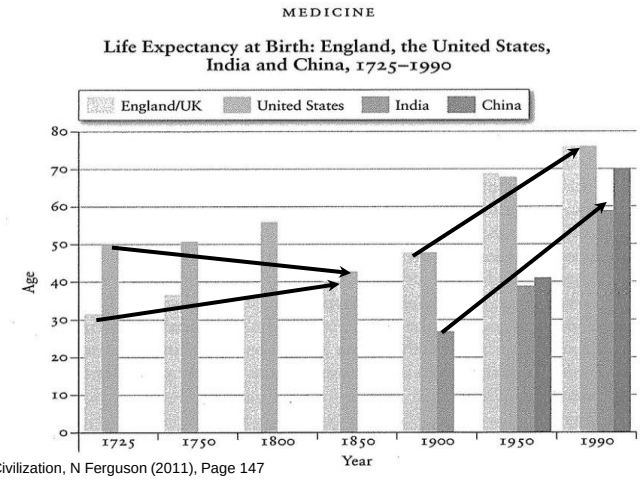
The Actuarial Profession
making financial sense of the future

Life Conference 2012
John Wilden, Global Health Futures
Daniel Ryan, Swiss Re

Who will live to 100?

6 November 2012

Increased longevity is a 20th century phenomena



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

"Forecasting" longevity in 20th 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)

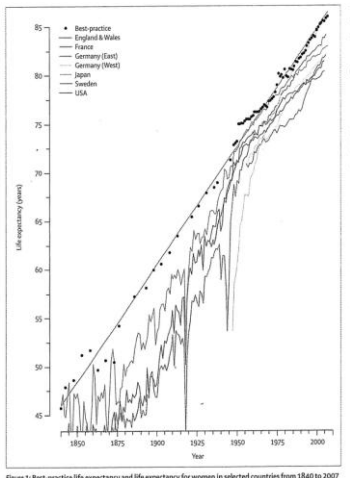
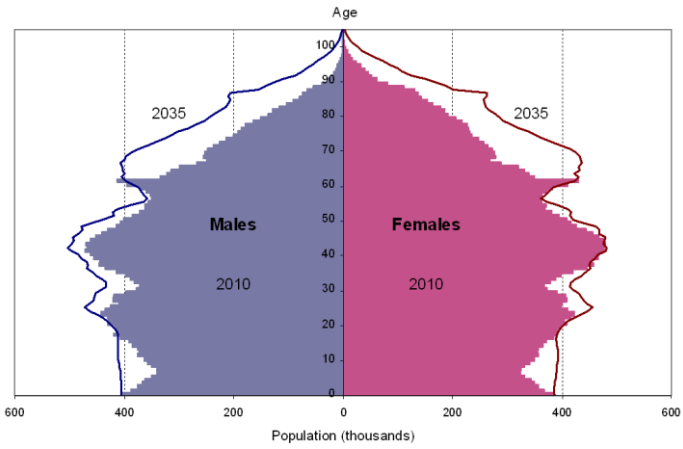


Figure 1: Best-practice life expectancy and life expectancy for women in selected countries from 1840 to 2007
Linear regression trend depicted by solid grey line with a slope of 0·24 per year. Data from supplementary material of reference 12 and the Human Mortality Database.

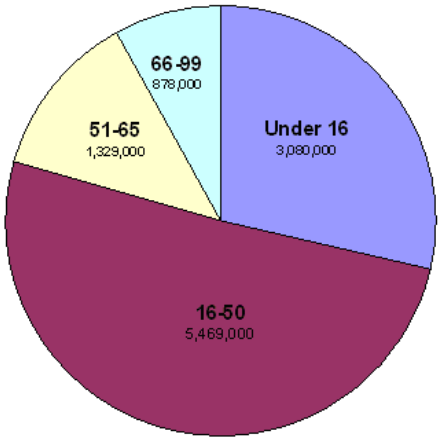
The future shape of our population

Estimated and projected age structure of the United Kingdom population, mid-2010 and mid-2035



Source: Office for National Statistics – 2010-based projections

Who are our future centenarians?



