

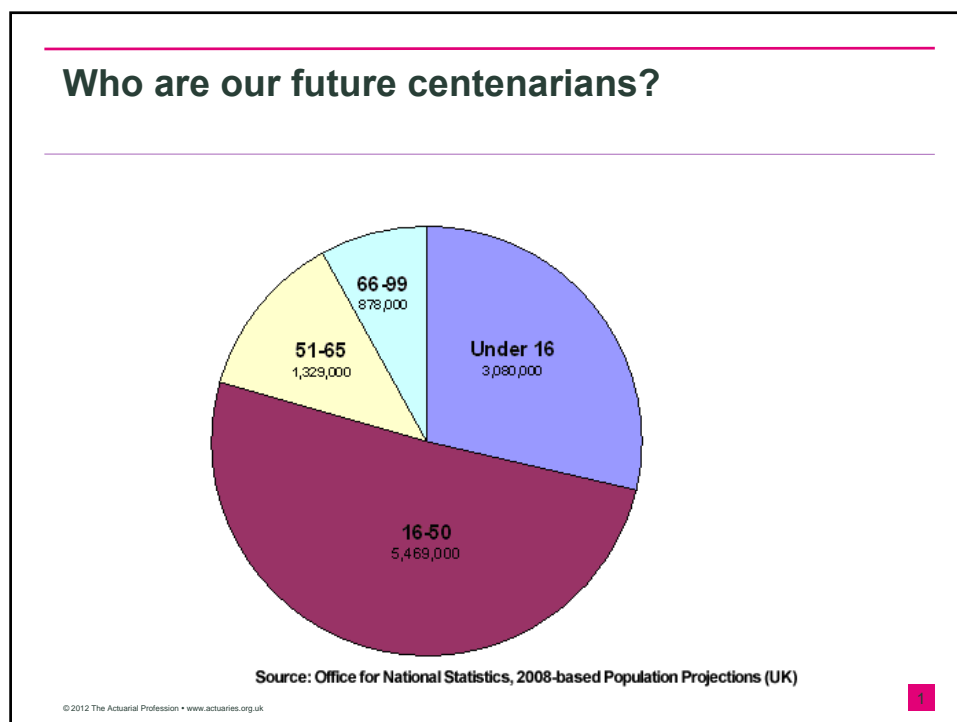
**The Actuarial Profession**  
making financial sense of the future

Highlights of the Life Conference 2012 seminars  
John Wilden, Global Health Futures  
Daniel Ryan, Swiss Re

# Who will live to 100?

7 March 2013

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## Why you might live to 100 (or not)

- GENES
- BEHAVIOUR
- Environment
- Societal pressures
- Accidents
- HEALTHCARE
- Stochastic variation / chance
- Historical trends
  - New England Centenarian study suggested dominant impact of genes in extreme longevity

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## Individual thought and decision-making



Mindspace report published in March 2010

Provides the operating framework for applying behavioural insight to public policy

*Behavioural Insights Team* established in the UK Prime Minister's Office

Paul Dolan, Michael Hallsworth, David Halpern, Dominic King, Ivo Vlaev

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## Concept of MINDSPACE explained



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## Importance of the messenger

### Advisor's Expertise

- People learn from experience to pay more attention to advisors who have given good advice in the past.
- Consumers are more influenced by better advisors
- Advisors have less influence on more experienced and knowledgeable consumers

### Advisor's Trustworthiness

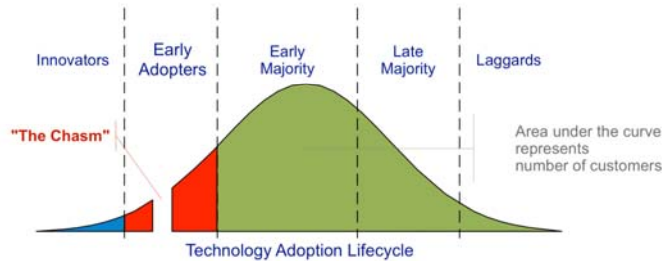
- People take more advice from trusted advisors
- Greater trust in advisors judged to have:
  - **Similar values**
  - **Shared goals**
  - **Similar intentions**
- Being of the **same sex and age** increases the attention paid to an advisor

