PROVIDING RESEARCH FINDINGS TO NON-PARTICIPANT THIRD PARTIES

EXPLORING SPECIFIC-BENEFICENCE OBLIGATIONS OF MEDICAL RESEARCHERS

U-M HEALTH SYSTEM CENTRAL BIOREPOSITORY

(UNDER CONSTRUCTION)

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Emerging research methods: genetic findings will implicate non-participants

- Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)
- Next-generation Sequencing (NGS)
- Methods in cancer research — can identify germ line (heritable) mutations
  - Well preserved tumor and surrounding tissue
  - “Encyclopedias” of germ line and somatic mutations
  - Multiple testing of single tumors

Case example 1: NIH ClinSeq Study

- Study goal: enroll 1500 participants, use WES and/or WGS to sequence most or all genes, then correlate genetic information with personal and family health histories

- Recontact to give option to receive particular findings, unless finding is especially serious (then no option)

Chan et al., AJOB 12:10, 1-8 (2012)

Case example 1: NIH ClinSeq Study

- Participant 1: four adult children, one sibling
- Recontact attempted 2 months after death; study team informed that some relatives had expressed interest in ClinSeq and findings
- Sample had undergone WES

Chan et al., AJOB 12:10, 1-8 (2012)

Case example 2: CTSA Consult Working Group/AJOB

- In 1990's, researchers observe small cohort with syndrome exhibiting blood cancers and infections — fatal in 50% of cases
- Over time, (1) observe syndrome is hereditary and (2) develop effective bone marrow transplant therapy
- In 2011, ID genotype — autosomal dominant

Taylor & Wilfond, AJOB 13:10, 61 (2013)

Case example 2: CTSA Consult Working Group/AJOB

- Analysis 1
  - Natural duty to warn — conditions: significance of potential harm; ease of warning
  - Actionable info, unique position, significant harm lead to *strong justification* for providing the information
  - Harms to decedents by confidentiality breach are unclear
  - Must show respect for wishes of proband, but overridable

Shah et al., AJOB 13:10, 62-63 (2013)

Case example 2: CTSA Consult Working Group/AJOB

- Analysis 2
  - If researcher is not proband's physician, no obligation
  - Primary duty is to advance knowledge, not provide benefits to individuals — physicians, in contrast, have duty to warn patients' families

Milner et al., AJOB 13:10, 66-67 (2013)

The Belmont Report: Boundaries Between Medical Practice & Medical Research

- Does distinction between medical practice and medical research rule out researcher obligations to individuals?

- "It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, **in order to know what activities ought to undergo review** for the protection of human subjects of research."

The Belmont Report: Boundaries Between Medical Practice & Medical Research

- Practice: “designed **solely** to enhance the well-being of an individual patient or client and [has] a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.”
- Research: “designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.”

Analyses 1 and 2: common ground

- Beneficence: acting for others' benefit
  - "requires us to abstain from intentionally injuring others, and to further the important and legitimate interests of others, largely by preventing or removing possible harms." (Faden & Beauchamp 1986)
- Scope of beneficence: obligatory vs. supererogatory

General vs. specific beneficence

- General: “directed to all persons”
  - Shah et al: “We all have a duty to warn others when we can easily provide information to protect them from significant harm.”
- Specific: “typically derive from special moral relationships with persons….[and] arise from implicit and explicit commitments…”

Beauchamp & Childress 2001

Case example 2: CTSA Consult Working Group/AJOB

- Analysis 3
  - Return to relatives motivated by beneficence may have harmful unintended consequences
  - HIPAA considerations

Rothstein, AJOB 13:10, 64-65 (2013)

- Observations so far (mirrors criteria identified in IF context by Gliwa & Berkman 2013):
  - Materiality component: validity, actionability — whether info could benefit the relatives
  - “Uniqueness of access” component — whether info is available through other means
  - Burden component — whether sharing info would unduly divert resources
- This points to something like a pro tanto obligation to share material genetic information
- Any specific-beneficence argument for this position? (This might enable us to identify an obligation to share rather than a justification to share)

- Do medical researchers — because they are medical researchers — have an obligation to share material genetic results with relatives of deceased participants?
    - Would they be blameworthy for not sharing (would it be wrong not to share) such results with the relatives?
    - Could family members, or someone else, legitimately demand that researchers share such results with the relatives?

