



Broken down by age and sex? Age moderation of individual differences in chronic medical illness burden

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Background: Chronic Medical Illness Burden

Impetus: to harmonize self-reported physical illness across IGEMS

Modified Cumulative Illness Rating Scale (Salvi et al., JAGS, 2008):

List of 14 body systems, including a comorbidity index that represents the number of categories with moderate disability or morbidity

Further adapted for IGEMS by dropping lower GI and genito-urinary (due to insufficient data across studies to score) and psychiatric (which was not included in the comorbidity index), while adding cancer (instead of scoring within each separate body system), and stroke (instead of including with neurological)

IGEMS-CIRS categories include: cardiac (heart), hypertension, vascular (circulatory), respiratory, EENT, upper GI, hepatic (liver), renal, musculoskeletal, neurological, endocrine/metabolic, cancer, and stroke.

Objectives

- Develop a harmonized measure of physical health
- Examine mean scores by age and sex and study
- Estimate variance components and test for age and sex moderation
- Evaluate the presence of G x E by applying a Fisher test

Participants: IGEMS Studies

- SATSA (Swedish)
- OCTO-Twin (Swedish)
- Gender (Swedish)
- LSADT (Danish)
- MADT (Danish)
- MTSADA (U.S.)
- VETSA (U.S.)
- MIDUS Twins (U.S.)
- FTC (Finnish)
- Over 50s (Australian)

