Data Sharing & Pragmatic Clinical Trials:
Navigating Ethical Challenges in a Changing Policy Landscape

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Project Background

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- **Project Team:** Jeremy Sugarman & Juli Bollinger (Hopkins); Kevin Weinfurt (Duke)

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Ethics challenges in sharing data from pragmatic clinical trials

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Abstract

Numerous arguments have been advanced for broadly sharing de-identified, participant-level clinical trials data, and trial sponsors and journals are increasingly requiring it. However, data sharing in pragmatic clinical trials presents ethical challenges related to the use of waivers or alterations of informed consent for some pragmatic clinical trials and corresponding limitations of informed consent to guide sharing decisions; the potential for data sharing in pragmatic clinical trials to present risks not only for individual patient-subjects, but also for health systems and the clinicians within them; sharing of data from electronic health records instead of data newly collected for research purposes; and researchers' limited capacity to control sensitive data within an electronic health record and potential implications of such limits for meeting obligations inherent to Certificates of Confidentiality. These challenges raise questions about the extent to which traditional research ethics governance structures are capable of guiding decisions about pragmatic clinical trial data sharing. This article identifies and examines these ethical challenges for pragmatic clinical trial data sharing. We suggest several areas for future empirical scholarship, including the need to identify patient and public attitudes regarding pragmatic clinical trial data sharing as well as to assess the demand for pragmatic clinical trial data and the correspondingly likely benefit of such sharing. Further conceptual work is also needed to explore how requirements to respect patient-subjects about whom data are shared in the context of pragmatic clinical trials should be understood, particularly in the absence of informed consent for initial research activities, and the appropriate balance between promoting the generation of socially valuable knowledge and respecting autonomy.

Keywords

Pragmatic clinical trials, ethics, data sharing, individual participant data

Key Stakeholder Interviews (N=40)

Role Type	# of Respondents
Research (PI, Co-I)	14
Human Research Protection Program	6
Data Science	6
Research Funder/Sponsor	5
Data Repository/Data Governance	4
Patient Advocate	3
Health Care System Leadership	2

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RESEARCH REPORT

Learning Health Systems

Stakeholder perspectives on data sharing from pragmatic clinical trials: Unanticipated challenges for meeting emerging requirements

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Abstract

Introduction: Numerous arguments have been advanced for broadly sharing de-identified, participant-level clinical trial data. However, data sharing in pragmatic clinical trials (PCTs) presents ethical challenges. While prior scholarship has described aspects of PCTs that raise distinct considerations for data sharing, there have been no reports of the experiences of those at the leading edge of data-sharing efforts for PCTs, including how these particular challenges have been navigated. To address this gap, we conducted interviews with key stakeholders, with a focus on the ethical issues presented by sharing data from PCTs.

Methods: We recruited respondents using purposive sampling to reflect the range of stakeholder groups affected by efforts to expand PCT data sharing. Through semi-structured interviews, we explored respondents' experiences and perceptions about sharing de-identified, individual-level data from PCTs. An integrated approach was used to identify and describe key themes.

Results: We conducted 40 interviews between April and September 2022. Five overarching themes emerged through analysis: (1) challenges in sharing data collected under a waiver or alteration of consent; (2) conflicting views regarding PCT patient-subject preferences for data sharing; (3) identification of respect-promoting practices beyond consent; (4) concerns about elevated risks or burdens from sharing PCT data; and (5) diverse views about the likely benefits resulting from sharing PCT data.

Key Themes

1. Challenges in sharing data collected under waiver/alteration of consent
2. Conflicting gatekeeper views regarding PCT patient-subject preferences for data sharing
3. Need for respect-promoting practices beyond consent
4. Concerns about elevated risks or burdens from sharing PCT data
5. Diverse views about likely benefits resulting from sharing PCT data

Key Themes

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5. Diverse views about likely benefits resulting from sharing PCT data

