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Prospective Longevity Risk Analysis

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Risk Management Solutions

Royal College of Physicians, Edinburgh: 22 October 2009

Outline

- The catastrophe insurance modelling approach
- Medical science-based mortality modelling
- Treatment of geroscience advancement

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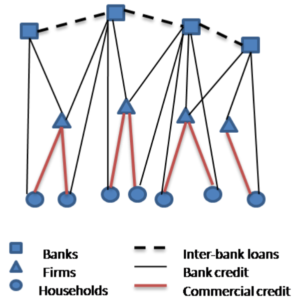
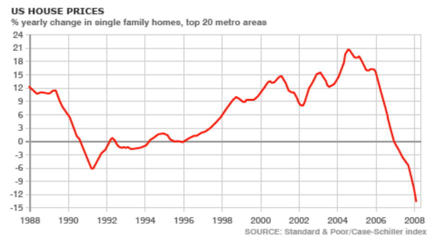
Probabilistic modelling of what might happen

*'To win back investor confidence, ratings must be more predictive, and must tell the market about **what might happen**, instead of what happened yesterday'.*

Stephen Joynt, Fitch Chief Executive, October 2008

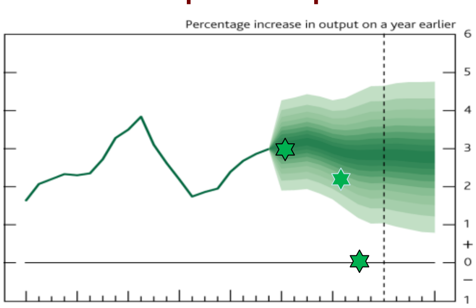
Santa Fe Institute
Modeling the complex structure of the US real estate market





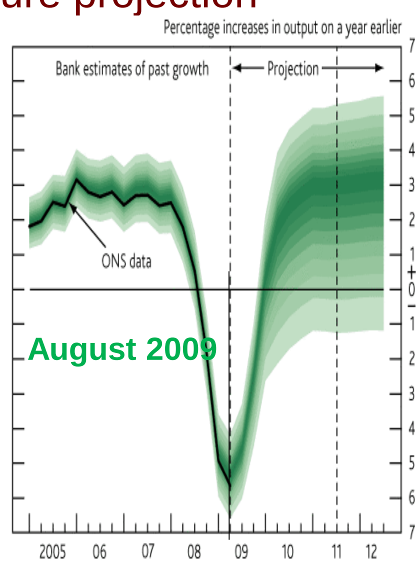
Contrast schematic mathematical modelling of the underlying complex dynamical structure, with elaborate statistical analysis of historical non-stationary time series.

Catastrophe impact on future projection



February 2007

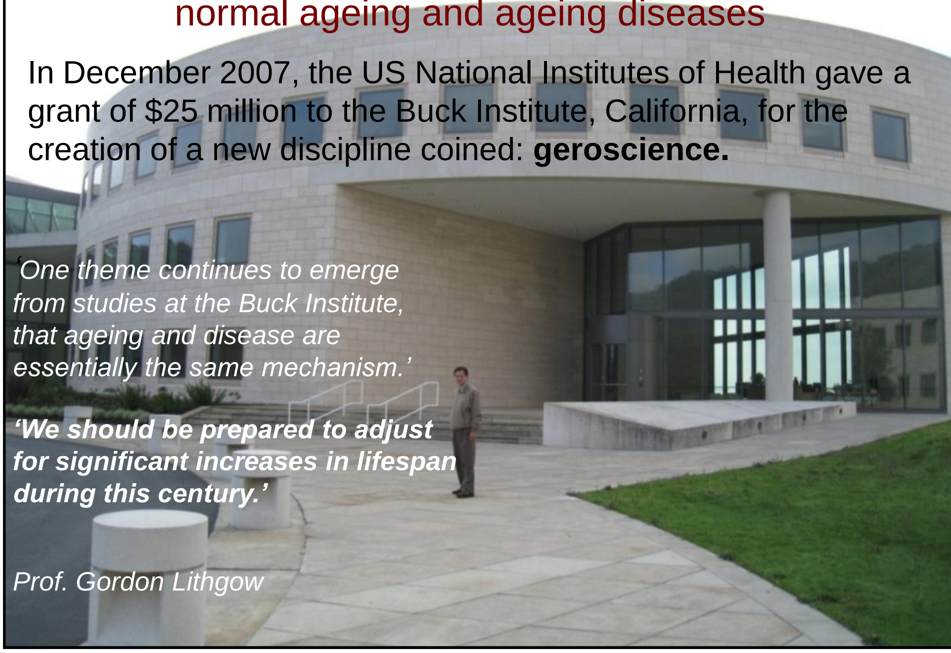
Bank of England GDP fan chart



August 2009

Geroscience: the study of the interface between normal ageing and ageing diseases

