

The Informed Consent Process for Human Research Must be Strengthened, Not Weakened

**HHS Meeting on Human Subjects Research
Studying “Standard of Care” Interventions**

August 28, 2013

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“Standard of Care” Research: a misnomer for an experiment

Testing comparative risks of subunits of a broad range of what may itself be a standard of care is really conducting an experiment. With subunit risks certainly differing from those of the broad range, subunits themselves can not be a standard of care.

The main source of conflict precipitating this meeting are contrasting views as to whether interventions in SUPPORT and similar studies are more like experiments, or more like the existing standards of care.

NEJM letter attacking OHRP conclusions confirms authors' stance on this conflict

“The infants...were randomly assigned to **oxygen-saturation targets that were consistent with standard clinical care** at the participating institutions. The conclusion of the OHRP that the study's **experimental evaluation of these otherwise routinely used oxygen-saturation levels** exposed subjects to additional risk (above the risks of routine clinical treatment) is not supported by the evidence.”

“Although we acknowledge that the permission forms could have been improved...”

Oxygen Experiment Known Uncertainty About Risk of Death

Cole et al., Resolving Our Uncertainty About Oxygen Therapy, Pediatrics 2003;112:1415-18:*

- “Several hundred patients...may be sufficient to demonstrate important difference in severe ROP. However, a much larger sample... will be needed to exclude smaller, important differences in outcomes such as mortality and disability to address real concerns about the safety of lower oxygen tensions.”

Standard of Care and informed consent

The underlying principle behind arguments opposing fully informed consent in such experiments is that it is necessary, via inadequately informed consent, to blur the line between research and standard of care to facilitate more consent and participation.

The origins of this thinking are not recent:

1993 Statement by noted British Neonatologist, Dr. Nina Modi

“To seek truly informed consent for participation in a research study is to oblige parents to listen to complex medical arguments that spell out the uncertainties of current practice. Although it might be argued that parents have a right to know about all aspects of their baby’s care, this would mean that, in many instances, distressed parents were forced to make decisions that they would not normally be asked to make.”⁶

Individualized care: Therapeutic Misconception

“Therapeutic misconception” was coined in 1982, when participants in several studies were found to be unaware of the difference between participating in a study and receiving personalized care in the clinical setting.

It was originally described as a “research participant’s failure to recognize how personal care (i.e. the obligation of physicians to make medical decisions solely with the patient’s interest in mind) may be compromised by research procedures.”

Individualized care: Therapeutic Misconception (cont'd)

A more recent study involved 225 participants who had previously consented to one of 25 clinical trials. 31.1% of participants expressed inaccurate beliefs regarding the degree of individualization of their treatment. As a result, they may have failed clearly to appreciate the risk/benefit ratio of the research project to which they were being asked to consent.

Misinformation about standard of care engenders Therapeutic Misconception

Blurring the distinction between standard of care and experiments such as SUPPORT is fostered by inappropriate, inaccurate portrayals of the experiment in the consent forms. Implicitly, the consenter can be led to believe that the experiment may involve individualized standard of care as seen in our analysis of 22 consent forms from SUPPORT.

SUPPORT Study Consent Forms Identifying Experimental Procedures

The sample consent form and 21/22 IRB-approved consent forms characterized the experimental oxygen arms in one or more of the following ways:

- “standard of care” (15/22)
- “within normal range” or “normal” (13/22)
- “within the range currently used” (7/22)
- “considered by some units to be the desired [or best] approach” (3/22)

SUPPORT Study Consent Forms

Risks of the Experimental Procedures

- Death and ROP were both components of the primary endpoint being assessed in the oxygen experiment and were reasonably foreseeable risks.
- 13/22 consent forms stated “Because all of the treatments proposed in this study are standard of care, there is no predictable increase in risk for your baby” or something very similar.
- None mentioned risk of death for the oxygen experiment.
- 20/22 consent forms failed to identify ROP or brain injury as a risk of the research.

Protecting Participants of Clinical Trials Conducted in the Intensive Care Unit*

“In the ICU....the investigator’s primary interest is to gain valid and generalizable knowledge from research, whereas the clinician’s primary interest is to benefit individual patients. However, the critically ill patient and their family, seeking a life-saving intervention, are dependent on their clinician and may attribute therapeutic intent to an investigational product or procedure.” (stated in the context of Therapeutic Misinformation)

Protecting Participants (cont'd)

- “the risk of therapeutic misconception could be reduced (though not eliminated) by using a ‘neutral discloser’, someone who has no direct involvement with the research study and who informs potential participants about how research participation would differ from clinical care. In the ICU setting using a neutral discloser might help ensure that participants or their surrogates understand how participation in research will affect clinical management of the patient.”

Protecting Participants (cont'd)

Other suggestions for protecting participants:

“While the protection of participants can be advanced through a variety of mechanisms—including codes of ethics, institutional policies, consensus statements from prestigious organizations that carry moral weight, and nonbinding federal agency guidance—many authors call for a more authoritative response through federal legislation or agency rule making, even though these routes are often the most difficult to navigate.”

Conclusions

The other remedies to the serious problem of misinformed consent/Therapeutic Misunderstanding must include enhancing surveillance and authority to enforce existing regulations, not weakening either the surveillance, authority or the regulations.

To do otherwise would be to sacrifice critical informed consent-dependent autonomy of patients' decisions about participation in research by deferring to researchers' autonomy to conduct trials with questionably ethical design and unquestionably unethical consent forms.