Ethical, Legal and Social Issues in Drug Development and Pharmacogenomics:

A Qualitative Study of the Perspectives of Canadian Stakeholders

Shannon Gibson, Prof. Trudo Lemmens & Dr. Hamid Raziee

University of Toronto, Faculty of Law

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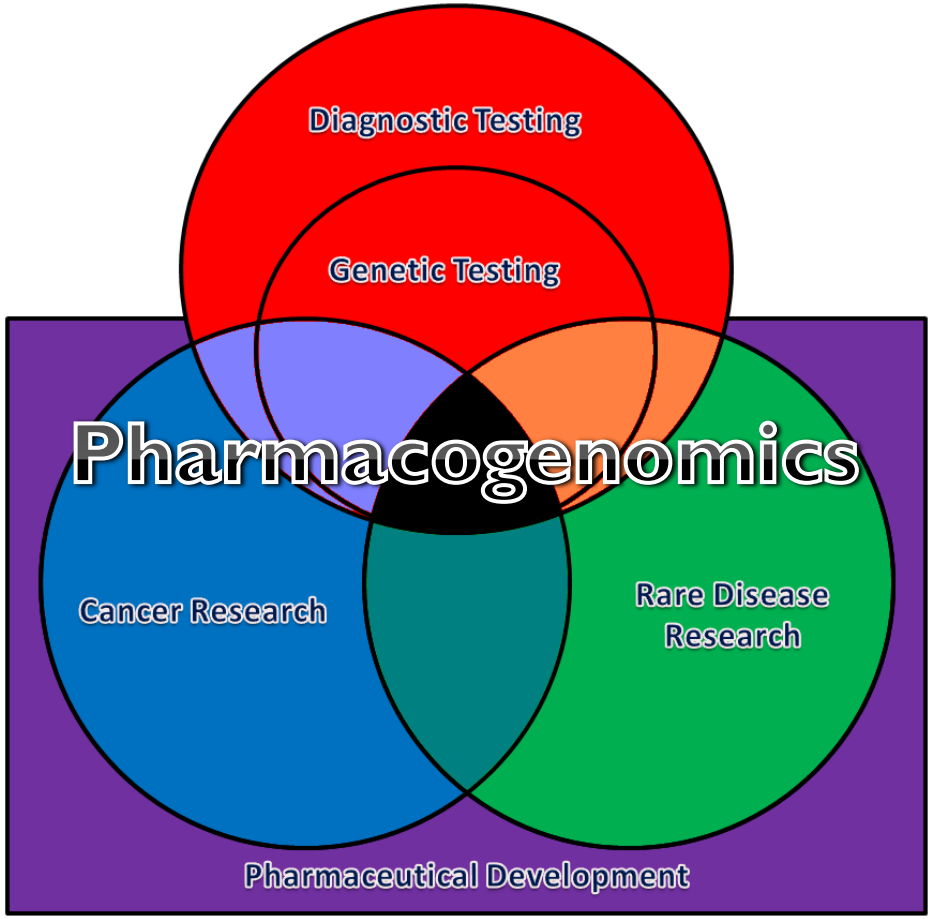
Introduction

- **Pharmacogenomics:** the study of the influence of genetic factors on drug response.
- Depending on each individual's genetic makeup:
  - Some drugs may work more or less effectively.
  - Some drugs may produce more or fewer side effects.
- Drug companies are developing an interest in increasing the efficacy of products by developing companion diagnostic tests.
- Ideally, the "one size fits all" model will give way to more "personalized" approaches where the "best-fit" drug can be identified at the outset.