In December 2007, the US National Institutes of Health gave a grant of $25 million to the Buck Institute, California, for the creation of a new discipline coined: **geroscience.**



'One theme continues to emerge from studies at the Buck Institute, that ageing and disease are essentially the same mechanism.'

'We should be prepared to adjust for significant increases in lifespan during this century.'

Prof. Gordon Lithgow

Property catastrophe risk analysis [pre-1990]

- Insurance market driven by supply and demand rather than risk awareness: *'An Act of God is an accident or event due to natural causes which no amount of human foresight could have guarded against.'*
- Race-to-the-bottom in exposure data quality:
  - Minimal exposure location data
  - Minimal information on property vulnerability to natural hazards
- Crude assessment of Probable Maximum Loss (PML)

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Key facets of catastrophe risk modelling

1. Minimize epistemic uncertainty by cleansing and mining portfolio exposure data.
2. Understand vulnerability at an individual insured level.
3. Explicitly construct an ensemble of future hazard scenarios, taking account of dynamic changes in the hazard environment not represented in historical time series.

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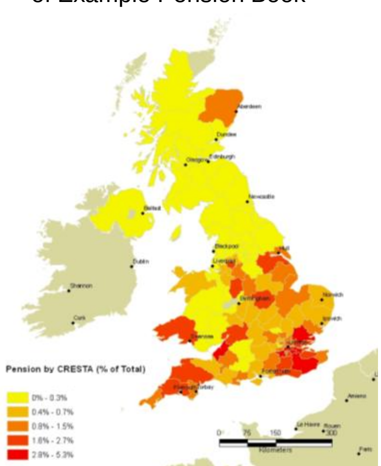
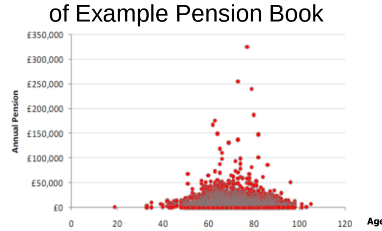
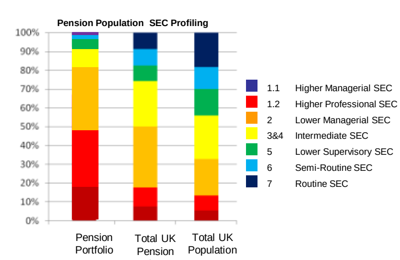
Portfolio analysis and data enrichment

Geographical Distribution of Example Pension Book



Age and Value Distribution of Example Pension Book





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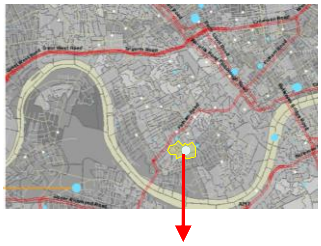
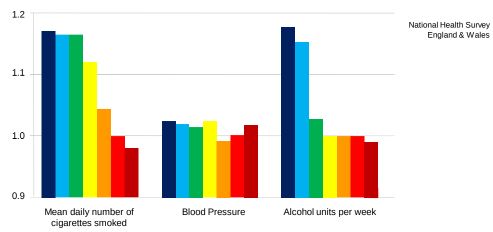
Postcodes, pensioners and health risk factors



- 1.1 Higher Managerial SEC
- 1.2 Higher Professional SEC
- 2 Lower Managerial SEC
- 3&4 Intermediate SEC
- 5 Lower Supervisory SEC
- 6 Semi-Routine SEC
- 7 Routine SEC

- Smoking prevalence
- Smoking severity
- Body Mass Index
- CVD prevalence
- Diabetes prevalence
- Cholesterol (TC/HDL Ratio)
- Blood Pressure
- Alcohol consumption
- Dietary habits
- Exercise patterns



