# INFORMED CONSENT

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# Disclaimer

- The views expressed are mine and do not necessarily represent the policies of the Department of Bioethics, National Institutes of Health, or the Department of Health and Human Services.

- I have no conflicts of interest to disclose

# Informed consent

- Well entrenched in American values, jurisprudence, medical practice, and clinical research.

- Informed consent is the bedrock principle on which most of modern research ethics rest…This was at the heart of the crucial ethical provision stated in the first words of the Nuremberg Code, and it remains equally compelling a half century later. Menikoff J, *Camb Quarterly* 2004 p 342

# Informed consent

- Authorization of an activity based on understanding what the activity entails.
- A legal, regulatory, and ethical requirement in health care and in most research with human subjects
- A process of reasoned decision making (not a form or an episode)
- One aspect of conducting ethical clinical research

# Ethical requirement

- Respect for autonomy - an individual's capacity and right to define his/her own goals and make choices consistent with those goals.

- "Informed consent is rooted in the fundamental recognition…that adults are entitled to accept or reject health care interventions on the basis of their own personal values and in furtherance of their own personal goals" Presidents Commission for the study of ethical problems…1982

# Informed consent in medical practice

# Informed consent in medical practice

- …informed consent in clinical practice is frequently inadequate…
- Physicians receive little training…
- Misunderstand requirements and legal standards…
- Time pressures and competing demands…
- Patient comprehension is often poor…
- Recent studies have demonstrated improvement in patient understanding of risks after teaching communication skills to physicians
- Schenker et al 2010; Matiasek et al. 2008; McClean et al. 2004, and others

# Research Informed consent: Regulatory requirements

- …no investigator may involve a human being as a subject in research ..unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative…(45CFR.46.116, 21CFR.50.20) (limited exceptions )

- Informed consent must be sought prospectively, and documented to the extent required under 45 CFR 46.117 and 21CFR50.27.

# Two senses of informed consent

(Faden & Beauchamp)

- An autonomous authorization:
  - "the intentional authorization of an activity based on substantial understanding and in the absence of control by others"
- Social rules of consent
  - An institutionally or legally effective authorization, as determined by prevailing rules

# Elements of informed consent

- Disclosure of information
- Understanding
- Voluntariness
- Consent authorization

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- *Disclosure of information*
- Understanding
- Voluntariness
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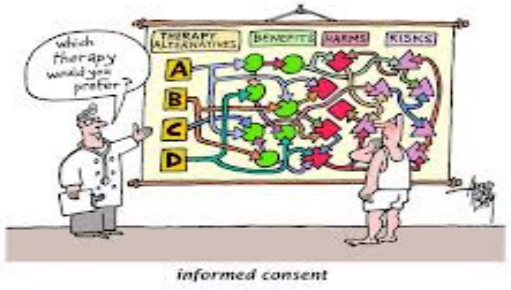
# Disclosure of information: Issues and challenges

- How much and what information should be disclosed?
- How should the information be presented?
- Circumstances and setting?



# Disclosure of information

- Written consent form
  - A summary of study information–explanation of what the study is about, the procedures, related risks and possible benefits, alternatives, rights;
- Advertisements, fliers, brochures
- Reviewed and approved by IRB

- Discussion with research team, other providers, other participants, etc.

# Disclosure- required elements

(from 45CFR46.116 and 21CFR50.25)

- Statement of research
- Purpose and procedures
- Foreseeable risks and discomforts
- Any benefits to subjects or others
- Appropriate alternatives
- Extent of confidentiality
- Treatment or compensation for injury
- Who to contact for answers to questions
- Participation is voluntary

- Additional elements

# Writing a consent form

- What  (and how much) information to include
- Making it readable and understandable
- Format
- Consideration of length and complexity


*"Whoa—way too much information!"*

# Studies of consent form readability

- **Reading level is high**
  - Consent forms and templates usually written at about the 11th grade level or higher LoVerde et al, 1989; Grossman et al 1994; Paasche-Orlow et al., 2003; Sharp 2004
- **Consent forms are long**
  - Consent documents have increased in length over time Baker and Taub, 1983; LoVerde et al 1989; Tarnowski et al 1990; Beardsley et al 2007, Albala et al. 2010
- **Missing required or relevant elements**
  - Silverman et al. *Critical Care Medicine* 2001; Horng et al, *NEJM* 2002; Beardsley et al. *JCO* 2007; Abeysena C et al *Ind J Med Ethics* 2012


*"Hey, no problem!"*

Once you've estimated how long it takes to read the consent form you can time how long subjects take to read the consent form during the consent process, or ask them how long it took them to read the consent form at home. Unfortunately, I suspect you'll find most subjects not taking adequate time to read the consent form, but are scanning it fairly quickly.

