ITHS Clinical Research Education Series

Innovations in Informed Consent

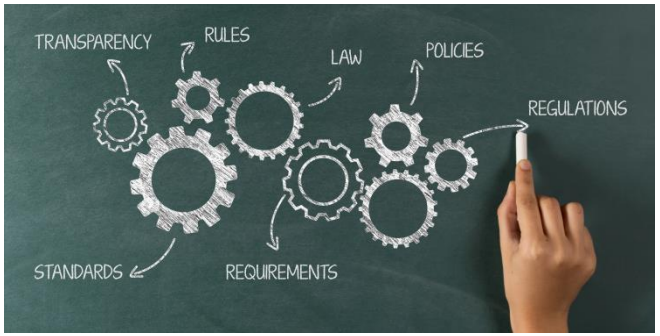
June 20, 2017

ITHS | Institute of Translational Health Sciences

Accelerating Research. Improving Health.

Institute of Translational Health Sciences

CLINICAL RESEARCH EDUCATION SERIES



We love to hear from you!

Please connect anytime.

Mandy Morneault

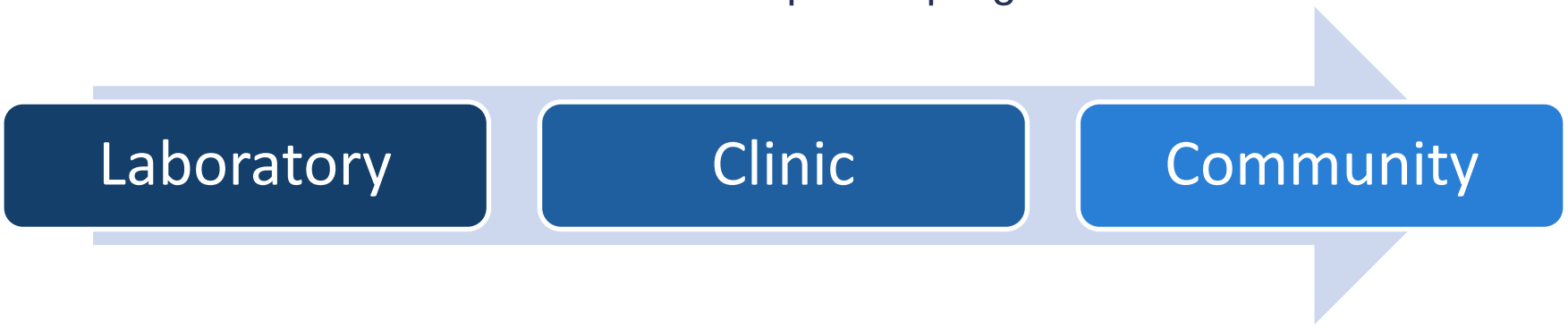
Manager for Regulatory Knowledge and Training, ITHS

vicka@uw.edu

206-616-6339

Our Focus

- Speeding science to the clinic for the benefit of patients and communities throughout WWAMI
- We promote the translation of scientific discovery to practice by:
  - ❑ Fostering innovative research
  - ❑ Cultivating transdisciplinary research partnerships
  - ❑ Ensuring a pipeline of next-generation researchers through robust education and career development programs



WORKSHOP AGENDA

8:30-9:40 Group	**Data on Informed Consent (Seema Shah)** **Dissolving the Monolith of Informed Consent (Adrienne Meyer)** **New Directions for Informed Consent (Bran LeFae)**
9:40-9:50 Break	**Transition to Breakout** • Restrooms are down the hall, to the right
9:50-11:20 Breakouts	**Comprehension** (Lyceum) **Plain Language** (145) **UW Consent Template** (238)
11:20-11:30 Break	**Transition to Closing Remarks** • Restrooms are down the hall, to the right
11:30-11:50 Group	**Closing Remarks** (Lyceum)

CONNECT FOUR

Meet someone from Bastyr	Meet someone who's done eConsent	Meet someone from SCCA	Meet someone who works at Fred Hutch
Meet someone from Swedish	Meet someone who works in Surgery	Meet someone who's tried Tiered Consent	Meet someone who works for ITHS
Meet someone who works in Behavioral Health	Meet someone who works in Global Health	Meet someone who works in Immunology	Meet someone who works at the VA
Meet someone from Seattle Children's	Meet someone who is a Nurse	Meet someone who is not a Research Coordinator	Meet someone who works in Genomics

How to play: Connect four dots in a row to win a small prize or fill three (or more) rows for a chance to win the grand prize!
Dots can be connected horizontally, vertically or diagonally.

PLEASE COMPLETE THE EVENT SURVEY AT THE CONCLUSION OF THE WORKSHOP.

THANK YOU!

Data on Informed Consent

Seema K. Shah, J.D.
Associate Professor, UW Department of Pediatrics
Faculty, Treuman Katz Center
Seattle Children's Research Institute
20 June 2017

ITHS | Institute of Translational Health Sciences
Accelerating Research. Improving Health.

Case Study

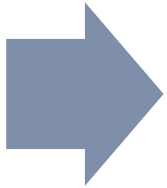
You are a research coordinator obtaining consent for a randomized controlled trial of a new breast cancer treatment vs. placebo (on top of standard of care)

During consent process, one woman is impatient and doesn't want to hear all the information

When you ask why not, she says she thinks the experimental treatment will work

Case Study

How can you tell if this potential subject understands enough to give valid informed consent?



What can you do to improve her understanding?

Learning Objectives

I. Where have we been?

Review the historical, ethical and legal importance of informed consent

II. How are we doing?

Discuss the data on informed consent

III. How can we improve?

Data on improving consent, needs for future research on informed consent

I. Where have we been?

The historical, ethical and legal importance of informed consent

Historical basis of informed consent

Slater v. Baker & Stapleton (1767):

Experimental surgery on an improperly healed broken bone

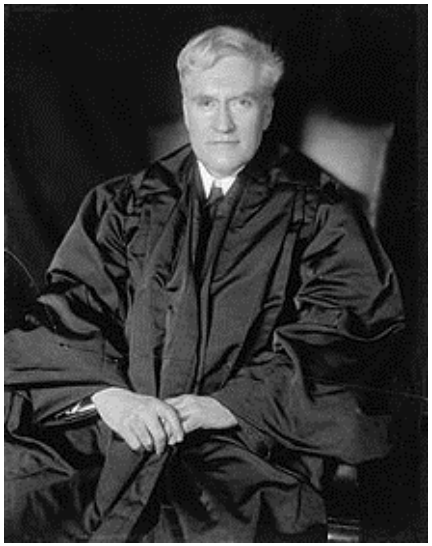
"improper to disunite the callous without consent"

Seeking consent was "the custom and usage of surgeons"

Failing to obtain consent before surgery was "contrary to the rule of the profession"

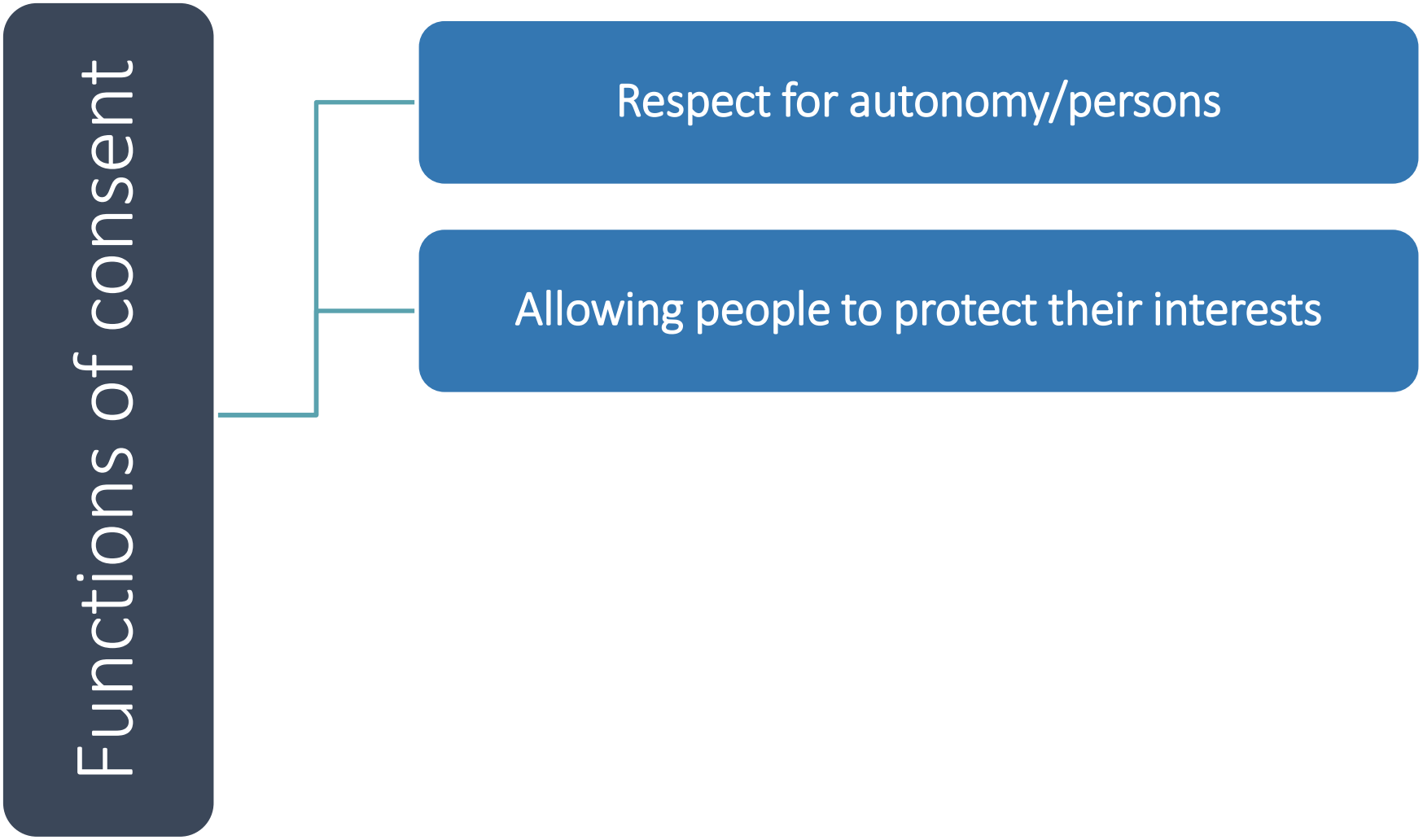
Legal basis for informed consent

"Every human being of adult years and sound mind has a right to determine what will be done with his body…."

