Study Protocol

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Randomized control trial of a decision aid for women considering elective egg freezing: The Eggsurance study protocol

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Abstract

Background: Uptake of elective egg freezing has increased globally. The decision to freeze eggs is complex, and detailed, unbiased information is needed. To address this, we developed an online Decision Aid for women considering elective egg freezing. Decision Aids are the standard of care to support complex health decisions.

Objectives: This study will measure the impact of the Decision Aid on decision-making (e.g. decisional conflict, engagement in decision-making, distress, and decision delay) and decision quality (e.g. knowledge, level of informed choice, and regret).

Methods and Analysis: A single-blinded two-arm parallel-group randomized controlled trial. Women considering elective egg freezing will be recruited using social media, newsletters, and fertility clinics. Data will be collected at baseline (recruitment), 6-month, and 12-month post-randomization. The primary hypothesis is that the intervention (Decision Aid plus Victorian Assisted Reproductive Technology Authority website) will reduce decisional conflict (measured using the Decisional Conflict Scale) at 12 months more than control (Victorian Assisted Reproductive Technology Authority website only). Secondary outcomes include engagement in decision-making (Perceived Involvement in Care Scale), distress (Depression, Anxiety, and Stress Scale), decision delay, knowledge, informed choice (Multi-dimensional Measure of Informed Choice), and decisional regret (Decisional Regret Scale).

Ethics: The study was approved by the University of Melbourne Human Research Ethics Committee (Ethics ID: 2056457). Informed consent will be obtained from all participants prior to enrolment.

Discussion: This is the first international randomized controlled trial that aims to investigate the effect of an elective egg freezing Decision Aid on decision-related outcomes (e.g. decisional conflict, informed choice, and regret). It is anticipated that participants who receive the Decision Aid will have better decision and health outcomes.

Registration details: ACTRN12620001032943: Comparing different information resources on the process and quality of decision-making in women considering elective egg freezing.

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Main text

Background

Live birth rates from frozen eggs are similar to fresh eggs, with younger age at egg collection and the number of eggs vitrified the main predictors for success.[1–4] Elective egg freezing (EEF) can potentially extend reproductive years for those planning to have children when their natural fertility is declining.[5] Qualitative literature has shown that the main driver for EEF is the fear of running out of time to form a conventional family, in large part due to not having a partner at the time of EEF, in case they do not have one when they are ready to become a parent, or they are in a situation where their current partner is unlikely to be the father of their future child (because he does not want to be a parent or the relationship is unlikely to last).[6,7] EEF provides a way to avoid future regret and blame.[6] Uptake of egg freezing has risen exponentially with cycles increasing between 2010 and 2016 by 378% in the United Kingdom, 507% in Australia and New Zealand, and 880% in the United States.[8–10] Most likely, this reflects growing public awareness of EEF, active promotion by service providers, increased access, improvements to egg freezing technology, and employee subsidization.[1,8,11–14]

Despite this rapid increase in EEF uptake, only 3%–38% of women have returned to use their frozen eggs within 15 years.[15–20] This may reflect overuse of the procedure,[21] limited long-term data about egg usage (anticipating greater use as time progresses), or that some women perceive EEF as a form of insurance and do not intend to use their frozen eggs.[22] Our data show that most women who have considered EEF have sizable uncertainty and spend a median of 2 years making their decision (Sandhu, 2022 unpublished). Given that the average age at egg freezing is 34.7 years,[8] this 2-year delay may result in lower egg yield and reduced pregnancy potential.[8,18] While qualitative work has reported low regret[23] and a UK survey study reported 9% (n = 85) of participants having some level of regret,[24] only two studies have measured regret about EEF using the validated Decisional Regret Scale. These include a US study which found moderate to severe decision regret in 16% (n = 33) of participants, with higher regret associated with insufficient provision of EEF information,[25] and a Turkish study which also reported moderate to severe regret in 16% of participants (n = 552), with higher regret associated with whether they believed that having a child was due to fate, trust in the efficacy of egg freezing, and emotional challenges while undergoing egg freezing.[26]