Study Objectives and Methods

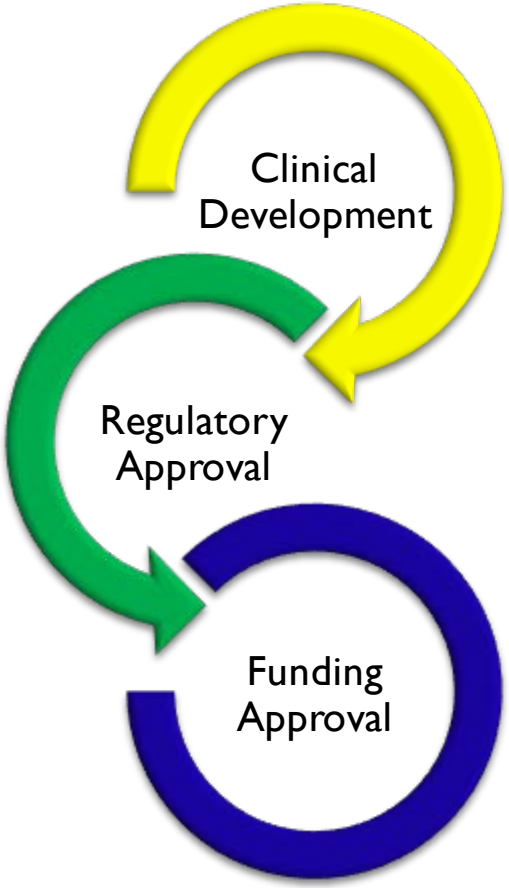
- **Objectives:**
  - Capture perspectives of key informants on the opportunities and challenges of pharmacogenomic drug development, particularly the ethical, legal and social issues involved.
  - Gain insight into the regulatory and policy responses necessary to achieve the successful—and hopefully sustainable—integration of pharmacogenomic therapies into the health care system.
- **Methods:** 34 semi-structured interviews with key stakeholders:
  - drug regulators ▸ drug funders ▸ health technology assessors
  - clinical researchers, ▸ patent experts ▸ drug policy experts
  - pharmaceutical industry representatives ▸ patient advocates

An Intersection of Contexts



Complexity of Pharmacogenomic Products

- Split regulatory authority over drug and test components.
- Lack of coordination between and across levels of government.



- Challenges in identifying useful biomarkers.
- Issues in diagnostic test development.

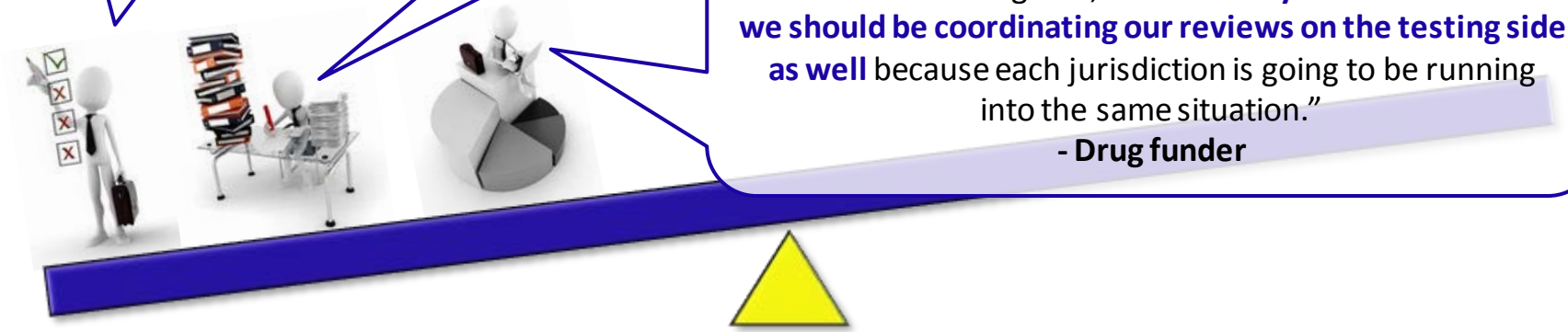
- Drugs and tests are often reviewed separately.
- Drugs and tests subject to different reimbursement models.

Need for Better Coordination

"We're not applying that same level of scrutiny on the testing side [as on the drug side]… **There needs to be a coordinated effort across the healthcare system to actually validate both of those pieces [together]."**
- Drug funder

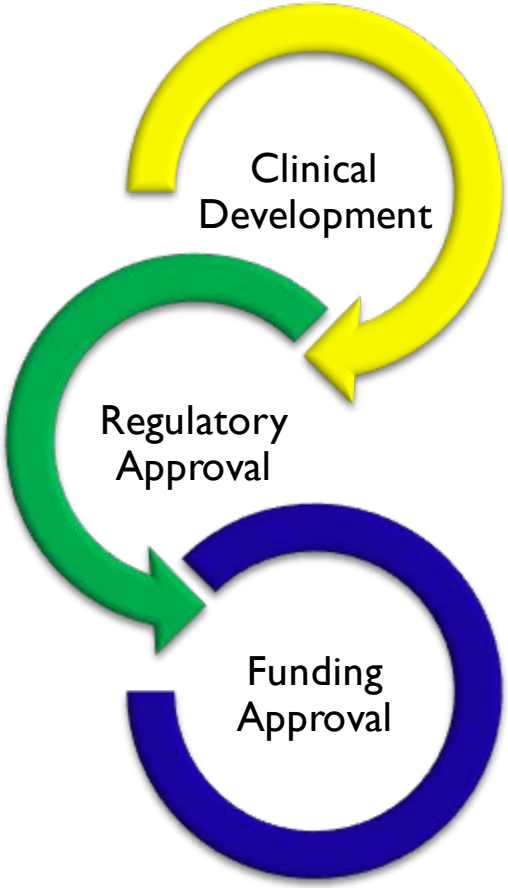
"[Drug funders] should be assessing the evidence behind the effectiveness and specificity and sensitivity of the test and how that relates to the treatment and then the effectiveness and cost-effectiveness of the treatment given the diagnostic test. At the moment that's not clear that that's being done."
- Health technology assessor