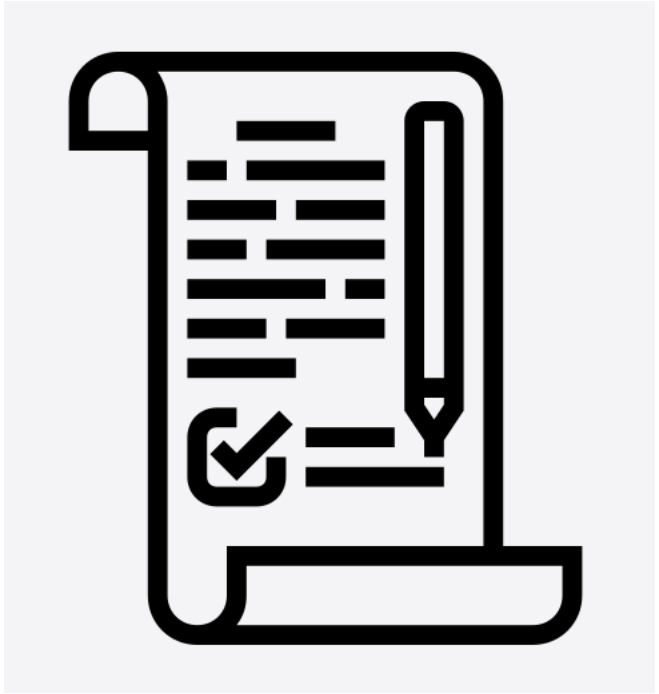
What does it mean to <u>respect</u> patient-subjects in the context of (not?) sharing data from a PCT—

especially for trials conducted under a waiver/alteration of informed consent?

