Trade off between resistance and tolerance to gastrointestinal nematodes in sheep

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Acknowledgement

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Gastrointestinal nematodes in sheep

➢ *Teladorsagia circumcincta*

- Most common in different climates

- Reduced performance in sheep

➢ Anthelmintic treatment

- Risk of anthelmintic resistant worms

➢ Breeding could be an option

Response to infection

- Resistance
    - Reduce or eliminate the invading pathogen

- Tolerance
    - Reduce the damage caused by a given pathogen burden

Response to infection

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        - Measured as change in pathogen burden during a certain period of time

- Tolerance
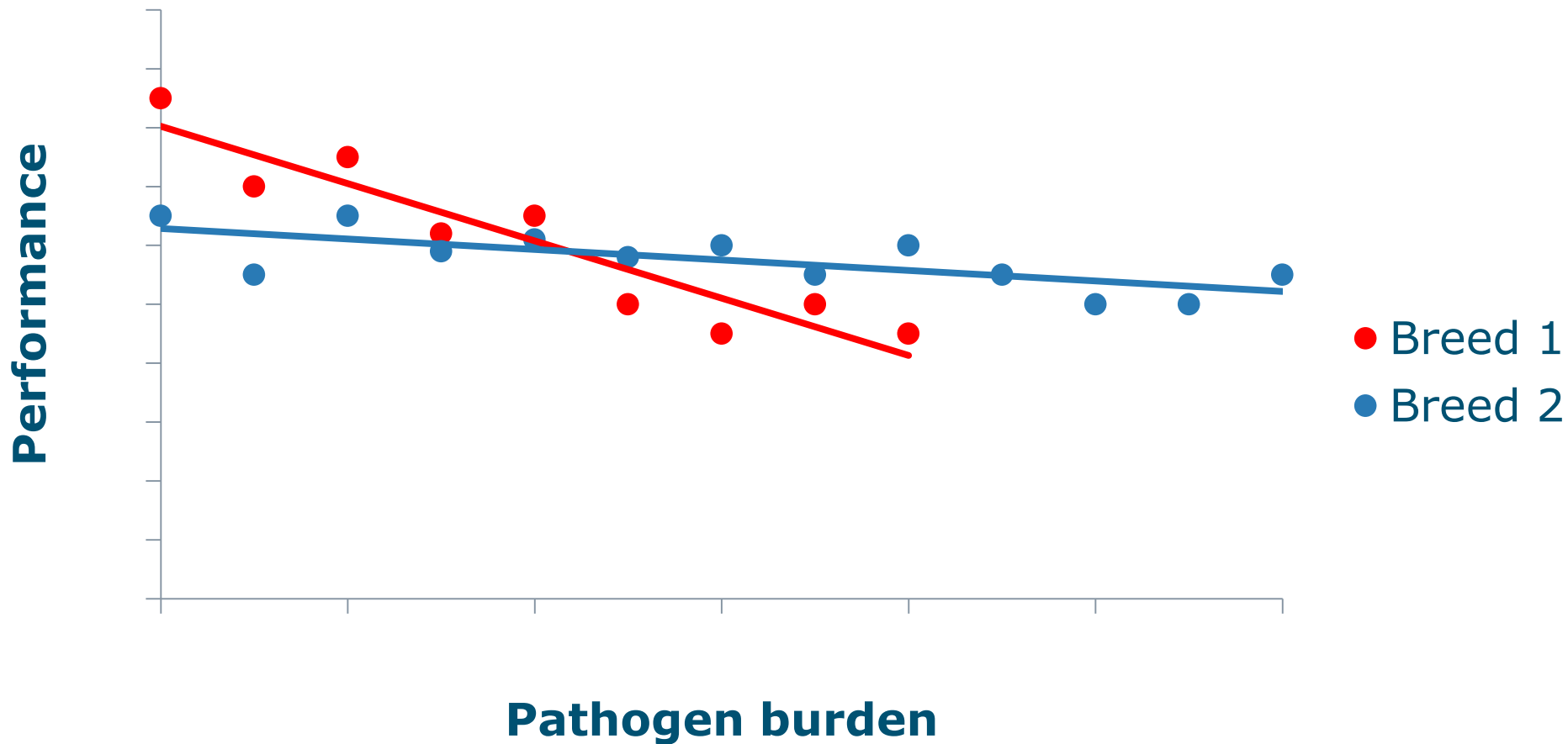   - Reduce the damage caused by a given pathogen burden
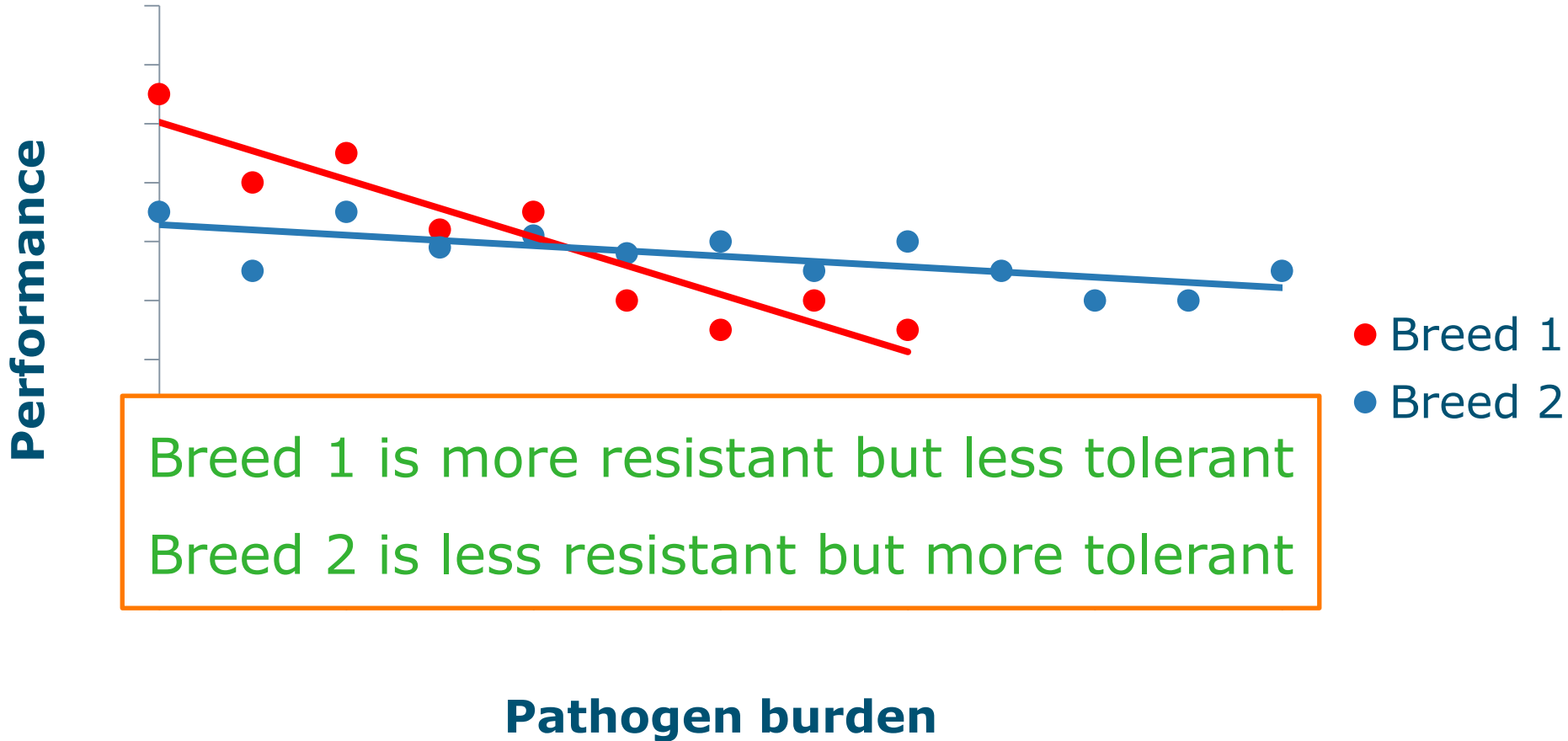
Response to infection

- Resistance
  - Reduce or eliminate the invading pathogen
    - Measured as change in pathogen burden during a certain period of time

- Tolerance
  - Reduce the damage caused by a given pathogen burden
    - Measured as reaction norm of performance on pathogen

