Lecture 13b

Real World of Evaluation

Ethics of Research with Human Subjects

Horror stories in research

- Tuskegee “Experiment”
- Milgram Experiments
- Drug trials in developing coutries

Belmont Report

- 1974 – National Research Act
  - Identify basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects
  - Develop guidelines which should be followed to assure that such research is conducted in accordance with those principles
    - See http://ohsr.od.nih.gov/guidelines/belmont.html and BB

Basic ethical principles

- Respect for persons
  - Individuals treated as autonomous agents
  - Those with diminished autonomy entitled to more protection
  - Respect=subjects enter into the research voluntarily and with adequate information
- Beneficence
  - Do no harm
  - Maximize possible benefits and minimize possible harms

Justice

- Who ought to receive the benefits of research and bear its burdens?
  - Justice=sense of fairness in distribution
  - Injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly
- Why apply principles of justice to scientific research?

Application of ethical principles

- Informed Consent (Respect)
  - Give opportunity to choose what shall or shall not happen to them
    - Standards for Informed Consent
      - Information
      - Comprehension
      - Voluntariness
- Assessment of Risks and Benefits
  - Minimal risks or small Benefits/Risks ratio
  - Privacy
- Selection of Subjects
  - Fairness in selection, equitable distribution of risks & benefits

NYU Human subjects application

- http://www.nyu.edu/ucaihs/forms/

Case study 1 in ethics

- CHEERS Study
- Responses

From the EPA…

- CHEERS: EPA-sponsored, with collaboration from Duval County, Florida Health Dept (Jacksonville) and CDC
  - Field monitoring study of the effects of pesticides (and other chemicals) on young children in the home environment.
  - Plans to recruit 60 young children with high pesticide use in the home. A comparison group of low pesticide use would also be recruited.
  - Parents would not be required to begin using pesticides or continue using pesticides. It was not an intentional dosing study.
    - In fact, the EPA would carefully screen participants to make sure that they were already using pesticides (if in that group).

Study procedures

- Extensive study procedures:
  - interviews
  - collecting samples around the home (level of pesticides)
  - taking blood and urine samples (presence of pesticides)
  - parents were required to videotape their children's activities and keep a pesticide purchasing and food journals.
- 5 home visits over a two-year period.
- Parents would be warned of any unsafe pesticide levels in blood or urine or unsafe pesticide practice.

Follow the money: incentives/funding

- Incentives:
  - Parents would be paid $970 to complete all of the activities
  - Got to keep video camera
  - Got t-shirts and mugs.

- Funding:
  - The American Chemistry Council (ACC) would pay $2 million to help support the study.

Responses

- Even though it was not an intentional dosing study, it was portrayed as such by the media.

- Soon reporters and blogs were describing it as an experiment in which parents would be paid to expose their children to pesticides.
  - No one bothered to check the original stories for accuracy.
  - The EPA did not respond effectively to these charges.

The story

- **Environmental and Children's Health groups protested the CHEERS study.**
- **CHEERS became a political cause and symbol of the Bush Administration's environmental policies.**
- **Congressional hearing were held, led by Sen. Barbara Boxer (D-Cal).**
- **CHEERS researchers were compared to the Nazis.**
- **Boxer and others threatened to stop the nomination of Steve Johnson as the new EPA director if he did not stop the CHEERS study.**
- **Johnson cancelled the study on April 9, 2005.**

Statement by Stephen L. Johnson, Acting Administrator of the EPA

On April 8, 2005, I cancelled the Children's Health Environmental Exposure Research Study. The Children's Health Environmental Exposure Research Study was designed to fill critical data gaps in our understanding of how children may be exposed to pesticides (such as bug spray) and chemicals currently used in households. Information from the study was intended to help EPA better protect children. EPA will continue to pursue the goal of protecting children's health.

Last fall, in light of questions about the study design, I directed that all work on the study stop immediately and requested an independent review. Since that time, many misrepresentations about the study have been made. EPA senior scientists have briefed me on the impact these misrepresentations have had on the ability to proceed with the study.

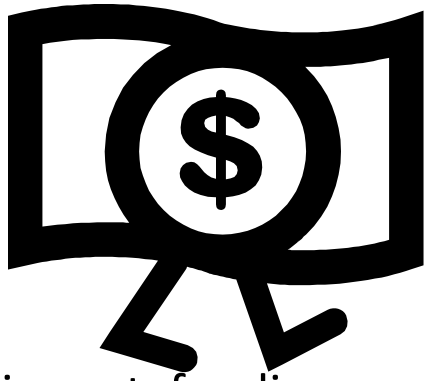
I have concluded that the study cannot go forward, regardless of the outcome of the independent review. EPA must conduct quality, credible research in an atmosphere absent of gross misrepresentation and controversy.

As a scientist and a 24-year employee of the EPA, I have a deep passion for the Agency's mission to protect human health and the environment. Continual review and reassessment is a fundamental aspect of scientific progress, and I am committed to ensuring that EPA's research is based on sound science with the highest ethical standards.