### Advisor's Personality

- Consumers are more influenced by **confident** advisors irrespective of advice quality
- **Dissenting** advisors are discounted unless they are historically better than the consensus
- People are better at taking advice when advisors are more **distinct** from one another

## Our divided attitudes to change

### Reactions of populations to emerging technology

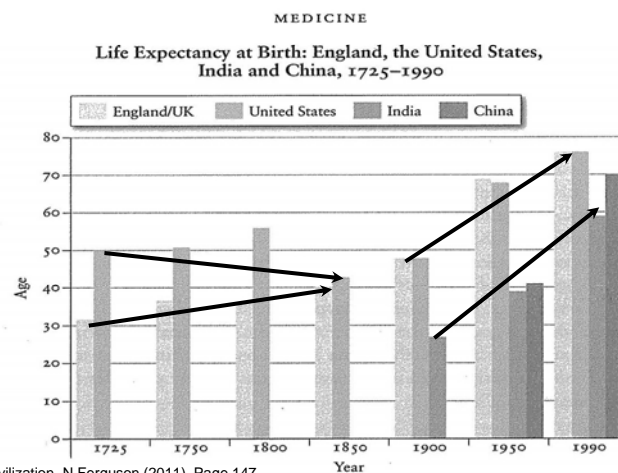


- Health technology is a discontinuous innovation
- Chasm exists because of characteristics of "early majority" or pragmatists
  - desire for integrated solutions at reasonable price
  - focus on delivery of existing healthcare
  - appetite for standard, tested solutions

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## Increased longevity is a 20<sup>th</sup> century phenomena



Source: Civilization, N Ferguson (2011), Page 147

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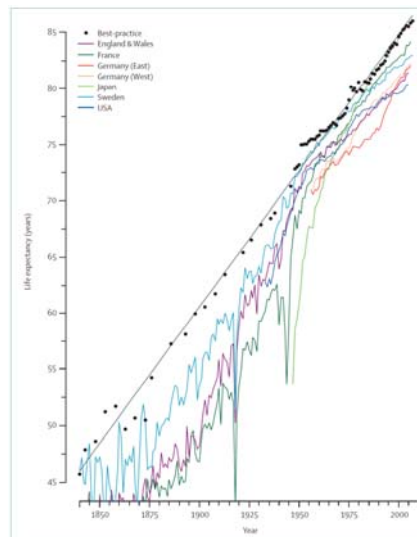
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## "Forecasting" longevity in 20<sup>th</sup> century

**"If the pace of increase in life expectancy in developed countries over the past two centuries continues through the 21st century, most babies born in 2000 in France, Germany, Italy, the UK, the USA, Canada, Japan, and other countries with long life expectancies will celebrate their 100th Birthdays".**

Professor Christensen  
Danish Ageing Research Centre,  
Denmark.  
Professor Vaupel  
Max Planck Institute, Germany.

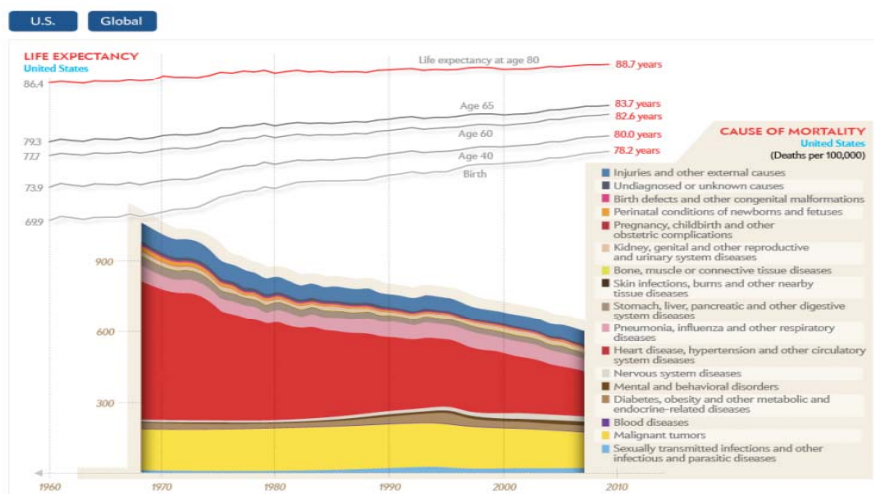
Source: Lancet: October 2009 (374: 1196)



