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An assessment of the societal and individual preferences for fertility treatment in Australia: study protocol for stated preference discrete choice experiments

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3 **An assessment of the societal and individual preferences for fertility treatment in**
4 **Australia: study protocol for stated preference discrete choice experiments**
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16

17 **Abstract**
18

19 **Introduction**
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21
22 In Australia, societal and individual preferences for funding fertility treatment remain largely
23 unknown. This has resulted in a lack of evidence about willingness to pay (WTP) for fertility
24 treatment by either the general population (the funders) or infertile individuals (who directly
25 benefit). Using a stated preference discrete choice experiment (SPDCE) approach has been
26 suggested as a more appropriate method to inform economic evaluations of fertility
27 treatment.
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32 We outline the protocol for an ongoing study which aims to assess fertility treatment
33 preferences of both the general population and infertile individuals and indirectly estimate
34 their WTP for fertility treatment.
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37 **Methods and analysis**
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40 Two separate but related SPDCEs will be conducted for two population samples — the
41 general population and infertile individuals — to elicit preferences for fertility treatment to
42 indirectly estimate willingness to pay. We describe the qualitative work to be undertaken to
43 design the SPDCEs. We will use D-efficient fractional experimental designs informed by
44 prior coefficients from the pilot surveys. The mode of administration for the SPDCE is also
45 discussed. The final results will be analysed using mixed logit (MXL) or latent class (LC)
46 models.
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51 **Ethics and dissemination**
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54 This study is being funded by the Australian National Health and Medical Research Council
55 (NHMRC) project grant AP1104543 and has been approved by the University of New South
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3 Wales Human Research Ethics Committee (HEC 17255) and a fertility clinic's Ethics
4 Committee. Findings of the study will be disseminated in peer-reviewed journals and
5 presented at various conferences. A lay summary of the results will be made publicly
6 available on the UNSW National Perinatal Epidemiology and Statistics Unit (NPESU)
7 website. Our results will contribute to the development of an evidence-based policy
8 framework for the provision of cost-effective and patient-centred fertility treatment in
9 Australia.
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Strengths and limitations of this study

- To our knowledge, this study will be the first to measure and quantify preferences for fertility treatment for the general population and infertile individuals in Australia.
- The study design is unique and capable of eliciting preferences from both the general population and individuals experiencing fertility treatment.
- The results will contribute to the development of an evidence-based policy framework for the provision of cost-effective and patient-centred fertility treatment in Australia.
- The SPDCE surveys will be undertaken in Australia, which could affect generalisability to other settings.

Introduction

One in six couples suffer infertility, causing significant personal suffering to possibly more than 50 million couples worldwide^{1 2 3}. Rates of infertility are predicted to increase with the trend to postpone childbearing, deteriorating sperm quality, and rising rates of obesity and some sexually transmitted diseases⁴.

Economic evaluations that consider outcomes of fertility treatment are scarce, mainly because the unique objective of fertility treatment is to create new life rather than extend or improve health-related quality of life (HRQoL), unlike other forms of medical care⁵. The outcomes of fertility treatment are also broader than those traditionally considered in healthcare and include substantial non-health related, such as family formation, existential meaning, and individual identity. Furthermore, process outcomes related to delivery of treatment, such as continuity of care, joint decision making, and convenience, are also important drivers of satisfaction with treatment⁶⁻¹¹.

These multiple and varied outcomes do not usually have a market price and cannot all be captured and valued in a conventional quality-adjusted life year (QALY) framework¹²⁻¹⁷. Fertility treatment involves multiple stakeholders, including the mother, father, donor, and society, which further makes the QALY measure unsuitable^{12 13 18-22}. Despite supportive public funding of fertility treatment in Australia through its universal health insurance scheme (Medicare), societal and individual preferences for funding fertility treatment remain largely unknown. This results in a lack of evidence about willingness to pay (WTP) for fertility treatment by either the general population (the indirect funders through tax

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3 contribution) or infertile individuals (who directly benefit). Without estimates of the shadow
4 price for fertility treatment, as expressed by WTP estimates, the economic value of fertility
5 treatment and its cost-effectiveness are lacking to inform policy and resource allocation
6 decision-making¹².
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10 Using stated preference discrete choice experiment (SPDCE) has been suggested as an
11 appropriate method for evaluating broad outcomes of fertility treatment in monetary terms¹³
12^{16 23 24}. This approach indirectly elicits willingness to pay (WTP) estimates for any treatment
13 attributes (characteristics) without being restricted to health outcomes alone.
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18 We outline a unique design of two separate but related SPDCEs to elicit treatment
19 preferences from the general population and infertile individuals to indirectly estimate WTP
20 values for the attributes and levels of fertility treatment. To our knowledge, this study will be
21 the first to measure and quantify preferences for fertility treatment for both the general
22 population and infertile individuals.
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26 27 **Aims**

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29 The specific objectives of the study are to assess WTP values for fertility treatment from the
30 general population and infertile individuals. The study will determine whether:
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- 33 1. The current level of Medicare expenditure for fertility treatment in Australia is in line
34 with the general population's and individuals' WTP for the treatment;
- 35 2. The general population's WTP for fertility treatment varies by patient characteristics
36 and family structures.
- 37 3. The general population's and patients' WTP for fertility treatment can be influenced
38 by the attributes of treatment.
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45 **Methods and analysis**

46 47 **Overview of SPDCE approach**

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49 The SPDCE approach is an attribute-based measure of value which can capture broader
50 aspects of an intervention, including outcomes not related to health, and process outcomes
51 related to delivery of treatment²⁵. SPDCEs have a theoretical basis on Random Utility
52 Theory (RUT) which assumes that individuals value an intervention based on the bundle of
53 its attributes as a whole²⁶ and that they prefer an intervention that gives them the highest level
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3 of satisfaction based on the individual attributes²⁷. In a SPDCE, respondents are presented
4 with specially designed hypothetical scenarios of treatment programs where at least one
5 attribute of the treatment is varied systematically in terms of its levels. Individuals are asked
6 to choose an option they prefer, including an 'opt-out'. The extent to which respondents
7 'trade-off' one set of attributes against one another is assessed through logistic regression
8 models^{28 29}. The dependent variable in the model represents the likelihood of choosing one
9 alternative with specific attributes and levels over another. The independent variables are the
10 attributes and levels of treatment. Heterogeneity can be accounted for using covariates or
11 their specification in a mixed logit (MXL) or latent class (LC) models^{30 31 32}. When a cost
12 attribute is included, it is possible to indirectly estimate WTP values for particular attributes
13 of treatment^{23 25 33 34}.

21 Crucial to the SPDCE process is the conduct of the following five stages: 1) identification of
22 attributes for fertility treatment; 2) assignment of levels to these attributes; 3) development of
23 an experimental design to define the choice alternatives to be presented to respondents; 4)
24 development and administration of questionnaires to collect data; and 5) data input and
25 analysis of responses from the surveys^{32 35-37}. In the following section, we summarise the
26 steps involved in our planned SPDCE.

