



EADGENE 


*From Infection to Inference:
 Interpreting animal health and disease data*



**Interpreting and Utilising Data
 Describing Nematode Infections**


Steve Bishop

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Aim of Talk

- Consider analysis & interpretation of nematode infection data
 - What are the biological properties?
 - What are the statistical properties?
 - Impact of properties on:
 - Experimental design
 - Disease control
 - Parasite evolution




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Indicator Traits

<u>Category</u>	
Level of infection	
Immune response	
'Pathology'	


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Indicator Traits

<u>Category</u>	<u>Example</u>
Level of infection	Worm burden FEC
Immune response	IgA, IgE, IgG Eosinophilia
'Pathology'	Pepsinogen Fructosamine Growth rate!


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Indicator Traits

<u>Category</u>	<u>Example</u>	<u>Factors</u>
Level of infection	Worm burden FEC	} Challenge + (Est., mort, fecund), Intake
Immune response	IgA, IgE, IgG Eosinophilia	
'Pathology'	Pepsinogen Fructosamine Growth rate!	} Worm burden, Immunity

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Dissecting FEC

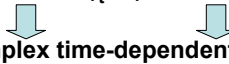
- $FEC_t \propto (\text{worm burden})_t \times (\text{worm fecundity})_t$

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Dissecting FEC

- $FEC_t \propto (\text{worm burden})_t \times (\text{worm fecundity})_t$

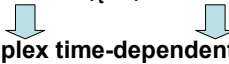

 complex time-dependent traits

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Dissecting FEC

- $FEC_t \propto (\text{worm burden})_t \times (\text{worm fecundity})_t$


 complex time-dependent traits

$$F = \left(\frac{F_{\max} \cdot (f_i \cdot PRQ_{imm})^2}{(f_i \cdot PRQ_{imm})^2 + (PAC_{imm} \cdot \sum L_i^*)^2} \right) + F_{\min}$$

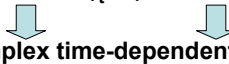
$$\epsilon = \left(\epsilon_{\max} \cdot e^{-K_i \left(\frac{PAC_{imm}}{PRQ_{imm}} \right) \sum L_i^*} \right) + \epsilon_{\min} \quad \mu = \left(\frac{\mu_{\max} \cdot (PAC_{imm} \cdot \sum L_i^*)^2}{(PRQ_{imm} \cdot mi)^2 + (PAC_{imm} \cdot \sum L_i^*)^2} \right) + \mu_{\min}$$

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Dissecting FEC

- $FEC_t \propto (\text{worm burden})_t \times (\text{worm fecundity})_t$


 complex time-dependent traits

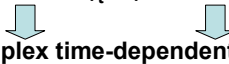
- Genetic consequence:
 - Many genes likely to be involved
 - “Confirmed” by difficulty of QTL studies

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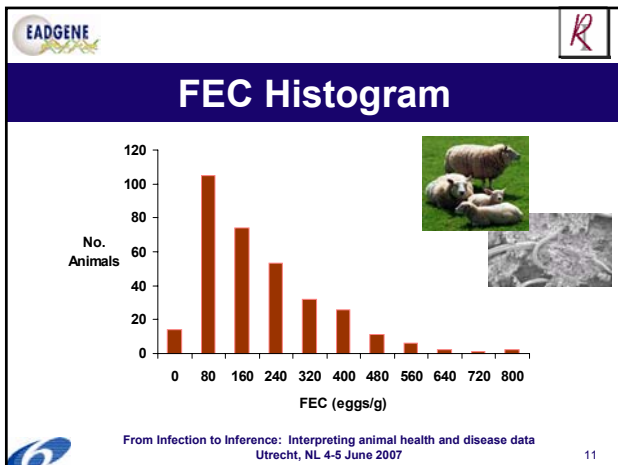
Dissecting FEC

- $FEC_t \propto (\text{worm burden})_t \times (\text{worm fecundity})_t$


 complex time-dependent traits

- Genetic consequence:
 - Many genes likely to be involved
- Statistical consequence:
 - Fecundity ~ Poisson
 - Worm burden ~ variable (e.g. exponential)
 - FEC ~ Negative Binomial

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Dissecting FEC Further

- Observed FEC = multiplicative trait

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Dissecting FEC Further

- Observed FEC = multiplicative trait
- $\text{Log}(\text{FEC}) = \text{Genotype} + \text{Environment}$

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Dissecting FEC Further

- Observed FEC = multiplicative trait
- $\text{Log}(\text{FEC}) = \text{Genotype} + \text{Environment}$

Permanent E. immune memory Temporary E. fluctuations in challenge True residual measurement error

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Dissecting FEC Further

- $\text{Log}(\text{FEC}) = g + \text{perm.}_e + \text{temp.}_e + \text{error}$

25%
5%
40%
30%

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Dissecting FEC Further

- $\text{Log}(\text{FEC}) = g + \text{perm.}_e + \text{temp.}_e + \text{error}$
- Genetic correlation of FEC over time:

25%
5%
40%
30%

Week

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Dissecting FEC Further

- $\text{Log}(\text{FEC}): \text{Genetics} + \text{Perm. E.} = 30\%$
 - Trait poorly correlated across time
 - EVEN if underlying genetics constant