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## Decomposition of changes in life expectancy USA men (1960-2010)



Source: Scientific American Sept 2012

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## Increasing longevity in 21<sup>st</sup> century

### The continued development of 2<sup>nd</sup> era of globalisation

- Economic prosperity, improved communication, transport
- Food production, water supply, air pollution
- Less smoking, improved diet, exercise
- Governance of financial institutions

### Eradication of disease

- A Biological Foundation of Cure

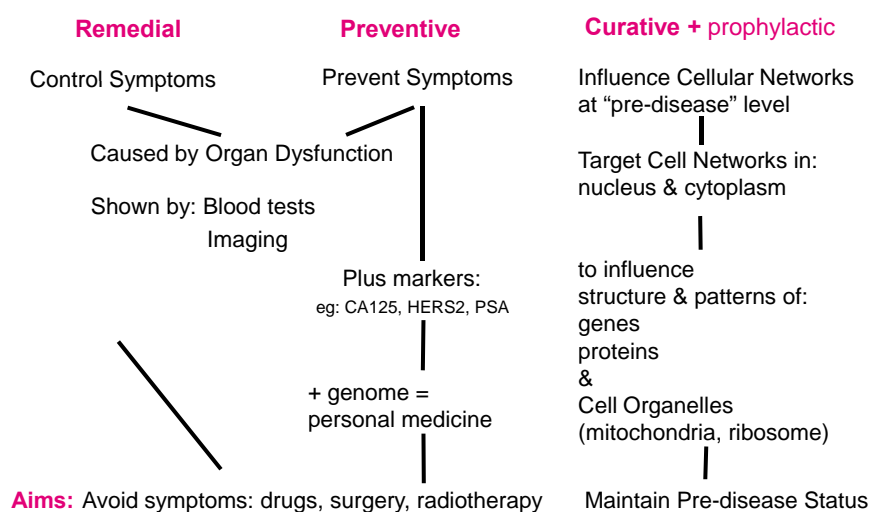
### Delivery of healthcare

- Nation: bound
- Efficient: effective & productive healthcare

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## The definitions of healthcare



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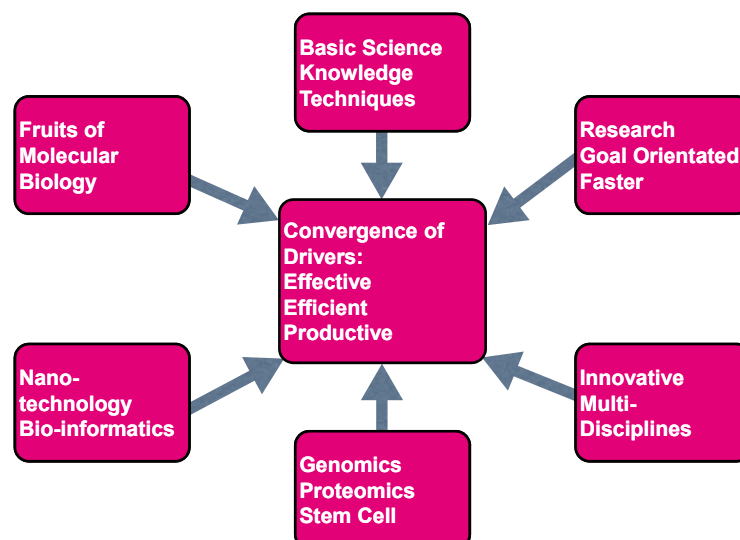
## Burdens of disease: remedial, preventive & curative

