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*International Society
for the Study of Pleura
and Peritoneum*



QUALITY OF LIFE & SURGICAL PALLIATION

Clinical Trial Endpoints: Quality of Life in Peritoneal Disease

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Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

Quality of Life: Research Methods

- Quantitative
 - Patient-reported outcomes (PROs)
 - Surrogate measures
- Qualitative
 - Patient interviews
 - Focus groups
 - Family interviews
 - Open-ended survey questions

Patient reported outcomes (PROs) - Subjective

- Subjective Measures
- Multiple surveys based on what is most meaningful
 - General (FACT-G; MDASI; COH-QOL; EOETC QLQ – C30)
 - Disease specific
 - Symptom specific (MD Anderson Symptom Inventory - GI, numerical analogue scales [e.g. pain])
 - Functional (SF-36)
 - Preference-based (EQ-5D; SF-6D)
 - PROMIS® (Patient-Reported Outcomes Measurement Information System)
<https://www.healthmeasures.net/explore-measurement-systems/promis>

Why Use PROMIS?

- Developed and validated with state-of-the-science methods to be psychometrically sound and to transform how life domains are measured
- Designed to enhance communication between clinicians and patients in diverse research and clinical settings
- Created to be relevant across all conditions for the assessment of symptoms and functions
- Available in multiple formats and easily integrated into diverse administration platforms
- Translations available in Spanish and many other languages
- **Strategic for Federal funding

Surrogate QOL Endpoints

- Objective measures
- Maybe most meaningful
- Multiple possible endpoints for peritoneal disease
 - Hospital Days
 - Hospitalizations
 - NG tube days
 - Morbidity
 - Procedures endured (ascites)
 - Amount of Carcinomatosis
 - Survival
 - Composite measure
 - e.g. Days out of hospital and alive

Qualitative endpoints

- Patient's own words
- Analysis time-consuming
- May be helpful in determining outcome importance (preparatory for clinical trial)
- Not useful as primary outcome in clinical trial, but can get meaningful information that can inform outcomes or next study

Choosing the correct primary endpoint

- Is it believable to the clinical/research community?
- Can it be funded?
- Is it important to the patient advocate community?
- Can it be reliably measured?
- What is the reasonable timeframe to evaluate?
- Will patients complete surveys? Will need surrogate to complete surveys?
- Are there secondary endpoints that are important (especially if primary outcome does not pan out)?

The Malignant Bowel Obstruction (MBO) Example

International Conference on Malignant
Bowel Obstruction (ICMBO)

PI: Robert S. Krouse, MD

NCI R13 CA110771

ICMBO Objectives

- 1. Using MBO as a model, explore clinical, research, ethical, and cultural issues related to implementing prospective studies for patients with advanced cancer.**
- 2. Through discussion and debate by relevant experts, develop an integrated methodological framework for prospective, randomized studies of patients with advanced cancer.**
- 3. Apply integrative palliative care research methods and an implementation framework in developing a prospective randomized trial for patients with MBO.**

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Organization



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Table 1 Domains and Selected Examples of Measures for Research in Palliative and End-of-Life Care^a

Domain	Measurement Tools
Symptom management	McGill Pain Questionnaire, Wisconsin Brief Pain Questionnaire, Brief Pain Inventory, Memorial Pain Assessment Card, Edmonton Symptom Assessment System, Memorial Symptom Assessment Scale, Profile of Mood States, Center for Epidemiologic Studies Depression Scale, and RAND Mental Health Inventory
Whole person and maintaining QOL	QUAL-E, McGill QOL Questionnaire, Missoula-VITAS QOL Index, European Organization for Research and Treatment of Cancer QOL Questionnaire Core 30, Functional Assessment of Cancer Therapy - General, and QODD
Functional aspects	Index of Independence in Activities of Daily Living Barthel Index, Physical Self-Maintenance Scale, Rapid Disability Rating Scale, Stanford Health Assessment Questionnaire, and Functional Independence Measure
Satisfaction	TIME After-Death Bereaved Family Member Interview, Quality of End-of-Life Care and Satisfaction with Treatment (QUEST), Medical Outcome Study Satisfaction Survey, Family Satisfaction in the Intensive Care Unit, Picker-Commonwealth Survey, and FAMCARE Scale
Relationships	Meaning in Life Scale, QODD, and TIME After-Death Bereaved Family Member Interview
Decision making and care planning	TIME After-Death Bereaved Family Member Interview, POS, and QUAL-E
Continuity and communication	POS, QODD, QUEST, Picker-Commonwealth Survey, Smith-Falvo Patient-Doctor Interaction Scale, and McCusker Scale
Family burden and well-being	Caregiver Strain Index, Caregiver Reaction Assessment, Grief Resolution Index, and Anticipatory Grief Scale
Quality of death and end-of-life experience	Spiritual Well-Being Scale, Spiritual Perspective Scale, Death Transcendence Scale, POS, QUAL-E, QODD, and TIME After-Death Bereaved Family Member Interview

