Why you will live to 100 (or not)
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 will live to 100 (or not)

- Genes
- Behaviours
- Environment
- Societal pressures
- Accidents
- Medical interventions
- Stochastic variation
- Historical trends
  - New England Centenarian study suggested dominant impact of genes in extreme longevity
Tips for healthy ageing
National Institute of Ageing

- Eat a balanced diet.
- Exercise regularly.
- Get check-ups on a regular basis.
- Do not smoke.
- Practice safety habits at home to prevent falls and bone fractures. Wear a seatbelt in the car.
- Stay in contact with family and friends.
- Avoid too much exposure to the sun or cold weather.
- Drink alcohol only in moderation.
- Keep personal and financial records in good order.
- Keep a positive attitude toward life. Do the things that bring happiness.

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Relative importance of genes and environment

![Diagram showing the relative importance of genes and environment](image)

- **Genotype**
  - Huntington’s
  - Cystic Fibrosis
  - Schizophrenia
  - Fam. breast cancer
  - Colon cancer syndrome
  - Huntington’s

- **Environment**
  - Non - Genetic
  - Thrombosis
  - Alzheimer
  - Diabetes
  - Asthma
  - Lung cancer
  - Car accident

**Spectrum of Disease**
### Genes associated with increased risk of disease

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Relative Risk ≥5.0 Family studies</th>
<th>Relative Risk ≥1.5 and &gt;5.0 Resequencing</th>
<th>Relative Risk ≥1.01 and &gt;1.5 Genome-wide association studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>RB1, TP53</td>
<td></td>
<td>rs1051730, rs8034191 (CHRNA3, CHRNA4, CHRNA5)</td>
</tr>
<tr>
<td>Breast</td>
<td>BRCA1, BRCA2, TP53, PTEN, SK11, CDH1</td>
<td>CHEK2, ATM, PALB2, BRIP1</td>
<td>CASP8, FGR2, MAP3K1, 8q24, 5p, TOX3, 2q, 6q22, LSP1</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>APC, MLH1, MSH2, MSH6, PMS2</td>
<td>APC (I1307K), BLM</td>
<td>MUTYH, CASP8, 8q24, 8q23 (EIF3H), 10p14, 11q23, CRAC1, SMAD7</td>
</tr>
<tr>
<td>Prostate</td>
<td>BRCA2</td>
<td>8q24</td>
<td>rs6501455, rs721048, NBS1, EHPB1, TCF2, CTBP2, JAZF1, MSMB, LMTK2, KLK3, SLC22A3</td>
</tr>
<tr>
<td>Pancreas</td>
<td>BRCA2, CDKN2A, STK11, TP53, PRSS1, SPINK1</td>
<td>BRCA1, MSH2, MLH1</td>
<td></td>
</tr>
</tbody>
</table>

Different approaches to considering the future
Converging or Diverging?

- "Projectionists" e.g. Vaupel – no current evidence of restrictions to improvements in life expectancy leading to expectations that medical advances will deliver – up to 0.25 years per calendar year
- "Realists" e.g. Olshansky – treatment of disease without affecting ageing process has limited potential to expand life expectancy, and not clear how "less healthy" cohorts will develop
- No current treatments affect ageing process and no biomarkers to determine effectiveness of treatments
- Acceptance of the possibility of future treatments that could slow ageing process
Understanding the potential for further improvements from disease-elimination models

Fig. 2. Percentage of reduction in the conditional probability of death for the United States (from 1985 levels) required to produce a life expectancy at birth from 80 to 120 years.

The impact of the ageing process

- Hand grip strength reduces by 45% by age 75
- Blood flow to brain reduces by 15-20% by age 70
- Sense of smell reduces to 50% of peak by age 80
- Maximum heart rate reduces by 15-20% by age 70
- Blood pressure of 50% population at age 65 is mild or worse hypertension
- Maximum breath capacity reduces by 40% by age 80
- Dementia affects 10% of those over age 65; 20% of those over age 85
Potential benefits from disease elimination and slowing of ageing process

![Image of table showing life expectancy at birth, at age 65, and at age 85 for males, females, and the total population for 2000, 2030, and 2050 under Network A (lower disease mortality) and Network B (slow aging).]

