Functional Medicine in the Age of Genomics, Biometrics, and Wearable Devices

Jeffrey Bland, PhD, FACN, FACB
Co-Founder, The Institute for Functional Medicine
Founder, Personalized Lifestyle Medicine Institute

www.facebook.com/jeffreyblandphd
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Where We Are
Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.

Christopher Murray, MD, DPhil
Institute Director, Institute for Health Metrics and Evaluation

“Ageing of the world’s population is leading to a substantial increase in the number of individuals with sequelae of disease and injuries. Rates of YLDs are declining much more slowly than mortality rates. The non-fatal dimensions of disease and injury will require more and more attention from health systems. The transition to non-fatal outcomes as the dominant source of burden of disease is occurring rapidly outside of sub-Saharan Africa. Our results can guide future health initiatives through examination of epidemiological trends and a better understanding of variation across countries.”

Lancet 2015; 386: 743-800
The History of the New Paradigm
Roger J. Williams, PhD
1883 - 1988

• Renowned Nutritional Biochemist
• Discoverer of Pantothenic Acid (Vitamin B5)
• Professor, University of Texas
• Known as the “Father” of the concepts of *Biochemical Individuality* and *Genetotrophic Disease*
• Introduced to me in 1975, an influential and inspirational figure to me since that time.
“Medicine is for Real People:
Statistical Humans are of Little Interest.”
Linus Pauling, PhD
1901 - 1994

• Two-time Nobel Laureate: Chemistry (1954) and Peace (1962)
• Molecular Medicine (1949)
• Orthomolecular Medicine (1968)
• My mentor and guide during my time at the Linus Pauling Institute of Science and Medicine (1982 – 1984)
1983: A Celebration of Linus Pauling’s 82nd Birthday
Roger Williams and Linus Pauling

Biochemical Individuality Meets Molecular Medicine

Houston, Texas - 1974
What We Have Learned About Chronic Disease
Health is personal.
LASTING HEALTH COMES FROM THE INTERACTION OF OUR GENES WITH OUR LIFESTYLE AND ENVIRONMENT. PERSONALIZING THIS CONNECTION IS THE FUTURE.

— JEFFREY BLAND, PHD

Founder & President, Personalized Lifestyle Medicine Institute
Founder, The Institute for Functional Medicine
A Global Social Movement is Underway:

A TRANSITION FROM THE AGE OF THE AVERAGE TO THE AGE OF THE INDIVIDUAL
The Creation of the Functional Medicine Model and The Institute for Functional Medicine

- Susan Bland organized two meetings in 1989 and 1990 to discuss the future of medicine.
- We invited thought leaders from different disciplines to come together for “white board” sessions and discussion.
- As a result of these gatherings, the concept of Functional Medicine as a systems biology approach to healthcare was conceived.
- The Institute for Functional Medicine was created in 1990.
• Founded 1991. More than 100,000 practitioners have now completed CME-approved courses.

• The interaction between our genes and our environment and lifestyle gives rise to our function.

• The question is not just what is the information that we have inherited in our genes, but also how is it being expressed?

• There are many potential ways our genes can be expressed in our function, from health to disease.

• How is the expression of our genes controlled?
Characteristics of the Functional Medicine Assessment

• Antecedents
• Triggers
• Mediators
• Signs and Symptoms
Health Can Only be Determined by Measuring Functional Status

- Physical
- Physiological
- Cognitive
- Psychological
Disease Model vs Functional Medicine Model

- Diagnostic
- Diagnosis Focused
- Abnormal compared to the group
- Pathway Focused
- Partitioned into specialties
- Pathology-based

- Functional
- Etiology Focused
- Abnormal compared to the individual themselves
- Network Focused
- Interconnected Organ Systems
- Determination of underlying dysfunctions leading to symptoms
The Functional Medicine Operating Model

- **Genes**
- **Environment**
- **Structure**
- **Assimilation/Elimination**
- **Energy** (Production & Utilization)
- **Detoxification**
- **Cellular Transport**
- **Immune Defense**
- **Cellular Communication** (Hormones)
- **Lifestyle Behaviors**
- **Personalized Lifestyle Healthcare/Medicine**
- **Diet**

**Commitment to Win Breaking Barriers**
Moving the Functional Medicine Model into Institutional Medicine

• The Functional Medicine Clinic at the Cleveland Clinic was established in 2014
• Founder: Mark Hyman MD / Head of Clinical Services: Patrick Hanaway, MD
• Personalized Lifestyle Medicine: Diet, medical nutrition therapy, exercise, stress management, environment, bioenergetics, Functional Medicine
• Research Focus
A Future Vision of Precision Personalized Lifestyle Medicine

• “While PM aims to incorporate individual variability in genes, environment, and lifestyle, the emphasis in current practice is on profiling risk”

• The future of PM will move us beyond “population risk” to that of understanding individual functional uniqueness
  – Less emphasis on “Risk” and more emphasis on “Opportunity”
The “Gene-Environment” Paradigm

Gene-environment interplay

The “Gene-Environment” Paradigm

The advent of incredibly powerful and innovative RNA sequencing methods is changing many aspects of genetics research. In particular, human genome sequencing is revolutionizing our understanding of many aspects of human biology and disease. However, we must be certain to extend our focus on future—environmental factors and disease also play important roles.

I recall a conversation with Nobel laureate Michael Brownstein at a scientific meeting some years ago when he described his opening lecture to a medical school human biology class.

“Ask the class,” he told them, “how would you prevent a rare genetic disease?” After listening to answers—“almost invariably based on inducing mutations, Dr. Brown smiled. The preferred answer:—would change the building codes so that no shortage would be taken in the test. This would, he said, be a ‘rare disease optimization’ that would be the result of more common in disease and would use other predisposing genetic factors for which variations are associated with all other conditions.”

The potential of such an approach is vast. Gene-environment interactions in health and disease.

