The Actuarial Profession
making financial sense of the future

Health and Care Conference 2011
Daniel Ryan, Swiss Re

Prevention versus treatment in driving future mortality improvements?

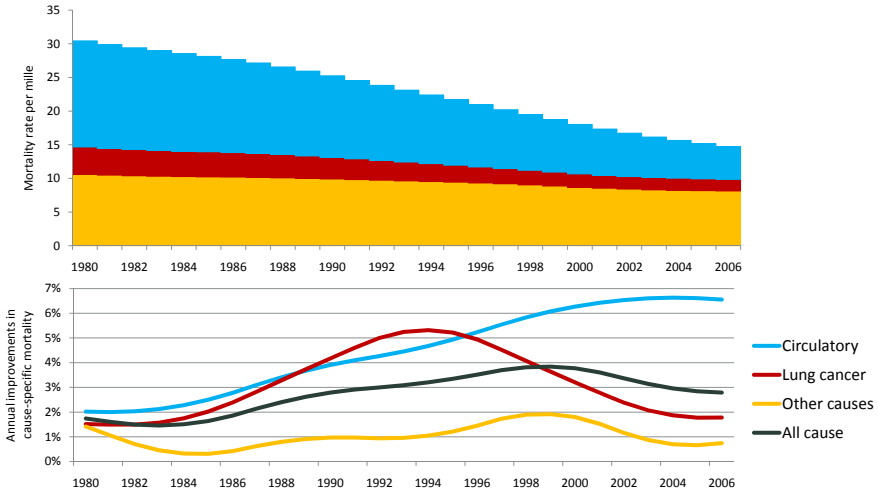
19th May 2011

Who wants us to live longer?

- Individuals – MIXED – clearly not all interested in maximising life span – examples would include smoking, obesity, lack of compliance with best clinical practice.
- Governments – MIXED - concerns over pension and healthcare costs after retirement, although have control over taxation policy and state retirement age
- Corporates/pension schemes – MIXED – potentially healthier workforce through concept of dynamic equilibrium, but major concerns over affordability of defined benefit schemes
- Pharmaceutical industry – YES – introduction of drugs and screening methodologies together with wider distribution of existing drugs
- Medical & nursing professions – YES – application and reinforcement of best practice guidelines, plus continual challenge to find solutions for those that die prematurely

