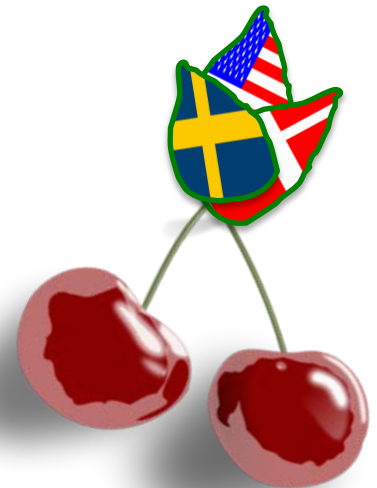


Longitudinal study of hand grip strength in twins

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- on behalf of the iGEMS consortium

Hand grip strength predicts...

Previous studies have demonstrated an inverse relation between grip strength and

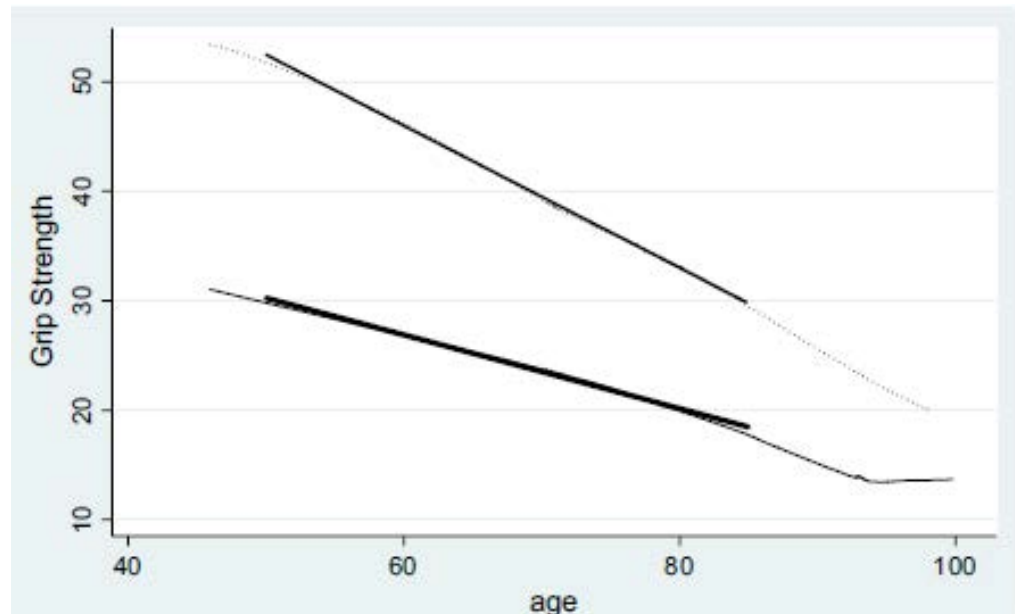
- Disability
- Length of hospital stay
- Mortality



Predictors of hand grip strength

- environmental factors

- Stature, BMI, birth weight
- Marital status, wealth, nationality
- Dementia, chronic diseases
- Occupation, physical activity (work & leisure)
- Alcohol, smoking
- **Age and sex**



