If we knew then what we know now: how Medical Advances have Influenced Longevity in the Past, Along with Expectations for the Future

Daniel Ryan
Head of Life & Health R&D
Swiss Re

19 June 2014
How well are we predicting future UK longevity

Period life expectancy

Projection base year


19 June 2014
Understanding past changes in CHD deaths

Risk Factors worse +13%
  Obesity (increase)  +3.5%
  Diabetes (increase)  +4.8%
  Physical activity (less)  +4.4%

Risk Factors better -71%
  Smoking  -41%
  Cholesterol  -9%
  Population BP fall  -9%
  Deprivation  -3%
  Other factors  -8%

Treatments -42%
  AMI treatments  -8%
  Secondary prevention  -11%
  Heart failure  -12%
  Angina: CABG & PTCA  -4%
  Angina: Aspirin etc  -5%
  Hypertension therapies  -3%
Debating the evidence for further reductions

The National Institute for Health and Care Excellence published draft guidance in February calling for their use to be extended to save more lives.

It could mean another five million people in England and Wales using them on top of seven million who already do.

Source: National Institute of Health & Clinical Excellence

Source: BBC News
Colour palette for PowerPoint presentations

- **Dark blue**
  - R17 G52 B88

- **Gold**
  - R217 G171 B22

- **Mid blue**
  - R64 G150 B184

Secondary color palette

- **Light grey**
  - R220 G221 B217

- **Pea green**
  - R121 G163 B42

- **Forest green**
  - R0 G132 B82

- **Bottle green**
  - R17 G179 B162

- **Cyan**
  - R0 G156 B200

- **Light blue**
  - R124 G179 B225

- **Violet**
  - R128 G118 B207

- **Purple**
  - R143 G70 B147

- **Fuscia**
  - R233 G69 B140

- **Red**
  - R200 G30 B69

- **Orange**
  - R238 G116 B29

- **Dark grey**
  - R63 G69 B72
How fit for purpose are our models?  
- experience for Dutch men

Actual Dutch improvements to 1992 then model projections to 2007\(^1\)

\(^1\) Projected using an Age-Period-Cohort (APC) model

Actual Dutch improvements to 1992 then model projections to 2007

Source: HMD, Swiss Re calculations

19 June 2014
How fit for purpose are our models? - experience for Dutch men

Actual Dutch improvements to 2007

Source: HMD, Swiss Re calculations

19 June 2014
Longevity catalysts working group

The Longevity Catalysts Working Group is the Actuarial Profession to answer the question: “What future events are we aware of that are likely to be coupled with a significant impact on human lifespan?” The situation is thus complex, yet this group aims to illustrate the even greater imperfections of ignoring future catalyst events that are now known.

Longevity Catalysts summary:
- Introduction of New Medicine
- Past Longevity Catalysts
- Breast Cancer
- Classification
- Longevity Catalysts summary
- Use of novel diagnostic biomarkers
- KRAS targeted cancer treatment
- Bowel cancer screening
- Stem cell therapy & Parkinson’s disease
- Polypharmacy
- Universal Influenza Vaccine
- Catalyst evolution

Classification:
Each catalyst is classified into one of eight broad groups.

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Aiming for a more holistic view of longevity

General drivers to diagnosis and survival

- Individual risk factors
  - Age, gender, diet, smoking
  - Taxes and restrictions
  - Current treatments (bupropion)
  - Future treatments (vaccines)

- Healthcare funding
  - Public vs private funding
  - Patient advocacy groups
  - Allocation of resources towards cure vs prevention

- Patient interaction
  - Health awareness
  - Trust and confidence
  - Use of clinical guidelines

- Research & development
  - Public/commercial sponsors
  - Regulators’ attitude
  - Disease-focused approach vs global impact of ageing

Disease types and disease progression

- Healthy
- Circulatory Stroke, angina, heart attack
- Respiratory Chronic obstructive pulmonary disease
- Multiple diseases
- Death

Factors involved in assessing specific example disease

- Risk factors
  - Family history
  - Obesity
  - Having children later in life
  - Not breast feeding

- Cancer
  - Lung, colorectal, prostate, breast

- Early detection
  - Digital mammography
  - MRI for high-risk
  - Gail algorithm (own factors)
  - Klaus algorithm (family history)

- Medical innovations
  - Tumour profiling
  - Clinical trials – Kadcyla from Phase III EMILIA

