# Implementing genomic selection in livestock species

Julius van der Werf

*CRC for Sheep Industry Innovation*
*School of Environmental and Rural Science, UNE, Armidale, NSW*

# Outline

1. Potential benefits of genomic selection in breeding programs

2. Can we predict the accuracy of genomic selection?

3. What information is needed for accurate predictions?

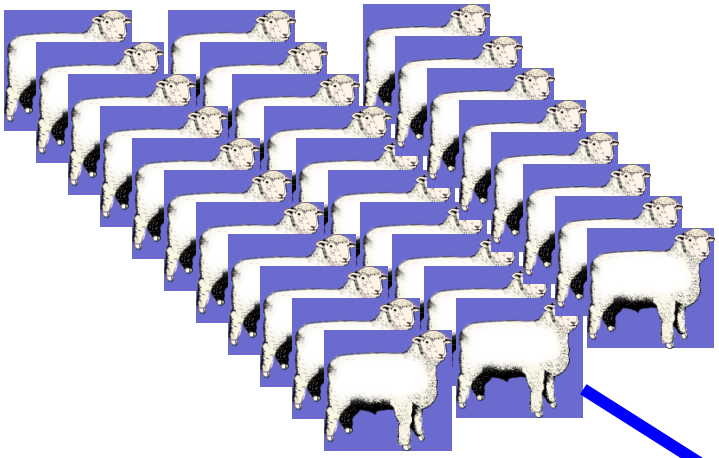
4. Requirements for the reference population

   how large, how related, how long-lasting, multi-breed?

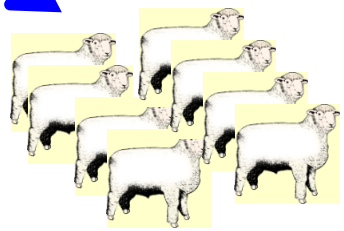
5. Strategies for genotyping

   low density chips, high density chips, sequence data?