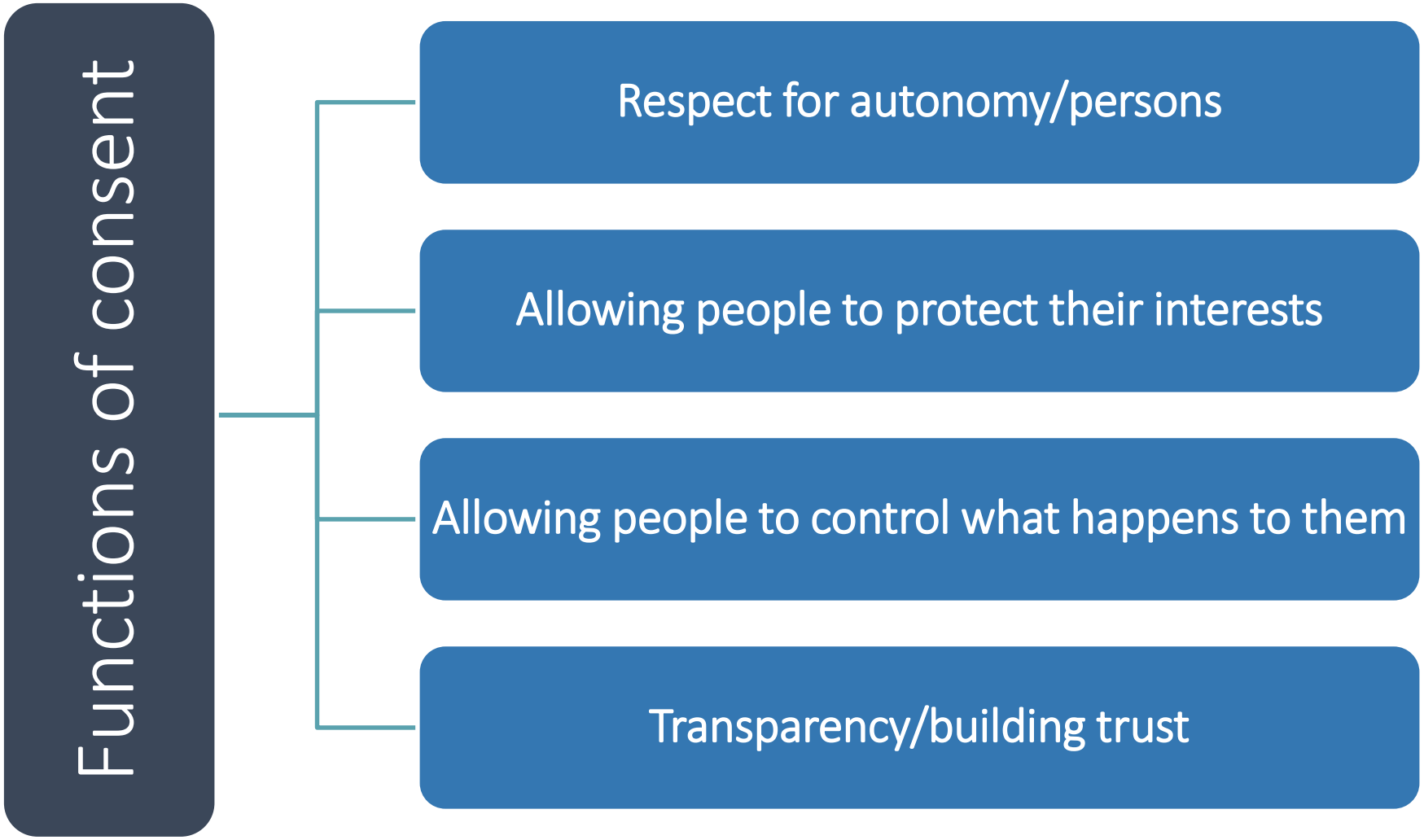


Justice Cardozo, *Schloendorff v. Society of New York Hospital* (1914)

Why is informed consent important?



Why is informed consent important?



How important is informed consent?

A legal and ethical requirement in medicine and in (most) research with human subjects

- Requirement for medical research in 84 countries
- Can be waived in some cases

A process—not a form or an episode

1. Collaborative partnership
2. Social value
3. Scientific validity
4. Fair Subject Selection
5. Favorable risk-benefit ratio
6. Independent review
7. Informed consent
8. Respect for enrolled subjects

What makes clinical research ethical? Emanuel et al. JAMA 2000; JID 2004.

1. Collaborative partnership
2. Social value
3. Scientific validity
4. Fair Subject Selection
5. Favorable risk-benefit ratio
6. Independent review
7. Informed consent
8. Respect for enrolled subjects

What makes clinical research ethical? Emanuel et al. JAMA 2000; JID 2004.

How important is informed consent?

Widely subscribed to, but imperfectly realized!

II. How are we doing?

Discuss the data on informed consent

Elements of informed consent

- Decision-maker with capacity to consent
- Disclosure of information
- Understanding
- Voluntariness
- Consent authorization

Data on elements of informed consent

~~Decision-maker with capacity to consent~~

Disclosure of information

Understanding

Voluntariness

~~Consent authorization~~

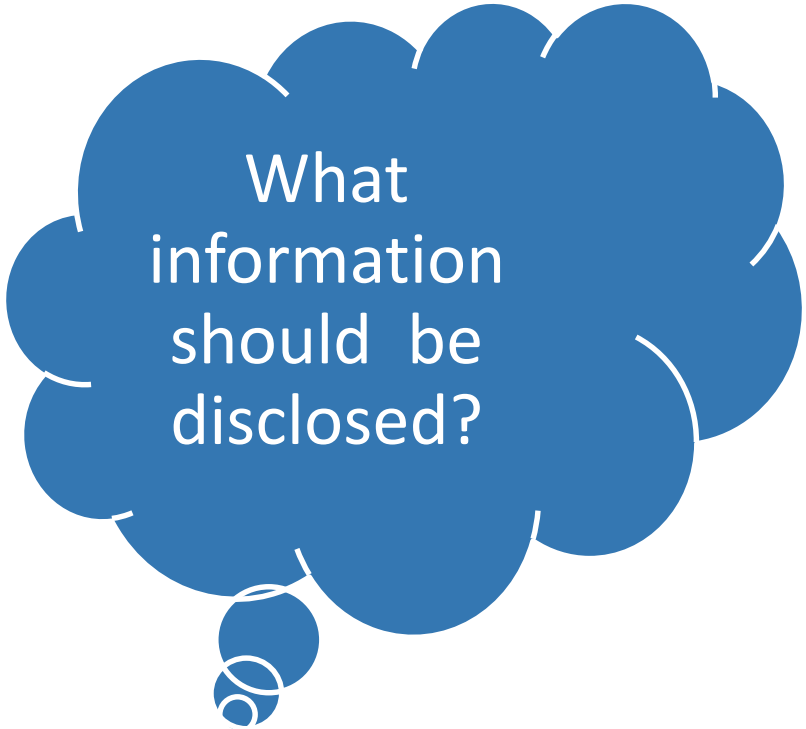
Data on elements of informed consent

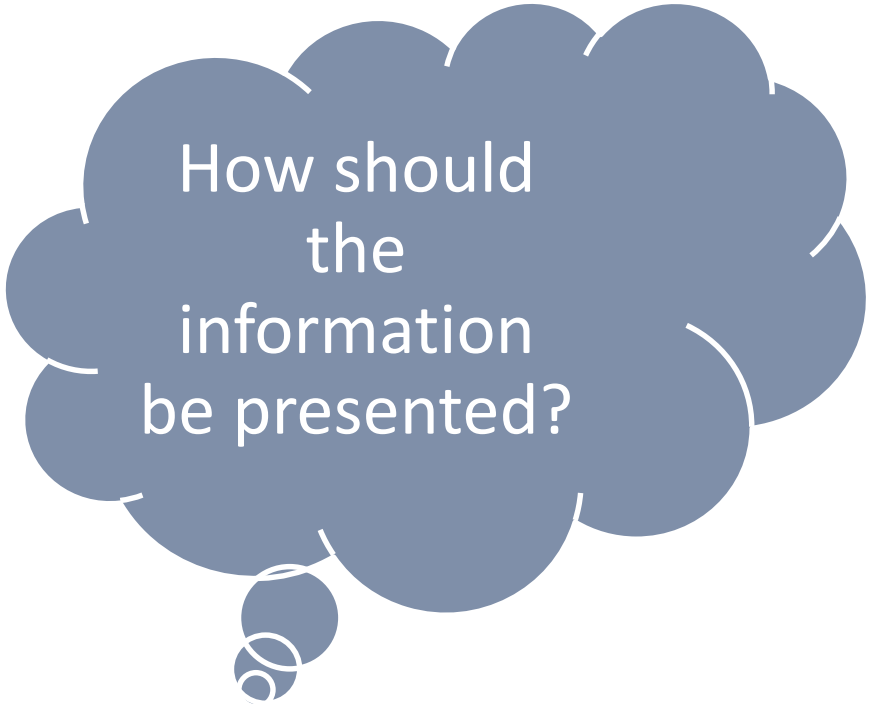
Disclosure of information

Understanding

Voluntariness

Disclosure of Information: Issues and Challenges





Disclosure of Information:

