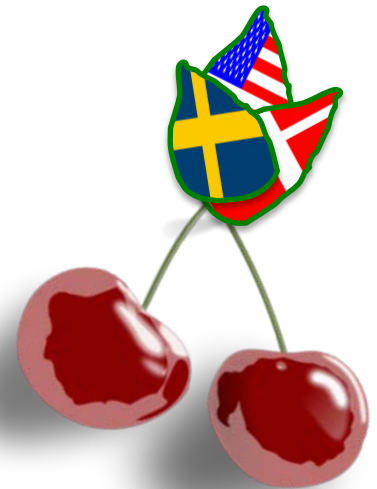


# Longitudinal study of hand grip strength in twins

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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

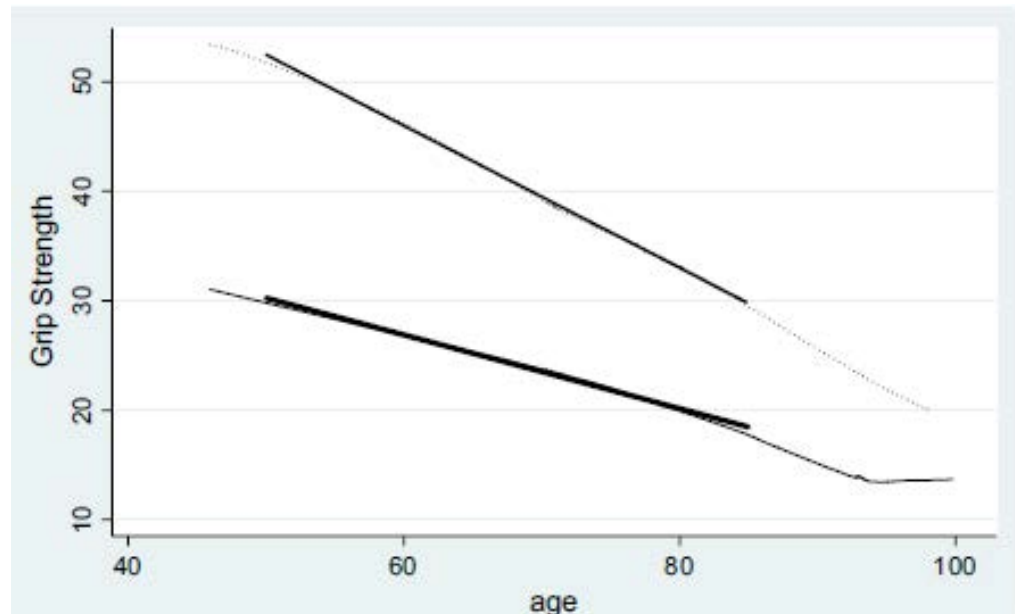
- Disability
- Length of hospital stay
- Mortality



