

# Ancillary care and post-trial access

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# The MOMS study

- 5 year observational study of malaria in children
- Blood samples taken at delivery, regular blood draws thereafter
- Childhood malarial bouts are severe, often fatal
- Moreover, HIV-prevalence in the local population was high
- No treatment available for HIV/AIDS
- Government health care spending US\$12/person/year

# What additional clinical care ought the researchers to provide for participants?

- None?
- Better malaria treatment than standard care at the hospital?
- Treatment for opportunistic infections?
- Provide anti-retrovirals?

# The problem

- Researchers are scientists, not physicians
- But in locations with poor health care facilities, they may be the only people who can help
- Many researchers feel obligated to do something

# Outline

1. Ancillary care
2. Post-trial access
  - 2.1. For research participants
  - 2.2. For host communities
3. Questions and discussion

# Disclaimer

The views expressed are my own and do not represent the views of the NIH, DHHS, or any other US government agency

# 1. *Ancillary Care*

# What is ancillary care?

- Ancillary care is medical care provided to participants in a trial that is not required for the trial's safety or scientific validity
- Focus on obligations of researchers and sponsors

# Guidelines



- The Council for International Organizations of Medical Sciences (CIOMS):
  - “Although sponsors are, in general, not obliged to provide health-care services beyond that which is necessary for the conduct of the research, it is morally praiseworthy to do so.” (Guideline 21)
- But many researchers feel that there is an obligation

# What is the extent of the obligations?

- Minimal view: nothing
- Maximalist view: researchers should do everything they can
- Something in-between?
  - We need to know what justifies the obligations in order to find out...

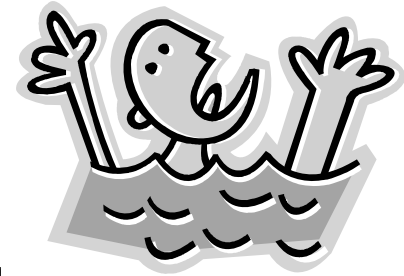
# Possible justifications for ancillary care obligations

1. Compensation for harm
2. Duty of rescue
3. Reciprocation for the participants' contribution
4. Relationship between researchers and participants

# Compensation for harm

- Almost all medical research poses risks to participants
- If I cause you harm, then I have a *prima facie* obligation to repair that harm
- When research participants do not have other health care, not to treat research related injuries (RRIs) would make research too risky

# Duty of rescue



- “If it is in our power to prevent something bad from happening, without thereby sacrificing anything morally significant, we ought, morally, to do it” (Singer)
- Researchers may be able to give life-saving treatment
- Participants may not have other sources of treatment



# Reciprocation

- Research participants contribute to medical knowledge
- They deserve reward in return for this contribution
- Additional medical care is an appropriate way to reward them

# Researcher-participant relationship

- During the research a relationship develops between researchers and their participants
- It is analogous to the doctor-patient relationship
- Participants entrust aspects of their health to the researchers

# Critical thoughts about ancillary care

- Other parties also have obligations
  - We all have a duty of rescue
  - It is not just the researchers who benefit from health research
- Unfairness
  - People who were excluded from research participation also get excluded from ancillary care
- There is no algorithm to calculate ancillary care

## The sources of ancillary care obligations

Research related injury	Compensate all harms caused by research
Rescue	Meet urgent medical needs, if low cost
Reciprocity	Provide reward proportional to contribution
Relationship	Provide care proportional to depth of relationship, and determined by scope of entrustment

# The MOMS study

- Any research related injuries should be treated
- HIV/AIDS treatment is urgent
  - Prophylactic treatment for opportunistic infections with co-trimoxazole was affordable
  - Treatment with antiretrovirals unaffordable
- Treatment for malaria is the focus of the study
  - Hence, malarial diseases within scope of entrustment
  - Coinvestigator supervised children's in- and out-patient malaria care

## **2. Post-trial Access**

# Two key questions

- Access to what?
  - Study intervention
  - Additional healthcare
- Access by whom?
  - Trial participants
  - Host community

## **2.1. Participant access to study intervention - International guidelines**

“At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.”

(Helsinki, Art. 33)



# Possible justifications for post-trial access

1. Compensation for harm: danger of taking participants off treatment
2. Duty of rescue: researchers are in a special position to help participants
3. Reciprocation for the participants' contribution or the risks they've taken
4. Relationship between researchers and participants

# Difficult cases

- Chronic conditions
  - Long-term, expensive care
- Not applicable to certain research
  - e.g. observational studies, Phase 1 trials
- Too late for the control group
  - e.g. Participants who acquire the disease during a prevention trial

# Access to additional healthcare

- When the study intervention cannot be supplied, alternative health care might meet the obligations
- Alternatively, researchers might partner with local health care providers
- The question of how much post-trial care should be given is controversial
  - E.g. HIV vaccine trials
  - Should researchers guarantee treatment for AIDS?

## 2.2. Community access to study intervention

- Ideally, where researchers, sponsors, participants and hosts are part of the same society, the fruits of research may be expected to benefit everyone
- New interventions will eventually be introduced into the national health care system
- But where the sponsors and hosts are in different societies this may not be the case

# Exploitation

- Exploitation occurs when one party takes unfair advantage of another
- Research conducted on one community for the benefit of another may be exploitative
- Exacerbated if host community is poor, and if the research excludes other research or healthcare

# Avoiding exploitation

- Two conditions allow international collaborative research to mimic national research:
  - Research is responsive to host community needs
  - Host community has access to successful interventions

# International guidelines

“Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:

- the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and
- any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.”

(CIOMS, Guideline 10)



# **Doubts about responsiveness and reasonable availability: the Malarone study**

- Placebo-controlled RCT of Malarone for malaria prophylaxis in recent immigrants to a malaria endemic region
- Participants and community will receive improved medical care
- The drug will be marketed mainly to travelers
- The local government supports the trial

# Problems with “reasonable availability”

- Narrow conception of benefits
  - Other health benefits may be more valuable
- Disregards community autonomy
  - e.g. choosing to host a trial in order to develop health care or research capacity
- Not applicable to certain research
  - e.g. observational studies, Phase 1 trials

# Fair benefits: an alternative proposal

- In addition to standard ethical requirements
- All benefits (and risks) of research are evaluated
  - To participants
  - To host community
- Trials must offer a fair total amount of benefits
- Free decision by community to host research on these terms

# Concerns about fair benefits

- Criticized for demanding too little of researchers, compared with “reasonable availability”
- Response: the *amount* of benefits may be the same or greater than “reasonable availability”
- We should be concerned about implementation
  - Guidance on how to decide fair benefits – what is a fair deal?
  - How to avoid bad deals

# Summary of ethical issues

## 1. Ancillary care

- Some additional clinical care should be given
- No simple algorithm to determine how much

## 2. Post-trial access

- Participant access may be impossible or impractical
- Problems with responsiveness and reasonable availability conditions for communities
- Can be resolved if benefits are not always in kind