Resistance vs. Tolerance

Performance

Pathogen burden

Breed 1
Breed 2

Resistance vs. Tolerance

Performance

Pathogen burden

● Breed 1
● Breed 2

Breed 1 is more resistant but less tolerant

Breed 2 is less resistant but more tolerant

Objectives

- Study tolerance as the reaction norm of lamb's body weight on faecal egg count

- Study genetic correlation between tolerance & resistance
  - Resistance indicators:
    - Faecal egg count ➔ Low resistance
    - IgA ➔ High resistance

Data

- Animals
  - Scottish Blackface sheep, commercial farm
    - 962 lambs
    - 30 sires x 380 dams
- Traits
  - Recorded at 5 months of age
    - Bodyweight (BW)
    - Faecal egg count (FEC)
    - IgA against nematodes

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FEC and IgA were log-transformed

Tolerance to nematode infection?

- Reaction norm of BW on FEC

$$BW = Xb + sire_{int} + sire_{sl} \times FEC + e$$

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Performance when FEC=0: Intercept

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Variation in slope ➜ Variation in tolerance

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Tolerance to nematode infection?

- Reaction norm of BW on FEC

$$BW = Xb + sire_{int} + sire_{sl} \times FEC + e$$

- Heterogeneous residual variance
  - Three levels of FEC (egg per gram)
    - Low (<50)
    - Medium (50-200)
    - High (>200)

Correlation between resistance and tolerance

- Bivariate analysis
  - Tolerance: reaction norm of BW on FEC
  - Resistance: sire effect on FEC and IgA

$$\begin{cases} \mathbf{BW} = \mathbf{Xb_1} + \mathbf{sire_{int}} + \mathbf{sire_{sl}} \times \mathbf{FEC} + \mathbf{e_1} \\ \\ \mathbf{FEC, IgA} = \mathbf{Xb_2} + \mathbf{sire} + \mathbf{e_2} \end{cases}$$

Results: Variance components of BW reaction norm on FEC

Source	Value
Intercept	1.77 (1.16)
Slope	0.09 (0.06)
Correlation	-0.85 (0.13)
Residual Low	11.60 (1.15)
Residual Medium	13.00 (1.27)
Residual High	15.36 (1.51)

➢ Intercept variance: Variation at zero FEC

➢ Slope variance: Variation in tolerance

> ➢ Likelihood ratio test (9.90) ➔ Significant slope ($P<0.01$)

➢ Negative correlation between intercept and slope: Higher BW at zero FEC ➔ Higher reduction of BW when FEC is high

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➢ Heterogeneous residual variance