The decision to freeze eggs is challenging. Outcomes for EEF are uncertain and vary between providers, and success declines with age at freezing.[15,27,28] In addition, EEF is expensive with providers often recommending >1 cycle to collect sufficient eggs to optimize the chances of a live birth. Cost is a common barrier to use.[23] There is variability around individual success from egg freezing, however, on average, ~14 eggs are collected per cycle which decrease with age, from ~17 for women aged <35 years to ~9 for women aged >42 years per cycle.[15] Live birth rates at 10- to 15-year follow-up are around 34%, and, while not statistically significant, it appears that having ⩽9 oocytes thawed results in a lower live birth rate (17%, mean = 6.7 oocytes, 95% confidence interval (CI) = 5.0–7.6) than having ⩾10 oocytes thawed (40%, mean = 18.6 oocytes, 95% CI = 16.6–20.6, p = 0.07).[15] Egg collection is generally safe with complication rates typically <1%; however, if they do occur, these complications can be serious with ~0.6% of patients requiring hospitalization.[21,29] There can also be an emotional impact from EEF, for instance, feelings of isolation,[23] that needs to be considered. Ultimately, many women considering EEF are weighing up their future parenting desires against their financial situation, relationship status, and personal values. The decision is made more complex by the lack of independent, personalized, and values-based support to guide choices.[30] Most women seek EEF information through media stories, social media, and fertility clinic websites.[31,32] However, media information is often limited and information on fertility clinic websites have been rated as low quality and strongly biased towards EEF.[12,27,30,33–38] Women who have previously frozen eggs have reported that their greatest desire was to have detailed EEF information, focusing specifically on women.[23]

To address this, we developed an online Decision Aid (DA) for women considering EEF. DAs are designed to support complex decisions about healthcare options.[39] A systematic review demonstrates that DAs improve patient outcomes by reducing uncertainty, improving engagement in decision-making, facilitating informed choice and reducing decision delay, and resulting in greater satisfaction and less decision regret.[39] DAs are recommended for complex health choices by the Australian Commission on Safety and Quality in Healthcare, the United Kingdom National Institute of Clinical Excellence (NICE), and the United States Affordable Care Act.[40–42] We developed this DA according to the International Patient Decision Aid Standards (IPDAS) guidelines, and in collaboration with experts in fertility, psychology, decision-making, women's health, and consumer representatives (Sandhu, 2021,

unpublished). This randomized controlled trial (RCT) aims to determine whether the DA improves the quality of EEF decisions, specifically by assessing the impact of the DA at 12 months (compared to the control) on Decisional Conflict (primary outcome), engagement in decision-making, distress, decision delay, knowledge, informed choice, and Decisional Regret, to inform future changes to public policy and clinical practice.

Methods and analysis

Study design

A single-blinded, two-arm parallel-group RCT, with participants individually randomized to a placebo-type control group (provided with the Victorian Assisted Reproductive Treatment Authority (VARTA) website: https://www.varta.org.au/) or intervention group (provided with the DA plus VARTA website). Participants will complete three surveys: at baseline (T_0), 6-month (T_1), and 12-month (T_2) post-randomization.

Hypotheses

Primary. In women considering EEF, the intervention group will have a greater reduction in Decisional Conflict (measured by the Decisional Conflict Scale, DCS)[43] about EEF at 12 months compared to control.

Secondary. Access to the intervention, compared to control, will at 12 months lead to:

1. Greater engagement in decision-making (measured by the Perceived Involvement in Care Scale).[44]
2. Less distress (measured by the Depression Anxiety Stress Scale).[45]
3. Faster decision-making about EEF (measured by decisional delay).
4. Greater improvements in EEF and female fertility knowledge (measured by a purpose-built knowledge scale).
5. Greater informed choice (measured by the Multidimensional Measure of Informed Choice).[46]
6. Less regret about their EEF decision, irrespective of decision made (measured by the Decisional Regret Scale).[47]

Recruitment

Participants will be recruited using multiple methods including paid Google advertising, Search Engine Optimization of the study's landing page, social media, newsletters and website posts by our partner organizations, and promotion via radio, podcasts, and print media interviews. Partner organizations include VARTA, Jean Hailes for Women's Health, and investigator affiliated universities, hospitals, and fertility clinics. For all recruitment methods, interested parties will be directed to the study's landing page (eggfreezing.org.au) for more information and an option to participate.

