JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Protection and Access

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Section A

Themes and Definitions

Themes

Protection and Access

- Protection from . . .
  - Harm
  - Exploitation
- Access to . . .
  - Potential benefits
  - Beneficial interventions

Continued

Themes

- Justice considerations relevant at every stage of a research project
  - Choosing a research question
  - Study design
  - Locale of study
  - Recruitment of subjects
  - Dissemination of results

Framework for Ethical Analysis

Justice

- Moral requirement
  - Equals should be treated equally
- Practical applications
  - Fair procedures for selection of study subjects (individual, social)
  - Gender/minority equity

Paradigms of Justice

- General definition
  - Equals must be treated equally and unequals must be treated unequally

Continued

Paradigms of Justice

- Procedural justice
  - Well-ordered
  - Agreement
  - Just procedures vs. just outcomes

Continued

Paradigms of Justice

- Oppression as a concern of justice
  - Power and political standing
  - Unfair distribution
  - Compensatory justice
    - Redress past wrongs

Continued

Paradigms of Justice

- Distributive justice
  - How should we allocate a given resource?
  - Applies to classes/groups
  - Who ought to receive the benefits and bear the burdens of research participation?

Continued

Paradigms of Justice

- Distributive justice
  - Historical perspective of Belmont
    - Burdens fell on one group
    - Benefits accrued to another

Continued

Paradigms of Justice

Belmont Report

- Subject selection
  - Individual level
  - Social level
- Patterns of injustice

CFR: Criteria for IRB Approval

- In order to approve research covered in this policy the IRB shall determine that all of the following requirements are satisfied:
  - Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

Source: 45 CFR 46.111

Continued

CFR: Criteria for IRB Approval

- In order to approve research covered in this policy, the IRB shall determine that all of the following requirements are satisfied:
  - When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Source: 45 CFR 46.111

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Section B

Vulnerable Populations

Definition of Vulnerable

- Someone incapable of providing informed consent, or . . .
  - Obvious
  - Determined
- If capable of providing informed consent, may not be in position to give voluntary consent

Conditions for Enrollment

- Subject may personally benefit from the research, or . . .
- The research is directly related to the specific conditions of the class involved
  - Alzheimer's disease study

Vulnerable Populations

- According to 45 CFR 46
  - Pregnant women/neonates/fetuses
  - Prisoners
  - Children

Continued

Vulnerable Populations

- Pregnant women/neonates/fetuses
  - Subpart B (1978, 2001)

Definition of Vulnerable

- Someone incapable of providing informed consent, or . . .
- If capable of providing informed consent, may not be in position to give voluntary consent

Fetus

- Purpose to meet health needs of fetus
- Risks minimized or minimal
- Consent from both parents

Pregnant Woman

- Purpose to meet health needs of mother
- Risks to fetus minimized or minimal
- Consent from both parents

Continued

Pregnant Woman

- No inducements
- No overlap between researchers and termination of pregnancy
- Researchers have no role in determining viability of fetus

Definition of Vulnerable

- Someone incapable of providing informed consent, or . . .
- If capable of providing informed consent, may not be in position to give voluntary consent

Pregnant Woman

- Influence of hormones
- Fetus has no voice
- Risk of harm

Continued

Pregnant Woman

- Clinton revisions
  - Presumption of inclusion
  - Consent of father no longer required

Continued

Pregnant Woman

- Bush revisions
  - Addition of neonates
  - Consent of father required when research directed at fetus alone

Prisoners

- Limits on voluntary consent
- Exposed to risk of enrollment

Continued

Prisoners

- Subpart C (1978)
- Permitted research
  - On topic related to interaction with system and no more than minimal risk/ inconvenience
  - On prisons or prisoners as group and more than minimal risk/inconvenience

Continued

Prisoners

- Permitted research
  - On conditions affecting prisoners as class
  - On practices with intent of improving health/well-being

Continued

Prisoners

- Additional safeguards
  - Limits on rewards for participation
  - Risks similar to what non-prisoners would accept
  - Selection fair
  - Information understandable
  - No role in parole
  - Adequate follow-up

Definition of Vulnerable

- Someone incapable of providing informed consent, or . . .
- If capable of providing informed consent, may not be in a position to give voluntary consent

Competence

- Mentally infirm
  - Decision-making ability
    - Incapacity
    - Developmental disability
    - Dementia
  - Surrogate decision-maker