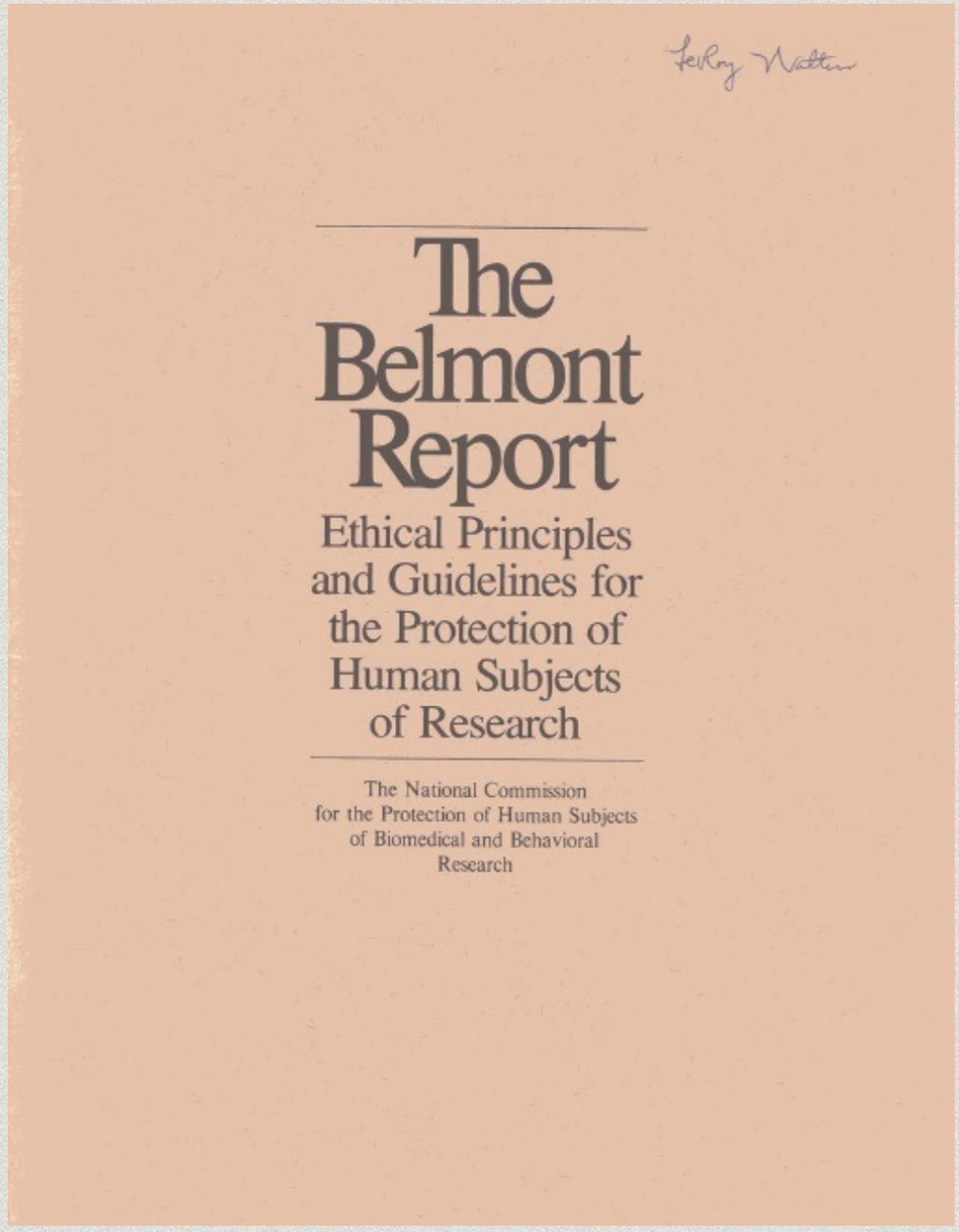
Legal obligations: undeveloped

- Canada: Liss v. Watters
- France: *Bioethics Law*
- United States:
  - Few state court decisions
  - HIPAA
  - Emergence of a standard of care

