Research with Vulnerable Persons & Groups, Undue inducement, coercion and motivation for participation

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Outline of Presentation

- Defining Vulnerability
- Levels
  - Countries
  - Institutions
  - Researchers
  - Groups
  - Individuals
- What can we do as researchers?

Defining Vulnerability

- History full of examples of abuse of groups in research
- Vulnerable groups are made of persons who are not able to fight for themselves
- They are susceptible to exploitation
- Vulnerability affects decision making
- Some entities traditionally defined as vulnerable
- New entities emerging

Analytical questions

- What are the common characteristics?
- What do these characteristics imply?
- What should we do as researchers in addressing the vulnerability?
- Researcher needs to take steps in the design of the protocol as a condition for proceeding.

Countries

- Are we vulnerable as developing Countries?
- Who sets the research agenda?
- “Ministry of Health pushes EC to approve a big grant”
- Parachute researchers
- Second scramble for Africa
- Negotiations with big pharmaceutical companies

Institutions

- In what ways are our institutions vulnerable?
- Head of institution pushes the EC
- Grants mean more to poorly supported institutions
- Conflict of interest
- ECs to rubber stamp institutional decisions
- How can we ensure that our institutions are less vulnerable?

Researchers

- As researchers do you feel vulnerable?
- In what ways?
- Grants?
- Publications?
- Specimen collectors/postal agencies
- Names used for purpose of winning grant
- How can researchers liberate themselves?

Vulnerable groups

- Desperately ill
- Elderly
- Institutionalised persons
- Captive populations – prisoners, students
- Sexual minorities
- Persons engaging in illegal/sensitive behaviours
- The poor
- No access to health
- The less educated/illiterate
- Children
- Military
- Mentally ill
- Homeless

Questions and questions?

- Do poor people participate so as to access better quality care?
- Do the poor participate for money?
- Do we also have the same situation in the North?
- Do poor people make a rational decisions?
- Do we have “Professional research participants?”
- What is our opinion on their involvement in research?

Illustrations Focusing on the following:

1. Research on substance abuse
2. Pediatric research
3. Research with adolescents

Research on substance abuse

- Some Research Features Raising Ethical Issues
  - Recruitment of research participants
  - Informed consent
  - Confidentiality of research data
  - ***Remuneration of research participants***

Substance Abuse Research Raises Particular Ethical Issues

- Stigma attached to substance use & abuse, especially of illegal drugs
- Confidentiality of sensitive data (e.g., illegal activity by participants)
- Addiction (loss of control over behavior) in research participants
- Participation of “vulnerable” participants: poor, marginalized, socially isolated

Informed Consent Issues

- Ability to give informed consent
  - Acute intoxication, withdrawal
  - Reading & language skills
- Assessment of competence
  - Psychological testing
- Assessment of comprehension
  - Post-consent quiz
- Voluntariness
  - No coercion, undue influence

Confidentiality Issues

- Do not release data without participant's consent
- Avoid inadvertent disclosure of sensitive data that might harm or embarrass subject
- Unlink data and personal identifiers, keep data coded, in secure location
- Protect data from court subpoena, police
- Disclose in consent form any limits to confidentiality, e.g., reporting child abuse

Subject Remuneration Issues

- Is large payment to poor participant “undue” influence?
- Will payments be used to buy substances?
  - Maximize beneficial use of payment
    - Should we limit amount & frequency of cash payments
    - Should we encourage payment in-kind, rather than in cash

Research Questions

- Do larger cash incentives precipitate new drug use?
- Are larger cash incentives perceived as more coercive?
- Do larger cash incentives increase satisfaction with research?
- Do larger cash incentives produce higher follow-up rates?

Pediatric Research

Children are Unique

- **Diseases**
- **Development**
- **Growth**
- **Metabolism**
- **Toxicity**

Why researchers avoid studies with Children?

- **High costs**
- **Complex consent process**
- **Limited economic gain**
- **High liability risk**

But Children Deserve Research, too

"Children are both vulnerable subjects in need of protection from research risks and a neglected class that needs better access to the benefits of research"*

Children and Adults

- When should we involve children:
  - Drugs aimed at children disease only?
  - Drugs aimed for diseases for both?
  - Drugs aimed at diseases for adults?
- What about Institutionalised children?
- When can we involve them?
- Don’t use institutionalized children to study intervention in a disease prevalent in non-institutionalized subjects
- But use of institutionalized children may be appropriate if disease primarily affects those children and the intervention cannot be studied any other way

Assent

- "…a child's affirmative agreement to participate in a clinical investigation. Mere failure to object may not, without affirmative agreement, be construed as assent"
- Only required when EC judges that the children involved are capable of assenting
- EC takes into account in making that determination:
  - Age
  - Maturity
  - Psychological state
- Determination can be made for all children in a trial or individually
- EC determines whether and how assent is documented

Elements of Assent

- **Awareness of the present illness**
- **What can be expected from the intervention**
- **Assessment of the child's understanding of her medical condition**
- **Solicitation of Assent**

Researcher's responsibilities - assent

- Help the child achieve a developmentally appropriate awareness of her condition
- Disclose the nature of the proposed intervention and child's likely experience
- Assess the child's understanding and any (coercive) factors influencing the child
- Solicit the child's willingness to accept the proposed intervention

Respecting a Child's Dissent

"To be used as a research subject may or may not involve a risk of harm to the child. For a child to be used as a research subject ...against her expressed persistent objection *does* involve doing her predictable harm."