Continued

Competence

- Unconscious (e.g. patient in ER)
- Educationally disadvantaged
  - Illiterate

Voluntariness

- Impoverished
- Military
- Dependent relationship

Competence and Voluntariness

- Terminally ill
- Resident of resource poor country

Vulnerability

- Cognitive/communicative
- Institutional
- Deferential

Source: NBAC (2001). Ethical and Policy Issues in Research Involving Human Subjects

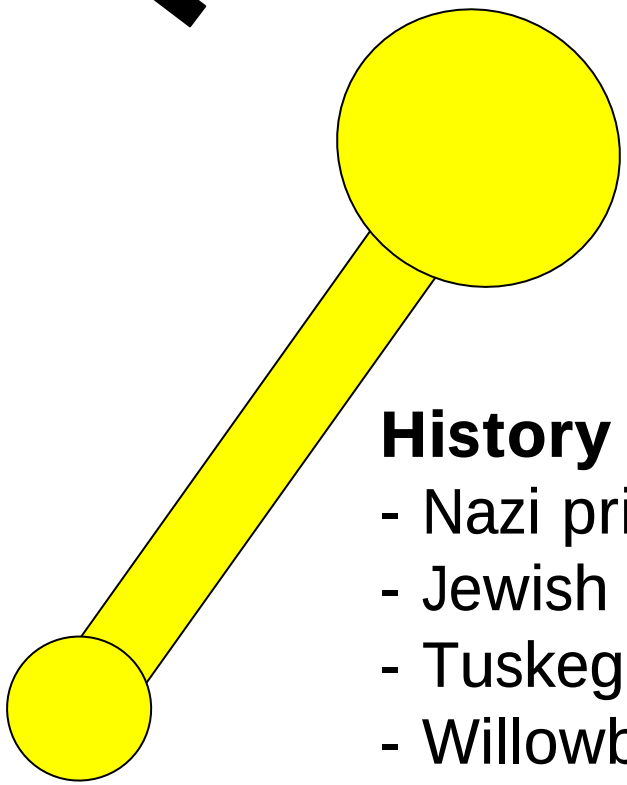
Continued

Vulnerability

- Medical
- Economic
- Social

Source: NBAC (2001). Ethical and Policy Issues in Research Involving Human Subjects

RESEARCH



History of Abuses

- Nazi prisoner experiments
- Jewish chronic disease hospital
- Tuskegee
- Willowbrook

PROTECTION

-From harm

-From exploitation

ACCESS

-To benefit

-To outcome

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Section C

Exclusion of Women from Clinical Research

History of Exclusion

- Food and drug acts—1906, 1938
- Thalidomide—1960s

Continued

History of Exclusion

- Food and drug act amendment—1962
- DES—1960s
- FDA regulations—1977

Continued

History of Exclusion

- “A woman of childbearing potential is defined as a pre-menopausal female capable of becoming pregnant. This includes women on oral, injectable, or mechanical contraception, women who are single, women whose husbands have been vasectomized, or whose husbands have received or are utilizing mechanical contraceptive devices.”

Source: Food and Drug Administration (1977)

Potential Harm to Offspring
- Thalidomide/DES

FDA Regulations

Study Design Considerations

Oppression

PROTECTION
-From harm
-From exploitation

ACCESS
-To benefit
-To outcome

Harms of Exclusion

- No share of potential benefits
- Lack of data to inform medical practice
  - Heart disease
  - HIV/AIDS

Continued

Harms of Exclusion

- Adverse effects burden
- Lack of treatment options

Demands for Inclusion

- Harms of exclusion
- Drug trials = health care
- Congressional interest

PROTECTION

-From harm

-From exploitation

ACCESS

-To benefit

-To outcome

Inclusion of Women

- Shift to inclusion and access
  - AIDS activism
  - Evidence about level of risk
  - Congressional interest

Continued

Demands for Inclusion

- Harms of exclusion
- Drug trials = health care
- Congressional interest

PROTECTION

-From harm

-From exploitation

ACCESS

-To benefit

-To outcome

Inclusion of Women

- Shift to inclusion and access
  - U.S. PHS Task Force—1985
  - NIH Policy—1986
  - FDA Guidelines—1988
  - GAO Report—1990

Continued

Inclusion of Women

- Shift to inclusion and access
  - ORWH created—1990
  - NIH policy—1990
  - WHI initiated—1991
  - GAO report—1992

Continued

Inclusion of Women

- Current policy
  - FDA revision—1993
  - NIH guidelines—1994
  - FDA regulation—1998
  - FDA regulation—2000

