Post-Study Arrangements

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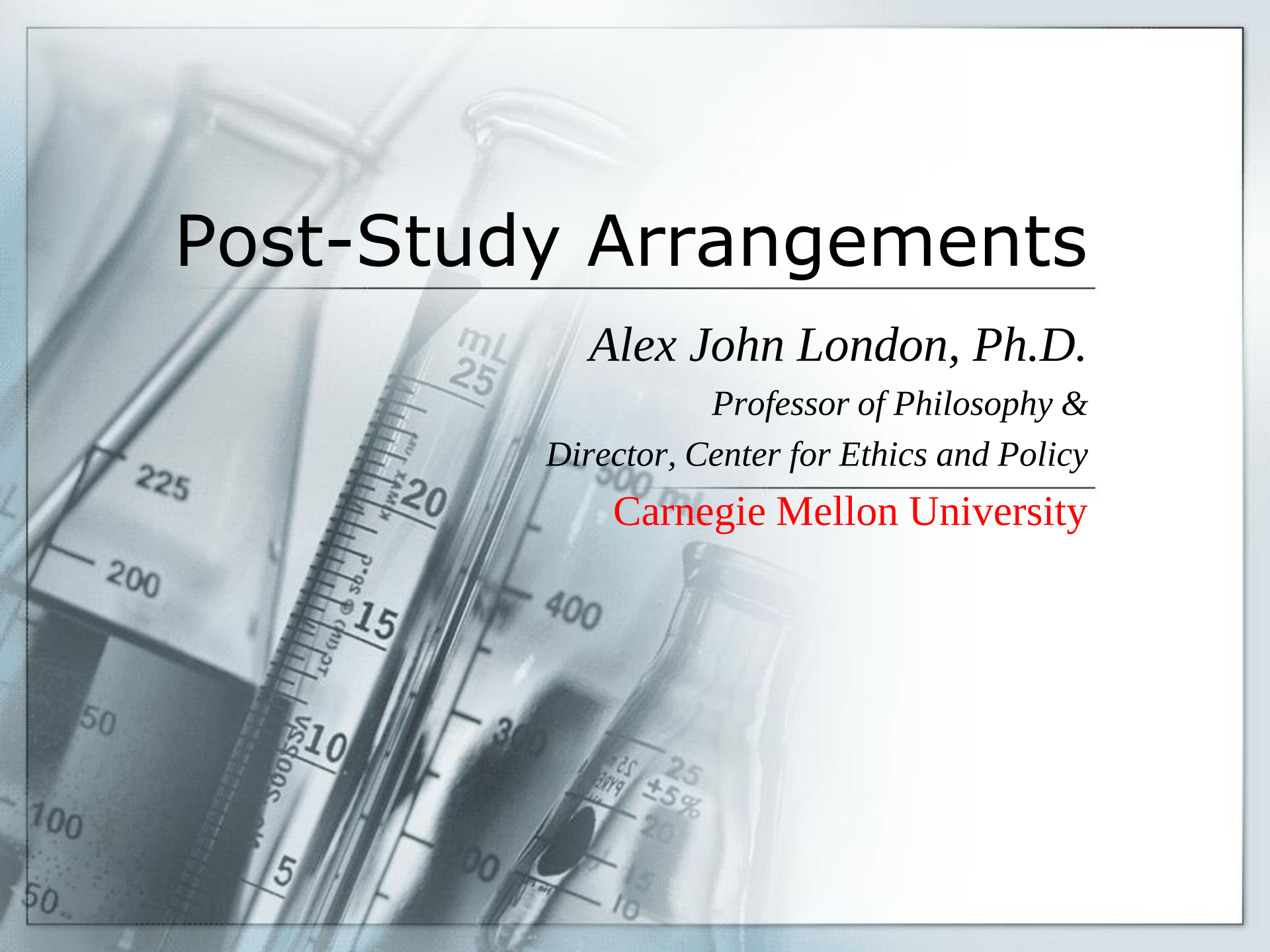

"Benefits" of Research

I. DoH 5: (Populations.) Access to research connected to the benefit of improved care.
II. DoH 17: (Populations.) "results of research" which could be new knowledge, information, practices, interventions, or profits.
III. DoH 33: (Participants.) Study findings
IV. DoH 14 & 33: (Participants.) Access to care or other benefits.

Research and Fairness

I. Research can overlap with, augment or supplant delivery of health services to participants.
   - Participants sometimes access improved standard of care
   - Assume research related risks
   - Care must be transferred back to providers after research.

II. Can reconfigure the way resources are used in a community during and after research:
   - Utilizes personnel, equipment, supplies, time, clinical space, treatment, funding and other resources.
   - Who benefits from this raises issues of equity and fairness
     - Participants / non-participants
     - Host countries / other countries

III. Has diverse connections to health system:
   - Shapes provider practice and patient expectation.
   - Affects entitlements.

