



Interpreting Patient Reported Outcomes: A Holistic Approach

Interpretation of data derived from a patient-reported outcome measure can be challenging, particularly with regard to understanding the meaning of what a change or difference in a score means clinically

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Remembering that patient-reported outcomes (PROs) are assessing outcomes from the perspective of the patient, any change in the score may or may not be related to a clinical outcome. As an example, patients with diabetes who have changed to an insulin treatment considered more convenient (but is the same in all other respects) are unlikely to report any improvement in clinical outcomes, but may well report that their quality of life has been enhanced as a result of the greater flexibility in their lives. A range of techniques exist for interpreting PRO data, which are:

- **Minimal important difference:** The smallest difference in a score that is considered to be worthwhile or important
- **Known groups:** The mean scores underlying particular clinical groups or clinical indicators which give rise to them and can be used as a clinically based benchmark to compare other groups
- **Normative and reference groups:** Mean scores from defined large populations to provide normative data (typical scores) called norms. Mean scores from a particular study can be compared with the population norms
- **Statistical significance:** The statistical significance of the probability of treatment A being better than treatment B
- **Effect size:** A way of quantifying the difference between two groups of patients that has many advantages over the use of statistical significance alone and emphasises the size of the difference rather than confounding this with sample size
- **Cumulative distribution functions (CDF):** The CDF shows a continuous plot of the proportion of patients experiencing change at that level or lower levels at each point along the continuum of the scale score

Other approaches include reference to the PRO content when interpreting its score, as well as comparing them with known clinical parameters such as days in hospital and illness severity or the proportion of patients whose PRO score improve or get worse after intervention.

McLeod *et al* point out that the final FDA PRO guidance admits that judgement is still required when evaluating whether each individuals' responses are meaningful (1). McLeod *et al* go on to briefly outline patient-based methods such as the concept of 'symptom-free days' as well as consensus-based methods.

The challenges, however, when bringing together both quantitative and qualitative data include:

- Developing an actionable framework to enable the combining of qualitative and quantitative evidence
- Developing frameworks to enable the incorporation of expert intuition into the data analysis process
- Bringing the analyst's knowledge and experience of the research craft (what works and what does not) that can enrich the interpretation of the data

The notion put forward here is that the understanding of PROs can be enhanced by bringing a methodological approach – a 'holistic' analysis – that provides a rounded view of what all the qualitative and quantitative evidence is saying, while retaining the integrity of the data (see Figure 1, page 22).

Starting at the End

It is essential that every analysis starts with making sure the right problem is being analysed by using a rigorous problem-identification process. This involves getting a full understanding of the desired outcomes and whether the primary and secondary endpoints and the conceptual model are relevant to the questions asked of the data.

Compensating for Imperfect Data

While there is a wealth of potential contextualising information available to enable a deeper interpretation of PRO results such as surveys, interviews with clinicians and patients, etc, some of this data is likely to fail the

