

CONDUCTING QUALITATIVE 'EXIT' INTERVIEWS FOLLOWING CLINICAL TRIALS OR OBSERVATIONAL STUDIES:

A VALUABLE METHOD FOR UNDERSTANDING THE PATIENT
EXPERIENCE, INFORMING MEASUREMENT STRATEGY AND AIDING
INTERPRETATION OF PATIENT-REPORTED OUTCOMES (PRO)

Presenters

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Workshop outline

Methodology, uses, and challenges and solutions for implementation in clinical trials

Refining COA instruments through cognitive debriefing in exit interviews

Use of exit interviews to aid interpretation of changes in Clinical Outcome Assessment (COA) scores

Understanding the disease experience, patient journey, and new product attributes

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Methodology, Uses, and Challenges and Solutions for Implementation in Clinical Trials

Robyn von Maltzahn

Scientist, Patient Centred Outcomes

GSK

What are exit interviews?

- > Exit interviews are very broad in scope
- > Exit interviews are designed to:
 - capture any reported symptom changes (benefits, tolerability and other unintended effects) throughout the trial
 - patients' evaluation of treatment received
 - patient experience of taking part in a clinical trial
 - providing a better understanding of the disease
- > This information can be used to:
 - Inform study design
 - Inform asset development
 - Assist in interpretation of PROs

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Exit interview methodology

- > Semi-structured qualitative interviews
- > Typically conducted in-person at final visit (study exit) or alternatively over the phone in a period post-final visit
 - Timings can vary depending on what information is being sort
- > One-on-one interviews
- > Conducted either by study site staff or expert interviewers from an external vendor

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Exit interview methodology cont.

- > Patient selection
 - Blinded study sample
 - Random vs. purposive e.g. gender
 - Early withdrawal participants
- > Analysis and reporting similar to other qualitative data
 - Saturation in blinded study

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Potential uses

- > Informing initial development or refining a clinical outcome assessment (COA) through cognitive interviews as part of a mixed method approach
- > Add greater depth to data in rare diseases (or possibly other diseases with not much patient input) where subtleties of patients' experiences may not be captured fully by existing COAs
- > Obtaining patient input on meaningful outcome or meaningful change/responder definition
 - Patient definition of control or improvement
 - Relating patient definition to an existing measure

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Potential uses cont.

- > Accessing the patient experience of being a participant in the trial
 - Understand participants' reasons for consent and participation
 - Possible trial design modifications for later phases
 - Patient centric
 - Logistics
 - Data capture methods e.g. eCOA

- > Understanding the patient experience of the drug/treatment
 - Participant experience of disease and treatment expectations
 - Anticipated and unintended symptoms and AEs
 - Viability of proposed dosing regiment
 - Informal cost/benefit trade-off of drug from patient perspective
 - Able to access qualitative aspects that emerge outside of pre-specified hard endpoints

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Challenges/Solutions for implementation alongside clinical trials

Logistics	
Contracting	Site training
<ul style="list-style-type: none"> > Subcontracting interviews separately to clinical trial > Timelines and complexity if added on to original trial as a protocol amendment > <i>Solution: logistics become easier as exit interviews become more common; internal roles and responsibilities become clearer; more awareness of benefits of exit interviews results in less amendments as teams proactively include them as a defined study procedure</i> 	<ul style="list-style-type: none"> > Additional/separate training to clinical trial site training > Multiple time points > <i>Solution: buy in from wider team on the role of training for quality data and ensuring there is enough time and budget for thorough training of sites</i>

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Challenges/Solutions for implementation alongside clinical trials

Logistics

Who (site staff or vendor) conducts the interviews and training

- > Extra burden on site staff; not all staff skilled in interviews (requires vendor monitoring and frequent training)
- > Scheduling, administration time and confidentiality – certain sites/countries cannot pass on contact details to a 3rd party vendor
- > *Solution: assess site's experience and complexity of interviews; site schedules interviews and a TC line is used to ensure no details are passed onto vendor*

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Challenges/Solutions for implementation alongside clinical trials

Implementation

Multinational study logistics

- > Translation, timings etc – consider number of interviews needed, number of sites to participate, number of countries/cultures to include
- > *Solution: Close work with clinical team; early planning*

Timing

- > Timing of interview and recall bias
- > *Solution: Timing needs to be dependent on best place to answer primary research question (as well as practicalities)*

