Risks of Standard of Care (Experimental Aspects of Study)

Patrick Herbison

Continuing Education for IRB Members

SUPPORT Study

- From OHRP letter to site (3/2013):

http://www.hhs.gov/ohrp/detrm_letrs/YR13/mar13a.pdf

- “extremely low birth weight infants”
- “comparing a lower versus a higher range of levels of oxygen saturation in such infants”

SUPPORT Study

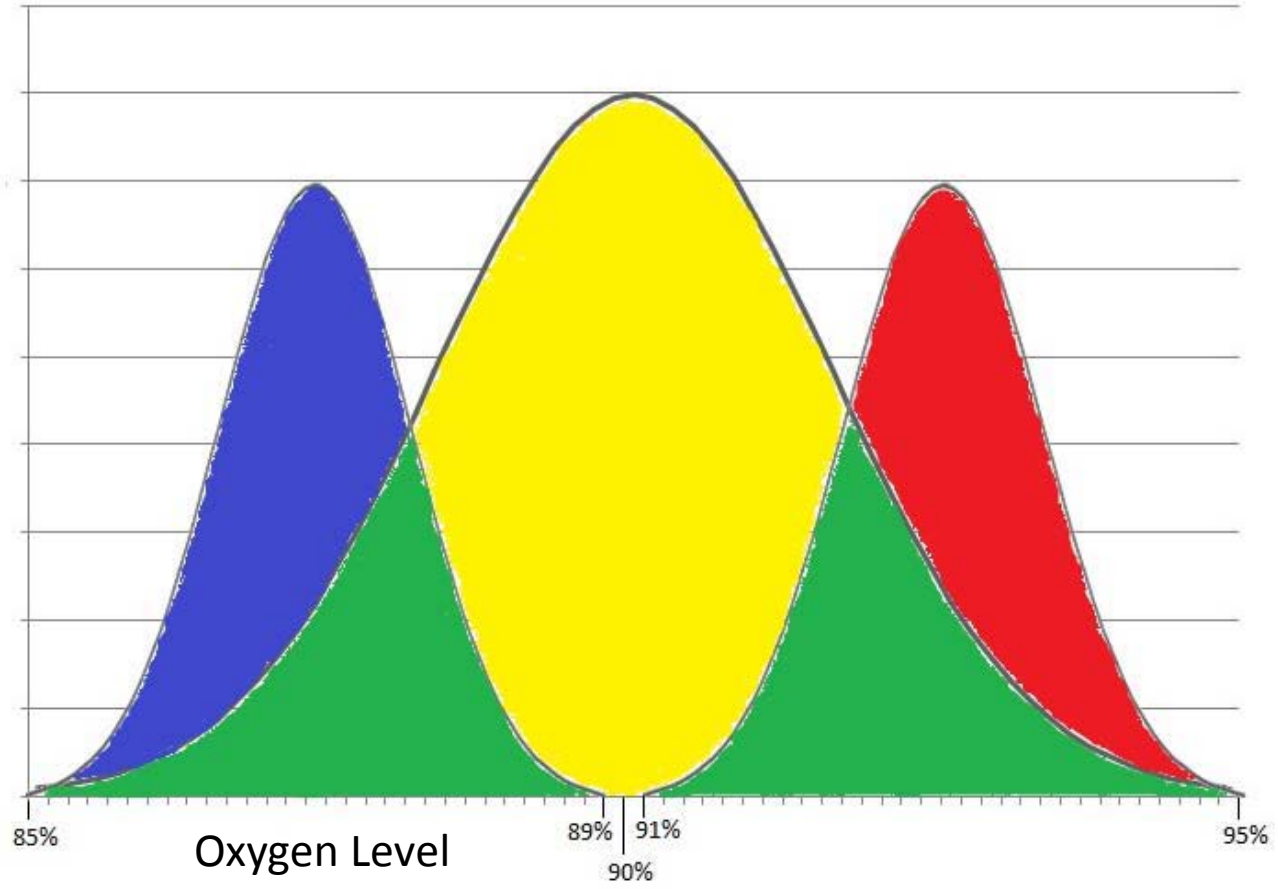
- From OHRP letter to site (3/2013):

