DEALING WITH ETHICS – ISSUES AND CHALLENGES

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PRESENTATION OUTLINE

- Outline
- Presenter's Background
- Introduction
- Ethical theories/principles
- Core ethical issues in DUR
- Ethics guidelines/regulatory agencies
- Ethical issues in DUR – practical examples
- Public perspective of ethics of DUR
- Conclusion
- References

MY BACKGROUND

- Medical Practitioner
- Post-graduate specialization in Internal Medicine
- Sub-specialization in Clinical Pharmacology and Therapeutics
- Masters degree in Bioethics (KU Leuven/University of Padova)

PRESENT STATUS

- Senior Lecturer in Pharmacology
- Consultant Physician/Clinical Pharmacologist
- Research mainly in the following areas:
  - Drug utilization
  - Adverse drug reactions

DEFINITIONS

- Ethics – branch of moral philosophy which addresses questions about morality,
- The concept of good and bad; right and wrong; justice; virtue etc
- Medical ethics – field of applied ethics
- Study of moral values and judgments as it applies to medicine
- Bioethics – a more encompassing discipline with application to biotechnology, life sciences, environment and society

INTRODUCTION

- Definitions
- Importance of Ethics in Research
- Ethics in Drug Utilization Research

IMPORTANCE OF ETHICS IN RESEARCH

- Nazi experimentation with human beings
- The Thalidomide case
- Advances in medicine such as organ transplantation, kidney dialysis and use of respirators
- End of life care – dementia, persistent vegetative state etc

IMPORTANCE OF ETHICS IN RESEARCH

- The Tuskegee syphilis experiment/ Public Health Service Syphilis Study
- Conducted in Alabama between 1932-1972
- Clinical study which recruited 399 poor African-Americans with syphilis
- The aim was to follow the progression of the disease
- They were not told that there was treatment for their condition
- They were not treated with Penicillin despite its availability

IMPORTANCE OF ETHICSIN DRUG UTILIZATION RESEARCH

- Pharmaco-epidemiological studies deal often with large number of people
- Usually observational, non-experimental studies
- Different from the regular clinical research or clinical trial
- Ensure protection of study participants
- May have impact on different segments of the society with the possibility of stigmatization

ETHICAL THEORIES

- Deontology
  - Otherwise known as Kantian theory
  - People should not be treated as a means to an end
  - Some actions are right or wrong regardless of the consequences (protection of research participants may lead to slowing down of research output)

ETHICAL THEORIES 2

- Utilitarianism
  - Aggregate or collective benefits to be maximized
  - “The benefit of all more important than individual benefits”
  - Provides justification for public health programs like compulsory vaccination and use of fluoride in water

PRINCIPLE OF BIOMEDICAL ETHICS

- Developed by Beauchamp and Childress first in 1978
- Introduced initially for ethical issues in clinical medicine
- Made of four components
  - Respect for autonomy- basis for informed consent
  - Beneficence – to do good
  - Non-maleficence – “primum no norcere” means to do no harm
  - Justice – equitable access to health care
- Useful framework for ethical decision-making

CASE- BASED APPROACH

- The principles cannot answer all ethical posers
- Casuistry (developed by Albert Jonsen)
- Decision takes place at the level of the particular case
- No reference to any particular theory
- Clear exposition of all facts surrounding the case
- A “maxim” or “rule to govern the case is decided usually through logical reasoning

INFORMED CONSENT

- A process through a fully informed patient / subject can participate in choices about their healthcare
- Has five components:
- Nature of the procedure/research
- Alternatives to the procedure/research
- Likely benefits and risks
- An assessment of the patient's understanding
- Obtaining the consent
- ESSENTIAL FOR CLINICAL PRACTICE AND RESEARCH
- MAY NOT BE POSSIBLE IN SOME INSTANCES IN PHARMACOEPIDEMIOLOGICAL RESEARCH

INFORMED CONSENT

- Essential for clinical practice and research
- Ethical imperialism or pluralism
- May not be possible in some instances in pharmacoepidemiological research
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BENEFICENCE/NON-MALEFISANCE

- Ethical obligation to maximize benefits and to minimize harms
- Risk-Benefit ratio to be assessed
- Qualified and competent investigators to safeguard welfare of participants
- No deliberate harm