   ➢ Residual variance increases by increasing FEC

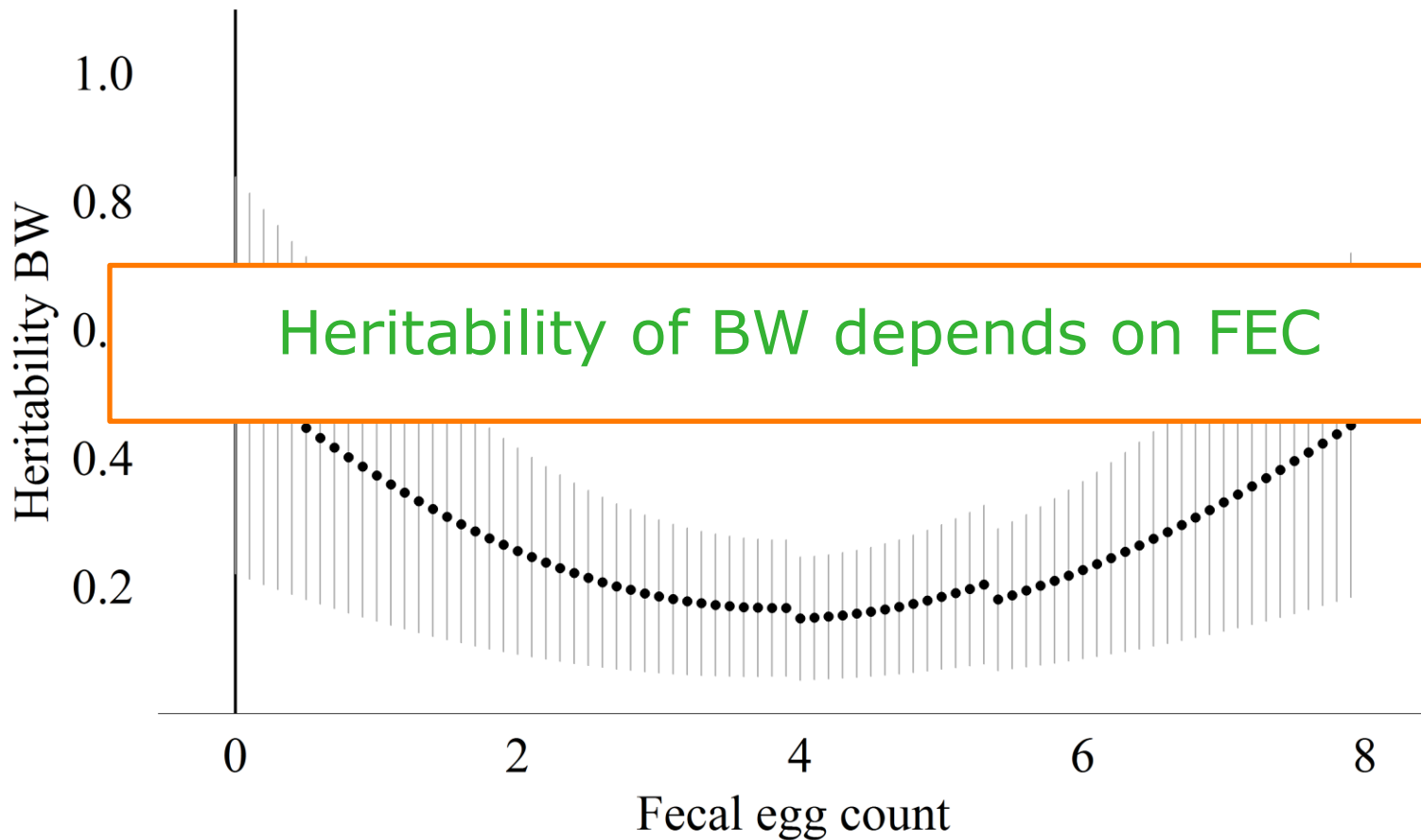WAGENINGEN UNIVERSITY
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