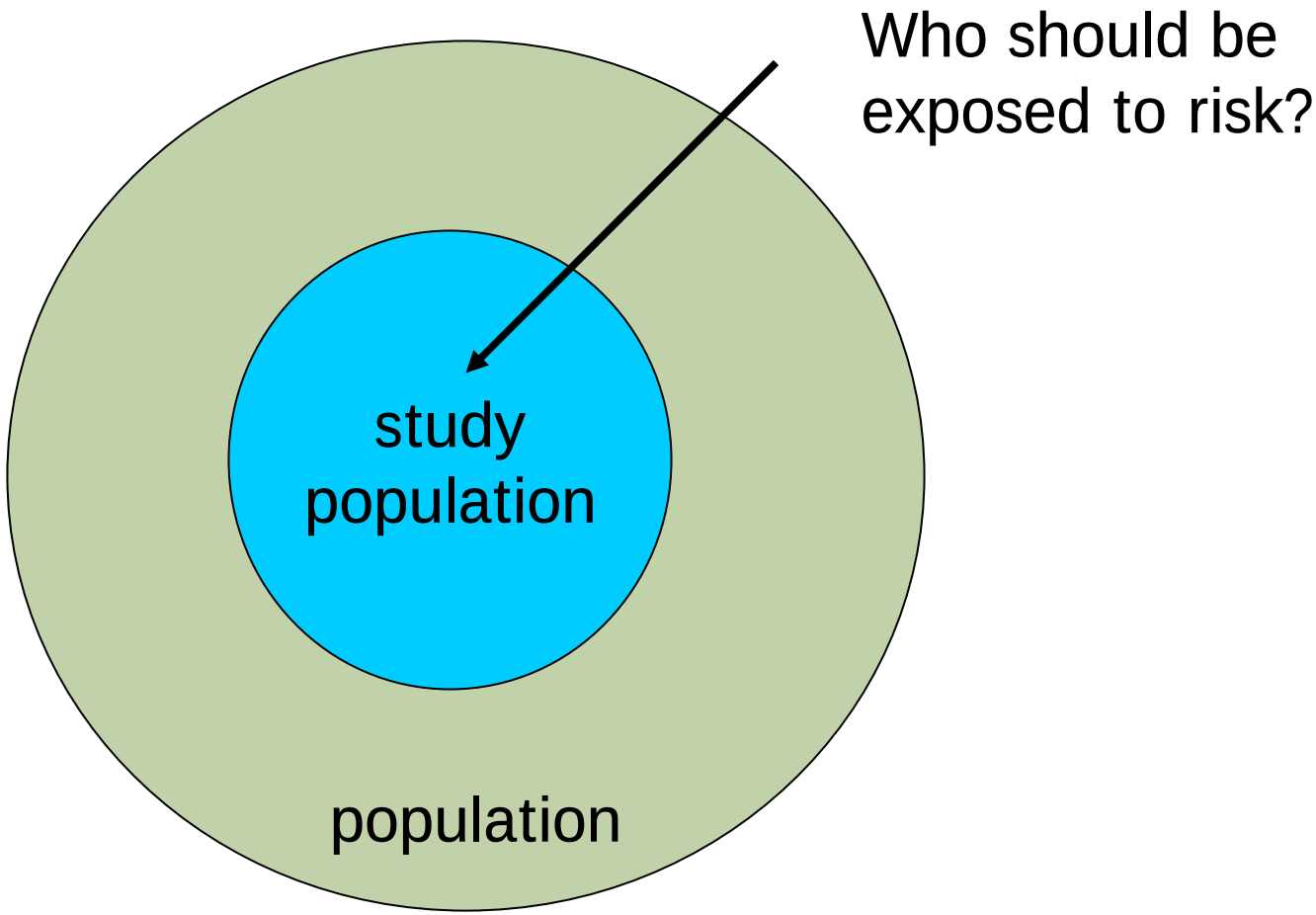
Continued

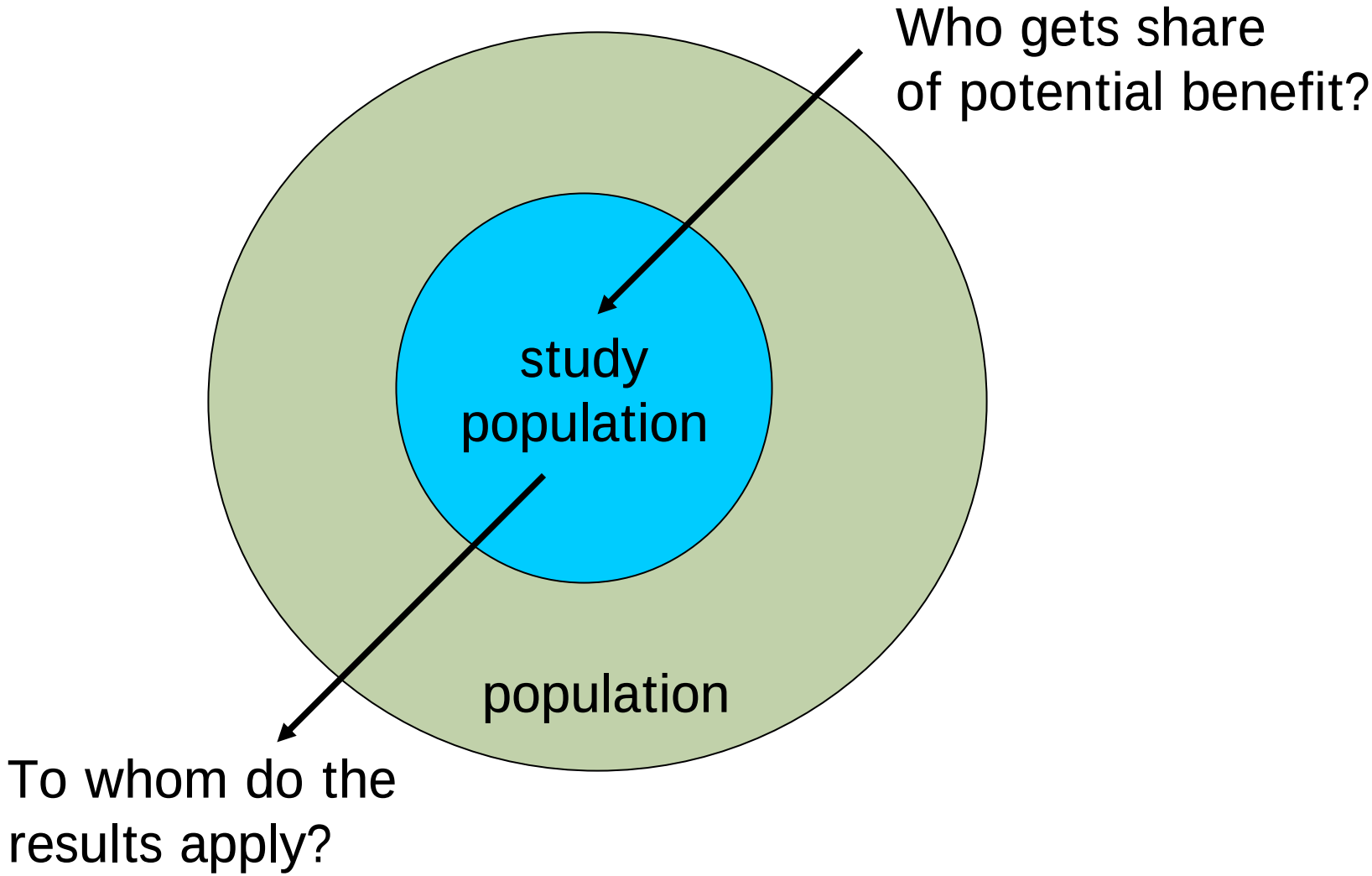
Inclusion of Women

- GAO report on NIH—2000
- NIH response—2001
- GAO report on FDA—2001
- AHRQ report—2003

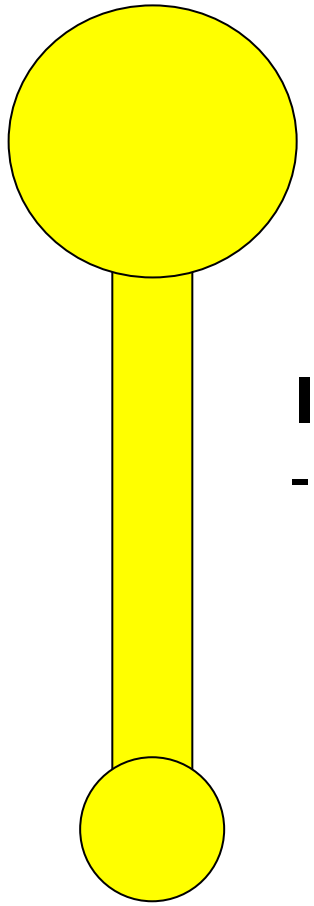
Inclusion of Minorities

- Causes for concern?
  - Perpetuates racism
  - Race is a marker for social conditions
    - Why spend time looking for biologic differences
  - Sample size inflation
  - Threats to voluntariness


Who should be
exposed to risk?
study
population
population


Who gets share
of potential benefit?
study
population
population
To whom do the
results apply?