Genetic variants that have evolved in the service of circumstances to be beneficial or neutral can be quite detrimental in other conditions. In many aspects of our metabolism, evolution has left conditions where certain traits or conditions are beneficial. For example, many aspects of our metabolism evolved under conditions where sugar was hard to come by. Now, in the era of obesity and the prevalence of type 2 diabetes, we face the challenge of obesity and other diseases. Evolution has shaped our bodies and health outcomes in the service of our survival.

In addition to elucidating genetic makeup, powerful genetic studies yield valuable information on understanding environmental effects on health. In this regard, the study of 

...genes alone do not determine our futures...

Even if traits are largely determined by genetics, environment—particularly in the form of lifestyle choices—continue to influence the development of chronic diseases. For example, waist circumference and physical activity levels are strongly associated with the risk of developing type 2 diabetes and cardiovascular disease. Understanding how these lifestyle choices interact with genetic factors can help us better prevent and treat chronic diseases.

Science 2016; 354:15.

- Creation of an actionable approach to chronic disease prevention and treatment
- Moves beyond “diagnosis” to “etiology”
- Sets stage for personalized, precision lifestyle medicine
Genes Viewed as “Risk Factors”
What If We Knew The Genetic Uniqueness of Each Person?

- Eric Topol
  - “The Patient Will See You Now”

“Omics” Tools
- Genomics
- Epigenomics
- Transcriptomics
- Proteomics
- Metabolomics
- Metagenomics
- Phenomics
- Biomarkers

Cell 2014; 157: 241-53,
There is Joy in our genes
The Connection of Functional Medicine to Systems Biology

P4 Medicine:
• Predictive
• Preventive
• Personalized
• Participatory

Leroy Hood, MD, PhD

Learn more:
www.systemsbiology.org
www.p4mi.org
The Institute for Systems Biology
Pioneer 100 Wellness Project

Source: Institute for Systems Biology
Technologies Powering the Revolution

- Genomics and its companion “omics” technologies
  - Full genome sequencing
  - Transcriptomics
  - Proteomics
  - Kinomics
  - Lipidomics
  - Metabolomics
  - Nutrigenomics
  - Exposomics
  - Epigenomics

- Informatics
  - Cloud based computing
  - Artificial Intelligence and Machine Learning
  - Precision Public Health (Clustering of Etiopathologies)

- Biometrics
  - Wearable devices and new biomarkers

- Social Media
  - Citizen Scientist
Biomarkers Used to Assess Aging

- Biological vs Chronological Aging
- Telomere Length
- Epigenetic Alterations of DNA
  - Methylation Patterns
- Mutational Markers in Genome
- Damaged Proteins
- Metabolites of Aging
The Quantified Human

Biometrics, Biohacking, Wearable Devices

• The BIG Six
  – Continuous Blood Sugar Monitoring
  – Continuous Blood Pressure Monitoring
  – Fitness Assessment
    • Strength
    • Flexibility
    • Endurance
  – Heart Rate Variability
  – Sleep Cycling
  – Functional Neurological Testing
    • Memory, Reaction time, Vibratory Sensation, Balance, Hearing, Taste/Smell
My Pioneer 100 Experience:
Making the “Omics” Revolution Personal
The Start of Making Wellness Personal and Precise

A wellness study of 108 individuals using personal, dense, dynamic data clouds

Nathan D Price 1,2,4, Andrew T Maggi3,5, John C Earl3,6, Gustavo Ghino1,5, Boaz Levy7, Christopher Lusteed8, David T McDonald3,5, Urike Koebele1,8, Christopher J Mencarini9, Shidlin Qin1, Robert J Morris1,3, Kristin Brego1, Gilbert S Omen1,6, Jennifer C Lovcevich1,9 & Leroy Hood2,3,4

Personal data for 108 individuals were collected during a 9-month period, including whole genome sequences, clinical tests, metabolomics, phenomics, and microbiomes at three time points, and daily activity tracking. Using all of these data, we generated a cross-referenced network that provided a novel view of correlated and causative biologics (e.g., genetic risk for inflammatory bowel disease was negatively correlated with plasma cytokine). Finally, behavioral coaching informed by personal data helped participants improve their clinical biomarkers. Our results show that management of personal data over time can improve our understanding of health and disease, including early transitions to disease states.

II: Why Personal?

We report the generation and analysis of personal, dense, dynamic data clouds for 108 individuals over the course of a 9-month study that we call the Pioneer Personal Wellness Project (PPWP). Our study included whole genome sequences, clinical tests, metabolomics, phenomics, and microbiomes at 3-month intervals and frequent activity measurements (i.e., wearing a fitness tracker). This study takes a different approach from previous studies in that it builds a whole-person biologics database on each individual to elucidate biological links between his health and his genes that we observed in previous clinical studies and tests were used as a starting point to identify actionable possibilities for behavioral coaching.

We report the cross-referenced and different data types and identify a large number of individuals in this project. This is the start of measuring the biological impact of the interactions identified from the data and the impact of personalized behavioral coaching on health and disease.

RESULTS

The PPWB study had four objectives. First, establish cost-efficient workflows for genotyping, storing, and analyzing multiple sources of data.
Pharmacogenomics and Detoxification

Pharmacogenomics is the study of the role of inherited and acquired genetic variation in drug response. Clinically relevant pharmacogenetic examples, mainly involving drug metabolism, have been known for decades, but recently, the field of pharmacogenetics has evolved into “pharmacogenomics,” involving a shift from a focus on individual candidate genes to genomewide association studies. Such studies are based on a rapid scan of markers across the genome of persons affected by a particular disorder or drug-response phenotype and persons who are not affected, with tests for association that compare genetic variation in a case–control setting. An example is provided in this issue of the Journal: McCormack and colleagues, testing for genomewide association, identified an HLA allele that is associated with hypersensitivity reactions to the anticonvulsant and mood-stabilizing drug carbamazepine in persons of European descent. Pharmacogenomics facilitates the identification of biomarkers that can help physicians optimize drug selection, dose, and treatment duration and avert adverse drug reactions. In addition, pharmacogenomics can provide new insights into mechanisms of drug action and as a result can contribute to the development of new therapeutic agents.

