Understanding hearing loss: Hearing research with the UK Biobank resource

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Why hearing?

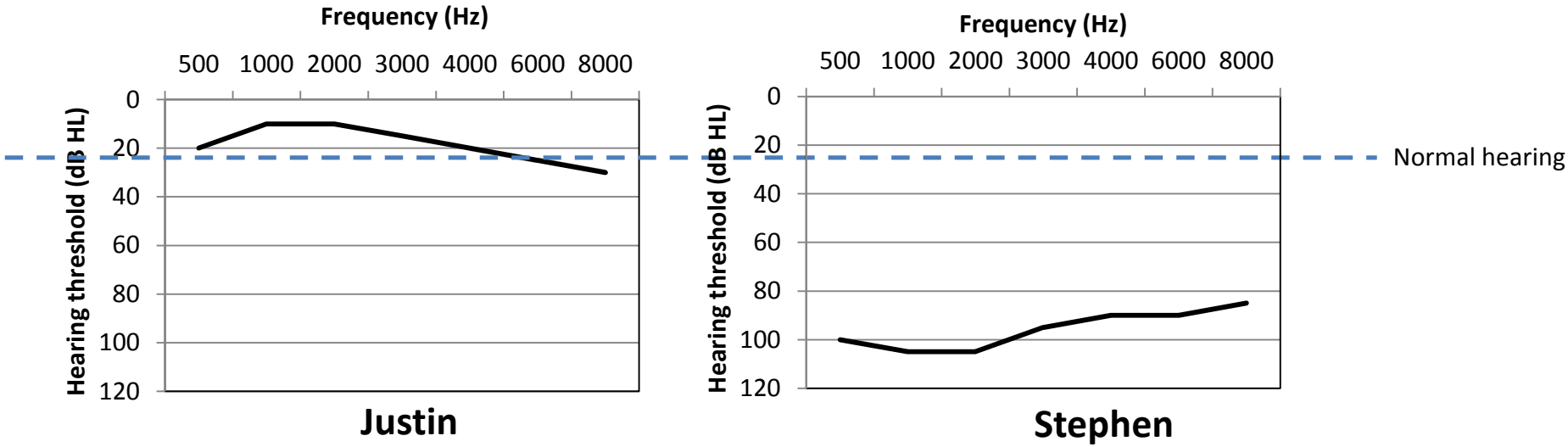
- Hearing loss very common, especially for older adults (currently >10 million in UK)
- Impacts on communication → social isolation, depression, poor quality of life
- High prevalence + impact → high cost (213 billion Euros per year)
- No drug treatment. Hearing aids of limited effectiveness; stigma; low uptake

→ Need to find ways to prevent and lessen the impact of hearing loss

- High prevalence of HL and significant impact

…..but evidence that HL may be preventable

1. Geographical variation; higher levels of HL in northern England
2. Age cohort; baby boomers have better hearing than their parents
3. Not all older people have poor hearing:



→ Suggests that hearing loss is avoidable, and that there could be modifiable factors that cause hearing loss

So why do people loose their hearing?

What can we do to prevent hearing loss?

biobank uk

Improving the health of future generations

- Prospective resource for epidemiology
- Environmental and genetic risk for disease
- 500,000 aged 40 to 69 years
- Questionnaire, physical measures, blood & urine sample (2007-2010)
- Link with NHS medical records

(First group; most website hits)

Hearing

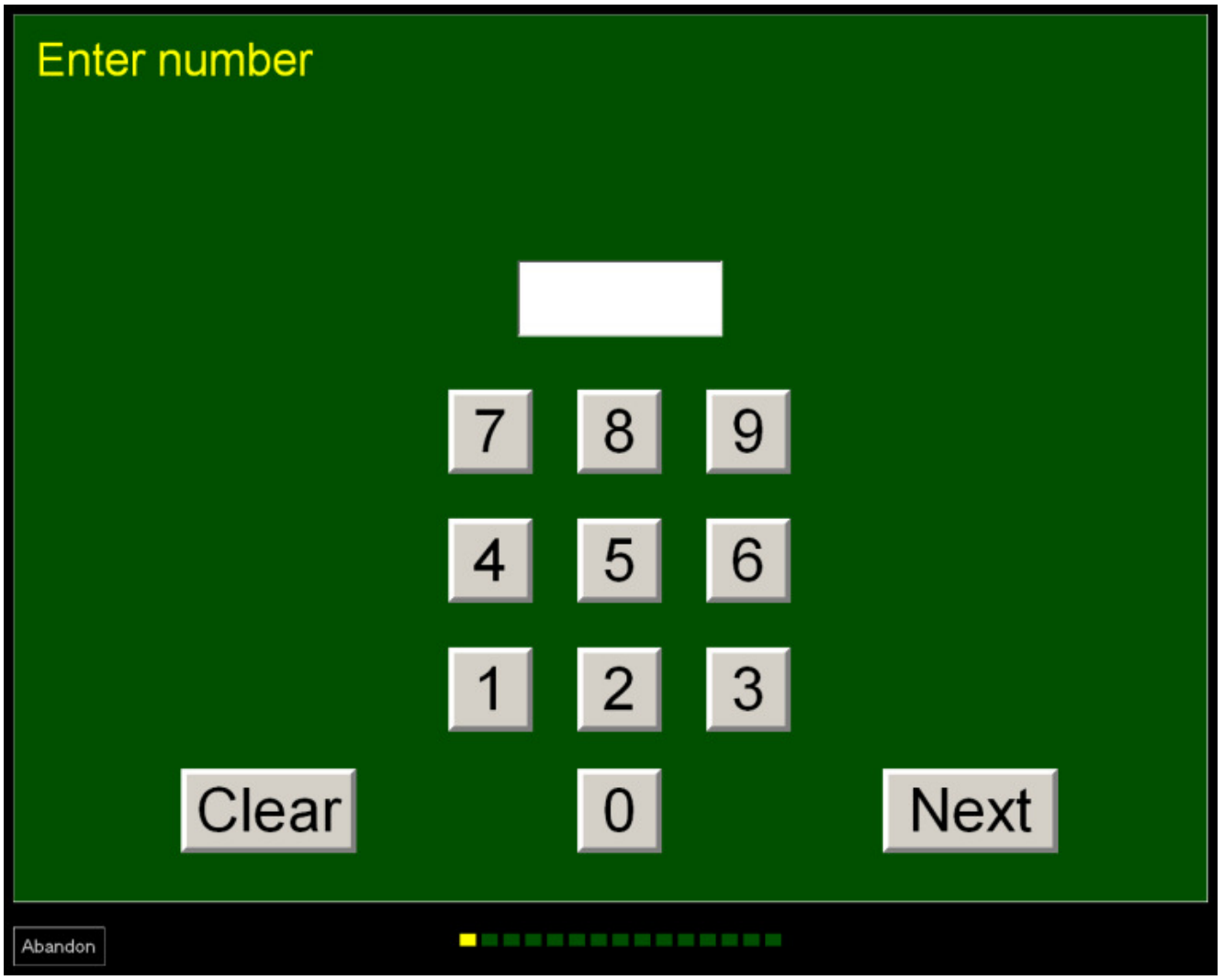
Self-report questions

- Hearing aid use
- Noise exposure (work and music)
- Tinnitus

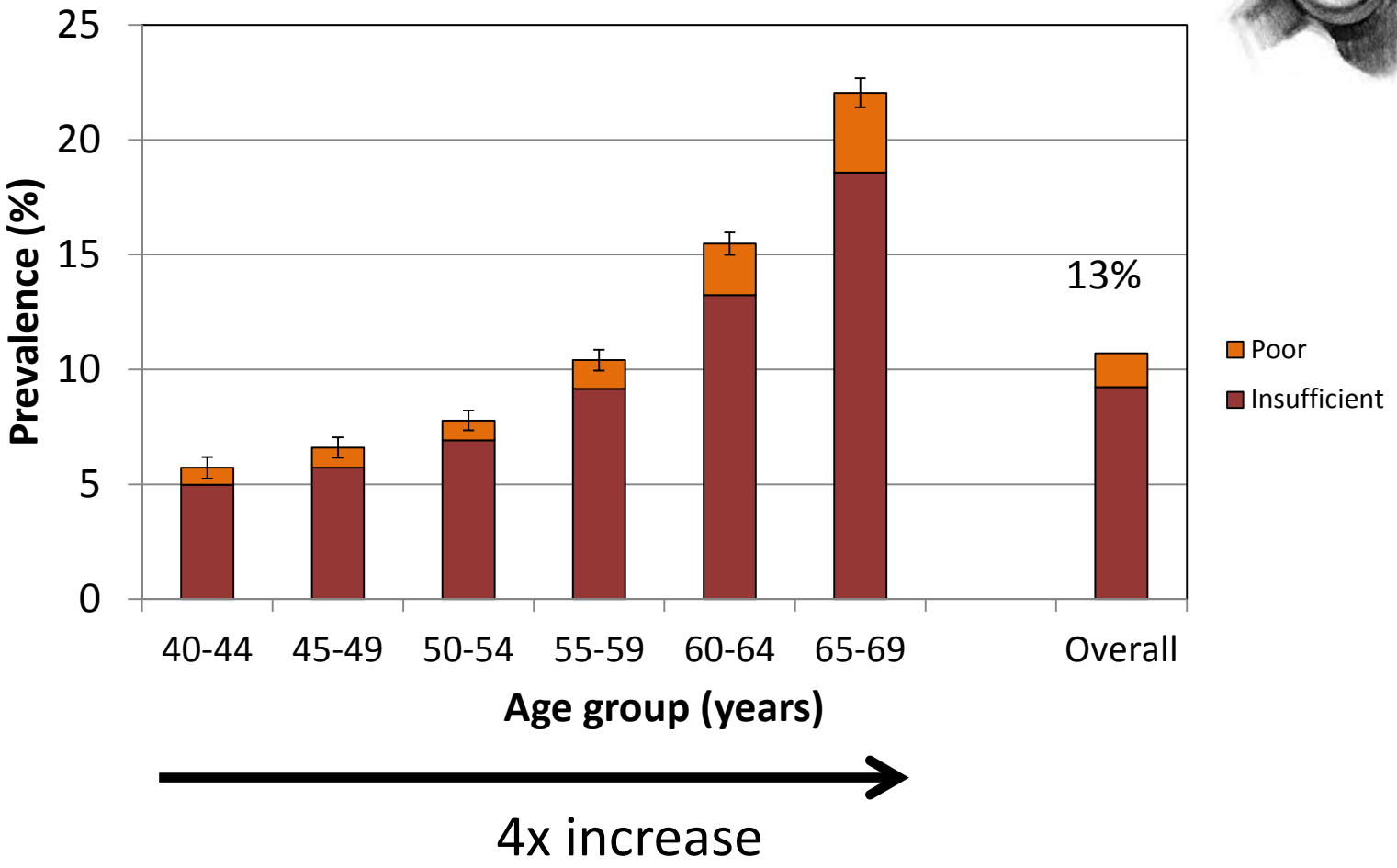
Digit Triplet Test (Smits, Kapteyn & Houtgast, 2004)

- E.g. “1, 6, 4”; vary noise level to track 50% correct
- Classify according to normal range performance, better ear
- 164,000 people

