

The Actuarial Profession
making financial sense of the future

Highlights of the Life Conference 2011
Peter Banthorpe



Stress testing and scenario modelling of longevity

7 March 2012

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Agenda

- Possible medical advances impacting longevity;
- Factors influencing time lines;
- Scenarios;

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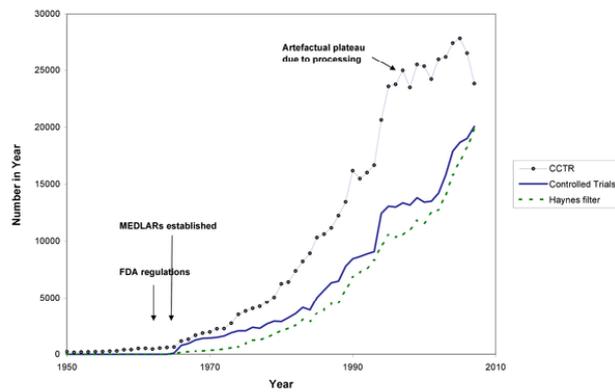
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Possible Medical Advances Affecting Longevity

Enhancing Longevity

- Lifestyle changes / optimisation
- Healthcare policy
- Specific disease based interventions
 - Cancer ←
 - Cardio-vascular
 - Neuro-degenerative
 - etc
- Regenerative medicine
- Anti-ageing technology ←

Pace of Medical Research Is Accelerating



Number of Published Trials, 1950 to 2007

Source : Seventy-Five Trials and Eleven Systematic Reviews a Day: How Will We Ever Keep Up? Bastian, et Al, 2010

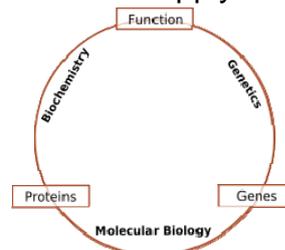
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Reducing Cancer Deaths

- Many avenues for advancement:
 - Prevention
 - Lifestyle changes
 - Vaccination
 - Early detection
 - Improved treatments
 - Post treatment care

Molecular Biological Techniques and Genetics could apply

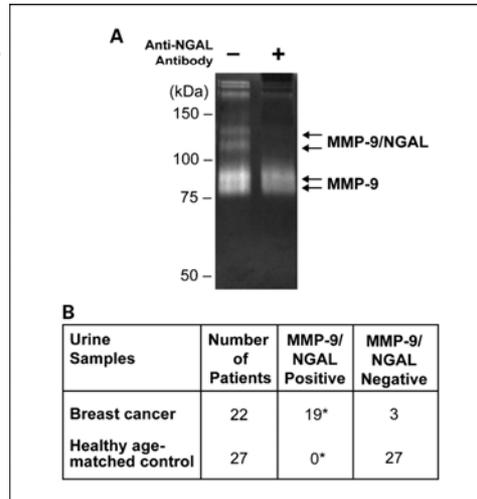


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Advances in Cancer Detection

Matrix Metalloproteinases (MMPs)

- Enzymes found in the Urine of Cancer patients;
- Tests for these are seeking approval.

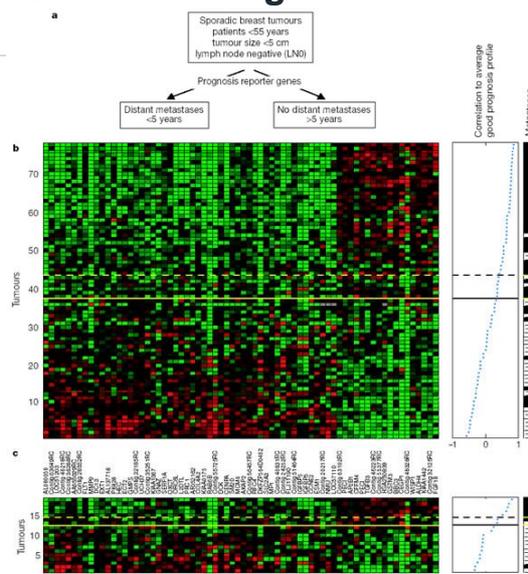


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Tumour Gene Expression Profiling

- Genes make proteins, 'via' RNA;
- Examining RNA from Tumour genes has prognostic value, e.g.:
 - Breast Cancer
 - Prostate Cancer
- Influences treatment strategy



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Potential Advances in Cancer Treatment – Example

- Genetically modified T cells, targeted to destroy Chronic Lymphoid Leukemia cells;
- NEJM, August 2011, reported 1 case of complete remission;
- 2 other cases, 1 complete remission, 1 partial response;
- Small clinical trial ongoing, due to complete 2014;
- European study is ATTACK (Adoptive Engineered T-Cell Targeting to Activate Cancer Killing)

