, satisfaction with the intervention and decision quality.

***Group education session followed by individual genetic counselling versus individual education and genetic counselling***

Low to high quality evidence indicated that a group education session (or DVD) preceding a shorter individual genetic counselling session was not inferior to individual education and counselling. Time taken for individual counselling, however, was not an outcome analysed in this evidence review.

***Decision support versus usual care in BRCA1/2 mutation carriers***

In terms of adverse effects such as anxiety, depression and cancer worry, High quality evidence showed no important difference between decision aids when compared to usual care for women who are *BRCA1/2* positive. However, moderate quality evidence showed better decision satisfaction with the decision aid.

***Education app versus usual care (pre genetic counselling)***

Moderate quality evidence from a single trial evaluating a mobile telephone app for educating women with ovarian cancer about genetic counselling showed no evidence of an important difference in terms of an increased uptake of counselling with use of the app. However, high quality evidence showed an important benefit of the app in terms of improved decision quality when compared to usual care.

See appendix F for full GRADE tables.

## Economic evidence

### Included studies

Two economic studies were identified which were relevant to this review (Manchanda 2016, Tutty 2019).

A single economic search was undertaken for all topics included in the scope of this guideline. See supplementary material 2 for details.

### Excluded studies

Economic studies not included in this review are listed and reasons for their exclusion are provided in Supplement 2.

## Summary of included economic evidence

The systematic search of the economic literature undertaken for the guideline identified the following studies:

***DVD-assisted genetic counselling for BRCA1/2***

- One UK study on the cost-minimisation of DVD-assisted genetic counselling for *BRCA1/2* in adult Ashkenazi-Jewish men and women (Manchanda 2016).

***Telephone pre- and post-test genetic counselling for BRCA1/2***

- One Australian study on the costs of telephone pre- and post-test genetic counselling for *BRCA1/2* in adult women with high-grade serous ovarian cancer (Tutty 2019).

See the economic evidence tables in appendix H. See Table 3 to Table **4** for the economic evidence profiles of the included studies.

**Table 3: Economic evidence profile for DVD-assisted genetic counselling (DVD-C) for *BRCA1/2* versus traditional face-to-face counselling (TC) only for *BRCA1/2***

| | | | | Incremental | | | |
|---|---|---|---|---|---|---|---|
| **Study** | **Limitations** | **Applicability** | **Other comments** | **Costs** | **Effect** | **Cost effectiveness** | **Uncertainty** |
| Manchanda 2016<br><br>UK<br><br>Cost-minimisation analysis | Minor [1] | Partially [2] | A cluster-randomised non-inferiority RCT (N=936), [Manchanda 2016]<br>Time horizon: Under 1 year<br>Outcome: Genetic testing uptake, change in cancer risk perception, increase in knowledge, counselling time, satisfaction | -£14 | DVD-C non-inferior to TC for increase in knowledge, counselling satisfaction, and change in risk perception.<br><br>DVD-C equivalent to TC for genetic testing uptake. | DVD-C preferred | -No significant differences in outcomes.<br>-Adjusting knowledge scores to account for the proportion of valid questions answered and missing answers and transforming Genetic Counselling Satisfaction Scores to account for skewness did not change the results.<br>-Using multiple imputation for missing data showed similar results. |

*Abbreviations: DVD-C: DVD assisted genetic counselling; N: number of people; RCT: Randomised controlled trial; TC: Traditional face-to-face counselling; UK: United Kingdom*
*[1] Time horizon (under one year), however, there is no difference in outcomes and extending the time horizon is unlikely to change the result; effectiveness from a single RCT (N=936), the baseline estimates are unlikely to reflect outcomes for people in the UK, as these were based on a single RCT*
*[2] UK study; substantial proportion were males; no quality-adjusted life-years (QALYs), however not a problem since equivalent outcomes, superior genetic testing uptake, and lower costs*

**Table 4: Economic evidence profiles for telephone pre- and post-test genetic counselling (TC) for *BRCA1/2* versus in-person pre- and post-test genetic counselling (SC) for *BRCA1/2***

| Study | Limitations | Applicability | Other comments | Incremental | | | Uncertainty |
|---|---|---|---|---|---|---|---|
| | | | | Costs [1] | Effect | Cost effectiveness | |
| Tutty 2019<br><br>Australia<br><br>Cost-analysis | Potentially serious [2] | Partially [3] | Time horizon: 1 year<br>Outcome: Cost savings | −£8 | NA | TC cost saving | NR |

*Abbreviations: NA: Not applicable; NR: Not reported; TC: Telephone genetic counselling*
*[1] Costs were converted to UK pounds using OECD purchasing power parities (PPPs)*
*[2] No statistical analysis on costs, costs from a case-control study (N=120)*
*[3] The non-UK study, has not considered comparative health outcomes*

## Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

## Evidence statements

### Economic

#### DVD-assisted genetic counselling for *BRCA1/2*

- Evidence from a cost-minimisation analysis conducted alongside a non-inferiority RCT (Manchanda 2016, N=936) suggests that DVD-assisted genetic counselling (DVD-C) for *BRCA1/2* is likely to be preferred to traditional face-to-face counselling (TC) for *BRCA1/2* alone in the general adult Ashkenazi-Jewish population (men and women) in the UK. DVD-C was non-inferior to TC for genetic testing uptake, change in cancer risk perception, increase in knowledge, counselling time and satisfaction and less costly than TC. The study is partially applicable to the NICE decision-making context and has minor limitations.

#### Telephone pre- and post-genetic counselling for *BRCA1/2*

- Evidence from a cost analysis (Tutty 2019) with costs from a case-control study (N=120) suggests that telephone pre- and post-genetic counselling is cost-saving compared with traditional face-to-face counselling in adult women with high-grade serous ovarian cancer. The study is partially applicable to the NICE decision-making context and has potentially serious limitations.

## The committee's discussion and interpretation of the evidence

### The outcomes that matter most

Preparation for active participation in making a health decision was a critical outcome because it reflects whether the interventions help increase people's confidence in making decisions about their own healthcare. Resolution of decisional needs was also a critical outcome because it indicates whether an intervention helps resolve the key uncertainties and conflicts that prevent people from making a healthcare decision. Adverse effects associated with decision making, both at the time of making the decision and afterwards, were the final critical outcomes. Decision regret, anxiety, depression, distress, grief or loss and cancer worry were identified as examples of such adverse effects.

Satisfaction with the decision support intervention was an important outcome as it reflects the acceptability of the intervention. Uptake of the management option being considered was also chosen as an important outcome because it indicates whether the intervention influenced decisions one way or another (increasing or decreasing the proportion of people choosing that option). Decision quality was an important outcome as it reflects whether people are making fully informed decisions based on a good understanding of the options. Quality of life was an important outcome too because it indicates whether interventions that support decision making have an overall impact on the person's life.

### The quality of the evidence

The quality of the evidence was assessed using GRADE and ranged from low to high, with most of the evidence being of moderate quality. Evidence was downgraded predominately due to risk of bias, imprecision, and inconsistency. There was no relevant evidence identified

for psychological support interventions and for some adverse effects related to decision making, such as distress, grief or loss and quality-of-life outcomes.

**Benefits and harms**

The committee reflected on the variety of approaches used to provide information and support for individuals preparing to make a healthcare decision related to genetic testing and management options to reduce their risk of ovarian cancer. They also noted that studies included various populations (for example, women with known *BRCA1/2* mutations, those with a personal or family history of breast or ovarian, women diagnosed with epithelial ovarian, primary peritoneal or fallopian tube cancer) and the differing follow-up periods (for example, 1 week and 2 years). They also noted that 2 studies included a small proportion of men. Despite these limitations the committee decided to use the evidence as well as their experience and expertise to draft recommendations.

The committee recommended that healthcare professionals in genetics services should provide ongoing information and support. The committee found that important because, according to the evidence report A which focuses on information and support, the majority of the evidence suggests that people generally thought that they did not receive all the information and support they hoped to receive.

Evidence indicated that, compared with usual care, genetic counselling was associated with a higher uptake of the options being considered (such as the uptake of genetic testing and risk-reducing surgery in those at potentially high risk of familial ovarian cancer) and better knowledge about ovarian cancer risk (enabling more informed decision making). The committee discussed that this evidence was low to moderate quality, but noted that this finding was consistent with their experience and they considered genetic counselling to be an essential component of care. So they decided that individuals who meet the criteria for genetic testing should be provided with information about referral for genetic counselling and testing. They agreed that during genetic counselling information would always be shared with the person that would aim to help decision-making. The committee noted that this should include topics such as genetic testing, risk-reducing surgery, fertility and whether the person wants to have children, and menopause and managing symptoms genetic testing, risk-reducing surgery, fertility and whether the person wants to have children, and menopause and managing symptoms. This would allow the person to make a fully informed decision.

Based on their experience, the committee recommended that a healthcare professional with skills and experience in information provision and shared decision making specifically related to genetics and cancer risk should offer genetic counselling to people who meet the referral criteria for genetic testing. They acknowledged that this professional may not always be a genetic counsellor because genetic counselling services are being integrated into routine healthcare settings. This means that oncologists or nurse specialists may also counsel a woman about the option of genetic testing. The committee agreed that the professional's experience in information provision and shared decision making in the context of genetics and cancer risk was vital to help the person to make informed decisions.

The committee discussed that, although very low to high quality evidence showed no important difference in outcomes with telephone and face-to-face genetic counselling, based on their experience of remote consultations since the COVID-19 pandemic, they recognised that this was now a far more common method of delivery and decided to recommend face-to-face or remote genetic counselling. They noted that there were factors to take into account when deciding whether a remote or a face-to-face consultation would be more appropriate. For example, they agreed that personal preferences should be considered because this could influence how engaged someone is in the process and how much information they take in. It was also discussed that there were many different types of decisions that will have to be made at different times and that some discussions were potentially more appropriate face-to-face than remote (for example, they discussed that risk-reducing surgery would better be

discussed in face-to-face meetings but did not want to be prescriptive about this). They noted that remote counselling could have some advantages related to access to services (for example, people living in rural areas) but potentially some disadvantages for people with language or communication needs or people who do not have digital access. There are other factors that should be taken into account, such as when people do not understand or speak English and a translator is required. For these people face-to-face counselling may be preferable so that a translators can facilitate consultations.

There was some evidence to support group information giving sessions, for example by watching an informational DVD as a group. The committee noted that this evidence was mostly of high quality and recommended group sessions as an efficient way to deliver generic information before the person receives an individual genetic counselling session tailored to their personal information and support needs. However, they agreed that in some circumstances providing information on an individual basis may still be preferable, so they recommended group sessions be considered. Despite the potential cost savings, the committee did not want to be prescriptive about this because circumstances can vary widely (for example, level of risk, level of distress or other factors such as communication or language difficulties), which may mean that an individual session may be preferable for some people.

There was some moderate quality evidence to support the use of decision aids as an adjunct to genetic counselling in the context of breast and ovarian cancer risk management for people with pathogenic variants associated with increased ovarian cancer risk. The committee noted that none of the studies provided sufficient detail to reuse the patient decision aids and some are not publicly available, however they agreed that the concept of a decision aid may be considered as an option to support decision making. The committee decided against recommending specific decision aids, due to concerns about their need to be kept up-to-date and requirements for validation.

The committee noted a lack of relevant evidence on psychological interventions to support decision making They thought that psychological support could play an important role in helping women to make informed decisions at a time of anxiety and distress and therefore agreed to make a research recommendation on the effectiveness of psychological interventions.

**Cost effectiveness and resource use**

The committee discussed that it is current practice to offer genetic counselling to people at high risk of familial ovarian cancer. They acknowledged that the potential widening of the eligibility criteria for genetic counselling might have implementation issues due to a need for more trained individuals to undertake genetic counselling. However, the committee explained that genetic counselling services are increasingly being integrated into routine healthcare settings. This integration enables not only genetic counsellors but also oncologists or nurse specialists to provide counselling regarding genetic testing.

There was one existing economic study on genetic testing models. It suggested that telephone genetic counselling was cost saving for *BRCA1/2* compared with in-person genetic counselling. The committee acknowledged that this evidence was non-UK and that this study partially applied to the NICE decision-making context and had potentially serious limitations. The committee noted that video rather than telephone delivery is the current practice for most services. This may impact outcomes and further limit the applicability of this evidence. For example, a video session may result in better engagement than a telephone session. The committee also noted that this study had short time horizon which may not be long enough to capture all important differences in costs. For example, people who are at risk of familial ovarian cancer are going through a lifelong journey and may have multiple consultations before deciding whether to have, for example, genetic testing. This may mean

that this study may have underestimated costs. It also has not considered effectiveness outcomes.

The committee also noted that the telephone model also provided an opportunity to access hard-to-reach populations. For example, individuals residing in rural areas who may face barriers in accessing in-person counselling services. The economic analysis did not consider such potential benefits of the telephone counselling approach. Overall the committee agreed that the telephone and in-person genetic counselling models were broadly similar.

The committee also discussed the possibility that telephone genetic counselling might be much more acceptable. For example, it may reduce travel costs and allow a person's family to be present during a digital consultation. This is generally not possible during an in-person consultation.

The committee explained that services currently use both video and in-person genetic counselling models. The recommendations in this area are not expected to represent a change in practice or require additional resources to implement.

The committee explained that group sessions which occur before an individual genetic counselling session where people get general information are not current practice. However, such models utilising group sessions are not inferior in terms of clinical outcomes. They result in shorter individual genetic counselling sessions and potential cost savings for the NHS. One supporting UK study suggested that DVD-assisted genetic counselling for small groups of people with *BRCA* variant resulted in reduced costs and non-inferior outcomes compared with traditional individual in-person counselling.

The committee noted that this evidence was only partially applicable to the review due to a sample comprising a large proportion of men. Nevertheless, the committee was of the view that the findings were encouraging and supported alternative genetic counselling models. The committee also noted that people might value mutual support from such group sessions and that such benefits have not been accounted for in the economic evaluation. The committee explained that since this is not current practice, their recommendation may require some service re-organisation. However, there is potential for further savings due to shorter individual genetic counselling sessions. Given the lack of suitably trained staff to deliver genetic counselling some capacity may also be created in the system and help address broader workforce shortages.

Overall, due to the broadening of genetic testing criteria, more people may be accessing support services, which could result in increased pressure on existing services. However, access to support services such as genetic counselling and psychological services is essential for decision-making and risk management uptake. Successful risk management will lead to fewer cancers and associated cost savings to services, outweighing any additional costs associated with investment in capacity within these services.

**Other factors the committee took into account**

The committee noted that genetic tests are now commercially available (known as direct-to-consumer testing) and discussed what would happen if a person accesses NHS services and presents with a positive genetic test result. They agreed that not all laboratories produce accurate test results or prepare people for their test results; therefore, positive test results for a pathogenic variant for which NHS testing is offered will need to be discussed with an NHS genetics service to decide if referral is needed. This is consistent with the joint guidance by the Royal College of GPs and the British Society for Genetic Medicine.

The committee explained that many services do not accept referrals from individuals who have undergone direct-to-consumer genomic testing primarily because of the unreliability of such tests. This direct-to-consumer testing leads to the unnecessary burden of confirming non-existent variants. The recommendation in this area may help to address this issue by

ensuring that only appropriate cases with reliable results are referred to genetic services. This is consistent with other guidance and should be current practice for most services.

The committee were aware of other relevant guidance and made cross reference to it: the NICE guideline on shared decision making and the recommendations on patient decision aids in the NICE guideline on shared decision making.

### Recommendations supported by this evidence review

This evidence review supports recommendations 1.2.7 to 1.2.11 as well as 1.3.2 and bullet 8 in Table 1 and bullet 6 in Table 2 and research recommendation 1 on psychological support interventions in the NICE guideline.

## References – included studies


**Effectiveness**

**Armstrong 2005**

Armstrong, K., Weber, B., Ubel, P. A. et al. Individualized survival curves improve satisfaction with cancer risk management decisions in women with BRCA1/2 mutations. Journal of Clinical Oncology 23(36): 9319-28,2005

**Calzone 2005**

Calzone, K. A., Prindiville, S. A., Jourkiv, O. et al. Randomized comparison of group versus individual genetic education and counselling for familial breast and/or ovarian cancer. Journal of Clinical Oncology 23(15): 3455-64, 2005

**Drescher 2016**

Drescher, C. W., Beatty, J. D., Resta, R. et al. The effect of referral for genetic counselling on genetic testing and surgical prevention in women at high risk for ovarian cancer: Results from a randomized controlled trial. Cancer 122(22): 3509-3518, 2016

**Green 2004**

Green, M. J., Peterson, S. K., Baker, M. W. et al. Effect of a computer-based decision aid on knowledge, perceptions, and intentions about genetic testing for breast cancer susceptibility: a randomized controlled trial. JAMA 292(4): 442-52, 2004

**Kinney 2014**

Kinney, A. Y., Butler, K. M., Schwartz, M. D. et al. Expanding access to BRCA1/2 genetic counselling with telephone delivery: a cluster randomized trial. Journal of the National Cancer Institute 106(12), 2014

**Lerman 1997**

Lerman, C., Biesecker, B., Benkendorf, J. L. et al. Controlled trial of pretest education approaches to enhance informed decision-making for BRCA1 gene testing. Journal of the National Cancer Institute 89(2): 148-57, 1997

**Manchanda 2016**

Manchanda, R., Burnell, M., Loggenberg, K. 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 53(7): 472-80, 2016

**Roussi 2010**

Roussi, P., Sherman, K. A., Miller, S. et al. Enhanced counselling for women undergoing BRCA1/2 testing: Impact on knowledge and psychological distress-results from a randomised clinical trial. Psychology & Health 25(4): 401-15, 2010

**Schwartz 2014**

Schwartz, M. D., Valdimarsdottir, H. B., Peshkin, B. N. et al. Randomized noninferiority trial of telephone versus in-person genetic counselling for hereditary breast and ovarian cancer. Journal of Clinical Oncology 32(7): 618-26, 2014

**Tiller 2006**

Tiller, K., Meiser, B., Gaff, C. et al. A randomized controlled trial of a decision aid for women at increased risk of ovarian cancer. Medical Decision Making 26(4): 360-72, 2006

**van Roosmalen 2004a**

van Roosmalen, M. S., Stalmeier, P. F., Verhoef, L. C. et al. Randomised trial of a decision aid and its timing for women being tested for a BRCA1/2 mutation. British Journal of Cancer 90(2): 333-42, 2004

**van Roosmalen 2004b**

van Roosmalen, M. S., Stalmeier, P. F., Verhoef, L. C. et al. Randomized trial of a shared decision-making intervention consisting of trade-offs and individualized treatment information for BRCA1/2 mutation carriers. Journal of Clinical Oncology 22(16): 3293-301, 2004

**Vogel 2019**

Vogel, R. I., Niendorf, K., Petzel, S. et al. A patient-centered mobile health application to motivate use of genetic counselling among women with ovarian cancer: A pilot randomized controlled trial. Gynecol Oncol 153(1): 100-107, 2019

**Wakefield 2008a**

Wakefield, C. E., Meiser, B., Homewood, J. et al. A randomized controlled trial of a decision aid for women considering genetic testing for breast and ovarian cancer risk. Breast Cancer Research & Treatment 107(2): 289-301, 2008

**Wakefield 2008b**

Wakefield, C. E., Meiser, B., Homewood, J. et al. A randomized trial of a breast/ovarian cancer genetic testing decision aid used as a communication aid during genetic counselling. Psycho-Oncology 17(8): 844-54, 2008

**Wang 2005**

Wang, C., Gonzalez, R., Milliron, K. J. et al. Genetic counselling for BRCA1/2: a randomized controlled trial of two strategies to facilitate the education and counselling process. American Journal of Medical Genetics. Part A 134a(1): 66-73, 2005

**Economic**

**Manchanda 2016**

Manchanda R, Burnell M, Loggenberg K, Desai R, Wardle J, Sanderson SC, Gessler S, Side L, Balogun N, Kumar A, Dorkins H., Cluster-randomised non-inferiority trial comparing DVD-assisted and traditional genetic counselling in systematic population testing for BRCA1/2 mutations. Journal of medical genetics, 53, 472-80, 2016

**Tutty 2019**

Tutty E, Petelin L, McKinley J, Young MA, Meiser B, Rasmussen VM, Forbes Shepherd R, James PA, Forrest LE., Evaluation of telephone genetic counselling to facilitate germline BRCA1/2 testing in women with high-grade serous ovarian cancer, European Journal of Human Genetics, 27, 1186-96, 2019

# Appendices

## Appendix A Review protocol

### Review protocol for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

**Table 5: Review protocol**

| ID | Field | Content |
|---|---|---|
| 0. | PROSPERO registration number | CRD42022336229 |
| 1. | Review title | Interventions to support decision making about management options for women at increased risk of ovarian cancer |
| 2. | Review question | Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options? |
| 3. | Objective | To establish the effectiveness of interventions to aid decision making about management options for those at risk of familial ovarian cancer |
| 4. | Searches | The following databases will be searched:<br>• Cochrane Central Register of Controlled Trials (CENTRAL)<br>• Cochrane Database of Systematic Reviews (CDSR)<br>• Embase<br>• MEDLINE, MEDLINE in Process & MEDLINE Epub Ahead of Print<br>• Epistemonikos<br>• International Health Technology Assessment (INAHTA) database<br>• PsycINFO<br><br>Searches will be restricted by:<br>• English language studies |

| | | |
|---|---|---|
| | | • Human studies<br><br>The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion.<br><br>The full search strategies for MEDLINE database will be published in the final review. |
| 5. | Condition or domain being studied | Familial ovarian cancer |
| 6. | Population | Inclusion: Women with familial ovarian cancer or at increased risk of ovarian cancer preparing to make a healthcare decision. For example:<br>• Women considering risk assessment<br>• Women deciding about genetic testing<br>• Women deciding about risk reducing treatment<br>• Those considering HRT, fertility treatment or contraception<br><br>Exclusion: Women preparing to make healthcare decisions about recognition and initial management of ovarian cancer |
| 7. | Interventions | Decision coaching for decision making such as:<br>• Health counselling (including genetic counselling)<br>• Psychological support<br>Evidence based information (including online tools) such as:<br>• Decision aids<br>Combination of decision coaching and evidence-based information |
| 8. | Comparator | • Interventions compared with each other<br>• Usual care (no formal method used to help with decision making) |
| 9. | Types of study to be included | • Systematic reviews of RCTs<br>• RCTs<br>If RCTs are not available for a given management decision (risk assessment, genetic testing, risk reducing treatment or hormonal treatments) comparative observational studies will be included |
| 10. | Other exclusion criteria | Inclusion criteria:<br>• Full text papers |

| | | |
|---|---|---|
| | | • Observational studies should adjust for baseline differences between people in different intervention groups in their analyses<br>• For studies in mixed populations of familial cancers at least 80% of the participants should have or be at increased risk of ovarian cancer<br><br>Exclusion criteria:<br>• Conference abstracts<br>• Papers that do not include methodological details will not be included as they do not provide sufficient information to evaluate risk of bias/study quality.<br>• Non-English language articles |
| 11. | Context | Women making decisions about suspected or diagnosed familial ovarian cancer with healthcare professionals in primary, secondary or tertiary care |
| 12. | Primary outcomes (critical outcomes) | • Preparation for active participation in making a health decision<br>• Resolution of decisional needs<br>• Adverse effects (during or after decision making) such as:<br>  ○ Decision regret<br>  ○ Anxiety<br>  ○ Depression<br>  ○ Distress<br>  ○ Grief or loss<br>  ○ Cancer worry |
| 13. | Secondary outcomes (important outcomes) | • Satisfaction with decision support intervention<br>• Uptake of the management option being considered<br>• Decision quality<br>• Quality of life |
| 14. | Data extraction (selection and coding) | All references identified by the searches and from other sources will be uploaded into EPPI-Reviewer and de-duplicated. |

| | | |
|---|---|---|
| | | Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol.<br><br>Dual sifting will be performed on at least 10% of records (or 300 records, whichever is smaller); 90% agreement is required. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary.<br><br>Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion.<br><br>A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer. |
| 15. | Risk of bias (quality) assessment | Quality assessment of individual studies will be performed using the preferred checklist as described in Appendix H of Developing NICE guidelines: the manual<br><br>• ROBIS tool for systematic reviews<br>• Cochrane RoB tool v.2 for RCTs and quasi-RCTs<br>• The non-randomised study design appropriate checklist. For example, Cochrane ROBINS-I tool for non-randomised controlled trials.<br>The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer. |
| 16. | Strategy for data synthesis | Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where possible, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the $I^2$ statistic. Alongside visual inspection of the point estimates and confidence intervals, $I^2$ values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup |

| | | | |
|---|---|---|---|
| | | analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled.<br><br>The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/.<br><br>Importance and imprecision of findings will be assessed against minimally important differences (MIDs). The following MIDs will be used: 0.8 and 1.25 for all relative dichotomous outcomes, for continuous outcomes any published validated MIDs, if none are available then +/- 0.5x control group SD. | |
| 17. | Analysis of sub-groups | Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:<br><br>• Groups identified in the equality considerations section of the scope<br>  ○ socioeconomic and geographical factors<br>  ○ age<br>  ○ ethnicity<br>  ○ disabilities<br>  ○ people for whom English is not their first language or who have other communication needs.<br>  ○ trans people (particularly trans men)<br>  ○ non-binary people<br>• Context of decision (for example, mainstreaming vs genetics counsellor)<br><br>Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others | |
| 18. | | ☒ | Intervention |

| | | | |
|---|---|---|---|
| | Type and method of review | ☐ | Diagnostic |
| | | ☐ | Prognostic |
| | | ☐ | Qualitative |
| | | ☐ | Epidemiologic |
| | | ☐ | Service Delivery |
| | | ☐ | Other (please specify) |
| 19. | Language | English | |
| 20. | Country | England | |
| 21. | Anticipated or actual start date | June 2022 | |
| 22. | Anticipated completion date | September 2023 | |
| 23. | Stage of review at time of this submission | **Review stage** | **Started** / **Completed** |
| | | Preliminary searches | ☑ / ☑ |
| | | Piloting of the study selection process | ☑ / ☑ |
| | | Formal screening of search results against eligibility criteria | ☑ / ☑ |
| | | Data extraction | ☑ / ☑ |
| | | Risk of bias (quality) assessment | ☑ / ☑ |
| | | Data analysis | ☑ / ☑ |
| 24. | Named contact | **5a Named contact**<br>National Institute for Health and Care Excellence (NICE) | |

| | | |
|---|---|---|
| | | **5b Named contact e-mail**<br>foc@nice.org.uk<br><br>**5c Organisational affiliation of the review**<br>National Institute for Health and Care Excellence (NICE) |
| 25. | Review team members | From Guideline Development Team NGA, Centre for Guidelines, National Institute for Health and Care Excellence (NICE):<br>• Senior systematic reviewer<br>• Systematic reviewer |
| 26. | Funding sources/sponsor | This systematic review is being completed by NICE |
| 27. | Conflicts of interest | All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline. |
| 28. | Collaborators | Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage]. |
| 29. | Other registration details | |
| 30. | Reference/URL for published protocol | https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=336229 |
| 31. | Dissemination plans | NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. |

| | | | |
|---|---|---|---|
| 32. | Keywords | Decision making, management, ovarian cancer | |
| 33. | Details of existing review of same topic by same authors | None | |
| 34. | Current review status | ☐ | Ongoing |
| | | ☐ | Completed but not published |
| | | ☒ | Completed and published |
| | | ☐ | Completed, published and being updated |
| | | ☐ | Discontinued |
| 35. | Additional information | None | |
| 36. | Details of final publication | https://www.nice.org.uk | |

*GRADE: Grading of Recommendations Assessment, Development and Evaluation; MID: minimally important difference; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation*