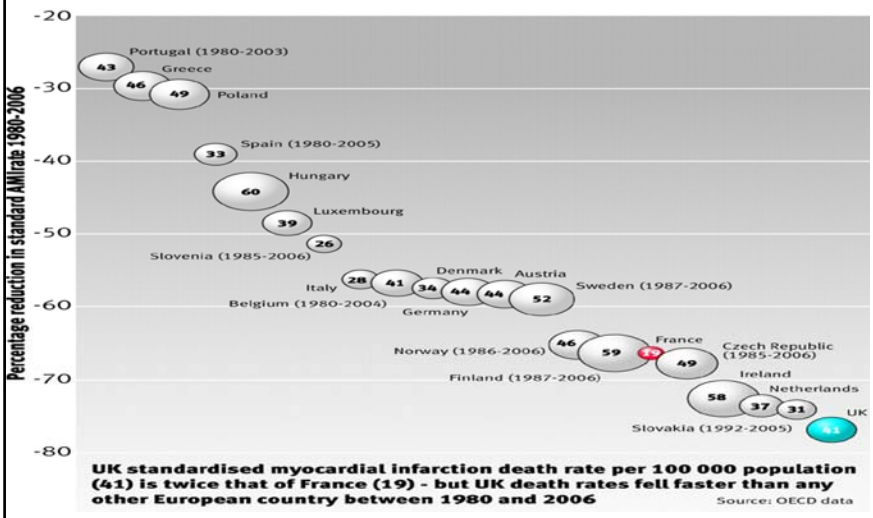
1

Recent dominance of mortality trends
Men aged 65 in England & Wales



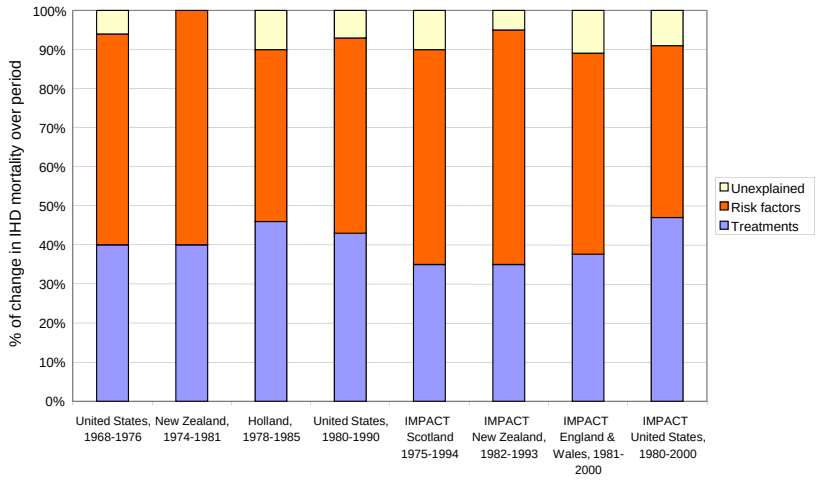
2

International trends in cause-specific mortality
Myocardial infarction (1980-2006)



3

Historical risk factors vs. treatments
CHD Impact & other studies



4

Focus on individual contributions
Cardiovascular mortality (1980-2000), E&W

Risk Factor	Effect	Treatments	Effect
Obesity	+3%	AMI	-8%
Diabetes	+5%	Secondary prevention	-11%
Blood Pressure	-10%	Heart failure	-13%
Smoking	-48%	Angina: CABG/PTCA	-7%
Cholesterol	-9%	Hypertension therapy	-3%
Physical activity	+4%		
Deprivation	-3%		
Total	-58%		-42%

CHD Impact model – University of Liverpool – England & Wales

5

Preventative medicine vs. curative medicine
Where should the focus lie?

- Preventative medicine – reduce risk of developing a disease or reduce risk of subsequent disease/disability
  - Primary – avoid disease
  - Secondary – detect and cure disease whilst asymptomatic
  - Tertiary – reduce impact or progression for those with disease
  - Importance of screening to primary and secondary prevention
- Curative medicine – elimination of disease
  - Rarely achieved except for acute infectious disease
  - Instead focus on various different modalities of treatment
- Key driver to change is perception that preventative medicine should be less expensive in aggregate – BUT is it?

Source of imbalance to treatment medicine?

- 90/10 split of funds in the USA
- Public health less eye-catching than recent technology and new hospitals
- Personalised medicine approach being adopted by pharmaceutical companies
- Highly specialised nature of many medical professional groups tends to lead to excessive focus on the disease rather than the individual
- Popular resistance to "nanny state" and science in general
- Fast developing networks of patients through social media with common disease leading to development of patient advocacy and pressure groups

Areas that would need to be addressed

- Changing public opinion
  - New dialogue with "healthy" population that educates and informs on the importance of different risk factors
  - Engage individuals over their health decisions rather than a passive recipient of different clinical guidance
- Rebalance existing structures
  - Boost role and status of General Practitioners/Public Health
  - Investigate remuneration/financial packages that place the GP at the centre of patient expenditure – VERY TOPICAL INDEED
  - Co-ordinate treatment of co-morbidity in the elderly
- Promote healthy activities
  - Policy initiatives to promote beneficial risk behaviours and penalise adverse risk behaviours – e.g. Gym vs, smoking

8

Role of screening in preventative medicine

- Initiated by doctor rather than patient
  - may have financial implications based on target % screened
- International criteria
  - Accepted treatment or intervention for patients with the disease.
  - Natural history of the disease should be adequately understood
  - Latent or early symptomatic stage
  - Suitable and acceptable screening test or examination
  - Treatment started at an early stage should be of more benefit than treatment started later
- Sensitivity & specificity are both key
  - extent of physical and psychological harm caused by investigation of false positives and dangers of false negatives

9

Is screening cheaper than treatment?

