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Why and How Are We Living Longer?

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Campus for Ageing and Vitality
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A Year of Anniversaries

800 years since Magna Carta



200 years since Waterloo



40 years since my first papers about ageing!

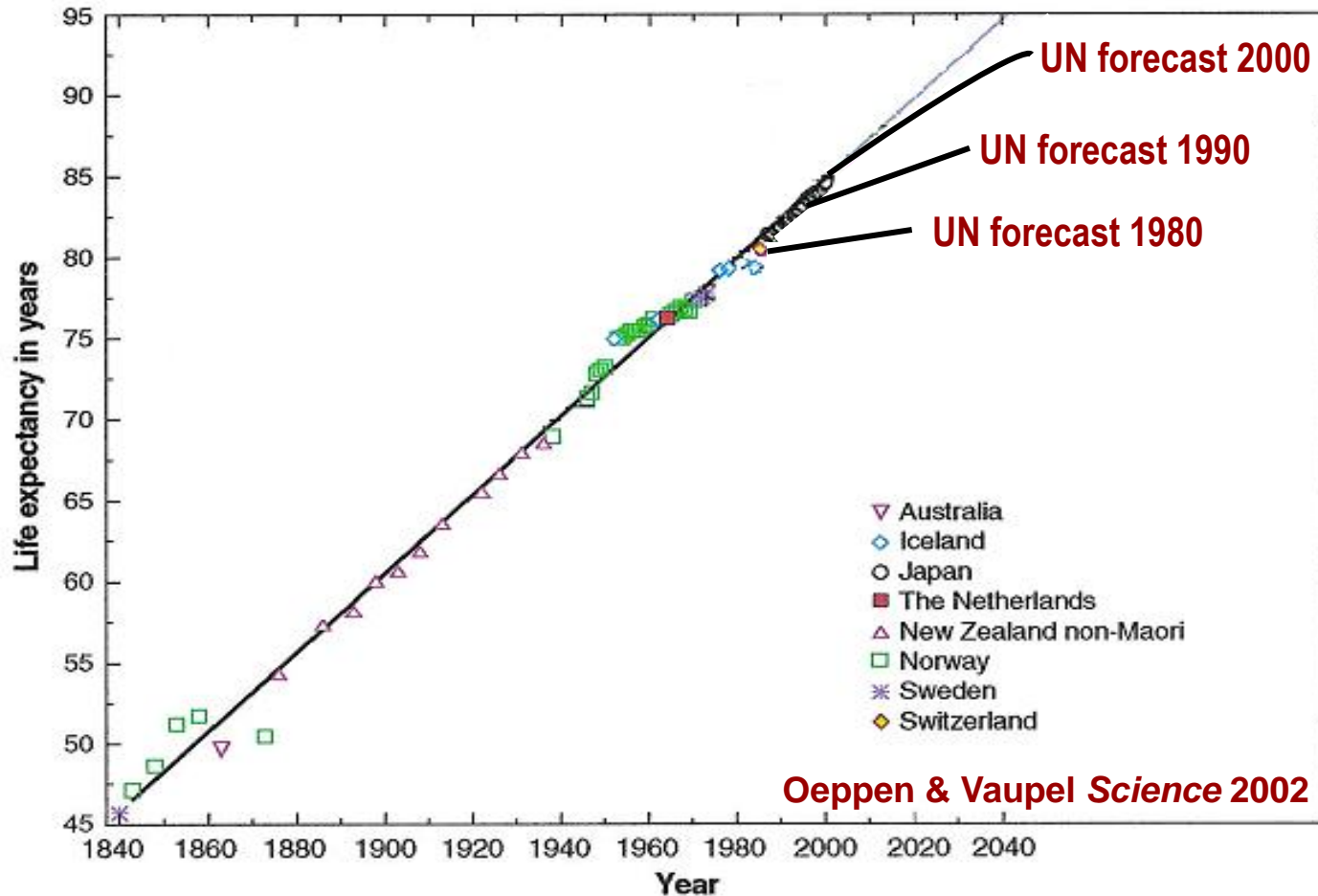
Big Questions about Living Longer

- Why has the continuing increase in longevity taken the world by surprise?
- Do we understand what is driving it?
- What are the consequences for health in old age?
- Where will it all end?
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The Increase in Human Life Expectancy