**Summary**

Even though typical consent forms require subjects to sign that "I have read and understood this consent form…" that signature does not guarantee that subjects took enough time to read the consent form. Subjects may want to believe that they have read and understood the consent form; researchers may want to believe that their subjects have read and understood the consent form. If so, both are engaging in self-deception. Unless more direct evidence shows that subjects actually have read the consent form, it's probably wise to assume that they have not. If so, future research needs to focus on what--if anything--can be done to encourage subjects to take the time needed to read the consent form.

**Table #2: Minutes to read a consent form**

| Consent Form Length (Words) | Very Slow Reading Speed (100 words/min) | Average Reading Speed (200 - 250 words/ min) | Fast Reading Speed (300 words/ min) |
|---|---|---|---|
| 2,000 | 20 minutes | 8 - 10 minutes | 7 minutes |
| 3,000 | 30 | 12 - 15 | 10 |
| 4,000 | 40 | 16 - 20 | 13 |
| 5,000 | 50 | 20 - 25 | 17 |
| 6,000 | 60 | 24 - 30 | 20 |
| 7,000 | 70 | 28 - 35 | 23 |
| 8,000 | 80 | 32 - 40 | 27 |
| 9,000 | 90 | 36 - 45 | 30 |
| 10,000 | 100 | 40 - 50 | 33 |
| 11,000 | 110 | 44 - 55 | 37 |
| 12,000 | 120 | 48 - 60 | 40 |

**References**


1. Davis, T.C., Holcombe, R.F., Berkel, H.J., et al. (1998) Informed Consent for Clinical Trials: a Comparative Study of Standard Versus Simplified Forms. *Journal National Cancer Institute*, 90, 668-674.
2. McNutt, L., Waltermaurer, E., Bednarcyk, R.A., et al (2008) Are We Misjudging How Well Informed Consent Forms Are Read? *Journal of Empirical Research on Human Research Ethics*, 3(1), 89-97.
3. Davis, T.C., Bocchini, J.A., Fredrickson, D., et al (1996) Parent comprehension of polio vaccine information pamphlets. *Pediatrics*, 97(6), 804-810.
4. Davis, T.C., Fredrickson, D.D., Arnold, C., et al (1998) A polio immunization pamphlet with increased appeal and simplified language does not improve comprehension to an acceptable level. *Patient Education and Counseling*, 33, 25-37.

# Challenges

- Research informed consent usually requires a written form
- It is hard to communicate clearly

  "Easy reading is damn hard writing."

  Nathaniel Hawthorne ~1840

  Maya Angelou ~2000
- Documentation of informed consent protects the institution
- IRBs make consent forms longer and more complex

# Easy-to-read informed consent documents

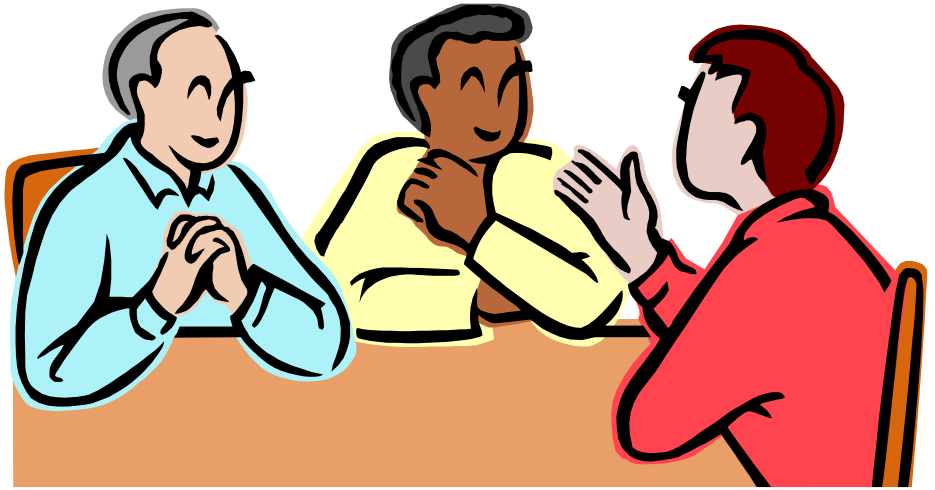
- Familiar, consistent words, Active voice and personal pronouns
- Short, simple, and direct sentences with limited line length
- Short paragraphs, one idea per paragraph.
- Clear and logically sequenced ideas
- Highlight Important points
- Avoid acronyms and abbreviations
- Format:
  - Titles, subtitles, simple headers
  - Balance white space with words and graphics
  - Font, style, spacing,
  - Underline, bold, or boxes (rather than all caps or italics) give emphasis.
- **From NCI Simplification of Informed Consent Documents, Appendix 3**. <http://www.cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/page1