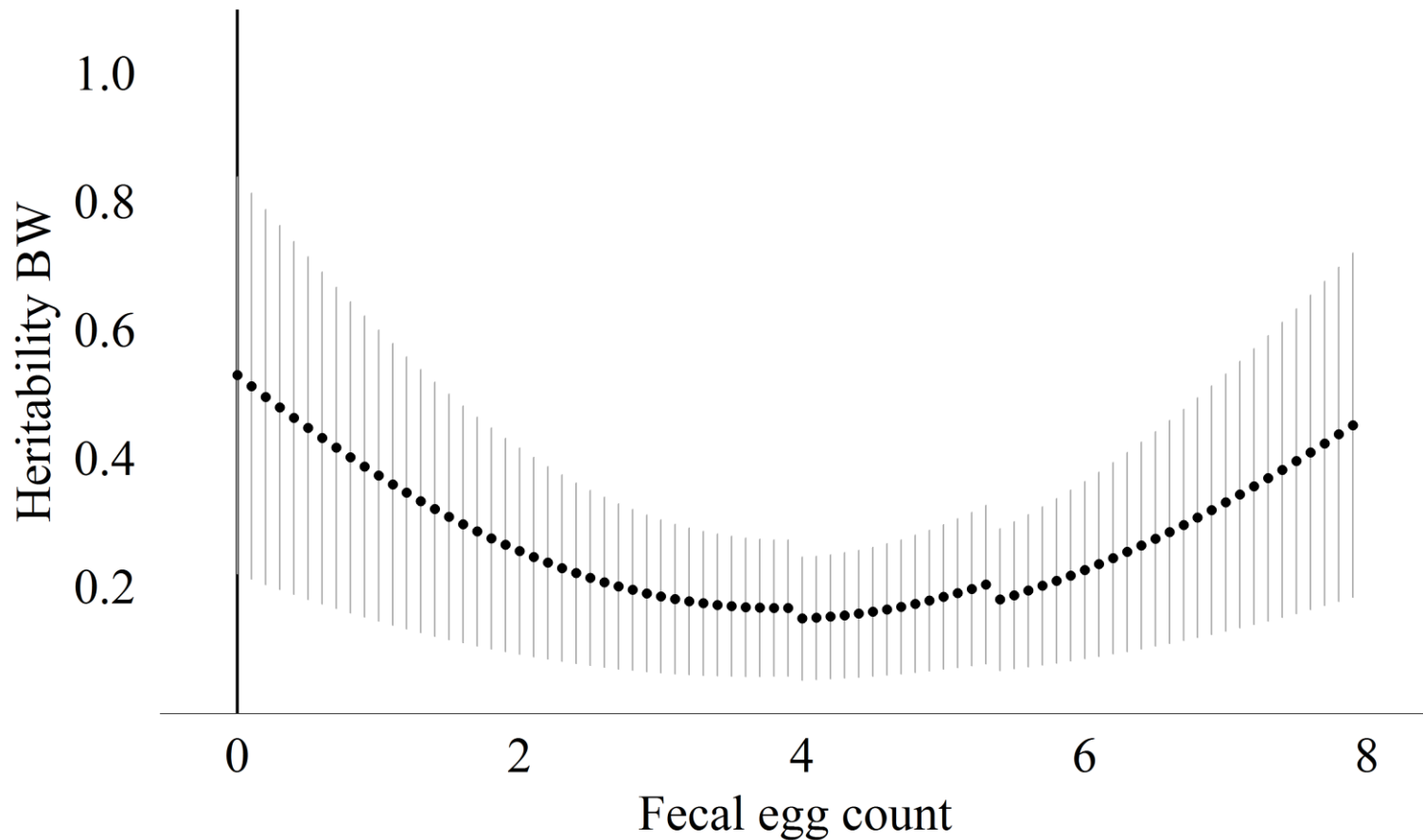
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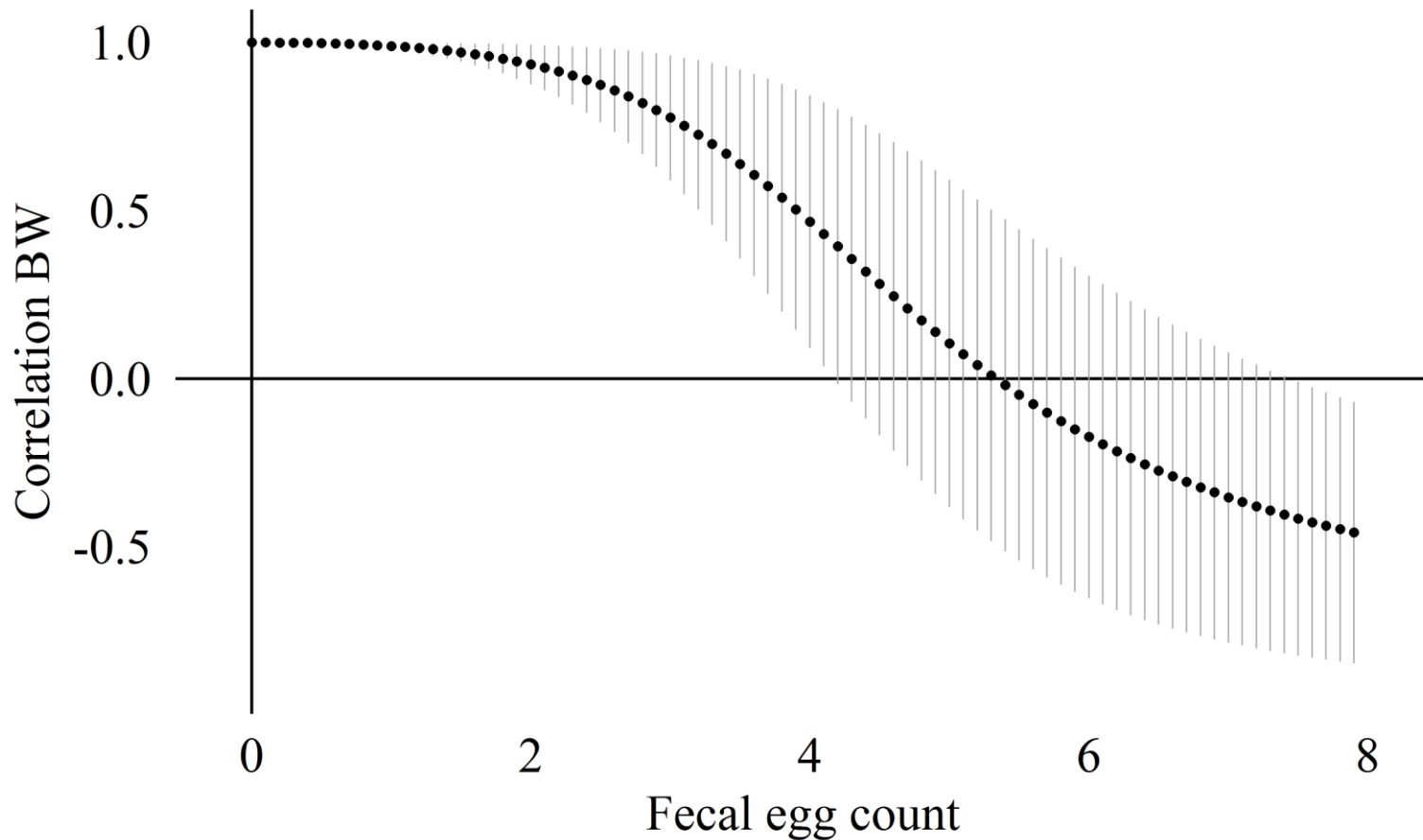