In 2003, two reviews of pharmacogenetics were published in the Journal. Since then, both genomic science and its application to drug response have undergone major advances. Here we review some of those advances, with an emphasis on discovery through genomewide association studies. We describe examples that highlight principles of pharmacogenomics that are relevant to a wide variety of drugs.

Constitutive or Inducible?
Phase 1 CYP 450 and Phase 2 Conjugases
Genetic Methylation Profile

Multiple Homozygous SNPs for MTRR, AHCY, CBS
Genetic Detox Profile

Multiple Homozygous SNPs for CYP1A1, CYP2D6, CYP2E1, NAT1, NAT2
Metabolic Data (measured every 3 months)

**INSULIN** is a hormone that helps your body's cells use glucose by promoting its absorption from the blood stream to the skeletal muscles for energy or fat tissue for storage. Insulin prevents the accumulation of glucose in the blood stream, which can have toxic effects. Elevated insulin is often associated with excess body weight and typically indicates insulin resistance by the cells.

**HbA1c** reflects your average blood glucose (sugar) level for the past two to three months. It measures the percentage of blood sugar attached to hemoglobin, the oxygen-carrying protein in red blood cells. The higher your blood sugar levels, the more hemoglobin you'll have with sugar attached and the higher your HbA1c.

**HOMA score** is a calculation of your insulin resistance. Insulin resistance is a condition in which the body produces insulin but does not use it effectively. When people have insulin resistance, glucose can build up in the blood stream instead of being absorbed by the cells, leading to type 2 diabetes or prediabetes.

High Stress
Mother in Hospital
Inflammatory Markers

Hs-CRP is a protein produced in the liver that increases in abundance in response to inflammation within the body. Its biological role is to bind and remove dead and dying cells. In large epidemiologic studies, elevated levels of hs-CRP have been shown to be a strong indicator of cardiovascular disease and have been implicated in chronic diseases, cancer and immune dysfunction.

IL-6, IL-8, AND TNF-ALPHA are all small proteins known as cytokines that act as signaling molecules to send messages through the body. All three act to stimulate the immune system to create an inflammatory response.

At healthy levels these proteins help the body fight viral infections, bacterial invasions, and cancerous cells. Extended signaling from these small proteins lead to chronic and harmful inflammation within the body.
## Blood Elemental Analysis

<table>
<thead>
<tr>
<th>Element</th>
<th>Reference Range</th>
<th>Reference Range</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper</td>
<td>0.531</td>
<td>0.466-0.721 mcg/g</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>55.3</td>
<td>30.1-56.5 mcg/g</td>
<td></td>
</tr>
<tr>
<td>Manganese</td>
<td>0.012</td>
<td>0.007-0.038 mcg/g</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>3.421</td>
<td>2.220-3.626 mcg/g</td>
<td></td>
</tr>
<tr>
<td>Selenium</td>
<td>0.46</td>
<td>0.25-0.76 mcg/g</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>7.5</td>
<td>7.8-13.1 mcg/g</td>
<td></td>
</tr>
</tbody>
</table>

### Nutrient Elements

The Elemental reference ranges are based on an adult population.

<table>
<thead>
<tr>
<th>Element</th>
<th>Reference Range</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead</td>
<td>0.025</td>
<td>&lt;= 0.048 mcg/g</td>
</tr>
<tr>
<td>Mercury</td>
<td>0.001</td>
<td>&lt;= 0.0039 mcg/g</td>
</tr>
<tr>
<td>Antimony</td>
<td>0.001</td>
<td>&lt;= 0.002 mcg/g</td>
</tr>
<tr>
<td>Arsenic</td>
<td>0.016</td>
<td>&lt;= 0.071 mcg/g</td>
</tr>
<tr>
<td>Cadmium</td>
<td>0.001</td>
<td>&lt;= 0.001 mcg/g</td>
</tr>
<tr>
<td>Tin</td>
<td>&lt;dl</td>
<td>&lt;= 0.0009 mcg/g</td>
</tr>
</tbody>
</table>

### Toxic Elements

Tuna Sushi
Nutritional Assessment

**Oxidative Stress Markers**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutathione (whole blood)</td>
<td>1.596 ± 669 micromol/L</td>
</tr>
<tr>
<td>Lipid Peroxides (urine)</td>
<td>micromol/g Creat.</td>
</tr>
<tr>
<td>8-OHdG (urine)</td>
<td>mcg/g Creat.</td>
</tr>
<tr>
<td>Coenzyme Q10, Ubiquinone (plasma)</td>
<td>0.46-1.72 mcg/mL</td>
</tr>
</tbody>
</table>

The Oxidative Stress reference ranges are based on an adult population.

**Vitamin D**

<table>
<thead>
<tr>
<th>Inside Range</th>
<th>Outside Range</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-OH Vitamin D</td>
<td>38</td>
<td>50-100 ng/mL</td>
</tr>
</tbody>
</table>

Vitamin D Receptor Polymorphism
### Essential Fatty Acid Analysis

#### Seattle Salmon

#### Omega 3 Fatty Acids

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Linolenic</td>
<td>&gt;= 0.09 wt %</td>
<td>0.17</td>
</tr>
<tr>
<td>Eicosapentaenoic</td>
<td>&gt;= 0.71 wt %</td>
<td>0.71</td>
</tr>
<tr>
<td>Docosapentaenoic</td>
<td>&gt;= 1.14 wt %</td>
<td>1.74</td>
</tr>
<tr>
<td>Docosahexaenoic</td>
<td>&gt;= 2.1 wt %</td>
<td>4.9</td>
</tr>
<tr>
<td>% Omega 3s</td>
<td>&gt;= 3.8</td>
<td>7.5</td>
</tr>
</tbody>
</table>

