Qualitative Research for Discrete Choice Experiments (DCEs): Towards Defining Gold Standards.

Samuel Aballéa[1,2], Nicola Germain[1], Linda Abetz-Webb[3]

1. Creativ-Ceutical, Paris, France
2. Public Health Department, Aix-Marseille University, Marseille, France
3. Patient-Centered Outcomes Assessment, Bollington, UK

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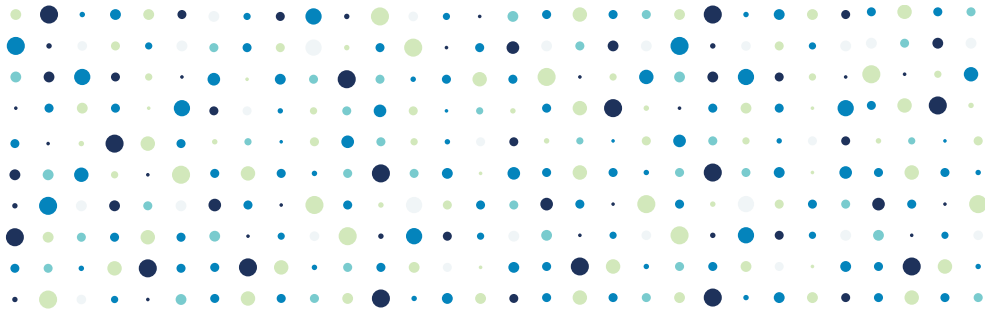


Agenda

1. Context
2. Qualitative Research in DCEs – challenges and experience
3. Standards for Qualitative Research
4. Discussion

Discrete choice experiments

- Discrete choice experiments (DCEs) are a stated-preference method
- DCEs use a survey to quantify individuals' preferences.
  - Respondents are asked to choose their preferred option from a series of hypothetical scenarios called choice-sets.
  - They are used to understand how consumers balance these attributes, and the relative importance of each attribute in their decision to consume.
- Frequently used method to quantify preferences in healthcare.

Preference data are increasingly being accepted for guiding regulatory decision making

US / FDA

- "Patient Preference Information (PPI) may be used to:
  - Provide estimates of how much different outcomes, endpoints or other attributes are valued by patients
  - Understand trade-offs that patients state or demonstrate they are willing to make

Development	Clinical trial design	Pre-marked benefit-risk assessment	Post-market
Understand what matters most to patients	Inform endpoint selection	Patient perspective on benefit-risk trade-offs	Inform interpretation and communicate benefit-risk assessment to patients

- The FDA publised guidance for PPI submission for devices citing DCEs as the favoured stated preference elicitation method.

Preference data are increasingly being accepted for guiding regulatory decision making

Europe / EMA

- The EMA has launched initiatives in patient preference
  - The **VALUE study** used novel software to elicit patient preferences for different outcomes in the treatment of multiple sclerosis
  - PROTECT project investigated the usefulness of different methodologies for more effectively capturing and communicating patient risk benefit analyses for use in regulatory decision making.
  - → The use of DCEs for this purpose was among their recommendations (Hughes *et al*. 2016).

Context | HTA bodies interested in patient preference data

Numerous agencies are interested in patient preference

Main US and European HTA bodies and payers interested in Patient Preference

Country	Organization
Belgium	Belgian Health Care Knowledge Centre (KCE)
England	National Institute for Health and Care Excellence (NICE)
Finland	Finnish Medicines Agency (Fimea)
France	High Authority of Health (HAS)
Germany	Institute for Quality and Efficiency in Health Care (IQWiG)
Scotland	Scottish Medicines Consortium (SMC)
The Netherlands	Care Institute Netherlands (CVZ)
USA	Centers for Medicare & Medicaid Services (CMS)

Van Overbeeke E, Whichello C, Janssens R, Veldwijk J, Cleemput I, Simoens S, Juhaeri J, Levitan B, Kübler J, de Bekker-Grob E, Huys I. Factors and situations influencing the value of patient preference studies along the medical product lifecycle: a literature review. Drug Discov Today. 2019 Jan;24(1):57-68

Methodological guidance for DCEs

Methodological guidance is limited!