UK Biobank Digit Triplets Test



Hearing



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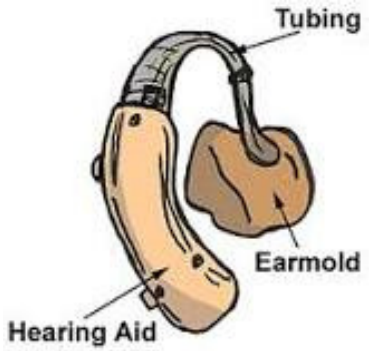
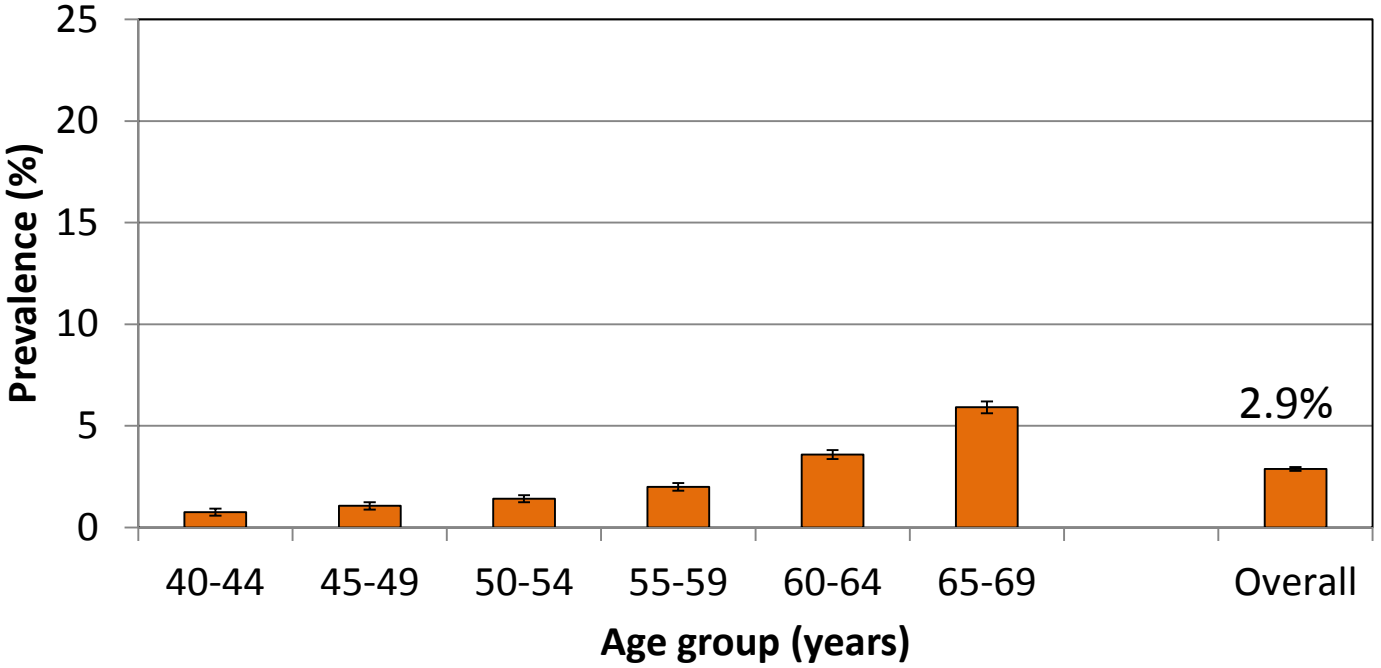
Hearing aid use





vs 22%HL

Cf 2.8% ownership in early 1980s

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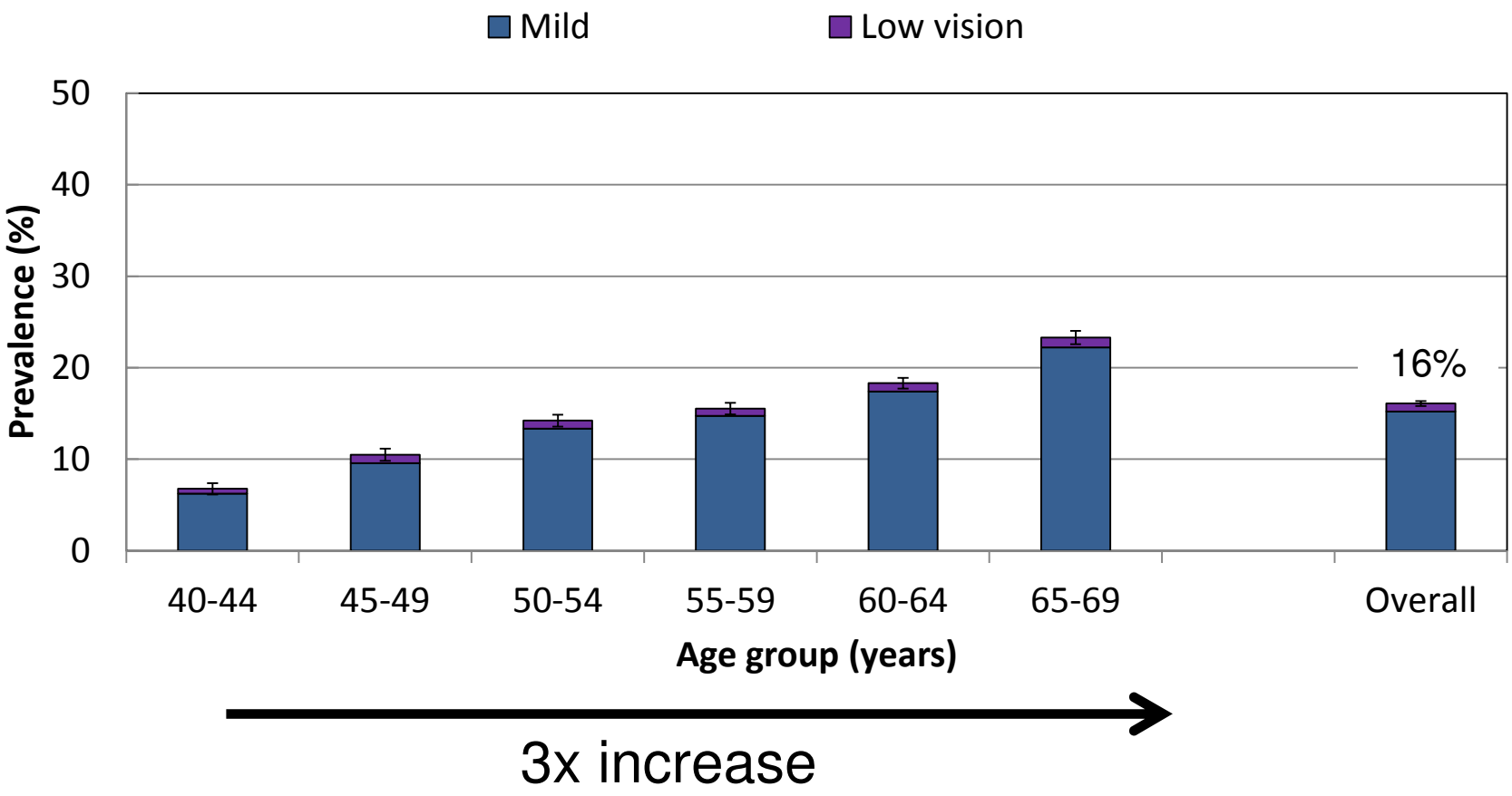
VISUAL ACUITY (WITH 'USUAL' GLASSES)



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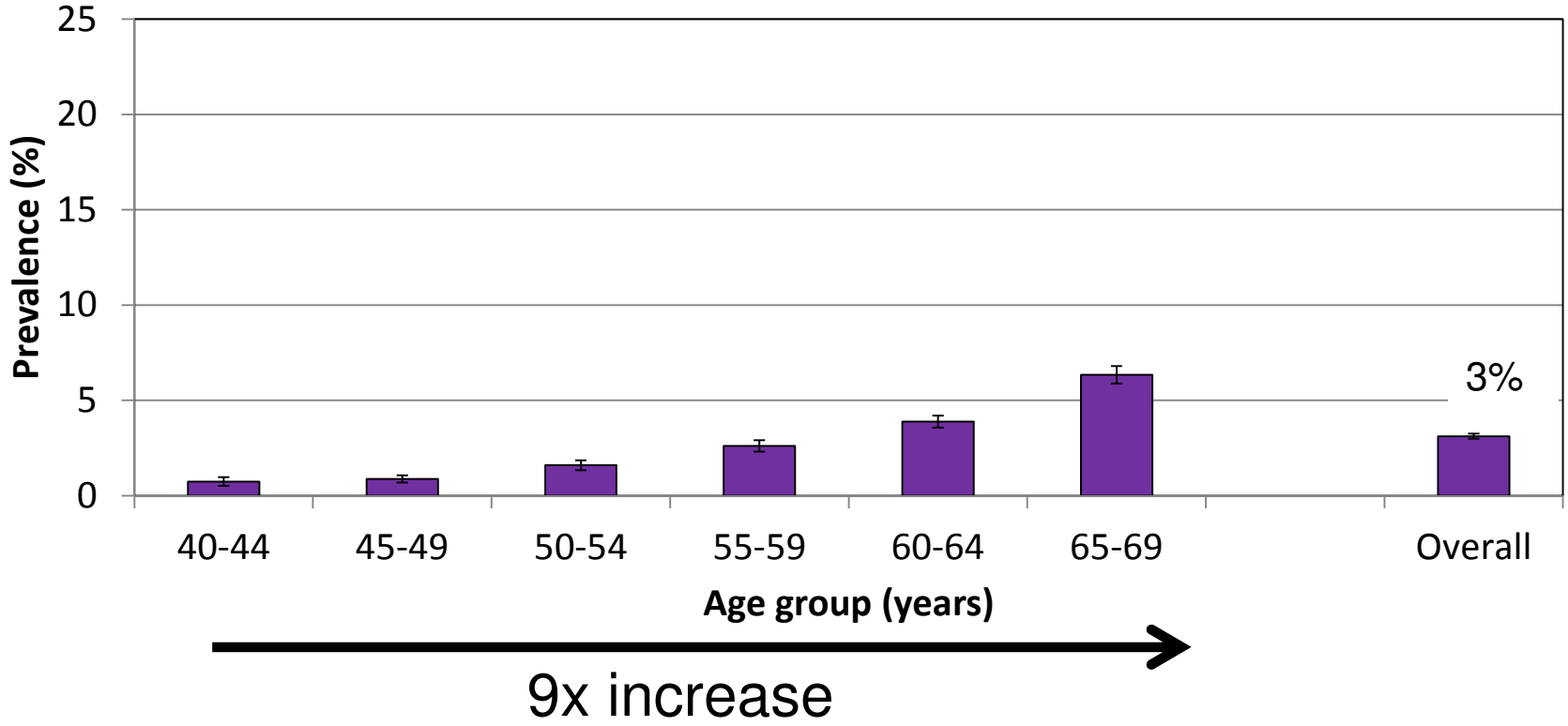
DUAL SENSORY PROBLEMS



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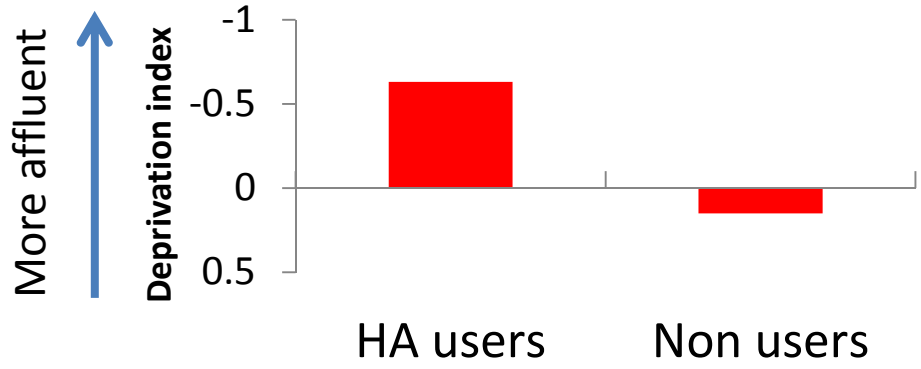
Lifestyle, demographics & hearing loss

- Noise exposure
- Diet
- Exercise
- Cardiovascular disease & diabetes
- Alcohol consumption & smoking
- Ethnicity & socioeconomic status
- Early life exposures

Statistical modelling: what is the unique contribution of each factor?