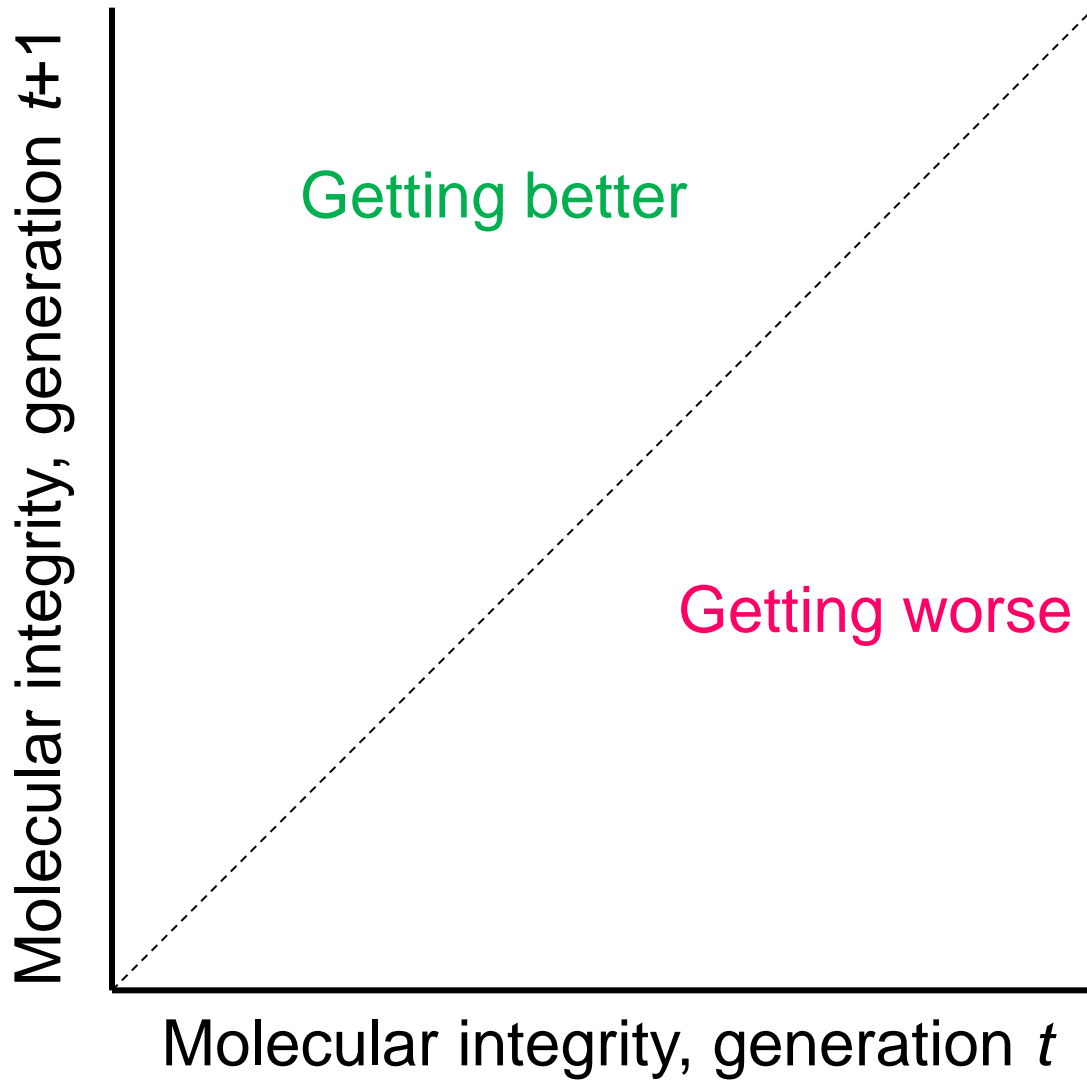
Declining early/mid-life mortality

Declining later-life mortality

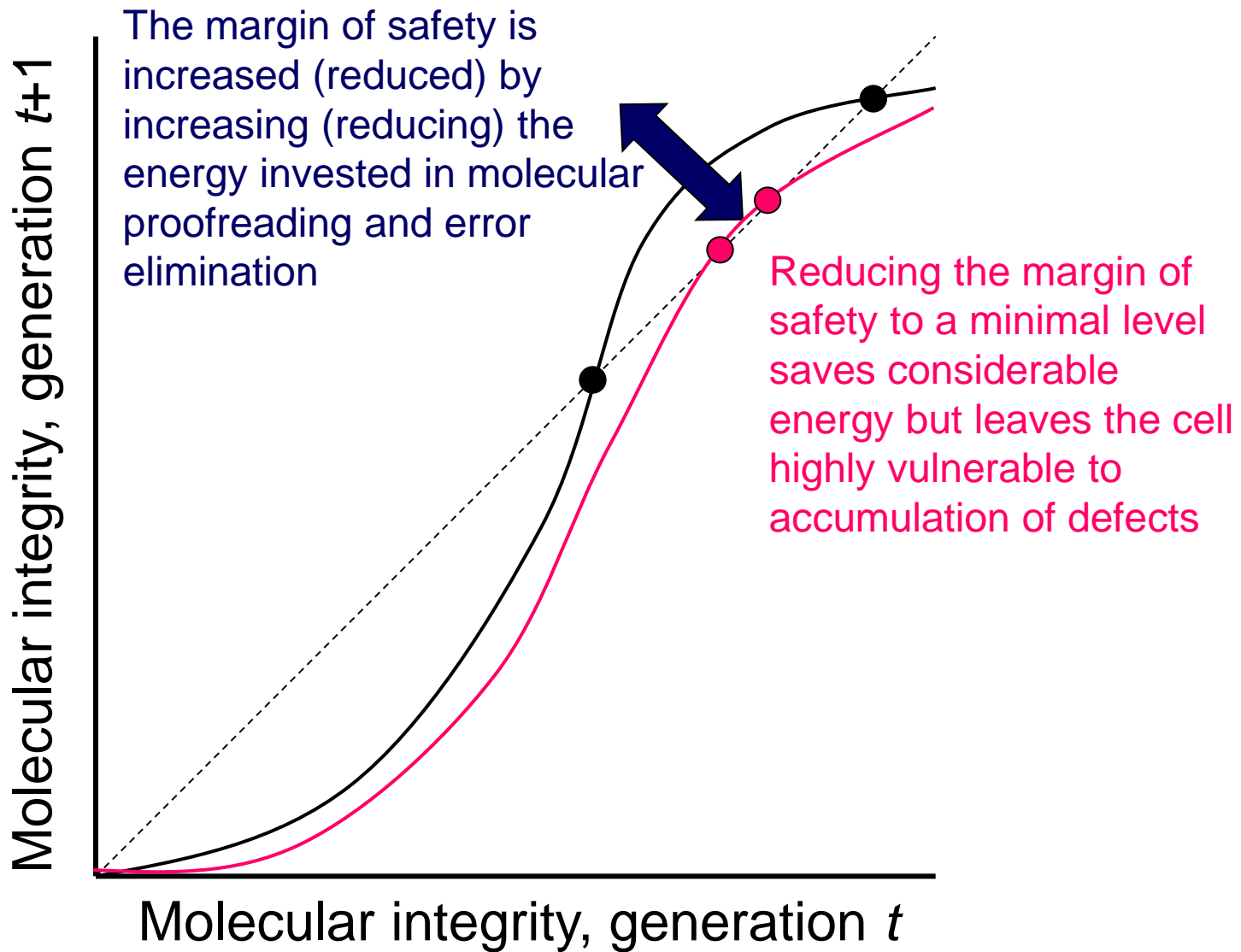
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Cellular Stability and Instability

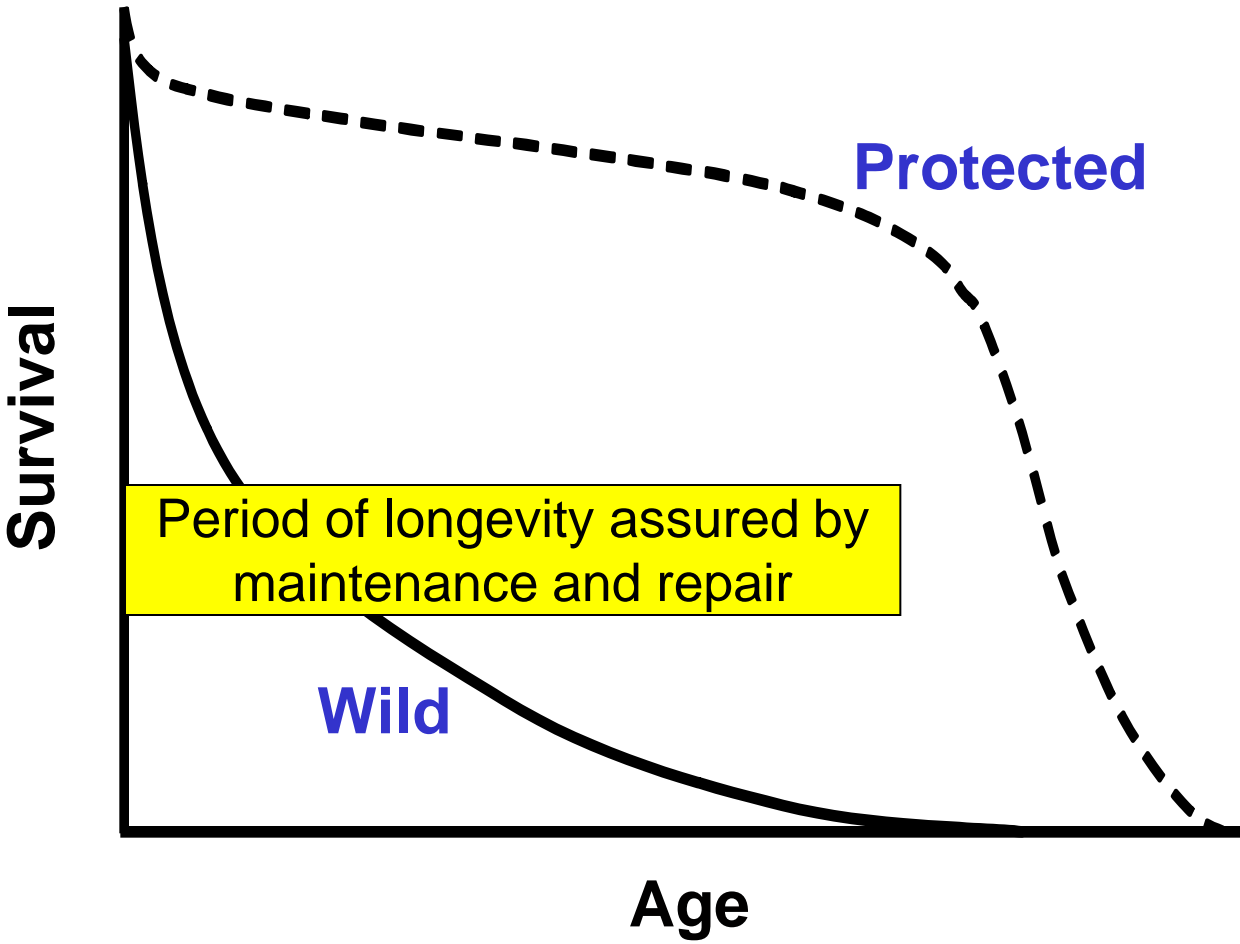


Cellular Stability and Instability



Disposable Soma Theory

Kirkwood *Nature* 1977



The Ageing Process

Functional Impairments in Organs and Tissues leading to Age-related Frailty, Disability, and Disease