http://www.hhs.gov/ohrp/detrm_letrs/YR13/mar13a.pdf

ENDPOINTS

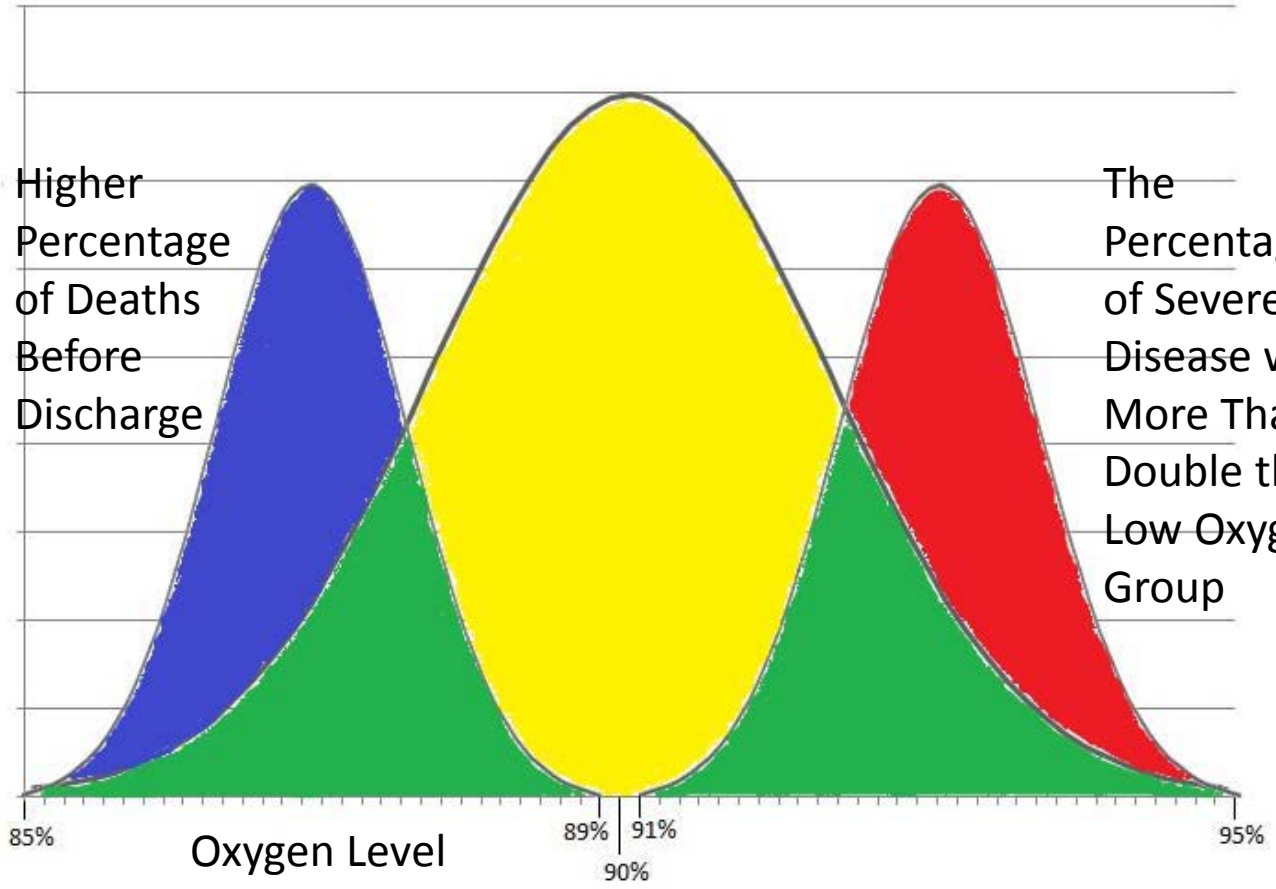
- "survival
- neurological development
- likelihood of developing retinopathy of prematurity (ROP), a serious - often blinding - visual disorder"