Frederiksen et al, Annal.Epidemiol., 2006

Hand grip strength

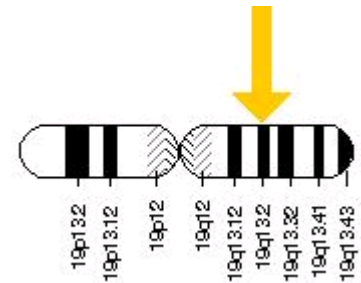
- heritability

- Level: 50-70%
 - remarkably flat across age ranges
- Decline: ~0%

Hand grip strength

- genes

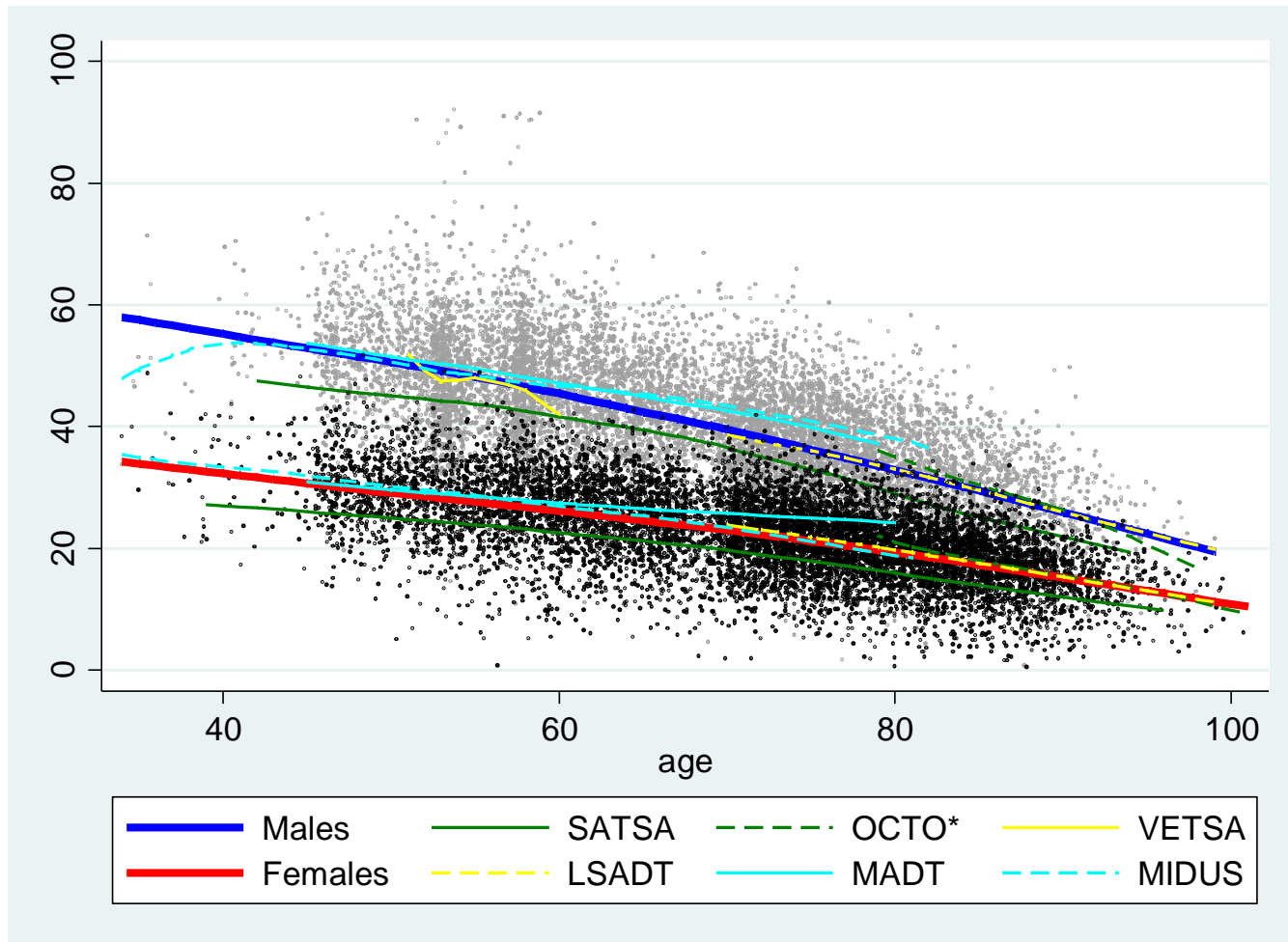
- APOE ϵ 4 vs APOE ϵ 3
 - higher grip strength level
- APOE ϵ 2 vs APOE ϵ 3
 - lower grip strength level
 - Less decline
- ACE, ACTN3, PPARA...



