Social position and DNA methylation age acceleration across the lifecourse

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Overview

- What is DNA methylation age?

- Why might it be relevant to health inequalities?

- DNA methylation age measures in Understanding Society (UKHLS)

- Associations with social position across the lifecourse

- Issues using the algorithms in mixed-age samples

- What now?

Genetics vs. epigenetics

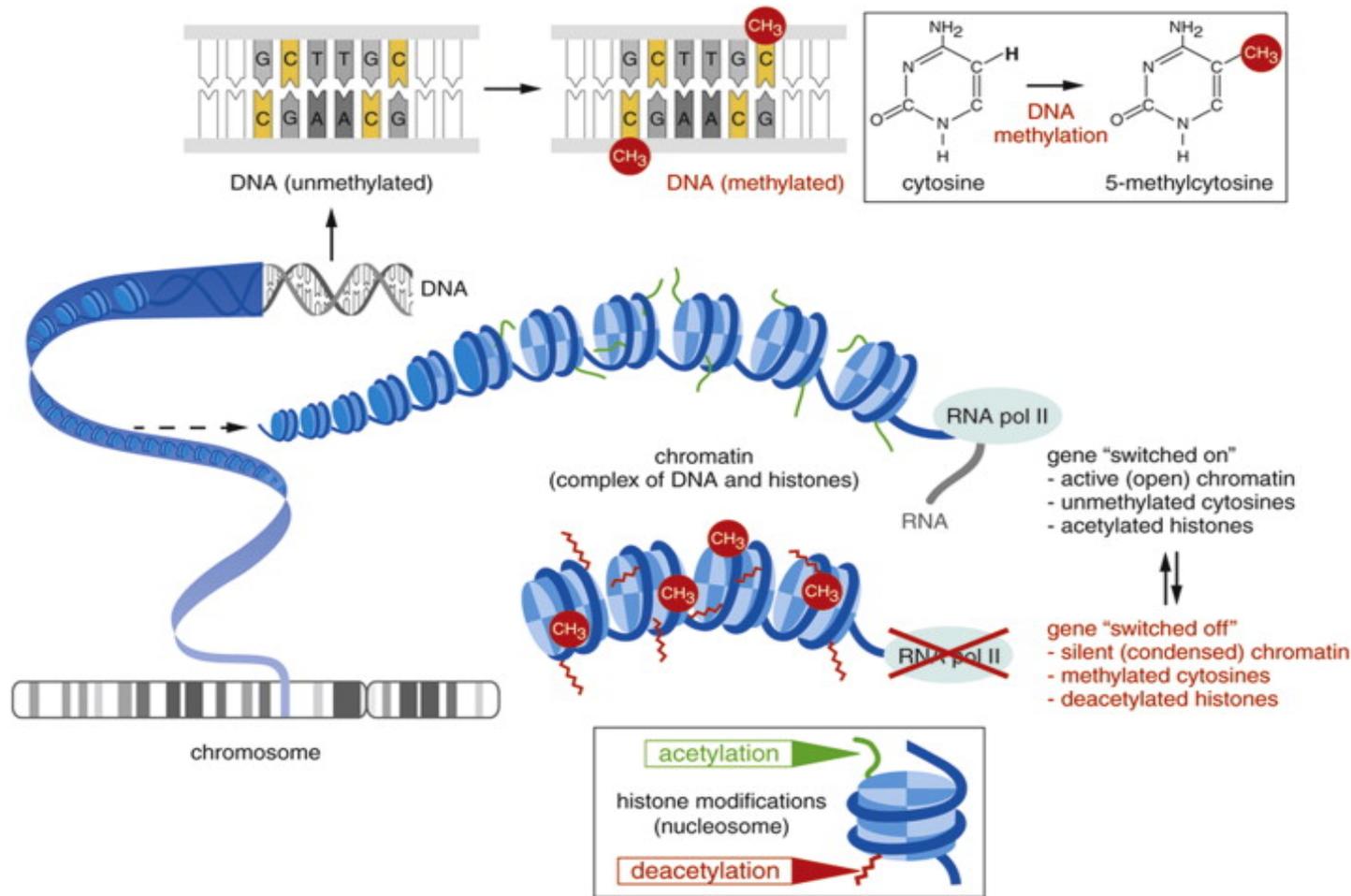Genes, made up of DNA, act as instructions to make proteins.
Humans have 20,000-25,000 genes
These vary in size: a few hundred DNA bases to >2 million bases
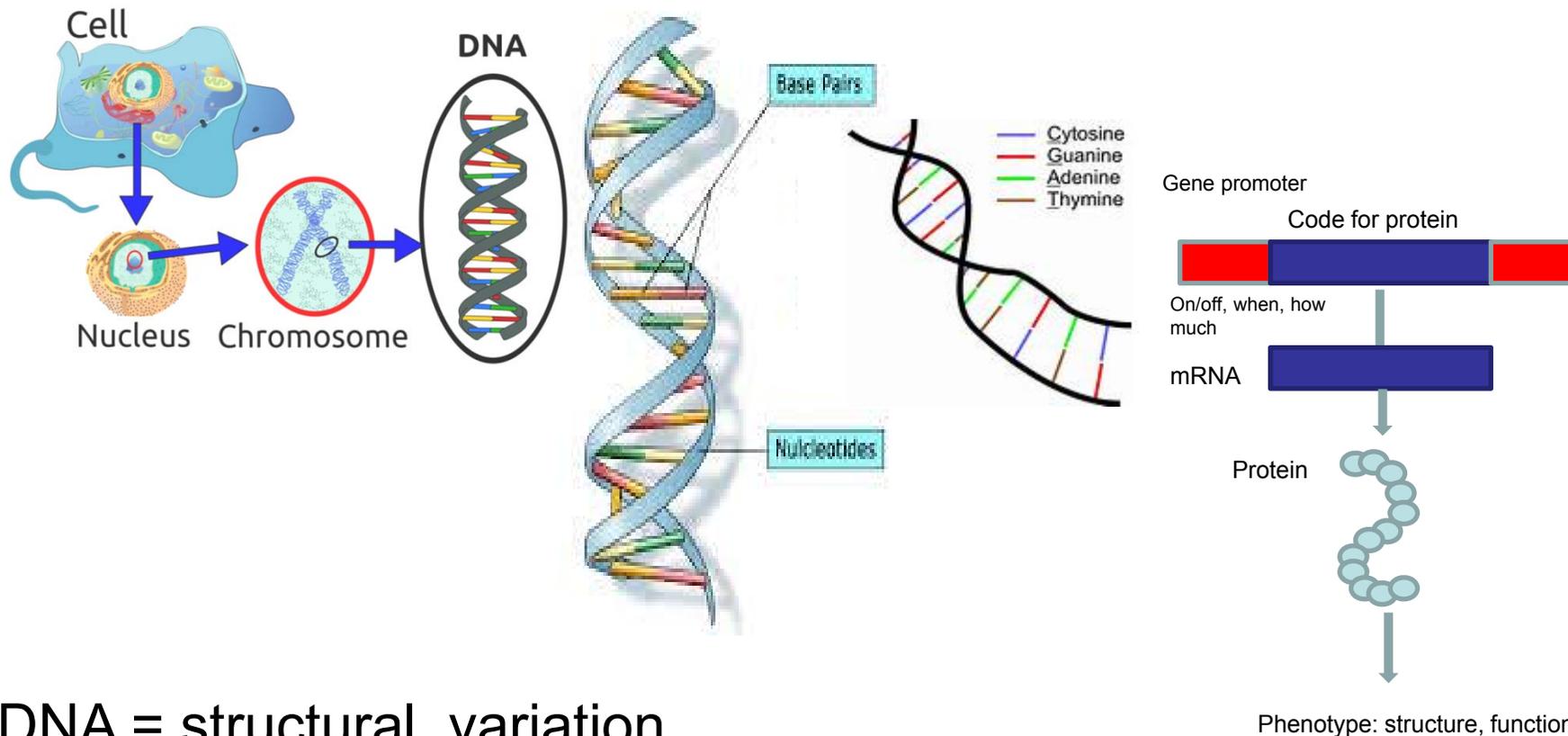
DNA = structural variation

Epigenetic modifications

Glossary:

Methylation
CpG islands

Histone
Acetylation

Epigenetics modifications: non-structural changes which affect gene expression (active versus inactive genes) → a change in *phenotype* without a change in *genotype*.