# Readable/understandable

- "The purpose of this study is to test the safety of XXX at different dose levels in patients with cancer who have different degrees of normal and abnormal liver function. XXX is an experimental drug that has not been approved by the FDA for use in patients with cancer. XXX was designed to enter cancer cells and block the activity of proteins that are important for cancer cell growth and survival. This is the first study in which XXX will be given to people with different degrees of liver function. We already know the safe dose for people with normal liver function…"

- We want to find out what dose of XXX is safe in patients with cancer whose livers are not working normally. XXX is an experimental drug that blocks the growth of cells related to cancer. It is not approved by the FDA for patients with cancer. We know the safe dose in patients with normal liver tests. This is the first time we will give XXX to people who have abnormal liver tests

# Presentation

# SETTING

# Data on investigator practices regarding consent

- Investigators (n=117) of a multinational HIV trial surveyed about consent practices
  - Provided a copy to read (99%)
  - Gave subjects opportunity to read before clinic (97%)
  - Provided a great deal of information about risks and purpose (>75%)
  - Emphasized randomization (<56%)
  - Formal assessment of understanding (8.6%)

Sabik et al. *IRB* 2005

# Summary- disclosure

- What, where, who, when, and how matter
- Consent documents
  - usually include relevant information,
  - not always compliant with regulations,
  - are long, complex and written at a high level
- Disclosure by investigators variable- very few studies *
- Limited training for investigators

# Elements of informed consent

- Disclosure of information
- *Understanding*
- Voluntariness
- Consent authorization

# Understanding: issues and challenges

- Factors that might affect understanding
- How is/should understanding be assessed?
- How much do subjects understand? How much should they understand?
- What happens (or should happen) when subjects don't understand?

# Factors that might affect understanding

- Age*
- Severity of illness and need
- Educational level*
- Cognitive capacity*
- Familiarity with research
- Language and customs
- Literacy

# What affects understanding?

- "Host" factors- Age, education, pain, cognitive impairment, capacity, literacy

- Expectations and familiarity
  - Trust in providers
  - Therapeutic misconception and related misunderstandings

- Process related factors
  - What is disclosed and how
  - How does the participant listen to/read the information?