Socioeconomic status (SES)

- Hearing: Low SES (bottom 15%) at 200% increased chance of poor hearing (vs top 15%)
- Hearing aids: Among those with poor hearing; 21% are HA users. Non-users have significantly more deprived background:



→strong association between SES and HL and HA use

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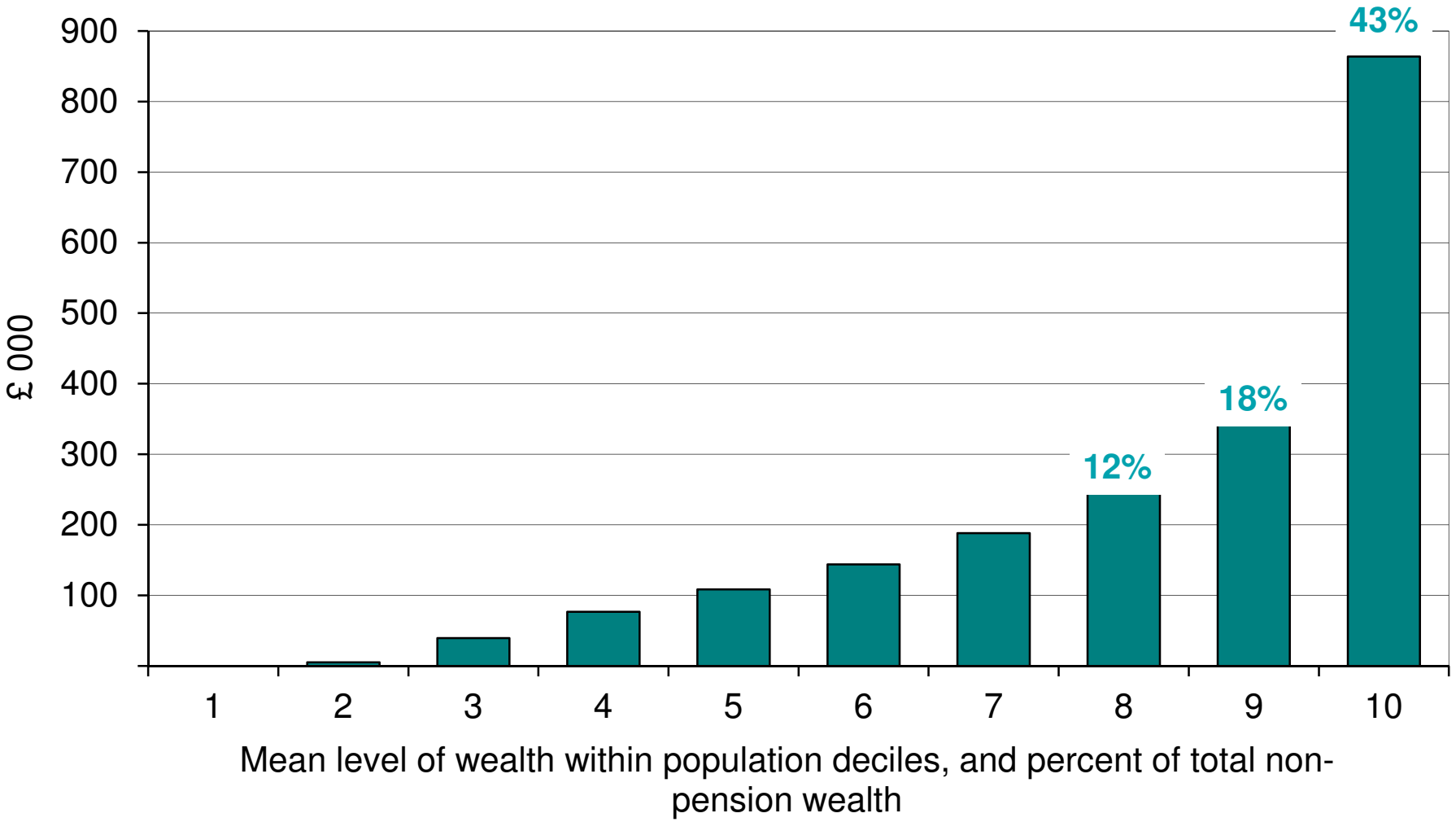
SES & health: English Longitudinal Study of Ageing

- >50 years, 6 waves of data collection every 2 years
- 11,400 at baseline
- Detailed content on: demographics, health, physical and cognitive performance, biomarkers, wellbeing, economics, housing, employment, social relationships, social civic and cultural participation, life history.

Marshall, A., Nazroo, J., Tampubolon, G. and Vanhoutte, B. (in press) 'Cohort differences in the levels and trajectories of frailty among older people in England', *Journal of Epidemiology and Community Health*

SES: The distribution of wealth in England



ELSA English Longitudinal Study of Ageing

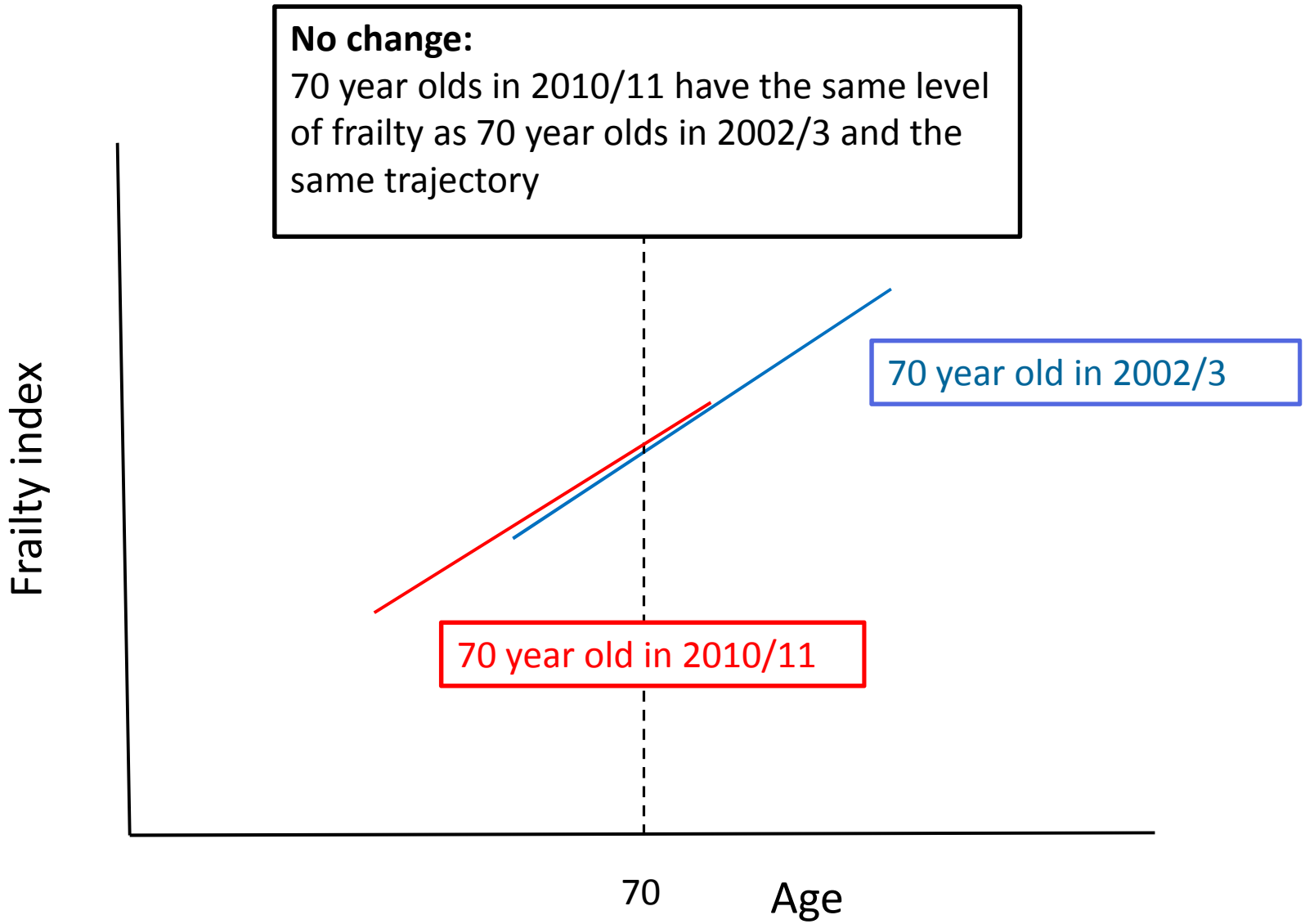
‘Frailty’

- ‘Frailty’ - an individual’s capacity for independent living and the risk of suffering a adverse event.
- non-specific state reflecting age-related declines in multiple systems.
- based on accumulation of ‘deficits’ (activities of daily living, mobility, cognitive function, chronic diseases, CVD, depression/mental health, **poor eyesight/hearing**, falls, fractures and joint replacements).

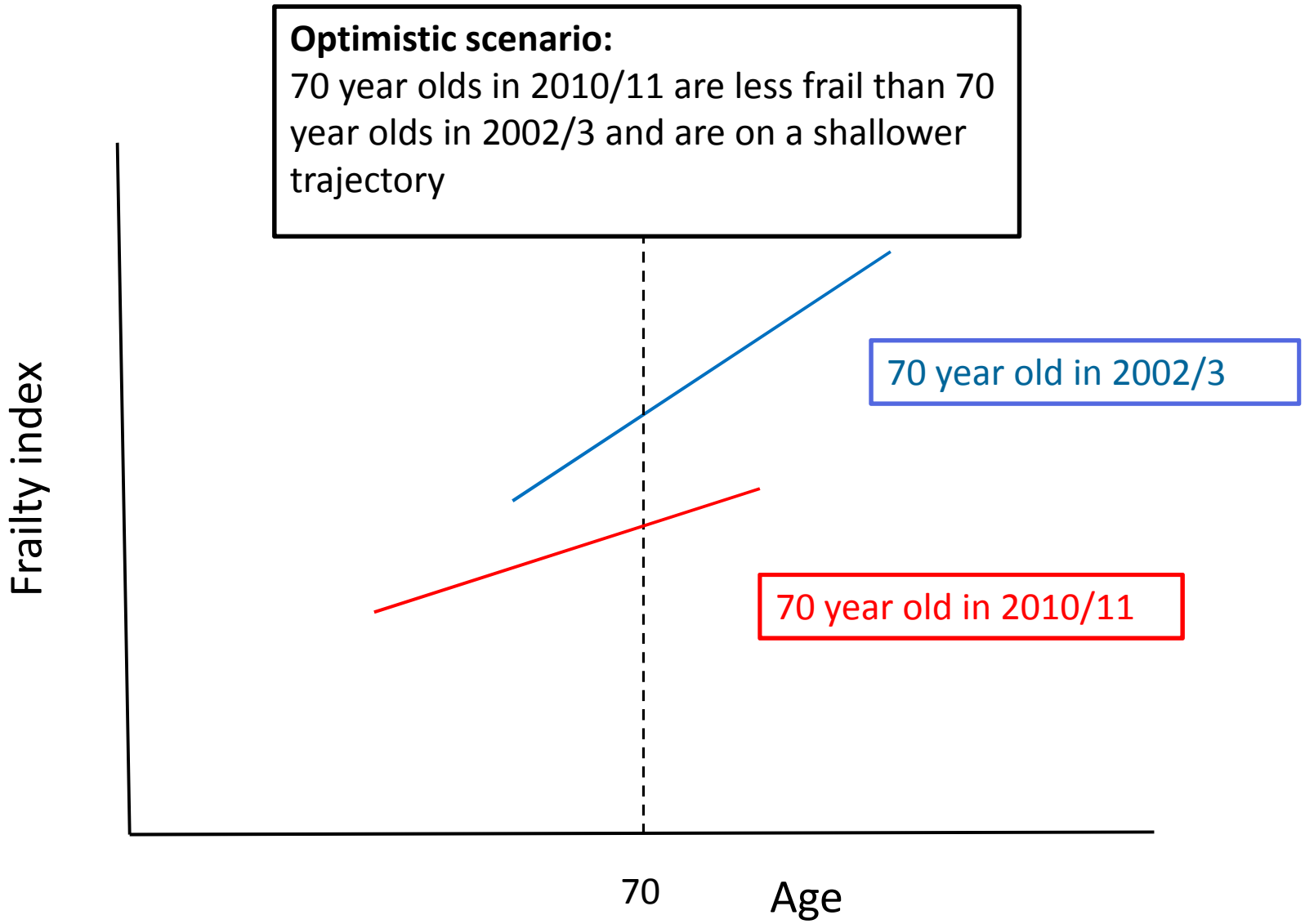
Frailty and SES

- Five waves of data
- Sample divided into five year age groups, resulting in cohorts whose ages overlap over eight years of observation.
- Model age related trajectories by cohort and socioeconomic position.
- Predicted trajectories are graphed by age cohort.