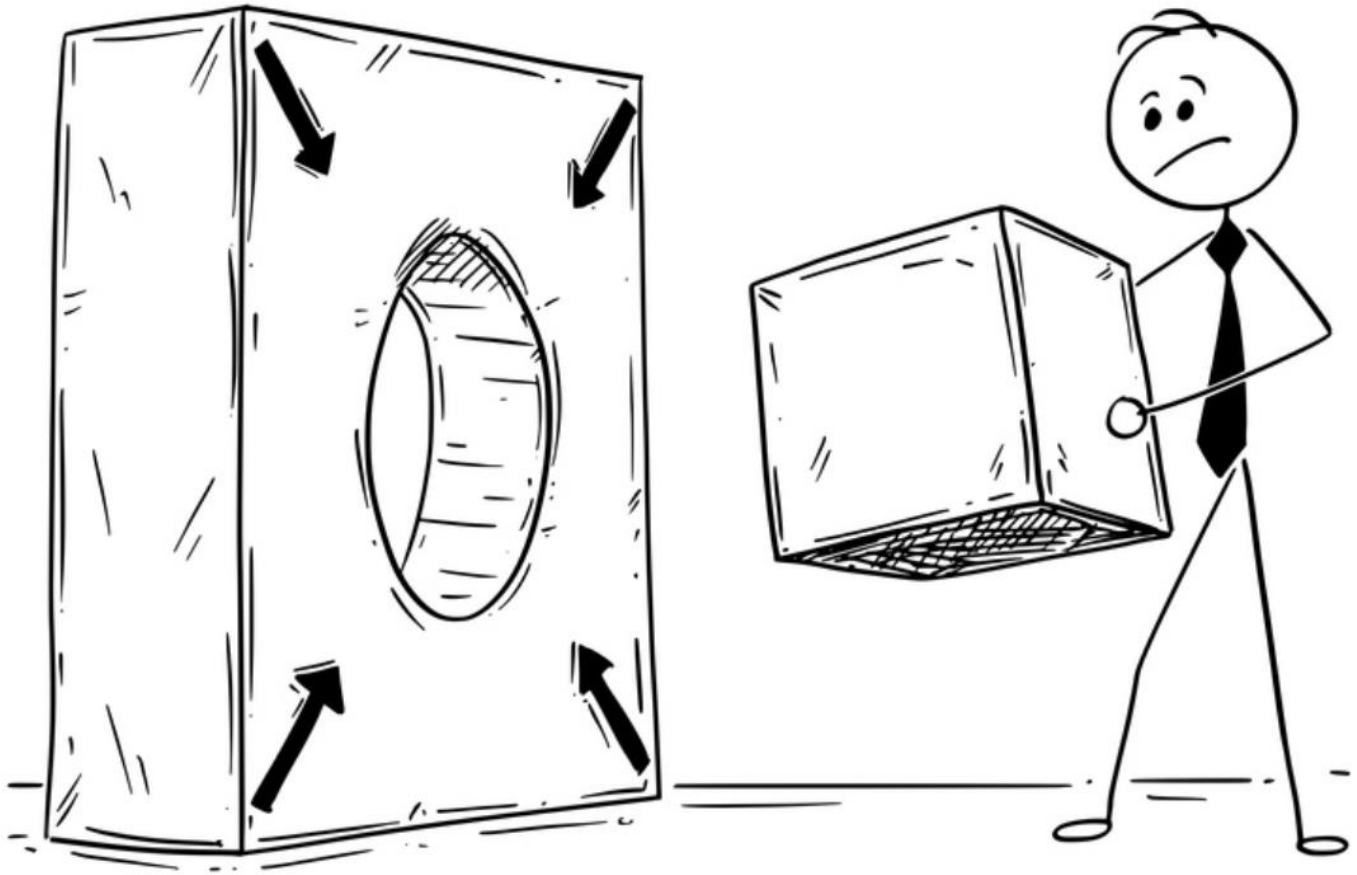
Data Sharing & Informed Consent

Traditionally…

- Heavy reliance on informed consent process
- Expectation that participants want and expect data to be shared



Sharing Data Collected Under Waiver/Alteration of Consent



Gatekeepers as Data Stewards

- IRBs/HRPPs
- Investigators
- Health system leaders

Yet divergent perceptions about patient-subject preferences…

"…if people know that you're doing research… for public good, and not for profit, ***people are generally enthusiastic*** *about [their] participation being used by others to learn more.*

-Health System Leader

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-Health System Leader

*"…**research participants want to be asked**…when we talk about downstream sharing of deidentified data it would probably run along the same lines of whether or not people…would be **bothered by the fact that they were in a study under a waiver in the first place**…."* –HRPP Director

Insight #1: Data Needed on Preferences

Use of waivers or alterations of informed consent

→

Elicit patient preferences about sharing PCT data—and about how to do consistent with principle of respect

Insight #2: Look Beyond Consent

Use of waivers or alterations of informed consent

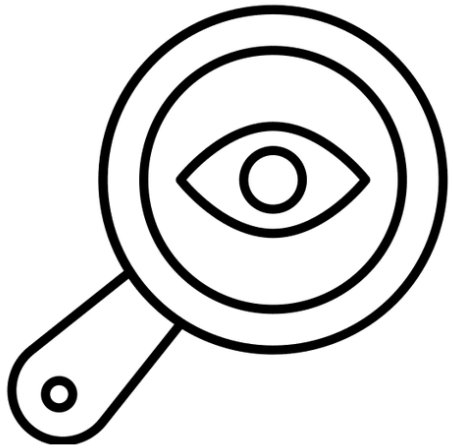
→

Look beyond informed consent processes to fulfill obligations of respect when sharing individual-level data from PCTs

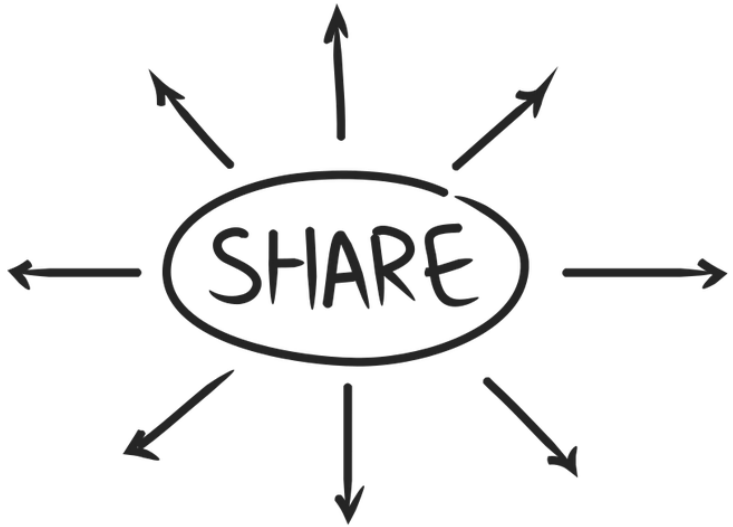
I think we tend to minimize how valuable just learning something or getting something back that was the result of …participating in a [research] experience.… Even just being able to say, “We've been conducting a PCT in your healthcare system for the last year, and here’s some of the information that we've learned about the people participating.” …

I think would give people the opportunity to appreciate that their participation …in research generates something, and that something could come back to them in a way that actually might be of interest to them.