DNA methylation age

- Patterns of DNA methylation change with age. 'Typical' methylation patterns for different ages allow prediction of chronological age from DNA methylation

- Horvath algorithm (353 CpG loci): based on >8000 individuals of different ages, multiple tissue types. (Horvath 2013)

- Hannum (71 CpG loci): Blood based predictor from 666 American adults (Hannum et al., 2013).

- These allow calculation of DNA methylation age 'acceleration': greater methylation age than chronological age (Δage)

- Terminology: DNA methylation (DNAm) age 'acceleration': not really acceleration (i.e., rate of change) but simply a difference

DNA methylation age and health

DNAm age acceleration has been linked with health and functioning in later life:

- walk speed, lung function and cognition (Marioni et al 2015a)

- All-cause mortality (Marioni et al 2015b, Dugué et al 2017)

- Applies even within pairs of twins(Christiansen et al 2016)

- Consistent with wider literature on 'biological ageing', e.g. allostatic load (Seeman et al 2010)

DNA methylation age and the social environment

DNA methylation age acceleration has been linked with:

- economic hardship (Simons et al, 2016)

- lifetime stress (Zannas et al, 2015)

- dietary factors (Quach et al, 2017)

- pollution (Nwanaji-Enwerem et al, 2017)

- education relative to peers (Fiorito et al, 2017).

- Relevance to health inequalities: DNAm age acceleration could plausibly mediate inequalities in health and functioning

Analysis in UKHLS Epigenetic Subsample

We investigate associations of DNAm age acceleration with multiple dimensions of SEP

Epigenetic subsample: 1099 UKHLS participants aged 28-98y

Horvath and Hannum Δage explored in relation to:

- Current household income (quartiles of equivalized net)
- Current employment status
- 'Lifetime' income measure (1999-2011): years in the lowest equivalized quartile
- Lifetime' unemployment (1999-2011): months unemployed
- Education, standardized by gender and 5-year age band
- Childhood social class (parents' RGSC at age 14)

Association of the algorithm with age: Horvath age vs chronological age

Non-parallel lines: participants consistently 'older' at younger ages and 'younger' at older ages