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Reducing Cancer Deaths – Other Examples

- Vaccines
 - E.g. HPV Vaccine to prevent cervical cancer
- Targeted Therapies
 - E.g. Gleevec, FDA approved since May 2001;
 - Time' magazine's "magic bullet" – targets a specific cancer protein (enzyme);
 - Now approved for 10 different cancers;
- Virotherapy

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Ageing in Humans and in Animal Models

- Human ageing expected to involve complex biological and biochemical pathways;
- In animals single gene mutations or simple environmental interventions can greatly extend healthy life span, e.g.:
 - Insulin/Insulin Like Growth Factor Signalling Pathways
 - Target of Rapamycin
- Role of these pathways in humans is not well understood;
- Work is underway on phenotypes and genotypes associated with human longevity

THE SUNDAY TIMES 06.11.11 9

Want \$10m? Find the secret to healthy old age

Robin Kinchen WHOSE are you got if you cross an independent Oscar winner and a 100-year-old find manager? The secret to a healthy old age and a \$10m prize, according to experts, lies in the genes of those who live extra old age without succumbing to chronic disease that will fight diabetes and stroke off America.

They have offered a \$10m prize to anyone who can make those genes a reality.

Specific genes common in the DNA of older people that help to protect them from Alzheimer's and elevate their production of good cholesterol have already been identified. Now, a competition has been launched to encourage scientists to derive even deeper insights into the genetic secrets of longevity.

The prize was organized by the Kinchen Foundation, a nonprofit organization that sets seemingly impossible scientific challenges. A prize of \$10m, provided by the Kinchen Foundation, is the largest prize in the world for a single scientific discovery.

It is the hope of the foundation that the prize will go to the scientists who can most accurately sequence the full genome of an centenarian in just 90 days and at a low cost.

Great Company, the director in charge of the competition, said, "We are trying to uncover what it is that makes these individuals unique, what it is in their genes that allows them to evade the diseases which affect so many people around the world."

Competition and his team are currently recruiting healthy centenarians from Britain and the rest of the world.

Alberto Luigi Kelly, with the oldest living financial investment professional, is one of the first volunteers. He will share the investment business he founded in his age and said, "Honestly I don't feel my age but I don't have to work that I did in my age."

Dr. Mark Smith, from the Albert Einstein College of Medicine, has been studying the genes of 100 healthy elderly people and is involved in examining the centenarians. Research showed that factors including smoking and obesity did not appear to affect those with specific genes, he said.

"They were protected against the environment by their genes so those things didn't matter," Smith said.

Another project, the Weizmann study, which is being conducted at the Scripps Research Institute, recently began to sequence the complete genomes of centenarians. A large study of people who have never suffered from chronic disease.

Research includes the Oscar-winning actress Celia Lovatt, 80, who shares the oldest living American centenarian on Broadway.

THE RAGE IS ON!

ARE YOU READY?

ARCHON GENOMICS XPRIZE PRESENTED BY medco

- Aim: To inspire breakthrough genome sequencing innovations and technologies with the potential to create a new era of personalized medicine.
- \$10 million will be awarded to the first team to rapidly, accurately and economically sequence 100 whole human genomes to an unprecedented level of accuracy.

Caloric Restriction with optimal nutrition

- Lab rodents – reducing food intake by 10% - 40% increases life span;
- Associated with favorable metabolic parameters in humans;
- Most find effective restricted diet intolerable



Canto, left, a 27-year-old rhesus monkey, is on a restricted diet. Owen, right, 29, is not. Canto looks much healthier. The two monkeys are part of a study of the links between diet and aging. Picture from Reuters.
(Colman et al. Science 10 July 2009; Vol. 325, no. 5937, pp. 201 - 204)



Groundbreaking Insights for Longer, Better Lives

In 1998, Washington University in St. Louis's internationally known School of Medicine teamed with Reinsurance Group of America, Incorporated, one of the world's leading life reinsurers, to create The Longer Life Foundation, an innovative partnership supporting independent research by medical and public health experts to improve long-term mortality prediction and promote longer, healthier lives.

LLF-funded research has led to advancements in the fields of:

Longevity	Mortality	Morbidity	Obesity
Genomics	Older-Age Cognition	Cancer	
Caloric Restriction	Public Health		

Since LLF's founding 13 years ago, more than USD \$3.1 million funded 61 research grants. These grants have led to more than 50 publications in peer-reviewed medical journals, and have seeded remarkable growth in new grants awarded to Washington University researchers and the number of academicians and scientists now engaged in longevity research.

LLF also sponsors several lectures, seminars and forums every year, and funds The *Longevity Research Program*, which supports collaborative research into caloric restriction's effects on healthy aging and longevity, and its potential benefits for the heart, the immune system, and cancer prevention.