N = 27742

54.8% female

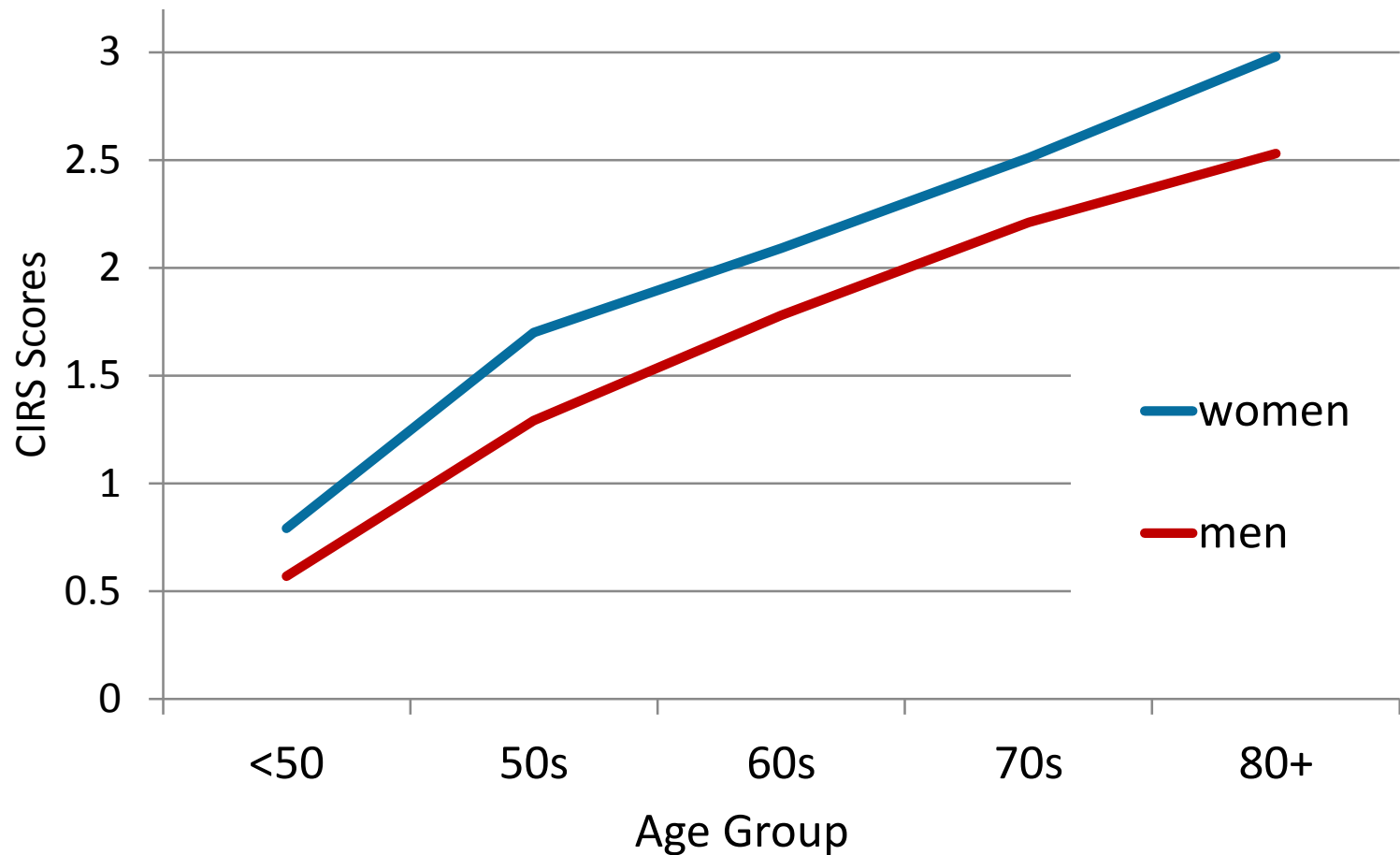
Complete pairs = 8743

- 3964 MZ
