Mining Dense Dynamic Personal Data Clouds for Scientific Wellness

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Institute for Systems Biology
Seattle, WA

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Disclosures

• Dr. Price is a Co-Founder of **Arivale**, a scientific wellness company that partially funded and may license discoveries resulting from the Hundred Person Wellness Project (to be described).

• Dr. Price is a Scientific Advisor to **Habit**, a new personalized nutrition company.
Nutrition health effects...

Multiple studies demonstrate nutritional effects on disease risk.
Nutrition health effects... are complex: Need context and personalization

Everything we eat both causes and prevents cancer

- Wine
- Tomatoes
- Tea
- Milk
- Eggs
- Corn
- Coffee
- Butter
- Beef

SOURCE: Schoenfeld and Ioannidis, American Journal of Clinical Nutrition
86% of Healthcare Costs Treat Chronic Disease

<table>
<thead>
<tr>
<th>Chronic Diseases</th>
<th>Prevalence (Millions)</th>
<th>Direct Cost ($ Billions)</th>
<th>Disease severity</th>
<th>Episodic or Steady state</th>
<th>Opportunities for DX Monitor</th>
<th>Cost Impact</th>
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<tbody>
<tr>
<td>Angina</td>
<td></td>
<td></td>
<td>High</td>
<td>Episodic</td>
<td>High</td>
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<tr>
<td>Anxiety disorders (social, etc.)</td>
<td></td>
<td></td>
<td>Medium</td>
<td>Episodic</td>
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<tr>
<td>Arthritis, Rheumatoid</td>
<td>1.3 M</td>
<td>$12.4 B</td>
<td>High</td>
<td>Episodic</td>
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<tr>
<td>Asthma</td>
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<td>Episodic</td>
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<td>Atrial Fibrillation</td>
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<td>Chronic Kidney Disease</td>
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<td>Steady Progression</td>
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<td>Congestive Heart Failure</td>
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<td>$32.9 B</td>
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<td>COPD/Emphysema</td>
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<td>Coronary Artery Disease</td>
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<td>Depression</td>
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<td>Diabetes</td>
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<td>$116.0 B</td>
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<td>Gastroesophageal Reflux Disease (GERD)</td>
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<td>Hypertension</td>
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<td>Medium</td>
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<td>Lupus (SLE)</td>
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<td>High</td>
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<td>Migraines</td>
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<td>Episodic</td>
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<td>High</td>
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<td>Multiple Sclerosis</td>
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<td>Medium</td>
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<td>Osteoarthritis</td>
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<td>Episodic</td>
<td>High</td>
<td>High</td>
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<tr>
<td>Osteoporosis</td>
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<td>$14.0 B</td>
<td>High</td>
<td>Steady Progression</td>
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<td>High</td>
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<td>Stroke</td>
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<td>$43.7 B</td>
<td>High</td>
<td>Episodic</td>
<td>High</td>
<td>High</td>
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</tbody>
</table>

Top 20 examples of chronic diseases out of 91 studied by EAC. Noted are 9 Chronic Diseases often seen as comorbidities of diabetes.
Determinants of Health in U.S.

- Genetics: 10%
- Behavior & environment: 60%
- Health Care: 30%

Nutrition!
Scientific Wellness → A New Industry

Wellness Industry

Scientific Wellness

U.S. Healthcare Spending
$3.8 Trillion (2014)
Proposing the 100K Wellness Project

Promoting Wellness & Demystifying Disease:
The 100K Project

Leroy Hood, M.D., Ph.D., and Nathan D. Price, Ph.D.

SYSTEMS BIOLOGY

Demystifying Disease, Democratizing Health Care

UNSUSTAINABLE COST INCREASES THREATEN THE GLOBAL HEALTH CARE SYSTEM, and further progress is stymied more by societal than technological factors. Only by engaging health care consumers (that is, patients) as pioneers who provide both health-related data and insights into pathophysiology can we meet those societal challenges and thus accelerate the pace of biomedical innovation.

In March 2014, the Institute for Systems Biology will launch a longitudinal, Framingham-like study (www.framingham2020.org) of 100,000 (100K) healthy individuals that we believe will be instrumental in bringing predictive, preventive, personalized, and participatory (P4) medicine to patients. Participatory medicine means that patients, researchers, physicians, and the entire health care community join forces to transform the practice of medicine to make it more proactive than reactive—and, in turn, less expensive and more effective (1).

PEOPLE POWER
A systems approach is necessary for the effective management of complex diseases (1). This fundamental component of P4 medicine is built on two central features. The first is a conviction that, in 5 to 10 years, each patient will have a dynamic data cloud consisting of billions of diverse types of data points and that medicine will be informed by computational analyses that reduce high-dimensional data to actionable hypotheses designed with the intent of optimizing wellness and minimizing disease in individual patients. The second feature is that integration of patient data will reveal biological networks that specify health and are altered in disease, and that through an understanding of these differences, one can gain fundamental insights into disease mechanisms. Such insights are essential for developing more effective diagnostic and therapeutic approaches. Indeed, such an approach has already provided powerful new technologies and strategies (2) that have brought us to the brink of P4 medicine (3).