Availability of guidance on design and conduct of patient preference studies

Topic	Availability of guidance
Good research practices	ISPOR method-specific good research practices
Choice of preference exploration/elicitation method	Lack of guidance reported
Selection of attributes	Lack of guidance reported
Whose preferences should be measured	Lack of guidance reported
Validity assessment	Janssen *et al.*: Improving the quality of discrete-choice experiments in health: how can we assess validity and reliability? Lack of guidance reported

Source: Overbeeke *et al*, 2019

ISPOR Good Research Practices reports for DCEs

- Conjoint analysis applications in health (2011)
  - *Researchers need to strike a balance between what may be important to the respondent and what is relevant to the particular policy- or decision-making environment.*
  - *Sources of evidence to support the inclusion or exclusion of attributes should include literature reviews and other evidence on the impact of the disease and the nature of the health technology being assessed. Consultation with clinical experts, qualitative research, or other preliminary studies can provide the basis for identifying the full set of attributes…*
  - *Discussion with experts and further pilot testing with subjects can be used to narrow the list of attributes*.
- Constructing Experimental Designs for Discrete-Choice Experiments (2013)
- Statistical Methods for the Analysis of Discrete-Choice Experiments (2016)

Use of qualitative methods in DCEs

Previous literature review (Vass *et al*, 2017)

Previous SLR shows inconsistent reporting of qualitative research and need for guidelines

- → 254 healthcare DCEs were included in the review (2001-2012)
  - → 44% did not report using any qualitative methods;
  - → 45% reported ‘‘basic’’ information;
  - → 11% reported or cited ‘‘extensive’’ use of qualitative methods
- → Studies reporting the use of qualitative methods
  - → to select attributes and/or levels (66%)
  - → to pilot the DCE survey (18%).
- → Popular qualitative methods included
  - → interviews (76%).
  - → focus groups (44%)
- → All responding authors (n = 50) found that qualitative methods added value to their DCE study, but many (44%) reported that journals were uninterested in the reporting of QR results.

Vass C, Rigby D, Payne K. The Role of Qualitative Research Methods in Discrete Choice Experiments. Med Decis Making. 2017

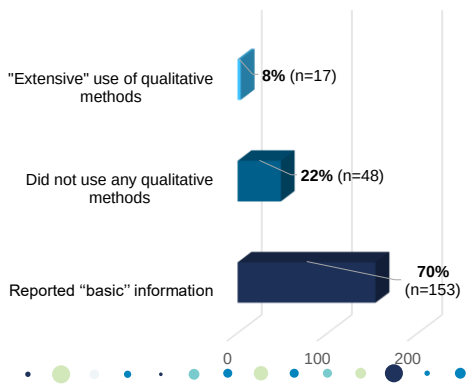
Use of qualitative methods in DCEs

Updated literature review (1)

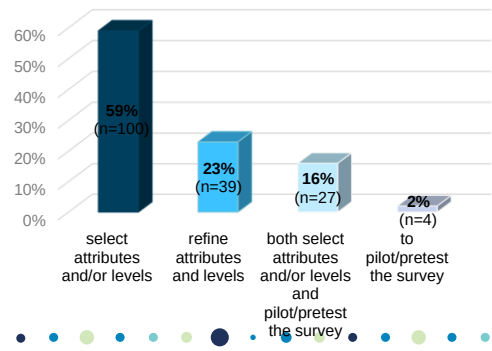
Updated literature review confirms conclusions of previous SLR

- → 218 healthcare DCEs were included in the review (2018-2019)
- → 13 of these were multi-country DCEs. None of these 13 studies reported use of qualitative methods in every study country.

Use of qualitative methods

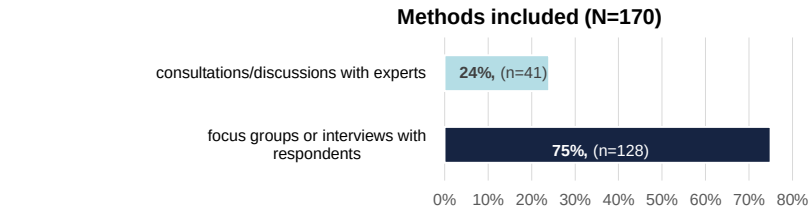


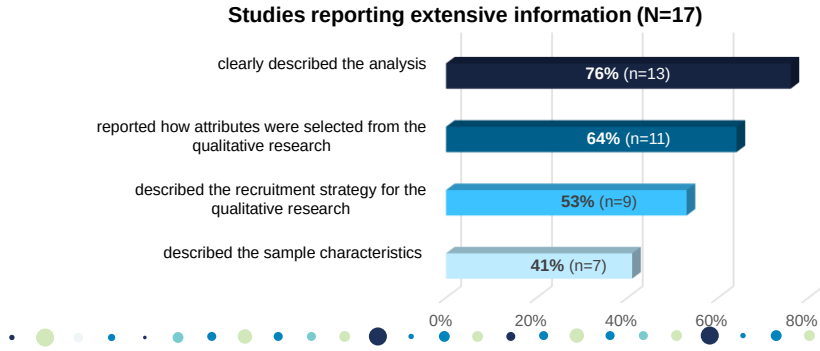
Studies reporting use of qualitative methods



Use of qualitative methods in DCEs

Updated literature review (2)





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Social Q&A

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Poll: Have you conducted DCE(s) / Do you conduct DCEs?

