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The basic concepts of research ethics

Part I. Case studies
Ethics: the most basic concepts

Judie and Mary

"Both Jodie and Mary, who were born on 8 August 2000,were pseudonyms given to conjoined twins, who were joined at the pelvis. The medical evidence indicated that Jodie was the stronger sibling who was sustaining the life of Mary. Mary had only survived birth due to a shared common artery that enabled her sister Jodie to oxygenate blood for both twins. If surgically separated Jodie had a 94% survival rate but Mary was guaranteed to die. However if they were left conjoined then Jodie's health, which was already rapidly deteriorating, was predicted to fail before they were six months old. Jodie's death would inevitably result in Mary's."

(source: Wikipedia)

Research involving human beings – the most basic concepts

Practice or research? I

Mr. P is a 55 years-old oncology patient, cured with no relapse. He had to undergo a chemotherapy treatment that resulted in cirrhosis, a progressive and irreversible disorder of the liver. In the later stages of cirrhosis, hemorrhages of the digestive tract (i.e. bleeding varices) are common. Majority of patients die during the first occurrence of hemorrhage. However, Mr. P has experienced 12 episodes of hemorrhages already. Last year Mr. P experienced another hemorrhage and ended up in the ICU. His condition was critical. The treatment prescribed for Mr. P was not successful, but after a week of inefficient management, the physician found out about a medicine (XYZ) that may help stop the bleeding. This medicine works for two hours and if during this time the wound is healed, bleeding would stop. The medicine was registered for hemophilia hemorrhage, but the physician wanted to take a risk and make an experiment."

(source: based on A. Smatanova's case from Erasmus Mundus Master of Bioethics 2010-2011)

Practice or research? II

„A major side-effect of chemotherapy is peripheral neuropathy. A new substance, compound S, has been shown in animal tests to have a protective effect on the peripheral nervous system when exposed to neurotoxic drugs. In Phase I studies on normal volunteers, compound S has not demonstrated any toxic side-effects. A placebo-controlled trial of its safety and efficacy at preventing peripheral neuropathy in patients with cancer receiving neurotoxic chemotherapy is planned. Matched population will receive at the time of standard intravenous chemotherapy additional infusions of either placebo

or compound S."
(source: B. Freedman, A. Fuks, C. Weijer, Demarcating research and treatment: a systematic approach for the analysis of the ethics of clinical research, Clinical research, 1992, vol. 40, no. 4, pp. 653-660.)

Practice or research? III

„A research study is organized by a group practice in pediatrics. Some physicians use antibiotic A for a common infection while others use B. Patients will be assign to A or B (randomly). After some interval patients' computer records will be checked to see, if any important differences appear. When testing head to head the efficacy of two treatments that fall within the range of standard practice as judge by an endpoint examined in standard practice. But the design of the study may achieve generalizable knowledge."
(source: B. Freedman, A. Fuks, C. Weijer, Demarcating research and treatment: a systematic approach for the analysis of the ethics of clinical research, Clinical research, 1992, vol. 40, no. 4, pp. 653-660.)

Practice or research? IV

46-year-old patient, Mr. T. is diagnosed with hypertension. His physician, dr. Wolfe prescribed him medicine X 2,5 mg o.d. However, the pressure of the patient still remained too high. Therefore dr. Wolfe decided to increase a dose to 5 mg o.d. Since T. complains also on digestive troubles, dr. Wolfe prescribed him additional medicines.

Practice or research? V

ABC is a new antihypertensive agent. Recruitment to a phase III, randomized, double-blind clinical trials has been started. In Phases I and II safety of the compound was determined. The efficacy and safety of ABC will be studies against two, already approved and registered drugs. Dr. Wolfe invites his patient Mr. T, to participate in the trial.

Dr. Pronovost's checklist

"Regulators in the Office for Human Research Protections (OHRP) – the US's highest office for the protection of human subjects. The allegation was that Pronovost and the 67 Michigan hospitals were using patients in human-subjects research without informed consent – obviously a serious allegation of an ethical violation. Pronovost's funded activities were part of a study to improve medical care; it was sponsored by the Michigan Hospital Association. The aim was to improve care in ICUs by strictly implementing preventive procedures that had already been recommended by the Centers for Disease Control and Prevention, such as washing hands, using certain infection-control precautions, and the like. The team Dr Peter Pronovost at the Johns Hopkins University was working with 103 ICUs in 67 Michigan hospitals to implement and evaluate, what had been established at Johns Hopkins and other intensive care units to be a very successful infection-control measure. However, the work was halted by federal studied the effect on infection rates of a careful implementation in practice of all the recommended procedures following a checklist. They found that infection rates fell substantially if the checklist is scrupulously followed. After a published report of the study, the OHRP received a complaint that there search violated US regulations. After investigating, the OHRP demanded that Johns Hopkins (and Michigan hospitals) correct this mistake and undertake full review of the study."
(source: T. L. Beauchamp, Why our conceptions of research and practicemay not serve the best interest of patients and

subjects, The Journal of Internal Medcine, 269; 383–391.)

Human tissue research

An investigator receives specimens from an institution she works at. The specimens: tissues from a pathology department, have been collected over the years in the institution. The specimens do not have links in any identifiable information. Does investigator conduct research involving human beings? Should she obtain an approval from an ethics committee?

Electronic health records

A researcher proposes to link de-identified data from different electronic health repositories. Although this is not a goal of a research project, there is potential that together information would allow to identify the individuals. Is that a research project involving human beings?

Part II – Excerpts from regulations

US. Federal Regulations. 45 CFR part 46. Section 102.

Definition of research:

(l) Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

Definition of a human subject:

(1)Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

(2)Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

(3)Interaction includes communication or interpersonal contact between investigator and subject.

(4)Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

(5)Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

(6)An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Exemption from Federal Regulations:

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512 […]

Declaration of Helsinki

Goal of research and physician's professional duties:

6. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

14. Physicians who combine medical research with medical care should involve their patients in

research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

Definition of research involving human beings:
32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. [….]

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