Source: Office for National Statistics, 2008-based Population Projections (UK)

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

Factors contributing to 20th century longevity

Industrialisation & capitalism

- Better homes & heating, providing equitable environment
- Industrial food production at affordable prices
- Safe preparation, cooking and storage of food stuffs
- Five-fold increase of income since 1930‘s in developed world

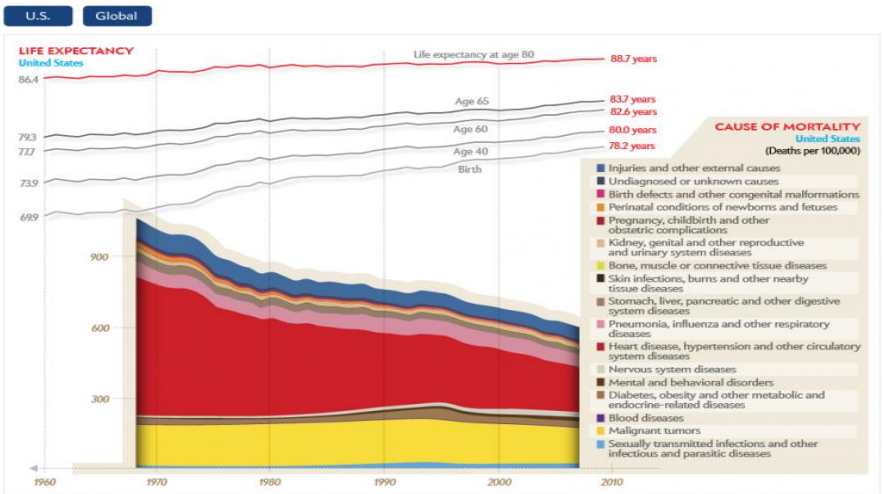
Public health standards

- Sanitation: safe drinking water and sewage disposal

Primary healthcare provision

- Anti-septic technique, vaccination, anti-bacterial agents

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



Source: Scientific American Sept 2012

Increasing longevity in 21st century

The continued development of 2nd 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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Future impact of longevity
Which lives benefit?

	50 year olds	70+ year olds
Preventive healthcare	Amenable, potentially beneficial	Less amenable, potentially less beneficial
Disability	Negligible	Already present
Quality of life	Good	Fair
Medically	Warrant treatment	Treatment less warranted
Adverse outcome	More tolerable	Less tolerable
Future financial/healthcare provision	Highest earning period	Limited or no earnings Dependent on state/private retirement provision

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Scientific approaches to evidence, prediction & risk

Evidence
Valid
Reliable
Accurate
Verifiable
Reproducible
Falsifiable
Analysable
Null Hypothesis

Risk
Unknown Unknowns
Known Unknowns
Known Knowns
Fat & Long Tails
Black Swans
Chaos

Prediction
Evidence
Risk
Statistical
Models
Strategies

Categories of Evidence
Conceptual
Topographical
Methodological
Factual

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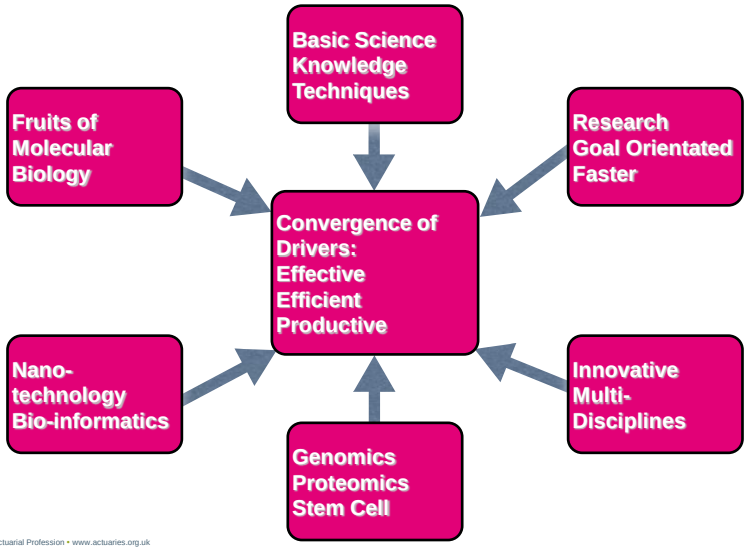
Future innovative healthcare drivers



