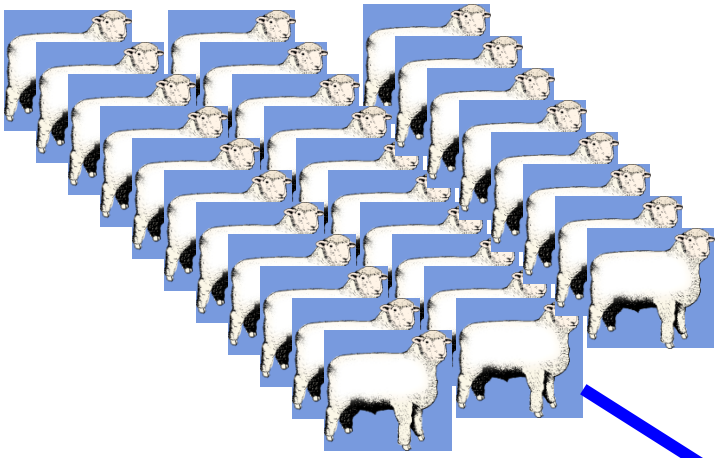
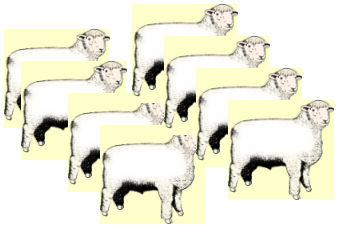
Genomic Prediction: basic idea



Reference population
measured and DNA tested



Young sires
Only DNA tested

To predict a trait EBV at a young age,

good for: late traits
hard to measure traits

The questions

- How many records are needed in the reference population to achieve a certain accuracy?

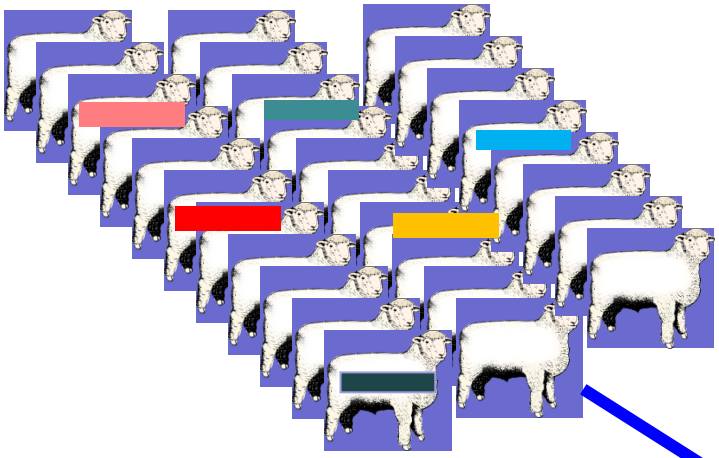
But also:

- What if you are more related to the reference?
- property of the reference population (heterogeneous, multi breed?
- the value of closer relatives

Genomic prediction accuracy

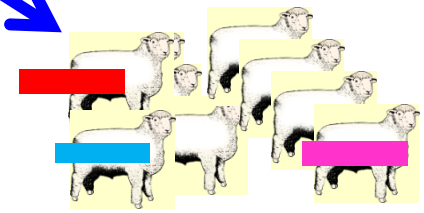
- Derive from the model, e.g. PEV from GBLUP mixed model equations
- Validate with other EBVs or phenotypes
  - Validation population
  - Cross-validation
- Predict in advance based on theory and assumptions about population

Genomic Prediction: basic idea



1) Reference population

diversity and length of segments → accuracy



2) young sire

Accuracy depends on:

- Linkage Disequilibrium
- Sharing haplotypes
- Genomic Relationships

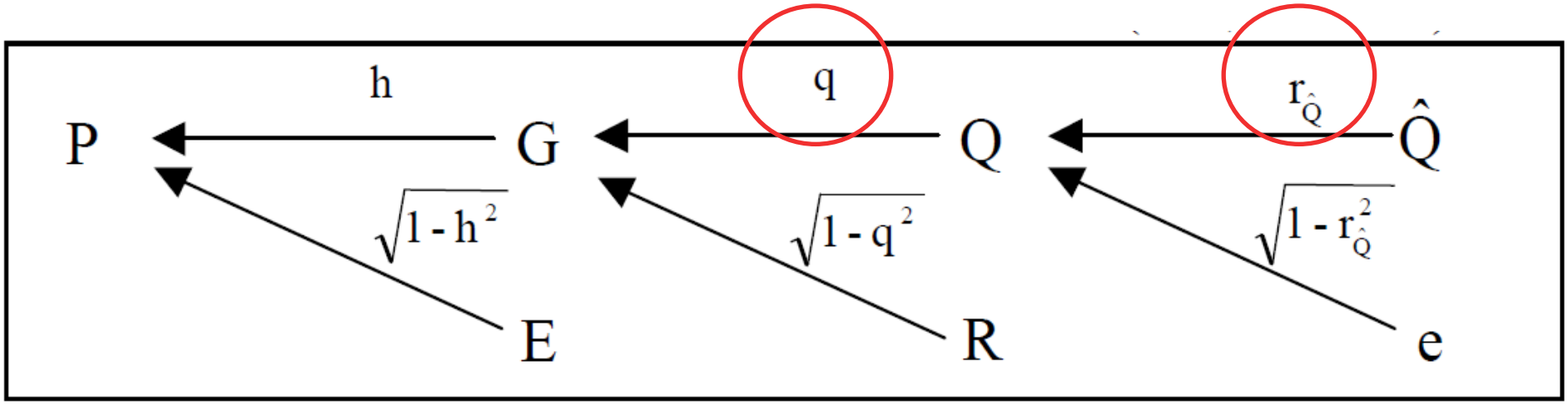
Genomic prediction accuracy *Using Goddard et al, 2011*

Depends on

i) Proportion of genetic variance at QTL captured by markers

i) Reliability of estimating marker effects

See also Dekkers 2007 (Path coefficient method)



Trait heritability = h^2

G = total BV

Q = genetic effects captured by marker(s)

R = residual polygenic effects

Model for phenotype: P = G + E

Model for BV: G = Q + R

Genomic prediction accuracy *Using Goddard et al, 2011*

Depends on

i) Proportion of genetic variance at QTL captured by markers q^2

i) Reliability of estimating marker effects r^2_{Qhat}

Accuracy = $\sqrt{(q^2 . r^2_{Qhat})}$

= $q . r_{Qhat}$

Genomic prediction accuracy *Using Goddard et al, 2011*

Depends on

i) Proportion of genetic variance at QTL captured by markers $q^2 = M/(M_e + M)$

↳ Depends on marker-QTL LD

↳ Depends on

M = # markers

M_e = 'effective number of chromosome segments'