# Appendix B Literature search strategies

## Literature search strategies for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

### Database: Ovid Medline ALL

### Date of last search: 23/01/2023

| # | Searches |
|---|---|
| 1 | exp Ovarian Neoplasms/ |
| 2 | (ovar* adj5 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 3 | or/1-2 |
| 4 | exp Breast Neoplasms/ |
| 5 | exp "Neoplasms, Ductal, Lobular, and Medullary"/ |
| 6 | ((breast* or mammary) adj5 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or dcis or ductal or infiltrat* or intraductal* or lobular or medullary or metasta*)).tw,kf. |
| 7 | or/4-6 |
| 8 | 3 or 7 |
| 9 | exp Genetic Predisposition to Disease/ |
| 10 | Pedigree/ |
| 11 | exp Neoplastic Syndromes, Hereditary/ |
| 12 | ((hereditary or inherit* or familial) adj3 (nonpolyposis or non polyposis) adj3 (colon or colorectal or bowel) adj3 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 13 | ((lynch or Muir Torre) adj2 (syndrome* or cancer*)).tw,kf. |
| 14 | HNPCC.tw,kf. |
| 15 | (peutz* or intestin* polyposis or STK11 or LKB1 or PJS or hLKB1 or (perior* adj1 lentigino*)).tw,kf. |
| 16 | ((hamartoma* or "polyps and spots" or cowden*) adj2 (syndrome* or polyp*)).tw,kf. |
| 17 | ((hereditary or inherit* or familial or adenomato* or attenuated) adj3 polyp* adj3 (coli or colon or colorectal or bowel or rectum or intestin* or gastrointestin* or syndrome* or multiple)).tw,kf. |
| 18 | gardner* syndrome*.tw,kf. |
| 19 | (MUTYH or MYH or FAP or AFAP or APC).tw,kf. |
| 20 | ((familial or inherit* or heredit* or predispos* or pre dispos* or susceptib* or ancestr* or genealog* or descent) adj2 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 21 | ("hereditary breast and ovarian cancer" or HBOC or Li Fraumeni syndrome or SBLA or LFS).tw,kf. |
| 22 | (famil* adj2 histor* adj2 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 23 | risk factors/ |
| 24 | ((risk* or probabil*) adj3 (high* or increas* or factor* or rais*) adj3 (mutat* or malignan* or gene* or variant*)).tw,kf. |
| 25 | ((carrier* or gene*) adj3 mutat*).tw,kf. |
| 26 | exp Genes, Tumor Suppressor/ |
| 27 | exp Tumor Suppressor Proteins/ |
| 28 | ((tumo?r* or cancer* or metastas?s or growth*) adj2 (suppress* adj1 (gene* or protein*))).tw,kf. |
| 29 | (anti oncogene* or antioncogene* or onco suppressor* or oncosuppressor*).tw,kf. |
| 30 | exp Fanconi Anemia Complementation Group Proteins/ |
| 31 | (Fanconi An?emia adj3 protein*).tw,kf. |
| 32 | (BRCA* or IRIS or PSCP or BRCC1 or BRIP1 or BACH1 or FANC* or PNCA* or RNF53 or PPP1R53 or FAD* or FACD or GLM3 or BRCC2 or XRCC11 or TP53 or P53 or PALB2 or RAD51* or R51H3 or BROVCA* or TRAD or BARD1 or MLH1 or MSH2 or MSH6 or PMS2).tw,kf. |
| 33 | ("breast cancer gene 1" or "breast cancer gene 2").tw,kf. |
| 34 | Rad51 Recombinase/ |
| 35 | Ataxia Telangiectasia Mutated Proteins/ |

| # | Searches |
|---|---|
| 36 | ((Ataxia telangiectasia adj1 mutated adj1 (protein* or kinase*)) or ATM or AT1 or ATA or ATC or ATD or ATDC or ATE or TEL1 or TELO1).tw,kf. |
| 37 | Checkpoint Kinase 2/ |
| 38 | (((checkpoint or check point or serine threonine) adj2 (protein* or kinase*)) or CHEK2 or CDS1 or CHK2 or HuCds1 or LFS2 or PP1425 or RAD53 or hCds1 or hchk2).tw,kf. |
| 39 | Carcinoma, Small Cell/ge [Genetics] |
| 40 | (small cell adj2 (cancer* or carcinoma*) adj2 gene*).tw,kf. |
| 41 | (SMARCA4 or BRG1 or CSS4 or SNF2 or SWI2 or MRD16 or RTPS2 or BAF190 or SNF2L4 or SNF2LB or hSNF2b or BAF190A or SNF2-beta).tw,kf. |
| 42 | exp Sertoli-Leydig Cell Tumor/ |
| 43 | (((Sertoli or leydig) adj3 (tumo?r* or adenoma* or cancer* or carcinoma* or neoplas* or metasta*)) or arrhenoblastoma* or andr?oblastoma* or SLCT or gynandroblastoma*).tw,kf. |
| 44 | (DICER?? or DCR1 or GLOW or MNG1 or aviD or HERNA or RMSE2 or K12H4?8-LIKE).tw,kf. |
| 45 | Epithelial Cell Adhesion Molecule/ |
| 46 | Epithelial cell adhesion molecule*.tw,kf. |
| 47 | (EPCAM* or EP CAM or ESA or KSA or M4S1 or MK-1 or DIAR5 or EGP??? or Ly74 or gp40 or CD326 or GA733?? or GA 733 or KS1?4 or MIC18 or TROP1 or BerEp4 or HNPCC8 or LYNCH8 or MOC-31 or Ber-Ep4 or TACSTD1).tw,kf. |
| 48 | or/9-47 |
| 49 | 8 and 48 |
| 50 | Decision Making/ or choice behavior/ or decision making, shared/ |
| 51 | decision support techniques/ |
| 52 | (decision* or decid* or choice* or choose or prefer*).ti,ab,kf. |
| 53 | risk assessment/ |
| 54 | or/50-53 |
| 55 | Genetic Counseling/ |
| 56 | exp Counseling/ |
| 57 | decision support systems clinical/ |
| 58 | Decision Making, Computer-Assisted/ |
| 59 | Health Education/ |
| 60 | Patient Education as Topic/ |
| 61 | Patient Participation/ |
| 62 | Physician-Patient Relations/ |
| 63 | "Referral and Consultation"/ |
| 64 | (assess* or coach* or guidance or counsel* or prepar*).ti,ab,kf. |
| 65 | Communication/ or Health Communication/ |
| 66 | Health Knowledge, Attitudes, Practice/ |
| 67 | Telemedicine/ |
| 68 | (telemedicine* or tele medicine* or telehealth* or tele health* or ehealth e health or mhealth or m health or mobile health).ti,ab,kf. |
| 69 | exp Communications Media/ or exp Social Networking/ or exp Internet/ |
| 70 | (app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or myspace or online or magazine* or mobile or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or telephone or text messag* or twitter or tweet* or video* or web* or wiki* or youtube*).ti,ab,kf. |
| 71 | or/55-70 |
| 72 | 54 and 71 |
| 73 | ((decision* or decid*) adj4 (manag* or aid* or tool* or instrument* or technolog* or technique* or system* or program* or algorithm* or process* or method* or intervention* or material*)).ti,ab,kf. |
| 74 | ((decision or decid* or choice* or choose or support*) adj4 (counsel* or psycholog* or psychosocial* or guide* or guidance)).ti,ab,kf. |
| 75 | (risk adj3 (information or communicat* or assessment or predict* or presentation or graphic* or tool* or method*)).ti,ab,kf. |
| 76 | (interactive adj2 (internet or online or graphic* or booklet*)).ti,ab,kf. |
| 77 | ((communicat* or advi?e* or provide* or provision* or inform*) adj4 (health or medical or electronic or virtual)).ti,ab,kf. |
| 78 | or/73-77 |

| # | Searches |
|---|---|
| 79 | 72 or 78 |
| 80 | 49 and 79 |
| 81 | letter/ |
| 82 | editorial/ |
| 83 | news/ |
| 84 | exp historical article/ |
| 85 | Anecdotes as Topic/ |
| 86 | comment/ |
| 87 | case reports/ |
| 88 | (letter or comment*).ti. |
| 89 | or/81-88 |
| 90 | randomized controlled trial/ or random*.ti,ab. |
| 91 | 89 not 90 |
| 92 | animals/ not humans/ |
| 93 | exp Animals, Laboratory/ |
| 94 | exp Animal Experimentation/ |
| 95 | exp Models, Animal/ |
| 96 | exp Rodentia/ |
| 97 | (rat or rats or mouse or mice or rodent*).ti. |
| 98 | or/91-97 |
| 99 | 80 not 98 |
| 100 | limit 99 to English language |
| 101 | randomized controlled trial.pt. |
| 102 | controlled clinical trial.pt. |
| 103 | pragmatic clinical trial.pt. |
| 104 | randomi#ed.ab. |
| 105 | placebo.ab. |
| 106 | drug therapy.fs. |
| 107 | randomly.ab. |
| 108 | trial.ab. |
| 109 | groups.ab. |
| 110 | or/101-109 |
| 111 | Clinical Trials as topic.sh. |
| 112 | trial.ti. |
| 113 | or/101-105,107,111-112 |
| 114 | Meta-Analysis/ |
| 115 | Meta-Analysis as Topic/ |
| 116 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 117 | ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. |
| 118 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 119 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 120 | (search* adj4 literature).ab. |
| 121 | (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. |
| 122 | cochrane.jw. |
| 123 | or/114-122 |
| 124 | 100 and (113 or 123) |
| 125 | Observational Studies as Topic/ |
| 126 | Observational Study/ |
| 127 | Epidemiologic Studies/ |
| 128 | exp Case-Control Studies/ |
| 129 | exp Cohort Studies/ |
| 130 | Cross-Sectional Studies/ |
| 131 | Controlled Before-After Studies/ |

| # | Searches |
|---|---|
| 132 | Historically Controlled Study/ |
| 133 | Interrupted Time Series Analysis/ |
| 134 | Comparative Study.pt. |
| 135 | case control$.tw. |
| 136 | case series.tw. |
| 137 | (cohort adj (study or studies)).tw. |
| 138 | cohort analy$.tw. |
| 139 | (follow up adj (study or studies)).tw. |
| 140 | (observational adj (study or studies)).tw. |
| 141 | longitudinal.tw. |
| 142 | prospective.tw. |
| 143 | retrospective.tw. |
| 144 | cross sectional.tw. |
| 145 | or/125-144 |
| 146 | 100 and 145 |

## Database: Ovid Embase

## Date of last search: 23/01/2023

| # | Searches |
|---|---|
| 1 | exp ovary tumor/ |
| 2 | (ovar* adj5 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 3 | or/1-2 |
| 4 | exp breast tumor/ |
| 5 | ((breast* or mammary) adj5 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or dcis or ductal or infiltrat* or intraductal* or lobular or medullary or metasta*)).tw,kf. |
| 6 | or/4-5 |
| 7 | 3 or 6 |
| 8 | exp genetic predisposition/ |
| 9 | pedigree/ |
| 10 | exp hereditary tumor syndrome/ |
| 11 | ((hereditary or inherit* or familial) adj3 (nonpolyposis or non polyposis) adj3 (colon or colorectal or bowel) adj3 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 12 | ((lynch or Muir Torre) adj2 (syndrome* or cancer*)).tw,kf. |
| 13 | HNPCC.tw,kf. |
| 14 | (peutz* or intestin* polyposis or STK11 or LKB1 or PJS or hLKB1 or (perior* adj1 lentigino*)).tw,kf. |
| 15 | ((hamartoma* or "polyps and spots" or cowden*) adj2 (syndrome* or polyp*)).tw,kf. |
| 16 | ((hereditary or inherit* or familial or adenomato* or attenuated) adj3 polyp* adj3 (coli or colon or colorectal or bowel or rectum or intestin* or gastrointestin* or syndrome* or multiple)).tw,kf. |
| 17 | gardner* syndrome*.tw,kf. |
| 18 | (MUTYH or MYH or FAP or AFAP or APC).tw,kf. |
| 19 | ((familial or inherit* or heredit* or predispos* or pre dispos* or susceptib* or ancestr* or genealog* or descent) adj2 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 20 | ((“hereditary breast and ovarian cancer”) or HBOC or Li Fraumeni syndrome or SBLA or LFS).tw,kf. |
| 21 | (famil* adj2 histor* adj2 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,kf. |
| 22 | risk factor/ |
| 23 | ((risk* or probabil*) adj3 (high* or increas* or factor* or rais*) adj3 (mutat* or malignan* or gene* or variant*)).tw,kf. |
| 24 | ((carrier* or gene*) adj3 mutat*).tw,kf. |
| 25 | tumor suppressor gene/ |
| 26 | exp tumor suppressor protein/ |
| 27 | ((tumo?r* or cancer* or metastas?s or growth*) adj2 (suppress* adj1 (gene* or protein*))).tw,kf. |

| # | Searches |
|---|---|
| 28 | (anti oncogene* or antioncogene* or onco suppressor* or oncosuppressor*).tw,kf. |
| 29 | Fanconi anemia protein/ |
| 30 | (Fanconi An?emia adj3 protein*).tw,kf. |
| 31 | (BRCA* or IRIS or PSCP or BRCC1 or BRIP1 or BACH1 or FANC* or PNCA* or RNF53 or PPP1R53 or FAD* or FACD or GLM3 or BRCC2 or XRCC11 or TP53 or P53 or PALB2 or RAD51* or R51H3 or BROVCA* or TRAD or BARD1 or MLH1 or MSH2 or MSH6 or PMS2).tw,kf. |
| 32 | ("breast cancer gene 1" or "breast cancer gene 2").tw,kf. |
| 33 | Rad51 protein/ |
| 34 | ATM protein/ |
| 35 | ((Ataxia telangiectasia adj1 mutated adj1 (protein* or kinase*)) or ATM or AT1 or ATA or ATC or ATD or ATDC or ATE or TEL1 or TELO1).tw,kf. |
| 36 | checkpoint kinase 2/ |
| 37 | (((checkpoint or check point or serine threonine) adj2 (protein* or kinase*)) or CHEK2 or CDS1 or CHK2 or HuCds1 or LFS2 or PP1425 or RAD53 or hCds1 or hchk2).tw,kf. |
| 38 | small cell carcinoma/ |
| 39 | genetics/ |
| 40 | 38 and 39 |
| 41 | (small cell adj2 (cancer* or carcinoma*) adj2 gene*).tw,kf. |
| 42 | (SMARCA4 or BRG1 or CSS4 or SNF2 or SWI2 or MRD16 or RTPS2 or BAF190 or SNF2L4 or SNF2LB or hSNF2b or BAF190A or SNF2-beta).tw,kf. |
| 43 | androblastoma/ or Sertoli cell tumor/ or Leydig cell tumor/ |
| 44 | (((Sertoli or leydig) adj3 (tumo?r* or adenoma* or cancer* or carcinoma* or neoplas* or metasta*)) or arrhenoblastoma* or andr?oblastoma* or SLCT or gynandroblastoma*).tw,kf. |
| 45 | (DICER?? or DCR1 or GLOW or MNG1 or aviD or HERNA or RMSE2 or K12H4?8-LIKE).tw,kf. |
| 46 | epithelial cell adhesion molecule/ |
| 47 | Epithelial cell adhesion molecule*.tw,kf. |
| 48 | (EPCAM* or EP CAM or ESA or KSA or M4S1 or MK-1 or DIAR5 or EGP??? or Ly74 or gp40 or CD326 or GA733?? or GA 733 or KS1?4 or MIC18 or TROP1 or BerEp4 or HNPCC8 or LYNCH8 or MOC-31 or Ber-Ep4 or TACSTD1).tw,kf. |
| 49 | or/8-37,40-48 |
| 50 | 7 and 49 |
| 51 | *decision making/ or *family decision making/ or *patient decision making/ or *shared decision making/ |
| 52 | exp *decision support system/ |
| 53 | (decision* or decid* or choice* or choose or prefer*).ti,ab,kf. |
| 54 | *risk assessment/ |
| 55 | or/51-54 |
| 56 | *genetic counseling/ |
| 57 | exp *counseling/ |
| 58 | *health education/ |
| 59 | *patient education/ |
| 60 | *patient participation/ |
| 61 | *doctor patient relationship/ |
| 62 | *patient referral/ |
| 63 | (assess* or coach* or guidance or counsel* or prepar*).ti,ab,kf. |
| 64 | *interpersonal communication/ or *medical information/ |
| 65 | *attitude to health/ |
| 66 | *telemedicine/ |
| 67 | (telemedicine* or tele medicine* or telehealth* or tele health* or ehealth e health or mhealth or m health or mobile health).ti,ab,kf. |
| 68 | exp *mass communication/ or exp *social network/ or exp *internet/ |
| 69 | (app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or myspace or online or magazine* or mobile or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or telephone or text messag* or twitter or tweet* or video* or web* or wiki* or youtube*).ti,ab,kf. |
| 70 | or/56-69 |
| 71 | 55 and 70 |

| # | Searches |
|---|---|
| 72 | ((decision* or decid*) adj4 (manag* or aid* or tool* or instrument* or technolog* or technique* or system* or program* or algorithm* or process* or method* or intervention* or material*)).ti,ab,kf. |
| 73 | ((decision or decid* or choice* or choose or support*) adj4 (counsel* or psycholog* or psychosocial* or guide* or guidance)).ti,ab,kf. |
| 74 | (risk adj3 (information or communicat* or assessment or predict* or presentation or graphic* or tool* or method*)).ti,ab,kf. |
| 75 | (interactive adj2 (internet or online or graphic* or booklet*)).ti,ab,kf. |
| 76 | ((communicat* or advi?e* or provide* or provision* or inform*) adj4 (health or medical or electronic or virtual)).ti,ab,kf. |
| 77 | or/72-76 |
| 78 | 71 or 77 |
| 79 | 50 and 78 |
| 80 | letter.pt. or letter/ |
| 81 | note.pt. |
| 82 | editorial.pt. |
| 83 | case report/ or case study/ |
| 84 | (letter or comment*).ti. |
| 85 | or/80-84 |
| 86 | randomized controlled trial/ or random*.ti,ab. |
| 87 | 85 not 86 |
| 88 | animal/ not human/ |
| 89 | nonhuman/ |
| 90 | exp Animal Experiment/ |
| 91 | exp Experimental Animal/ |
| 92 | animal model/ |
| 93 | exp Rodent/ |
| 94 | (rat or rats or mouse or mice or rodent*).ti. |
| 95 | or/87-94 |
| 96 | 79 not 95 |
| 97 | (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. |
| 98 | 96 not 97 |
| 99 | limit 98 to English language |
| 100 | random*.ti,ab. |
| 101 | factorial*.ti,ab. |
| 102 | (crossover* or cross over*).ti,ab. |
| 103 | ((doubl* or singl*) adj blind*).ti,ab. |
| 104 | (assign* or allocat* or volunteer* or placebo*).ti,ab. |
| 105 | crossover procedure/ |
| 106 | single blind procedure/ |
| 107 | randomized controlled trial/ |
| 108 | double blind procedure/ |
| 109 | or/100-108 |
| 110 | systematic review/ |
| 111 | meta-analysis/ |
| 112 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 113 | ((systematic or evidence) adj2 (review* or overview*)).ti,ab. |
| 114 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 115 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 116 | (search* adj4 literature).ab. |
| 117 | (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. |
| 118 | ((pool* or combined) adj2 (data or trials or studies or results)).ab. |
| 119 | cochrane.jw. |
| 120 | or/110-119 |
| 121 | 99 and (109 or 120) |
| 122 | Clinical study/ |

| # | Searches |
|---|---|
| 123 | Case control study/ |
| 124 | Family study/ |
| 125 | Longitudinal study/ |
| 126 | Retrospective study/ |
| 127 | comparative study/ |
| 128 | Prospective study/ |
| 129 | Randomized controlled trials/ |
| 130 | 128 not 129 |
| 131 | Cohort analysis/ |
| 132 | cohort analy$.tw. |
| 133 | (Cohort adj (study or studies)).tw. |
| 134 | (Case control$ adj (study or studies)).tw. |
| 135 | (follow up adj (study or studies)).tw. |
| 136 | (observational adj (study or studies)).tw. |
| 137 | (epidemiologic$ adj (study or studies)).tw. |
| 138 | (cross sectional adj (study or studies)).tw. |
| 139 | case series.tw. |
| 140 | prospective.tw. |
| 141 | retrospective.tw. |
| 142 | or/122-127,130-141 |
| 143 | 99 and 142 |

**Database: Cochrane Database of Systematic Reviews, Issue 1 of 12, January 2023 & Cochrane Central Register of Controlled Trials, Issue 1 of 12, January 2023**

**Date of last search: 23/01/2023**

| # | Searches |
|---|---|
| #1 | MeSH descriptor: [Ovarian Neoplasms] explode all trees |
| #2 | (ovar* NEAR/5 (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)):ti,ab,kw |
| #3 | #1 OR #2 |
| #4 | MeSH descriptor: [Breast Neoplasms] explode all trees |
| #5 | MeSH descriptor: [Neoplasms, Ductal, Lobular, and Medullary] explode all trees |
| #6 | ((breast* or mammary) NEAR/5 (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or dcis or ductal or infiltrat* or intraductal* or lobular or medullary or metasta*)):ti,ab,kw |
| #7 | {OR #4-#6} |
| #8 | #3 OR #7 |
| #9 | MeSH descriptor: [Genetic Predisposition to Disease] explode all trees |
| #10 | MeSH descriptor: [Pedigree] this term only |
| #11 | MeSH descriptor: [Neoplastic Syndromes, Hereditary] explode all trees |
| #12 | ((hereditary or inherit* or familial) NEAR/3 (nonpolyposis or "non polyposis") NEAR/3 (colon or colorectal or bowel) NEAR/3 (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)):ti,ab,kw |
| #13 | ((lynch or "Muir Torre") NEAR/2 (syndrome* or cancer*)):ti,ab,kw |
| #14 | HNPCC:ti,ab,kw |
| #15 | (peutz* or intestin* NEXT polyposis or STK11 or LKB1 or PJS or hLKB1 or (perior* NEAR/1 lentigino*)):ti,ab,kw |
| #16 | ((hamartoma* or "polyps and spots" or cowden*) NEAR/2 (syndrome* or polyp*)):ti,ab,kw |
| #17 | ((hereditary or inherit* or familial or adenomato* or attenuated) NEAR/3 polyp* NEAR/3 (coli or colon or colorectal or bowel or rectum or intestin* or gastrointestin* or syndrome* or multiple)):ti,ab,kw |
| #18 | gardner* NEXT syndrome*:ti,ab,kw |
| #19 | (MUTYH or MYH or FAP or AFAP or APC):ti,ab,kw |
| #20 | ((familial or inherit* or heredit* or predispos* or pre NEXT dispos* or susceptib* or ancestr* or genealog* or descent) NEAR/2 (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)):ti,ab,kw |
| #21 | ("hereditary breast and ovarian cancer" or HBOC or "Li Fraumeni syndrome" or SBLA or LFS):ti,ab,kw |

| # | Searches |
|---|---|
| #22 | (famil* NEAR/2 histor* NEAR/2 (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)):ti,ab,kw |
| #23 | MeSH descriptor: [Risk Factors] this term only |
| #24 | ((risk* or probabil*) NEAR/3 (high* or increas* or factor* or rais*) NEAR/3 (mutat* or malignan* or gene* or variant*)):ti,ab,kw |
| #25 | ((carrier* or gene*) NEAR/3 mutat*):ti,ab,kw |
| #26 | MeSH descriptor: [Genes, Tumor Suppressor] explode all trees |
| #27 | MeSH descriptor: [Tumor Suppressor Proteins] explode all trees |
| #28 | ((tumor* or tumour* or cancer* or metastasis or metastases or growth*) NEAR/2 (suppress* NEAR/1 (gene* or protein*))):ti,ab,kw |
| #29 | (anti NEXT oncogene* or antioncogene* or onco NEXT suppressor* or oncosuppressor*):ti,ab,kw |
| #30 | MeSH descriptor: [Fanconi Anemia Complementation Group Proteins] explode all trees |
| #31 | (("Fanconi Anemia" or "fanconi anaemia") NEAR/3 protein*):ti,ab,kw |
| #32 | (BRCA* or IRIS or PSCP or BRCC1 or BRIP1 or BACH1 or FANC* or PNCA* or RNF53 or PPP1R53 or FAD* or FACD or GLM3 or BRCC2 or XRCC11 or TP53 or P53 or PALB2 or RAD51* or R51H3 or BROVCA* or TRAD or BARD1 or MLH1 or MSH2 or MSH6 or PMS2):ti,ab,kw |
| #33 | ("breast cancer gene 1" or "breast cancer gene 2"):ti,ab,kw |
| #34 | MeSH descriptor: [Rad51 Recombinase] this term only |
| #35 | MeSH descriptor: [Ataxia Telangiectasia Mutated Proteins] this term only |
| #36 | (("Ataxia telangiectasia" NEAR/1 mutated NEAR/1 (protein* or kinase*)) or ATM or AT1 or ATA or ATC or ATD or ATDC or ATE or TEL1 or TELO1):ti,ab,kw |
| #37 | MeSH descriptor: [Checkpoint Kinase 2] this term only |
| #38 | (((checkpoint or "check point" or "serine threonine") NEAR/2 (protein* or kinase*)) or CHEK2 or CDS1 or CHK2 or HuCds1 or LFS2 or PP1425 or RAD53 or hCds1 or hchk2):ti,ab,kw |
| #39 | MeSH descriptor: [Carcinoma, Small Cell] this term only and with qualifier(s): [genetics - GE] |
| #40 | ("small cell" NEAR/2 (cancer* or carcinoma*) NEAR/2 gene*):ti,ab,kw |
| #41 | (SMARCA4 or BRG1 or CSS4 or SNF2 or SWI2 or MRD16 or RTPS2 or BAF190 or SNF2L4 or SNF2LB or hSNF2b or BAF190A or "SNF2 beta"):ti,ab,kw |
| #42 | MeSH descriptor: [Sertoli-Leydig Cell Tumor] explode all trees |
| #43 | (((Sertoli or leydig) NEAR/3 (tumor* or tumour* or adenoma* or cancer* or carcinoma* or neoplas* or metasta*)) or arrhenoblastoma* or androblastoma* or andreoblastoma* or SLCT or gynandroblastoma*):ti,ab,kw |
| #44 | (DICER* or DCR1 or GLOW or MNG1 or aviD or HERNA or RMSE2 or "K12H48 LIKE"):ti,ab,kw |
| #45 | MeSH descriptor: [Epithelial Cell Adhesion Molecule] this term only |
| #46 | Epithelial cell adhesion NEXT molecule*:ti,ab,kw |
| #47 | (EPCAM* or "EP CAM" or ESA or KSA or M4S1 or "MK 1" or DIAR5 or EGP* or Ly74 or gp40 or CD326 or GA733* or GA 733 or KS14 or MIC18 or TROP1 or BerEp4 or HNPCC8 or LYNCH8 or "MOC 31" or "Ber Ep4" or TACSTD1):ti,ab,kw |
| #48 | {OR #9-#47} |
| #49 | #8 AND #48 |
| #50 | MeSH descriptor: [Decision Making] this term only |
| #51 | MeSH descriptor: [Choice Behavior] this term only |
| #52 | MeSH descriptor: [Decision Making, Shared] this term only |
| #53 | MeSH descriptor: [Decision Support Techniques] this term only |
| #54 | (decision* or decid* or choice* or choose or prefer*):ti,ab,kw |
| #55 | MeSH descriptor: [Risk Assessment] this term only |
| #56 | {OR #50-#55} |
| #57 | MeSH descriptor: [Genetic Counseling] this term only |
| #58 | MeSH descriptor: [Counseling] explode all trees |
| #59 | MeSH descriptor: [Decision Support Systems, Clinical] this term only |
| #60 | MeSH descriptor: [Decision Making, Computer-Assisted] this term only |
| #61 | MeSH descriptor: [Health Education] this term only |
| #62 | MeSH descriptor: [Patient Education as Topic] this term only |
| #63 | MeSH descriptor: [Patient Participation] this term only |
| #64 | MeSH descriptor: [Physician-Patient Relations] this term only |
| #65 | MeSH descriptor: [Referral and Consultation] this term only |
| #66 | (assess* or coach* or guidance or counsel* or prepar*):ti,ab,kw |
| #67 | MeSH descriptor: [Communication] this term only |

| # | Searches |
|---|---|
| #68 | MeSH descriptor: [Health Communication] this term only |
| #69 | MeSH descriptor: [Health Knowledge, Attitudes, Practice] this term only |
| #70 | MeSH descriptor: [Telemedicine] this term only |
| #71 | (telemedicine* or tele NEXT medicine* or telehealth* or tele NEXT health* or ehealth "e health" or mhealth or "m health" or "mobile health"):ti,ab,kw |
| #72 | MeSH descriptor: [Communications Media] 1 tree(s) exploded |
| #73 | MeSH descriptor: [Social Networking] explode all trees |
| #74 | MeSH descriptor: [Internet] explode all trees |
| #75 | (app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e NEXT mail* or facebook or facetime or "face time" or forum* or handout* or hand-out* or hand NEXT out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or myspace or online or magazine* or mobile or newsletter* or pamphlet* or palm NEXT pilot* or personal NEXT digital NEXT assistant* or pocket NEXT pc* or podcast* or poster or posters or skype* or smartphone* or smart NEXT phone* or "social media" or social NEXT network* or sms or telephone or text NEXT messag* or twitter or tweet* or video* or web* or wiki* or youtube*):ti,ab,kw |
| #76 | {OR #57-#75} |
| #77 | #56 and #76 |
| #78 | ((decision* or decid*) NEAR/4 (manag* or aid* or tool* or instrument* or technolog* or technique* or system* or program* or algorithm* or process* or method* or intervention* or material*)):ti,ab,kw |
| #79 | ((decision or decid* or choice* or choose or support*) NEAR/4 (counsel* or psycholog* or psychosocial* or guide* or guidance)):ti,ab,kw |
| #80 | (risk NEAR/3 (information or communicat* or assessment or predict* or presentation or graphic* or tool* or method*)):ti,ab,kw |
| #81 | (interactive NEAR/2 (internet or online or graphic* or booklet*)):ti,ab,kw |
| #82 | ((communicat* or advise* or advice* or provide* or provision* or inform*) NEAR/4 (health or medical or electronic or virtual)):ti,ab,kw |
| #83 | {OR #78-#82} |
| #84 | #77 OR #83 |
| #85 | #49 AND #84 |
| #86 | conference:pt or (clinicaltrials or trialsearch):so |
| #87 | #85 NOT #86 |