Eligibility

Inclusion criteria

- Premenopausal women aged ⩾18 years;
- Currently considering egg freezing;
- Residing in Australia for the next 12 months;
- Proficiency in the English language; and
- Access to the Internet.

Exclusion criteria

- Postmenopausal women;
- Already frozen eggs;
- Considering egg freezing for medical reasons (e.g. before chemotherapy); or
- Reviewed any of our previous information resources about EEF.

Enrolment

Women interested to participate in the trial will be directed from the study's landing page to the 'Participant Information and Consent Form'. This contains a detailed participant information sheet (Supplementary Material 1) including the research team's contact information for those with any queries about the study. Eligibility will be confirmed, and consent collected. Participants will then be directed to complete the baseline survey.

Randomization

Participants will be randomized (1:1) using a list of randomly permuted blocks computer-generated by an independent statistician and stratified by Australian state/territory (8 levels: Victoria, New South Wales, Tasmania, Queensland, South Australia, Western Australia, Northern Territory, and Australian Capital Territory) and whether they had consulted an in vitro fertilization (IVF) specialist about EEF (two levels: yes, no) to control for state-based healthcare and population differences.

Control group. Participants allocated to the control arm will receive a link to the VARTA website (www.varta.org.au). The VARTA is a statutory authority, funded by the Victorian Department of Health and Human Services. It provides independent information and support for individuals, couples and health professionals about fertility and issues relating to assisted reproductive treatment. Information about EEF includes reasons for freezing, steps involved, storage time, success rates, associated potential risks, financial implications, and important questions to ask a doctor.

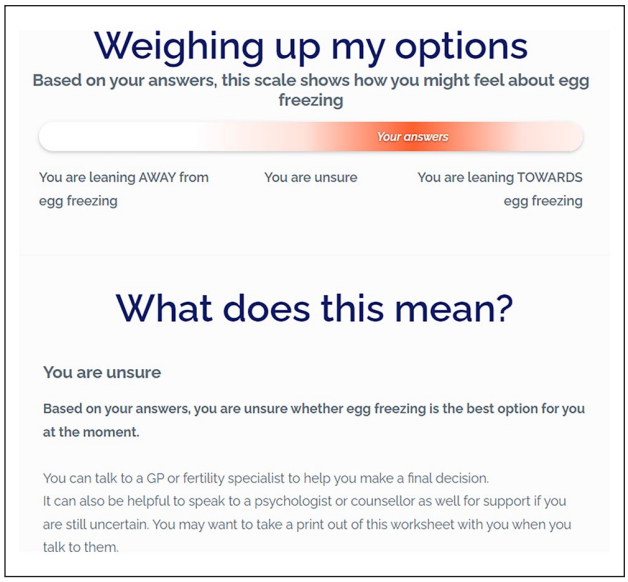

Figure 1. Results image from the values clarification exercise.

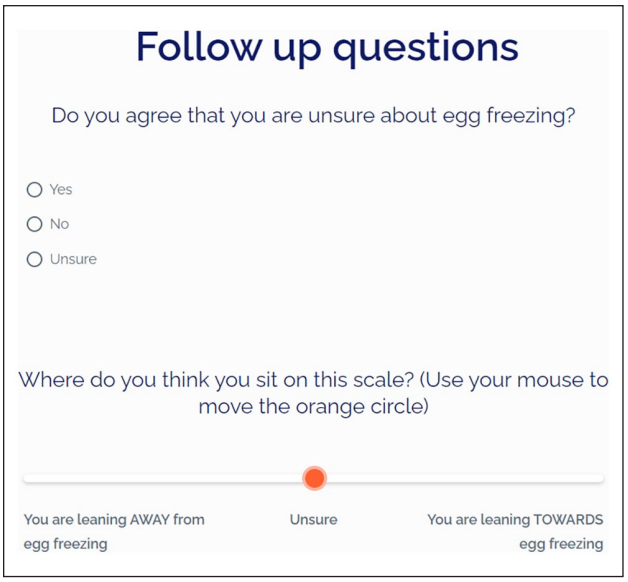

Figure 2. Values clarification exercise confirmatory questions.