$M_e = 2N_eLk/\ln(2N_e)$

or is it…?

i) Reliability of estimating marker effects

$r^2_{Qhat} = V_{qhat}/V_q = N/(N+\lambda)$

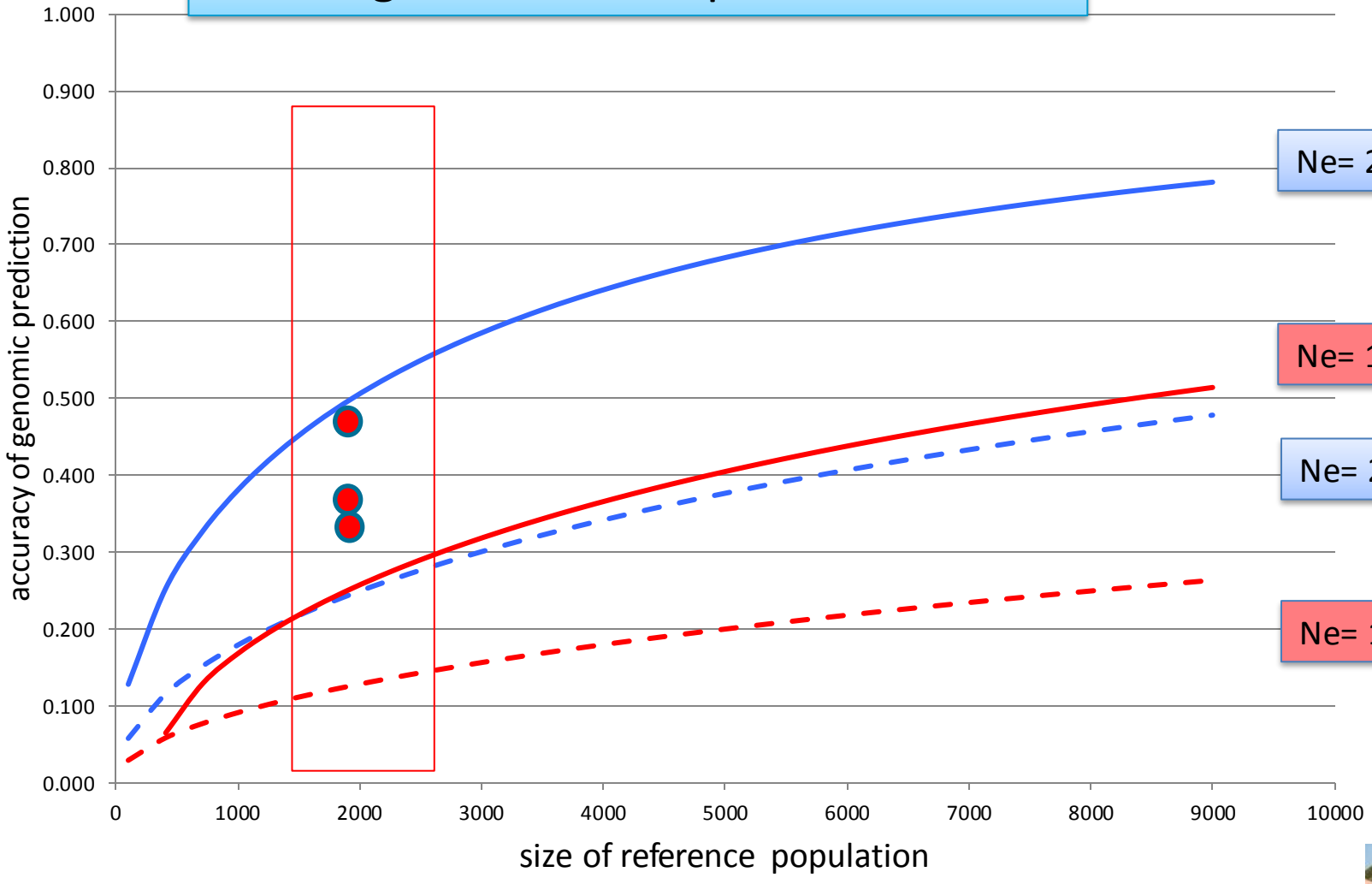
$\lambda = M_e/q^2.h^2$

Accuracy = $\sqrt{(q^2.\ r^2_{Qhat})}$

$= q.\ r_{Qhat}$

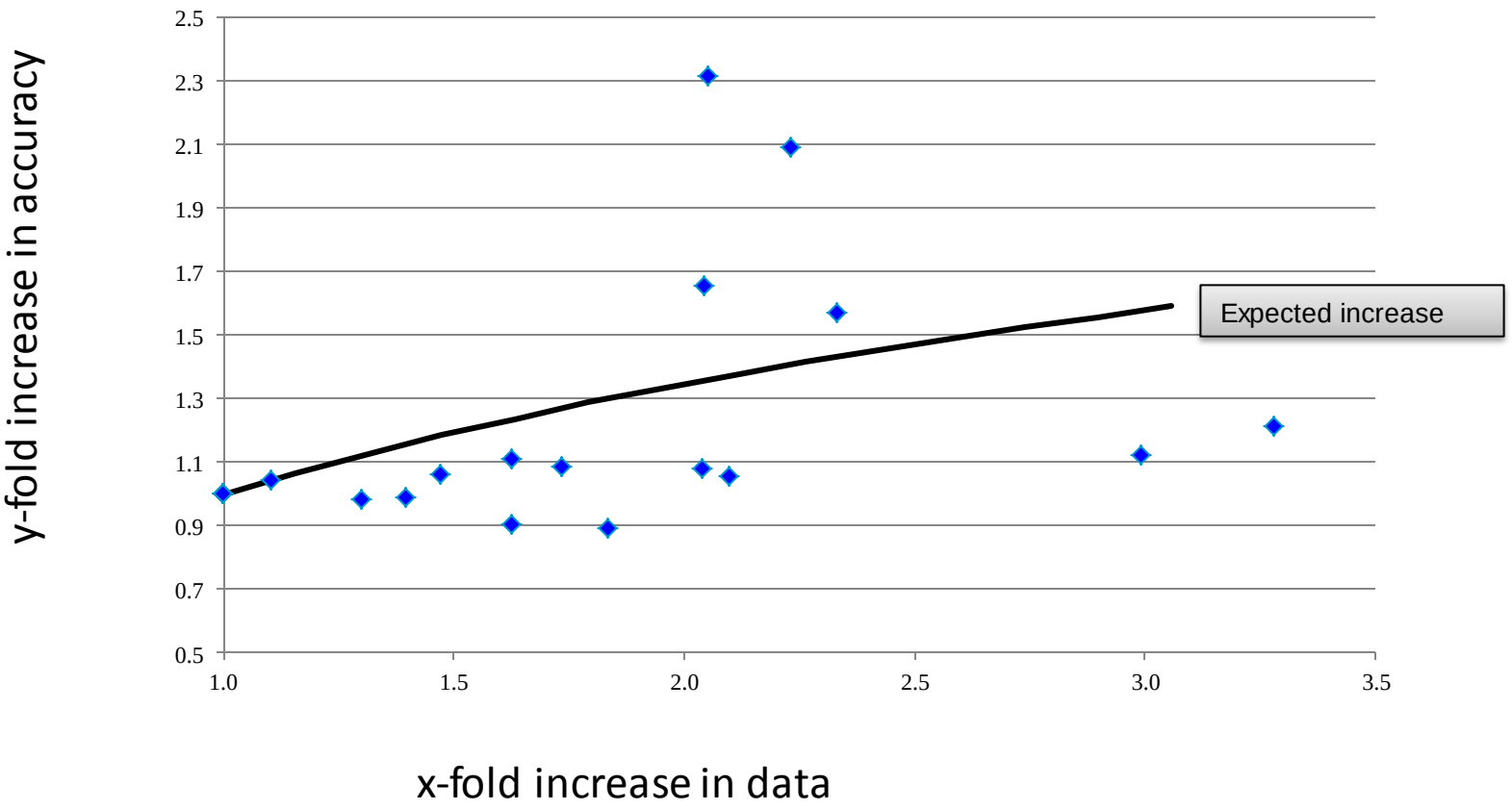
Genomic prediction accuracy *Using Goddard et al, 2011*

Did we get what we expected?



Validating ‘Genomic Prediction Accuracy’

More data: does accuracy increase as expected?



Relationship with reference population

