

Cohort Commons Meeting

The value of long term follow-up

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Health ABC Cohort

- 3075 men and women (50%), 45% African American – Pittsburgh, Memphis, UCSF CC and NIA
- Focus – weight, body comp and physical disability
- 6 Annual exams with body comp, performance, morbidity assessment
- Two additional exams and continued phone follow-up
- Adjudicated mortality and weight related health conditions
- Biorepository

- Some key questions about aging
 - Longevity
 - Healthy Aging
- Potential to address with ideas about consortia

What does it take to live a long and healthy life?

- Women > Men – Why?
- What is the role of the life course?
 - What are the key periods for exposure?
 - Fetal origins
 - Key points for intervention
- How important is physiologic reserve to the period of disability-free survival?
 - When and how to optimize reserve?
- What determines the rate of aging?
 - Can it be slowed down in humans?
 - Onset delayed vs. change in rate

Long term follow-up of existing cohorts

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A Meta-analysis of Four Genome-Wide Association Studies of Survival to Age 90 Years or Older: The Cohorts for Heart and Aging Research in Genomic Epidemiology Consortium

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GWAS of Longevity in CHARGE Consortium Confirms *APOE* and *FOXO3* Candidacy

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2010

Cases:

1,836 longevity cases, age 90+

Comparison:

1,955 died between the ages of 55 and 80

2014

Cases:

6,036 longevity cases, age 90+

Comparison:

3,757 died between ages 55 and 80

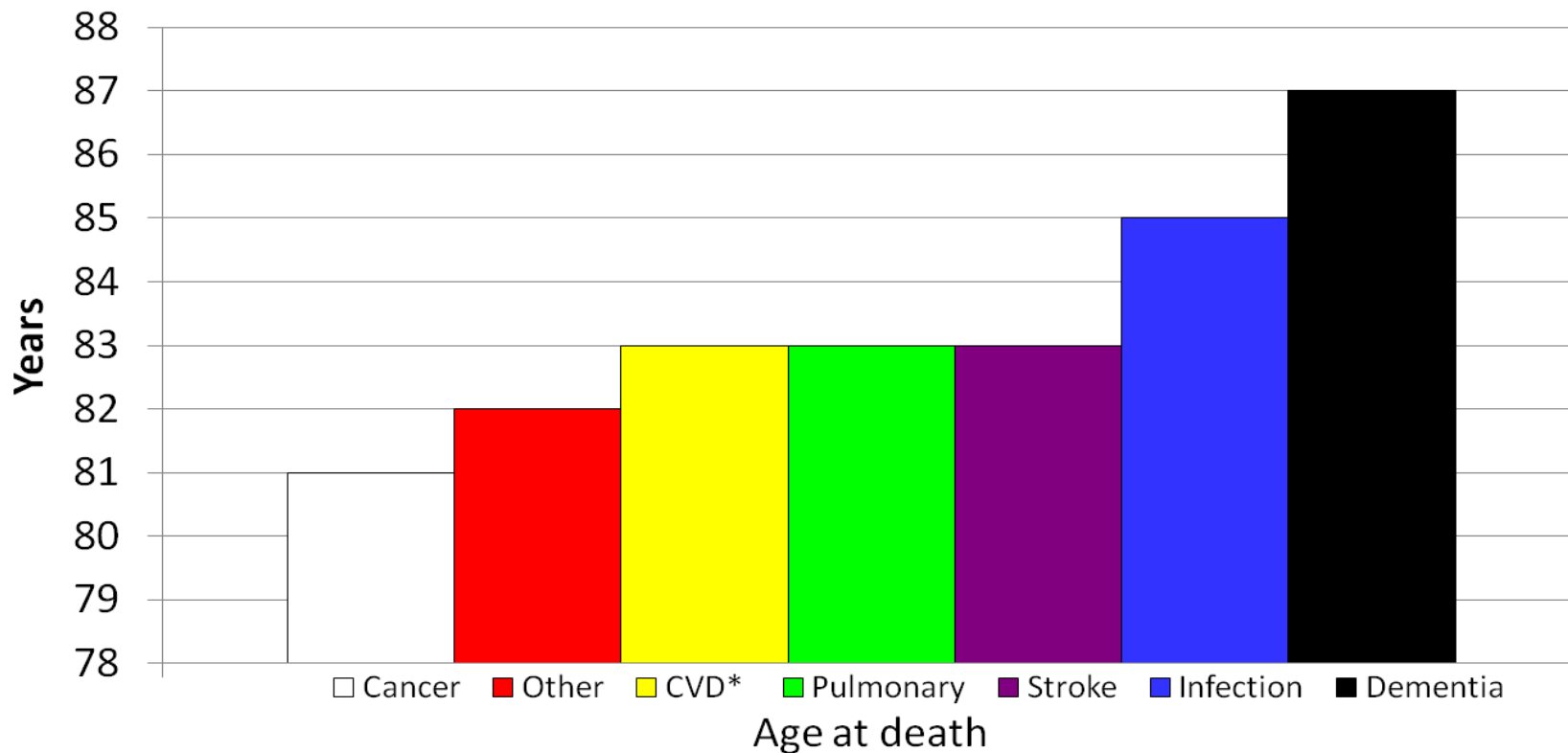
Longevity research

- CHARGE GWAS Longevity
 - Illustrates the opportunity
 - Sample size for longevity is growing
- Few genetic factors identified
 - *ApoE4*
 - *FOXO3a*
- Rare Variation?
- Epigenetics?
- Environment? Birth cohort?

Longevity \neq Healthy Aging

- Risk/protective factors for longevity
 - Cardiovascular risk factors predominate (Newman 2003, Terry 2005, Willcox 2006, Yates 2008, Britton 2008, Sun 2009, Baer 2011, Walter 2012)
 - Delay onset of functional decline with CVD prevention
- Multimorbidity and competing risk
- Time sequence of events
 - $\text{Age}_{\text{cancer}} < \text{Age}_{\text{CVD}} < \text{age}_{\text{dementia}}$

Mean Age at Death by Cause of Death in CHS – 15 year follow-up



Newman AB, Sachs MC, Arnold AM, Fried LP, Kronmal R, Cushman M, Psaty BM, Harris TB, Robbins JA, Burke GL, Kuller LH, Lumley T. Total and Cause Specific Mortality in the Cardiovascular Health Study. *J Gerontol A Biol Sci Med Sci.* 2009;64A(12):1251-126. PMID: PMC2773812.

Need for new or expanded studies

- Increasing proportions surviving to very old ages
- Environmental factors predominate
- Birth cohort trends difficult to discern in individual cohort studies
- Key parameters of aging often not measured in early and midlife in most cohort studies
- Little information on achievement of peak development in studies of adults – birth to early adulthood

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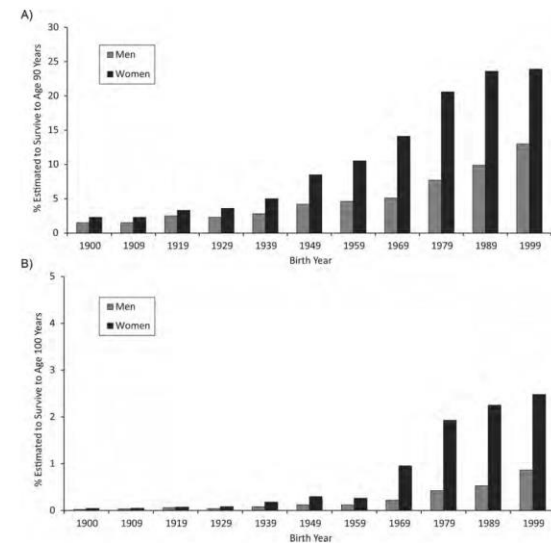


Figure 1. Survivorship to ages 90 years (A) and 100 years (B) for the 1900–1999 birth cohorts, by sex, United States. Data were obtained from Arias (3).

Grip Strength across the Life Course: Normative Data from Twelve British Studies

Richard M. Dodds^{1*}, Holly E. Syddall¹, Rachel Cooper², Michaela Benzeval³, Ian J. Deary⁴, Elaine M. Dennison¹, Geoff Der⁵, Catharine R. Gale^{1,4}, Hazel M. Inskip¹, Carol Jagger⁶, Thomas B. Kirkwood⁶, Debbie A. Lawlor⁷, Sian M. Robinson¹, John M. Starr⁴, Andrew Steptoe⁸, Kate Tilling⁷, Diana Kuh², Cyrus Cooper¹, Avan Aihie Sayer¹