Intervention group. Participants allocated to the intervention arm will receive access to the DA and a link to the VARTA website. The development and content of the DA will be reported in detail elsewhere (Sandhu, 2022, unpublished). In brief, it includes information about: common causes of female infertility (including age); the pros and cons of EEF; the EEF process; success rates; patient experience narratives; options for using frozen eggs; health, social, and psychological implications; and a values clarification exercise to help guide decisions. The values clarification exercise will ask participants to allocate a level of importance (not, somewhat, or very) to four benefits (e.g. 'Doing something about your fertility now rather later') and level of worry (not, somewhat, or very) to four egg freezing drawbacks (e.g. 'Egg freezing does not guarantee a baby when I am ready to have one'). Participants will have the option to add additional benefits and drawbacks specific to their experience. Each rating will be allocated a score (from 0 to ± 2). Total scores will be averaged, and a standard deviation (SD) is calculated. These will be on a scale showing if they are leaning towards or against egg freezing (Figure 1). Participants will then be asked if they agree with their results (Figure 2).

Allocation concealment and blinding

Allocation will be achieved using an automated randomization module in REDCap (Research Electronic Data Capture tool) after completing the baseline survey. The research coordinator will then send participants a 'welcome' email with their relevant website link(s) and an account activation email to intervention group participants to access the DA. Participants will be blinded to their allocation (e.g. told that they are comparing information resources but not specifically comparing a DA against existing website information). The research coordinator and Principal Investigator (PI) will not be blinded as they will send participants their relevant information and address any queries that arise regarding the websites. The study statistician will remain blinded to the allocation until the database is clean and locked before breaking the blind.

Follow-up data collection

Participants will be emailed their 6-month (T_1) and 12-month (T_2) surveys, for completion within five business days. For those requiring follow-up, a maximum of three attempts will be made within 28 days.

Study completion

Participants will be sent a thank you email after completing the T_2 survey. Those who complete all surveys will also be given an AU$50 gift card to cover their time taken for study participation. A result summary will be sent upon completion of the study to those who requested it. If the objectives of this trial have been met, a link to the tool will also be provided to all participants.

The coronavirus (COVID-19) pandemic

In response to the global COVID-19 pandemic, the study plan was changed to mitigate potential risks compromising the validity of findings. We anticipated that COVID-19 could affect outcomes such as information-seeking and EEF uptake, and thus added questions to measure this. Changes to the study regarding COVID-19 were approved by ethics (22 March 2021, Protocol version 2) and are outlined in

accordance with the CONSORT (Consolidated Standards of Reporting Trials) and SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) and the SPIRIT Extension for RCTs Revised in Extenuating Circumstances (Supplemental Tables 1 and 2).[48]

Measures

Supplemental Table 3 outlines all adaptations made to instruments.

Demographic and baseline data

Demographic and Reproductive Data (24-items): at baseline, data will be collected on participants' recruitment source, date of birth, country of birth, ethnicity, sexual orientation, religion, length of time living in Australia, postcode, first language, language spoken at home, Indigenous Australian ancestry, the highest education level, annual income, health-related training, employment, profession, number of existing children, how they have researched EEF, plans for having children, reason for considering EEF, maximum age they would be willing to have a baby, and whether they consulted a fertility specialist about EEF (when and the outcome). Relationship status will be assessed at all three time points. At T_2, three questions will assess if pregnancy had been attempted in the prior 12 months, time spent attempting conception, and the outcome.

Control Preferences (1-item): adapted from an interview-style question, will assess participants' preferences for control when making healthcare decisions (e.g. active vs passive decision-makers).[49]

Information Preference Style (3-items): this scale, adapted to specifically address EEF decisions, will assess at baseline desire for information. How proactive participants have been in seeking information will also be assessed. It has satisfactory internal consistency ($\alpha = 0.6$).[50,51]

Anti-Müllerian Hormone (AMH, 6-items): at baseline and T_2, data will be collected on whether participants had undertaken a serum AMH test, when, who ordered it, the result, their understanding of it, and whether this influenced their EEF decision.

