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making financial sense of the future

Life Conference 2011  
Peter Banthorpe, Joseph Lu



# Stress testing and scenario modelling of longevity

22 November 2011

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## Agenda

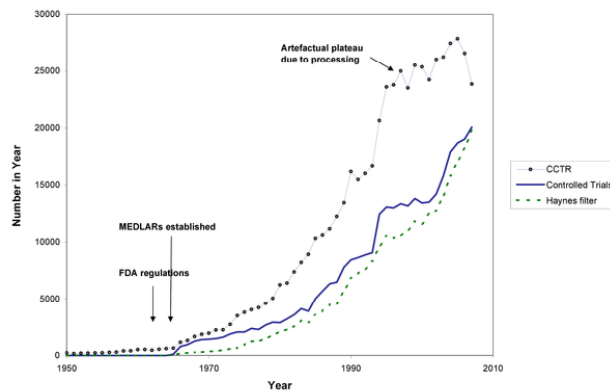
- Possible medical advances impacting longevity;
- Factors influencing time lines;
- Scenarios;

## 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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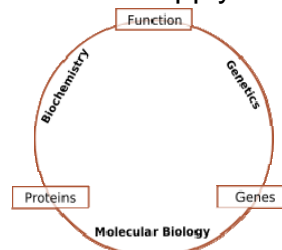
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## Reducing Cancer Deaths

- Many avenues for advancement:

- Prevention
  - Lifestyle changes
  - Vaccination
- Early detection
- Improved treatments
- Post treatment care

Molecular Biological  
Techniques and Genetics  
could apply

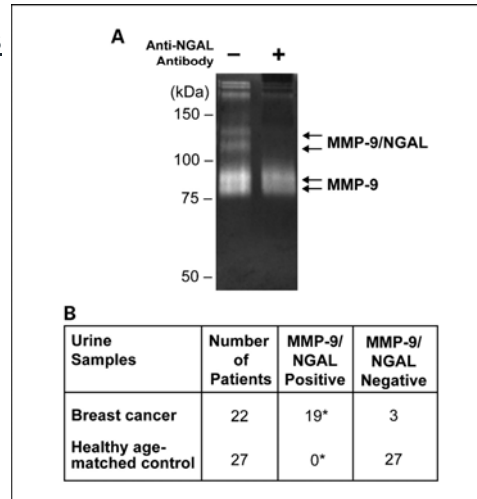


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## Advances in Cancer Detection

### Matrix Metalloproteinases (MMPs)

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

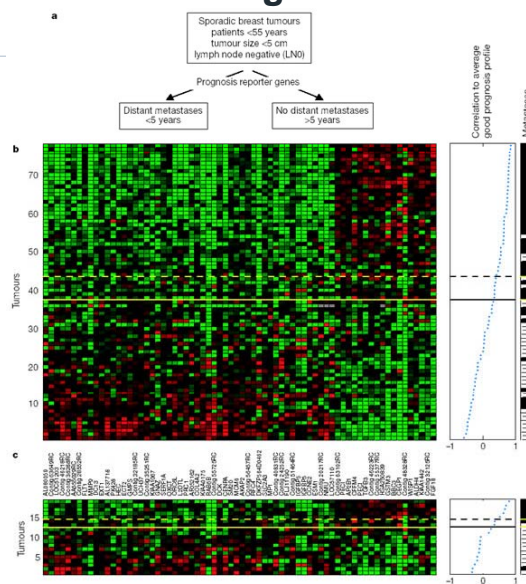


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## Tumour Gene Expression Profiling

- 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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## 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 ages more slowly and Owen



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.

(Corman et al., Science 10 July 2009; Vol. 325, no. 5937, pp. 201 - 204)

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# Longer Life Foundation

An RGA/Washington University Partnership

### 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.

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Please visit [www.longerlife.org](http://www.longerlife.org)

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## 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?