|                                     | Remedial                          | Preventive                        | Curative<br>Cell Network Level |
|-------------------------------------|-----------------------------------|-----------------------------------|--------------------------------|
| <b>Heart Attacks &amp; Strokes:</b> | >70% reduction in lumen of artery | <70% reduction in lumen of artery | ?                              |
| <b>Common Cancers:</b>              | >80% life cycle                   | < 80% life cycle                  | ?                              |
| <b>Diabetes:</b>                    | >90% insulin cells destroyed      | <90% insulin cells destroyed      | ?                              |
| <b>Duration of Practice</b>         | 25 Centuries                      | 3-4 Decades                       | ? 1-2 years                    |
|                                     | Vaccination: 2 Centuries          |                                   |                                |

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## Future innovative healthcare drivers



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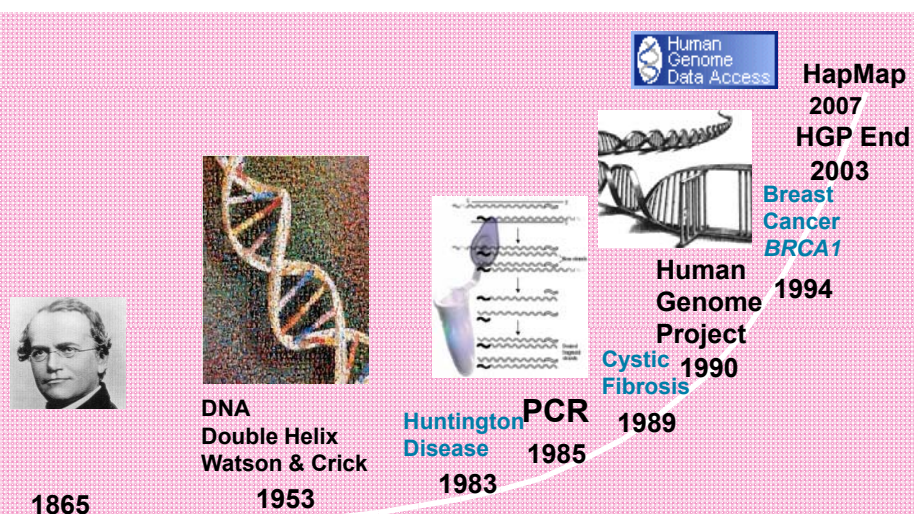
## The futures of separate cell types and organs

| Cell types               | Stem cells<br>Experimental | Stem cells<br>Clinical implantation |
|--------------------------|----------------------------|-------------------------------------|
| Skin                     | Yes                        | Yes                                 |
| Cartilage                | Yes                        | Yes                                 |
| Arteries & Veins         | Yes                        |                                     |
| Trachea                  | Yes                        | Yes                                 |
| Eye (Retinal Cells)      | Yes                        | Yes                                 |
| Pancreas (insulin cells) | Yes                        | Yes                                 |
| Brain (dopamine cells)   | Yes                        | Yes                                 |
| Red Blood Cells          | Yes                        | Yes                                 |
| Lung                     | Yes                        |                                     |
| Heart                    | Yes                        |                                     |
| Liver                    | Yes                        |                                     |
| Small intestine          | Yes                        |                                     |

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## Genetic information & technology have grown exponentially

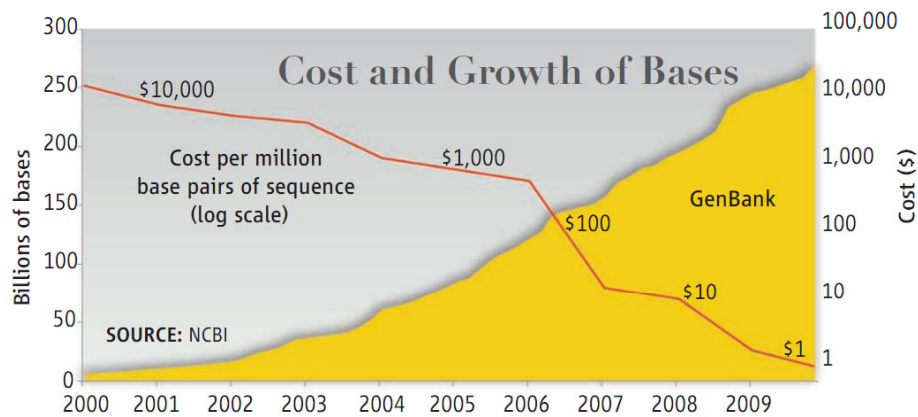


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## DNA sequencing costs are decreasing at exponential rates



