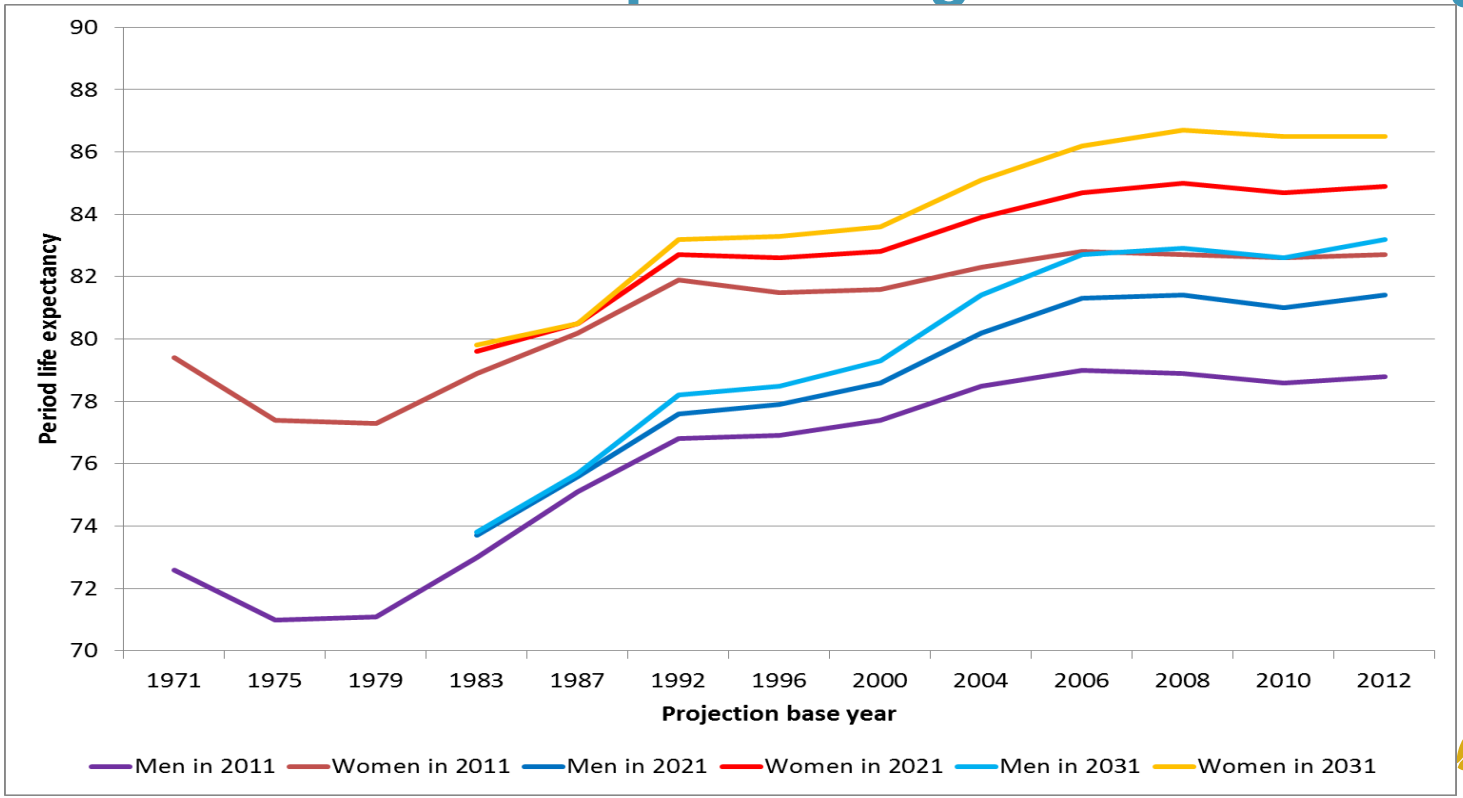
Institute and Faculty of Actuaries

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

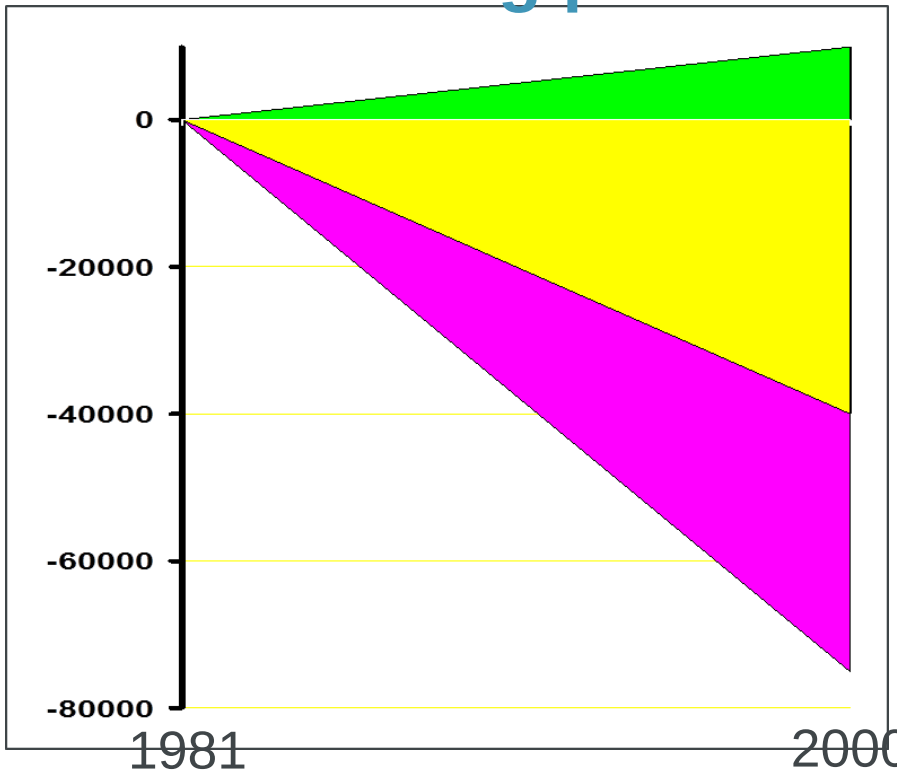
19 June 2014

How well are we predicting future UK longevity



Institute and Faculty of Actuaries

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%

Unal, Critchley & Capewell
Circulation 2004 109(9) 1101

Institute and Faculty of Actuaries

Debating the evidence for further reductions

By checking this box you are agreeing to the NICE Terms and Conditions

NICE National Institute for Health and Care Excellence

Find guidance | NICE Pathways | Quality standards

The new NICE website will be launch

	CVD events avoided	
*18	**Total number of CVD events avoided**	
*18	**Distribution of CVD events**	
	Angina aged over 69	
	Angina aged under 70	
	MI without complications	
	MI with complications	
	TIA aged over 69	
	TIA aged under 70	
	Stroke aged over 69	
	Stroke aged under 70	
	CVD or CHD death	
*19	**Cost of cardiovascular events avoided**	
	Angina aged over 69	1,946
	Angina aged under 70	1,451
	MI without complications	6,538
	MI with complications	8,589
	TIA aged over 69	1,831
	TIA aged under 70	1,064
	Stroke aged over 69	4,614
	Stroke aged under 70	3,015
	CVD or CHD death	-
	Resource impact of cardiovascular events avoided	
*20	**Net resource impact of lipid modification guideline (excluding risk assessments)**	
*21	Less net resource impact already identified in NICE technology appraisal guidance 94	
	Net additional resource impact of lipid modification guideline (excluding risk	

Source: National Institute of Health & Clinical Excellence

Proposals to extend the use of statin drugs should be scrapped, a group of leading doctors and academics says.

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.

