Ethical Issues in Personalized Medicine: Selection and Privacy

Jan C. Heller, PhD
Director, Ethics and Spiritual Care
5 June 2013
Presentation Outline

• Introduction
  – Two disclaimers

• Background
  – Some definitions, characteristics, and terminology

• Selected Ethical Issues
  – Two ethically important distinctions
  – Assessing emerging biomedical technologies ethically
  – Selection and privacy issues in personalized medicine

• Questions and discussion
Two Disclaimers

• It is difficult to give enough attention to the fascinating science and technologies driving personalized medicine…
  – They’re too complex and too diverse to do them justice in a brief time
  – They’re developing very rapidly
  – Nevertheless, certain ethical issues arise with the science and technology that will require clarification in discussion

• There are lots of warnings in the literature, from both researchers and observers, about the “hype” associated with this research
  – Not our focus today, but we must try to sort this out when making our ethical assessments…
  – Will try to avoid being overly optimistic or overly cautious
What Counts as Personalized Medicine?

• Some argue that *all* medicine is and always has been personalized…but today we’re considering applications like some of the following:
  
  – *Certain vaccines and anti-viral therapies developed on basis of genetic research*
  
  – *Certain gene therapies*
  
  – *Oncology tests that better predict cancer growth or therapies that attack tumors directly on basis of genetic knowledge*
  
  – *Transplantation therapies using patient’s own stem cells or for better selection of candidates (discussed below)*
Some Definitions

• The fundamental intention of guiding personalized medicine is to reduce the medical uncertainty that arises with human genetic variability…

• At least three (working) “definitions” in use, not all equally helpful
  – Taking advantage of human genetic variation to benefit human health and cure diseases (emphasis added)
  – The use of molecular analysis to achieve optimal medical outcomes for individuals
  – Medicine that is predictive, preventive, participatory, and personalized (so-called “P4 Medicine”)
Four Characteristics

• Personalized medicine…
  – Uses molecular characterization to create a medical decision-making system for disease risk management, diagnostics, prognosis monitoring, and treatment outcome predictions
  – Creates interventions based on an individual’s “genetic/biochemical fingerprint”
  – Shifts traditional focus from relief of symptoms to proactive measures aimed at reducing disease risks, preventing disease onset, and reversing the course of disease progression
  – Aims to minimize harmful side effects of “one size fits all” treatments and medications

  » JY Chen, et al., 2011, p. 3.
Some Issues with Terminology

• Personalized vs. individualized vs. tailored medicine, and a new term: “precision” medicine
  – In practice, terms are used almost interchangeably
  – Realistically, some “personalized” or “tailored” medical treatments (e.g., medications) are or will be, in fact, “relatively individualized”
  – Most will be used with small or limited groups of patients having the relevant markers

More Terminology

- *Pharmacogenetics*, the study of effects of *genotypic* variation on drug response and drug interaction

- *Pharmacogenomics*, the study of the effects of variation on the *expression* of individual genes in cells of particular tissues on drug response
  - *Aim for more effective medications, with fewer adverse effects and safer dosage*
Two Ethically Important Distinctions

• You know these, but it is important not to forget them…

• Research/therapy and subject/patient
  – *Research is aimed at developing new knowledge that may or may not benefit individual human subjects* (it may even harm them); benefits usually enjoyed, if at all, by future patients

  – *Therapy is aimed at benefiting an individual patient*

  – *Research supporting the development of personalized medicine, in particular, tends to blur the distinction between subject and patient*
Assessing Biomedical Technologies

- Ethicists *generally* assess emerging biomedical technologies under four categories, and by comparing results to existing technologies:
  - **Efficacy**
  - **Safety**
  - **Cost**
    - (E.g., see here E. Mardis, “The $1,000 genome, the $100,000 analysis? *Genome Medicine* 2010, 2:84)
  - **Access**

- With the safety of gene therapy being the notable exception (e.g., Jesse Gelsinger’s death), most of the ethical attention with personalized medicine is focused on cost and access
Selection Issues

• E.g.: Renal transplantation
  – *Scarcity is a given: Not every one who needs an organ will get one*
  – *Inherent and ongoing ethical tension in current transplantation decisions*
    • Promoting equal access, based on some notion of fairness (equity) vs...
    • Maximizing efficacy, based on allocating organs to recipients who are most likely to benefit (in terms of longer life, lower rejection rates, etc.)
  – *Personalized medicine aims to get “the right treatment to the right patient at the right time.” How might this affect transplantation ethics?*
Selection Issues