OHRP 45CFR46.116 and FDA 21CFR50.25

Data on Disclosure

Consent documents

- Content
- Readability and Length

Discussion

- Content
- Quality of interaction

Disclosure: Content of Consent Forms

Only 3/16 consent forms had all required elements

Silverman et al. Critical Care Medicine 2001

Most Phase I oncology consent forms (n=267) were found to include the required elements

- Purpose (92%)
- Right to withdraw (99%)
- Risk of death (67%)
- Unknown risks (84%)
- Cure as a possible benefit (5%)

Horng et al. NEJM 2002

Review of IC form content for 27 trials across 4 hospitals (abbreviated)

Table 1. Information Frequently Missing From PICFs

Type of Information	PICFs Missing Information (%)
Basic information	
Specific cancer being studied	12
Reason for research	12
Notice of voluntary participation	6
Options and further discussion	
Other treatment options available	12
Suggestion to discuss all options with doctor	24
Risks	
Potential for sterility	29
Irreversibility of risks	26

Beardsley et al. JCO 2007

Readability and Length

Reading level is too high

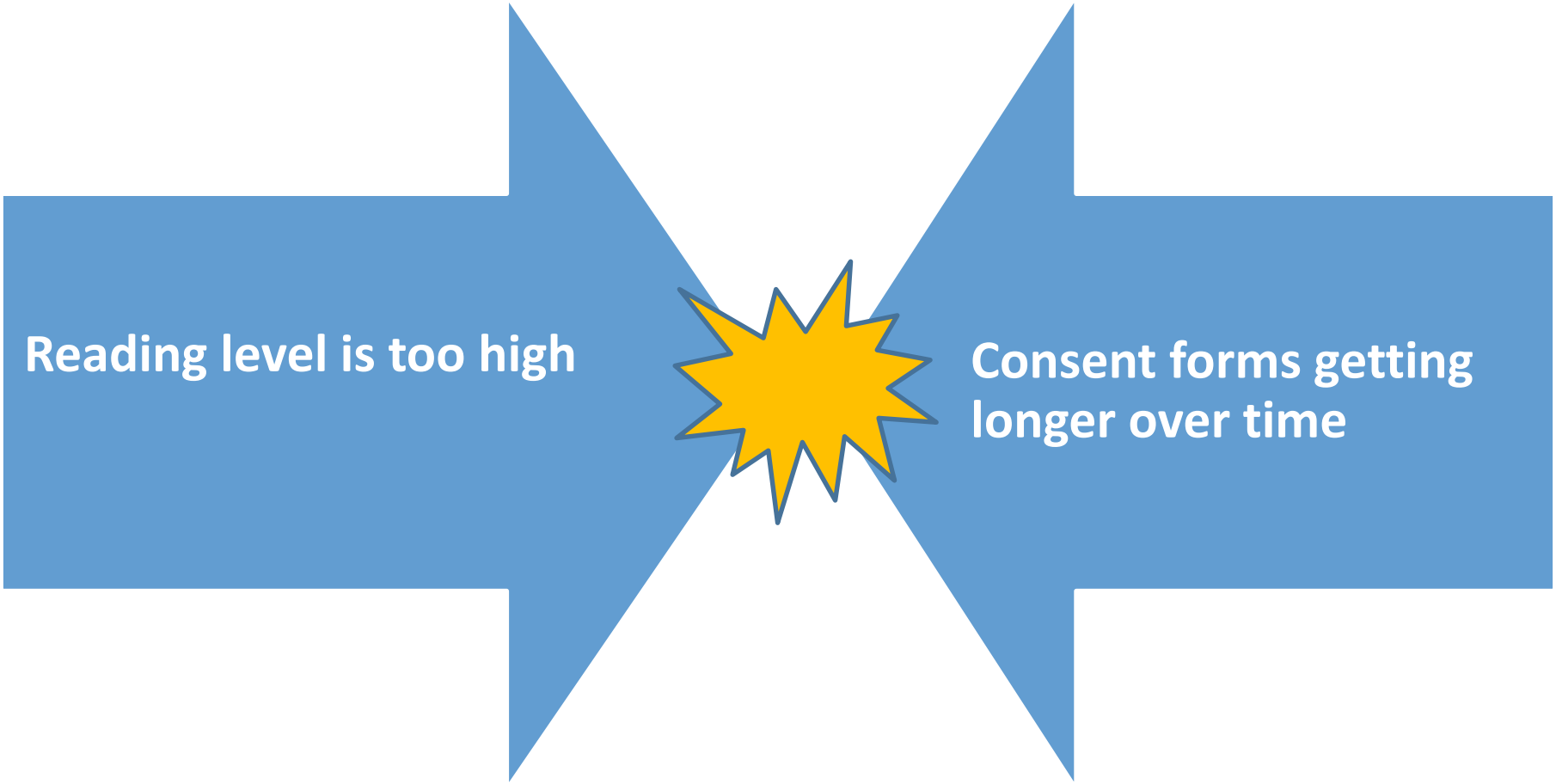
LoVerde et al, 1989, Grossman et al 1994, Paasche-Orlow et al., 2003, Sharp 2004

- Recommendations to write form at 8th grade level
- Consent forms and templates usually written at 11th grade level or higher

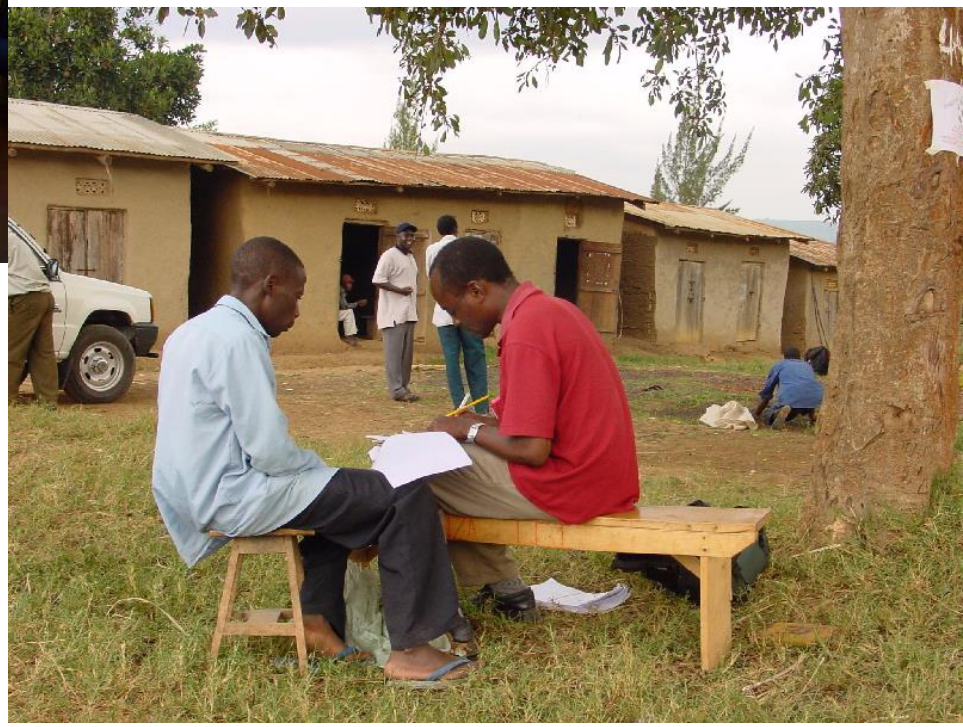
Consent forms getting longer over time

Baker and Taub, 1983; LoVerde et al 1989; Tarnowski et al 1990; Beardsley et al 2007, Albala et al. 2010

Readability and Length



Huge variation in quality of interaction



Disclosure: Interaction

Videotaped oncologists	Survey of investigators of 12 multi-center RCTs
N=12	N=60
• 92% described study purpose & reviewed treatment, tests, procedures • 82% reviewed alternatives	• 58% gave full information • 12% did not inform patients prior to randomization • 38% did not always tell the patient about randomization • 5% did not seek consent at all
Albrecht et al. 1999	*Williams & Zwitter 1994*

