The Healthy Ageing Phenotype:
a meeting, a concept and its application

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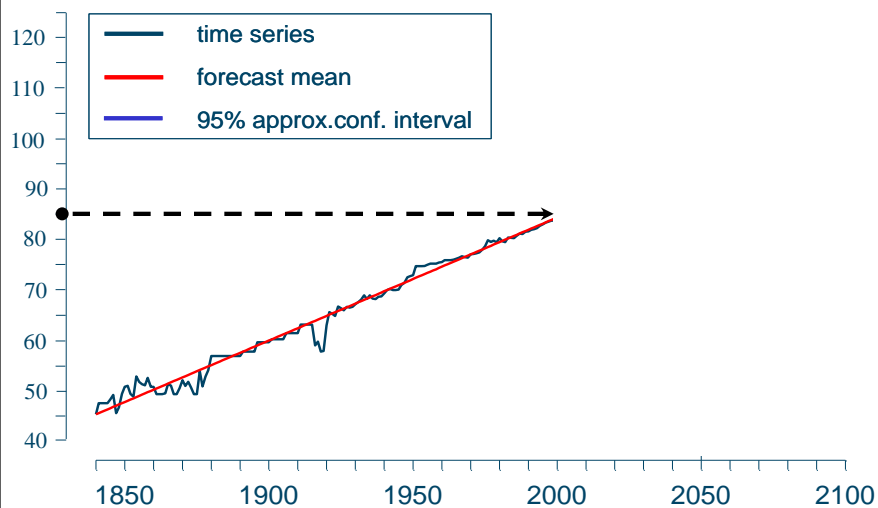
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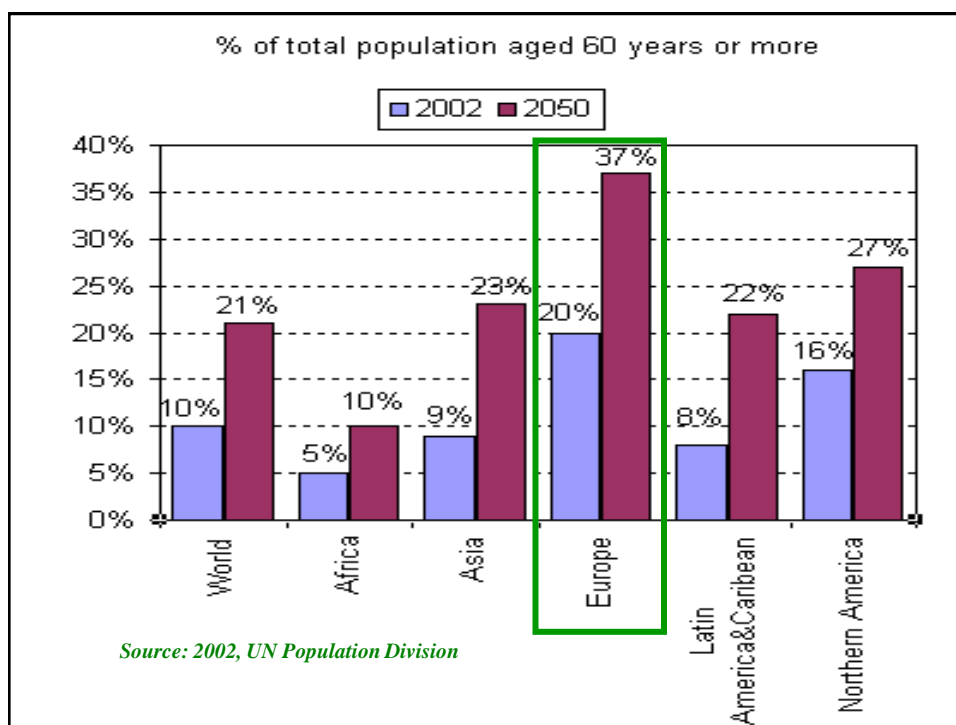