Virtual cohort –
Multiple
harmonized
cohorts

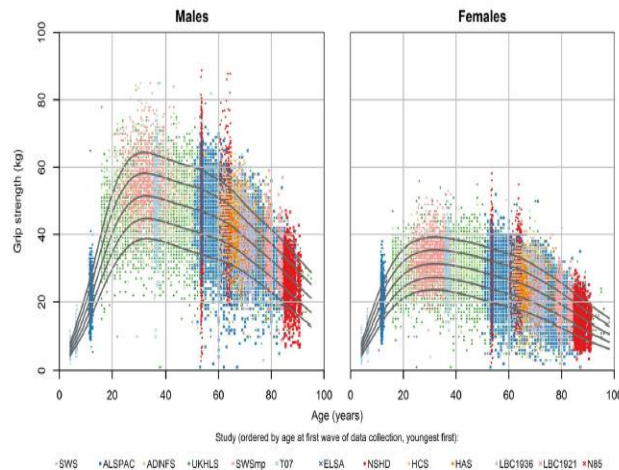


Figure 1. Cross-cohort centile curves for grip strength. Centiles shown 10th, 25th, 50th, 75th and 90th. ADNFS Allied Dunbar National Fitness Survey, ALSPAC Avon Longitudinal Study of Parents and Children, ELSA English Longitudinal Study of Ageing, HAS Hertfordshire Ageing Study, HCS Hertfordshire Cohort Study, LBC1921 and LBC1936 Lothian Birth Cohorts of 1921 and 1936, N85 Newcastle 85+ Study, NSHD Medical Research Council National Survey of Health and Development, SWS Southampton Women's Survey, SWSmp mothers and their partners from the SWS, T-07 West of Scotland Twenty-07 Study, UKHLS Understanding Society: the UK Household Panel Study.

doi:10.1371/journal.pone.0113637.g001

Consortium Ideas

- Assemble cross-sectional data by age and birth cohort – “Virtual Cohort”
 - Birth – old age
 - Birth cohort effects?

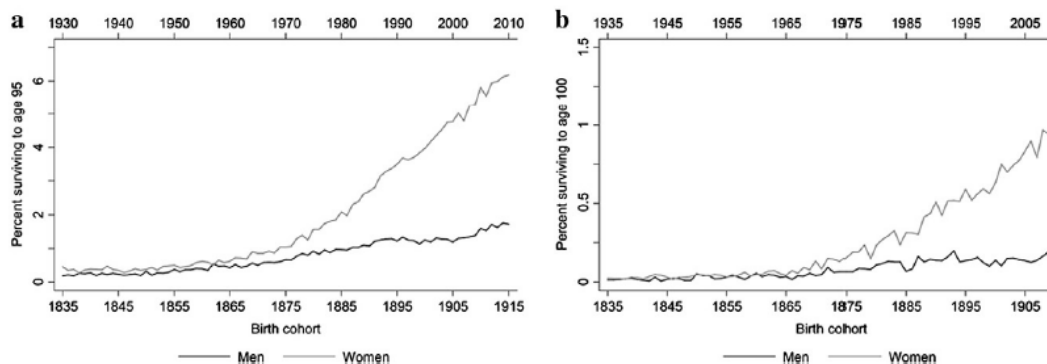


Fig. 1. The probability of surviving in Denmark from birth to age 95 in the period 1835 to 1915 (a) and from birth to age 100 in the period 1835 to 1910 (b).