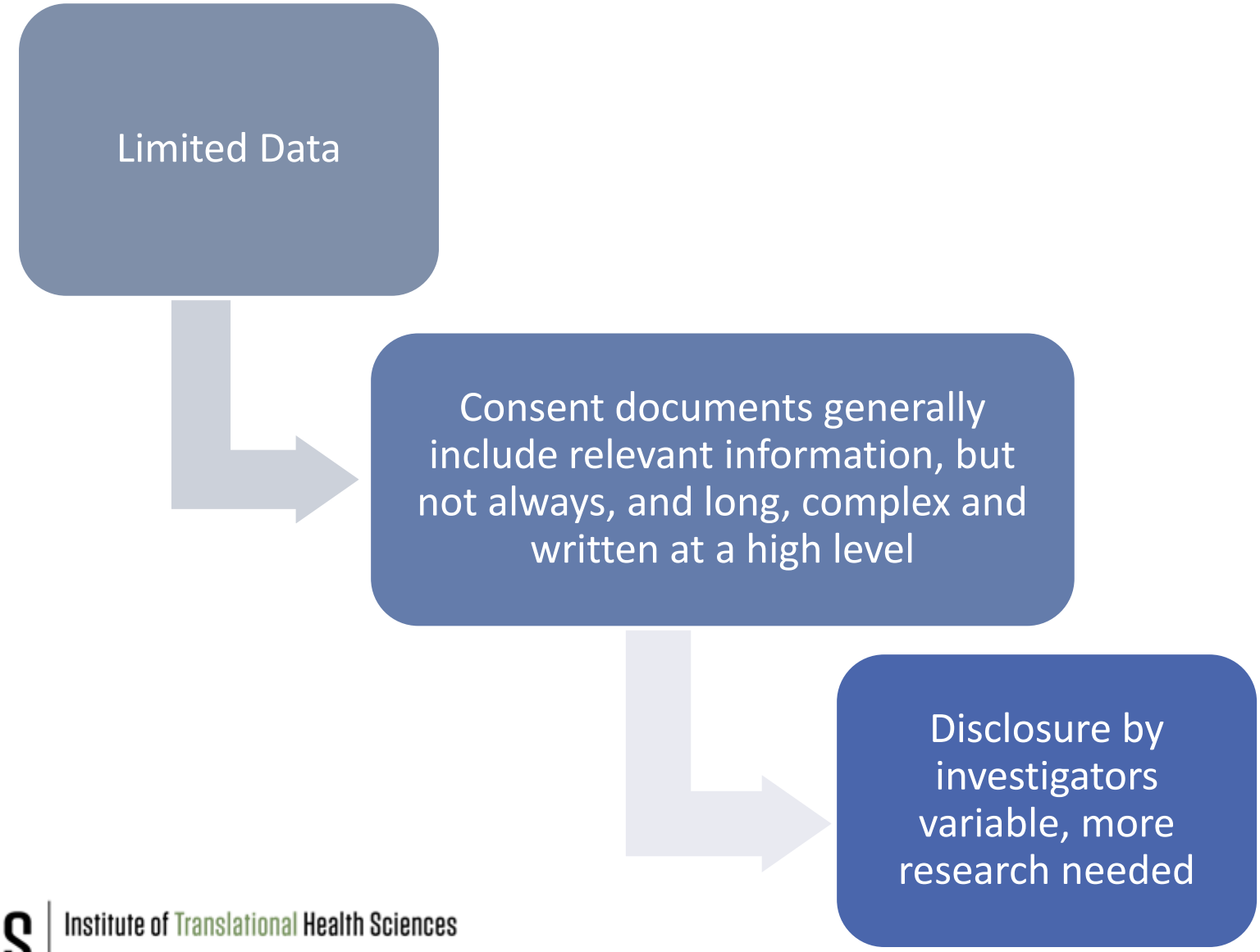
Disclosure: Interaction

Survey of investigators (n=117) of multinational HIV trial

- 99% gave copy of IC document to read
- 97% gave opportunity to read before clinic
- 75% provided “a great deal” of information about risks & purpose
- <56% emphasized randomization
- 8.6% did formal assessment of understanding

Sabik et al. IRB 2005

Summary of Data on Disclosure



Data on elements of informed consent

Disclosure of information

Understanding

Voluntariness

Overview of data on understanding

Data are limited, hard to compare

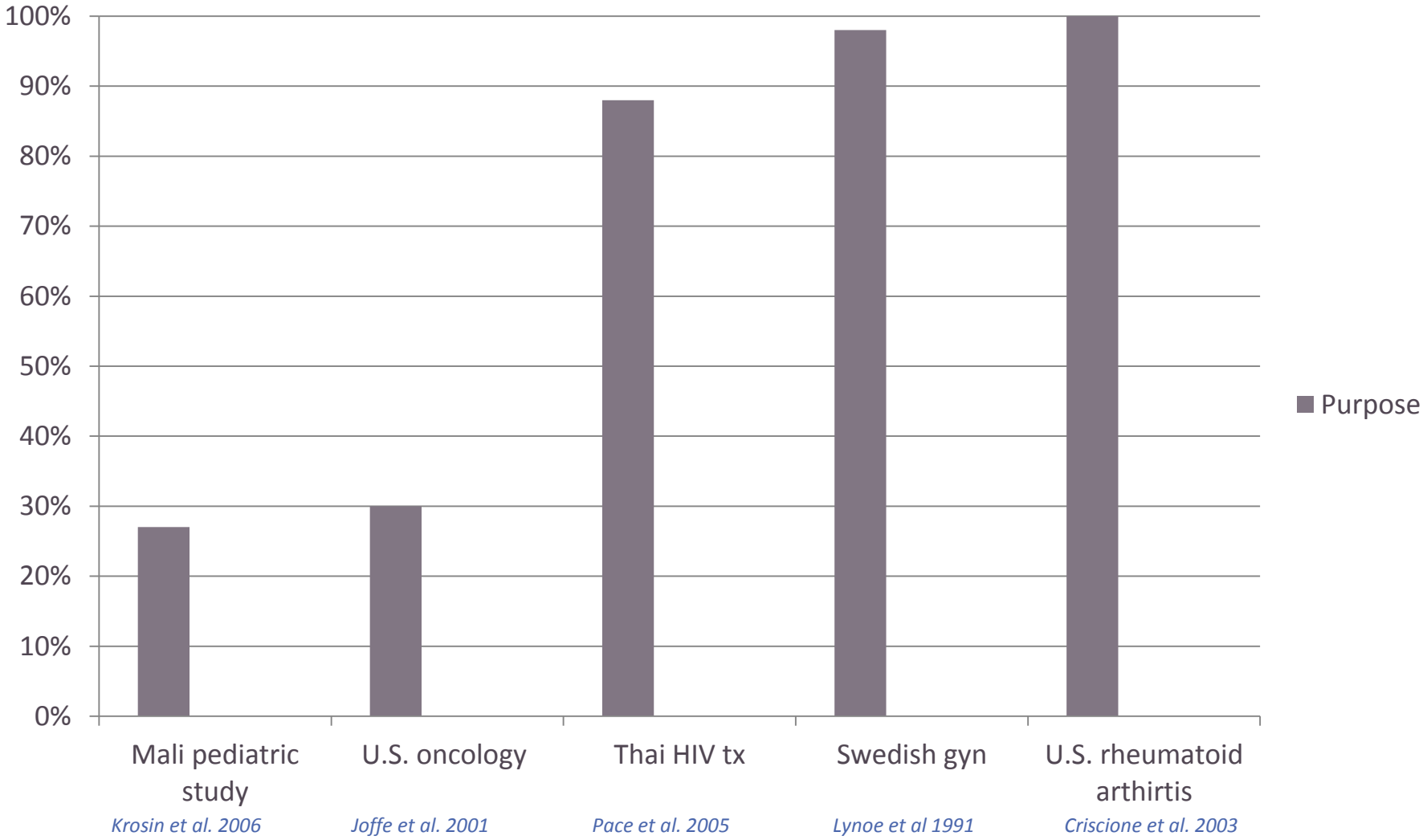
Data show that understanding is variable