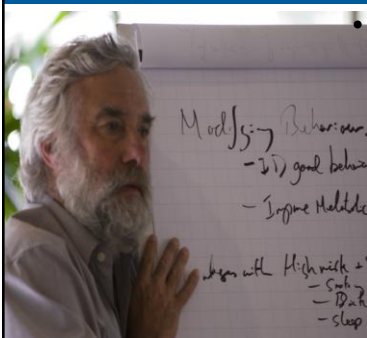# The Healthy Ageing Phenotype:
the meeting, Amsterdam 2007

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Forecast of record LE

time series
forecast mean
95% approx.conf. interval

Source: Vaupel

% of total population aged 60 years or more

■ 2002 ■ 2050

Source: 2002, UN Population Division

➢ The recent history of human longevity demonstrates that the ageing process is highly malleable.

➢ Ageing is a multi-factorial process:
  ➢ Genetic predisposition explain approx 25% of differences in lifespan
  ➢ Environmental and lifestyle factors such as pollution, infection, stress, sleep, physical activity, psychological wellbeing, diet, health infra-structure and financial security account for the remainder.
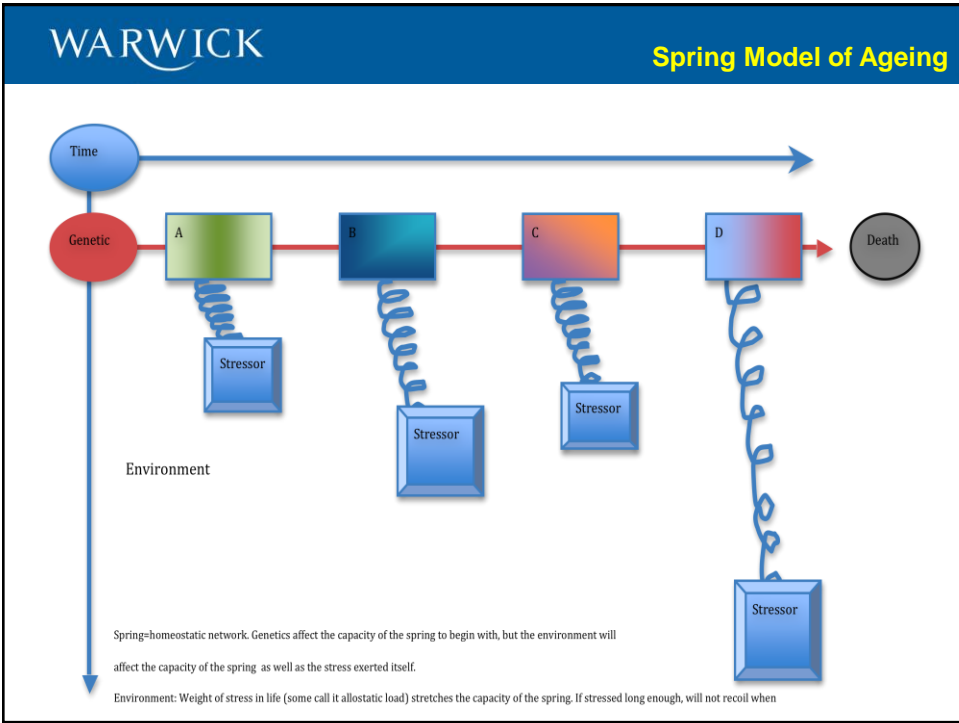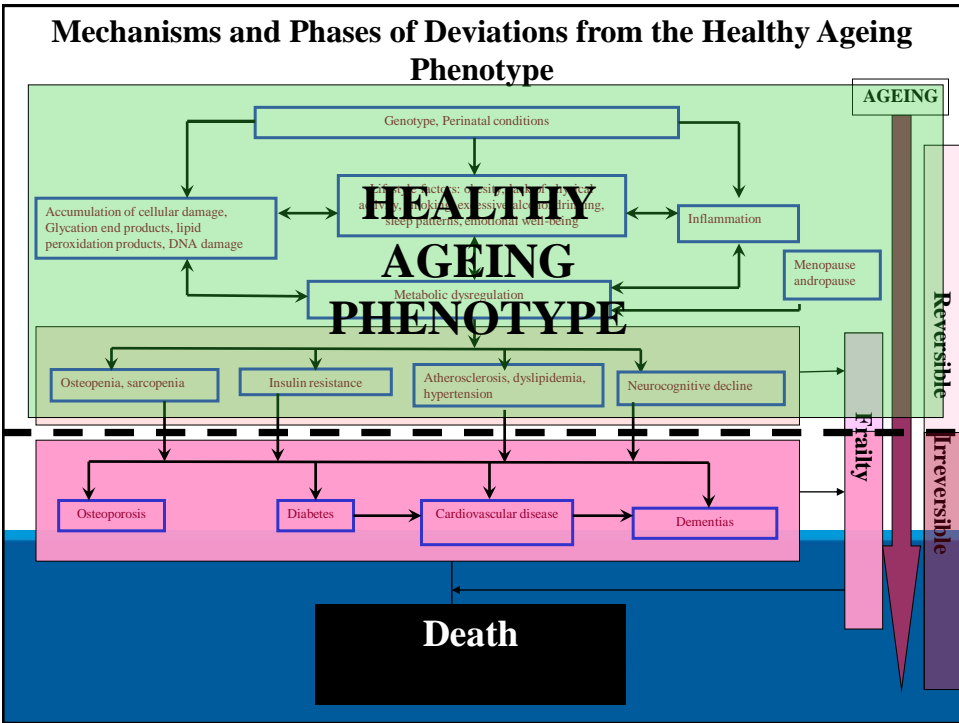
• To find clear attributes and definitions of the "Healthy Ageing Phenotype"