(Interviewee 43; Patient Advocate)



Transparency about research underway in health system



Sharing research findings with patient-subjects

Toward Meeting the OBLIGATION of Respect for Persons in Pragmatic Clinical Trials

by STEPHANIE R. MORAIN, STEPHANIE A. KRAFT, BENJAMIN S. WILFOND, AMY MCGUIRE, NEAL W. DICKERT, ANDREW GARLAND, and JEREMY SUGARMAN

Embedding research in clinical care offers multiple benefits, including the opportunity to evaluate the effectiveness of interventions under real-world conditions. Yet the traditional informed consent process may be an inappropriate or insufficient mechanism for respecting prospective or actual subjects in pragmatic clinical trials. Several dimensions of demonstrating respect for persons—including maximizing agency and minimizing burdens—should be considered in designing, conducting, and overseeing such trials.

Patients, clinicians, and other stakeholders need high-quality evidence to guide health care decisions. Yet numerous barriers impede the ability of health care systems to efficiently generate needed evidence that is responsive to real-world needs. To overcome these barriers, many have advocated shifting toward learning health systems, in which clinical trials are embedded into clinical care, trial results are deliberately integrated into clinical care decisions, and clinical care informs the development of subsequent trials.[1] One aspect of advancing the learning health system vision involves pragmatic clinical trials, or PCTs, which are designed to efficiently evaluate the effectiveness of interventions under real-world conditions, to produce results that can be broadly generalized, and to inform both care delivery and policy development.[2]

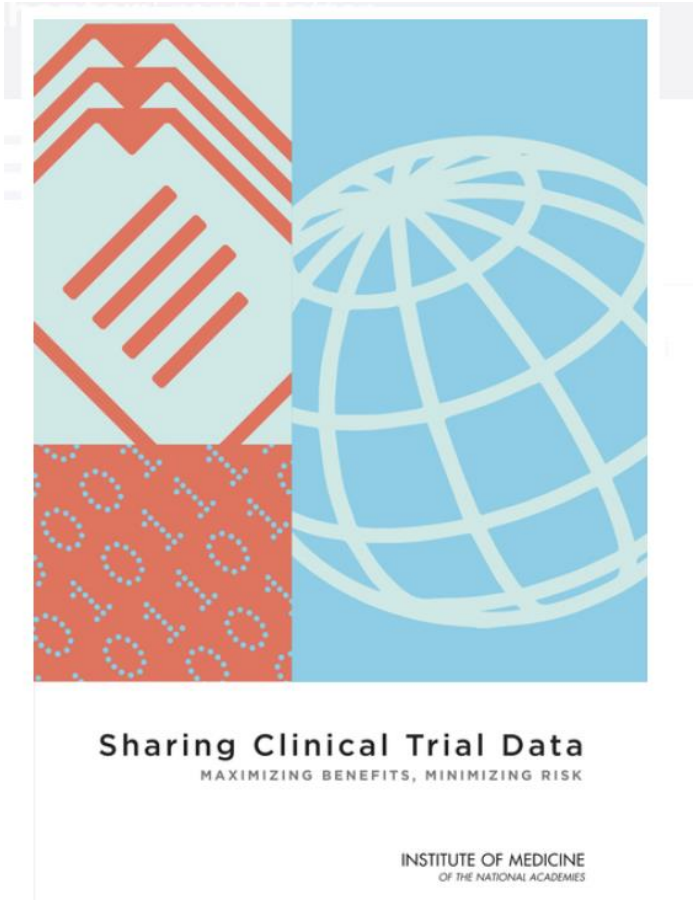
To achieve these goals, PCTs are often embedded into routine clinical practice settings, which can both support the efficiency of research by eliminating the need for a separate research infrastructure and help ensure the generalizability of results. While embedding research into clinical care offers several advantages, it also presents ethical and regulatory challenges.[3] Research has historically been understood as a distinct activity entailing distinct normative commitments, including the commitment to obtain explicit informed consent from individual participants for specific research projects. The deliberate integration of research into routine clinical practice settings challenges this paradigm, calling

