Every person is different, so why should your medication be the same?

Ruslan Dorfman, PhD, MBA GeneYouIn Inc.
Adjunct Professor - Department of Anesthesia, McMaster University
  Director of Personalized Medicine Strategy at Mount Sinai Hospital Toronto (2012)
  Personalized Medicine Consultant for Bridgepoint Health (2011)

PhD, genetics, Weizmann Institute of Science - 34 publications
  Pharmacogenetic strategy
  Pain Genetics
  23andme debate

Founder and CEO of GeneYouIn – a Personalized Medicine company
  *PillCheck* – pharmacogenetic genome annotation platform – 10 genes
  *VitaSeq* – complete genome analysis for disease risk – 20,000 genes
What is Precision Medicine?
Types of genetic tests
Getting personal beyond cancer
Mental health treatment optimization
Precision Medicine & adherence to treatment
Breaking the silos – cost of medication vs disability management cost
Current PGx projects in Canada, USA and Europe
Patient privacy & consumer protection
Full circle of care – role of pharmacists and EAPs
“Medicine acts as both remedy and poison” Socrates

- 200,000 reported Adverse Side Reactions annually
- 30% of drug spending is ineffective
- 50% of prescriptions are unfilled by patients
Promises and pitfalls of Precision Medicine

The White House
Office of the Press Secretary:

“Most medical treatments have been designed for the “average patient.” As a result of this “one-size-fits-all-approach,” treatments can be very successful for some patients but not for others.”

http://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative
### Types of genetic tests

<table>
<thead>
<tr>
<th>Disease risk</th>
<th>Treatment optimization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRCA1&amp;2</strong> for breast &amp; ovarian cancer</td>
<td>HER, BRAF, CYP P450</td>
</tr>
<tr>
<td>High risk of catastrophic illness</td>
<td>Predictive of treatment outcome</td>
</tr>
<tr>
<td>Rare occurrence</td>
<td>Very common</td>
</tr>
<tr>
<td>Confirmatory in most cases</td>
<td>Prospective</td>
</tr>
<tr>
<td>High value for disease prevention</td>
<td>High value for disease management</td>
</tr>
<tr>
<td>Privacy &amp; insurability concerns</td>
<td>Treatment reimbursement</td>
</tr>
</tbody>
</table>
Why focus on Precision Medicine?

**Average cost of cancer treatment:** $65,000 per patient

*Herceptin*®  HER2 Positive Breast or Gastric cancer:
Treatment $70,000 + $200 test  = savings $52,000 per patient

*Kalydeco*® - treatment of cystic fibrosis in patients with p.G551D or other specific mutations
$360,000

*Harvoni*® -
treatment of Hepatitis C – high rate of cure $90,000

*Evolocumab* -
new PCSK9 biologic drug for cholesterol

## Importance of widely used drugs

<table>
<thead>
<tr>
<th>Cause of death in Canada (2011)*</th>
<th>Number</th>
<th>%</th>
<th>Cost of disease*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>72,476</td>
<td>29.9</td>
<td>$157B</td>
</tr>
<tr>
<td>Heart disease</td>
<td>47,627</td>
<td>19.7</td>
<td>$193B</td>
</tr>
<tr>
<td>Stroke</td>
<td>13,283</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Chronic lower respiratory diseases</td>
<td>11,184</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>Accidents</td>
<td>10,716</td>
<td>4.4</td>
<td>$176B</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7,194</td>
<td>3</td>
<td>$109B</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>6,356</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>Influenza and pneumonia</td>
<td>5,767</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Suicide</td>
<td>3,728</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Kidney disease</td>
<td>3,294</td>
<td>1.4</td>
<td>$157B</td>
</tr>
</tbody>
</table>

* [http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/hlth36a-eng.htm](http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/hlth36a-eng.htm)  

* [http://www.cdc.gov/chronicdisease/overview/](http://www.cdc.gov/chronicdisease/overview/)
Impact of Chronic Diseases

- 17.4% of health care spending, $29.8B is drug costs
- 18 prescriptions per year filled by every Canadian
- 6 of Top 10 drug classes used for chronic conditions

<table>
<thead>
<tr>
<th>Percentage of adult diagnoses</th>
<th>Age 45 to 64 Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Blood Pressure</td>
<td>High Blood Pressure</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Arthritis</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>Heart Disease</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Cancer</td>
<td>Cancer</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>Chronic Pain</td>
</tr>
<tr>
<td>Asthma</td>
<td>Asthma</td>
</tr>
<tr>
<td>Depression</td>
<td>Depression</td>
</tr>
<tr>
<td>Emphysema or COPD</td>
<td>Emphysema or COPD</td>
</tr>
</tbody>
</table>

Canadian Survey of Experiences With Primary Health Care, 2008, Statistics Canada; CIHI
Why are some medications not effective?