• To identify potential mechanisms and interventions to improve healthy life expectancy of the population

• To highlight areas on ageing research that should be prioritised in the future

Mechanisms and Phases of Deviations from the Healthy Ageing Phenotype

AGEING

Genotype, Perinatal conditions

HEALTHY AGEING PHENOTYPE

Lifestyle factors: physical activity, diet, smoking, excessive alcohol drinking, sleep patterns, emotional well-being

Inflammation

Accumulation of cellular damage, Glycation end products, lipid peroxidation products, DNA damage

Menopause andropause

Metabolic dysregulation

Osteopenia, sarcopenia

Insulin resistance

Atherosclerosis, dyslipidemia, hypertension

Neurocognitive decline

Reversible

Frailty

Irreversible

Osteoporosis

Diabetes

Cardiovascular disease

Dementias

Death

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Spring Model of Ageing

Time

Genetic

A B C D

Death

Stressor

Stressor

Stressor

Stressor

Environment

Spring=homeostatic network. Genetics affect the capacity of the spring to begin with, but the environment will

affect the capacity of the spring as well as the stress exerted itself.

Environment: Weight of stress in life (some call it allostatic load) stretches the capacity of the spring. If stressed long enough, will not recoil when

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The Healthy Ageing Phenotype can be defined as:

➢ condition of having highly preserved functioning metabolic, hormonal and neuro-endocrine control systems at the organ, tissue and molecular level.

➢ It is further characterised by a higher degree of physiological complexity, for instance, in heart rate variability, of neuronal structure and bone architecture.

➢ This translates into optimal reserves and biological resilience to respond to and accommodate day to day environmental stressors.

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Recommendations/Observations I

➢ Ageing over the lifecourse is not necessarily a steady decline from optimal health. Physiological resilience along ageing reduces the negative effects of external stressors Further research is required to understand the nature of this resilience and how to prevent permanent dysregulation as we age.

➢ The future development of interventions and preventive strategies should also acknowledge the holistic nature of human health. Research has shown that many age-related conditions share common underlying pathways, and thus to maximise the benefits of intervention and prevention strategies, it may be appropriate to target common pathways.

➢ The scope of lifestyle interventions towards the prevention of morbidity and mortality should incorporate positive modifications of diet, exercise, sleep and behavioural patterns as well as the preservation of emotional well being.