Tassé, 39 J.L. Med. & Ethics 621 (2011)

Pursuit of generalizable knowledge

- Research is “designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships).”
- Yet: “Nobody quite knows what the term means.” (Beauchamp, 11/07/13)



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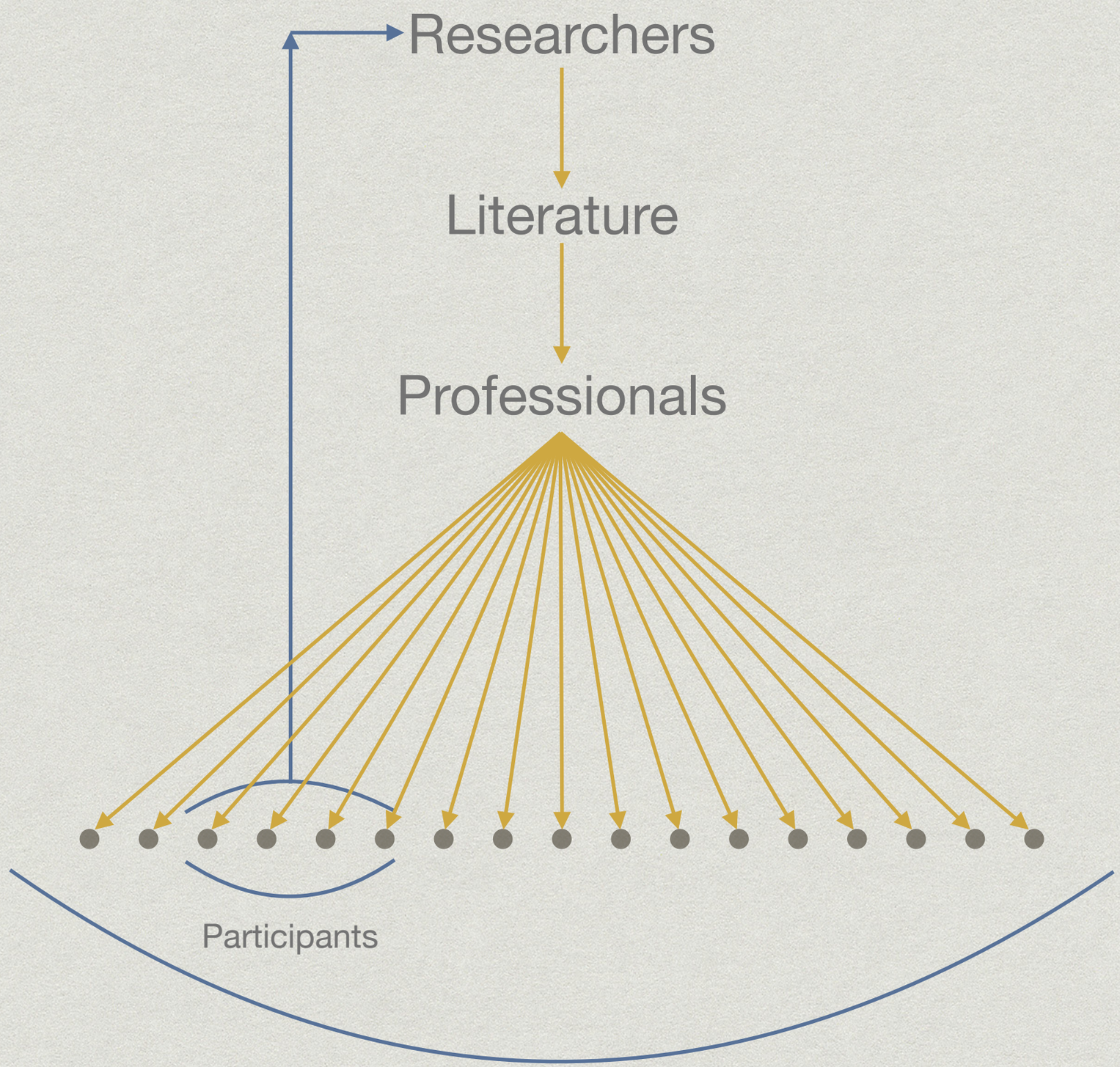
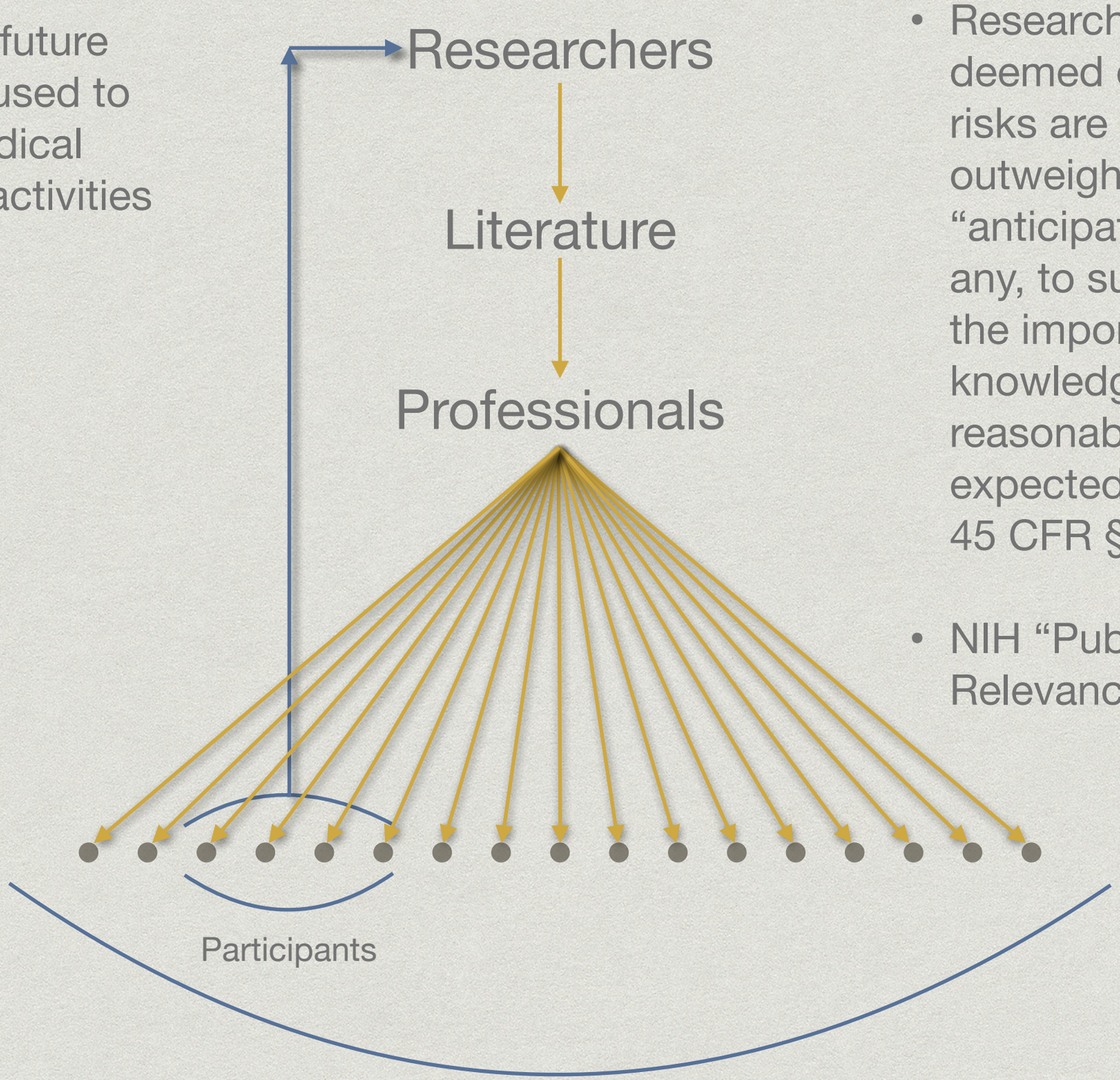