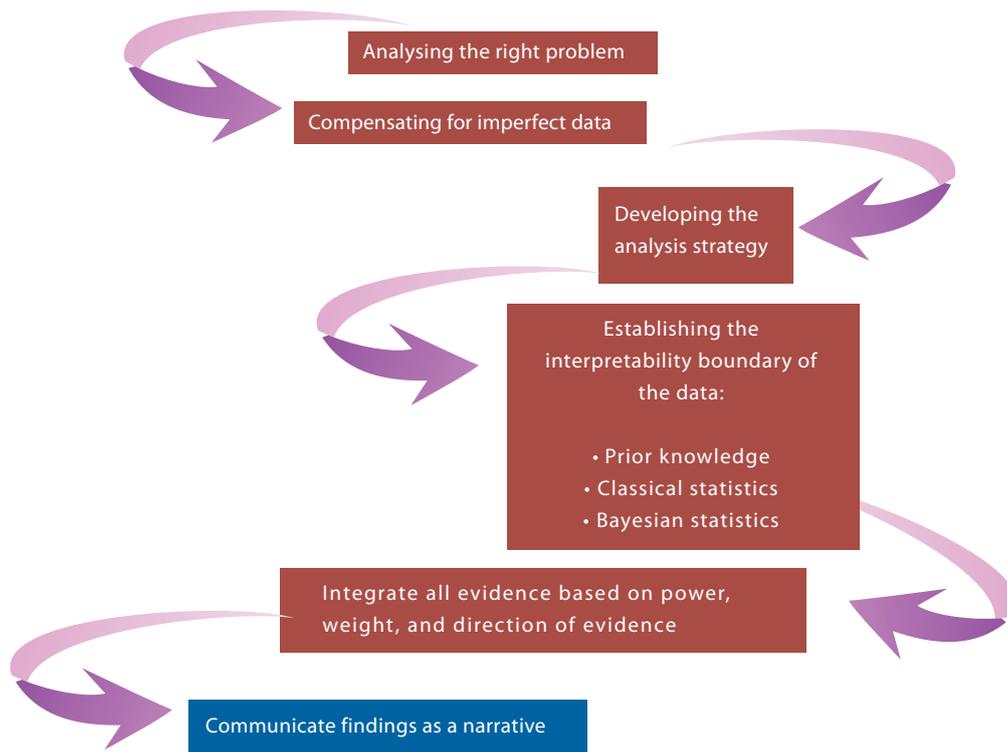


Figure 1: The holistic data analysis framework

criteria of the hypothetico-deductive model of enquiry and classical statistics. However, for the holistic analysis, this information is nonetheless important in the interpretation of the total picture. Therefore, the first requirement is deciding on the level of compensation required in dealing with less-than-perfect data and how this might impact on the quality of the results and will include asking questions of the data such as:

- Did the context in which the research was conducted affect the responses?
- Was the sample representative?
- Were the questions asked neutral and unbiased?

Developing an Analytical Strategy

Here, the focus is on developing a detailed analysis strategy that specifically demonstrates how the various

stakeholders' decisions to be made will be addressed (see Figure 2, page 24). The approach is, first, to get a picture of the total sample, followed by looking at subgroup variations and differences.

Establishing the Interpretation Boundary of the Data

This is the process of establishing, the more statistically derived constraints first (eg, study design, statistical significance of the quantitative data, sampling error) which must be worked within. The 'enablers' are then applied to determine how far the statistically driven assessments can be legitimately stretched (in the interpretation of the data through the application of a set of user-friendly general principles drawn from Bayesian thinking), where significance testing becomes one of a simple probability that any differences are likely to be significant.