# Genomic Prediction: basic idea



1) Somebody (else) measures lots of sheep, and their DNA
→ Reference population



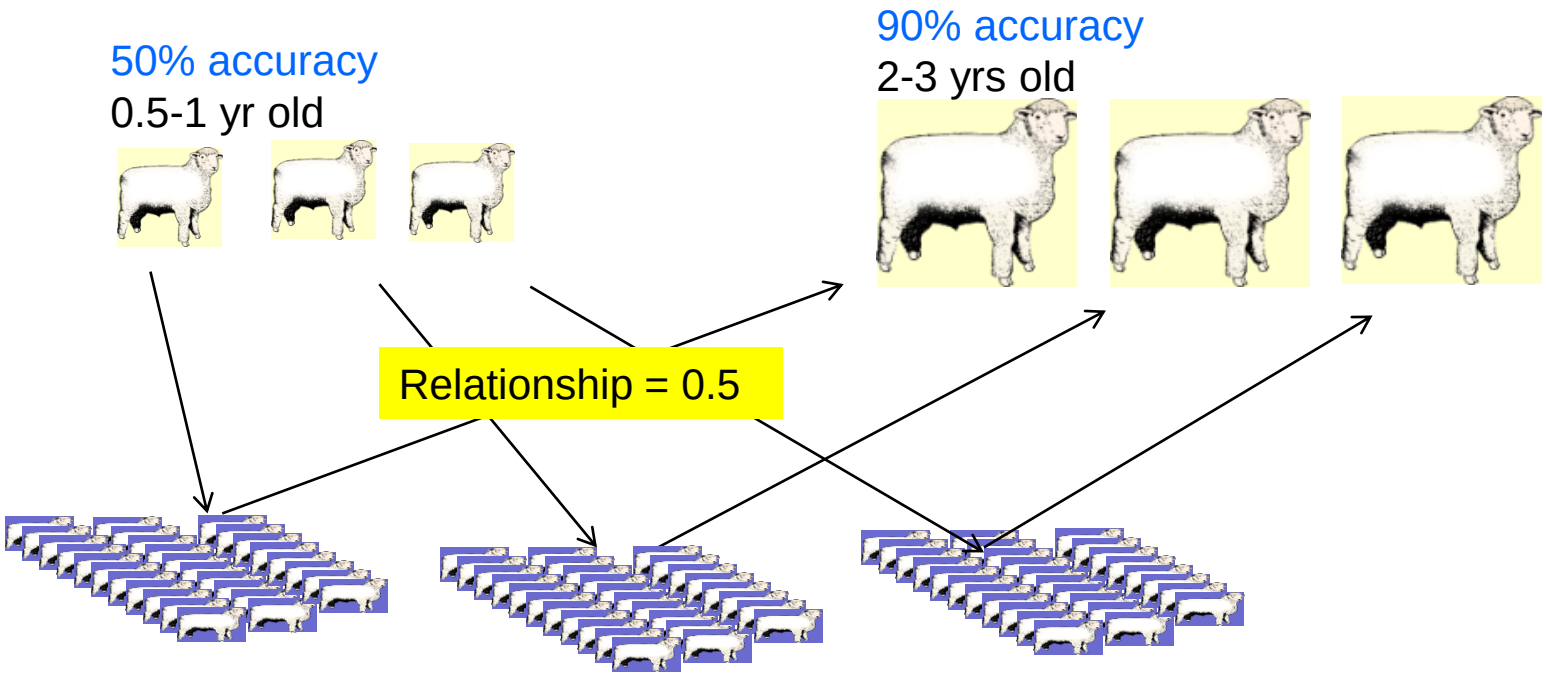
2) A breeder tests DNA on young rams

Prediction from DNA → genomic breeding values - GBV

GBV + Current ASBV → Improved ASBV

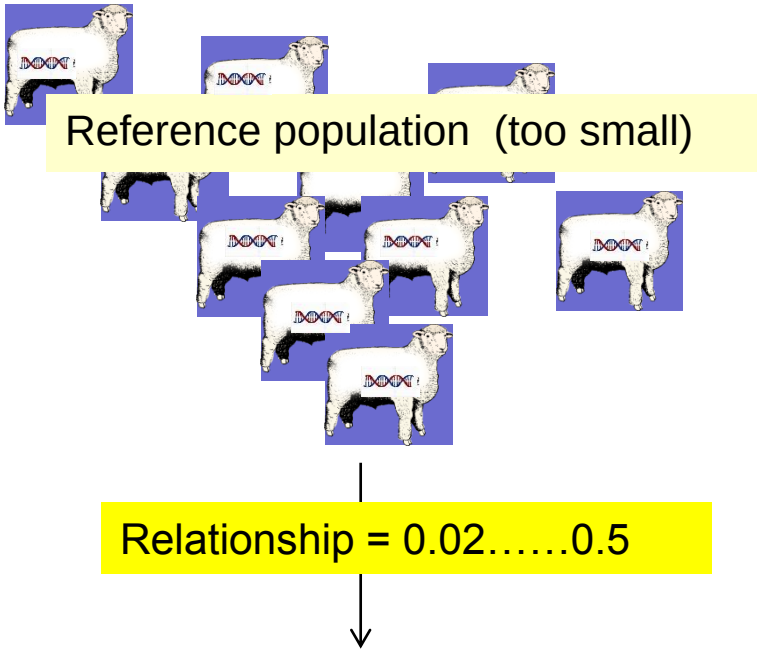
Merit depends on trait measurability

# Compare: Progeny Testing



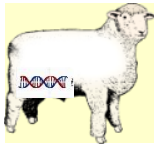

Each progeny group only informs one sire

# Genomic Testing

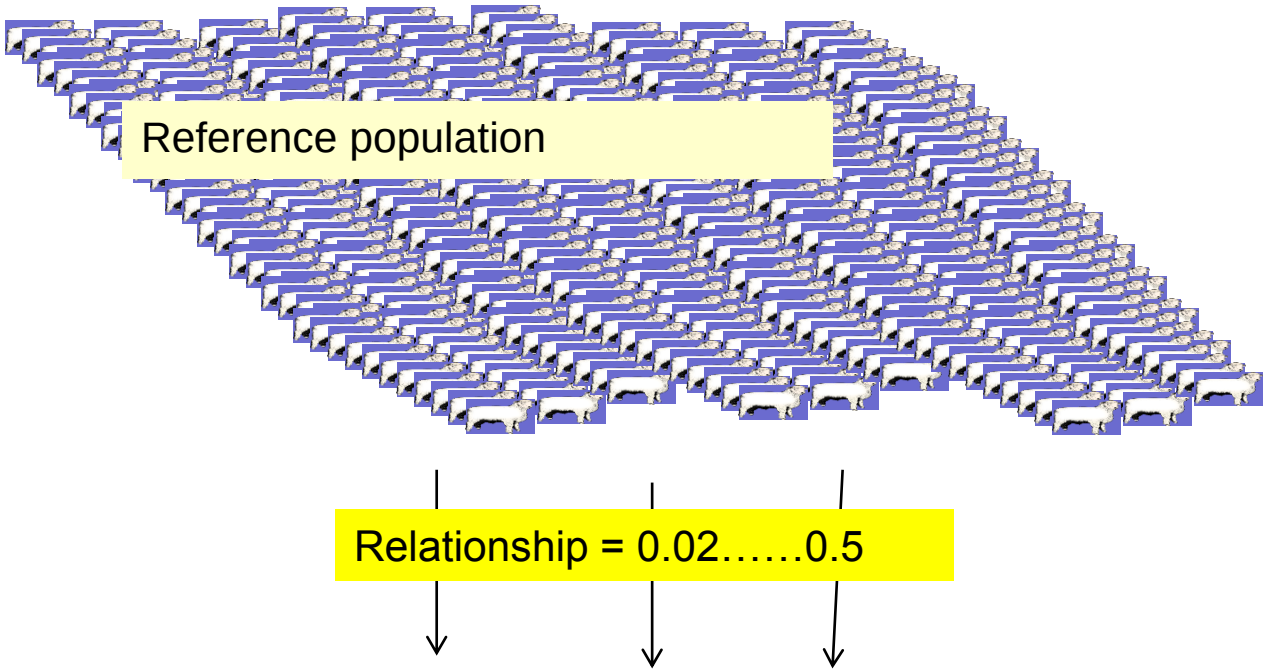



use information on “relatives” while sire is still young

51% accuracy
0.5-1 yrs old

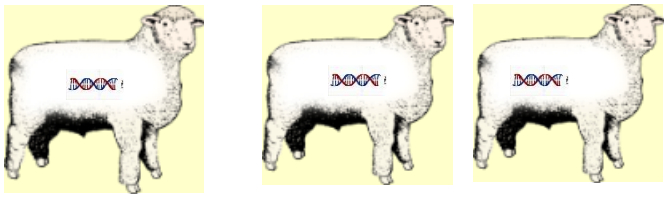


# Genomic Testing




70% accuracy

0.5-1 yrs old



# Summarizing Genomic Prediction

## - What information is used?

- Based on very many small – genomic- relationships
- Does not require ‘direct relatives’ to be tested
- Can be based on distant relatives ‘some generations away’
- …..but the number of small relatives needs to be large (thousands)
- Can not predict across breed

# Setting up reference populations

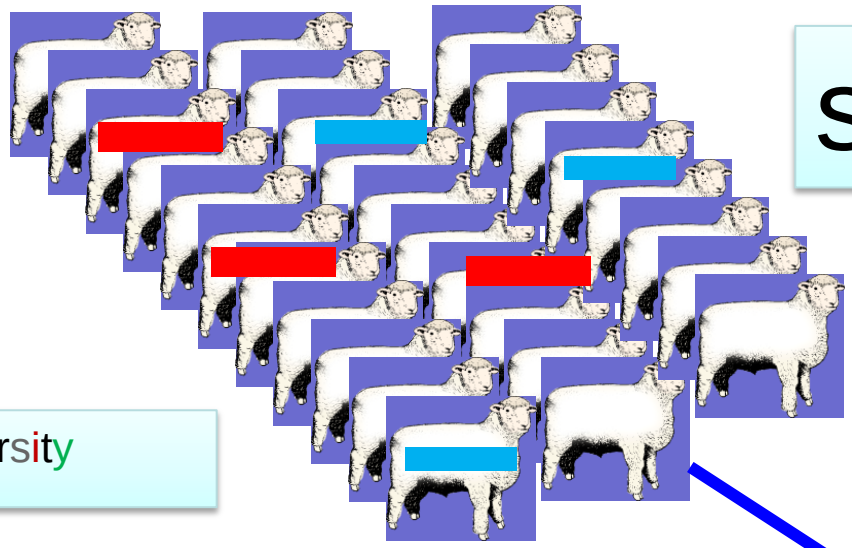
| Trait is already measured | Early measurement | Late Measurement |
|---|---|---|
| YES | No Need | Use industry data (milk, fertility, late wool) |
| NO | Create Reference population (slaughter) | Create Reference population |

Genomic selection has affected the need for phenotyping !

more…not less

Who pays?