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

UK standardised myocardial infarction death rate per 100,000 population (41) is twice that of France (19) - but UK death rates fell faster than any other European country between 1980 and 2006

Source: OECD data
## Relative importance of risk factors and treatment

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

Source: CHD Impact model – University of Liverpool – England & Wales
Obesity trends among U.S. adults 1985

(*BMI ≥30, or ~ 30 lbs overweight for 5’ 4” person)

Source: CDC
Obesity trends in U.S. adults
1990

Source: CDC
Obesity trends in U.S. adults
1995

Source: CDC

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Obesity trends in U.S. adults 2000

Source: CDC
Obesity trends in U.S. adults 2005

Source: CDC
Obesity trends in U.S. adults 2010

Source: CDC
United States: The Revis family of North Carolina
Food expenditure for one week $341.98
Italy: The Manzo family of Sicily
Food expenditure for one week: 214.36 Euros or $260.11
Egypt: The Ahmed family of Cairo
Food expenditure for one week: 387.85 Egyptian Pounds or $68.53
Bhutan: The Namgay family of Shingkhey Village
Food expenditure for one week: 224.93 ngultrum or $5.03
What do we want from our healthcare systems

- Fast access to reliable health advice
- *Effective treatment delivered by trusted professionals*
- Involvement in decisions and respect for preferences
- Clear, comprehensible information and support for self-care
- Attention to physical and environmental needs
- Emotional support, empathy and respect
- Involvement of, and support for, family and carers
- Continuity of care and smooth transitions

Source: Picker Institute Europe based on patient interviews
Healthcare expenditure at end of life Survivors and deceased in regional study in Italy

## Comparisons of different treatments
### Breast cancer

### Hazard ratios for mortality

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparator</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>Observation</td>
<td>0.66 (0.57, 0.77)</td>
</tr>
<tr>
<td>Docetaxel[TAC]</td>
<td>FAC</td>
<td>0.70 (0.53, 0.93)</td>
</tr>
<tr>
<td>Anastrazole[HR +ve]</td>
<td>Tamoxifen</td>
<td>0.97 (0.83, 1.14)</td>
</tr>
<tr>
<td>Exemestane</td>
<td>Tamoxifen</td>
<td>0.83 (0.67, 1.02)</td>
</tr>
<tr>
<td>Letrozole</td>
<td>Tamoxifen</td>
<td>0.86 (0.70, 1.06)</td>
</tr>
<tr>
<td>Gemcitabine[GT]</td>
<td>Paclitaxel(T)</td>
<td>0.82 (0.67, 1.00)</td>
</tr>
</tbody>
</table>

Based on: NICE Technology Appraisals, 2005 to 2010
Comparisons of different treatments
Breast cancer

Modelled life expectancy with and without interventions

- Gemcitabine
- Letrozole
- Exemestane
- Anastrazole
- Docetaxel
- Trastuzumab

- Mean survival without intervention
- Additional survival with intervention

Based on: NICE Technology Appraisals, 2005 to 2010
Guidance over use of different treatments
% of breast cancers

Based on: NICE Technology Appraisals, 2005 to 2010
Evaluating cost-effectiveness of treatments
Co-ordinated stroke care in different locations

## Clinical trials – scope and timeframe

<table>
<thead>
<tr>
<th>Time</th>
<th>Preclinical testing</th>
<th>Phase I Trials</th>
<th>Phase II Trials</th>
<th>Phase III Trials</th>
<th>Filing/approval</th>
<th>Phase IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study subject</strong></td>
<td>Laboratory and animal studies</td>
<td>20 - 80 healthy volunteers</td>
<td>100 - 300 patient volunteers</td>
<td>1’000 - 3’000 patient volunteers</td>
<td>—</td>
<td>open, according to indication</td>
</tr>
<tr>
<td><strong>Study aim</strong></td>
<td>Assess safety &amp; biol. activity</td>
<td>Determine safety &amp; max. dose</td>
<td>Evaluate effective dose, side effects</td>
<td>Verify efficacy, monitor long term</td>
<td>Review process</td>
<td>Post marketing safety monitoring</td>
</tr>
</tbody>
</table>

Source: CDC
Clinical trials – approval rates by therapeutic class

Table 3  Phase transition and clinical approval probabilities by therapeutic class for self-originated compounds first tested in humans from 1993 to 2004