Clark et al 2011

Method	**Close** Ped 0 - 0.25 Genom 0.08 – 0.35	**Distant** 0 - 0.125 0.08 – 0.26	**Unrelated** 0 - 0.05 0.08 – 0.16
BLUP- Shallow pedigree	0.39	0.00	0.00
BLUP- 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

Selection Index principles

Single Trait selection index calculation using genomic testing

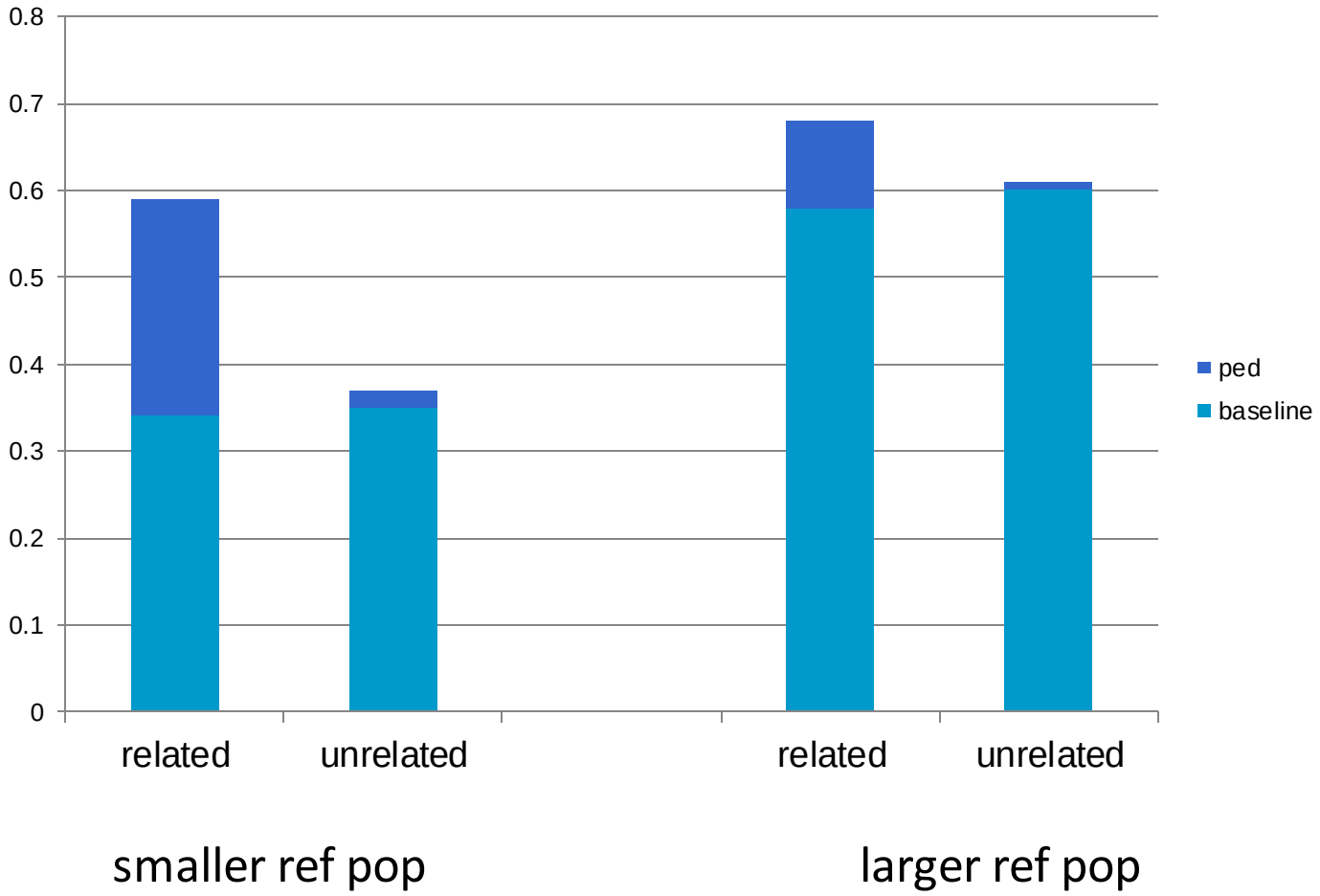
Parameters	
Heritability	0.3
Repeatability of subsequent records	0.3
c-squared (among full sibs)	0.15
Reliability of genomic test (prop expl)	0.09091