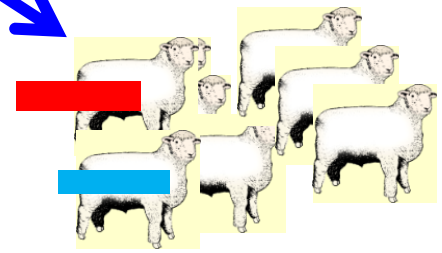
# Design of reference populations



size

diversity

relatedness



Select on impact → merit

→ diversity

Multi-breed
Across breed?
Longevity of RefPop?

# Outline: Sheep Genomic Analysis

- What information is used?
- How useful is this information?
- How to use it?

# Genomic Selection: Benefit

Overall:

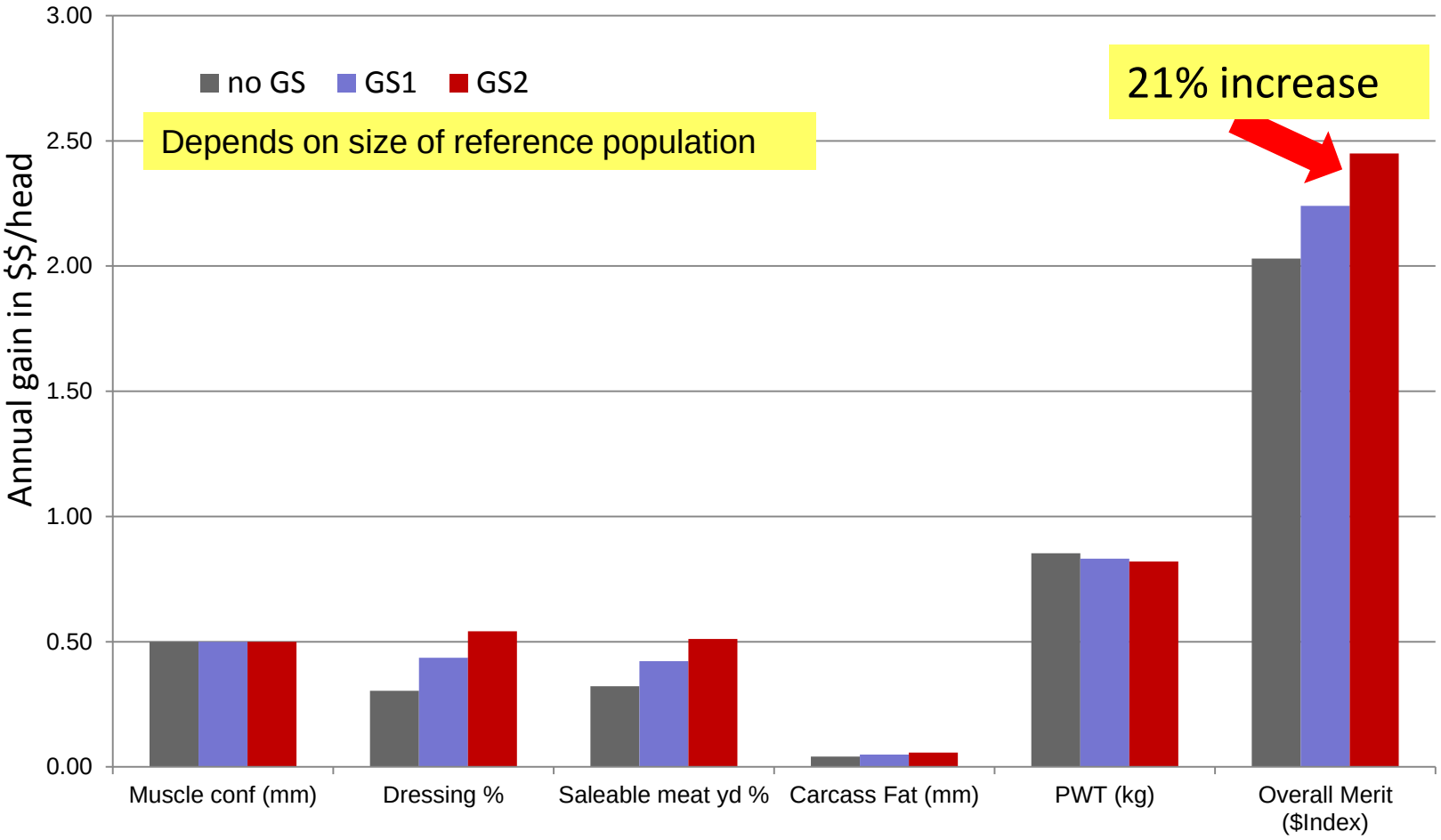
More accurate prediction of genetic merit for breeding objective

Specific:

Traits that are usually difficult to improve

- difficult or expensive to measure
- can not be measured early
- low heritability

# Possible Benefits



# Modeling genomic selection in breeding programs

1. Selection index approach: multiple information, multiple traits

   Accuracy component

2. Optimizing selection across age classes

   Generation Interval component

3. For specific breeding objectives

# Percent increase in rate of genetic gain when using genomic selection

Selection on a single trait

Predicted accuracy of Molecular EBV = 55% *(VQTL=30%)*

| Trait Measurability | Heritability | |
|---|---|---|
| | 0.10 | 0.50 |
| Measured < 1 year, males and female | 37 | 6 |
| Measured > 1 year, males and females | 64 | 18 |
| Measured >1 year, females only | 109 | 39 |
| Measured on Correlated Trait, Genetic Correlation = 0.9 | 48 | 11 |
| Measured on Correlated Trait, Genetic Correlation = 0.5 | 143 | 62 |