- Balance in economic costs between different approaches
  - Screening costs include the cost of applying the test to the target population (which could be all population) and the cost of further investigation of true and false positives
  - Potentially long-term treatment and support costs for those that develop disease
- Comparative analysis of frequency of screening and target age groups
- Maybe more expensive if incidence of disease is low and screening costs are more substantial
- Key question would be the proportion of additional years of life that are expected to be in good health – otherwise extension of life may lead to significantly greater overall medical/social costs

Use of biomarkers in general

- Historical basis of assessing risk is through risk algorithms based on epidemiological data e.g. total cholesterol, HDL cholesterol, LDL cholesterol, blood pressure, BMI, waist circumference
- Biomarkers are measurable characteristics or alterations that indicate normal or pathogenic processes or responses to intervention
- Different biomarkers could reflect:
  - Environmental exposure - e.g. industrial pollutant concentrations
  - Genetic susceptibility - e.g. APOE in Alzheimer's disease
- Potential roles in accelerating pharmaceutical development
  - Screening new compounds
  - Accelerating proof of concept
  - Evaluate drug efficacy in clinical trials

Use of biomarkers for cardiovascular disease

- Imaging of atherosclerosis as ideal solution but impractical for primary prevention
- Biomarkers already well established in the diagnosis of acute cardiovascular disease
  - myoglobin, CK-MB, troponin (T, I or C)
- Concentrations of troponins with ECG and clinical changes used to categorise patients based on severity of disease
- Newer markers offer more detailed categorisation, assessing disease burden and potential indicators of restoration of function – example markers used with heart failure
  - BNP
  - NT-proBNP

12

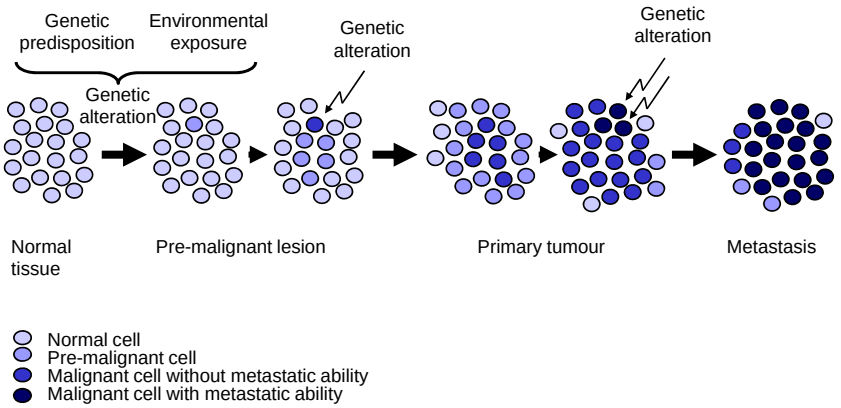
Potential biomarkers for cardiovascular disease

- MMP (metalloproteinases) & MPO (myeloperoxidases)
  - plaque destabilisation through macrophage activity on protective collagen layer
  - importance of shearing forces from arterial blood
  - markers of inflammation
- sCD40L (soluble CD40 ligand), PlGF (placental growth factor), PAPP-A (pregnancy-associated plasma protein A)
  - plaque rupture
- IMA (ischaemia-modified albumin) – increases within minutes of ischaemia, normal within 24 hours
- BUT all of above are either not unique to cardiovascular disease or affected by treatments – The Search Continues

Lex – The Future of Cardiac Biomarkers. Temple University School of Medicine, USA

13

Natural history of cancer as staged process



14

Estimates of contribution of risk factors to cancer

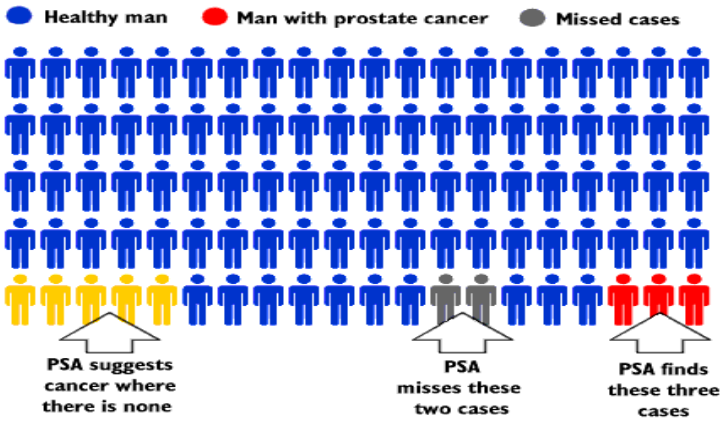
Factor or class of factors	Percentage of all cancer deaths	
	Best estimates	Range of acceptable estimates
Tobacco	**30**	**25–40**
Alcohol	**3**	**2–4**
Diet	**35**	**10–70**
Food additives	<1	-5* to -2
Reproductive and sexual behaviour	7	1–13
Occupation	4	2–8
Pollution	2	<1–5
Industrial products	<1	<1–2
Medicines and medical procedures	1	0.5–3
Geophysical factors	3	2–4
Infection	10?	1–?
Unknown	?	?