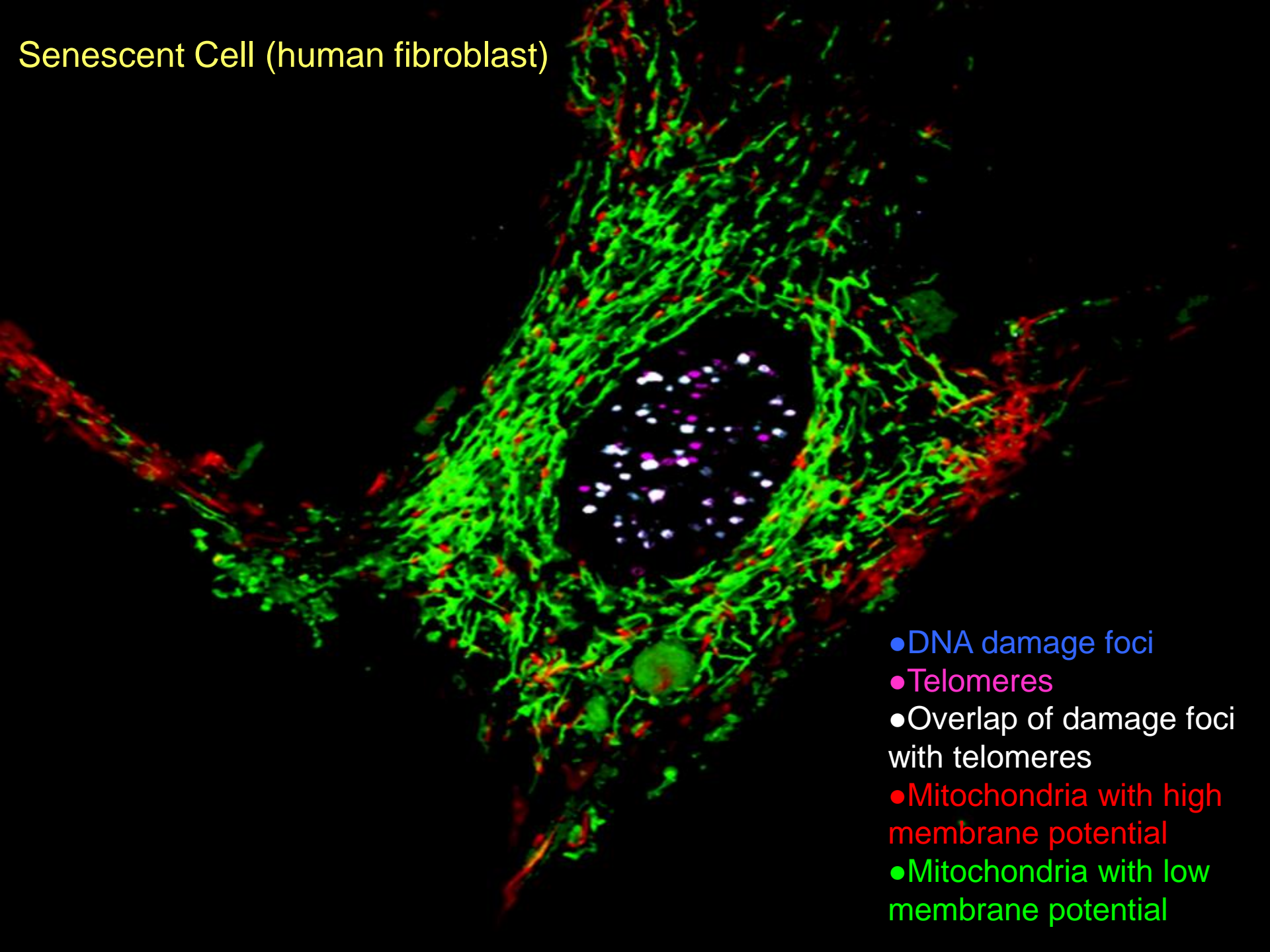


Accumulation of Cellular Defects



Random Molecular Damage

Senescent Cell (human fibroblast)

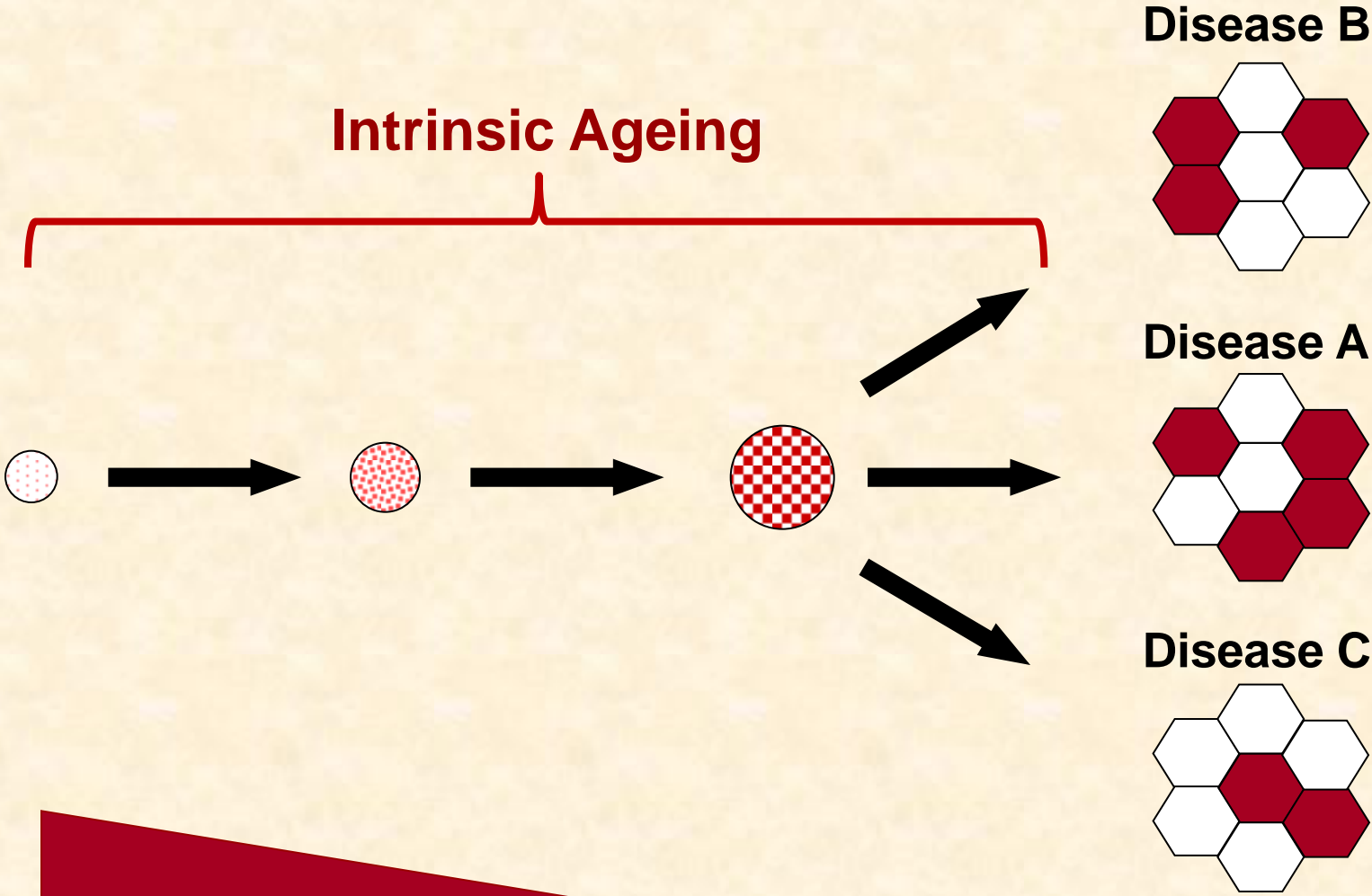


- DNA damage foci
- Telomeres
- Overlap of damage foci with telomeres
- Mitochondria with high membrane potential
- Mitochondria with low membrane potential

