Prof. Dr. D.L. Knook Lecture

Ede, Netherlands, 3 November 2017

Why and How Are We Living Longer?

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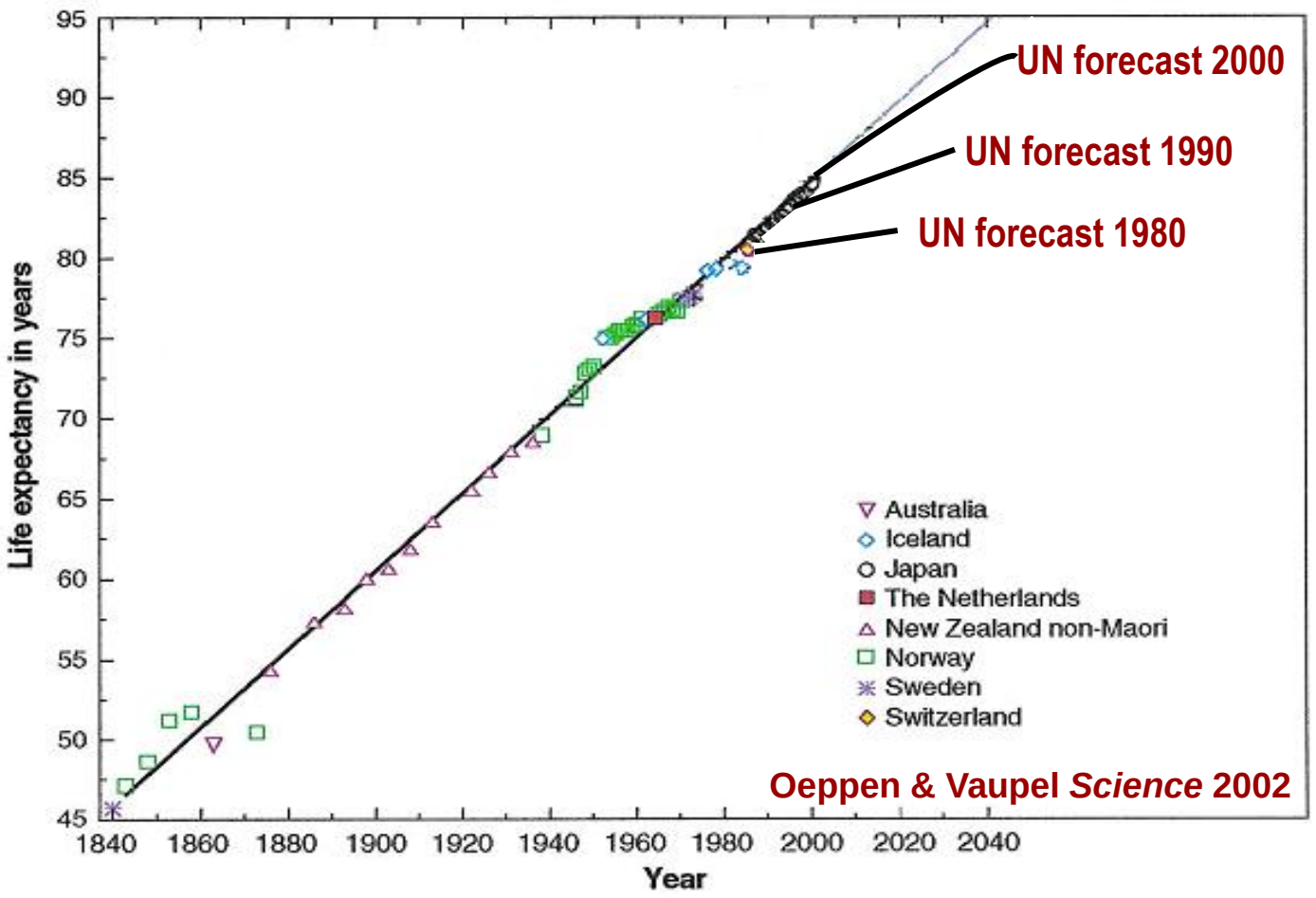
The Increase in Human Life Expectancy