Most subjects know they are in research

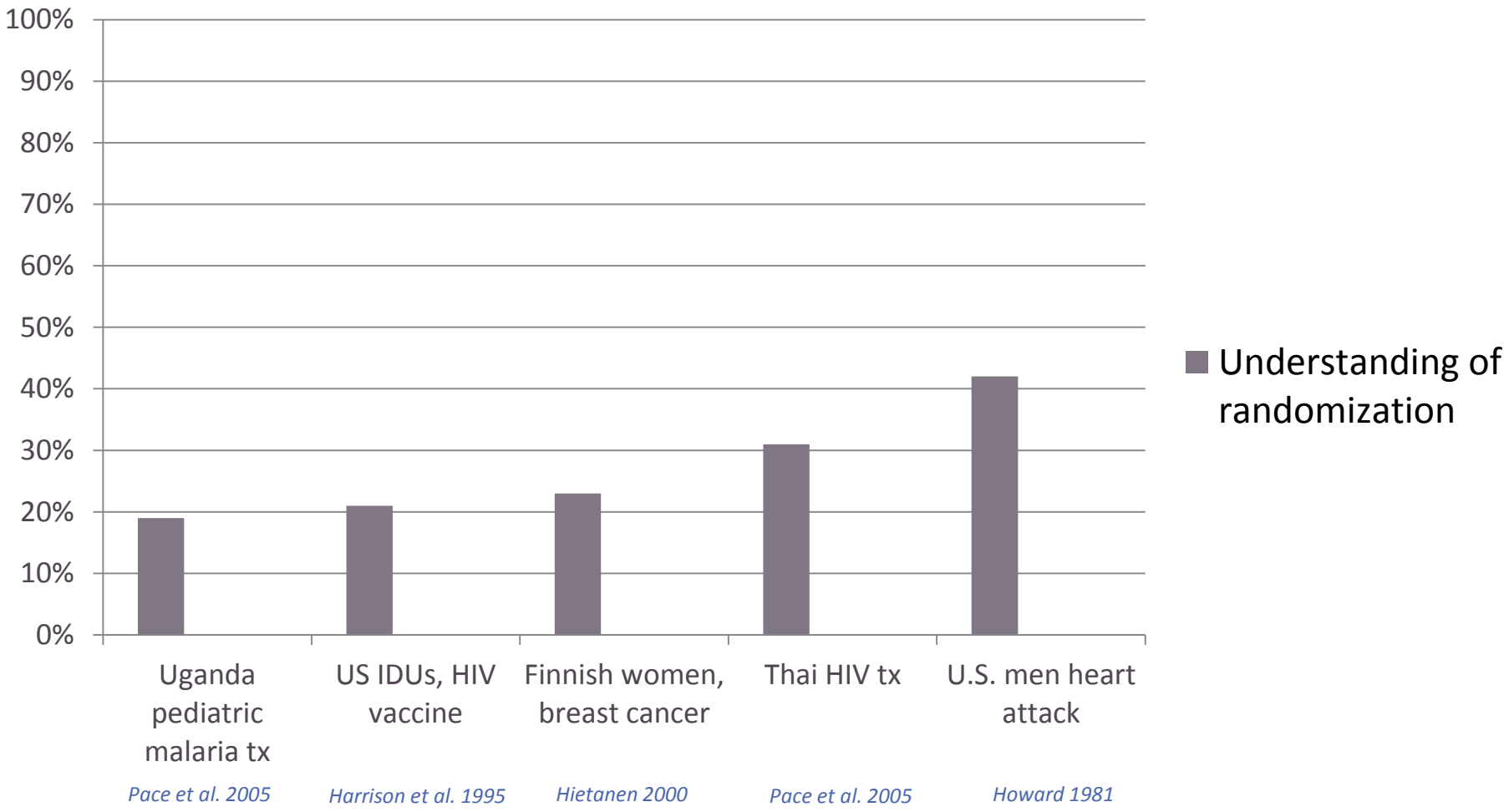
Randomization is poorly understood

Age & education sometimes affect understanding

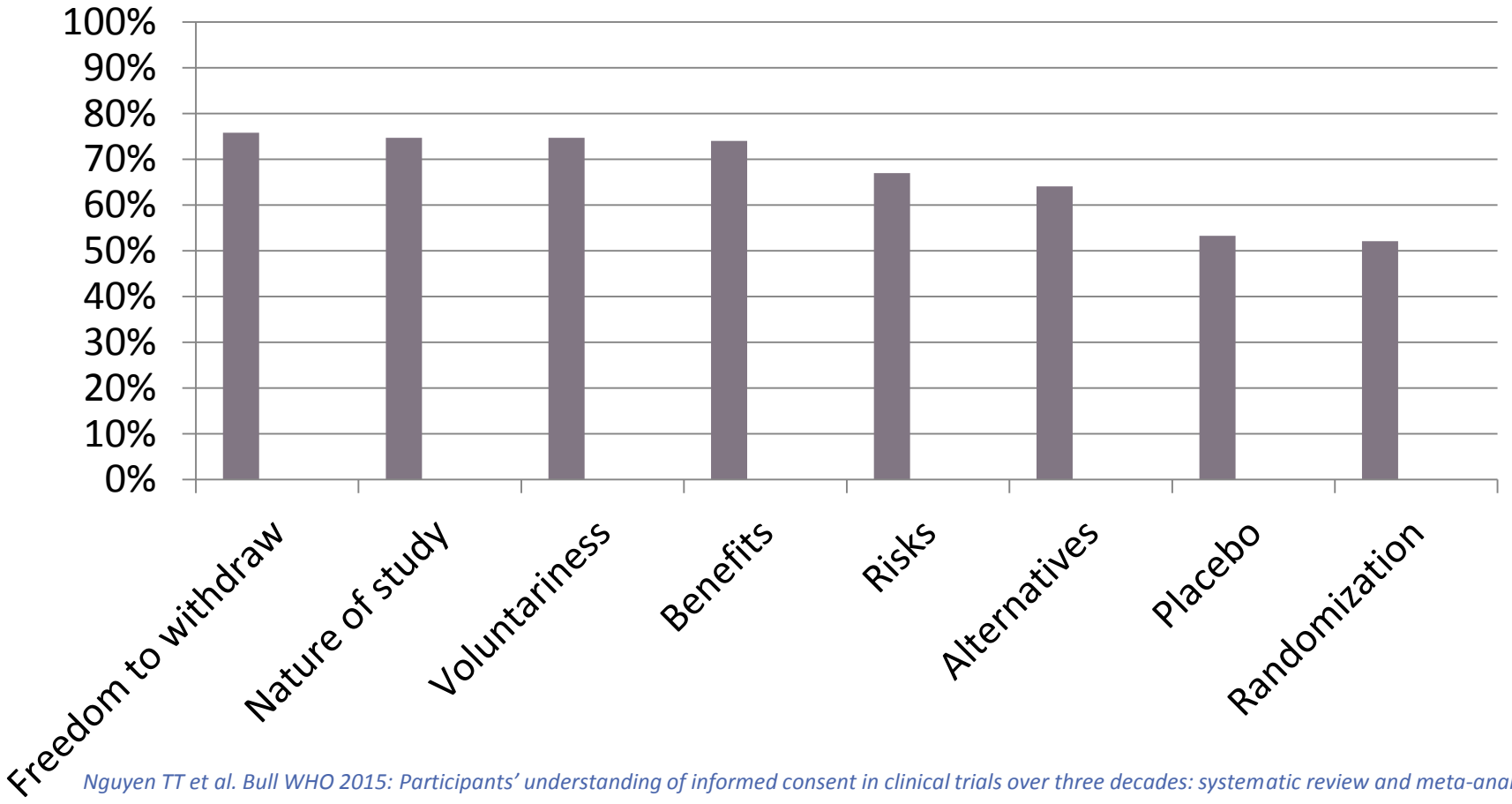
Understanding of research purpose



Randomization



Meta-analysis of data on understanding



Nguyen TT et al. Bull WHO 2015: Participants' understanding of informed consent in clinical trials over three decades: systematic review and meta-analysis

Variation by context?

Most variation in understanding appears to be **concept-specific**, not context-specific

No systematic difference in understanding across most concepts

Randomization especially hard to understand in U.S. and internationally

Exception: Right to withdraw might be less understood in developing countries

Mandava et al. JME 2012

Understanding vs. appreciation

Difference between:

Comprehension of relevant information	Appreciation of how it applies

E.g., **67%** of US participants in rheumatoid arthritis trial knew some people would get a placebo

- ***50%*** *knew they may not get active drug*
- ***53%*** *knew treatment would not be decided based on symptoms*

Criscione et al. 2003

Data on elements of informed consent

Disclosure of information

Understanding

Voluntariness

Voluntariness

Able to make a (free) choice

No coercion, undue influence

How to measure voluntariness?

Did individuals choose *not* to participate?

Did participants feel pressure to join?

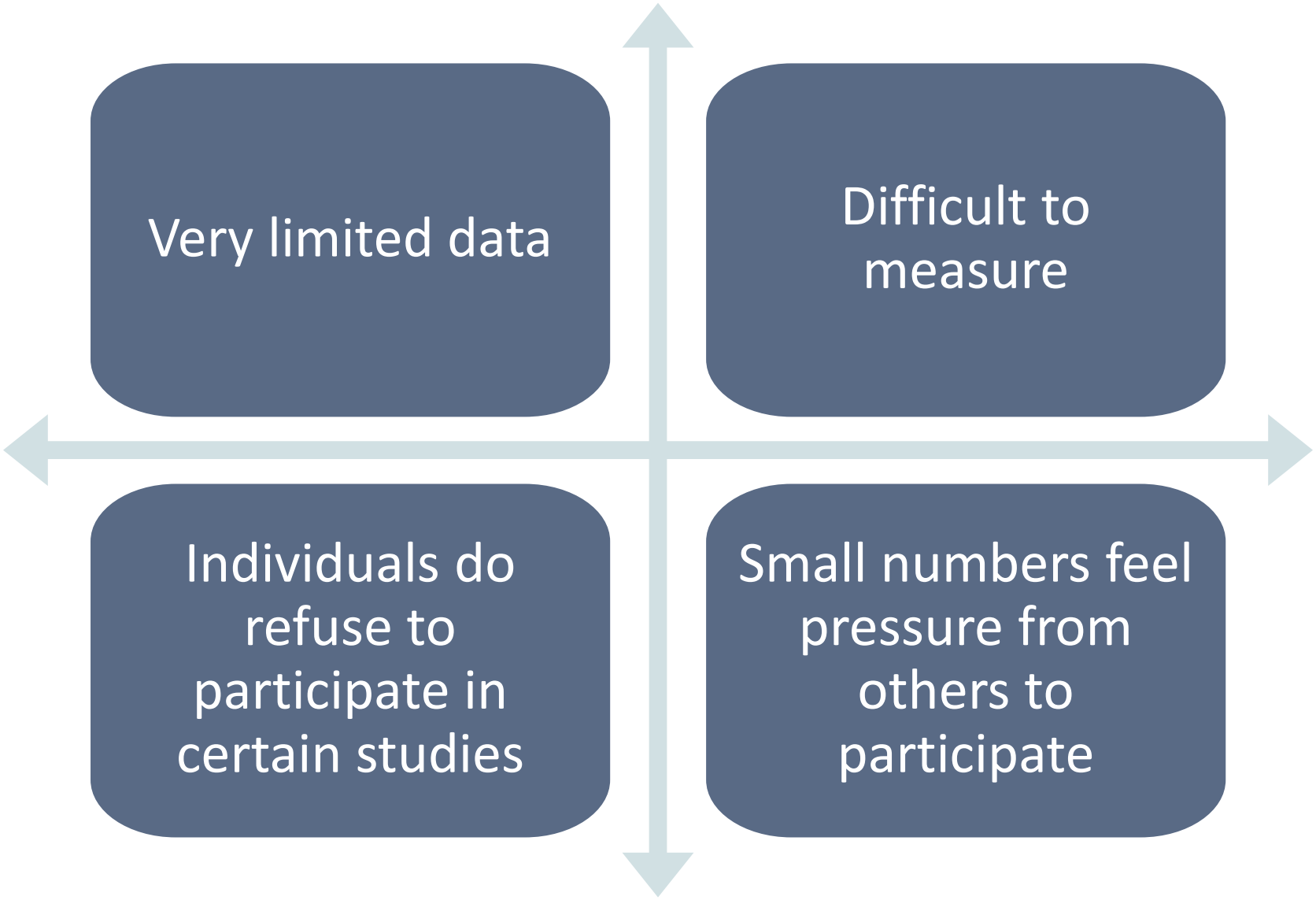
Chose not to participate?

Study population	% who declined to participate	Cite
Cardiac intervention studies	7% (range 1-21%)	Gross et al. 2002
Breast conserving treatment trial	9%	Bijker et al. Brit J Ca 2002
Long observational study (NHANES)	18.9% for interviews, 14.7% for blood samples	NHANES
Adolescents in intensive diabetes tx study	43%	Terryak et al. Diabetes Care 1998
Guarani indians in genetics study	58%	Benitez 2002

Felt pressure to join?

