PRO'S in Clinical Trials

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Inclusion of PRO's in Clinical Trials

Key Factors for Success

- Integral part of trial
  - a priori inclusion in protocol
  - clear hypothesis, sample size
  - entry requirement for trial
  - part of DQM
- Adequately funded
- PRO Trial subcommittee
- "Culture" embraces importance of PRO

PRO's in Clinical Trials

Instrument Selection

- Tailored to study question/intervention
- Reasonable respondent burden
- Validated
- Clinical significance - distribution-based
  - anchor-based

PRO's in Clinical Trials

The BEST Study

- RCT of group psychosocial support (vs. no support) in metastatic breast cancer
- n=235
- 1° outcome - survival
- 2° outcome - POMS*
  - IES
  - EORTC QLQ-C30
  - PAIS
  - PAIN*

Goodwin PJ NEJM 345:1719-26, 2001

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The BEST Study Outcomes

1. Survival → no significant effects

2. PRO's → POMS* - significant ↓ distress (TMD)

   Pain - significant ↓ suffering from pain

   (interaction with baseline score – effect greatest in most distressed women)

   Others - no significant effects

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The BEST Study – Missing Data (EORTC QLQ-C30)

		% Complete (alive)
Baseline		100%
Follow-up	**- 4 months**	60%
	- 8 months	46%
	-12 months	48%

- no difference in completion rate between study arms (< 1% missing items/subscales on completed questionnaires)
- missingness related to poor QOL, imminent death (2 months)
- outcome of analysis not related to missingness – (CCA, available case analysis, various simple imputations, multiple imputations)

Bordeleau L et al. JCO 2003

PRO's in Clinical Trials

The BEST Study – Relative Efficiency

	Group Intervention	Improved Mood*	Disease Progression**
POMS TMD	1.0	1.0	1.0
IES Total	0.01	0.05	0.3
PAIS Total	0.56	0.03	3.8
EORTC EF **QOL**	0 0.12	0.15 0.08	0.03 6.5
PAIN	0.16	0.01	3.1

* improved TMD ≥ 0.2 ES @ 6 months

** death within 6 months