Clinical Trials in Developing Countries: The Role of Culture & Tradition

Session: - International Clinical Trials

by

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Scope of the Dilemma

- Research is a Global business, funders are international organizations, agencies, industries
- World is of diverse economies, cultures and traditions
- Can we apply the universal principles of Ethics in these diversity?
Figure: Population Living in Poverty (% below $1 a Day)

<table>
<thead>
<tr>
<th>Year</th>
<th>Africa</th>
<th>Developing Countries</th>
<th>Developed Countries</th>
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<tbody>
<tr>
<td>2000</td>
<td>46.7%</td>
<td>23.0%</td>
<td>20.0%</td>
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Death Rates in Developing Countries

52 million die annually worldwide

In developing Countries:

- 16m affected - infections & parasitic diseases
- 55% of 10m affected - circulatory diseases
- 3.5% of 6m affected - malignant disease
- 80% of Global burden of disease in DALYs
Africa Poverty Syndrome

- 33 of 50 world poorest countries are in Africa
- 690 million Africans rep 10% of world pop. living on <1% GNP
- 2/3 of Africans live in abject poverty
- 50% lack safe water
- 70% without proper sanitation

Consequential disease prone and a need to embrace research benefits.
Figure 4: % of Population with Access to Safe Water and Health Services, 2000

- **Safe Water**
  - Africa: 62.1
  - Developing Countries: 78
  - Developed Countries: 100

- **Health Services**
  - Africa: 61.7
  - Developing Countries: 80
  - Developed Countries: 100
Africa Disease Syndrome

Africa has:

- 80% of global HIV-positive
- 90% of 2m worldwide annual malaria deaths
  
  \(90\% \text{ of these are malaria deaths of young children}\)
- 22% of global deaths
- 34% of global DALYS from Tuberculosis
- 24% of global DALYS from malnutrition

No of unnecessary deaths equiv. to 10 Hiroshima & Nagasaki bombs annually.

- DALYS – Disability Adjusted Life Years.
Figure 2: Infant Mortality Trend (per 1000 live births)

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<tr>
<td>2002</td>
<td>86.9</td>
<td>62.4</td>
<td>7.7</td>
</tr>
<tr>
<td>2003</td>
<td>85.8</td>
<td>61.4</td>
<td>7.7</td>
</tr>
<tr>
<td>2004</td>
<td>84.7</td>
<td>60.4</td>
<td>7.6</td>
</tr>
<tr>
<td>2005</td>
<td>83.6</td>
<td>59.4</td>
<td>7.5</td>
</tr>
<tr>
<td>2006</td>
<td>82.5</td>
<td>58.3</td>
<td>7.4</td>
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PROGRESSION OF POVERTY IN DEV. COUNTRIES

20% Developed wealthiest countries vs 20% poorest.

- Early 20th Cent. - 9ce richer
- 1960 - 30ce richer
- 1990 - 60ce richer
- 1997 - 70ce richer

*Progression of poverty impact on disease is staggering*
Consequences of Profile of Dev. Countries

- Poor resource base
- Poor environmental facilities
- High Child & Adult mortality
- *Clinical Trials & Research Essential in Developing countries*
Ethical Merit of Research

- Understanding the nature and purpose of research
- Effective communication
- Opportunity to have their pertinent questions answered
- Can truly informed consent
- Can make uncoerced decisions for participation
Merits in Clinical Trials

- **Respect** for the dignity of participants/
  *Respect their integrity, privacy, safety, human rights*

- **Beneficence/ Non Maleficence**
  Balance risks against benefits
  - Recompense for time
  - Compensation for injury
  - Protect confidentiality
  - Avoidance of conflict on interest

- **Justice**
  Justification for the Clinical Trials and the outcome
  **VOLUNTARY INFORMED CONSENT IS KEY**
Ethical Relativism in Clinical Trials

- Cultural ethical or descriptive relativism
- Normative ethical relativism
- Metaethical relativism
- Contextual relativism
- Risk – benefit relativism

- Ruth Matlin – Albert Einstein College of Medicine
Cultural Ethical Relativism

- Customs, traditions, moral values varying worldwide
- Cultural norms & tradition guide the views of individuals, communities & society
- Shapes Actions of individuals communities & Societies for right and wrong
Normative Ethical Relativism

- What is right in one society may be wrong in another
- Normative Ethical relativism justifies cultural relativism
- No absolutely valid Universal ethical principle
- Criticism and imposition of a cultures ethical norms on another is unethical
Metaethical I – Conceptual & methodological relativism

- Culture lacking concept of individual human rights
- Culture lacking concept of gender equality cannot understand, accept or respect, voluntary concept of individual even more so gender equality in informed consent.
Cultures where authority of leaders is basis of judgment

Cultures with believes of ancient or religious texts cannot accept modern international concepts for decisions.
Risk benefit relativism

- Research not ethically acceptable in a low disease country may be acceptable in one with high prevalence

  e.g. Rotavirus vaccine trial in US vs dev. Counties.