Normal Distribution Curves for SOC and SUPPORT Trial Arms Oxygen Levels



Adapted from: The SUPPORT Trial and Beyond: Ethical Perspectives on Comparative Effectiveness Studies, Julie Kaneshiro and Ivor Pritchard, Office for Human Research Protections , October 24, 2014

Normal Distribution Curves for SOC and SUPPORT Trial Arms Oxygen Levels



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SUPPORT Study

- From OHRP letter to site (3/2013):

http://www.hhs.gov/ohrp/detrm_letrs/YR13/mar13a.pdf

- "the low oxygen group had a higher percentage of deaths before discharge"
- "In the high oxygen arm, more than double that percentage of infants developed severe eye disease"

SUPPORT Study

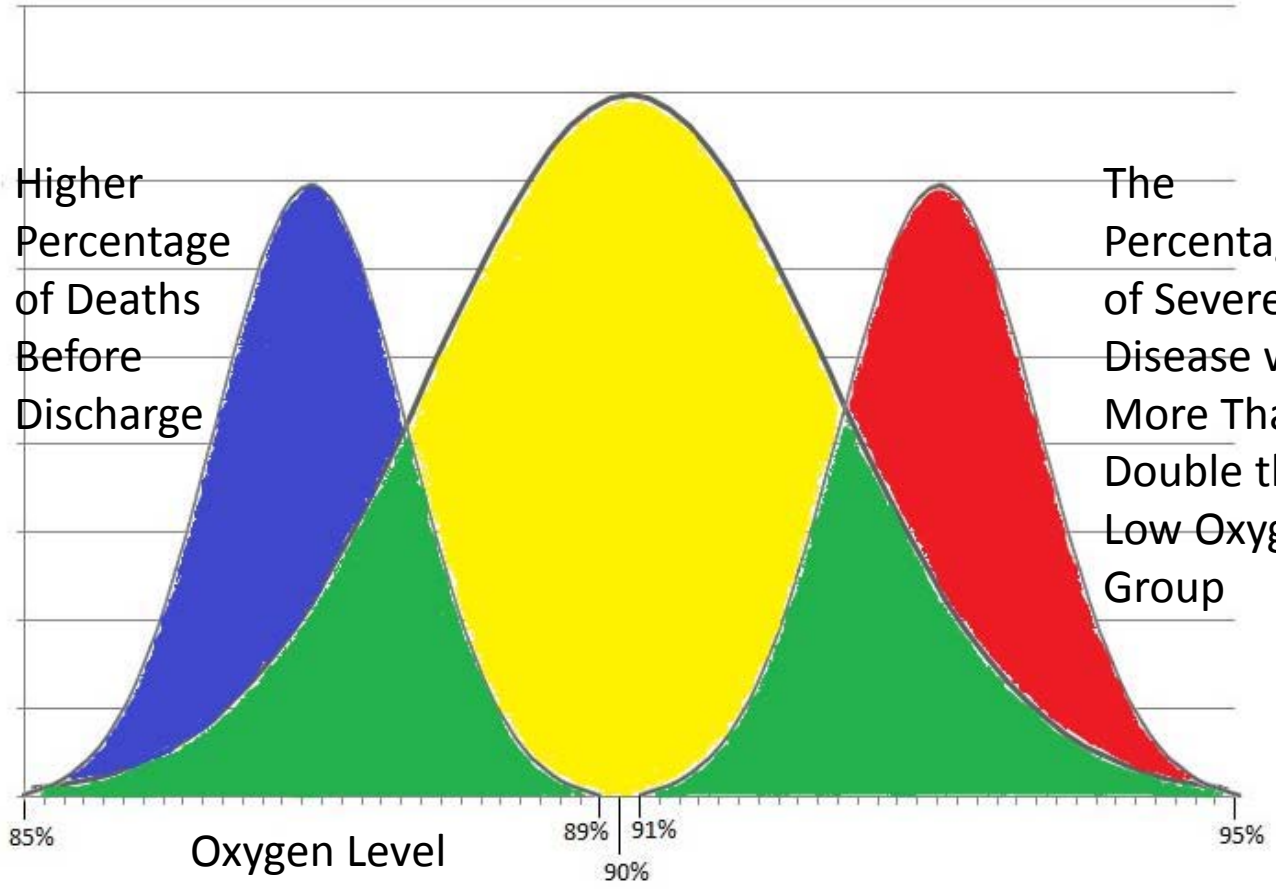
(Violated Regulations)