## Database: Ovid PsycINFO

## Date of last search: 23/01/2023

| # | Searches |
|---|---|
| 1 | ovaries/ |
| 2 | exp neoplasms/ |
| 3 | 1 and 2 |
| 4 | (ovar* adj5 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,id. |
| 5 | 3 or 4 |
| 6 | exp Breast Neoplasms/ |
| 7 | ((breast* or mammary) adj5 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or dcis or ductal or infiltrat* or intraductal* or lobular or medullary or metasta*)).tw,id. |
| 8 | 6 or 7 |
| 9 | 5 or 8 |
| 10 | exp genetic disorders/ |
| 11 | ((hereditary or inherit* or familial) adj3 (nonpolyposis or non polyposis) adj3 (colon or colorectal or bowel) adj3 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,id. |
| 12 | ((lynch or Muir Torre) adj2 (syndrome* or cancer*)).tw,id. |
| 13 | HNPCC.tw,id. |
| 14 | (peutz* or intestin* polyposis or STK11 or LKB1 or PJS or hLKB1 or (perior* adj1 lentigino*)).tw,id. |
| 15 | ((hamartoma* or "polyps and spots" or cowden*) adj2 (syndrome* or polyp*)).tw,id. |
| 16 | ((hereditary or inherit* or familial or adenomato* or attenuated) adj3 polyp* adj3 (coli or colon or colorectal or bowel or rectum or intestin* or gastrointestin* or syndrome* or multiple)).tw,id. |
| 17 | gardner* syndrome*.tw,id. |

| # | Searches |
|---|---|
| 18 | (MUTYH or MYH or FAP or AFAP or APC).tw,id. |
| 19 | ((familial or inherit* or heredit* or predispos* or pre dispos* or susceptib* or ancestr* or genealog* or descent) adj2 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,id. |
| 20 | ("hereditary breast and ovarian cancer" or HBOC or Li Fraumeni syndrome or SBLA or LFS).tw,id. |
| 21 | (famil* adj2 histor* adj2 (cancer* or neoplas* or carcino* or malignan* or tumo?r* or adenocarcinoma* or sarcoma* or angiosarcoma* or lymphoma* or leiomyosarcoma* or metasta*)).tw,id. |
| 22 | Risk Factors/ |
| 23 | ((risk* or probabil*) adj3 (high* or increas* or factor* or rais*) adj3 (mutat* or malignan* or gene* or variant*)).tw,id. |
| 24 | ((carrier* or gene*) adj3 mutat*).tw,id. |
| 25 | ((tumo?r* or cancer* or metastas?s or growth*) adj2 (suppress* adj1 (gene* or protein*))).tw,id. |
| 26 | (anti oncogene* or antioncogene* or onco suppressor* or oncosuppressor*).tw,id. |
| 27 | (Fanconi An?emia adj3 protein*).tw,id. |
| 28 | (BRCA* or IRIS or PSCP or BRCC1 or BRIP1 or BACH1 or FANC* or PNCA* or RNF53 or PPP1R53 or FAD* or FACD or GLM3 or BRCC2 or XRCC11 or TP53 or P53 or PALB2 or RAD51* or R51H3 or BROVCA* or TRAD or BARD1 or MLH1 or MSH2 or MSH6 or PMS2).tw,id. |
| 29 | ("breast cancer gene 1" or "breast cancer gene 2").tw,id. |
| 30 | ((Ataxia telangiectasia adj1 mutated adj1 (protein* or kinase*)) or ATM or AT1 or ATA or ATC or ATD or ATDC or ATE or TEL1 or TELO1).tw,id. |
| 31 | (((checkpoint or check point or serine threonine) adj2 (protein* or kinase*)) or CHEK2 or CDS1 or CHK2 or HuCds1 or LFS2 or PP1425 or RAD53 or hCds1 or hchk2).tw,id. |
| 32 | (small cell adj2 (cancer* or carcinoma*) adj2 gene*).tw,id. |
| 33 | (SMARCA4 or BRG1 or CSS4 or SNF2 or SWI2 or MRD16 or RTPS2 or BAF190 or SNF2L4 or SNF2LB or hSNF2b or BAF190A or SNF2-beta).tw,id. |
| 34 | (((Sertoli or leydig) adj3 (tumo?r* or adenoma* or cancer* or carcinoma* or neoplas* or metasta*)) or arrhenoblastoma* or andr?oblastoma* or SLCT or gynandroblastoma*).tw,id. |
| 35 | (DICER?? or DCR1 or GLOW or MNG1 or aviD or HERNA or RMSE2 or K12H4?8-LIKE).tw,id. |
| 36 | Epithelial cell adhesion molecule*.tw,id. |
| 37 | (EPCAM* or EP CAM or ESA or KSA or M4S1 or MK-1 or DIAR5 or EGP??? or Ly74 or gp40 or CD326 or GA733?? or GA 733 or KS1?4 or MIC18 or TROP1 or BerEp4 or HNPCC8 or LYNCH8 or MOC-31 or Ber-Ep4 or TACSTD1).tw,id. |
| 38 | or/10-37 |
| 39 | 9 and 38 |
| 40 | decision making/ |
| 41 | decision support systems/ |
| 42 | (decision* or decid* or choice* or choose or prefer*).ti,ab,hw,id. |
| 43 | risk assessment/ |
| 44 | or/40-43 |
| 45 | genetic counseling/ |
| 46 | exp counseling/ |
| 47 | health education/ |
| 48 | client education/ |
| 49 | client participation/ |
| 50 | Professional Referral/ |
| 51 | Professional Consultation/ |
| 52 | (assess* or coach* or guidance or counsel* or prepar*).ti,ab,hw,id. |
| 53 | communication/ |
| 54 | health knowledge/ |
| 55 | exp telemedicine/ |
| 56 | (telemedicine* or tele medicine* or telehealth* or tele health* or ehealth e health or mhealth or m health or mobile health).ti,ab,hw,id. |
| 57 | exp communications media/ or exp social networks/ or exp internet/ |
| 58 | (app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or myspace or online or magazine* or mobile or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or telephone or text messag* or twitter or tweet* or video* or web* or wiki* or youtube*).ti,ab,hw,id. |
| 59 | or/45-58 |

| # | Searches |
|---|---|
| 60 | 44 and 59 |
| 61 | ((decision* or decid*) adj4 (manag* or aid* or tool* or instrument* or technolog* or technique* or system* or program* or algorithm* or process* or method* or intervention* or material*)).ti,ab,hw,id. |
| 62 | ((decision or decid* or choice* or choose or support*) adj4 (counsel* or psycholog* or psychosocial* or guide* or guidance)).ti,ab,hw,id. |
| 63 | (risk adj3 (information or communicat* or assessment or predict* or presentation or graphic* or tool* or method*)).ti,ab,hw,id. |
| 64 | (interactive adj2 (internet or online or graphic* or booklet*)).ti,ab,hw,id. |
| 65 | ((communicat* or advi?e* or provide* or provision* or inform*) adj4 (health or medical or electronic or virtual)).ti,ab,hw,id. |
| 66 | or/61-65 |
| 67 | 60 or 66 |
| 68 | 39 and 67 |
| 69 | (letter or editorial or comment reply).dt. or case report/ |
| 70 | (letter or comment*).ti. |
| 71 | or/69-70 |
| 72 | exp randomized controlled trial/ |
| 73 | random*.ti,ab. |
| 74 | or/72-73 |
| 75 | 71 not 74 |
| 76 | animal.po. |
| 77 | (rat or rats or rodent* or mouse or mice).ti. |
| 78 | or/75-77 |
| 79 | 68 not 78 |
| 80 | limit 79 to English language |
| 81 | clinical trial.md. |
| 82 | Clinical trials/ |
| 83 | Randomized controlled trials/ |
| 84 | Randomized clinical trials/ |
| 85 | assign*.ti,ab. |
| 86 | allocat*.ti,ab. |
| 87 | crossover*.ti,ab. |
| 88 | cross over*.ti,ab. |
| 89 | ((doubl* or singl*) adj blind*).ti,ab. |
| 90 | factorial*.ti,ab. |
| 91 | placebo*.ti,ab. |
| 92 | random*.ti,ab. |
| 93 | volunteer*.ti,ab. |
| 94 | trial?.ti,ab. |
| 95 | or/81-94 |
| 96 | (meta analysis or "systematic review").md. |
| 97 | META ANALYSIS/ |
| 98 | SYSTEMATIC REVIEW/ |
| 99 | (meta analy* or metanaly* or metaanaly*).ti,ab. |
| 100 | ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. |
| 101 | (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. |
| 102 | (search strategy or search criteria or systematic search or study selection or data extraction).ab. |
| 103 | (search* adj4 literature).ab. |
| 104 | cochrane.jw. |
| 105 | ((pool* or combined) adj2 (data or trials or studies or results)).ab. |
| 106 | (medline or pubmed or cochrane or embase or psychlit or psyclit or cinahl or science citation index or bids or cancerlit).ab. |
| 107 | or/96-106 |
| 108 | 80 and (95 or 107) |
| 109 | FOLLOWUP STUDY/ |

| # | Searches |
|---|---|
| 110 | followup study.md. |
| 111 | TREATMENT OUTCOMES/ |
| 112 | treatment outcome.md. |
| 113 | CLINICAL TRIALS/ |
| 114 | clinical trial.md. |
| 115 | chang$.tw. |
| 116 | evaluat$.tw. |
| 117 | reviewed.tw. |
| 118 | prospective$.tw. |
| 119 | retrospective$.tw. |
| 120 | baseline.tw. |
| 121 | cohort.tw. |
| 122 | case series.tw. |
| 123 | (compare$ or compara$).tw. |
| 124 | or/109-123 |
| 125 | 80 and 124 |

### Database: Epistemonikos

### Date of last search: 23/01/2023

| # | Searches |
|---|---|
| 1 | ((advanced_title_en:((ovar* AND (cancer* OR neoplas* OR carcino* OR malignan* OR tumor* OR tumour* OR adenocarcinoma*))) OR advanced_abstract_en:((ovar* AND (cancer* OR neoplas* OR carcino* OR malignan* OR tumor* OR tumour* OR adenocarcinoma*)))) |
| 2 | ((advanced_title_en:((familial OR inherit* OR heredit* OR predispos* OR susceptib*)) OR advanced_abstract_en:((familial OR inherit* OR heredit* OR predispos* OR susceptib*))) |
| 3 | (advanced_title_en:((BRCA1 OR BRCA2 OR TP53 OR P53)) OR advanced_abstract_en:((BRCA1 OR BRCA2 OR TP53 OR P53))) |
| 4 | #2 or #3 |
| 5 | #1 and #4 |
| 6 | (((advanced_title_en:((decision* OR decid* OR choice* OR choose OR prefer*)) OR advanced_abstract_en:((decision* OR decid* OR choice* OR choose OR prefer*)) |
| 7 | (advanced_title_en:((assess* OR coach* OR guidance OR counsel* OR prepar*)) OR advanced_abstract_en:((assess* OR coach* OR guidance OR counsel* OR prepar*)) |
| 8 | #6 and #7 |
| 9 | #5 and #8 |
| 10 | (((advanced_title_en:(((breast* OR mammary) AND (neoplas* OR cancer* OR tumo?r* OR carcino* OR adenocarcinoma* OR sarcoma* OR dcis OR ductal OR infiltrat* OR intraductal* OR lobular OR medullary OR metasta*))) OR advanced_abstract_en:(((breast* OR mammary) adj5 (neoplas* OR cancer* OR tumo?r* OR carcino* OR adenocarcinoma* OR sarcoma* OR dcis OR ductal OR infiltrat* OR intraductal* OR lobular OR medullary OR metasta*))))) |
| 11 | (((advanced_title_en:((decision* OR decid* OR choice* OR choose OR prefer*)) OR advanced_abstract_en:((decision* OR decid* OR choice* OR choose OR prefer*))) |
| 12 | (advanced_title_en:((assess* OR coach* OR guidance OR counsel* OR prepar*)) OR advanced_abstract_en:((assess* OR coach* OR guidance OR counsel* OR prepar*)))) |
| 13 | #11 and #12 |
| 14 | #10 and #13 |
| 15 | #9 or #14 |

### Database: INAHTA INTERNATIONAL HTA DATABASE

### Date of last search: 23/01/2023

| # | Searches |
|---|---|
| 1 | "Ovarian Neoplasms"[mhe] |
| 2 | ((ovar* AND (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma*)))[Title] OR ((ovar* AND (cancer* or neoplas* or carcino* or malignan* or tumor* or tumour* or adenocarcinoma*)))[abs] |
| 3 | #1 OR #2 |
| 4 | "Breast Neoplasms"[mhe] |

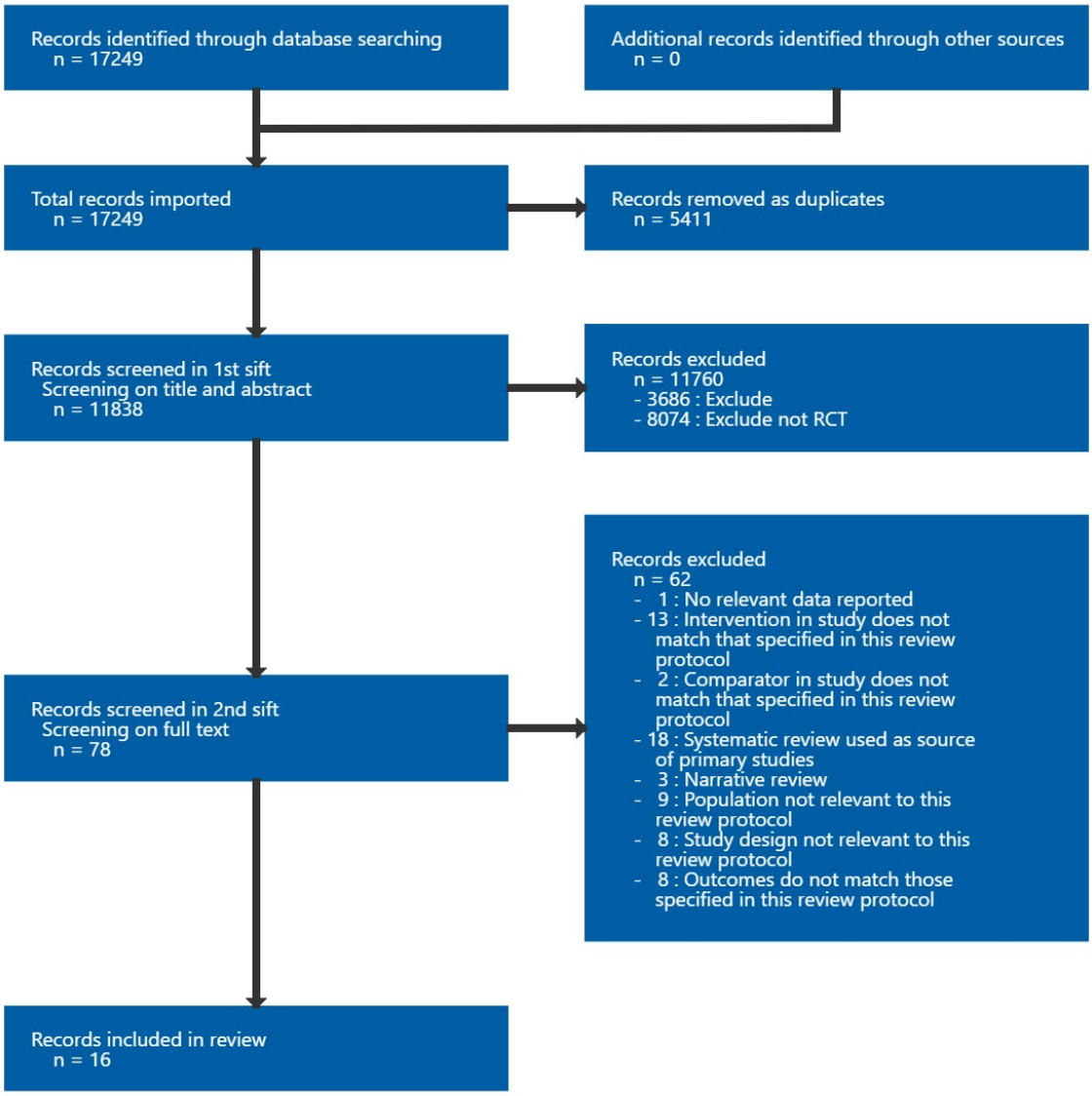
| # | Searches |
|---|---|
| 5 | "Neoplasms, Ductal, Lobular, and Medullary"[mhe] |
| 6 | "Breast"[mhe] |
| 7 | "Neoplasms"[mhe] |
| 8 | #6 AND #7 |
| 9 | (((breast* or mammary) AND (neoplas* or cancer* or tumo?r* or carcino* or adenocarcinoma* or sarcoma* or dcis or ductal or infiltrat* or intraductal* or lobular or medullary or metasta*)))[Title] OR (((breast* or mammary) AND (neoplas* or cancer* or tumo?r* or carcino* or adenocarcinoma* or sarcoma* or dcis or ductal or infiltrat* or intraductal* or lobular or medullary or metasta*)))[abs] |
| 10 | #4 OR #5 OR #8 OR #9 |
| 11 | #3 OR #10 |
| 12 | "Decision Making"[mh] |
| 13 | "Choice Behavior"[mh] |
| 14 | "Decision Making, Shared"[mh] |
| 15 | "Decision Support Techniques"[mh] |
| 16 | ((decision* or decid* or choice* or choose or prefer*))[Title] OR ((decision* or decid* or choice* or choose or prefer*))[abs] |
| 17 | "Risk Assessment"[mh] |
| 18 | #12 OR #13 OR #14 OR #15 OR #16 #17 |
| 19 | "Genetic Counseling"[mh] |
| 20 | "Counseling"[mhe] |
| 21 | "Decision Support Systems, Clinical"[mh] |
| 22 | "Decision Making, Computer-Assisted"[mh] |
| 23 | "Health Education"[mh] |
| 24 | "Patient Education as Topic"[mh] |
| 25 | "Patient Participation"[mh] |
| 26 | "Physician-Patient Relations"[mh] |
| 27 | "Referral and Consultation"[mh] |
| 28 | ((assess* or coach* or guidance or counsel* or prepar*))[Title] OR ((assess* or coach* or guidance or counsel* or prepar*))[abs] |
| 29 | "Communication"[mh] |
| 30 | "Health Communication"[mh] |
| 31 | "Health Knowledge, Attitudes, Practice"[mh] |
| 32 | "Telemedicine"[mh] |
| 33 | ((telemedicine* or tele medicine* or telehealth* or tele health* or ehealth e health or mhealth or m health or mobile health))[Title] OR ((telemedicine* or tele medicine* or telehealth* or tele health* or ehealth e health or mhealth or m health or mobile health))[abs] |
| 34 | "Communications Media"[mhe] |
| 35 | "Social Media"[mhe] |
| 36 | "Internet"[mhe] |
| 37 | ((app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or myspace or online or magazine* or mobile or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or telephone or text messag* or twitter or tweet* or video* or web* or wiki* or youtube*))[Title] OR ((app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or myspace or online or magazine* or mobile or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or telephone or text messag* or twitter or tweet* or video* or web* or wiki* or youtube*))[abs] |
| 38 | #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR 35 OR #36 OR #37 |
| 39 | #18 AND #38 |
| 40 | (((decision* or decid*) AND (manag* or aid* or tool* or instrument* or technolog* or technique* or system* or program* or algorithm* or process* or method* or intervention* or material*)))[Title] OR (((decision* or decid*) AND (manag* or aid* or tool* or instrument* or technolog* or technique* or system* or program* or algorithm* or process* or method* or intervention* or material*)))[abs] |
| 41 | (((decision or decid* or choice* or choose or support*) AND (counsel* or psycholog* or psychosocial* or guide* or guidance)))[Title] OR (((decision or decid* or choice* or choose or support*) AND (counsel* or psycholog* or psychosocial* or guide* or guidance)))[abs] |

| # | Searches |
|---|---|
| 42 | ((risk AND (information or communicat* or assessment or predict* or presentation or graphic* or tool* or method*)))[Title] OR ((risk AND (information or communicat* or assessment or predict* or presentation or graphic* or tool* or method*)))[abs] |
| 43 | ((interactive AND (internet or online or graphic* or booklet*)))[Title] OR ((interactive AND (internet or online or graphic* or booklet*)))[abs] |
| 44 | (((communicat* or advi?e* or provide* or provision* or inform*) AND (health or medical or electronic or virtual)))[Title] OR (((communicat* or advi?e* or provide* or provision* or inform*) AND (health or medical or electronic or virtual)))[abs] |
| 45 | #40 OR #41 OR #42 OR #43 OR #44 |
| 50 | #39 OR #45 |
| 51 | #11 and #50 |

# Appendix C Effectiveness evidence study selection

## Study selection for: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

### Figure 1: Study selection flow chart



# Appendix D Evidence tables

**Evidence tables for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?**

**Table 6: Evidence tables**

**Armstrong, 2005**

| | |
|---|---|
| **Bibliographic Reference** | Armstrong, K.; Weber, B.; Ubel, P. A.; Peters, N.; Holmes, J.; Schwartz, J. S.; Individualized survival curves improve satisfaction with cancer risk management decisions in women with BRCA1/2 mutations; Journal of Clinical Oncology; 2005; vol. 23 (no. 36); 9319-28 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | November 2000 and September 2003 |
| **Inclusion criteria** | • women who underwent *BRCA1/2* testing through the Cancer Risk Evaluation Program at the University of Pennsylvania between November 2000 and September 2003 and<br>• who had undergone either oophorectomy or mastectomy in the past |
| **Exclusion criteria** | • women who did not have significant residual breast or ovarian cancer risk (that is, they had already undergone both bilateral oophorectomy and bilateral mastectomy)<br>• if they had ovarian cancer or metastatic breast cancer |
| **Patient characteristics** | **Age (mean [range], years):** intervention 45 [30-59]; control 42 [26-54]<br><br>**Breast cancer diagnosis:** intervention 46%; control 50%<br><br>**Unilateral mastectomy:** intervention 23%; control 0% |

| | |
|---|---|
| | **Bilateral mastectomy:** intervention 46%; control 36%<br><br>**White ethnicity:** intervention 100%; control 100%<br><br>**Socioeconomic and geographical factors:** not reported<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** not reported<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | Participants in both groups had a one-on-one meeting with the research study coordinator that included a structured review of an educational booklet and completion of several questionnaires. The educational booklet was developed for the trial and reviewed general information about the cancer risks associated with *BRCA1/2* mutations and the alternative management options.<br><br>**Individualised treatment information:** a tailored decision support system (DSS) that provides individualized survival and cancer incidence curves specific to expected outcomes of alternative management strategies. The content of the DSS was tailored to the participant's past medical history by adjusting the transition probabilities in the Markov model and by presenting only the survival and incidence curves for options that remained relevant<br><br>**Usual care (educational booklet):** see above |
| **Duration of follow-up** | 6 weeks |
| **Sources of funding** | Not reported |
| **Sample size** | N=27 women enrolled, n=27 completed follow-up (n=14 in the intervention arm, n=13 in the control arm) |

**Study arms**

**Individualised information (N = 14)**

**Educational booklet (usual care) (N = 13)**

**Outcomes**

**Study timepoints**

- 6 week

**Resolution of decision needs**

| Outcome | Individualised information, N = 14 | Educational booklet (usual care), N = 13 |
|---|---|---|
| **Decision regret**<br>Decision satisfaction score, range 0 to 48, higher better)<br><br>Mean (SD) | 31.2 (5.99) | 26.2 (5.99) |

**Critical appraisal - Cochrane RoB 2.0 - standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Some concerns<br>*(statistical difference between intervention and control groups in terms of unilateral mastectomy: 23% had unilateral mastectomy in the intervention group and none in the control group)* |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(participants and outcome assessors blinded, but the research coordinator who generated and administered the decision support system for each participant was not blinded to group assignment)* |

| Section | Question | Answer |
|---|---|---|
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Low |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Low |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | none |