Ethical / Commercial Challenges

- Gems (2011) concluded the benefits of “freeing people” from ageing outweighed social consequences.
- However, commercial challenges do exist (Evans 2011)
 - Trials over a long-period;
 - Involving older lives;
 - Multiple chronic conditions
 - Many medications
 - Frailty is not a recognised medical problem;
 - Would a broad improvement in health be sufficient motivation for a drug trial?

Factors Influencing Timelines

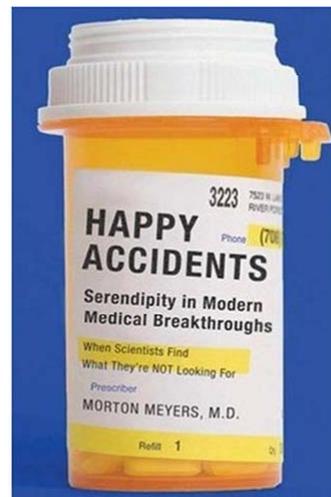
Steps to new medical treatments

- Research
- Discovery
- Approval
- Uptake

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Some medical discoveries are random.....

- ...so it is hard to predict when break-throughs will occur;
- Examples:
 - Penicillin
 - Heparin,
 - Viagra etc
- But also consider, for example, rational drug design



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...and predicting winners is hard

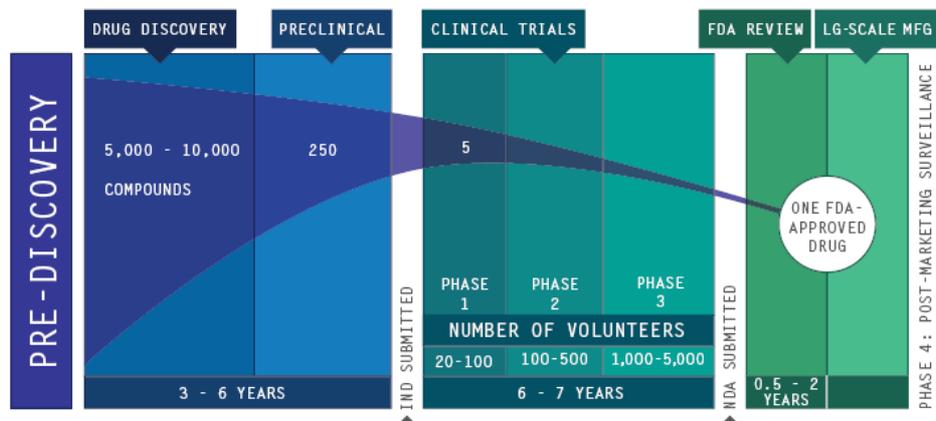
- April 2008
 - GSK acquire Sirtris Pharmaceuticals
 - c£362m
 - Sirtris were world leaders in Sirtuin research;
- Late 2009
 - Evidence emerges that Sirtris' compounds are 'problematic';



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Drug Development Process



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Summary of FDA Drug Approval Process

Pre-Clinical	Clinical			Approval	Market
	Phase I	Phase II	Phase III	New Drug Application	Phase IV / Postmarket surveillance
Purpose	Safety	Safety dosing efficacy	safety efficacy side effects		
Expenses (\$m)	15.2	23.4	86.5		
Time (months)	21.6	25.7	30.5		
Total Time	6 to 11 years			0.6 to 2 years	11 to 14 years
Overall probability of success					
	30%	14%	9%	8%	

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Source: Dimasi, Hansen, Grabowski (2003)

