

Empiricism and Bioethics: Can This Help Accelerate Transition of Candidate Genomics Applications to Practice?

Vural Ozdemir, MD, PhD

Associate Professor

Centre of Genomics and Policy

Department of Human Genetics

Faculty of Medicine, McGill University



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ELSI Research: Connecting the Past and the Future

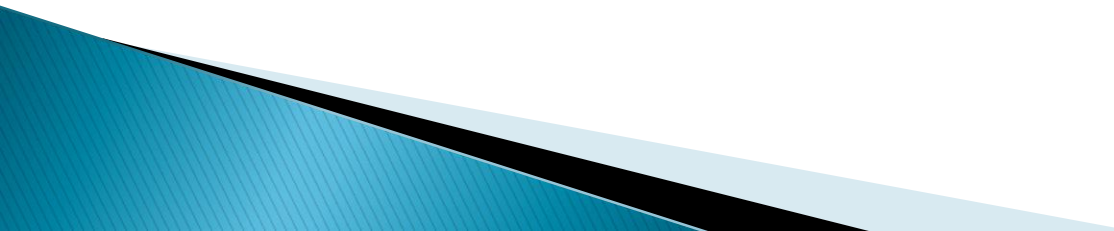
The Human Genome Project allocated 3% to 5% of their annual budgets toward studying the ethical, legal, social issues (ELSIs) surrounding availability of genetic information.

“One of the challenges in the evaluation of genomic applications to healthcare is the integration of studies of the ethical, legal and social implications (ELSI) with those of clinical outcomes.

Scientific and clinical evaluation are considered separately from the [ELSI] of a test, ***without guidance as to how these different spheres should inform each other.***”

How can ELSI research better inform science, medicine and technology evidence base (and *vice versa*)?

How best to identify the “novel ELSIs” that might emerge from newer omics applications (e.g., pharmacoproteomics)?



Genomics and Personalized Medicine (GPM)

Question 1: *Where is the ethics in GPM?*

Defining the **scope** beyond the usual suspects:

GPM evidence gap – An ethical issue?

If yes, how and by whom this should be addressed?

Question 2: *What is the extent of GPM evidence gap?*

Question 3: *What is upstream bioethics?*

Making ethical reasoning and decision-making processes explicit and transparent (e.g., similar to sensitivity analyses)

Genomics and Personalized Medicine (GPM)

Question 1: *Where is the ethics in GPM?*

Defining the **scope** beyond the usual suspects:

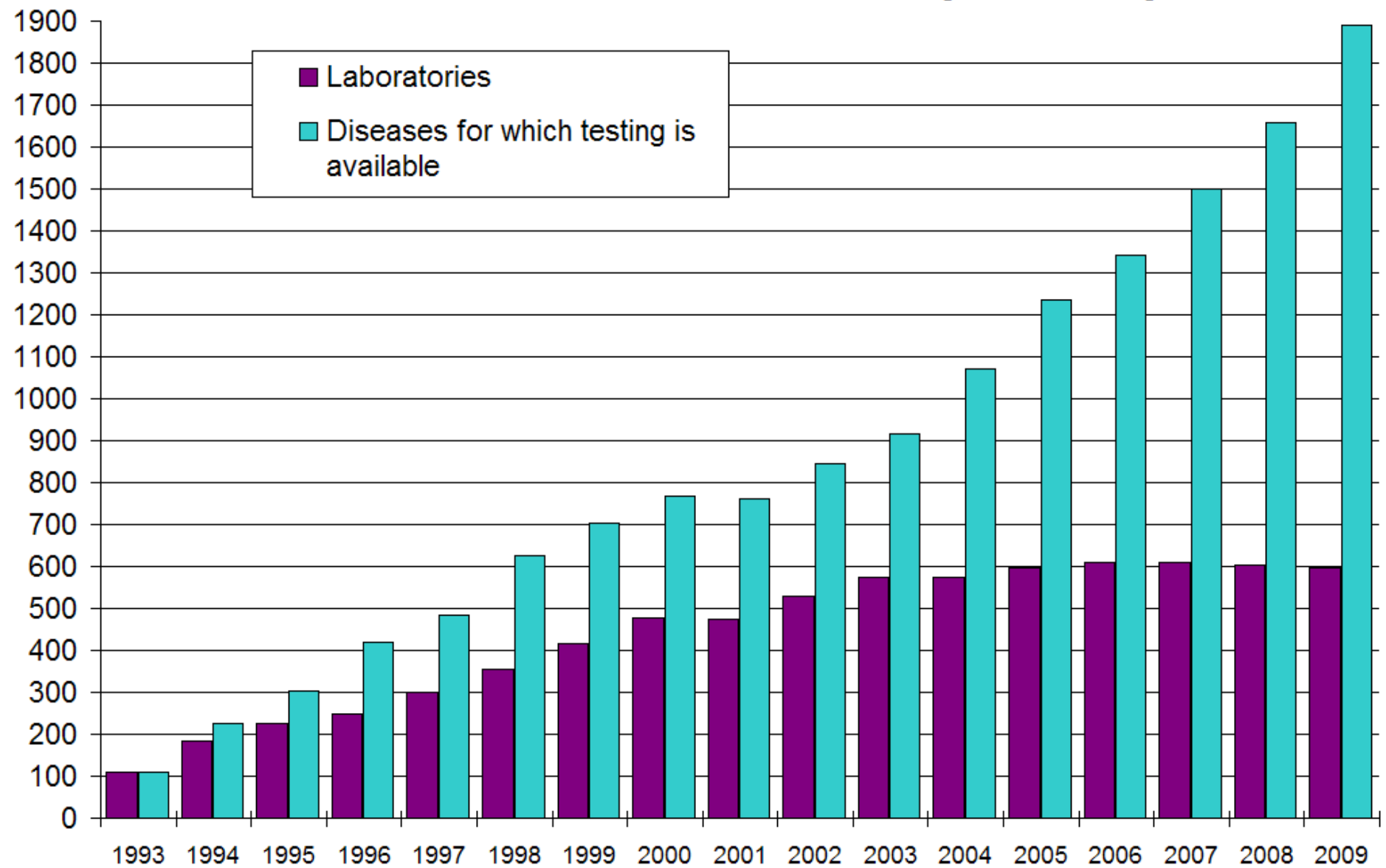
GPM evidence gap – An ethical issue?