Doll and Peto (1981) J Natl Cancer Inst 66(6):1191-308.

15

Dilemma posed by original PSA test

For every 100 men over the age of 50 who have the PSA test



16

Advances in prostate cancer diagnosis

- PLCO trials – 155,000 screened by 2006 and followed up for 10 years
- Must not overlook aggressive prostate cancers that represent threat
- Improvements to PSA test
  - PSA velocity – suggested value of 0.35ng/ml per year
  - PSA density – comparison of PSA level and prostate volume
  - Free/bound PSA – prostate cancer has more bound PSA than benign prostatic hypertrophy (BPH)
  - Variation in cut-off values by age (as opposed to 4.0ng/ml)
- New strategies under research
  - Pattern recognition – microRNA, proteomics, metabolomics
  - Epigenetic gene alterations or characteristic gene fusions
  - PCA3 – prostate specific RNA - increased expression in cancer

17

Difference of opinion on colo-rectal cancer
Prevent occurrence or detect and treat early

- Conflicting opinions on how invasive initial screening should be:
  - American Cancer Society/American College of Radiology/US Multi-Society Task Force on Colorectal cancer stressed value of tests that detect and remove polyps to prevent cancer
  - US Preventive Services Task Force supported stool tests
- Choice of high initial costs with more lives saved vs low initial costs with fewer lives saved
- Most countries with screening programs use fecal occult blood test – the simpler option
- However, higher false positives from a simpler test leads to more colonoscopy surveillance if best practice guidelines on follow-up followed – potentially a false economy over the longer term

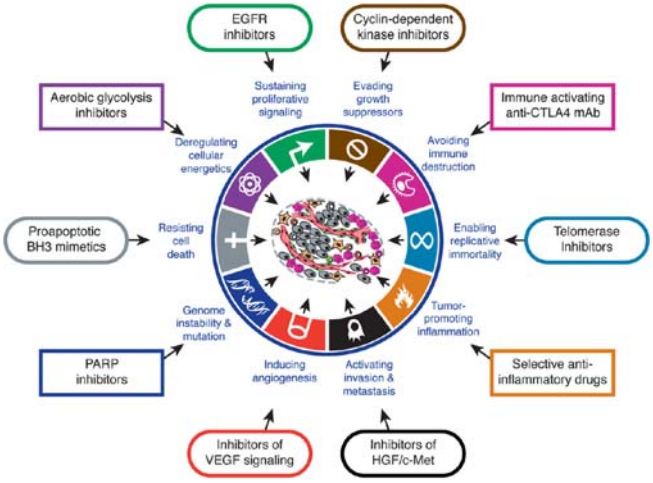
18

Screening vs. treatment for breast cancer
Historical importance to cause-specific mortality

- Original meta-analysis produced by WHO in 2002 suggested that screening women aged 50 to 69 years reduced breast cancer mortality was responsible for 25% of the decline in mortality rates.
- Norwegian study of a combined group of 40,000 screened and non-screened women found 28% survival change in mortality rates over the period of the investigation. Further analysis suggested that the impact of scenarios was only 8%, with the bulk of the change likely to be associated with the use of tamoxifen.
- UK has significantly higher long-term mortality experience after breast cancer diagnosis. This is believed to be as a result of small seedling metastases which might not have developed if more extensive investigation was routinely carried out.