# Understanding is variable

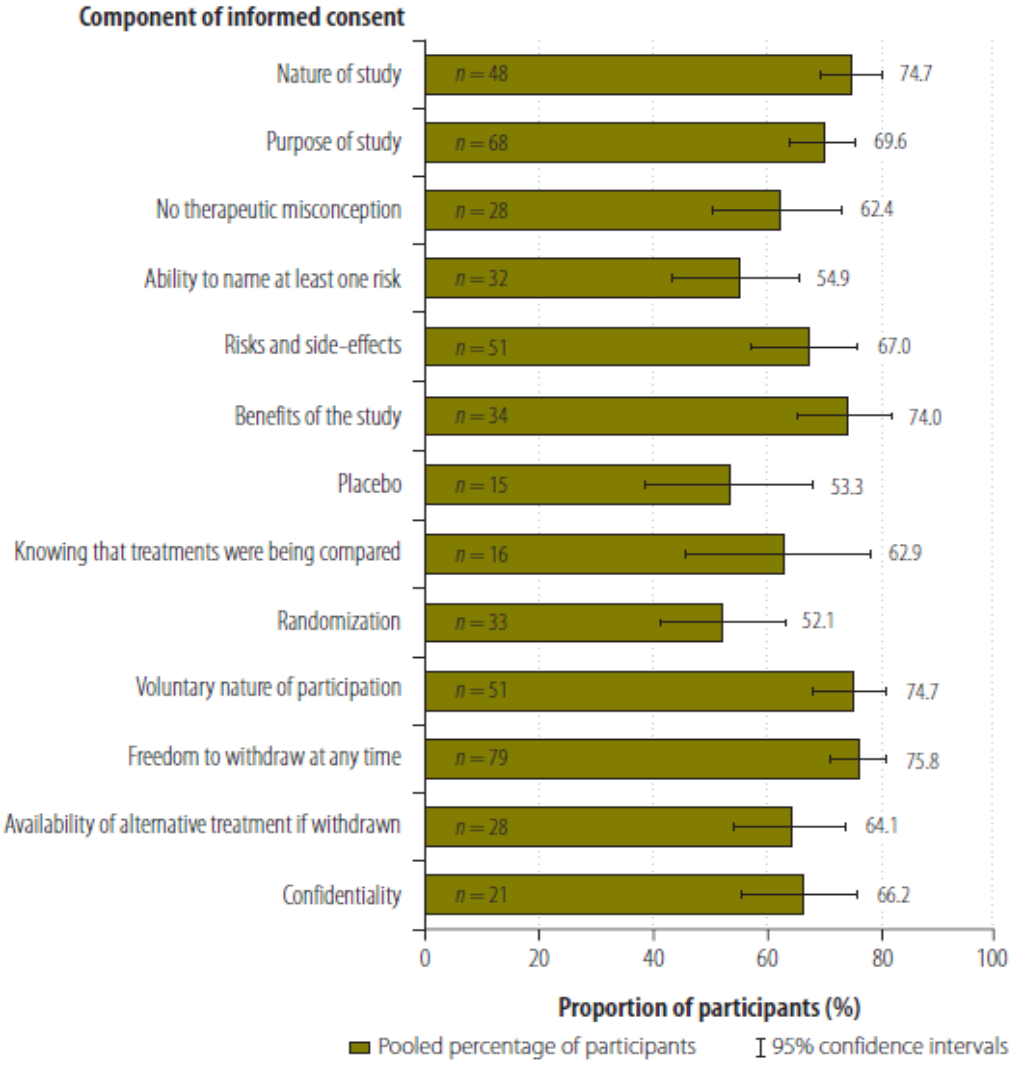
- Studies continue to show that research participants often have limited understanding of study information

e.g. Mandava A et al *J Med Ethics* 2012

# Participant Understanding: Research Purpose/ Nature, Risks, and Randomization

- Range of understanding about the purpose and nature of research (27% -100%) Krosin et al 2006; Joffe et al 2001; Pace et al. 2005; Criscione et al. 2003
- Range of understanding about research risks (28%-100%) Bergler 1980; Joffe et al. 2001; Leach et al, 1999; Dougherty et al 2000
- Range of understanding about randomization (21%-42%) Harrison et al 1995; Hietanen 2000; Pace et al. 2005; Howard 1981

Fig. 2. **Participants' understanding of components of informed consent in clinical trials, by meta-analysis[a]**




[a] The number of studies included in the evaluation of each component is given.