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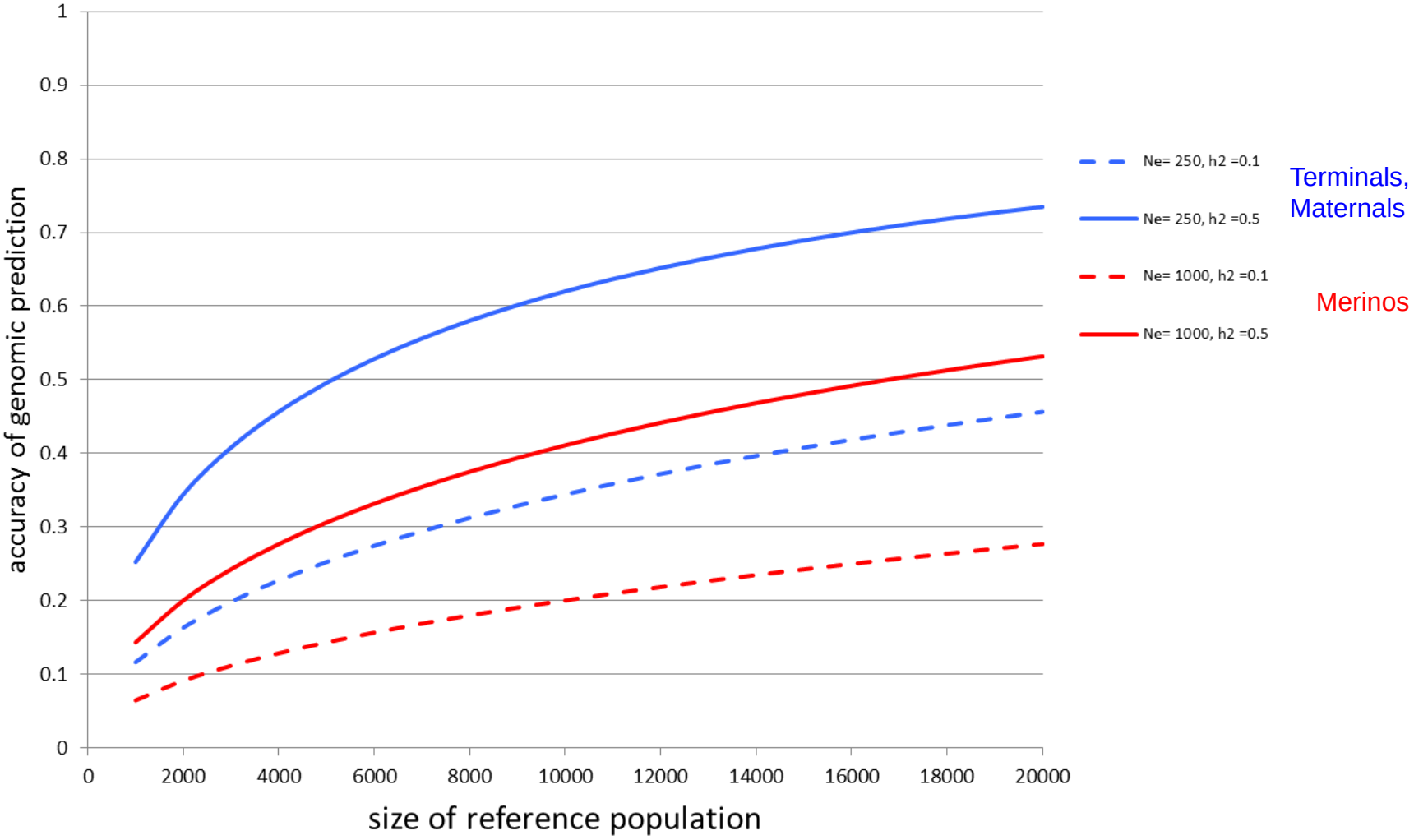
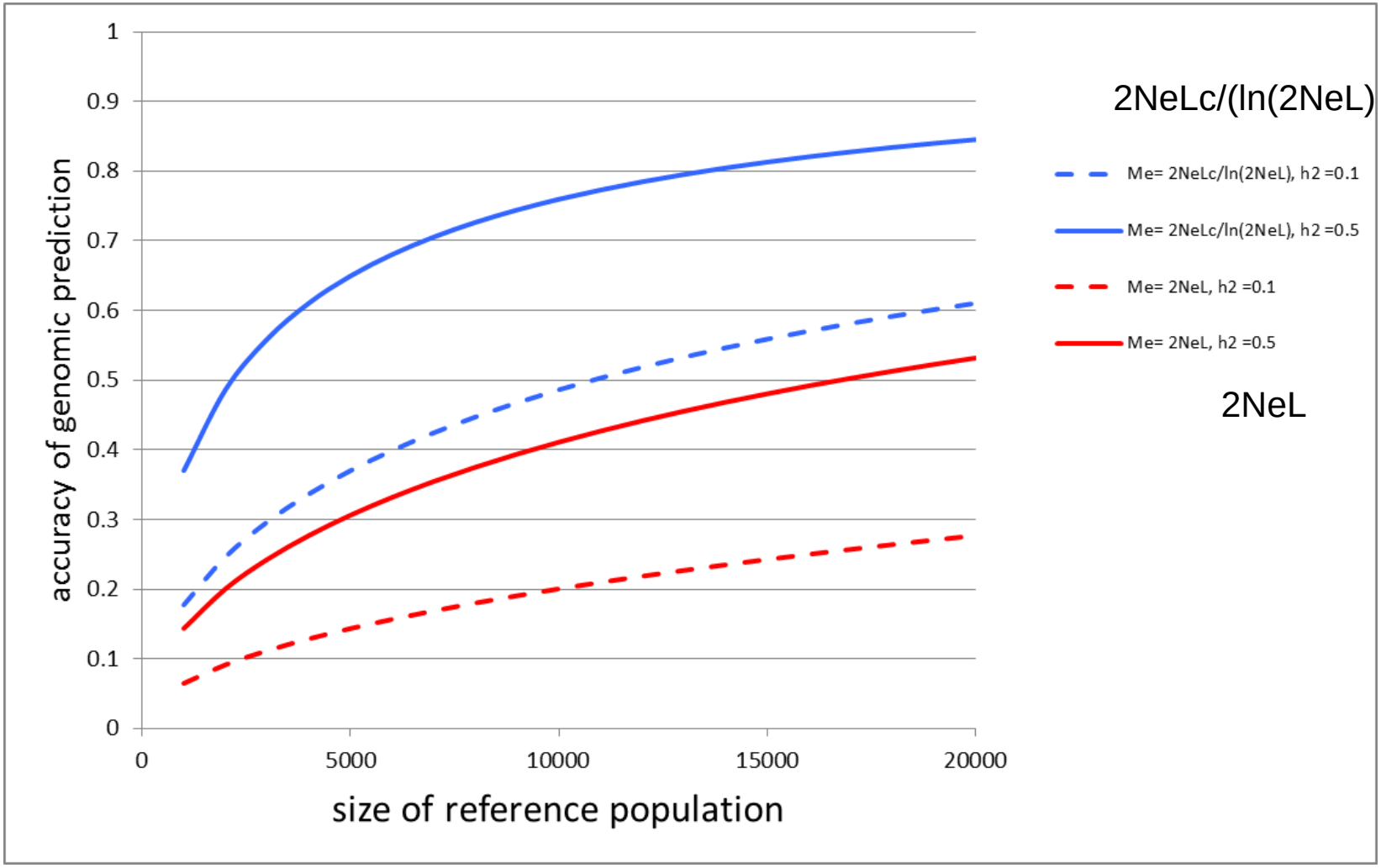
# Accuracy of genomic prediction depending on size of reference population