If yes, how and by whom this should be addressed?

Genetic tests have been developed for more than 2084 diseases (*GeneTests*, NCBI)

- ▶ Of which 1816 are currently available for use in clinical settings (Accessed May 26, 2010)
- ▶ Most tests concern single genes and are used to diagnose rare genetic disorders. However, a growing number of tests are being developed for multiple genes that may increase or decrease a person's risk of common complex diseases, such as cancer or diabetes, or response to medicines. (NOPHG, CDC Accessed May 26, 2010)

GENETests: Growth of Laboratory Directory



May 26, 2010

Premature Translation Lost in Translation

“..In the absence of a robust evaluation strategy, a trial-and-error process of innovation occurs.

This approach is evident in direct-to-consumer and -physician marketing of genetic/genomics tests... and represents a potential drain on healthcare resources.

There is also a risk that effective innovations will not be implemented, or implemented haphazardly.”

Genet Med 2006; 8: 451-8.

Genomics and Personalized Medicine (GPM)

Question 2: *What is the extent of GPM evidence gap?*

Utilizing the new concept of **ethics epidemiology**

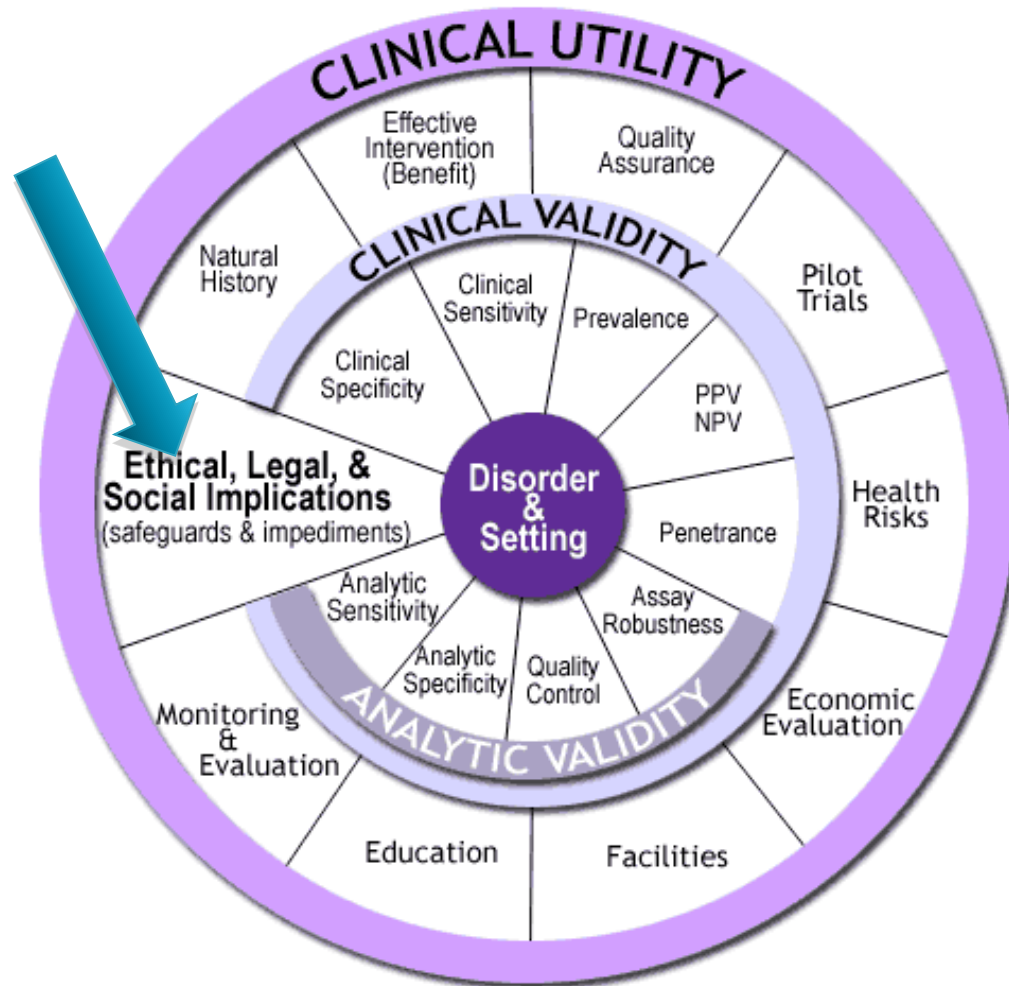
Identifying the knowledge gaps where translation
research and research funding are most warranted.