Declining early/mid-life mortality

Declining later-life mortality

Change is coming fast even in the poorest regions

ORS: Oral Rehydration Salts

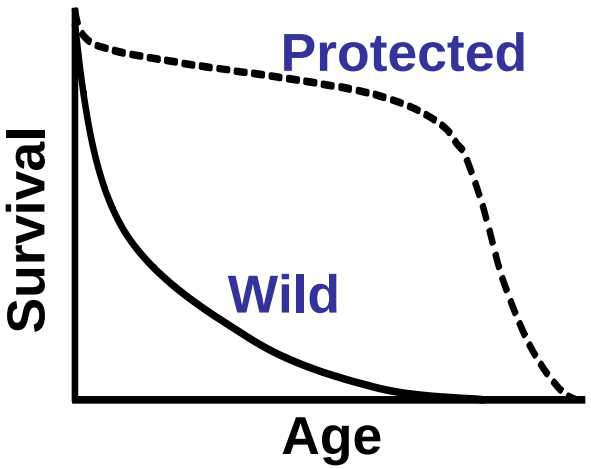
Photo: Immigration hut at border between Burkina Faso and Ghana

- Why does ageing occur at all?
- What explains the individuality of ageing trajectories?
- What is life really like for today's older people?
- Changing expectations of life.

Why does ageing occur at all?

Absence of a Program for Ageing

Contrary to widely held belief, the body is NOT programmed to age and die.



- Animals in the wild rarely live long enough to display signs of old age.

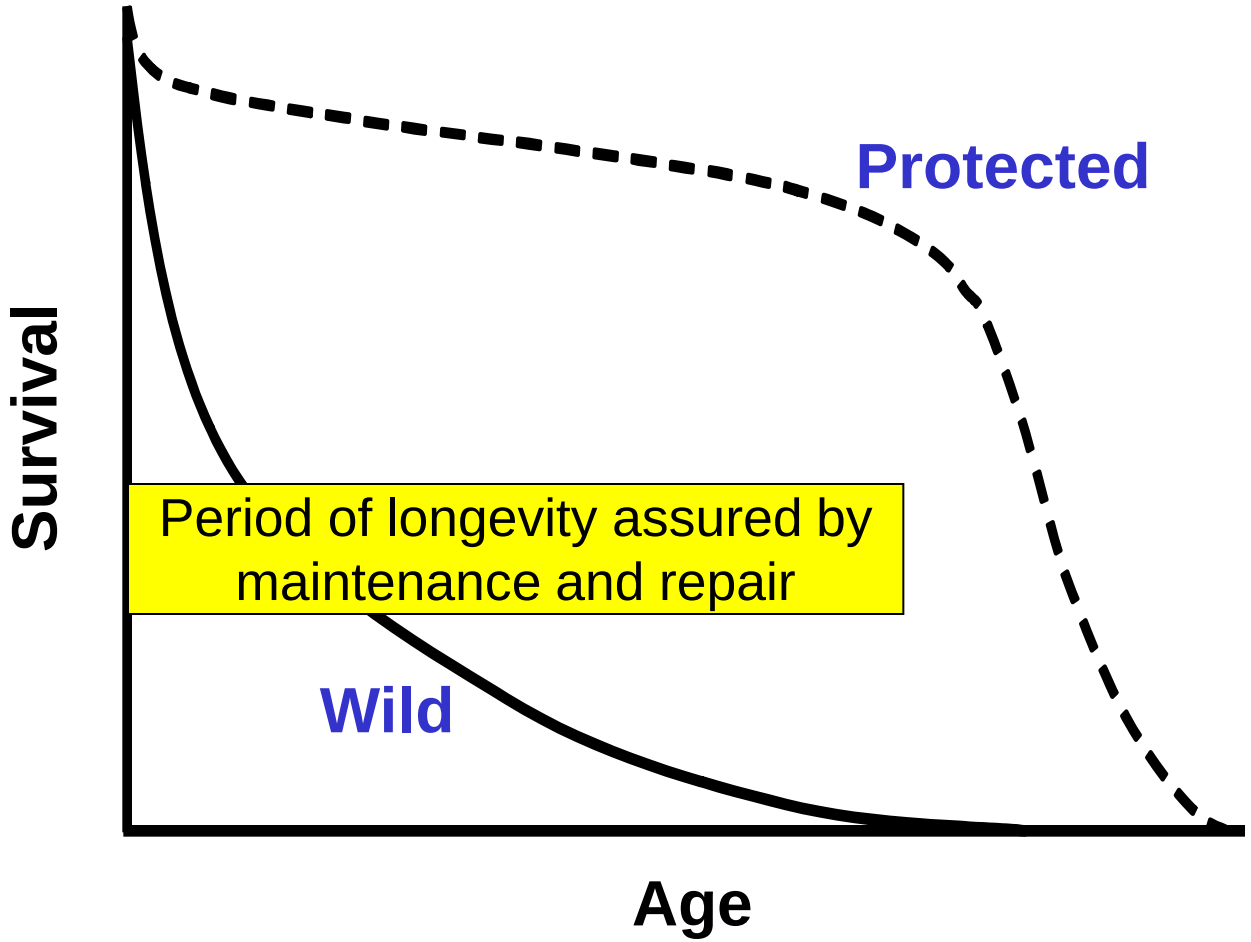
- Other things being equal, natural selection will oppose any programme for death.