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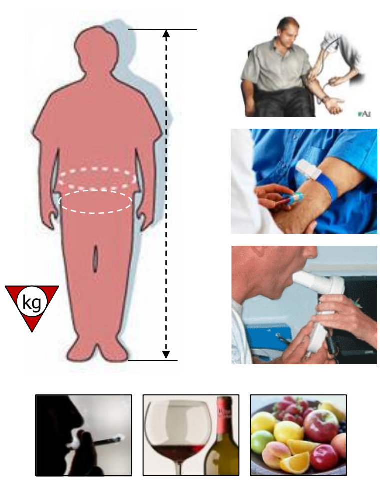
Individual risk factors



Risk Factors for a Person
Age
Gender
Occupation
Current diseases
Blood pressure (SBP/DBP)
Pulse rate
Weight/Height/BMI
Waist/Hip circumference
Blood Lipids (Cholesterol, Triglycerides, Apolipoproteins)
Haemoglobin A1c (HbA1c)
Lung function tests (PEFR/FEV1/FEV%)
Left ventricular hypertrophy on ECG (LVH)
Smoking history (consumption/pack yrs/age commenced)
Alcohol consumption
Leisure activities

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Quantifying the effect of risk factors

- An individual's mortality risk from a disease depends on a range of health and lifestyle risk factors.
  - e.g. blood pressure, cholesterol level, diabetes, smoking
- Based on medical science knowledge, it is possible to estimate an individual's risk of disease during a specified time range. The change in risk associated with changes in risk factor levels can be quantified via survival curves.

Construction of an odds model of coronary heart disease using published information: the Cardiovascular Health Improvement Model (CHIME)

Christopher J Martin, **Paul Taylor** and **Henry WW Potts**

BMC Medical Informatics and Decision Making 2008, **8:**49doi:10.1186/1472-6947-8-49

Framingham risk equations

$$\mu = \sum_i \beta_i x_i \qquad \sigma = \theta_0 + \mu\theta_1$$

Different values of $\beta_i, \theta_0, \theta_1$ are used for coronary heart disease (CHD), stroke and cardiovascular disease (CVD).

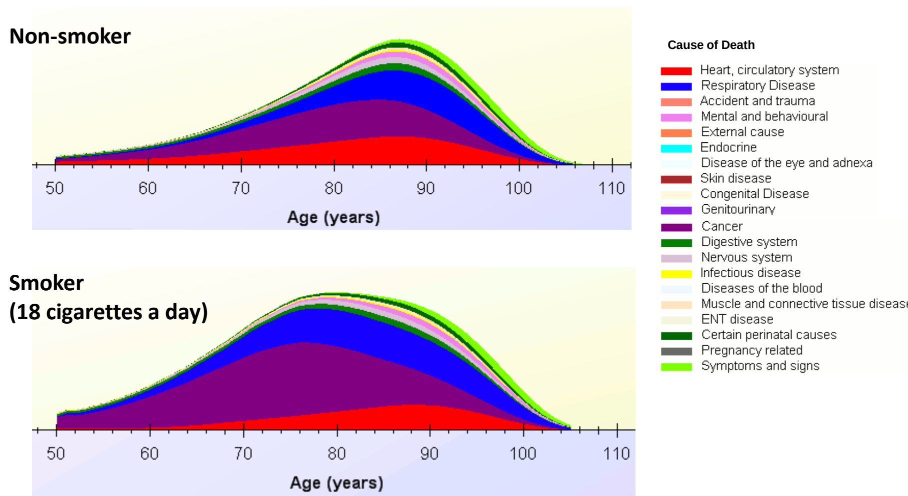
Chance of surviving T years is: $\exp(-T * \exp(-\mu / \sigma))$

Risk Factors
Age
Gender
Smoking
Blood Pressure
Cholesterol ratio
Diabetic
etc.

→

e.g. 10 Year Risk	
CVD event	12%
CVD death	9%
CHD event	8%
CHD death	5%
Stroke event	3%
MI event	7%

Comparison of probability of age of death by cause in an average smoking and non-smoking man aged fifty



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Projections of the future

- Instead of directly forecasting the time series for mortality from historical data, as in the Lee-Carter model, RMS is modeling stochastically the underlying causative time series for future geroscience advancements.
- There are ‘catastrophe’ 21st century medical technology scenarios, which have no historical precedent.
- Conversely, standard medical search methods for effective drugs may possibly have diminishing returns.
- At any future time, the impact of existing geroscience advancements on mortality can be assessed using the RMS mortality model.

