REVOLUTIONIZING THE PATIENT JOURNEY AND CATALYZING COMMERCIAL INNOVATION WITH TECHNOLOGY

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Percent of the Patient Population for Which a Particular Drug is Ineffective, On Average

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-depressants (SSRIs)</td>
<td>38%</td>
</tr>
<tr>
<td>Asthma Drugs</td>
<td>40%</td>
</tr>
<tr>
<td>Diabetes Drugs</td>
<td>43%</td>
</tr>
<tr>
<td>Arthritis Drugs</td>
<td>50%</td>
</tr>
<tr>
<td>Alzheimer’s Drugs</td>
<td>70%</td>
</tr>
<tr>
<td>Cancer Drugs</td>
<td>75%</td>
</tr>
</tbody>
</table>

Source: Personalized Medicine Coalition
Increasing Number of Breakthrough Drugs

Multiple Myeloma

Takeda gets FDA approval for multiple myeloma pill

Bristol-Myers and AbbVie win FDA approval for a 'breakthrough' myeloma treatment

Boston Globe, Nov 20, 2015

Fierce Biotech, Nov 10, 2015
U.S. health care costs for the aged are sky high

December 13, 2009
By Mark Roth / Pittsburgh Post-Gazette

*Similar per capita expenditures as Germany or UK would reduce total US healthcare costs by 40%
TOP-DOWN, RULES-BASED SELECTION

Identifies patients using pre-defined events to trigger interventions
Averaging Health Leads to Below-Average Health at High Costs

- Asthma Drugs: 40%
- Arthritis Drugs: 50%
- Cancer Drugs: 75%

No Benefit

Benefit
Traditional Healthcare Data Sources

Claims
Medical & Pharmacy

Lab Results

Family History

Demographics
Human Genome Project

- Formally launched in 1990
- Declared complete in 2003
- Allows insight into the genetic basis for human health and discovery of pathways of various diseases
Consumer Data & Wearables

20% Adoption rates of wearables is on pace with that of tablets

“70% of consumers say they would wear employer provided wearables streaming anonymous data to a pool in exchange for a break on their insurance premiums”
Electronic Medical Records

• EMRs are used by **77% of primary health doctors** in Canada and **73% of specialists**

• **99 %** of Canadians have at least one clinical report, or other health record, available in electronic form

• **78.4%** of US doctors have some type of EMR system in place (2013)
New Emerging Big Data

- Imaging
- Electronic Medical Record (EMR)
- Genomic & Molecular
- Claims
- Activity Tracker
- Consumer
- Participation
- Laboratory
A Retrospective Analysis of Precision Medicine Outcomes in Patients with Advanced Cancer Reveals Improved Progression-Free Survival Without Increased Health Care Costs

- **Purpose:** The advent of genomic diagnostic technologies such as next-generation sequencing has recently enabled the use of genomic information to guide targeted treatment in patients with cancer, an approach known as precision medicine. However, clinical outcomes, including survival and the cost of health care associated with precision cancer medicine, have been challenging to measure and remain largely unreported.

- **Patients and Methods:** We conducted a matched cohort study of 72 patients with metastatic cancer of diverse subtypes in the setting of a large, integrated health care delivery system. We analyzed the outcomes of 36 patients who received genomic testing and targeted therapy (precision cancer medicine) between July 1, 2013, and January 31, 2015, compared with 36 historical control patients who received standard chemotherapy (n = 29) or best supportive care (n = 7).

- **Results:** The average progression-free survival was 22.9 weeks for the precision medicine group and 12.0 weeks for the control group ($P = .002$) with a hazard ratio of 0.47 (95% CI, 0.29 to 0.75) when matching on age, sex, histologic diagnosis, and previous lines of treatment. In a subset analysis of patients who received all care within the Intermountain Healthcare system (n = 44), per patient charges per week were $4,665 in the precision treatment group and $5,000 in the control group ($P = .126$).