# Association of the algorithm with age: Hannum age vs chronological age
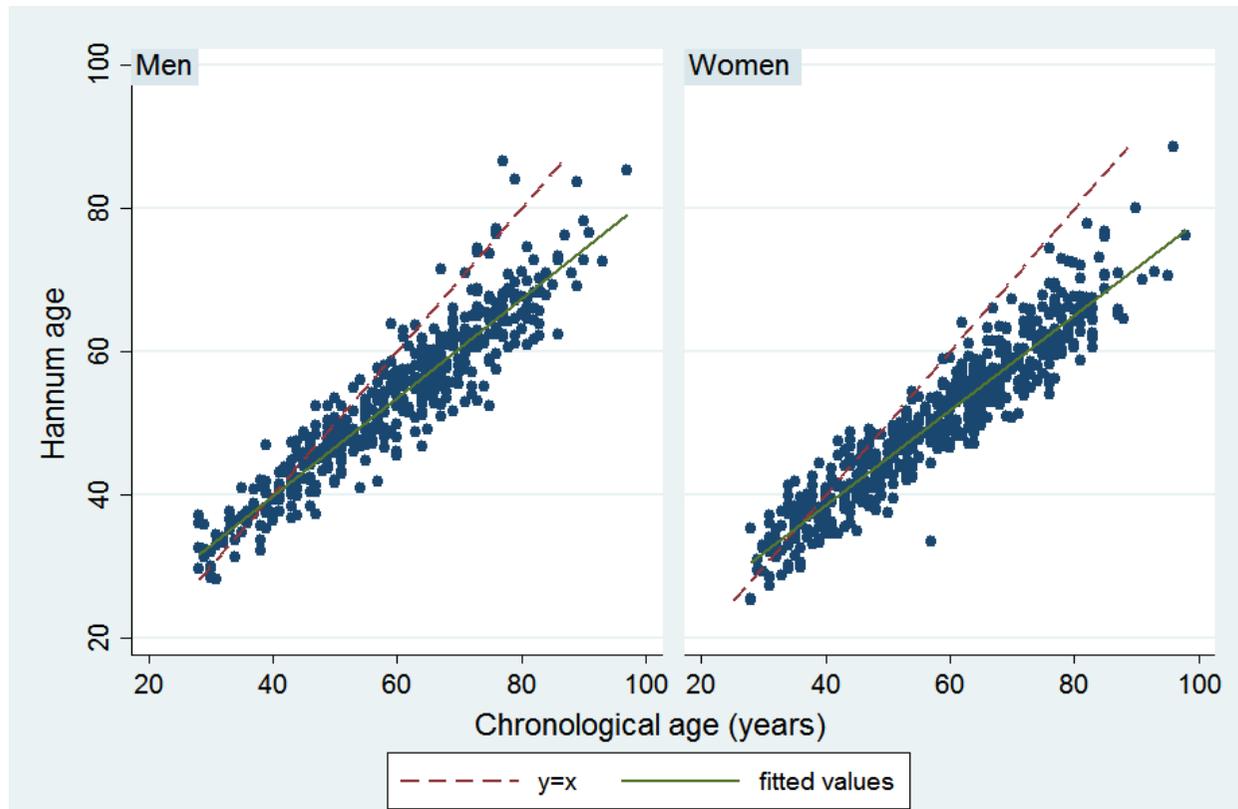
Similar results for Hannum: better (predictive) performance at younger ages

Association of Horvath Δage with social position

No association with income measures, educational attainment, current employment status or total unemployment.

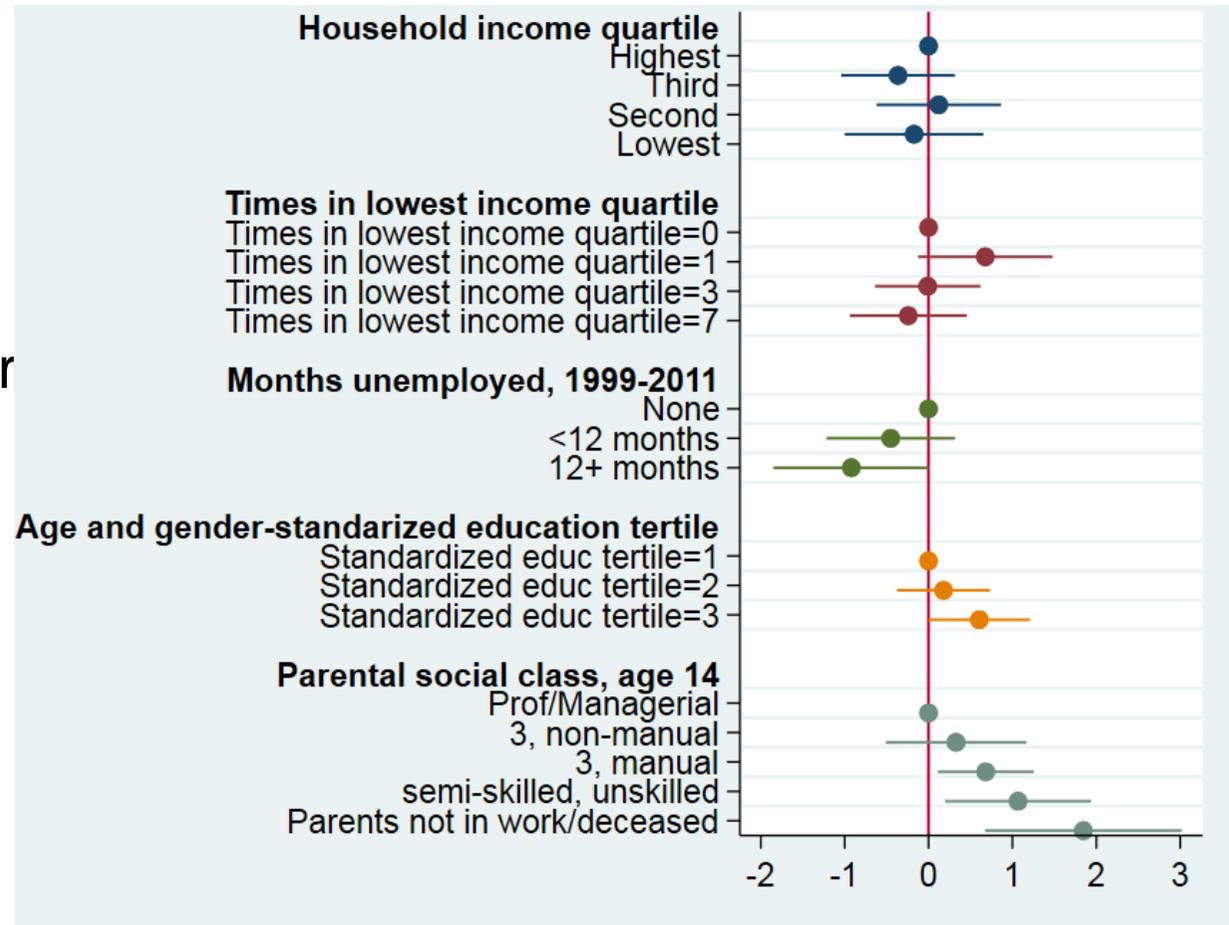Possible association with childhood social class.