19

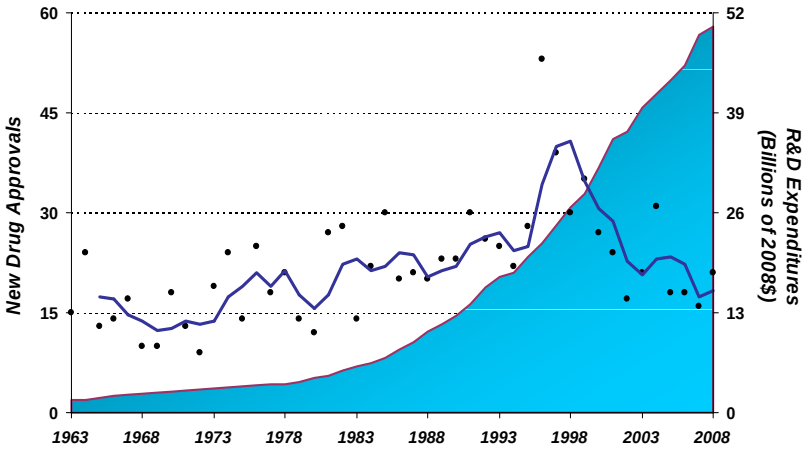
Therapeutic targeting of the hallmarks of cancer
Many avenues vs. single vaccine



D. Hanahan and R. Weinberg, Cell, 144 (646-674), 2011

20

Limited return on increasing R&D expenditure



Kaitin, Clin Pharmacol Ther, 2010;87:356-361

21

New directions: vaccines in non-infectious disease

- Cytos originally developed the Immunodrug platform
- Cytos has since gone into partnership on specific treatments with Pfizer and Novartis..
- Two of the most advanced substances have completed Phase II trials and these are on smoking cessation and hypertension.

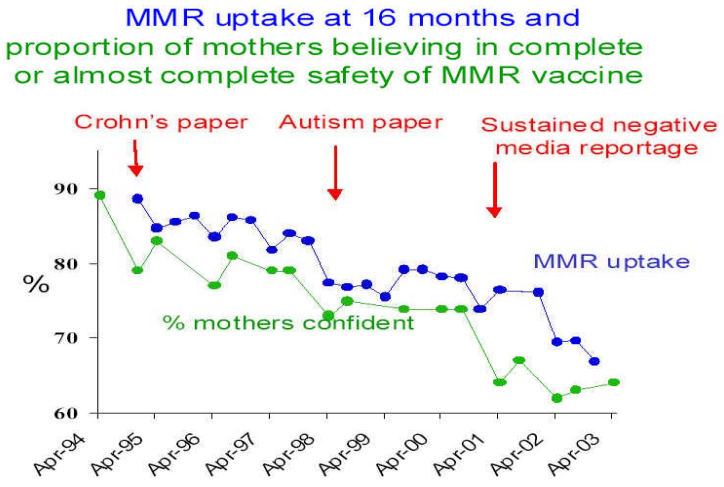
Product Pipeline **February 2011**

		Preclinical	Phase I	Phase II	Phase IIb
Respiratory	CYT003-QbG10 for allergic rhinoconjunctivitis				
	CYT003-QbG10 for allergic asthma				
	VLP-IgE vaccine for allergic diseases	*partnered with Pfizer*			
	NIC002 for smoking cessation	*partnered with Novartis*			
Cardiovascular	CYT006-AngQb for hypertension				
Nervous system	CAD106 for Alzheimer's disease	*partnered with Novartis*			
Metabolic	CYT013-IL1bQb for type II diabetes				
Inflammation / Autoimmunity	CYT020-TNFQb for inflammation				
	CYT017-IL17Qb for multiple sclerosis/psoriasis				
Infectious diseases	Influenza Vaccine Qb-Flu	*partnered with Singapore*			
	Malaria Vaccine	*collaboration with NIH*			

In addition, Immunodrug™ collaborations are ongoing with Pfizer on undisclosed human and animal health applications.

22

Levels of distrust in UK vaccination



Brian Deer – Sunday Times

23

Concluding remarks

- Original contention was that preventative medicine would be in the interest of the patients and more cost-efficient that curative medicine.
- Actually dependent on the underlying incidence of the disease and relative screening and treatment costs.
- Evolution of existing screening programs to include a wider range of ages, but no national programmes other than breast, cervical and colon-rectal cancers in UK.
- Evaluation of new and better biomarkers
- Attitudes of press and public towards medical or technological discoveries – reduction in MMR vaccine uptake in response to scare stories demonstrates the issue.

Questions or comments?