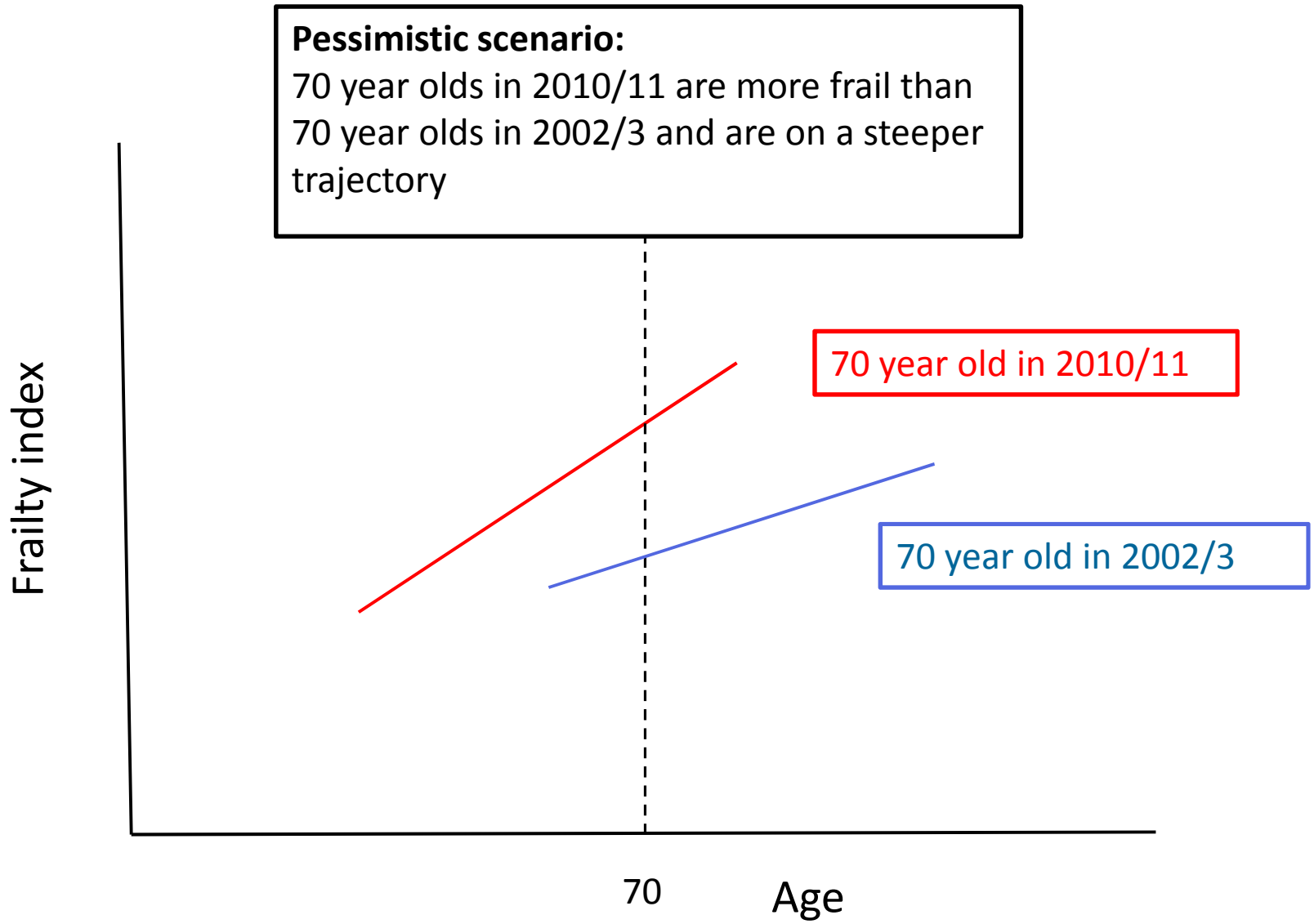
Modelling frailty trajectories by age cohort



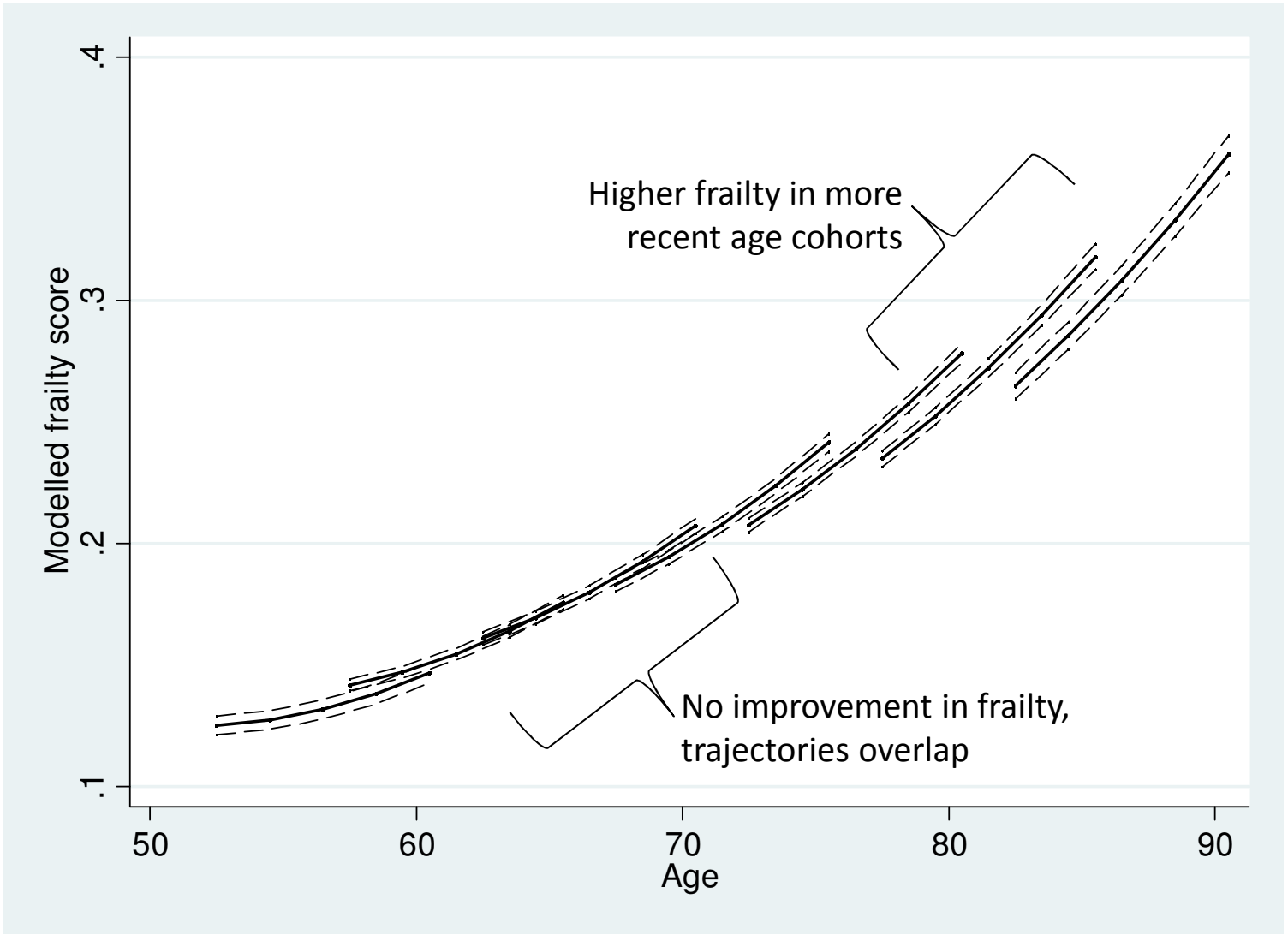
Modelling frailty trajectories by age cohort



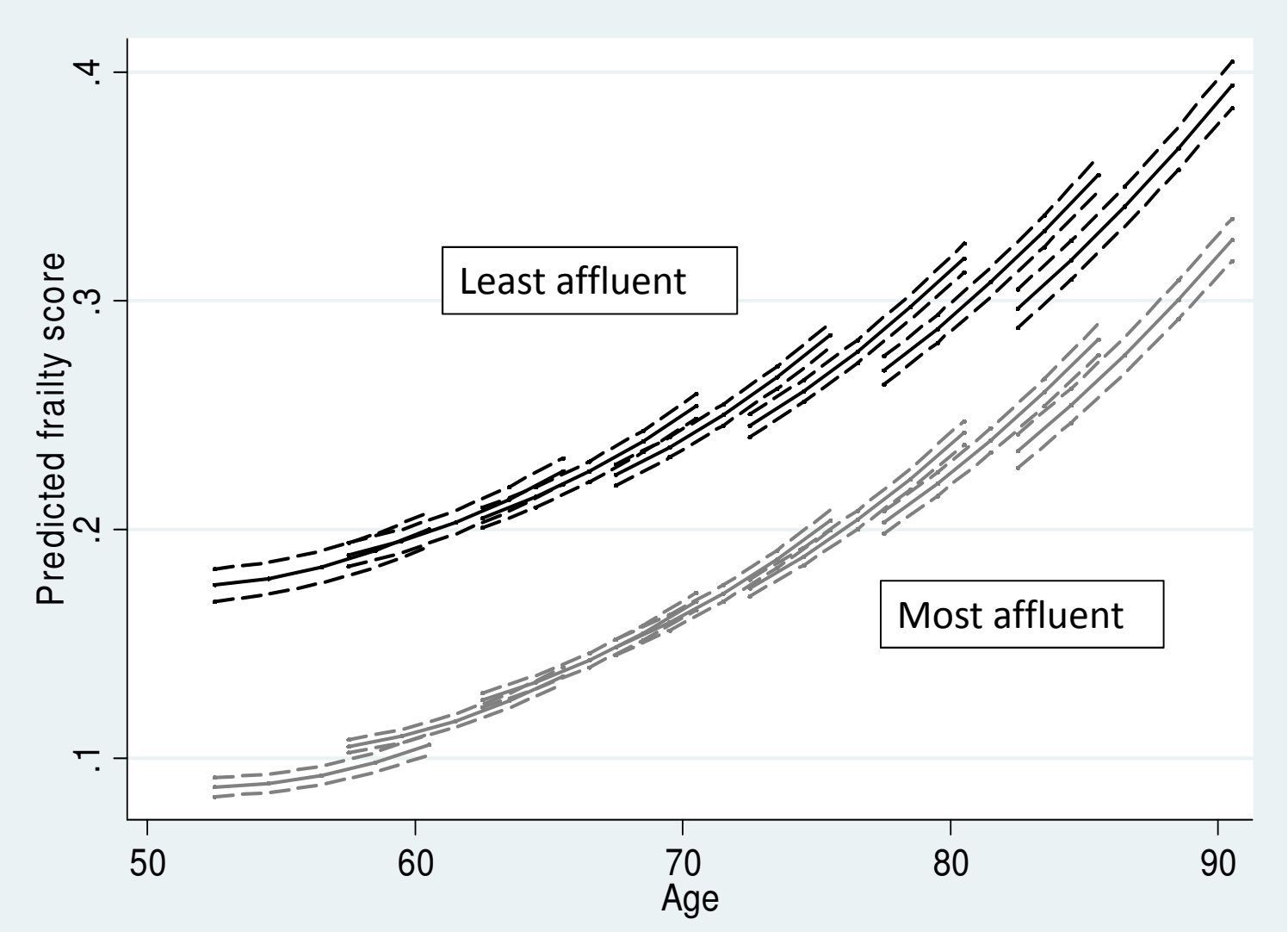
Modelling frailty trajectories by age cohort