Bartholome (1996)

- "The dissent of the child subject should be binding in all but the most exceptional circumstances. There are few, if any, clinical situations in which a child's participation in research is *the only* means of responding to the child's healthcare needs." (Bartholome, 1996)

When can Assent be Waived by EC?

- Capability of the subjects to understand is limited
- Generally, below the age of 6
- The investigation is considered minimal risk
- The waiver will not adversely affect the rights and welfare of the participant
- The investigation could not be conducted without the waiver
- Study holds direct therapeutic benefit for the child
- Parental Consent is still required

Benefits of Assent to Child

- Assent reminds us that children should be treated with dignity and respect
- Permitting children a shared role in decision making benefits their development as autonomous individuals
- Requirement of assent serves to remind parents and investigators that children are persons with interests and not mere vessels for the purpose of research
- An assent requirement offers school-age children the opportunity to learn the meaning of respect for others

Diekema DK. Taking Children Seriously: What's so Important about Assent? American Journal of Bioethics 3(4):25-26 (2003)

Are children being exploited?

- Are children being exploited in some settings?
  - When trials are being conducted in one location because they could not be conducted elsewhere?
  - When there is no intention to make the therapy available to the population in which the test is being conducted?
  - When trial might be considered unethical in another country?

Ethics of Investigator Payments

- Finder's fees or bonuses for enrolling a specific number of children are unethical and should not be permitted.

Minimizing Distress

- Studies designed by personnel experienced with children
- Use of appropriate formulations and routes of administration
- Studies designed for pediatric populations, don’t copy adult
- Use personnel skilled in pediatric procedures
- Physical setting - furniture, activities, toys, food appropriate for age
- Use familiar environment where participants normally receive care
- Catheters instead of repeated venipunctures
- Piggybacking sample collections
- If child becomes upset by procedure, researchers should accept this as a valid refusal

Improving Pediatric Expertise of IRBs

- ECs reviewing pediatric studies should have expertise in child health care and research
- At least a member with pediatric expertise should be present (and voting) when a pediatric research protocol is reviewed.
- When appropriate, ECs should consult child health experts, parents, children, adolescents, and community members who can provide relevant perspectives
- ECs should include at least one nonscientist, unaffiliated member who can represent *explicitly* the perspectives of parents and children

From: Ethical Conduct of Clinical Research Involving Children, Recommendation 8.3 (IOM 2004)

Other categories of young persons

- Under age mothers
- Street kids
- Orphan headed households
- Mature minors
- Emancipated minors

Adolescent research & Parental Consent

Do we need to obtain parental consent for adolescent research?

More issues……

- Issues that ethics committees and researchers have to deal with:
  - Exploitation
  - Inducement
  - Coercion
  - Deception

Questions?

- Are inducements bad?
- Is deception in research ever acceptable?

Consider Important Terms

- Compensation
- Reimbursement
- Inducement
- Undue inducement
- motivation
- Coercion

Why pay research participants?

- Money enables participation
- It is reasonable to pay someone for their work.
- It takes time to participate in research.
- Time is money.
- But then - What is the value of time for the person in the study?”

In reality…….

- It is cheap to conduct research in Africa
- TS5000 vs $100
- Are we looking at humanitarian efforts or exlpoitation???
- How can we address this?

Coercive Circumstances & factors

- Poverty
- Lack of access to care
- The authority of physicians and researchers
- Involvement of community leaders

And even more challenges

- Adherence – the carrot approach.
  - Use incremental scale
  - Different levels for different types of visits
- Currency differentials
- Lotto tickets approach

Other views

- Reimbursements as a way of redistributing wealth
- As source of income for poor communities
- Professional research participants
- Pure trade – blood for cash – research participants have some products and services to offer.

Summary (1)

- Vulnerable groups require special measures to shield from undue risk
- Studies properly designed to insure quality and interpretability
- Participants expected to benefit except under special circumstances
- ECs approving research have members knowledgeable in ethical, clinical, and psychosocial issues
- Recruitment free from inducements to participants or guardians

Summary (2)

- Compensation must be approved by EC
- Consent/assent from participant if capable and permission from legal guardian
- Use of least vulnerable population in which research can be conducted
- Minimize distress by actions and environment
- Need to give thought to “fair compensation” for disadvantaged research participants