33 **Qualitative component to inform the development of attributes and levels**

35 The attributes and levels of the SPDCEs will be developed based on a qualitative component
36 of the study, which includes a literature review and focus group discussions (FGDs)^{36 38-43}.
37 The latter will involve two distinct sample groups: general population and infertile
38 individuals (n=8-16), respectively. The general population will be recruited using a poster
39 advertisement placed on notice-boards in public places such as shopping centres and libraries,
40 and an online classified advertisement placed on social media and advertising websites such
41 as 'Gumtree'. Infertile individuals will be recruited from a fertility clinic in Sydney through a
42 poster advertisement which will be placed in the clinic. These participants will be a mix of
43 those who are considering, currently using, or have previously used fertility treatment.

50 For both population groups, individuals who are interested in participating in the FGD are
51 asked to respond to the study advertisements by contacting the research team through email
52 or telephone for more information. Following contact, a member of the research team will
53 provide additional information on the purpose of the FGDs to ensure participants have
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adequate knowledge and understand what their participation would involve. At the same time, potential participants will be screened for eligibility. All participants must be aged 18 years or older, able to speak English, Australian citizens or residents, and with the ability to provide consent. There are no eligibility criteria related to gender or marital status. If they meet the set inclusion criteria, prospective participants will be asked to provide an email address for the researchers to send them an invitation with the details of the FGD and the Participant Information Sheet and Consent Form (PISCF). Both FGDs will be facilitated by two researchers and will last approximately 1-1.5 hours. The discussions will be audio recorded and later transcribed without any identifying information.

The FGDs will use a Nominal Group Technique (NGT)^{42 44-46} where a facilitator will ask participants to think about the important features of fertility treatment and whether the way it is provided might matter to them or other individuals when choosing one fertility treatment over another. Participants will be asked to silently generate a list of the attributes of fertility treatment. One participant at a time will be asked to state a single attribute to the group which will be recorded verbatim on a whiteboard. This process will continue until saturation after which attributes will be clarified and similar attributes grouped together by FGD participants. Following this, participants will be asked to rank order the identified attributes privately based on personal preferences for the attributes. In case the cost attribute is not identified during the FGDs, it will, nevertheless, be included to allow the indirect estimation of willingness to pay (WTP) through marginal rate of substitution (MRS)^{33 47-50}.

Selection of attributes and levels for the SPDCE

A comprehensive list of potential attributes and levels from this qualitative work will be broadly categorised into two groups: attributes related to the outcomes of treatment; and attributes related to the process, delivery or provision of treatment^{6 7 11 51-55}. A consensus group of experts in fertility treatment will help synthesise the attributes, assign levels to the attributes (where they were not identified by the FGDs) and refine the wording for clarity. The number of attributes to include in the SPDCE model will be limited to eight each with two to four levels based on the rules-of-thumb used in many studies^{35 41 56-58}. Using too many attributes and levels increases the complexity of the choice tasks for respondents which may result in individuals not trading-off the attributes or in respondent fatigue^{59 60}.

SPDCE design

The consolidated attributes and levels of fertility treatment will be used in the initial orthogonal fractional experimental design. This will define the choice alternatives for a pilot survey of both the general population and infertile individuals⁵⁰. This design will have no prior information about preferences for fertility treatment.⁵⁰ Subsequently, the coefficients from the pilot surveys will be used as prior information to inform the construction of optimal or efficient fractional experimental designs for the final surveys of the two sample groups^{58 61 62}. The SPDCE designs will be unlabelled^{35 63 64} and will follow design principles stipulated by Huber and Zwerina⁶⁵. Ngene software will be used for constructing experimental designs⁶⁶.

Questionnaire development and administration

The choice tasks in the SPDCE questionnaire for the pilot surveys will be similar for the two sample groups, developed using the output of the fractional experimental designs without prior information on preferences. These choice tasks will differ in the final surveys as they will be built using the coefficients obtained from the results of the pilot surveys, which will differ between the two groups. The format of the questionnaire will follow guidelines which suggest the provision of an introduction; an explanation of the context of the survey, the attributes and their levels; an example of the choice task; an emphasis on respondents' time commitment and the importance of their participation and confidentiality⁵⁰. Respondents will be guided on where to direct any queries on the survey and how to proceed answering the choices questions. The questionnaire will also include additional follow-up questions which will include an evaluation of the level of difficulty of the choice tasks on a five-point scale of very easy, easy, ok, difficult and very difficult; and respondents' socio-demographic characteristics.

The SPDCE questionnaire will be tested for face and theoretical validity. Face validity will be done with a small group of individuals to refine the phrasing and comprehension, while theoretical validity will be explored in the pilot surveys through sign and significance of the parameter estimates to ensure that they conform to a priori expectations, especially for the time or cost attribute which would normally show a monotonic relationship⁶⁷. Two additional choice sets will also be included to act as consistency and reliability checks^{57 67 68}. A consistency check is a theoretically dominant choice set on attribute-levels which is used to

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3 test the rationality of the respondents, while a reliability check is simply a re-insertion of a
4 choice set from the experimental design to somewhere later in the design.
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6 **Sampling and recruitment**

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9 Sample size calculation in SPDCE studies has not been fully developed, with most studies
10 still using the 'rules-of-thumb' or relying on the use of efficient experimental designs. This
11 has the potential benefit of reducing confidence intervals of parameter estimates in a SPDCE
12 model, hence permitting the use of reduced sample sizes^{58 69-71}.
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16 A sample size of 20 respondents has been suggested as adequate to be able to estimate a
17 SPDCE model³⁵. Previous studies have generally shown that sample sizes of 40-100
18 respondents may be sufficient for reliable statistical analysis⁷². Orme⁷⁰ proposes a total of
19 300 respondents for robust quantitative research and a minimum of 200 per group for
20 subgroup analysis. This study will benefit both from using sample sizes well above the rules-
21 of-thumb and efficient experimental designs for the final surveys, in order to have robust
22 results.
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28 All surveys will be administered online with a sample size of 30 participants for pilot surveys
29 of the general population and infertile individuals, respectively. Participants for both pilot
30 surveys will be recruited using the same methods as used for the FDGs. For the two samples,
31 interested participants will respond to the study advertisements by contacting researchers
32 either by email or phone. Following screening for eligibility, potential participants will be
33 emailed a survey invitation and Participant Information Sheet and Consent Form (PISCF)
34 with a link to the online pilot survey. By completing and submitting the survey, participants
35 will be providing their consent.
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42 The final survey for the general population will be administered by a commercial survey
43 company, recruiting 3000 participants from a panel of the Australian population. Recruitment
44 of infertile individuals will be through a fertility organisation's clinics and a national
45 infertility consumer organisation (n=250-300). Interested individuals will respond to the
46 study advertisements by email or telephone and will be emailed the invitation and PISCF
47 with a link to an online survey. Clicking on a link within the consent form will imply consent
48 to start the survey and they can withdraw at any time. Full consent will be deemed after they
49 complete and submit the entire survey.
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Data analysis plan