Sample

Study	N	Male (%)	Age range (median)	Repeated measures – max (median)
SATSA	851	41%	39-88 (63)	7 (4)
OctoTwin	640	34%	79-99 (82)	5 (3)
VETSA	1,215	100%	51-60 (54)	1 (1)
LSADT	2,873	45%	70-97 (75)	4 (3)
MADT	4,274	51%	45-77 (56)	2 (2)
MIDUS	379	41%	34-82 (53)	1 (1)
TOTAL	9,853	48%	34-99 (72)	7(2)

Age- and sex- trajectories



* Rescaled due to different measuring device

Fisher's test

- heterogeneity

Monozygotic twin pairs only!

d = within twin pair difference

$$h = \overline{d^2} - \frac{\pi}{2} \bar{d}^2$$

$$\text{s.e.} = \frac{\overline{d^2}}{\sqrt{n}} \sqrt{2\pi - 6}$$

Significant test indicates a mixture of distributions
- which again might indicate presence of GxE
interaction

Fisher's test

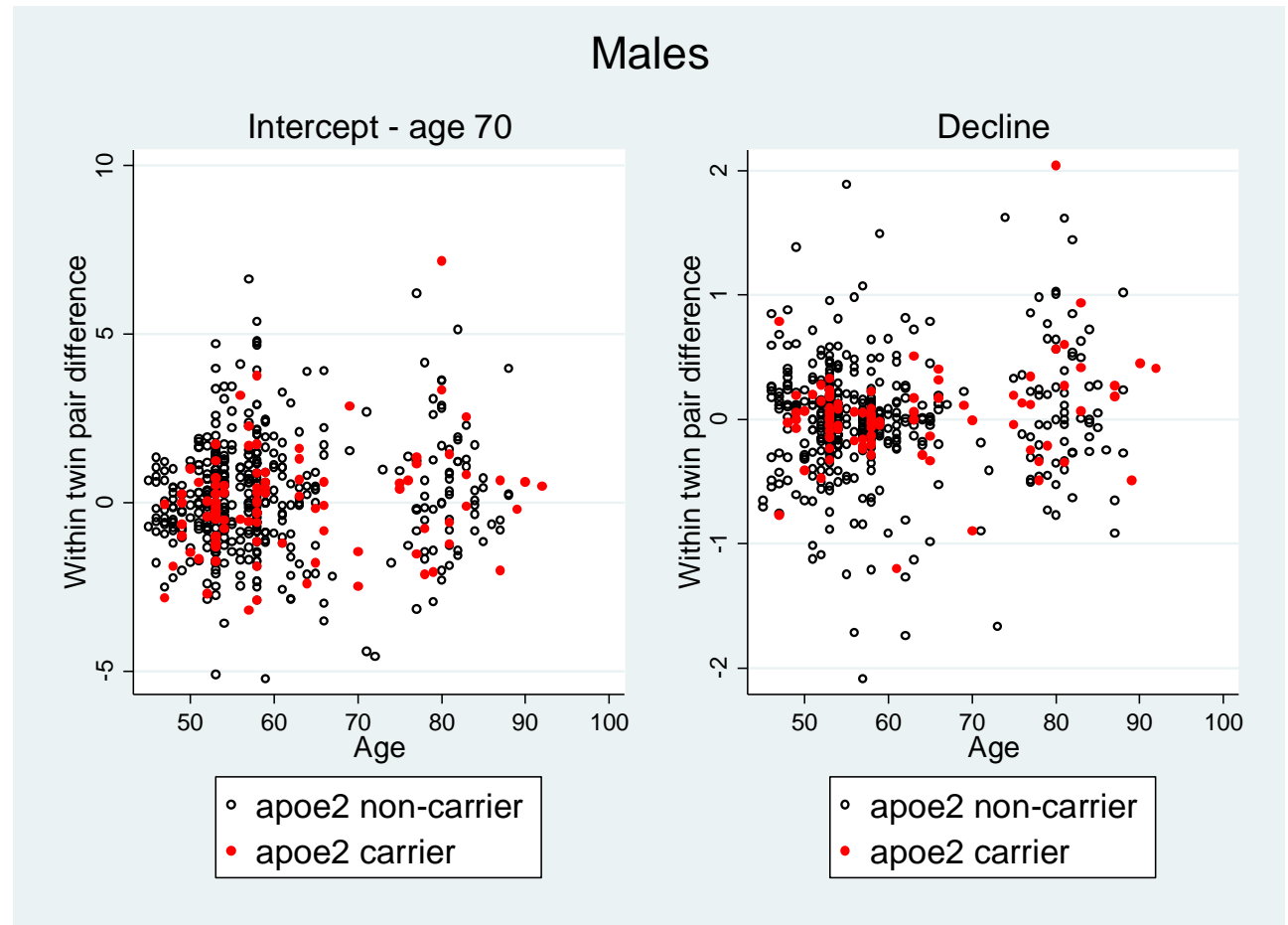
All studies	<i>N</i>	<i>t</i>	<i>p</i>
MALES			
Intercept	915	8.84	<0.001
Decline	915	19.50	<0.001
FEMALES			
Intercept	701	5.89	<0.001
Decline	701	16.65	<0.001