#### Omega 6 Fatty Acids

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic</td>
<td>10.5-16.9 wt %</td>
<td>15.4</td>
</tr>
<tr>
<td>γ-Linolenic</td>
<td>0.03-0.13 wt %</td>
<td>0.12</td>
</tr>
<tr>
<td>Dihomo-γ-Linolenic</td>
<td>&gt;= 1.19 wt %</td>
<td>1.34</td>
</tr>
<tr>
<td>Arachidonic</td>
<td>15-21 wt %</td>
<td>15</td>
</tr>
<tr>
<td>Docosatetraenoic</td>
<td>1.50-4.20 wt %</td>
<td>1.29</td>
</tr>
<tr>
<td>Eicosadienoic</td>
<td>&lt;= 0.26 wt %</td>
<td>0.33</td>
</tr>
<tr>
<td>% Omega 6s</td>
<td>33.8</td>
<td>30.5-39.7</td>
</tr>
</tbody>
</table>

#### Omega 9 Fatty Acids

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oleic</td>
<td>10-13 wt %</td>
<td>14</td>
</tr>
<tr>
<td>Nervonic</td>
<td>2.1-3.5 wt %</td>
<td>2.9</td>
</tr>
<tr>
<td>% Omega 9s</td>
<td>17.4</td>
<td>13.3-16.6</td>
</tr>
</tbody>
</table>

#### Saturated Fatty Acids

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmitic</td>
<td>18-23 wt %</td>
<td>19</td>
</tr>
<tr>
<td>Stearic</td>
<td>14-17 wt %</td>
<td>17</td>
</tr>
<tr>
<td>Arachidic</td>
<td>0.22-0.35 wt %</td>
<td>0.27</td>
</tr>
<tr>
<td>Behenic</td>
<td>0.02-1.68 wt %</td>
<td>0.07</td>
</tr>
<tr>
<td>Tricosanoic</td>
<td>0.12-0.18 wt %</td>
<td>0.19</td>
</tr>
<tr>
<td>Lignoceric</td>
<td>2.1-3.8 wt %</td>
<td>0.19</td>
</tr>
<tr>
<td>Pentadecanoic</td>
<td>0.07-0.15 wt %</td>
<td>0.09</td>
</tr>
<tr>
<td>Margaric</td>
<td>0.22-0.37 wt %</td>
<td>0.27</td>
</tr>
<tr>
<td>% Saturated Fats</td>
<td>35.7</td>
<td>39.8-43.6</td>
</tr>
</tbody>
</table>

#### Monounsaturated Fats

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmitoleic</td>
<td>&lt;= 0.64 wt %</td>
<td>0.28</td>
</tr>
<tr>
<td>Vaccenic</td>
<td>&lt;= 1.13 wt %</td>
<td>0.67</td>
</tr>
<tr>
<td>% Trans Fat</td>
<td>0.33</td>
<td>&lt;= 0.59 wt %</td>
</tr>
</tbody>
</table>

#### Delta-6 Desaturase Activity

- Upregulated: Functional
- Impaired: Not functional

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linoleic / DGLA</td>
<td>6.0-12.3</td>
<td>11.5</td>
</tr>
</tbody>
</table>

#### Cardiovascular Risk

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Reference Range</th>
<th>Seattle Salmon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega 6s / Omega 3s</td>
<td>3.4-10.7</td>
<td>4.8</td>
</tr>
<tr>
<td>AA / EPA</td>
<td>12-125</td>
<td>21</td>
</tr>
<tr>
<td>Omega 3 Index</td>
<td>&gt;= 4.0</td>
<td>5.6</td>
</tr>
</tbody>
</table>
Adrenal-Stress Indication

Salivary Cortisol and DHEA

Reference Range
- 1 Hour After Rising
  7AM - 9AM: 0.27-1.18 mcg/dL
  11AM - 1PM: 0.10-0.41 mcg/dL
  3PM - 5PM: 0.05-0.27 mcg/dL
  10PM - 12AM: 0.03-0.14 mcg/dL
Influence of Lifestyle on My Resting Heart Rate
Medical Devices, Innovation, Point of Care Measurements and Empowerment

- Do-it-yourself health technologies were rated a number 1 in the top 10 health industry developments in 2015
- Optimism must be balanced with realism
  – Case Study: Theranos
- Accuracy, Precision and Sensitivity are Important
- Different biometric measurements have different precision standards

Do-It-Yourself Medical Devices — Technology and Empowerment in American Health Care

In recent years, do-it-yourself (DIY) health care technology has become a topic of speculation in medical and financial journals, as smart devices and wearable technologies promise to transform homes, workplaces, and mobile phones into more accessible sites for health monitoring and intervention. The auditing and consulting firm PricewaterhouseCoopers ranked DIY health care number 1 in its top 10 health industry developments of 2015, and the wireless-telecommunications giant Qualcomm recently began final judging rounds on its Tricorder XPRIZE, a $10 million global competition to "stimulate innovation and integration of precision diagnostic technologies, helping consumers make their own reliable health diagnoses anywhere, anytime." Yet "do-it-yourself" is rarely defined, and novelty claims in this arena require a decided short-sighted view of history. An examination of past and current DIY medical technologies suggests that over time, different approaches to these devices have been linked to different concepts of empowerment, with very different implications for benefit, cost, and risk for consumers.

Half a century ago, the Journal published "Electrocardiography by Do-It-Yourself Radio-telemetry" by Captain Frederick Fascenelli of Brooks Air Force Base in Texas. Fascenelli, concerned that the potential impact of telecommunications technologies in research and medical care was limited by high costs, provided circuit diagrams and parts lists to enable interested readers to build their own cardiac telemetry devices from supplies available at their local Radio Shack (see fig. 1). In place of commercial systems that cost up to $3,500 per telemetry channel, this shareable technology could be "built by any interested person in four hours for under $15." Twenty cents of that price tag consisted of two 10-cent coins to be used as electrodes. Fascenelli assumed that any jour-

NEJM 2016; 374: 305-07
Wearables as Medical Devices

What is a “medical device” in the 21st century?
- Sleep assessment
- Neurological Functional assessment
- Cardiac Function
- Blood Sugar
- Mood Assessment
- Blood Pressure
- Oxidative Stress
- Dietary Assessment by Urinary Excretion of Metabolites

JAMA 2018; 320: 139-41
Can Wearable Fitness Monitoring and Telephone Coaching Improve Peripheral Artery Disease?