Tam T et al. Bull of WHO 2015

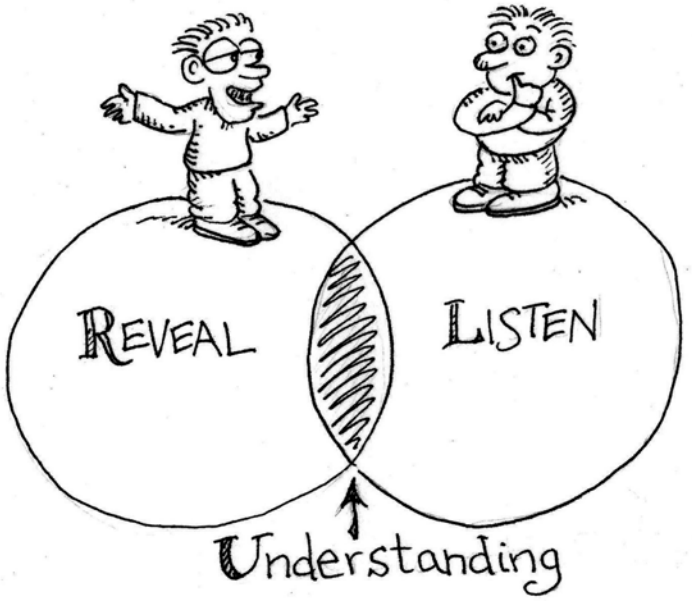
# Challenges

- The complexities of scientific endeavors
- Health literacy and capacity
- Measuring understanding- How do we know when someone doesn't understand?
- Different kinds of "mis-understanding"
  - Misconception
  - Mis-estimation
  - Optimism

    Horng & Grady *IRB* 2003
- Knowledge v. appreciation

# Understanding

- Knowledge of relevant information
- Appreciation of how it applies
- Therapeutic misconception



# Therapeutic Misconception

- When a research participant fails to recognize how individualized medical care (i.e. physician obligation to make medical decisions in the patient's best medical interests) may be compromised by research procedures Appelbaum et al. IRB 2004

- Failure to recognize the differences between research and ordinary care negate the ability to provide meaningful informed consent. Appelbaum et al. KIE 2006

# Studies of strategies to improve understanding

- Multimedia (e.g. audiotapes, videotapes, interactive computers)
- Enhanced consent form (e.g. modified style, format or length)
- Extended discussion ( with team member or neutral educator)
- Test/feedback (e.g. quizzes and review)
  - Flory and Emanuel *JAMA* 2004

# Studies of strategies to improve understanding: Audio visual interventions

- 4 trials (3 RCT) involving data from 511 people, conducted in USA and Canada.

- Audio-visual interventions
  - No consistent increase in understanding
  - 1 study showed better retention of knowledge
  - Transient increase in willingness to participate in trials, not sustained at 2-4 weeks

- Ryan RE, Prictor MJ, McLaughlin KJ, Hill SJ. *Cochrane Database of Systematic Reviews* 2008.

## Studies of strategies to improve understanding: consent form

- Enhanced consent form (e.g. modified style, format or length)
  - 6 of 15 showed significant increase in understanding Flory et al 2004
  - Variable interventions, measurements, and populations studied

## Strategies to improve understanding

- Limited data suggest that extended discussions (3/5) , test/feedback strategies (5/5) may help improve understanding Flory and Emanuel *JAMA* 2004

- Haiti: Case-control study of HIV transmission
  - To enroll, prospective participants had to pass a T/F quiz on study purpose, voluntary participation, risks, benefits and HIV prevention.
  - 20% passed when attended single consent meeting; 80% passed when attended 3 information sessions and a consent meeting

    Fitzgerald et. al. Lancet 2002; 360: 130

## Strategies to improve understanding

- Multimedia (e.g. audiotapes, videotapes, interactive computers)
- Enhanced consent form (e.g. modified style, format or length)
- Extended discussion ( with team member or neutral educator)
- Test/feedback (e.g. quizzes and review)
- Mixed and miscellaneous (e.g. online presentations, supplementary vignettes, etc)

Nishimura A et al. *BMC Medical Ethics* 2013

# Strategies to improve understanding

- Significant increase in understanding with enhanced consent form compared to controls (meta-analysis).

- "The question of whether "shorter forms are better (or no worse than) longer" for participant understanding is still an open question…need for direct comparison in randomized studies…"

Nishimura A et al. *BMC Medical Ethics* 2013

# Strategies to improve understanding

- Randomized participants to either a concise or standard consent form.
- Does a simpler, more concise consent form affect study understanding or satisfaction with consent?
  - Healthy volunteers: Flu vaccine studies, Phase 1 drug development. Stunkel et al *IRB* 2010; Enama et al *Cont Clin Trial* 2012
  - Patient volunteers: Multinational HIV study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ETHICS & HUMAN RESEARCH

Comprehension and Informed Consent: Assessing the Effect of a Short Consent Form

IN THE FIELD

Assessing the Readability of Non-English-Language Consent Forms: The Case of Kiswahili for Research Conducted in Kenya

Comprehension and Informed Consent:
*Assessing the Effect of a Short Consent Form*