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Poll: Did/Do you use qualitative research?

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Poll: Did/Do you report qualitative methods in your publication(s)?

Standards for qualitative research & relevance to DCE

ISPOR, Copenhagen, Denmark, 6 November 2019

Written by: Linda Abetz- Webb

E-mail: linda.abetz-webb@p-coa.com

WWW.P-COA.COM

Getting the patient's voice heard.

Objectives

- To review current standards for qualitative research
- To assess the appropriateness of the standards for DCEs

Purpose of qualitative research

- Identify relevant concepts for patients or other key stakeholders (concept elicitation)
  - Exploratory and unbiased
- To assess clarity and understanding (cognitive debriefing)
- When used along with quantitative methods (mixed methods) , may understand the complexities of a given situation & implications of quantitative data

Key standards used

- Protocol including:
  - Rationale/objectives
  - Methods
    - Patient population and Recruitment
    - Interview method and logistics
    - Informed consent/data protection
    - Interview guide in appendix
- Ethics approval
- Analysis
- Detailed reporting
- Publications

Methods: Patient population & Recruitment

- Inclusion/exclusion criteria
  - Mimic trial or
  - Widest possible population
- Sampling
  - Minimum threshold to achieve saturation (the point at which no new information arises)
  - Quotas that may reflect the population or where differences are expected
    - E.g. lower educational level for cognitive debriefing
- Recruitment
  - Fieldwork agencies
    - Databases, advertisements, clinician contacts
  - Patient advocacy groups

Interview methods: In-depth interview vs focus group

- Focus groups
  - Provide quick, high level information from a larger sample
    - normally 4-8 focus groups of up to 10 (7-8 ideal) people
    - stratified by type of patient (e.g. severity level, gender etc as required)
    - Not appropriate for cognitive debriefing
    - Requires very experienced moderator to ensure all participate
- Interviews
  - Provide more in-depth information
  - Normally at least 12 people per type to achieve saturation
  - Allows more in-depth analysis by different characteristics
  - Can be used for both concept elicitation and cognitive debriefing
  - Requires experienced interviewer

Interview method: Discussion guides

- Concept elicitation interview or focus group guide
  - Open-ended, un-biased questioning
    - Probes can help the interviewer/moderator focus on key areas of interest
- Cognitive debriefing
  - Open-ended but more prescribed
    - Interpretation of items, responses, recall periods and instructions
    - Perceptions of formatting
- Typically no more than 60-90 minutes

Interview method: logistics

- Interviewer/moderator
  - Training
- Place of interview
  - In-person: Market research site, clinic, home, other
  - Skype or phone
    - Not ideal for cognitive debriefing
  - On-line

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Methods: Ethics and data protection

- Ethics approval is usually sought for questionnaire and trial related interviews
  - For any study where publication is likely
  - Remember translations of key documents may be required
- Informed consent is sought and confidentiality assured
- Data protection methods specified in protocol

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Analysis-Concept elicitation

- Verbatim transcripts
- Analysis using software
  - E.g. Atlas Ti, MaxQDA, etc
- Analyze first 2-3 interviews
  - Develop codebook (can be changed throughout analysis)
  - Coding generally takes 3-4 hours per 1 hour interview
  - Once coded, analyse themes and sub-themes for total sample and by age group
  - Assess saturation

Analysis- cognitive debriefing

- Verbatim transcripts best
- Can analyse using software or excel
- Analyze using a grid format

Reporting

- Introduction, Objectives, Methods
- Results
  - Sample demographics and clinical characteristics
  - Concept elicitation
    - Concepts and sub-concepts with illustrative quotes
    - Highlight differences by sub-group (and similarities)
    - N's and % are also included
    - Saturation table
    - Conceptual model – mapping to previous model and/or to questionnaires
  - Cognitive debriefing
    - Number of items understood as intended
    - Description of reasons not well understood, with illustrative quotes
    - Highlight differences by sub-group (especially demographics)
    - Suggestions for changes; ideally retest any changes
    - Item tracking matrix
- Discussion
  - Key findings
  - Key limitations
  - Future research
- Appendices

Do we really need to do all that for DCE?