Study population	% who felt pressure	Cite
Cardiology and oncology studies in US (n=570)	2%	ACHRE 1996
Dutch parents in anticonvulsant study	25%	Van Stuijvenberg 1998
Ugandan parents in malaria tx trial	15% from others; 58% from child's illness	Pace et al. AJPH 2005

Overview of data on voluntariness



III. How can we do better?

Data on improving consent, needs for future research on informed consent

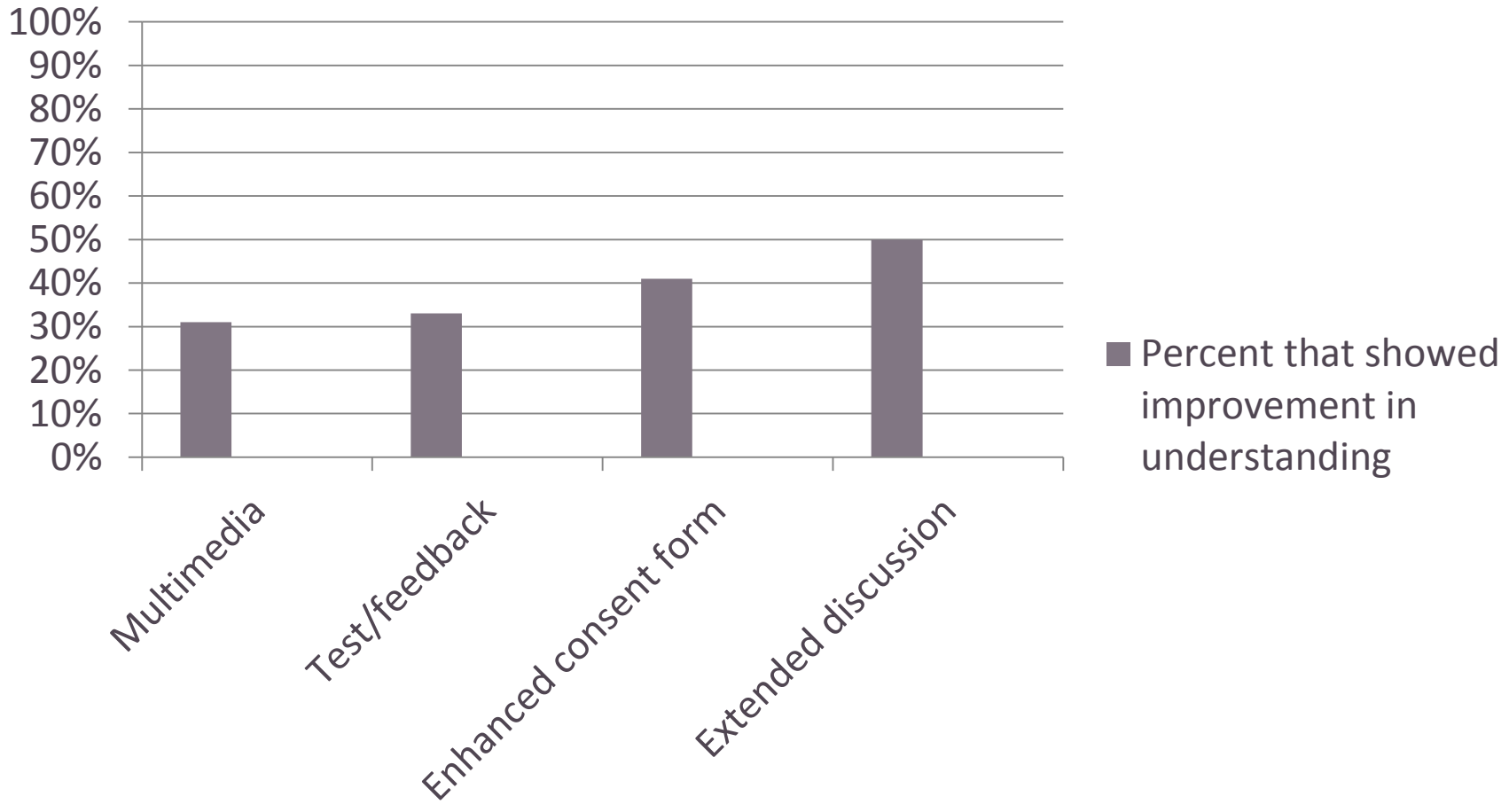
Studies of strategies to improve consent

Data suggest extended discussion, test/feedback strategies help improve understanding

Evidence about multimedia strategies improving understanding less compelling

Flory and Emanuel JAMA 2004; Ryan et al. Cochrane Database of Systematic Reviews 2008; Nishimura et al. BMC Med Ethics 2013; Synnot et al. Cochrane Database of Systematic Reviews 2014

Meta-analysis of interventions to improve understanding



Nishimura et al. BMC Med Ethics 2013

Audiovisual strategies to improve consent

"Low to very low quality evidence" that A/V interventions can improve knowledge or understanding "slightly"

Do not necessarily make a difference in terms of participation rate, willingness to participate

Not enough evidence about anxiety or satisfaction

Synnot et al. Cochrane Database of Systematic Reviews 2014

Data on informed consent: Remaining challenges

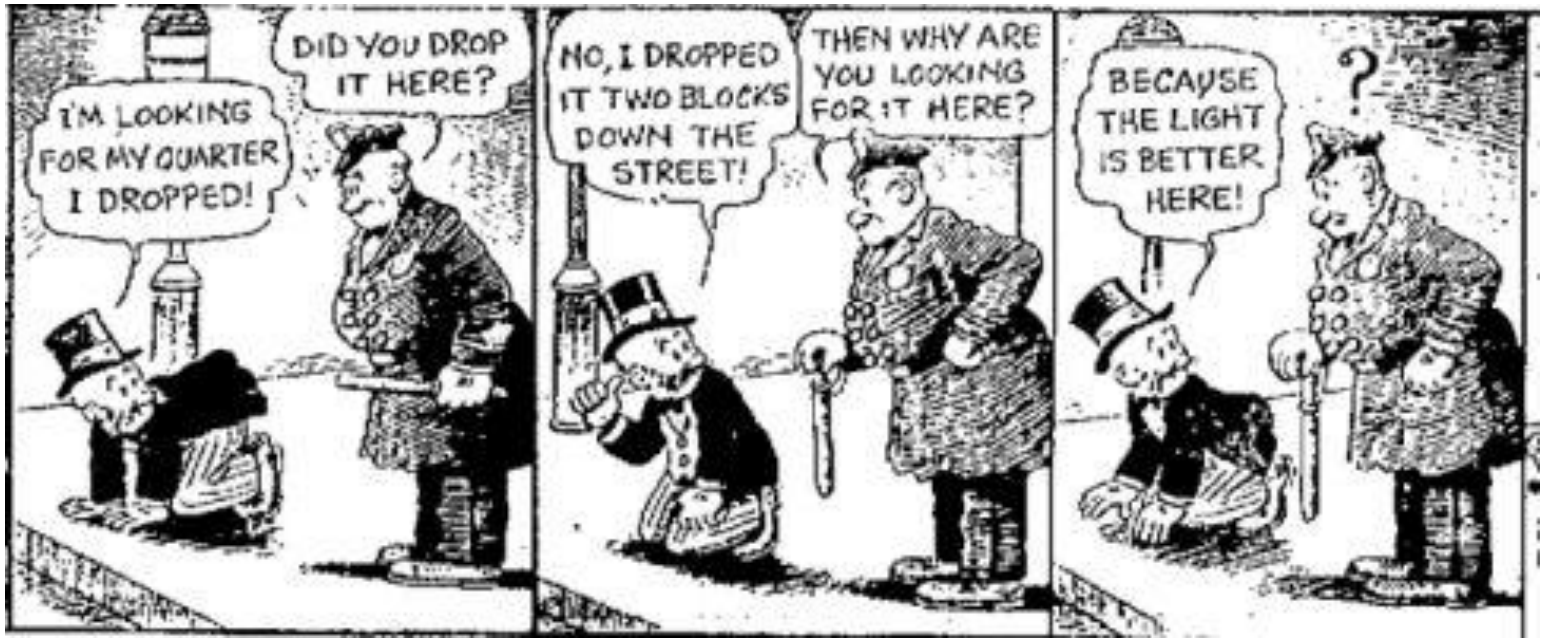
Hard to compare data; lack of standardized metrics or questions, sources of variation

What metrics should we use to measure understanding, voluntariness?

How to study other functions of consent?

When do people actually learn about research & make decisions?

Data on informed consent



Conclusions

I. Informed consent long recognized by physicians

II. Ethically important, imperfectly realized

III. Available data suggest: 1. Consent forms are long and complex 2. Understanding is variable 3. Spending more time may enhance understanding

IV. Need innovative ethics research with standardized metrics to understand how research decisions are made, can be improved

Case Study

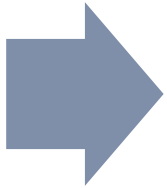
You are a research coordinator obtaining consent for a randomized controlled trial of a new breast cancer treatment vs. placebo (on top of standard of care)

During consent process, one woman is impatient and doesn't want to hear all the information

When you ask why not, she says she thinks the experimental treatment will work

Case Study

How can you tell if this potential subject understands enough to give valid informed consent?



What can you do to improve her understanding?