Building a Systematic Chain of Evidence: the **ACCE** Framework

- ▶ Technical performance of the test (**Analytic validity**)
- ▶ Strength of the association between a genotype and phenotype of interest, i.e., the test's ability to diagnose a disorder or drug treatment outcomes, (**Clinical validity**)
- ▶ Evidence that test impacts patient management decisions and improve *net health outcomes* considering the balance of *benefits* and *harms* (**Clinical utility**)
- ▶ Consideration of **E**thical, legal, and social implications (**ELSI**) as integral to all components of evaluation

- GPM Evidence gap is multidimensional and “**co-constructed**” by technical, scientific, ethical and social dimensions.

ACCE Framework



21st Century Biomedical Ethics: Time for an Empirical Turn?

There is a wider range of issues [than what is usually discussed in bioethics literature] emerging from the daily practice of science and biotechnology.

Innovations are Ecosystems with Many “Moving Parts”

Past few years have seen a conceptual shift towards empirical study of innovations as **ecosystems** with many “***moving parts***” (Guston, 2008), and components that interact in more than one way (cooperation, competition, pre-competitive collaboration).

This has profound implications for empirical approaches to bioethics and establishing evidentiary thresholds to transition candidate genomics applications to practice.

Genomics and Personalized Medicine (GPM)

Question 3: *What is upstream bioethics?*

Upstream ethics: Making ethical reasoning and decision-making processes explicit and transparent

American Journal of Bioethics 2010; 10(6): 42-44.

20th Century Biomedical Ethics

Biomedical ethics and research ethics rose to prominence in the second half of the twentieth century as a response to, for example, abuse of human subjects in medical research (Belmont Report, 1978).

20th Century Biomedical Ethics

Decision-making in biomedical and research ethics has primarily relied on the theme of '**protection**' and normative analyses using principles from moral philosophy:

Respect for autonomy: respecting the decision-making capacities of autonomous persons;

Beneficence: balancing benefits against risks and costs;

Nonmaleficence: avoiding the causation of harm;

Justice: distributing benefits, risks and costs fairly.

21st Century Biomedical Ethics: Time for an Empirical Turn?

In western bioethics practice, **autonomy principle** has come to dominate over-and-above other bioethics principles.

This can be problematic as pharmacogenomics research is now truly global in nature crossing national, political, geographical and cultural borders. Many countries in the Asia-Pacific region are becoming significant contributors to genomics and the science of personalized medicine.

While autonomy may be appealing in a western context, **other bioethics principles may be more important in different societies and contexts** (Burton 2002).

For example, in the process of collection of genetic samples from the **South Pacific island of Tonga**, the **individual informed consent procedure** was met with opposition for failing to address the traditional Tongan role of the extended family in decision-making.

Upstream Ethics: When does ethical reasoning actually start?