Run

			Index Wght		Value of Variate	
Information used	Nr.Records	Genotyped	Pheno	Geno	Pheno	Geno
nr of own records	1	1	0.214	0.550	14.7%	2.7%
nr. of records on dam	1	0	0.082	-	2.1%	-
nr of records on sire	1	0	0.030	-	0.2%	-
nr of fulls sib records	4	0	0.186	-	3.3%	-
nr. of half sib records (excl. full sibs)	40	0	0.347	-	3.0%	-
nr. of progeny	0	0	-	-	-	-

Accurcay of EBV	**0.707**
Accuracy of Pheno EBV	0.689
Accuracy of MBV	0.302
correlation EBV FS	0.797
correlation EBV HS	0.440

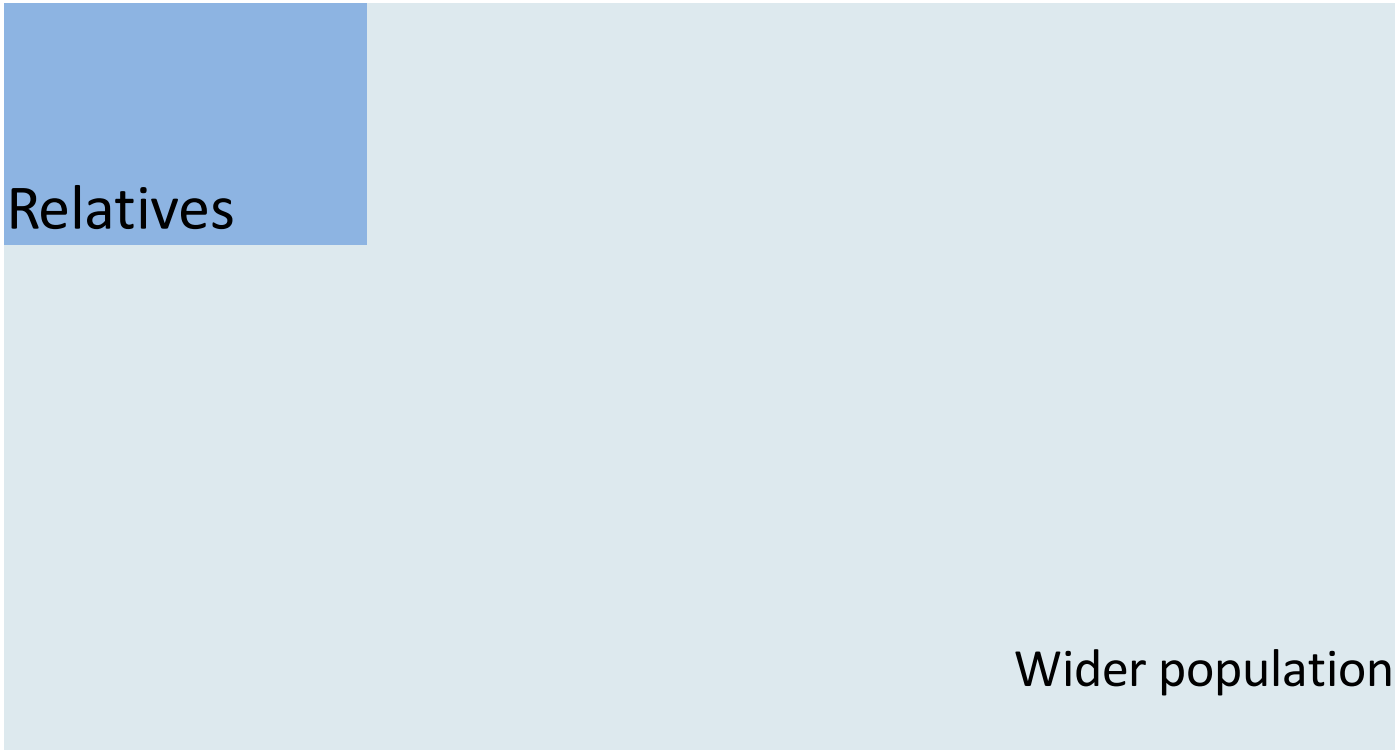
Relatedness matters more if the reference population is smaller



(hypothesis)

Van der Werf AAABG 2011

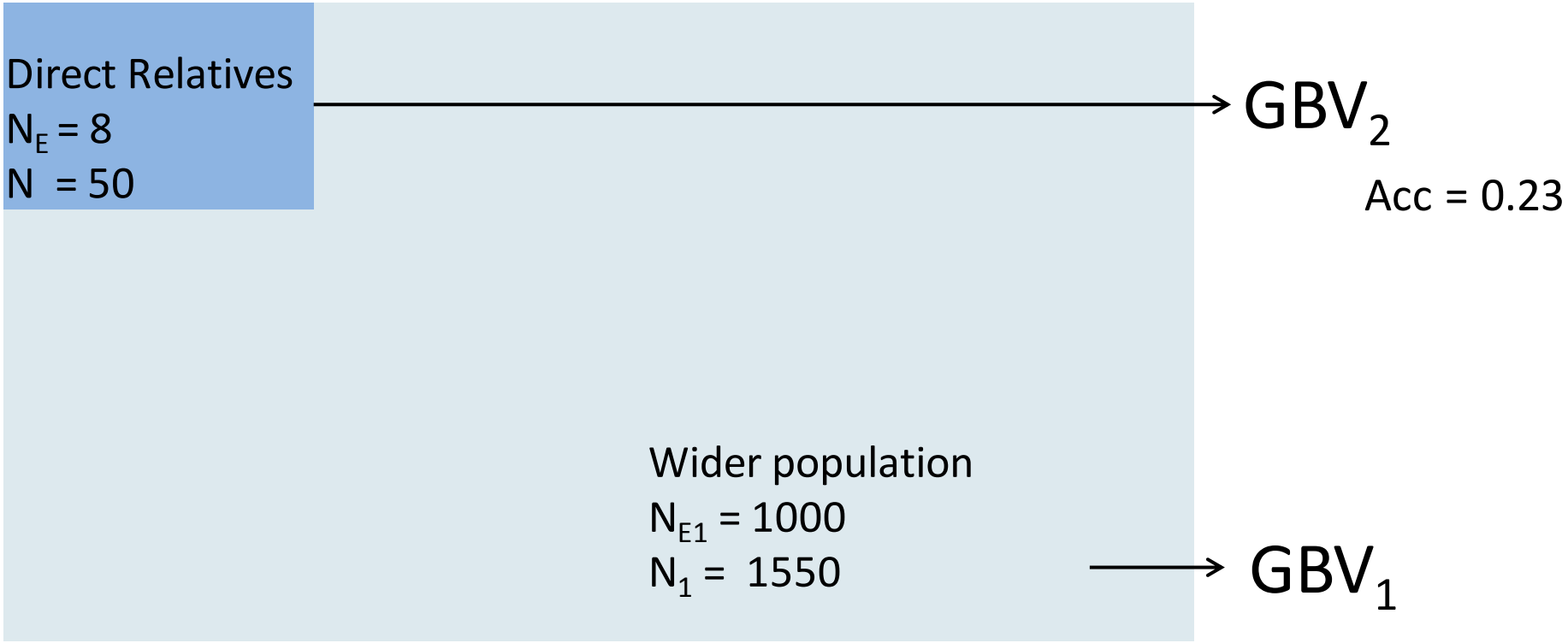
A reference population may have relatives