**Calzone, 2005**

| | |
|---|---|
| **Bibliographic Reference** | Calzone, K. A.; Prindiville, S. A.; Jourkiv, O.; Jenkins, J.; DeCarvalho, M.; Wallerstedt, D. B.; Liewehr, D. J.; Steinberg, S. M.; Soballe, P. W.; Lipkowitz, S.; Klein, P.; Kirsch, I. R.; Randomized comparison of group versus individual genetic education and counselling for familial breast and/or ovarian cancer; Journal of Clinical Oncology; 2005; vol. 23 (no. 15); 3455-64 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |

| | |
|---|---|
| **Study dates** | Not reported |
| **Inclusion criteria** | English-speaking men and women aged 25 to 68 years who met at least one of the following criteria:<br><br>• had a known deleterious *BRCA1/2* mutation documented in their family;<br>• were diagnosed with breast cancer or ductal carcinoma-in-situ at age ≤45 years or diagnosed with ovarian cancer at age ≤ 50 years;<br>• were men diagnosed with breast cancer at any age;<br>• were affected with either breast or ovarian cancer and had a family history of cancer consistent with a prior probability of harbouring a mutation of at least 10% by any peer-reviewed prior probability model<br>• Eligible men had to have a documentation of deleterious *BRCA1/2* mutation in the family or have a documented history of male breast cancer. |
| **Exclusion criteria** | None reported |
| **Patient characteristics** | **Gender:** Group Counselling (GC) male 4/71, female 67/71; Individual Counselling (IC) male 3/71, female 68/71<br><br>**Age, median years**: GC 40; IC 41<br><br>**Ethnicity:** GC White 64/71, Black 3/71, Hispanic 3/71, Asian 1/71; IC White 62/71, Black 5/71, Hispanic 2/71, Asian 2/71;<br><br>**Socioeconomic and geographical factors:** Income > $75K GC 40/71; IC 34/71; education at least college GC 48/72; IC 42/71<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** only English speakers included<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | **Group education + brief individual counselling:** Group education sessions ranged from two to 10 patients and were conducted by genetic advanced-practice nurses who had training in cancer genetics. The education session followed a detailed script with visual aides consisting of slides. Specific information regarding risk factors for breast and ovarian |

| | |
|---|---|
| | cancer and the risks, benefits, and limitations of *BRCA* testing was discussed in detail during the education session s. Immediately after the group education session, all participants had a brief individual counselling session with one of the genetic advanced practice nurses who had conducted and/or attended the education session. This individual session provided the patient with an opportunity to privately address personal concerns that were not amenable to group discussion, such as sexuality or body image issues. The individual session also reviewed personal risk and family history information and addressed questions as well as any other concerns associated with the education session and/or genetic testing<br><br>**Individual education + counselling:** The individual education and counselling session followed the detailed script and content as above but reproduced on a flip chart. The difference was any personal issues or questions that arose during the education part could be discussed straight away. |
| **Duration of follow-up** | Outcomes measured at baseline (before interventions), immediately after education and counselling, at 3 months, 6 months and 12 months |
| **Sources of funding** | National Cancer Institute; The Chief, Navy Bureau of Medicine and Surgery, Washington, DC, Clinical Investigation Program No. B99-015. |

**Study arms**

**Group education session followed by shorter genetic counselling (N = 71)**

**Individual education and genetic counselling (N = 71)**

**Outcomes**

**Study timepoints**

- Baseline
- 3 month
- 1 hour (Immediately after counselling and education)

**Group vs individual education & counselling**

| Outcome | Group education session followed by shorter genetic counselling, 3 month vs Baseline, N = 71 | Group education session followed by shorter genetic counselling, 1 hour vs Baseline, N = 71 | Individual education and genetic counselling, 3 month vs Baseline, N = 71 | Individual education and genetic counselling, 1 hour vs Baseline, N = 71 |
|---|---|---|---|---|
| **Adverse effects: cancer worry**<br>IES scale, range 0 to 75<br><br>Mean (SD) | -4.63 (12.1) | *empty data* | -1.38 (9.12) | *empty data* |
| **Uptake of the option being considered**<br>Rate of genetic testing<br><br>No of events | n = 63; % = 89 | *empty data* | n = 63; % = 89 | *empty data* |
| **Decision quality**<br>Objective knowledge, range 0 to 10<br><br>Mean (SD) | *empty data* | 1.76 (1.82) | *empty data* | 1.94 (2.01) |

Adverse effects: cancer worry - Polarity - Lower values are better
Decision quality - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 - standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Some concerns<br>*(no information whether the allocation sequence was concealed until participants were enrolled and assigned to interventions)* |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(participants were blinded but not reported if staff were blinded; not reported if ITT analysis was done)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Some concerns<br>*(participants were blinded but not reported if staff was)* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns<br>*(not reported if staff was blinded)* |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable<br>*(however, there were 4/71 and 3/71 men in the intervention and control groups, respectively)* |
| Overall bias and Directness | Risk of bias variation across outcomes | low for decision quality outcome; some concerns for the other outcomes |

**Drescher, 2016**

| | |
|---|---|
| **Bibliographic Reference** | Drescher, C. W.; Beatty, J. D.; Resta, R.; Andersen, M. R.; Watabayashi, K.; Thorpe, J.; Hawley, S.; Purkey, H.; Chubak, J.; Hanson, N.; Buist, D. S. M.; Urban, N.; The effect of referral for genetic counselling on genetic testing and surgical prevention in women at high risk for ovarian cancer: Results from a randomized controlled trial; Cancer; 2016; vol. 122 (no. 22); 3509-3518 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | Enrolment from 2008 to 2009 |
| **Inclusion criteria** | Eligible women were identified from a mammography database which included details about family cancer history. Women had to meet the NCCN 2013 pedigree criteria for referral to a genetic counsellor. |
| **Exclusion criteria** | Women were ineligible if they had a history of prior ovarian cancer or bilateral salpingo-oophorectomy (BSO), had tested negative for a previously identified family germline mutation, were unable or unwilling to provide informed consent; or could not identify a primary care physician to receive reports from the genetic counsellor. Women were not excluded based on prior genetic counselling or testing. |
| **Patient characteristics** | **Socioeconomic and geographical factors:** at least college educated: Genetic counselling group (GC) 77%; Usual care group (UC) 77%<br><br>**Age, mean (SD)**: GC 54 (10) years; UC 53 (10 ) years<br><br>**Ethnicity**: Race: GC 0% black, 67% white, 4% Asian; UC 1 black, 71% white, 4% Asian. Ashkenazi Jewish ethnicity: GC 15%; UC 16%<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** not reported<br><br>**Trans people (particularly trans men):** not reported |

| | |
|---|---|
| | **Non-binary people:** not reported |
| **Intervention(s)/control** | **Genetic counselling:** Women were invited to participate in a standard clinical genetic counselling session, of around one hour and including a face-to face consultation with a certified genetic counsellor. Counselling included review of the lifetime risk of breast and ovarian cancer for all women, an individualized discussion tailored to the participant's personal medical and family history, and determination of the need for genetic testing for the participant and/or her affected relative. Advantages and disadvantages of genetic testing were covered.<br><br>**Usual care:** women received routine care as directed by their primary healthcare provider, with no study-related intervention except follow-up outcome assessments. The study did not give these women personalized risk assessment information, general information about ovarian cancer risk factors, or advice regarding ovarian cancer risk. |
| **Duration of follow-up** | Follow up for genetic testing and BSO rates was up to 2 years. |
| **Sources of funding** | CDC 1R18DP001142; NIH/NCI P50CA083636 |
| **Sample size** | 458 |

**Study arms**

**Genetic counselling (N = 228)**
A standard clinical genetic counselling session of approximately one hour and including a face-to face consultation with a certified genetic counsellor.

**Usual care (N = 230)**
Routine care as directed by their primary healthcare provider, with no study-related intervention except follow-up outcome assessments.

**Outcomes**

**Study timepoints**
- 2 year

**Uptake of the option being considered**

| Outcome | Genetic counselling, 2-year, N = 228 | Usual care, 2-year, N = 230 |
|---|---|---|
| **Genetic testing**<br><br>No of events | n = 74 | n = 20 |
| **BSO**<br><br>No of events | n = 10 | n = 3 |

**Critical appraisal - Cochrane RoB 2.0 - standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns *(participants were not blinded)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Some concerns *(participants were not blinded)* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Low |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |

| Section | Question | Answer |
|---|---|---|
| Overall bias and Directness | Risk of bias variation across outcomes | none |

**Green, 2004**

| | |
|---|---|
| **Bibliographic Reference** | Green, M. J.; Peterson, S. K.; Baker, M. W.; Harper, G. R.; Friedman, L. C.; Rubinstein, W. S.; Mauger, D. T.; Effect of a computer-based decision aid on knowledge, perceptions, and intentions about genetic testing for breast cancer susceptibility: a randomized controlled trial; JAMA; 2004; vol. 292 (no. 4); 442-52 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | Enrolment from 2000 to 2002 |
| **Inclusion criteria** | 18 years or older; able to read, write, and speak English; referred for genetic counselling for evaluation of personal or family history of breast cancer; and able to give informed consent. |
| **Exclusion criteria** | Women who previously had undergone genetic counselling or testing for inherited breast cancer susceptibility were excluded. |
| **Patient characteristics** | **Socioeconomic and geographical factors:** at least college degree Computer + Genetic counselling group (CGC) 62%; genetic counselling group (GC) 50%<br><br>**Age, mean (SD not reported):** CGC 45 years; GC 44 years<br><br>**Ethnicity:** white: CGC 95%; GC 90%, African American GCG 2%; GC 6%, Hispanic CGC 2%; GC 4%<br><br>**Disabilities:** not reported |

| | |
|---|---|
| | **People with communication needs (for example, not English 1st language):** English language comprehension was an inclusion criterion<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | **Computer education followed by genetic counselling:** An interactive, multimedia CD-ROM–based decision aid designed to educate women about breast cancer, heredity, and the benefits and limitations of genetic testing. This was followed by genetic counselling as described below.<br><br>**Genetic counselling:** standard genetic counselling session provided by genetic counsellors or an advanced practice nurse with specialty training in cancer genetics. Counsellors (but not the computer program) provided individualized risk estimates for the likelihood of carrying a genetic mutation and of developing breast cancer. The counselling (but not the computer program) included a psychosocial component to address emotional concerns if they were raised during discussions of breast cancer risk and genetic testing. |
| **Duration of follow-up** | outcomes were measured at baseline, immediately after the intervention and at 1- and 6-months post-intervention. The computer group also had outcomes measured after the computer education session but before their genetic counselling session. |
| **Sources of funding** | Supported by grants R03CA70638 and R01CA84770 from the National Cancer Institute and the National Human Genome Research Institute, National Institutes of Health, Bethesda, Md. |
| **Sample size** | 211 |

**Study arms**

**Computer education followed by genetic counselling (N = 106)**

**Genetic counselling (N = 105)**

**Outcomes**

**Study timepoints**

- Baseline

- 1 hour (Immediately after the intervention)
- 1 month
- 6 month

**Adverse effects: anxiety**

| Outcome | Computer education followed by genetic counselling, 1 hour vs Baseline, N = 106 | Genetic counselling, 1 hour vs Baseline, N = 105 |
|---|---|---|
| **Anxiety (STAI state scale)**<br>Scale 20 to 80<br><br>Mean (SD) | -3.53 (8.68) | -4.42 (10.44) |

Anxiety (STAI state scale) - Polarity - Lower values are better

**Uptake of the option being considered**

| Outcome | Computer education followed by genetic counselling, Baseline, N = 106 | Computer education followed by genetic counselling, 1 hour, N = 106 | Computer education followed by genetic counselling, 1 month, N = 85 | Computer education followed by genetic counselling, 6-month, N = 76 | Genetic counselling, Baseline, N = 105 | Genetic counselling, 1 hour, N = 105 | Genetic counselling, 1 month, N = 87 | Genetic counselling, 6-month, N = 80 |
|---|---|---|---|---|---|---|---|---|
| **Uptake of genetic testing**<br><br>No of events | *empty data* | *empty data* | n = 20 | n = 33 | *empty data* | *empty data* | n = 16 | n = 28 |

**Decision quality**

| Outcome | Computer education followed by genetic counselling, 1 hour vs Baseline, N = 106 | Genetic counselling, 1 hour vs Baseline, N = 105 |
|---|---|---|
| **Objective knowledge test** (%)<br>Scale 0 to 100<br><br>Mean (SD) | 36.11 (75.55) | 29 (60.82) |

Objective knowledge test - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 - standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(no information about the blinding; not reported if ITT analysis was done)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Some concerns<br>*(no information about the blinding)* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns<br>*(not reported if investigators were blinded)* |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |

| Section | Question | Answer |
|---|---|---|
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | low for decision quality outcome; some concerns for the other outcomes |

**Kinney, 2014**

| | |
|---|---|
| **Bibliographic Reference** | Kinney, A. Y.; Butler, K. M.; Schwartz, M. D.; Mandelblatt, J. S.; Boucher, K. M.; Pappas, L. M.; Gammon, A.; Kohlmann, W.; Edwards, S. L.; Stroup, A. M.; Buys, S. S.; Flores, K. G.; Campo, R. A.; Expanding access to BRCA1/2 genetic counselling with telephone delivery: a cluster randomized trial; Journal of the National Cancer Institute; 2014; vol. 106 (no. 12) |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Cluster randomised controlled trial |
| **Study dates** | 2010 to 2012 |
| **Inclusion criteria** | Women 25 to 74 years of age with personal or family histories of breast or ovarian cancer, telephone access and who were able to travel to one of 14 outreach clinics. |
| **Exclusion criteria** | Women who had prior genetic counselling and/or *BRCA1/2* testing, who did not appear mentally competent to give informed consent as determined by study staff during screening, or who could not speak and read English. |
| **Patient characteristics** | **Gender:** Women<br><br>**Age, mean years:** 56.1 (SD 8.2)<br><br>**Ethnicity:** Non-Hispanic white 94%, Hispanic 3%, other 3%; Self-reported Ashkenazi Jewish 1% |

| | |
|---|---|
| | **Socioeconomic and geographical factors: at least college educated:** at least college educated 78%; household income >$70K 45%; rural residence 15%<br><br>**Disabilities**: not reported<br><br>**People with communication needs (for example, not English 1st language):** study excluded those who could not speak or read English.<br><br>**Trans people (particularly trans men)**: not reported<br><br>**Non-binary people:** not reported<br><br>**Cluster unit:** family<br><br>**Mean cluster size**: 1.02<br><br>**ICC:** not reported (authors assumed 0.05) |
| **Intervention(s)/control** | In-person and telephone counselling were delivered by the same five board-certified genetic counsellors using a semi-structured protocol.<br><br>**Telephone genetic counselling:** Participants randomly assigned to telephone counselling were mailed packets that included a sealed envelope containing an educational brochure about HBOC genetic counselling with visual aids. At the time of their session, participants opened their envelope and counsellors used the visual aids to explain breast-ovarian cancer genetics.<br><br>**In-person genetic counselling:** Women receiving in-person genetic counselling were given the same educational brochure during their session at the community clinic. |
| **Duration of follow-up** | Outcomes were measured at baseline one week after pretest and post-test counselling and six months after the last counselling session. Genetic testing uptake was assessed within 3 months of counselling. |
| **Sources of funding** | Supported grants from the National Cancer Institute at the National Institutes of Health (1R01CA129142 to AYK and U01 CA152958, K05 CA096940, and U01 CA183081 to JSM) and the Huntsman Cancer Foundation. The project was also supported by the Shared Resources (P30 CA042014) at Huntsman Cancer Institute (Biostatistics and Research Design, Genetic Counselling, Research Informatics, and the Utah Population Database [UPDB]); the Utah Cancer Registry, which is funded by Contract No. HHSN261201000026C from the National Cancer Institute's Surveillance, Epidemiology |

| | |
|---|---|
| | and End Results (SEER) Program with additional support from the Utah State Department of Health and the University of Utah; the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant 8UL1TR000105 (formerly UL1RR025764). |
| **Sample size** | 998 family clusters (1012 individuals)<br><br>Telephone counselling: 494 families (510 individuals)<br>In person counselling: 494 families (502 individuals) |

**Study arms**

**Telephone Genetic Counselling (N = 502)**

**Genetic Counselling (N = 510)**

**Outcomes**

**Study timepoints**

- Baseline
- 1 week (1 week after pretest counselling)
- 3 month
- 6 month

**Telephone versus in-person genetic counselling**

| Outcome | Telephone Genetic Counselling, Baseline, N = 502 | Telephone Genetic Counselling, 1 week, N = 449 | Telephone Genetic Counselling, 3-month, N = 464 | Telephone Genetic Counselling, 6-month, N = 385 | Genetic Counselling, Baseline, N = 510 | Genetic Counselling, 1 week, N = 416 | Genetic Counselling, 3-month, N = 437 | Genetic Counselling, 6-month, N = 369 |
|---|---|---|---|---|---|---|---|---|
| **Resolution of decisional** | *empty data* | *empty data* | *empty data* | 35.9 (8.96), n=383 | *empty data* | *empty data* | *empty data* | 35.4 (8.76), n=366 |

| Outcome | Telephone Genetic Counselling, Baseline, N = 502 | Telephone Genetic Counselling, 1 week, N = 449 | Telephone Genetic Counselling, 3-month, N = 464 | Telephone Genetic Counselling, 6-month, N = 385 | Genetic Counselling, Baseline, N = 510 | Genetic Counselling, 1 week, N = 416 | Genetic Counselling, 3-month, N = 437 | Genetic Counselling, 6-month, N = 369 |
|---|---|---|---|---|---|---|---|---|
| **needs** Decisional conflict scale, range 0 to 100<br><br>Mean (SD) | | | | | | | | |
| **Adverse effects: anxiety** BSI-18, 0 to 24<br><br>Mean (SD) | *empty data* | 2.3 (3.23) | *empty data* | *empty data* | *empty data* | 2.2 (3.11) | *empty data* | *empty data* |
| **Adverse effects: cancer worry** Impact of Events Scale, range 0 to 75<br><br>Mean (SD) | *empty data* | 12.9 (13.99), n=447 | *empty data* | *empty data* | *empty data* | 12.5 (13.41), n=411 | *empty data* | *empty data* |
| **Adverse effects: decision regret** | *empty data* | *empty data* | *empty data* | 20.53 (18.07), n=377 | *empty data* | *empty data* | *empty data* | 18.5 (17.34), n=359 |

| Outcome | Telephone Genetic Counselling, Baseline, N = 502 | Telephone Genetic Counselling, 1 week, N = 449 | Telephone Genetic Counselling, 3-month, N = 464 | Telephone Genetic Counselling, 6-month, N = 385 | Genetic Counselling, Baseline, N = 510 | Genetic Counselling, 1 week, N = 416 | Genetic Counselling, 3-month, N = 437 | Genetic Counselling, 6-month, N = 369 |
|---|---|---|---|---|---|---|---|---|
| Decision regret scale, range 0 to 100<br><br>Mean (SD) | | | | | | | | |
| **Uptake of the option being considered** Genetic testing rate<br><br>No of events | *empty data* | *empty data* | n = 101; % = 21.8 | *empty data* | *empty data* | *empty data* | n = 139; % = 31.8 | *empty data* |
| **Decision quality** Objective knowledge test, range 0 to 10<br><br>Mean (SD) | *empty data* | 8 (1.05), n=423 | *empty data* | *empty data* | *empty data* | 8.4 (2.03), n=398 | *empty data* | *empty data* |

Adverse effects: anxiety - Polarity - Lower values are better
Adverse effects: cancer worry - Polarity - Lower values are better
Decision quality - Polarity - Higher values are better
Adverse effects: decision regret - Polarity - Lower values are better
Resolution of decisional needs - Polarity - Lower values are better

**Critical appraisal - Cochrane RoB 2.0 – cluster RCT**

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 1. Was the allocation sequence random? | Yes<br>*(using a computer-generated allocation algorithm on the basis of a randomized blocks method using four, six, or eight patients in each block)* |
| 1a. Bias arising from the randomisation process | 1a. 2. Is it likely that the allocation sequence was subverted? | Probably no |
| 1a. Bias arising from the randomisation process | 1a. 3. Were there baseline imbalances that suggest a problem with the randomisation process? | No |
| 1a. Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 1. Were all the individual participants identified before randomisation of clusters (and if the trial specifically recruited patients were they all recruited before randomisation of clusters)? | Yes |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 2. If N/PN/NI to 1b.1: Is it likely that selection of individual participants was affected by knowledge of the intervention? | No<br>*(Staff who conducted the baseline assessments were blinded to the identity of participating relatives)* |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 3. Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation | Low |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | 2.1a Were participants aware that they were in a trial? | No information |
| 2. Bias due to deviations from intended interventions | 2.1b If Y/PY/NI to 2.1a: Were participants aware of their assigned intervention during the trial? | No information<br>*(not clear if participants were blinded)* |
| 2. Bias due to deviations from intended interventions | 2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial? | No information<br>*(not clear if personnel were blinded)* |
| 2. Bias due to deviations from intended interventions | 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5a Were any clusters analysed in a group different from the one to which they were assigned? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5b Were any participants analysed in a group different from the one to which their original cluster was randomised? | Probably No |
| 2. Bias due to deviations from intended interventions | 2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group? | Not applicable |
| 2. Bias due to deviations from intended interventions | Risk of bias judgement for deviations from intended interventions | Some concerns<br>*(not clear if participants and personnel were blinded)* |
| 3. Bias due to missing outcome data | 3.1a Were outcome data available for all, or nearly all, clusters randomised? | No information |

| Section | Question | Answer |
|---|---|---|
| 3. Bias due to missing outcome data | 3.1b Were outcome data available for all, or nearly all, participants within clusters? | Probably no |
| 3. Bias due to missing outcome data | 3.2 If N/PN/NI to 3.1a or 3.1b: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups? | Probably Yes |
| 3. Bias due to missing outcome data | 3.3 If N/PN/NI to 3.1a or 3.1b: Is there evidence that results were robust to the presence of missing outcome data? | Probably No |
| 3. Bias due to missing outcome data | Risk of bias judgement for missing outcome data | Some concerns<br>*(71% to 75% completed follow-up assessments)* |
| 4. Bias in measurement of the outcome | 4.1a Were outcome assessors aware that a trial was taking place? | No information |
| 4. Bias in measurement of the outcome | 4.1b If Y/PY/NI to 4.1: Were outcome assessors aware of the intervention received by study participants? | No information |
| 4. Bias in measurement of the outcome | 4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received? | Probably no |
| 4. Bias in measurement of the outcome | Risk of bias judgement for measurement of the outcome | Some concerns<br>*(not clear if outcome assessors were blinded)* |
| 5. Bias in selection of the reported result | 5.1 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple outcome measurements (for example, scales, definitions, time points) within the outcome domain? | No information<br>*(not reported if study protocol was registered in a central trials registry)* |

| Section | Question | Answer |
|---|---|---|
| 5. Bias in selection of the reported result | 5.2 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple analyses of the data? | No/Probably no |
| 5. Bias in selection of the reported result | Risk of bias for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Low |
| Overall bias and Directness | Overall Directness | Directly applicable |

**Lerman, 1997**

| | |
|---|---|
| **Bibliographic Reference** | Lerman, C.; Biesecker, B.; Benkendorf, J. L.; Kerner, J.; Gomez-Caminero, A.; Hughes, C.; Reed, M. M.; Controlled trial of pretest education approaches to enhance informed decision-making for BRCA1 gene testing; Journal of the National Cancer Institute; 1997; vol. 89 (no. 2); 148-57 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | Not reported |
| **Inclusion criteria** | Women aged 18-75 years who had had at least one first-degree relative with breast and/or ovarian cancer. |
| **Exclusion criteria** | Personal history of cancer (except basal cell or squamous cell skin cancers). |
| **Patient characteristics** | **Socioeconomic and geographical factors:** Income > $50,000: Education group (E) 65%; Education + Counselling (EC) 63%; Waiting list (WL) 60% |

| | |
|---|---|
| | **Age:** >50 years: E 30%, EC 25%, WL 30%<br><br>**Ethnicity:** White: E 74%, EC 75%, WL 66%. Black E 25%, EC 23%, WL 30%.<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** not reported<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | **Education:** individual session with oncology nurse or genetic counselor covering the following topics: individual risk factors for breast and ovarian cancers, patterns of inheritance, benefits, risk and limitations of genetic testing, risk reducing treatments and surveillance.<br><br>**Education plus counselling:** Women received the above education session plus non-directed counselling covering: experience with cancer in the family, anticipated impact of test results or deciding not to be tested, perceived coping resources and skills to adapt to different testing outcomes; and intentions on communication of test results to family, friends, and others<br><br>**Waiting list control:** subjects received the education intervention - but at the end of the trial after outcomes had been measured. |
| **Duration of follow-up** | 1 month. |
| **Sources of funding** | Public Health Service grants (RO1MH/HG54435) from the National Institutes of Mental Health and the National Center for Human Genome Research, National Institutes of Health Department of Health and Human Services. |
| **Sample size** | 400 |

**Study arms**

**Education (N = 114)**

**Education + counselling (N = 122)**

**Waiting list control (N = 164)**

**Outcomes**

**Study timepoints**

- Baseline
- 1 month (1 month after intervention)

**Uptake of the management option being considered**

| Outcome | Education, Baseline, N = | Education, 1 month, N = 114 | Education + counselling, Baseline, N = | Education + counselling, 1 month, N = 122 | Waiting list control, Baseline, N = | Waiting list control, 1 month, N = 164 |
|---|---|---|---|---|---|---|
| **Intention to get *BRCA1* test**<br><br>No of events | *empty data* | n = 65; % = 57 | *empty data* | n = 74; % = 61 | *empty data* | n = 87; % = 53 |

**Decision quality**

| Outcome | Education, 1 month vs Baseline, N = 114 | Education + counselling, 1 month vs Baseline, N = 122 | Waiting list control, 1 month vs Baseline, N = 164 |
|---|---|---|---|
| **Objective knowledge**<br>Scale 0 to 11<br><br>Mean (SD) | 1.84 (1.37) | 1.74 (1.33) | -0.54 (1.44) |

Objective knowledge - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Some concerns<br>*(no information on the randomisation procedure)* |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(participants were not blinded; not clear if personnel were blinded)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Low |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Some concerns<br>*(overall response rate was 76%; for education/education plus 65%)* |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | High |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | none |

**Manchanda, 2016**

| | |
|---|---|
| **Bibliographic Reference** | Manchanda, R.; Burnell, M.; Loggenberg, K.; Desai, R.; Wardle, J.; Sanderson, S. C.; Gessler, S.; Side, L.; Balogun, N.; Kumar, A.; Dorkins, H.; Wallis, Y.; Chapman, C.; Tomlinson, I.; Taylor, R.; Jacobs, C.; Legood, R.; Raikou, M.; McGuire, A.; Beller, U.; Menon, U.; Jacobs, I.; Cluster-randomised non-inferiority trial comparing DVD-assisted and traditional genetic counselling in systematic population testing for BRCA1/2 mutations; J Med Genet; 2016; vol. 53 (no. 7); 472-80 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | UK |
| **Study type** | Cluster randomised controlled trial |
| **Study dates** | 2009 to 2010 |
| **Inclusion criteria** | Participants were recruited from within a population screening trial. Criteria were age > 18 years and Ashkenazi Jewish ethnicity. |
| **Exclusion criteria** | Known *BRCA1/2* mutation, previous *BRCA1/2* testing or first-degree relative of a *BRCA1/2* carrier. |
| **Patient characteristics** | **Socioeconomic and geographical factors:** income > £50K DVD+GC 52%; GC 50%<br><br>**Gender:** DVD+GC men 35% women 65%; GC men 32% women 68%<br><br>**Age, mean (SD) years**: DVD+GC 53.9 (14.9), GC 53.9 (15.1)<br><br>**Ethnicity:** Ashkenazi Jewish<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** not reported<br><br>**Trans people (particularly trans men):** not reported |

| | |
|---|---|
| | **Non-binary people:** not reported<br><br>**Cluster unit:** clinic<br><br>**Mean cluster size**: 3.8<br><br>**ICC:** counselling satisfaction, 0.0005; counselling time, 0.15; uptake of testing, 0.21; gain in knowledge, 0.007 |
| **Intervention(s)/control** | **DVD + genetic counselling (DVD+GC):** Groups of participants (from 2 to 5 people) watched a DVD on risks/benefits/implications/purpose of genetic-testing. This was followed by an individual genetic counselling session as below.<br><br>**Genetic counselling (GC):** An individual non-directive pre-genetic test genetic counselling session provided by a qualified genetic-counsellor covering: interpretation of family history, knowledge about risk, inheritance, management options, advantages, disadvantages and psychosocial implications to promote informed choice and adaptation. |
| **Duration of follow-up** | Outcomes were assessed at baseline and post-consultation. |
| **Sources of funding** | The Eve Appeal charity |
| **Sample size** | 936<br><br>DVD+GC: n=409; 122 clusters; mean cluster size 3.4<br><br>GC: n=527 134 clusters; mean cluster size 3.8 |