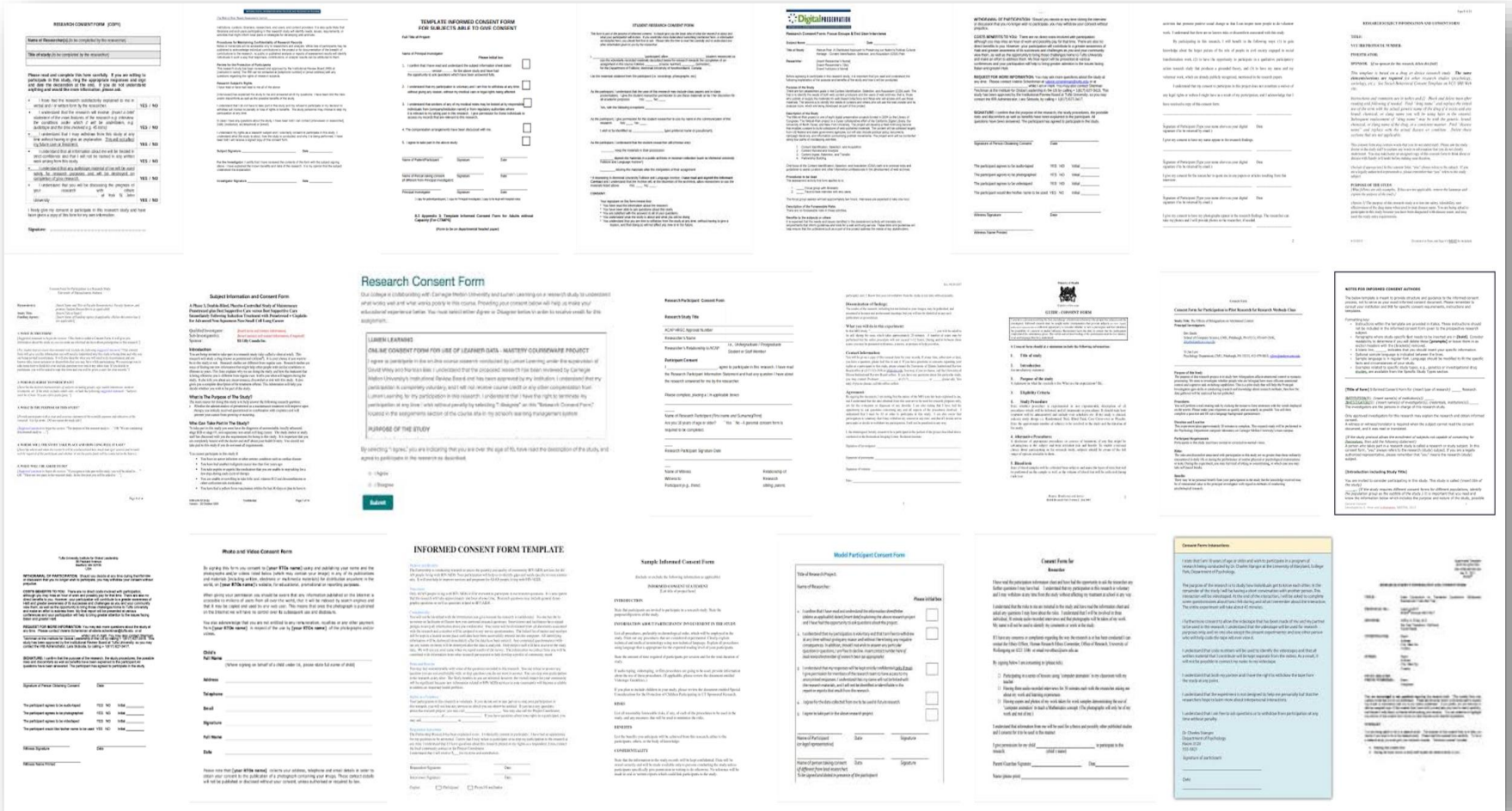
Acknowledgments

- Thanks to Christine Grady, Chief of the Department of Bioethics at NIH, for sharing data and slides

Dissolving the monolith of informed consent

Adrienne Meyer, MPA
Assistant Director, UW Human Subjects Division

ITHS | Institute of Translational Health Sciences
Accelerating Research. Improving Health.



RESEARCH CONSENT FORM (CORT)

TEMPLATE INFORMED CONSENT FORM FOR SUBJECTS ABLE TO GIVE CONSENT

STUDENT RESEARCH CONSENT FORM

DigitalHumanities

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

Subject Information and Consent Form

Research Consent Form

Our college is collaborating with Carnegie Mellon University and Lumen Learning on a research study to understand what works well and what works poorly in this course. Providing your consent below will help us make your educational experience better. You have select either Agree or Disagree below in order to receive credit for this assignment.

LUMEN LEARNING
ONLINE CONSENT FORM FOR USE OF LEARNER DATA - MASTERY COURSEWARE PROJECT

I agree or participate in the on-line course research conducted by Lumen Learning under the supervision of David Wiley and Norman Bier. I understand that the proposed research has been reviewed by Carnegie Mellon University's Institutional Review Board and has been approved by my institution. I understand that my participation is completely voluntary and I will not receive course credit or any other compensation from Lumen Learning for my participation in this research. I understand that I have the right to terminate my participation at any time I wish without penalty by selecting "I disagree" on this "Research Consent Form," located in the assignments section of the course site in my school's learning management system.

PURPOSE OF THE STUDY

By selecting "I agree," you are indicating that you are over the age of 18, have read the description of the study, and agree to participate in the research as described.

○ I Agree
○ I Disagree

Submit

GUIDE - CONSENT FORM

NOTES FOR UNFUNDED CONSENT AUTHORS

Photo and Video Consent Form

INFORMED CONSENT FORM TEMPLATE

Sample Informed Consent Form

Model Participant Consent Form

Consent Form for Research

Consent Form Interactions

The first crack in the monolith

In order to approve research:

- An IRB shall require that **information given to subjects** as part of informed consent is **in accordance with §46.116**.
- An IRB shall require **documentation of informed consent** or **may waive** documentation **in accordance with §46.117**.

What does this mean?

Informed consent is conceived of in the Common Rule as primarily in relation to the information given to subjects

When a written consent form is referred to, it is primarily referred to as a way to document consent

Another little crack

The consent form may be either of the following:

- A **written consent** document that embodies the **elements** of informed consent **required by §46.116**.
- A **short form** written consent document stating that the **elements** of informed consent **required by §46.116** have been **presented orally** to the subject or the subject's legally authorized representative.

What does this mean?

There are already two types of written consent forms described in the regulations

There is no definition in the regulations for "written consent form"

One more tap of the hammer

An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

- That the only record linking the subject and the research would be the consent document and the **principal risk** would be potential harm resulting from a **breach of confidentiality**.
- That the research presents no more than **minimal risk of harm** to subjects and involves **no procedures** for which written consent is **normally required** outside of the research context.

What does this mean?

For minimal risk research, written documentation of consent can almost always be waived

For some research greater than minimal risk, written consent can also be waived.

Let's open up another crack

An IRB may approve a consent procedure which does not include (or which alters)
some or all of the elements of informed consent…
…or waive the requirement to obtain informed consent
provided the IRB finds and documents that:

- The research involves no more than minimal risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

What does this mean?

FOR MINIMAL RISK RESEARCH:

If the research cannot practicably be carried out under the requirements for obtaining consent, the IRB can:

Waive the need to obtain consent at all

Waive the need for subjects to be provided with certain pieces of information

What about the FDA?

YES!

Waiver of written documentation for **minimal risk** research

NO

General waiver of consent or elements

YES!

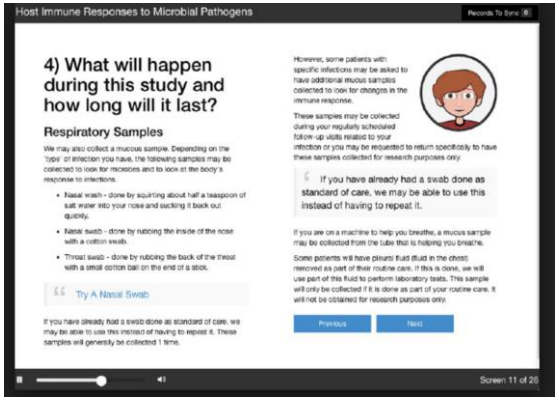
Waiver of consent for **emergency medicine** research

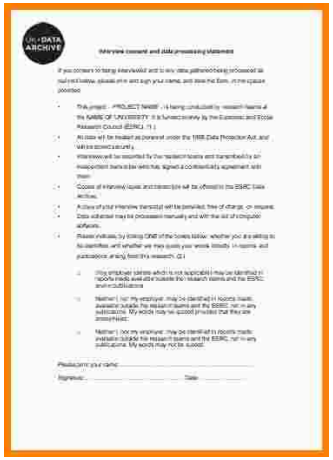
The IRB may even give you a hammer

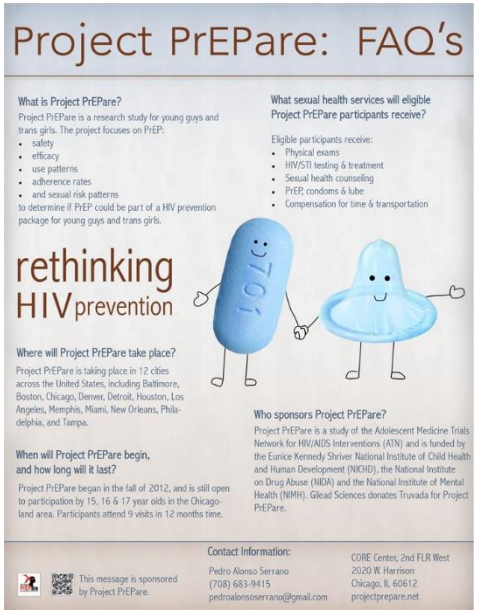
3.2 UW Consent Form Templates. Though it is not an absolute requirement, researchers are encouraged to use one of the UW consent templates when drafting a consent form. Use of the templates ensures compliance with federal and state regulatory requirements as well as UW-specific issues. However, the UW IRB recognizes that there are some circumstances where a significantly different form, organization, and/or approach may be more appropriate.