RESEARCH



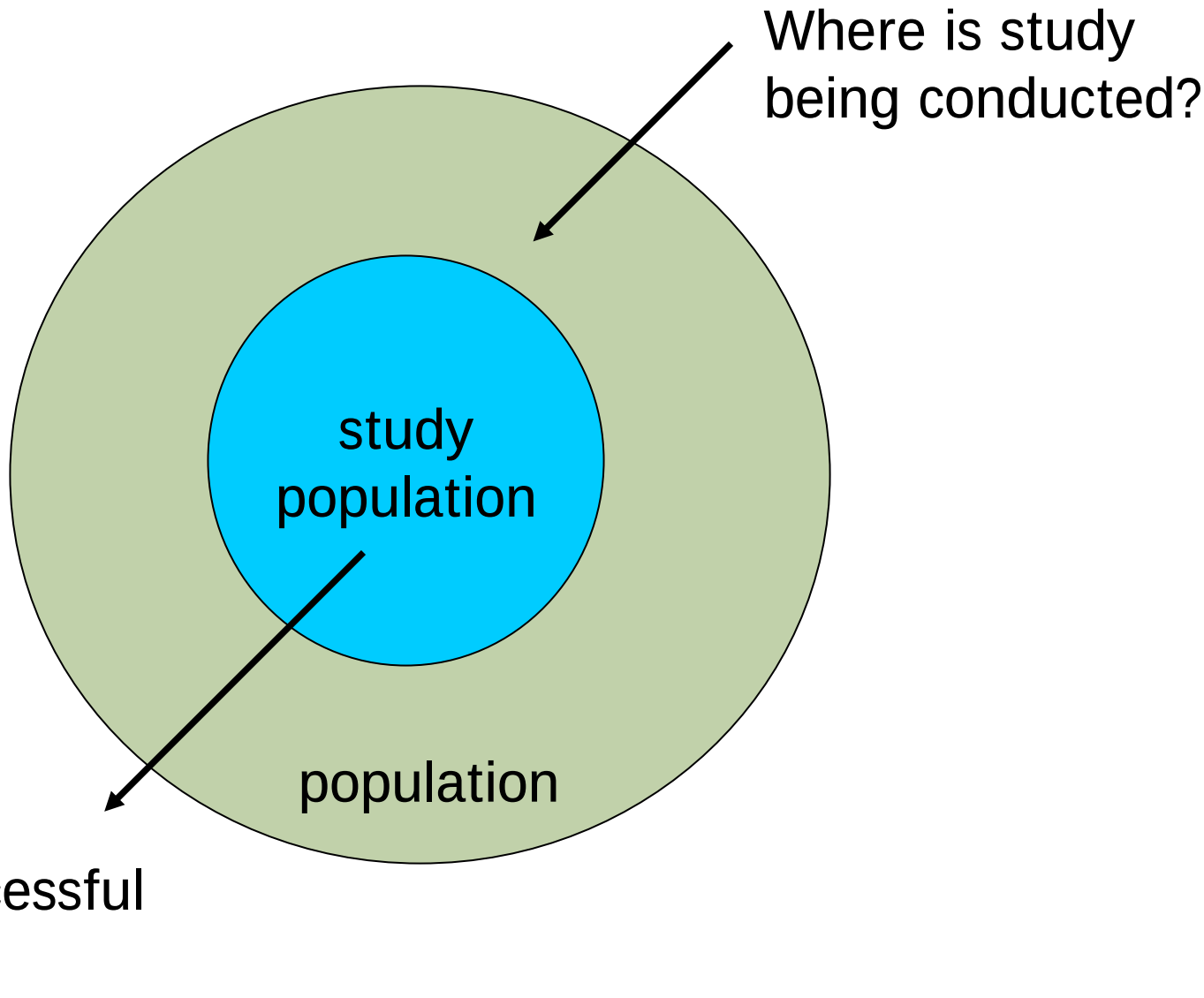
International Trials
- Short course AZT

Domestic Trials
-Gene therapy (Gelsinger)
-Healthy volunteer (Roche)

International Trials
- Short course AZT

PROTECTION
-From harm
-From exploitation

ACCESS
-To benefit
-To outcome


Where is study being conducted?
study population
population
Who will have access to successful intervention?