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# The Quality of Informed Consent: What do the data show?

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**The views expressed here are mine and do not represent the views of the Department of Bioethics, the NIH or of the Department of Health and Human Services.**

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# Informed consent

- A legal, regulatory, and ethical requirement of most research with human subjects
  - One aspect of conducting ethical clinical research
  - A process (not a form or an episode)
  - Widely subscribed to, but imperfectly realized
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# Elements of informed consent

- Capacity to consent
  - Disclosure of information
  - Understanding
  - Voluntariness
  - Consent authorization
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# Research on informed consent

- Data on the quality of informed consent
    - Disclosure
    - Readability of forms
    - Understanding
    - Motivations
  - Data comparing consent strategies
    - To improve understanding and satisfaction
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# Research on Informed Consent

- Important to improve our understanding of:
    - The process
    - The written information
    - Participants' experience
    - Participants' understanding
    - Participants' decision making process
    - Strategies that work best
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## **Disclosure of information:**

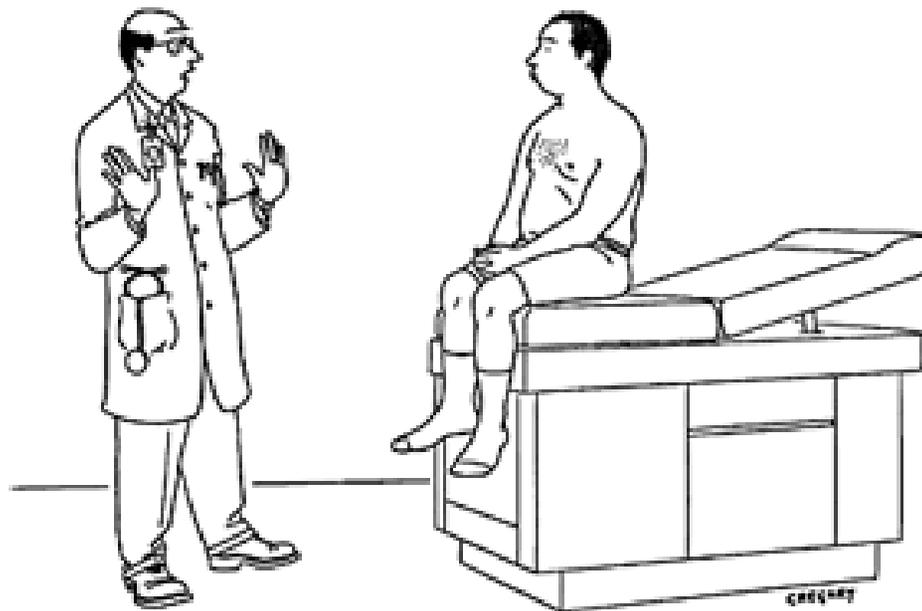
considerations

- What information should be disclosed?
  - How should the information be presented?
  - Accounting for circumstances and setting?
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# Disclosure of information

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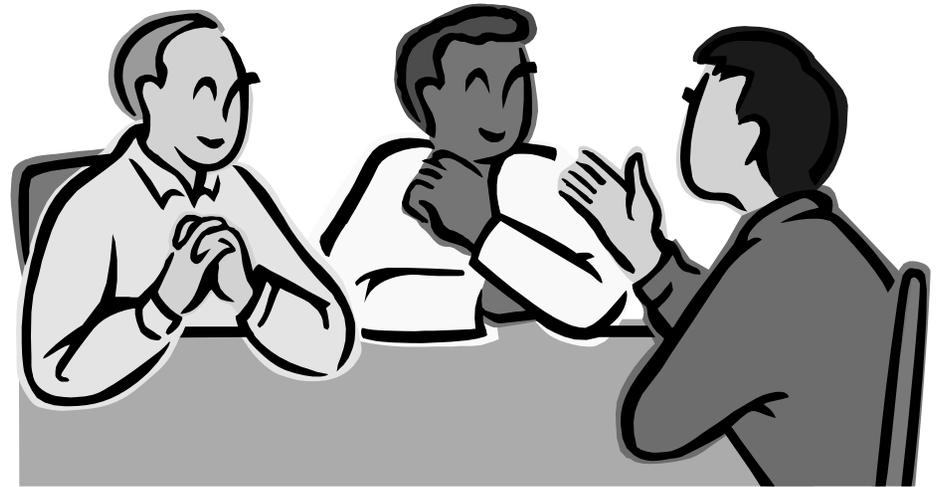