Heritability of BW depends on FEC

Results: Correlation at zero FEC with other levels of FEC

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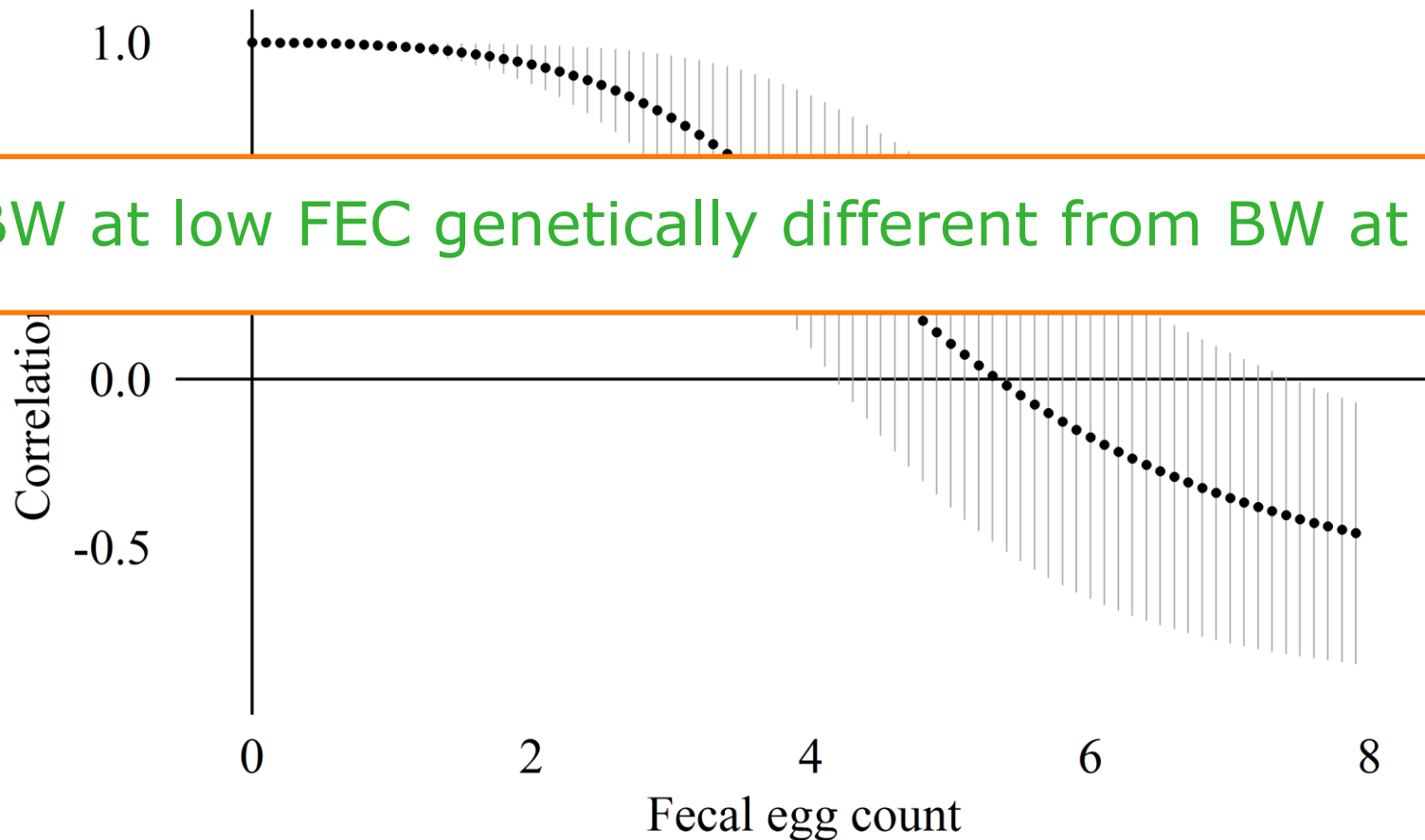
BW at low FEC genetically different from BW at high FEC