• Role of personalized medicine in transplantation…
  – “…immunological and genetic characteristics predispose recipients to respond differently to immunosuppressive treatment” after transplantation
  – Research aim: to quantify these immunological and genetic risk factors, along with others (clinical, psychosocial), to help predict which potential recipient should get the available organ, when all who need one can’t be served
  • Current research may bias selection toward maximizing efficacy over equity or fair access to those on the transplant waiting list…
Selection Issues

• Questions and issues to consider…
  – How to “balance” efficacy and equity concerns (but should we balance them or deliberately value one over the other?)
  – Who should decide to introduce this technology into a clinical setting (physicians, patients, ethicists, society?)
  – Ongoing concern about clinical judgment (will clinical judgment be aided, overruled, or nullified by quantifiable selection criteria?)
  – Positive and negative implications for physician-patient relationship (better informed, evidence-based choices vs. diminished clinical discretion of physicians, more patient resentment if excluded)

Selection Issues

• From an ethics perspective, it’s worth asking if any of these questions are new…
  – *I don’t think they are, though certain problems may be made more acute*

  • Assuming we can better predict patient outcomes, it seems to value efficacy over equity. Should this be resisted?
  • Might we end up systematically excluding certain populations on a genetic basis?
  • Could this concern be generalized to other scarce treatments? Selection for research trials? To evidence-based medicine generally?
Privacy Concerns

- Background: Privacy vs. Confidentiality
  - *Privacy refers to a “zone of protected activity” attached to our persons that should be free from interference by others*
    - Includes certain information about us
  - *Confidentiality exists when a person discloses private information to a second person, or the second person somehow learns private information about the first person, and the second person does not disclose that information without explicit consent from the first person*
    - Confidentiality assumes some loss of privacy
    - Places constraints on us concerning retention and sharing of information, and on processes used to protect information
    - It is possible to breach privacy without breaching confidentiality (e.g., anonymous case presentations without permission)
Privacy Concerns

- Long-term concern that the *sheer volume* of information generated by genomic (and other “omic”) research and technologies would overwhelm our ability to protect privacy and confidentiality
  - *Personalized medicine depends on integrating new biological and medical analytical tools with computer modeling techniques*
    - E.g., only about 25,000 genes in human genome, but they produce ~1 million proteins, of which ~10,000 can currently be detected
    - One patient’s genome requires ~300 gigabytes of raw data storage space
    - ~30 million single-nucleotide polymorphisms (SNPs), with most not characterized and their relation to phenotype (traits) remains to be established
    - Can now routinely do functional genomic, proteomic, and metabolomic analyses, but often can’t integrate results without use of advanced informatics tools (i.e., so-called Systems Biology)
Privacy Concerns

• All of the above for individuals *also* needs to be analyzed in relation to growing database of “publicly accumulated knowledge of genes, proteins, functional annotations, molecular interactions, and molecular measurements…” to “help interpret molecular functions and bridge molecular understanding of human diseases.”

• Much of this public information is stored in biobanks…
  – *Repositories of human biological material that are linked to electronic health databases, used particularly to explore relationship between genotype and phenotype*
    • Viewed as a “prerequisite to personalized medicine”
    • Primary intended for research purposes
Privacy Concerns

- To “translate” biobanks’ information into clinical practice, we’ll also need “genetically literate” clinicians and clinicians who can communicate highly complex information to patients and families.

  - *Testing on an individual patient is predicted to generate raw data “at the Gigabyte or Terabyte level, orders of magnitude bigger than his entire medical record coded in text”*

  - *Described as the “incoming tidal wave of data” of which many clinicians are unaware and for which they are not prepared*

    - Chen, p. 6.
Privacy Concerns

• Concerns:
  – Anonymizing individual patients in biobanks may no longer be technically feasible due to the SNP data that can easily be extracted from large databases
    • Tension between advancing research and protecting individual privacy
  – Some argue we should change the “opt-in” informed consent process to an “opt-out” policy for the large databases
  – On-going concern with conflict between family members about learning information they don’t want to know or needing to contribute genetic material for others when they don’t want to
  – For hospital use, health care professionals will need to learn how to permit their colleagues access to relevant portions of the genomic data in the electronic health record
Questions and Discussion

• Sir William Osler, 1892

  “If it were not for the great variability among individuals, medicine might well be a science and not an art.”

  » Quoted (without source) in JY Chen, et al., 2011, p. 10.