History of the Ethical Principles Underlying Conduct of Research with Human Subjects

IRB 101

Alaska Native Tribal Health Consortium
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Hy’shqe siam (Lummi) - Thank you, respected teachers

- Community Institutional Review Board (IRB) members
  - Sam Deloria, Lisa Preston, Kathleen Alexis, many others
- Native IRB leaders
  - Francine Gachupin, Dave Oreiro, Barbara Juarez, many others
- IRB staffs
  - Helen McGough, Ada Sue Selwitz, Shannon Sowards, many others
- Participants in research projects
- Researchers who walk their talk
  - Tessa Evans-Campbell, Jaime Donatuto, Stacy Rasmus, others
- "Indigenous Research Methods in Public Health"
  - Graduate Course U MT 595.54-34884 – by Lori Lambert
- Wife - Carolyn Robbins

WWII unethical research: Nazis

- concentration & killing camps (Dachau, Auschwitz)
  - Immersed prisoners in cold water
    - until they died – the intent of the research
  - Decompressed prisoners in high-altitude chambers
    - until they died – the intent of the research
  - Injected many prisoners with typhus
    - many died
  - Experiments about fatal infections on healthy identical twins
    - 1 twin killed by infection -> ID twin killed to do comparative autopsy
- Nuremberg Medical Trial, 1946-47
  - tried 23 defendants (20 physicians) - convicted 15
- Nuremberg Code, 1947: 10 rules for research
US Unethical research: PHS Syphilis Study

- Natural history of untreated syphilis: 399 African American men, dirt-poor sharecroppers Tuskegee, AL 1932
- Researchers lied to the men — “treated for bad blood”
- Not secret! — updates published about every 5 years!
- Continued in spite of: unclear scientific question (10 was answered by 1937); better Rx (penicillin) available 1945
- Highly “successful” (= “the men stayed with it”) – dropout rate only 1% over 40 years
- https://www.cdc.gov/tuskegee/timeline.htm

Q. Why was it so “successful”?  
Please answer this question yourself before discussing

Why was the Syphilis Study “successful”?

- NOTE: key reason for keeping 99% for 40 years was that the study was:
  - free burials,
  - African American doctors & nurses
- NOTE 2: “Culturally sensitive: can mask – even be used by – highly unethical research
- LESSON: being “culturally sensitive” is not sufficient by itself to make a research project ethical

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

- By the 1974 National Research Act
- First, it proposed regulations:
  - required Institutional Review Boards (IRBs)
  - for research done or conducted by HEW (now DHHS)
  - 45 CFR 46 (Title 45 Code of Federal Regulations Chapter 46)
- Applied to all types of human research
  - not just “experiments” or “biomedical research”
  - PHS Syphilis Study in Tuskegee: observational research
Then issued The Belmont Report

The three basic ethical principles underlying its proposed regulations (and their application):

- **Respect for persons** (application: Informed Consent)
- **Beneficence** (application: Assessment of potential risks [harm] and benefits)
- **Justice** (Equitable selection of people in the research)

(The Belmont Report in effect asked: “Under what circumstances is research ethical?” Its answer:

“When, & only when, the research complies with all 3 principles by applying them.”


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The Good, the Bad, & the Ugly …

Bad (unethical) research with AI/AN-1

- **Social science in the service of eugenics**
  - In Vermont [VT], the first third of 20th century
  - Surveys of “dumb” or “delinquent” children and their families
  - “Dumb” or “delinquent” families were usually poor Abenaki Indians +/- Catholic French Canadians +/- migrants

- **VT sterilized some “dumb” or “delinquent” children identified by the research – “to protect the gene pool”**

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Bad (unethical) research with AI/AN-2

- **Research with radioactive iodine (I131)**
  - early 1950s, USAF
  - “Do ANs survive the cold by having higher metabolism?”

- **Gave I\(^{131}\) to Alaska Native people**
  - same amount as then used for thyroid scan

- **Long safety of I\(^{131}\) thyroid scan unknown then**
  - almost all ANs did not speak English
  - 3 AN women in research were breast feeding children!
    - No-one has followed up with their children

- (Answer: ANs not higher metabolism; ANs simply know how to dress and eat in the Arctic!)
Bad (unethical) research with AI/AN-3

- Navajo uranium miners, 1950s
- Dust in U mines known to cause lung cancer
  - AEC refused to regulate mining
- PHS study, “natural history”
  - Health exam every 2 years, tracked deaths
  - “Pile up bodies at the door”
  - Did not inform participants of known health effects or reason for study
    - U Mine owners would refuse access if miners had been told
- Bodies piled up by early 1960s
- Research led to regulation of mining

Bad (unethical) research with AI/AN-4

- AI children of upper Midwest Reservation early ’60s
- Epidemic of impetigo causing temporary kidney disease (acute glomerulonephritis [AGN]) in kids
  - University nearby brought 30+ kids (most with impetigo) to U. Hospital to study them with urine and blood tests
  - Microscopy of early AGN had never been done
- Did kidney biopsies by needle in 31 AI children – 27 with impetigo + 4 without (“controls”), 4 repeated
- Needle kidney biopsy was new then, larger needles
  - Youngest age 1 year 4 months
- Put young kids at significant risk to do microscopy of early & pre-acute glomerulonephritis

Bad (unethical) research with AI/AN-5

Research on effects of alcoholism in Barrow, Alaska

- 1970s, researchers from northeastern US
- Announced findings in press conference at their U.
- Barrow was floating bonds on Wall St. -> BIG news
  - Bond ratings on Wall Street adversely affected
- The worst & longest-lasting harm?
- Internal stigmatization by people from Barrow & nearby communities
- NOTE: harms were done by dissemination of results & the researcher’s interpretation
Bad (unethical) research with AI/AN-6

Havasupai Tribe
- early 1990, Tribal Council approved a diabetes study including genetic analysis, by Arizona State University
- Tribal Council was not informed about and did not approve any other research
- BUT other research was done using specimens:
  - HLA
  - inbreeding.
  - migration genetic research
- Value of the research on diabetes for Havasupai?
  - no NLM-listed journal articles on genetic analysis of diabetes among Havasupai, one article on nutrition

The Good, the Bad, & the Ugly …

UGLY research with AI/AN

Havasupai Tribe [yes,… there is more]
- concurrently with diabetes study was schizophrenia study
- But:
  - neither tribe nor individual participants told or consented
  - information from clinic charts was obtained illegally, after hours, with no approval by anyone
- This is prime example of ugly research with AI/AN
  - major publicity adverse to ASU & all research in Arizona
  - major law suit by the Havasupai, settled Apr 21, 2010
- Could a good IRB system have prevented this?
- Could Tribal review have prevented this!

The Good, the Bad, & the Ugly …

GOOD research with AI/AN

People Awakening Project, Alaska, mid-1990s
- "What strengths & resiliency do AN people have re: alcohol & alcoholism"
- People who had never drank or in stable recovery
- People interviewed for their life history
- Patterns of individual, family, & village/community strengths & resiliency
- Led directly to an intervention now proven effective
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