Impact of poor informed consent processes on clinical trials: From the practical to the sublime

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Basic components of informed consent

• Disclosing adequate information to allow for an informed decision about research participation
• Facilitating comprehension
• Providing adequate opportunity to ask questions and to consider participation
• Obtaining voluntary agreement
Complexities of studying Informed consent

• Complex process of learning activities
• Clinical research is diverse
• Study populations differ: Does this affect the implementation of adequate informed consent, and if so, how?
• Data derived from various components of informed consent processes are heterogeneous (setting, timing of data collection, types and quality of methodology used, ability to generalize to other groups)
Practical concerns

• **Failure to describe the nature of the research and the scientific reasons for it:**
  – Reduced recruitment?
  – Affects on retention: Important to do an exit interview to ascertain why participants withdraw and whether improvements in research conduct are needed

• **Long and complex forms may:**
  – Inhibit reading and processing
  – Increase resource burdens
  – Delay research start-up time, particularly for multi-site research
Practical concerns

• Decreased understanding by research participants may affect data integrity:
  – Impacting participants’ ability to follow study procedures
  – Perpetuating the therapeutic misconception, which may:
    • Promote a bias in favor of efficacy
    • Lead to under-reporting of adverse effects
Aspirational goals of informed consent

• Honoring self-determination
• Empowering the potential participant to decide whether the risk/benefit ratio is acceptable to that individual, and remains acceptable throughout the research
• Respecting potential participants as true partners in the research endeavor
• Maintaining an ongoing dialogue (before research initiation, during and after study completion)
• Protecting individuals with diminished autonomy (e.g., assent, LAR, adjusting the informed consent process to accommodate diminished decisional-capacity)
“Sublime” concerns

• Failure to provide contextual meaning to the research may degrade the participant’s autonomy and decision-making abilities
  – (Brian Zikmund-Fisher: “. . . Not just to recognize the number, but also to draw the meaning they need from the number to make the choices the need to make.”)

• Failure to engage participants as true partners in the research enterprise may lead to a sense of objectification or “commoditization”

• Failure to accurately describe the nature of the research enterprise may promote distrust/anger on an individual or group level
Further discussion needed . . .

• Studies show that research participants have limited understanding of aspects of research after standard informed consent.

• Studies show that interventions to improve understanding are not effective or are of limited/inconsistent effectiveness.

  – Flory, Wendler, Emanuel: Looked at 42 trials of consent processes involving an intervention (e.g., multimedia, extended discussions, test/feedback, enhanced forms). “Person-to-person interactions, especially the extended discussion interventions, may be more effective in improving understanding.”
Enhanced consent forms

*Flory, Wendler, Emanuel*

- Reduced length, simplification of content, inclusion of graphics, revised formatting
- 6 of the 15 studies showed “significant gains in understanding” but 9 did not.
- Of the 6 studies: 5 were simulated consent processes with no discussion
- Of the 9 studies: 4 were randomized controlled trials of actual consent processes
- Lower educational levels, mental illness and advanced age are associated with poorer understanding.
Further discussion needed . . .

• Evidence-based research on informed consent interventions is essential.
  – Quality data is challenging to obtain.
  – Generalizability of the results across disparate study populations will need to be assessed.
  – Validation and quality of tools to measure understanding and participant satisfaction need to be ascertained.
  – Consider nested informed consent studies (i.e., consent sub-study of an actual clinical study)
Further discussion needed . . .
What do participants want/need to know?

• Patient-centered informed consent mechanisms, tools and learning strategies (e.g., partnerships between investigators and patients/disease-based advocacy groups)
  – Dana Farber-improving informed consent for palliative chemotherapy (Deborah Schrag presentation to SACHRP, 7/21/14): Participants recommended, “Organizing IC by regimen rather than individual drug”; “Including patient voices” (e.g., what can be done to alleviate AER)
A Randomized, Controlled Study Comparing NCI’s Original and Revised Informed Consent Templates (Massett, HA., et.al. Abstract ID #6523)

• NCI, revised its informed consent template for its late phase clinical trials, based on expert input from MDs, RNs, IRB reps, industry reps, FDA, OHRP, ethicists, lawyers, patient advocates, communication experts.

• The newer ICD was:
  – 2 pages shorter, 25% fewer words, 32% fewer sentences, 36% fewer sentences per paragraph, 10% fewer passive sentences, 7% more paragraphs
A Randomized, Controlled Study Comparing NCI’s Original and Revised Informed Consent Templates

(Massett, HA., et.al. Abstract ID #6523)

• Compared knowledge means and participant satisfaction for colorectal cancer survivors (not research participants).
• No difference in satisfaction
• Higher education predicted greater knowledge items
• Familiarity with clinical trials were more likely to consider a clinical trial in the future
• [Should all clinical trial participants be provided general knowledge about clinical trials as part of the informed consent process?]
Further discussion needed . . .

Going beyond “the informed consent form”

- Educating rather than simply informing
- Understanding it is a continuous process rather than a single event (which should include return of aggregate results)
- Reflecting the diversity of research (One approach to informed consent may not be suitable for all types of research)
  - A minimal risk survey study --- a study of a permanently implantable investigational device
  - A Phase 1 study of an investigational drug --- a comparative effectiveness study of standard-of-care drugs
  - A first-in-human stem cell transplant --- CER
- Restructuring the organization of the informed consent form (e.g., summary information first, followed by more detailed appendices)
For further discussion . . .
Going beyond the individual

• Role of the community (e.g., patient-advocacy groups, community-based advisory boards, disease-specific foundations)
  – FDA commitment to patient-focused drug development under the 5th reauthorization of the Prescription Drug User Fee Act
    • HIV “Cure” Research, 6/14/13

• Role of subject advocates
For further discussion . . .
Reaching out to other disciplines

• Co-opting successful research tools from other applicable fields (e.g., socio-behavioral sciences, decisional science, psychology)

• Co-opting successful teaching techniques from educators and others
  – Teach back, teach-to-goal

• Co-opting successful communication skills to provide periodic updates during ongoing research
Information sharing

• **HIPAA**
  – Current misunderstandings and burdens associated with applying HIPAA to the research context
  – Pros and cons to stand-alone HIPAA authorization forms and compound forms

• **Sharing “big data”**
  – Multiple data sets from different sources that are pooled to answer a new question(s)
  – Data may consist of billions to trillions of records of millions of people from different sources
  – Data may be updated periodically
  – May be multi-national
  – May be obtained when a person seeks medical care or other goods and services (Consent?)
Information sharing

• **Future use of biospecimens**
  – Existing concerns accentuated for genetic and genomic information
  – Is de-identification, given current computer technology, a safeguard of privacy?
  – FDA Guidance on clinical pharmacogenomics (2013) recommends that “DNA samples should be collected from all patients in all arms of clinical trials in all phases of drug development.”
  – Tracking of initially expressed wishes
  – Barnes and Heffernan: “The NCI formulation [tiered-approach] has the benefit of treading a line between being inaccurately specific and impermissibly vague.”
Information sharing

• What does privacy mean in today’s highly matrixed and technologically sophisticated world?
• How would the public balance protection of individual privacy vs. utilitarian benefits to public health from future use of linked data sets and/or biospecimens?
• How should differing national concerns and sensitivities be bridged?
• Ultimately, what is the optimal manner to present this information in an informed consent process?
• Fundamentally, there is an epistemological problem(s) with informed consent.
Partnerships: Public dialogue & education coupled with evidence-based research on informed consent
Suggested references

• Sugarman, et.al., *Evaluating the quality of informed consent*, Clinical Trials (2005);2:3-4.
Suggested references


Thank you

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