- 4578 SS DZ
- 1652 OS DZ

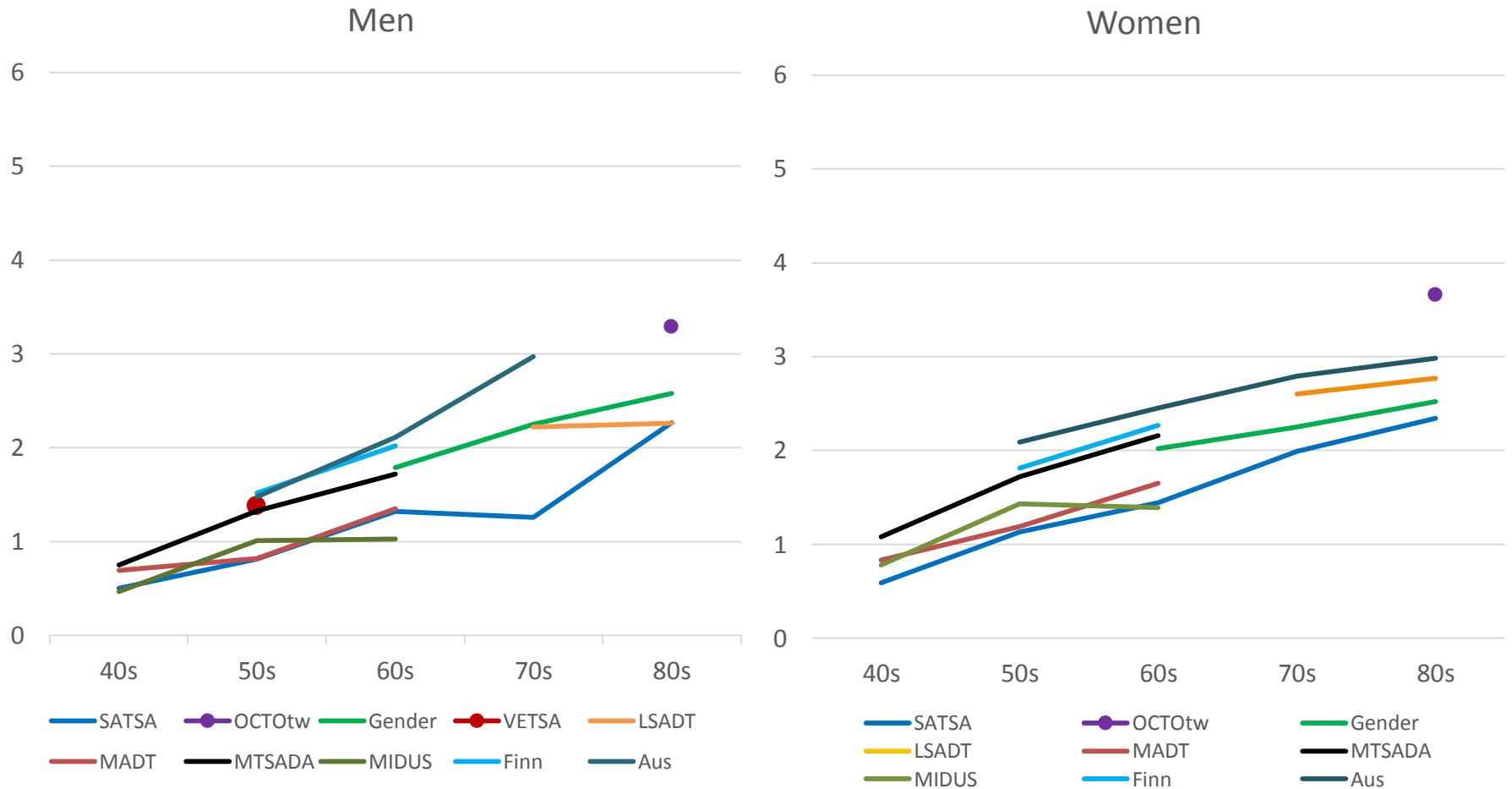
Age Range: 25-102

(M = 62.8 SD = 11.6)