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GASP model

- **GEROSCIENCE:** The interdisciplinary science of aging, and age-related diseases, provides the knowledge basis for future longevity scenarios
- **ADVANCEMENT:** Future advancement in medical technology and healthcare is taken into account in forward modeling.
- **STOCHASTIC:** The evolution of future longevity involves intrinsic randomness and is fundamentally stochastic.
- **PROCESS:** Developments in longevity are process-driven.

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Five categories of future longevity change

A. Lifestyle
- Personal choice: smoking, diet, drinking, exercise

B. Health Environment
- Sanitation, hygiene, health awareness and education, testing and screening

C. Disease Reduction
- Drug discovery and treatments to reduce the incidence of major causes of premature death

D. Regenerative Medicine
- New treatments to prolong life for people who are suffering a life-threatening condition e.g.: Transplant techniques, Individualized Gene Therapy, Stem Cell Therapy, Nanomedicine

E. Life Extension
- Changing the biology of ageing to extend healthy life

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Modeling of GASP future trajectories

- Geroscience advancement scenarios are modelled as trajectories spanning decades into the future.
- Each geroscience advancement defines a stochastic process: $G_k(t)$.
- A standardized universal metric for geroscience advancement may be taken to be the aggregate mortality reduction associated with a range of diseases.
- Progress is gauged in terms of mortality reduction relative to the maximum potential improvement.

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Mortality reduction

Type of disease	Mortality reduction
Infectious diseases	R[1: t]
Neoplasms	R[2: t]
Blood diseases	R[3: t]
Endocrine and metabolic diseases	R[4: t]
Nervous system diseases	R[5: t]
Circulatory system diseases	R[6: t]
Cerebrovascular diseases	R[7: t]
Respiratory system diseases	R[8: t]
Digestive system diseases	R[9: t]
Genitourinary diseases	R[10: t]
Etc……….	……….

Relative progress in mortality reduction at time t is:

$$G_k(t) = \sum_j R[j:t] / \sum_j R[j:\infty]$$

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Medical discovery as a stochastic process

- The search for therapeutic chemical compounds involves a sizeable heuristic trial-and-error component.
- Serendipity and luck have played a key role in past medical discoveries.
- '*Serendipity is the art of finding what we are not looking for by looking for what we are not finding*' (Quéau, 1986).

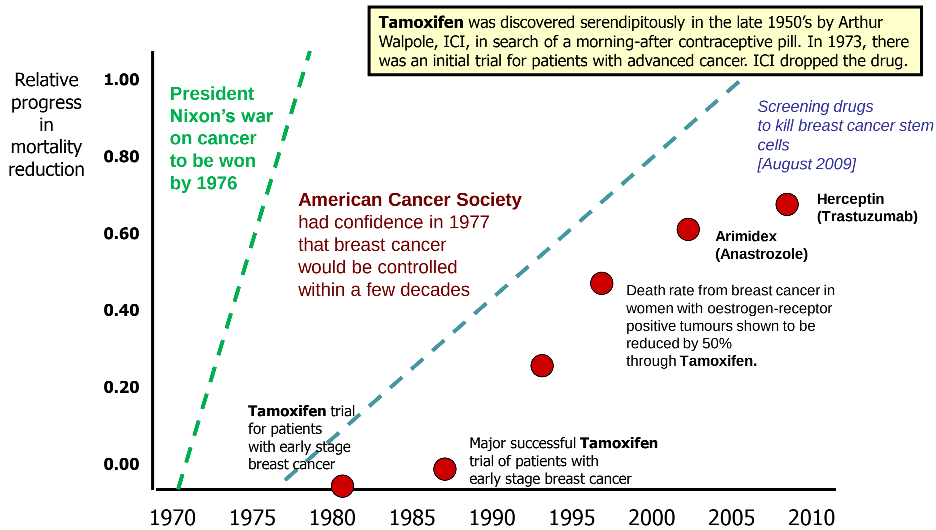
Problem **1** [**No** solution] → Problem **2** [solution]

> *'Medical research is still more a game of pool than billiards. You score points regardless of which pocket the ball goes into'.*
>
> Arthur Kornberg
> Nobel laureate in medicine

Modeling randomness in medical discovery

- Investigations that seemed totally irrelevant to any practical objective have yielded *most* of the major discoveries of medicine.
- Medical discovery has the characteristics of a random walk superposed on a rising trend towards making progress, but with the possibility of setbacks.
- This progress trend is dependent on a number of increasing variables:
  - global funding for medical research;
  - the number of major medical research institutes; international scientific researchers, publications etc..
  - the power of technology.