- From OHRP letter to site (3/2013):

http://www.hhs.gov/ohrp/detrm_letrs/YR13/mar13a.pdf

- Consent form "does not identify any specific risk relating to randomizing infants to a high or low range of oxygen"

Normal Distribution Curves for SOC and SUPPORT Trial Arms Oxygen Levels



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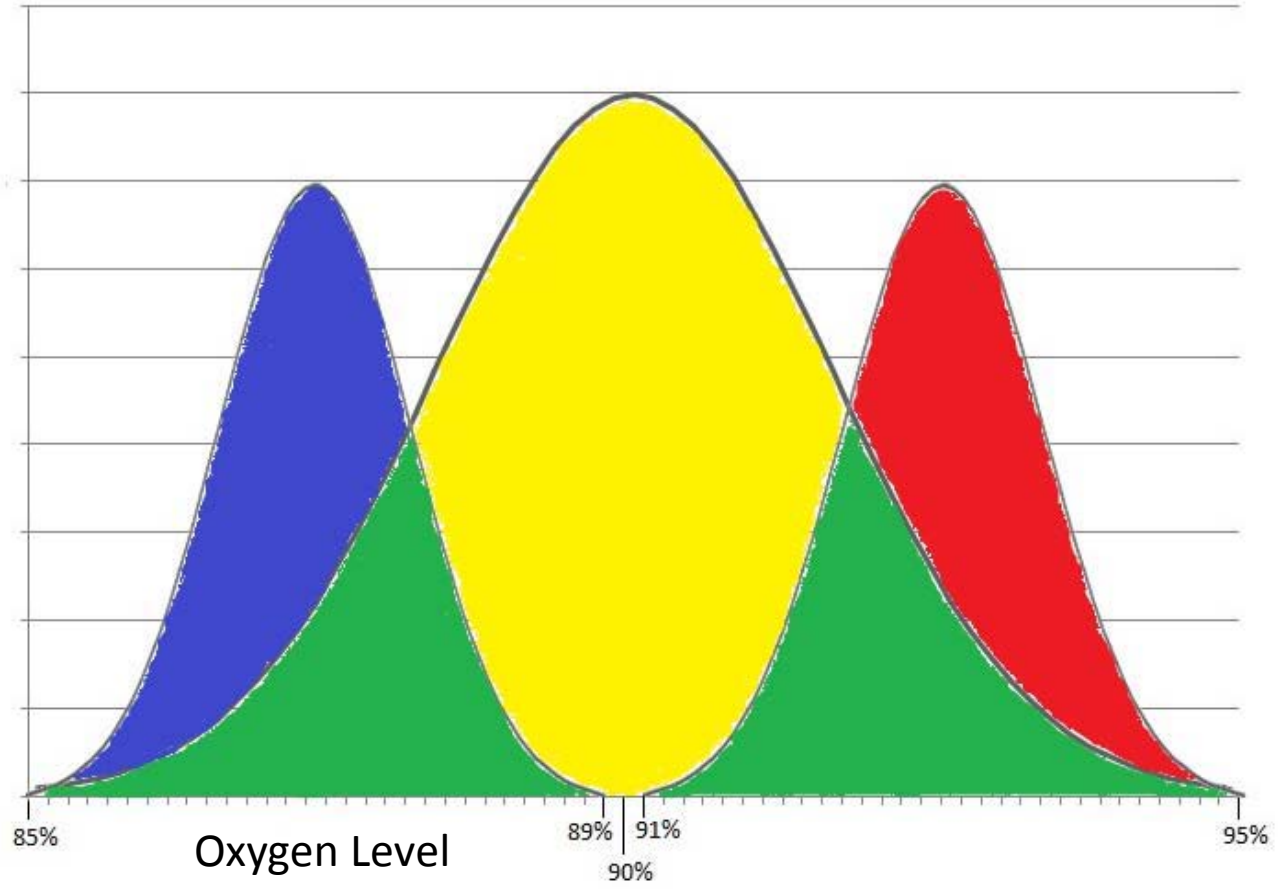
OHRP Draft Guidance