Intrinsic Ageing and Age-Related Disease

Accumulation of Molecular and Cellular Damage

Initiating Processes

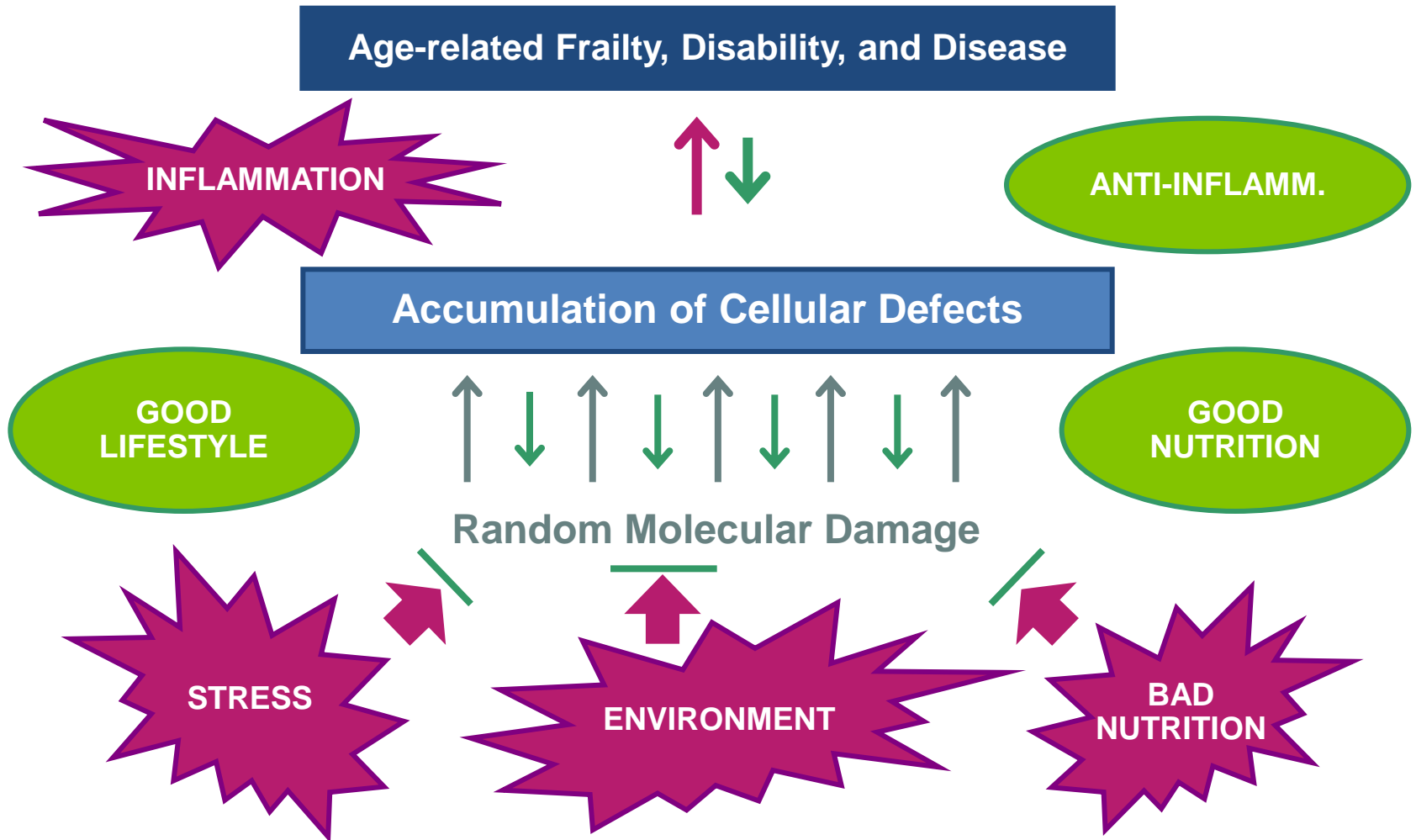


End-Stage Pathology

Likely Effectiveness of Interventions

HUMAN AGEING AND ITS MALLEABILITY

Kirkwood *Cell* 2005



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Factors Influencing Health Trajectories in Old Age

Newcastle 85+ Study; prospective study in 1000+ individuals born in 1921

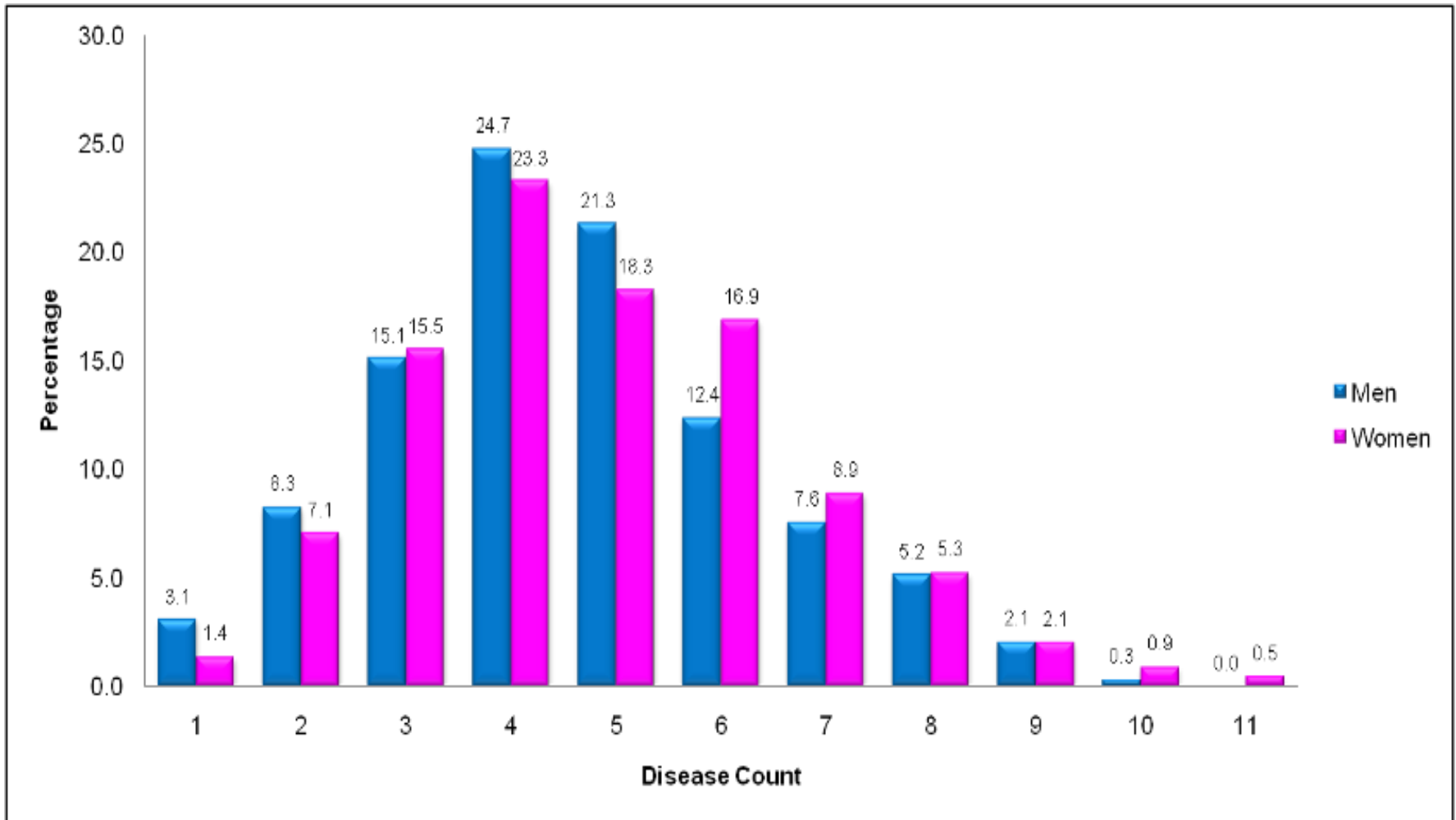
Comprehensive study of the complex biological, medical and psychosocial factors affecting ageing trajectories of 85+ year olds.

Domains of assessment: health (nurse assessment and GP record review); cognitive and physical function; nutrition; activity; sleep; sensory function; psychology; socioeconomic; biological markers; genetics.

Exceptionally high rates of recruitment and retention through nurse-led development and refinement of procedures.