Drug treatments for breast cancer



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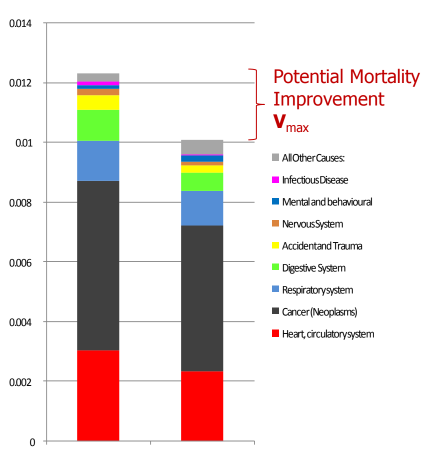
Stem cell transplant impact on future mortality

Estimated impact on mortality if stem cell transplant treatment became standard practice



Diseases amenable to stem cell therapy

- Diseases that involve a loss of tissue:
  - ischaemic heart disease
  - stroke
- Disease where there is a loss of specialized cells:
  - some forms of diabetes
  - Parkinson's disease.
- Recovery from other treatments that would otherwise be lethal:
  - bone marrow replacement after whole body radiotherapy in leukaemia

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General stem cell therapy projections

- Regenerative medicine and stem cell technologies are estimated to become a US$ 500 billion market over the next 20 years.
- The number of stem cell articles doubled in the decade since 1995 from about 1600 to over 3200.
- *"The potential of adult stem cells for regenerative medicine is great; it is likely that these various cells will find clinical application in the upcoming decades."* (National Institutes of Health, 2006).

"Engineering a trachea is the holy grail of tracheal replacement"

Dr. Paolo Macchiarini,
The Journal of Thoracic and Cardiovascular Surgery, **2004**

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Organ replacement projections

- Professor Martin Birchall, Bristol University, who helped grow the cells for the first windpipe transplant, said (11/08): "In 20 years, this will be the most common form of surgery, virtually any transplant organ could be made in this way. The commonest operations will be regenerative procedures to replace organs and tissues."
- Patrick Warnke, a surgeon at the University of Kiel, who is also growing patients' tissues from stem cells for transplants, predicts that doctors might one day be able to produce organs in the laboratory from patients' own stem cells. *"That is still years away, but we need pioneering approaches like this to solve the problem."*
- Dr. Allan Kirk of the American Society of Transplantation commented: *"It's an important advance, but constructing an entire organ is still a long way off."*

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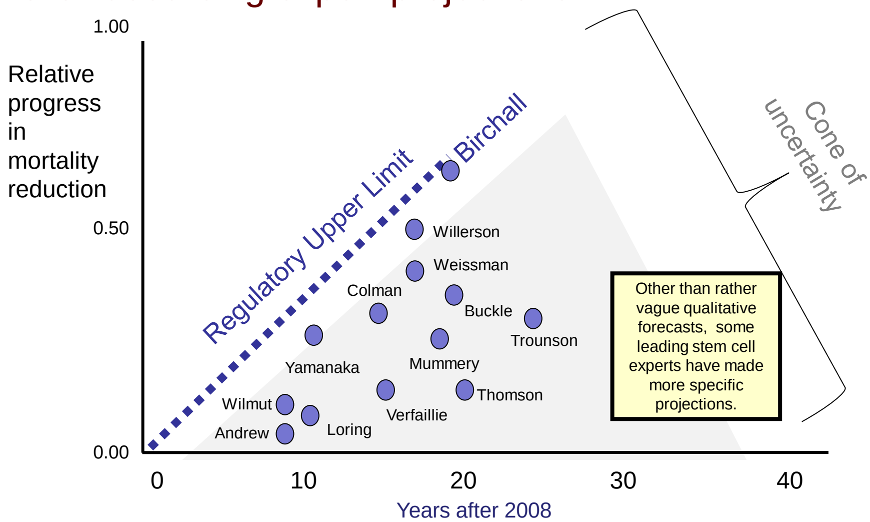
Regenerative medicine:
Crowdsourcing expert projections



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Modeling randomness in medical discovery

The procedure for simulating a trajectory for a GASP medical discovery stochastic process $G(t)$ is based on the general dynamical equation below.