Kirkwood & Melov *Current Biology* 2011
Kowald & Kirkwood *Aging Cell* 2016

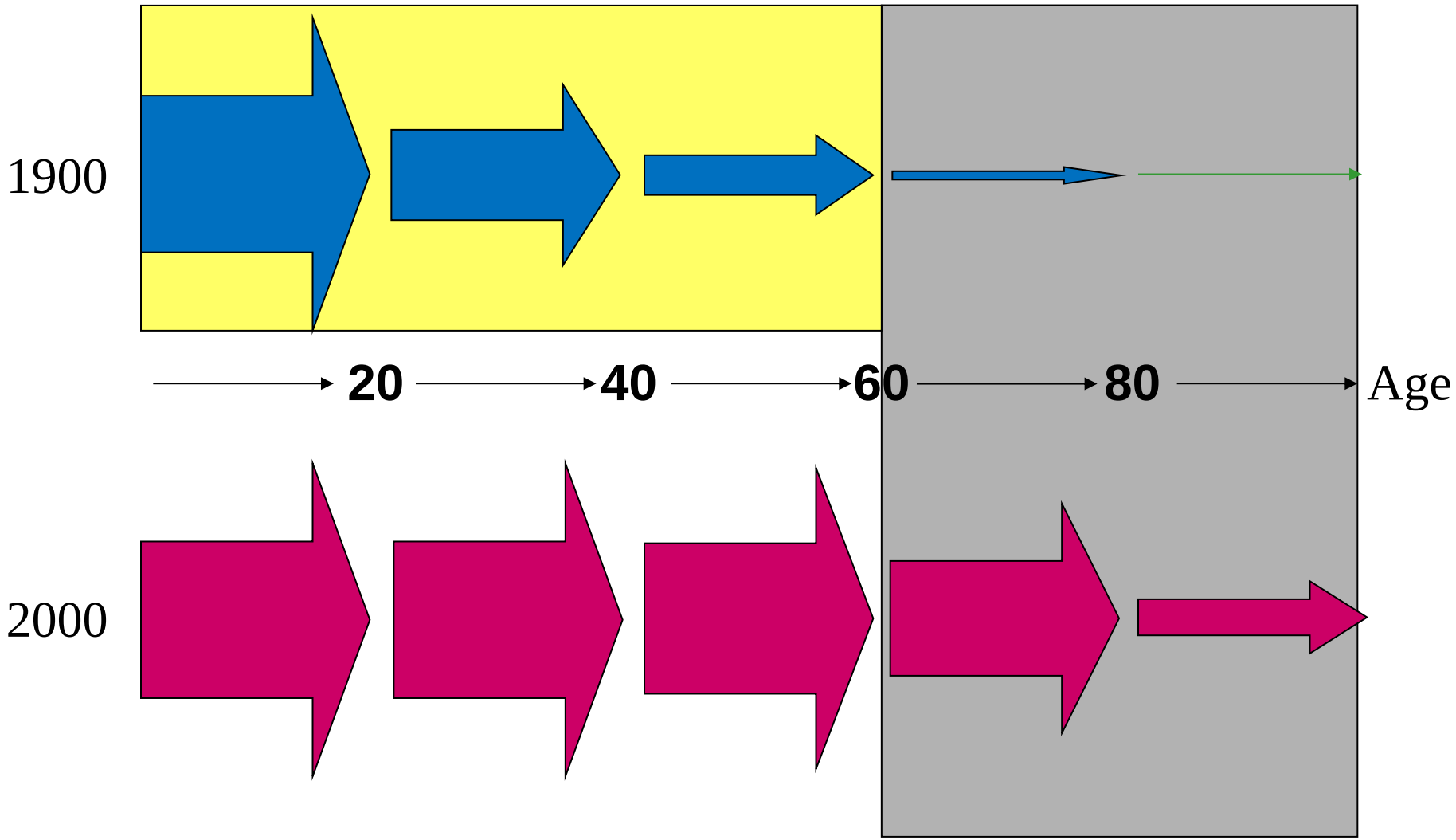
Natural selection dictates that organisms optimise their allocation of metabolic resources