Researchers
Literature
Professionals
Participants
Class described by research

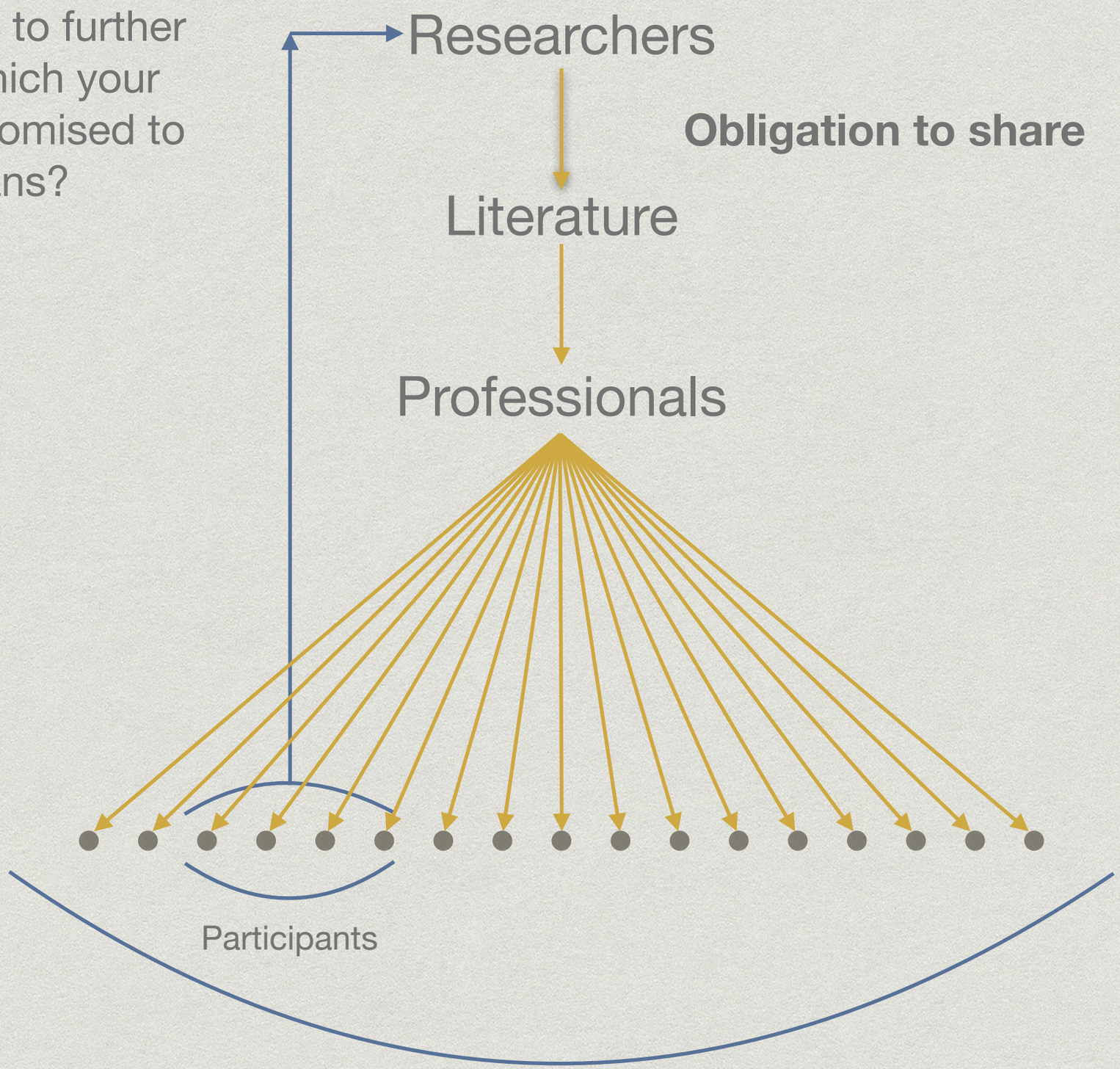
"Benefit to future patients" is used to <u>justify</u> medical researchers' activities