➤ Understanding life-course trajectories followed by those living to old age maintaining a satisfactory level of health and functionality could constitute a helpful route to identify and design optimal preventive strategies.

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

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Review

Changing course in ageing research: The Healthy Ageing Phenotype☆

Oscar H. Franco[a,b,*], Kavita Karnik[a], Gabrielle Osborne[a], Jose M. Ordovas[c], Michael Catt[a], Frans van der Ouderaa[a]

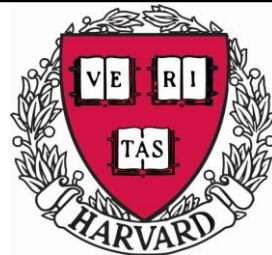[a] Unilever Corporate Research, Colworth Park, Sharnbrook, Bedfordshire, UK
[b] Health Sciences Research Institute, University of Warwick, Coventry, United Kingdom
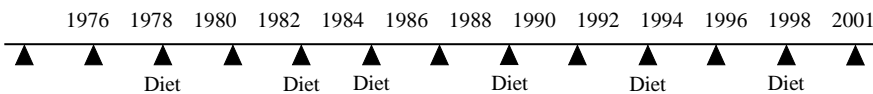[c] Nutrition and Genomics Laboratory, Jean Mayer-US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA

The Healthy Ageing Phenotype:
applying the concept

In collaboration with Harvard School of Public Health:
Qi Sun, Mary K. Townsend, Olivia I. Okereke, Frank B. Hu, and Francine Grodstein

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Slide 1

1976 1978 1980 1982 1984 1986 1988 1990 1992 1994 1996 1998 2001

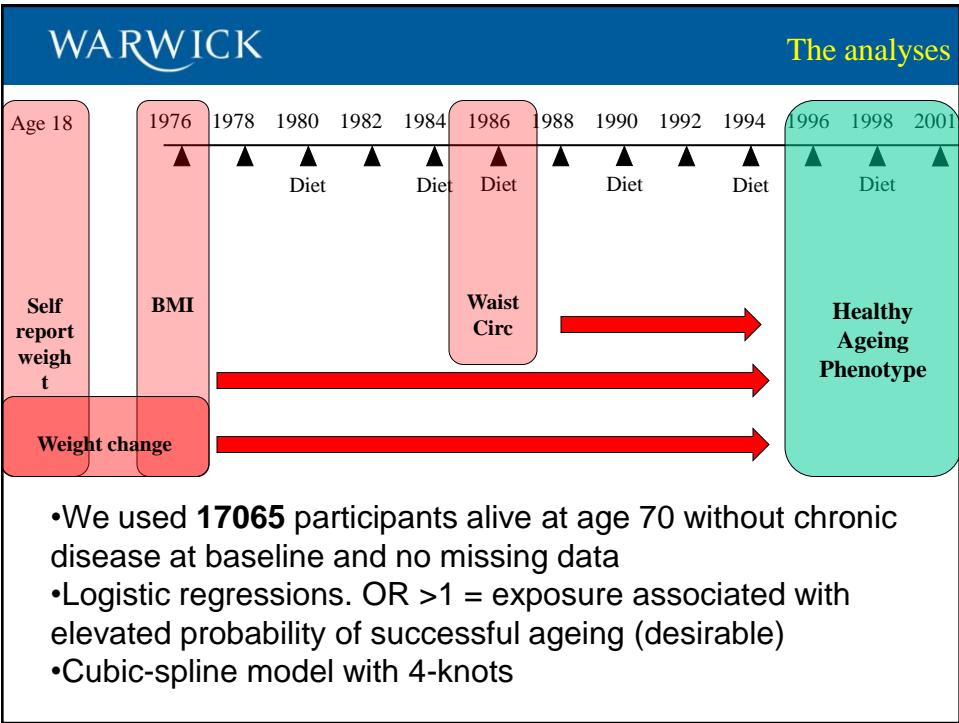Diet   Diet Diet   Diet   Diet   Diet

- 121,700 registered nurses
- Baseline is 1976
- Every 2 years: follow-up questionnaire
- Every 2-4 years: FFQ
- High follow-up rate (>95% by 2002)
- Blood samples collected in 1989 and 1990: 33,000 women