*“Whoa—way too much information!”*

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# Presentation



Context



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# 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
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# Informed consent document

- **Question 1:** Is it written at a reading level understandable to research subjects?
  - **Question 2:** Is the document formatted well? Does it have headings which break the text into short sections?
  - **Question 3:** Does the document contain the basic elements for informed consent and are they presented in a clear, easy-to-understand way?
  - **Question 4:** Can the document be shortened without compromising clarity or other requirements
    - <http://ohsr.od.nih.gov/info/sheet6.html>
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# Data on disclosure

- Consent documents
    - Readability
    - Content
  
  - Discussion
    - Content
    - Interaction
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# Consent form readability

- **Reading level is high**

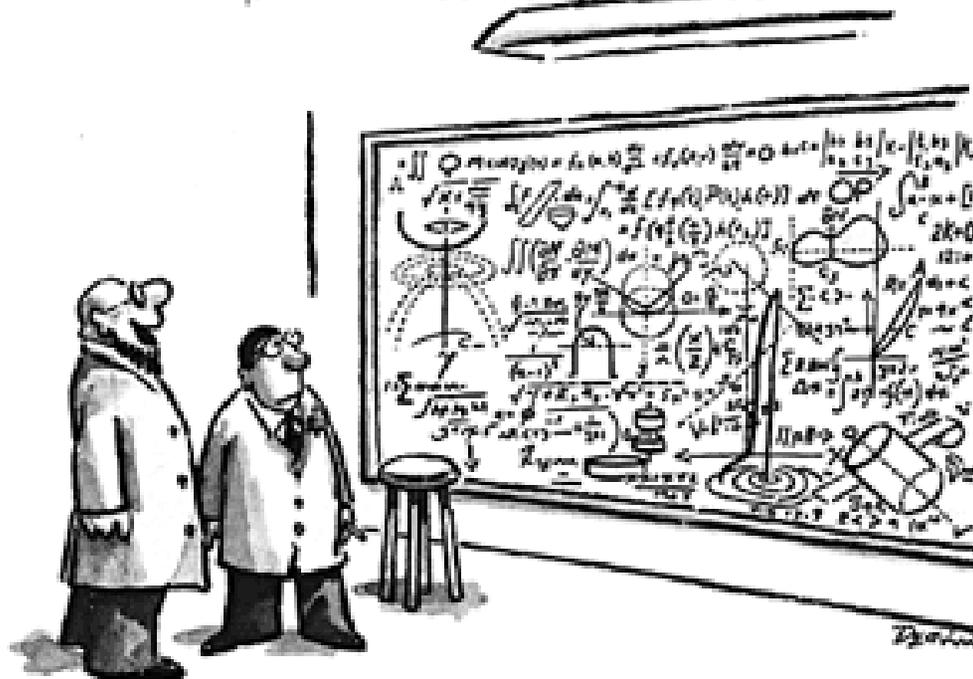
- College level (Denver VA (n=88); LoVerde, 1989)
- 11<sup>th</sup> grade (Flesch-Kincaid) to college level (Gunning Fog Index) (JHU phase 1-3 oncology consent forms, Grossman et al, JCO 1994)
- Average 10.6 grade (Flesch-Kincaid) on consent templates from websites of 114 US medical schools, (Paasche-Orlow et al. NEJM 2003)
- Average grade level 11.9 (Gunning Fog), none < 8<sup>th</sup> grade level (Emory oncology consent forms, Sharp, Am J Clin Onc 2004)

- **Consent forms are long**

- Studies have shown that consent documents have increased in length over time (Baker and Taub, JAMA 1983; LoVerde et al J Gen Int Med 1989; Tarnowski et al Pediatrics 1990 Beardsley et al JCO 2007)
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# Reading consent forms

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*"Hey, no problem!"*

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# Disclosure- content of forms

- 267 Phase I oncology consent forms were found to include:
  - The trial was research (99%)
  - The purpose as safety testing (92%)
  - The right to withdraw (99%)
  - Death as a risk (67%), unknown risks (84%)
  - Cure as a possible benefit (5%)