Related Stories

Statins side effects claims probed

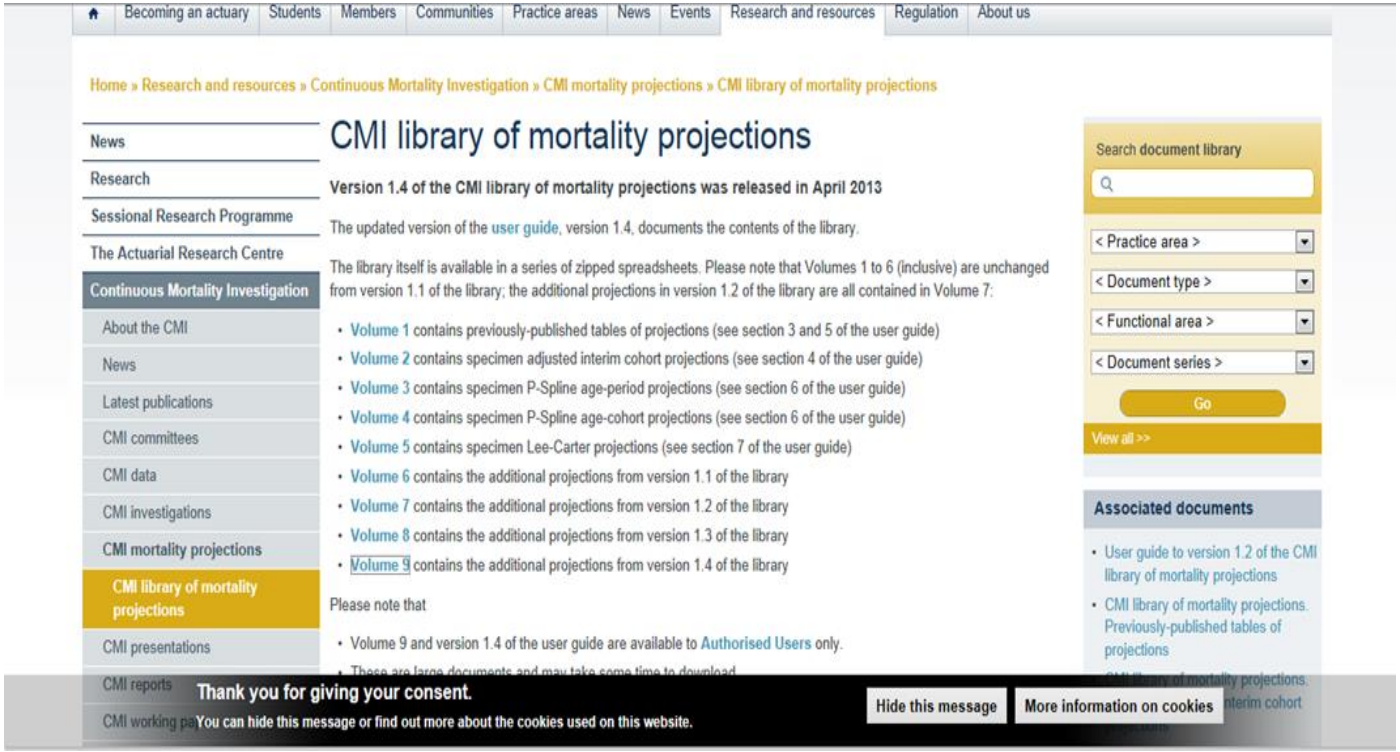
Statins: Are they safe?

'Millions more should take statins'