Source: E. Pennisi Science 2011 331; 666-8

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## Genome-wide association to identify genes involved in disease

| Cancer site      | Relative Risk $\geq 5.0$<br>Family studies | Relative Risk $\geq 1.5$ and $> 5.0$<br>Resequencing | Relative Risk $\geq 1.01$ and $> 1.5$<br>Genome-wide association studies         |
|------------------|--|--|--|
| Lung             | RB1, TP53                                  |  | rs1051730, rs8034191 (CHRNA3, CHRNA4, CHRNA5)                                    |
| Breast           | BRCA1, BRCA2, TP53, PTEN, SK11, CDH1       | CHEK2, ATM, PALB2, BRIP1                             | CASP8, FGFR2, MAP3K1, 8q24, 5p, TOX3, 2q, 6q22, LSP1                             |
| Colon and rectum | APC, MLH1, MSH2, MSH6, PMS2                | APC (I1307K), BLM                                    | MUTYH, CASP8, 8q24, 8q23 (EIF3H), 10p14, 11q23, CRAC1, SMAD7                     |
| Prostate         | BRCA2                                      | 8q24   | rs6501455, rs721048, NBS1, EHBP1, TCF2, CTBP2, JAZF1, MSMB, LMTK2, KLK3, SLC22A3 |
| Pancreas         | BRCA2, CDKN2A, STK11, TP53, PRSS1, SPINK1  | BRCA1, MSH2, MLH1                                    |  |

Source: Foulkes W; N Engl J Med; 2008;359:2143-2153

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## Increasing numbers of genetic tests in clinical practice

September 2011

### GeneTests

2,433 disease-genes  
1,171 tests in clinics  
602 laboratories  
541 GeneReviews

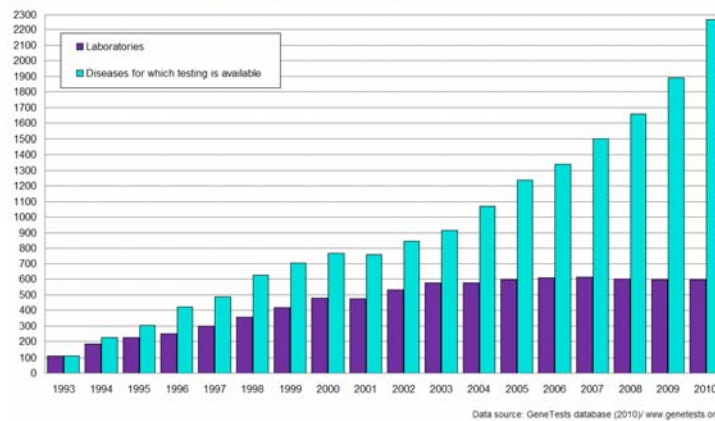
### ACCE Framework

- Analytical validity
- Clinical validity
- Clinical utility
- Ethical, legal, social

### UKGTN

541 genetic diseases  
tested in UK Genetic  
Testing Network

### GeneTests: Growth of Laboratory Directory



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## 23andme – Colorectal cancer marker

### Karen Jacobs

0.21 out of 100

people of European ethnicity who share Karen Jacobs's genotype will get Colorectal Cancer between the ages of 30 and 49.

### Average

0.26 out of 100

people of European ethnicity will get Colorectal Cancer between the ages of 30 and 49.

### 8q24 region

Marker: rs6983267

This SNP occurs in a hypothetical gene called LOC727677. Little is known about the gene's function; however, it is located in a region of DNA that often acquires extra copies in colorectal cancers. This suggests that the SNP is linked to a change in the activity of a nearby gene that influences cancer development.