# 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

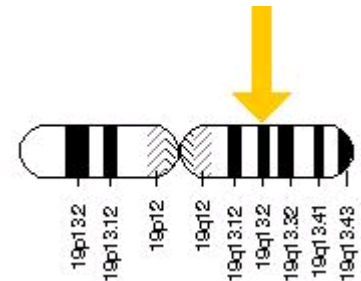
- heritability

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

# Hand grip strength

- genes

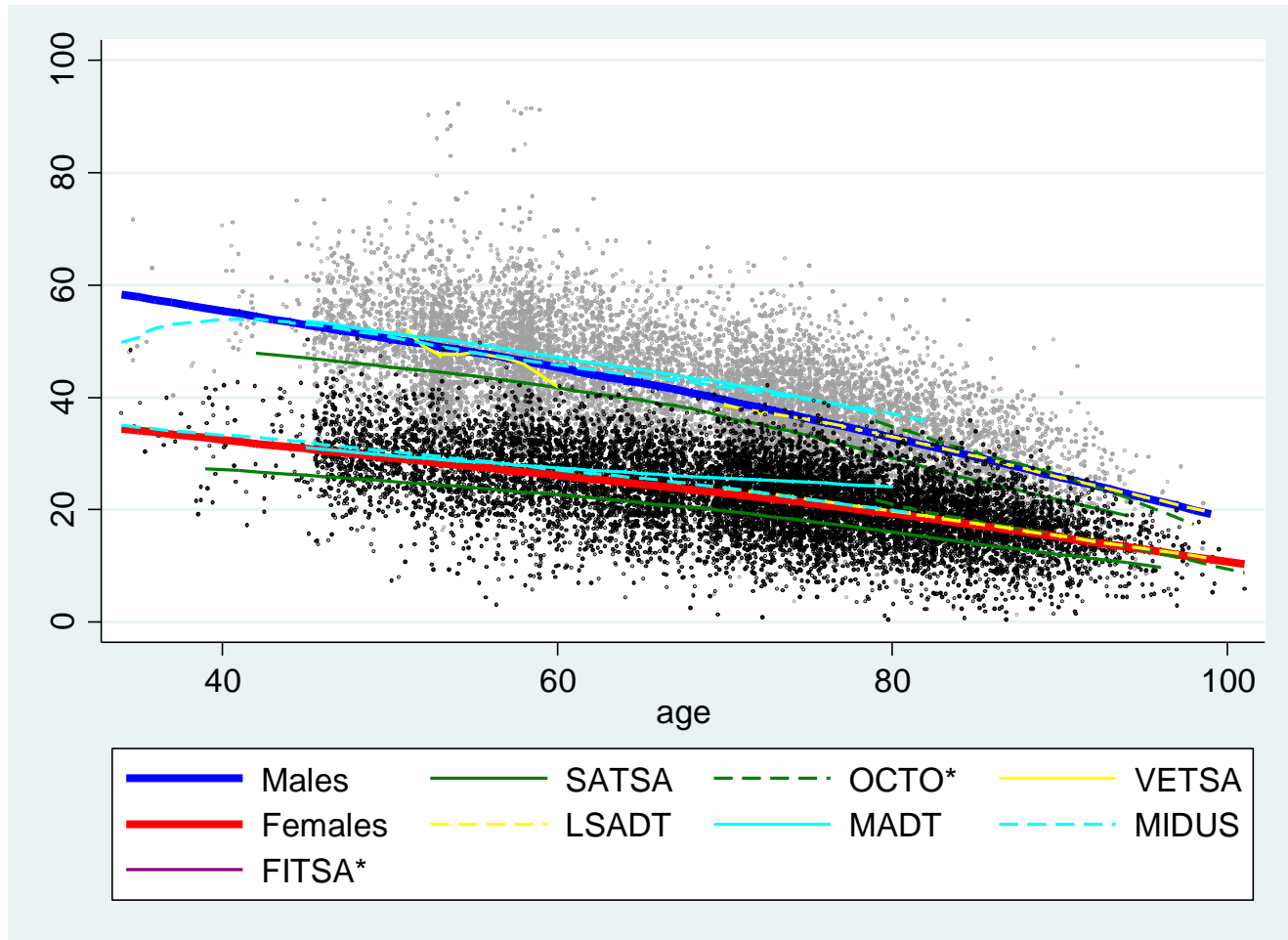
- APOE $\epsilon$ 4 vs APOE $\epsilon$ 3
  - APOE $\epsilon$ 4 carriers have higher grip strength level
- APOE $\epsilon$ 2 vs APOE $\epsilon$ 3
  - APOE $\epsilon$ 2 carriers lower grip strength level
  - APOE $\epsilon$ 4 carriers less decline
- ACE, ACTN3, PPARA...