Source: BBC News

Institute and Faculty of Actuaries

CMI Mortality Projections Library

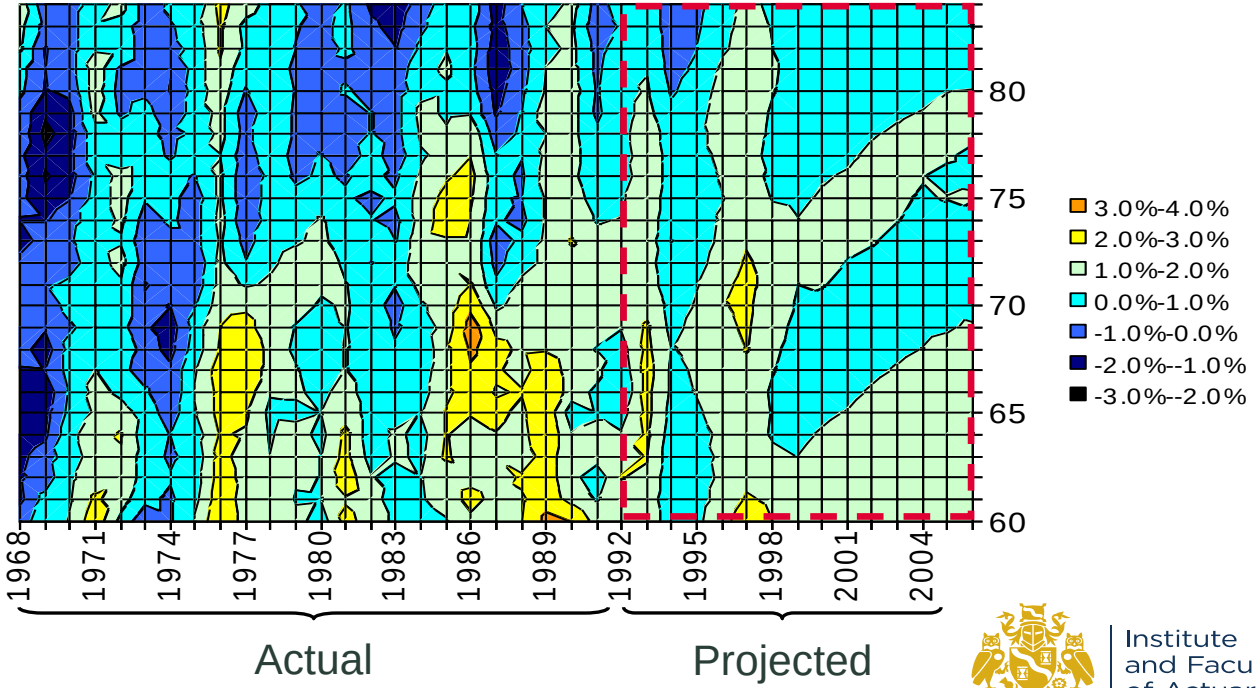


Institute and Faculty of Actuaries

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

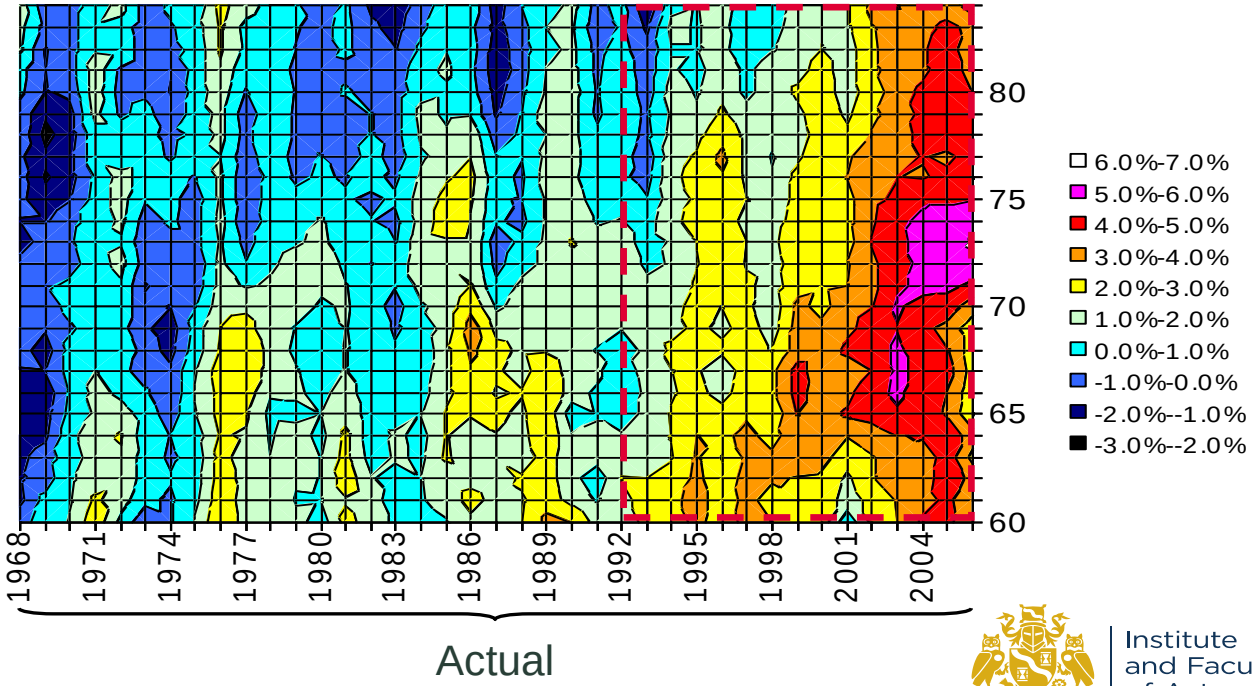


Source: HMD, Swiss Re calculations

Institute and Faculty of Actuaries

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

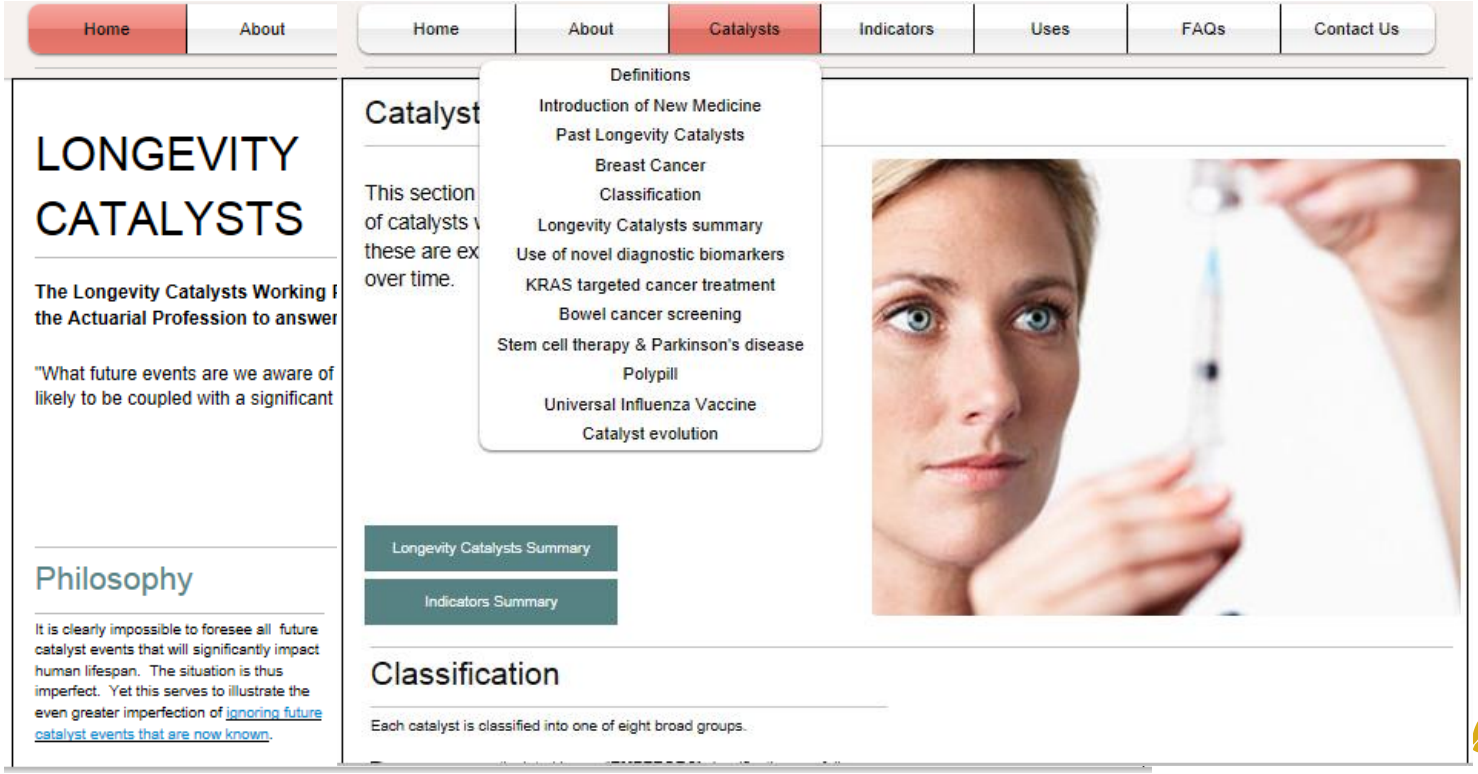
Actual Dutch improvements to 2007



Source: HMD, Swiss Re calculations

Institute and Faculty of Actuaries

Longevity catalysts working group



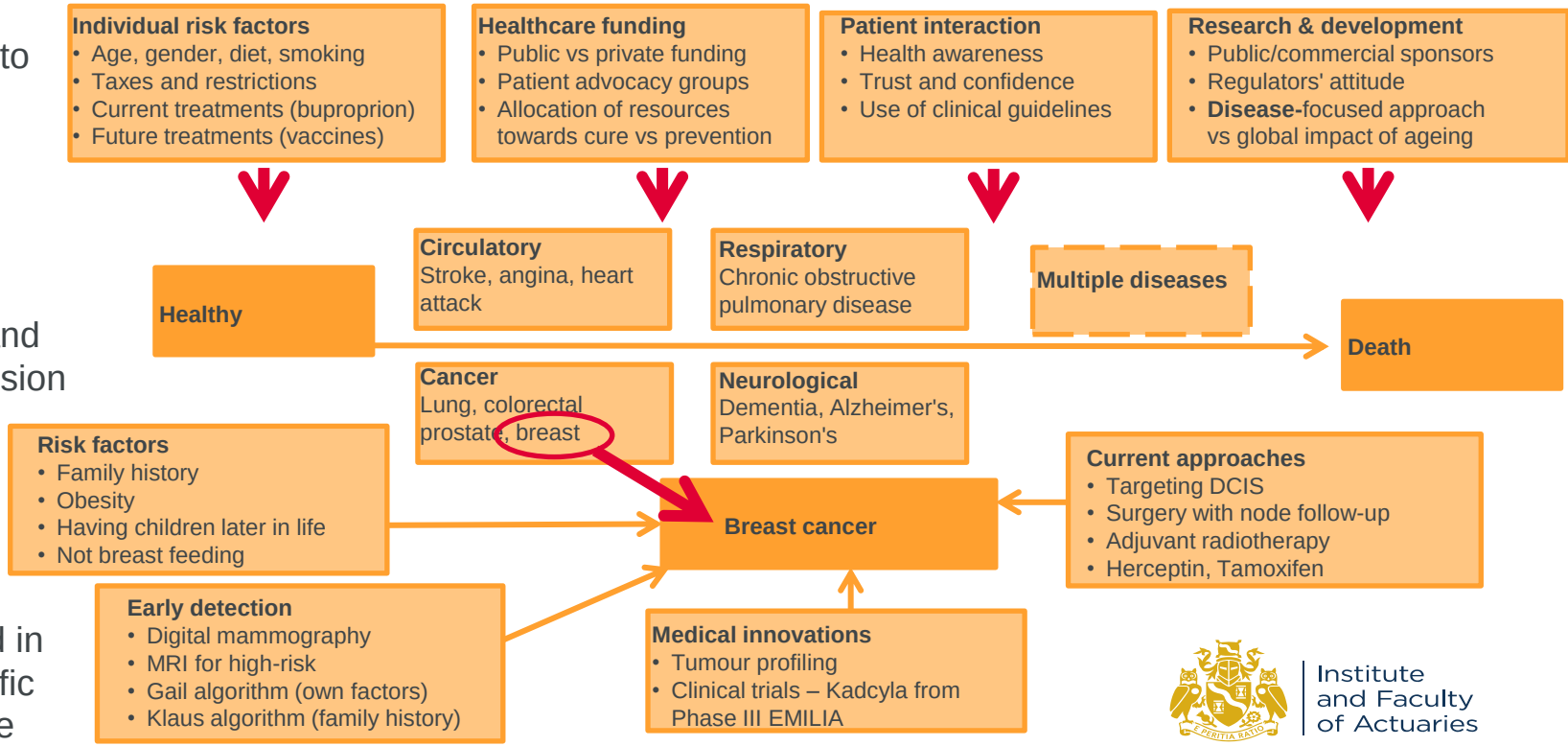
Institute and Faculty of Actuaries

Aiming for a more holistic view of longevity

General drivers to diagnosis and survival

Disease types and disease progression

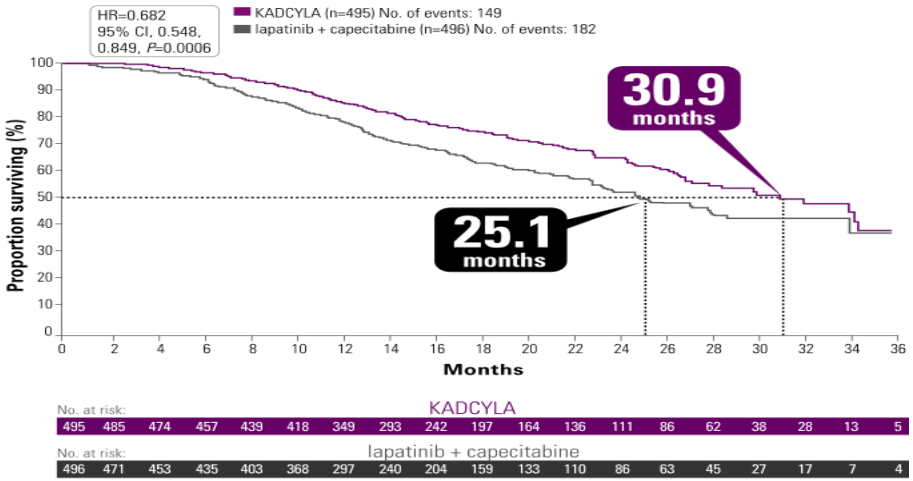
Factors involved in assessing specific example disease

