Informed Consent: What do the data show?

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The views expressed here are the author's own and do not reflect the position of the National Institutes of Health or of the Department of Health and Human Services.

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)

Informed Consent

- Widely subscribed to, but
- Imperfectly realized

Elements of informed consent

- Disclosure of information
- Understanding
- Voluntariness
- Consent

Research on Informed Consent

- Important to improve our understanding of:
  - The process
  - The written information
  - The experience of participants
  - The understanding of participants
  - The decision making process of participants
  - Strategies that work best

Research on Informed Consent: Challenges

- Conceptually- what to measure
  - Understanding versus appreciation
  - Voluntariness
- Design issues
  - Hypothetical vs. observation vs. surveys

Research on Informed Consent: Challenges

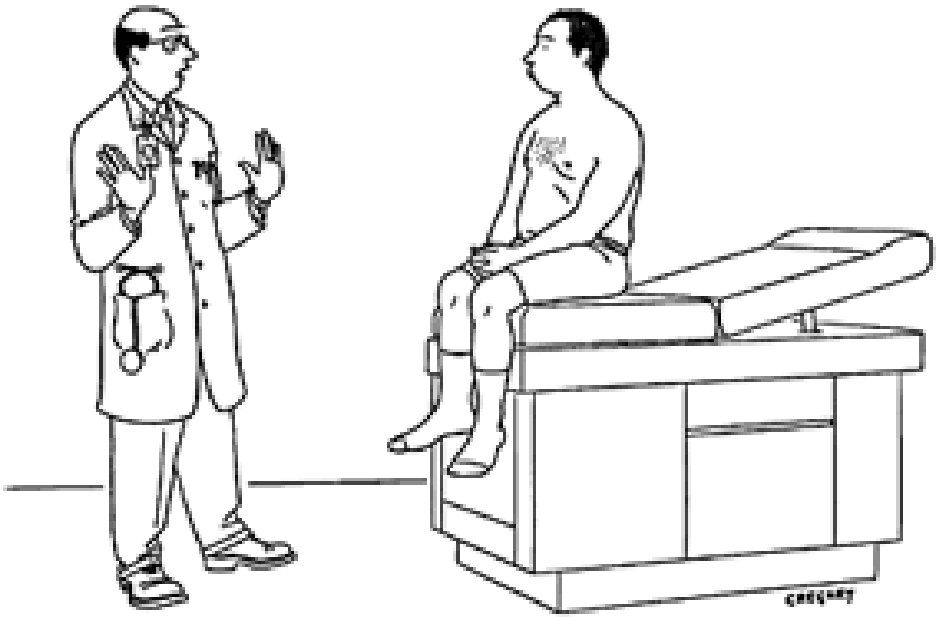
- Measurement issues
  - Standardization of questions
  - Timing of questions
  - Size of cohort
- See, for e.g. Informed consent supplement in IRB: Ethics and Human Research, Sept/Oct. 2003

Research on Informed Consent: Challenges

- IRB approval
- Collaboration with clinical investigators
- Disruption of flow/enrollment
- Obtaining informed consent
- Intervening?

Research on informed consent

- Current data:
  - The quality of informed consent
  - Strategies to improve informed consent
- Small sample size
- Single site studies
- Varied questions (no standardization,
- ? Comparability)
- Varied timing



"Whoa—way too much information!"

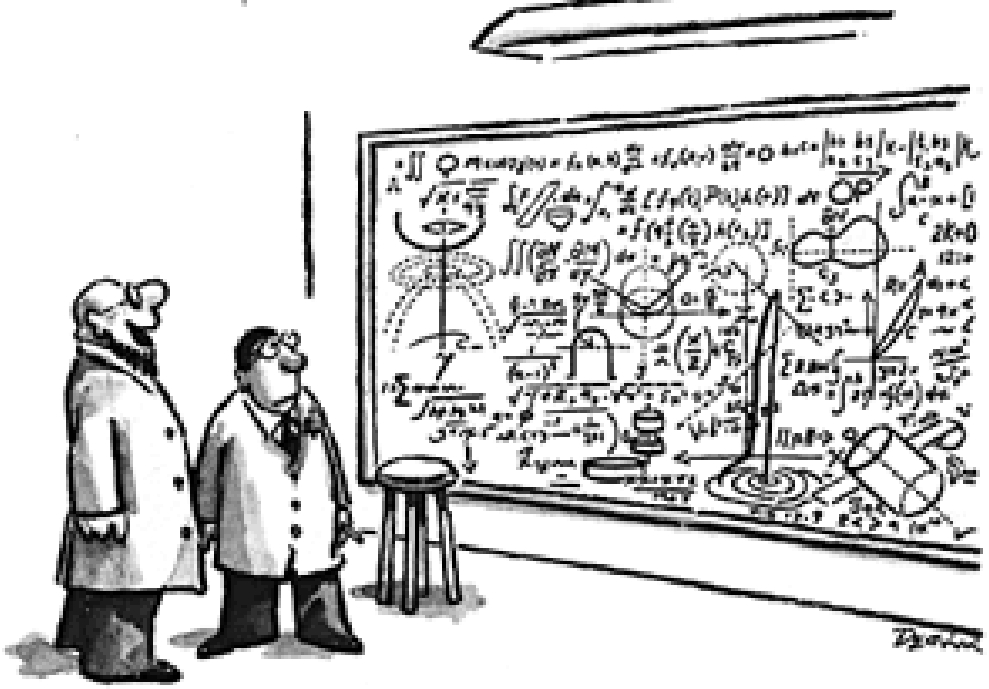
Elements of informed consent

- Disclosure of information
- Understanding
- Voluntariness
- Consent

Data on disclosure

- What information is given to subjects and how?
- Consent documents
  - Readability
  - Content
- Discussion
  - Content
  - Interaction

Reading consent forms



"Hey, no problem!"