- From OHRP Draft Guidance on Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care (10/2014)

http://www.hhs.gov/ohrp/newsroom/rfc/comstdofcare.html

- (Paraphrased) If the risks of the research are different than what the subject would normally be exposed to, the risks must be in the consent form.

Normal Distribution Curves for SOC and SUPPORT Trial Arms Oxygen Levels



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New England Journal of Medicine Editorial

- (Paraphrased) The OHRP guidance will interfere with conducting research.

- The consent form should “make it clear that the purpose of the research study is to determine whether in fact the net benefits or harms of the treatments now thought to be equivalent are in fact so”

OHRP and Standard-of-Care Research: n engl j med 371;22, november 27, 2014
http://www.nejm.org/doi/full/10.1056/NEJMe1413296

PRIM&R Response to OHRP Guidance

(Public Responsibility in Medicine and Research)

Consent form should describe:

- 1. What is being studied (e.g. comparing the risks and benefits)
- 2. Why it is being studied (e.g. to improve clinical care)
- 3. How the study differs from standard of care
- 4. How the intervention is assigned (e.g. randomly - that they or the investigator can't choose the assignment)

http://primr.blogspot.com/2015/01/prim-response-to-ohrps-draft-guidance_22.html

PRIM&R Response to OHRP Guidance

Consent form should describe:

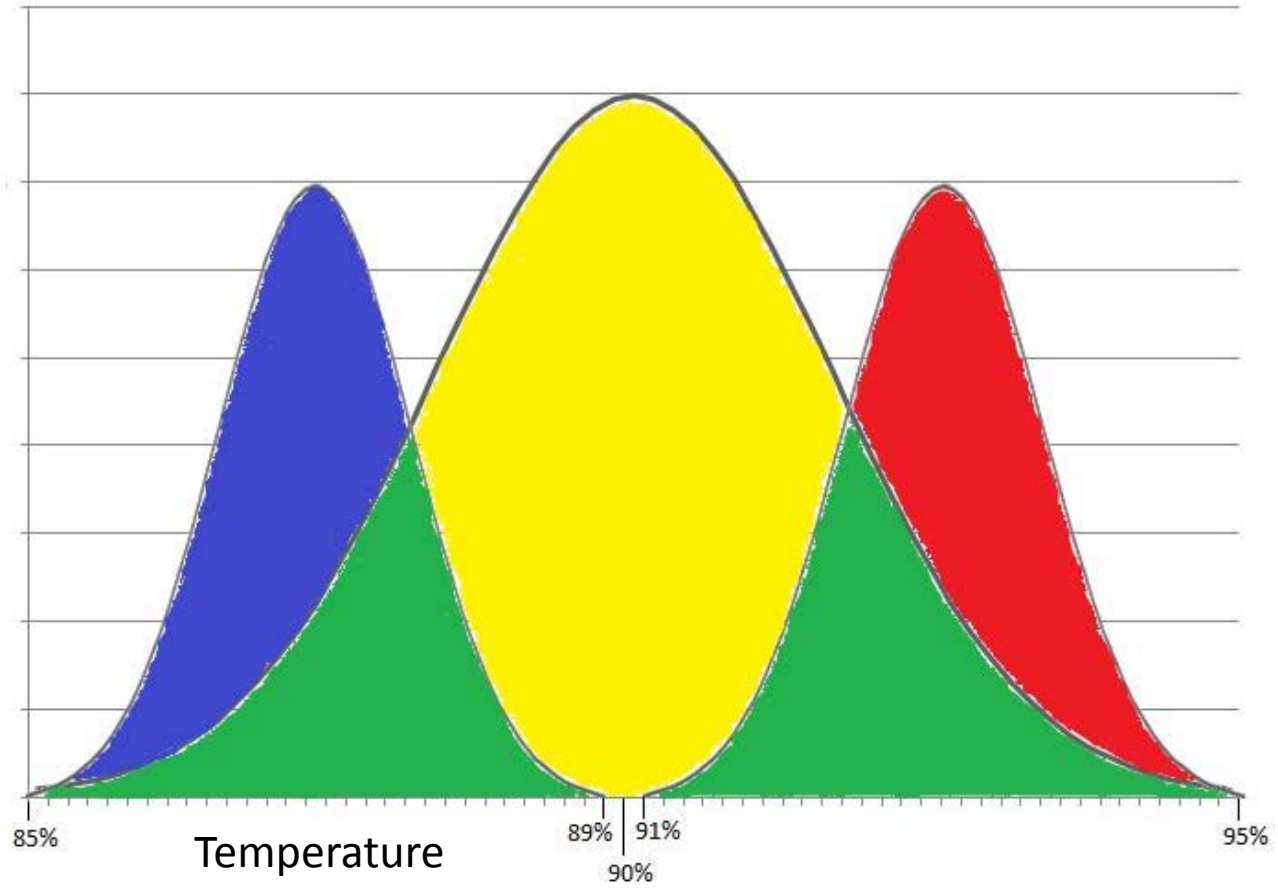
- 1. What is being studied (e.g. comparing the risks and benefits) - Purpose
- 2. Why it is being studied (e.g. to improve clinical care) - Purpose
- 3. How the study differs from standard of care – Experimental Aspect
- 4. How the intervention is assigned (e.g. randomly - that they or the investigator can't choose the assignment) – Probability of Random Assignment (ICH)

Study at Jefferson - Consent

- Maintaining 2 different body temperatures after a stroke.
- “following serious heart attack” the “two temperature ranges have become acceptable standards”
- “This is the first time this is being studied in stroke victims”