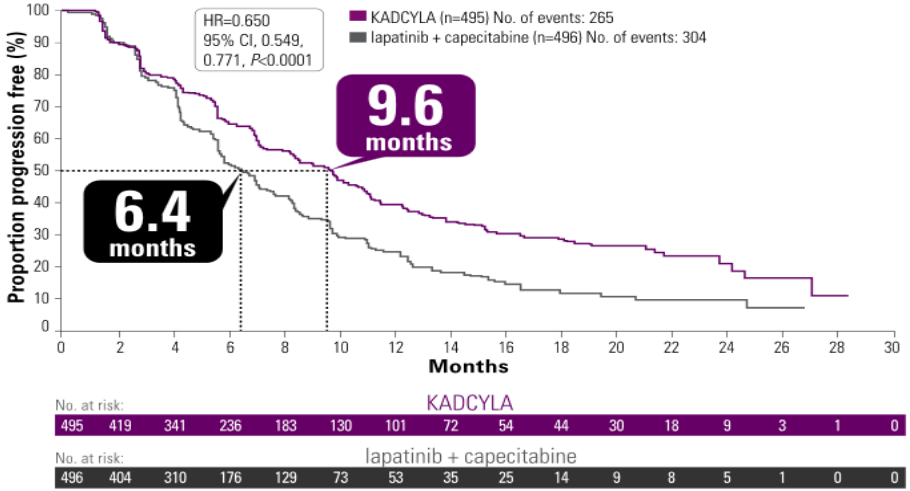


Institute and Faculty of Actuaries

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

Institute and Faculty of Actuaries

The true cost of pharmaceutical research

Company	Ticker	Number of drugs approved	R&D Spending Per Drug ($Mil)	Total R&D Spending 1997-2011 ($Mil)
AstraZeneca	AZN	5	11,790.93	58,955
GlaxoSmithKline	GSK	10	8,170.81	81,708
Sanofi	SNY	8	7,909.26	63,274
Roche Holding AG	RHHBY	11	7,803.77	85,841
Pfizer Inc.	PFE	14	7,727.03	108,178
Johnson & Johnson	JNJ	15	5,885.65	88,285
Eli Lilly & Co.	LLY	11	4,577.04	50,347
Abbott Laboratories	ABT	8	4,496.21	35,970
Merck & Co Inc	MRK	16	4,209.99	67,360
Bristol-Myers Squibb Co.	BMY	11	4,152.26	45,675
Novartis AG	NVS	21	3,983.13	83,646
Amgen Inc.	AMGN	9	3,692.14	33,229

Sources: InnoThink Center For Research In Biomedical Innovation; Thomson Reuters Fundamentals via FactSet Research Systems

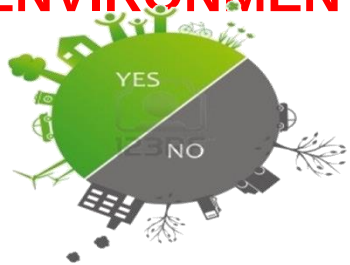
Institute and Faculty of Actuaries

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

GENES

BEHAVIOUR

ENVIRONMENT



HEALTHCARE

SOCIETAL PRESSURES

Institute and Faculty of Actuaries

Risk factors linking across disease

Global Burden of Disease

Ranking legend
1–5 | 6–10 | 11–15 | 16–20 | 21–25 | 26–30 | 31–35 | 36–40 | >40

Risk factor	Global	High-income Asia Pacific	Western Europe	Australasia	High-income North America	Central Europe	Southern Latin America	Eastern Europe	East Asia	Tropical Latin America	Central Latin America	Southeast Asia	Central Asia	Andean Latin America	North Africa and Middle East	Caribbean	South Asia	Oceania	Southern sub-Saharan Africa	Eastern sub-Saharan Africa	Central sub-Saharan Africa	Western sub-Saharan Africa
High blood pressure	1	1	2	3	4	1	2	2	1	2	4	1	1	2	1	1	3	6	2	6	5	6
Tobacco smoking, including second-hand smoke	2	2	1	2	1	3	3	3	2	4	5	2	3	5	3	3	2	3	5	7	12	10
Alcohol use	3	3	4	4	3	2	4	1	6	1	1	6	2	1	11	5	8	5	1	5	6	5
Household air pollution from solid fuels	4	42	..	..	..	14	23	20	5	18	11	3	12	7	13	9	1	4	7	2	2	2
Diet low in fruits	5	5	7	7	7	5	6	5	3	6	7	4	5	10	6	8	5	9	8	8	11	13
High body-mass index	6	8	3	1	2	4	1	4	9	3	2	9	4	3	2	2	17	2	3	14	18	15
High fasting plasma glucose	7	7	6	6	5	7	5	10	8	5	3	5	7	6	4	4	7	1	6	10	13	11
Childhood underweight	8	39	38	37	39	38	38	38	38	32	23	13	25	18	21	14	4	8	9	1	1	1
Ambient particulate matter pollution	9	9	11	26	14	12	24	14	4	27	19	11	10	24	7	19	6	32	25	16	14	7
Physical inactivity and low physical activity	10	4	5	5	6	6	7	7	10	8	6	8	9	8	5	7	11	7	11	15	15	16
Diet high in sodium	11	6	10	11	11	9	11	9	7	9	13	7	6	13	8	15	14	16	13	21	17	18
Diet low in nuts and seeds	12	11	9	8	8	8	8	8	12	10	8	15	8	12	9	10	13	13	16	22	16	21
Iron deficiency	13	20	32	21	35	22	17	21	19	14	12	12	17	4	12	6	9	11	10	4	4	4
Suboptimal breastfeeding	14	..	..	..	..	..	27	..	24	22	15	14	16	9	15	13	10	10	4	3	3	3
High total cholesterol	15	12	8	9	9	10	9	6	13	11	10	16	14	16	10	16	20	14	19	28	27	30
Diet low in whole grains	16	10	16	16	17	11	12	11	11	12	14	26	13	17	14	12	15	15	32	24	19	24
Diet low in vegetables	17	14	13	12	13	13	10	12	15	16	20	10	11	14	18	11	16	12	15	23	23	20
Diet low in seafood omega-3 fatty acids	18	17	15	13	16	16	14	13	17	17	18	19	15	23	16	17	18	20	23	27	25	25
Drug use	19	13	14	10	10	20	13	17	18	13	16	18	20	11	19	18	22	19	12	19	24	22
Occupational risk factors for injuries	20	24	24	20	25	26	16	25	20	19	22	23	21	21	23	31	12	22	22	20	22	17

Understanding the drivers of future longevity
- transition from remedial to curative medicine

