IRB / Ethics Committee Requirements for Pediatric Studies & How These May Affect Drug Research

Alison Bateman-House, PhD, MPH, MA
Assistant Professor, Division of Medical Ethics
Alison.Bateman-House@nyulangone.org
@ABatemanHouse

NYU Grossman School of Medicine

2 different sets of (overlapping) concerns…

Ethical concerns – how to do the most transparent and voluntary, benefit-maximizing and risk-minimizing research for the best possible outcomes for patients and the advancement of science

2 different sets of (overlapping) concerns…

Ethical concerns – how to do the most transparent and voluntary, benefit-maximizing and risk-minimizing research for the best possible outcomes for patients and the advancement of science

- Ethicists, national/regional/state ethics bodies
- All of us!

2 different sets of (overlapping) concerns…

Ethical concerns – how to do the most transparent and voluntary, benefit-maximizing and risk-minimizing research for the best possible outcomes for patients and the advancement of science

- Ethicists, national/regional/state ethics bodies
- All of us!

Regulatory/Legal concerns – how to conform to the relevant laws, policies, and guidelines about what types of research may be conducted on whom, subject to what review and with what safeguards

2 different sets of (overlapping) concerns…

Ethical concerns – how to do the most transparent and voluntary, benefit-maximizing and risk-minimizing research for the best possible outcomes for patients and the advancement of science

- Ethicists, national/regional/state ethics bodies
- All of us!

Regulatory/Legal concerns – how to conform to the relevant laws, policies, and guidelines about what types of research may be conducted on whom, subject to what review and with what safeguards

- Institutional review boards (IRBs), research compliance, national ethics bodies
- All of us!

Ethical concern

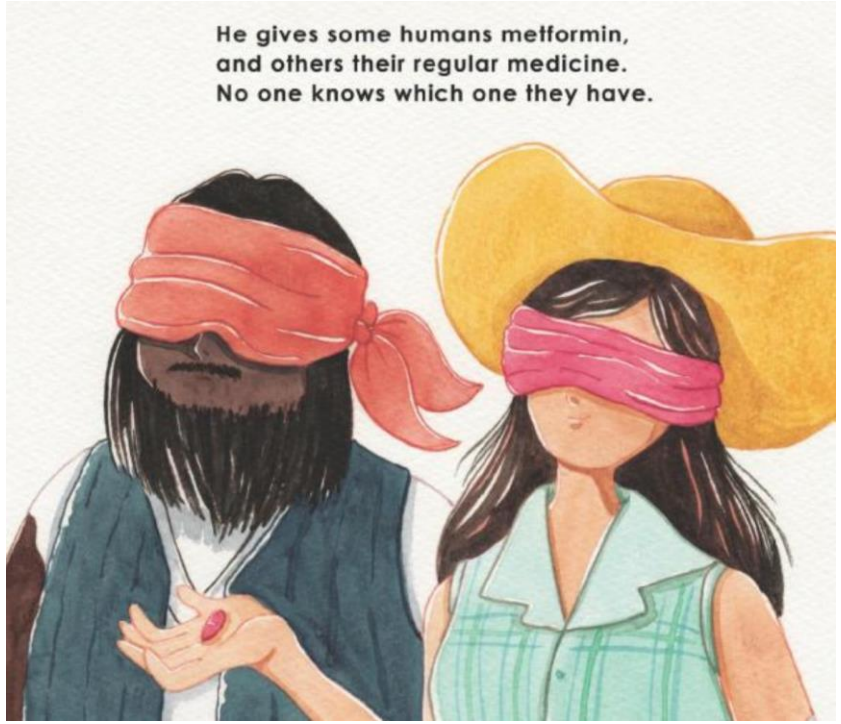
Autonomy

- We should allow individuals to engage in self-directed decisionmaking
    - Informed
    - Voluntary (non-coerced, non-pressured)

But…these are children!

While parent/guardian has legal authority to enroll minor in research, child's assent should still be sought (especially older children).