- Current approaches
  - Targeting DCIS
  - Surgery with node follow-up
  - Adjuvant radiotherapy
  - Herceptin, Tamoxifen

General drivers to diagnosis and survival

- Individual risk factors
- Healthcare funding
- Patient interaction
- Research & development

Disease types and disease progression

- Healthy
- Circulatory Stroke, angina, heart attack
- Respiratory Chronic obstructive pulmonary disease
- Multiple diseases
- Death

Factors involved in assessing specific example disease

- Risk factors
- Cancer
- Early detection
- Medical innovations
- Current approaches

19 June 2014
Understanding potential of cancer treatments

- Kadcyla for HER2-positive, late-stage metastatic breast cancer
- EMILIA phase III trial results

- FDA approval Feb. 2013; EMA approval Nov. 2013
# The true cost of pharmaceutical research

<table>
<thead>
<tr>
<th>Company</th>
<th>Ticker</th>
<th>Number of drugs approved</th>
<th>R&amp;D Spending Per Drug ($Mil)</th>
<th>Total R&amp;D Spending 1997-2011 ($Mil)</th>
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Sources: InnoThink Center For Research In Biomedical Innovation; Thomson Reuters Fundamentals via FactSet Research Systems

19 June 2014
Understanding the drivers of future longevity
- common risk factors across diseases

GENES

ENVIRONMENT

HEALTHCARE

BEHAVIOUR

SOCIETAL PRESSURES
## Risk factors linking across disease

Global Burden of Disease

### Table of Risk Factors

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<tr>
<th>Risk Factor</th>
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<th>Western Europe</th>
<th>Australasia</th>
<th>High-income North America</th>
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<th>South Asia</th>
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<th>Central Europe</th>
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19 June 2014
Understanding the drivers of future longevity
- transition from remedial to curative medicine

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19 June 2014
If we knew then what we know now: how Medical Advances have Influenced Longevity in the Past, Along with Expectations for the Future

Aubrey de Grey
Chief Science Officer
SENS Research Foundation
aubrey@sens.org  http://www.sens.org/

19 June 2014
The aging population

Source: UN World Population Prospects 2008

* Source: http://esa.un.org/wpp/unpp/panel_population.htm
If historical rates continue, US healthcare spending will be 34% of GDP by 2040. Source: http://www.whitehouse.gov/administration/eop/cea/TheEconomicCaseforHealthCareReform

In 2010, the US spent $1.186 trillion on healthcare for people 65+. Source: http://sambaker.com/econ/classes/nhe10/
Most infectious diseases have been easily prevented

- Sanitation
- Vaccines
- Antibiotics
- Carrier control

Age-related diseases have not. Why not?
Well… what is ‘aging’, exactly?

Aging is:

The life-long accumulation of “damage” to the body that occurs as an intrinsic side-effect of the body’s normal operation.

The body can tolerate some damage, but too much of it causes disease and disability.
Age-related diseases are caused by aging!

Thus, they are:

- widespread now that infections are “rare”
- staggeringly costly
- universal if you live long enough
- not medically curable, in the strict sense

But they, and aging itself, are nonetheless:

- medical problems
- medically preventable in principle
## ARDs and aging: conventional view

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<tr>
<th>Diseases</th>
<th>Aging</th>
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### ARDs and aging: correct view

<table>
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<th>Diseases</th>
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</table>
Even though 90% of US deaths and at least 80% of US medical costs are caused by aging:

- National Institutes of Health budget (M) ~30,000
- National Institute of Aging budget ~1,000
- Division of Aging Biology budget ~150
- Spent on translational research (max) ~10
- SENS Research Foundation budget ~5
How age-related disease is addressed today