Results: Genetic correlation between resistance and tolerance

Resistance	Correlation	
	Intercept	**Slope**
FEC	-0.76 (0.32)	0.60 (0.33)
IgA	0.48 (0.32)	-0.63 (0.25)

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➢ **High BW at zero FEC ➔ High resistance (Low FEC)**

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➢ High BW at zero FEC ➡ High resistance (Low FEC)

➢ **High BW at zero FEC ➡ High resistance (High IgA)**

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FEC	-0.76 (0.32)	**0.60 (0.33)**
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➤ **Low resistance (High FEC) ➔ High tolerance**

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➢ Low resistance (High FEC) ➔ High tolerance

➢ **High resistance (High IgA) ➔ Low tolerance**

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High resistance = Low tolerance

Implication

↑ Resistance increase $1 \times \sigma_{A_{res}}$ = ↓ Tolerance decrease $0.60 \times \sigma_{A_{res}}$

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Resistance and tolerance should be put in selection index

Summary

- Significant genetic variation in tolerance

- Change of heritability of bodyweight across different levels of FEC

- Bodyweights at two extreme levels of nematode infection are genetically different traits

- Negative genetic correlation between resistance and tolerance

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Summary   Thank you!

- Significant genetic variation in tolerance

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Check the results from the reaction norm model: Trivariate analysis

$$\begin{bmatrix} \mathbf{BW}_l \\ \mathbf{BW}_m \\ \mathbf{BW}_h \end{bmatrix} = \begin{bmatrix} \mathbf{X}_l & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_m & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{X}_h \end{bmatrix} \begin{bmatrix} \mathbf{b}_l \\ \mathbf{b}_m \\ \mathbf{b}_h \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_l & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_m & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{Z}_h \end{bmatrix} \begin{bmatrix} \mathbf{a}_l \\ \mathbf{a}_m \\ \mathbf{a}_h \end{bmatrix} + \begin{bmatrix} \mathbf{e}_l \\ \mathbf{e}_m \\ \mathbf{e}_h \end{bmatrix}$$

FEC level	Low	Medium	High
Low	**0.39 (0.25)**	0.10 (0.30)	-0.17 (0.57)
Medium		**0.25 (0.21)**	0.51 (0.61)
High			**0.32 (0.22)**

Goodness of fit

- Akaike information criterion (AIC):

  ➢ Univariate mixed model

$$BW = Xb + sire + e$$

  ➢ Reaction norm model

$$BW = Xb + sire_{int} + sire_{sl} \times FEC + e$$

- Likelihood ratio test (LRT) between the models

Goodness of fit

Model	AIC	LRT	5% threshold
Univariate	2474.92		
		9.90	5.14
Reaction norm	2469.02		

➤ Reaction norm model fits better

➤ Models are significantly different

slope variance is significant

Implication

Correlated response

$$R_{tol,res} = r_g \frac{\sigma_{A_{tol}}}{\sigma_{A_{res}}} R_{res}$$

↑ Resistance increase $1 \times \sigma_{A_{res}}$ = ↓ Tolerance decrease $0.60 \times \sigma_{A_{res}}$