The responses from the SPDCE surveys will initially be analysed using logistic regression with a multinomial logit (MNL) model in Stata or Nlogit software. To estimate WTP, the results of a mixed logit (MXL) or latent class (LC) models which account for preference heterogeneity will be used. The success rate, time and cost attributes of fertility treatment will be modelled as continuous variables in order to apply the MRS. Differences in preferences between individual groups will be explored through the interaction between the attributes or levels and the socio-demographic characteristics. Figure 1 presents a flowchart of activities for our study:

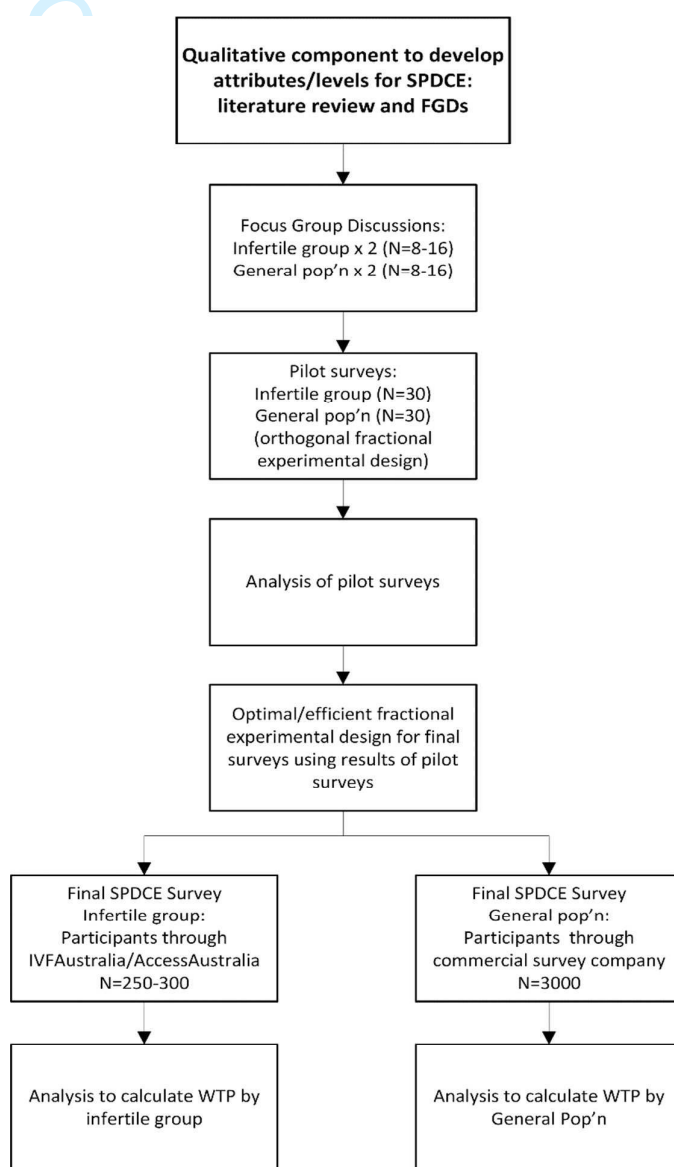


Figure 1: A flowchart of activities

Ethics and dissemination

The ethics approval was obtained from the University of New South Wales Human Research Ethics Committee (HEC 17255) and a fertility clinic's Ethics Committee. All participants will be provided with a Participant Information Sheet and Consent Form (PISCF) before undertaking any study activity. There will be no incentive payment of any form to participants. Findings of the study will be disseminated in peer-reviewed journals and presented at various conferences. A lay summary of the results will be made available publicly on the UNSW National Perinatal Epidemiology and Statistics Unit (NPESU) website. The results will be used to contribute to the development of an evidence-based policy framework for the provision of cost-effective and patient-centred fertility treatments in Australia.

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Competing interests None declared.

Ethics approval University of New South Wales Human Research Ethics Committee (HEC 17255).

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An assessment of the societal and individual preferences for fertility treatment in Australia: study protocol for stated preference discrete choice experiments

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An assessment of the societal and individual preferences for fertility treatment in Australia: study protocol for stated preference discrete choice experiments

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Abstract

Introduction

In Australia, societal and individual preferences for funding fertility treatment remain largely unknown. This has resulted in a lack of evidence about willingness to pay (WTP) for fertility treatment by either the general population (the funders) or infertile individuals (who directly benefit). Using a stated preference discrete choice experiment (SPDCE) approach has been suggested as a more appropriate method to inform economic evaluations of fertility treatment.

We outline the protocol for an ongoing study which aims to assess fertility treatment preferences of both the general population and infertile individuals and indirectly estimate their WTP for fertility treatment.

Methods and analysis

Two separate but related SPDCEs will be conducted for two population samples — the general population and infertile individuals — to elicit preferences for fertility treatment to indirectly estimate willingness to pay. We describe the qualitative work to be undertaken to design the SPDCEs. We will use D-efficient fractional experimental designs informed by prior coefficients from the pilot surveys. The mode of administration for the SPDCE is also discussed. The final results will be analysed using mixed logit (MXL) or latent class (LC) models.

Ethics and dissemination

This study is being funded by the Australian National Health and Medical Research Council (NHMRC) project grant AP1104543 and has been approved by the University of New South

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3 Wales Human Research Ethics Committee (HEC 17255) and a fertility clinic's Ethics
4 Committee. Findings of the study will be disseminated in peer-reviewed journals and
5 presented at various conferences. A lay summary of the results will be made publicly
6 available on the UNSW National Perinatal Epidemiology and Statistics Unit (NPESU)
7 website. Our results will contribute to the development of an evidence-based policy
8 framework for the provision of cost-effective and patient-centred fertility treatment in
9 Australia.
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Strengths and limitations of this study

- To our knowledge, this study will be the first to measure and quantify preferences for fertility treatment for the general population and infertile individuals in Australia.
- The study design is unique and capable of eliciting preferences from both the general population and individuals experiencing fertility treatment.
- The results will contribute to the development of an evidence-based policy framework for the provision of cost-effective and patient-centred fertility treatment in Australia.
- The SPDCE surveys will be undertaken in Australia, which could affect generalisability to other settings.

Introduction

One in six couples suffer infertility, causing significant personal suffering to possibly more than 50 million couples worldwide^{1 2 3}. Rates of infertility are predicted to increase with the trend to postpone childbearing, deteriorating sperm quality, and rising rates of obesity and some sexually transmitted diseases⁴.

Economic evaluations that consider outcomes of fertility treatment are scarce, mainly because the unique objective of fertility treatment is to create new life rather than extend or improve health-related quality of life (HRQoL), unlike other forms of medical care⁵. The outcomes of fertility treatment are also broader than those traditionally considered in healthcare and include substantial non-health related, such as family formation, existential meaning, and individual identity. Furthermore, process outcomes related to delivery of treatment, such as continuity of care, joint decision making, and convenience, are also important drivers of satisfaction with treatment⁶⁻¹¹.