- “Among Patient with PAD a home-based exercise intervention consisting of a wearable activity monitor and telephone coaching compared with usual care did not improve walking distance”
  - Do you need personal coaching interaction?
  - Was the functional decline too great to have an impact?
Effect of Wearable Technology Combined with Lifestyle Intervention on Long-Term Weight Loss

- “Devices that monitor and provide feedback on physical activity may not offer an advantage over standard behavioral weight loss approaches”
  - Why not?
  - Is the device effectively incorporated into an effective patient-centered approach?

JAMA 2018; 319: 1665-70
CONTINUOUS GLUCOSE MONITORING

Continuous Glucose Monitoring (CGM) gives you a more complete picture of your glucose levels, which can lead to better lifestyle decisions and better glucose control.

EXPLORE CGM OPTIONS  GET STARTED

WHAT IS CGM?

Continuous Glucose Monitoring is an advanced way for people living with diabetes to check glucose readings in real-time or monitor glucose readings over a period of time. By using a continuous glucose monitor, your CGM system will automatically receive glucose readings every 5 minutes allowing you to fingerstick less often. CGM can be used with or without an insulin pump.†

What is Smart CGM?
Smart CGM predicts future high and low sensor glucose events up to 60 minutes in advance and provides access to additional algorithms and insights that can inform you of clinically relevant glucose patterns.†
Continuous Blood Glucose Monitoring of a Type 2 Diabetic on Insulin

**Daily Patterns** (with Ambulatory Glucose Profile)
September 7, 2015 – September 20, 2015 (14 days)

Estimated A1c 7.8%, or 62 mmol/mol

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Chaotic Blood Glucose of a Type 2 Diabetic on Insulin
Jeff Bland’s Blood Glucose on a Metabolic Program

Glucose Trend: Bland, Jeffrey [SM71704120]
Jeff Bland’s Blood Glucose over 7 Days

Patterns: Bland, Jeffrey [SM71704120]

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Jeff Bland’s Average Blood Glucose Each Hour of the Day

Hourly Stats: Bland, Jeffrey [SM71704120]

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Totals</th>
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<th>4:00am</th>
<th>5:00am</th>
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<th>7:00am</th>
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</table>
Jeff Bland’s Diet and Lifestyle Versus Blood Glucose Over the Day
Continuous Blood Pressure Monitoring
## Best Heart Rate Variability Monitor

### HRV Devices (Quick Comparison Table)

<table>
<thead>
<tr>
<th>HRV Brand</th>
<th>Battery Life</th>
<th>iOS &amp; Android App</th>
<th>Sensor Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polar H7</td>
<td>200 hours</td>
<td>Yes</td>
<td>Chest strap</td>
</tr>
<tr>
<td>Polar H10</td>
<td>400 hours</td>
<td>Yes</td>
<td>Chest strap</td>
</tr>
<tr>
<td>Garmin Premium Heart Rate Monitor Strap</td>
<td>4.5 years (1 hour per day)</td>
<td>Yes</td>
<td>Chest strap</td>
</tr>
<tr>
<td>4iiii V100 Innovations Vital Heart Rate Monitor</td>
<td>160 hours</td>
<td>Yes</td>
<td>Chest strap</td>
</tr>
<tr>
<td>LifeTrak Zoom HRV Intensity &amp; Recovery Trainer</td>
<td>5 days before recharging battery</td>
<td>Yes</td>
<td>Wrist strap, forearm strap, upper arm strap, or ankle strap sensor</td>
</tr>
</tbody>
</table>
Heart rate variability: A new way to track well-being

POSTED NOVEMBER 22, 2017, 10:00 AM

Marcelo Campos, MD
Contributor

The easiest and cheapest way to check HRV is to buy a chest strap heart monitor (Polar, Wahoo) and download a free app (Elite HRV is a good one) to analyze the data. The chest strap monitor tends to be more accurate than wrist or finger devices. Check your HRV in the mornings after you wake up, a few times a week, and track for changes as you incorporate healthier interventions.
The One Wearable To Rule Them All? Oura Ring Review
Evaluation of smartphone-based testing to generate exploratory outcome measures in a phase 1 Parkinson's disease clinical trial.


Abstract

BACKGROUND: Ubiquitous digital technologies such as smartphone sensors promise to fundamentally change biomedical research and treatment monitoring in neurological diseases such as PD, creating a new domain of digital biomarkers.

OBJECTIVES: The present study assessed the feasibility, reliability, and validity of smartphone-based digital biomarkers of PD in a clinical trial setting.

METHODS: During a 6-month, phase 1b clinical trial with 44 Parkinson participants, and an independent, 45-day study in 35 age-matched healthy controls, participants completed six daily motor active tests (sustained phonation, rest tremor, postural tremor, finger-tapping, balance, and gait), then carried the smartphone during the day (passive monitoring), enabling assessment of, for example, time spent walking and sit-to-stand transitions by gyroscopic and accelerometer data.

RESULTS: Adherence was acceptable. Patients completed active testing on average 3.5 of 7 times/week. Sensor-based features showed moderate-to-excellent test-retest reliability (average intraclass correlation coefficient = 0.64). All active and passive features significantly differentiated PD from controls with P < 0.005. All active test features except sustained phonation were significantly related to corresponding International Parkinson and Movement Disorder Society-Sponsored UPRDS clinical severity ratings. On passive monitoring, time spent walking had a significant (P = 0.005) relationship with average postural instability and gait disturbance scores. Of note, for all smartphone active and passive features except postural tremor, the monitoring procedure detected abnormalities even in those Parkinson participants scored as having no signs in the corresponding International Parkinson and Movement Disorder Society-Sponsored UPRDS items at the site visit.

CONCLUSIONS: These findings demonstrate the feasibility of smartphone-based digital biomarkers and indicate that smartphone-sensor technologies provide reliable, valid, clinically meaningful, and highly sensitive phenotypic data in Parkinson's disease. © 2018 The Authors. Movement Disorders published by Wiley Periodicals, Inc. on behalf of International Parkinson and Movement Disorder Society.
Reversal of Alzheimer’s Disease?