Tylenol 3 = acetaminophen (500 mg) + codeine (30mg)

- Codeine
  - CYP2D6
  - Morphine
    - Pain relief

- Codeine
  - CYP2D6
  - NO
    - pain relief

- Codeine
  - 2 x CYP2D6
  - Short-term pain relief, delirium

The CYP2D6 metabolizes:
- Oxycodone
- Percocet
- Tramadol

Vuilleumier et al. Pharmacogenomics and Personalized Medicine 2012:5; 73-87
This is Ann today

Had a heart attack
“Trial and error” prescribing:
- Clopidogrel & aspirin
- Statin
- Antihypertensive

Secondary stroke
8-20% probability

Rehab for 6 months

>$50,000* cost to payer

FDA issued Black Box warning on Clopidogrel label
- Diminished effectiveness in CYP2C19 Poor Metabolizers
- 12%-25% of Population are Poor Metabolizers

Labeling is also done by the European Medicines Agency & Pharmaceuticals and Medical Devices Agency (PMDA), Japan

* Goeree at al., 2005
Clinical evidence shows that drug response **varies** from person to person!

Genetic test predicts a person’s response to a medication.
FDA has genetic biomarkers on 150 drug labels

http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm
FDA has genetic biomarkers on 150 drug labels

- Oncology (>80)
- Antidepressants (25)
- Cardiovascular (12)
- Opioids
- Antivirals

- CTP codes for CYP2D6, CYP2C19

- Specific medications reimbursed by Medicare etc…
PharmGKB & CPIC

http://www.pharmgkb.org
Limitations of Precision Medicine

- Requires integration into clinical and administrative workflows: EMR, PBM adjudication application, pharmacy systems
- PGx - better than guessing but not a magic bullet
- Not all drugs are metabolized by CYPs
- Need to identify reliable biomarkers (Humira, Remicade, Neulasta?)
- PGx test cost x sensitivity = cost effectiveness
- Rare variations in downstream genes can affect drug response
Medco/AMA Nationwide Physician Survey

Key Findings

- 97.6% believe genetics affects drug response
- 29.0% have PGx training in med school or postgraduate
- 10.3% feel adequately informed about genetic testing
- 12.9% ordered a PGx test in last 6 mo.
- 26.4% anticipate ordering PGx test in next 6 mo.
- 57.0% test not ordered due to not enough info

Adherence to treatment reduces disease management cost

Total health care costs go down as diabetes medication adherence goes up.\(^7\)

\[\text{Sokol MC, et al. 2005 Medical Care 43; 521-530}\]
PGx testing improves adherence to treatment

- 50% of patients are not adherent to treatment
- 20% experience adverse effect to medications
- 5% are intolerant to statins
- candidates for Evolocumab

[Bar chart showing persistence to statin therapy after 6 months:]

Adapted from Charland et al., The Pharmacogenomics Journal (2014) 14, 272–280;
Why PGx testing is improving compliance?

Jerome, 19: “No way I’m taking any meds”

I was prescribed citalopram (Cipralex) for depression.

I looked it up online. One of the common side effects of Cipralex is erectile dysfunction. This is just way too much for me.

Mom ordered PGx test for me, which showed that I am a normal metabolizer and likely won’t experience side effects.

I took the test results to my doctor and he came up with a drug regiment and recommended a therapist.

6 weeks later… I feel that the blanket of gloom is no longer there!

- PGx testing helps to remove fear of side effects
- Improves confidence of medication’s efficacy
- Empowers through patient-physician dialog
What is the impact of PGx testing?

- Significant improvement in depression scores
- Higher response rates
- Higher remission rates
- Higher physician and patient satisfaction

### MEAN SYMPTOM IMPROVEMENT AT WEEK 8

<table>
<thead>
<tr>
<th>Scale</th>
<th>Reduction in Score from Baseline (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QIDS-C16</td>
<td>44.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HAM-D17</td>
<td>46.9%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>40.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TAU</td>
<td>26.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>19.5%</td>
<td></td>
</tr>
</tbody>
</table>

Where are the cost savings for employers?