These multiple and varied outcomes do not usually have a market price and cannot all be captured and valued in a conventional quality-adjusted life year (QALY) framework¹²⁻¹⁷. Fertility treatment involves multiple stakeholders, including the mother, father, donor, and society, which further makes the QALY measure unsuitable^{12 13 18-22}. Despite supportive public funding of fertility treatment in Australia through its universal health insurance scheme (Medicare), societal and individual preferences for funding fertility treatment remain largely unknown. This results in a lack of evidence about willingness to pay (WTP) for fertility treatment by either the general population (the indirect funders through tax

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3 contribution) or infertile individuals (who directly benefit). Without estimates of the shadow
4 price for fertility treatment, as expressed by WTP estimates, the economic value of fertility
5 treatment and its cost-effectiveness are lacking to inform policy and resource allocation
6 decision-making¹².
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10 Using stated preference discrete choice experiment (SPDCE) has been suggested as an
11 appropriate method for evaluating broad outcomes of fertility treatment in monetary terms¹³
12^{16 23 24}. This approach indirectly elicits willingness to pay (WTP) estimates for any treatment
13 attributes (characteristics) without being restricted to health outcomes alone.
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18 We outline a unique design of two separate but related SPDCEs to elicit treatment
19 preferences from the general population and infertile individuals to indirectly estimate WTP
20 values for the attributes and levels of fertility treatment. To our knowledge, this study will be
21 the first to measure and quantify preferences for fertility treatment for both the general
22 population and infertile individuals.
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26 27 **Aims**

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29 The specific objectives of the study are to assess WTP values for fertility treatment from the
30 general population and infertile individuals. The study will determine whether:
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- 33 1. The current level of Medicare expenditure for fertility treatment in Australia is in line
34 with the general population's and individuals' WTP for the treatment;
- 35 2. The general population's WTP for fertility treatment varies by patient characteristics
36 and family structures.
- 37 3. The general population's and patients' WTP for fertility treatment can be influenced
38 by the attributes of treatment.
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45 **Methods and analysis**

46 47 **Overview of SPDCE approach**

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49 The SPDCE approach is an attribute-based measure of value which can capture broader
50 aspects of an intervention, including outcomes not related to health, and process outcomes
51 related to delivery of treatment²⁵. SPDCEs have a theoretical basis on Random Utility
52 Theory (RUT) which assumes that individuals value an intervention based on the bundle of
53 its attributes as a whole²⁶ and that they prefer an intervention that gives them the highest level
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3 of satisfaction based on the individual attributes²⁷. In a SPDCE, respondents are presented
4 with specially designed hypothetical scenarios of treatment programs where at least one
5 attribute of the treatment is varied systematically in terms of its levels. Individuals are asked
6 to choose an option they prefer, including an 'opt-out'. The extent to which respondents
7 'trade-off' one set of attributes against one another is assessed through logistic regression
8 models^{28 29}. The dependent variable in the model represents the likelihood of choosing one
9 alternative with specific attributes and levels over another. The independent variables are the
10 attributes and levels of treatment. Heterogeneity can be accounted for using covariates or
11 their specification in a mixed logit (MXL) or latent class (LC) models^{30 31 32}. When a cost
12 attribute is included, it is possible to indirectly estimate WTP values for particular attributes
13 of treatment^{23 25 33 34}.

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21 Crucial to the SPDCE process is the conduct of the following five stages: 1) identification of
22 attributes for fertility treatment; 2) assignment of levels to these attributes; 3) development of
23 an experimental design to define the choice alternatives to be presented to respondents; 4)
24 development and administration of questionnaires to collect data; and 5) data input and
25 analysis of responses from the surveys^{32 35-37}. In the following section, we summarise the
26 steps involved in our planned SPDCE.
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33 **Qualitative component to inform the development of attributes and levels**

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35 The attributes and levels of the SPDCEs will be developed based on a qualitative component
36 of the study, which includes a literature review and focus group discussions (FGDs)^{36 38-43}.
37 The latter will involve two distinct sample groups: general population and infertile
38 individuals (n=8-16), respectively. The general population will be recruited using a poster
39 advertisement placed on notice-boards in public places such as shopping centres and libraries,
40 and an online classified advertisement placed on social media and advertising websites such
41 as 'Gumtree'. Infertile individuals will be recruited from a fertility clinic in Sydney through a
42 poster advertisement which will be placed in the clinic. These participants will be a mix of
43 those who are considering, currently using, or have previously used fertility treatment.
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51 For both population groups, individuals who are interested in participating in the FGD are
52 asked to respond to the study advertisements by contacting the research team through email
53 or telephone for more information. Following contact, a member of the research team will
54 provide additional information on the purpose of the FGDs to ensure participants have
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adequate knowledge and understand what their participation would involve. At the same time, potential participants will be screened for eligibility. All participants must be aged 18 years or older, able to speak English, Australian citizens or residents, and with the ability to provide consent. There are no eligibility criteria related to gender or marital status. If they meet the set inclusion criteria, prospective participants will be asked to provide an email address for the researchers to send them an invitation with the details of the FGD and the Participant Information Sheet and Consent Form (PISCF). Both FGDs will be facilitated by two researchers and will last approximately 1-1.5 hours. The discussions will be audio recorded and later transcribed without any identifying information.

The FGDs will use a Nominal Group Technique (NGT)^{42 44-46} where a facilitator will ask participants to think about the important features of fertility treatment and whether the way it is provided might matter to them or other individuals when choosing one fertility treatment over another. Participants will be asked to silently generate a list of the attributes of fertility treatment. One participant at a time will be asked to state a single attribute to the group which will be recorded verbatim on a whiteboard. This process will continue until saturation after which attributes will be clarified and similar attributes grouped together by FGD participants. Following this, participants will be asked to rank order the identified attributes privately based on personal preferences for the attributes. In case the cost attribute is not identified during the FGDs, it will, nevertheless, be included to allow the indirect estimation of willingness to pay (WTP) through marginal rate of substitution (MRS)^{33 47-50}.

Selection of attributes and levels for the SPDCE

A comprehensive list of potential attributes and levels from this qualitative work will be broadly categorised into two groups: attributes related to the outcomes of treatment; and attributes related to the process, delivery or provision of treatment^{6 7 11 51-55}. A consensus group of experts in fertility treatment will help synthesise the attributes, assign levels to the attributes (where they were not identified by the FGDs) and refine the wording for clarity. The number of attributes to include in the SPDCE model will be limited to eight each with two to four levels based on the rules-of-thumb used in many studies^{35 41 56-58}. Using too many attributes and levels increases the complexity of the choice tasks for respondents which may result in individuals not trading-off the attributes or in respondent fatigue^{59 60}.

SPDCE design

The consolidated attributes and levels of fertility treatment will be used in the initial orthogonal fractional experimental design. This will define the choice alternatives for a pilot survey of both the general population and infertile individuals⁵⁰. This design will have no prior information about preferences for fertility treatment.⁵⁰ Subsequently, the coefficients from the pilot surveys will be used as prior information to inform the construction of optimal or efficient fractional experimental designs for the final surveys of the two sample groups^{58 61 62}. The SPDCE designs will be unlabelled^{35 63 64} and will follow design principles stipulated by Huber and Zwerina⁶⁵. Ngene software will be used for constructing experimental designs⁶⁶.