Kirkwood (1981) in *Physiological Ecology: An Evolutionary Approach to Resource Use* (eds Townsend & Calow)

DISPOSABLE SOMA THEORY

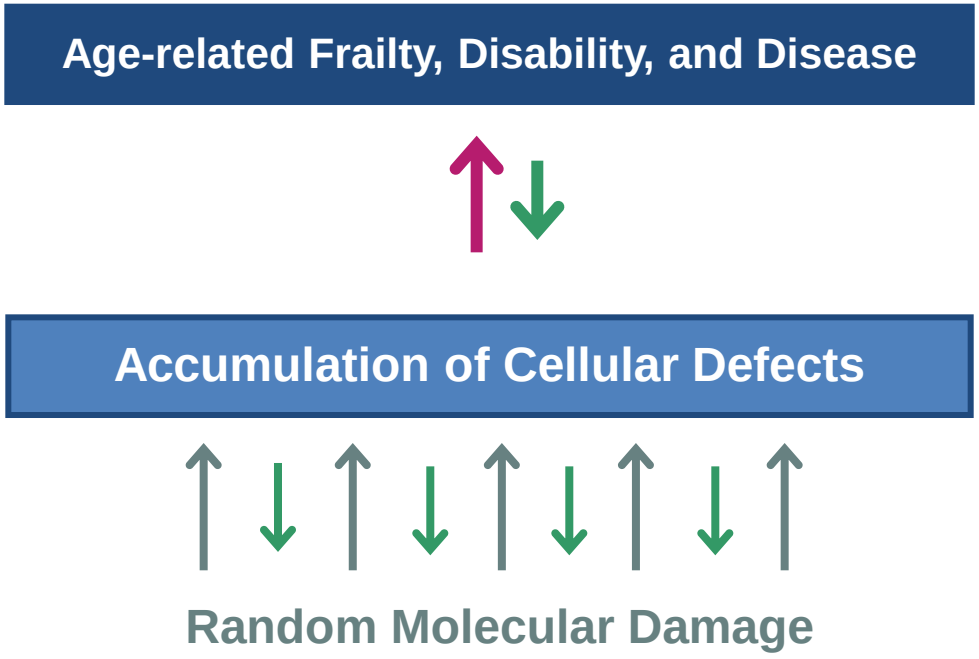