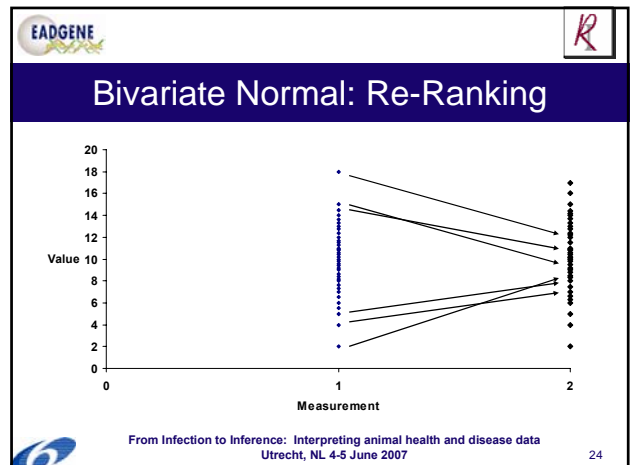
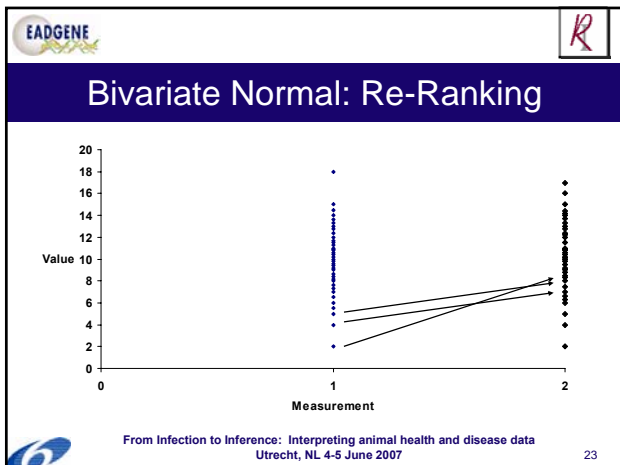
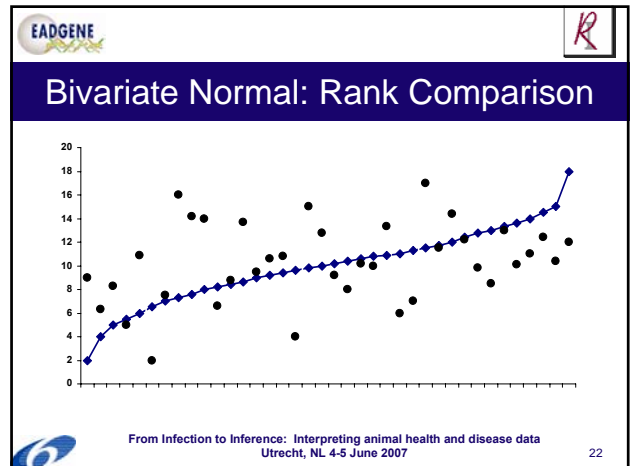
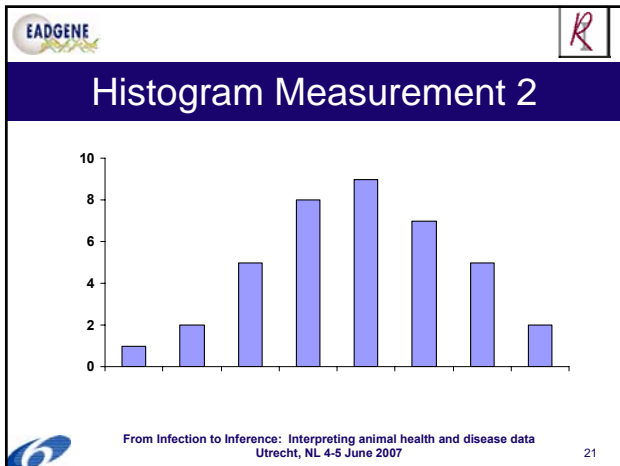
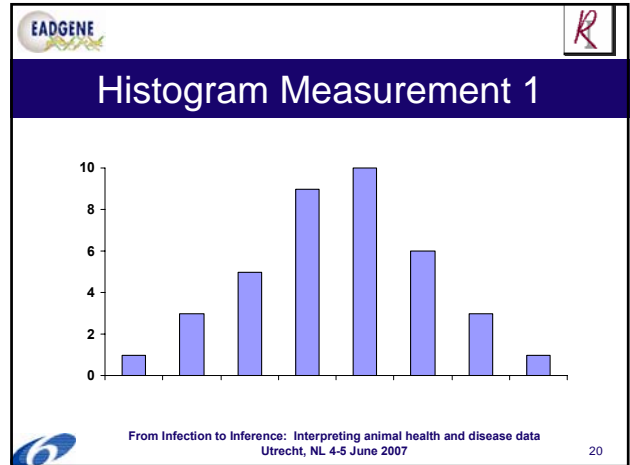
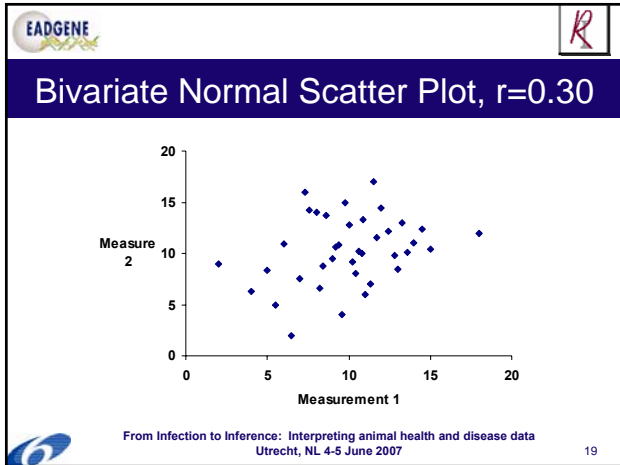
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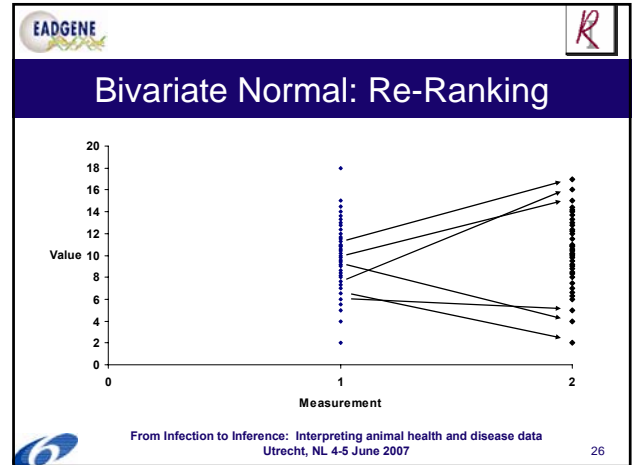
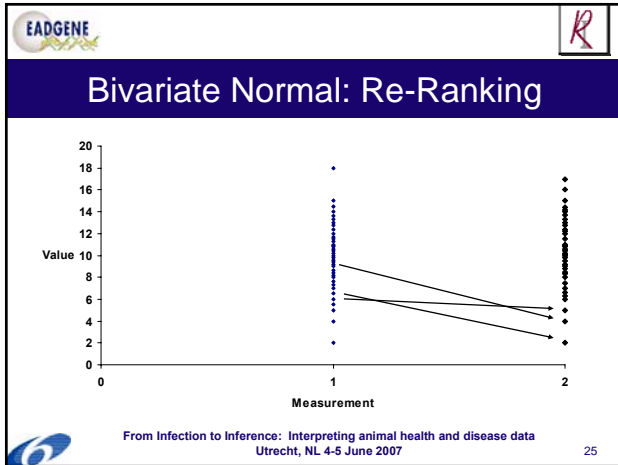
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Dissecting FEC Further