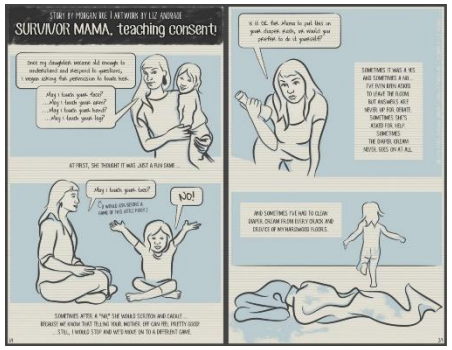
...and a chisel

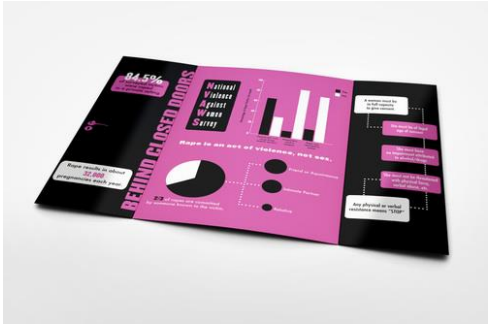
3.7.3 "Researcher" signature. The person who obtained consent from the subject must also sign and date the consent form if the research involves more than minimal risk to subjects. The signature cannot pre-date the subject's signature. The purpose of the signature is to document that the person has explained the research to the subject and answered the subject's questions.











ITHS | Institute of Translational Health Sciences
Accelerating Research. Improving Health.

Carve something great

New Directions for Informed Consent

Bran LeFae
Medical Writer, Seattle Genetics

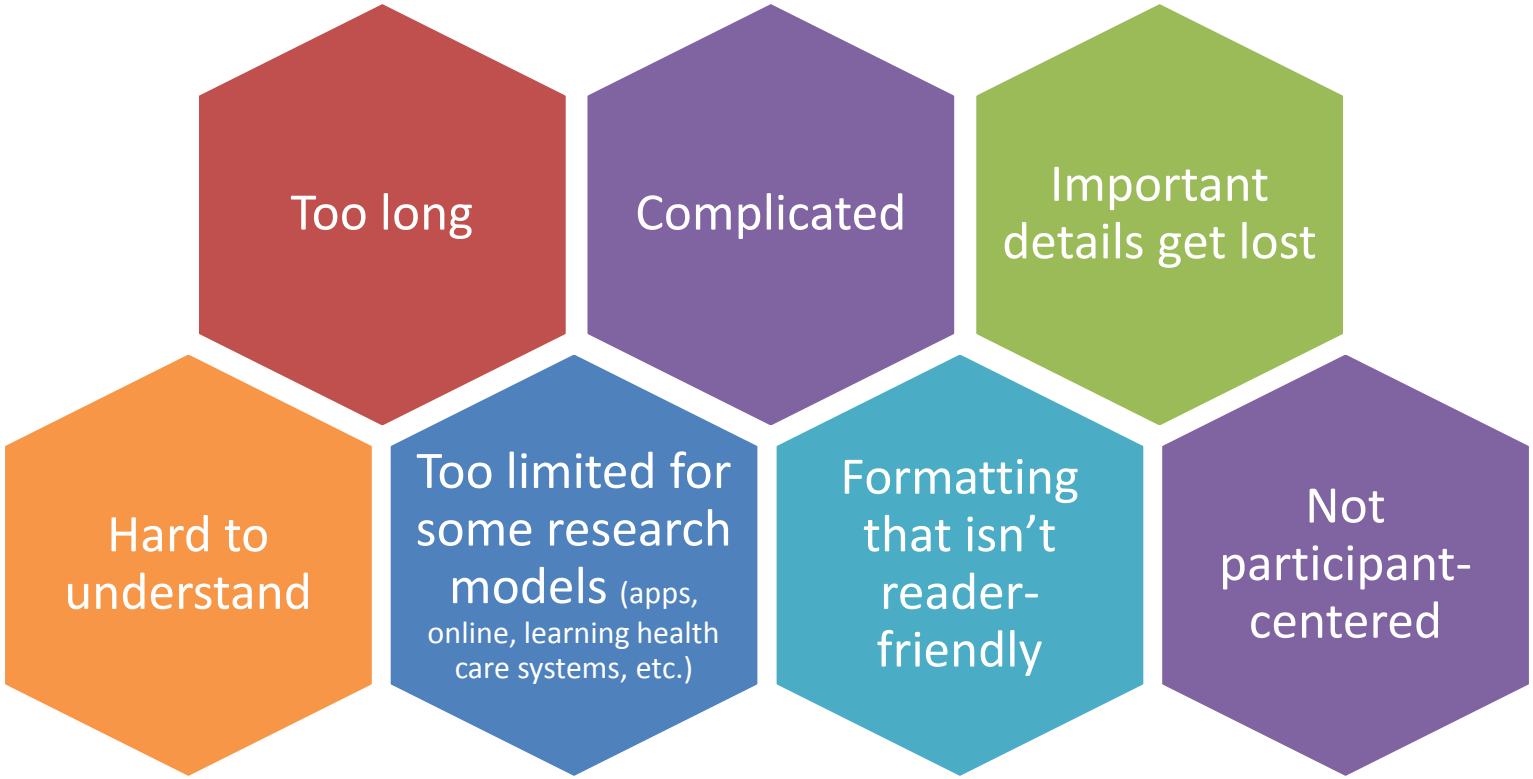
ITHS | Institute of Translational Health Sciences
Accelerating Research. Improving Health.

All opinions expressed in the course of this presentation are mine alone. This presentation does not include any information about current Seattle Genetics practices.

What is Informed Consent?

"…a process of providing potential participants with relevant information that they understand and use to make informed and voluntary decisions…"[1]

Traditional Paper Consent – Challenges and Limitations



Emerging Models of Informed Consent

eConsent[2]

Tiered consenting[3,4]

Staged consenting[5]

Tools for enhanced consenting

Visual aids[6]

Plain language

eConsent

Plenty of interest at the sponsor level and at sites

IRBs are starting to review studies using eConsent

Early days – so far, only used by a small number of studies

In December 2016, FDA issued "Use of Electronic Informed Consent, Questions and Answers. Guidance for Institutional Review Boards, Investigators, and Sponsors."

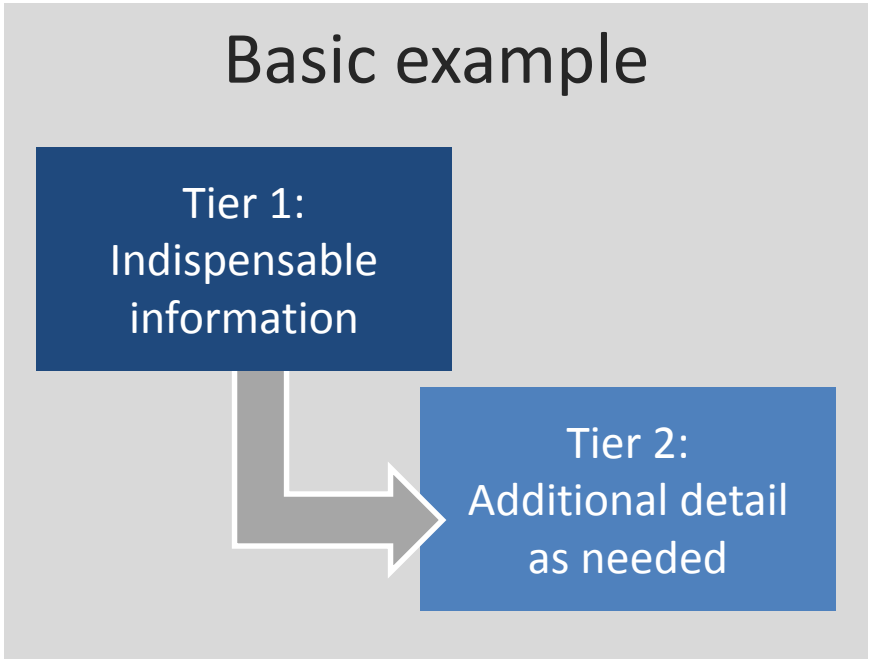
- Essentially who, what, when, where, and how
- Electronic signatures
- Confidentiality
- IRB review (materials needed, etc.)

eConsent

Pros	Cons
Hotlinks can give participants the ability to get a word defined, learn more about a phrase, or access visual, video, or live chat options.	Not all participants find electronic consent inviting. Some populations have a strong preference for paper documents over electronic.
Easy to set up for a tiered or staged consenting approach.	Potentially decreased interaction with the study team and physician or investigator.
Can be used to consent remotely for certain studies.	Still have to give a paper copy to participants.

Tiered Consent

Emerging model that allows the potential participant to guide the level of detail for any given item while still meeting all required elements of consent.



Tiered Consent

Pros
May pair well with an electronic platform, allowing the participant to dig into more detail through hotlinks, video, and diagrams.
This model can serve as a way to get broad consent for an overarching study (ex: genetic analysis) with the participant offering further consent for each specific test.
Participants who are consenting for a complicated or frightening study can control how much detail they receive in the consenting discussion.
Participants can give continued informed consent by agreeing to take part in the greater study and consenting at each visit to the tests and procedures.
Cons
As a new model, there is no data to tell us if this informs participants more or less than a traditional full consent approach

Staged Consenting

Model often used in pediatric oncology studies, where patients start with a standard of care treatment. During treatment, parents and physicians have a series of consenting discussions to explore the clinical trial.

Pros
Parents have a longer period to consider the clinical trial, more chances to ask questions, and time to weigh the risks and benefits.
Cons
The study design has to allow for a longer consenting period. This is not a one size fits all consenting model.

Visual Aids

The eye and brain react to the visual display of communication as well as the content.

Graphics can be used to increase understanding of a concept and to bridge health literacy gaps in communication.

Visual tools must be created with the audience in mind.

Engaging the audience for feedback is often essential, given the inherent limitations of understanding how other people interpret visual information.

Many people are challenged in understanding and working with numbers. Graphics can help bridge this gap.

Plain Language

Are we meeting that standard?

Regulations and best practices require us to use language that is "…as non-technical as practical and should be understandable to the subject…" (Good Clinical Practice) and write consents "…in language understandable to the subject…" (Common Rule 45 CFR 46.111).

Health literacy research data created communication standards, eventually packaged as "plain language".

Plain language techniques use simple tools to create clear, engaging communication.

Regardless of consent model or platform, plain language helps you reach your patient or participant by bridging any health literacy gaps.

Questions?