# Sample

<b>Study</b>	<b>N</b>	<b>Male (%)</b>	<b>Age range (median) at baseline</b>	<b>Repeated measures – max (median)</b>
<b>SATSA</b>	851	41%	39-88 (63)	7 (4)
<b>OctoTwin</b>	640	34%	79-99 (82)	5 (3)
<b>VETSA</b>	1,215	100%	51-60 (54)	1 (1)
<b>MIDUS</b>	379	41%	34-82 (53)	1 (1)
<b>LSADT</b>	2,886	45%	70-97 (75)	4 (3)
<b>MADT</b>	4,276	51%	45-77 (56)	2 (2)
<b>FITSA</b>	434	0%	63-79 (69)	2 (1)
<b>TOTAL</b>	10,681	51%	34-99 (66)	7(1)

# 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

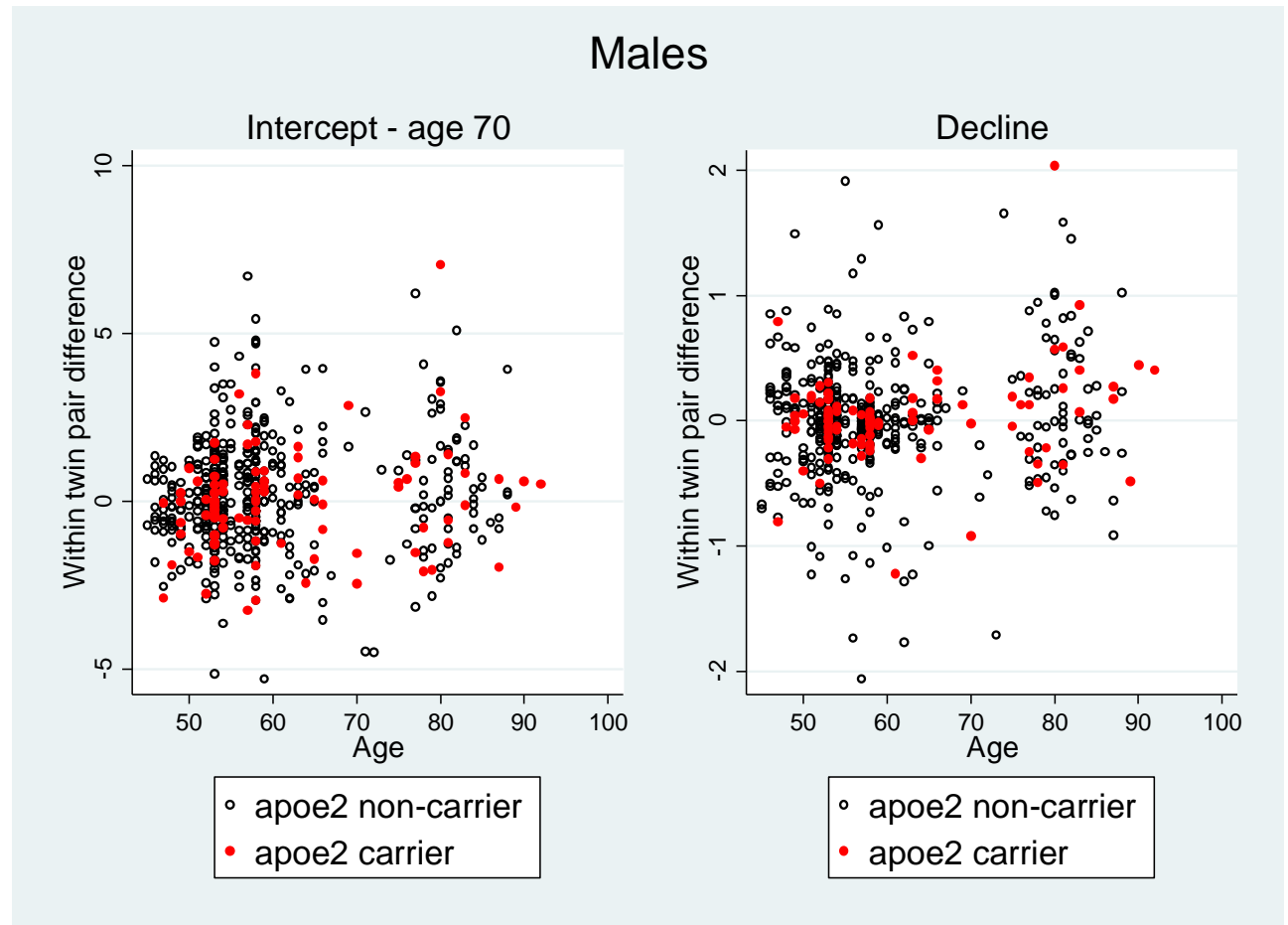
All studies	<i>N</i>	<i>t</i>	<i>p</i>
<b>MALES</b>			
Intercept	917	9.18	<0.001
Decline	917	19.79	<0.001
<b>FEMALES</b>			
Intercept	807	5.30	<0.001
Decline	807	18.47	<0.001