‘Relatedness’ can be represented by effective size

Hayes et al 2009

Information from different subsets can be combined

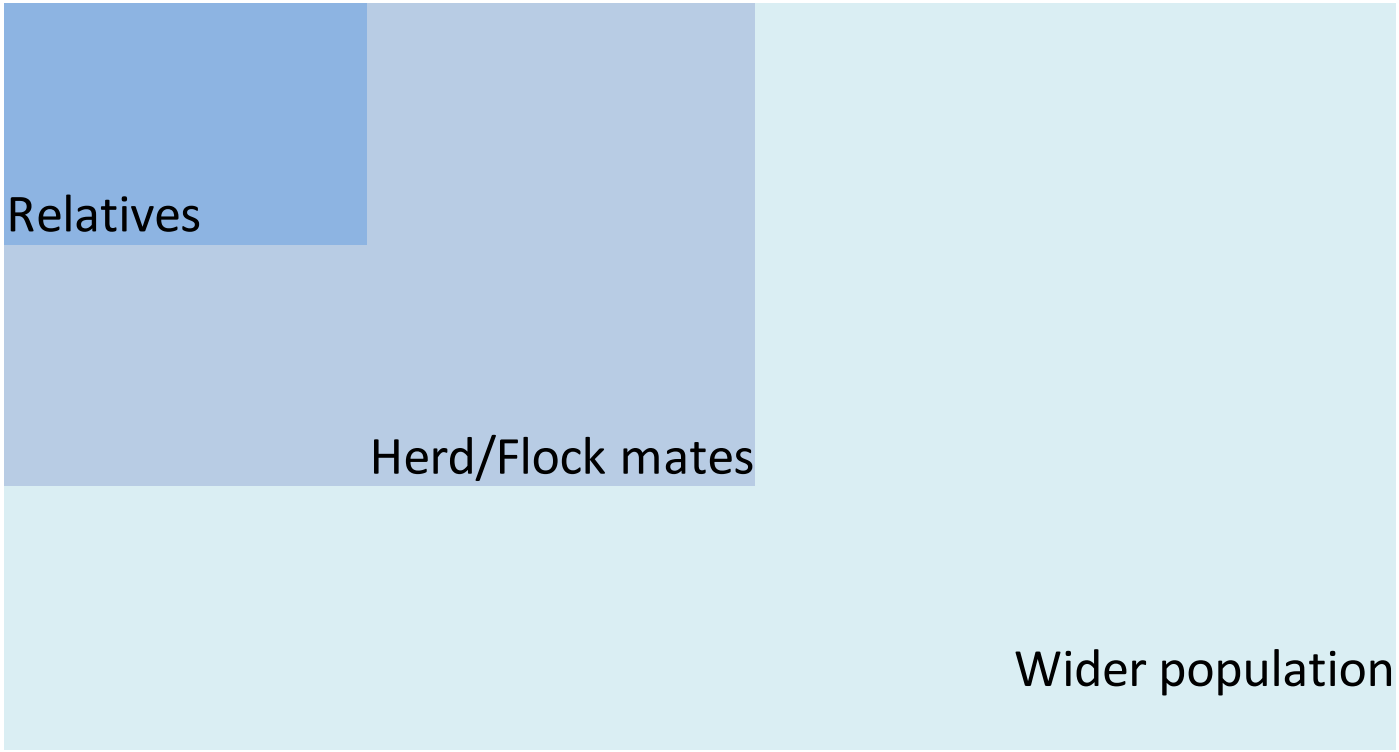


Calculate overall accuracy using selection index

$$GBV = \sum b_i GBV_i$$