Kirkwood *Nature* 1977

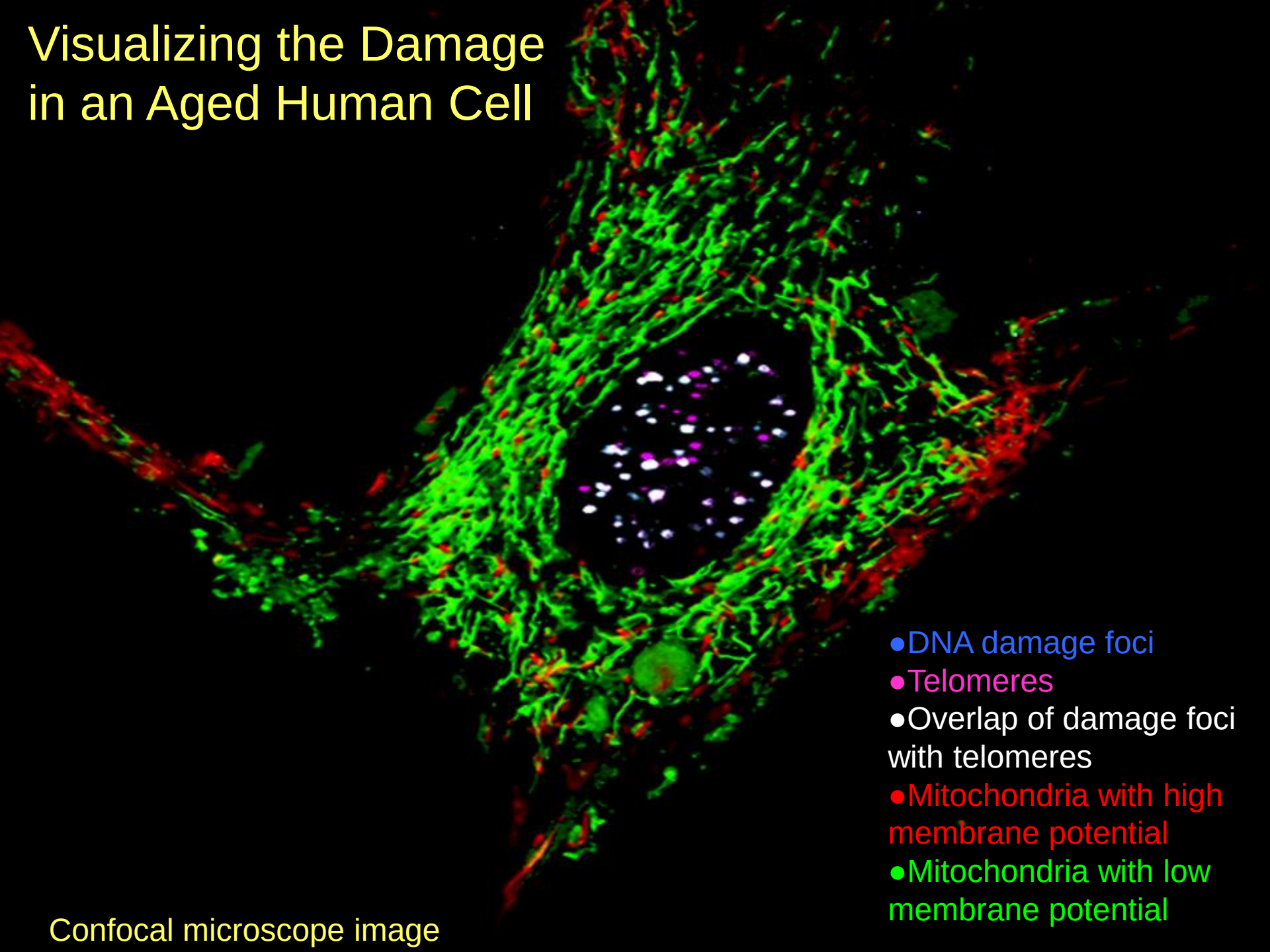


Differences in survival using death rates from Registrar-General of England & Wales for 1900 (blue) and 2000 (pink)