Integrity of a Social Good

I. From person-to-person relations to research as a system of social interaction.

II. System in which diverse stakeholders, who may have differing and even conflicting mandates, pursue diverse interests and goals.

   a. access to care

   b. profit / personal advancement

   c. scientific advance

   d. improving standard of care

An Adequate Research Ethics

III. Set terms under which diverse stakeholders can participate in the research enterprise and be assured that the pursuit of private or personal interests does not compromise its ability to produce the unique social good of new knowledge and interventions that enable health systems to better meet health needs of the people they serve.*

*London AJ. 2012. A Non-Paternalistic Model of Research Ethics and Oversight: Assessing the Benefits of Prospective Review. Journal of Law, Medicine, and Ethics forthcoming.

*London AJ, Carlisle B and Kimmelman J. 2012. Rethinking Research Ethics: The Case of Postmarketing Trials. Science 336 (May 4):544-545.

*London AJ. 2005. "Justice and the Human Development Approach to International Research." The Hastings Center Report 35(1):24-37.

An Adequate Research Ethics

I. Secure the rights and welfare of participants.
   - Traditional research ethics focus.

II. Safeguard the integrity and reliability of research from various parochial interests.
   - Registration, publication, and oversight.

III. Preserve the connection between research and the health systems that rely on it for new knowledge and interventions.
   - Equity and fairness in resource use, access to research (DoH 5), and improved health systems.

Information as a Benefit

I. Treatment of information in the DoH has some exemplary features. A model for interventions.
   a. Recognized as a central benefit of research.
   b. Emphasis on responsiveness and access.
   c. Issues dealt with across the lifecycle of research.
   d. Requirements identified related to preserving the integrity of research.
      1. Registration.
      2. Publication, including negative findings.
   e. Fuller range of stakeholders identified.

II. Access to other benefits—which may also be important—should not eclipse the centrality of the connection between research and health systems.

Information Across the Research Lifecycle

I. Access to research affects the ability of health systems to improve care for populations (DoH 5).

II. Study should be relevant to the health needs and priorities of the host community (DoH 17).
   - Responsibility of: researchers, sponsors, and local / national health authorities.

III. Trial publically registered (DoH 19)
   - Responsibility of: Researchers and sponsors.

IV. Participants should be informed of study outcomes (DoH 33)
   - Responsibility of: Researchers and sponsors.

V. Findings (including negative) should be published (DoH 30)
   - Responsibility of: researchers and sponsors, editors.

VI. Information should be integrated into health practices and policies.
   - Responsibility of: Local and national health authorities with assistance from sponsors or other development entities.

Suggested Language Para 5.

New text is in italics:

Medical progress is based on research that ultimately must include studies involving human subjects. *Research should be designed and conducted in ways that do not degrade, and are likely to enhance, the capacity of local and national health institutions to provide equitable access to effective health services*. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.

Rationale

- Explicitly connects access to research with improvements in health systems.
- Assurance that research will not be conducted in ways that leave communities worse off.

Suggested Language Para 17

Medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit ~~from the results of the research~~. *from the knowledge, practices, or interventions that result from the research*.

Rationale

- 5 & 17: communities should reasonably expect to benefit from research via the questions it addresses and the interventions it assesses.

Suggested Language Para 14

…The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care ~~or benefits~~. *This information should also be disclosed to participants during the informed consent process*.

Suggested Language Para 33

At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.

I agree with the Macklin's proposed revisions to paragraph 33:

"*In advance of a clinical trial, sponsors, researchers, and host-country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the study. All study participants should be informed about the outcome of the study*."

Participant Welfare

I. When researchers and sponsors assume responsibility for participant care, they assume some fiduciary responsibilities to participants.

II. The force of responsibility may vary according to:

   a. Severity of the health consequences for participants and others (e.g., drug resistance).

   b. The ease of transitioning the care of participants to another provider (e.g., the local or national health system).

   c. The availability of the intervention or adequate alternatives.

Appropriate Continuity of Care

III. When participant health requires continuing treatment, researchers, sponsors, and local health authorities have a duty to ensure ***appropriate continuity of care***.

IV. This should normally be understood as a duty of researchers and sponsors to facilitate continued provision of care until that responsibility can be discharged within the relevant local or national health system.

Justice and Equity

IV. Equitable provision of health services is the function of the health system.
    a. Prior to regulatory approval or sale, sponsors may need to facilitate access to study interventions.
V. In low-resource settings, inequitable resource allocation in the health system may result if disproportionate share of host community resources are diverted to fulfill post-trial obligations to participants.

Justice and Equity

VI. Sponsors, researchers, and host governments should negotiate mechanisms to avoid inequitable resource allocation in under-resourced settings.

a. Pricing / licensing
b. Funding commitments
c. Partnerships

Conclusion

- Communities should reasonably expect research:
  - to address questions and study interventions that are likely to expand the capacity of their health institutions to meet community health needs.
  - To be carried out in a way that improves capacity of health institutions.
- Participants should reasonably expect:
  - Respect for their rights and welfare.
  - Appropriate continuity of care.