Research vs. Standard of Care
Considerations for the Design & Implementation of your Study

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ITHS: Clinical Research Education Series (CRES)
June 2012
Issues to be Considered in Research vs. Standard of Care

The Nuremberg Code (1947)
Declaration of Helsinki (1964)
The Belmont Report (1979)
Clinical Equipoise

… we will look at the critical aspects and how to operationalize them.
Objectives

• What is the difference between research and standard of care?
• How do you define this difference in the study protocol?
• How can you balance the roles and responsibilities of research vs. standard of care?
Research vs. Standard of Care

Jazz

Classical
What is the difference between research and standard of care?
STANDARD

Anything serving as a type or pattern to which other like things must conform (Stedman’s Medical Dictionary)

STANDARD OF CARE

The level at which the average, prudent provider in a given situation would managed the patient’s care under the same or similar circumstances. (Webster’s New World Medical Dictionary)
standard of care  (STAN-durd ... kayr)

Treatment that experts agree is appropriate, accepted, and widely used.

Also called best practice, standard medical care, and standard therapy.
research study  (reh-SERCH STUH-dee)

A scientific study of nature that sometimes includes processes involved in health and disease. For example, clinical trials are research studies that involve people. These studies may be related to new ways to screen, prevent, diagnose, and treat disease. They may also study certain outcomes and certain groups of people by looking at data collected in the past or future.
Research is done to help find out if a treatment or procedure is good for a large group of people with a certain disease or condition. Research helps to answer questions for the future health of those populations. Standard medical care, however, focuses on individual needs in the present.
What is the difference between research and standard of care?

- Line is sometimes unclear, but it is an important distinction.
- Important not to confuse research with standard of care.
- Departure from standard of care is not necessarily research.
Line is sometimes unclear, but it is an important distinction.
Departure from standard of care is not necessarily research.
What is the difference between research and standard of care?

• **Practice** refers to interventions designed solely to benefit an **individual patient** and have a reasonable expectation of **success**.

• **Research** is an activity designed to test a **hypothesis** and contribute to **generalizable knowledge**.
What makes Research different from “Standard of Care”

- Involves human subjects
- Tests an “intervention” – be it a product, procedure or health care system....in order to improve standard of care!
- Measures effects over a period of time
- Most have a comparison CONTROL group
- Must have method to measure intervention
  - this is captured in the protocol and this must be stuck to meticulously if the question is to be answered!!
- Focuses on unknowns: effect of intervention
- Must be done before a treatment is part of standard of care
- Standard of Care is all about clinical judgement decision/flexibility – research need to stick with the protocol, no deviation – within your clinical judgement
Case Example

The New England Journal of Medicine

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*
History of the ARDS Network

In order to hasten the development of effective therapy for Acute Respiratory Distress Syndrome (ARDS), the National Heart, Lung, and Blood Institute, National Institutes of Health, initiated a clinical network to carry out multi center clinical trials of ARDS treatments. The ARDS Network was established as a contract program in 1994 following a national competition.
Chest X-ray of ARDS patient

Normal

ARDS
ARDS network study

Acute Onset of:
1. PaO2/FiO2 <= 300
2. Bilateral infiltrates consistent with pulmonary edema on frontal chest radiograph
3. Requirement for positive pressure ventilation via endotracheal tube.
4. No evidence of left atrial hypertension.

Patients age > 18 with no exclusion criteria were randomized to tidal volumes of 12 mL/kg or 6 ml/kg.
Study Results

• Study stopped after 2nd interim analysis (861 subjects).

• Reduction of mortality by 22%.

First treatment for ARDS other than supportive care.
After Publication

The “Control” group that was used in the study was challenged.

But, the Network demonstrate how they defined it in subsequent publications.
How do you define this difference in the study protocol?
PROTOCOL???

Research Question

Methods and Analysis

Protocol

Literature review

Methodology & Ethical Issues
Where in the protocol is SOC discussed?

• **Background and Significance**

Briefly give the background to the present proposal, critically evaluate existing knowledge, and specifically identify the gaps which the project is intended to fill. Cite literature and include a list of references.
Defining Standard of Care

THE EVIDENCE PYRAMID

- Systematic Reviews and Meta-analyses
- Randomized Controlled Double Blind Studies
- Cohort Studies
- Case Control Studies
- Case Series
- Case Reports
- Ideas, Editorials, Opinions
- Animal research
- In vitro ('test tube') research
Websites Used for Standard of Care

• www.nhlbi.nih.gov
• www.ahrq.gov
• www.guideline.gov
• www.americanheart.org
• www.nice.org.uk
Clinical Research Protocol

Clearly define the standard of care (SOC) of the population from the beginning.

- Would the subject receive this care absent the clinical trial?
- Can you back yourself up in the literature?
- Does local SOC differ from national standards/guidelines?
- Documentation of protocol deviations
Documentation of Protocol Deviations

• 21 CFR 3 12.23(a)(6)(ii) states, "A protocol for a Phase 2 or 3 investigation should be designed in such a way that if the sponsor anticipates that some deviation from the study design may become necessary as the investigation progresses, alternatives or contingencies to provide for such deviation are built into the protocols at the outset. For example, a protocol for a controlled short-term study might include a plan for an early crossover of nonresponders to an alternative therapy."
Documentation of protocol deviations

Subject safety is #1.
What do you need to do to protect the subject?

• **Expected** protocol deviations
  – If the possibility of certain deviations are known then include them in the protocol – track them

• **Unexpected** protocol deviations
  – Track them extra carefully – look for a pattern
How can you balance the roles and responsibilities of research vs. standard of care?
Conflict of Interest

Clinician?

Clinician Researcher?
Clinician

✓ acting in the best interests of the individual patient medically
Clinical researcher

✓ answering questions
✓ testing hypotheses

To benefit humanity in general.
You have a great responsibility not only to the subjects in front of you but to patients you will never meet.
Questions