Impact of COVID-19 (14-items): data on the perceived impact of COVID-19 on employment will be collected. The perceived impact of COVID-19 on participants' EEF decision, ability to seek information and/or see a doctor, family planning, and anything else they wish to disclose will be collected all time points.

Primary outcome

Low Literacy Decisional Conflict Scale (DCS, 11 items): at all time points, the 10-item DCS measures perceived uncertainty about a decision and the modifiable factors that contribute to this uncertainty (feeling uninformed, unsupported, and unclear about personal values).[43] Scores >37.5 indicate high decisional conflict which is associated with decision delay. Scores <25 are associated with implementing decisions. The DCS has good internal consistency ($\alpha = 0.86$) and correlates with constructs of knowledge, Decisional Regret, and discontinuance. A question preceding the DCS scale will identify which option participants prefer: (1) freeze eggs now, (2) freeze eggs later, (3) not freeze eggs at all, (4) reconsider egg freezing in the future, (5) try to get pregnant now naturally or with fertility treatment, (6) try to get pregnant in the future naturally or with fertility treatment, (7) not have children at all, (8) adoption/fostering, (9) freeze embryos, and (10) unsure.

Secondary outcomes

Perceived Involvement in Care (17 items): the original 13-item scale, adapted to address EEF, will assess at T_1 and T_2 involvement in treatment decisions and interactions with healthcare providers among those who consulted a doctor about EEF.[44] It has acceptable internal consistency ($\alpha = 0.73$). Information about their experiences in obtaining clinical advice will also be collected.

Depression, Anxiety, and Stress Scale (DASS, 21-items): this scale measures distress at all time points. Scores >13 for depression, >9 for anxiety, and >18 for stress indicate moderate to severe emotional states. The scale has good to excellent internal consistency ($\alpha_{anxiety} = 0.8$, $\alpha_{stress} = 0.84$, and $\alpha_{depression} = 0.91$).[45]

Knowledge about Female Fertility and Egg Freezing (13-items): a purposively developed knowledge scale (with true/false/unsure response options), adapted from our previous studies (Sandhu, 2021, unpublished), will assess at all time points, participants understanding of egg freezing, its rationale, benefits, risks and side effects, alternatives, and female fertility. Responses will be scored (1 = correct, 0 = incorrect or unsure) and tallied. A total knowledge score above the midpoint ($\geqslant 7$) will be classified as 'good knowledge'.

Multi-dimensional Measure of Informed Choice (MMIC, 7-items): the MMIC will assess at T_1 and T_2 whether participants made an informed choice.[46,52] Informed choice will be determined by having either (1) good knowledge AND positive attitudes (assessed using seven items included in the MMIC) AND freezing eggs (uptake at T_1 or T_2) or (2) good knowledge AND negative attitudes AND not freezing eggs. All other combinations will be considered 'uninformed'. The MMIC has good internal consistency ($\alpha = 0.81$).

Decisional Regret Scale (DRS, 5-items): among those who made a decision, the DRS will measure remorse (scores ⩾30 will indicate high decisional regret) at T_1 and T_2.[47] The DRS has good to excellent internal consistency ($\alpha = 0.81–0.92$) and discriminatory validity.

Decision Delay (1-item): one purposive item will assess the time taken to decide.

Other decision process-related variables

Decision Self-Efficacy Scale (11-items): this scale adapted for EEF decisions will assess at T_1 and T_2 self-confidence in one's abilities to make a decision[53] (Supplemental Table 3). Higher scores indicate higher self-efficacy. The scale has high internal consistency ($\alpha = 0.92$) and is correlated with the DCS feeling informed ($r = 0.47$) and supported ($r = 0.45$) subscales.

Stage of Decision-Making (1-item): will assess at all time points readiness to engage in decision-making.[54] It is associated with DCS (early stages of decision-making are associated with high DCS, and later stages with lower DCS). Another item will assess inclination to freeze eggs (or not).