**Study arms**

**DVD plus genetic counselling (N = 409)**

**Genetic counselling (N = 527)**

**Outcomes**

**Outcomes: DVD + genetic counselling versus genetic counselling**

| Outcome | DVD plus genetic counselling, N = 409 | Genetic counselling, N = 527 |
|---|---|---|
| **Counselling satisfaction**<br>GCSS Score (range 5 to 30)<br><br>Mean (SD) | 25.03 (5.27) | 25.59 (4.45) |
| **Counselling time** (Minutes)<br><br>Mean (SD) | 21.3 (8.4) | 46 (49.7) |
| **Uptake of the management option being considered (genetic testing)**<br>Cluster RCT (mean cluster size 3.6, ICC = 0.21 so divide by 1.55 for effective sample size)<br><br>No of events | n = 357 | n = 470 |
| **Decision quality: objective knowledge (change from baseline to post counselling)**<br>Scale 0 to 10<br><br>Mean (SD) | 1.64 (2.14) | 1.89 (2.29) |

Counselling satisfaction - Polarity - Higher values are better
Counselling time - Polarity - Lower values are better
Objective knowledge (change from baseline to post counselling) - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – cluster RCT**

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 1. Was the allocation sequence random? | Yes |
| 1a. Bias arising from the randomisation process | 1a. 2. Is it likely that the allocation sequence was subverted? | No |
| 1a. Bias arising from the randomisation process | 1a. 3. Were there baseline imbalances that suggest a problem with the randomisation process? | No |
| 1a. Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 1. Were all the individual participants identified before randomisation of clusters (and if the trial specifically recruited patients were they all recruited before randomisation of clusters)? | Yes |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 2. If N/PN/NI to 1b.1: Is it likely that selection of individual participants was affected by knowledge of the intervention? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 3. Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation | Low |
| 2. Bias due to deviations from intended interventions | 2.1a Were participants aware that they were in a trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.1b If Y/PY/NI to 2.1a: Were participants aware of their assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial? | Yes |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5a Were any clusters analysed in a group different from the one to which they were assigned? | No |
| 2. Bias due to deviations from intended interventions | 2.5b Were any participants analysed in a group different from the one to which their original cluster was randomised? | No |
| 2. Bias due to deviations from intended interventions | 2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group? | No |
| 2. Bias due to deviations from intended interventions | Risk of bias judgement for deviations from intended interventions | Low |
| 3. Bias due to missing outcome data | 3.1a Were outcome data available for all, or nearly all, clusters randomised? | Yes |
| 3. Bias due to missing outcome data | 3.1b Were outcome data available for all, or nearly all, participants within clusters? | Yes |
| 3. Bias due to missing outcome data | 3.2 If N/PN/NI to 3.1a or 3.1b: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups? | Probably Yes |
| 3. Bias due to missing outcome data | 3.3 If N/PN/NI to 3.1a or 3.1b: Is there evidence that results were robust to the presence of missing outcome data? | Yes |
| 3. Bias due to missing outcome data | Risk of bias judgement for missing outcome data | Low |
| 4. Bias in measurement of the outcome | 4.1a Were outcome assessors aware that a trial was taking place? | Yes |

| Section | Question | Answer |
|---|---|---|
| 4. Bias in measurement of the outcome | 4.1b If Y/PY/NI to 4.1: Were outcome assessors aware of the intervention received by study participants? | Not applicable |
| 4. Bias in measurement of the outcome | 4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received? | Probably no |
| 4. Bias in measurement of the outcome | Risk of bias judgement for measurement of the outcome | Some concerns |
| 5. Bias in selection of the reported result | 5.1 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple outcome measurements (for example, scales, definitions, time points) within the outcome domain? | No/Probably no |
| 5. Bias in selection of the reported result | 5.2 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple analyses of the data? | No/Probably no |
| 5. Bias in selection of the reported result | Risk of bias for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Low |
| Overall bias and Directness | Overall Directness | Directly applicable |

**Roussi, 2010**

| | |
|---|---|
| **Bibliographic Reference** | Roussi, P.; Sherman, K. A.; Miller, S.; Buzaglo, J.; Daly, M.; Taylor, A.; Ross, E.; Godwin, A.; Enhanced counselling for women undergoing BRCA1/2 testing: Impact on knowledge and psychological distress-results from a randomised clinical trial; Psychology & Health; 2010; vol. 25 (no. 4); 401-15 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | Enrolment 1998 to 2000 |
| **Inclusion criteria** | Women who contacted a family risk assessment program, who were 21 years of age and had a family history consistent with possible hereditary breast and/or ovarian cancer. |
| **Exclusion criteria** | None reported |
| **Patient characteristics** | **Gender:** Women<br><br>**Age:** 47% aged over 50 years<br><br>**Ethnicity:** 97% White<br><br>**Socioeconomic and geographical factors:** 58% at least college educated<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** not reported<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | **Enhanced genetic counselling (EGC):** Women had a standard genetic counselling session. This was followed by a 45-minute session with a health educator to encourage participants to systematically “pre-live” the possible testing scenarios and to anticipate their personal reactions to each potential outcome.<br><br>**Standard genetic counselling (GC):** Women had a standard genetic counselling session followed by 45 minutes of general health information. |
| **Duration of follow-up** | Participants were assessed at baseline, one week after enhanced or standard counselling, and one week after disclosure of the test result. |

| | |
|---|---|
| **Sample size** | 134 |

**Study arms**

**Enhanced genetic counselling (N = 69)**

**Genetic counselling (N = 65)**

**Outcomes**

**Study timepoints**

- Baseline
- 10 week (1 week post intervention)
- 34 week (1 week post test result)

**Enhanced versus standard genetic counselling**

| Outcome | Enhanced genetic counselling, Baseline, N = | Enhanced genetic counselling, 10-week, N = 43 | Enhanced genetic counselling, 34-week, N = | Genetic counselling, Baseline, N = | Genetic counselling, 10-week, N = 39 | Genetic counselling, 34-week, N = |
|---|---|---|---|---|---|---|
| **Decision quality: objective knowledge**<br><br>Mean (95% -I) | *empty data* (*empty data* to *empty data*) | 7.68 (7.14 to 8.22) | *empty data* (*empty data* to *empty data*) | *empty data* (*empty data* to *empty data*) | 7 (6.53 to 7.47) | *empty data* (*empty data* to *empty data*) |

**Critical appraisal - Cochrane RoB 2.0 – standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Low |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Low |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | High |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Low |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | High |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | none |

**Schwartz, 2014**

| | |
|---|---|
| **Bibliographic Reference** | Schwartz, M. D.; Valdimarsdottir, H. B.; Peshkin, B. N.; Mandelblatt, J.; Nusbaum, R.; Huang, A. T.; Chang, Y.; Graves, K.; Isaacs, C.; Wood, M.; McKinnon, W.; Garber, J.; McCormick, S.; Kinney, A. Y.; Luta, G.; Kelleher, S.; Leventhal, K. G.; Vegella, P.; Tong, A.; King, L.; Randomized noninferiority trial of telephone versus in-person genetic counselling for hereditary breast and ovarian cancer; Journal of Clinical Oncology; 2014; vol. 32 (no. 7); 618-26 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | 2005 to 2012 |
| **Inclusion criteria** | Women aged 21 to 85 years, with a minimum 10% risk for a *BRCA1/2* mutation who lived within the catchment area of a study site. |
| **Exclusion criteria** | Newly diagnosed (4 weeks) or metastatic cancer, those who lacked the cognitive capacity to provide informed consent, or those who were candidates for genetic counselling for another hereditary cancer syndrome |
| **Patient characteristics** | **Gender:** Women<br><br>**Age, mean (SD) years:** Telephone counselling (TC) 47.7 (13.1); Usual care (UC) 48.4 (14.2)<br><br>**Ethnicity:** White: TC 85.1%; UC 87.3%; Ashkenazi Jewish: TC 27.5%; UC 29.9%<br><br>**Socioeconomic and geographical factors: at least college educated:** At least college educated: TC 80%; UC 79.3%; Full time employment: TC 59.4%; UC 54.8%<br><br>**Disabilities**: not reported<br><br>**People with communication needs (for example, not English 1st language):** not reported<br><br>**Trans people (particularly trans men)**: not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | **Telephone genetic counselling (TC)**: before the TC session, participants were mailed visual aids for use during the session. TC was delivered over the telephone by the same genetic counsellors who delivered in-person counselling and with comparable content. After the initial session, participants could provide DNA at a physician's office, a local laboratory (blood kit supplied by the study), or the study site. Participants were posted a clinical summary letter outlining guidelines and recommendations. |

| | |
|---|---|
| | **In person genetic counselling (usual care):** participants received standard *BRCA1/2* genetic counselling and result disclosure delivered in person by board-certified/board-eligible genetic counsellors. Participants could provide DNA for testing at the conclusion of the initial counselling session. Participants were posted a clinical summary letter outlining guidelines and recommendations. |
| **Duration of follow-up** | Outcomes were measured at baseline, at 2 weeks (after pretest genetic counselling) and at 3 months. |
| **Sources of funding** | Supported by Grants No. R01 CA108933, U01 CA152958, and P30 CA051008 from the National Cancer Institute; by the Lombardi Comprehensive Cancer Center Biostatistics and Bioinformatics Shared Resource; and by the Jess and Mildred Fisher Center for Familial Cancer Research. |
| **Sample size** | 669 |

**Study arms**

**Telephone Genetic Counselling (N = 335)**

**In person Genetic Counselling (N = 334)**

**Outcomes**

**Study timepoints**

- Baseline
- 2 week
- 3 month

**Telephone versus in person genetic counselling**

| Outcome | Telephone Genetic Counselling, Baseline, N = 335 | Telephone Genetic Counselling, 2-week, N = 272 | Telephone Genetic Counselling, 3-month, N = 298 | In person Genetic Counselling, Baseline, N = 334 | In person Genetic Counselling, 2-week, N = 282 | In person Genetic Counselling, 3-month, N = 302 |
|---|---|---|---|---|---|---|
| **Resolution of decisional needs** | *empty data* | 7.5 (13.4) | *empty data* | *empty data* | 6.7 (13.2) | *empty data* |

| Outcome | Telephone Genetic Counselling, Baseline, N = 335 | Telephone Genetic Counselling, 2-week, N = 272 | Telephone Genetic Counselling, 3-month, N = 298 | In person Genetic Counselling, Baseline, N = 334 | In person Genetic Counselling, 2-week, N = 282 | In person Genetic Counselling, 3-month, N = 302 |
|---|---|---|---|---|---|---|
| Decisional Conflict Scale<br><br>Mean (SD) | | | | | | |
| **Adverse effects: cancer worry**<br>IES scale, range 0 to 76<br><br>Mean (SD) | *empty data* | 17.3 (15.1) | *empty data* | *empty data* | 17 (15.5) | *empty data* |
| **Satisfaction with decision support intervention**<br>Genetic counselling satisfaction scale<br><br>Mean (SD) | *empty data* | 26.8 (3.1) | *empty data* | *empty data* | 27 (3.3) | *empty data* |
| **Uptake of the option being considered**<br>Rate of genetic testing<br><br>No of events | *empty data* | *empty data* | n = 251; % = 84.2 | *empty data* | *empty data* | n = 272; % = 90.1 |

Resolution of decisional needs - Polarity - Lower values are better
Adverse effects: cancer worry - Polarity - Lower values are better
Satisfaction with decision support intervention - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Some concerns<br>*(not reported if the allocation sequence was concealed until participants were enrolled and assigned to interventions)* |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(no blinding)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Some concerns<br>*(no blinding)* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Some concerns<br>*(80% to 85% completed the follow-up assessments)* |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns<br>*(no blinding)* |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | low for the decision quality outcome, some concerns for the other outcomes |

**Tiller, 2006**

| | |
|---|---|
| **Bibliographic Reference** | Tiller, K.; Meiser, B.; Gaff, C.; Kirk, J.; Dudding, T.; Phillips, K. A.; Friedlander, M.; Tucker, K.; A randomized controlled trial of a decision aid for women at increased risk of ovarian cancer; Medical Decision Making; 2006; vol. 26 (no. 4); 360-72 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | Australia |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | Not reported |
| **Inclusion criteria** | Women from high-risk families who approached 1 of 6 participating familial cancer clinics in New South Wales and Victoria, Australia. Age 30 or older and proficient in English language. |
| **Exclusion criteria** | Proven noncarriers of ovarian-cancer-related gene mutations (that is, predictive genetic testing had identified the individual did not carry the *BRCA1/2* or HNPCC gene mutation), those who had already undergone a bilateral oophorectomy and those with personal history of ovarian cancer. |
| **Patient characteristics** | **Gender:** women<br><br>**Age, mean years:** Decision aid group (DA) 45.8; control group (C) 46.3<br><br>**Ethnicity:** not reported<br><br>**Socioeconomic and geographical factors:** at least college educated: DA 71%; C 71%<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** those not proficient in English were excluded<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported |

| | |
|---|---|
| **Intervention(s)/control** | **Decision aid intervention:** consisted of a booklet and a separate values clarification exercise. The booklet contained information on the risk factors for ovarian cancer, the impact of family history on risk, issues of genetic testing, 4 options for managing increased risk (watchful waiting, screening, OCP, prophylactic oophorectomy), and the benefits and risks associated with each option. The values clarification exercise took the information presented in the booklet one step further by asking women to rate the importance of each risk and benefit as "leaning" toward each of the 4 management options, and was included to facilitate a decision in line with personal values<br><br>**Control group:** received a general educational pamphlet which was a summary of the information in the booklet above - but without the values clarification exercise. |
| **Duration of follow-up** | Follow-up questionnaires were mailed 2 weeks and 6 months postintervention. |
| **Sources of funding** | Project Grant No. 209504 from the National Health and Medical Research Council of Australia (NHMRC) |
| **Sample size** | 131 |

**Study arms**

**Decision aid + genetic counselling (N = 68)**

**Genetic counselling (N = 63)**
Women in the control group also received an information leaflet.

**Outcomes**

**Study timepoints**
- Baseline
- 2 week
- 6 month

**Decision aid + genetic counselling versus genetic counselling (plus leaflet)**

| Outcome | Decision aid + genetic counselling, 2 week vs Baseline, N = 59 | Decision aid + genetic counselling, 6 month vs Baseline, N = 61 | Genetic counselling, 2-week vs Baseline, N = 53 | Genetic counselling, 6-month vs Baseline, N = 56 |
|---|---|---|---|---|
| **Resolution of decisional needs**<br>Decisional conflict scale, range 1 to 5<br><br>Mean (SD) | -0.63 (0.36), n=58 | -0.8 (0.36), n=51 | -0.39 (0.36), n=61 | -0.5 (0.36), n=55 |
| **Adverse effects: anxiety**<br>STAI state scale, range 20 to 80<br><br>Mean (SD) | -1.7 (8.97), n=58 | -4.2 (9.24), n=53 | -1.1 (9.58), n=60 | -2.8 (9.19), n=55 |
| **Adverse effects: depression**<br>HADS score, range 0 to 21<br><br>Mean (SD) | -0.6 (3.48), n=58 | -1.4 (3.26), n=50 | -0.6 (3.96), n=61 | -1.3 (3.96), n=56 |
| **Uptake of the option being considered**<br>Rates of risk reducing surgery<br><br>Nominal | *empty data* | 18 | *empty data* | 17 |
| **Decision quality: o*bjective knowledge***, scale 0 to 10<br><br>Mean (SD) | 2.8 (1.62), n=59 | 1.6 (1.4), n=40 | 2.2 (1.28), n=61 | 1.2 (1.27), n=47 |

Decision quality - Polarity - Higher values are better

Adverse effects: anxiety - Polarity - Lower values are better
Adverse effects: depression - Polarity - Lower values are better
Resolution of decisional needs - Polarity - Lower values are better

**Critical appraisal - Cochrane RoB 2.0 – standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Some concerns<br>*(no information whether the allocation sequence was random)* |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Low |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Low |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns<br>*(outcome assessors were aware of the intervention received by study participants)* |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | none |

**van Roosmalen, 2004a**

| | |
|---|---|
| **Bibliographic Reference** | van Roosmalen, M. S.; Stalmeier, P. F.; Verhoef, L. C.; Hoekstra-Weebers, J. E.; Oosterwijk, J. C.; Hoogerbrugge, N.; Moog, U.; van Daal, W. A.; Randomised trial of a decision aid and its timing for women being tested for a BRCA1/2 mutation; British Journal of Cancer; 2004; vol. 90 (no. 2); 333-42 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | The Netherlands |
| **Study type** | Cluster randomised controlled trial |
| **Study dates** | Enrolment from 1999 to 2001 |
| **Inclusion criteria** | People at increased risk of carrying a pathogenic variant: women with or without a personal history of breast or ovarian cancer, who provided a blood sample for *BRCA1/2* testing at the Family Cancer Clinics of the University Hospitals of Nijmegen. |
| **Exclusion criteria** | Cognitive disorder that precluded informed consent, insufficient knowledge of the Dutch language, distant metastases, had undergone both bilateral mastectomy and oophorectomy, treatment with chemotherapy, radiotherapy, or surgery for breast or ovarian cancer less than 1 month before blood sampling. |
| **Patient characteristics** | **Gender:** Women<br><br>**Age mean (SD):** DA group 43.7 (11.3) years; Usual care group 43.5 (10.4) years<br><br>**Ethnicity:** not reported<br><br>**Socioeconomic and geographical factors**: DA group 37% at least college education and 65% employed ; Usual care group 32% at least college education and 65% employed<br><br>**Disabilities**: - people with learning disabilities excluded<br><br>**People with communication needs (for example, not English 1st language):** - people with difficulty communicating in Dutch were excluded |

| | |
|---|---|
| | **Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported<br><br>**Cluster unit:** family<br><br>**Mean cluster size**: 1.16<br><br>**ICC:** not reported – assumed 0.05 |
| **Intervention(s)/control** | All participants had opted for genetic tests following genetic counselling<br><br>**Decision aid:** a decision aid (14-page brochure and 45 min. video) with detailed information on risk reducing treatment, surveillance and consequences. The video included patient stories from 8 *BRCA1/2* carriers. The DA was viewed at home 2 weeks after the person had blood taken for genetic tests.<br><br>**Control group:** usual care |
| **Duration of follow-up** | 4 weeks after blood sampling for genetic tests - 2 weeks after the decision aid intervention. |
| **Sources of funding** | Not reported. |
| **Sample size** | 368 |

**Study arms**

**Decision aid (N = 184)**

**Usual care (N = 184)**

**Outcomes**

**Study timepoints**

- Baseline
- 4 week (2 weeks after the decision aid intervention, 4 weeks after baseline measurements)

**Decision aid versus treatment as usual. Changes from baseline.**

| Outcome | Decision aid, 4-week vs Baseline, N = 176 | Usual care, 4-week vs Baseline, N = 175 |
|---|---|---|
| **Resolution of decisional needs**<br>Decision conflict scale, range 1-5<br><br>Mean (SD) | -0.1 (0.66), n=157 | -0.1 (0.67), n=162 |
| **Adverse effects: anxiety**<br>STAI scale, 20 to 80<br><br>Mean (SD) | -0.6 (7.18) | -1 (6.7), n=174 |
| **Adverse effects: depression**<br>CESD scale, range 0 to 60<br><br>Mean (SD) | -0.6 (5.54) | -0.6 (4.72) |
| **Adverse effects: cancer worry**<br>Impact of event scale, range 0 to 75<br><br>Mean (SD) | -1.3 (9.4), n=169 | -1.3 (8.7), n=174 |

Adverse effects: anxiety - Polarity - Lower values are better
Adverse effects: depression - Polarity - Lower values are better
Adverse effects: cancer worry - Polarity - Lower values are better
Resolution of decisional needs - Polarity - Lower values are better

**Decision aid versus treatment as usual. Final values.**

| Outcome | Decision aid, Baseline, N = 184 | Decision aid, 4-week, N = 184 | Usual care, Baseline, N = 184 | Usual care, 4-week, N = 184 |
|---|---|---|---|---|
| **Satisfaction with decision support intervention**<br>Scale 1 to 6<br><br>Mean (SD) | *empty data* | 3.8 (0.9) | *empty data* | 3.2 (1) |
| **Uptake of the option being considered**<br>treatment choice prophylactic oophorectomy<br><br>Nominal | 112 | 122 | 105 | 107 |
| **Uptake of the option being considered**<br>treatment choice ovarian cancer screening<br><br>Nominal | 36 | 24 | 44 | 48 |
| **Uptake of the option being considered**<br>treatment choice undecided<br><br>Nominal | 21 | 21 | 20 | 14 |

Satisfaction with decision support intervention - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – cluster RCT**

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 1. Was the allocation sequence random? | Yes<br>*(the randomization schedule, stratified by* |

| Section | Question | Answer |
|---|---|---|
| | | *medical history of breast/ovarian cancer and by timing of the informative DA, was generated by computer in blocks of 10)* |
| 1a. Bias arising from the randomisation process | 1a. 2. Is it likely that the allocation sequence was subverted? | Probably no |
| 1a. Bias arising from the randomisation process | 1a. 3. Were there baseline imbalances that suggest a problem with the randomisation process? | No |
| 1a. Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 1. Were all the individual participants identified before randomisation of clusters (and if the trial specifically recruited patients were they all recruited before randomisation of clusters)? | No information |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 2. If N/PN/NI to 1b.1: Is it likely that selection of individual participants was affected by knowledge of the intervention? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 3. Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation | Low |
| 2. Bias due to deviations from intended interventions | 2.1a Were participants aware that they were in a trial? | Yes |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | 2.1b If Y/PY/NI to 2.1a: Were participants aware of their assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice? | No information |
| 2. Bias due to deviations from intended interventions | 2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5a Were any clusters analysed in a group different from the one to which they were assigned? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5b Were any participants analysed in a group different from the one to which their original cluster was randomised? | Probably No |
| 2. Bias due to deviations from intended interventions | 2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group? | Not applicable |
| 2. Bias due to deviations from intended interventions | Risk of bias judgement for deviations from intended interventions | Some concerns<br>*(neither study participants nor members of the study staff were blinded to intervention assignment)* |
| 3. Bias due to missing outcome data | 3.1a Were outcome data available for all, or nearly all, clusters randomised? | Yes |

| Section | Question | Answer |
|---|---|---|
| 3. Bias due to missing outcome data | 3.1b Were outcome data available for all, or nearly all, participants within clusters? | Yes |
| 3. Bias due to missing outcome data | 3.2 If N/PN/NI to 3.1a or 3.1b: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups? | Probably Yes |
| 3. Bias due to missing outcome data | 3.3 If N/PN/NI to 3.1a or 3.1b: Is there evidence that results were robust to the presence of missing outcome data? | Probably Yes |
| 3. Bias due to missing outcome data | Risk of bias judgement for missing outcome data | Low |
| 4. Bias in measurement of the outcome | 4.1a Were outcome assessors aware that a trial was taking place? | Yes |
| 4. Bias in measurement of the outcome | 4.1b If Y/PY/NI to 4.1: Were outcome assessors aware of the intervention received by study participants? | Yes |
| 4. Bias in measurement of the outcome | 4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received? | Probably no |
| 4. Bias in measurement of the outcome | Risk of bias judgement for measurement of the outcome | Some concerns<br>*(neither study participants nor members of the study staff were blinded to intervention assignment)* |
| 5. Bias in selection of the reported result | 5.1 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple outcome measurements (for example, scales, definitions, time points) within the outcome domain? | No/Probably no |

| Section | Question | Answer |
|---|---|---|
| 5. Bias in selection of the reported result | 5.2 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple analyses of the data? | No/Probably no |
| 5. Bias in selection of the reported result | Risk of bias for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Low |
| Overall bias and Directness | Overall Directness | Directly applicable |

**van Roosmalen, 2004b**

| | |
|---|---|
| **Bibliographic Reference** | van Roosmalen, M. S.; Stalmeier, P. F.; Verhoef, L. C.; Hoekstra-Weebers, J. E.; Oosterwijk, J. C.; Hoogerbrugge, N.; Moog, U.; van Daal, W. A.; Randomized trial of a shared decision-making intervention consisting of trade-offs and individualized treatment information for BRCA1/2 mutation carriers; Journal of Clinical Oncology; 2004; vol. 22 (no. 16); 3293-301 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | The Netherlands |
| **Study type** | Cluster randomised controlled trial |
| **Study dates** | 1999 to 2001 |
| **Inclusion criteria** | Women affected and unaffected with breast/ovarian cancer who had chosen to undergo DNA testing were eligible. The women were part of another RCT (see van Roosmalen 2004a). Those whose genetic tests showed they were *BRCA1/2* positive were randomised for this trial. |

| | |
|---|---|
| **Exclusion criteria** | Women were excluded if they were unable to give informed consent, had insufficient knowledge of the Dutch language, were diagnosed with distant metastases, had undergone both bilateral mastectomy and oophorectomy, or had been treated with chemotherapy, radiotherapy, or surgery for breast/ovarian cancer less than 1 month before blood sampling. |
| **Patient characteristics** | **Gender:** Women<br><br>**Age mean (SD) years**: Shared Decision Making group (SDMI) 39.1 (9.7): Control group (C) 39.9 (10.4)<br><br>**Ethnicity:** not reported<br><br>**Socioeconomic and geographical factors:** employed SDMI 68% C 73%; college or higher SDMI 39% C 34%<br><br>**Disabilities:** not reported<br><br>**People with communication needs (for example, not English 1st language):** knowledge of the Dutch language was an inclusion criterion<br><br>**Trans people (particularly trans men):** not reported<br><br>**Non-binary people:** not reported<br><br>**Cluster unit:** family<br><br>**Mean cluster size**: 1.16<br><br>**ICC:** not reported – assumed 0.05 |
| **Intervention(s)/control** | **Decision aid:** this was a shared decision making intervention (SDMI) provided by a trained research assistant and consisted of three sessions with an interval of 1 to 2 weeks. In the first session, individual values for the treatment options (screening and prophylactic surgery) were assessed in a face-to-face interview. The second session covered the same assessment but was done by telephone. Decision analysis was used to arrive at individualized treatment information and then in the third session, individualized treatment information was shared with the women using two bar charts, presenting the treatment options relative to each other. |

| | |
|---|---|
| | **Usual care:** the control group received usual care - and had the SDMI (as above) later (after the first set of outcomes had been measured) |
| **Duration of follow-up** | Baseline was 2 weeks after positive genetic test, the SDMI intervention was 2 months later and outcomes were measured again 3 and 9 months later. |
| **Sources of funding** | Grant from the Dutch Cancer Society (grant No. 98-1585) |
| **Sample size** | 88 |

**Study arms**

**Decision aid (N = 44)**

**Usual care (N = 44)**

**Outcomes**

**Study timepoints**

- Baseline
- 3 month (3 months from baseline measures but 1 month after intervention started (the intervention took between 2 to 4 weeks))

**Shared decision making intervention versus control**

| Outcome | Decision aid, 3 month vs Baseline, N = 43 | Usual care, 3 month vs Baseline, N = 43 |
|---|---|---|
| **Adverse effects: anxiety**<br>STAI -state, range 20 to 80<br><br>Mean (SD) | -4.1 (7.56) | -3.9 (7.64) |
| **Adverse effects: depression**<br>CESD scale, range 0 to 60<br><br>Mean (SD) | -4.3 (5.95) | -3 (6.32) |

| Outcome | Decision aid, 3 month vs Baseline, N = 43 | Usual care, 3 month vs Baseline, N = 43 |
|---|---|---|
| **Adverse effects: cancer worry**<br>Impact of Event Scale, range 0 to 75<br><br>Mean (SD) | -3.8 (5.83) | -2.3 (5.42) |

Adverse effects: anxiety - Polarity - Lower values are better
Adverse effects: depression - Polarity - Lower values are better
Adverse effects: cancer worry - Polarity - Lower values are better
Decision uncertainty and related outcomes were not reported for ovarian cancer management decisions - the authors noted "With respect to the decision-related outcomes for the ovaries, no effects were found, neither in the short nor in the long term (data not shown)."