  Complication risk ratio 1:80
Challenges to consent seeking in Clinical Trials

- Poor handling of
  - informed consent
  - Confidentiality
  - Conflict of Interest
  - Standard of care
  - Lack of honest reporting of data
  - Misconduct & professional incompetence of researchers
  - Clearly defined benefits to the research host community
Probing Questions by Research participants -1 in Developing Countries

- Who are these people conducting the trial?
- What is their real interest?
- Why are health care facilities so inadequate in our community?
- Why is such a large team with huge facilities interested in studying us?
Probing Questions by Research participants—II in Developing Countries

- Is this for the researcher’s benefit or ours?
- How will our lives change if tests are positive for enumeration in research?
- What happens to us if we refuse to participate?
- What happens to us after clinical trials if we accept participation?
Probing Questions by Research participants -III in Developing Countries

- Will we be better off if we participate?
- What effect will clinical trials have on our babies (if not breast feed in HIV test cases)?
- What will our spouses (husbands) say about participation?
- Who can we consult for answers to these myriads of questions?
- Can we rely on all explanations by the researchers?
Probing Questions by Research participants IV in Developing Countries

- Should we consult the leaders in our communities?
- Should the community play a role in deciding if our members should participate in the trial or must we decide all by ourselves?
- If researchers encourage us to participate, how will the decision affect our relationship with our communities?
Resolution of Participants mindset

- Do Researchers bother about the mindset of participants as to their view of researchers and the privileged world?
- Have researchers tried to understand the mindset of potential research participants?
- Have resource been allocated to train health care workers to constructively evaluate these probing questions of participants?
- Do researchers merely want to get research done quickly and economically?
- Do these issues if not well addressed go well with
Clinical Trials and Cultural Relativism

- Can the Principles of research ethics be totally universally applied?
- Respect for persons
- Communities that do not respect or accept autonomy of each individual but believes in the community leadership cannot absolutely embrace the international concept
Hierarchical Consent in African Country setting

- In many communities in Africa, first contact must be tribal chiefs, community leaders, council elders for permission to enter and approach individuals.

- Process is mistaken and adjudged as consent for participation by the individuals but is not consent for enrolment of participants simply permission to enter.
Ethical relativism in informed consent

- Some cultures require signature of husbands before wives can participate in research.
- Some cultures, patients *never make decisions*.
  - As all uncertainties must be held back from them (yet this is the bedrock of randomisation).
  - Existence of alternative therapies.
  - No mention of placebo to participants as there will be no enrolment.
  - No informed consent is requested at all to remove suspicion.
Procedural Ethical ‘uniformity’

- Fundamental Principles of Respect Beneficence Justice
- Every adult must give individual consent usually in addition to other gatekeepers
- Complete disclosure of clinical trial aims & objectives, methodology, expected risks and outcome of research.
Procedural Ethical ‘Variability’

- Cultural challenges may induce variability including
  - Written Consent process severally signed (chiefs, leaders, husbands, in-laws etc)
  - Verbal recorded consent may be admissible
  - Composition and rules of procedure of ERC
Way Forward 1

Achieving Universality in Ethical Standards

- Examine:
  - What constitutes the best interest of subjects with individual culture & traditions preferences worldwide.
  - Differences between truly universal & imperialistic notions
  - Consideration of contextual issues on moral grounds.
Way Forward 2

- Develop Expertise & Infrastructure to
  - Evaluate ethical problems
  - Educate practitioners & researchers
  - Facilitate development of policy

- Address the gap between motives of external funders/researchers, and those of local institutions/researchers.

- Address international Scientific worldview gap compared with the mindset of the research participants requires attention.
Way Forward 3
Host Country Participation

- CIOMS Guidelines 3. An external sponsoring organisation and individual investigation should submit research protocol for ethical and scientific review in the country of the sponsoring organisation, and the ethical standards applied should be no less stringent than they would be for research carried out in that country.
Way Forward 4

Strengthening Consent-Giving

- NBAC Recommendation 3.2. Researchers should develop culturally appropriate ways to disclose information that is necessary for adherence to the substantive ethical standard of informed consent, with particular attention to disclosures relating to diagnosis, risks, research design and possible post trial benefits.
The Way Forward 5

“Justice must be seen to be done”

- Focus must be to improve the lives of the vulnerable and disadvantaged in developing countries.
- Appreciation of the place of exploitation through selective promotion of interest of researchers & sponsors and exclusive ownership of data and IPRs.
- Building adequate capacity in research ethics.
- Research into diseases of developing countries which are of limited interest to the industrialised world e.g. Sickle Cell Disease etc. must be encouraged.
- Inclusion of Developing World in collaborative process to improve local capacity and collective understanding of the reasoning process not simply for project execution.
Way Forward -6

“Justice must be seen to be done”

- Individuals, Community & Society hosting clinical trials must have
  - Adequate compensation
  - Post Trial Benefits
“Justice must be seen to be done”

- Host countries:
- Corrective positive policies in research put in place not simply “complain”
- Special attention paid to women in Dev. Countries for better income generation to improve capacity building and social support networks for clinical trials.
- Encourage IPRs in research in their countries to break poverty & disease syndromes
References

- CIOMS 1993
- Benatar SR. Reflections & recommendations on research ethics in developing countries. Social science & medicine 54( 2002) 1131 – 1141
- Ruth Macklin,Albert Einsten College of Medicine