Benefit/risk

- Benefit to society
  - Better knowledge of how pesticides affect people can lead to better regulation of pesticides, which can improve public health.
  - Can help the EPA establish safe levels of pesticide exposure.
  - Industry is hoping that the studies will provide evidence for increasing allowable exposures, but the studies might support the opposite conclusion.
    - The studies could lead to tougher regulation of pesticides.
  - Studies could improve public health by enhancing our general understanding of how pesticides affect people.
    - Animal studies offer useful data, but they can only go so far.

Conflict of interest



- Since pesticide industry (Assoc Chemical Companies), in part, funding CHEERS study, COI major issue.
- CON: The sponsors will find ways of biasing the studies to promote their own interests and short-change the public.
- PRO: Steps can be taken to prevent bias, such as independent design and monitoring of studies, independent analysis of data, and no restrictions on publication.
  - Companies should not be allowed to skew the data or suppress unwanted results.
- However, the ACC would not have been significantly involved in the design of the study, interpretation of the data, or dissemination of results.
- Nevertheless, the appearance of a COI was a cause for concern.

Power and ethics

- Some of the studies submitted to the EPA by industry may have been statistically underpowered (sample size too small).

- Any studies should have the appropriate sample size (not too large or too small).
  - Too large (unnecessary exposure to risk)
  - Too small (may not produce statistically significant results).

- Question: can we learn anything useful from small samples? Maybe.

Vulnerable populations

- CHEERS was classified as minimal risk because it was not viewed as an intentional dosing study.
- The risks were the risks of data collecting procedures, not the risks of exposure to pesticides in the home.
- Whose kids? Which households?

Case study 2 in ethics

- Corruption in India

Bertrand, Djankov, Hanna, Mullainathan

- Explore corruption in the process of getting a drivers license.
- Would-be drivers assigned into one of 3 groups:
  - bonus (offered a financial reward if they could obtain their license fast),
  - lesson (offered free driving lessons upfront), and
  - control.
- Conducted surprise driving tests to see who could drive.

The control group

- 34 percentage points of individuals in the control group obtained a license without taking the legally required licensing exam (i.e. 71% of the 0.48 of individuals obtaining a license).
- Close to 30% (14%age points relative to 0.48 getting a license) of the control group obtained a license *and* automatically failed an independent driving test.
- Getting a license involves extra-legal payments. The control group pays well above the legislated fees to get a license. Specifically, the average license getter in the control group paid Rs 1,120, or about 2.5 times the official fee of Rs 450, to obtain his driving license.
  - Yet, causality is hard to assign. Do these distortions result from bureaucrats sacrificing social benefits in order to cater to individuals? private willingness to pay? Do these distortions imply that bureaucrats ignore social considerations?

The bonus treatment

- Find that the system responds to private needs: the bonus group is 24%age points more likely to obtain a license than the control group (i.e. 0.72 vs. 0.48).
- *"To ensure no social costs to the study, participants in the control and bonus groups were offered free driving lessons upon completion of the final survey and driving test."*
- However, this response comes at a social cost: the bonus group is 18%age points (relative to 0.14) more likely to both obtain a license *and* fail the independent driving test.
- Individuals in the bonus group are 13 percentage points more likely than the control group to obtain a license while also not taking the legally required driving exam.
- We also find that the bonus group pays on average Rs 178 more in extra-legal fees (*i.e., bribes?*).

The lesson treatment

- The lesson group is 12 percentage points more likely to obtain a license than the control group. But, the lesson group does not pay less than the control for their license, despite their superior driving ability, suggesting that extra-legal payments might be an essential part of getting a license.

Is it corruption?

- They find almost no evidence of *direct* bribes to bureaucrats in any of the groups. Instead, the extra-legal payments are payments to agents, professionals who assist individuals in the process of obtaining their driving license.

Food for thought

- Does the experiment pay people to engage in corruption? Is this ethical?
- Does this put more bad drivers on the road? Is this ethical?

Case study 3 in ethics: Repair and Maintenance Study (JHU)

- Evaluate low-cost abatement in old homes with peeling paint
  - Sample
    - 108 homes occupied when study began
    - In other homes, landlords who had agreed to participate in study were encouraged to rent to families with young children
  - Design
    - 3 experimental groups
      - 25 homes had minimal lead abatement
      - 25 had middle level of abatement
      - 25 had extensive abatement
    - 2 control groups
      - All lead hazards eliminated
      - Homes that never had lead paint
  - Time
    - 2 years of blood, dust, and water samples to measure contamination

Court case

- May 1994, Ms Higgins moved into a rented house that was part of study with 4 yr old son.
  - Later, her son tested positive for high levels of lead contamination leading to neurological problems.
  - Ms. Higgins had enrolled in the study but says no one ever told her about the levels of lead in the house (minimal abatement house)
    - Several other families claimed similar experiences
- Court
  - Enticed families into potentially lead-tainted households
  - Researchers intended that the children be canaries in the mines
- All research suspended at JHU