Compare to Jefferson Study

How is it Different from Standard of Care



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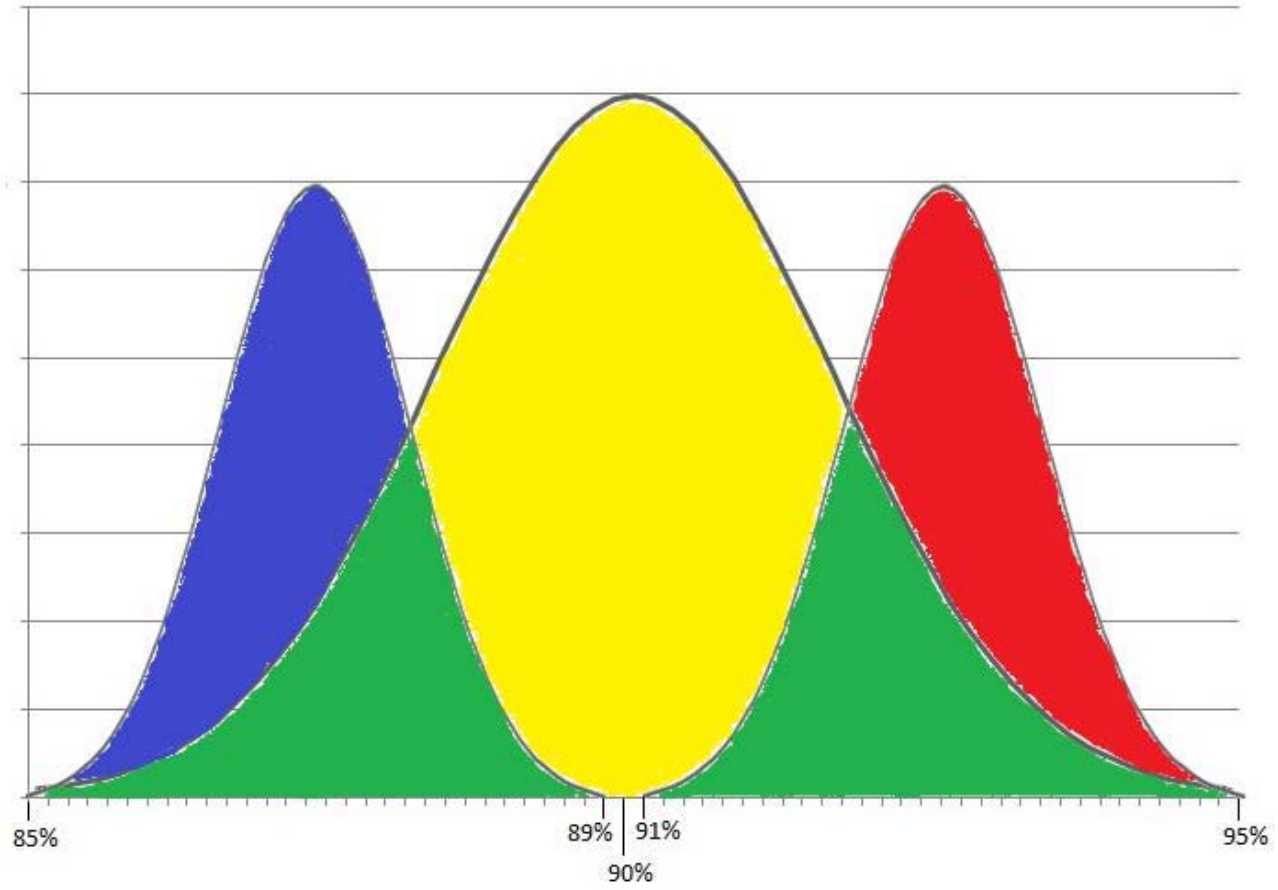
Temperature Ranges Do Not Reflect Those Used in the Study

Consent Form Text

Existing: “try to determine which range actually works best”

Suggested: The goal of this study is to find out if one of the two temperature ranges being tested results in fewer bad effects from the stroke. Depending on which group you are assigned to, you may or may not have more of the bad effects caused by a stroke.