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# Disclosure- content of forms

- Multicenter trial with common protocol for 16 sites
  - 3 of 16 consent forms contained all basic elements 45CFR.46

Silverman et al. Critical Care Medicine 2001

- Review of 27 trials across 4 hospitals found significant information missing from PICFs

Beardsley et al. JCO 2007

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# Disclosure-interaction

- 48 videotaped physician-patient interactions with 12 oncologists were found to include:
  - Description of the study purpose (92%)
  - Review of the treatments, tests and procedures involved (92%)
  - Review of alternatives (82%)

Albrecht et al. 1999

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# Disclosure practices

- Investigators (n=60) of 12 multi-center RCTs asked about obtaining consent
- 58% reported giving full information, 42% only on the proposed treatment arm
- 12% did not inform patients about the trial prior to randomization
- 38% did not always tell the patient about randomization
- 5% did not seek consent at all

Williams and Zwitter, *Eur J Cancer* 1994

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# Disclosure practices

- Investigators (n=117) of a multinational HIV trial surveyed about consent practices
  - Provided subject with a copy to read (99%)
  - Subjects had opportunity to read before coming to clinic for signing (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

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# Summary- data on disclosure

- Limited data
  - Consent documents seem to include relevant information but are long and high level
  - Information is complex
  - Disclosure by investigators variable
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# Understanding

- Factors that might affect understanding
  - How is/should understanding assessed?
  - How much should subjects understand?
  - What happens when subjects don't understand? (or should happen?)
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# Subject characteristics to consider

- Age
  - Severity of illness and need
  - Educational level
  - Cognitive capacity
  - Familiarity with research
  - Language and customs
  - Capacity for free choice
  - Literacy
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## Data: Understanding research purpose/ nature

- 27% of Malian parents knew that study involved unproven malaria vaccine. Krosin et al 2006
  - 30% of U.S. Phase I, II, III oncology trial participants knew the treatments were unproven Joffe et al 2001
  - 88% of Thai HIV treatment participants knew study purpose Pace et al. 2005
  - 98% of Swedish women in a gyn trial knew it was research Lynoe et al 1991
  - 100% of rheumatoid arthritis RCT participants knew they were in a medical experiment Criscione et al. 2003
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## Data: Understanding risks/side effects

- 28% of subjects in a Hypertension trial remembered 2 side effects two hours after consent. Bergler 1980
  - 37% of US Cancer patients were aware of research risks Joffe et al. 2001
  - 56% of Gambian mothers could name  $\geq 1$  side effect of Hib vaccine Leach et al, 1999
  - 100% of US cancer patients could name  $\geq 1$  side effect of their Phase I trial Dougherty et al 2000
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# Data: Understanding Randomization

- 19% of mothers in a pediatric malaria treatment trial knew that not all children would get the same treatment. Pace et al 2005
  - 21% of US IDUs in an HIV vaccine trial knew that not everyone would get the vaccine Harrison et al 1995
  - 23% of Finnish women in a breast cancer trial remembered that treatment was chosen randomly. Hietanen 2000
  - 31% of Thai participants in HIV treatment trial knew that only half would get the experimental treatment Pace et al. 2005
  - 42% of US men in beta blocker heart attack trial were aware of the existence of a control group and of the fact that assignment was based on chance Howard 1981
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## Data: Understanding placebo controls

- 10% of Gambian mothers understood placebo design for vaccine trial Leach et al 1999
  - 67% of US participants in a rheumatoid arthritis trial knew that some people would get a placebo, but only 50% knew they were not certain to get active drug, and 53% that treatment would not be decided based on symptoms Criscione et al 2003
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# Knowledge vs. appreciation

- Therapeutic misconception
  - Immediately after consent psychiatric subjects (40%) said assignment would be based on therapeutic needs, and dosage (50%) would be adjusted according to their need. Appelbaum, 1982
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# Data on what affects understanding

