Definition of Ethics (1)

• The discipline of dealing with what is good and bad, with moral duty and obligation

• A set of moral principles or values

• The principle of conduct governing an individual or group

• Webster’s Ninth New Collegiate Dictionary
Definition of Ethics (2)

A Dictionary of Epidemiology, 4th ed, 2001
(J.M. Last (ed))

The branch of philosophy that deals with distinctions between right and wrong – with the moral consequences of human actions
ETHICS

• Medical ethics (patient-centered)
• Public health ethics – (community/population-centered)
• Research ethics (subject-centered)
Ethics

There is no right decision – only a least-worst decision
REQUIRED ETHICAL PROCEDURES FOR INTERNATIONAL RESEARCH (U.S. PUBLIC HEALTH SERVICE)
Institutions that want to engage in research that do not have an IRB/IEC may submit a Federalwide Assurance (FWA) form that designates one or more approved IRBs that are already registered with the Office of Human Research Protection (OHRP).
Reliance on another institution's IRB/IEC must be documented by a written agreement that is available for review by OHRP upon request.
Research project must be supported by US dollars, reviewed by an appropriate IRB/IEC, have an approval letter issued listing the IRB number and the FWA number of the institution conducting the research, and be signed by the IRB/IEC chair.
All investigators must complete an approved ethics training course and obtain a certificate of completion.
RESEARCH IN POPULATIONS AND COMMUNITIES WITH LIMITED RESOURCES
TWO RESPONSIBILITIES

- Prior to conducting research in a population or community with limited resources the researcher/sponsor should:
  1) Ensure the research responds to the health needs and priorities of the target community
  2) Ensure any product or benefit developed will be made available to the community
RESPONSIVENESS TO COMMUNITY HEALTH NEEDS

• Research to determine disease prevalence that should lead to intervention

• If successful interventions result from the research they must be made available to the community

• If this is not done, the research is exploitative
MAKING A PRIOR AGREEMENT

• Before the research begins, a plan should be offered in which the proposed product is made available to the host nation upon completion of the study.

• Investigators should include representatives of the nation’s government, local authorities, community members, and NGO groups in planning.
COMPREHENSIVENESS OF THE AGREEMENT

• The agreement should include decisions about payments, royalties, distribution costs, subsidies, technology, and intellectual property

• In some cases, international organizations, public and private, may also be included in the discussions.
RESEARCH CONTROVERSIES IN DEVELOPING COUNTRIES

• Are placebo groups ethical?
• Should placebos reflect international or local standards of care?
• Should participants be assured care beyond the trials – if so, for how long?
• Should care be provided to the trial community?
• Should trials be evaluated for scale-up feasibility before implementation?
REQUIREMENTS FOR COMMUNITY APPROVAL

- Community must have legitimate, empowered spokesperson(s)
- Community must have a common health-related culture
- A communication network for the community must be in place
FACTORS INFLUENCING VOLUNTARY CONSENT

- Vulnerability to incentives
- Impact of community pressure (routine community testing)
- Power of investigators to influence
- Ability of participants to understand goals and risks
INVESTIGATOR’S RESPONSIBILITIES (UCLA IRB) (1)

- Identify and ensure compliance with all applicable laws, regulations, and guidelines for human subjects research in the country(ies) where the research will be conducted.
- Provide the IRB with the necessary information.
- Provide a scientific and ethical justification for conducting the research in an international setting.
INVESTIGATOR’S RESPONSIBILITIES (UCLA IRB) (2)

Local Situation:

- Identify each collaborating site/agency/institution and describe their role.

- Identify the appropriate local permissions required for the conduct of the research.

- Identify each collaborator, his/her institutional affiliation, specify their role in the research, and outline their scientific qualifications.

- Identify the institution(s)/government(s) who will have access to the data, and specify the level of data which they will access (anonymous, coded, individual-level identified, etc.).
The IRB application should:

1) Include discussion of planned or completed community consultation activities regarding the consent process, consent documentation, study instruments;

2) Identify the participants in the planned or completed community consultation; and

3) Describe the methods, discussions, and meetings

4) Describe the literacy level of the population, and discuss how subjects' comprehension of the consent process will be maximized

5) Explain how the cultural appropriateness of the consent process and consent document (if applicable), study instruments, etc. has been determined.
INVESTIGATOR’S RESPONSIBILITIES (UCLA IRB) (4)

Women and Children:

Discuss the status of women in the local community/country

• How will you **ensure women's voluntary participation** in the research?

• If women's consent will be supplemented by a male (spouse, brother, father, etc.), **explain why it is impossible to conduct the research without obtaining supplemental male permission** for female subjects.