THE AGEING PROCESS



Visualizing the Damage in an Aged Human Cell

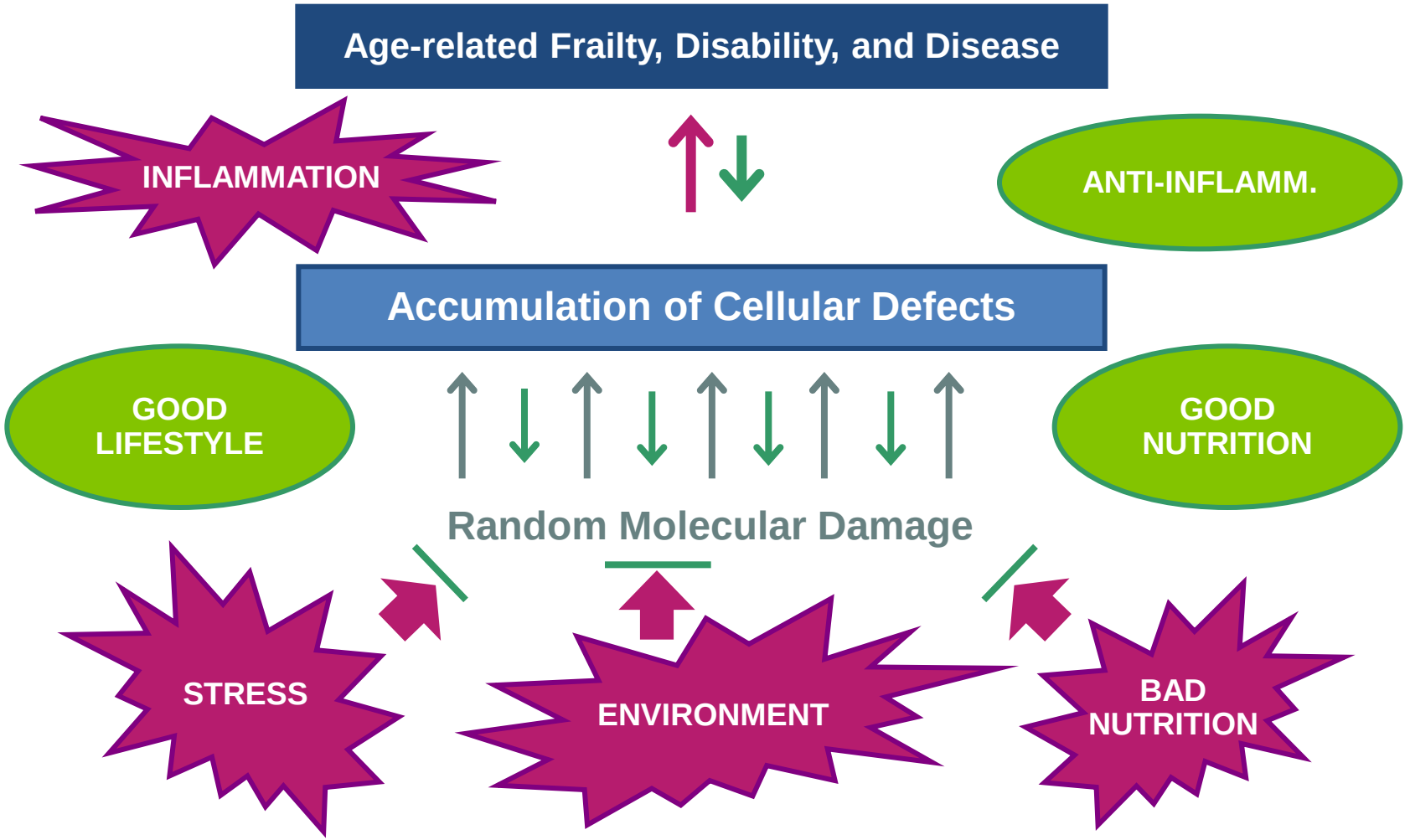


- DNA damage foci
- Telomeres
- Overlap of damage foci with telomeres
- Mitochondria with high membrane potential
- Mitochondria with low membrane potential

Confocal microscope image

HUMAN AGEING AND ITS MALLEABILITY

Kirkwood *Cell* 2005



What explains the individuality of ageing trajectories?

Factors Influencing Health Trajectories in Old Age

- Genes
- Nutrition
- Physical activity
- Lifestyle
- Environment
- Socioeconomic status
- Attitude
- Chance

Genetics of Human Longevity

Twin Studies	Coefficient of heritability
McGue et al (1993)	0.22
Herskind et al (1996)	0.25
Ljungquist et al (1998)	<0.33

►Genes account for about 25% of what determines human longevity

The relevant genes are numerous, mostly of small individual effect, and they influence somatic maintenance and metabolism.

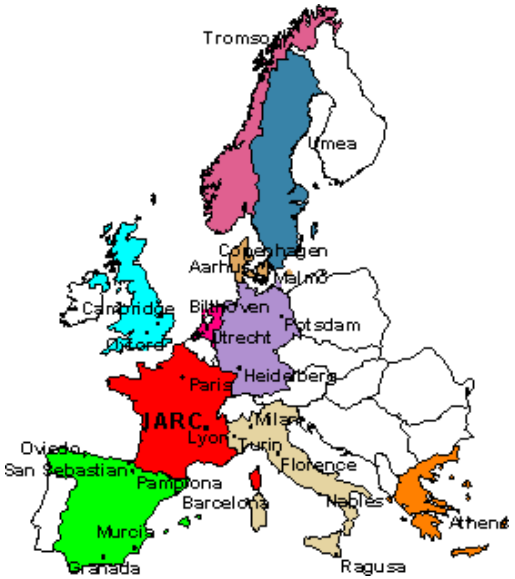
Schächter, Cohen, Kirkwood *Hum Genet* 1993
Kirkwood, Cordell, Finch *Trends Genet* 2011
Beekman et al *Aging Cell* 2013
Deelen et al *Hum Mol Genet* 2014