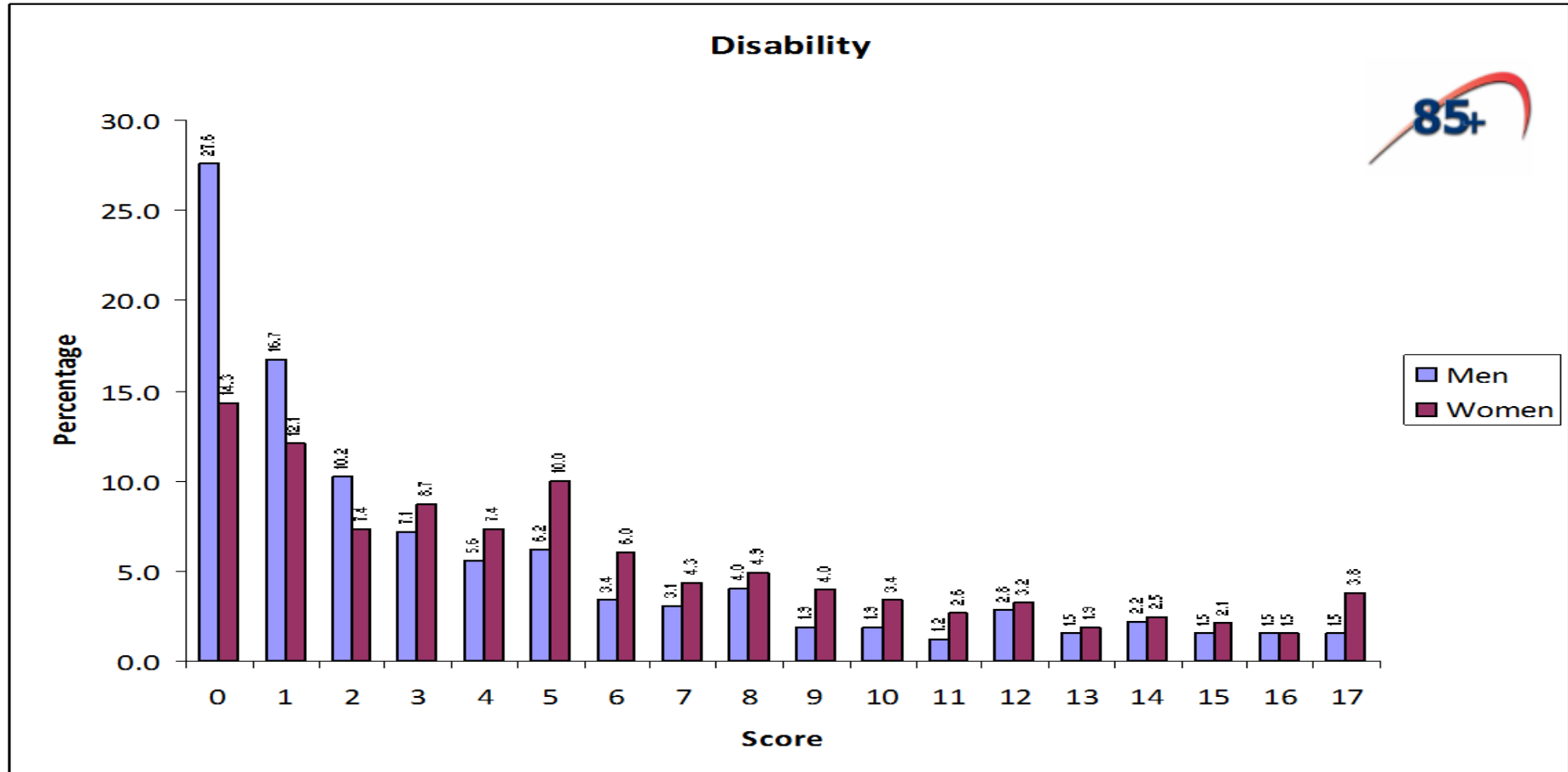
Multi-Morbidity is the Norm



No one has perfect medical health at age 85.

Yet, 78% rated their health compared with others of the same age as “good” (34%), “very good” (32%) or “excellent” (12%).

Capability and Dependency



A quarter of men and a sixth of women have no important functional limitation at age 85.

Can we relate health status
to intrinsic biological markers
of ageing?

Biomarker Domains in Newcastle 85+ Study

Anthropometry, blood pressure and physical function

- Weight, body fat percentage, body fat mass, fat free mass and total body water
- Diastolic and systolic blood pressures
- Right and left hand-grip strength
- Timed Up-and-Go (TUG) test; 7-day continuous activity monitoring
- Respiratory function

Blood-based biomarkers

- Haematology and biochemistry:
- Nutritional markers
- Inflammatory response
- Lymphocyte subpopulations
- Telomere length
- DNA Damage and Repair
- Plasma isoprostanes

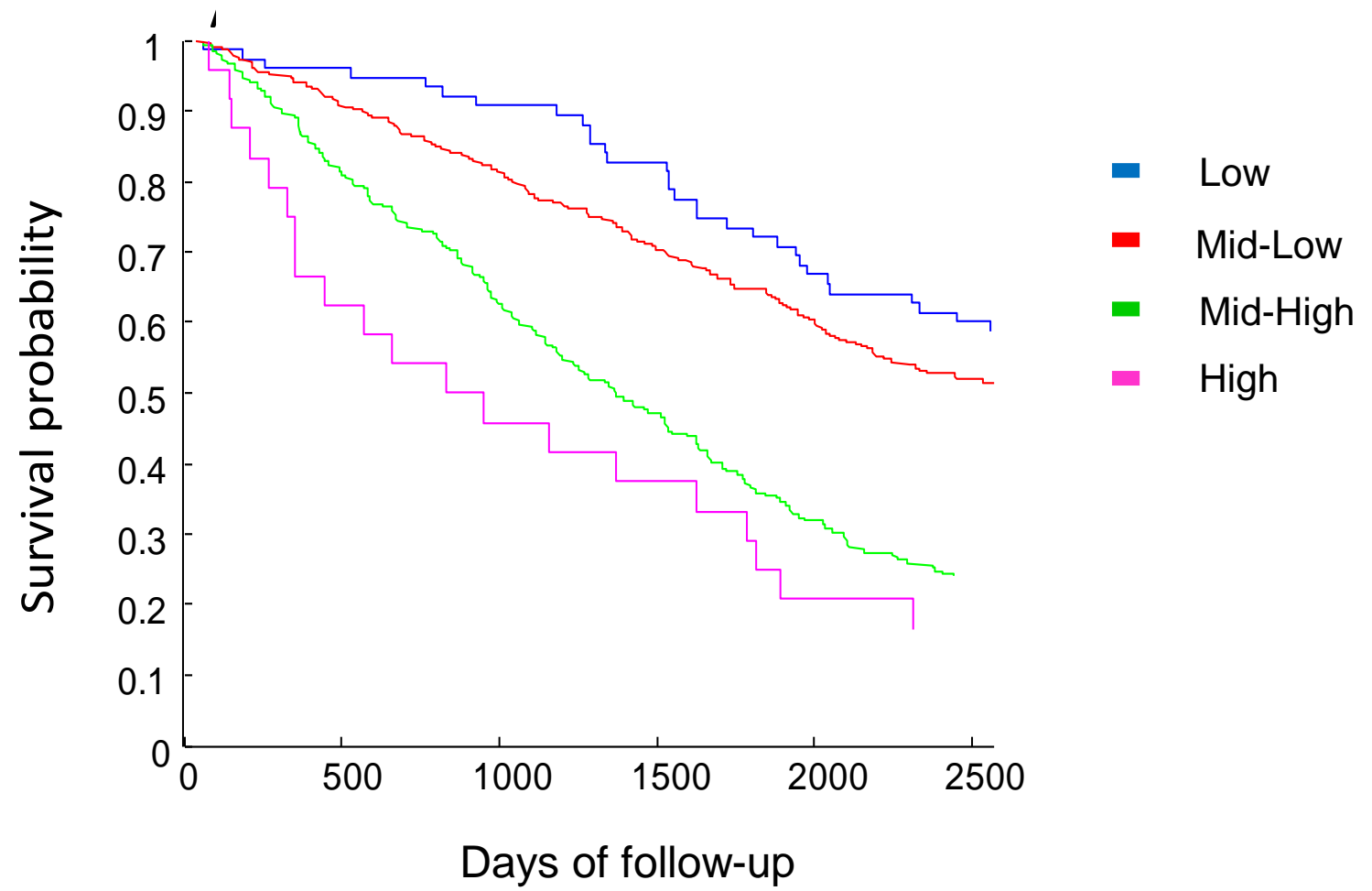
Frailty Index

(Searle et al *BMC Geriatrics* 2008, Clegg et al *Lancet* 2013)

Each biomarker was dichotomized into 'deficit' vs. 'no deficit' using empirically determined cut-points.