Impact of Information (6-items): at T_1 and T_2, these items will measure use of information provided and other resources accessed to support their decision. At T_2, participants will be asked if the information led them to consider single motherhood, any other option for parenthood, and not having any children/more children, and perceptions on when someone considering EEF should be provided with this information.

Other decision quality-related variables

Realistic Expectations (2-items): at all time points, these items, adapted from a validated measure,[55] will assess participant's perceived chances of (1) having a baby naturally now and (2) having a baby from frozen eggs in the future if their eggs were frozen now. Responses will be compared with published success data.

Preparation for Decision-Making (PDM, 10-items): At T_1, this scale adapted for EEF will evaluate usefulness of the information provided in facilitating communication with healthcare providers[56] (Supplemental Table 3). Higher scores indicate a higher level of preparation. The PDM has high internal consistency ($\alpha = 0.92–0.96$), item-total correlation (0.75–0.81), total-test reliability (0.944), and discriminates between different decision support interventions (effect size = 1.8).

Values (8-items): at T_1 and T_2, this scale adapted for EEF evaluates the importance placed on benefits and risks of an option[57] (Supplemental Table 3). The scale has acceptable test–retest coefficients (0.79–0.91).

Satisfaction with Decision Scale (SWD, 6-items): the validated SWD, adapted for EEF (Supplemental Table 3), will measure decision satisfaction.[58] Higher scores indicate greater satisfaction. The scale has good internal consistency ($\alpha = 0.85$).

Utility of the Values Clarification Exercise(2-items): participants in the intervention group who complete the DA's values clarification exercise will be asked at the end of the exercise (1) if they agree with the outcome provided (e.g. leaning towards/against egg freezing) and (2) where they feel they sit on the scale towards/against EEF. Data will be evaluated at T_1 and T_2.

Table 1 outlines the timeline of assessment.

Sample size

When comparing the intervention and control groups at 12 months, a total sample size of 200 participants (100 in each arm) will allow for an effect size (Cohen's d) of 0.4 in the DCS scores to be detected with 80% power at a two-sided significance level of 0.05. This assumes equal SDs in both groups and no correlation between baseline and 12-month measures (conservative). This sample size is based on a magnitude of improvement in the decision-making process, which represents a change that women perceive as beneficial and would result in worthwhile implementation. An effect size of 0.4 will discriminate between those who make and those who delay decisions.[62,63] Assuming that women in the control group will have a mean DCS score of 48.3 units (SD = 31.9),[64] and assuming the same SD in the intervention group, a reduction in DCS score that is 0.4 of the SD will result in a mean score for the intervention group of 35.5 units which is below the standardized cut-off (37.5). It will also result in less decision delay and higher decision implementation.[63] This effect size is considered to be a 'visible' difference and worth implementing.[62] Based on similar studies,[65] the maximum attrition rate is anticipated to be 30% at 12 months. Therefore, 286 women will be recruited (143 in each arm).

Data analyses

Data analyses will be undertaken according to a pre-specified detailed statistical plan that will be finalized before unblinding. Available data of the participants will be analysed in the group they were randomized to, regardless of deviation from study protocol. Decisional Conflict will be analysed using a likelihood-based longitudinal data analysis model.[66] The outcome (dependent variable) will consist of the baseline and post-baseline values. The model will assume a common baseline mean across the two groups due to random allocation. The variance-covariance among the repeated measurements will be defined as unstructured and in the case of non-convergence, alternative structures will

Table 1. Timing of study measures.