- College education, speaking only English at home  
Joffe et al 2001
  - Education and age Bergler et al 1981
  - Education and age Hietanen et al 2000
  - Neither education nor age Miller et al. 1994
  - Neither education nor previous research experience  
Pace et al 2005
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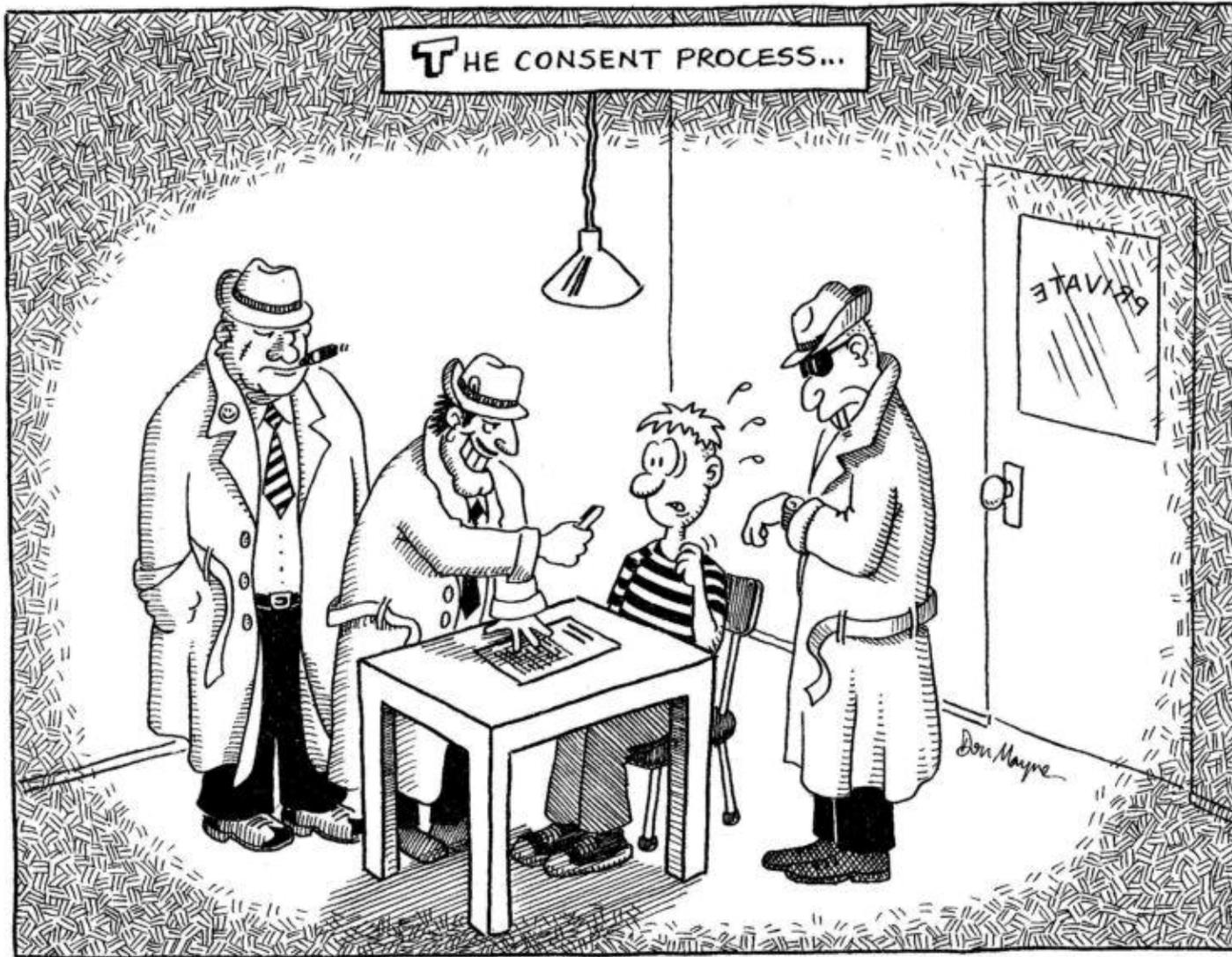
# Summary: data on understanding

- Understanding is variable
  - Most subjects know they are in research
  - Randomization is poorly understood
  - Understanding  $\neq$  appreciation
  - Age and education affect understanding, but not always
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# Voluntariness

- Able to make a (free) choice
  - No coercion or undue influence
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# Voluntary participation: possible influences

- Illness
  - Dependent position
  - Power relationship
  - Trust in health care provider
  - Restricted choices
  - Family pressures
  - Incentives
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# Measuring voluntariness

- Choose not to participate
  - Feel pressure to join
  - Know one can refuse or withdraw
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# Voluntariness- refusal

- 9% of women refused participation in breast conserving treatment trial for breast cancer.