"If we are coordinating our [health technology assessment] reviews on the drug side, **I think it only makes sense that we should be coordinating our reviews on the testing side as well** because each jurisdiction is going to be running into the same situation."
- Drug funder



Impact of Rarity and Specialized Markets

- Intense pressure to fast-track approval where few or no alternative treatment options available.
- Particularly acute for serious or life-threatening diseases.



- Inherently limited patient base may result in smaller clinical trials.
- Enrichment strategies raise issues around validating drug use drug outside of the biomarker group.

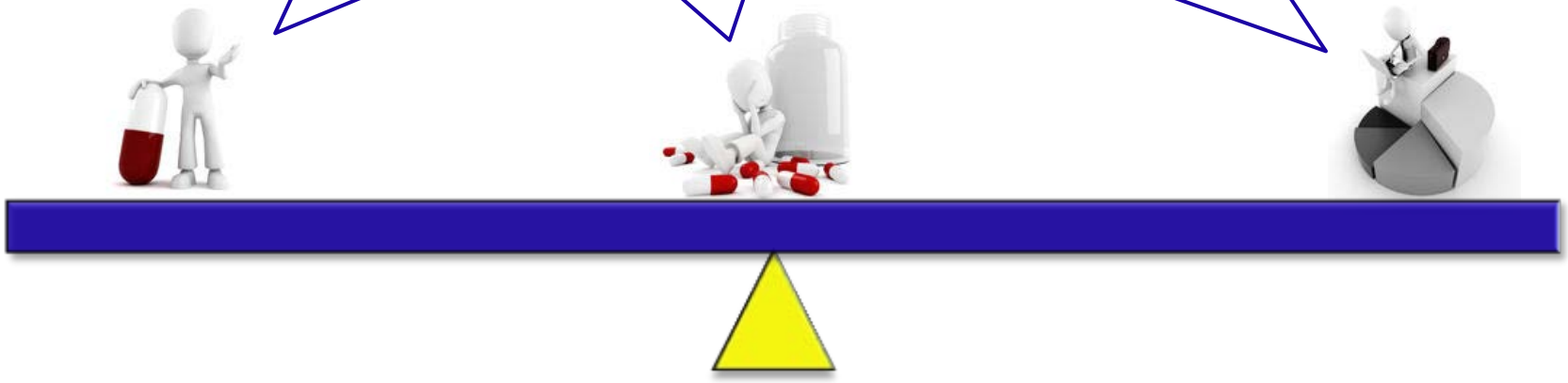
- Intense pressure to extend coverage where few or no alternative treatment options available.
- Lack of competition = high prices and little negotiating power.

Rewarding Innovation vs. Sustainability

"Payers are always going to be trying to drive down price... [People] want cost control but they also want better health care. **If your sole priority is driving down cost, I'm not sure you're going to get an ecosystem that's going to reward innovation."**
- Pharmaceutical industry representative

"More and more people are being treated with these medication and **we have to know that we're spending money on the right medications and were getting the benefit the medications say they are [providing]."**
– Patient Advocate

"The niche-busters seem to be working on the basis that while it's a small patient population, and industry is saying we can't defray our costs across a large population and therefore keep the prices down. **They're really using the political economy of rarity, if you like, to justify very significant payment."**
- Health technology assessor



The Importance of Evidence

"The idea of progressive licensing is absolutely fantastic because it recognizes that even with the best clinical development, the real life level of uncertainty is huge and we don't have a crystal ball… **It makes sense to make a call based on the available evidence and then amend [the license] as we accumulate experience."**