- Ensure that concepts are relevant and important
  - Concept elicitation
- Ensure are understood as intended
  - Cognitive debriefing
- But what about the most time intensive elements?
  - Protocol
  - Ethics
  - Transcripts
  - Saturation, quotas
  - Detailed analysis
  - Tracking matrix

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Qualitative Research in DCEs | Experience & Challenges

Conducting Qualitative Research

What?
- Qualitative Research Methods

How:
- Protocol / Interview guide / Recruitment or identification of respondents / Interviews or Focus Groups / Analysis / Reporting

Why?
- Attribute Development
- Pilot testing/cognitive debriefing

DCE in general population

Study: DCE to explore drivers of preference for making curative cancer treatment available in France

Population: General Population

Challenge: Knowledge of treatments is limited – not the patient population

Consequences: Treatment characteristics cited often "irrelevant/incorrect/unrealistic" E.g. Country in which a treatment is developed, Number of employees of a pharmaceutical company, Duration of treatment

Solution implemented: Review of literature influenced choice of attributes more than respondent interviews

Characteristics of a treatment not yet on the market

Study: DCE to explore drivers of preference for endometriosis treatment

Population: Women with endometriosis in the UK

Challenge: New treatment (future first in market for mode of administration) to be included in DCE

Consequences: Input very hypothetical – respondents unable to speak of own experience

Solution implemented: Explanation of new treatment included in DCE – attributes for new treatment not based on respondent input.

Using Semi-Directive Interview Techniques

Study: DCE to explore drivers of preference for convenience-related characteristics of devices in COPD

Population: Moderate to Severe Population COPD in France

Challenge: Patients report incorrect device characteristics e.g. dose confirmation for a device for which no dose confirmation exists - challenging as device experience is key

Consequences: Semi-directive approach means large portions of the interviews are “wasted” on exploring experiences that cannot be used

Solution implemented: Directive techniques were used to obtain patients’ input to ensure that characteristics could be sufficiently explored

Demonstrating Sufficient Sample Size

Study: DCE to explore drivers of preference for making curative cancer treatment available in France

Population: General Population

Challenge: No clear subgroups to drive sample size; Saturation not relevant because respondents have no experience of the subject so are not expected to address all characteristics.

Consequences: Risk of not capturing all relevant characteristics

Solution implemented: Sample size based on experience with qualitative research & DCEs, as well as ensuring a diverse range of ages, education & income levels, and equal balance of genders

Difficulty of Choice Tasks

Studies: DCE to quantify role played by different adverse events in preference for antipsychotic treatment for schizophrenia / DCE to explore drivers of preference for convenience-related characteristics of devices in COPD

Populations: Respondents with a diagnosis of schizophrenia in the US / Moderate to Severe Population COPD in France

Challenge: Respondents had difficulty understanding choice tasks

Consequences: Some respondents understood that they were to identify their treatment/device among the treatment profiles or that there was a “right” answer

Solution implemented: An example scenario was added and tested in a second pilot wave. Instructions were simplified and re-formatted. Instructions were repeated at the top of each choice task. Implementation of a “test scenario” to identify respondents who may not have understood.

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Recruitment

Studies: DCE to quantify role played by different adverse events in preference for antipsychotic treatment for schizophrenia / DCE to explore drivers of preference for convenience-related characteristics of devices in COPD / DCE to explore drivers of preference for endometriosis treatment

Populations: Respondents with a diagnosis of schizophrenia in the US / Moderate to Severe Population COPD in France / Women with endometriosis in the UK

Challenge: Clinician confirmation of diagnosis is not feasible for DCE given the sample sizes required

Consequences: Risk of including respondents that do not meet inclusion/exclusion criteria – recruitment often through panels

Solution implemented: Screening questions included in upfront medical history/socio-demographic questions – aim both to confirm diagnosis/treatments taken and to “catch out” respondents who make false claims about diagnoses.
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Difficulty of Opt-Out

Study: DCE to explore drivers of preference for endometriosis treatment

Population: Women with endometriosis in the UK

Challenge: Opt-out worded “Neither of these treatments”, understood as continuing current treatment whereas it was intended to mean no treatment

Consequences: Bias towards selection of opt-out to avoid risk

Solution implemented: Opt-out changed to be presented as 3rd option and described using attributes and levels

Difficulty understanding Risk (1)

Study: DCE to quantify role played by different adverse events in preference for antipsychotic treatment for schizophrenia

Population: Respondents with a diagnosis of schizophrenia in the US

Experience: Pilot Phase 1- risk levels were phrased in percentages, with icon arrays in the shape of people, showing the numbers affected per 100 patients

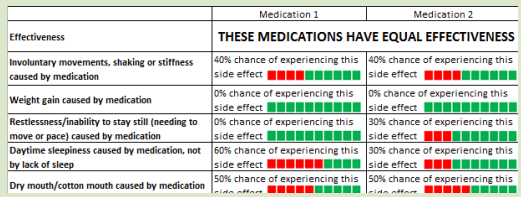
- Negative impact of space taken up by these icons outweighed positive impact of the visual cue

Icon arrays were deleted for pilot phase 2. The risk levels were rephrased as, for example, “Three in ten patients taking this medication experience this side effect”.

