Frailty and mortality: Investigating sex differences and socioeconomic influences using Swedish twins

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Objective

To investigate sex differences in frailty and the relationship with socioeconomic factors. Using same-sex and opposite-sex twins provides an unique opportunity to study the relationship between SES, frailty, and mortality - and how it may differ between men and women.

Introduction

- Frailty is a state of increased vulnerability which has several clinical representations, related to cognitive and physical vulnerability and disability.
- The prevalence of frailty is not equally distributed within the aging population and socioeconomic factors, sex, and genetic influences are suggested to be important in the development of frailty.

Measurements

- Data were retrieved from the Screening Across the Lifespan Twin study (SALT), from same-sex and opposite-sex twin pairs, born 1886-1958 (n=43,636).
- Frailty was operationalized using the Frailty Index (FI). The FI was created from 44 items of health indicators, such as symptoms, diagnoses and functional status. Mean FI was 0.13 (SD 0.09, min 0 - max 0.76).
- Two attained socioeconomic indicators were used, social class (SEI) and education.

Statistical analyses

- (1) To investigate potential familial influences on sex differences in FI, we created clusters of artificial opposite-sex twin pairs (unrelated) derived from the same-sex twin pairs. Each cluster contained unrelated males and females with the same birth year and same level of parental social class. Sex differences in frailty were estimated in a linear regression by comparing the sample of unrelated clusters to a sample restricted to opposite-sex twin pairs.
- (2) Linear regression was used to estimate the effect of social class and education on frailty.
- (3) Cox proportional hazard models were applied to investigate socioeconomic influences on mortality risk by level of frailty.
- (4) To investigate possible differences between belonging to same-sex or opposite-sex twin pairs, we compared same-sex with opposite-sex females and same-sex with opposite-sex males.
- Co-twin control methods were used to evaluate familial confounding. By utilizing information from discordant twin pairs, we compared the population effect to the within-pair effect. The within-pair effect indicates if the effect of the exposure remains when familial factors are taken into account.

Intra-pair correlations of the Frailty Index

	Correlations		
	MZ	SSDZ	OSDZ
Frailty index (total sample)	.52 (0.01)	.27 (0.02)	0.20 (0.02)
Males	.45 (0.03)	.21 (0.02)	
Females	.53 (0.02)	.28 (0.02)	

Note. MZ=Monozygotic twins, SSDZ=Same-sex dizygotic twins, and OSDZ=Opposite-sex dizygotic twins

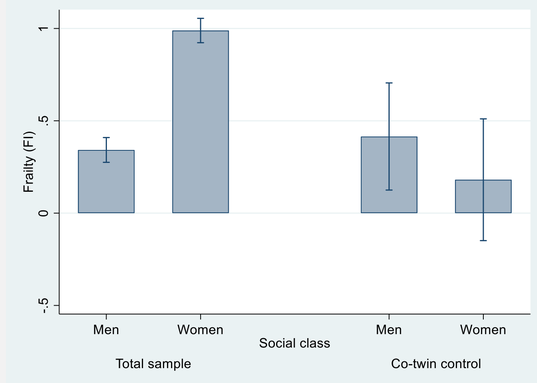
Conclusions

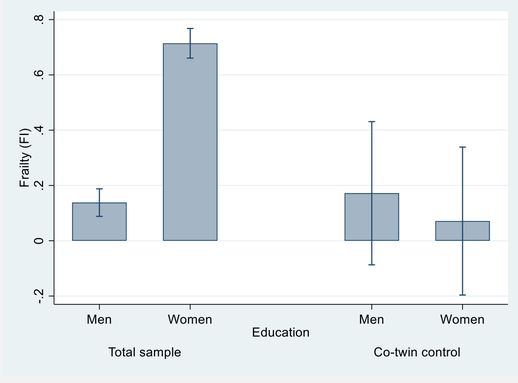
- Our results indicate that frailty may be different for men and women, where socioeconomic factors are more important for the development of frailty in men, while genetic and early-life factors account for the relationship between SES and FI in women. It is possible that these results reflect a familial selection into social class and educational levels for women but not for men in our sample to the same extent.
- We found support for the male-female health-survival paradox in the relationship between frailty and mortality, with higher levels of frailty in women but a stronger relationship between frailty and mortality in men - independent of SES, age and familial factors