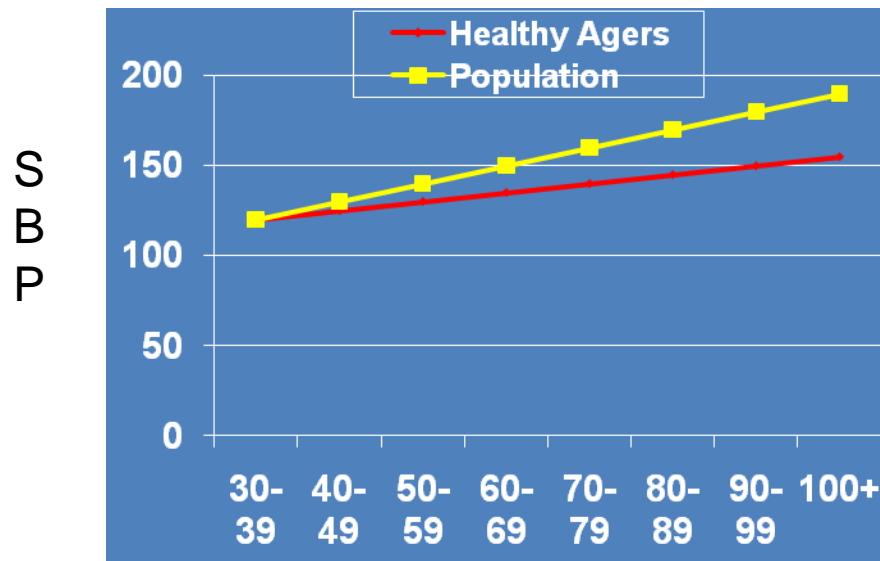
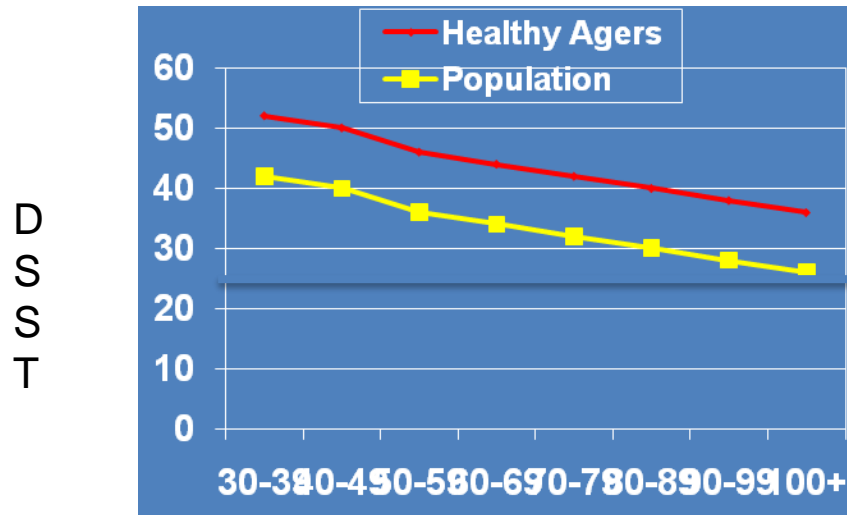
Nygaard, Marianne, et al. "Birth cohort differences in the prevalence of longevity-associated variants in APOE and FOXO3A in Danish long-lived individuals." *Experimental gerontology* 57 (2014): 41-46.

Consortium Ideas

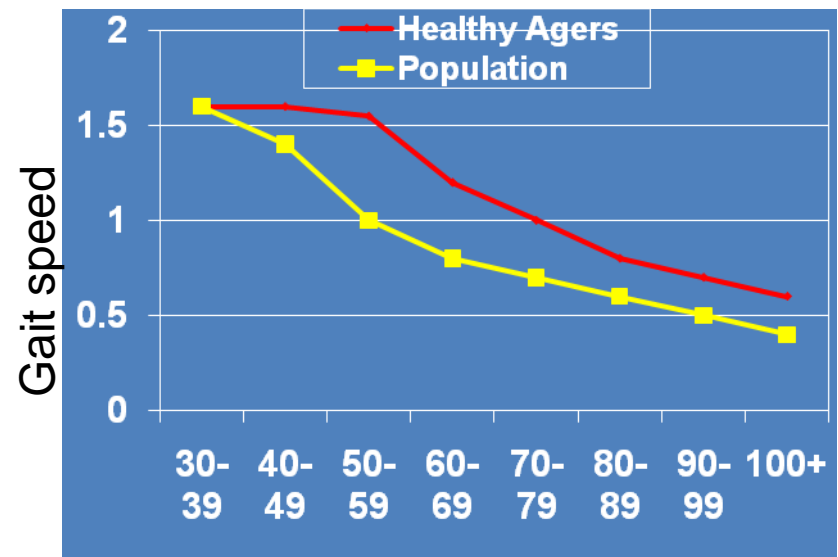
- Assemble new life course cohort
 - From existing?
 - Assess development and decline
 - Add measures that are age sensitive and longitudinal
 - Distinguish phenotypes
 - Greater reserve from
 - rate of decline or
 - onset of decline

Hypothetical Trajectories – Different Phenotypes

1. Greater reserve (same rate of decline)



3. Later onset of decline



2. Slower rate of rise

Consortium Ideas

- Multigenerational cohort
 - Children of cohorts?
 - Secular/birth cohort trends
 - Fetal origins

Primordial prevention to optimize aging

- Lipids, BP
- Muscle function
- Bone density
- Vision
- Hearing
- Dementia - ?

Value of long term follow-up

- Studies should be:
 - Lifelong
 - Multigenerational
 - Preconception
 - Interventional
- To address:
 - Multiple diseases simultaneously
 - In the context of their major risk factor: Aging