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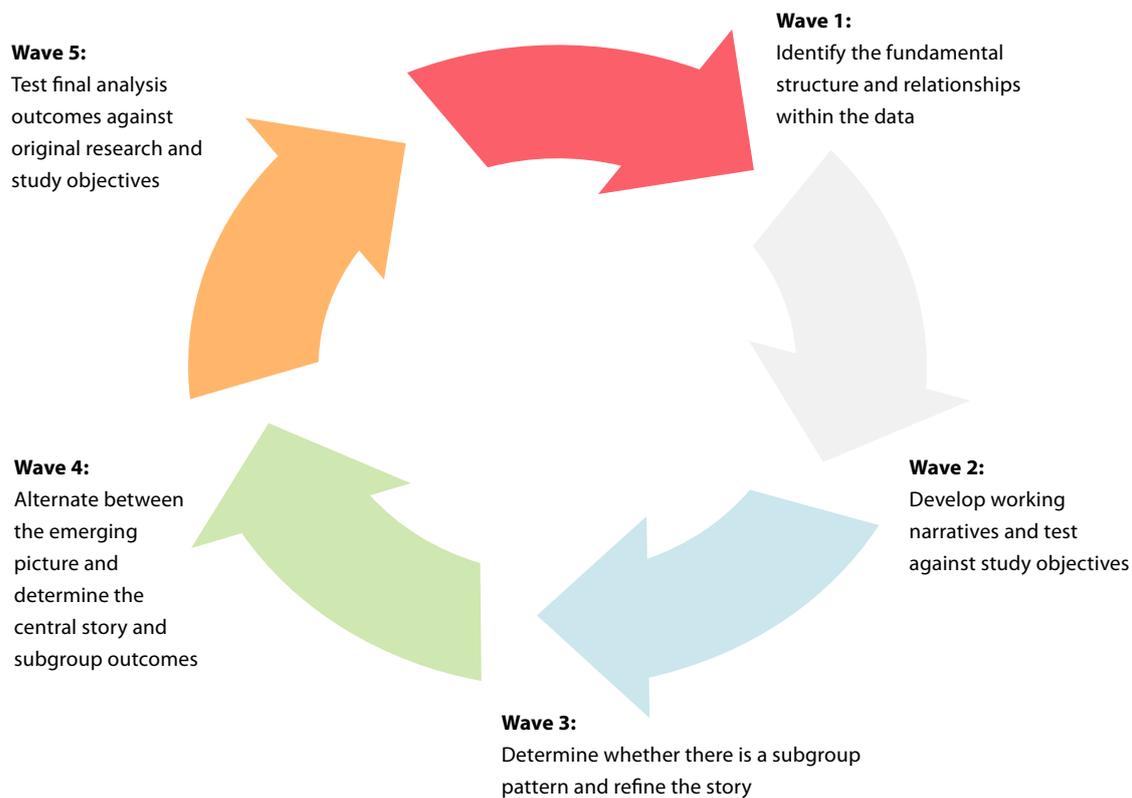


Figure 2: The holistic approach

Integrating all the Evidence

The stage of combining the qualitative and quantitative datasets follows with the need to examine the evidence within a framework of weight, power, and direction.

Assessments of examples of the qualitative and quantitative datasets are:

Weight

- Balance of opinion: The proportion of the dataset numerically in favour, for example, of an improvement in symptoms score, number of symptom-free days, etc
- Depth of feeling: This is the depth or strength of feeling about the topic and can be based on either quantitative or qualitative assessments

Power of Evidence

- Prior knowledge: How does the data fit into the wider context of what is known, eg, contraindications, symptoms, ad hoc evidence?
- Integrity of the data: What is known about the data, eg, can it be a good predictor of outcome or is it in need of careful interpretation?

Direction of Evidence

- Internal consistency: The level of consistency within each dataset
- External consistency: The level of consistency across the datasets (see Figure 3, page 25)

Communicating the Research Findings as a Narrative

In sharp contrast to the building block approach where the evidence is listed, experimentation is executed with the narrative approach, which identifies the key issues relating to the problem under investigation and focuses on these with supporting evidence as the narrative unfolds.

However, while checks and balances will need to be applied to ensure the integrity of the data, presentation of research findings through a compelling narrative can:

- Help communicate the complex whole: Linking together key relationships and experiences
- Aid comprehension: Presenting data in a coherent narrative form is more likely to be understood, absorbed, and recalled
- Enhance action: Reduces barriers to change and brings potential actions to life
- Facilitate buy-in: If the narrative is seen as relevant and timely, it is more likely to be communicated, absorbed, and recalled

Ending Interpretation

More often than not, researchers believe that, to be meaningful, evidence must meet the criteria of classic statistical significance. However, by viewing everything through that narrow statistical lens, are researchers more

Externally consistent across datasets, eg, prodata, attitudes, in-depth interviews