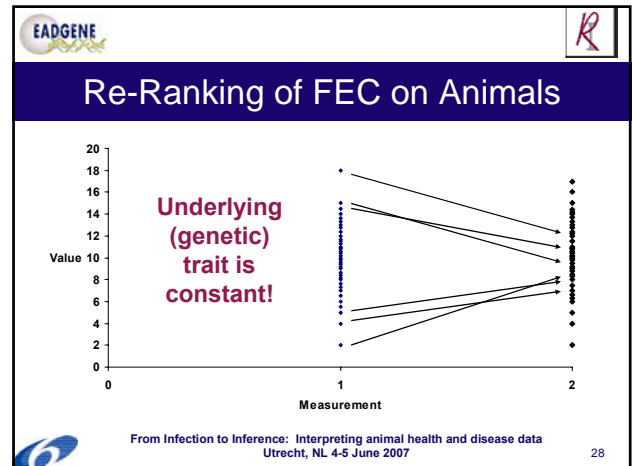
- $\text{Log}(\text{FEC}): \text{Genetics} + \text{Perm. E.} = 30\%$
 - Trait poorly correlated across time
 - EVEN if underlying genetics constant
 - APPARENT re-ranking of animals
 - *** Warning! ***
- $\text{Log}(\text{FEC}): \text{very variable}$
 - *** Warning! ***

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- FEC Statistical Consequences**
- FEC is variable**
 - Avoid small experimental sample sizes
 - Results will be non-reproducible!
 - $R \sim 0.3 \rightarrow$ experiments on selected extremes will disappoint
 - At time 2, 'extreme' animals are not extreme!
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- Simple Statistical Solutions**
- Don't do little experiments!
 - Design with CV (trait) of 100%
 - Replicate measurement
 - To assess ascertainment error
 - Replicate over time
 - To assess permanent environ & genetic correl'n
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- Simple Statistical Solutions**
- Don't do little experiments!
 - Design with CV (trait) of 100%
 - Replicate measurement
 - To assess ascertainment error
 - Replicate over time
 - To assess permanent environ & genetic correl'n
 - Genetic studies
 - more animals > more measures per animal
 - Epidemiological studies
 - Balance animals vs. measure per animal
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