Questionnaire development and administration

The choice tasks in the SPDCE questionnaire for the pilot surveys will be similar for the two sample groups, developed using the output of the fractional experimental designs without prior information on preferences. These choice tasks will differ in the final surveys as they will be built using the coefficients obtained from the results of the pilot surveys, which will differ between the two groups. The format of the questionnaire will follow guidelines which suggest the provision of an introduction; an explanation of the context of the survey, the attributes and their levels; an example of the choice task; an emphasis on respondents' time commitment and the importance of their participation and confidentiality⁵⁰. Respondents will be guided on where to direct any queries on the survey and how to proceed answering the choices questions. The questionnaire will also include additional follow-up questions which will include an evaluation of the level of difficulty of the choice tasks on a five-point scale of very easy, easy, ok, difficult and very difficult; and respondents' socio-demographic characteristics.

The SPDCE questionnaire will be tested for face and theoretical validity. Face validity will be done with a small group of individuals to refine the phrasing and comprehension, while theoretical validity will be explored in the pilot surveys through sign and significance of the parameter estimates to ensure that they conform to a priori expectations, especially for the time or cost attribute which would normally show a monotonic relationship⁶⁷. Two additional choice sets will also be included to act as consistency and reliability checks^{57 67 68}. A consistency check is a theoretically dominant choice set on attribute-levels which is used to

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3 test the rationality of the respondents, while a reliability check is simply a re-insertion of a
4 choice set from the experimental design to somewhere later in the design.
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6 **Sampling and recruitment**

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9 Sample size calculation in SPDCE studies has not been fully developed, with most studies
10 still using the 'rules-of-thumb' or relying on the use of efficient experimental designs. This
11 has the potential benefit of reducing confidence intervals of parameter estimates in a SPDCE
12 model, hence permitting the use of reduced sample sizes^{58 69-71}.
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16 A sample size of 20 respondents has been suggested as adequate to be able to estimate a
17 SPDCE model³⁵. Previous studies have generally shown that sample sizes of 40-100
18 respondents may be sufficient for reliable statistical analysis⁷². Orme⁷⁰ proposes a total of
19 300 respondents for robust quantitative research and a minimum of 200 per group for
20 subgroup analysis. This study will benefit both from using sample sizes well above the rules-
21 of-thumb and efficient experimental designs for the final surveys, in order to have robust
22 results.
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28 All surveys will be administered online with a sample size of 30 participants for pilot surveys
29 of the general population and infertile individuals, respectively. Participants for both pilot
30 surveys will be recruited using the same methods as used for the FDGs. For the two samples,
31 interested participants will respond to the study advertisements by contacting researchers
32 either by email or phone. Following screening for eligibility, potential participants will be
33 emailed a survey invitation and Participant Information Sheet and Consent Form (PISCF)
34 with a link to the online pilot survey. By completing and submitting the survey, participants
35 will be providing their consent.
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42 The final survey for the general population will be administered by a commercial survey
43 company, recruiting 3000 participants from a panel of the Australian population. Recruitment
44 of infertile individuals will be through a fertility organisation's clinics and a national
45 infertility consumer organisation (n=250-300). Interested individuals will respond to the
46 study advertisements by email or telephone and will be emailed the invitation and PISCF
47 with a link to an online survey. Clicking on a link within the consent form will imply consent
48 to start the survey and they can withdraw at any time. Full consent will be deemed after they
49 complete and submit the entire survey.
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Data analysis plan

The responses from the SPDCE surveys will initially be analysed using logistic regression with a multinomial logit (MNL) model in Stata or Nlogit software. To estimate WTP, the results of a mixed logit (MXL) or latent class (LC) models which account for preference heterogeneity will be used. The success rate, time and cost attributes of fertility treatment will be modelled as continuous variables in order to apply the MRS. Differences in preferences between individual groups will be explored through the interaction between the attributes or levels and the socio-demographic characteristics. Figure 1 presents a flowchart of activities for our study:

(Figure 1)

Ethics and dissemination

The ethics approval was obtained from the University of New South Wales Human Research Ethics Committee (HEC 17255) and a fertility clinic's Ethics Committee. All participants will be provided with a Participant Information Sheet and Consent Form (PISCF) before undertaking any study activity. There will be no incentive payment of any form to participants. Findings of the study will be disseminated in peer-reviewed journals and presented at various conferences. A lay summary of the results will be made available publicly on the UNSW National Perinatal Epidemiology and Statistics Unit (NPESU) website. The results will be used to contribute to the development of an evidence-based policy framework for the provision of cost-effective and patient-centred fertility treatments in Australia.

Limitations of SPDCE approach in the context of this study

The SPDCE approach offers great potential for informing policy and addressing resource allocation questions related to the provision of fertility treatment. However, there are a number of methodological limitations that are common to all SPDCEs. In the context of our study, the first challenge relates to selecting a limited number of attributes and levels that are both practically feasible to include in a SPDCE and define the fertility treatment. There are likely multiple attributes and levels that could influence choices of fertility treatment from the perspective of both the general population and patients. However, only up to eight each with

two to four levels are ideal^{35 57}. Too many attributes and levels can affect the statistical quality of the SPDCE design, and result in too great a cognitive burden on respondents to answer an excessive number of choice sets^{56 58}.

Furthermore, the SPDCE surveys will be undertaken in Australia, which could affect generalisability to other settings. Australia is a developed country with a relatively supportive funding environment for fertility treatment through the universal insurance scheme (Medicare). Finally, the choices made by the participants based on the hypothetical scenarios presented in the SPDCE may not reflect real-life choices. However, the focus group discussions, careful development of the experimental design and analyses will minimise this risk, plus the comparison of the results of the SPDCE to the revealed preferences reflected by fertility treatment utilisation rates and government rebate will provide a mechanism for validating the results.

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Competing interests None declared.

Ethics approval University of New South Wales Human Research Ethics Committee (HEC 17255).