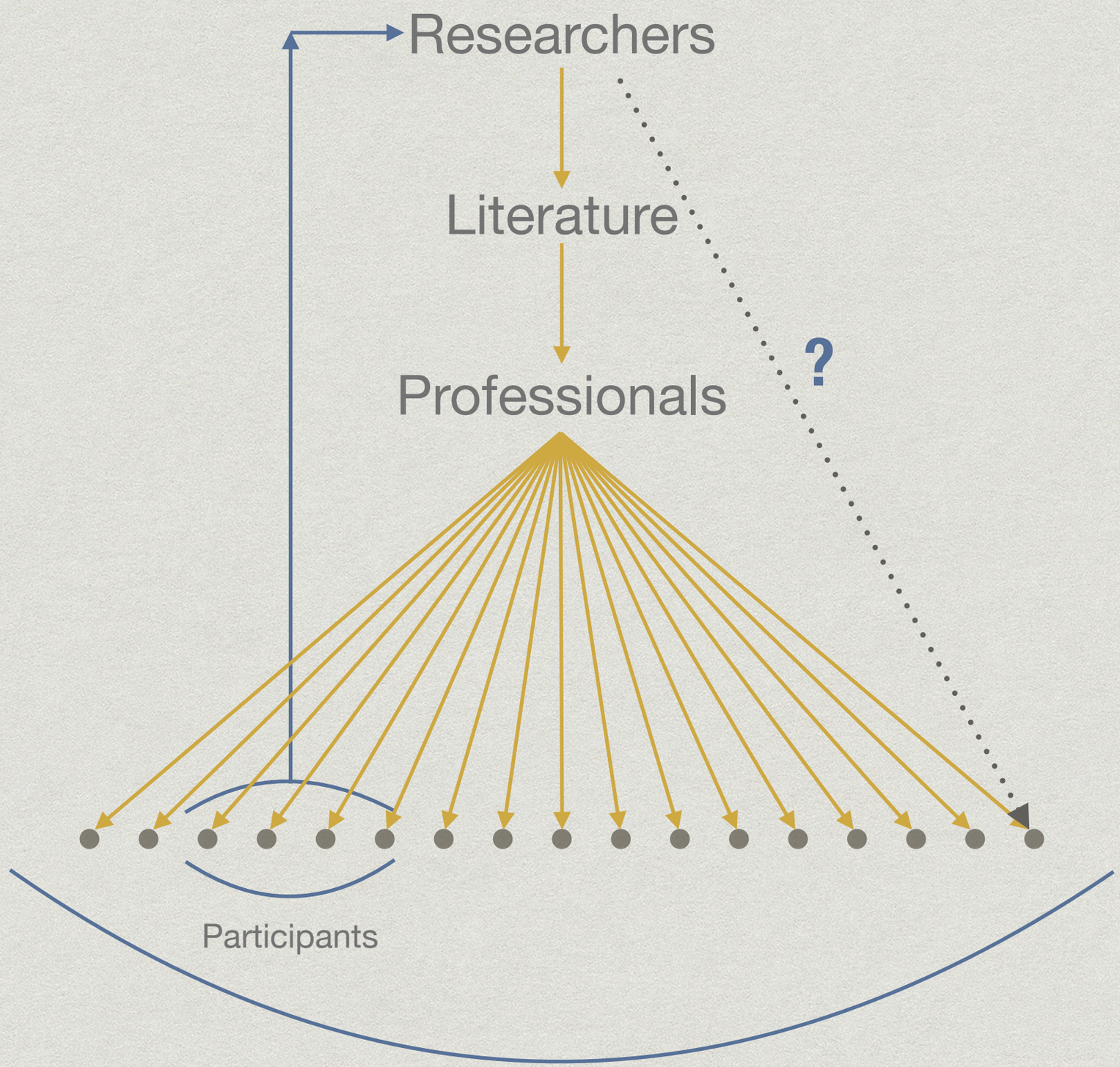
- Research is to be deemed ethical only if risks are balanced or outweighed by "anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result." 45 CFR § 46.111(a)(2)

- NIH "Public Health Relevance" Statement

Any obligations to further the end for which your activities are promised to be a means?