*Goddard 2009*



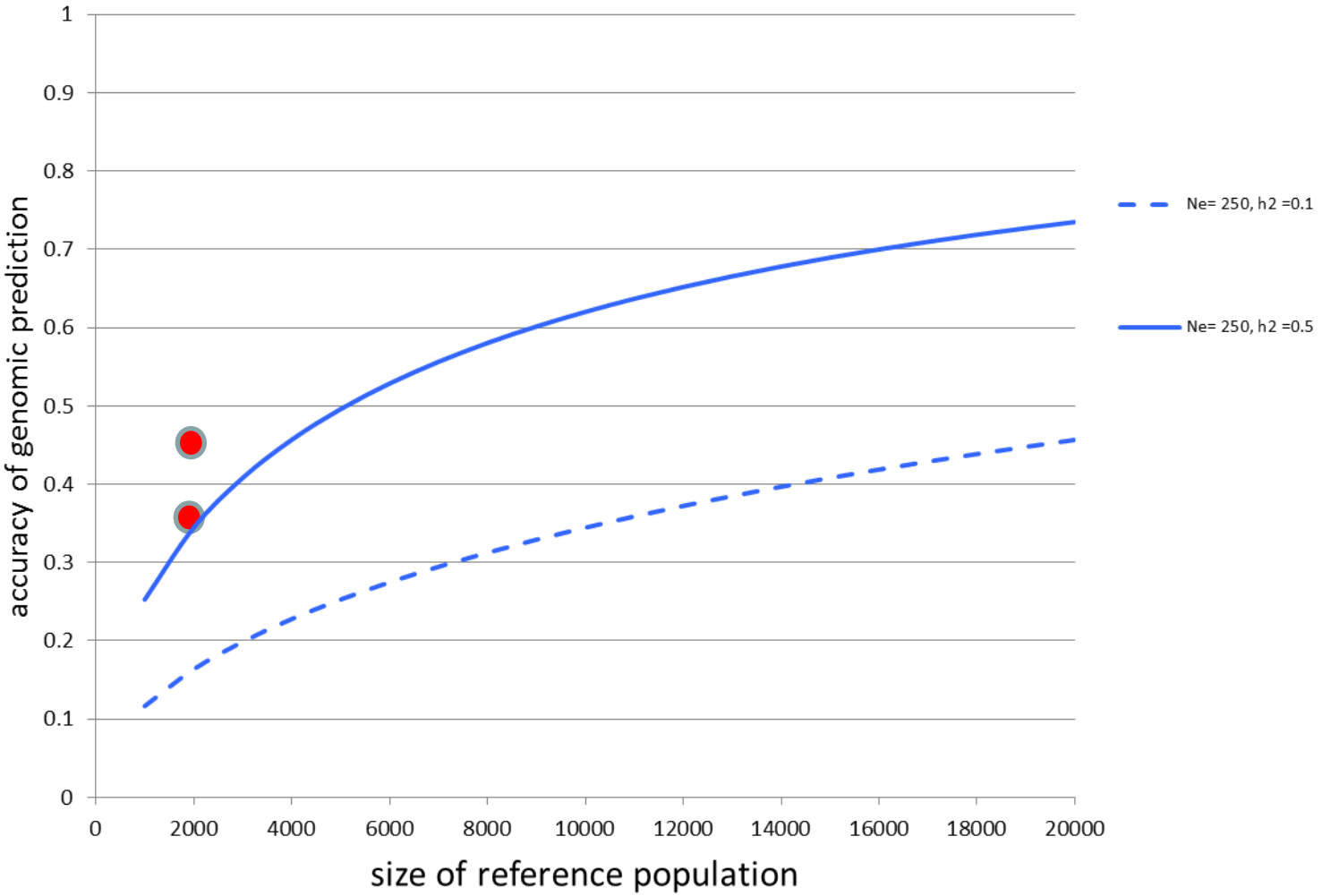
# Accuracy, depending on how Me is approximated



