

Measuring Real-World Outcomes

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What is An Outcome?

- Potential target of an intervention
- Potential result of an exposure
- A future or current event or state
- Can be good or bad – e.g. cure versus adverse event
- Can be clinically meaningful or surrogate

A Variety of Outcomes

- Health events – e.g. an MI
- States – e.g. Quality of Life, disease ratings
- Physiologic measures – e.g. blood pressure
- Laboratory results – e.g. kidney function tests
- Disease response – e.g. tumour size post therapy
- Costs or resource use

Real World Outcomes

- Include measures of health, well-being, system effectiveness, drug effects good and bad as seen in the real world etc
- Differs from outcomes measured on very selected populations under controlled circumstances
- Should reflect things that matter to patients, practitioners and decision makers

Impactful Real World Outcomes?

- POR is generally at the applied end of health research
- Ideally your real world outcome will clearly be intended to improve policy, practice, system effectiveness, patient health (defined very broadly) or experience demonstrable through KT
- Earlier phase research that can clearly lead to a more definitive study may be OK if the KT plan is appropriate

Keeping You Honest

- Specify a primary outcome – should be the most important, should be used in sample size estimation, should be measured carefully
- Can also list secondary outcomes –
 - explanatory,
 - exploratory,
 - supportive

Desirable Characteristics

- Meaningful to patients, providers or payers – e.g. survival change versus serum sodium change
- Readily measured & interpreted
- Potentially modifiable
- Linked to intervention or exposure by likely pathogenetic mechanisms
- Acceptable to measure and not too costly

Ascertainment

- Active versus passive
- Objective versus subjective
- Importance of definition
- Primary sources versus secondary data
- A role for blinding?

Ascertainment and Assignment

- For important and primary outcomes
 - Use clear predefined measures
 - Specify how and when the measures will be made
 - Train all observers
 - Do audits to assess accuracy of measures
 - Assignment of outcome status may require blinded adjudication by experts reviewing the best available data

Timelines

- Consider disease course
- Time required to see response to exposure or intervention
- Arrange appropriate follow up
- Tension between need to know now versus having to wait to find out (and risking drop-outs and drop-ins)

“Contrast” CIAKI v. Hep B Vaccine

- Case 1. Radiocontrast may cause acute kidney injury – do we count cases that need dialysis or measure change in serum creatinine and when?
- Case 2. A new vaccine is tested to prevent Hepatitis B. Do we measure protective antibody levels post vaccine or count cases of Hepatitis B and when?

Consider Core Outcome Sets

e.g. Current best evidence
recommendations on measurement
and interpretation of physical function
in patients with chronic kidney disease
Koufaki, P. Kouidi, E.

If you Google “Core Outcome Sets” & the name of a common disease you may find that someone has done the work for you

Use Standardized Measures When Possible








- Generic or condition specific scales that have known reliability, validity and sensitivity
- Allows easier interpretation and comparison across studies
- Likely to provide more “true” results

Examples of Standardized Measures

- For QoL – SF-36, WHO-QUAL_Bref
- For utilities – HUI, EQ-5D
- For Asthma – Asthma Control Questionnaire
- For Crohns disease – CD Activity Index
- For psoriasis – P Area & Severity Index
- For Rheumatoid arthritis – ACR20 i.e. 20% improvement
- For MS – Extended Disability Status Scale

A favourite For Irritable Bowel Disease

Bristol Stool Chart

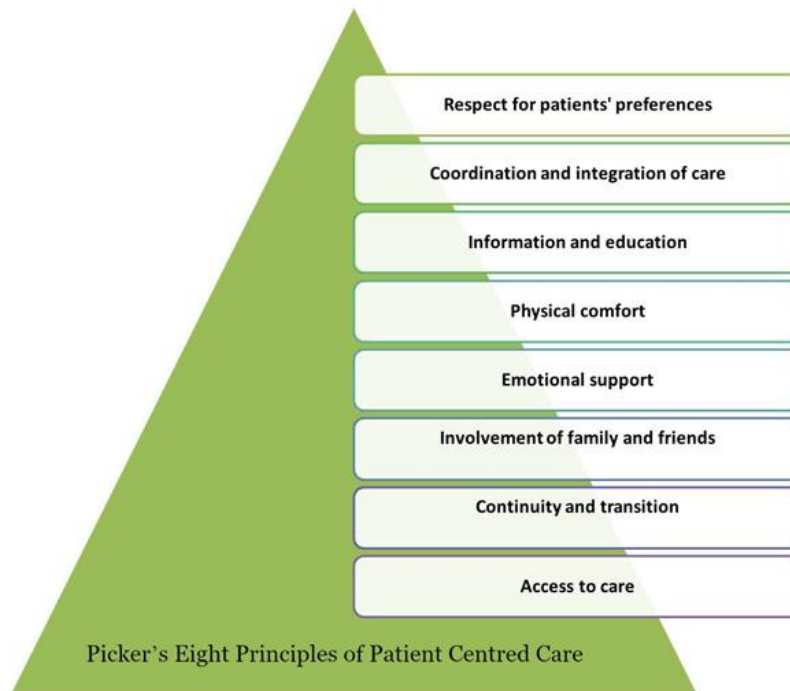
Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

PROMs & PREMs

PROMs	PREMs
Measures impact of an illness or health condition from the patient's perspective	Captures the patient's view of what happened during their healthcare visit (process of healthcare)
Examples: quality of life, symptom severity, functional status, health status	Examples: Communication and trust in staff, cleanliness, timeliness
Used to monitor the progress of a health condition or whether a treatment has been effective by comparing results over time	Used to evaluate and monitor service delivery

Note: these correlate only a little $r = 0.2$

Basis for Outcomes?



Guidelines for PROMS

- COMET – Prinsen CAC et al, How to select outcome measurement instruments for outcomes included in a “Core Outcome Set”- a practical guideline. *Trials* 2016;17:449.
- COSMIN – Mokkink LB. The COSMIN checklist for evaluating the methodological quality of studies on measurement properties. *BMC Med Res Methodol* 2010;10:22

Surrogate Outcomes

- Used mainly when feasibility of measuring the clinically relevant outcome is poor
- This might be an issue of expense, timing, or just rarity
- A surrogate is a marker that would be expected to change in anticipation of the clinical event e.g. a tumour marker, LDL level, serum sodium or the like

Valid Surrogates Must

- Predict clinically important outcomes
- Predict changes in these outcomes when the surrogate changes with intervention
- Be on the causal pathway between the therapy and the clinical outcome
- Have a similar dose response to therapy as does the clinical outcome

Caution

- Many surrogates have not been adequately validated
- A surrogate may only be valid for a set population, intervention and outcome



Some Additional Resources

- <https://www.youtube.com/watch?v=gJWVj0okmmQ>
- <https://www.youtube.com/watch?v=dSmOsikZg8I>
- <http://www.healthmeasures.net/explore-measurement-systems/promis>