<table>
<thead>
<tr>
<th>Therapeutic class</th>
<th>Phase I–II (%)</th>
<th>Phase II–III (%)</th>
<th>Phase III–RR (%)</th>
<th>RR–approval (%)</th>
<th>Clinical approval success rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antineoplastic/immunologic</td>
<td>71.8</td>
<td>49.0</td>
<td>55.3</td>
<td>100</td>
<td>19.4</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>62.9</td>
<td>32.4</td>
<td>64.3</td>
<td>66.7</td>
<td>8.7</td>
</tr>
<tr>
<td>CNS</td>
<td>59.6</td>
<td>33.0</td>
<td>46.4</td>
<td>90.0</td>
<td>8.2</td>
</tr>
<tr>
<td>GI/metabolism</td>
<td>67.5</td>
<td>34.9</td>
<td>50.0</td>
<td>80.0</td>
<td>9.4</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>72.4</td>
<td>35.2</td>
<td>80.0</td>
<td>100</td>
<td>20.4</td>
</tr>
<tr>
<td>Respiratory</td>
<td>72.5</td>
<td>20.0</td>
<td>85.7</td>
<td>80.0</td>
<td>9.9</td>
</tr>
<tr>
<td>Systemic anti-infective</td>
<td>58.2</td>
<td>52.2</td>
<td>78.6</td>
<td>100</td>
<td>23.9</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>62.8</td>
<td>48.7</td>
<td>69.8</td>
<td>91.3</td>
<td>19.5</td>
</tr>
</tbody>
</table>

Through June 2009.
CNS, central nervous system; GI, gastrointestinal; RR, regulatory review.

Source: DiMasi et al. Nature (March 2010), 87, 3, 272-7
Regenerative medicine: gene therapy

http://en.wikipedia.org/wiki/Gene_therapy
Regenerative medicine: cell therapy

Nature Reviews Neuroscience 2002
Genetic information:
Revolutionary developments from DNA sequencing

Source: E. Pennisi, Science 2011, 331, 666-8
Combining different elements in a forward-looking approach to assessing future mortality

General drivers to diagnosis and survival

- **Individual risk factors**
  - Age, gender, diet, smoking – smoking considerations:
    - Taxes and restrictions
    - Current treatments (bupropion)
    - Future treatments (vaccines)

- **Healthcare funding**
  - Public vs private funding
  - Disease-based patient advocacy groups’ influence
  - Allocation of resources towards cure vs prevention

- **Patient interaction**
  - Health awareness
  - Trust and confidence in advice given
  - Use of clinical guidelines to improve quality of care

- **Research & development**
  - Public vs commercial sponsors
  - Regulators’ attitude to developments
  - Disease-focused approach vs global impact of ageing

Disease types and disease progression

- Healthy
- Cancer: Lung, colorectal, prostate, breast
- Neurological: Dementia, Alzheimer’s, Parkinson’s
- Circulatory: Stroke, angina, heart attack
- Respiratory: Chronic obstructive pulmonary disease

Factors involved in assessing specific example disease

- Risk factors:
  - Family history
  - Obesity
  - Having children later in life
  - Not breast feeding

- Early detection:
  - Digital mammography
  - MRI for high-risk
  - Gail algorithm (own factors)
  - Klaus algorithm (family history)

- Medical innovations:
  - Growth factor inhibition
  - Future of personalised medicine (e.g., tumour profiling)

- Current approaches:
  - Targeting DCIS
  - Surgery with node follow-up
  - Adjuvant radiotherapy
  - Herceptin, Tamoxifen

- Clinical trials pipeline:
  - Phase II (230 trials*)
  - Phase III (56)
  - e.g., pertuzumab (limits cancer growth)
Education of future medical professionals
Implications of an ageing society
Teaching Geriatric in Medical Education study (TeGeMe)

- Collaborative study of WHO and International Federation of Medical Students' Associations
- WHO intends healthy/active ageing and promotion of long term health to form education of all future young doctors
- Promotion of life course in graduate training and later
- 41% of medical school curricula refer explicitly to geriatrics
- GERIND index calculated by medical school and averaged across country – separation of geriatrics teaching and quality of ageing science being taught
- Central hypothesis is that countries with higher percentage of older persons are more likely to have separate high-quality teaching on geriatric medicine – not always true
TeGeMe – GERIND index vs. age of population

Source: World Health Organisation
A new relationship between doctor & patient

- Classic asymmetrical relationship based on knowledge
- Medical and surgical specialisation driven or required because of technical information & procedures
- Doctors facing information overload
- Transforming effects of internet as clinical guidance becomes more comprehensive
- Two key roles for doctors
  - Patient advocate – facilitate patient-based healthcare and act as guide to new technological breakthroughs
  - Scientist/technician – maintain pace of development

A new functional divide across the profession
Some thoughts for holders of longevity risk

- Continuing differences in schools of thought over future longevity
- Conflicting forces between risk behaviours and treatment
- Impending revolution in genetic information
- Increasing demands from regulators for justification
- No market as yet in longevity risk

Holders of longevity risk have several options –
- Transfer risk
- Invest in further research and understanding
- Wait and see
Thank you