# design of reference population

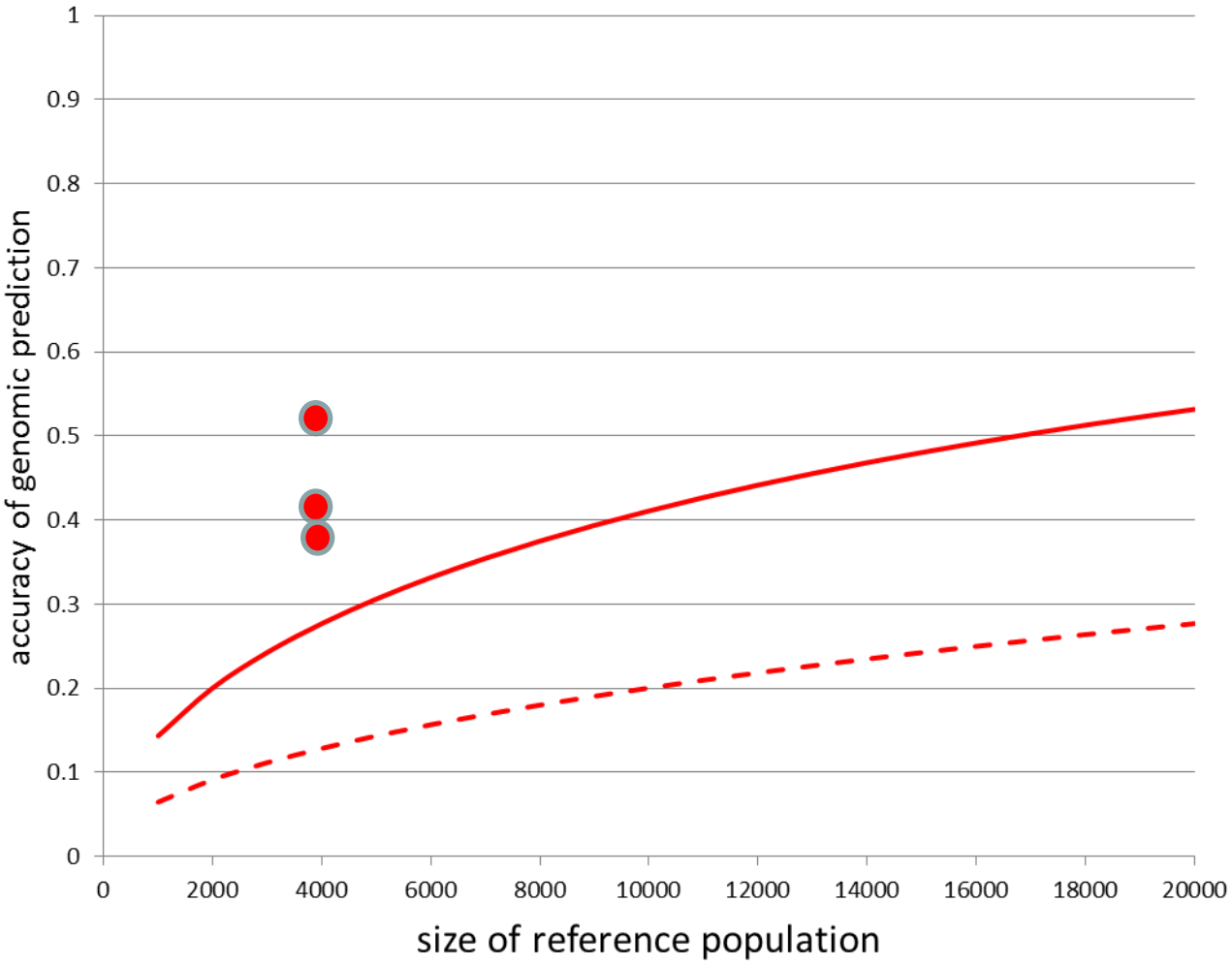
- Relatedness between reference population and selection candidates
- Across breeds or lines?
- Number of sires, nr of progeny per sire, which dams?

# Realized accuracy 1




Terminals,
Maternals

# Realized accuracy 2




Merino

# Accuracy of genomic prediction for Post Weaning Weight from a mixed breed reference population

| Reference population | | GEBV accuracy | |
|---|---|---|---|
| | | G1 | |
| **Type** | **Size** | **BL** | **Merino** |
| (1) = Merino | 1000 | -0.02 [a] | 0.53 [b] |
| (2) = Merino | 2000 | -0.04 [a] | 0.57 [bc] |
| (3) = Merino | 3000 | -0.08 [a] | 0.59 [c] |
| BLxMerino | 1514 | 0.49 [c] | 0.45 [a] |
| BLxMerino + (1) | 2514 | 0.42 [bc] | 0.56 [bc] |
| BLxMerino + (2) | 3514 | 0.37 [b] | 0.54 [bc] |
| BLxMerino + (3) | 4514 | 0.36 [b] | 0.56 [bc] |

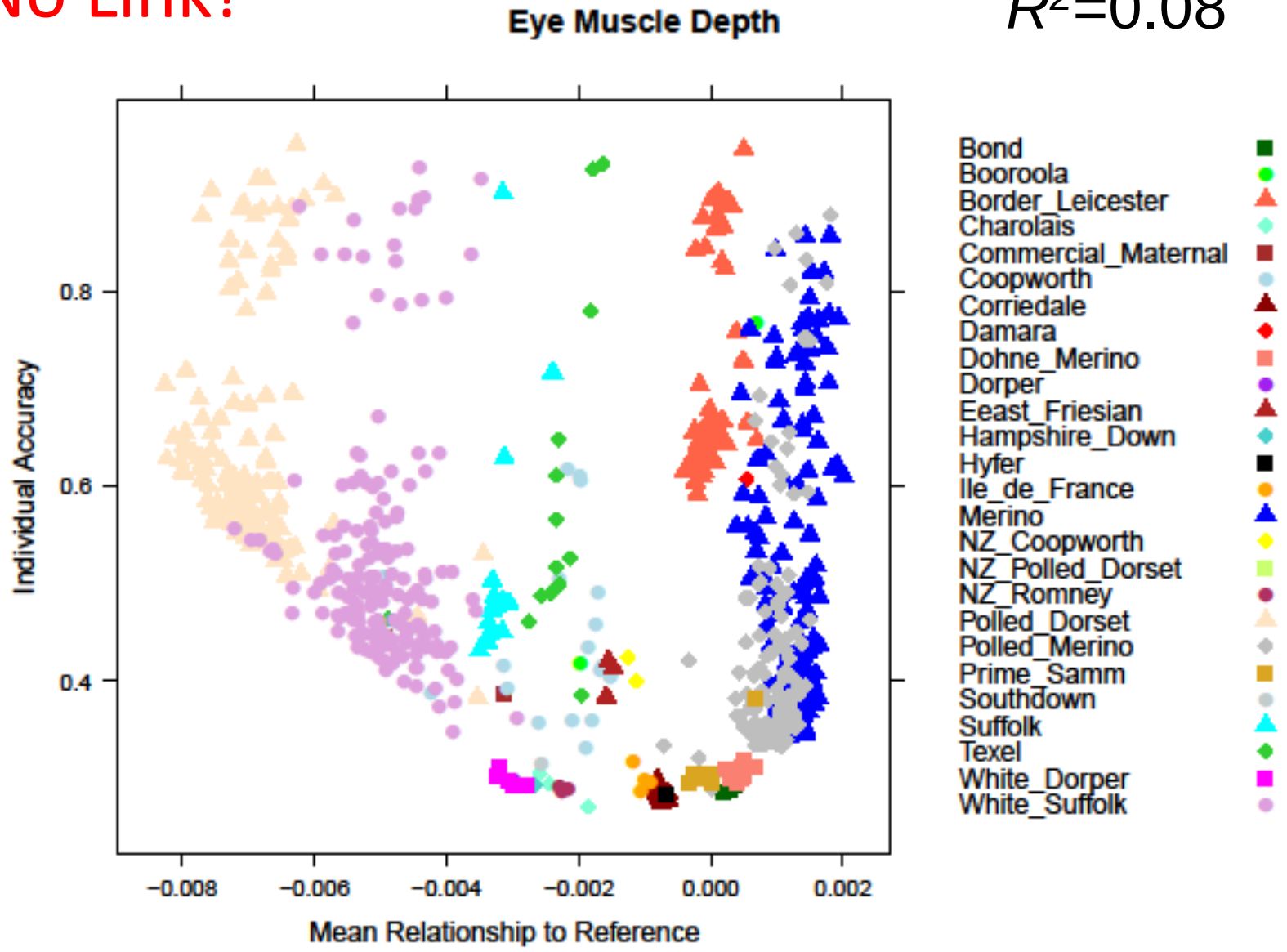
Moghaddar, van der Werf and Swan, 2013 AAABG)

une

# Accuracy and Mean Relationship to Ref

→ No Link!