• Explain why failure to conduct the research **could deny its potential benefits to women** in the host country.

• Outline **the measures to respect women's autonomy to consent**.

• Provide written justification for why a competent adult woman should be enrolled in research solely upon the permission of another person.

Discuss the status of children in the local community/country.
INVESTIGATOR’S RESPONSIBILITIES (UCLA IRB) (5)

Describe how the research may address an important scientific question regarding the host community/country

Describe how the proposal is responsive to local health needs of the host community/country

Describe both the standard of care in the USA and the available standard of care/alternatives in the host community/country
INVESTIGATOR’S RESPONSIBILITIES (UCLA IRB) (6)

Responsibilities to participants and host country (continued):

The investigator should:

(1) Minimize the likelihood subjects will believe mistakenly that the purpose of the research is solely to provide treatment.

(2) Assure continued access for all subjects to needed experimental interventions that have been proven effective at the conclusion of the project.

(3) Explain how the investigator will secure continued access (for subjects) to needed experimental interventions or explain why the investigator has not secured continued access (for subjects).

(4) Will the procedures will be available to some or all of the host country population? Also explain why the research procedures (if effective) will NOT be made available to the host country's population.
A CASE FOR EXPLOITATIVE RESEARCH
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Student athletes</td>
<td>It is often said that universities exploit their student athletes when they gain income, entertainment, and loyalty from alumni, whereas athletes get little education and relatively few receive their degrees or go on to play professional sports</td>
</tr>
<tr>
<td>Lumber</td>
<td>If there is a hurricane in Florida and lumber retailers were to raise their prices, we might say that they were exploiting their customers</td>
</tr>
<tr>
<td>Strip club</td>
<td>It is often said that strip clubs exploit the women they employ or women as a group</td>
</tr>
<tr>
<td>Volunteer army</td>
<td>It is sometimes claimed that the volunteer army exploits those citizens who lack decent civil career opportunities: “A society as unjust as ours must draft its military to avoid unfair exploitation…”</td>
</tr>
<tr>
<td>Scenario</td>
<td>Description</td>
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<tr>
<td>Rescue</td>
<td>Suppose that B’s car slipped into a snow bank on a rural road late at night. A can pull B out by attaching a rope to his four-wheel drive pickup truck. A offers to help B for $500.</td>
</tr>
<tr>
<td>Surrogacy</td>
<td>Commercial surrogacy involves exploitation of the surrogate mothers</td>
</tr>
<tr>
<td>Kidneys</td>
<td>The sale of bodily organs, such as kidneys, involves the exploitation of impoverished persons e.g. China</td>
</tr>
<tr>
<td>Interns</td>
<td>Hospitals exploit interns by requiring them to work long hours for relatively low pay.</td>
</tr>
<tr>
<td>Inducements</td>
<td>Medical researchers exploit people when they offer inducements to participate in research</td>
</tr>
<tr>
<td>Scenario</td>
<td>Description</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Embryonic stem cells</td>
<td>Embryonic stem cell research treats “nascent human life as raw material to be exploited as a mere natural resource.”</td>
</tr>
<tr>
<td>Unfair surgery</td>
<td>“B” needs life-saving surgery. “A” is the best surgeon available. “A” proposes to perform the surgery for $200,000 when the normal fee is $15,000</td>
</tr>
</tbody>
</table>
ETHICAL RATIONALE FOR “EXPLOITATIVE” RESEARCH (1)

Participants:
1. Benefit from incentive/compensation
2. Incentive may be low by Western standards, but “good” for poor country
3. Receive better medical care, albeit temporary
4. Country benefits from income (cost of doing study/trial)
5. Consent freely (needed income vs. exploitation) = mutually advantageous consensual exploitation
ETHICAL RATIONALE FOR “EXPLOITATIVE” RESEARCH (2)

Study might not be done if not allowed in developing country (cost, logistics, enrollment problems)
- ethics of not doing a necessary/essential study/trial

Researcher not responsible for historical injustices to developing country

Not ethical to deny participants the opportunity for mutually advantageous consensual exploitation
STIGMATIZATION, PRIVACY, AND CONFIDENTIALITY
STIGMATIZATION

Stigmatization = characterizing or branding (a person) as disgraceful or ignominious

RESEARCH MUST NOT INCREASE RISK OF STIGMATIZATION
STIGMATIZED GROUPS (examples)

• Marginalized groups
  - The poor
  - Ethnic minorities
  - Sex workers
  - Drug users
  - The uneducated (illiterate)
  - Men/women who have sex with persons of the same gender
STIGMATIZED GROUPS (2)

- HIV-infected persons
- Persons infected with sexually transmitted organisms
- Sexually promiscuous persons
Lack of confidentiality creates a risk of stigmatization.

