Scientific Wellness and the Future of Health and Nutrition

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American College of Nutrition
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Disclosures

• Dr. Price is a Co-Founder of Arivale, which 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
After participating in this presentation, learners should be better able to:

• Understand the scale of omic data collection that can inform nutrition and wellness.
• Understand the role of wellness coaches in interpreting data and motivating action.
• Understand new emerging field of 'scientific wellness'.
Nutrition health effects are complex: Need context and personalization

Everything we eat both causes and prevents cancer

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

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

Diagram:
- Diabetes with Comorbidities (Vary by Age and Ethnicity)
  - ~23% Obstructive Sleep Apnea, Neuropathy
  - ~33% Dyslipidemia (LDL, HDL or Trig)
  - ~38% Kidney Disease
  - ~75% Hypertension
  - ~45% Cardiovascular Disease, Congestive Heart Failure, Coronary Artery Disease, Angina
  - ~25% Depression, Osteoporosis, GERD

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™
Determinants of Health in U.S.

- Nutrition!
- 60% Behavior & environment
- 30% Genetics
- 10% Health Care
Scientific Wellness → A New Industry

Wellness Industry

Scientific Wellness

U.S. Healthcare Spending $3.8 Trillion (2014)
Conceptual Themes of P4 Medicine

P4 Medicine
- Predictive
- Preventive
- Personalized
- Participatory

Wellness Quantified

Disease Demystified

Scientific Wellness Industry

Disease Industry
Proposing the 100K Wellness Project

Hood and Price, Clinical Omics, (2014)

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 these 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.framinghamheartstudy.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 foundation, 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-
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).
• 108 participants
• Age range: 20s to 88+
• 9-month study launched March 2014
• IRB approved
• Evaluation / insights for next phase

• Whole genome sequence
• Detailed blood, urine, saliva measurements 3x
• Gut microbiome 3x
• Continual self-tracking and lifestyle monitoring
• Data integration & correlations
• Monthly coaching sessions on actionable data
• Discovery research
• Events and education
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

Database of actionable possibilities that will grow over time

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April May June July August September October November December
Intro Round 1 Coaching Sessions Round 2 Coaching Sessions Round 3 Coaching Sessions
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

<table>
<thead>
<tr>
<th>Category</th>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Improved by 6%</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>Improved by 33%</td>
<td></td>
<td></td>
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<tr>
<td>Inflammation</td>
<td>Improved by 12%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutrition</td>
<td>Improved by 21%</td>
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</tbody>
</table>
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%
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
Identifying inter-related molecular modules
Cholesterol is positively associated with alpha-tocopherol (Vitamin E).

Cholesterol is negatively associated with endogenous thyroxine.

A beneficial side effect of the drug thyroxine (Synthroid) is lowering LDL cholesterol.
The largest molecular community: related to cardiometabolic health
We can determine your genetic risk for at least 60 diseases.
GWAS variants have been determined for about 60 diseases and traits:

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<thead>
<tr>
<th>ADHD</th>
<th>COPD</th>
<th>Myopia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's disease</td>
<td>Crohn's disease</td>
<td>Obesity</td>
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<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>
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<tr>
<td>Bipolar disorder</td>
<td>Hypertension</td>
<td>Primary biliary cirrhosis</td>
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<tr>
<td>Blood pressure</td>
<td>Hypothyroidism</td>
<td>Prostate cancer</td>
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<tr>
<td>Bone mineral density</td>
<td>Inflammatory bowel disease</td>
<td>Psoriasis</td>
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<tr>
<td>Inflammation</td>
<td>Iron levels</td>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Calcium</td>
<td>Lung Cancer</td>
<td>Schizophrenia</td>
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<td>Cardiovascular disease</td>
<td>Lupus</td>
<td>Stroke</td>
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<tr>
<td>Celiac disease</td>
<td>Macular degeneration</td>
<td>Type 1 Diabetes</td>
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<tr>
<td>Cholesterol levels</td>
<td>Magnesium levels</td>
<td>Type 2 Diabetes</td>
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<tr>
<td>Chronic kidney disease</td>
<td>Metabolic syndrome</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>Migraine</td>
<td>Urate levels</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>Multiple sclerosis</td>
<td></td>
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</table>
Your genome affects metabolite concentrations in your blood.