- Entails explaining the research procedure, intent, & possible risks/ benefits in a way accessible to the child



Page from Nikhil Radha Krishnan's book "If You Give A Mouse Metformin"

How does parent/guardian not feel pressured to participate if:

- There are no therapeutic options?
- If offer comes from their child's clinician?

Regulatory/legal concerns

- To ensure these autonomy-related issues have been addressed proactively
  - Ex: inform parent/guardian child's care will not be impacted by decision to not participate in research

- To ensure the proposed study meets the relevant local laws and rules
  - Multinational research can be difficult, due to differences (e.g., in age of consent)

- To perform ongoing review of study and address ethical issues as they arise; to revise consent forms as new findings add more information; etc.

Ethical concern

Beneficence	We should do good

What kind of good?

- How weigh immediate vs long-term benefits?
- Medical benefits are only one type of benefit

Good for whom?

(especially since we may not be able ask the child participant what they consider a good outcome)

- Direct benefit to the child research participant?
- Possibility of direct benefit to the child research participant?
- Possibility of direct benefit to similar children, but perhaps not this one?
- Possibility of advancing science, but perhaps not with direct benefits to children with this condition?

Ethical concern

Non-maleficence	We should avoid causing harm *

* Not a complete prohibition of causing harm, or else much of medical research could not happen

What counts as harm? What harm is considered justifiable in light of expected/possible benefits?

- Physical harm (temporary/lasting; minor/severe)
- “Fiscal toxicity”
- Opportunity costs (re other possibilities, current and future)
- Downstream or dignitary harm (e.g., loss of privacy)
- What about harm from poorly designed research?
  - In US, IRBs do not review scientific validity of research
- What about harm from research that doesn’t reflect the priorities of patients or caregivers?
  - Sponsor, regulator, KOL have input into endpoints; what about patients, caregivers, payers?

Regulatory/legal concerns

- To ensure these harm-related issues have been addressed proactively & in compliance with law / regulations / norms

  - “If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children…consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.” (45 CRF 46)

  - To evaluate benefit holistically, must have different perspectives
    - US IRBs required to have one non-scientist, one community member

Ethical concern(s)

Justice	We should evenly distribute benefits and harms amongst persons/ groups
Solidarity	Concern for the common good

Role of IRB (US)

- Has largely been limited to preventing exploitation of vulnerable subjects (as defined in the regulations) and the poor (re what is felt to be compensation of an irresistible amount)
- Result of history from whence bioethics and research regulation arose; view of research as something to be protected from
- Focus on the individual participant, not “bystanders” (e.g., family)

Pendulum has moved too far in the opposite direction – overprotection has led to harm

(e.g., lack of approved drugs, lack of evidence-based treatments)

- Children
- Pregnant Women
- Prisoners
- Decisionally-Incompetent Persons

Ethical concern(s)

Justice	We should evenly distribute benefits and harms amongst persons/ groups
Solidarity	Concern for the common good

How?

- Inequities in trial design impact who can participate in a trial
  - E.g., location of trial sites, ease of access to trial sites, time required at trial sites all impact who can participate

- Inequities in research may be reproduced in access post-approval
  - Is the research sample a good proxy for the larger patient population?
  - Will regulators or payers extrapolate data from the trial participants to the larger patient population?

What IRBs/compliance bodies review:

- Protocol and any protocol changes that occur over course of study
- Text of recruitment materials
- Consent form

What do IRBs not review?

- Justice concerns
- Risk/benefit ratio from the vantage point of all different stakeholders
- Scientific validity of research
- Utility of research question

Take-aways

- Regulatory/compliance bodies are meant to ensure compliance with local laws/regulations. [Poses challenge for multi-site/ multinational research.]

- Overprotecting children deprives them of the possible benefits of research, both short and long-term.

- Can't view regulatory/compliance bodies as 100% guarantors of ethical research, particularly with regard to issues not in the regulations.
  - If you disagree with IRB/research ethics body, make your case!

- Reach out, often and early, to IRB/ethics bodies, regulators, patient advocacy groups, parents/children to learn what you don't know, to make your trial the best it can be in real time and to have the most desirable downstream impact.

Thank you!

Alison.Bateman-House@nyulangone.org

@ABatemanHouse