Stephanie R. Morain, Stephanie A. Kraft, Benjamin S. Wilfond, Amy McGuire, Neal W. Dickert, Andrew Garland, and Jeremy Sugarman, "Toward Meeting the Obligation of Respect for Persons in Pragmatic Clinical Trials," *Hastings Center Report* 52, no. 3 (2022): 9-17. DOI: 10.1002/hast.1391

Table 1.
Eight Dimensions of Demonstrating Respect for Persons in PCTs

Dimension	*Respect-promoting practice(s)*
Engaging patients and communities	Actively involve patients and communities throughout the lifecycle of research.
Promoting transparency and open communication	Provide information about research activities and the study purpose and communicate about study progress.
Maximizing agency	Recognize and promote the decisional rights of individuals, including but not limited to decisions about research enrollment.
Minimizing burdens and promoting accessibility	Minimize perceived subject burdens and facilitate research enrollment by those with differing abilities and situational contexts.
Protecting privacy and confidentiality	Ensure that data is shared only "under appropriate conditions, [with] appropriate parties, and for appropriate reasons."[1]
Valuing interpersonal interactions	Show kindness and appreciation in interactions with patient-subjects and take interest in their perspectives.
Providing compensation	Offer payment as reimbursement for costs incurred as result of research participation or as compensation for additional time, effort, or inconvenience.
Maximizing social value	Deliberately design research to enhance the likelihood that it can generate future improvements in health or well-being.

Insight #3: Health Systems/Institutions as Key Players



BOX 3-1
Key Stakeholders Involved in Sharing Clinical Trial Data

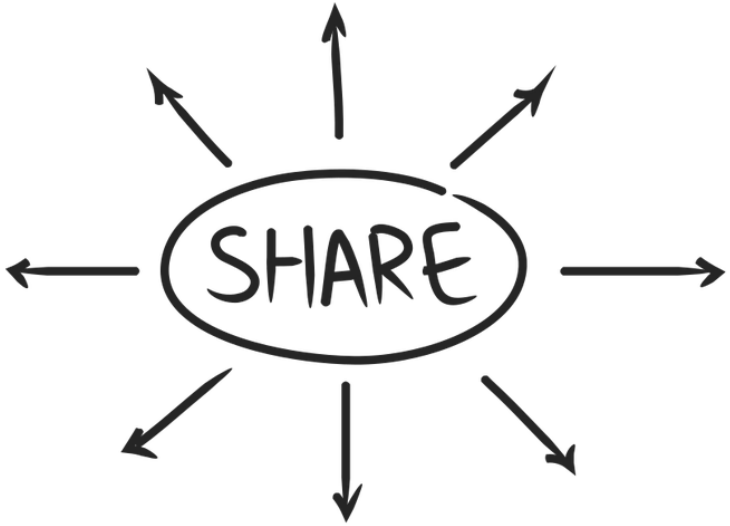
- **Participants in clinical trials**
  - Individual patients and healthy volunteers*
  - Research Ethics Committees (termed Institutional Review Boards [IRBs] in the United States)
  - Data Monitoring Committees (DMCs), also called Data and Safety Monitoring Boards (DSMBs)
  - Disease advocacy organizations
- **Funders and sponsors of trials**
  - Public and nonprofit funders/sponsors (including disease advocacy organizations in this role)
  - Industry sponsors (including large and small private sponsors of pharmaceutical, device, and biologic clinical trials)
- **Regulatory agencies**
  - European Medicines Agency (EMA)
  - U.S. Food and Drug Administration (FDA)
- **Investigators**
  - Clinical trialists
  - Secondary users (e.g., reanalysts, meta-analysts)
- **Research institutions and universities**
- **Journals**
- **Professional societies**

Insight #4: The Public Can't Support What it Doesn't Know Exists

"…the public does not fully understand the benefits and value of data sharing, and the demand is not commensurate with the need for change."

"Engendering support for data sharing will require greater awareness of how the use of electronic health care data has led to improved outcomes…"

Sharing clinical trials data



Sharing research findings with patient-subjects

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