From Populations to Molecules
What’s new in medical science

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Investigating Future Mortality: Blending Medical & Actuarial Science for Life & Longevity Risk Management

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A Brief History of Wine

And Human Health
Wine’s Medicinal Past

Early History

Serendipitous Discovery

Anecdotal Evidence
2200 BC

Fall from Grace

Step 1: A glass with a friend
Step 2: A glass to keep the cold out
Step 3: A glass too much
Step 4: Drunk and riotous
Step 5: The summit attained
Jolly companions.
A confirmed drunkard
Step 6: Poverty and disease
Step 7: Forsaken by friends
Step 8: Desperation and crime
Step 9: Death by suicide

French Paradox

Interaction and Side Effects
19th and 20th Century

Complex Interactions
Population – Individual–Molecule
1990’s to Present
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Complex Interactions
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1990’s to Present
Is Wine Good for my Health?

1. Do you already drink?
   - Yes
   - No, Don’t Start

2. Do you have a history of addiction, head and neck, breast, or digestive cancers?
   - Yes
   - No

3. Are you Male?
   - Yes
   - No

4. Are you over 50?
   - Yes
   - No

5. Do you exercise and have normal BMI and cholesterol?
   - Yes
   - No, Jury’s still out. Depends on individual genetics

6. Do you have a family history of breast cancer?
   - Yes
   - No

7. Do you have a variant ALDH2 gene?
   - Yes
   - No, inability to metabolism alcohol

8. Any history of CVD or family history of CVD?
   - Yes
   - No

9. Drinking is associated with increased cancer risk

10. Moderate consumption recommended

11. Alcohol will increase risk
Old Biomedical Paradigm

Epidemiology and Public Health

Population

Environment

Individual

Medicine

Molecular

Genetic

Cellular

Biotechnology
The Promise of Genetic Medicine

Population

Environment

Individual

Molecular

Genetic

Cellular
## The Vision of Genetic Medicine

<table>
<thead>
<tr>
<th>Condition</th>
<th>Your percentile (^1)</th>
<th>Your estimated lifetime risk (^2)</th>
<th>Average lifetime risk (^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal aneurysm</td>
<td>75% - 100%</td>
<td>1.9%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>74% - 98%</td>
<td>37%</td>
<td>17%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>57% - 75%</td>
<td>25%</td>
<td>23%</td>
</tr>
<tr>
<td>Brain aneurysm</td>
<td>75% - 100%</td>
<td>1.1%</td>
<td>0.90%</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>68% - 70%</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>5% - 7%</td>
<td>0.02%</td>
<td>0.11%</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>59% - 64%</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>81% - 83%</td>
<td>0.75%</td>
<td>0.54%</td>
</tr>
<tr>
<td>Diabetes, type 2</td>
<td>2% - 4%</td>
<td>18%</td>
<td>30%</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>77% - 100%</td>
<td>7%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Graves' disease</td>
<td>39% - 64%</td>
<td>2.4%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Heart attack</td>
<td>71% - 87%</td>
<td>28%</td>
<td>25%</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>0% - 62%</td>
<td>extremely low risk</td>
<td>N/A</td>
</tr>
<tr>
<td>Lactose intolerance</td>
<td>0% - 95%</td>
<td>low risk</td>
<td>N/A</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>33% - 80%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Lupus</td>
<td>46% - 48%</td>
<td>0.18%</td>
<td>0.26%</td>
</tr>
<tr>
<td>Macular degeneration</td>
<td>39% - 48%</td>
<td>1.3%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>0% - 61%</td>
<td>1.6%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>75% - 93%</td>
<td>1.3%</td>
<td>0.77%</td>
</tr>
</tbody>
</table>

*Example Report taken from Navigencs
The Reality of Genetic Medicine

Population

Epigenomics
Proteomics

Molecular

Genetic
Transcriptomics
Structural Genomics

Exposome
Nutrigenomics

Individual

Cellular

Environment

Toxicogenomics
Developments across the Medical Landscape

1) Sirtuins
2) Cardiac Stem Cells
3) One drug to shrink tumors
4) Awakening HIV
5) Technology and Medicine

- Retardation of Aging
- Regenerative Medicine
- CVD
- Medical Intervention
- Cancer
- Lifestyle
- Health Environment

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Retardation of Aging:
A Step Back for Sirtuin

- Encompasses discoveries that directly affect the human aging process, and decrease the biological age relative to the chronological age.
- Not likely to have any near term impact, but could cause a paradigm shift in longevity and ageing in the future.
In 1999 it was discovered that an extra copy of the sirtuin gene led to an up to 30% increase in the longevity of yeast.