Dale Bredesen, MD

UCLA Department of Neurology
Director, Mary Easton Center for Alzheimer’s Disease Research

www.impactaging.com

Reversal of cognitive decline: A novel therapeutic program

Dale E. Bredesen1, 2

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2 Buck Institute for Research on Aging, Novato, CA 94945.

Key words: Alzheimer’s, dementia, mild cognitive impairment, neurobehavioral disorders, neuroinflammation, neurodegeneration, systems biology

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Abstract: This report describes a novel, comprehensive, and personalized therapeutic program that is based on the underlying pathogenesis of Alzheimer’s disease, and which involves multiple modalities designed to achieve metabolic enhancement for neurodegeneration (MEND). The first 10 patients who have utilized this program include patients with memory loss associated with Alzheimer’s disease (AD), amnestic mild cognitive impairment (aMCI), or subjective cognitive impairment (SCI). Nine of the 10 displayed subjective or objective improvement in cognition beginning within 3-6 months, with the one failure being a patient with very late stage AD. Six of the patients had to discontinue working or were struggling with their jobs at the time of presentation, and all were able to return to work or continue working with improved performance. Improvements have been sustained, and at this time the longest patient follow-up is two and one-half years from initial treatment, with sustained and marked improvement. These results suggest that a larger, more extensive trial of this therapeutic program is warranted. The results also suggest that, at least early in the course, cognitive decline may be driven in large part by metabolic processes. Furthermore, given the failure of monotherapeutics in AD to date, the results raise the possibility that such a therapeutic system may be useful as a platform on which drugs that would fail as monotherapeutics may succeed as key components of a therapeutic system.
Genetic Expression is Regulated by the Epigenome

- All cells of the body have essentially the same DNA
- Cell types differ in their expression of the genetic message as dictated by epigenetic marks
- Most of the epigenetic marks are placed during embryogenesis, but there are a few that are metastable epialleles that can change with lifestyle and environmental exposure
- Methylation is a key epigenetic modulator

NEJM 2018; 378: 1324-32
Emerging evidence suggests that epigenetics regulates telomere dynamics in adults. However, the relationship between these pathways in children and youth remains unknown. Thus, we examined this association in 542 healthy adolescents aged 14 to 18 years old (44.8% African Americans; 55.2% females). Global DNA methylation level (-government-mC) was quantified using ELISA method. Leukocyte telomere length (LTL) was defined as relative telomere to single copy gene (T/S) ratio. Multiple linear regression models, adjusted for age, gender, ethnicity, Tanner stage, BMI, PA, and batch effect, revealed that 96% mC was associated with LTL (adjusted $\beta = 0.17$, $p < 0.01$). 96% mC accounted for 5.0% of the variation for LTL. A significant gender interaction was identified ($p < 0.01$). There was an association between %65 mC and LTL in females (all $ps < 0.01$), but not in males. Further sensitivity analyses by race revealed similar associations in African Americans and whites (all $ps < 0.03$). The present study, for the first time, shows that lower levels of global DNA methylation are associated with shorter telomere lengths in youth, which may decrease genome stability and augment the susceptibility to diseases. Longitudinal studies are warranted to establish the effects of global DNA methylation on LTL maintenance over time.
**Test Belongs To:**
Name: Jeffrey Bland
Age: 72
Sample Collected on: 06-May-2018
Sex: Male
Health Provider: Cynthia Taylor
Date of Birth: 21-Mar-1946
Received on: 10-May-2018
Clinic: PWN Health
TeloYears Customer ID #: 18042816084740
Reported on: 25-May-2018
Clinic Phone #: 844-457-9844
Accessory #: 18003954
Clinic ID #: PWNHealth

**About this Test:**
TeloYears is a genetic test that measures the length of your telomeres, the dynamic, protective caps on the ends of your DNA strands that tend to shorten with age. The test provides your Average Telomere Length (ATL) as well as your current age in TeloYears, or your “cellular” age based on your telomere length. Your age in TeloYears is the actual age of a typical man or woman whose telomere length is similar to yours.

**Your Results:**
Your Average Telomere Length is 0.94 (T/S ratio), which puts you in the 73rd percentile. This means that your telomeres are longer than 73% of men your age.\(^1\)

Your expected telomere length: 0.86
Your actual age: 72 years

The age of your cells: 61 TeloYears
Principles of DNA methylation and their implications for biology and medicine

Yuval Dor, Howard Cedar

DNA methylation represents an annotation system for marking the genetic text, thus providing instruction as to how and when to read the information and control transcription. Unlike sequence information, which is inherited, methylation patterns are established in a programmed process that continues throughout development, thus setting up stable gene expression profiles. This DNA methylation paradigm is a key player in medicine. Some changes in methylation closely correlate with age providing a marker for biological ageing, and these same sites could also play a part in cancer. The genome continues to undergo programmed variation in methylation after birth in response to environmental inputs, serving as a memory device that could affect ageing and predisposition to various metabolic, autoimmune, and neurological diseases. Taking advantage of tissue-specific differences, methylation can be used to detect cell death and thereby monitor many common diseases with a simple cell-free circulating-DNA blood test.
Methylation Patterns In Aging

[Diagram showing methylation patterns across different stages: embryo, 20 year old, 70 year old, and cancer.]