^aSee TIME (<http://www.chcr.brown.edu/pcoc/toolkit.htm>) and end-of-life care and outcomes summary (www.ahrq.gov/clinic/epcs/sums/eolsum.htm) for additional measures and information.^{18,27,30}

Mularski RA, et. al. Measuring Outcomes in Randomized Prospective Trials in Palliative Care, JPSM 2007

Table 2 Categories and Example of Palliative and End-of-Life Care Outcomes in a Trial of MBO Therapies

Condition-related outcomes	Patient-related outcomes	Family related outcomes
Survival duration	Ability to return home	Caregiving burden
Symptoms	QOL (physical, emotional, social, spiritual)	Emotional distress
Impairment to eating	Satisfaction with decision making	Financial burden
Resource use (hospital days, rehospitalization rates)	Overall patient satisfaction	Family perception of the quality of patient's care
Medical expenses	Rating of worth of intervention	Family satisfaction

Mularski RA, et. al. Measuring Outcomes in Randomized Prospective Trials in Palliative Care, JPSM 2007

Outcome measures

Primary Outcome measure

- Number of “good days” as defined by days outside the hospital without an NG tube or IV hydration (a difference of two weeks in 10 week time period)
- 68 patients per arm (total 136)
 - 90% power to detect a mean difference of 14 “good days”
 - based on a t-test at the two-sided 0.05 significance level

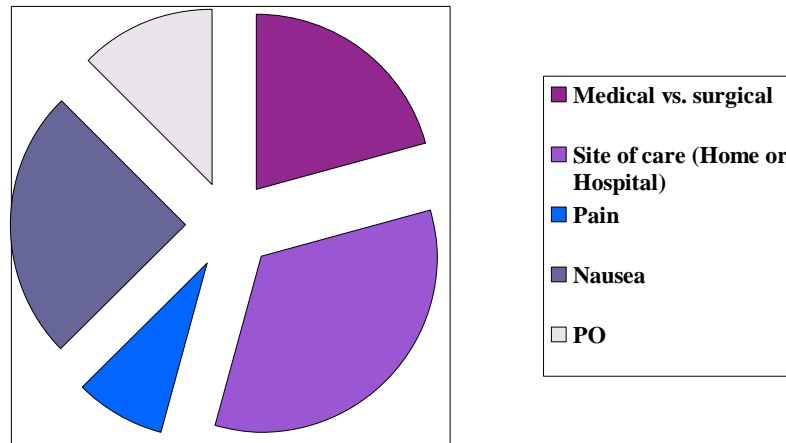
Secondary Outcome measures

- QOL
- Nutrition
- Recurrence of obstruction
- Economic
- Morbidity/Mortality
- Survival

Anthony T, et. al., Report of the Clinical Protocol Committee: Development of Randomized Trials for Malignant Bowel Obstruction, JPSM 2007

Outcome preference for patients with MBO

- Relative importance of 5 key goals (n=28):



Casarett, U of Penn, unpublished.

Importance of Outcome

The primary endpoint is “Days out of the hospital and alive”. There is ample evidence that the primary goal for patients with end stage disease is to be at home/out of the hospital.