JUSTICE

- Refers to equitable distribution of burdens and benefits
- Differences in the distribution of burdens is allowed with “vulnerable” population
- Research conducted in developing countries should be responsive to the needs ot their communities
- Exploitation of research participants from low-resource settings is discouraged

KEY PRINCIPLES

Principle	**Application**
1. Respect for persons	1. Informed consent
2. Beneficence	2. Assessment of risks/benefits
3. Justice	3. Fair selection of subjects

- Notable in that research ethics guidelines were expanded to cover all research

Basis for different approach to ethics of DUR

Individual Health

Bioethics = human rights, civil liberties and individual autonomy approach, medicalized system, confidentiality, privacy, personalized

Population Health

Public health = utilitarian, paternalistic, social and legal responsibility to protect the public health, community orientation, accountability, universal, governmental responsibility

CORE ETHICAL ISSUES IN DUR

- Informed consent
- Confidentiality and privacy
- Beneficience/Non-maleficence
- Communication of results

INFORMED CONSENT

- May be waived under the following circumstances:
  - conducted in the interest of the public's health
  - direct harm to the individual is extremely unlikely
  - individually identifiable data are not made public
  - the use of personally identifiable materials with special justification
  - the use of personally non-identifiable materials
  - large databases are being used making obtaining informed consent almost impossible

CONFIDENTIALITY/PRIVACY

- Risk of exposure of sensitive information
- May lead to stigmatization of individuals and communities
- May also be associated with job loss, insurance issues etc
- Who has access to the data and under what condition?
- Secondary use of data
- Cross-national exchange of data

CONFIDENTIALITY

- All steps that will be taken to protect the confidentiality of research participants should be documented in the research protocol
- These include:
  - Limited access (locking up of folders)
  - Limiting access (number of people)
  - Removing identifiers
  - Encryption of information

CONFIDENTIALITY

- There should be international legal backing for cross-national transfer of data (European Union Data Privacy)
- All studies that use identifiable data (prospective) should get ethical approval from the research ethics committee (REC) or IRB
- The REC has the responsibility to monitor use of confidential data by investigators

BENEFICENCE/NON-MALEFICENCE

- Though the physical risk associated with DUR is negligible, investigators must take note of the following:
  - Potential stigmatization of individuals and communities
  - Other socio-economic consequences such as job loss, insurance issues

ETHICAL GUIDELINES/REGULATION

- Declaration of Helsinki
  - Developed by the World Medical Association for the medical community regarding human experimentation
  - The foundation document of human research ethics
- Council of International Organizations of Medical Sciences (CIOMS)
  - Developed together with WHO the "*International Ethical Guidelines for Biomedical Research Involving Human Subjects*"
  - Latest review in 2009
  - More flexible towards research in different cultural contexts

NHREC Code

- National Health Research Ethics Committee is the regulatory body for human subject research in Nigeria
- NHREC Code was released in 2007
- Research Ethics Guidelines adapted to our cultural and national context
- Developed on the background of the DoH and CIOMS guidelines

OTHER REGULATORY CODES

- South Africa- Guidelines on Ethics for medical Research – General Principles (MRC)
- UK - **MRC Ethics Guide :**Research involving human participants in developing societies
- International Epidemiological Association (IEA) Good Epidemiological Practice (GEP)
- International Ethical Guidelines for Epidemiological Studies (CIOMS)
- ISPE **Guidelines for Good Pharmacoepidemiology Practices (GPP)**

THE ROLE OF RESEARCH ETHICS COMMITTEE

- Definition: An independent body , consisting of healthcare professionals and non-medical members, whose responsibility it is to protect the rights, safety and wellbeing of human subjects involved in research and to provide public assurance of that protection
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FUNCTIONS OF THE RESEARCH ETHICS COMMITTEE

- To maintain ethical standards of practice in research;
- To protect research participants and investigators from harm or exploitation;
- To preserve the research participant's rights, which take preference over society's rights
- To provide reassurance to society that this is being done

ETHICS COMMITTEE – COMPOSITION GCP GUIDELINES, 1996

- The IRB/IEC should consist of a reasonable number of members, who collectively have the qualifications and experience to review and evaluate the science, medical
- aspects, and ethics of the proposed trial.
- It is recommended that the IRB/IEC should include:

- a) At least five members.
- b) At least one member whose primary area of interest is in a non-scientific area.
- c) At least one member who is independent of the institution/trial site.