**Critical appraisal - Cochrane RoB 2.0 – cluster RCT**

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 1. Was the allocation sequence random? | Yes<br>*(the randomization schedule, stratified by medical history of breast/ovarian cancer and by timing of the informative DA, was generated by computer in blocks of 10)* |
| 1a. Bias arising from the randomisation process | 1a. 2. Is it likely that the allocation sequence was subverted? | Probably no |
| 1a. Bias arising from the randomisation process | 1a. 3. Were there baseline imbalances that suggest a problem with the randomisation process? | No |
| 1a. Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| 1b. Bias arising from the timing of identification and recruitment of | 1b. 1. Were all the individual participants identified before randomisation of clusters (and if the trial specifically recruited | No information |

| Section | Question | Answer |
|---|---|---|
| individual participants in relation to timing of randomisation | patients were they all recruited before randomisation of clusters)? | |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 2. If N/PN/NI to 1b.1: Is it likely that selection of individual participants was affected by knowledge of the intervention? | Probably no |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 3. Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation | Low |
| 2. Bias due to deviations from intended interventions | 2.1a Were participants aware that they were in a trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.1b If Y/PY/NI to 2.1a: Were participants aware of their assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? | Probably no |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | 2.5a Were any clusters analysed in a group different from the one to which they were assigned? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5b Were any participants analysed in a group different from the one to which their original cluster was randomised? | Probably No |
| 2. Bias due to deviations from intended interventions | 2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group? | Not applicable |
| 2. Bias due to deviations from intended interventions | Risk of bias judgement for deviations from intended interventions | Some concerns<br>*(neither study participants nor members of the study staff were blinded to intervention assignment)* |
| 3. Bias due to missing outcome data | 3.1a Were outcome data available for all, or nearly all, clusters randomised? | Yes |
| 3. Bias due to missing outcome data | 3.1b Were outcome data available for all, or nearly all, participants within clusters? | Yes |
| 3. Bias due to missing outcome data | 3.2 If N/PN/NI to 3.1a or 3.1b: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups? | Probably Yes |
| 3. Bias due to missing outcome data | 3.3 If N/PN/NI to 3.1a or 3.1b: Is there evidence that results were robust to the presence of missing outcome data? | Probably Yes |
| 3. Bias due to missing outcome data | Risk of bias judgement for missing outcome data | Low |
| 4. Bias in measurement of the outcome | 4.1a Were outcome assessors aware that a trial was taking place? | Yes |

| Section | Question | Answer |
|---|---|---|
| 4. Bias in measurement of the outcome | 4.1b If Y/PY/NI to 4.1: Were outcome assessors aware of the intervention received by study participants? | Yes |
| 4. Bias in measurement of the outcome | 4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received? | Probably no |
| 4. Bias in measurement of the outcome | Risk of bias judgement for measurement of the outcome | Some concerns<br>*(neither study participants nor members of the study staff were blinded to intervention assignment)* |
| 5. Bias in selection of the reported result | 5.1 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple outcome measurements (for example, scales, definitions, time points) within the outcome domain? | No/Probably no |
| 5. Bias in selection of the reported result | 5.2 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple analyses of the data? | No/Probably no |
| 5. Bias in selection of the reported result | Risk of bias for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Low |
| Overall bias and Directness | Overall Directness | Directly applicable |

**Vogel, 2019**

| | |
|---|---|
| **Bibliographic Reference** | Vogel, R. I.; Niendorf, K.; Petzel, S.; Lee, H.; Teoh, D.; Blaes, A. H.; Argenta, P.; Rivard, C.; Winterhoff, B.; Lee, H. Y.; Geller, M. A.; A patient-centered mobile health application to motivate use of genetic counselling among women with ovarian cancer: A pilot randomized controlled trial; Gynecol Oncol; 2019; vol. 153 (no. 1); 100-107 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | 2016 to 2018 |
| **Inclusion criteria** | Women with a diagnosis of epithelial ovarian, primary peritoneal or fallopian tube cancer who had not previously received or scheduled genetic counselling or testing related to cancer. 18 years old or older, able to read and write in English and no known major psychiatric or neurological diagnosis |
| **Exclusion criteria** | None reported |
| **Patient characteristics** | **Gender:** Women<br><br>**Age, mean (SD) years:** App group (A) 60.9 (10.7) Control group (C) 62 (12.0)<br><br>**Ethnicity:** white non-Hispanic A 90.6%, C 88.2%<br><br>**Socioeconomic and geographical factors:** employed A 53%, C 43%; at least college educated A 51%, C 50%<br><br>**Disabilities:** not reported but major psychiatric or neurological diagnosis excluded<br><br>**People with communication needs** (for example, not English 1st language): ability to read and write in English was an inclusion criterion<br><br>**Trans people (particularly trans men)**: not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | **mAGIC app:** an iOS mobile Application for Genetic Information on Cancer (mAGIC) intervention aimed to persuade women with ovarian cancer to pursue genetic counselling. Over 7 days the app covered education topics on genetic counselling, genetic testing, cancer genetics and personal health, impact on family, self-care and preparation for a genetic counselling appointment.<br><br>**Usual care:** all participants (including those in the mAGIC app group) received a pamphlet on hereditary cancer risk and genetic counselling at the time of study entry and were provided with information on both the genetic counselling |

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|---|---|
| | services in the clinic along with other genetic counsellors throughout the state for patients who preferred appointments near their home. |
| **Duration of follow-up** | Outcomes measured at baseline, 1 week and 3 months. |
| **Sources of funding** | Department of Defense Ovarian Cancer Research Program [A-18144] |
| **Sample size** | 104 |

**Study arms**

**mAGIC intervention (N = 53)**

**Usual care (N = 51)**

**Outcomes**

**Study timepoints**

- Baseline
- 1 week
- 3 month

**mAGIC app versus usual care**

| Outcome | mAGIC intervention, Baseline, N = 53 | mAGIC intervention, 1 week, N = 47 | mAGIC intervention, 3-month, N = 46 | Usual care, Baseline, N = 51 | Usual care, 1 week, N = 48 | Usual care, 3-month, N = 45 |
|---|---|---|---|---|---|---|
| **Uptake of the option being considered**<br>Rate of genetic counselling<br><br>No of events | *empty data* | *empty data* | n = 25; % = 54.5 | *empty data* | *empty data* | n = 17; % = 38.6 |

| Outcome | mAGIC intervention, Baseline, N = 53 | mAGIC intervention, 1 week, N = 47 | mAGIC intervention, 3-month, N = 46 | Usual care, Baseline, N = 51 | Usual care, 1 week, N = 48 | Usual care, 3-month, N = 45 |
|---|---|---|---|---|---|---|
| **Decision quality: objective knowledge tes**t, range 0 to 10<br><br>Mean (SD) | *empty data* | 9.4 (1) | *empty data* | *empty data* | 7.1 (1.5) | *empty data* |

Decision quality - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(not clear if participants and personnel were blinded)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Some concerns<br>*(not clear if participants and personnel were blinded)* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns<br>*(not clear if outcome assessors were blind)* |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |

| Section | Question | Answer |
|---|---|---|
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | Low for decision quality outcome; some concerns for the other outcomes |

**Wakefield, 2008a**

| | |
|---|---|
| **Bibliographic Reference** | Wakefield, C. E.; Meiser, B.; Homewood, J.; Peate, M.; Taylor, A.; Lobb, E.; Kirk, J.; Young, M. A.; Williams, R.; Dudding, T.; Tucker, K.; Group, A. GenDA Collaborative; A randomized controlled trial of a decision aid for women considering genetic testing for breast and ovarian cancer risk; Breast Cancer Research & Treatment; 2008; vol. 107 (no. 2); 289-301 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | Australia |
| **Study type** | Cluster randomised controlled trial |
| **Study dates** | Not reported |
| **Inclusion criteria** | Women who contacted one of five Australian familial cancer clinics. They had to be eligible for genetic testing in Australia (a family history consistent with a dominantly inherited hereditary breast/ovarian cancer syndrome who have an affected, living relative willing to provide a blood sample), able to give informed consent, able to read English and at least 18 years old. |
| **Exclusion criteria** | Males. Women with a personal history of cancer. |
| **Patient characteristics** | **Gender:** Women<br><br>**Age, mean years:** Decision aid plus genetic counselling group (DA+GC) 45.8; genetic counselling group (GC) 49.6 |

| | |
|---|---|
| | **Ethnicity:** not reported<br><br>**Socioeconomic and geographical factors: at least college educated:** DA+GC 36.9%; GC 32.4%<br><br>**Disabilities**: not reported<br><br>**People with communication needs (for example, not English 1st language):** study excluded those who could not read English.<br><br>**Trans people (particularly trans men)**: not reported<br><br>**Non-binary people:** not reported<br><br>**Cluster unit:** family<br><br>**Mean cluster size**: not reported – likely to be 1.2 or less based on other studies<br><br>**ICC:** not reported – assumed 0.05 |
| **Intervention(s)/control** | **Decision aid + genetic counselling:** a 40 page decision aid including background information about cancer and cancer-related genes, a description of the testing process, possible test results and a discussion of the potential impact of testing on the individual and their family. The decision aid was given to women after their first consultation with a genetic counsellor and taken home by the woman.<br><br>**Genetic counselling:** women received a general information pamphlet at their first consultation with a genetic counsellor to take home with them. |
| **Duration of follow-up** | The first questionnaire was completed within 1 week of the intervention. A second questionnaire was done at 6 months. |
| **Sources of funding** | Project grant from The Cancer Council of New South Wales (Project Grant 300441) |
| **Sample size** | 145 enrolled, 119 returned 1st questionnaire ,110 returned 2nd questionnaire |

**Study arms**

**Decision aid + genetic counselling (N = 73)**

**Genetic counselling (N = 73)**

**Outcomes**

**Study timepoints**

- 1 week

**Decision aid + genetic counselling versus genetic counselling**

| Outcome | Decision aid + genetic counselling, 1 week, N = 56 | Genetic counselling, 1 week, N = 63 |
|---|---|---|
| **Resolution of decisional needs**<br>Decisional conflict scale. 1 to 5<br><br>Mean (SD) | 1.64 (0.24) | 1.68 (0.32) |
| **Decision quality**<br>Objective knowledge, 0 to 8<br><br>Mean (SD) | 7.19 (1.01) | 6.74 (1.32) |
| **Uptake of the option being considered**<br>Rate of genetic tests<br><br>No of events | n = 53; % = 94.3 | n = 52; % = 90.2 |

Resolution of decisional needs - Polarity - Lower values are better
Decision quality - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – cluster RCT**

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 1. Was the allocation sequence random? | Yes<br>*(participants were randomized according to family-wise randomization: all participants who were the first of their family to attend the clinic were randomly allocated to the control or DA condition. Subsequent members of the same family attending the same clinic were then assigned to the same condition as their other family members to prevent potential contamination across groups)* |
| 1a. Bias arising from the randomisation process | 1a. 2. Is it likely that the allocation sequence was subverted? | Probably no |
| 1a. Bias arising from the randomisation process | 1a. 3. Were there baseline imbalances that suggest a problem with the randomisation process? | Probably no |
| 1a. Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 1. Were all the individual participants identified before randomisation of clusters (and if the trial specifically recruited patients were they all recruited before randomisation of clusters)? | Probably yes |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 2. If N/PN/NI to 1b.1: Is it likely that selection of individual participants was affected by knowledge of the intervention? | Probably yes |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in | 1b. 3. Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms? | No |

| Section | Question | Answer |
|---|---|---|
| relation to timing of randomisation | | |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation | Low |
| 2. Bias due to deviations from intended interventions | 2.1a Were participants aware that they were in a trial? | Probably yes |
| 2. Bias due to deviations from intended interventions | 2.1b If Y/PY/NI to 2.1a: Were participants aware of their assigned intervention during the trial? | Probably yes |
| 2. Bias due to deviations from intended interventions | 2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice? | No information |
| 2. Bias due to deviations from intended interventions | 2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5a Were any clusters analysed in a group different from the one to which they were assigned? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5b Were any participants analysed in a group different from the one to which their original cluster was randomised? | Probably No |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | 2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group? | Probably no |
| 2. Bias due to deviations from intended interventions | Risk of bias judgement for deviations from intended interventions | Some concerns<br>*(not clear if participants were blinded; personnel were not blinded)* |
| 3. Bias due to missing outcome data | 3.1a Were outcome data available for all, or nearly all, clusters randomised? | Yes |
| 3. Bias due to missing outcome data | 3.1b Were outcome data available for all, or nearly all, participants within clusters? | Yes |
| 3. Bias due to missing outcome data | 3.2 If N/PN/NI to 3.1a or 3.1b: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups? | Yes |
| 3. Bias due to missing outcome data | 3.3 If N/PN/NI to 3.1a or 3.1b: Is there evidence that results were robust to the presence of missing outcome data? | Yes |
| 3. Bias due to missing outcome data | Risk of bias judgement for missing outcome data | Low |
| 4. Bias in measurement of the outcome | 4.1a Were outcome assessors aware that a trial was taking place? | Probably yes |
| 4. Bias in measurement of the outcome | 4.1b If Y/PY/NI to 4.1: Were outcome assessors aware of the intervention received by study participants? | Probably yes |

| Section | Question | Answer |
|---|---|---|
| 4. Bias in measurement of the outcome | 4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received? | Probably no |
| 4. Bias in measurement of the outcome | Risk of bias judgement for measurement of the outcome | Some concerns<br>*(not clear if participants were blinded; personnel were not blinded)* |
| 5. Bias in selection of the reported result | 5.1 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple outcome measurements (for example, scales, definitions, time points) within the outcome domain? | No/Probably no |
| 5. Bias in selection of the reported result | 5.2 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple analyses of the data? | No/Probably no |
| 5. Bias in selection of the reported result | Risk of bias for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Low |
| Overall bias and Directness | Overall Directness | Directly applicable |

**Wakefield, 2008b**

| | |
|---|---|
| **Bibliographic Reference** | Wakefield, C. E.; Meiser, B.; Homewood, J.; Taylor, A.; Gleeson, M.; Williams, R.; Tucker, K.; Australian, GENetic testing Decision Aid Collaborative Group; A randomized trial of a breast/ovarian cancer genetic testing decision aid used as a communication aid during genetic counselling; Psycho-Oncology; 2008; vol. 17 (no. 8); 844-54 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | Australia |
| **Study type** | Cluster randomised controlled trial |
| **Study dates** | Enrolment from 2004 to 2006 |
| **Inclusion criteria** | Women who contacted one of five Australian familial cancer clinics. They had to be eligible for genetic testing in Australia, able to give informed consent, able to read English and at least 18 years old. |
| **Exclusion criteria** | Males - no other criteria reported. |
| **Patient characteristics** | **Gender:** Women<br><br>**Age, mean years:** Decision aid plus genetic counselling group (DA+GC) 49.2; genetic counselling group (GC) 48.2<br><br>**Ethnicity:** not reported<br><br>**Socioeconomic and geographical factors: at least college educated:** DA+GC 39.6%; GC 33.3%<br><br>**Disabilities**: not reported<br><br>**People with communication needs (for example, not English 1st language):** study excluded those who could not read English.<br><br>**Trans people (particularly trans men)**: not reported<br><br>**Non-binary people:** not reported<br><br>**Cluster unit:** family<br><br>**Mean cluster size**: not reported – likely to be 1.2 or less based on other studies<br><br>**ICC:** not reported – assumed 0.05 |
| **Intervention(s)/control** | **Decision aid + genetic counselling:** a 40 page decision aid including background information about cancer and cancer-related genes, a description of the testing process, possible test results and a discussion of the potential impact |

| | |
|---|---|
| | of testing on the individual and their family. The decision aid was given to women at the beginning of their first consultation with a genetic counsellor, used during counselling, and then taken home by the woman.<br><br>**Genetic counselling:** women received a general information pamphlet at the beginning of their first consultation with a genetic counsellor to take home with them. |
| **Duration of follow-up** | Outcomes measured just after the intervention. |
| **Sources of funding** | Project grant from The Cancer Council of New South Wales (Project Grant 300441) |
| **Sample size** | 148 enrolled; 110 returned 1st questionnaire; 105 returned 2nd questionnaire. |

**Study arms**

**Decision aid + genetic counselling (N = 63)**

**Genetic counselling (N = 60)**
The control arm also received a general information leaflet.

**Outcomes**

**Study timepoints**
- Just after intervention

**Decision aid + genetic counselling versus genetic counselling**

| Outcome | Decision aid + genetic counselling, After intervention, N = 55 | Genetic counselling, After intervention, N = 55 |
|---|---|---|
| **Resolution of decisional needs**<br>Decisional conflict scale. 1 to 5<br><br>Mean (SD) | 1.6 (0.21) | 1.69 (0.36) |

| Outcome | Decision aid + genetic counselling, After intervention, N = 55 | Genetic counselling, After intervention, N = 55 |
|---|---|---|
| **Uptake of the option being considered**<br>Rate of genetic tests<br><br>No of events | n = 46; % = 92 | n = 48; % = 94.2 |
| **Decision quality**<br>Objective knowledge, 0 to 8<br><br>Mean (SD) | 7.05 (1.04) | 6.68 (1.3) |

Resolution of decisional needs - Polarity - Lower values are better
Decision quality - Polarity - Higher values are better

**Critical appraisal - Cochrane RoB 2.0 – cluster RCT**

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 1. Was the allocation sequence random? | Yes<br>*(participants were randomized according to family-wise randomization: all participants who were the first of their family to attend the clinic were randomly allocated to the control or DA condition. Subsequent members of the same family attending the same clinic were then assigned to the same condition as their other family members to prevent potential contamination across groups)* |
| 1a. Bias arising from the randomisation process | 1a. 2. Is it likely that the allocation sequence was subverted? | Probably no |

| Section | Question | Answer |
|---|---|---|
| 1a. Bias arising from the randomisation process | 1a. 3. Were there baseline imbalances that suggest a problem with the randomisation process? | No |
| 1a. Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 1. Were all the individual participants identified before randomisation of clusters (and if the trial specifically recruited patients were they all recruited before randomisation of clusters)? | Probably yes |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 2. If N/PN/NI to 1b.1: Is it likely that selection of individual participants was affected by knowledge of the intervention? | Probably yes |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | 1b. 3. Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms? | No |
| 1b. Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomisation | Risk of bias judgement for the timing of identification and recruitment of individual participants in relation to timing of randomisation | Low |
| 2. Bias due to deviations from intended interventions | 2.1a Were participants aware that they were in a trial? | Probably yes |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | 2.1b If Y/PY/NI to 2.1a: Were participants aware of their assigned intervention during the trial? | Probably yes |
| 2. Bias due to deviations from intended interventions | 2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial? | Yes |
| 2. Bias due to deviations from intended interventions | 2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice? | No information |
| 2. Bias due to deviations from intended interventions | 2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5a Were any clusters analysed in a group different from the one to which they were assigned? | Probably no |
| 2. Bias due to deviations from intended interventions | 2.5b Were any participants analysed in a group different from the one to which their original cluster was randomised? | Probably No |
| 2. Bias due to deviations from intended interventions | 2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group? | Probably no |

| Section | Question | Answer |
|---|---|---|
| 2. Bias due to deviations from intended interventions | Risk of bias judgement for deviations from intended interventions | Some concerns<br>*(not clear if participants were blinded; personnel were not blinded)* |
| 3. Bias due to missing outcome data | 3.1a Were outcome data available for all, or nearly all, clusters randomised? | Probably yes |
| 3. Bias due to missing outcome data | 3.1b Were outcome data available for all, or nearly all, participants within clusters? | No |
| 3. Bias due to missing outcome data | 3.2 If N/PN/NI to 3.1a or 3.1b: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups? | Yes |
| 3. Bias due to missing outcome data | 3.3 If N/PN/NI to 3.1a or 3.1b: Is there evidence that results were robust to the presence of missing outcome data? | Probably No |
| 3. Bias due to missing outcome data | Risk of bias judgement for missing outcome data | Low |
| 4. Bias in measurement of the outcome | 4.1a Were outcome assessors aware that a trial was taking place? | Probably yes |
| 4. Bias in measurement of the outcome | 4.1b If Y/PY/NI to 4.1: Were outcome assessors aware of the intervention received by study participants? | Probably yes |
| 4. Bias in measurement of the outcome | 4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received? | Probably no |

| Section | Question | Answer |
|---|---|---|
| 4. Bias in measurement of the outcome | Risk of bias judgement for measurement of the outcome | Some concerns<br>*(not clear if participants were blinded; personnel were not blinded)* |
| 5. Bias in selection of the reported result | 5.1 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple outcome measurements (for example, scales, definitions, time points) within the outcome domain? | No/Probably no |
| 5. Bias in selection of the reported result | 5.2 Are the reported outcome data likely to have been selected, on the basis of the results, from multiple analyses of the data? | No/Probably no |
| 5. Bias in selection of the reported result | Risk of bias for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Low |
| Overall bias and Directness | Overall Directness | Directly applicable |

**Wang, 2005**

| | |
|---|---|
| **Bibliographic Reference** | Wang, C.; Gonzalez, R.; Milliron, K. J.; Strecher, V. J.; Merajver, S. D.; Genetic counselling for BRCA1/2: a randomized controlled trial of two strategies to facilitate the education and counselling process; American Journal of Medical Genetics. Part A; 2005; vol. 134a (no. 1); 66-73 |

**Study details**

| | |
|---|---|
| **Country/ies where study was carried out** | USA |
| **Study type** | Randomised controlled trial (RCT) |
| **Study dates** | 2000-2002 |
| **Inclusion criteria** | Women attending the Breast and Ovarian Cancer Risk Evaluation Program (BOCREP) at the University of Michigan Comprehensive Cancer Centre. |
| **Exclusion criteria** | None reported. |
| **Patient characteristics** | **Gender:** Women<br><br>**Age, mean years:** 44-45<br><br>**Ethnicity:** White 93%, African American 2%, Hispanic 1%, Asian 1%, Other 3%<br><br>**Socioeconomic and geographical factors:** at least college educated: 58%; income >$60K 66%<br><br>**Disabilities**: not reported<br><br>**People with communication needs (for example, not English 1st language):** study excluded those who could not read English.<br><br>**Trans people (particularly trans men)**: not reported<br><br>**Non-binary people:** not reported |
| **Intervention(s)/control** | 4 trial arms:<br><br>**CD-ROM + Genetic counselling:** women viewed part or all of a 40 minute CD-ROM ‘‘Understanding Cancer and Genetics’’ covering 5 topics: Basic Genetics, Cancer and Genetics, Genes Associated With Breast Cancer, Genetic Testing, and Managing Risk. They could view at least one of the introductory topics Basic Genetics, Cancer and Genetics and viewed other topics if they had time. Following this they had a genetic counselling session with either a genetic counsellor or medical oncologist. |

| | |
|---|---|
| | **Feedback + Genetic counselling:** women took a knowledge test on cancer and genetics. Following this they had a genetic counselling session with either a genetic counsellor or medical oncologist who used the feedback checklist to tailor the information to the woman's understanding.<br><br>**CD-ROM+ Feedback + Genetic counselling:** a combination of the 2 above interventions.<br><br>**Genetic counselling:** a genetic counselling session with either a genetic counsellor or medical oncologist. |
| **Duration of follow-up** | Outcomes were measured at baseline - before the intervention and Immediately following genetic counselling, women were asked to complete an exit questionnaire. Rates of genetic testing were determined up to 1 year later from medical records. |
| **Sample size** | 198 |

**Study arms**

**CD-ROM (± Feedback )+ Genetic counselling (N = 100)**

**Genetic counselling (N = 48)**

**Outcomes**

**Study timepoints**

- Baseline
- 1 hour (Outcomes were assessed immediately after genetic counselling)
- 1 year

**CD-ROM + Genetic counselling (± feedback) versus genetic counselling**

| Outcome | CD-ROM (± Feedback )+ Genetic counselling, Baseline, N = | CD-ROM (± Feedback) + Genetic counselling, 1 hour, N = 100 | CD-ROM (± Feedback) + Genetic counselling, 1 year, N = | Genetic counselling, Baseline, N = | Genetic counselling, 1 hour, N = 48 | Genetic counselling, 1 year, N = |
|---|---|---|---|---|---|---|
| **Time taken for face-to-face counselling** (Minutes)<br><br>Mean (SD) | *empty data* | 59.5 (16.92) | *empty data* | *empty data* | 68 (17) | *empty data* |

**CD-ROM + Genetic counselling (± feedback) versus genetic counselling (± feedback)**

| Outcome | CD-ROM (± Feedback) + Genetic counselling, Baseline, N = | CD-ROM (± Feedback) + Genetic counselling, 1 hour, N = | CD-ROM (± Feedback) + Genetic counselling, 1 year, N = 100 | Genetic counselling, Baseline, N = | Genetic counselling, 1 hour, N = | Genetic counselling, 1 year, N = 98 |
|---|---|---|---|---|---|---|
| **Uptake of the option being considered** Rate of genetic testing<br><br>No of events | *empty data* | *empty data* | n = 33; % = 33 | *empty data* | *empty data* | n = 46; % = 47 |

**Critical appraisal - Cochrane RoB 2.0 – standard RCT**

| Section | Question | Answer |
|---|---|---|
| Domain 1: Bias arising from the randomisation process | Risk of bias judgement for the randomisation process | Low |

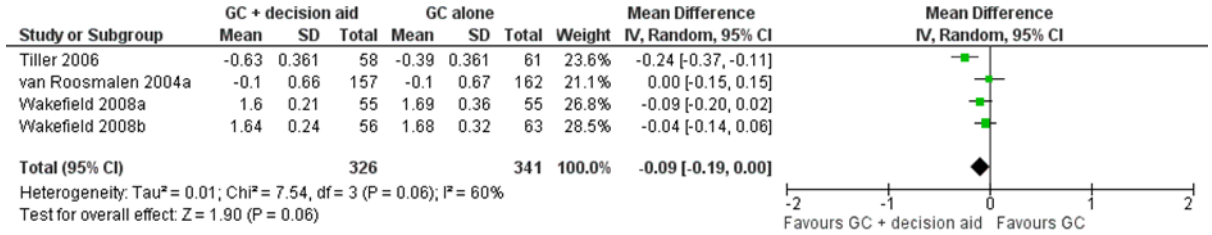
| Section | Question | Answer |
|---|---|---|
| Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention) | Risk of bias for deviations from the intended interventions (effect of assignment to intervention) | Some concerns<br>*(not clear if participants were blinded; efforts were made to maximize the likelihood of the counsellor remaining blind to the experimental condition)* |
| Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention) | Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention) | Some concerns<br>*(not clear if participants were blinded; efforts were made to maximize the likelihood of the counsellor remaining blind to the experimental condition)* |
| Domain 3. Bias due to missing outcome data | Risk-of-bias judgement for missing outcome data | Low |
| Domain 4. Bias in measurement of the outcome | Risk-of-bias judgement for measurement of the outcome | Some concerns<br>*(not clear if outcome assessors aware of the intervention received by study participants)* |
| Domain 5. Bias in selection of the reported result | Risk-of-bias judgement for selection of the reported result | Low |
| Overall bias and Directness | Risk of bias judgement | Some concerns |
| Overall bias and Directness | Overall Directness | Directly applicable |
| Overall bias and Directness | Risk of bias variation across outcomes | low for decision quality outcome; some concerns for the other outcomes |