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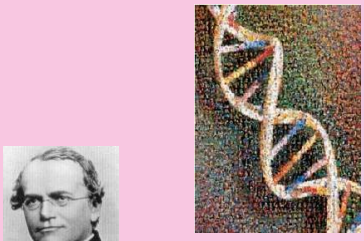
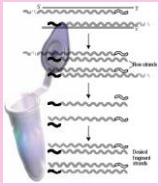
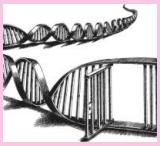
Genetic information & technology have grown exponentially







1865

DNA
Double Helix
Watson & Crick
1953

Huntington
Disease
1983

PCR
1985

Cystic
Fibrosis
1989

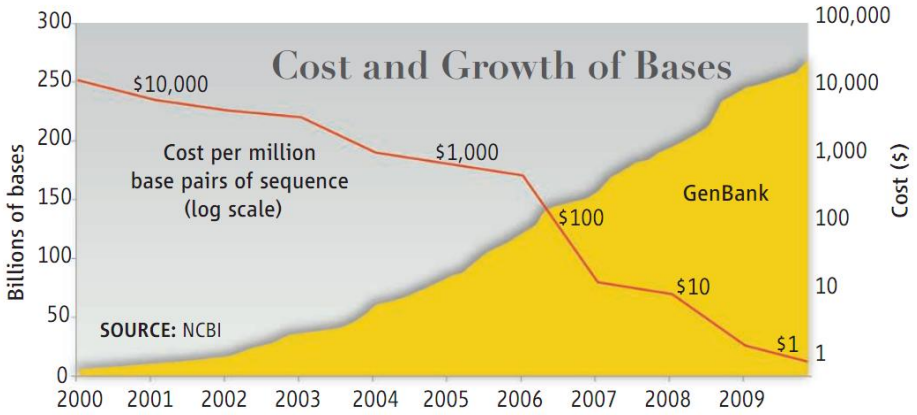
Human
Genome
Project
1990

Breast
Cancer
BRCA1
1994

HapMap
2007

HGP End
2003

DNA sequencing costs are decreasing at exponential rates



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

Genome-wide association to identify genes involved in disease

Cancer site	Relative Risk ≥5.0 Family studies	Relative Risk ≥1.5 and >5.0 Resequencing	Relative Risk ≥1.01and >1.5 Genome-wide association studies
Lung	RB1, TP53		rs1051730, rs8034191 (CHRNA3, CHRNB4, 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

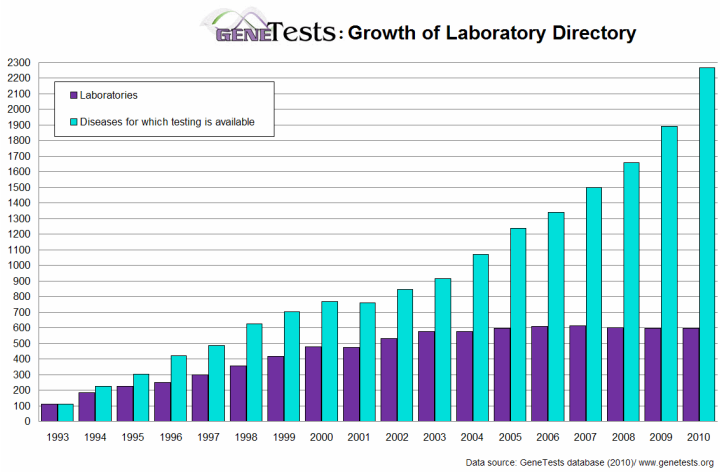
Increasing numbers of genetic tests in clinical practice

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



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..

Tomlinson 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):984-988.

Zanke et al. (2007) . "Genome-wide association scan identifies a colorectal cancer susceptibility locus on chromosome 8q24." *Nat Genet* 39(8):989-994.