Consent form readability

- Analysis of 88 forms from the Denver VA:
  - Reading levels ranged from 9th to 17th grade
  - The mean reading level required college-level reading ability
  - Length had increased by 58% since a similar study 7 years earlier

LoVerde, 1989

Consent form readability

- Analysis of 137 oncology consent forms (phase I, II, and III trials) at Johns Hopkins Oncology Center
  - Mean grade reading level was 11.1 using Flesch-Kincaid formula and 14.1 using Gunning Fog index
    - Grossman et al, JCO 1994

Consent form readability

- Readability scores computed for informed consent templates from the websites of 114 US medical schools
  - Average readability score (Flesch-Kincaid) for text provided as templates was at the 10.6 grade level, exceeding the stated standard by an average of 2.8 grade levels

    - Paasche-Orlow et al. NEJM 2003

Disclosure- content of forms

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

Horng et al, NEJM 2002

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

Disclosure

- Investigators of 12 multi-center RCTs were asked about their practice of obtaining consent in these RCTs.
- Of 60 respondents
  - 12% did not inform their patients about the trial prior to randomization, and 38% did not always tell the patient about randomization
  - 5% did not seek consent at all
  - Only 58% of clinicians reported giving full information on all aspects of the trial.
  - 42% gave information on the proposed treatment arm only.

Williams, 1994

Elements of informed consent

- Disclosure
- **Understanding**
  - Knowledge of the relevant information
  - Appreciation of how study information applies
- Voluntariness
- Consent

Data: Understanding research purpose/ nature

- 98% of Swedish women in a gyn trial knew it was research Lynoe et al 1991
- 30% of U.S. Phase I, II, III oncology trial participants knew the treatments were unproven Joffe et al 2001
- 80% of Thai HIV vaccine trial participants knew that the vaccine might not work Pitisuttithum et al. 1997
- 100% of participants in an RCT for rheumatoid arthritis knew they were participating in a medical experiment Criscione et al. 2003

Data: Understanding risks/side effects

- 56% of Gambian mothers could name ≥ 1 side effect of HIB vaccine Leach et al, 1999
- 100% of cancer patients could name ≥ 1 side effect of their Phase I trial Dougherty et al 2000
- 28% of subjects in a Hypertension trial remembered two side effects two hours after consent. Bergler 1980
- 52.4% of subjects in an analgesia study did not remember any of 12 side-effects 60 days after consent. Miller 1994

Data: Understanding Randomization

- 23% of Finnish women in a breast cancer trial remembered that treatment was chosen randomly. Hietanen 2000
- 21% of US IDUs in an HIV vaccine trial knew that not everyone would get the vaccine Harrison et al 1995
- 31% of Thai participants in HIV treatment trial knew that only half would get the experimental treatment Pace et al. 2003
- 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

Data: Understanding

- 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

Knowledge vs. appreciation

- 40% of psychiatric subjects interviewed immediately after consent stated that assignment would be made on the basis of their therapeutic needs.

- 50% incorrectly believed that their dosage would be adjusted according to their individual need.

Appelbaum, 1982

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 2003

Voluntariness

- Able to make a (free) choice
- No coercion or undue influence

Data: Voluntariness

- 88% of Thai HIV vaccine trial participants knew they could “refuse at any time” Pitisuttithum 1997
- 48% of Bangladeshi pregnant women in an iron supplement trial knew they could quit Lynoe 2001
- 90% of U.S. oncology patients in Phase I, II, or III trials knew they could quit Joffe et al 2001

Data: Voluntariness

- 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
- 44% of Swedish women in a gyn trial knew they could quit Lynoe et al 1991
- 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

Data: Voluntariness

- 2% of 570 U.S. participants in cardiology and oncology studies felt pressure to join ACHRE 1996
- 25% of Dutch parents of children in an anticonvulsant study “felt obliged” to participate
  Van Stuijvenberg 1998
- 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, unpublished data

Data: Voluntariness

- 58% of Guarani Indians refused to participate in a genetics study Benitez 2002
- 43% of adolescents refused participation in an intensive therapy trial for diabetes Terryak et al Diabetes Care 1998
- 9% of women refused participation in breast conserving treatment trial for breast cancer. Bijker et al Brit J Ca 2002

Consent

- Decision
- Authorization
- Usually documented by signature

Consent

- Paraguay: Genetic population study among Guarani Indians with high illiteracy rates
  - Consent form translated to Guarani and read to prospective participants
  - Bilingual Q&A session
  - Participants gave individual oral consent and signed or fingerprinted a written form.
  - All was documented by triple media recording (“audiovisual documentation of consent”)

Benitez et al. Lancet 2002; 359: 1406-07

Informed consent-conclusions

- Informed consent in research is important, but imperfect
- Data is limited (both in quality and quantity)
- More data and more rigorous data needed

Quality of informed consent

- Available data suggest:
  - Consent forms are complex, but complete
  - Participants are generally satisfied
  - Participant understanding is variable, and lacking in certain areas (e.g. randomization and side effects)
  - Many do not know/feel they can quit

Trials of strategies to improve consent

- Success measured in improved understanding or improved satisfaction
- Audiotapes, videotapes, interactive computers, telephone follow up, additional time with study team, post-tests, competence assessment, simpler forms

Trials of strategies to improve consent

- Mixed results
- “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