BY LEANNE STUNKEL, MEREDITH BENSON, LOUISE MCLELLAN, NINET SINAII, GABRIELLA BEDARIDA, EZEKIEL EMANUEL, AND CHRISTINE GRADY


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Randomization to standard and concise informed consent forms: Development of evidence-based consent practices☆

Mary E. Enama, Zonghui Hu, Ingelise Gordon, Pamela Costner, Julie E. Ledgerwood, Christine Grady and the VRC 306 and 307 Consent Study Teams

ARTICLE INFO

ABSTRACT

# Adequate understanding?

- Truog R et al. Is Informed Consent Always Necessary for Randomized, Controlled Trials**?** *N Engl J Med* 1999; 340:804-807

- Srinivasan G. Does informed consent to research require comprehension? *The Lancet* 2003; 362 (9400):2016–2018.

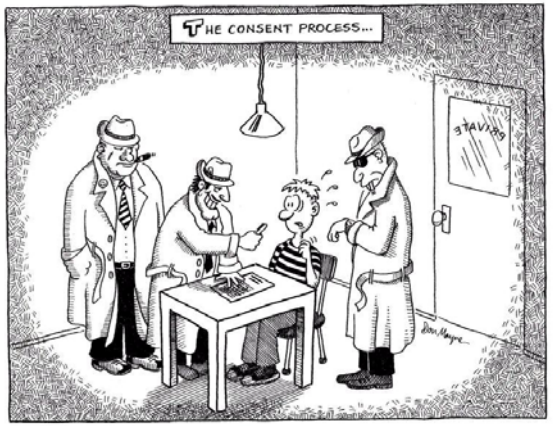
- Wendler D, Grady C. What should research participants understand to understand they are participants in research? *Bioethics* 2008; 22(4):203-8

# Elements of informed consent

- Disclosure of information
- Understanding
- *Voluntariness*
- Consent authorization

# Voluntariness

- Able to make a voluntary choice?
- No deception, coercion, undue influence

# Possible influences on voluntariness

- Dependent position
- Power relationship
- Pressure from others (family, friends)
- Trust in health care provider
- Restricted choices
- Illness
- Incentives

# Voluntariness

- Pressure from others
  - 2%- 25% (ACHRE 1996, van Stuvensten et al 1998, Pace et al 2005)
  - 58% from child's disease (Pace et al 2005)

- Knew they could quit
  - 44% Swedish women in gyn trial, 88% Thai HIV vaccine participants, 90% US Cancer patients (Lynoe et al 1991 and 2001, Pitisuttithum et al 1997, Joffe et al 2001)

# Voluntariness: Data on refusal

| Study | Refusal rate |
| --- | --- |
| Cardiac intervention studies | 7% (range 1-21%) |
| Breast conserving treatment trial | 9% |
| NHANES interviews and samples | 18.9 %, 14.7% |
| Intensive diabetes therapy- adolescents | 43% |
| Genetics study Guarani Indians | 58% |

# Summary: voluntariness

- Limited Data
- Measurement of voluntariness difficult
- Few feel pressure from others
- Many say they cannot quit or could not say no
- Individuals  refuse participation at variable rates

- "Is Informed Consent Broken?"
  - Overemphasis on the form and not the process
  - Inadequate understanding of the difference between research and treatment
  - Overemphasis on respect for persons
  - Flawed institutional enforcement
  - Changes in research

Henderson G, *American Journal of Medical Sciences*, October 2011

# Deciding for others

- Consent versus Permission
- Capacity
- Legal age of consent
- Legally authorized representatives
- Consent and assent

# Informed consent-conclusions

- Informed consent in research is ethically important, but imperfectly realized

- Data suggest:
  - Consent forms are long and complex,
  - Understanding is variable, and lacking in certain areas (e.g. randomization)
  - Many participants do not know/feel they can quit
  - Spending more time may enhance understanding

- More (and rigorous) data are needed
  - to improve our understanding of informed consent
  - Improve the process in a variety of settings
  - Enhance participants' experience, understanding, and decision making

# Informed consent

- More is not always better
- Timing matters
- Technology can help


Schenker Y and Meisel A, *JAMA 2011*

# Informed consent-conclusions

- Clarity about the purpose(s) of informed consent in research
- Quality training of researchers, research teams, and IRBs
- Creativity