Bijker et al Brit J Ca 2002

- 43% of adolescents refused participation in an intensive therapy trial for diabetes

Terryak et al  
Diabetes Care 1998

- 58% of Guarani Indians refused to participate in a genetics study

Benitez 2002

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# Voluntariness- pressure to join

- 2% of 570 U.S. participants in cardiology and oncology studies felt pressure to join ACHRE 1996
  - 15% of Ugandan parents felt pressure from others to enroll their child in a malaria treatment trial; 58% felt pressure because of their child's illness. Pace et al. AJPH 2005
  - 25% of Dutch parents of children in an anticonvulsant study "felt obliged" to participate Van Stuijvenberg 1998
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## Voluntariness- free to withdraw

- 44% of Swedish women in a gyn trial knew they could quit Lynoe et al 1991
  - 48% of Bangladeshi pregnant women in an iron supplement trial knew they could quit Lynoe 2001
  - 88% of Thai HIV vaccine trial participants knew they could “refuse at any time” Pitisuttithum 1997
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## Data: Voluntariness

- 90% of U.S. oncology patients in Phase I, II, or III trials knew they could quit Joffe et al 2001
  - 96% of US participants in a rheumatoid arthritis study knew they did not have to stay in the trial if they didn't want to Criscione et al 2003
  - 93% of South African women in an HIV transmission study knew they were free to quit; but 98% said the clinic would not let them quit  
Karim 1998
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# Trials of strategies to improve consent

## ■ Interventions

- 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)

## ■ Success measured in improved understanding or improved satisfaction

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- Flory and Emanuel *JAMA* 2004

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# Trials of strategies to improve consent

- Neither multimedia strategies nor enhanced consent forms consistently improved understanding
- However:
  - May be as good as usual process
  - May be more appropriate for certain populations
  - May be useful in standardizing disclosure
  - May improve satisfaction

Flory and Emanuel *JAMA* 2004

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# Trials of strategies to improve consent: Audio visual interventions

- 4 trials (3 RCT) involving data from 511 people, conducted in USA and Canada.
- Audio-visual interventions
  - did not consistently increase participants' levels of knowledge/understanding
  - 1 study showed better retention of knowledge amongst intervention recipients.
  - may transiently increase people's willingness to participate in trials, but this was not sustained at two to four weeks
- Considerable uncertainty remains about the effects of audio-visual interventions, compared with standard forms of information provision

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

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# Trials of strategies to improve consent

- Limited data suggest that more person-to-person contact (through extended discussions (3/5) , test/feedback strategies (5/5)) may help improve understanding

Flory and Emanuel *JAMA* 2004

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# Trials of strategies to improve consent

“None of the intervention studies clearly identified... methods...to increase knowledge,... satisfaction, or to affect actual decisions”

*IRB: Ethics and Human Research* Informed consent supplement  
Sept/Oct. 2003

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# Research on Informed Consent: Challenges

## ■ **Conceptual issues**

- Understanding versus appreciation
- Voluntariness

## ■ **Design issues**

- Real vs. simulated
- Survey

## ■ **Measurement issues**

- Standardization of questions
  - Timing of questions
  - Size of cohort
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# Research on Informed Consent: Challenges

- IRB approval
  - Collaboration with clinical investigators
  - Possible disruption of flow/enrollment
  - Obtaining informed consent
  - Intervening?
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# Research on informed consent

- Current data:
    - Most are small samples
    - Single site studies
    - Variable timing
    - Non standard questions
  - Comparability ?
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# Informed consent-conclusions

- Informed consent in research is ethically important, but imperfectly realized
  - More (and rigorous) data are needed
  - Available data suggest:
    - Consent forms are complex,
    - Understanding is variable, and especially lacking in certain areas (e.g. randomization and side effects)
    - Many do not know/feel they can quit
    - Spending more time may enhance understanding
-