RECS IN PRACTICE IN NIGERIA

- Research ethics committees are present in teaching hospitals/universities/research institutes
- Involved mainly in review of research protocols
- Composed usually of scientists, doctors, clergy, lawyers and laymen
- Usually meets once in a month

ETHICAL CHALLENGES IN DUR AND RESOLUTIONS

PRACTICAL EXAMPLES

SOUTH AFRICA – Truter et al,2001

- Retrospective study using computerized medical records from 3 private healthcare organization
- Investigated drug utilisation in hyperlipidaemia. DM and TCAs
- Study was not sponsored by any drug company
- It was not possible to trace any patient
- Not possible to identify prescribing physician
- Data confidentiality and privacy was protected at all times

UK –Evans et al, 2001

- Study using record-linkage technique to form databases
- Study involved anonymization of data
- Also ethical approval was sought from relevant bodies
- Introduced the concept of “Caldicott Guardian”
- This is a senior person responsible for protecting the confidentiality of a patient and service-user information and enabling appropriate information-sharing.

BRAZIL- de Castro et al, 2001

- Evaluated two studies
  - Medication adherence among hypertensives
  - Evaluated inadequate use of vancomycin
- Prescriptions were collected from the pharmacy (Privacy issues)
- For the adherence study, the ability of the patients to understand inform consent document was the main issue

How were these problems resolved?

- Removal of personal identifiers from the forms used for data analysis
- The research ethics committee scrutinized the informed consent document and approved its readability

NIGERIA – Fadare et al, 2014

- Prospective study among psychiatric outpatients
- Investigated medication adherence and patient satisfaction
- Informed consent – some patients only speak the local language
- Administered study instruments – some patients interview

CHALLENGES AND RESOLUTION

- Informed consent: Translation and back translation was done
- The research ethics committee approved the informed consent approach for the study
- Issue of coercion; the interview was conducted after the regular clinic appointment
- Patients who refused to participate had already being attended to

CHALLENGES AND RESOLUTION

- Data protection: From case notes
- Patient identifiers were inputted in the data collection forms
- Patients' interview, data entry and analysis was compartmentalized
- All data from the study was stored under lock and key with limited access

STUDY 2: Fadare et al, 2013

- Cross-sectional study among elderly outpatients
- Medical records of 220 patients were used
- Data confidentiality and privacy was ensured through the following means:
  - Removing all identifiers from the data collection form
  - Data collection, entry and analysis was done by different people

STUDY 2: Fadare et al, 2013

- Access to the data was also limited to the principal investigator
- The study protocol was approved by the research ethics committee before commencement .

STUDY 3 – Tamuno et al, 2011

- Retrospective cross-selection study
- 500 prescriptions collected from the pharmacy
- Personal identifiers excluded during transfer of data to collection form
- Researchers did not have access to patients' case notes
- Data confidentiality was maintained at all times

PATIENTS' OPINION ABOUT USE OF MEDICAL INFORMATION

UK – Parkin et al, 2011

- Citizen jury to determine public view on use of private information for post-marketing survellance
- Concluded that researchers should be allowed to use identifiable information without individual consent PROVIDED that
- Relevant ethical guidelines are followed
- This shows that an informed public does not place personal privacy above societal benefit

Australia – King et al, 2012

- A 2 stage qualitative and quantitative research
- Measured attitudes towards privacy, medical research and consent
- Also investigated privacy concern about sharing one's health information for research
- Result showed tremendous support for research (98%)
- At the same time, respondents were worried about privacy of their health information(66%)

Australia – King et al, 2012

- 92% would prefer to be asked when their personal information is being used for other purposes outside medical treatment
- 83% would like to know the nature of the research and the organization conducting the research before giving approval
- 42-60% had concerns about linkage of their identities to situations not related to medical treatment
- These include: STDs, mental illness, genetic problems, drug and alcohol use etc

CONCLUSION

- Drug utilization research is essential for the promotion of public health
- The principal ethical concerns are confidentiality and privacy
- Researchers should abide by existing national and international guidelines in this regard
- The role of research ethics committee as “guardians” is also highlighted

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