Nutrition and Survival: The EPIC-Ageing Study

76,707 men and women aged 60+

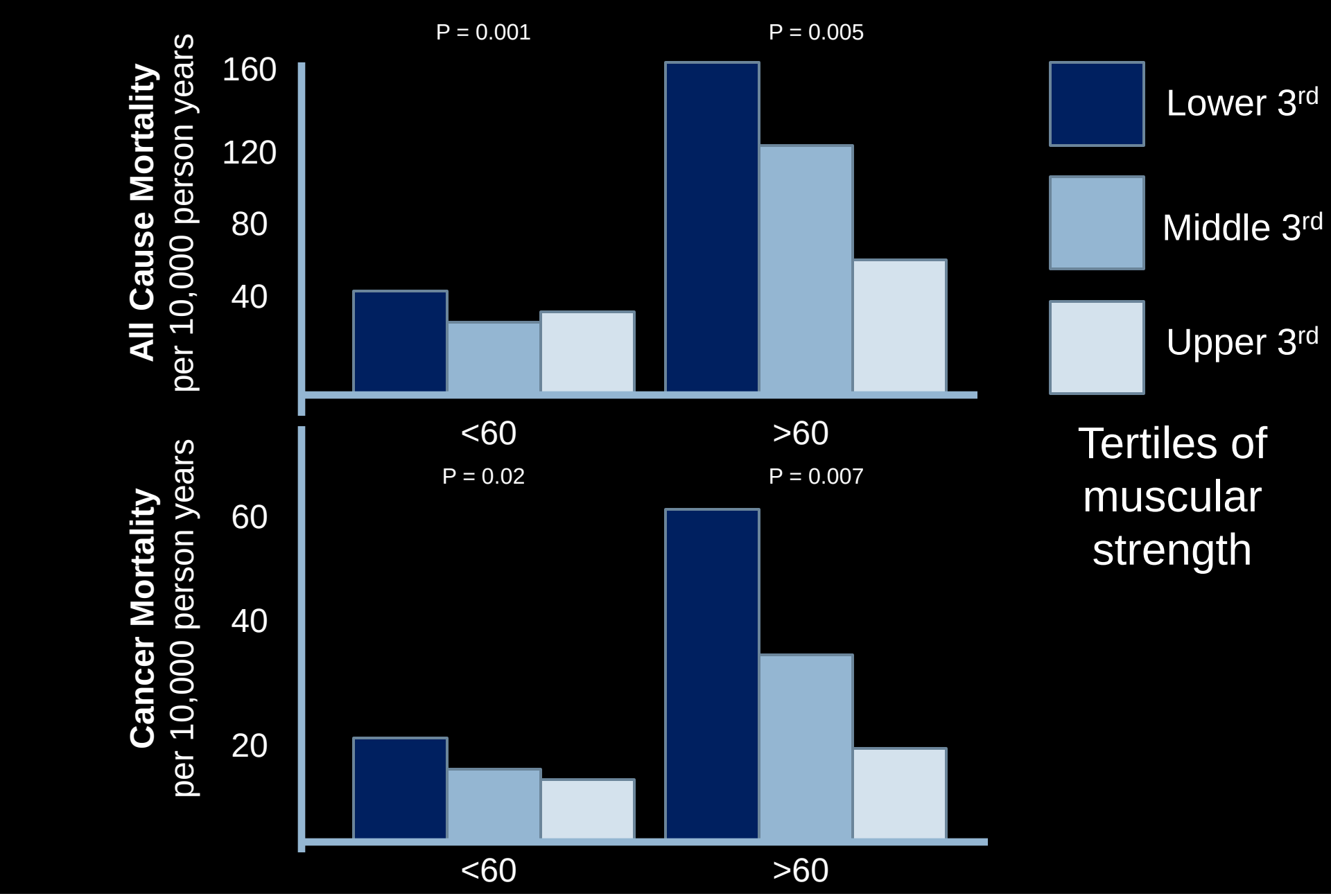
Followed for 7.5 years

Adherence to Mediterranean diet assessed on 10-point scale:
0 (poor)…9 (high)



2 unit increase in 'Mediterranean-ness' of diet results in 8% reduction of overall mortality