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

# Within twin pair differences

- APOE $\epsilon$ 2

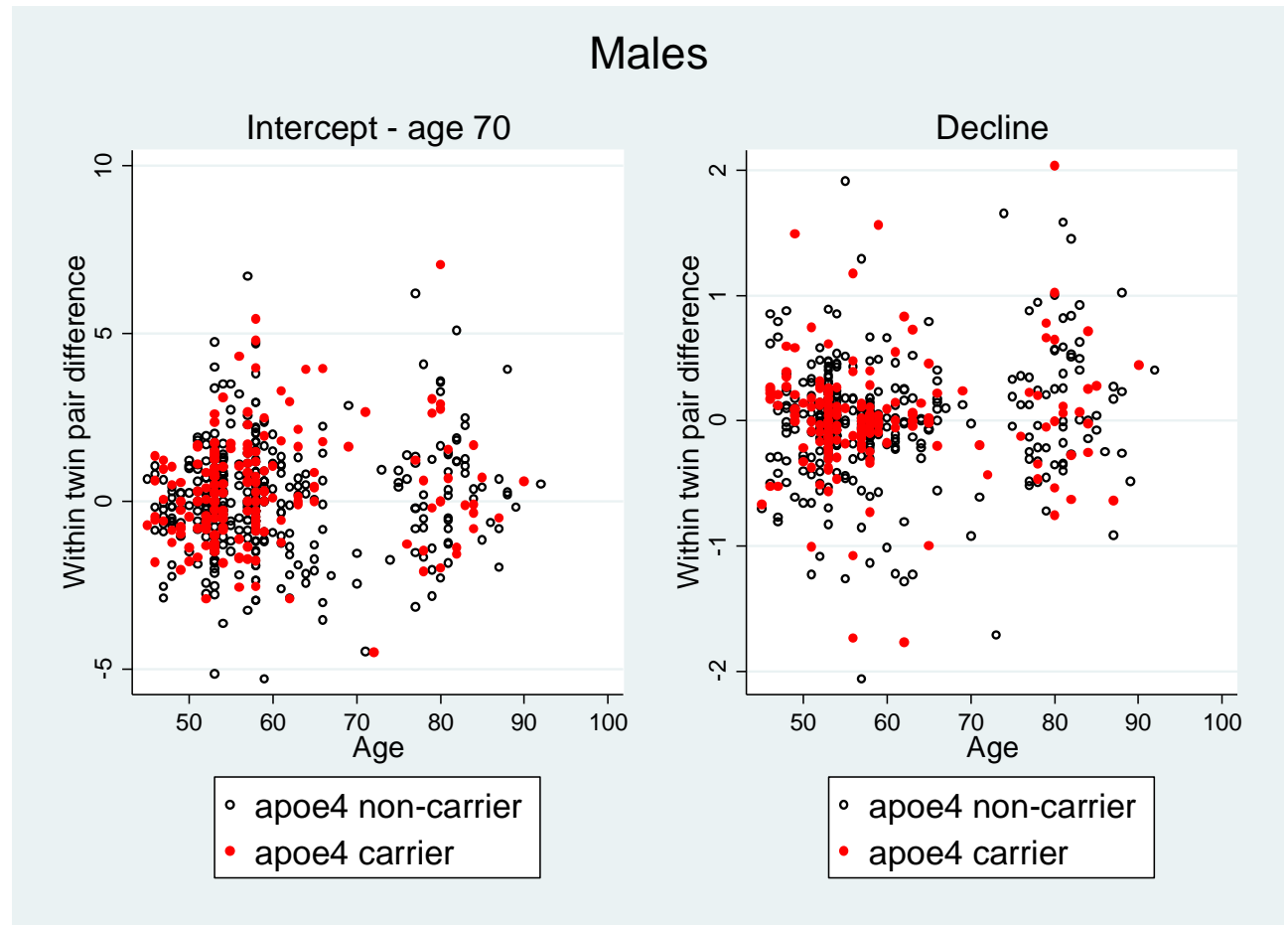
Less variability  
in APOE $\epsilon$ 2 carriers  
compared with  
non-carriers