Time point	T_0	T_1	T_2
Month	0	6	12
Enrolment/baseline			
Confirm eligibility	X		
Informed consent	X		
Randomization: intervention (DA + VARTA website) or control (VARTA website)	X		
Assessments			
Demographic and Baseline Data (24-items):			
Age, postcode, ethnicity, parity, attitudes to childbearing, education	X		
Relationship status	X	X	X
Anti-Müllerian Hormone (6-items)	X		X
Control Preferences (1-item)[a,b]	X		
Information Preference Style (3-items)[a]	X		
Impact of COVID-19 (14-items):			
On employment	X		
On their decision, ability to seek information and/or clinical care, family planning, and any other impacts	X	X	X
Primary outcome:			
Low Literacy Decisional Conflict Scale (DCS, 11 items)[a,b]	X	X	X
Secondary outcomes:			
Perceived Involvement in Care (17-items)[a,b]		X	X
Depression, Anxiety, and Stress Scale (DASS, 21-items)[a]	X	X	X
Knowledge about Female Fertility and Egg Freezing (13-items)[b]	X	X	X
Multi-dimensional Measure of Informed Choice (MMIC, 7-items)[a,b]		X	X
Decisional Regret Scale (DRS, 5-items)[a,b]		X	X
Decision Delay (1-item)[b]	X	X	X
Other Decision Process-Related Variables:			
Decision Self-Efficacy Scale (11-items)[a,b]	X	X	X
Stage of Decision-Making (2-items)[a,b]	X	X	X
Impact of Information (6-items)		X	X
Other Decision Quality-Related Variables:			
Realistic Expectations (2-items)	X	X	X
Preparation for Decision-Making (PDM, 10-items)[a,b]		X	
Values (8-items)[a,b]		X	X
Satisfaction with Decision Scale (SWD, 6-items)[a]		X	X
Utility of the Values Clarification Exercise(2-items)		X	X

[a]Validated measure.
[b]Assessments recommended by the International Patient Decision Aid Standards.[59–61]

be considered. This model will provide valid inference if data are missing at random. The primary hypothesis will be examined by obtaining an estimate and two-sided 95% CI of the absolute difference between the groups in mean changes from baseline to 12 months. We will also obtain an adjusted treatment effect by accounting for potential confounders in the primary model. Heterogeneity of treatment effect will be explored for subgroups defined by age categories, relationship status, and promotion source.

Secondary and other continuous outcomes will be analysed using a similar model. Secondary and other binary outcomes will be analysed using a logistic regression model, accounting for repeated measures when applicable. All statistical analyses will present two-sided 95% CIs and p-values.

Commentary provided in the surveys' free-text fields will be analysed qualitatively in accordance with the framework of Miles and Huberman.[67] Coding will be conducted as an iterative process: starting with broad themes before coding into hierarchical categories and subthemes. Patterns across the themes and subthemes and the relevance of these patterns to the research question and inquiry will be explored.

Patient and public involvement

The Eggsurance Collaborative Group has three consumer members (two women who froze their eggs and one who decided not to freeze eggs). These consumers were involved from trial conception. Their role includes

providing feedback on study documents – including the research question, study design and conduct, choice of outcome measures, methods for recruitment, and the DA content. They will also provide input into the study's summary of findings and approaches to disseminate the results. Furthermore, the DA underwent phase 1 testing to obtain feedback on its content and usability among 26 women interested in EEF. The DA was adapted in response (Sandhu, 2021, unpublished).

Ethics and dissemination

Ethical and safety considerations

The University of Melbourne, Australia Human Research Ethics Committee initially approved this study (Ethics ID: 2056457) on 3 June 2020 (Supplemental Table 4 outlines the ethics amendment and approval schedule). All relevant parties will be notified by the study team of important protocol modifications.

Participants will provide informed consent before enrolment in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), Good Clinical Practice (GCP)[68] and Declaration of Helsinki 2000[69] guidelines, and local regulatory requirements. Participants will be made aware of their rights to access their results in accordance with the Australian National Statement on Ethical Conduct in Human Research.[70] Participants will also be informed about plans to disseminate the research findings, including the publication and presentation to the broader scientific community and the public. All participants will be free to withdraw from the study at any time.

Any identifiable participant information will remain confidential and securely stored. Only the PI and research coordinator will have to access this information. It will only be used for this research project, and only disclosed with the participants' permission, except as required by law. In any publication and/or presentation, participant data will be de-identified.