Acc = 0.31

Using a stratified reference population -populations are not homogeneous



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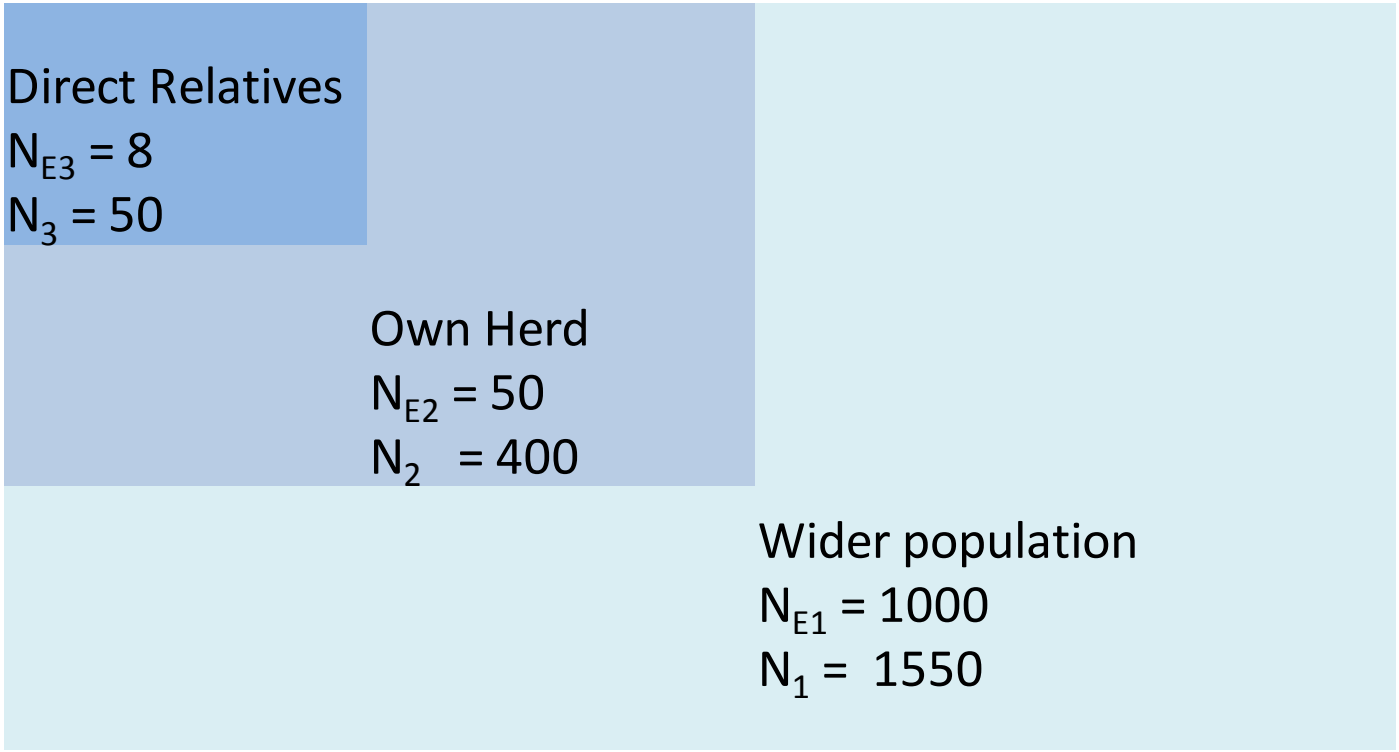
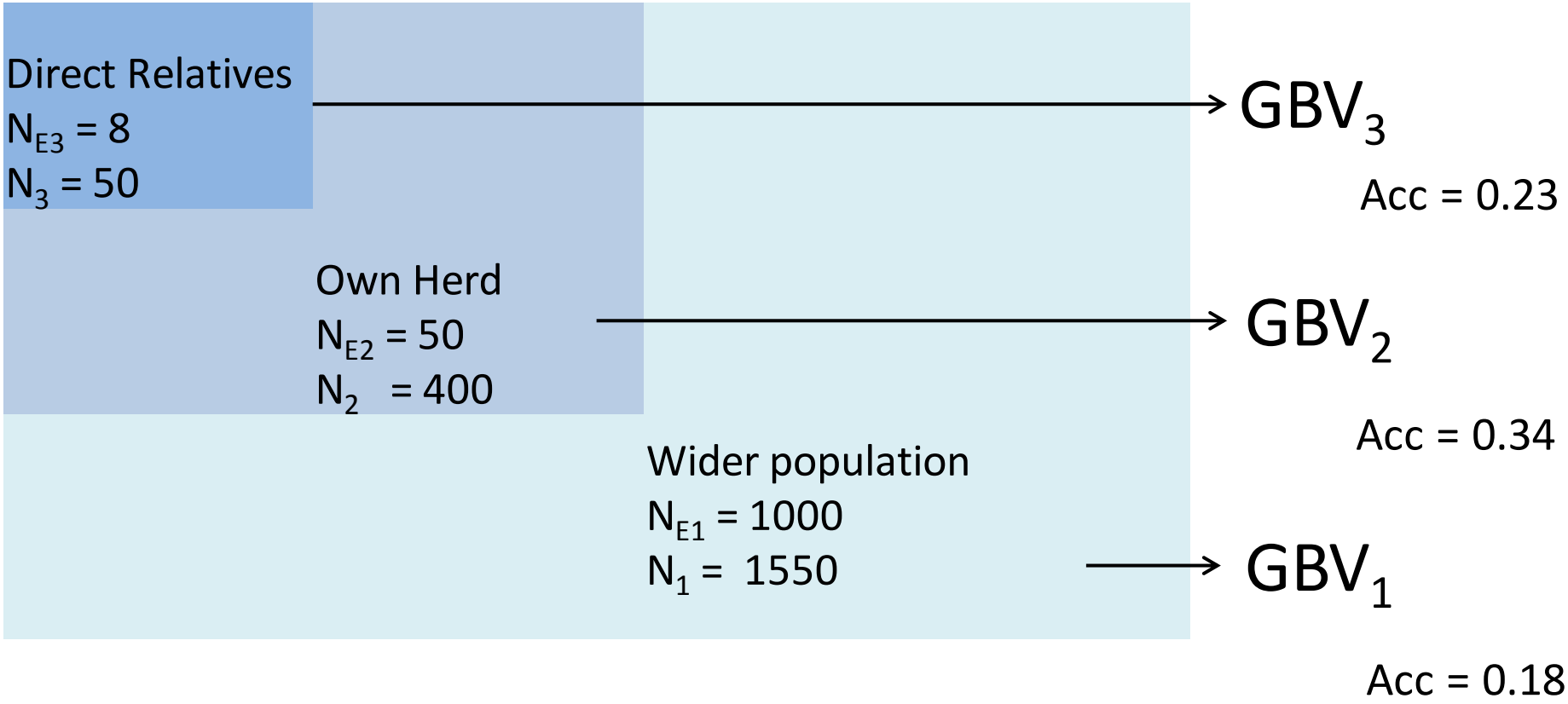