# Appendix E Forest plots

**Forest plots for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?**

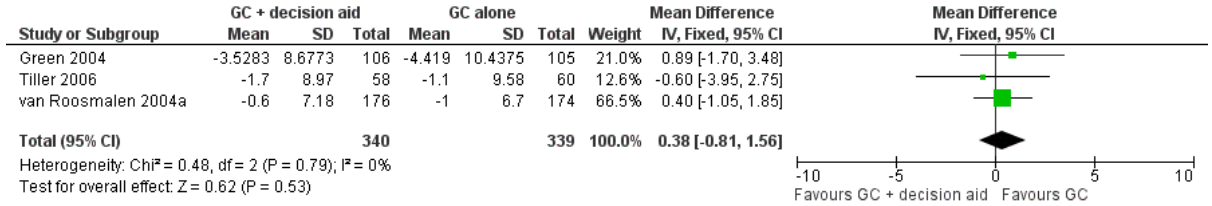
This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

**Figure 2: Comparison 2: Decision support interventions as an adjunct to genetic counselling. Resolution of decisional needs. Measured with decision conflict scale (range 1 – 5; lower better)**



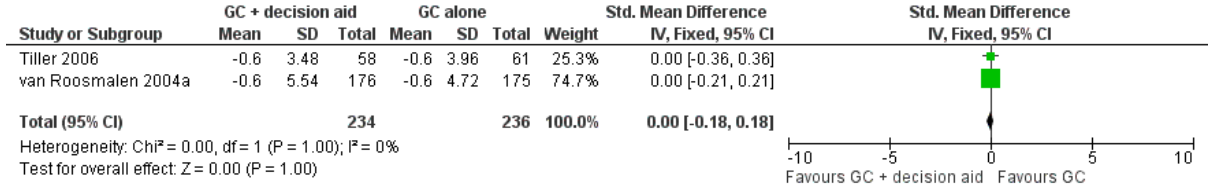

*Van Roosmalen 2004a, Wakefield 2008a and Wakefield 2008b are cluster RCTs but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 3: Comparison 2: Decision support interventions as an adjunct to genetic counselling. Adverse effects: anxiety. Measured with STAI-state score (range 20 – 80; lower better)**



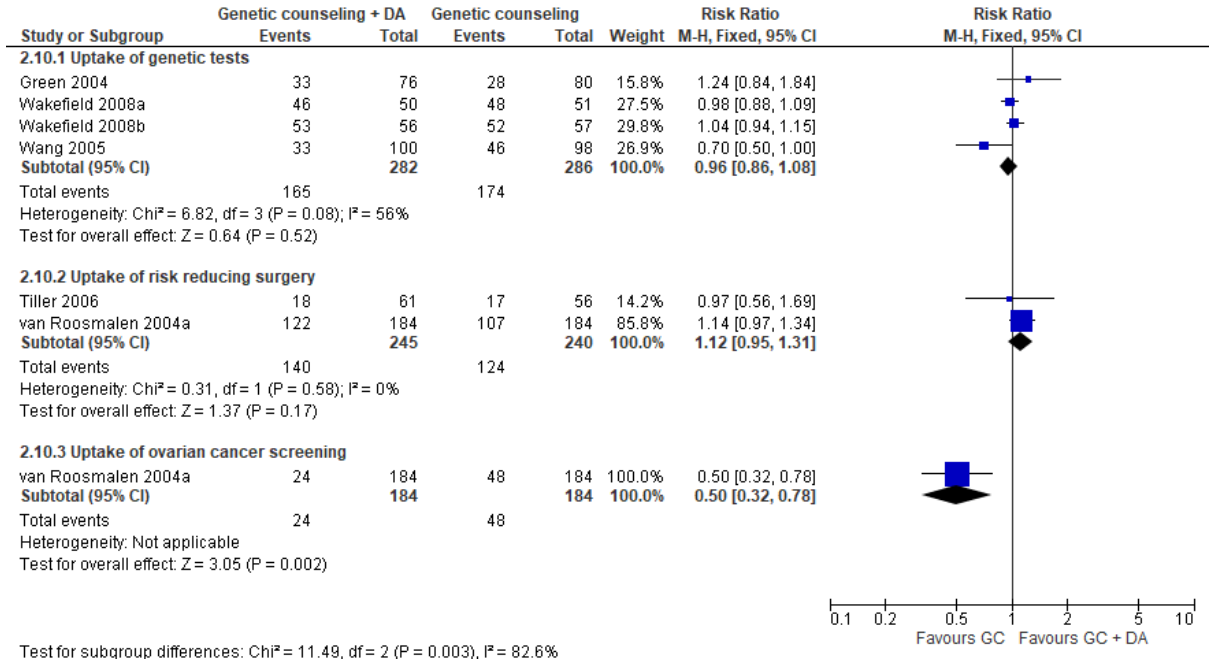

*Van Roosmalen 2004a is a cluster RCT but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 4: Comparison 2: Decision support interventions as an adjunct to genetic counselling. Adverse effects: depression. Measured with standardised mean difference, lower better**



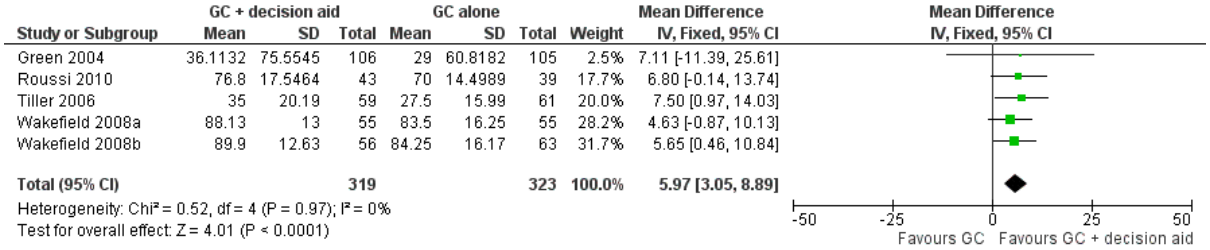

*Van Roosmalen 2004a is a cluster RCT but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 5: Comparison 2: Decision support interventions as an adjunct to genetic counselling. Uptake of the management option being considered**



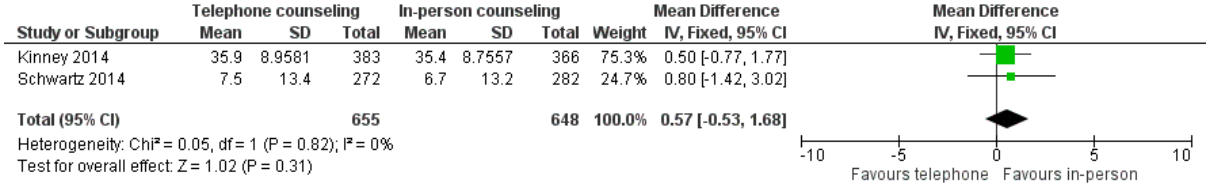

*Van Roosmalen 2004a, Wakefield 2008a and Wakefield 2008b are cluster RCTs but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 6: Comparison 2: Decision support interventions as an adjunct to genetic counselling. Decision quality. Measured with objective knowledge test (range 0 to 100, higher better)**



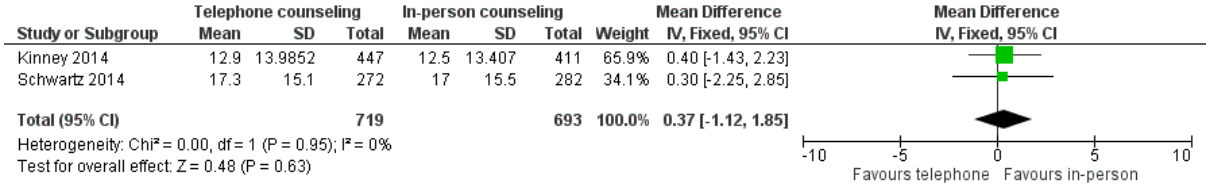

*Wakefield 2008a and Wakefield 2008b are cluster RCTs but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 7: Comparison 3: telephone versus in-person genetic counselling. Resolution of decisional needs. Measured with decision conflict scale (range 0 – 100; lower better)**



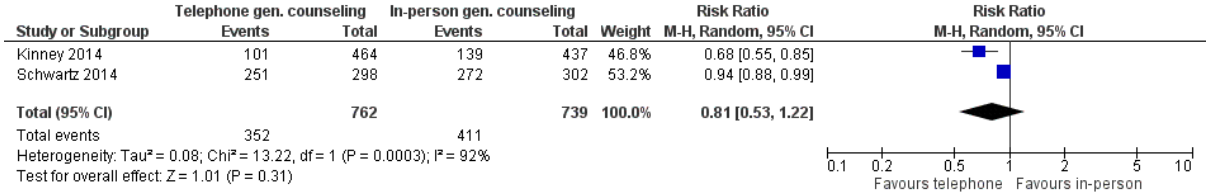

*Kinney 2014 is a cluster RCT but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 8: Comparison 3: telephone versus in-person genetic counselling. Adverse effects: cancer worry. Measured with Impact of Event scale (range 0 to 75; lower better)**



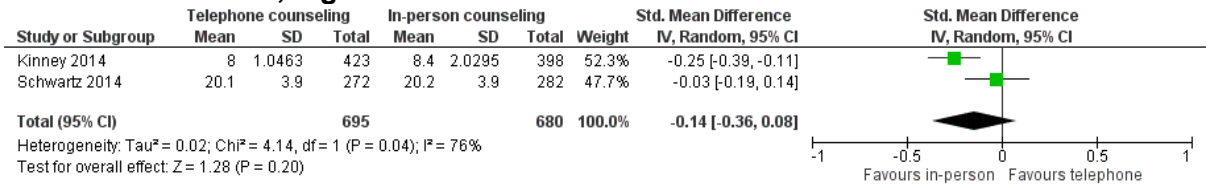

*Kinney 2014 is a cluster RCT but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 9: Comparison 3: telephone versus in-person genetic counselling. Uptake of the management option being considered**




*Kinney 2014 is a cluster RCT but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 10: Comparison 3: telephone versus in-person genetic counselling. Decision quality. Measured with objective knowledge test, standardised mean difference, higher better**

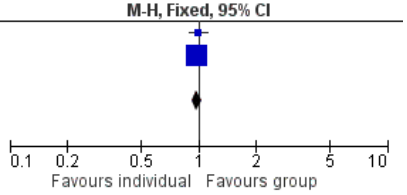



*Kinney 2014 is a cluster RCT but cluster size is small enough that adjusting for intra class correlation does not affect sample size*

**Figure 11: Comparison 4: Group education followed by shorter individual genetic counselling versus individual education and genetic counselling. Uptake of the management option being considered**

| Study or Subgroup | Group edu + ind. couns. Events | Total | Individual couns. Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Calzone 2005 | 63 | 71 | 63 | 71 | 19.2% | 1.00 [0.89, 1.12] |
| Manchanda 2016 (1) | 230 | 264 | 303 | 340 | 80.8% | 0.98 [0.92, 1.04] |
| **Total (95% CI)** | | **335** | | **411** | **100.0%** | **0.98 [0.93, 1.04]** |
| Total events | 293 | | 366 | | | |

Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.68 (P = 0.50)

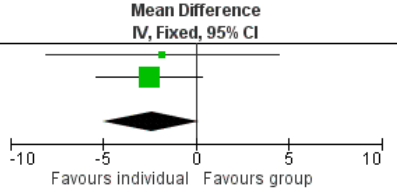



Footnotes
(1) Adjusted sample size due to cluster RCT design.

**Figure 12:Comparison 4: Group education followed by shorter individual genetic counselling versus individual education and genetic counselling. Decision quality. Measured with objective knowledge test (range 0 to 100, higher better)**

| Study or Subgroup | Group edu + ind. couns. Mean | SD | Total | Individual couns. Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Calzone 2005 | 17.6 | 18.2 | 71 | 19.4 | 20.1 | 71 | 16.9% | -1.80 [-8.11, 4.51] |
| Manchanda 2016 (1) | 16.4 | 21.38 | 409 | 18.9 | 22.8 | 527 | 83.1% | -2.50 [-5.34, 0.34] |
| **Total (95% CI)** | | | **480** | | | **598** | **100.0%** | **-2.38 [-4.97, 0.21]** |

Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%
Test for overall effect: Z = 1.80 (P = 0.07)




Footnotes
(1) Adjusted sample size due to cluster RCT design

# Appendix F GRADE tables

## GRADE tables for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

### Table 7: Evidence profile for comparison 1. Genetic counselling versus usual care

| Quality assessment | | | | | | | Number of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Genetic counselling | Usual care | Relative (95% CI) | Absolute (95% CI) | | |
| **Uptake of the option being considered (follow-up: 2 years; assessed with: Uptake of genetic testing in those at high risk of familial ovarian cancer)** | | | | | | | | | | | | |
| Drescher 2016 | randomised trial | serious[1] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 74/228 (32.5%) | 20/230 (8.7%) | RR 3.73 (2.36 to 5.90) | 237 more per 1,000 (from 118 more to 426 more) | MODERATE | IMPORTANT |
| **Uptake of the option being considered (follow-up: 1 months; assessed with: Intention to get genetic test in those with low to moderate risk of familial ovarian cancer)** | | | | | | | | | | | | |
| Lerman 1997 | randomised trial | very serious[2] | no serious inconsistency | no serious indirectness | serious[3] | none | 74/122 (60.7%) | 87/164 (53.0%) | RR 1.14 (0.93 to 1.40) | 74 more per 1,000 (from 37 fewer to 212 more) | VERY LOW | IMPORTANT |
| **Uptake of the option being considered (follow-up: 2 years; assessed with: Uptake of risk reducing salpingo-oophorectomy in those at high risk of familial ovarian cancer)** | | | | | | | | | | | | |
| Drescher 2016 | randomised trial | serious[1] | no serious inconsistency | no serious indirectness | serious[3] | none | 10/228 (4.4%) | 3/230 (1.3%) | RR 3.36 (0.94 to 12.06) | 31 more per 1,000 (from 1 fewer to 144 more) | LOW | IMPORTANT |
| **Decision quality (follow-up: 1 months; assessed with: Change from baseline in knowledge score (higher better); Scale from: 0 to 11)** | | | | | | | | | | | | |
| Lerman 1997 | randomised trial | very serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 122 | 164 | - | MD 2.38 higher (2.05 higher to 2.71 higher) | LOW | IMPORTANT |

*CI: confidence interval; MID: minimal important difference; MD: mean difference; RoB: risk of bias; RR: risk ratio*

*1 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
*2 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
*3 95% CI crosses 1 MID*

**Table 8: Evidence profile for comparison 2. Genetic counselling plus decision support intervention versus genetic counselling.**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Genetic counselling plus decision support intervention | Genetic counselling | Relative (95% CI) | Absolute (95% CI) | | |
| **Preparation for active participation in making a health decision (follow-up: 2 weeks; assessed with: Preference for decision making scale (higher better); Scale from: 1 to 5)** | | | | | | | | | | | | |
| van Roosmalen 2004a | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 155 | 159 | - | MD **0**.1 higher (0.03 lower to 0.23 higher) | HIGH | CRITICAL |
| **Resolution of decisional needs (follow-up: 2 weeks; assessed with: Decisional Conflict Scale (lower better); Scale from: 1 to 5)** | | | | | | | | | | | | |
| 4[1] | randomised trial | no serious risk of bias | serious[2] | no serious indirectness | no serious imprecision | none | 326 | 341 | - | MD 0.09 lower (0.19 lower to 0) | MODERATE | CRITICAL |
| **Adverse effects: anxiety (follow-up: 2 weeks; assessed with: (change from baseline STAI scale (lower better); Scale from: 20 to 80)** | | | | | | | | | | | | |
| 3[3] | randomised trial | serious[4] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 340 | 339 | - | MD 0.38 higher (0.81 lower to 1.56 higher) | MODERATE | CRITICAL |
| **Adverse effects: depression (follow-up: 2 weeks; assessed with: Change from baseline)** | | | | | | | | | | | | |
| 2[5] | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 234 | 236 | - | SMD 0 (0.18 lower to 0.18 higher) | HIGH | CRITICAL |
| **Adverse effects: cancer worry (follow-up: 2 weeks; assessed with: Impact of event scale (lower better); Scale from: 0 to 75)** | | | | | | | | | | | | |
| van Roosmalen 2004a | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 169 | 174 | - | MD 0 (1.92 lower to 1.92 higher) | HIGH | CRITICAL |

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Genetic counselling plus decision support intervention | Genetic counselling | Relative (95% CI) | Absolute (95% CI) | | |
| **Satisfaction with intervention (follow-up: 2 weeks; assessed with: Satisfaction scale (higher better); Scale from: 1 to 6)** | | | | | | | | | | | | |
| van Roosmalen 2004a | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | serious[6] | none | 176 | 171 | - | MD 0.6 higher (0.4 higher to 0.8 higher) | MODERATE | IMPORTANT |
| **Uptake of the option being considered (follow-up: range 6 months to 1 years; assessed with: Uptake of genetic testing)** | | | | | | | | | | | | |
| 4[7] | randomised trial | serious[4] | serious[2] | no serious indirectness | no serious imprecision | none | 165/282 (58.5%) | 174/286 (60.8%) | RR 0.96 (0.86 to 1.08) | 24 fewer per 1,000 (from 85 fewer to 49 more) | LOW | IMPORTANT |
| **Uptake of the option being considered (follow-up: range 1 months to 6 months; assessed with: Uptake (or treatment choice) of risk reducing surgery)** | | | | | | | | | | | | |
| 2[8] | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | serious[9] | none | 140/245 (57.1%) | 124/240 (51.7%) | RR 1.12 (0.95 to 1.31) | 62 more per 1,000 (from 26 fewer to 160 more) | MODERATE | IMPORTANT |
| **Uptake of the option being considered (follow-up: 4 weeks; assessed with: Treatment choice of ovarian cancer screening)** | | | | | | | | | | | | |
| van Roosmalen 2004a | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 24/184 (13.0%) | 48/184 (26.1%) | RR 0.50 (0.32 to 0.78) | 130 fewer per 1,000 (from 177 fewer to 57 fewer) | HIGH | IMPORTANT |
| **Decision quality (follow-up: range 1 days to 10 weeks; assessed with: Objective knowledge test (higher better); Scale from: 0 to 100)** | | | | | | | | | | | | |
| 5[10] | randomised trial | serious[4] | no serious inconsistency | no serious indirectness | serious[6] | none | 319 | 323 | - | MD 5.97 higher (3.05 higher to 8.89 higher) | LOW | IMPORTANT |

*CI: confidence interval; MD: mean difference; RoB: risk of bias; RR: risk ratio; SMD: standardised mean difference*

*1 Tiller 2006; van Roosmalen 2004a; Wakefield 2004a; Wakefield 2004b*
*2 Serious heterogeneity unexplained by subgroup analysis*
*3 Green 2004; Tiller 2006; van Roosmalen 2004a*
*4 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
*5 Tiller 2006; van Roosmalen 2004a*
*6 95% CI crosses 1 MID (0.5x control group SD, for satisfaction scale = 0.5, for objective knowledge test = 8.0)*
*7 Green 2004; Wakefield 2004a; Wakefield 2004b; Wang 2005*
*8 Tiller 2006; van Roosmalen 2004a*
*9 95% CI crosses 1 MID*
*10 Green 2004; Roussi 2010; Tiller 2006; Wakefield 2004a; Wakefield 2004b*

**Table 9: Evidence profile for comparison 3. Telephone genetic counselling versus in-person genetic counselling**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No of studies** | **Design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Telephone genetic counselling** | **In-person genetic counselling** | **Relative (95% CI)** | **Absolute (95% CI)** | | |
| **Resolution of decisional needs (follow-up: range 1 weeks to 2 weeks; assessed with: Decision conflict scale (lower better); Scale from: 0 to 100)** | | | | | | | | | | | | |
| 2[1] | randomised trial | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 655 | 648 | - | MD 0.57 higher (0.53 lower to 1.68 higher) | MODERATE | CRITICAL |
| **Adverse effects: decision regret (follow-up: 6 months; assessed with: Decision regret scale (lower better); Scale from: 0 to 100)** | | | | | | | | | | | | |
| Kinney 2014 | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 377 | 359 | - | MD 2.03 higher (0.53 lower to 4.59 higher) | HIGH | CRITICAL |
| **Adverse effects: anxiety (follow-up: 1 weeks; assessed with: BSI-18 (lower better); Scale from: 0 to 24)** | | | | | | | | | | | | |
| Kinney 2014 | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | serious[3] | none | 449 | 416 | - | MD 0.1 higher (0.32 lower to 0.52 higher) | MODERATE | CRITICAL |
| **Adverse effects: cancer worry (follow-up: 1 weeks; assessed with: Impact of Events Scale (lower better); Scale from: 0 to 75)** | | | | | | | | | | | | |

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Telephone genetic counselling | In-person genetic counselling | Relative (95% CI) | Absolute (95% CI) | | |
| 2[1] | randomised trial | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 719 | 693 | - | MD 0.37 higher (1.12 lower to 1.85 higher) | MODERATE | CRITICAL |
| **Uptake of the option being considered (follow-up: 3 months; assessed with: Uptake of genetic testing)** | | | | | | | | | | | | |
| 2[1] | randomised trial | serious[2] | very serious[4] | no serious indirectness | serious[5] | none | 352/762 (46.2%) | 411/739 (55.6%) | RR 0.81 (0.53 to 1.22)[6] | 106 fewer per 1,000 (from 261 fewer to 122 more) | VERY LOW | IMPORTANT |
| **Satisfaction with intervention (follow-up: 2 weeks; assessed with: Genetic counselling satisfaction scale (higher better))** | | | | | | | | | | | | |
| Schwartz 2014 | randomised trial | serious[2] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 272 | 282 | - | MD 0.2 lower (0.73 lower to 0.33 higher) | MODERATE | IMPORTANT |
| **Decision quality (Objective knowledge test, higher better) (follow-up: range 1 weeks to 2 weeks)** | | | | | | | | | | | | |
| 2[1] | randomised trial | no serious risk of bias | serious[3] | no serious indirectness | no serious imprecision | none | 695 | 680 | - | SMD 0.14 lower (0.36 lower to 0.08 higher) | MODERATE | IMPORTANT |

*CI: confidence interval; MD: mean difference; RoB: risk of bias; RR: risk ratio; SMD: standardised mean difference*
*1 Kinney 2014; Schwartz 2014*
*2 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
*3 95% CI crosses 1 MID (0.5x control group SD, for BSI-18 = 1.4,)*
*4 Very serious heterogeneity unexplained by subgroup analysis*
*5 95% CI crosses 1 MID*
*6 Both studies show reduced uptake of tests with telephone counselling but, pooled result is significant for fixed effects model but not random effects*

**Table 10: Evidence profile for comparison 4. Group education session followed by individual genetic counselling versus individual education and genetic counselling**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Group education followed by individual counselling | Individual counselling | Relative (95% CI) | Absolute (95% CI) | | |
| **Adverse effects: cancer worry (follow-up: 3 months; assessed with: IES score (lower better); Scale from: 0 to 75)** | | | | | | | | | | | | |
| Calzone 2005 | randomised trial | serious[1] | no serious inconsistency | no serious indirectness | serious[2] | none | 71 | 71 | - | MD 3.25 lower (6.77 lower to 0.27 higher) | LOW | CRITICAL |
| **Satisfaction with intervention (follow-up: 1 days; assessed with: Genetic Counselling Satisfaction Scale (higher better); Scale from: 5 to 30)** | | | | | | | | | | | | |
| Manchanda 2016 | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 409 | 527 | - | MD **0**.56 lower (1.2 lower to 0.08 higher) | HIGH | IMPORTANT |
| **Uptake of the option being considered (follow-up: range 1 days to 3 months; assessed with: Uptake of (or consent to) genetic testing)** | | | | | | | | | | | | |
| 2[3] | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 293/335 (87.5%) | 366/411 (89.1%) | RR 0.98 (0.93 to 1.04) | 18 fewer per 1,000 (from 62 fewer to 36 more) | HIGH | IMPORTANT |
| **Decision quality (follow-up: 1 days; assessed with: Objective knowledge test (higher better); Scale from: 0 to 100)** | | | | | | | | | | | | |
| 2[3] | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 480 | 598 | - | MD 2.38 lower (4.97 lower to 0.21 higher) | HIGH | IMPORTANT |

*CI: confidence interval; MD: mean difference; RoB: risk of bias; RR: risk ratio*
*1 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*
*2 95% CI crosses 1 MID (0.5x control group SD, for IES = 5.35)*
*3 Calzone 2005; Manchanda 2016*

**Table 11: Evidence profile for comparison 5. Decision support versus usual care in *BRCA1/2* mutation carriers**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | *BRCA1/2* positive: Decision aids | Usual care | Relative (95% CI) | Absolute (95% CI) | | |
| **Adverse effects: decision regret (follow-up: 6 weeks; assessed with: Decision satisfaction score, (higher better); Scale from: 0 to 48)** | | | | | | | | | | | | |
| Armstrong 2005 | randomised trial | serious[1] | no serious inconsistency | no serious indirectness | no serious imprecision | none | 14 | 13 | - | MD 5 higher (0.48 higher to 9.52 higher) | MODERATE | CRITICAL |
| **Adverse effects: anxiety (follow-up: 1 days; assessed with: STAI - state, (lower better); Scale from: 20 to 80)** | | | | | | | | | | | | |
| van Roosmalen 2004b | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 43 | 43 | - | MD 0.2 lower (3.41 lower to 3.01 higher) | HIGH | CRITICAL |
| **Adverse effects: depression (follow-up: 1 days; assessed with: CESD (lower better); Scale from: 0 to 60)** | | | | | | | | | | | | |
| van Roosmalen 2004b | randomised trial | not serious | no serious inconsistency | no serious indirectness | no serious imprecision | none | 43 | 43 | - | MD 1.3 lower (3.89 lower to 1.29 higher) | HIGH | CRITICAL |
| **Adverse effects: cancer worry (follow-up: 1 days; assessed with: IES (lower better); Scale from: 0 to 75)** | | | | | | | | | | | | |
| van Roosmalen 2004b | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 42 | 43 | - | MD 1.5 lower (3.89 lower to 0.89 higher) | HIGH | CRITICAL |

*CI: confidence interval; MD: mean difference; RoB: risk of bias*
*1 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2*

**Table 12: Evidence profile for comparison 6. Education app versus usual care (pre genetic counselling)**

| Quality assessment | | | | | | | No of patients | | Effect | | Quality | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No of studies | Design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Pre-counselling: Education app | Usual care | Relative (95% CI) | Absolute (95% CI) | | |
| **Uptake of the option being considered (follow-up: 3 months; assessed with: Uptake of genetic counselling)** | | | | | | | | | | | | |
| Vogel 2019 | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | serious[2] | none | 25/46 (54.3%) | 17/45 (37.8%) | RR 1.44 (0.91 to 2.28) | 166 more per 1,000 (from 34 fewer to 484 more) | MODERATE | IMPORTANT |
| **Decision quality (follow-up: 1 weeks; assessed with: Objective knowledge test (higher better); Scale from: 0 to 10)** | | | | | | | | | | | | |
| Vogel 2019 | randomised trial | no serious risk of bias | no serious inconsistency | no serious indirectness | no serious imprecision | none | 47 | 48 | - | MD 2.3 higher (1.79 higher to 2.81 higher) | HIGH | IMPORTANT |

*CI: confidence interval; MD: mean difference; RoB: risk of bias; RR: risk ratio*
*1 95% CI crosses 1 MID*

# Appendix G Economic evidence study selection

### Study selection for: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

One global search was undertaken – please see Supplement 2 for details on study selection.

