

SAMPLE SIZE, GROUNDED THEORY, AND SATURATION IN COA DEVELOPMENT

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May 23, 2018
ISPOR 2018 Baltimore



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1

Guidance for Industry: Sample size

- › Does not make any specific sample size recommendations
- › Stresses the importance of:
 - Saturation ← **Key element!**
 - Interview quality
 - Patient diversity

Sources: US Department of Health and Human Services Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH). Guidance for industry. Patient-reported outcome measures: use in medical product development to support labeling claims (2009)
Kerr, C. (2010). Assessing and demonstrating data saturation in qualitative inquiry supporting patient-reported outcomes research. *Expert Review of Pharmacoeconomics & Outcomes Research*, 10(3), 269-281.
doi:10.1586/erp.10.30



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2

Saturation in PROs

- ▶ What is it?
- ▶ Why is it necessary to achieve it?
- ▶ When do you start thinking about it?
- ▶ How do researchers know when they achieve it?
- ▶ How do we present findings to indicate that saturation has been achieved



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3

When To Start Thinking About Saturation

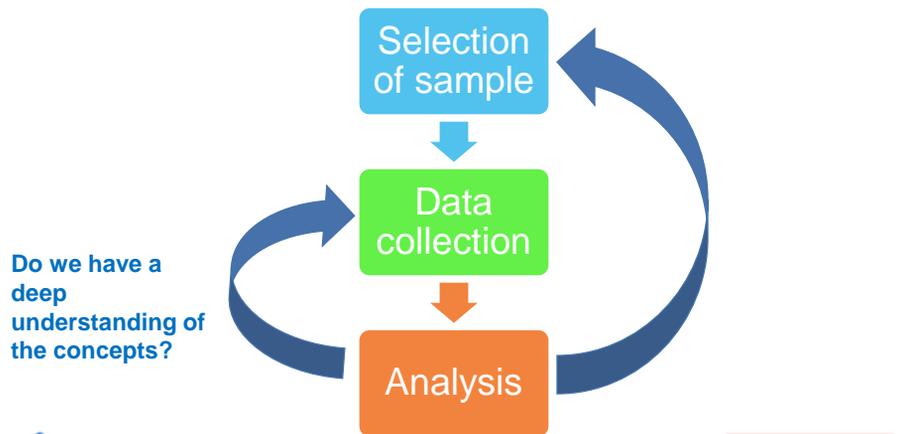
- ▶ When you formulate your research question
- ▶ **When you select your sample?**
 - **Homogeneous? Heterogeneous?**
- ▶ When you develop your discussion guide?
- ▶ When you iteratively develop a coding scheme (what do the codes mean?; when are codes reflecting distinct concepts?)
- ▶ When you conduct data analysis and if necessary, further data collection
 - Need to also search for disconfirming evidence and assure maximum variation – negative case



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Developing a PRO instrument: Data collection and analysis



Source: Kerr, C. (2010). Assessing and demonstrating data saturation in qualitative inquir supporting patient-reported outcomes research. *Expert Review of Pharmacoeconomics & Outcomes Research*, 10(3), 269-281. doi:10.1586/erp.10.30

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Phenomenological Theoretical Framework

- ▶ Accessing a concept through the eyes of a person experiencing the concept
 - Not constrained by preconceived theories
 - Not taken from an instrument
 - Open-ended questions
 - “What is it like for you to have diabetes?”



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6

Grounded Theory Methods

- ▶ Set of data collection and analysis methods whereby the meaning of a concept is discovered in the words and actions of participants from the ground up – not from application of a priori theory or concepts
- ▶ Application to COA: Help investigators develop a conceptual framework that can be used to design a questionnaire and/or quantitatively test a PRO instrument (reliability, psychometric properties, responsive)
- ▶ Inductive rather than deductive reasoning
- ▶ Simultaneous and iterative data collection and analysis
- ▶ Reliability through multiple coders and harmonization
- ▶ Achievement of **saturation**



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7

What is Saturation?