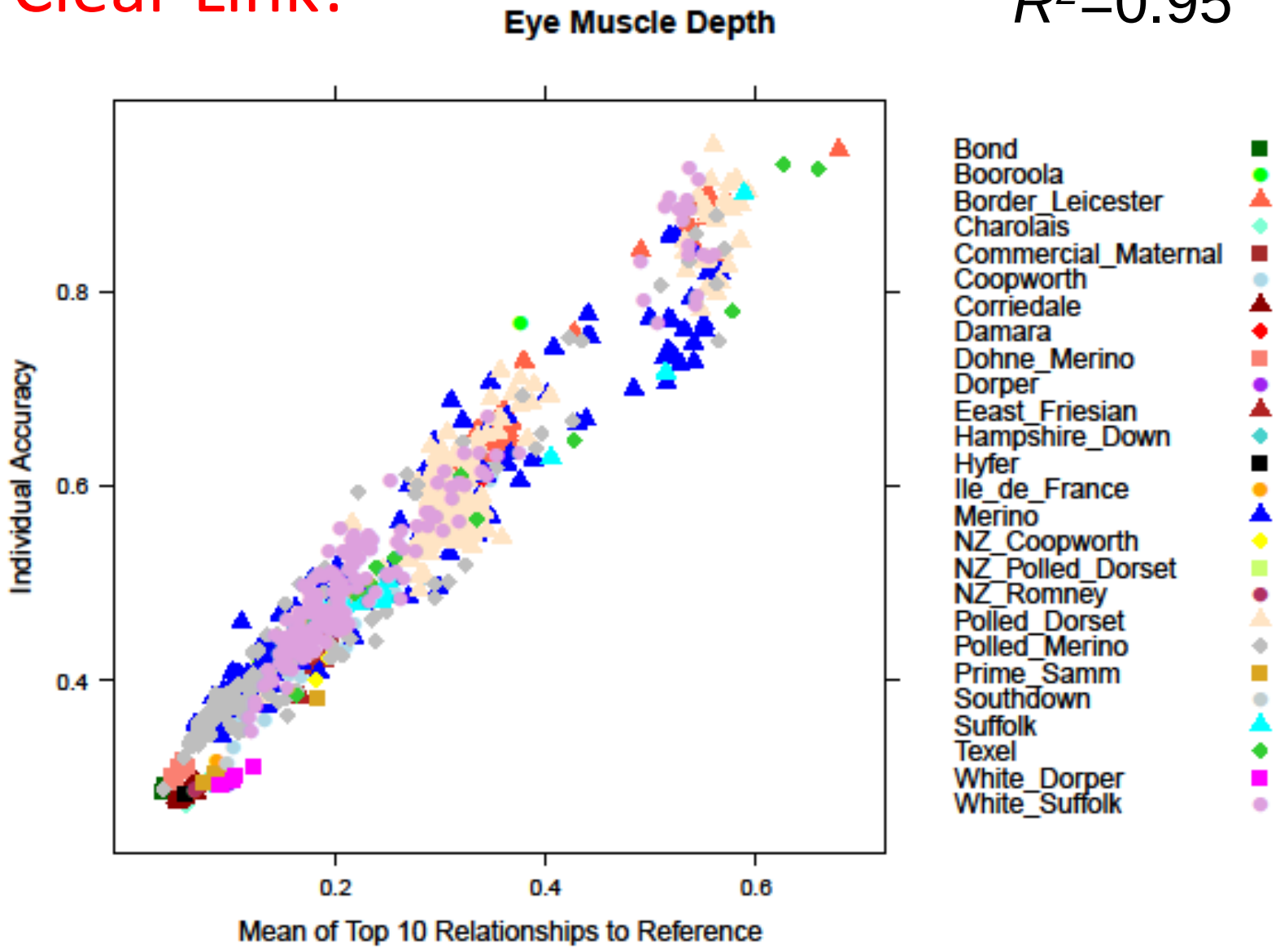
$R^2$=0.08



# Accuracy and Mean of Top 10 Relationships

→ Clear Link!

$R^2$=0.95



# Genomic prediction

$$\begin{bmatrix} X'X & X'X & 0 \\ Z'X & Z'Z + G^{11} & G^{12} \\ 0 & G^{21} & G^{22} \end{bmatrix} \begin{bmatrix} b \\ g_1 \\ g_2 \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ 0 \end{bmatrix}$$

$\hat{g}_2 = -(G^{22})^{-1} G^{21} \hat{g}_1$

Genomic regression

Example:
Data on sire 1, sons 2 and 3, 4 unrelated, want to predict 5

A-matrix (pedigree-based)

| | | | | |
|---|---|---|---|---|
| 1 | 0.5 | 0.5 | 0 | 0.5 |
| 0.5 | 1 | 0.25 | 0 | 0.25 |
| 0.5 | 0.25 | 1 | 0 | 0.25 |
| 0 | 0 | 0 | 1 | 0 |
| 0.5 | 0.25 | 0.25 | 0 | 1 |

G-matrix (DNA-based)

| | | | | |
|---|---|---|---|---|
| 1 | 0.5 | 0.5 | 0.02 | 0.5 |
| 0.5 | 1 | 0.20 | 0.015 | 0.20 |
| 0.5 | 0.20 | 1 | 0.025 | 0.30 |
| 0.02 | 0.015 | 0.025 | 1 | 0.025 |
| 0.5 | 0.20 | 0.30 | 0.025 | 1 |

BLUP

$\hat{u}_5 = 0.1136.y_1 + 0.0455.y_2 + 0.0455.y_3$

GBLUP

$\hat{g}_5 = 0.1135.y_1 + 0.0328.y_2 + 0.0591.y_3 + 0.00519.y_4$

# Genomic prediction

$$\begin{bmatrix} X'X & X'X & 0 \\ Z'X & Z'Z + G^{11} & G^{12} \\ 0 & G^{21} & G^{22} \end{bmatrix} \begin{bmatrix} b \\ g_1 \\ g_2 \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ 0 \end{bmatrix}$$