Evidence of a GxE interaction for level and decline of grip strength in males and females

Within twin pair differences

- APOE ϵ 2

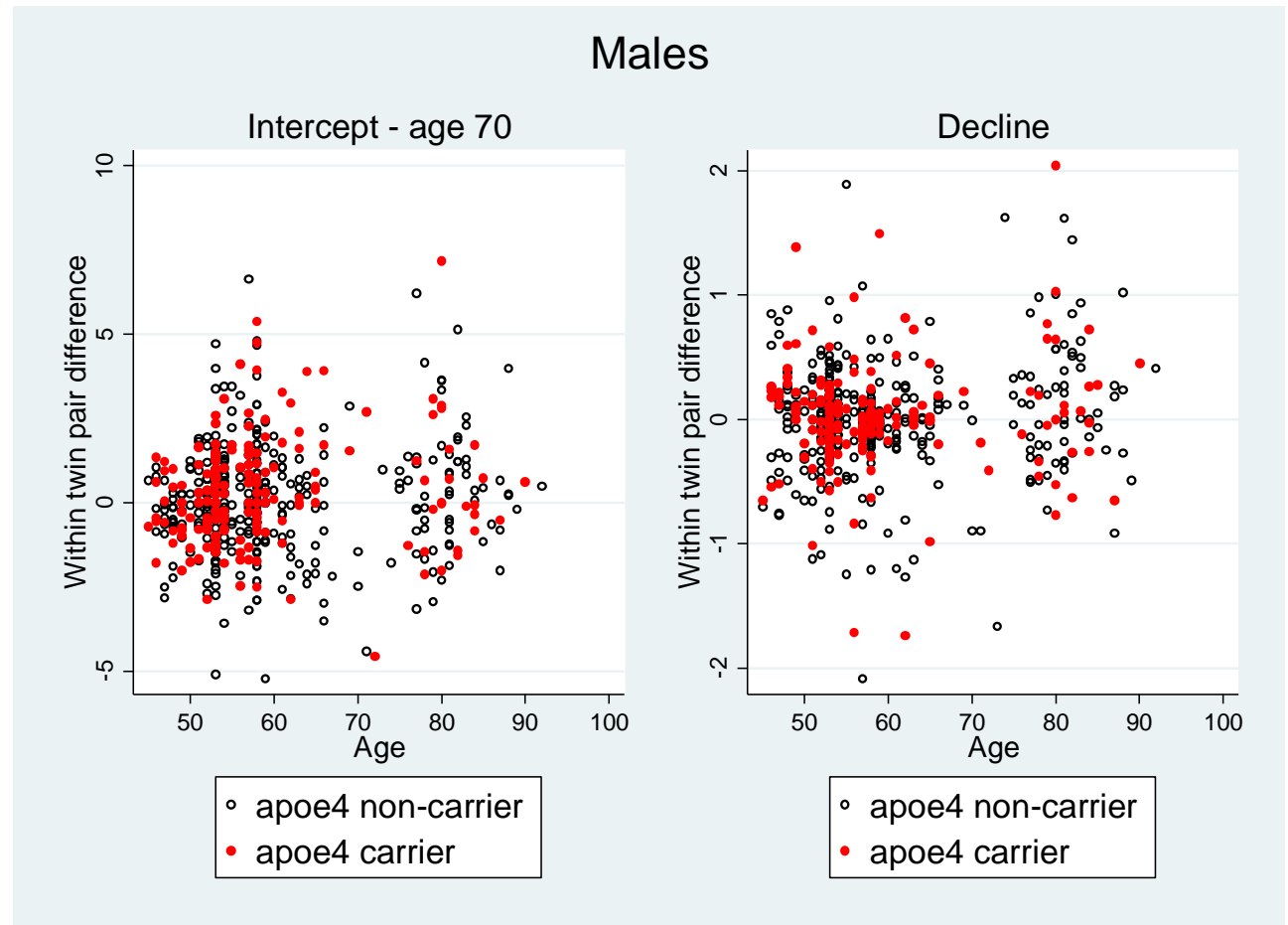
Less variability
in APOE ϵ 2 carriers
compared with
non-carriers