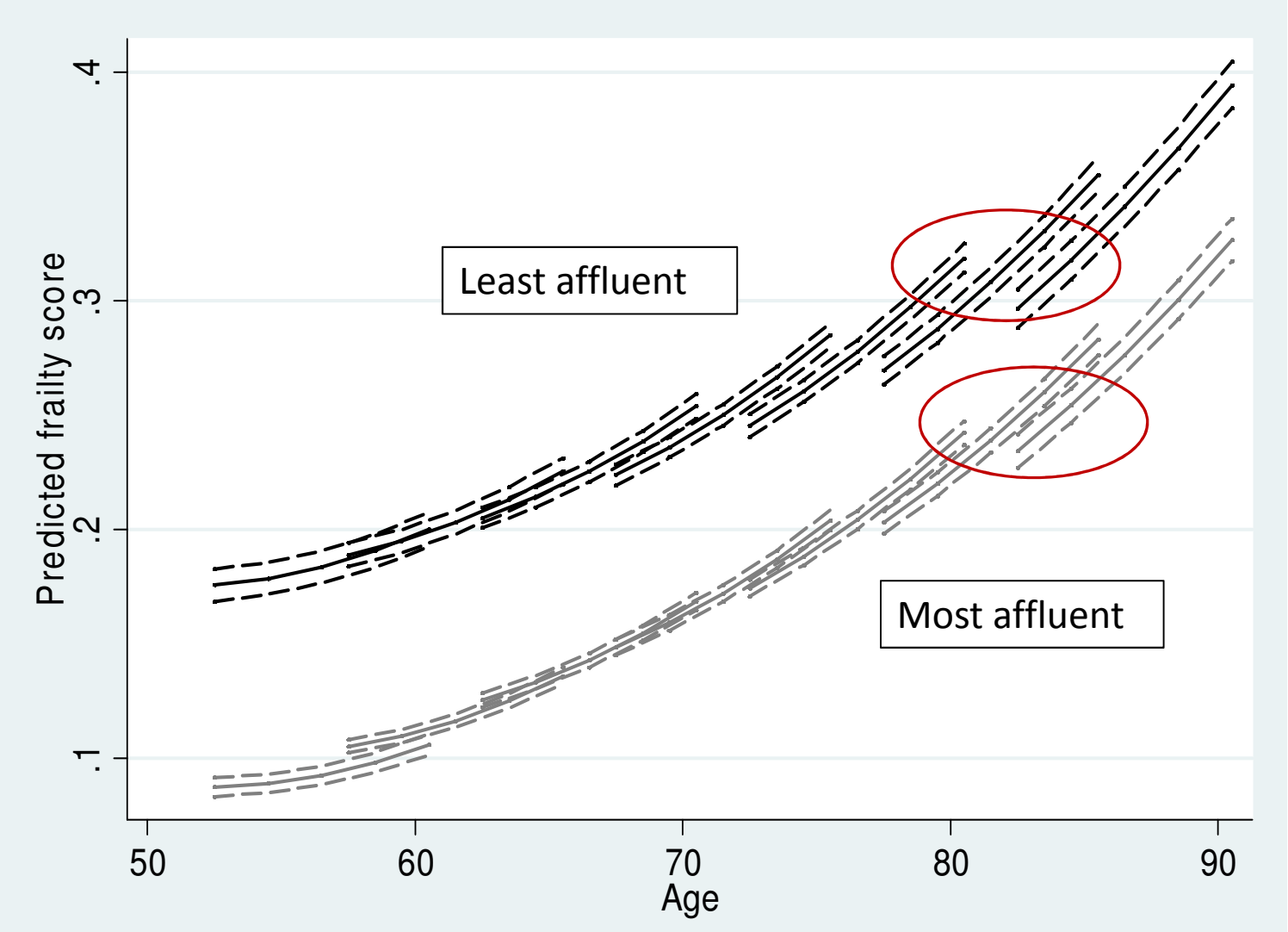
Frailty trajectories by age cohort



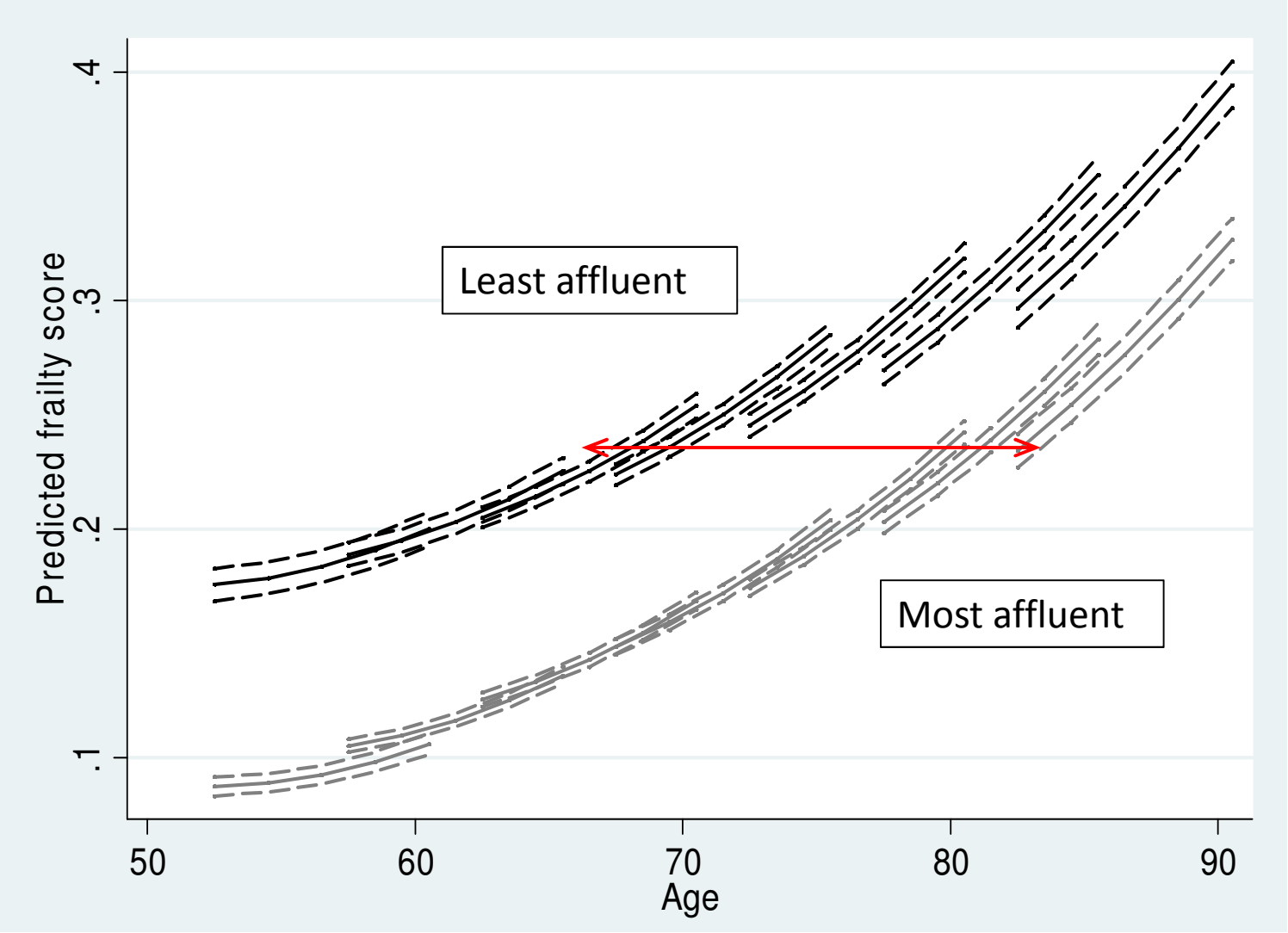
Frailty trajectories by cohort and wealth



Frailty trajectories by cohort and wealth



Frailty trajectories by cohort and wealth



Socioeconomic status & hearing

- People from low SES background have poorer hearing (UKB)
- Strong effect of SES on frailty (ELSA)

→Worsening hearing in younger generations, especially for people from low SES background

Ethnicity

- Non-white → 540% increased chance of hearing loss (3/10 vs 1/10)
- HA use 50% lower among people with non-White ethnic background
- Non-white ethnicity a risk due to particular subgroups being at particular risk

Ethnic subgroup	
Bangladeshi	(710%)
Black African	(700%)
Pakistani	(540%)
Black Other	(530%)
Asian Other	(500%)

- Agrees with findings of poorer general health within ethnic minorities in the UK

- Reasons: culture and lifestyle, socioeconomic factors, reduced uptake of services and biological susceptibility

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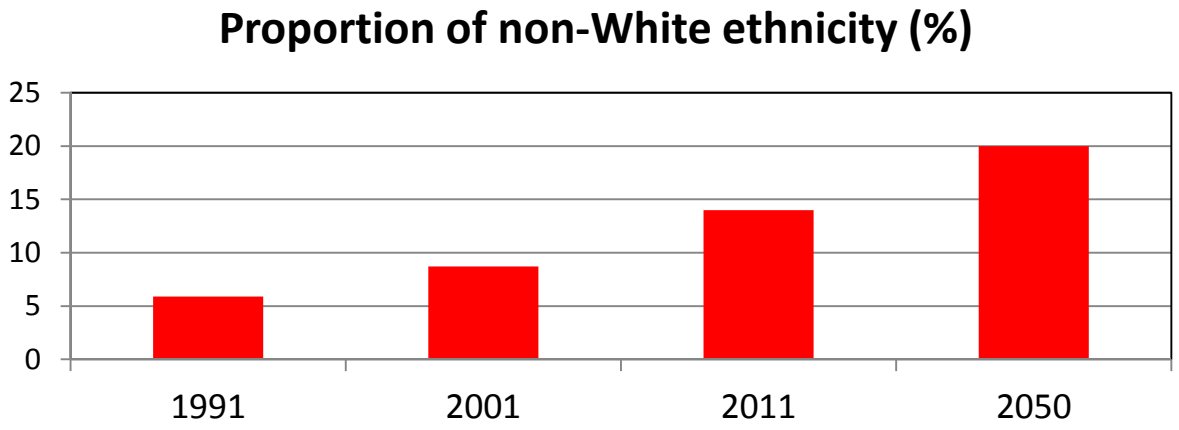
Ethnicity



- Proportion of non-White due to quadruple from 1991 levels
- non-White ethnic minority groups are presently younger than the White British section

→the oldest section of our community (where hearing loss is more prevalent) will become more ethnically diverse as the ethnic minority section of the population ages

→Increasing prevalence of HL, lower HA uptake

SES & ethnic hearing health inequality

- Low SES and ethnic minority background strongly linked to HL and HA use

→increasing levels of HL and lower levels of HA uptake

- Health inequality a focus of research attention; little work in relation to hearing
- Similar demographic trends in other countries

→a priority to understand and address hearing health inequality

Noise

Work noise

Have you ever worked in a noisy place where you had to shout to be heard?

>5 years exposure → 240% increased chance of poor hearing (vs no exposure)

5.5 million people work in the agricultural, mining and manufacturing industries (~10% of population)

Music

Have you ever listened to music for more than 3 hr per week at a volume which you would need to shout to be heard or, if wearing headphones, someone else would need to shout for you to hear them?

>5 years exposure → 20% increased chance of poor hearing (vs no exposure)

***inconsistent association, small increased risk for highest level of exposure*

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Alcohol

- Previous health research

Protective effect of alcohol consumption on cardiovascular disease

But maybe due to inclusion of ‘sick-quitters’ in non-drinking group?

Alcohol

- Lower risk of poor hearing for drinkers
- Those who consume alcohol were less likely to have a hearing loss than **lifetime teetotalers**
- Similar association across three levels consumption:

  lightest 25% (<15 units/wk); -39%

  middle 50% (15-24 units/wk); -38%

  heaviest 25% (>24 units/wk); -35%

Alcohol consumption reduces risk of CV disease, so impact of alcohol on hearing via CV disease

Dawes, P., Cruickshanks, K. J., Moore, D., Edmondson-Jones, M., McCormack, A., Fortnum, H., & Munro, K. (2014). Smoking, passive smoking, alcohol consumption and hearing loss. *JARO-Journal of the Association for Research in Otolaryngology*.

Smoking

- Passive smoke exposure:

+28% risk

- Dose-dependent:
  - 1hr/wk – no extra risk
  - 2-9hrs/wk +28%
  - 10+ hs/wk +39%

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Smoking

- Current smokers: +30%

- Dose-dependant (pack-years);
  - Bottom 25% -
  - Middle 50% +11%
  - Top 25% +30%

- Ex-smokers: no extra risk than non-smokers

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Summary: Smoking and alcohol

- Alcohol consumption associated with protective effect

Higher levels of consumption may be harmful

- Tobacco smoking & passive exposure to smoke is associated with risk of HL
- Benefit associated with reducing and/or stopping smoking

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Diet, exercise

- Detailed diet data just released
  - Examine dietary patterns & hearing

- Exercise based on accelerometer and fitness test (ECG bike test) Q1 2016

Early life exposure

- Pre-natal environmental exposures → critical effect on long-term adult health
- Well-established link between early development and diabetes and CV disease in adulthood
- Developmental programming of physiology via foetal under nutrition, hormonal action and/or alterations in gene expression

Early life: Cognition

Children

- Lots of research linking early development to cognitive ability in childhood & adolescence

Adults

- Richards et al (BMJ, 2001) 1946 British birth cohort (n=3900): Birth weight was positively associated with cognitive ability at 8, 11, 15 and 26 years, though ns association at 43 years.
- Raikkonen et al (Plos one, 2013) larger BW linked to better cognition at age 67 (n=931 men, Finland)

Early life: Cognition & large BW

- Poorer outcomes for very large babies?