A: CpG island (bound by polycomb) and CpG island Lamin
B: Correlation plot with DNA methylation age vs. age, showing a correlation of 0.88, p = 5.3x10^{-24}.
Effect of Testosterone on Genomic Methylation Patterns in Mice

<table>
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<tr>
<th>Tissue</th>
<th>Liver</th>
<th>Control</th>
<th>Castration</th>
<th>Castration + Testosterone</th>
<th>Control</th>
<th>Testosterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn mice</td>
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<tr>
<td>20-week-old male mice</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-week-old female mice</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Disease Diagnosis by Methylated DNA in the Plasma

- Graph showing the correlation between cardiac cell-free DNA levels and disease status.
- Table comparing DNA levels across different tissues for healthy and myocardial infarction patients:
  - Heart: Low
  - Kidney: Low
  - Muscle: Low
  - Brain: Low
  - Liver: High
  - Lung: Low
  - Colon: Low
  - Pancreas: Low
- Statistical significance indicated by p<0.0001.
Dnmt3a is an epigenetic mediator of adipose insulin resistance

Abstract Insulin resistance results from an intricate interaction between genetic make-up and environment, and thus may be orchestrated by epigenetic mechanisms like DNA methylation. Here, we demonstrate that DNA methyltransferase 3a (Dnmt3a) is both necessary and sufficient to mediate insulin resistance in cultured mouse and human adipocytes. Furthermore, adipose-specific Dnmt3a knock-out mice are protected from diet-induced insulin resistance and glucose intolerance without accompanying changes in adiposity. Unbiased gene profiling studies revealed Fgf21 as a key negatively regulated Dnmt3a target gene in adipocytes with concordant changes in DNA methylation at the Fgf21 promoter region. Consistent with this, Fgf21 can rescue Dnmt3a-mediated insulin resistance, and DNA methylation at the FGF21 locus was elevated in human subjects with diabetes and correlated negatively with expression of FGF21 in human adipose tissue. Taken together, our data demonstrate that adipose Dnmt3a is a novel epigenetic mediator of insulin resistance in vitro and in vivo.
DNA methylation directs functional maturation of pancreatic $\beta$ cells

Pancreatic $\beta$ cells secrete insulin in response to postprandial increases in glucose levels to prevent hyperglycemia and inhibit insulin secretion under fasting conditions to protect against hypoglycemia. $\beta$ cells lack this functional capability at birth and acquire glucose-stimulated insulin secretion (GSIS) during neonatal life. Here, we have shown that during postnatal life, the de novo DNA methyltransferase DNMT3A initiates a metabolic program by repressing key genes, thereby enabling the coupling of insulin secretion to glucose levels. In a murine model, $\beta$ cell–specific deletion of Dnmt3a prevented the metabolic switch, resulting in loss of GSIS. DNMT3A bound to the promoters of the genes encoding hexokinase 1 (HK1) and lactate dehydrogenase A (LDHA) – both of which regulate the metabolic switch – and knockdown of these two key DNMT3A targets restored the GSIS response in islets from animals with $\beta$ cell–specific Dnmt3a deletion. Furthermore, DNA methylation–mediated repression of glucose-secretion decoupling genes to modulate GSIS was conserved in human $\beta$ cells. Together, our results reveal a role for DNA methylation to direct the acquisition of pancreatic $\beta$ cell function.
Point Mutation Analysis
Allele Quantification
SNP Genotyping
Pyrosequencing Technology

Welcome to EpigenDx
EpigenDx is a genomic and epigenomic research company dedicated to providing superior products and laboratory services. Our technical expertise and focus on quality and rapid turnaround time have made us a dependable partner to our customers worldwide since 2006.

"Our experience with EpigenDx has been excellent – their technical staff will succeed even with difficult genomic regions."

-Dr. Benjamin Tycko, MD/PhD
Bisulfite Sequencing (Methyl-Seq) Service

Methylation Box Plot

Methylation Tracks

Red: hypermethylated, Blue: hypomethylated
Association of Altered DNA Methylation in Children with Fetal Alcohol Syndrome Using Bisulfite Analysis

Epigenomics 2015; 7: 1259-74
Plant Phytochemicals and Their Epigenetic Influence
**Epigenetic effects of nutrition**

**Methyl donors**
- Vitamin B12
- Folate
- Choline
- Betaine
- Methionine
- Serine
- Glycine

**Fatty acids**
- Butyrate
- Arachidonic acid
- Docosahexaenoic acid
- Eicosapentaenoic acid

**Vitamins**
- Retinol
- Tocopherols
- Vitamin C

**Phytochemicals**
- Genistein
- Soy Isoflavones
- Curcumin
- Resveratrol
- Sulforaphane
- Polyphenols

**Epigenetic control gene expression**

**Epimutations - EpiSNPs**

**Disease Specific Genes:**
- Involved in Metabolic Syndrome & Inflammaging

**ADME Genes:**
- Phase I enzymes
- Phase II Transporters
- Metabolisation DNA repair

*For example*
- PITX2, BRCA1, GPX3, MGMT, PLK2, TFAP2E,
- DSCP1, SFRP5, RASSF1A
- MPO, CFTR, ...
- CYP members, GSTM family
- GSTP / GSTA variants
- UGT / SLC22 variants
- SULT2 / SULF variants
- ABCA / ABCG variants
- ABCB / GPX variants
- ALDH variants, etc.

**Disease risk**
- Diagnosis
- Prognosis

**Metabolisation**
- Adverse effects
- Strong/weak response

**Personalized Epigenetic Biomarkers**
- Cancer, CVD, CNS, Inflammaging

**Personalized Nutrition**
Urinary excretions of 34 dietary polyphenols and their associations with lifestyle factors in the EPIC cohort study

Urinary excretion of 34 dietary polyphenols and their variations according to diet and other lifestyle factors were measured by tandem mass spectrometry in 475 adult participants from the European Prospective Investigation into Cancer and Nutrition (EPIC) cross-sectional study. A single 24-hour urine sample was analysed for each subject from 4 European countries. The highest median levels were observed for phenolic acids such as 4-hydroxyphenylacetic acid (157 µmol/24 h), followed by 3-hydroxyphenylacetic, ferulic, vanillic and homovanillic acids (20–50 µmol/24 h). The lowest concentrations were observed for equol, apigenin and resveratrol (<0.1 µmol/24 h). Urinary polyphenols significantly varied by centre, followed by alcohol intake, sex, educational level, and energy intake. This variability is largely explained by geographical variations in the diet, as suggested by the high correlations (r > 0.5) observed between urinary polyphenols and the intake of their main food sources (e.g., resveratrol and gallic acid ethyl ester with red wine intake; caffeic, protocatechuic and ferulic acids with coffee consumption; and hesperetin and naringenin with citrus fruit intake). The large variations in urinary polyphenols observed are largely determined by food preferences. These polyphenol biomarkers should allow more accurate evaluation of the relationships between polyphenol exposure and the risk of chronic diseases in large epidemiological studies.
Polyphenol Levels Are Inversely Correlated with Body Weight and Obesity in an Elderly Population after 5 Years of Follow Up (The Randomised PREDIMED Study)