**Graph 1:**
- $R = 0.50$ $p_{adj} = 3.41 \times 10^{-14}$
- $\rho = 0.48$ $p_{adj} = 1.26 \times 10^{-12}$
- $\tau = 0.34$ $p_{adj} = 1.26 \times 10^{-12}$

**Graph 2:**
- $R = 0.48$ $p_{adj} = 3.67 \times 10^{-13}$
- $\rho = 0.45$ $p_{adj} = 1.13 \times 10^{-10}$
- $\tau = 0.31$ $p_{adj} = 9.50 \times 10^{-11}$
Nutrient measurements correlate with genetic predisposition for IBD

Where are we going?
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
Arivale: Scientific Wellness at Scale

Founders
- Clayton Lewis, CEO and Co-founder
  Maveron, MarketLeader, Harborview Medical Center, Capitol Hill
- Lee Hood, MD, PhD, Co-founder, SAB Chair
  ISB, Amgen, National Academies, Presidential Medal
- Nathan Price, PhD, Co-founder, BOD
  ISB, University of Illinois, Urbana-Champaign, UCSD, UW

Customer Acquisition & Engagement
- Grant Ries, Chief Revenue Officer
  Founder: Bluekai; Oracle, AdReady, YuMe
- Alicia Nakamoto, Director, Community
  RealSelf, Amazon, Bing, HP
- Stewart Meyer, Director, Client Experience
  Amazon, Razorfish, Kinetix, Best Buy

Computational Bioscience & Software Development
- Bryan Wheeler, MS, Director, Software Development
  Amazon, MSNBC.com, Microsoft
- Andrew Magis, PhD, Senior Bioinformatics Scientist
  ISB, University of Illinois, Urbana-Champaign

Behavioral Coaching
- Jennifer Lovejoy, PhD, Chief Translational Science Officer
  Alere/Free & Clear, Bastyr Dean, Pennington Biomedical Research Center (LSU) Endowed Professorship
- Sandi Kaplan, MS, RD, Director, Coaching Services
  Alere/Free & Clear, founder Zing Bars

Operations & Finance
- Sean Bell, Chief Business Officer
  ISB, Alere/Free & Clear, LexisNexis
- Kern Maresca, Director of Finance
  Alere/Free & Clear, MindMyBody

External Affairs
- Gretchen Sorensen
  ISB, Clinton Administration, Turner Broadcasting, Capitol Hill

Capital Raised: $39M
Scaling Up: Building the Research Portal

From 108 to Thousands to Millions

Data

Impact of recommendations

Scientifically Validated Metrics

Breadth \( \times \) Depth \( \times \) Width =
PROVIDENCE-ISB AFFILIATION

Tens of millions of EMRs
Have access to patient samples
Can work with Providence to design clinical trials
Provides avenue to implement P4 Medicine
TRANSLATIONAL MEDICINE
PILLAR:
SCIENTIFIC
WELLNESS
TRANSLATIONAL MEDICINE
PILLAR:
BREAST
CANCER
SURVIVOR
WELLNESS
TRANSLATIONAL MEDICINE PILLAR:
ALZHEIMER’S DISEASE
TRANSLATIONAL MEDICINE
PILLAR:
(PRE)DIABETES
Dense, Dynamic Personal Data Clouds

These personalized data clouds are the foundation of Precision Medicine and Precision Nutrition.
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

Project Management

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

Participant Engagement

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

Communications

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

Medical Advisory Board

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

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After participating in this presentation, clinicians should be better able to:

• Discuss the power of data in driving clinical focus towards disease prevention and wellness optimization.