Cesur and Rashad (2008):

- Academic performance in junior school (n=19,280 children)
- either low or high birth weight had poorer academic performance vs normal range of birth weight.

Early life: hearing & vision

Olsen et al (Epdidemiology, 2001)

- 4,300 Danish male conscripts; Small birth weight associated with reduced visual acuity and poorer hearing

Barrenas (BMJ, 2003)

- 479 Swedish male workers and 500 conscripts; short adult height was associated with poorer hearing

Ecob et al (Longitudinal & Life Course Studies, 2011)

- 12,069 UK adults from 1958 British Birth Cohort; no association between birth weight and hearing at age 45 years.

Causal association?

- Association due to confounding?
- Difficulty with controlled studies with humans
- Experimental evidence from animal studies supports observational studies in humans

→ Causal link is plausible.

Mechanism?

- under-nutrition impacts on development of the brain and sensory organs
- alterations in gene expression that affect cognitive and sensory function
- glucocorticoid hormones or growth factors modulated by early experience and impact on neurosensory development
- effect is via increased susceptibility to diabetes and cardiovascular disease

Rice, D., & Barone Jr, S. (2000). Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. , 108(Suppl 3), 511. *Environmental health perspectives, 108*((Suppl 3)), 511-533.

Early life questions:

- Contribution of early life to adult cognitive, hearing and sensory function?
- What about change in function?
- Need very large sample to detect small effects, control for confounds
- Pre-natal vs early childhood effects?
- Effect via CV disease/diabetes?

Fluid intelligence

If Truda's mother's brother is Tim's sister's father, what relation is Truda to Tim?

Select from:
- Aunt
- Sister
- Niece
- Cousin
- No relation

Hearing

Digit triplet test, better ear

Vision

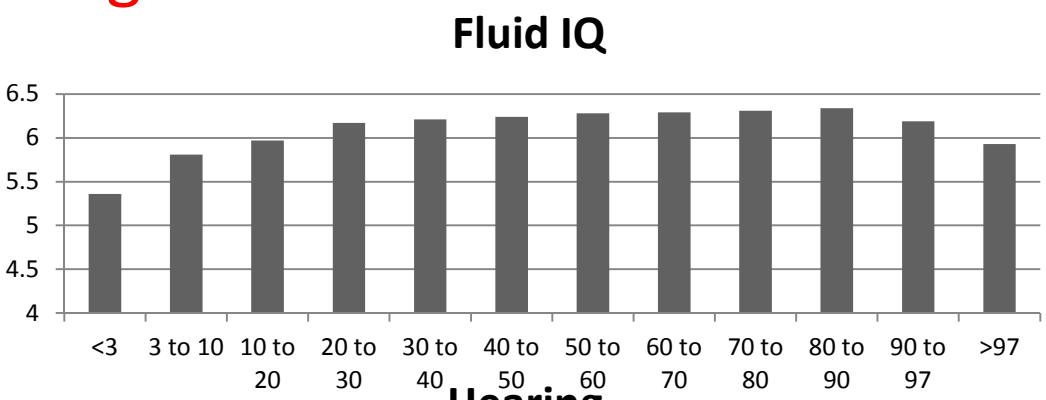
Visual acuity, better eye

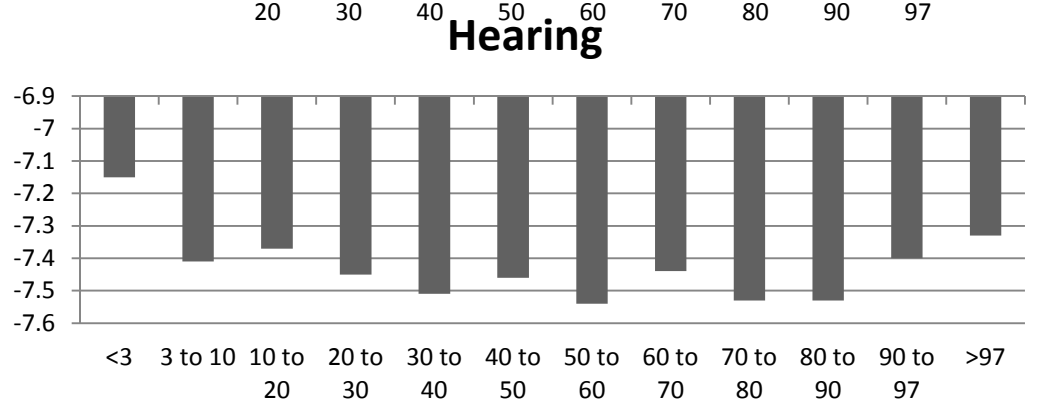
- Birth weight
  - Proxy measure of pre-natal growth
- Adult height
  - Proxy measure of childhood growth

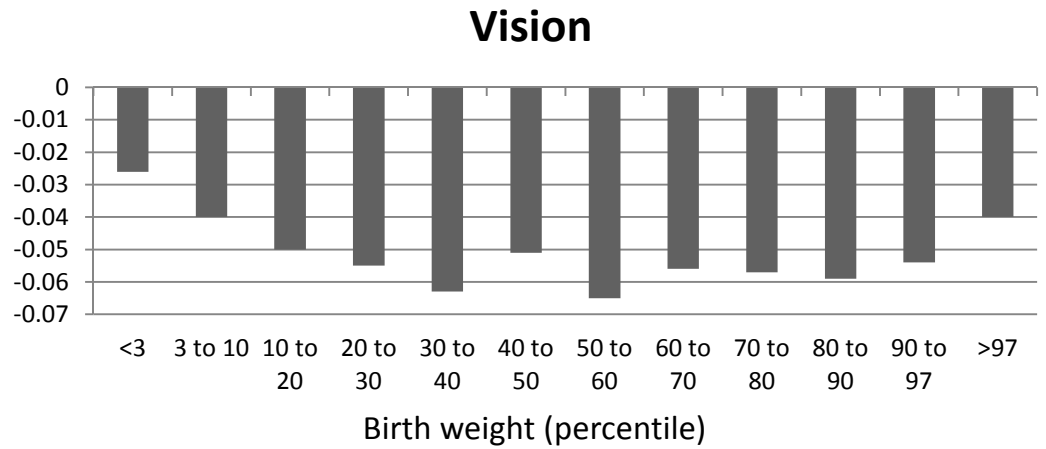
→Percentile rank (males and females separately)

- Examine hearing, vision and cognitive function (and 4 year change in function) in middle age (40-69 years)

Birth weight







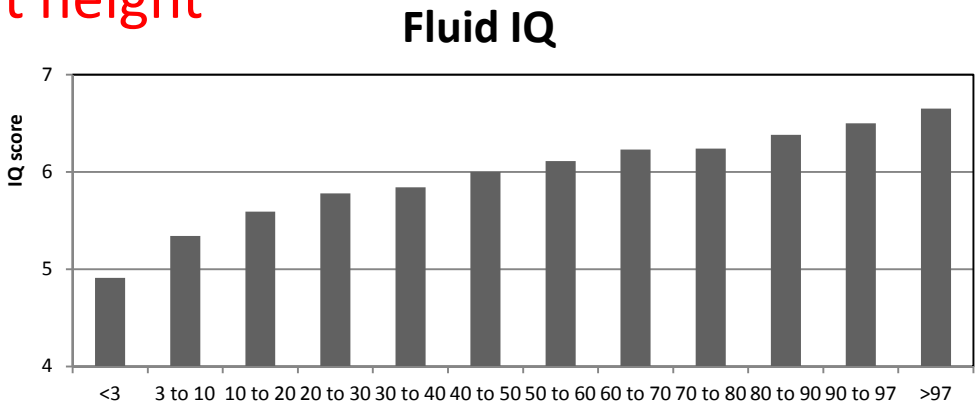
Similar pattern for cognitive performance, hearing and vision

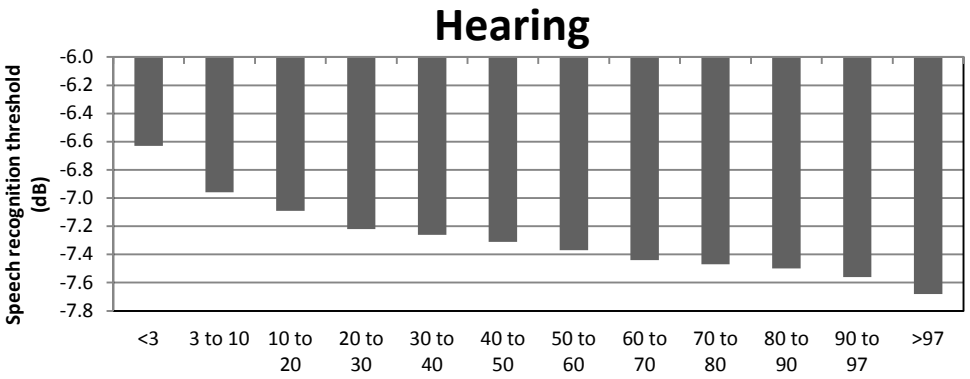
Very small or very large babies tend to be worse

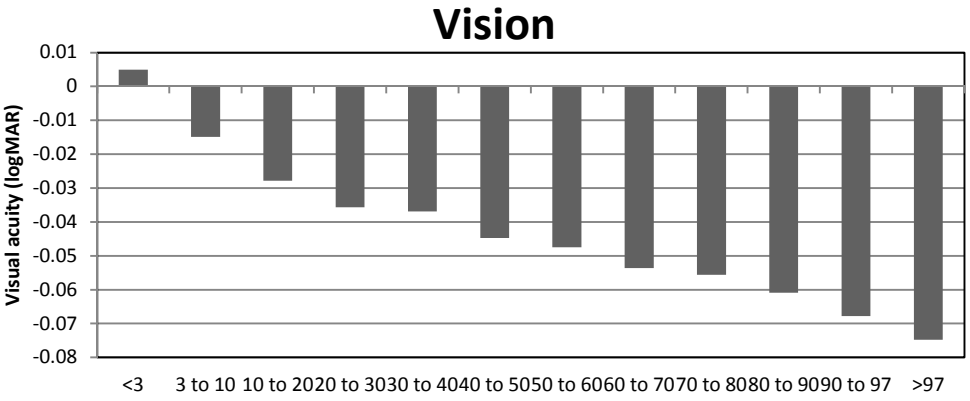
Within normal range, larger = better

6-14% of variance

Adult height





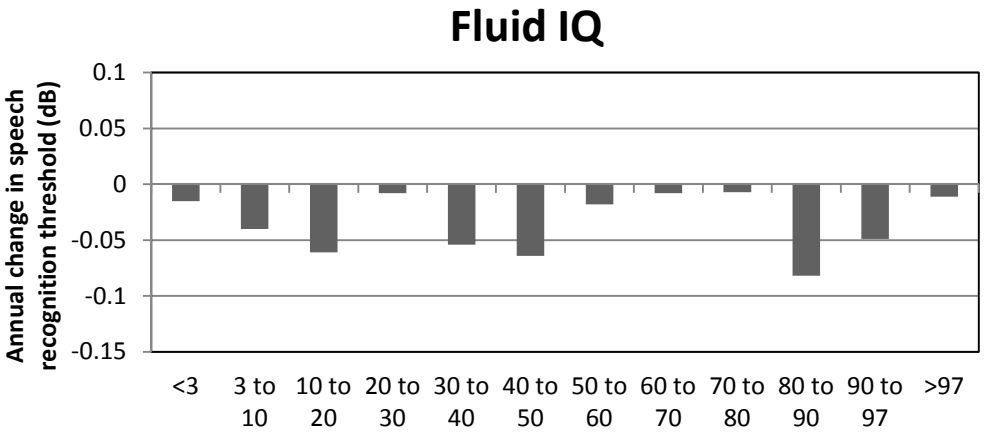


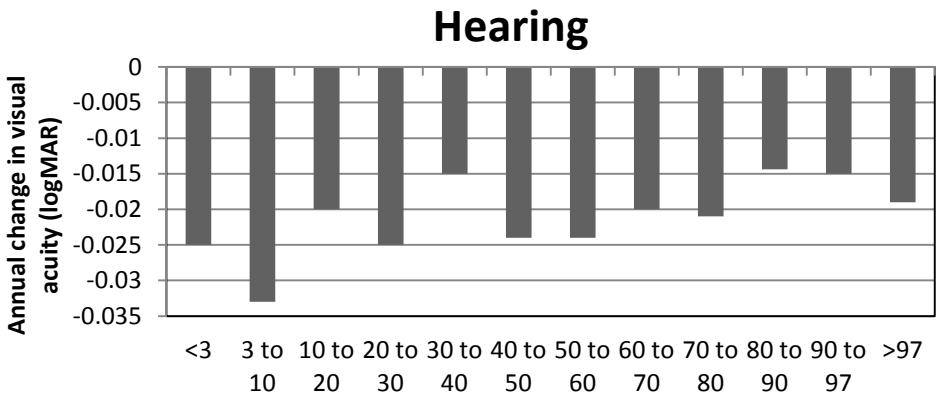
Similar pattern for cognitive performance, hearing and vision