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Example:
Data on sire 1, sons 2 and 3, 4 unrelated, want to predict 5

A-matrix (pedigree-based)

| | | | | |
|---|---|---|---|---|
| 1 | 0.5 | 0.5 | 0 | 0.5 |
| 0.5 | 1 | 0.25 | 0 | 0.25 |
| 0.5 | 0.25 | 1 | 0 | 0.25 |
| 0 | 0 | 0 | 1 | 0 |
| 0.5 | 0.25 | 0.25 | 0 | 1 |

G-matrix (DNA-based)

| | | | | |
|---|---|---|---|---|
| 1 | 0.5 | 0.5 | 0.02 | 0.5 |
| 0.5 | 1 | 0.20 | 0.015 | 0.20 |
| 0.5 | 0.20 | 1 | 0.025 | 0.30 |
| 0.02 | 0.015 | 0.025 | 1 | 0.025 |
| 0.5 | 0.20 | 0.30 | 0.025 | 1 |

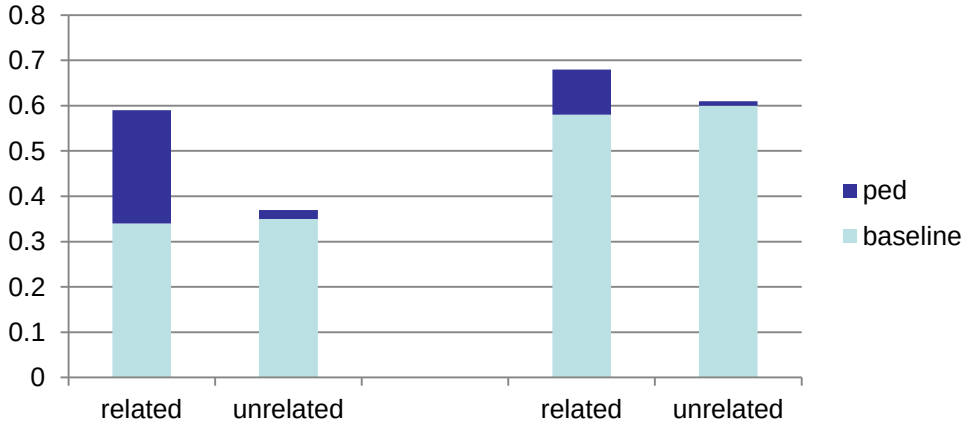
BLUP uses: Family Info

GBLUP uses: Family Info
Segregation within family
Info on 'unrelated'

# Sources of information contributing to GBV accuracy

| | BLUP | GBLUP | half life |
|---|---|---|---|
| 1. Variation between families | ++ | ++ | 1 gen |
| 2. Variation within families | 0 | + | 1 gen |
| 3. Markers tracking effects of genome segments/LD | 0 | ++.+ | several gen's |

*Info on 'unrelated'*




smaller ref pop

larger ref pop

Depending on size of reference population

# Results – Simulation

Sam Clark

| **Method** | **Close**<br>Ped 0 - 0.25<br>Genom 0.08 – 0.35 | **Distant**<br>0 - 0.125<br>0.08 – 0.26 | **Unrelated**<br>0 - 0.05<br>0.08 – 0.16 |
|---|---|---|---|
| BLUP-<br>Shallow pedigree | 0.39 | 0.00 | 0.00 |
| BLUP-<br>Deep Pedigree | 0.42 | 0.21 | 0.04 |
| gBLUP | **0.57** | 0.41 | 0.34 |

Additional accuracy from family info

'baseline accuracy': graphs predict 0.36 for Ne=100, N=1750, $h^2$=0.3

# Accuracy Real Data (INF) Sam Clark

| | Close related sires | | Distantly related sires | |
|---|---|---|---|---|
| Method | Empirical Acc<br>actual correlation with ASBV | Predicted Acc<br>correlation derived from gBLUP | Empirical Acc | Predicted Acc |
| BLUP-S | ? | ? | 0.00 | 0.00 |
| BLUP-D | 0.62 | 0.37 | 0.02 | 0.05 |
| gBLUP | 0.65 | 0.41 | 0.27 | 0.19 |

# Genomic prediction FAQ

- How well can we predict distantly related individuals?
  - Ok if reference population is large enough
  - Can NOT predict across breed *Daetwyler et al., 2011*
- How quick does the genomic prediction erode?
  - Fast if based on relationships, slower if based on 'distant relatives
- Do we need relatives?
  - Relatives give more accuracy, but not everyone can have them
- How large does a reference population need to be?
  - Design based as if prediction is based on 'unrelated'

# Reference Pop: How many are needed?

$\%V_A$ explained by GBV

| Breed | merino | WS, PD | BL |
|---|---|---|---|
| Ne | 1000 | 250 | 100 |
| Size of reference pop'n | 30,000 | 10,000 | 5,000 |
| Progeny measured per year[1] | 3750 | 1250 | 625 |
| h2=0.1 | 0.33 | 0.34 | 0.35 |
| h2=0.3 | 0.51 | 0.53 | 0.54 |
| h2=0.5 | 0.60 | 0.62 | 0.63 |
| Predicted benefit in dG | 40% | 20% | ? |

$\cong h^2$

*assuming the reference population is 'refreshed' every 8 years*

# Reference Pop: How many are needed?

$\%V_A$ explained by GBV

| Breed | merino | WS, PD | BL |
|---|---|---|---|
| Size of reference pop'n | 12,000 | 4,000 | 2,000 |
| Progeny measured per year[1] | 1500 | 500 | 250 |
| h2=0.1 | 0.22 | 0.23 | 0.23 |
| h2=0.3 | 0.36 | 0.37 | 0.38 |
| h2=0.5 | 0.44 | 0.46 | 0.47 |
| Predicted benefit in dG | 20% | 10% | ? |

$\cong \frac{1}{2} h^2$

*assuming the reference population is 'refreshed' every 8 years*

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# Implication

- To predict a selection candidate
  - It needs to have relatives in reference populations
  - We can afford a lower degree of relationship than with BLUP
    - » Can predict several generations away
  - Need large reference population

# Optimal Genotyping Strategies

- If genotyping is expensive
  - Genotype males only
  - Genotype only ‘best’ males
  - multi-stage selection
  - But enough to be able to select!

# Acknowledgements


| | |
|---|---|
| DPI Vic: | Hans Daetwyler, Ben Hayes |
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*Thanks*