- $1.50 a day – little change in cost of medications
- $200 per day of absenteeism & disability

http://genesight.com/education/clinical-studies/
Estimated cost savings for Mental Health

**84 patients with depression per 1000 employees**

**Standard of care**
- **First Line Therapy**
  - 28 DAYS: Select treatment based on trial & error, No response
- **Increase Dose of First Line Therapy**
  - 56 DAYS: No response, Side effects emerging
- **Switch Therapy**
  - 84 DAYS: Symptoms improve

**Precision Medicine with PGx testing**
- **Diagnosis**
  - Genetic Testing
    - 48 hours: Select treatment based on unique gene profile
- **Most Effective Therapy**
  - 30 DAYS: Symptoms improve

**Winner et al., Discov Med. 2013 Nov;16(89):219-2**
## Precision Medicine can improve patient outcomes

<table>
<thead>
<tr>
<th>Current</th>
<th>With PGx</th>
</tr>
</thead>
<tbody>
<tr>
<td>‣ Trying too many drugs</td>
<td>✓ Use only effective medications</td>
</tr>
<tr>
<td>‣ Multiple physician visits to adjust drug dose</td>
<td>✓ Reduce time on disability</td>
</tr>
<tr>
<td>‣ Adding new medications to address drug’s side effects</td>
<td>✓ Reduce treatment burden</td>
</tr>
<tr>
<td>‣ Poor patient compliance</td>
<td>✓ Reduce risk of ADRs</td>
</tr>
<tr>
<td></td>
<td>✓ Improve adherence</td>
</tr>
</tbody>
</table>

Savings compound over time as DNA does not change
Where PGx is in Canada?

- BC pharmacies – PGx of warfarin dosing
- AssureX & CAMH PGx of depression & psychiatry
- TGH & Mayo clinic – clopidogrel PGx
- Montreal Heart Institute
- SickKids
Ann tomorrow

Had a heart attack
- Evidence-based prescription
- No adverse event
- Reduced cost of treatment
- Quicker return to work

EMR -> Eligibility + Test requisition
Sample shipping & management
Genetic testing
Analytics & report

Pharmacogenetics driven treatment optimization can save
- up to 20% of disability costs
- 2-3% of drug costs

*Proprietary model from RL Analytics
Key applications and payer impact

- Specialty Drugs - integration into Prior Authorization process
- High claimants (polypharmacy & deprescribing)
- Broad range deployment of disease specific programs (mental health, diabetes)

Education & plan design with Employers and Unions

- Plan member education required
- Stratification and targeting of employees populations

Partnerships with pharmacies

- Administer test and handle genetic data to protect employee privacy
- Provide consultation and optimize treatment
- Calling physicians when needed
PGx testing fits workflow of Pharmacists

- Understand the PGx lingo
- Ready to help patients and adopt the technology #
- Automated adjudication increases uptake
- Pharmaceutical Opinion
- MedsCheck
- Enhanced dialogue with prescribing physicians
- Better informed patient with better health outcomes

PGx in Psychiatry

# De Denus et al., Pharmacogenomics. 2013 Jan;14(2):165-75
Employers need to contain growing costs of specialty drugs

**Specialty drug costs cancel out generic drug savings**
Specialty drugs to account for up to 60% of new approvals

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**US specialty drug spending will quadruple by 2020**
Projected specialty drug spending from 2012 to 2020

<table>
<thead>
<tr>
<th>Year</th>
<th>Spending Amount (in US$ billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>$87.1</td>
</tr>
<tr>
<td>2016</td>
<td>$192.2</td>
</tr>
<tr>
<td>2020</td>
<td>$401.7</td>
</tr>
</tbody>
</table>

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**Employer survey shows a strong interest in increasing employee cost sharing through plan design changes**

85% of employers have already implemented or are considering an increase in employee cost sharing through plan design changes over the next 3 years.

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Employer engagement and individual consumers are powerful and growing forces in the health ecosystem. To succeed, healthcare organizations should fashion strategies around new demands for value.

Concluding remarks

- Affordable & pervasive technology
- Learn how to apply it sensibly
- Consumerism in healthcare
- Break down the silos
- P4 medicine:
  - Predictive, Preventive, Personalized & Participatory
  - http://www.p4mi.org

“Employer engagement and individual consumers are powerful and growing forces in the health ecosystem. To succeed, healthcare organizations should fashion strategies around new demands for value.”

PWC Medical Cost Trend 2013
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647.868.1812