- **Conclusion:** These findings suggest that precision cancer medicine may improve survival for patients with refractory cancer without increasing health care costs. Although the results of this study warrant further validation, this precision medicine approach may be a viable option for patients with advanced cancer.

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Moore’s Law

1. The accelerating pace of change...
   - Agricultural Revolution: 8,000 years
   - Industrial Revolution: 120 years
   - Light-bulb: 90 years
   - Moon landing: 22 years
   - World Wide Web: 9 years
   - Human genome sequenced: 10^6

2. ...and exponential growth in computing power...
   - Computer technology, shown here climbing dramatically by powers of 10, is now progressing more each hour than it did in its entire first 90 years
   - UNIVAC I: The first commercially marketed computer, used to tabulate the U.S. Census, occupied 943 cu. ft.

3. ...will lead to the Singularity
   - Apple II: At a price of $1,298, the compact machine was one of the first massively popular personal computers
   - Power Mac G4: The first personal computer to deliver more than 1 trillion floating-point operations per second

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Cloud Computing

- Expenditures on the cloud made up **60%** of total IT spending growth in 2015 \(^1\)

Cloud Disrupting Traditional IT

- [Graph showing cloud computing infrastructure and platform market growth from 2013 to 2018 with projected figures (key: '13', '14', '15e', '16e', '17e', '18e').]
- [Graph showing as a % of total enterprise IT spending from 2013 to 2018 with projected figures (key: '13', '14', '15e', '16e', '17e', '18e').]

Source: Goldman Sachs (goldmansachs.com)
The Perfect Opportunity

Interventions
Massive increase in number and cost of interventions

Machine Learning
Breakthroughs in machine learning & cloud computing

Data
Exponential increase in data and investments to leverage it
Machine Learning & Simulation: “What If”?

- Predictive modeling: What will happen next?
- Forecasting/extrapolation: What if these trends continue?
- Statistical analysis: Why is this happening?
- Standard reports: What happened?
WHAT’S THE POINT

PREDICTING THE FUTURE

IF YOU CAN’T CHANGE IT?
Machine Learning & Simulation: “What If”? 

Tom Davenport  
*Competing on Analytics 2007*
Causality vs. Correlation

**Correlation**

We cannot distinguish causality from pairs of variables

\[
P(A) \cdot P(B|A) = P(B) \cdot P(A|B)
\]

**Causation**

Observing three or more variables enables us to score the most likely causal structures

\[
P(C) \cdot P(A|C) \cdot P(B|A) \neq P(C) \cdot P(B|C) \cdot P(A|B) \neq P(A) \cdot P(B) \cdot P(C|A,B)
\]
Matching Treatments to Patients From Data-Driven Models

- Emerging (mobile health) Data
- Genomic and ‘omic Data
- Clinical Data
- EMR, Consumer and Geographic Data

GNS REFS™ PLATFORM

Does treatment Y improve the outcomes & lower costs for patient X?

Large & Diverse Population-Based Causal Models

- Intervention
- Clinical Outcomes
- Member Characteristics
- Economic Outcomes

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ADVANCED ILLNESS
Understanding Advanced Illness

Occurring when one or more conditions become serious enough that **general health and functioning decline**, and **treatments begin to lose their impact**. This process continues to the end of life.¹

**4.5%** of Medicare population likely to pass in the next 12 months

- **70%**
  - Patient Wishes
  - The vast majority of patients want to spend their final days in their own homes.

- **63%**
  - Hospital
  - But instead, the majority of patients spend the end of their lives in hospitals or other institutions

- **17%**
  - Institutions

- **25**
  - Outlays
  - A quarter of cost outlays are in the last year of life, often for unwanted treatments

¹CTAC via [http://www.aha.org/about/org/aim-strategies.shtml](http://www.aha.org/about/org/aim-strategies.shtml)
Matching Wishes to Reality

Identification
Which members can be impacted?