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19 **Figure 1: A flowchart of activities**
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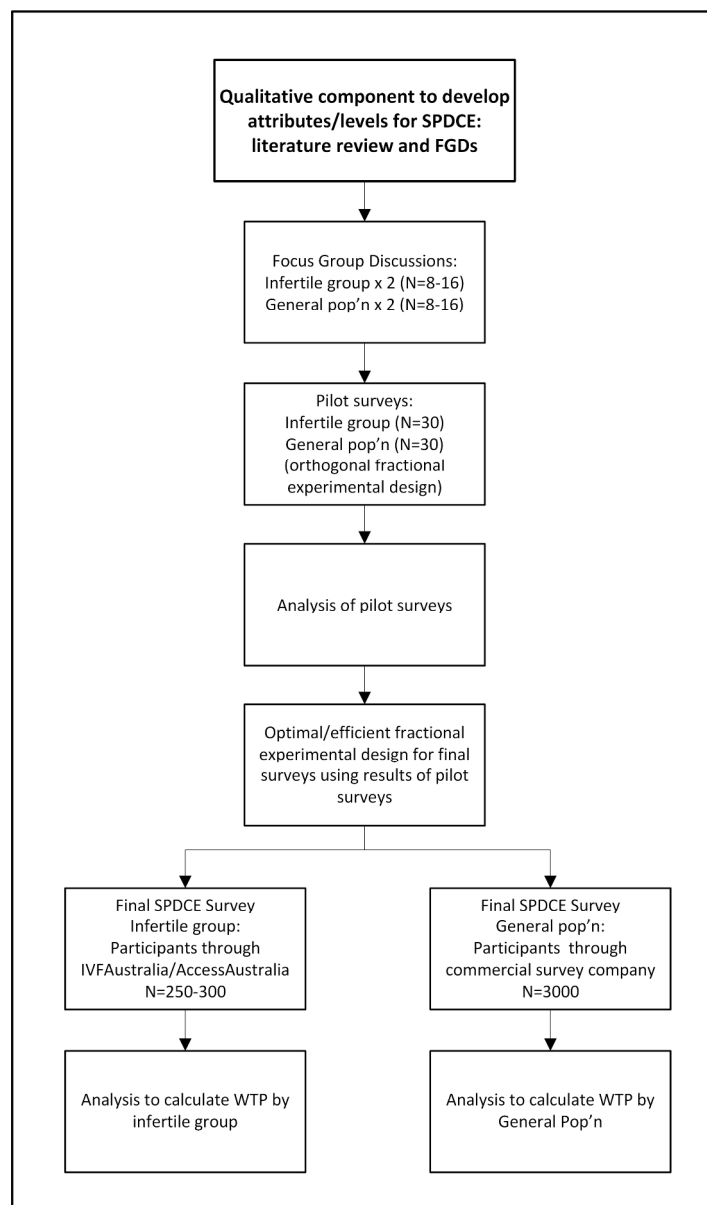


Figure 1: A flowchart of activities

187x318mm (300 x 300 DPI)

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An assessment of the societal and individual preferences for fertility treatment in Australia: study protocol for stated preference discrete choice experiments

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Manuscripts

An assessment of the societal and individual preferences for fertility treatment in Australia: study protocol for stated preference discrete choice experiments

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Abstract

Introduction

In Australia, societal and individual preferences for funding fertility treatment remain largely unknown. This has resulted in a lack of evidence about willingness to pay (WTP) for fertility treatment by either the general population (the funders) or infertile individuals (who directly benefit). Using a stated preference discrete choice experiment (SPDCE) approach has been suggested as a more appropriate method to inform economic evaluations of fertility treatment.

We outline the protocol for an ongoing study which aims to assess fertility treatment preferences of both the general population and infertile individuals and indirectly estimate their WTP for fertility treatment.

Methods and analysis

Two separate but related SPDCEs will be conducted for two population samples — the general population and infertile individuals — to elicit preferences for fertility treatment to indirectly estimate willingness to pay. We describe the qualitative work to be undertaken to design the SPDCEs. We will use D-efficient fractional experimental designs informed by prior coefficients from the pilot surveys. The mode of administration for the SPDCE is also discussed. The final results will be analysed using mixed logit (MXL) or latent class (LC) models.

Ethics and dissemination

This study is being funded by the Australian National Health and Medical Research Council (NHMRC) project grant AP1104543 and has been approved by the University of New South

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3 Wales Human Research Ethics Committee (HEC 17255) and a fertility clinic's Ethics
4 Committee. Findings of the study will be disseminated in peer-reviewed journals and
5 presented at various conferences. A lay summary of the results will be made publicly
6 available on the UNSW National Perinatal Epidemiology and Statistics Unit (NPESU)
7 website. Our results will contribute to the development of an evidence-based policy
8 framework for the provision of cost-effective and patient-centred fertility treatment in
9 Australia.
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For peer review only

Strengths and limitations of this study

- To our knowledge, this study will be the first to measure and quantify preferences for fertility treatment for the general population and infertile individuals in Australia.
- The study design is unique and capable of eliciting preferences from both the general population and individuals experiencing fertility treatment.
- The results will contribute to the development of an evidence-based policy framework for the provision of cost-effective and patient-centred fertility treatment in Australia.
- The SPDCE surveys will be undertaken in Australia, which could affect generalisability to other settings.

Introduction

One in six couples suffer infertility, causing significant personal suffering to possibly more than 50 million couples worldwide^{1 2 3}. Rates of infertility are predicted to increase with the trend to postpone childbearing, deteriorating sperm quality, and rising rates of obesity and some sexually transmitted diseases⁴.

Economic evaluations that consider outcomes of fertility treatment are scarce, mainly because the unique objective of fertility treatment is to create new life rather than extend or improve health-related quality of life (HRQoL), unlike other forms of medical care⁵. The outcomes of fertility treatment are also broader than those traditionally considered in healthcare and include substantial non-health related, such as family formation, existential meaning, and individual identity. Furthermore, process outcomes related to delivery of treatment, such as continuity of care, joint decision making, and convenience, are also important drivers of satisfaction with treatment⁶⁻¹¹.

These multiple and varied outcomes do not usually have a market price and cannot all be captured and valued in a conventional quality-adjusted life year (QALY) framework¹²⁻¹⁷. Fertility treatment involves multiple stakeholders, including the mother, father, donor, and society, which further makes the QALY measure unsuitable^{12 13 18-22}. Despite supportive public funding of fertility treatment in Australia through its universal health insurance scheme (Medicare), societal and individual preferences for funding fertility treatment remain largely unknown. This results in a lack of evidence about willingness to pay (WTP) for fertility treatment by either the general population (the indirect funders through tax contribution) or infertile individuals (who directly benefit). Without estimates of the shadow

price for fertility treatment, as expressed by WTP estimates, the economic value of fertility treatment and its cost-effectiveness are lacking to inform policy and resource allocation decision-making¹².

Using stated preference discrete choice experiment (SPDCE) has been suggested as an appropriate method for evaluating broad outcomes of fertility treatment in monetary terms¹³¹⁶²³²⁴. This approach indirectly elicits willingness to pay (WTP) estimates for any treatment attributes (characteristics) without being restricted to health outcomes alone.

We outline a unique design of two separate but related SPDCEs to elicit treatment preferences from the general population and infertile individuals to indirectly estimate WTP values for the attributes and levels of fertility treatment. The general population sample will be representative of the Australian population which includes members of the lesbian, gay, bisexual, transgender, intersex and queer (LGBTIQ) community. Infertile individuals will be patients recruited from fertility clinics who may also include members of the LGBTIQ community who have access to a variety of treatment options such as donor and egg sharing programs. To our knowledge, this study will be the first to measure and quantify preferences for fertility treatment for both the general population and infertile individuals.

Aims

The specific objectives of the study are to assess WTP values for fertility treatment from the general population and infertile individuals. The study will determine whether:

1. The current level of Medicare expenditure for fertility treatment in Australia is in line with the general population's and individuals' WTP for the treatment;
2. The general population's WTP for fertility treatment varies by patient characteristics and family structures.
3. The general population's and patients' WTP for fertility treatment can be influenced by the attributes of treatment.