GENES

BEHAVIOUR

ENVIRONMENT

HEALTHCARE

SOCIETAL PRESSURES

Institute and Faculty of Actuaries

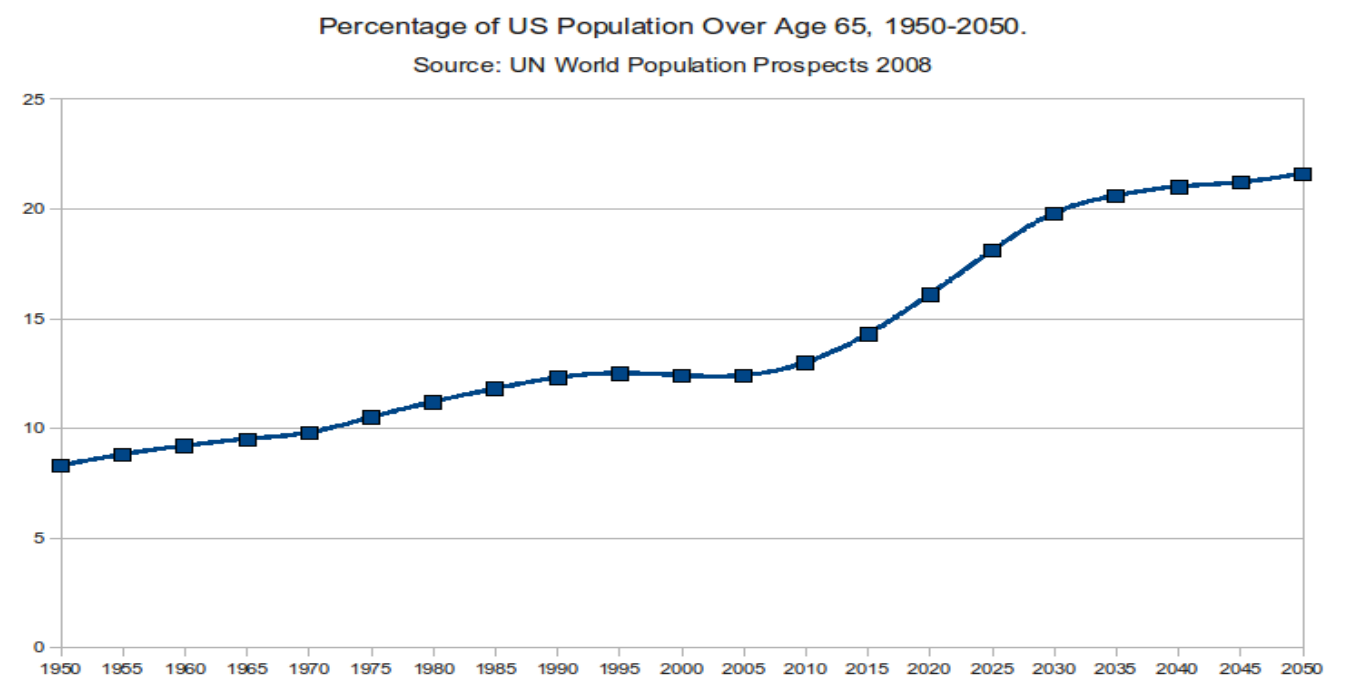
Institute and Faculty of Actuaries

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/

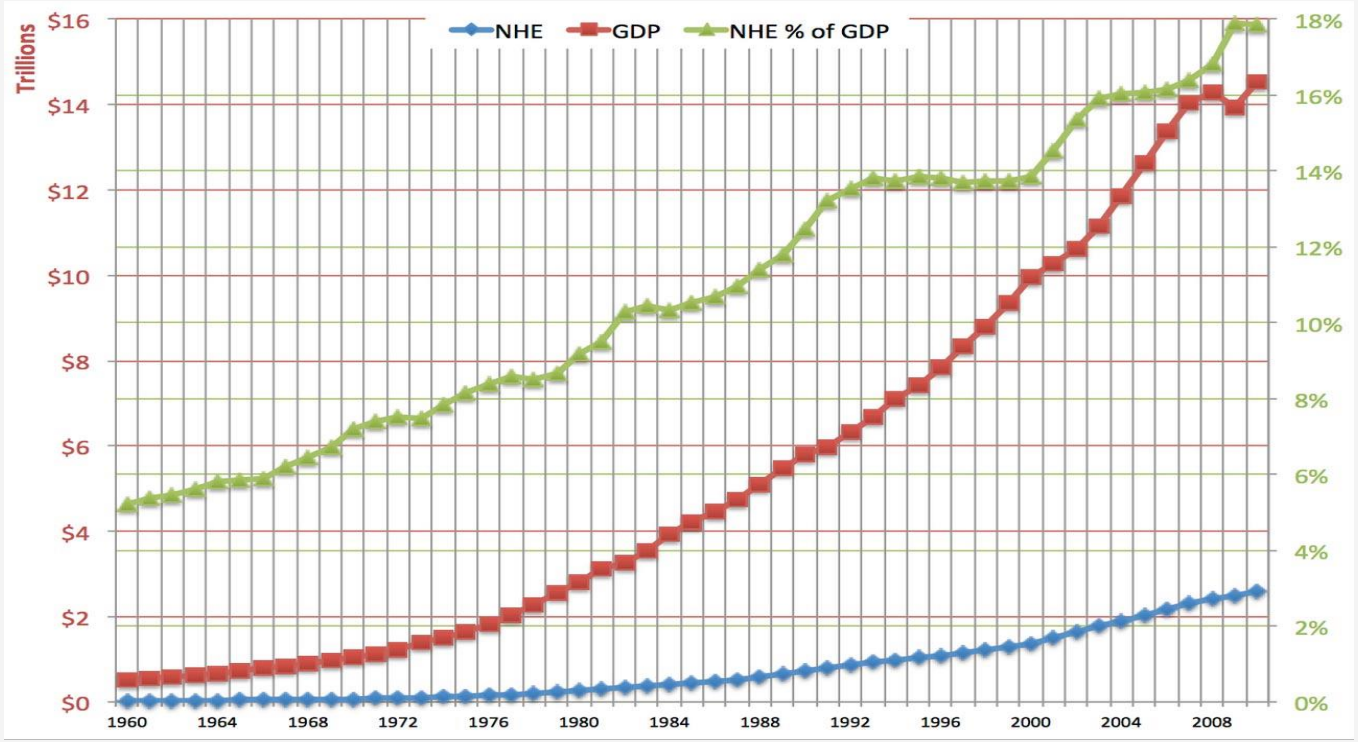
19 June 2014

The aging population



* Source: http://esa.un.org/wpp/unpp/panel_population.htm

The economics of aging



Source: http://sambaker.com/econ/classes/nhe10/

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://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_dchs_2012_hidden_costs112712.pdf

Age-related vs. infectious diseases

- 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.

A bizarrely underappreciated truth

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

Diseases			Aging
Communicable	Congenital	Age-related	
Tuberculosis Malaria HIV …	Tay-Sachs MELAS Li-Fraumeni ...	Alzheimer's Cancer Atherosclerosis …	Frailty Sarcopenia Immunosenescence …

ARDs and aging: correct view

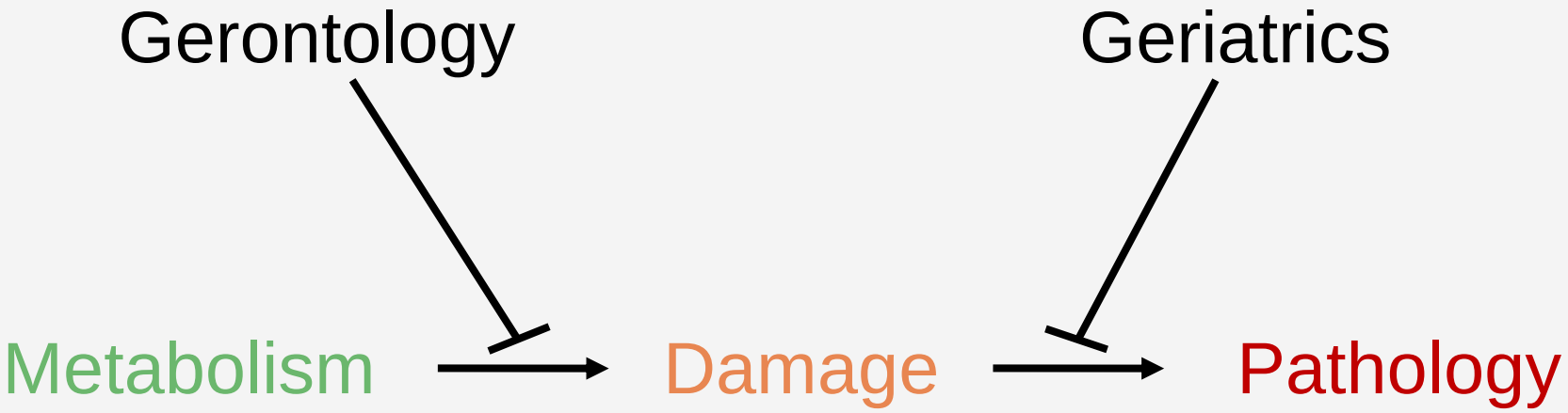
Diseases		Aging	
Communicable	Congenital	Specific	General
Tuberculosis Malaria HIV …	Tay-Sachs MELAS Li-Fraumeni ...	Alzheimer's Cancer Atherosclerosis …	Frailty Sarcopenia Immunosenescence …