Hughes et al., under review
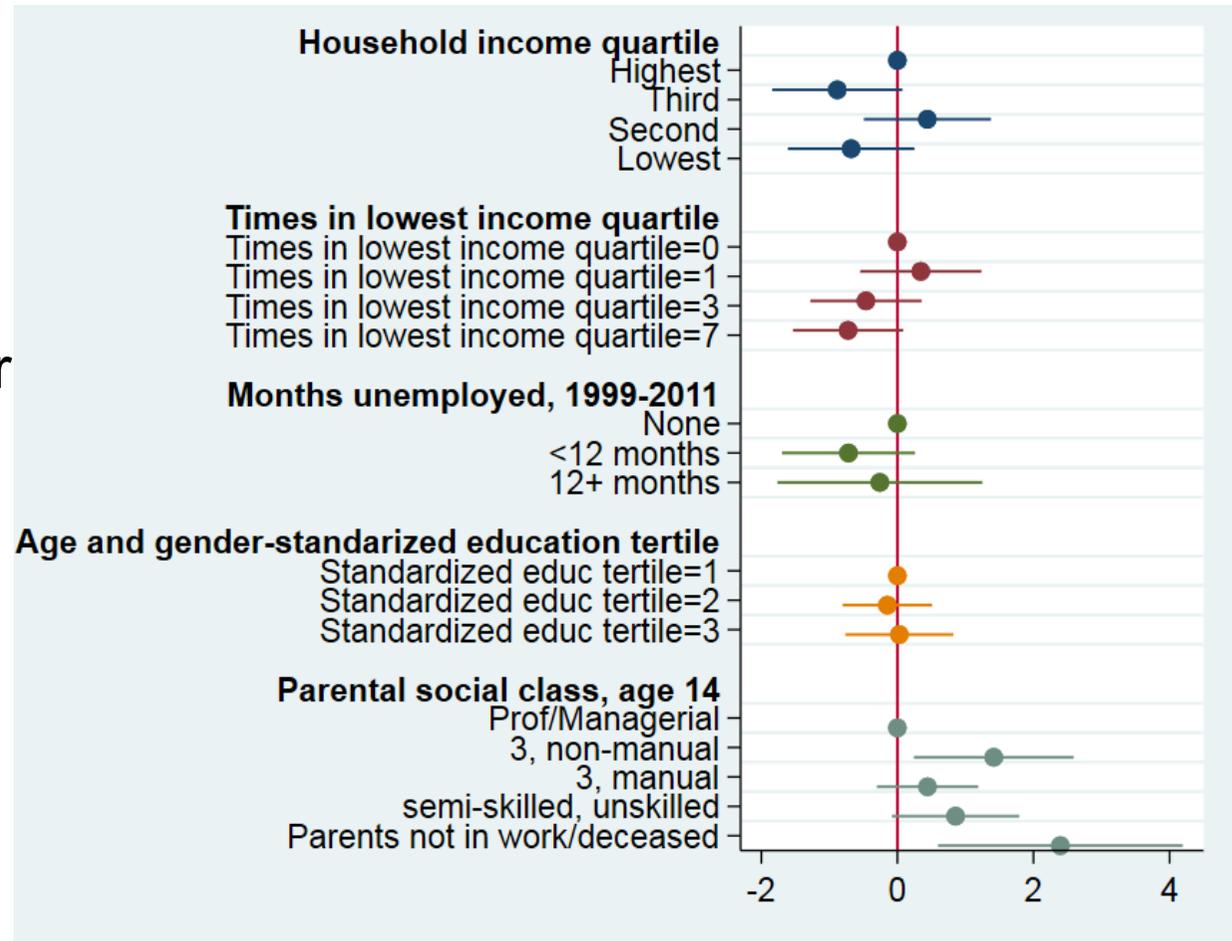
Association of Hannum Δage with social position