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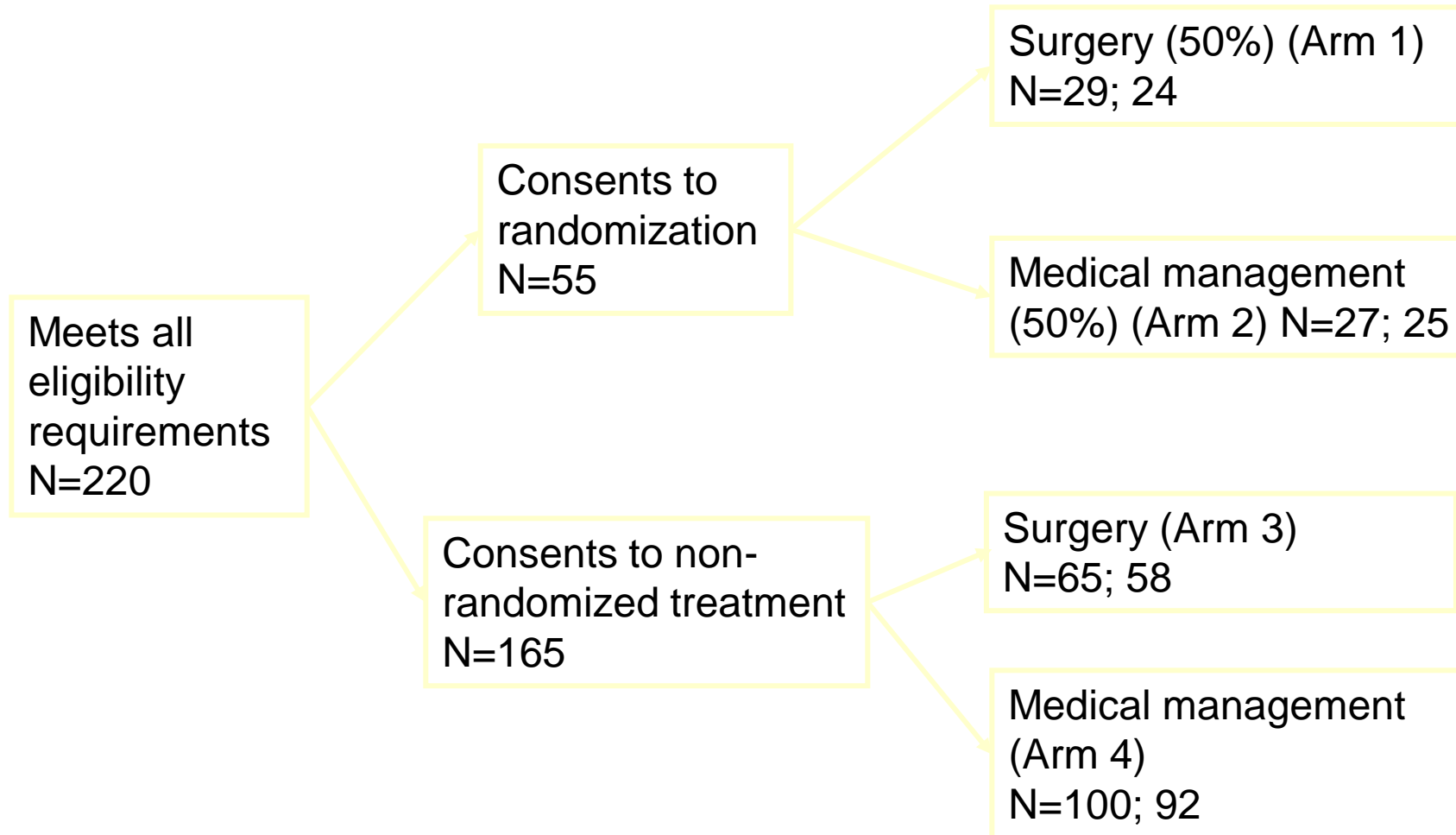
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S1316 Schema (revised)*



*Initially 200, revised to 220 to attain randomization goal (white), **final accrual 221; eligible 199**.

The S1316 Example: Primary Endpoint

“Good days” = days out of the hospital and alive in the first 91 days (13 weeks) after registration

Secondary Endpoints

- **Days with NG**
- **Days eating (Diet recalls)**
- **HRQOL (MDASI-GI, EQ-5D-5L)**
- **Morbidity/Mortality**
- **Survival**

Dietary Recall

- Self-reported diet measurement methods
- Relies on patient or caregiver to report foods consumed in prior 24-hour period
- Collected by Arizona Diet, Behavior, Quality of Life Assessment Lab through phone contact

What are the most important QOL outcomes in peritoneal disease?

- PRO
 - Overall QOL
 - Preference-based QOL
 - Nausea
 - Vomiting
 - Bloating
 - Pain
 - Constipation
 - Function
- Surrogate
 - Ascites
 - Carcinomatosis
 - Morbidity (Fistula; Wounds)
 - Eating
 - Hospitalization (Days; Admissions)
 - Healthcare utilization
 - Survival

Conclusions

- There is no defined quality of life endpoints for peritoneal disease trials
- There are many important quality of life endpoints for peritoneal trials
- Consensus from the clinical community must define ultimate primary outcomes
- Collecting meaningful secondary outcomes is imperative
- Ultimate question to ask when designing trial: Will the results change clinical practice?