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Challenges/Solutions for Implementation alongside clinical trials

Reporting	
Results	AE reporting
<ul style="list-style-type: none">> Inclusion of interviews in analysis plan and report or reported separately> <i>Solution: internal teams need to decide where best to place reports i.e. Appendices to clinical study reports etc</i>	<ul style="list-style-type: none">> Accurately capture AEs without omitting or double counting> <i>Solution: Follow internal protocol on this key issue; ensure vendor is aware of process and the importance of capturing and/or reconciling the AEs in the trial for safety report and not as unrelated Medwatch data</i>

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Refining COA instruments through cognitive debriefing in exit interviews

Chris Marshall

Senior Research Manager, Patient-Centered Outcomes
Adelphi Values

Refining COA instruments through cognitive debriefing in exit interviews

In the context of COA instrument development, exit interviews can be used to evaluate:



Content validity

- > Further explore the content validity of the PRO instrument (items, instructions, response scale) in the exact Context of Use.
- > Mixed methods approach to support item finalization in a validation study



Usability and feasibility

- > Usability of device in Context of Use, adequacy of instructions, training
- > Confirm feasibility of completion throughout a quantitative study
- > Inform changes to format of instrument



Meaningful change thresholds

- > Explore what level of change participants consider a meaningful and important
- > Timing of interviews may allow reflection on actual score change during trial
- > Ability to reflect on potential change due to treatment

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When is cognitive debriefing through exit interviews most valuable?

When:

- > **timelines are tight**
- > **working in rare diseases**
- > **multiple phase 2 trials** are planned
- > **item deletion is anticipated**
- > Using a new **mode of administration**

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Cognitive debriefing: who to interview?

Random subset of trial participants

- > Beware of potential for bias in who is willing to participate
- > Inclusion in trial protocol versus separate study

Typical sample

- > 20-30 patients but can vary widely (e.g. rare condition, patient subgroup representation)
- > Sample size determined based on budget, perceived importance, and diversity

Inclusion of patients only?



- > Clinicians and study nurses: Insights into **feasibility** and **practicality** of collecting PRO data, adequacy of **instructions** and **training**
- > Caregivers: Where patient report is not appropriate or substantiate

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Timing of cognitive debriefing or meaningful change exit interviews

During or directly after trial participation

Benefits

- > Better recall, immediate feedback
- > Patient engagement benefit

Risks/negatives

- > Risk of biasing trial data
- > Feasibility of interviewing quickly enough

After completion of validation analyses

Benefits

- > Can explore issues identified through quantitative analyses
- > e.g. reasons for missing data, floor or ceiling effects

Risks/negatives

- > Recall could be a problem
- > Practical challenges of re-contacting patients

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Refining COA instruments through cognitive debriefing in exit interviews: case study in asthma

Background

- > Exit interviews with patients following pilot testing of an electronic PRO diary assessment of asthma symptoms

Objective

- > Obtain feedback on the **feasibility** and **usability** of the ePRO device in the **context of use** of a quantitative study and further evaluate **content validity**

Methods

- > Semi-structured telephone interviews with a subset of **adolescents (n=14)** and **adults (n=10)** who participated in the 10-day quantitative study.
- > Interviews explored the **conceptual coverage** and potential **overlap** between PRO items, and debriefed an **additional question**.
- > Also used to explore opinions on the **response scale**, **usability**, and **feasibility** of the **ePRO device**.

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Refining COA instruments through cognitive debriefing in exit interviews: case study in asthma

Results

Understanding

- > The majority (22/24, 91.7%) had no difficulty understanding or responding to any of the PRO items – consistent with previous findings.
- > *Benefit: Confirmation items are acceptable and clear when completed over a number of days (i.e. more naturalistic than the typical cognitive interview setting)*

Usability and Feasibility

- > Patients were able to navigate the ePRO diary and had few issues fitting the morning and afternoon completions into daily routines.
“Um, well it wasn’t really... too much. Um, you know, I felt that twice a day was perfectly fine.”
- > *Benefit: Provides insight into the practicalities of completing COA instruments and inform future trial implementation and design.*

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Refining COA instruments through cognitive debriefing in exit interviews: case study in asthma