Abstract: Overweight and obesity have been steadily increasing in recent years and currently represent a serious threat to public health. Few human studies have investigated the relationship between polyphenol intake and body weight. Our aim was to assess the relationship between urinary polyphenol levels and body weight. A cross-sectional study was performed with 573 participants from the PREDIMED (Prevención con Dieta Mediterránea) trial (ISRCTN35739639). Total polyphenol levels were measured by a reliable biomarker, total urinary polyphenol excretion (TPE), determined by the Folin-Ciocalteu method in urine samples. Participants were categorized into five groups according to their TPE at the fifth year. Multiple linear regression models were used to assess the relationships between TPE and obesity parameters; body weight (BW), body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR). After a five years follow up, significant inverse correlations were observed between TPE at the 5th year and BW (β = −1.004; 95% CI: −1.634 to −0.375, p = 0.002), BMI (β = −0.320; 95% CI: −0.541 to −0.098, p = 0.005), WC (β = −0.742; 95% CI: −1.326 to −0.158, p = 0.013), and WHtR (β = −0.408; 95% CI: −0.788 to −0.028, p = 0.036) after adjustments for potential confounders. To conclude, a greater polyphenol intake may thus contribute to reducing body weight in elderly people at high cardiovascular risk.
Table 3. Multiple linear regression analyses with obesity indexes and quintiles of TPE at the fifth year for male, female, and total participants.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>β</th>
<th>SE</th>
<th>Beta</th>
<th>Significance</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>BW (kg)</td>
<td>Male</td>
<td>Model 1</td>
<td>-1.446</td>
<td>0.440</td>
<td>-0.198</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Model 2</td>
<td>-1.259</td>
<td>0.440</td>
<td>-0.170</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Model 3</td>
<td>-0.959</td>
<td>0.461</td>
<td>-0.131</td>
<td>0.039</td>
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<tr>
<td></td>
<td>Female</td>
<td>Model 1</td>
<td>-1.103</td>
<td>0.415</td>
<td>-0.153</td>
<td>0.008</td>
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<tr>
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<td></td>
<td>Model 2</td>
<td>-0.756</td>
<td>0.415</td>
<td>-0.105</td>
<td>0.069</td>
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<td></td>
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<td>Model 3</td>
<td>-0.757</td>
<td>0.431</td>
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<tr>
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<td>Total</td>
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<td>-2.350</td>
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<td>-0.285</td>
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<td></td>
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<td>Model 2</td>
<td>-1.070</td>
<td>0.315</td>
<td>-0.130</td>
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<tr>
<td></td>
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<td>Model 3</td>
<td>-1.004</td>
<td>0.320</td>
<td>-0.124</td>
<td>0.002</td>
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<td>BMI (kg/m²)</td>
<td>Male</td>
<td>Model 1</td>
<td>-0.405</td>
<td>0.135</td>
<td>-0.179</td>
<td>0.003</td>
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<td></td>
<td></td>
<td>Model 2</td>
<td>-0.370</td>
<td>0.136</td>
<td>-0.164</td>
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<td>Model 3</td>
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<td>-0.344</td>
<td>0.156</td>
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<td>0.028</td>
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<td>Model 2</td>
<td>-0.296</td>
<td>0.160</td>
<td>-0.110</td>
<td>0.064</td>
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<td>Model 3</td>
<td>-0.332</td>
<td>0.163</td>
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<td>Total</td>
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<td>0.104</td>
<td>-0.118</td>
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<td>0.110</td>
<td>-0.131</td>
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<td>-0.320</td>
<td>0.113</td>
<td>-0.129</td>
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<td>WC (cm)</td>
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<td>-0.769</td>
<td>0.364</td>
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<td>0.034</td>
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<td>0.378</td>
<td>-0.087</td>
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<tr>
<td></td>
<td>Female</td>
<td>Model 1</td>
<td>-0.546</td>
<td>0.409</td>
<td>-0.078</td>
<td>0.183</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Model 2</td>
<td>-0.527</td>
<td>0.419</td>
<td>-0.075</td>
<td>0.209</td>
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<tr>
<td></td>
<td></td>
<td>Model 3</td>
<td>-0.701</td>
<td>0.434</td>
<td>-0.101</td>
<td>0.108</td>
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<tr>
<td></td>
<td>Total</td>
<td>Model 1</td>
<td>-1.500</td>
<td>0.296</td>
<td>-0.208</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
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<td>-0.721</td>
<td>0.293</td>
<td>-0.100</td>
<td>0.014</td>
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<tr>
<td></td>
<td></td>
<td>Model 3</td>
<td>-0.742</td>
<td>0.297</td>
<td>-0.104</td>
<td>0.013</td>
</tr>
<tr>
<td>WHtR (cm/m)</td>
<td>Male</td>
<td>Model 1</td>
<td>-0.340</td>
<td>0.220</td>
<td>-0.093</td>
<td>0.124</td>
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<tr>
<td></td>
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<td>Model 2</td>
<td>-0.385</td>
<td>0.223</td>
<td>-0.105</td>
<td>0.085</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Model 3</td>
<td>-0.258</td>
<td>0.229</td>
<td>-0.072</td>
<td>0.261</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Model 1</td>
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<td>Model 2</td>
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<td>0.282</td>
<td>-0.070</td>
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<td>Model 3</td>
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What Might the 21st Century Functional Health Assessment Look Like?

- Polygenic Analysis of SNPS of Family of Methylation Related Genes
- Tissue Specific Genomic Methylation Profile
- Genomic Stability Assessment
- Telomere Length
- Metagenome Analysis
- Inflammation Biomarkers
- Oxidative Stress Biomarkers
- Urinary Polyphenol Analysis