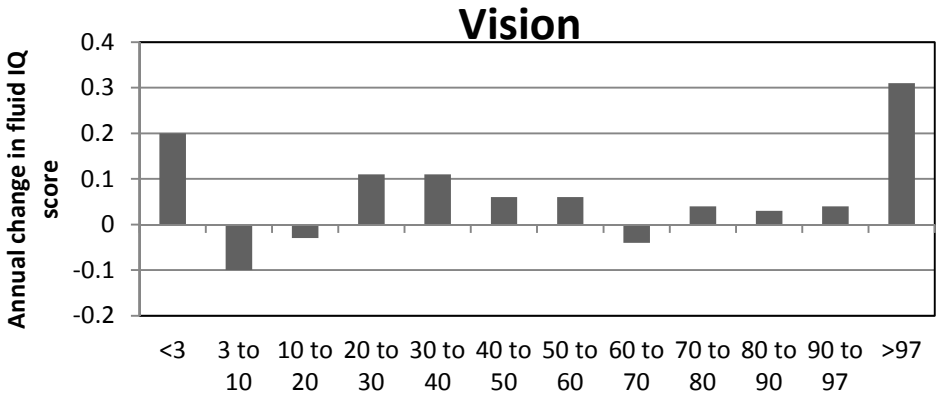
Taller = better

5-12% of variance

Birth weight and CHANGE in function







No association with change in function and BW or height

→no effect on rate of decline

Birth weight

- small/large → poorer than normal range
- Within normal birth weight range (10-90%), a linear association between BW and performance

Height

- Linear association between height and performance

(after age, sex, SES, educational level, smoking, maternal smoking, diabetes and CV disease)

→ Significant effect of pre-natal and childhood development on adult neurosensory function

Dawes, P., Cruickshanks, K., Moore, D. R., Fortnum, H., Edmondson-Jones, M., McCormack, A., & Munro, K. (2015). The effect of prenatal and childhood development on hearing, vision and cognition in adulthood. *PloS one, 10*(8). doi: 10.1371/journal.pone.0136590

An important determinant of neurosensory function

- Small effects (5-14% of variance)
- But observed across the range of BW and height

→universal exposure

Not significant at individual, clinical level

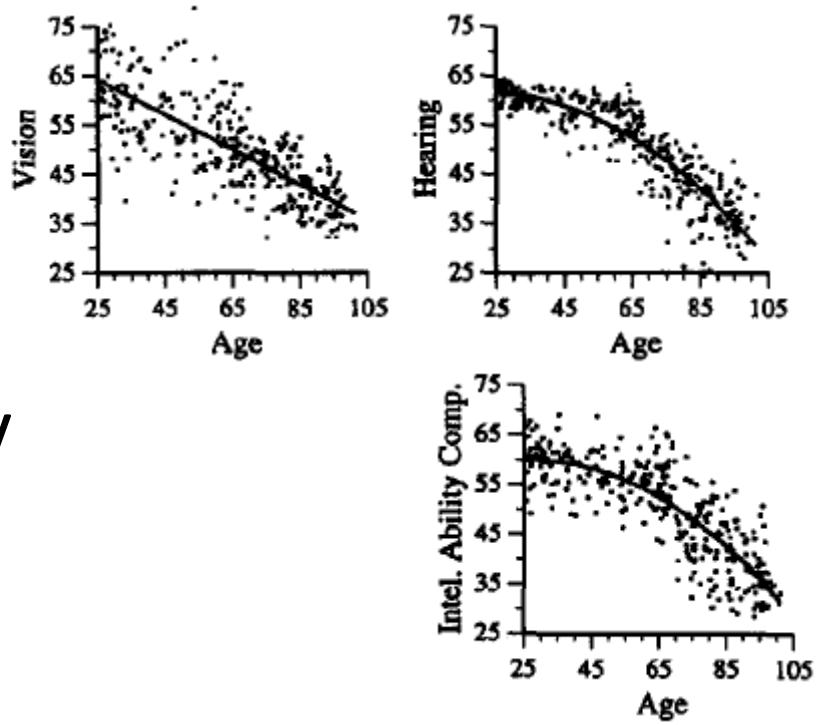
But important determinant at population level

Explains hearing-cognition association

- Berlin aging study
- 687 people aged 25-103
- Intelligence
- Vision and hearing acuity
- Sensory function: 12.6%

age-independent variance

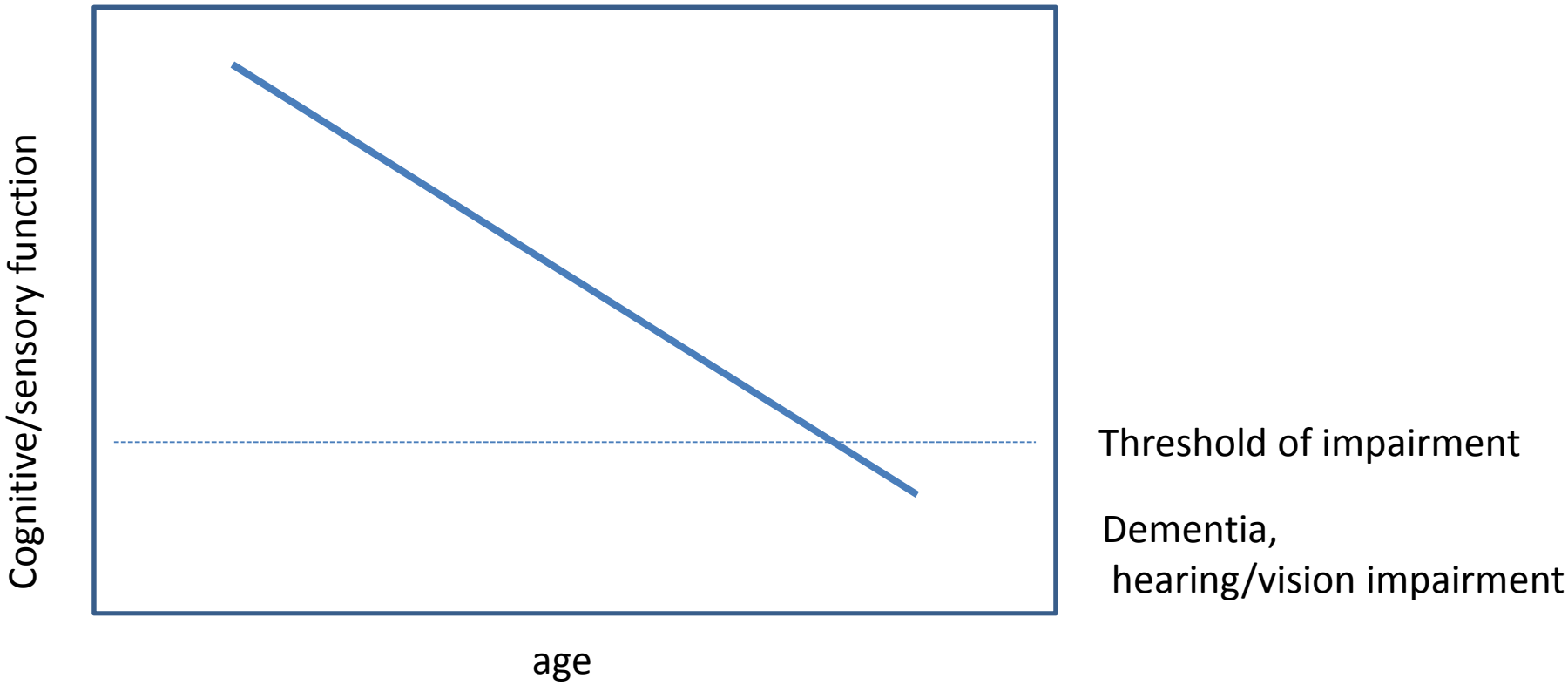
(vs Early life: 5-14% variance)



Lindenberger, U., & Baltes, P. B. (1994). Sensory functioning and intelligence in old age: a strong connection. *Psychology and aging, 9(3), 339.*

Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: a new window to the study of cognitive aging? *Psychology and aging, 12, 12-21.*

Adverse early life development a risk for hearing, vision and cognitive impairment



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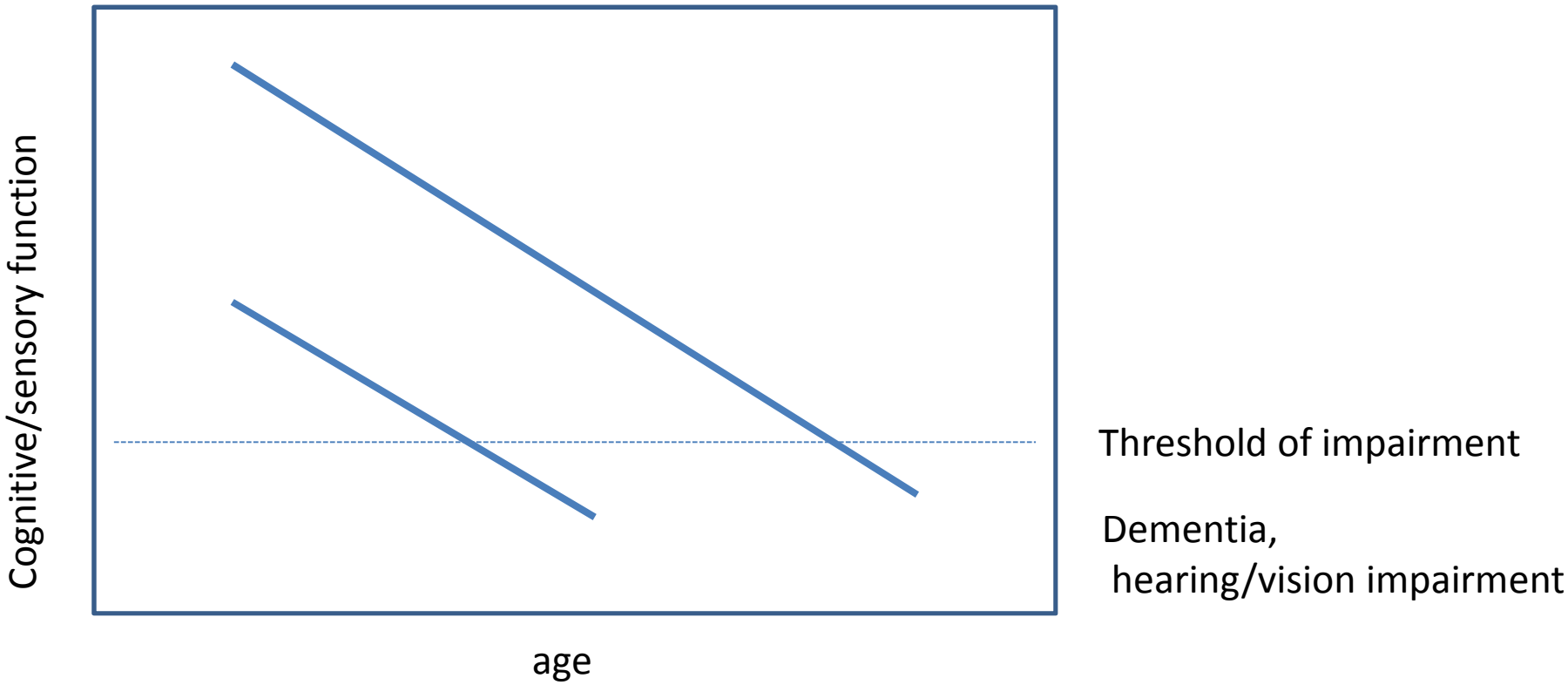
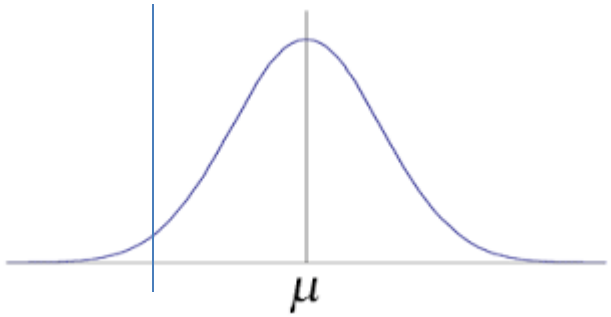