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## Factors Influencing Timelines

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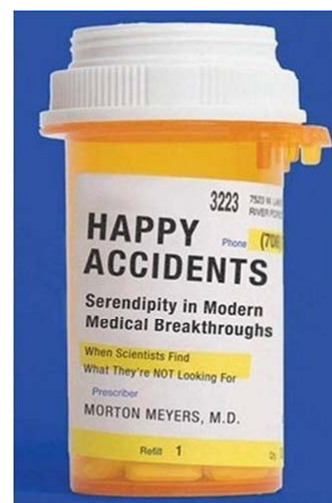
## Steps to new medical treatments

- 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

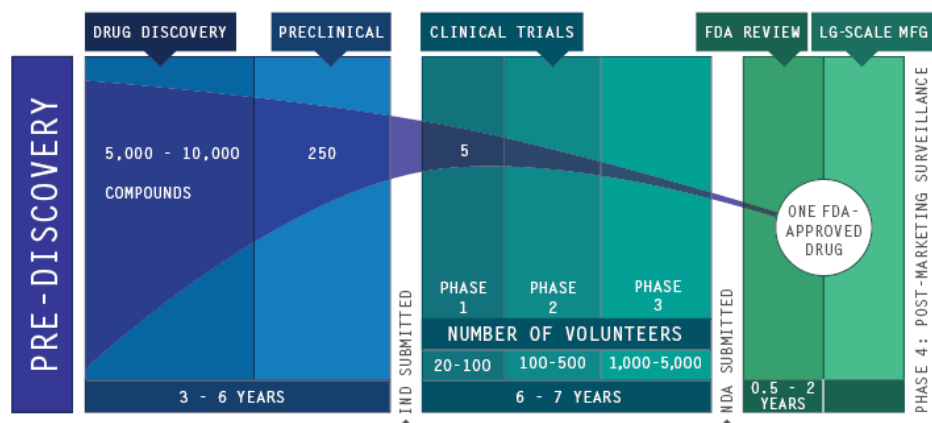
- April 2008
  - GSK acquire Sirtris Pharmaceuticals
  - c£362m
  - Sirtris were world leaders in Sirtuin research;
- Late 2009
  - Evidence emerges that Sirtris' compounds are 'problematic';



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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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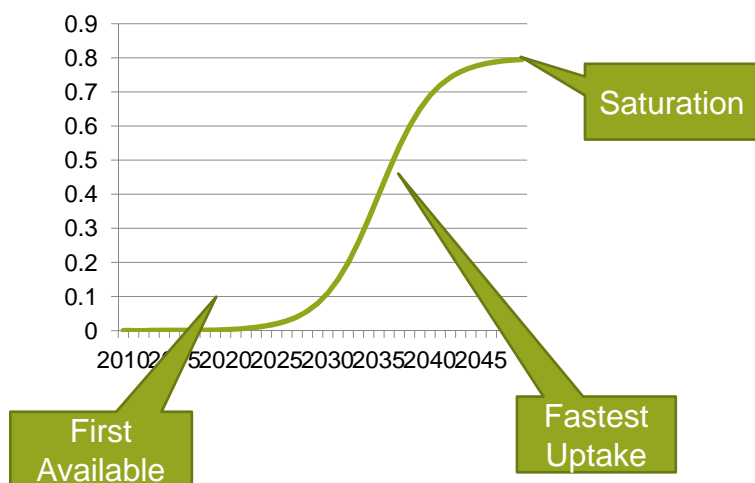
## Example: FDA Approval of Gleevec

- 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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## Population Uptake



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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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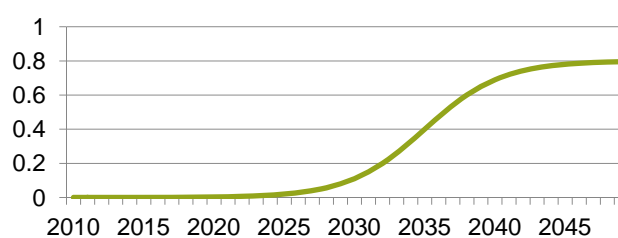
## Anti-aging Base Scenario: Efficacy

- 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?

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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 presenter.