Frailty Index = Total number of deficits/Number of biomarkers evaluated.

Biomarker-based Frailty Index Predicts 7-year Mortality



So although we cannot measure biological age precisely, we can see that there are many biological factors that relate to increasing frailty and mortality.

How can we relate this to the evident malleability of the ageing process?

As life expectancy increases:

- do biomarkers show changes later?
- do diseases develop later?
- do we see compression of morbidity?

Two-decade comparison of prevalence of dementia

Matthews et al *Lancet* 2013

Cognitive Function and Ageing Study (CFAS).

Three geographical regions of England.

CFAS I – 1989-1994 (7635 people aged 65 and over)

CFAS II – 2008-2011 (7796 people aged 65 and over)

- Using CFAS I age and sex specific prevalence estimates, 8.3% of the CFAS II study population would be expected to have dementia.
- However, the actual prevalence of dementia in CFAS II was 6.5%.

Getting to Grips with Changes in Health Expectancy

- Despite the importance of health expectancy in policy, monitoring trends both within and between countries is problematic.
- Lack of harmonisation of health measures remain the major limitation, together with differences in survey design and calculation methods.
- The Global Burden of Disease programme has to some extent overcome these deficiencies using complex modelling techniques to estimate healthy life expectancy for 187 countries worldwide (Salomon et al. *Lancet* 2012).
- Latest data suggest an expansion of ill-health and disability in the UK, France, Netherlands, Japan and the USA but not in Belgium, Sweden or Switzerland (where LE gains appear smaller).

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THE END OF AGE

Lecture 5 – New Directions

“Every revolution has a turning point - a time when the original impetus for change has run its course.

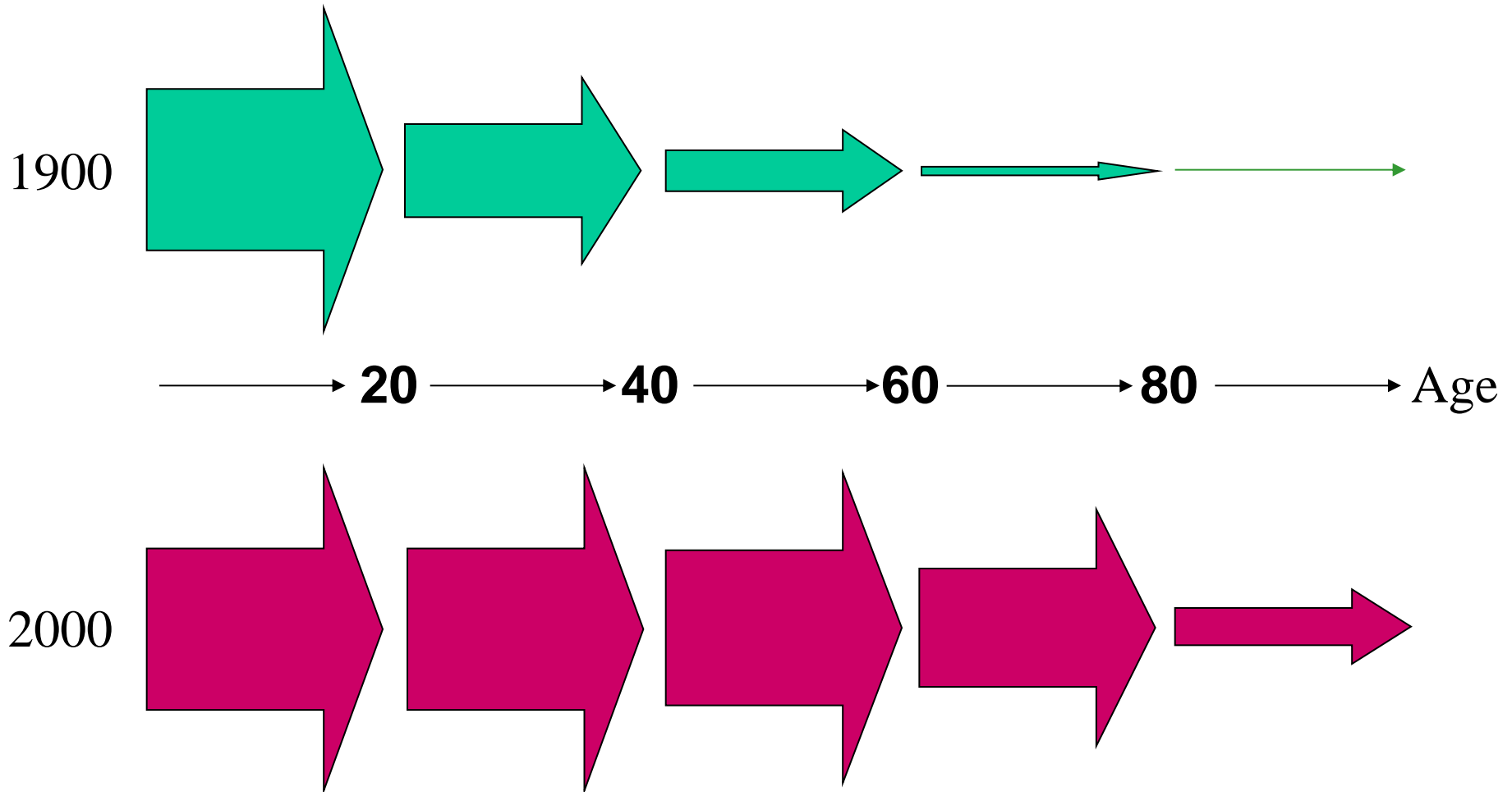
The longevity revolution is no exception.

We know where we've come from and why, but we don't have a clear plan of where to go now.

Ours has been a revolution from - from the terrible waste of life caused by premature death - not a revolution to.

We are at our turning point now.”

Our Changing Pattern of Survival – the UK's Greatest Success Story



What Should Be The Objectives of Medicine in Old Age?

Increase the Health Span?

- More good years and just deal with the bad stuff when it happens.

Compress Age-Related Morbidity?

- Condense the bad stuff into a shorter time.

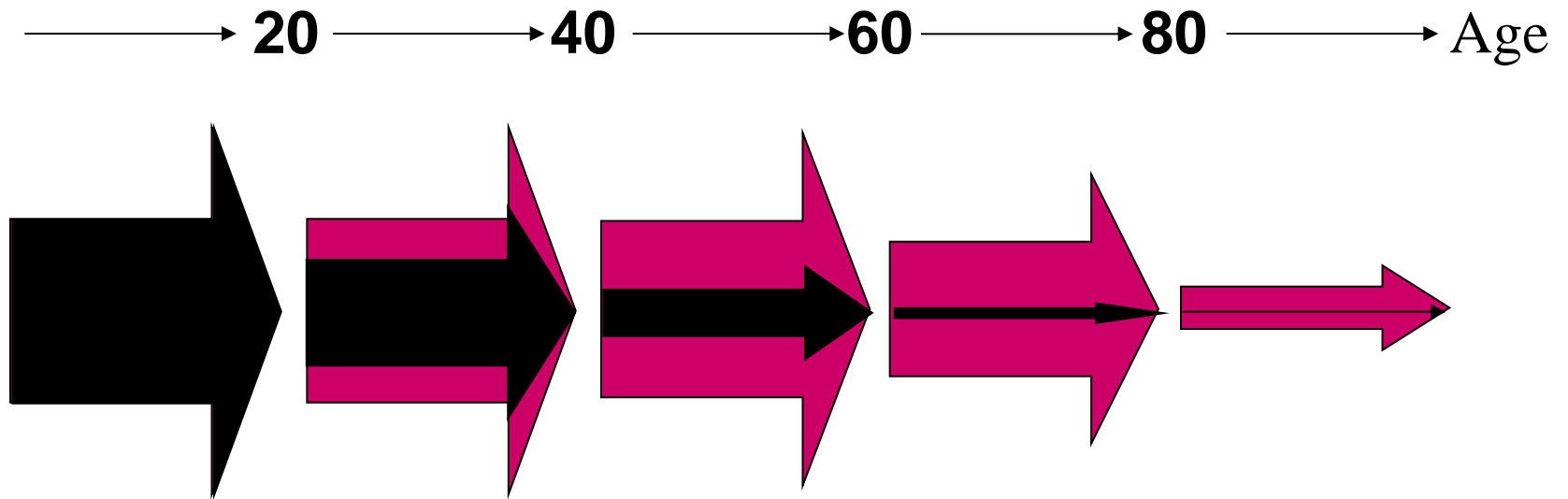
Selectively Postpone the Onset of the Least Desirable Diseases?