We aimed to evaluate the impact of obesity and weight change in the probability of achieving the healthy ageing phenotype

Slide 2

1. **Age≥70 years**
2. **No history of chronic diseases**
   1. CVD (cardiovascular disease)
   2. cancer
   3. diabetes
   4. kidney failure
   5. COPD
   6. Parkinson's disease
   7. multiple sclerosis
   8. amyotrophic lateral sclerosis
3. **No major physical limitations:** Limitation:
   1. limited at least "a little" on moderate activities or
   2. limited "a lot" in more difficult physical performance items.
4. **No cognitive impairment:** TICS (Telephone interview for cognitive status) >31
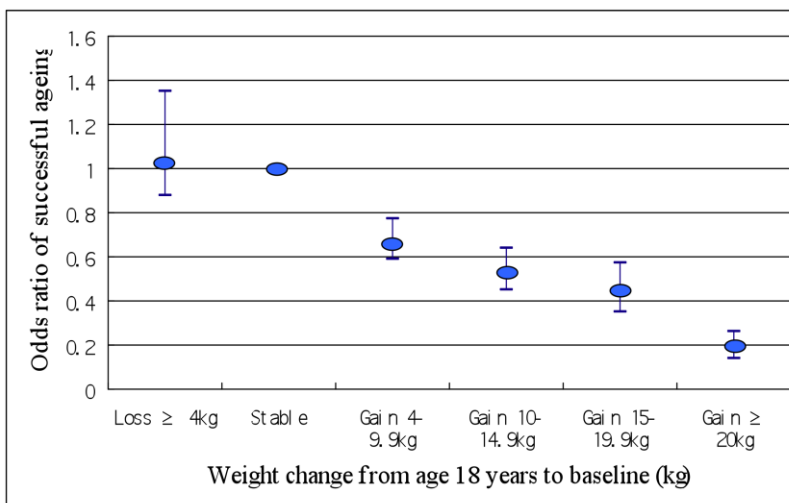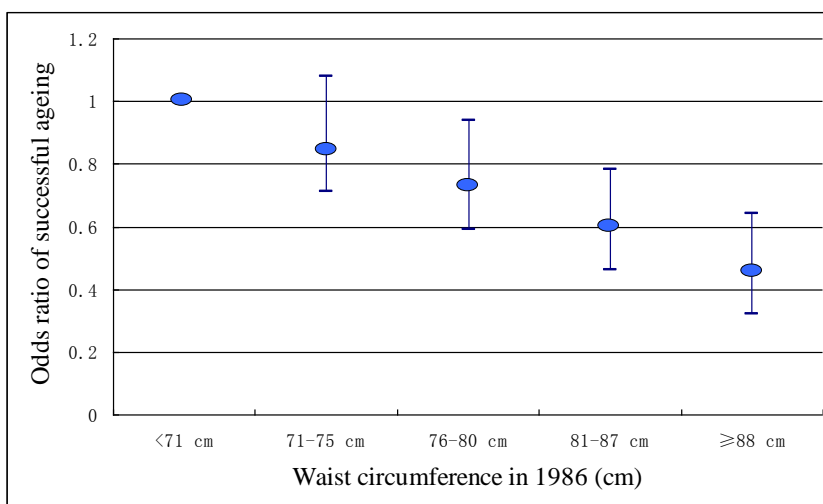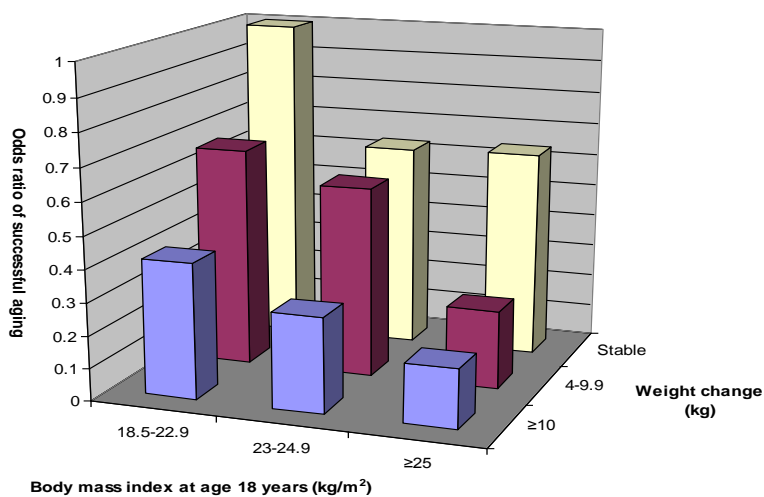5. **No mental health issues**: SF-36, mental health score above median (84)