Large impact

- Small shifts in population mean

→dramatic affect on N within the range of clinical impairment.

e.g. a decrease in the mean IQ of the population by 5 points on a standard distribution would double the number of people with an IQ <70



Impaired threshold

Effective early intervention

- interventions in adulthood are relatively limited
- intervention in a developmentally more plastic period has larger impact in altering metabolic trajectory and preventing disease

→ To reduce the burden of cognitive decline and sensory impairment, research attention should identify interventions to optimise foetal growth and childhood development

→ Early life factors are a EU and US national research priority in relation to dementia, diabetes and cardiovascular health. Should also be a priority in relation to hearing and vision impairment

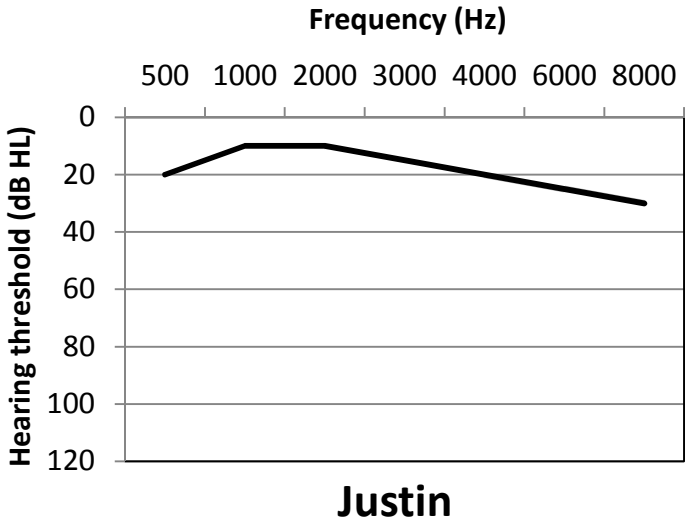
Hendrie, H. C., Albert, M. S., Butters, M. A., Gao, S., Knopman, D. S., Launer, L. J., . . . Wagster, M. V. (2006). The NIH cognitive and emotional health project: report of the critical evaluation study committee. *Alzheimer's & Dementia, 2*(1), 12-32.

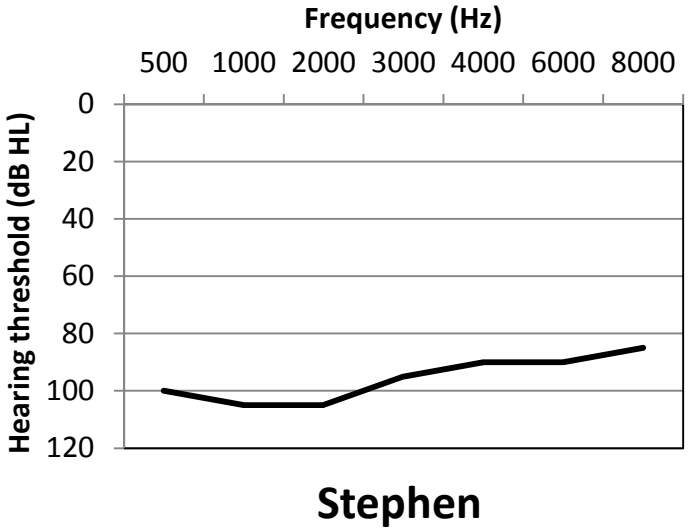
European Parliament. (2011). Futurage. A roadmap for European ageing research Retrieved October, 2014, from http://www.thehealthwell.info/node/99612

Hanson M, Gluckman P (2011) Developmental origins of non-communicable disease: Population and public health implications. American Journal of Clinical Nutrition 94: 1754S–1758S. doi: 10.3945/ajcn. 110.001206 PMID: 21525196

Environment affects hearing

- Evidence for association between HL and modifiable environmental factors
- Not just environmental exposures & lifestyle in adulthood, but also early in development could set us up to have good hearing (vision & cognition), better quality of life with age





Thanks

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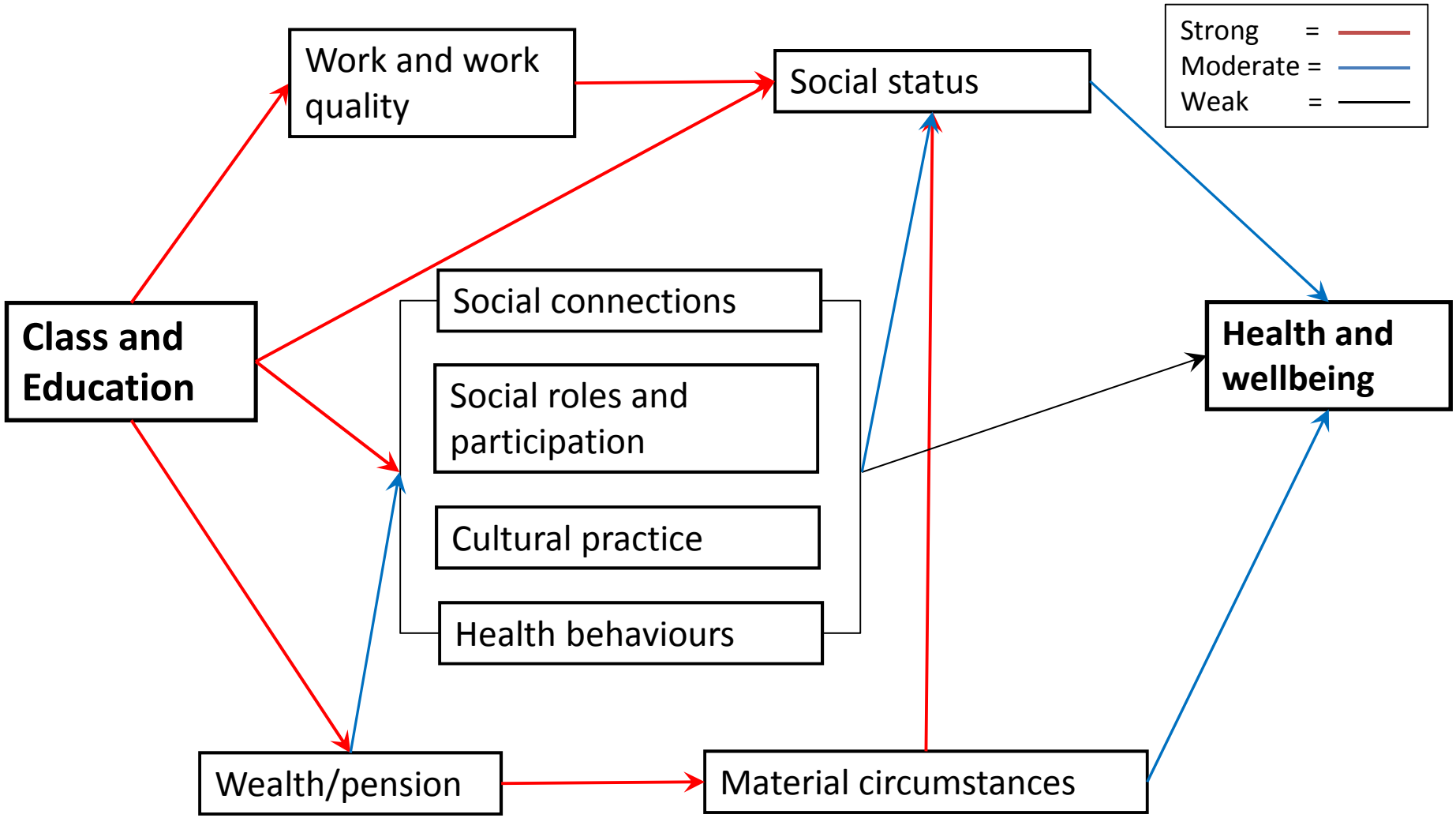
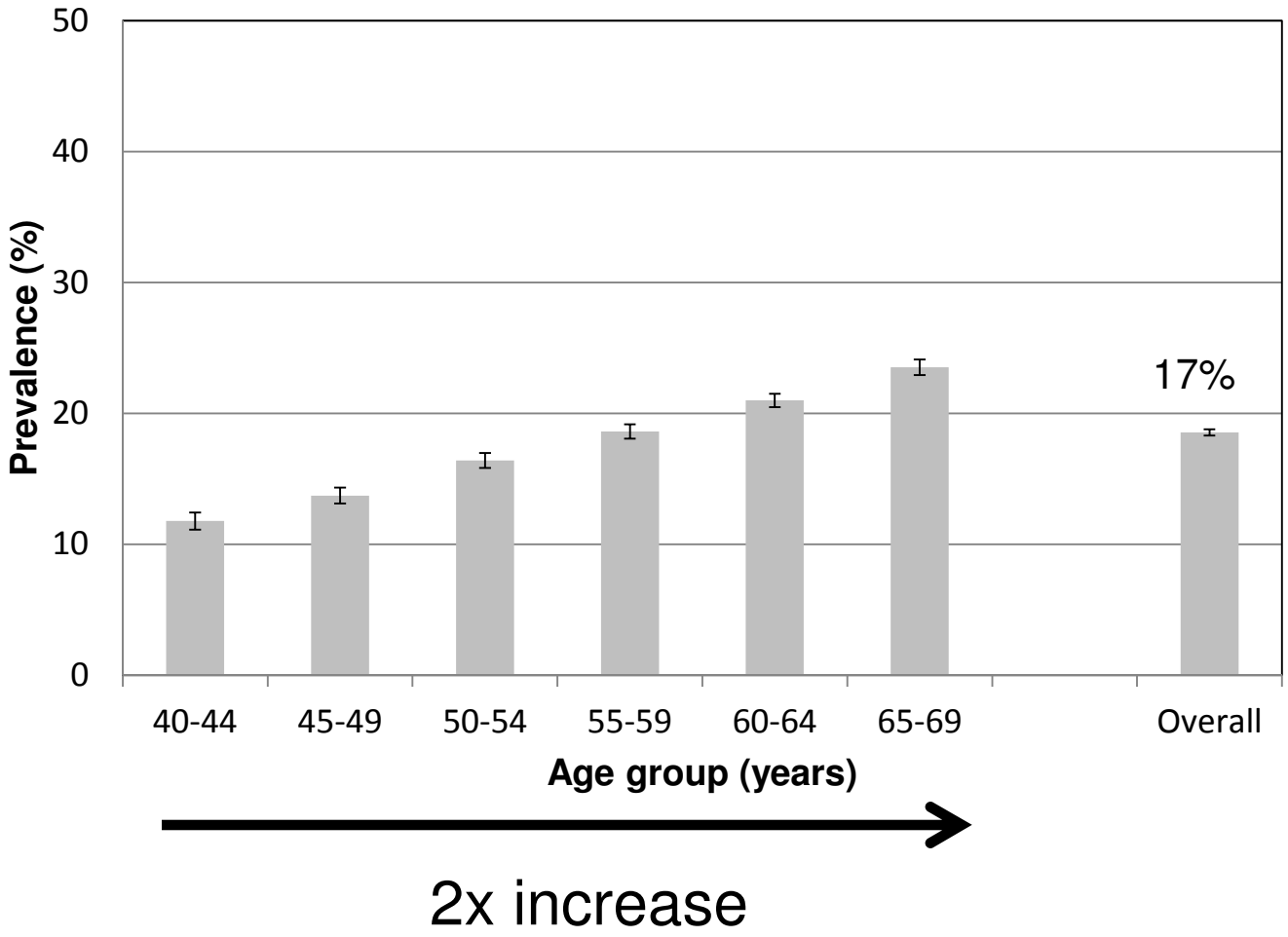
An empirical investigation of class-related (theoretical) pathways in later life



ELSA English Longitudinal Study of Ageing

TINNITUS



NSH= 15% over similar age

Genetics

- Strong heritability of HL (>70%)
- But few genes identified
- ‘Missing variance’; likely to be many genes with small effects, interactions with environmental factors

Need a powerful study; establish reliable genetic associations and explore G*E interactions

→ UK HearGene consortium