Using a stratified reference population -populations are not homogeneous



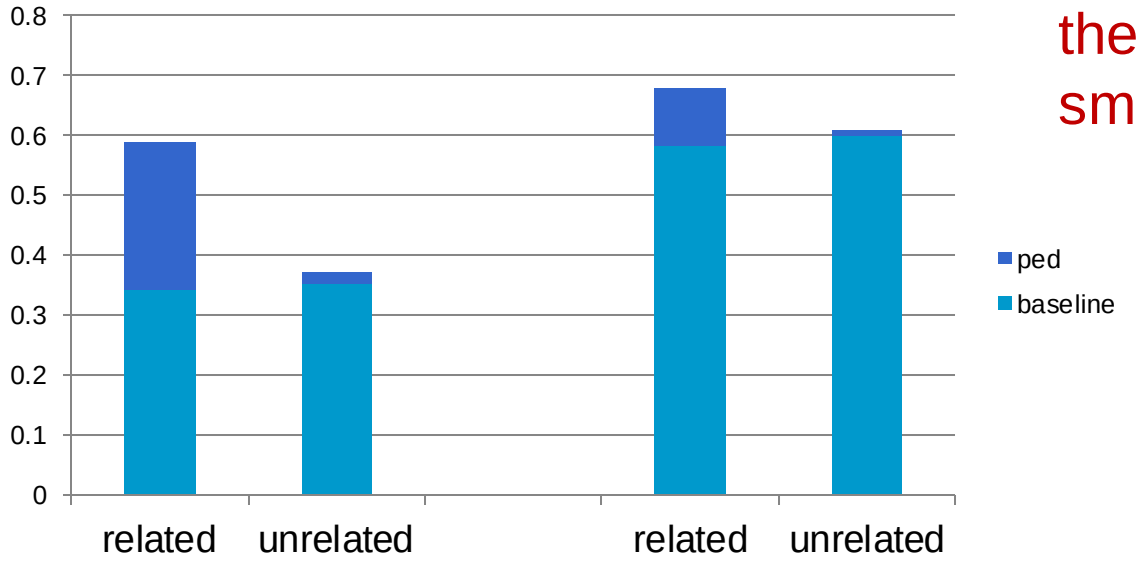
Calculate overall accuracy using selection index

$$GBV = \Sigma b_i GBV_i$$

Acc = 0.42

NE_1 = 1000

	Value of information source			GBV accuracy		
N_1	breed (N1)	flock **(400)**	relatives **(50)**	all info	breed only	diff
2,000	16%	52%	21%	0.43	0.22	95%
5,000	31%	39%	15%	0.47	0.32	48%
10,000	45%	26%	10%	0.53	0.42	26%



Relatedness matters more if the reference population is smaller

hypothesis confirmed

Van der Werf AAABG 2011

$NE_1 = 1000$

	Value of information source			GBV accuracy		
N_1	breed (N1)	flock 400	relatives 50	all info	breed only	diff
2,000	16%	52%	21%	0.43	0.22	95%
5,000	31%	39%	15%	0.47	0.32	48%
10,000	45%	26%	10%	0.53	0.42	26%
N_1	breed (N1)	flock 100	relatives 10	all info	breed only	diff
2,000	48%	36%	48%	0.28	0.21	36%
5,000	68%	19%	68%	0.36	0.31	15%
10,000	79%	11%	79%	0.45	0.41	7 %

With fewer relatives the reliance on the reference population increases

$NE_1 = 1000$

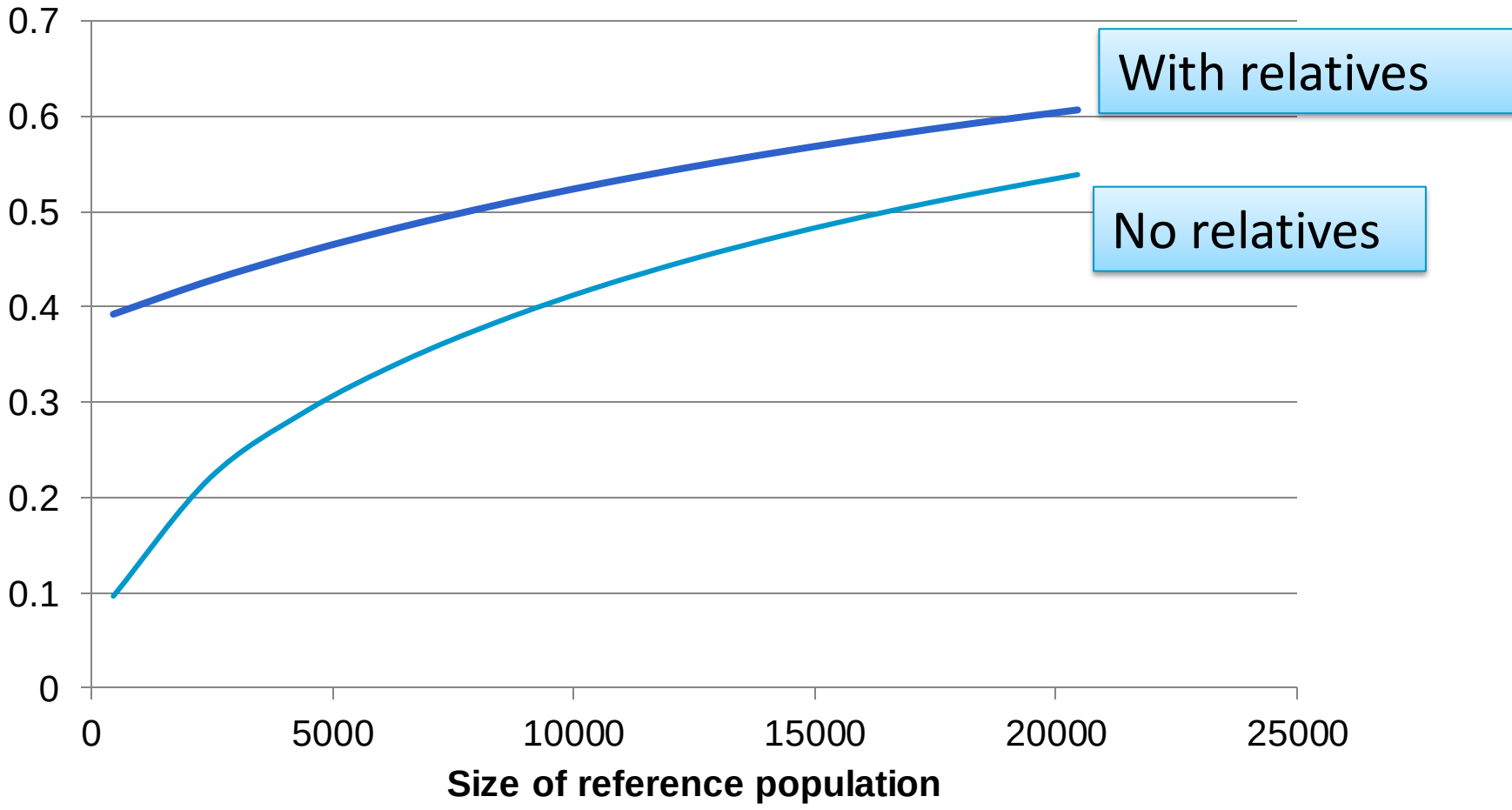
	Value of information source			GBV accuracy		
N_1	breed (N1)	flock **(400)**	relatives **(50)**	all info	breed only	diff
2,000	16%	52%	21%	0.43	0.22	95%
5,000	31%	39%	15%	0.47	0.32	48%
10,000	45%	26%	10%	0.53	0.42	26%