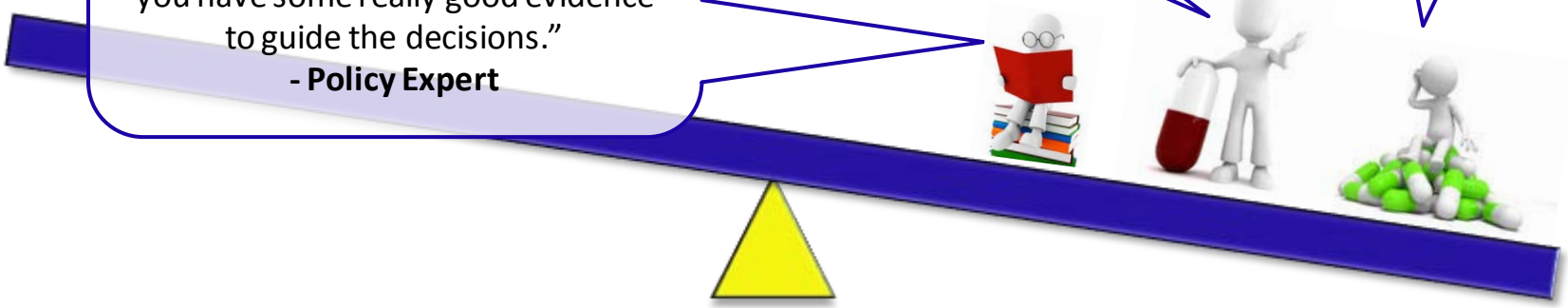
- Pharmaceutical industry representative

"As patient advocates, **we're all in favour of programs with evidence development** and were in favour of getting the **innovative drugs to market faster."**

– Patient Advocate

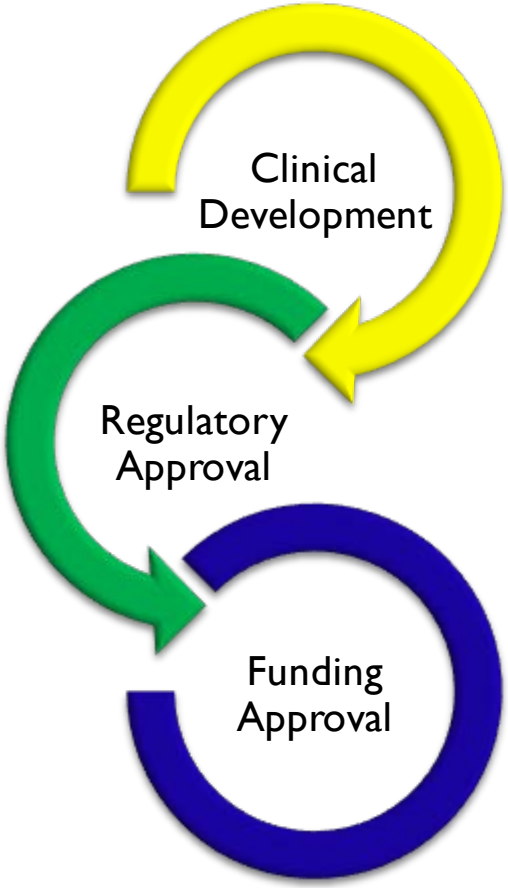
"More than anything, it's generating the evidence. Evidence-based medicine just can't take hold until you have some really good evidence to guide the decisions."

- Policy Expert



Justifying Inclusion and Exclusion

- Shortcomings in clinical trial design impact approved uses of the drug.
- Concerns about off-label prescribing.



- Issues around strength of correlation between biomarker and drug response.
- Enriched trials that exclude certain biomarker groups may be problematic.

- Clinical trial results and approved indications impact reimbursement.
- Controversy around strict criteria on reimbursement based on biomarker status.

Autonomy vs. Oversight

"Patients should have all the power to assess their risk… Patients are the ones who are taking all the risk—we're the ones taking the drug into our body."
– Patient Advocate

"Until we have a much better picture – comprehensive perspective – on the genome instead of just these little snapshots, **I really dislike the thought of overpromising to the public that genomics can really help them make meaningful decisions in their life, about their health.** It's disingenuous at best, it's dangerous at worst**."**
- Policy Expert

"A lack of evidence does not necessarily mean a lack of benefit… and were dealing here in a world where there isn't a whole lot of evidence."
– Patient Advocate

Conclusion

- Pharmacogenomics is complex!
  - There are no easy generalizations in the pharmacogenomic context.
  - Decision-making context varies for each drug, and for each patient.
- Remember the First Law of Technology:
  - **"We invariably overestimate the short-term impacts of new technologies and underestimate their longer-term effects."** Francis Collins, "Has the Revolution Arrived?" (2010) 464:7289 Nature 674-75.