Within twin pair differences

- APOE ϵ 4

Similar variability
in APOE ϵ 4 carriers
and non-carriers



Variance ratio test

- Males

	APOE ϵ 2				APOE ϵ 4			
	N-	N+	carrier/non-carrier	p-value	N-	N+	carrier/non-carrier	p-value
Intercept	530	107	0.95	0.75	433	204	1.04	0.74
Decline			0.73	<0.05			1.01	0.91
<70								
Intercept	459	83	0.74	0.09	366	176	0.90	0.45
Decline			0.48	<0.001			0.88	0.34
>=70								
Intercept	71	24	0.95	0.91	67	28	1.18	0.57
Decline			0.66	0.26			0.66	0.22

Variance ratio test

- Females

	APOE ϵ 2				APOE ϵ 4			
	N-	N+	carrier/non-carrier	p-value	N-	N+	carrier/non-carrier	p-value
Intercept	330	71	0.78	0.20	276	125	1.20	0.22
Decline			0.55	<0.01			1.59	<0.01
<70								
Intercept	205	45	0.70	0.16	174	76	1.07	0.71
Decline			0.54	0.02			1.46	0.04
>=70								
Intercept	123	26	0.91	0.81	100	49	1.51	0.08
Decline			0.79	0.50			0.81	0.43

Differences in intercept and decline predicted by APOE ϵ 2 and specific environmental factors

- DK females only

	N	G		E		GxE	
		Intercept	Decline	Intercept	Decline	Intercept	Decline
Height	254	X	X	X	✓	X	X
Depression symp. score	254	X	X	✓	X	X	X
Smoke (pack-year)	249	X	X	X	X	X	X
Peak flow	140	X	X	X	X	X	X
Chair stand	182	X	X	X	X	X	X

Differences in intercept and decline predicted by APOE ϵ 4 and specific environmental factors

- DK females only

	N	G		E		GxE	
		Intercept	Decline	Intercept	Decline	Intercept	Decline
Height	254	X	X	X	X	X	X
Depression symp. score	254	X	X	X	X	X	X
Smoke (pack-year)	249	X	X	X	X	X	✓
Peak flow	140	X	X	X	X	X	X
Chair stand	182	X	X	X	X	X	X

Conclusion

- Evidence of GxE for level as well as decline of grip strength based on tests of MZ twin pair differences in grip strength
- APOE ϵ 2 decreases variability of the decline of grip strength in males and females (age < 70 years)
- APOE ϵ 4 increases variability of the decline of grip strength in females (age < 70 years)
- In DK studies: no evidence that APOE ϵ 2/APOE ϵ 4 interact with pair differences of environmental factors* in relationship with pair dissimilarity of level and change of grip strength

* height, depression, pack-years, peak-flow, chair stand

Acknowledgements

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