- Pick'n'mix geriatrics.

Intervene in Selected Diseases to Palliate their Effects?

- Biologically manage symptoms and their causes.

Now Living – Formerly Dead



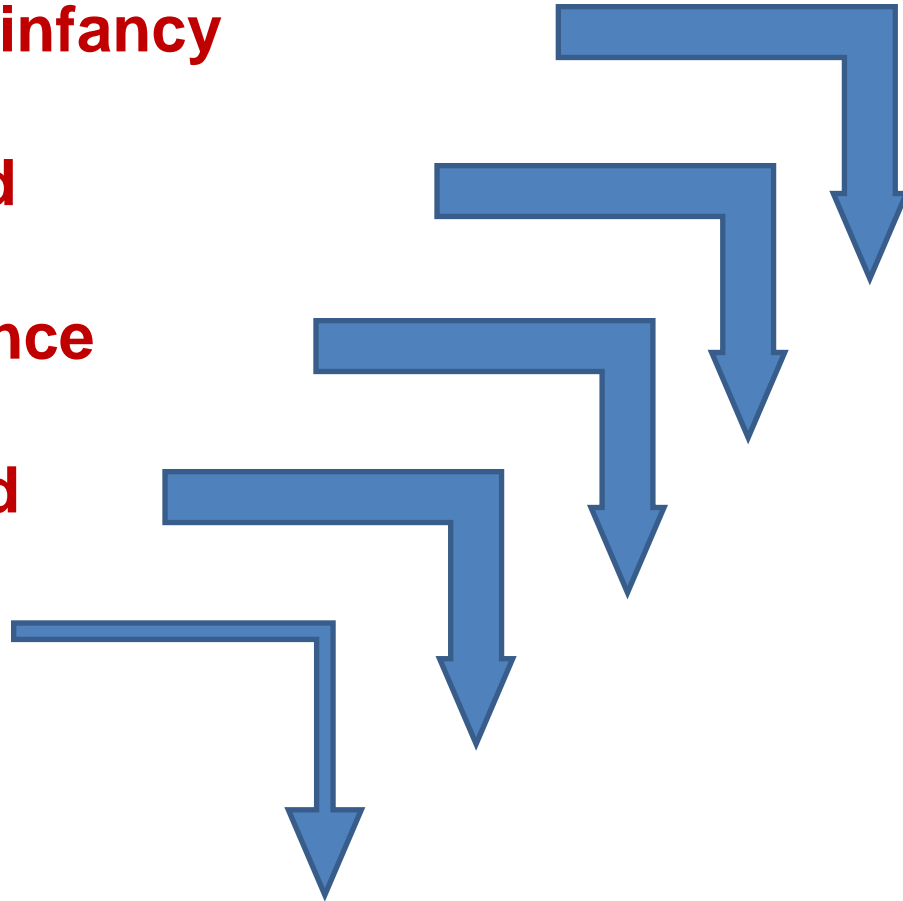
Birth and infancy

Childhood

Adolescence

Adulthood

Old Age



Death

Usually from a single, specific cause in an otherwise healthy individual

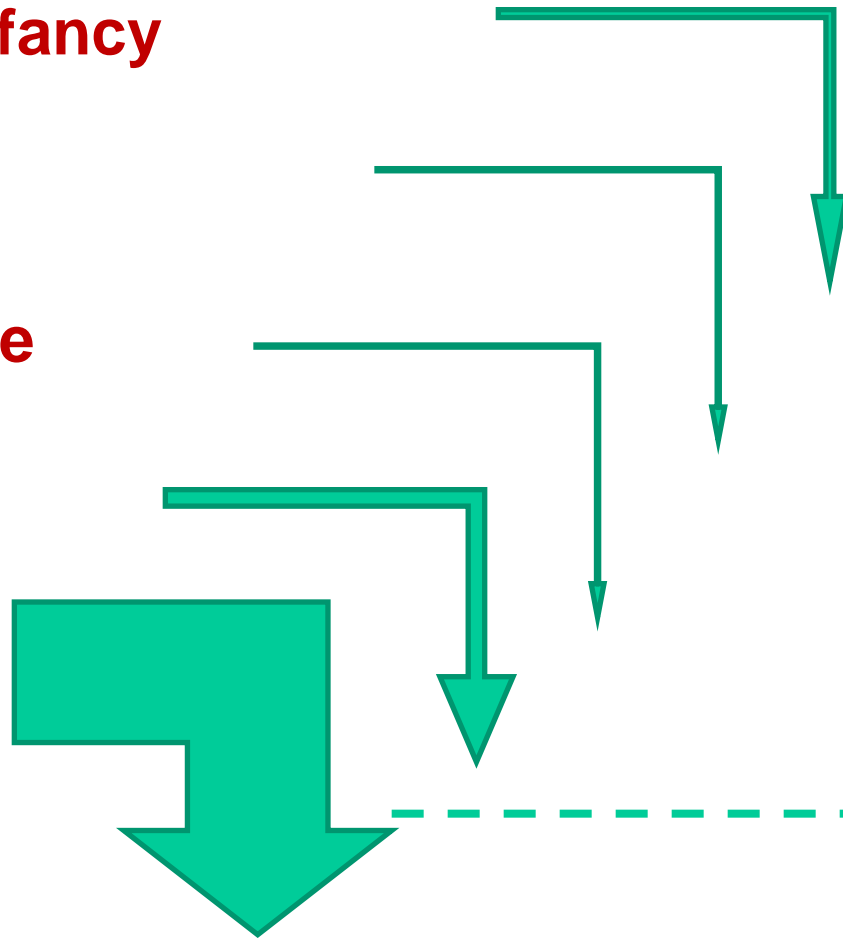
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Usually via a sequence of multi-morbidity and age-related frailty

Death

The 'Good Death' in the 21st Century

- The great majority of deaths are now the result of the ageing process
- Most of us will experience significant multi-morbidity as we advance into old age
- Old age is surprising. Perspectives continually change.
- Frailty, cognitive and sensory impairments are common but not universal features of advanced old age.
- Confusion and fear are common, and may lead to misunderstanding and lack of consistency.
- Transitions are a common feature in the later stages in life and are too often badly handled due to lack of preparation.
- Be prepared. Be flexible.