Results: missing data

- > 14/20 who were asked missed at least one diary entry
 - 5/20 missed two or more
- > Consistent with the quantitative study data, the frequency of skipping items within an entry was reported to be very low.
- > Reasons for missed entries varied, but were either:
 - **personal** issues (**forgetfulness, lack of time**), reported by 8/14,
 - **device-related** issues (problems **logging in, sending or saving data**), reported by 6/14.
 - **None** suggested difficulty or lack of acceptability of items
- > *Benefit: Insights that missing data was due to reasons other than problems with the items.*

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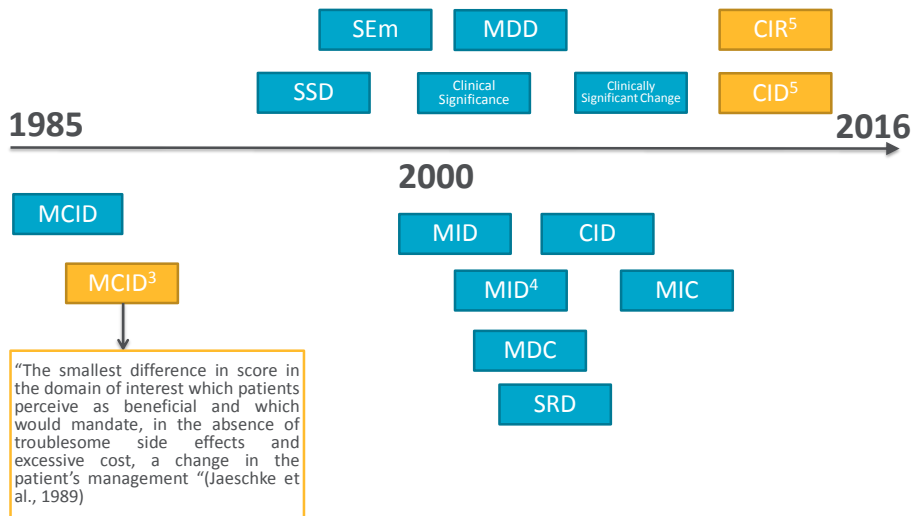
Use of exit interviews to aid interpretation of changes in Clinical Outcome Assessment (COA) scores

Rob Arbuckle

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History of terms^{1,2}



(¹King et al., 2011; ²Shields et al., 2015)

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Use of exit interviews to explore patient perspectives of meaningful change

- > There are well established quantitative methods for defining meaningful change through statistical analysis
 - Anchor based methods
 - Examining score change for change groups based on an external anchor
 - Distribution based methods e.g.:
 - ½ Standard deviation
 - Standard Error of Measurement
- > Getting direct patient perspective on meaningful change thresholds is increasingly valued

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Use of exit interviews to explore patient perspectives of meaningful change

- > Different methods can be used to capture patient perspective
- > But this often requires **hypothetical** thinking or recall over a long time period
- > Exit interviews provide an opportunity for a patient to reflect on **actual change** experienced due to an intervention
- > Can then link **qualitative comments** to PRO **score changes** experienced
- > The ultimate aim is then to **triangulate** the qualitative findings with quantitative findings

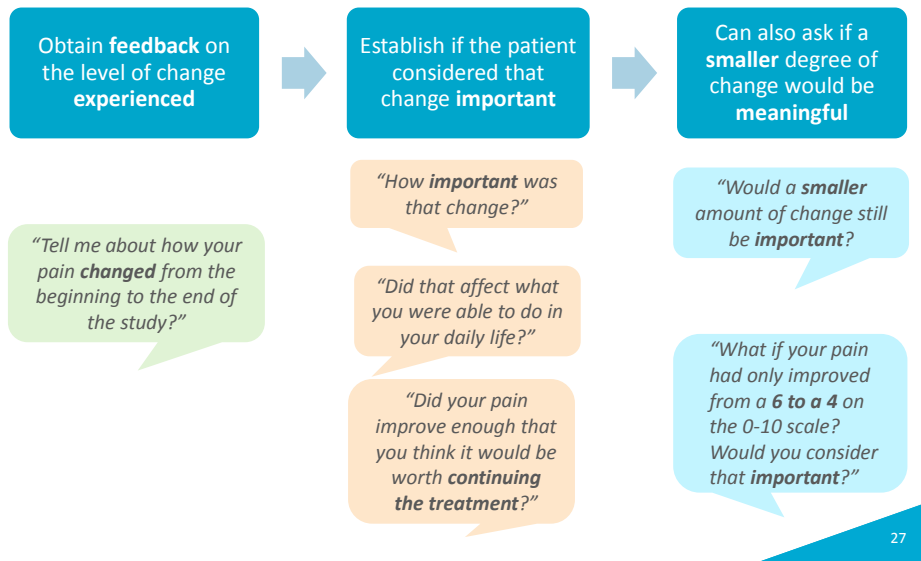
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How to talk to patients about the importance of change

