

Ethics and the EMBLEM Study

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Right to withdraw without penalty

- Valid consent requires being informed and being rational
- Valid withdrawal does not require being informed or being rational to anywhere near the same degree

Justifying “Right to Withdraw Without Penalty”

- Respect for persons, or for freedom, or for autonomy, etc., might explain “right to withdraw” but it does not explain “without penalty”
- “without penalty” reflects that biomedical research is trustworthy

Why Would a Research Participant Withdraw?

- Continued participation is inconvenient
- Actual adverse effects
- Belief that great harm will occur — e.g., the blood draw takes too much blood
- Belief that the researchers cannot be trusted

Two Kinds of Withdrawals

1. Prospective – research participant withdraws from all future involvement with the study and with all further data gathering
2. Total – prospective withdrawal plus withdrawing all records, data, and samples that have been acquired in the study

The Case for Allowing Total Withdrawal

- Some argue: the data and any biological samples extracted nevertheless are the property of the research participants and so they have the right to dispose of them as they wish
- The data or samples could be used in future studies. Research participants might not want to give consent to some future study and so they must have the right of Total Withdrawal



The Case Against Allowing Total Withdrawal

- Some argue: The data and samples belong to the researchers. They extracted the data, and the samples are essentially abandoned (or donated) material
- Excessive burden on researchers. They do not always have control over future studies that would use the data, etc.
- Allowing Total Withdrawal can affect scientific validity; if the withdrawals are not random, the findings could be biased.



EMBLEM Offers Total Withdrawal?

From the consent form (emphasis added):

- “You or your child can withdraw from the study in the future without penalty. ... When your request to withdraw is received, it will be sent to the PI at NCI, who will write to you to confirm that your information was deleted from the study files and your samples were removed and destroyed.”
- “You or your child can ask the local study staff to be removed from future comparisons using the procedures explained below.”



Informed Consent

- Justification: respect for people & their authority (self-determination) over their own lives
- Primary challenges concern implementation
 - How informed must people be in order for consent to be valid?
 - How can we be assured that people are not improperly influenced in their consent?
 - How should informed consent be documented?
 - What should be done when an eligible participant is incapable of giving informed consent?



Research on Children and Minors

- Informed consent is not possible
- Some argue that since informed consent not possible, research on children is not permitted
- Most argue for a special protection, a 2-key approach (2 keys needed to start the study)



The Two Keys in Pediatric Research

- First key: Informed Permission from parent or legal guardian
- Second key: the Assent of the child



First Key: Informed Permission

- The requirement of Informed Permission are similar to the requirements of Informed Consent
- Permission is given by someone who has the acknowledged responsibility to protect the child's interests

Second Key: Assent of the Child

- If parents have given permission, why is the child's assent needed?
- How is assent different from consent?

Standard Models of Assent: "Quasi-Consent"

- Assent is obtained when the child consents to the study or procedures based on his or her limited understanding ("quasi understanding") of the study or procedures
- Purpose is to provide protection similar to that of Informed Consent

Standard Models of Assent: "Quasi-Consent"

Problems:

- many scholars hold that this model can apply only to children > 14.
- Little agreement over how "quasi" the understanding can be before it is simply too little understanding

Standard Models of Assent: "Engagement"

- Assent is obtained by engaging the child in small decisions regarding procedures — e.g., "From which arm should blood be drawn?"
- Purpose is to show that the child deserves respect

Standard Models of Assent: "Engagement"

Problems:

- How to distinguish engaging with a child from pretending to engage with a child
- If child's decisions are limited to inconsequential ones, how does this show respect for the child?

"Capacity to Dissent" Model

Effort to combine the protection quasi-consent tries to offer with the respect that engagement tries to offer

“Capacity to Dissent” Model

- A child who lacks the capacity to give valid consent can nevertheless have the capacity to exercise valid withdrawal
- If the child has the capacity to withdraw from the study, the child therefore has the capacity to dissent from entering the study

“Capacity to Dissent” Model

- Simply determining if the child expresses dissent is inadequate. Lack of dissent can arise from shyness, passivity, etc.
- Actively seeking assent gives the child the best opportunity to express dissent

Seeking Assent

- Salient challenge is distinguishing manifesting distress from expressing dissent; the younger the child, the more difficult this is
- The researcher needs to be advised and guided by the parent who knows the child
- Many argue that this distinction cannot in general be made for children < 7; consequently, assent is not sought from young children

Further Considerations Regarding Assent

- Does the research expose the child to greater than minimal risk?
- Does the research offer the prospect of direct, therapeutic benefit?
- Affirmative answers to either of the above can affect the importance placed on assent and the significance parents should place on expressions of distress

Ethical Challenge of Incidental Findings

- An incidental finding is a finding that is relevant to the health of the individual research participant but goes beyond the aims of — is incidental to — the research study
- What are the researcher’s obligation when the study uncovers an incidental finding?

The Obligation of Ancillary Care

Many have argued:

- IF the incidental finding has clinical utility, and
- IF intervention would be an “easy rescue,”
- THEN the researcher is obligated to see that appropriate care is provided



EMBLEM and Ancillary Care

- If HIV infection detected, counseling and treatment is provided at no cost
- If parasites detected in stools, treatment is provided



Ethical Challenge of Incidental Findings

- The issue of incidental findings can go beyond the question of providing ancillary care.
- When should incidental findings (or individual research results) be returned to research participants?



For Returning Individual Research Results

- Some argue: research participants have a right to all of the information about them
- Many more argue: a necessary condition for returning individual results is that they have clinical utility



Against Returning Individual Research Results

- Excessive burden on researchers to track down research participants, especially if clinical utility is discovered many years later
- Encourages the Therapeutic Misconception — that the aim of the research is the health care of the participant rather than generalizable knowledge



EMBLEM on Returning Individual Results

From the consent form:

“The results for the 30,000 genes will not be returned to you because they will not change your child’s medical care.”



EMBLEM on Returning Individual Results

Concerns:

1. Given rapid development in genomic medicine, what is the evidence for claiming that the results from examining 30,000 genes “will not change your child’s medical care”?
2. Is the impact on child’s medical care the only reason for returning results? (e.g., Should information whether the child is a sickle cell carrier be returned?)



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