At its foundations, P4 medicine is about quantifying wellness and demystifying disease. Individual data clouds will let us predict future wellness and disease. The preventive element focuses on how well we can improve individual wellness and take actions to stop or de-
Scientific Wellness:
Two Integrated Directions

**Arivale**
- A consumer facing scientific wellness company
- 5,000 individuals in the first 18 months
- Transform how biotech industry operates

**ISB-Providence**
- Dense, dynamic, personal data clouds
- Research to validate wellness metrics
- Research for better assays
- Optimize wellness
- Study wellness to disease transitions
- Study disease progression, response to therapy and transition to wellness
The 100K Wellness Project was initiated in 2014 with the generation of dynamic data clouds for 108 individuals. These data provided spectacular insights into what it is to be well and the nature of wellness to disease transitions (and vice versa).
Assays / Measurements—108 Pioneers

Creating dense and dynamic personal data clouds

**GENOME**

Whole Genome Sequencing.
SNPs Millions

**LABS**

Detailed lab tests 3x (blood, urine, saliva)
Clinical chem. 150
Metabolites 700
Proteins 400

**SELF-TRACKING**

Continual self-tracking & lifestyle monitoring

**MICROBIOME**

Gut Microbiome 3x
Wellness coaching for participants

Wellness Coach

Sandi Kaplan, MS, RD

Study Physician

Craig Keebler, MD
Clinical Labs Discovery: Improvements in blood health with behavioral coaching

% change in out-of-range measurements

- Cardiovascular: Improved by 6%
- Diabetes: Improved by 33%
- Inflammation: Improved by 12%
- Nutrition: Improved by 21%
Clinical Labs Discovery:
Significant pre-diabetes improvements

Seven participants with pre-diabetes were completely normalized in six months

- **HbA1c (Glycated hemoglobin)**: Improved by 38%
- **Fasting glucose**: Improved by 19%
- **HOMA (Insulin resistance)**: Improved by 55%
- **Insulin**: Improved by 56%

*Baseline 3 months 6 months*
Diet modification to reduce heavy metal toxicity

1. Baseline: High mercury levels in blood

2. Coached to modify diet - eight weeks of eating salmon sushi vs. tuna sushi (3x a week)

3. Reduced mercury levels in three months
A wellness to disease transition—genetics plus environment—an actionable possibility
Blood + Genetics illuminated the effects of increasing copies of the Hemochromatosis variant.

Left untreated, this disorder could lead to cartilage damage, liver cancer, diabetes, and heart disease: Easily treated by regular blood donations to reduce the iron stores.

One participant ALREADY had cartilage damage from his undiagnosed disease.

Subsequent family genetic testing detected other family members at risk.

Genetics and Clinical Labs: Hemochromatosis
Detected risk of a deadly disease in two participants.
Deriving Insights from Data: New Frontiers
Nutrient measurements correlate with genetic predisposition for IBD

We can determine your genetic risk for at least 60 diseases.
GWAS variants have been determined for about 60 diseases and traits:

<table>
<thead>
<tr>
<th>ADHD</th>
<th>COPD</th>
<th>Myopia</th>
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</thead>
<tbody>
<tr>
<td>Alzheimer's disease</td>
<td>Crohn's disease</td>
<td>Obesity</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Esophageal cancer</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Asthma</td>
<td>Gout</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Grave's disease</td>
<td>Ovarian cancer</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>Hematocrit</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>Hypertension</td>
<td>Pancreatic cancer</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Hypothyroidism</td>
<td>Primary biliary cirrhosis</td>
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<tr>
<td>Bone mineral density</td>
<td>Inflammatory bowel disease</td>
<td>Prostate cancer</td>
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<tr>
<td>Inflammation</td>
<td>Iron levels</td>
<td>Psoriasis</td>
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<tr>
<td>Calcium</td>
<td>Lung Cancer</td>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Cardiovascular disease</td>
<td>Lupus</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Macular degeneration</td>
<td>Stroke</td>
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<tr>
<td>Cholesterol levels</td>
<td>Magnesium levels</td>
<td>Type 1 Diabetes</td>
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<tr>
<td>Chronic kidney disease</td>
<td>Metabolic syndrome</td>
<td>Type 2 Diabetes</td>
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<tr>
<td>Colorectal cancer</td>
<td>Migraine</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>Multiple sclerosis</td>
<td>Urate levels</td>
</tr>
</tbody>
</table>
Enabling Individuals to take Responsibility for their Own Wellness (and Disease)

Individuals taking responsibility for their own health – with informed personalized nutrition – will dramatically reduce the cost of healthcare.
ISB Hundred Person Wellness Project: Team

Special thanks to our funders: Robert Wood Johnson Foundation and M.J. Murdock Charitable Trust

Project Leadership
- Leroy Hood, MD, PhD
- Nathan Price, PhD
- Sean Bell, Business Director

Data Analytics
- Nathan Price, PhD – Analytics Lead
- Gustavo Glusman, PhD, Genomics
- Andrew Magis, PhD, Multi-omics
- John Earls, Data integration

Participant Engagement
- Jennifer Lovejoy, PhD, VP Clinical Affairs
- Sandi Kaplan, Wellness Coach
- Craig Keebler, MD, Study Physician

Project Management
- Kristin Brogaard, PhD Project Manager
- Sara Mecca, Project Assistant
- Mary Brunkow, PhD, Project Coordinator

Medical Advisory Board
- Robert Green, MD
- Jane Guiltinan, ND
- Michael Raff, MD
- Sarah Speck, MD

Communications
- Gretchen Sorenson, Consultant
- Hsiao-Ching Chou, Commun. Director

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