Comparison of Different Approaches for Notification and Authorization in Pragmatic Clinical Research Evaluating Commonly Used Medical Practices

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The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.
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Types of Trials

• **Explanatory**
  
  “primarily designed to determine the effects of an intervention under ideal circumstances”

• **Pragmatic**

  “primarily designed to determine the effects of an intervention under the usual conditions in which it will be applied”

Attributes of PCTs

1) an intent to inform decision-makers (patients, clinicians, administrators, and policy makers), as opposed to elucidating a biological or social mechanism;

2) an intent to enroll a population relevant to the decision in practice and representative of the patients/populations and clinical settings for whom the decision is relevant;

3) a focus on outcomes of relevance to patients and clinicians; and

4) either an intent to
   (a) streamline unnecessary procedures and data collection so that the trial can focus on adequate power for informing the clinical and policy decisions targeted by the trial or
   (b) measure a broad range of outcomes.

Background Conditions

• Broad moral claim to obtain evidence to improve clinical practice since most decisions are now made without reliable evidence to know which choices optimize health

• Technology permits conducting large scale research and cohort finding for rare diseases and special populations, often with minimal incremental risks and burdens and less cost

Clinical Trials Special Series
Guest Editors: Jeremy Sugarman and Robert Califf

Informed consent
Defining minimal risk
Data monitoring
Research/quality improvement distinction
Vulnerable subjects
IRB harmonization
Identifying direct and indirect subjects
Gatekeepers
FDA-regulated products
Nature of intervention
Privacy

http://ctj.sagepub.com/content/early/recent
NIH Ethics Supplements

CTSA (University of Washington & Stanford)

NIH Collaboratory

TiME (University of Pennsylvania)

ABATE (University of California - Irvine)

Coordinating Center (Duke & Hopkins)
Ethics of research in usual care settings: Data on point

Patients' views concerning research on medical practices: Implications for consent

Alternative consent models for comparative effectiveness studies: Views of patients from two institutions

Patient and physician views about protocolized dialysis treatment in randomized trials and clinical care

The patient's perspective on the need for informed consent for minimal risk studies: Development of a survey-based measure

Adrift in the gray zone: IRB perspectives on research in the learning health system
What’s been done?

• **Qualitative**
  • Focus groups with patients/parents of patients
  • Interviews with IRB members and researchers
  • Focus groups with QI professionals and CER investigators
  • Deliberative engagement with patients
  • Interviews with dialysis patients and nephrologists
  • Focus groups with IRB members

• **Quantitative**
  • Instrument development regarding QI and consent
  • Two national web-based surveys

What do we know?

• At least a substantial minority of patients wants to be engaged in making decisions about participating in research in usual care settings, regardless of whether this may not be the norm for certain health care activities or the activity poses minimal risk.

• It is unclear whether this would still be the case if the nature of the research was clearly communicated and understood and patients could be sure that their best interests would not be compromised by the research.

• Currently available reports rely in large part on hypothetical examples and choices, which necessarily has limited verisimilitude to actual practices and limits validity.

Objective

For different types of CER study designs, compare different models for notification and authorization (N&A) with respect to . . .

- Participation in the research
- Acceptability of the notification & authorization approach
- Understanding
- Perception of personal risks/benefits
- Trust
- Perceived amount of information
Methods
(Brief)
Sample

U.S. adults from GfK KnowledgePanel

English-speaking

Have seen a health care provider at least once in the past year

Probability-weighted to allow inference to U.S. population
Each person randomized to “experience” and react to 1 of 24 different research scenarios
CER Designs Tested

Pharmacotherapy

Medical Record Review

Individual Randomization

Devices Used at the Institution (Cluster randomization)
CER Designs Tested

- Pharmacotherapy
- Devices Used at the Institution (Cluster randomization)

Medical Record Review

Individual Randomization

Multiple approaches to notification and authorization tested for each design
Approaches to Notification & Authorization

- Written consent (with clinical risks included)
- Written consent
- Oral consent + Info sheet
- Oral consent
- General notification (with opt-out)
- Post-notification after study done
Survey/Materials Development

Plausibility of notification/authorization materials (approx 120 pages)

Reviewed by 2 IRB members (1 chair) from 6 different institutions

Cognitive interviews to evaluate scenario descriptions and survey questions

5 rounds with 31 participants (!)
4879 sampled

2994 completed

2955 Final N

39 excluded for speeding or missing > 1/3 items

61.4% completion rate
Key Findings & Implications
1. People have significant difficulty understanding aspects of pragmatic trials of commonly used medical practices.
Randomization
No extra things required
SCENARIO 29

You go to the local clinic for a routine checkup. There is a sign on the waiting room wall describing a research study in which the clinic is participating.