Participants will have the option to skip questions, stop the survey, or withdraw from the study. Contact details for the PI, research coordinator, and relevant ethics committee(s) will be provided. The research team will monitor participants' questions or concerns and adapt as needed. Although unlikely, if participants experience distress, they will be referred to the Australian 24-h Beyond Blue phone-based counselling service (www.beyondblue.org.au) and the incident will be documented. In the unlikely occurrence of serious adverse events (SAEs), the research team will initiate an appropriate response including reporting the SAE to the lead ethics committee. Complaints relating to the research will be comprehensively recorded and addressed in accordance with the relevant ethics committee/s policy.

Potential conflicts of interest (COIs) will be clearly stated in the Plain Language Statement (PLS) for each investigator. In addition, the PLS will outline that the study investigators with potential COIs will not be involved in the day-to-day activities of this project, data collection or analysis, and they will not have final authority when making study-related decisions. These investigators will not have access to any participant data and any results provided to them will be in a de-identified or aggregate format.

Data deposition and curation

Access to study data will be limited to the research coordinator and PI. Participant data will be securely stored in password-protected electronic databases on the University of Melbourne server, and backed up daily. Each participant will be allocated a unique study ID so data analysis is performed using non-identifiable information. Only the PI and research coordinator will have access to the information linking participants' study IDs to their corresponding personal information. Information will be held for at least 7 years (post-trial completion) according to the National Health and Medical Research Council, and for 5 years after publication. All information will then be destroyed via the University of Melbourne Records Retention and Disposal Authority.

Data management

The consent process and all surveys will be administered and managed using REDCap hosted at the University of Melbourne.[71,72] REDCap is a secure, web-based software platform designed to support data capture for research studies.

Monitoring

As this study does not address mortality or disease progression, a Data Safety Monitoring Board is not warranted.[73] Instead, the number of participants who report questions or concerns will be monitored and the Trial Management Group (M.P., S.S., M.H., S.B., and R.L.) will meet monthly to provide oversight of the data relating to quality, protocol adherence, patient retention rates, and respond to adverse events (in the unlikely event that one occurs).

Dissemination plan

Aggregated data will be submitted to peer-reviewed journals for publication and presented at national and international conferences. Authorship will be determined in accordance with the International Committee of Medical Journal Editors guidelines.[74] A summary of results will be distributed to participants and displayed on the research unit's website. Findings will also be

communicated through a media release and our research partner's communication channels.

Strengths and limitations

Strengths of this study include that this is the first RCT to investigate the effect of an EEF DA on decision-related outcomes (e.g. decisional conflict, informed choice, and regret). The study and DA were developed using participatory design (i.e. in cooperation with all stakeholders, including consumers) and measures used are in accordance with the International Patient Decision Aids Standards for the evaluation of DA.[60] Additional strengths include using a placebo-type control to minimize bias and having a 12-month follow-up period which allows for assessment of the sustained effects from the DA. Although using broad recruitment approaches, a consequence is an inability to count total eligible population reached (and consequent study uptake). Other limitations include the potential bias from the type of person who participates in online studies. Also, the adaption of some measures to improve suitability for the study population may impact their validity.

Future directions

If proven effective, this will provide support for the utility of similar DAs for other aspects of fertility treatment, such as decisions around the disposition of stored material or for egg donors and recipients.

Declarations

Ethics approval and consent to participate

The University of Melbourne, Australia Human Research Ethics Committee initially approved this study (Ethics ID: 2056457) on 3 June 2020. Participants will provide informed consent before enrolment in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), Good Clinical Practice (GCP) and Declaration of Helsinki 2000 guidelines, and local regulatory requirements.

Consent for publication

As this paper reports on the study protocol (and does not include any patient data), consent for publication is not applicable.

Author contribution(s)

Michelle Peate: Conceptualization; Funding acquisition; Methodology; Project administration; Supervision; Writing – original draft; Writing – review & editing.
Sherine Sandhu: Methodology; Project administration; Supervision; Writing – review & editing.
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Martha Hickey: Conceptualization; Funding acquisition; Methodology; Supervision; Writing – review & editing.

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Competing interests

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Availability of data and materials

Not applicable.

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Supplemental material

Supplemental material for this article is available online.

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