Differences Can be Subtle



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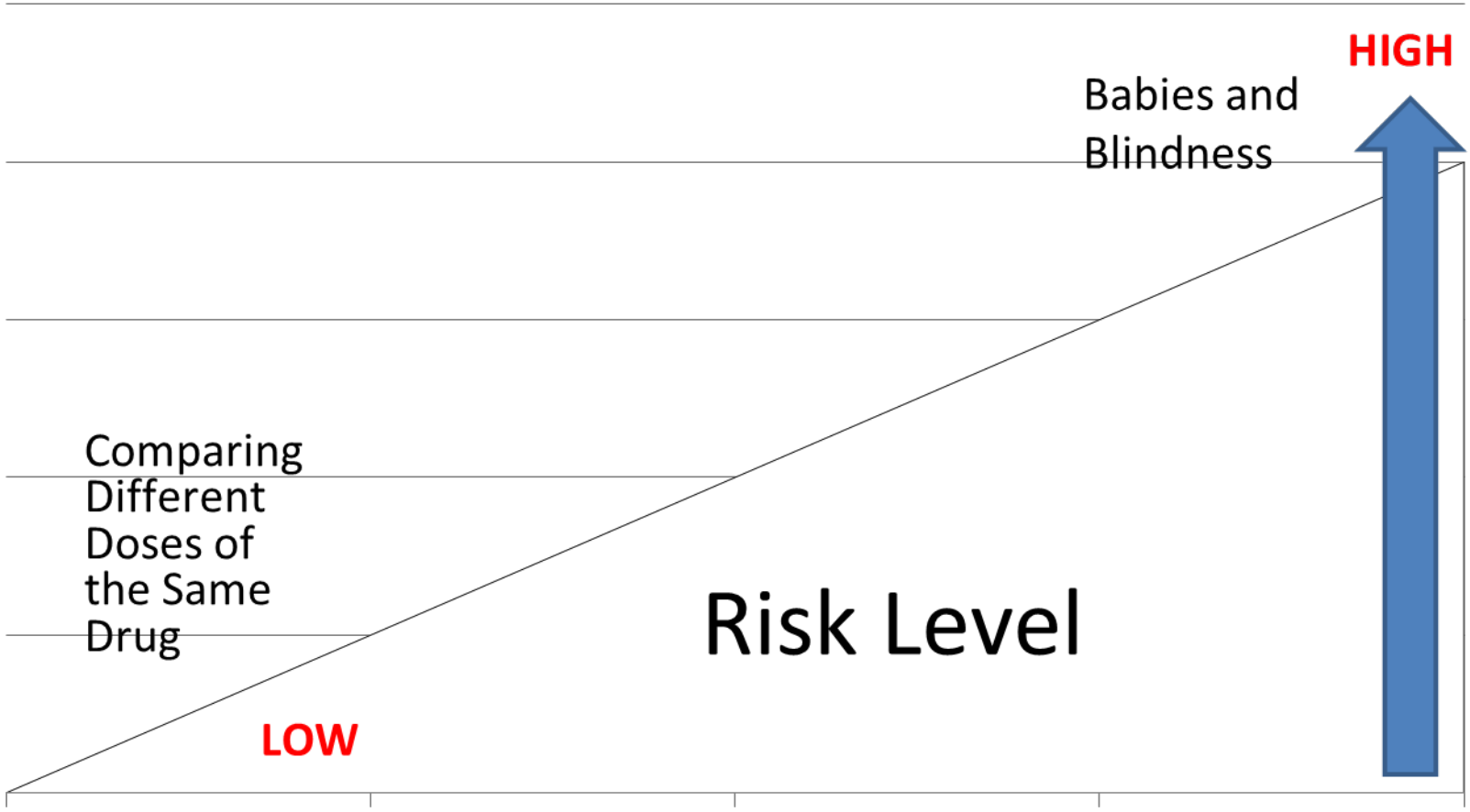
Risk of Not Addressing in Consent



Action

When reviewing consent forms please consider:

Keeping in Mind: Risks of standard of care that the patient would receive outside of research may not need to be included in the consent form.

1. Is a purpose of the study to determine which intervention has fewer or greater risks/benefits?
2. How does the intervention differ from standard of care?
3. Even small changes from standard of care should be described (e.g. randomization).

Modified from PRIM&R List

Consent form should describe:

1. What is being studied (e.g. comparing the risks and benefits)
2. Why it is being studied (e.g. to improve clinical care)
3. How the study differs from standard of care
4. How the risk is different from standard of care
5. How the intervention is assigned (e.g. randomly - that they or the investigator can’t choose the assignment)

- Questions or Comments?