(1) Frailty index as a function of sex, comparing opposite-sex twins with a matched sample of unrelated opposite-sex twins

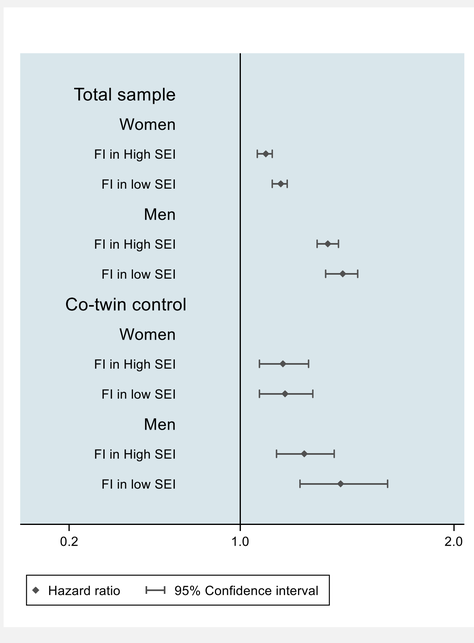
	Model 1		Model 2		Model 3	
	β (CI)	Diff. p	β (CI)	Diff. p	β (CI)	Diff. p
Sex	2.05 (1.70, 2.39)	0.077	1.84 (1.50, 2.21)	0.112	2.09 (1.75, 2.43)	0.081
By age groups						
Age ≤50	2.10 (1.51, 2.68)	0.644	2.02 (1.42, 2.61)	0.626	2.25 (1.66, 2.84)	0.667
Age 51-60	2.18 (1.65, 2.71)	0.160	1.95 (1.40, 2.49)	0.225	2.25 (1.72, 2.79)	0.224
Age 61-70	1.51 (0.73, 2.29)	0.567	1.33 (0.52, 2.14)	0.882	1.47 (0.68, 2.25)	0.602
Age 71-80	2.31 (1.12, 3.51)	0.597	2.04 (0.70, 3.37)	0.622	2.10 (0.90, 3.30)	0.664
Age ≥81	3.41 (-0.09, 6.91)	0.293	2.39 (-2.07, 6.85)	0.279	3.43 (-0.27, 7.13)	0.326

Note. Model 1: Adjusted for age at interview, Model 2: Adjusted for age at interview and attained social class, Model 3: Adjusted for age at interview and attained education

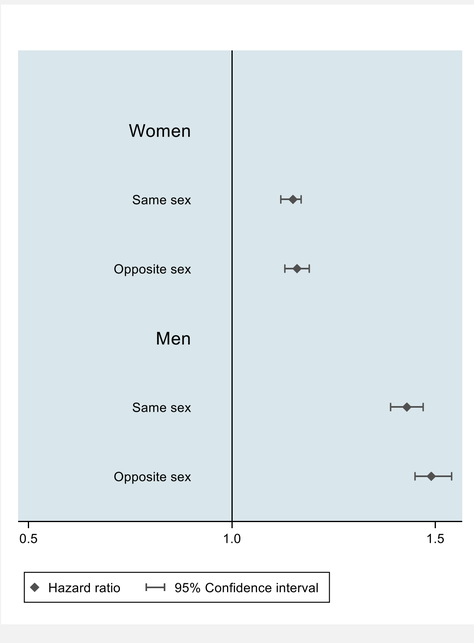




(2) Frailty as a function of attained social class and education in men and women, adjusted age and birth cohort (born before or after 1925).
Note. The estimates indicate units of increase in FI at one unit increase of the socioeconomic indicators.



(3) Hazard ratios in all-cause mortality by 10 percent increase in FI, stratified by sex and high vs low social class and education.



(4) Hazard ratios in all-cause mortality by 10% increase in FI, comparing same-sex with opposite-sex twins by sex.

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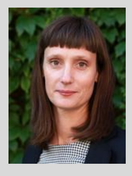

Funding
FORTE 2013-02292
VR 2013-08689
NIH R01 AG037985, R01 AG059329

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