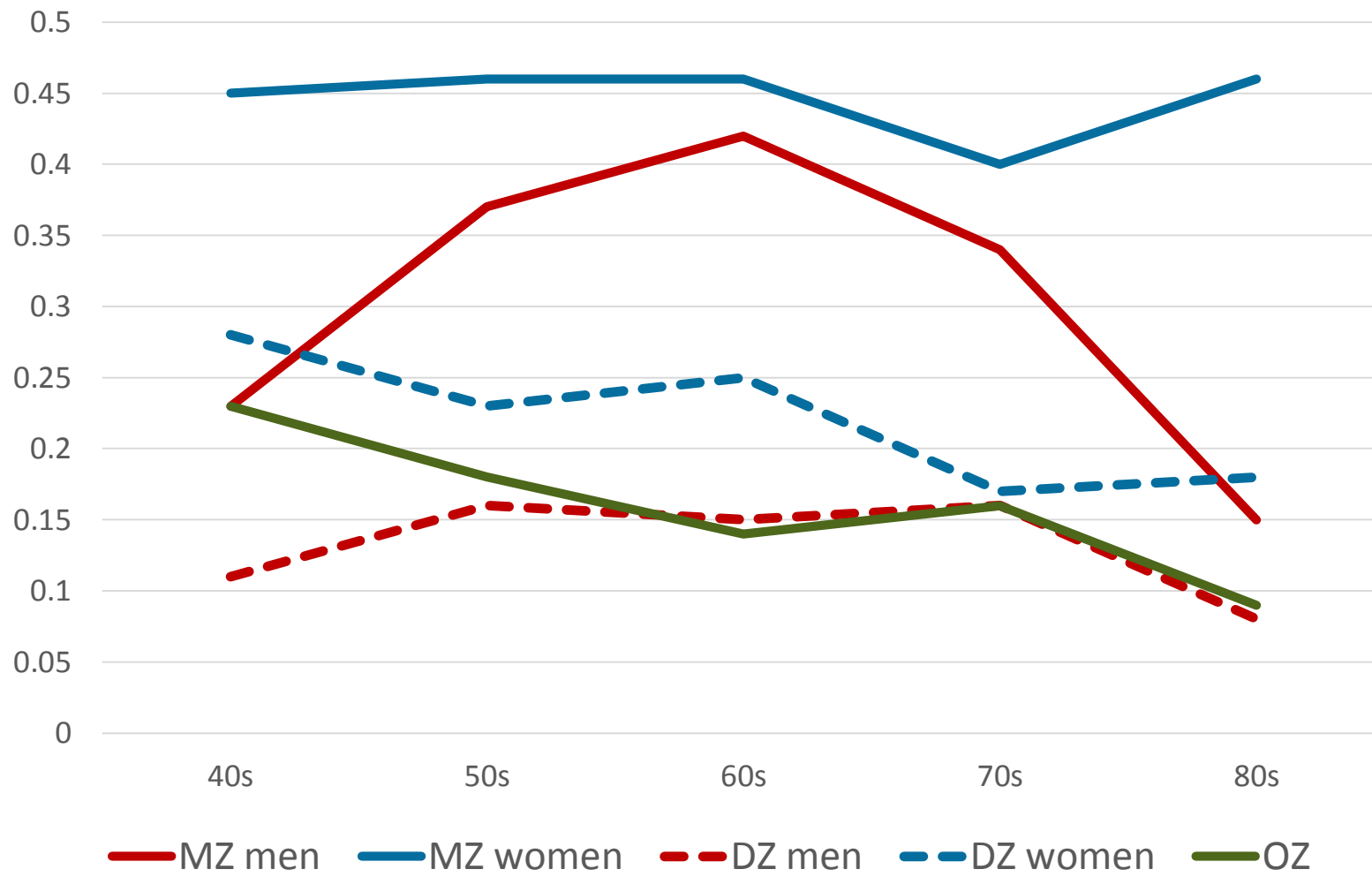
CIRS mean scores by age and sex



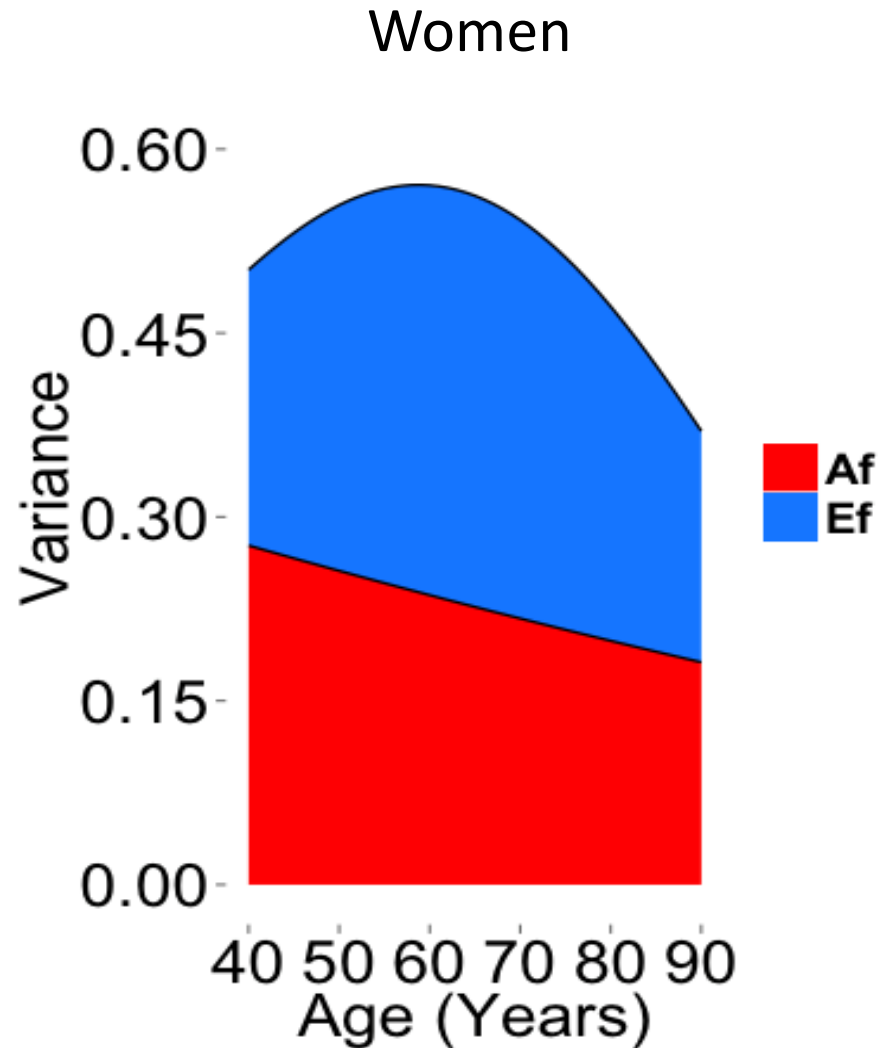