# Appendix H Economic evidence tables

## Economic evidence tables for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

**Table 13: Economic evidence table for DVD-assisted genetic counselling for *BRCA1/2***

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Manchanda 2016<br><br>UK<br><br>Cost-minimisation analysis<br><br>Source of funding: The Eve Appeal charity | Intervention<br>DVD-assisted genetic counselling (DVD-C) for *BRCA1/2*<br>-A DVD presentation to small groups (2-5 people) at a time,<br>-DVD-C participants subsequently saw a genetic counsellor for an individual genetic-counselling session (post-DVD) at the same appointment.<br><br>Comparator<br>Traditional face-to-face counselling (TC) only for *BRCA1/2*.<br><br>A qualified genetic counsellor undertook genetic counselling with clinical/counselling supervision provided by a Regional Genetics Centre and a clinical fellow | Unselected adult Ashkenazi-Jewish population (men and women, 66.8% women) from North-London community, mean age 53.9 years, approximately 13% reported family history of cancer<br><br>A cluster-randomised non-inferiority RCT (Manchanda 2016)<br><br>Source of effectiveness data: RCT (N=936, TC=527, DVD-C=409, missing data NR)<br><br>Source of cost data: (N=936, TC=527, DVD-C=409, missing data NR) | Costs: Filming the DVD, burning blank DVD, genetic counselling, psychological appointment<br><br>Mean cost per participant<br>DVD-C: £19<br>TC: £33<br>Difference: -£14<br><br>Primary outcome measure: Genetic testing uptake, change in cancer risk perception, increase in knowledge, counselling time and satisfaction.<br><br>DVD-C is non-inferior for TC for the increase in knowledge, counselling satisfaction, | DVD-C preferred based on cost-minimisation<br><br>Probability of being cost-effective: NA<br><br>Subgroup analysis: NA<br><br>Sensitivity analysis:<br>Adjusting knowledge scores to account for the proportion of valid questions answered and missing answers, and transforming Genetic Counselling Satisfaction Scores to account for skewness had no impact on the results. | Perspective: Narrow NHS<br>Currency: GBP £<br>Cost year: 2010<br>Time horizon: Under 1 year<br>Discounting: NA<br>Applicability: Partially<br>Limitations: Minor<br><br>Other comments:<br>General Ashkenazi-Jewish population, high proportion of men. |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| | experienced in cancer genetics risk assessment and management.<br><br>Counselling was undertaken at high-street/community-based centres.<br><br>Counselling covered: interpretation of family history, knowledge about risk, inheritance, management options, advantages, disadvantages, and psychosocial implications to promote informed choice and adaptation.<br><br>Family history and baseline questionnaires were collected before the DVD presentation or seeing the genetic counsellor.<br><br>Post counselling questionnaires were filled out and collected after the genetic counselling session.<br><br>Individuals deciding to undergo *BRCA1/2* genetic testing were consented after genetic counselling. | Source of unit cost data: National sources (Personal Social Services Research Unit [PSSRU]) | and change in risk perception.<br><br>DVD-C is equivalent to TC for genetic testing uptake. | | |

*Abbreviations: DVD-C: DVD assisted genetic counselling; N: number of people; NA: Not applicable; NHS: National Health Service; NR: Not reported; PSSRU: Personal Social Services Research Unit; RCT: Randomised controlled trial; TC: Traditional face-to-face counselling; UK: United Kingdom*

**Table 14: Economic evidence tables for telephone pre- and post-test genetic counselling (TC) for *BRCA1/2***

| Study<br>Country<br>Study type | Intervention & comparator | Study population<br>Study design<br>Data sources | Costs: description and values<br>Outcomes: description and values | Results | Comments |
|---|---|---|---|---|---|
| Tutty 2019<br><br>Australia<br><br>Cost-analysis<br><br>Source of funding: National Health and Medical Research Council | Intervention<br>Telephone pre- and post-test genetic counselling (TC) for *BRCA1/2*<br>Oncological referral for TC,<br>Genetic counsellor provides pre-test counselling,<br>Patients receive forms/test kit and gives blood sample locally,<br>Genetic counsellor receives *BRCA1/2* results,<br>Positive or variant unknown significance with complex family history cases reviewed with geneticist,<br>Genetic counsellor provides post-test TC,<br>Genetic counsellor informs referring oncologist.<br><br>Comparator<br>In-person pre- and post-test genetic counselling (SC) for *BRCA1/2* | Women aged 45-89 (mean: 66.9) years with high-grade serous ovarian cancer<br><br>Source of effectiveness data: NA<br><br>Source of cost data: case control study (N=50 SC, N=70 TC)<br><br>Source of unit cost data: national sources (Victoria state rates and market prices) | Costs: Pre-test counselling telephone interview, pre-test genetic counselling, appointment letters, shipping of blood collection kits, post-test genetic counselling, time for unspecified additional contacts and tasks performed as recorded in the clinical database<br><br>Mean cost per participant<br>TC: $91<br>SC: $107<br>Difference: −$16 | TC cost saving<br><br>Probability of being cost effective: NA<br><br>Subgroup analysis: NR<br><br>Sensitivity analysis: NR | Perspective: Healthcare payer<br>Currency: AUD<br>Cost year: 2017<br>Time horizon: 1 year<br>Discounting: NA<br>Applicability: Partially<br>Limitations: Potentially serious<br><br>Other comments:<br>Reported non-comparative effectiveness and acceptability data for TC from case series (N=107) |

*Abbreviations: IES: Impact of Event Scale; N: number of people; NA: Not applicable; NHS: National Health Service; NR: Not reported; QALY: Quality-adjusted life year; RCT: Randomised controlled trial; SC: Standard care; SF-12: Short Form-12 questionnaire; TC: Telephone genetic counselling; UK: United Kingdom; US: United States*
*[1] Actual rates of genetic testing and disclosure for in-person and telephone counselling arms were 90.7% and 83.9%, respectively, so only these proportions of patients accrue testing costs (and post-test disclosure) in the sensitivity analyses*

# Appendix I Economic model

### Economic model for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

No economic analysis was conducted for this review question.

# Appendix J Excluded studies

## Excluded studies for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?

### Excluded effectiveness studies

**Table 15: Excluded studies and reasons for their exclusion**

| Study | Reason for exclusion |
|---|---|
| Banegas, Matthew Patrick (2013) Prediction, communication, and distribution of breast cancer risk. Dissertation Abstracts International: Section B: The Sciences and Engineering 73(12be) | Study design not relevant to this review protocol |
| Baroutsou, V., Underhill-Blazey, M. L., Appenzeller-Herzog, C. et al. (2021) Interventions Facilitating Family Communication of Genetic Testing Results and Cascade Screening in Hereditary Breast/Ovarian Cancer or Lynch Syndrome: A Systematic Review and Meta-Analysis. Cancers 13(4): 23 | Systematic review used as source of primary studies |
| Brain, K., Gray, J., Norman, P. et al. (2000) Randomized trial of a specialist genetic assessment service for familial breast cancer. J Natl Cancer Inst 92(16): 1345-51 | Intervention in study does not match that specified in this review protocol |
| Brain, K., Norman, P., Gray, J. et al. (2002) A randomized trial of specialist genetic assessment: psychological impact on women at different levels of familial breast cancer risk. British Journal of Cancer 86(2): 233-8 | Intervention in study does not match that specified in this review protocol |
| Braithwaite, D., Emery, J., Walter, F. et al. (2004) Psychological impact of genetic counselling for familial cancer: A systematic review and meta-analysis. Journal of the National Cancer Institute 96(2): 122-133 | Systematic review used as source of primary studies |
| Butrick, M., Kelly, S., Peshkin, B. N. et al. (2015) Disparities in uptake of BRCA1/2 genetic testing in a randomized trial of telephone counselling. Genet Med 17(6): 467-75 | Post-hoc analysis of Schwartz 2014 trial |
| Fournier, D. M.; Bazzell, A. F.; Dains, J. E. (2018) Comparing Outcomes of Genetic Counselling Options in Breast and Ovarian Cancer: An Integrative Review. Oncology Nursing Forum 45(1): 96-105 | Systematic review used as source of primary studies |
| Gao, J. P., Jin, Y. H., Yu, S. F. et al. (2020) Evaluate the effectiveness of breast cancer decision aids: A systematic review and meta-analysis of randomize clinical trails. Nursing open | Systematic review used as source of primary studies |
| Gray, S. W., O'Grady, C., Karp, L. et al. (2009) Risk information exposure and direct-to-consumer genetic testing for BRCA mutations among women with a personal or family history of breast or ovarian cancer. Cancer Epidemiology, Biomarkers & Prevention 18(4): 1303-11 | Population not relevant to this review protocol |
| Green, M. J., McInerney, A. M., Biesecker, B. B. et al. (2001) Education about genetic testing for breast cancer susceptibility: patient preferences for a computer program or genetic counselor. American Journal of Medical Genetics 103(1): 24-31 | Comparator in study does not match that specified in this review protocol |
| Grimmett, C., Pickett, K., Shepherd, J. et al. (2018) Systematic review of the empirical investigation of resources to support decision-making regarding BRCA1 and BRCA2 | Systematic review used as source of primary studies |

| Study | Reason for exclusion |
|---|---|
| genetic testing in women with breast cancer. Patient Education & Counselling 101(5): 779-788 | |
| Halbert, C. H., Wenzel, L., Lerman, C. et al. (2004) Predictors of participation in psychosocial telephone counselling following genetic testing for BRCA1 and BRCA2 mutations. Cancer Epidemiology, Biomarkers & Prevention 13(5): 875-81 | Comparator in study does not match that specified in this review protocol |
| Helmes, A. W.; Culver, J. O.; Bowen, D. J. (2006) Results of a randomized study of telephone versus in-person breast cancer risk counselling. Patient Education & Counselling 64(13): 96-103 | Population not relevant to this review protocol |
| Hilgart, J. S.; Coles, B.; Iredale, R. (2012) Cancer genetic risk assessment for individuals at risk of familial breast cancer. Cochrane Database of Systematic Reviews | Systematic review used as source of primary studies |
| Hooker, G. W., Leventhal, K. G., DeMarco, T. et al. (2011) Longitudinal changes in patient distress following interactive decision aid use among BRCA1/2 carriers: a randomized trial. Medical Decision Making 31(3): 412-21 | No relevant data reported |
| Howard, A. F.; Balneaves, L. G.; Bottorff, J. L. (2009) Women's decision making about risk-reducing strategies in the context of hereditary breast and ovarian cancer: A systematic review. Journal of Genetic Counselling 18(6): 578-597 | Systematic review used as source of primary studies |
| Interrante, M. K., Segal, H., Peshkin, B. N. et al. (2017) Randomized Noninferiority Trial of Telephone vs In-Person Genetic Counselling for Hereditary Breast and Ovarian Cancer: A 12-Month Follow-Up. JNCI Cancer Spectrum 1(1): pkx002 | Outcomes do not match those specified in this review protocol |
| Kaufman, E. M., Peshkin, B. N., Lawrence, W. F. et al. (2003) Development of an Interactive Decision Aid for Female BRCA1/BRCA2 Carriers. Journal of Genetic Counselling 12(2): 109-29 | Study design not relevant to this review protocol |
| Kautz-Freimuth, S., Redaelli, M., Rhiem, K. et al. (2021) Development of decision aids for female BRCA1 and BRCA2 mutation carriers in Germany to support preference-sensitive decision-making. BMC Medical Informatics & Decision Making 21(1): 180 | Study design not relevant to this review protocol |
| Kinney, A. Y., Steffen, L. E., Brumbach, B. H. et al. (2016) Randomized Noninferiority Trial of Telephone Delivery of BRCA1/2 Genetic Counselling Compared With In-Person Counselling: 1-Year Follow-Up. Journal of Clinical Oncology 34(24): 2914-24 | Outcomes do not match those specified in this review protocol |
| Korfage, I. J., Fuhrel-Forbis, A., Ubel, P. A. et al. (2013) Informed choice about breast cancer prevention: randomized controlled trial of an online decision aid intervention. Breast Cancer Research 15(5): r74 | Intervention in study does not match that specified in this review protocol |
| Krassuski, L. M., Kautz-Freimuth, S., Vennedey, V. et al. (2021) Decision Aids for Preventive Treatment Alternatives for BRCA1/2 Mutation Carriers: a Systematic Review. Geburtshilfe und Frauenheilkunde 81(6): 679-698 | Systematic review used as source of primary studies |
| Krassuski, L., Vennedey, V., Stock, S. et al. (2019) Effectiveness of decision aids for female BRCA1 and BRCA2 mutation carriers: a systematic review. BMC Medical Informatics & Decision Making 19(1): 154 | Systematic review used as source of primary studies |
| Kukafka, Rita, Pan, Samuel, Silverman, Thomas et al. (2022) Patient and Clinician Decision Support to Increase Genetic Counseling for Hereditary Breast and Ovarian Cancer | Intervention in study does not match that specified in this review protocol |

| Study | Reason for exclusion |
|---|---|
| Syndrome in Primary Care: A Cluster Randomized Clinical Trial. JAMA network open 5(7): e2222092 | |
| LeCompte, C.G., McDougall, J., Walters, S.T. et al. (2022) Understanding Cancer Genetic Risk Assessment Intentions in a Tailored Risk Communication Intervention Randomized Controlled Trial. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 31(7): 1513-1514 | Outcomes do not match those specified in this review protocol |
| Lee, S. I., Patel, M., Dutton, B. et al. (2020) Effectiveness of interventions to identify and manage patients with familial cancer risk in primary care: a systematic review. Journal of Community Genetics 11(1): 73-83 | Outcomes do not match those specified in this review protocol |
| Lobb, E., Butow, P., Meiser, B. et al. (2002) The use of audiotapes in consultations with women from high risk breast cancer families: a randomised trial. Journal of medical genetics 39(9): 697-703 | Outcomes do not match those specified in this review protocol |
| Matloff, E. T., Moyer, A., Shannon, K. M. et al. (2006) Healthy women with a family history of breast cancer: impact of a tailored genetic counselling intervention on risk perception, knowledge, and menopausal therapy decision making. Journal of Women's Health 15(7): 843-56 | Population not relevant to this review protocol |
| McCuaig, J. M., Tone, A. A., Maganti, M. et al. (2019) Modified panel-based genetic counseling for ovarian cancer susceptibility: A randomized non-inferiority study. Gynecologic Oncology 153(1): 108-115 | Intervention in study does not match that specified in this review protocol |
| McGahan, L., Kakuma, R., Ho, C. et al. (2006) BRCA1 and BRCA2 predictive genetic testing for breast and ovarian cancers: a systematic review of clinical evidence | Intervention in study does not match that specified in this review protocol |
| McGahan, L., Kakuma, R., Ho, C. et al. (2006) A clinical systematic review of BRCA1 and BRCA2 genetic testing for breast and ovarian cancers | Intervention in study does not match that specified in this review protocol |
| McInerney-Leo, A., Biesecker, B. B., Hadley, D. W. et al. (2004) BRCA1/2 testing in hereditary breast and ovarian cancer families: effectiveness of problem-solving training as a counselling intervention. American Journal of Medical Genetics. Part A 130a(3): 221-7 | Intervention in study does not match that specified in this review protocol |
| Meilleur, K. G. and Littleton-Kearney, M. T. (2009) Interventions to improve patient education regarding multifactorial genetic conditions: a systematic review. American Journal of Medical Genetics. Part A 149a(4): 819-30 | Systematic review used as source of primary studies |
| Meisel, S. F., Freeman, M., Waller, J. et al. (2017) Impact of a decision aid about stratified ovarian cancer risk-management on women's knowledge and intentions: a randomised online experimental survey study. BMC Public Health 17(1): 882 | Population not relevant to this review protocol |
| Metcalfe, K. A., Dennis, C. L., Poll, A. et al. (2017) Effect of decision aid for breast cancer prevention on decisional conflict in women with a BRCA1 or BRCA2 mutation: a multisite, randomized, controlled trial. Genetics in Medicine 19(3): 330-336 | Intervention in study does not match that specified in this review protocol |
| Miller, S. M., Fleisher, L., Roussi, P. et al. (2005) Facilitating informed decision making about breast cancer risk and genetic counselling among women calling the NCI's Cancer Information Service. Journal of Health Communication 10suppl1: 119-36 | Outcomes do not match those specified in this review protocol |

| Study | Reason for exclusion |
|---|---|
| Miller, S. M., Roussi, P., Daly, M. B. et al. (2005) Enhanced counselling for women undergoing BRCA1/2 testing: impact on subsequent decision making about risk reduction behaviors. Health Education & Behavior 32(5): 654-67 | Narrative review |
| Miller, S. M., Roussi, P., Daly, M. B. et al. (2010) New strategies in ovarian cancer: uptake and experience of women at high risk of ovarian cancer who are considering risk-reducing salpingo-oophorectomy. Clinical Cancer Research 16(21): 5094-106 | Systematic review used as source of primary studies |
| Nelson, H. D., Fu, R., Goddard, K. et al. (2013) Risk assessment, genetic counselling, and genetic testing for BRCA-related cancer in women: a systematic review to update the U.S. Preventive Services Task Force recommendation. Agency for Healthcare Research and Quality: 12 | Systematic review used as source of primary studies |
| Nelson, H. D., Fu, R., Goddard, K. et al. (2014) Risk assessment, genetic counselling, and genetic testing for BRCA-related cancer: systematic review to update the U.S. preventive services task force recommendation | Systematic review used as source of primary studies |
| Nelson, H. D., Pappas, M., Cantor, A. et al. (2019) Risk Assessment, Genetic Counselling, and Genetic Testing for BRCA-Related Cancer in Women: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 322(7): 666-685 | Systematic review used as source of primary studies |
| Nelson, H. D., Pappas, M., Cantor, A. et al. (2019) Risk Assessment, Genetic Counselling, and Genetic Testing for BRCA1/2-Related Cancer in Women: A Systematic Review for the U.S. Preventive Services Task Force [Internet]. Agency for Healthcare Research and Quality: 08 | Systematic review used as source of primary studies |
| Obeidat, R.; Finnell, D. S.; Lally, R. M. (2011) Decision aids for surgical treatment of earlystage breast cancer: a narrative review of the literature. Patient education and counselling 85(3): e311-21 | Population not relevant to this review protocol |
| Owens, R. G., Ashcroft, J. J., Leinster, S. J. et al. (1987) Informal decision analysis with breast cancer patients: an aid to psychological preparation for surgery. Journal of Psychosocial Oncology 5: 23-33 | Population not relevant to this review protocol |
| Peshkin, B. N., Kelly, S., Nusbaum, R. H. et al. (2016) Patient Perceptions of Telephone vs. In-Person BRCA1/BRCA2 Genetic Counselling. Journal of Genetic Counselling 25(3): 472-82 | Outcomes do not match those specified in this review protocol |
| Pruthi, S.; Gostout, B. S.; Lindor, N. M. (2010) Identification and Management of Women With BRCA Mutations or Hereditary Predisposition for Breast and Ovarian Cancer. Mayo Clinic Proceedings 85(12): 1111-20 | Narrative review |
| Roshanai, A. H., Rosenquist, R., Lampic, C. et al. (2009) Does enhanced information at cancer genetic counselling improve counselees' knowledge, risk perception, satisfaction and negotiation of information to at-risk relatives?-a randomized study. Acta Oncologica 48(7): 999-1009 | Population not relevant to this review protocol |
| Schwartz, M. D., Peshkin, B. N., Isaacs, C. et al. (2018) Randomized trial of proactive rapid genetic counselling versus usual care for newly diagnosed breast cancer patients. Breast Cancer Research & Treatment 170(3): 517-524 | Intervention in study does not match that specified in this review protocol |
| Schwartz, M. D., Peshkin, B. N., Tercyak, K. P. et al. (2005) Decision making and decision support for hereditary breast- | Narrative review |

| Study | Reason for exclusion |
|---|---|
| ovarian cancer susceptibility. Health Psychology 24(4 SUPPL.): S78-S84 | |
| Skrovanek, E., Dunbar-Jacob, J., Dunwoody, C. et al. (2020) Integrative Review of Reproductive Decision Making of Women Who Are BRCA Positive. JOGNN - Journal of Obstetric, Gynecologic, & Neonatal Nursing 49(6): 525-536 | Systematic review used as source of primary studies |
| Stacey, D., Légaré, F., Lewis, K. et al. (2017) Decision aids for people facing health treatment or screening decisions. Cochrane Database of Systematic Reviews | Systematic review used as source of primary studies |
| Stalmeier, P. F. and Roosmalen, M. S. (2009) Concise evaluation of decision aids. Patient Education & Counselling 74(1): 104-9 | Intervention in study does not match that specified in this review protocol |
| Tea, M. M., Tan, Y. Y., Staudigl, C. et al. (2018) Improving comprehension of genetic counselling for hereditary breast and ovarian cancer clients with a visual tool. PLoS ONE [Electronic Resource] 13(7): e0200559 | Study design not relevant to this review protocol |
| Tutty, E., Petelin, L., McKinley, J. et al. (2019) Evaluation of telephone genetic counselling to facilitate germline BRCA1/2 testing in women with high-grade serous ovarian cancer. Eur J Hum Genet 27(8): 1186-1196 | Study design not relevant to this review protocol |
| Waljee, J. F.; Rogers, M. A.; Alderman, A. K. (2007) Decision aids and breast cancer: do they influence choice for surgery and knowledge of treatment options? Journal of clinical oncology official journal of the American Society of Clinical Oncology 25(9): 1067-73 | Population not relevant to this review protocol |
| Wang, Catharine Chia-Ling (2003) Decision making in the context of genetic testing for hereditary breast and ovarian cancer: Key predictors and influences. Dissertation Abstracts International: Section B: The Sciences and Engineering 64(6b) | Study design not relevant to this review protocol |
| Wevers, M. R., Aaronson, N. K., Bleiker, E. M. A. et al. (2017) Rapid genetic counselling and testing in newly diagnosed breast cancer: Patients' and health professionals' attitudes, experiences, and evaluation of effects on treatment decision making. Journal of Surgical Oncology 116(8): 1029-1039 | Intervention in study does not match that specified in this review protocol |
| Widmer, Colin L., Wolfe, Christopher R., Reyna, Valerie F. et al. (2015) Tutorial dialogues and gist explanations of genetic breast cancer risk. Behavior Research Methods 47(3): 632-648 | Population not relevant to this review protocol |
| Williams, L., Jones, W., Elwyn, G. et al. (2008) Interactive patient decision aids for women facing genetic testing for familial breast cancer: a systematic web and literature review. Journal of Evaluation in Clinical Practice 14(1): 70-4 | Systematic review used as source of primary studies |
| Witt, J., Elwyn, G., Wood, F. et al. (2014) Adapting the coping in deliberation (CODE) framework: a multi-method approach in the context of familial ovarian cancer risk management. Patient Education & Counselling 97(2): 200-10 | Study design not relevant to this review protocol |
| Zhao, A., Larbi, M., Miller, K. et al. (2021) A scoping review of interactive and personalized web-based clinical tools to support treatment decision making in breast cancer. Breast (Edinburgh, Scotland) 61: 43-57 | Intervention in study does not match that specified in this review protocol |
| Zilliacus, E. M., Meiser, B., Lobb, E. A. et al. (2011) Are videoconferenced consultations as effective as face-to-face consultations for hereditary breast and ovarian cancer genetic counselling? Genet Med 13(11): 933-41 | Study design not relevant to this review protocol |

### Excluded economic studies

See Supplement 2 for the list of excluded studies across all reviews.

# Appendix K Research recommendations – full details

**Research recommendations for review question: Which interventions are effective for supporting women at increased risk of ovarian cancer to make decisions about management options?**

## J1.1 Research recommendation

What is the effectiveness of psychological interventions to support decision making for people who meet the referral criteria for genetic testing?

### Why this is important

Currently those referred to be tested for a pathogenic variant associated with familial ovarian cancer are seen by a genetics counsellor for pre-testing counselling. This is an opportunity to discuss risk, the outcomes of the test and implications of a positive result. However, as rates of germline testing increase, genetic counselling services will become unable to meet the demand. This could lead to a delay in the diagnostic pathway which in turn could have detrimental management implications.

Therefore, there is a need to explore other means that can either supplement or replace the traditional model. This could be in form of psychological digital tools or other psychological interventions that aid decision making. There is limited data to support moving from the traditional method of pre-testing genetic counselling for the germline testing of high-risk ovarian cancer pathogenic variants. To date there are no randomised control trials to inform either clinicians or patients as to the utility of psychological interventions in supporting decision making. Such studies could find alternative methods in which women could be supported to make informed decisions around germline testing which would remove pressure on clinical genetic services without an increased psychological distress or decreased satisfaction in the decision making.

### Rationale for research recommendation

**Table 16: Research recommendation rationale**

| | |
|---|---|
| **Importance to 'patients' or the population** | Understanding the implications of undergoing a germline test to identify a gene change that could increase an individual's lifetime risk of ovarian cancer is complex. Risk is not a straightforward concept and the degree of risk that is specific to an individual is often opaque. Currently women get limited time with a counsellor to discuss and appreciate these concepts before they are offered germline testing. The use of psychological interventions could enable women more time to better understand these crucial concepts and make a more informed decision around testing. |
| **Relevance to NICE guidance** | Improving quality of life by promoting physical and psychological wellbeing is central to NICE guidance. Finding effective psychological interventions to support decision making is relevant to this since it could these interventions could be used to help people when they must make choices that may impact their own and their families' lives. |
| **Relevance to the NHS** | Correctly identifying women at an increased lifetime risk of ovarian cancer would empower women to take steps to reduce their cancer risk or seek medical attention earlier if concerned about symptoms. This is relevant to the NHS because of the emphasis of early detection and diagnosis in the NHS long term plan for cancer and NHS Clinically-led review of NHS cancer standards: models of care and management. Whilst these are not specifically mentioning ovarian cancer the aim is to |

| | |
|---|---|
| | focus the attention on prevention and diagnosis which would include assessing and managing the risk of cancer. |
| **National priorities** | Prevention and diagnosis of cancer is a national priority because it saves lives. |
| **Current evidence base** | There was no evidence identified for psychological interventions that support decision-making in relation germline testing for high risk gene changes for ovarian cancer |
| **Equality considerations** | The guideline equality assessment identified socioeconomic inequalities in access to tests as well as inequalities in access to services for tans men and non-binary people. Therefore, research addressing such inequalities would be particularly welcome. |

## Modified PICO table

### Table 17: Research recommendation modified PICO table

| | |
|---|---|
| **Population** | Women who are trying to decide if they wish to undergo a germline test for a pathogenic variant associated with familial ovarian cancer or women with a known pathogenic variant who have to make decisions about risk reducing surgery.<br><br>• women with a known pathogenic variant in their family<br>• women with a strong family history suggestive of a pathogenic variant in their family but without any germline confirmation<br>• women without a strong family history suggestive of a pathogenic variant in their family<br>• women without any family history suggestive of a pathogenic variant in their family<br><br>There is also a particular research gap in people born with some or all of the following organs: ovaries; fallopian tubes; and uterus who do not identify as women. Or people with protected characteristics. |
| **Intervention** | psychological interventions, for example:<br>• cognitive behavioural therapy |
| **Comparator** | • usual care without psychological interventions<br>• each other |
| **Outcome** | • Preparation for active participation in making a health decision<br>• Resolution of decisional needs<br>• Uptake of germline testing<br>• Adverse effects (during or after decision making) such as:<br>  ○ Decision regret<br>  ○ Anxiety<br>  ○ Depression<br>  ○ Distress<br>  ○ Grief or loss<br>  ○ Cancer worry |
| **Study design** | Randomised controlled trial |
| **Timeframe** | 5 Years |
| **Additional information** | None. |