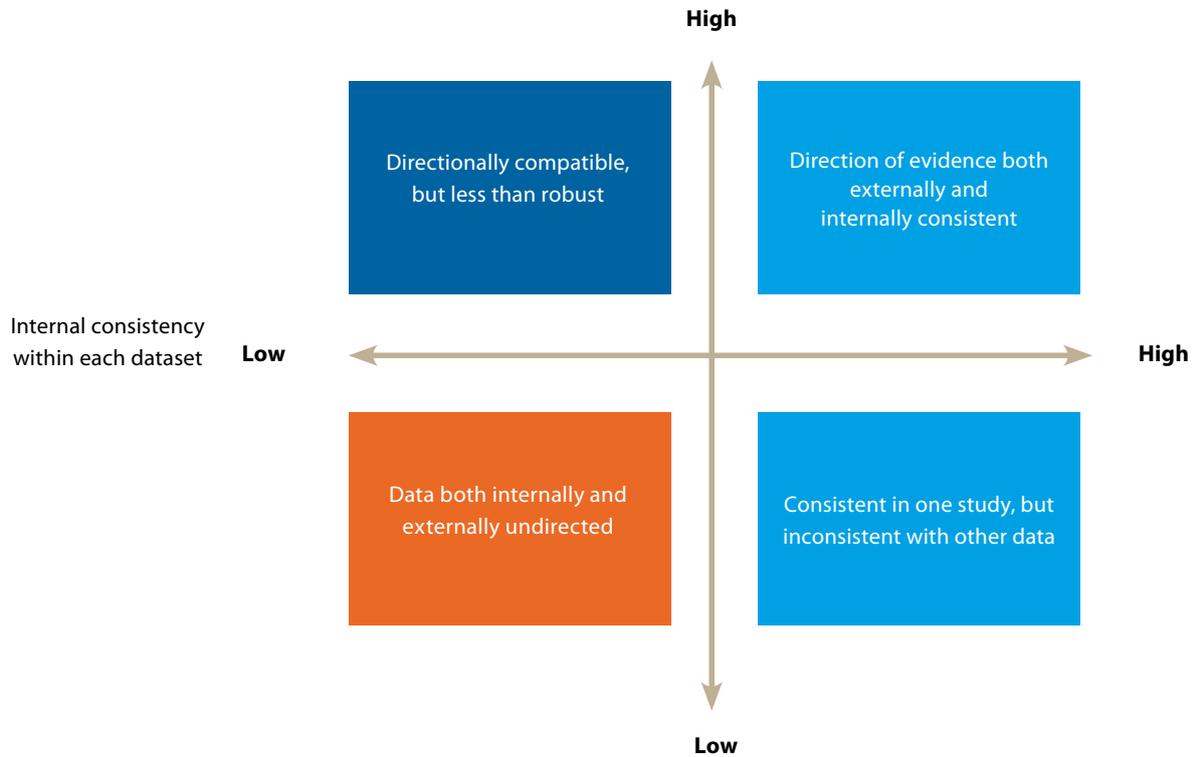


Figure 3: The direction of evidence

likely to miss those vital connections that are essential for identifying insight? Asking such a question is particularly relevant in a world of multiple datasets.

This article has described an analytical strategy that shifts researchers from being purveyors of outcome data to one in which real insight into PROs and experience is delivered. To achieve this, researchers need to move from a ‘box ticking’ analysis culture to one that is a blend of creativity and analysis, drawing on the integrating of multiple datasets and, in doing so, accepting that often these datasets, both quantitative and qualitative, will be imperfect.

Acknowledgement

Dr Keith Meadows would like to acknowledge that the premise of this article is based on the original work by David Smith and drawing on both personal communications and the content of his book *The Art and Science of Interpreting Market Research Evidence*.

References

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2. Visit: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf

3. Smith DVL and JH Fletcher, *The Art and Science of Interpreting Market Research Evidence: 2004*

About the author



Dr Keith Meadows holds a PhD in psychology from the University of London, UK, and has held academic posts at a number of universities conducting health and market research across Europe. He has more than 30 years’ experience in the development and evaluation of clinical outcome assessment measures, qualitative research, and survey design. Keith founded Health Outcomes Insights (formally DHP Research & Consultancy) to help healthcare agencies and pharmaceutical companies across a range of conditions get targeted answers to patient behaviour, experience, and outcomes using both traditional and innovative approaches.

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