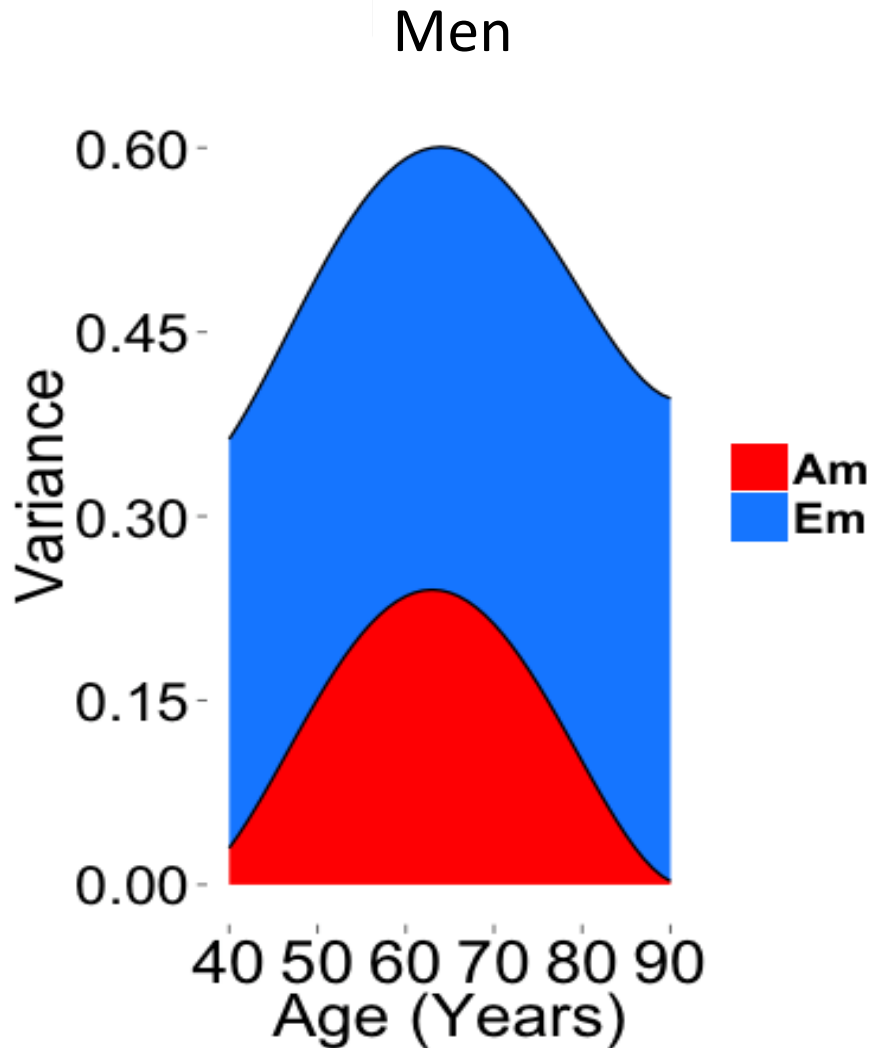
CIRS mean scores by age and study