This includes a noise factor $W(t)$, which reflects the inherent randomness in each stochastic process.

$$\frac{dG(t)}{dt} = f(t,G(t)) + \sigma(t,G(t)).W(t)$$

The complexity of this model should be commensurate with knowledge about the medical discovery process. The key characteristics can be captured with a basic stochastic model.

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Numerical model of G(t)

$$G(t+\Delta)-G(t)=f(t,G(t))\Delta+\sigma(t,G(t))W(t)\Delta$$

An appropriate and practical discretization time interval for longevity risk simulation Δ is several years. Given regulatory healthcare oversight, this is a time frame in which notable developments in mortality improvement can take place.

A parsimonious random walk model has a minimal set of parameters: an average trend superposed upon which are stationary independent Gaussian fluctuations.

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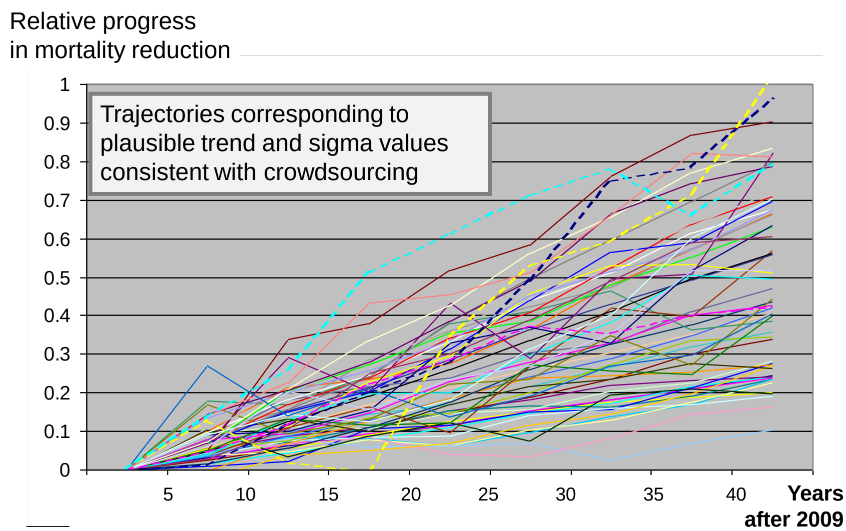
Regenerative medicine: random walk with trend



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Stochastic simulation of mortality reduction

- For the k'th geroscience advancement $G_k(t)$, an ensemble of simulations can be generated from the underlying stochastic dynamics.
- For each simulation, the collective mortality reduction of the set of scenarios $\{G_1(t), G_2(2), G_3(3)....\}$, at a given future time t can be evaluated from the mitigation of diseases targeted by these advancements.
- The updated disease rates at time t can then be input into PrognoSys.
- The outcome from the ensemble of simulations defines longevity risk over future decades.

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GASP model simulation flow

Simulate a future 50-year trajectory for each of the set of Geroscience Advancement Scenarios: *lifestyle, healthcare environment, disease treatment, regenerative medicine, life extension*

↓

Estimate the collective scenario impact on mortality reduction at 5-year time intervals over the next fifty years, using PrognoSys

↓

Compute longevity risk for the next fifty years from the ensemble of stochastic simulations of the set of Geroscience Advancement Scenarios

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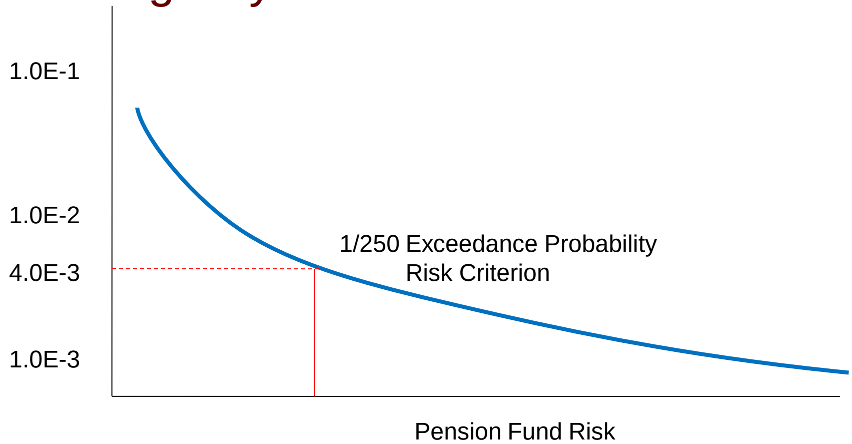
Exceedance probability curve for longevity risk



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