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

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 exploitation??
• 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