CIRS intrapair correlations by age



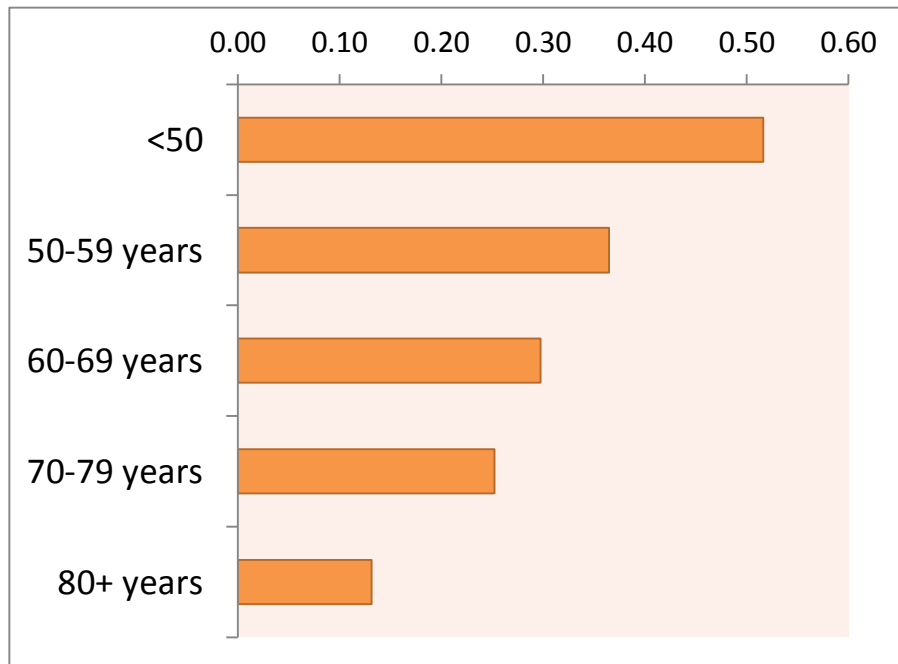
Model fitting results



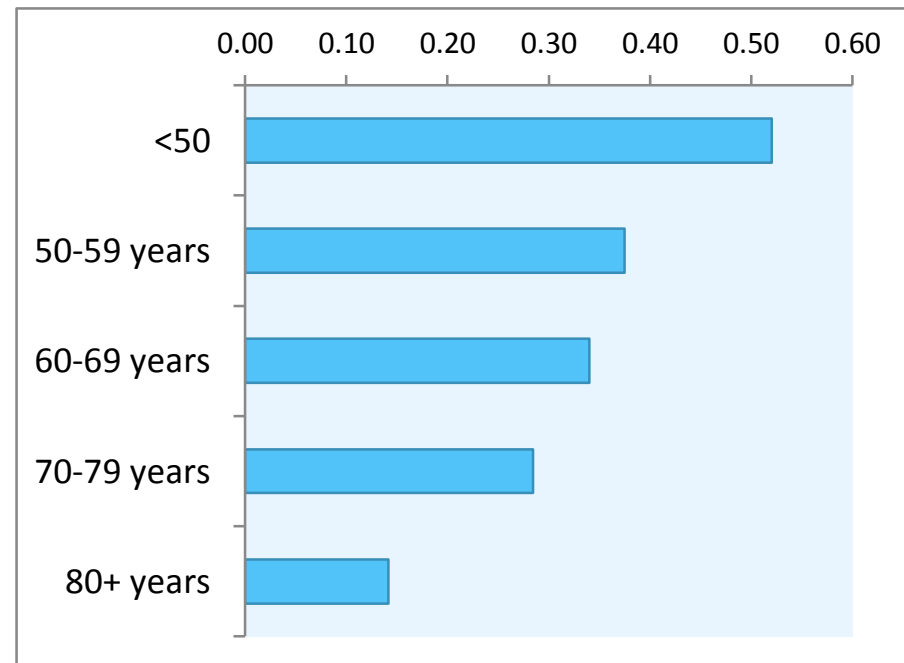
Age moderation is incorporated into the model by allowing the effects of A, C and E to be a function of age and squared age, with age 40-90 as a continuous variable. Can drop C parameter. Same model could not be fitted for men and women.

Fisher test: effect sizes

Men



Women



The Fisher test evaluates the difference between mean squared pair differences and the mean absolute pair differences squared in the MZ twins. A one-tailed *t*-test evaluates significance, with effect sizes calculated from the *t*-tests.

Summary/Conclusions

- IGEMS-CIRS score levels showed expected age and sex trends, with similar age and sex trends across studies
- Age moderation was significantly different by sex. Compared to men, women had a greater contribution from genetic variance and less age moderation. For men, genetic contribution to raw variance showed an inverted U-shaped curve peaking around age 65. For women, non-shared environmental variance showed an inverted U-shaped curve peaking around age 60
- Fisher test showed decreasing G x E with age

Limitations

- Cross sectional design
- Data did not permit rating severity of physical conditions
- Limited ethnic diversity

References

Fisher RA. (1925). The resemblance between twins, a statistical examination of Lauterbach's measurements. *Genetics* 10, 569–579.

Purcell S. (2002). Variance components models for gene-environment interaction in twin analysis. *Twin Res.* 5(6): 554-571.

Salvi F, Miller MD, Grilli A, Giorgi R, Towers AL, Morichi V, Spazzafumo L, Mancinelli L, Espinosa E, Rappelli A, Dessì-Fulgheri P. (2008). A manual of guidelines to score the modified cumulative illness rating scale and its validation in acute hospitalized elderly patients. *J Am Geriatr Soc.* 56(10): 1926-1931.