$NE_1 = 200$

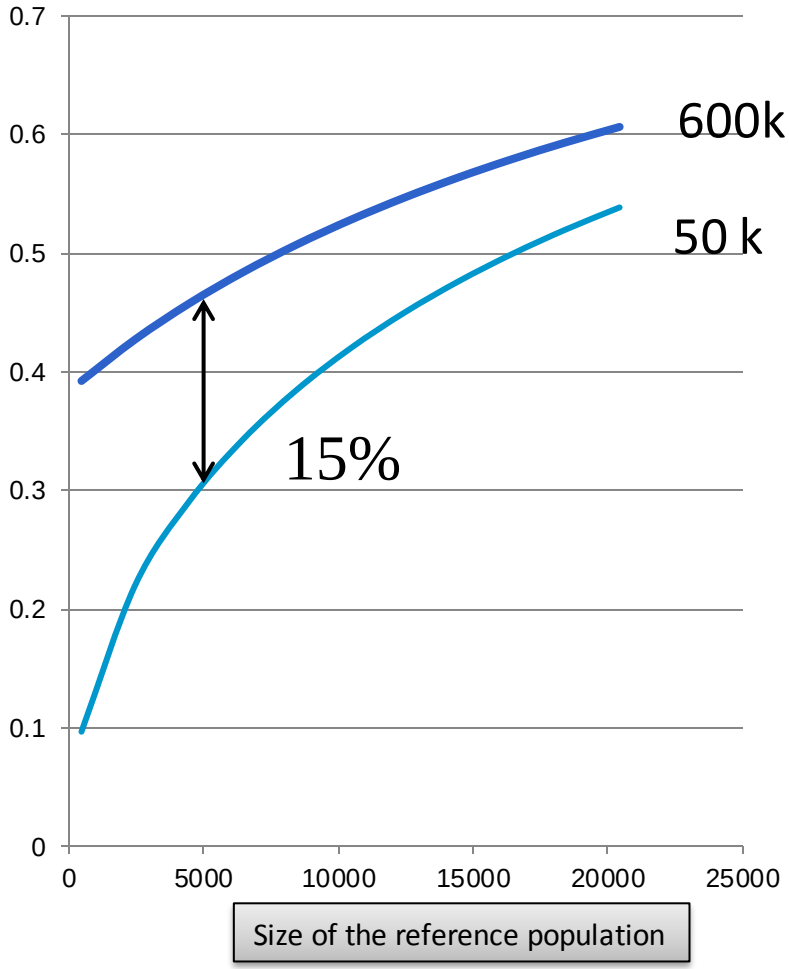
N_1	breed (N1)	flock **(400)**	relatives **(50)**	all info	breed only	diff
2,000	45%	26%	10%	0.53	0.45	18%
5,000	62%	12%	5%	0.64	0.60	7%
10,000	72%	5%	2%	0.74	0.72	3%

With less diverse populations the relatives matter a lot less

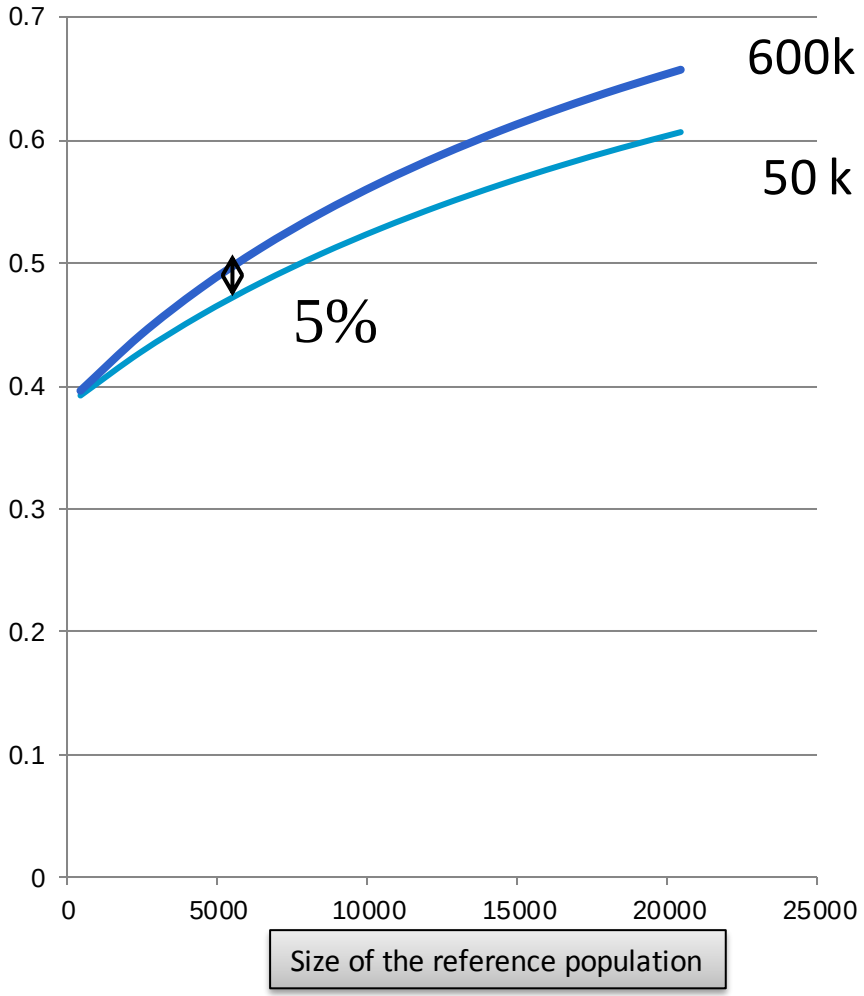
The effect of a larger reference population.



The effect of denser marker panels



No relatives



With relatives

Conclusions

- Theory exists to predict genomic prediction accuracy in advance: depends on population diversity, nr records
- Reference populations are heterogeneous, with closer as well as distant relatives
- Relatives will increase accuracy and decrease reliance on wider reference population (and denser marker) but that information has a shorter life