- > No one best approach
- > Start with a very qualitative **open discussion** of their symptoms before, during and after treatment and how **important** those changes were to them
- > Ask the participant to talk about how symptom changes affected **functioning**, coping strategies
- > Can talk about **numbers of days** with symptoms and how much difference that makes
- > For simpler instruments you can then move to talking more specifically about **actual score changes** on the PRO
- > The questions/approaches that work best may **vary** across a sample

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Example interview guide questions



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Some concepts and instruments are more challenging than others...

- > Exploring change in a single domain, assessed by a single item is relatively straight forward
 - Pain assessed through a 0-10 numerical rating scale
 - Frequency of bowel movements
 - Frequency and severity epileptic seizures
- > Where the PRO assesses multiple symptoms/concepts with a multi-item summary score it's more challenging

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Incorporating with quantitative findings

- > Qualitative exploration of meaningful change is still less established than quantitative methods
 - Treat as secondary and supportive to anchor-based methods... for now...
- > Supportive evidence that responder definitions defined primarily using anchor-based methods represent change that is important to patients, clinicians and/or caregivers

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Understanding the Disease Experience, Patient Journey & New Product Attributes

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Patient Interviews Alongside Clinical Trials

Opportunities for Incorporation of Patient Perspective Early & Throughout Drug Development

- 1 Enhance understanding of patient disease experience & treatment journey
- 2 Expand understanding of product/device benefits & risks to identify areas of differentiation
- 3 Assist in development & interpretation of PROs
- 4 Inform future trial design

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Patient Interviews Alongside Clinical Trials

Opportunities for Incorporation of Patient Perspective Early & Throughout Drug Development

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1 Enhance understanding of patient disease experience & treatment journey

- > Patient disease experience & treatment journey often unknown
- > Clinical trial population is a convenient sample to understand patient perspective
 1. Expand understanding of relevant concepts beyond clinical trial measurement strategy:
 - Core signs/symptoms
 - Related symptoms & co-morbid conditions
 - Impact on quality of life
 - Moderators/covariates
 - Additional dimensions relevant to patients
 2. Identify unmet needs & opportunity for new product differentiation through patient perception of prior treatment
 3. Identify patient-centric factors influencing treatment satisfaction and treatment adherence

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1 Enhance understanding of patient disease experience & treatment journey

Example Interview Questions: Disease Experience & Patient Journey

- > What symptoms do you experience? How do those symptoms make you feel?
- > Which symptoms are most bothersome?
- > Which symptoms would make you take a treatment for your condition?
- > Which symptoms would lead you to make a doctor's appointment?

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1 Enhance understanding of patient disease experience & treatment journey

Example Interview Questions: Ideal Treatment Attributes

- > Describe for me what an ideal treatment for condition X would be like.
 - Which symptoms are most important to improve with treatment?
 - How often would you be prepared to take the treatment?
- > Include rating exercise for treatment attributes

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2 Expand understanding of product/device benefits & risks to identify areas of differentiation

- > Clinical trial participants are the **only direct** source of product experience prior to approval
- > Methodology minimizes patient burden within trial AND offers an opportunity to understand risk/benefit profile for an investigational drug:
 1. Patient experience beyond outcomes measured
 2. Patient perceptions regarding change on key clinical and safety outcomes
 3. Patient-centric product value attributes & perceived risks
 4. Identify pressure points for future trial design and commercialization (eg, dosing regimen, route of administration, trial experience)
 5. Compare patient-reported study drug experience to patient perceptions of prior treatment experience

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2 Expand understanding of product/device benefits & risks to identify areas of differentiation

Example Interview Questions: Study Drug Experience

- > Tell me about how **satisfied** you were with the study medication while you were taking it.
 - Which symptoms did it improve the most? How about the least?
 - Was there anything about the study medication that you did not like?
 - How convenient was it to take?
 - What about the frequency of taking it?
 - How did it taste?
 - Did you worry about taking it at all? Why?
- > How does the study drug compare to _____ (*other treatments*)?
- > If given the opportunity to take _____ [*ask for each treatment they've taken before*] or study drug at equal cost, which treatment would you choose? Why?