# Within twin pair differences

- APOE $\epsilon$ 4

Similar variability  
in APOE $\epsilon$ 4 carriers  
and non-carriers



# Variance ratio test

- Males

	APOEε2				APOEε4			
	N-	N+	carrier/non-carrier	p-value	N-	N+	carrier/non-carrier	p-value
Intercept	531	107	0.94	0.69	434	204	1.04	0.71
Decline			0.71	<b>0.03</b>			1.06	0.64
<b>&lt;70</b>								
Intercept	460	83	0.79	0.19	367	176	1.00	0.99
Decline			0.42	<b>&lt;0.001</b>			1.13	0.32
<b>&gt;=70</b>								
Intercept	71	24	1.01	0.92	67	28	1.26	0.44
Decline			0.92	0.86			0.97	0.97

# Variance ratio test

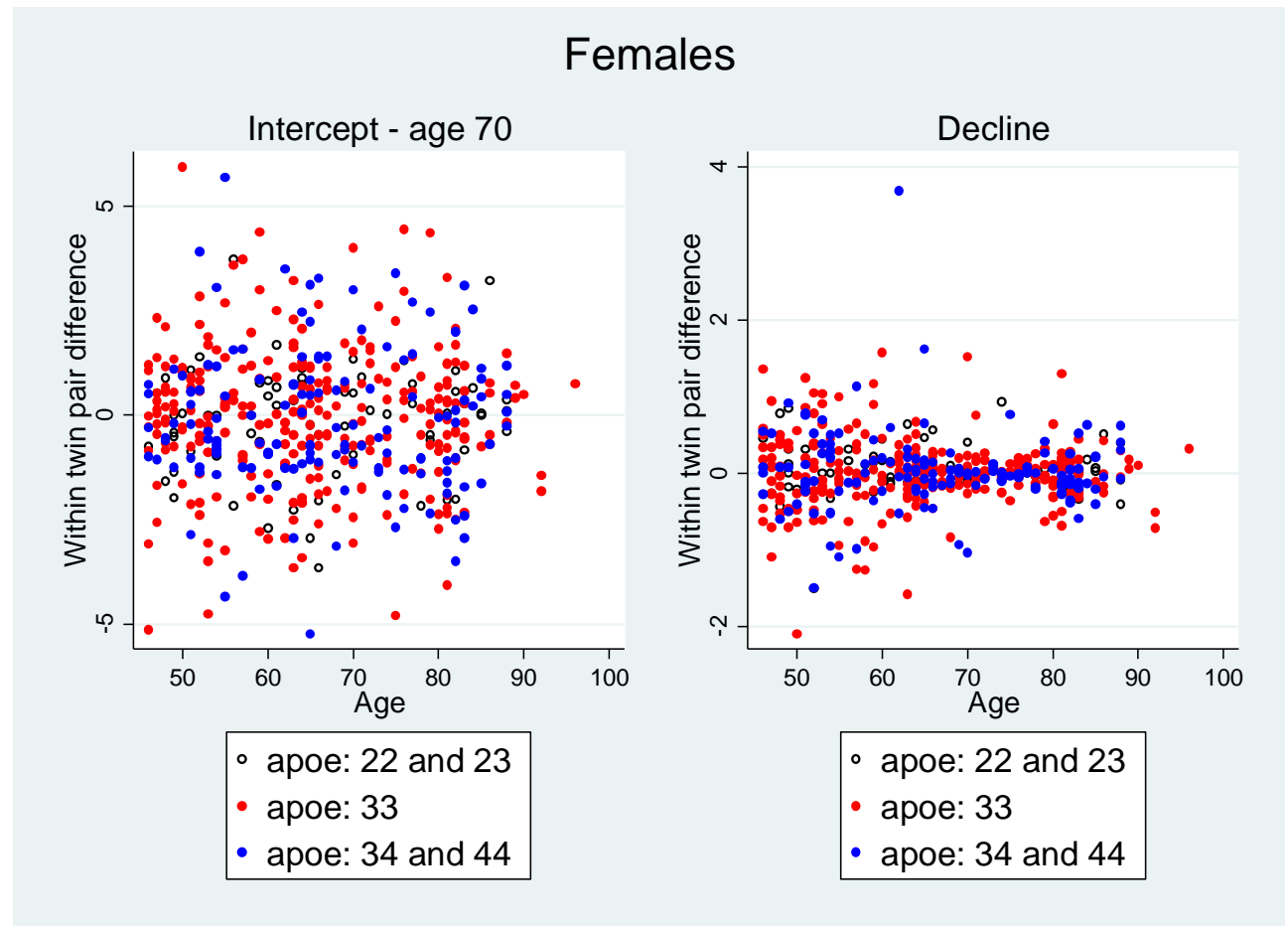
- Females

	APOEε2				APOEε4			
	N-	N+	carrier/non-carrier	p-value	N-	N+	carrier/non-carrier	p-value
Intercept	420	84	0.79	0.19	350	154	1.25	0.10
Decline			0.60	<b>&lt;0.01</b>			1.48	<b>&lt;0.01</b>
<b>&lt;70</b>								
Intercept	262	52	0.74	0.19	221	93	1.16	0.39
Decline			0.57	<b>0.02</b>			1.67	<b>&lt;0.01</b>
<b>&gt;=70</b>								
Intercept	158	32	0.67	0.68	129	61	1.40	0.11
Decline			0.78	0.41			0.91	0.69

# Within twin pair differences

- APOE $\epsilon$ 2/3/4