One group found that the riskier version of this SNP is associated not only with an increased risk of colorectal cancer, but also with formation of the precancerous adenomatous polyps. This suggests that the SNP is linked to a gene that affects the very early stages of colorectal cancer.

### Citations

Haiman et al. (2007). "A common genetic risk factor colorectal and prostate cancer." *Nat Genet* 39(8):954-6.

Towninson et al. (2007). "A genome-wide association scan of tag SNPs identifies a susceptibility variant for colorectal cancer at 8q24.21." *Nat Genet* 39(8):964-968.

Zanke et al. (2007). "Genome-wide association scan identifies a colorectal cancer susceptibility locus on chromosome 8q24." *Nat Genet* 39(8):969-994.

### Genes vs. Environment

35 %  
Attributable to  
Genetics

The heritability of colorectal cancer is estimated to be 35%. This means that environmental factors contribute more to differences in risk for this condition than genetic factors. Genetic factors that play a role in colorectal cancer include both unknown and known factors. Known factors include rare mutations in the MSH2 and MLH1 genes that appear in familial cases of colon cancer (which 23andMe does not genotype), and the SNP we describe here. Other factors include a history of previous colorectal cancer, colorectal polyps, or inflammatory bowel disease, being an Ashkenazi Jew or of African descent, a diet high in animal fat, physical inactivity, obesity, smoking, heavy alcohol use, and diabetes. (Note: The contribution of the SNP reported by 23andMe to inherited colorectal cancer risk is minor. If you have a strong family history of early-onset colon cancer, you should consider mutation testing of MSH2 and MLH1.) (sources)



Source: <http://www.23andme.com>

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## Further advances in genomic sequencing Oxford Nanopore

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## The futures of innovative technologies Critical periods & pivotal phases

### Critical periods in laboratory research

**Stem cell:** Induced pluri-potent stem cell from adult cell Gurdon 1962 Yamanaka 2006  
**Synthetic biology:** Mycoplasma Mycoides: Venter & Smith. 1995 - 2010

**Gene mapping:** Encode: 80% of the human gene is Important. 2007 - 2012  
 Nanopore gene mapping 1990s

**Convergence technologies:**  
 Opto-genetics for neurological disease. August 2012

### Critical periods in clinical research

**Low tech:** Single use self destructible syringes for vaccination

**High tech:** Molecular imaging: PET scan Florbetapir F18 for imaging amyloid  
 Gene mapping of foetal cells from mother's blood  
 Single gene therapy for multiple melanoma

**Convergence technologies:**  
 Nano-tubule + stem cells to produce heart muscle  
 Oxford Nanopore 2012. Gene mapping for \$1,000  
 Genes + Nanotechnology = Vaccines for hypertension

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## Futures of hypertension

### Remedial Healthcare

#### Hypertension

Monitor & control by drugs  
Investigate & removal of  
causes:

Vascular

Hormonal

Tumours etc

#### After Heart Attack

Medical: drugs to help strengthen the heart

Surgical: stents for coronary arteries

Stem cells to preserve & restore heart muscle

Heart transplantation

#### After Stroke

Carotid bifurcation

Endarterectomy

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## Futures of hypertension

### Preventive Healthcare

#### Heart & Arteries

Monitor blood pressure, sugar, lipids

Image coronary arteries for narrowing and atheroma:

CT scan measurement of cardiac calcification index

Venous MRI coronary angiography

#### Brain

Monitor blood pressure, sugar, lipids

Image carotid, vertebral & cerebral Arteries

Doppler ultrasound

Medical & surgical treatments as  
required

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## Futures of hypertension

### Curative Healthcare

#### Vaccinate against hypertension

Modifying kidney and brain regulatory systems  
Renin - Angiotensin - Aldosterone System

#### Modify heart & blood vessels

Modify elastic properties of vessels: remodel  
extracellular matrix  
Modify blood vessel surfaces eroded by blood flow

**"All of above in experimental stages"**

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## Futures of diabetes

### Remedial Healthcare

#### Patient

Frequent blood sugar analysis  
Diet  
Weight control

#### Medical Profession

Monitoring of essential organs  
Supervision of treatment

#### Medical Treatments

Oral hypoglycaemic drugs

Administration of insulin:

Injection: subcutaneous or implantable pump, sugar with auto-regulation

Oral, nasal, buccal: nano-delivery of Insulin

Stem cell therapy

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## Futures of diabetes

### Preventive Healthcare

Family history

Gene mapping: lipids, mutations, immune profiles

In utero testing: maternal blood

Blood sugars

Pancreatic measurements of insulin cells

Mitochondrial gene mapping

**"Some of above only in experimental stages"**

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## Futures of diabetes

### Curative Healthcare

Genomic conversion of Alpha (Exocrine Cells) to Beta Insulin for Types I & II

Genomic modification of mitochondria for Types I & II

Genomic delivery of immunotherapy for Type I

Irisin release for obesity

Genomic delivery via viral, nano-particles or synthetic biology

**"All of above in experimental stages"**

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## In Summary

**Build on 20<sup>th</sup> century success in public health**

**Remedial model of healthcare is unsustainable**  
– not just economically

**Biological foundations of cure are important part of 21<sup>st</sup> century longevity**

**Most important components of curative healthcare**  
Critical periods & Pivotal phases  
Effective & commoditisable & fair value

**Who is going to implement?**

**Who is going to benefit?**

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Multi-author. 400 researchers, over 300 institutions, across 50 countries

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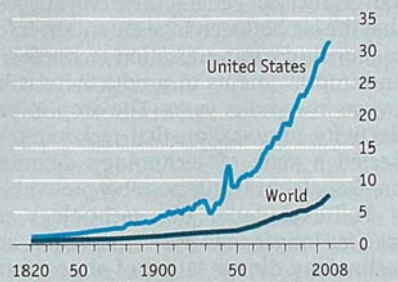
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## Further thoughts on the pace of progress IT & productivity

### Rising tide

GDP per person, 1990 \$'000\*

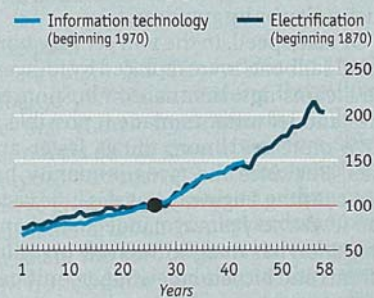


Source: Angus Maddison,  
University of Groningen

\*At purchasing-power parity

### Echoing electrification

US labour productivity, year 26=100

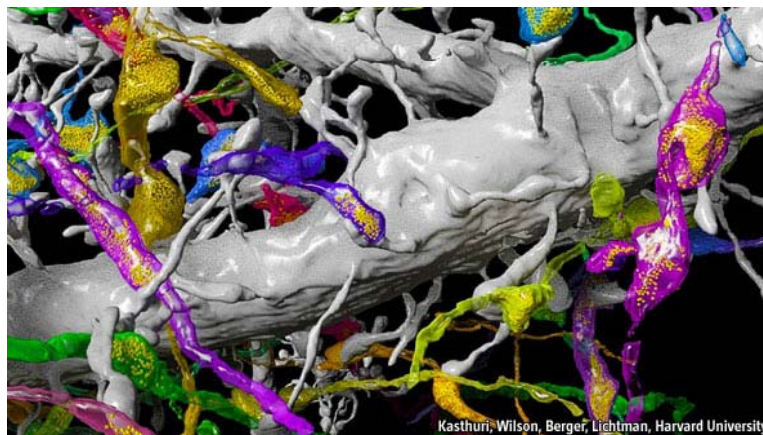


Source: Chad Syverson, University of Chicago

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## Further thoughts on the pace of progress Brain activity map



Kasthuri, Wilson, Berger, Lichtman, Harvard University

Source: Economist 23.02.13, Jeff Lichtman, Harvard, 100 microns wide, from 2,000 slices, Terabyte data

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## Questions or comments?

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Expressions of individual views by members of The Actuarial Profession and its staff are encouraged.

The views expressed in this presentation are those of the presenters.