Investigator has the responsibility to guarantee freedom from stigmatization for all participants.
PRIVACY

PRIVACY = FREEDOM FROM UNSANCTIONED INTRUSION

PRIVACY (2)

• Respect for persons guarantees the participants’ RIGHT to privacy
• Lack of privacy causes unwillingness to participate in research
• Assertion of investigator that privacy is guaranteed is insufficient
• Participant must perceive that privacy is guaranteed
CONFIDENTIALITY VS. ANONYMITY
CONFIDENTIALITY

• Name and identifying information are recorded

• Investigator guarantees that identifying information will not be shared with unauthorized persons

• Guarantee of confidentiality is only as good as the integrity and care of the investigator and staff
ANONYMITY

• Name and identifying information are not recorded

• Impossible to trace back results to informant
ETHICS

The ethics of taking action vs. the ethics of avoiding action
THREE CASE STUDIES
CASE 1: CLINICAL TRIAL TO PREVENT MATERNAL/CHILD TRANSMISSION OF HIV

- Without treatment, 30+% of infants born to HIV-infected mothers will be infected
- Long-term treatment used in rich countries costs several thousand dollars per mother
- Poor countries cannot afford long-term treatment
- Can short-term treatment reduce transmission?
CLINICAL TRIAL TO PREVENT MATERNAL/CHILD HIV TRANSMISSION

Ethical issues

• Is a trial of short-term treatment ethical when it is known that long-term treatment is effective?
• Is it ethical to have a control group?
• What should the control group receive?
• What are the ethical responsibilities of the investigator towards participants, particularly in the control group?
CASE 2: PRE-EXPOSURE PROPHYLAXIS

• 90% of sex workers become HIV-infected within the first year of work
• Many clients reluctant to wear condoms
• No female controlled microbicide available
• Tenofovir is cheap, effective and not known to have many side effects
• Is a clinical trial of prophylactic tenofovir ethical?
A TRIAL OF PROPHYLACTIC TENOFOVIR USE

- Intervention group = sex workers – daily tenofovir
- Placebo = no medication
- Counseling and condoms to avoid HIV infection provided
- Outcome variable = HIV infection rate
- Approved by IRBs in UCSF and NCHADS
- Infected sex workers receive two years of treatment with tenofovir
- Trial proceeding in other developing countries
PRE-EXPOSURE PROPHYLAXIS

Ethical concerns

• Is a clinical trial in poorly educated sex workers in a developing country exploitation?
• Should there be a control group?
• What should the control group receive, if anything?
• What responsibility does the investigator have for sex workers who become infected?
Cambodian Leader Throws Novel Prevention Trial Into Limbo

AIDS prevention for sex workers is crucial, and last March, the World Health Organization said they would give anti-AIDS drugs to volunteers over the next five years, a period they aim to protect them against possible HIV infection. However, the Cambodian leader has ordered the trial to be put on hold.

Prevention intervention. Oxfam’s Rosanna Barbero led opposition to the study.

SEX WORKER DEMANDS

- Lifetime care if she becomes HIV-infected or suffers side-effects
- Health insurance for 30 years
- More counseling
- Free female condoms
CASE 3: ETHICAL TO TEST RX AS PREVENTION IN HETEROSEXUALS?
As part of the strategy of **treatment as prevention** (in light of recent studies demonstrating essentially no transmission from HAART-treated HIV+ individuals), it is essential to implement testing to reduce the numbers of individuals unknowingly spreading HIV and provide them with effective treatment. Therefore, you intend to conduct a study to determine the prevalence of HIV among high-risk (long-distance) truck drivers and their primary sex partner/wife in Namakhal, India to determine if truck drivers are a high-risk group and are transmitting HIV.
1. Should the testing of drivers be “opt-out”?
2. Should return of testing results to truck drivers be optional?
3. Should those testing positive be referred to treatment or be treated by you? If referred, should you follow up to assure that they are receiving treatment?
4. Should treatment of HIV+ drivers be mandatory?
5. Should the primary sex partner/wife of the HIV+ drivers be informed that their husband may infect or already has infected them?

6. Should wives of HIV+ drivers be tested? Opt out?

7. Should HIV-infected wives be referred for care or treated by you? If referred, do you follow up to assure that they are receiving treatment?

8. Should uninfected wives of HIV+ drivers be given prophylactic treatment?
CONFLICTING PUBLIC HEALTH GOALS

- Protect the uninfected
- Protect the infected