Gerontology

Metabolism → Damage

Geriatrics

Damage → Pathology
Targeting pathology: tricky

presbycusis
osteoporosis
osteoarthritis
autoimmunity
grey hair
presbyopia
cataract
glaucoma
temporal arteritis
polymyalgia rheumatica
wringling
Alzheimer’s disease
Pick’s disease
corticobasal degeneration
progressive supranuclear palsy
Parkinson’s disease
multiple system atrophy
dementia with Lewy bodies
sarcopenia
glomerulonephritis
senile cardiac amyloidosis
atherosclerosis
arteriosclerosis
age-related macular degeneration
cardiomyopathy
diastolic heart failure
cancer
systemic inflammation
oxidative stress
reduced coronary blood flow
loss of cardiac reserve
andropause
thymic involution
reduced plasma renin activity
reduced aldosterone
reduced melatonin diurnal rhythm

reduced light adaptation
reduced ethanol metabolism
altered drug pharmacokinetics
somatopause
loss of cardiac adaptability
incontinence
impaired wound healing
idiopathic axonal polyneuropathy
autonomic neuropathy
arrhythmia
chronic obstructive pulmonary disorder
benign prostatic hypertrophy
menopause
leukoaraiosis
stroke
vascular dementia
frontotemporal dementia
immunosenesence
anosmia
cachexia
anorexia of aging
systolic hypertension
ageusia
erectile dysfunction
orthostatic hypotension
impaired adaptive beta-cell proliferation
fibroblast collapse
anergic T-cell clones
cellular senescence
vascular calcification
impaired transdermal absorption
impaired thermoregulation
reduced tactile acuity
impaired vasoconstriction
loss of neuromuscular junctions
delayed withdrawal reflex

impaired pH maintenance
reduced chemical clearance
altered dermal immune cell residence and function
aberrant allergic and irritant reactions
loss of skin elasticity
impaired vitamin D synthesis
reduced renal reserve
renal cortex atrophy
gut dysbiosis
loss of jejunal villus height
impaired response to vaccination
impaired thirst
lentigo senilis
thinning hair
impaired proprioception
impaired balance
reduced vital capacity
reduced cardiorespiratory endurance
impaired sweat response
impaired blood distribution
nutrient malabsorption
diverticular disease
presbyphagia
increased reflux
alveolar loss
neuronal loss
senile emphysema
degenerative disc disease
joint calcification
pinalal calcification
aberrant differentiation
gait instability
frontal demyelination
axonal atrophy
impaired functional connectivity
impaired working memory
Targeting metabolism: also tricky
Claim: unlike the others, the maintenance approach can deliver a big extension of human healthy lifespan quite soon.
Comparison: car maintenance
# Categorizing damage

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<th>Details</th>
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</thead>
<tbody>
<tr>
<td>Cell loss, cell atrophy</td>
<td></td>
</tr>
<tr>
<td>Division-obsessed cells</td>
<td></td>
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<tr>
<td>Death-resistant cells</td>
<td></td>
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<tr>
<td>Mitochondrial mutations</td>
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<tr>
<td>Intracellular junk</td>
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<td>Extracellular junk</td>
<td></td>
</tr>
<tr>
<td>Extracellular matrix stiffening</td>
<td></td>
</tr>
</tbody>
</table>

No new type of damage confirmed since 1982

And, I’ve said so without challenge since 2002
## Diseases by damage type

### Damage type

- Cell loss, cell atrophy
- **Division-obsessed cells**
- Death-resistant cells
- Mitochondrial mutations
- Intracellular junk
- Extracellular junk
- Extracellular matrix stiffening

*Cancer*
# Diseases by damage type

## Damage type

- Cell loss, cell atrophy
- Division-obsessed cells
- Death-resistant cells
- Mitochondrial mutations
- Intracellular junk
- Extracellular junk
- Extracellular matrix stiffening

### Heart Disease

- Obsessed cells
- Intracellular junk
- Extracellular junk
- Extracellular matrix stiffening
## Diseases by damage type

### Damage type

- Cell loss, cell atrophy
- Division-obsessed cells
- Death-resistant cells
- Mitochondrial mutations
- Intracellular junk
- Extracellular junk
- Extracellular matrix stiffening

![Graph showing relationships between damage types and Alzheimer's disease](image-url)
Frailty shares the same causes

**Damage type**

- Cell loss, cell atrophy
- Division-obsessed cells
- Death-resistant cells
- Mitochondrial mutations
- Intracellular junk
- Extracellular junk
- Extracellular matrix stiffening