Am J Bioethics 2010;10(6):42-44

Considers what happens before normative statements are made (e.g., an ethical/unethical technology)

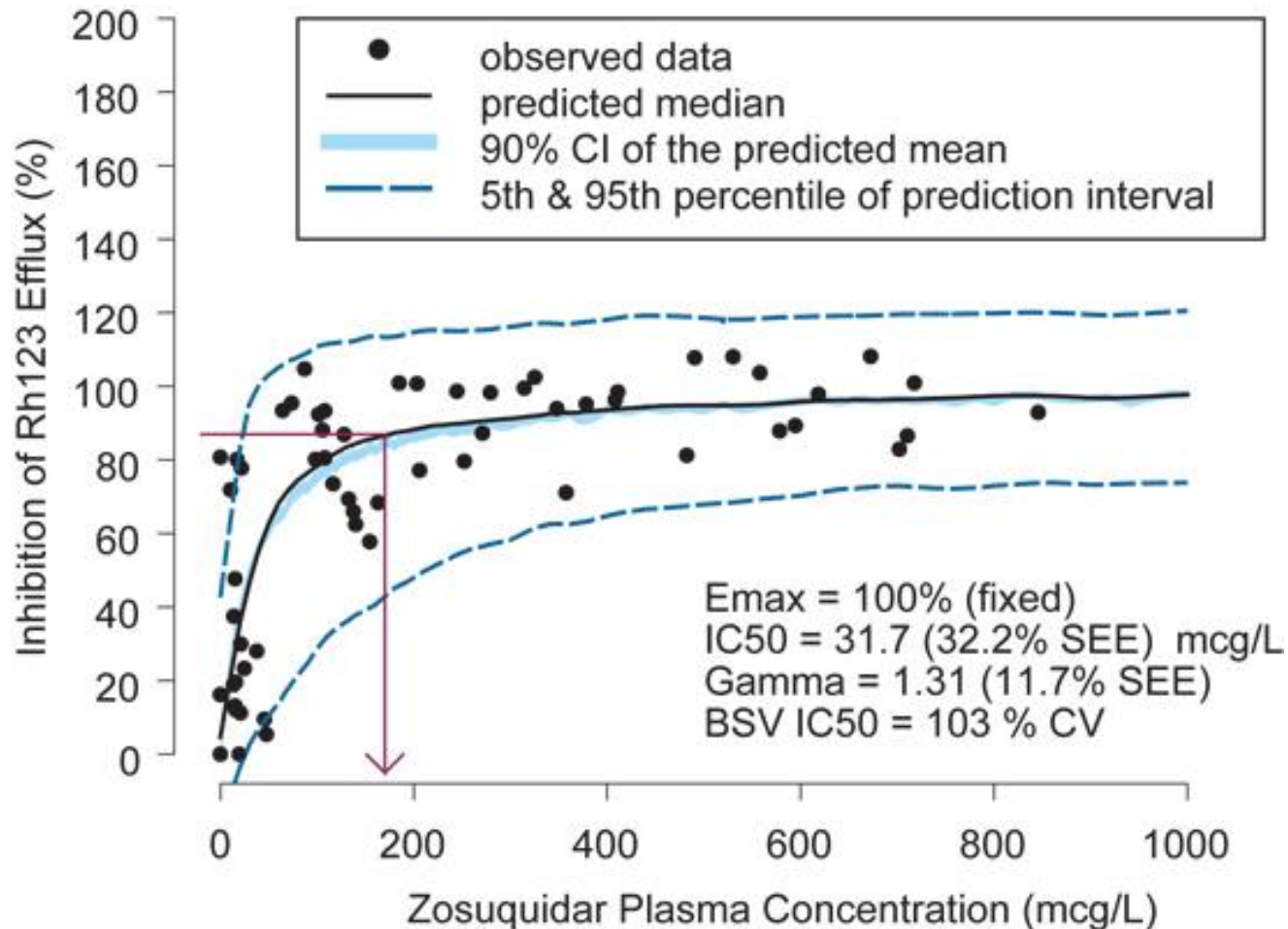
Emphasizes:

- ▶ the **context** in which an ELSI is embedded,
- ▶ rigour and transparency in **pre-normative selection** of bioethics principles when different principles compete or conflict with each other.

“Upstream Ethics as the *Backstage*”: The Side the Audience Does Not See...



Upstream ethics: Why is this similar to statistical genetics and pharmacokinetic models?



(note: arrows denotes target plasma concentration at 90% inhibition)



Future of Genomics and Personalized Medicine:

“From cell to society and public policy”

Thank you for your attendance!

Merci pour votre participation!

Gracias por su participación!

ご参加いただき、ありがとうございます

感謝您參與

Tesekkürler