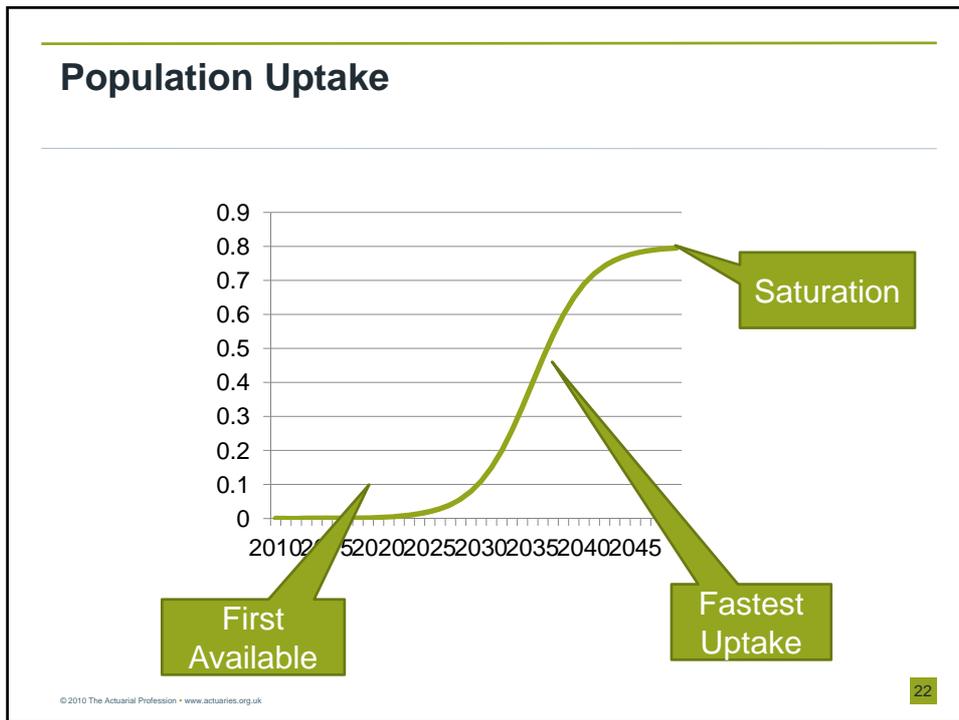
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Example: FDA Approval of Gleevec

- 1980's – understanding that the protein BCR-ABL 'causes' Leukemia;
- 1993 – first laboratory studies of compounds that could block BCR-ABL
- 1996 – Gleevec (STI571) shown to inhibit growth of BCR-ABL expressing cells;
- 1998 – First tested in a small study of patients
- 1999 – preliminary results on 31 patients;
- February 2001 – Application for approval submitted
- April 2001 – Study results published for 81 patients (phase 1)
 - Patients enrolled from June 1998 – May 2000
- May 2001 – FDA Approval

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Scenarios

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Anti-aging Base Scenario: Base Assumptions

- To think about stresses you need to know what you are stressing...
- This is the default behaviour until the stress takes place;
- We assume CMI(2011) [1%], which we believe is broadly equivalent to:
 - Significant attenuation of current level of CV, Lung Cancer and “other causes” improvements over the next 20 years;
 - No change in “Other Cancer” improvements over the next 20 years;
 - No material change in population risk factors;

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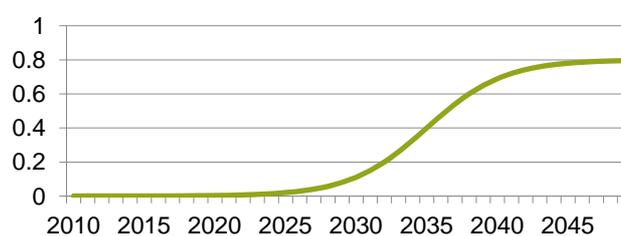
Anti-aging Base Scenario: Efficacy

- Fall in mortality for ages below 60:
 - 90% of the impact shown in animal trials
 - 65% reduction shown in trials (assumed from Colman et al, 2009)
- Impact on lives aged over 60, linear interpolation between
 - Effect as above for age 60,
 - 0% by age 100

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Anti-aging Base Scenario: Timing and Take-up

Parameter	Value
Drug ready for human trials in	2020
Drug first released in	2025
Drug 50% take-up in	2035
Drug maximum take-up in	2045
Maximum take-up % of Pop	80%



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Anti-aging Base Scenario: Conclusions

- Male Life Expectancies
- Expressed as CMI2011[x%]

Age in 2011	40	60	80
CMI2011[x]	2%	1.25%	1%
x – 1% (base)	+1%	+0.25%	-

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Anti-Aging Scenarios: Examples Scenarios Illustrating different outcomes

- For a male Life aged 60 now:
- To obtain a CMI 2011[2%] equivalent:
 - Quicker availability and quicker take up
 - Available from 2018, maximum take up in 2035
- To obtain a CMI 2011[3%] equivalent:
 - No tapering of efficacy;
 - Quicker availability and take up
 - Available from 2018, maximum take up in 2035
 - Maximum life span extended

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Cancer Elimination Scenarios

- Assumptions
 - Independence with other causes of death;
 - Elimination takes place over a staged process over y years

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Cancer Elimination Scenario: Conclusions

- Male Life Expectancies
- Expressed as CMI2011[x%]

Age in 2011	CMI2011[x%]
Full Elimination over 10 years	3%
80% Elimination over 20 years	2%

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Overall Conclusions / Opinions

- Many avenues are being explored which could drive longevity improvements;
- Predicting the outcome of this research is difficult both in terms of efficacy and timelines;
- Considering these two drivers of mortality improvements independently, CMI2011[3%] scenarios appear very ambitious
 - but well within 1 in 200 years event parameters;

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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 presenter.