What this misguidedness means in $$

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

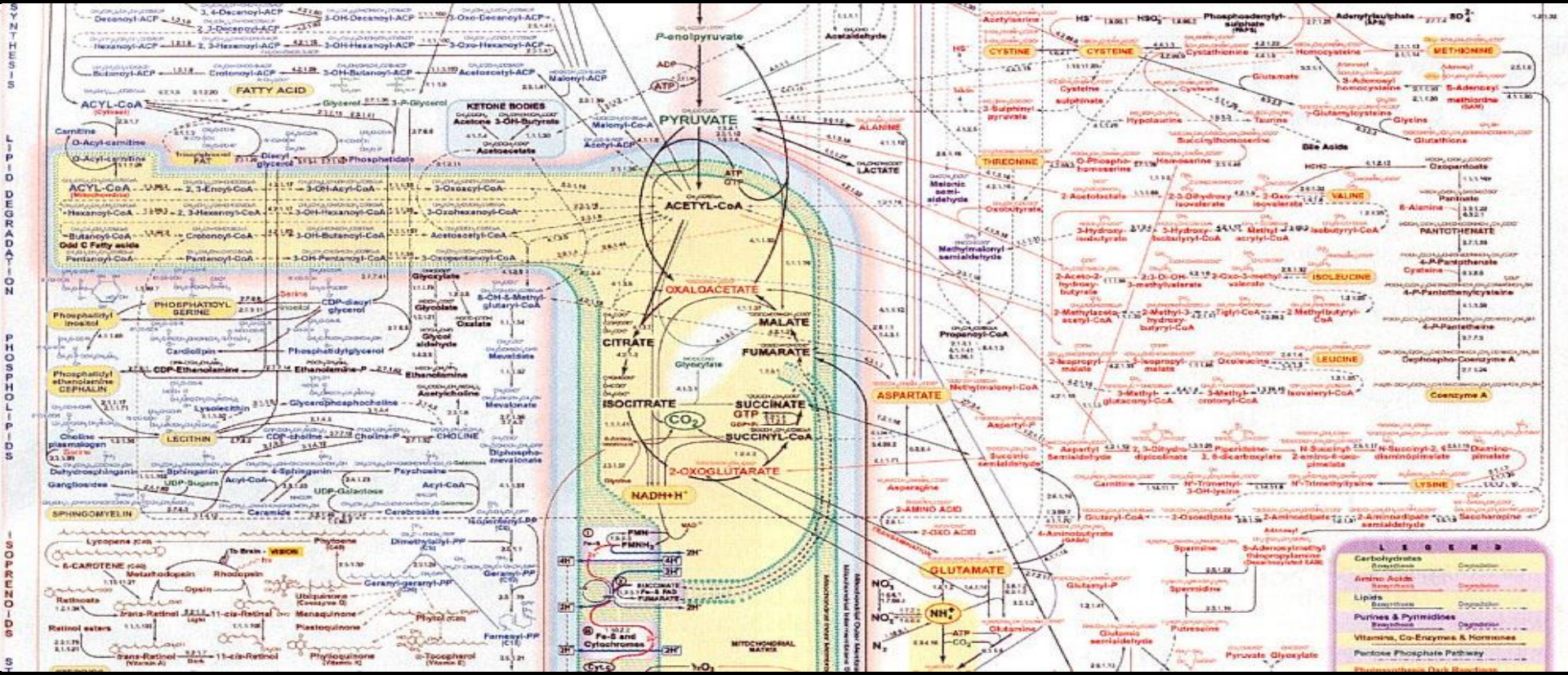
How age-related disease is addressed today



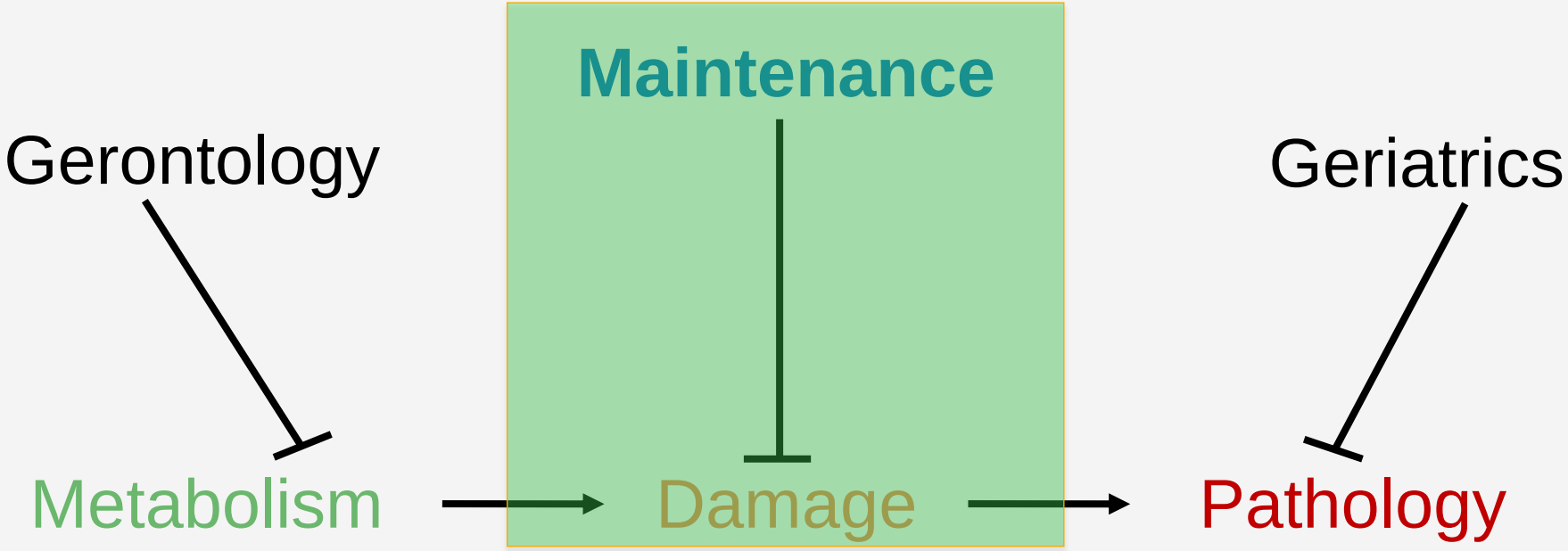
Targeting pathology: tricky

presbycusis
osteoporosis
osteoarthritis
autoimmunity
greying hair
presbyopia
cataract
glaucoma
temporal arteritis
polymyalgia rheumatica
wrinkling
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
immunosenescence
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
pineal calcification
aberrant differentiation
gait instability
frontal demyelination
axonal atrophy
impaired functional connectivity
impaired working memory

Targeting metabolism: also tricky



Maintenance: targeting damage



Claim: unlike the others, the maintenance approach can deliver a big extension of human healthy lifespan quite soon

Comparison: car maintenance

Categorizing damage

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

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

Diseases by damage type

Damage type

Cell loss, cell atrophy

Division-obsessed cells

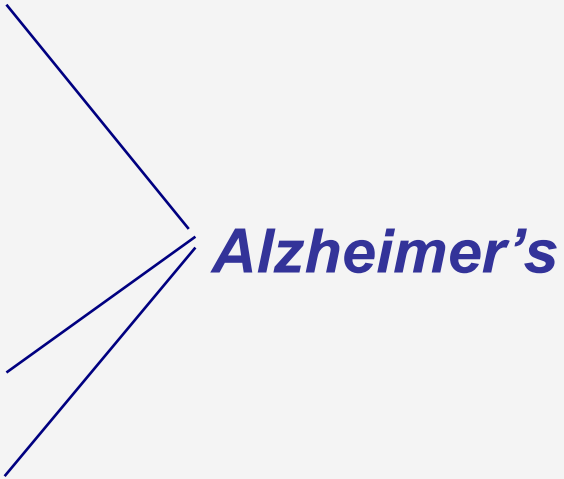
Death-resistant cells

Mitochondrial mutations

Intracellular junk

Extracellular junk

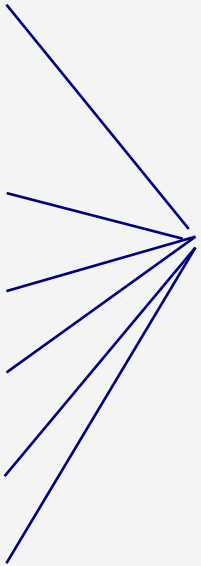
Extracellular matrix stiffening



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

Damage type	The maintenance approach
Cell loss, cell atrophy	Cell therapy, mainly
Division-obsessed cells	Telomerase/ALT gene deletion plus periodic stem cell reseeding
Death-resistant cells	Suicide genes, immune stimulation
Mitochondrial mutations	Allotopic expression of 13 proteins
Intracellular junk	Transgenic microbial hydrolases
Extracellular junk	Phagocytosis by immune stimulation
Extracellular matrix stiffening	AGE-breaking molecules/enzymes

How BIG is the longevity side-benefit?