Class described by research



Class described by research

- Complications:
  - **Means/end**: Obligation to further the end for which your activities are promised to be a means?
  - **Part/whole**: Obligation to group entail obligations to its members?
  - **Choice of available routes**: Obligation to take reasonably clear opportunities to share most efficiently?

Health Insurance Portability and Accountability Act (1996)

- Covered entities: health plans, health care clearinghouses, and any "health care provider who transmits any health information in electronic form in connection with a transaction covered by this subchapter." (45 CFR § 160.102(a))

- Disclosing PHI (individually identifiable health information) generally prohibited: "A covered entity … may not use or disclose protected health information without an authorization…" (45 CFR § 164.508(a))

- Decedents: "A covered entity must comply with the requirements of this subpart with respect to the protected health information of a deceased individual for a period of 50 years following the death of the individual." (45 CFR § 164.502(f))

Health Insurance Portability and Accountability Act (1996)

- To be valid, the authorization must include “the name or other specific identification of the person(s), or class of persons, to whom the covered entity may make the requested use or disclosure.” (45 CFR § 164.508(c)(1)(iii))

- Consent should include authorization to disclose genetic information to family members who could benefit from them after participant has died.

Final thoughts

- Providing material genetic information to relatives of deceased participants is one opportunity for medical researchers to treat being beneficent as part of being medical researchers.
- The conception of medical research as a completely distinct activity for which accountability can be made purely ex ante is unrealistic and untenable. Research is fast outpacing top-down regulation.

Anne Marie Tassé, The return of results of deceased research participants, 39 J. L. Med. & Ethics 621 (2011).

Ben Chan, et al., Genomic inheritances: Disclosing individual research results from whole-exome sequencing to deceased participants' relatives, The American Journal of Bioethics, 12:10, 1-8 (2012).

Catherine Gliwa & Benjamin E. Berkman, Do researchers have an obligation to actively look for genetic incidental findings?, The American Journal of Bioethics, 13:2, 42-42 (2013).

Department of Health, Education, and Welfare, The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research. (Washington, DC: OPRR Reports 1979).

Federal regulations at 45 C.F.R. §§ 46, 160, and 164.

Holly A. Taylor & Benjamin S. Wilfond, The ethics of contacting family members of a subject in a genetic research study to return results for an autosomal dominant syndrome, The American Journal of Bioethics, 13:10, 61 (2013).

And responses:

Lauren C. Milner, et al., Relationships matter: Ethical considerations for returning results to family members of deceased subjects, The American Journal of Bioethics, 13:10, 66-67 (2013).

Mark A. Rothstein, Should researchers disclose results to descendants?, The American Journal of Bioethics, 13:10, 64-65 (2013).

Seema K. Shah, et al., What does the duty to warn require?, The American Journal of Bioethics, 13:10, 62-63 (2013).

Kenneth Offit, et al., The "duty to warn" a patient's family members about hereditary disease risks, Journal of the American Medical Association, 292:12 (September 22/29, 2004).

Liss c. Watters, [2010] QCCS 3309 (Quebec Superior Court) and Watters c. White, [2012] QCCA 257 (Quebec Court of Appeal).

Tom Beauchamp, "The increasingly blurry distinction between medical research and practice: Implications for ethical oversight" (address to Public Responsibility in Medicine and Research conference, November 7, 2013, Boston, MA).

Tom L. Beauchamp & James F. Childress, Principles of Biomedical Ethics (Oxford University Press: 5th edition, 2001).