**Non-specific Decrepitude**
The “how” of preventative maintenance

- Replace
- Remove
- Repair
- Reinforce
# Addressing each category

<table>
<thead>
<tr>
<th>Damage type</th>
<th>The maintenance approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell loss, cell atrophy</td>
<td>Cell therapy, mainly</td>
</tr>
<tr>
<td>Division-obsessed cells</td>
<td>Telomerase/ALT gene deletion plus periodic stem cell reseeding</td>
</tr>
<tr>
<td>Death-resistant cells</td>
<td>Suicide genes, immune stimulation</td>
</tr>
<tr>
<td>Mitochondrial mutations</td>
<td>Allotopic expression of 13 proteins</td>
</tr>
<tr>
<td>Intracellular junk</td>
<td>Transgenic microbial hydrolases</td>
</tr>
<tr>
<td>Extracellular junk</td>
<td>Phagocytosis by immune stimulation</td>
</tr>
<tr>
<td>Extracellular matrix stiffening</td>
<td>AGE-breaking molecules/enzymes</td>
</tr>
</tbody>
</table>
Western mortality rate at age 20-30 is under $10^{-3}$/y
If it didn’t rise with age (and in fact it will very probably fall), most people would live to over 1000
Rejuvenation therapies may never be perfect; first-generation version may give “only” ~30y extra life
However, that would buy us time to develop better ones with which to re-rejuvenate the same people, and so on (“longevity escape velocity”)
Period life expectancy will very suddenly become incalculable (literally!)
How NEAR is the longevity side-benefit?

- This is pioneering technology, so we don’t know
- Guess: 50% chance in 20-25y if funding rises soon
- At least 10% chance it’ll take >100y
- That’s for the therapies I’ve mentioned today
- They will probably give around 30yr extra life
- LEV thenceforth seems inevitable to me…
- Everyone will understand the above this decade
Read the (semi-technical) book.
Available at Amazon and all good book stores.
Paperback is cheaper, and has an extra chapter!

Visit us on the web at
http://www.sens.org/

Drop us a line at
foundation@sens.org
www.sens.org
aubrey@sens.org
If we knew then what we know now: how Medical Advances have Influenced Longevity in the Past, Along with Expectations for the Future

Daniel Ryan
Head of Life & Health R&D
Swiss Re

19 June 2014
Understanding the drivers of future longevity
- the individual & social networks

GENES

ENVIRONMENT

HEALTHCARE

BEHAVIOUR

SOCIAL PRESSURES
1 billion will die from smoking in 21\textsuperscript{st} century

Source: Tobacco Cancer Atlas
Why do we engage in unhealthy behaviours?

10. Peer pressure
9. Social rewards
8. Risk-taking behaviour
7. Parental influence
6. Misinformation
5. Genetic predisposition
4. Advertising
3. Self-medication
2. Media influences
1. Stress relief

Source: Vape Lab in Shoreditch High Street, London
We live in an increasingly connected world
We are redefining our social networks

http://www.brafton.com/infographics/social-media-horse-race
Social physics – how good ideas spread

- Professor Alex Pentland – MIT Human Dynamics Lab
- How flow of ideas and information translates into changes in behaviour
- Promoting the development and sharing of social interactions from Living Labs

Source: 2013 Sense Networks - mClick-to-Visit™ Analytics
Source: 2008 Sense Networks – San Francisco Tribes
Source: Big Data comes to the Office, The New Yorker
How we can influence behaviour on future benefits

• We all know we should save for retirement - but we don't

• How about saving a proportion of your next pay increase?

• Professor Benartzi developed Save More Tomorrow™ (SMarT), which led to savings rates increased from 3.5% to 13.6% over three and a half years

• Save More Tomorrow™ is now offered by approximately half of the large retirement plans in the U.S. and many in UK
Promoting healthy behaviour

Salience

Yellow tape was placed across a shopping cart indicating where fruit and vegetables should be placed. Result: 102% increase in sales of fruit and vegetables.

Norms

Google cafeteria hid unhealthy food out of sight and out of reach and placed healthy food more centrally. Result: fat consumption from chocolate decreased by 11%.

Incentives

19 June 2014
Immediate feedback on impact of choices

Wearable sensors

Smart lenses

Smart garments

Handheld medical scanner

Smart Pill
Putting it all together

• Models of longevity must consider the underlying drivers
• Learnings from behavioural economics & social physics will lead to more effective health interventions and communication
• Continuous collection of biomedical data will link choices to health impact
• Necessary transition from remedial healthcare to curative healthcare over coming decades - benefits focused on pre-retirement population
• Future of longevity is more uncertain than ever before – key factors are individual engagement, societal attitudes & pace of technological change
Expressions of individual views by members of the Institute and Faculty of Actuaries and its staff are encouraged.

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