Similar effects were found in fruit flies, the roundworm (C. elegans) and mice.

The possibility of reducing aging and age associated diseases became closer reality in 2003 when revesterol (the compound in red wine) was discovered.

In 2011 a group of researchers lead by a team at the University of London cast serious doubt on the relationship when they redid the experiments controlling for genetic effects and transgene insertion.
Medical Intervention (CVD) and Regenerative Medicine: Cardiac Stem Cells Treat Heart Failure

- CVD is the number one cause of death in the UK, but has the most room for mortality improvement with current technologies.
- Regenerative medicine encompasses techniques for repairing and renewing cells and organs, like stem cell therapy and nanomedicine and could lead to another wave in CVD improvement.
2011 saw the first phase 1 clinical trial of cardiac stem cells in patients with heart failure.

Cardiac stem cells were taken from the patients during bypass surgery purified and then injected back several months later.

The 14 patients with severe heart failure patients receiving cardiac stem cells showed a 30% decrease in dead heart muscle after one year compared with no improvement in controls.

Medical Intervention (Cancer):
A Drug to Shrink All Tumors

- Cancer is poised to become the leading cause of death as CVD continues to decline.
- The multitude of etiologies make it a much more difficult problem to solve than CVD, but medical advances are turning some cancer into manageable conditions and miracle cures are becoming a more common occurrence.
A decade ago a Stanford researcher discovered that leukemia cells produce high levels of the protein CD47 relative to normal cells.

CD47 is used by healthy blood cells and tumor cells as a “Don’t eat me sign” for macrophages.

CD47 is produced by every primary tumor they have tested.

In just published anti-CD47 mouse trials implanted with human tumors:
- 10 of 10 untreated mice had cancer that spread to their lymph nodes compared to only one of the 10 mice treated with anti-CD47.
- Colon cancers transplanted into the mice shrank on average to less than one-third of their original size.
- In five mice with breast cancer tumors all of the animals remained cancer-free 4 months after the treatment.
Antibiotics, vaccines, and hygiene have revolutionized human mortality from infectious disease, but recently we have discovered the relationship is far more complex and infectious agents are deeply embedded in human evolution.
Retroviruses are adept at hiding in cells and integrating themselves into the genome

Human endogenous retroviruses, remnants of old viral infections, make up 5-8% of the human genome*

Latent HIV turns off the expression of its genes and just exists as viral DNA integrated into the chromosome host cell

Cancer drug lures HIV out of its hiding place, so it can be targeted by antiviral compounds

Our lifestyle choices and the environment in which we live is still the most important factor in individual and population health.

Genetic pre-determinism is only causal for rare disease and fundamentally we control how we interact with our health.
Private genetic screening company identifies 2 genetic variations present in Parkinson's disease in only a year and a half

Gamers deciphered the three-dimensional structure of a protein that allows the AIDS virus to infect cells

The rise of the quantified self movement

Smartphones ubiquitous in medicine

- 80% of physicians are carrying smartphones in 2012
- Consumers are using smartphones for health communication, diagnosis, and tracking
Observational Medicine in the Technological Era

Cognitive Function Score

Month of Observation

Illness

Doctor’s Visits
A Crystal Ball

- Blockbuster drugs coming off patent continue the changing model of drug development
- Miracle cures will become more common for small populations
- More cancers and chronic diseases will be found to have infectious disease origins
- Cancer will be increasingly treated with vaccines
- Revolutions in treatment will focus of life quality
- Doctors will become less important in medicine