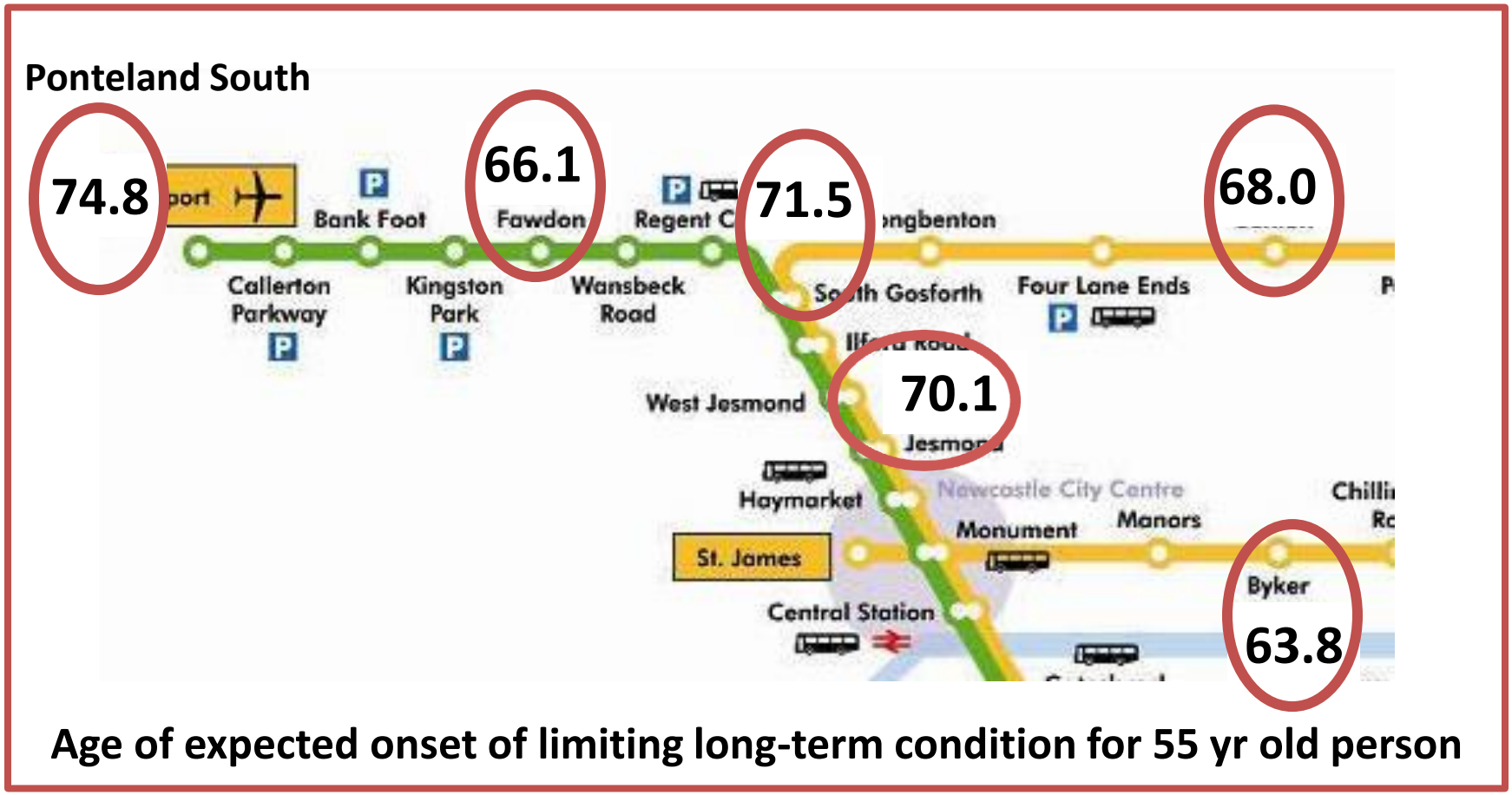
Trichopoulou A *et al.* (2005) *BMJ* 330, 991-997



8762 men

Ruiz J, et al. BMJ 19: 150-151 (2008)

The ‘social gradient’ in healthy life expectancy



Age of expected onset of limiting long-term condition for 55 yr old person

Courtesy Prof Peter Gore/Prof Carol Jagger/ONS

What is life really like for today's older people?