- Our clinic, along with other clinics around the country, is taking part in a research study.
- Researchers want to find out the best method for taking blood for routine tests. Clinics typically collect blood using one of two different types of needles. Researchers want to know if one type of needle is better than the other in terms of the number of attempts (times patients need to be stuck with a needle) needed to get enough blood.
- As part of the study, different clinics have been randomly selected to use one type of needle or the other. This means that some clinics were selected to use the first type of needle, and all the doctors and nurses there are using that type, while other clinics were selected to use the second type of needle, so all the doctors and nurses there are using that type.
- Later on, to see if one type works better than the other, researchers will look at specific parts of patients' medical records to see how many attempts were needed to get enough blood.
- Researchers have to follow the same rules that are already in place to protect health information and keep it secure.
- There will be no extra follow-up calls or visits that patients need to do related to the study.
- If you have any questions, please contact Dr. Smith at 123-4567.

The doctor does an exam and orders some basic lab tests. After the doctor finishes your exam, a nurse comes in to collect a small amount of blood for the tests.
There will be no extra follow-up calls or visits that patients need to do related to the study.
Later on, to see if one type works better than the second type of needle, so all the doctors agree on which parts of patients' medical records to see how much blood to draw enough for the research. Researchers have to follow the same rules that protect information and keep it secure.

There will be no extra follow-up calls or visits from the doctor does an exam and orders some basic labs in to collect a small amount of blood for the research.

If you have any questions, please contact Dr. Smith.
Therapeutic Misconception?
There could be nontrivial consent bias, but it’s the same for all approaches for N&A.
28 to 49% who declined to participate
Most of the public currently view less active approaches* to N&A as unacceptable for some types of pragmatic research.

*No notification and general notification
% people receiving general notification who were unaware they were in research and could opt out
21 to 36% people receiving general notification who were unaware they were in research and could opt out
WHAT ARE THE RISKS OF THE STUDY?

In this study, researchers must follow laws to protect health information and keep it secure. However, there is a very small chance that information about you might become known to people outside of the study.

Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of City Medical Center.
WHAT ARE THE RISKS OF THE STUDY?

You might have a complication from the blood clot, or a side-effect from one of the medicines. This could also happen if you were not in a study. Common side effects for both medicines include bleeding, bruising, skin rash, headaches, cold symptoms, skin breakdown, purple toes, elevated liver enzymes, and/or upset stomach. The doctor can tell you more about how often these occur and how serious they could be.

In this study, researchers must follow laws to protect health information and keep it secure. However, there is a very small chance that information about you might become known to people outside of the study.

Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of City Medical Center.
For written consent, including descriptions of background clinical risks increased length of form but did not change any outcome (including understanding and perception of risk).
Active alternatives to written consent—such as oral consent—may not be expected to compromise consent quality.
Acceptability of the consent model
Understanding
Perception of personal risks/benefits
Trust
Perceived amount of information

Oral consent
Oral consent + info sheet
Written consent (with or without clinical risks)
Acceptability of the consent model

Understanding

Perception of personal risks/benefits

Trust

Perceived amount of information

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<th>Oral consent</th>
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<tr>
<td>Oral consent</td>
<td>+ info sheet</td>
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Limitations

Hypothetical nature of scenarios

Artificial nature of notification & authorization
Conclusions
1. Difficulty understanding aspects of pragmatic trials of accepted medical practices

2. Nontrivial consent bias, but it’s the same for all approaches for N&A.

3. Less active approaches to N&A viewed as unacceptable for some types of pragmatic research including descriptions of background clinical risks increased length of form, but did not change any outcome

4. Active alternatives to written consent—such as oral consent—may not be expected to compromise consent quality.