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Value of Patient Interviews Alongside Clinical Trials: Applications

- > **Disease Experience**
 - Develop patient-centric disease conceptual model
 - Compare patient-reported experience with literature & diagnostic criteria
 - Identification of most bothersome/impactful signs & symptoms
- > **Prior Treatment Experience & Expectations**
 - Identify unmet needs and levels of satisfaction with prior therapies
 - Evaluate “ideal” treatment attributes and key factors driving treatment satisfaction and adherence

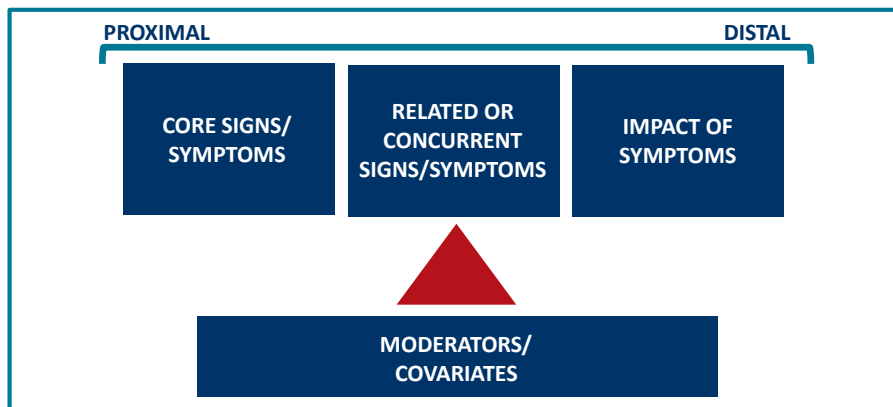
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Value of Patient Interviews Alongside Clinical Trials: Applications

- > **Study Drug Risks/Benefits**
 - Identify how changes in signs/symptoms relate to meaningful change in patients' ability to function
 - Compare patient experience with prior treatments to study drug
 - Understand patient perceptions of treatment benefit vs. adverse outcomes
 - Evaluate reasons for study withdrawal
- > **Outcome Assessment Alignment**
 - Validate current measurement strategy
 - Identify new outcomes relevant to patients
 - Identify new concepts for potential product differentiation

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Example Disease Conceptual Model: Patient Perspective, Diagnostic Criteria, Literature



Utility of Conceptual Model:

1. Aligns patient perspective with literature & diagnostic criteria
2. Inform measurement strategy
3. Comparison of perceived patient benefits/risks on study drug

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Patient Interviews Alongside Clinical Trials:

Lessons Learned & Potential Future Uses

> Lessons Learned

- Limit time between trial participation & interview
- Ensure appropriate procedures and training for AE reporting
- Consider incorporation into earlier phase trials
- Align internally on use of data from patient interviews
- Collaborate closely with GHEOR and clinical team

> Future uses for patient interviews

- Implement at other timepoints (ie, baseline)
- Incorporate patient interviews in real-world studies
- Expand interviews to evaluate ePRO data collection feasibility and overall trial experience

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Summary and conclusions

Conclusions

- > Exit interviews are a method which can add considerable value to clinical development programs, providing insight into:
 - Experience of participating in a trial (patient centricity)
 - Treatment experience/treatment satisfaction
 - COA content validity, usability and feasibility
 - Interpretation of changes in COA scores
- > BUT there are many study design and logistical considerations that must be decided
 - Incorporated into trial protocol vs separate study
 - Timing
 - Sample size
 - Practicalities of recruitment and patient selection

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Conclusions

- > As with many decisions that have to be made in clinical development, the answer to the question “**What is the best approach?**” is “**It depends....**”
- > It depends on:
 - Disease and context of use
 - Research question
 - Company policies and comfort of clinical colleagues
 - Timing
 - Budget
 - Among others...
- > As always **early planning** is critical to maximise success

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Questions?

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Thank you!