- ▶ Limited research
- ▶ Originates in Grounded Theory
 - Methodological and analytical approach to qualitative research
 - Theory evolves during actual research, and it does this through **continuous interplay between analysis and data collection**
 - Iterative process of sampling, data collection, and analysis
- ▶ When have you reached saturation?
 - Concepts cannot be further specified with additional analysis or new data collection
 - No new codes
 - Saturation table

Sources: Kerr, C. (2010). Assessing and demonstrating data saturation in qualitative inquiry supporting patient-reported outcomes research. *Expert Review of Pharmacoeconomics & Outcomes Research*, 10(3), 269-281. doi:10.1586/erp.10.30

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Lasch, K. E., Marquis, P., Vigneux, M., Abetz, L., Arnould, B., & Bayliss, M. (2010). PRO development: Rigorous qualitative research as the crucial foundation. *Quality of Life Research*, 19(8), 1087-1096. doi:10.1007/s11136-010-9677-6



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8

Looking for the Essence in Concepts: An Analogy

- Through **rigorous, detailed, documented, and transparent** work Rosalind Franklin, a British biophysicist, identified **the essence** of the DNA molecule with an X-ray diffraction photograph 1953.



- The DNA story involved describing the essence of the molecule, mixing methods to describe and test its structure, and multidisciplinary effort.



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9

Developing a PRO: Study Design

- Criteria for sample diversity
 - Diversity of patients with different characteristics to cover breadth of context
 - Variations in disease severity
 - Epidemiology of disease (rare/common, subtypes based on genetic factors) and subtypes based on prior and/or future treatments (first line, second line chemotherapy, stem cell transplant (eligible, not eligible)
 - Representative of the population of interest (age, ethnicity, gender)
- Types of Coding
 - Open (examining, comparing conceptualizing, categorizing data)
 - Axial (reassembling data into groupings based on relationships and patterns within and among the categories identified)
 - Selective (identifying and describing the central phenomenon or core category)



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10

Providing Evidence of Saturation

Dimension	Concept	1 vs. 2	1- 2 vs. 3	1-3 vs. 4	Total	Saturation
	Bloating	1 vs. 1	2 vs. 1	3 vs. 1	4	Merged, yes
	Distension	0 vs. 1	1 vs. 0	1 vs. 1	2	
Other Discomfort	Tightness	0 vs. 1	1 vs. 1	2 vs. 1	3	Merged, yes
	Heavy	0 vs. 1	1 vs. 1	2 vs. 1	3	
	Fullness	1 vs. 1	2 vs. 1	3 vs. 1	4	
	Itching	1 vs. 0	1 vs. 0	1 vs. 0	1	No
	Abdominal pressure	1 vs. 1	2 vs. 0	2 vs. 1	3	Yes

Merged concepts= As you develop a deeper understanding of the patient experience, codes/concepts that have the same meaning to patients may be merged

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Hypothetical Saturation of IBS (first 2 focus groups)

Rectal pain
 Bloating
 Fullness
 Abdominal pain
 Flatulence
 Cramping
 Distension
 Frequent bowel movements
 Incomplete evacuation
 Rectal bleeding



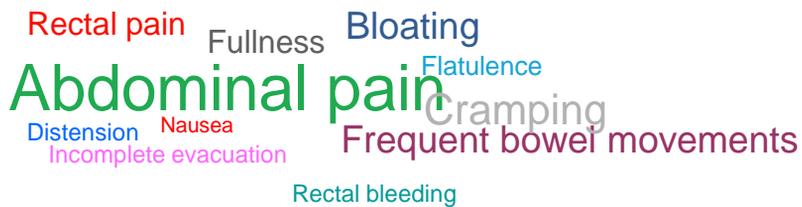
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Hypothetical Saturation of IBS (first 4 focus groups)



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Hypothetical Saturation of IBS (first 6 focus groups)



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Mixing qualitative AND Quantitative methods analogous to DNA Structure and process

- ▶ Qualitative data can be tapped throughout life cycle of the development and use of the PRO
- ▶ During cognitive interviews one often goes back to the concept elicitation data for clarification and comparison purposes
- ▶ Development of scoring algorithms and responder definitions often require further insight from the qualitative data (e.g., developing composite scores of symptom clusters)
- ▶ Interaction with the FDA/EMA may either require re-analysis of qualitative data or **collection of additional qualitative data**
- ▶ Quantitative analysis will describe and test the structure of the data; if additional qualitative data is collected, will need to show responder definition is still supported
- ▶ Analysis of efficacy and effectiveness results may be further explicated with qualitative research



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15



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16