No association with income measures, educational attainment, current employment status or total unemployment.

Clear association with childhood social class.

Hughes et al., under review

Summary of findings: DNAm age and SEP

- Early life social position is associated with greater biological than chronological age assessed by DNA methylation

- Clearer results for Hannum clock than Horvath clock. Because Hannum was trained on blood, Horvath trained on a mix of tissues? Or because sites involved are differentially influenced by exposures?

- Association of educational attainment and Δage explained by social class at 14y, but not vice-versa.

- Consistent with prior research on importance of early life influences, e.g. from 1958 cohort

- Current/adult measures of social position are not associated with Δage using either Horvath or Hannum

Words of caution when analysing these algorithms

- In social science, many social exposures are likely to have cohort/period effects. The association of Δage with age may therefore confound associations considerably. We recommend that the association of age with Δage be considered in all analyses.

- Several 'clock' algorithms exist; Horvath most widely adopted but others available or being developed. They vary by tissue type (blood, saliva etc.) and this needs to be considered when designing your study.
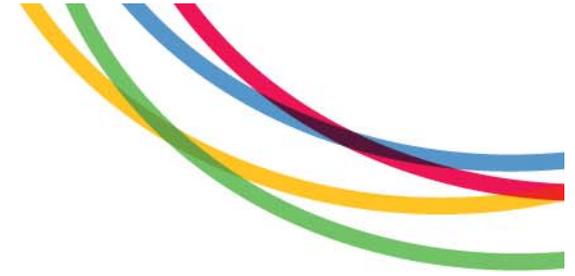
What now?

UKHLS: Further investigation of biology of ageing (with Leo Schalkwyk)

UKHLS: Other projects: eg. sleep/shiftwork (biomarker fellow)

In other mixed-age samples: similar association of age with Δage?

In the Birth Cohorts: analysis of environmental differences where age is held constant!

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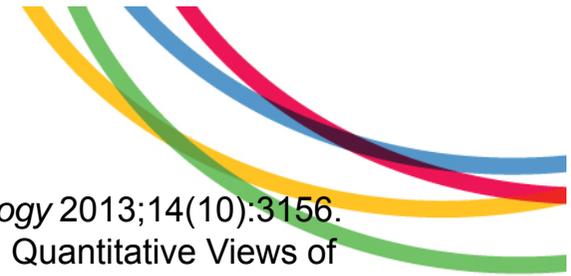
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