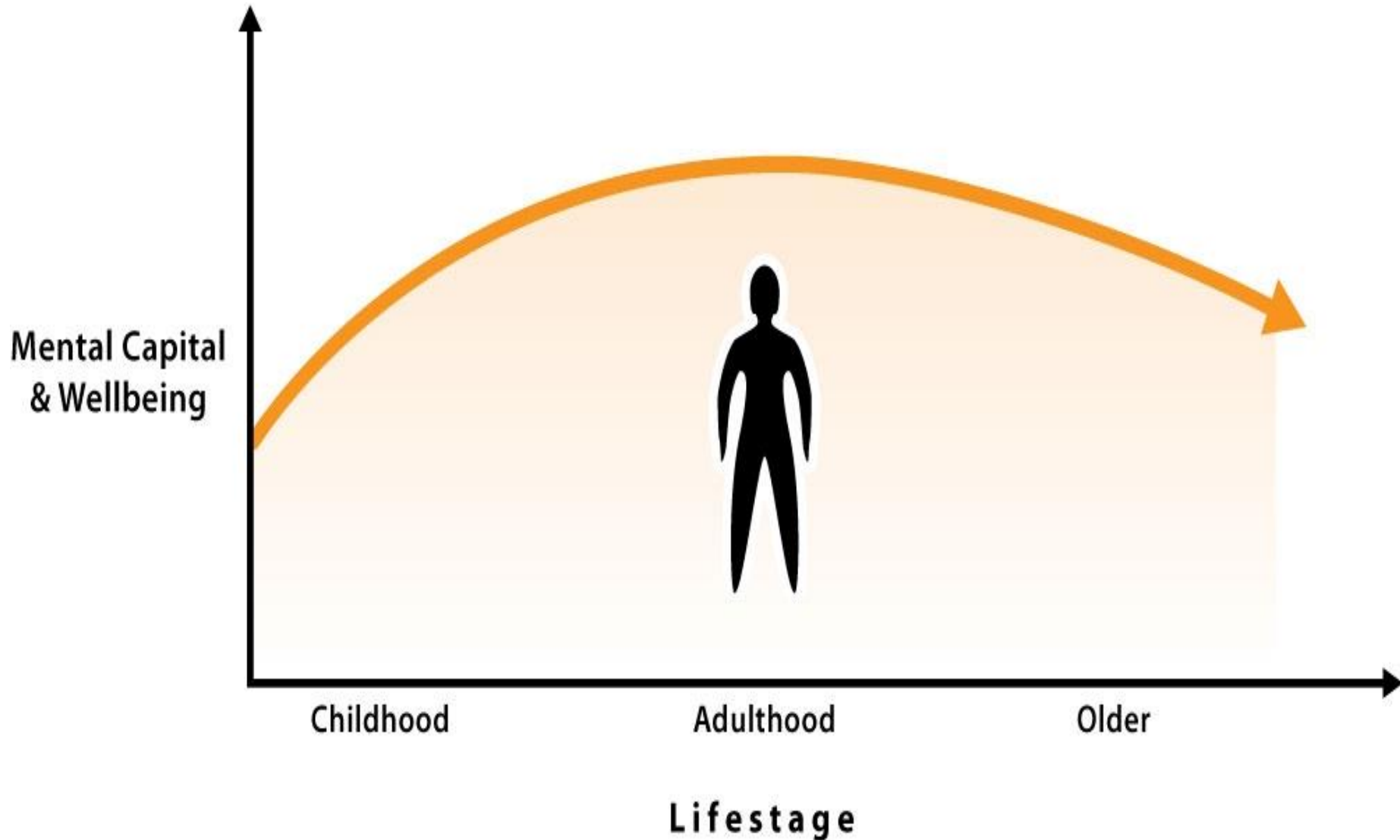
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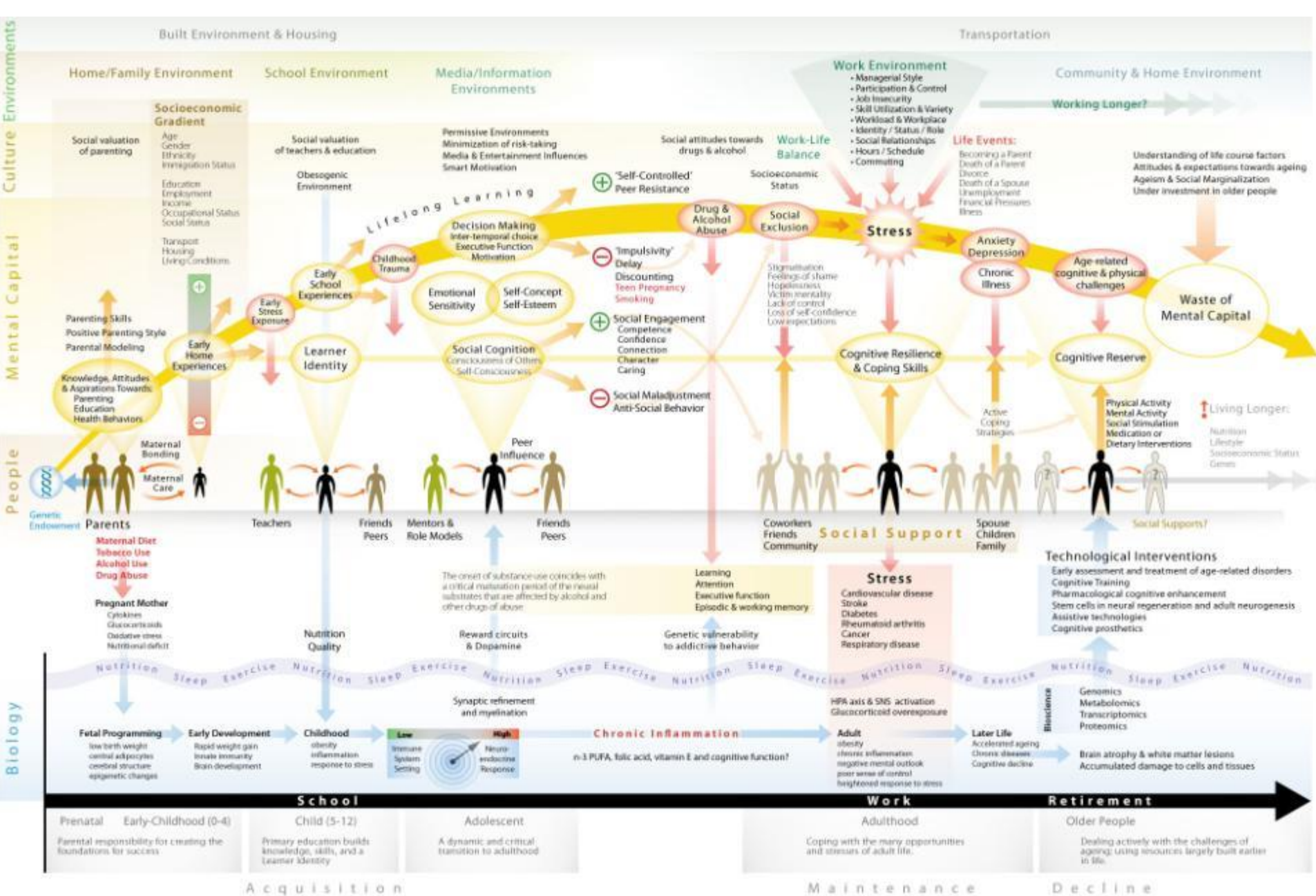
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Barriers to Achieving the Necessary Progress

- Fatalism
- Prejudice (explicit and implicit)
- Reluctance to address complexity
- Narrowness of vision
- Short-termism
- Funding constraints

The Life Course Trajectory of Mental Capital and Wellbeing





Beddington et al. The mental wealth of nations. *Nature*. 2008;455:1057-60.

UN Draft Sustainable Development Goals

Goal 3: Ensure healthy lives and promote well-being for all at all ages.

Target 3.4: By 2030 reduce by one-third premature* mortality from non-communicable diseases (NCDs) through prevention and treatment, and promote mental health and wellbeing.

*Before age 70.

“A premature mortality target for the SDG for health is ageist.”

Lloyd-Sherlock et al *Lancet* 2015

Key Questions and Implications

- Can we identify the precise factors contributing to the malleability of longevity and health in old age?
- Can we improve understanding of age-related multimorbidity?
- Can we use such knowledge further to promote health in old age and to reduce frailty and dependency?
- What mechanisms do we need to set in place to track trends in incidence of age-related diseases?
- How can we develop genuinely cross-disciplinary efforts to address the challenges of longevity?



Thank you

**Centre for Integrated Systems Biology of
Ageing and Nutrition**

Newcastle 85+ Study team

Institute for Ageing and Health (now NUIA)