WARWICK — The analyses

| Age 18 | 1976 | 1978 | 1980 | 1982 | 1984 | 1986 | 1988 | 1990 | 1992 | 1994 | 1996 | 1998 | 2001 |

Diet   Diet   Diet   Diet   Diet   Diet

Self report weight   **BMI**   **Waist Circ**   **Healthy Ageing Phenotype**

Weight change

- We used **17065** participants alive at age 70 without chronic disease at baseline and no missing data
- Logistic regressions. OR >1 = exposure associated with elevated probability of successful ageing (desirable)
- Cubic-spline model with 4-knots

WARWICK — Results 1

Definition	N (%)
Successful survivors	1,686 (9.9%)
Usual survivors	15,379 (90.9%)
Having chronic disease(s) only	511 (3.3%)
Having limitation(s) only	9,156 (59.5%)
Having both chronic disease(s) and limitation(s)	5,712 (37.1%)

WARWICK — Effects of BMI levels on odds of the HAP
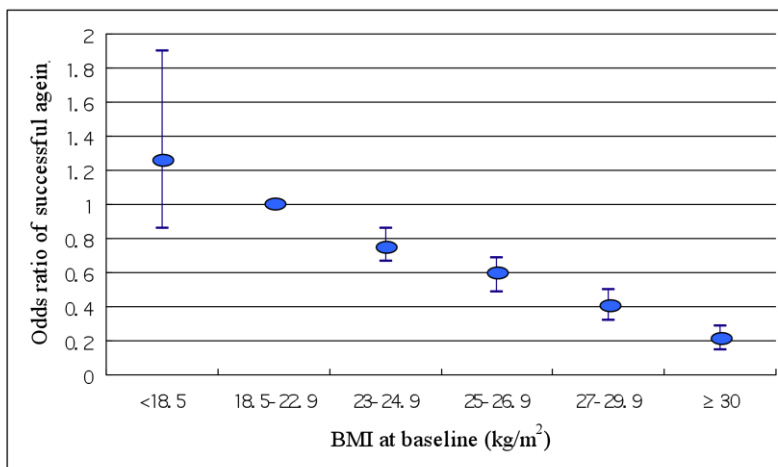
Adjusted for age, education, marital status, postmenopausal hormone use, smoking, family history of heart disease, diabetes, or cancer, vigorous physical activity, P:S ratio, intakes of trans fat, alcohol, and cereal fiber, and intakes of fruits and vegetables and red meat.

WARWICK — Effects of weight change on odds of the HAP

WARWICK Combined effects of BMI & weight change

WARWICK Effects of waist circumference on odds of the HAP

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WARWICK Conclusions

•Adiposity in mid-life and weight gain are strongly related to reduced probability of successful ageing.

•A new society, with novel characteristics and new needs is emerging and research into healthy longevity requires an innovative approach: multifactorial prevention and treatment of frailty, disability and disease seems the most appropriate way to steer the population to a healthier phenotype.

Paper in press in BMJ

Thank you for your attention