- 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?

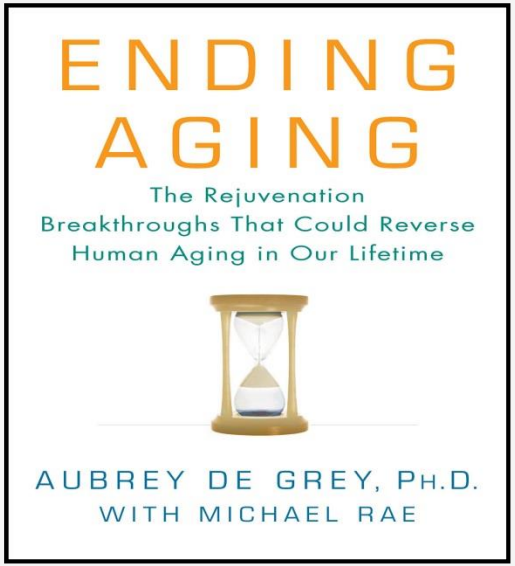
- This is pioneering technology, so we don’t know
- Guess: 50% chance in 20-25y if funding rises soon
- At least 10% chance it’ll take >100y
- That’s for the therapies I’ve mentioned today
- They will probably give around 30yr extra life
- LEV thenceforth seems inevitable to me…
- **Everyone will understand the above this decade**

Learn more

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

http://www.sens.org/outreach/conferences/rejuvenation-biotechnology-conference-2014

www.sens.org

aubrey@sens.org

Institute and Faculty of Actuaries

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

BEHAVIOUR

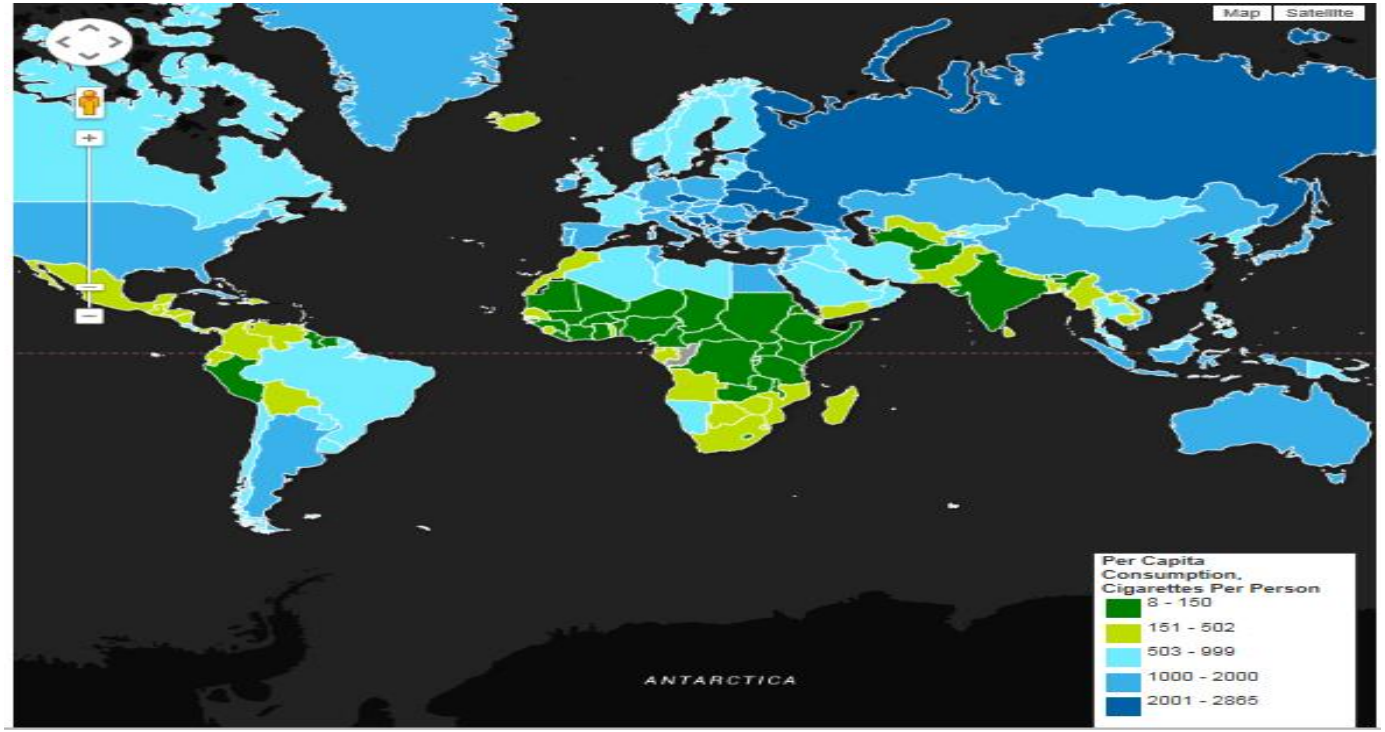
ENVIRONMENT

HEALTHCARE

SOCIETAL PRESSURES

Institute and Faculty of Actuaries

1 billion will die from smoking in 21st century



Source: Tobacco Cancer Atlas

Institute and Faculty of Actuaries

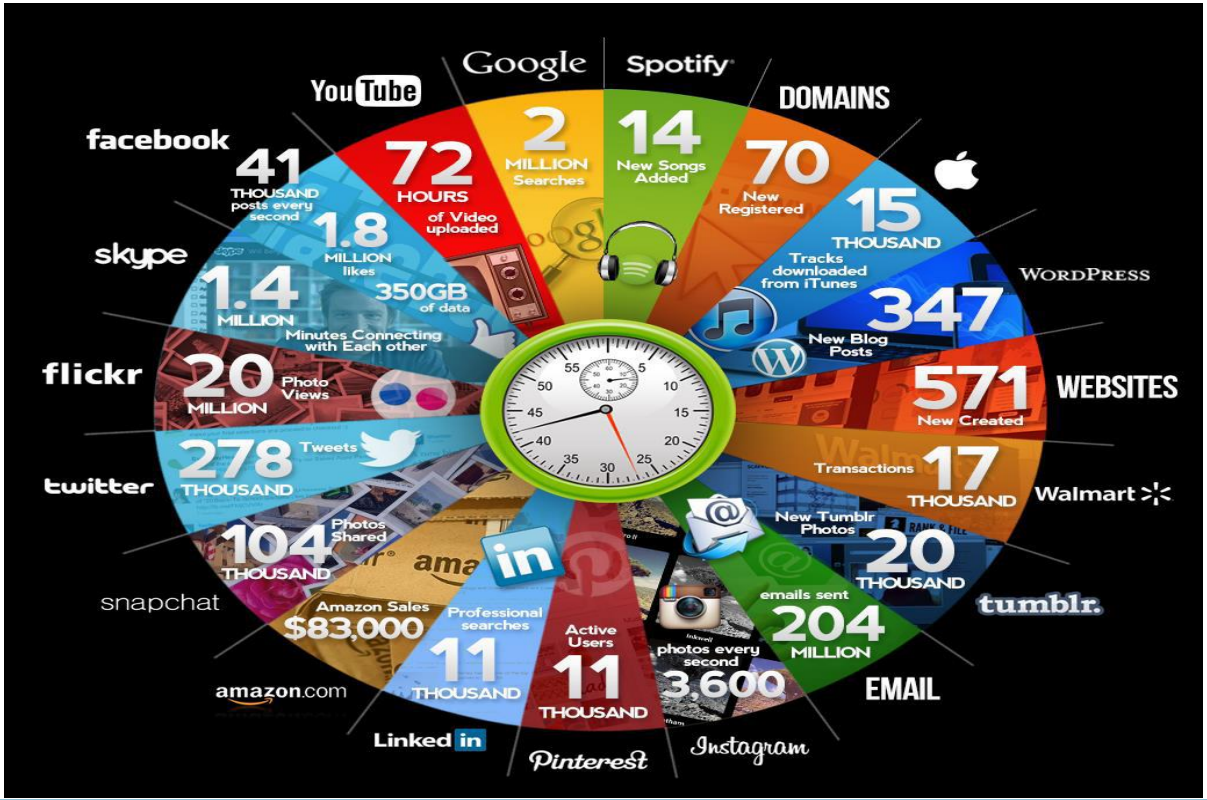
Why do we engage in unhealthy behaviours?