Optimization
Which intervention will change trajectory?

Case Management
Expertise, implementation & feedback

Optimal Solution
Combines the best of both steps
Causal Identification

Using GNS Causal Models, you can identify **50% more members** than the current methods with **90% accuracy**.
Prospective Solution Validations

Validations performed between January 1, 2016 and June 30, 2016

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Recall</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>20%</td>
<td>1.00</td>
</tr>
<tr>
<td>Health Plan 1 Medicare Advantage</td>
<td>27%</td>
<td>1.34</td>
</tr>
<tr>
<td>Health Plan 2 Medigap</td>
<td>35%</td>
<td>1.76</td>
</tr>
</tbody>
</table>

**Recall**: the proportion of predicted events that are expected to occur across the events that are measured

**Factor**: the percent of decedents identified
Operational Work Flow

Client Data Warehouse → Measurebase®™

REFS
- Models & Analytics
- Efficacy
- Risk
- Engagement
- Intervention
- ROI

Targeted Lists → Client Workflow

Interventions
Enable Well-Being

- Understand and respect member’s wishes and empower them with personalized information
- Improve quality of life and satisfaction
- Explore and offer alternatives to unwanted hospitalizations and interventions
CoMMpass Trial Dataset (NCT0145429)

- 1,500+ patients followed longitudinally from diagnosis
- Data collected every 3 months
- Tumor samples analyzed at time of recurrence or progression
- Treatments: bortezomib, combined bortezomib/IMIDs, carfilzomib, combined bortezomib/carfilzomib, combined bortezomib/IMIDs/carfilzomib, IMIDs
Automated Causal Model Building

GNS REFS™ Machine Learning Platform

Ensemble of models yields a distribution of predictions that quantify both the prediction & its uncertainty

<table>
<thead>
<tr>
<th></th>
<th>High Risk under baseline MELK</th>
<th>High Risk under overexpression MELK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.5</td>
<td>15.0</td>
</tr>
<tr>
<td></td>
<td>5.8</td>
<td>15.7</td>
</tr>
<tr>
<td></td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td></td>
<td>5.2</td>
<td>14.6</td>
</tr>
</tbody>
</table>

Ensemble of Models

Patient Demographics | Clinical Parameters | Immunoglobulin Profile
Clinical Study Data | RNAseq | Somatic Copy Number
Somatic Variants | Cytogenetic | Treatment
Outcomes Data

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>MELK</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>Male</td>
<td>7.2</td>
<td>?</td>
</tr>
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GNS Multiple Myeloma Disease Model

Simulations to identify Drivers of Treatment Outcomes

Drivers of High Risk
- Disease progression before 18 months

Drivers of Durable Response
- Treatment response that lasts over a year

Systematic Perturbations to Model Variables

Drivers of High Risk
- Disease progression before 18 months

Drivers of Durable Response
- Treatment response that lasts over a year
Drivers of High Risk

- Pathway of cell cycle regulation that drives high risk when overexpressed
- Top genetic drivers:
  - CDK1
  - MELK
  - NEK2
  - PKMY1
- Known targets of inhibitor drugs

**MELK inhibitor:**
- OTSSP167

**CDK Inhibitors**
- IBRANCE® (palbociclib)
- Dinaciclib
- AT7519

**Pathway of cell cycle regulation that drives high risk when overexpressed**

**Top genetic drivers:**
- CDK1
- MELK
- NEK2
- PKMY1

**Known targets of inhibitor drugs**
Identification of Patient Subpopulation Characteristics and Therapeutic Targets for Multiple Myeloma

Simulation of response to stem cell transplant for newly diagnosed patients

Translocation not present

Translocation present
The Future!

Comparative Effectiveness Treatment Algorithms

*Improving Outcomes and Reducing Costs Means Being Patient-Centric: There is a “Right Treatment” for the Right Patient at the Right Time*

Ex. Treatment Landscape for Multiple Myeloma