Difficulty Understanding Risk (2)

Pilot phase 2 interviews revealed
- Respondents had greater difficulty understanding this wording as expressing risk: “I’m trying to work out if I’m one of these 3 people.”,
- Too difficult to obtain an overview of the levels of risk given number of attributes and the lack of visual cues.

Solution implemented:
- Return to percentages, expressed as “chance” rather than “risk”
- Icon dot arrays that take up less space



	Medication 1	Medication 2
Effectiveness	THESE MEDICATIONS HAVE EQUAL EFFECTIVENESS	
Involuntary movements, shaking or stiffness caused by medication	40% chance of experiencing this side effect	40% chance of experiencing this side effect
Weight gain caused by medication	0% chance of experiencing this side effect	0% chance of experiencing this side effect
Restlessness/inability to stay still (needing to move or pace) caused by medication	0% chance of experiencing this side effect	30% chance of experiencing this side effect
Daytime sleepiness caused by medication, not by lack of sleep	60% chance of experiencing this side effect	30% chance of experiencing this side effect
Dry mouth/cotton mouth caused by medication	50% chance of experiencing this side effect	50% chance of experiencing this side effect

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Qualitative Research in DCEs | Experience & Challenges

Discussion – Audience Experience

Discussion:

Similar Experiences?

Multi-study DCEs?

Key learnings?

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Is it necessary to have a protocol?

Suggestions

- A protocol for the qualitative research element of a DCE must be written
- It should include details on
  - Recruitment approach
  - Inclusion/Exclusion criteria
  - Sample size
  - Conduct of interviews/focus groups
  - Analysis and Reporting methods
  - Maintaining respondent anonymity/data protection

Audience poll

- Is a protocol relevant for qualitative research in DCEs?

Discussion

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Poll: Is a protocol relevant for qualitative research in DCEs?

Is it necessary to demonstrate saturation/justify sample size?

Suggestions

- Demonstration of saturation not relevant.
- But need to demonstrate that
  - Respondents are same as future DCE respondents
  - All subgroups are represented

Audience poll

- Is demonstration of saturation relevant for qualitative research in DCEs?

Discussion

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Poll: Is demonstration of saturation relevant for qualitative research in DCEs?

Is it necessary to produce word-for-word transcripts of exploratory interviews and carry out in-depth analyses?

Suggestions

- Word-for-word transcripts and analysis not necessary but can have an added value
- But need to demonstrate respondents' wordings are used for formulation of attributes and levels *or justify why they are not used*

Audience poll

- Are word-for-word transcripts relevant for qualitative research in DCEs?
- Are in-depth analysis relevant for qualitative research in DCEs?

Discussion

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Poll: Are word-for-word transcripts relevant for qualitative research in DCEs?

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Poll: Are in-depth analysis relevant for qualitative research in DCEs?

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Is it necessary to do cognitive debriefings, and how many?

Suggestions

- Cognitive debriefings are essential
- Respondents who have had difficulty with choice tasks, and respondents with lower educational levels should be included
- Sample size should be determined by demonstrating inclusion of subgroups and those who have difficulty with choice tasks.
- Two rounds of cognitive debriefings are recommended when changes are more than minor (definition?)

Audience poll

- Are cognitive briefings essential for qualitative research in DCEs?
- Is one round of cognitive debriefings sufficient?

Discussion

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Poll: Are cognitive briefings essential for qualitative research in DCEs?

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Poll: Is one round of cognitive debriefings sufficient?

How should qualitative methods be implemented for multi-country studies?

Suggestions

- If possible, all qualitative components should be implemented in all countries.
- When this is not possible, cognitive debriefings must be carried out in every country.

Audience poll

- Is it essential to conduct qualitative research in all study countries for DCEs?

Discussion

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Poll: Is it essential to conduct qualitative research in all study countries for DCEs?

How much detail on qualitative methodologies should be reported in publications ?

Suggestions

- Methods, analysis and results should be reported
- Moving from results to formulation of attributes and levels should be reported.

Audience poll

- Is it essential to report qualitative research in publications for DCEs?

Discussion

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Conclusions

- Guidelines for qualitative research for DCEs need to be drawn up based on today's discussion
- Scientific journals should require DCE authors to report details of qualitative steps and make

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The enlightened decision

Thank you