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

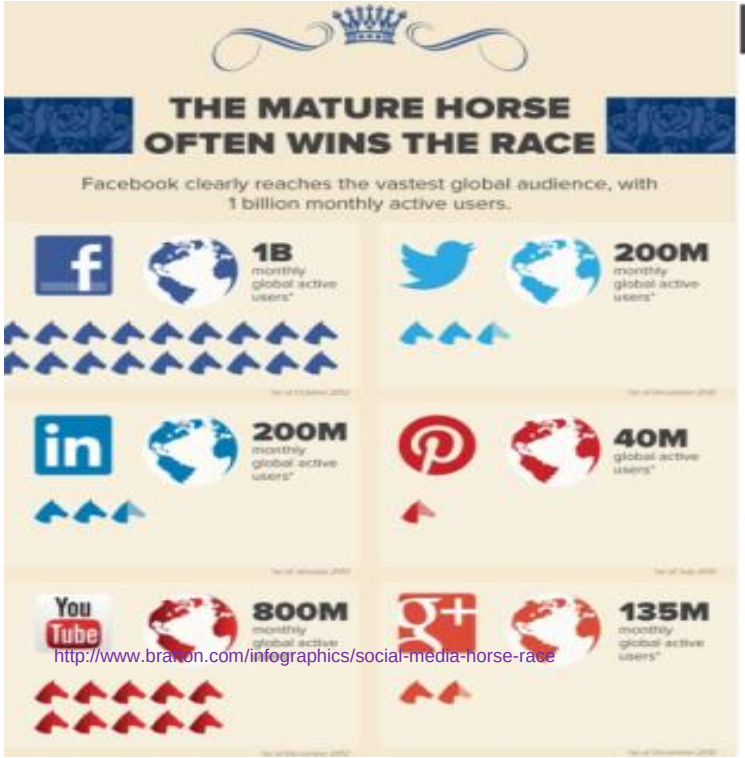
Institute and Faculty of Actuaries

We live in an increasingly connected world



Institute and Faculty of Actuaries

We are redefining our social networks

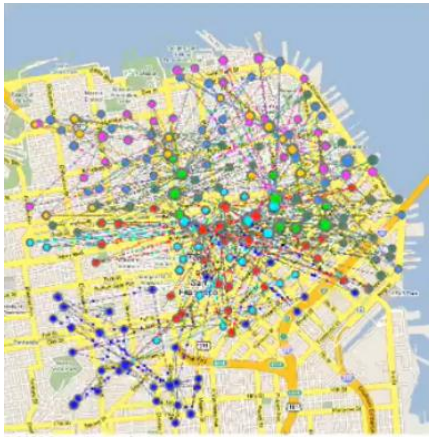


Institute and Faculty of Actuaries

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**



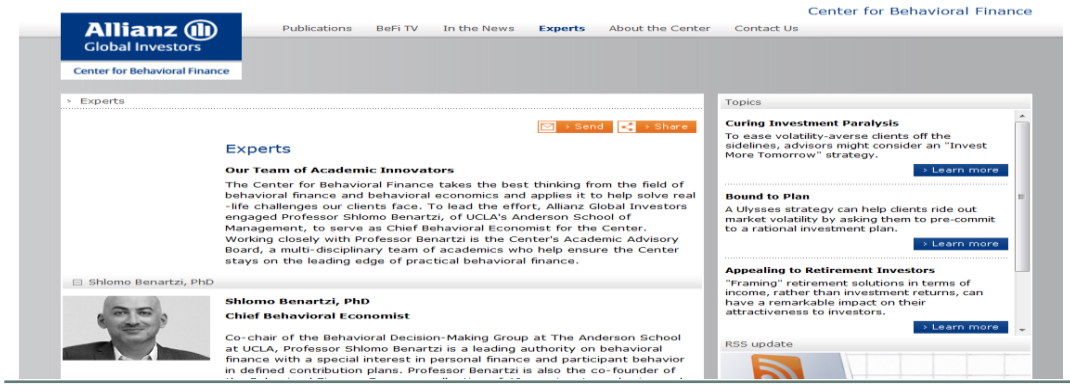
Source: 2008 Sense Networks – **San Francisco Tribes**

Source: Big Data comes to the Office, The New Yorker

Institute and Faculty of Actuaries

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



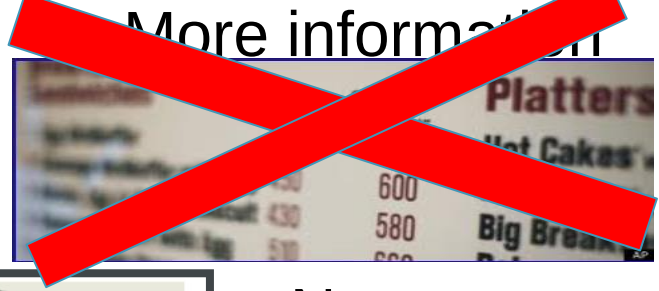
Shlomo Benartzi: Saving for tomorrow, tomorrow

TED@AllianzGI
Behavioral Finance

In November 2011, Professor Shlomo Benartzi, of the UCLA Anderson School of Management and Chief Behavioral Economist of the Allianz Global Investors

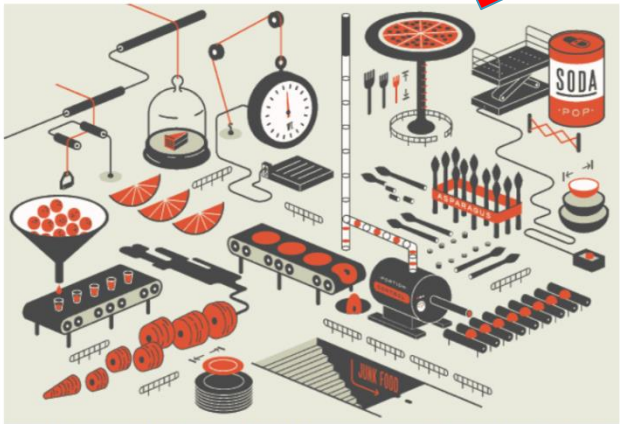
Institute and Faculty of Actuaries

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.



At Google's cafeteria, junk food is out of sight, and pizza is (almost) out of reach. *(Credit: Mike McQuade)*

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%.

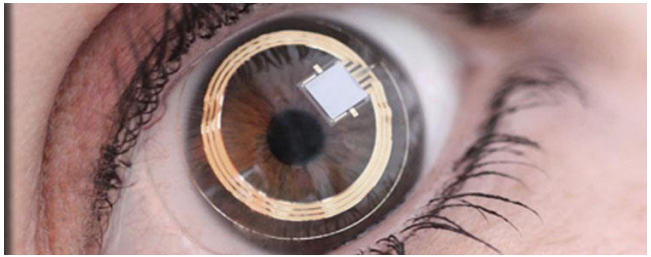
Norms

Incentives

Institute and Faculty of Actuaries

Immediate feedback on impact of choices

Wearable sensors



Smart lenses

Smart Pill

Smart garments

Handheld medical scanner

Institute and Faculty of Actuaries

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

Questions

Comments

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.

Institute and Faculty of Actuaries