Methods and analysis

Overview of SPDCE approach

The SPDCE approach is an attribute-based measure of value which can capture broader aspects of an intervention, including outcomes not related to health, and process outcomes related to delivery of treatment²⁵. SPDCEs have a theoretical basis on Random Utility

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3 Theory (RUT) which assumes that individuals value an intervention based on the bundle of
4 its attributes as a whole²⁶ and that they prefer an intervention that gives them the highest level
5 of satisfaction based on the individual attributes²⁷. In a SPDCE, respondents are presented
6 with specially designed hypothetical scenarios of treatment programs where at least one
7 attribute of the treatment is varied systematically in terms of its levels. Individuals are asked
8 to choose an option they prefer, including an 'opt-out'. The extent to which respondents
9 'trade-off' one set of attributes against one another is assessed through logistic regression
10 models^{28 29}. The dependent variable in the model represents the likelihood of choosing one
11 alternative with specific attributes and levels over another. The independent variables are the
12 attributes and levels of treatment. Heterogeneity can be accounted for using covariates or
13 their specification in a mixed logit (MXL) or latent class (LC) models^{30 31 32}. When a cost
14 attribute is included, it is possible to indirectly estimate WTP values for particular attributes
15 of treatment^{23 25 33 34}.

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24 Crucial to the SPDCE process is the conduct of the following five stages: 1) identification of
25 attributes for fertility treatment; 2) assignment of levels to these attributes; 3) development of
26 an experimental design to define the choice alternatives to be presented to respondents; 4)
27 development and administration of questionnaires to collect data; and 5) data input and
28 analysis of responses from the surveys^{32 35-37}. We are currently in the first stage of
29 identifying attributes of fertility treatment. The whole study is estimated to take 18 months
30 from June 2017 when ethical approval was obtained. In the following section, we summarise
31 the steps involved in our planned SPDCE.
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40 **Qualitative component to inform the development of attributes and levels**

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42 The attributes and levels of the SPDCEs will be developed based on a qualitative component
43 of the study, which includes a literature review and focus group discussions (FGDs)^{36 38-43}.
44 The latter will involve two distinct sample groups: general population and infertile
45 individuals (n=8-16), respectively. The general population will be recruited using a poster
46 advertisement placed on notice-boards in public places such as shopping centres and libraries,
47 and an online classified advertisement placed on social media and advertising websites such
48 as 'Gumtree'. Infertile individuals will be recruited from a fertility clinic in Sydney through a
49 poster advertisement which will be placed in the clinic. These participants will be a mix of
50 those who are considering, currently using, or have previously used fertility treatment.
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3 For both population groups, individuals who are interested in participating in the FGD are
4 asked to respond to the study advertisements by contacting the research team through email
5 or telephone for more information. Following contact, a member of the research team will
6 provide additional information on the purpose of the FGDs to ensure participants have
7 adequate knowledge and understand what their participation would involve. At the same
8 time, potential participants will be screened for eligibility. All participants must be aged 18
9 years or older, able to speak English, Australian citizens or residents, and with the ability to
10 provide consent. There are no eligibility criteria related to gender or marital status. If they
11 meet the set inclusion criteria, prospective participants will be asked to provide an email
12 address for the researchers to send them an invitation with the details of the FGD and the
13 Participant Information Sheet and Consent Form (PISCF). Both FGDs will be facilitated by
14 two researchers and will last approximately 1-1.5 hours. The discussions will be audio
15 recorded and later transcribed without any identifying information.

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17 The FGDs will use a Nominal Group Technique (NGT)^{42 44-46} where a facilitator will ask
18 participants to think about the important features of fertility treatment and whether the way it
19 is provided might matter to them or other individuals when choosing one fertility treatment
20 over another. Participants will be asked to silently generate a list of the attributes of fertility
21 treatment. One participant at a time will be asked to state a single attribute to the group which
22 will be recorded verbatim on a whiteboard. This process will continue until saturation after
23 which attributes will be clarified and similar attributes grouped together by FGD participants.
24 Following this, participants will be asked to rank order the identified attributes privately
25 based on personal preferences for the attributes. In case the cost attribute is not identified
26 during the FGDs, it will, nevertheless, be included to allow the indirect estimation of
27 willingness to pay (WTP) through marginal rate of substitution (MRS)^{33 47-50}.

28 **Selection of attributes and levels for the SPDCE**

29 A comprehensive list of potential attributes and levels from this qualitative work will be
30 broadly categorised into two groups: attributes related to the outcomes of treatment; and
31 attributes related to the process, delivery or provision of treatment^{6 7 11 51-55}. A consensus
32 group of experts in fertility treatment will help synthesise the attributes, assign levels to the
33 attributes (where they were not identified by the FGDs) and refine the wording for clarity.
34 The number of attributes to include in the SPDCE model will be limited to eight each with
35 two to four levels based on the rules-of-thumb used in many studies^{35 41 56-58}. Using too many
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3 attributes and levels increases the complexity of the choice tasks for respondents which may
4 result in individuals not trading-off the attributes or in respondent fatigue^{59 60}.

6 7 **SPDCE design**

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9 The consolidated attributes and levels of fertility treatment will be used in the initial
10 orthogonal fractional experimental design. This will define the choice alternatives for a pilot
11 survey of both the general population and infertile individuals⁵⁰. This design will have no
12 prior information about preferences for fertility treatment.⁵⁰. Subsequently, the coefficients
13 from the pilot surveys will be used as prior information to inform the construction of optimal
14 or efficient fractional experimental designs for the final surveys of the two sample groups^{58 61}
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24 25 **Questionnaire development and administration**

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27 The choice tasks in the SPDCE questionnaire for the pilot surveys will be similar for the two
28 sample groups, developed using the output of the fractional experimental designs without
29 prior information on preferences. These choice tasks will differ in the final surveys as they
30 will be built using the coefficients obtained from the results of the pilot surveys, which will
31 differ between the two groups. The format of the questionnaire will follow guidelines which
32 suggest the provision of an introduction; an explanation of the context of the survey, the
33 attributes and their levels; an example of the choice task; an emphasis on respondents' time
34 commitment and the importance of their participation and confidentiality⁵⁰. Respondents will
35 be guided on where to direct any queries on the survey and how to proceed answering the
36 choices questions. The questionnaire will also include additional follow-up questions which
37 will include an evaluation of the level of difficulty of the choice tasks on a five-point scale of
38 very easy, easy, ok, difficult and very difficult; and respondents' socio-demographic
39 characteristics.
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49 The SPDCE questionnaire will be tested for face and theoretical validity. Face validity will
50 be done with a small group of individuals to refine the phrasing and comprehension, while
51 theoretical validity will be explored in the pilot surveys through sign and significance of the
52 parameter estimates to ensure that they conform to a priori expectations, especially for the
53 time or cost attribute which would normally show a monotonic relationship⁶⁷. Two
54 additional choice sets will also be included to act as consistency and reliability checks^{57 67 68}.