- Similar variability in APOE $\epsilon$ 3 and APOE $\epsilon$ 4 carriers
- Less variability in APOE $\epsilon$ 2 carriers



# Variance of APOEε2, APOEε3, and APOEε4 carriers

Genotype	Intercept - age 70		Decline	
	Variance	p-value*	Variance	p-value*
<b>MALES</b>				
APOEε22/ 23	2.38 (1.52-3.23)	0.74	0.17 (0.09-0.24)	<b>0.02</b>
APOEε33	2.70 (2.00-3.41)		0.34 (0.24-0.44)	
APOEε34/ 44	2.89 (2.09-3.70)		0.29 (0.18-0.40)	
<b>FEMALES</b>				
APOEε22/ 23	1.74 (1.06-2.42)	<b>0.05</b>	0.12 (0.04-0.19)	<b>&lt;0.001</b>
APOEε33	2.65 (2.13-3.17)		0.19 (0.14-0.25)	
APOEε34/ 44	2.95 (2.19-3.72)		0.27 (0.07-0.46)	

\* Bartlett's test

**NB: same trend but NOT statistically significant when outliers are removed**

# 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 $\epsilon$ 2 decreases variability of the decline of grip strength in males and females (age < 70 years)
- APOE $\epsilon$ 4 increases variability of the decline of grip strength in females (age < 70 years)



# Acknowledgements

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