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

Further advances in genomic sequencing
Oxford Nanopore

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

The futures of separate cell types and organs

Cell types	Stem cells Experimental	Stem cells 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	

The futures of healthcare

Curative Healthcare

Eradication of disease
Recurrence possible
Minimal disease burden

Preventive Healthcare

Before symptoms
Pathological disease present

Remedial Healthcare

70, 80, 90% rule
Disease burden before symptoms
Vascular disease - heart attacks, strokes: 70%
Some major cancers: 80%
Diabetes: 90%

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

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

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"

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

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"

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

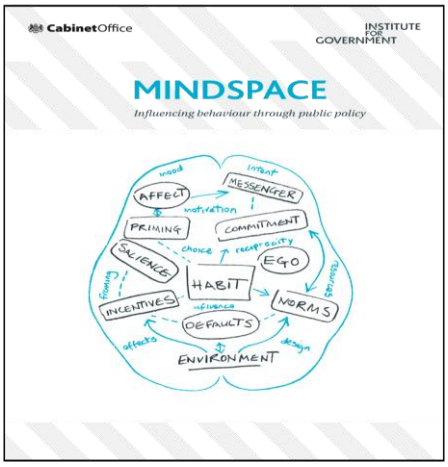
Genomic delivery of immunotherapy for Type I

Irisin release for obesity

Genomic delivery via viral, nano-particles or synthetic biology

"All of above in experimental stages"

Individual thought and decision-making



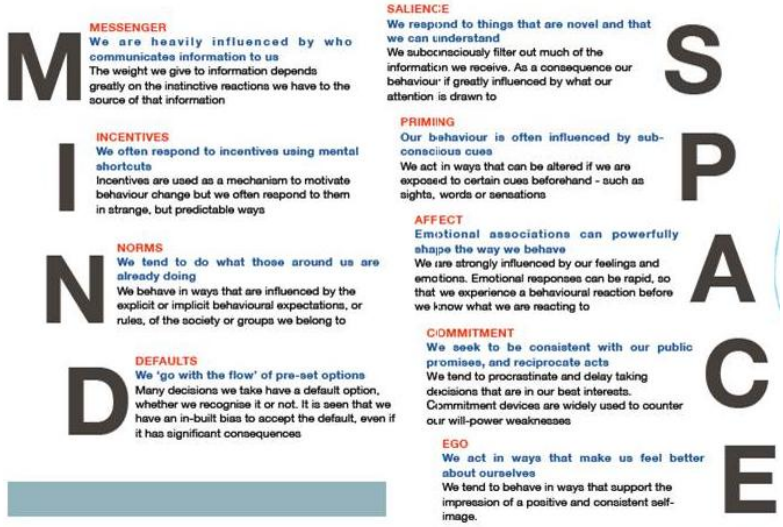
Mindspace report published in March 2010

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

Concept of MINDSPACE explained



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

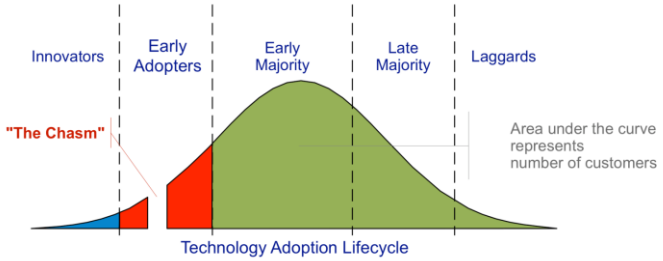
Advisor's Trustworthiness

- 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

Who will live to 100?
10 conclusions to ponder

1. The methodological science of predicting longevity is in its infancy
2. 20th Century longevity is not predictive of 21st century longevity
3. Controlling just One Biological Parameter can change longevity
4. Curing Disease in the 21st century will be a powerful driver of longevity
5. Some age groups and segments of society will benefit more than others
6. The management of evidence and risk will drive the science of prediction
7. The convergence of Healthcare Drivers of Innovation on a multi-disciplinary basis quickens change
8. The Futures of Innovative Techniques applied to separate organs and diseases will translate to unhealthy and healthy populations
9. The strategies to manage many possible futures will drive who lives to 100
10. Each lifetime is a unique and unrepeatable experiment with many influences

Questions or comments?

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.