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3 A consistency check is a theoretically dominant choice set on attribute-levels which is used to
4 test the rationality of the respondents, while a reliability check is simply a re-insertion of a
5 choice set from the experimental design to somewhere later in the design.
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8 **Sampling and recruitment**

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10 Sample size calculation in SPDCE studies has not been fully developed, with most studies
11 still using the 'rules-of-thumb' or relying on the use of efficient experimental designs. This
12 has the potential benefit of reducing confidence intervals of parameter estimates in a SPDCE
13 model, hence permitting the use of reduced sample sizes^{58 69-71}.
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17 A sample size of 20 respondents has been suggested as adequate to be able to estimate a
18 SPDCE model³⁵. Previous studies have generally shown that sample sizes of 40-100
19 respondents may be sufficient for reliable statistical analysis⁷². Orme⁷⁰ proposes a total of
20 300 respondents for robust quantitative research and a minimum of 200 per group for
21 subgroup analysis. This study will benefit both from using sample sizes well above the rules-
22 of-thumb and efficient experimental designs for the final surveys, in order to have robust
23 results.
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27 All surveys will be administered online with a sample size of 30 participants for pilot surveys
28 of the general population and infertile individuals, respectively. Participants for both pilot
29 surveys will be recruited using the same methods as used for the FDGs. For the two samples,
30 interested participants will respond to the study advertisements by contacting researchers
31 either by email or phone. Following screening for eligibility, potential participants will be
32 emailed a survey invitation and Participant Information Sheet and Consent Form (PISCF)
33 with a link to the online pilot survey. By completing and submitting the survey, participants
34 will be providing their consent.
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38 The final survey for the general population will be administered by a commercial survey
39 company, recruiting 3000 participants from a panel of the Australian population. Recruitment
40 of infertile individuals will be through a fertility organisation's clinics and a national
41 infertility consumer organisation (n=250-300). Interested individuals will respond to the
42 study advertisements by email or telephone and will be emailed the invitation and PISCF
43 with a link to an online survey. Clicking on a link within the consent form will imply consent
44 to start the survey and they can withdraw at any time. Full consent will be deemed after they
45 complete and submit the entire survey.
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Data analysis plan

The responses from the SPDCE surveys will initially be analysed using logistic regression with a multinomial logit (MNL) model in Stata or Nlogit software. To estimate WTP, the results of a mixed logit (MXL) or latent class (LC) models which account for preference heterogeneity will be used. The success rate, time and cost attributes of fertility treatment will be modelled as continuous variables in order to apply the MRS. Differences in preferences between individual groups will be explored through the interaction between the attributes or levels and the socio-demographic characteristics. Figure 1 presents a flowchart of activities for our study:

(Figure 1)

Ethics and dissemination

The ethics approval was obtained from the University of New South Wales Human Research Ethics Committee (HEC 17255) and a fertility clinic's Ethics Committee. All participants will be provided with a Participant Information Sheet and Consent Form (PISCF) before undertaking any study activity. There will be no incentive payment of any form to participants. Findings of the study will be disseminated in peer-reviewed journals and presented at various conferences. A lay summary of the results will be made available publicly on the UNSW National Perinatal Epidemiology and Statistics Unit (NPESU) website. The results will be used to contribute to the development of an evidence-based policy framework for the provision of cost-effective and patient-centred fertility treatments in Australia.

Limitations of SPDCE approach in the context of this study

The SPDCE approach offers great potential for informing policy and addressing resource allocation questions related to the provision of fertility treatment. However, there are a number of methodological limitations that are common to all SPDCEs. In the context of our study, the first challenge relates to selecting a limited number of attributes and levels that are both practically feasible to include in a SPDCE and define the fertility treatment. There are likely multiple attributes and levels that could influence choices of fertility treatment from the perspective of both the general population and patients. However, only up to eight each with

two to four levels are ideal^{35 57}. Too many attributes and levels can affect the statistical quality of the SPDCE design, and result in too great a cognitive burden on respondents to answer an excessive number of choice sets^{56 58}.

Furthermore, the SPDCE surveys will be undertaken in Australia, which could affect generalisability to other settings. Australia is a developed country with a relatively supportive funding environment for fertility treatment through the universal insurance scheme (Medicare). Finally, the choices made by the participants based on the hypothetical scenarios presented in the SPDCE may not reflect real-life choices. However, the focus group discussions, careful development of the experimental design and analyses will minimise this risk, plus the comparison of the results of the SPDCE to the revealed preferences reflected by fertility treatment utilisation rates and government rebate will provide a mechanism for validating the results.

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19 **Figure 1: A flowchart of activities**
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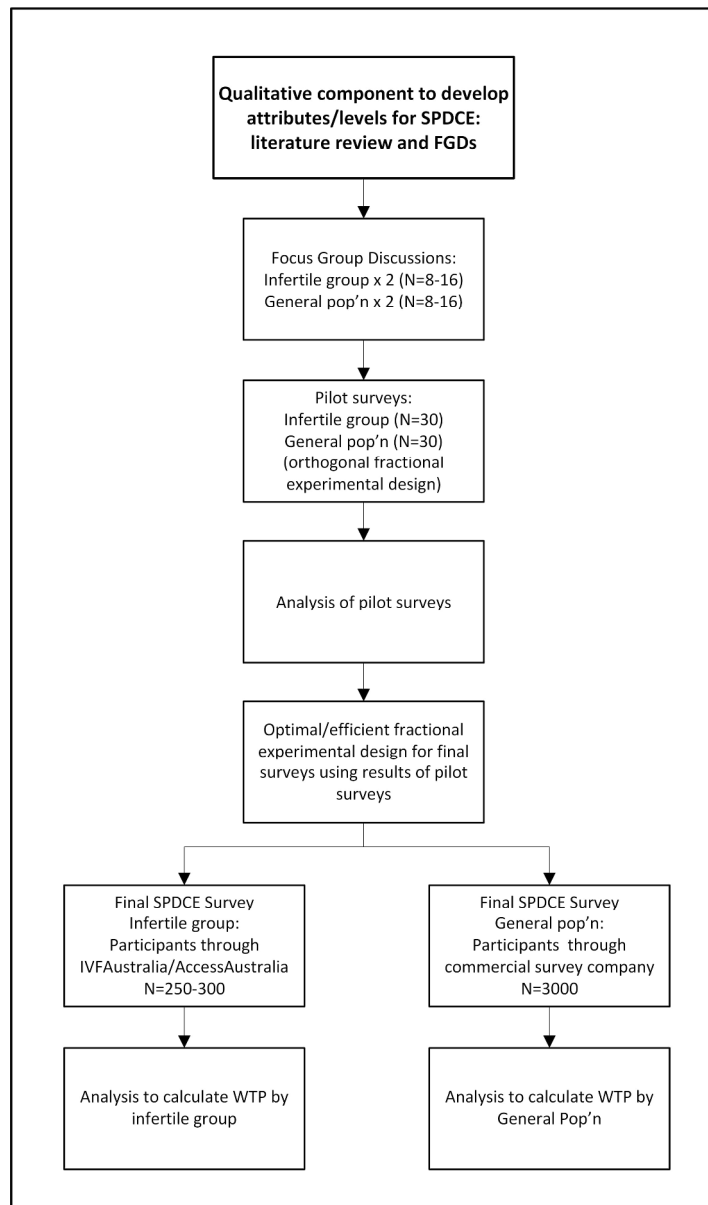


Figure 1: A flowchart of activities

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