Opportunities to optimize the role of functional traits in dairy breeding goals using genomic information

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Introduction

- Breeding goal and selection indexes have changed in many countries, with increasing weights on functional traits (fertility, health and longevity)
- Several reasons:
  - Unfavorable trends in functional traits have become clear and limiting
  - Interbull has provided international EBVs for more and more traits, facilitating this change

Introduction

- However, relative genetic responses in goal traits are not the same as indicated by the relative economic weights!
  - Depends on **amount of information and heritability**
- Large difference between accuracies for production traits (h^2=0.3) and functional traits (sometimes h^2=0.05)
- For mass selection, accuracy would be 0.55 vs 0.22: relative value **2.45**

Introduction

- For sire selection the difference in accuracy becomes lower
- The difference decreases with increasing number of daughters

Accuracies

Number of daughters	h^2 0.30	h^2 0.05	Relative
50	0.90	0.62	1.44
100	**0.94**	**0.75**	**1.26**
150	0.96	0.81	1.19
200	0.97	0.85	1.15
2000	1.00	0.98	1.02

Introduction

- However, relative genetic responses in goal traits are not the same as indicated by the relative economic weights!
  - Depends on **genetic correlation**

Trait	Econ wts 1:1	
	rg = 0	rg = -0.3
Milk	0.492	0.488
Functional trait	0.051	-0.012

h^2 0.3 and 0.05; 100 daughters, econ wts per phen SD

Introduction

- However, relative genetic responses in goal traits are not the same as indicated by the relative economic weights!
  - Depends on **generation interval**
- Longevity and performance in later lactations most clearly affected
- If selection takes place very early in lactation (based on TDM for milk) also to some extent fertility and traits expressed late in lactation

Potential Advantages of Genomic Selection

Potential Advantages of Genomic Selection

- Accuracies of GBVs based on sires with many daughters
  - High “heritability” of both production and functional traits, 0.95 and 0.75 respectively
  - “Phenotypes” are daughter averages
  - Accuracy depends mainly on number of bulls, N_p

$$r^2_{g\hat{g}} = \frac{N_p h^2}{N_p h^2 + M_e}$$

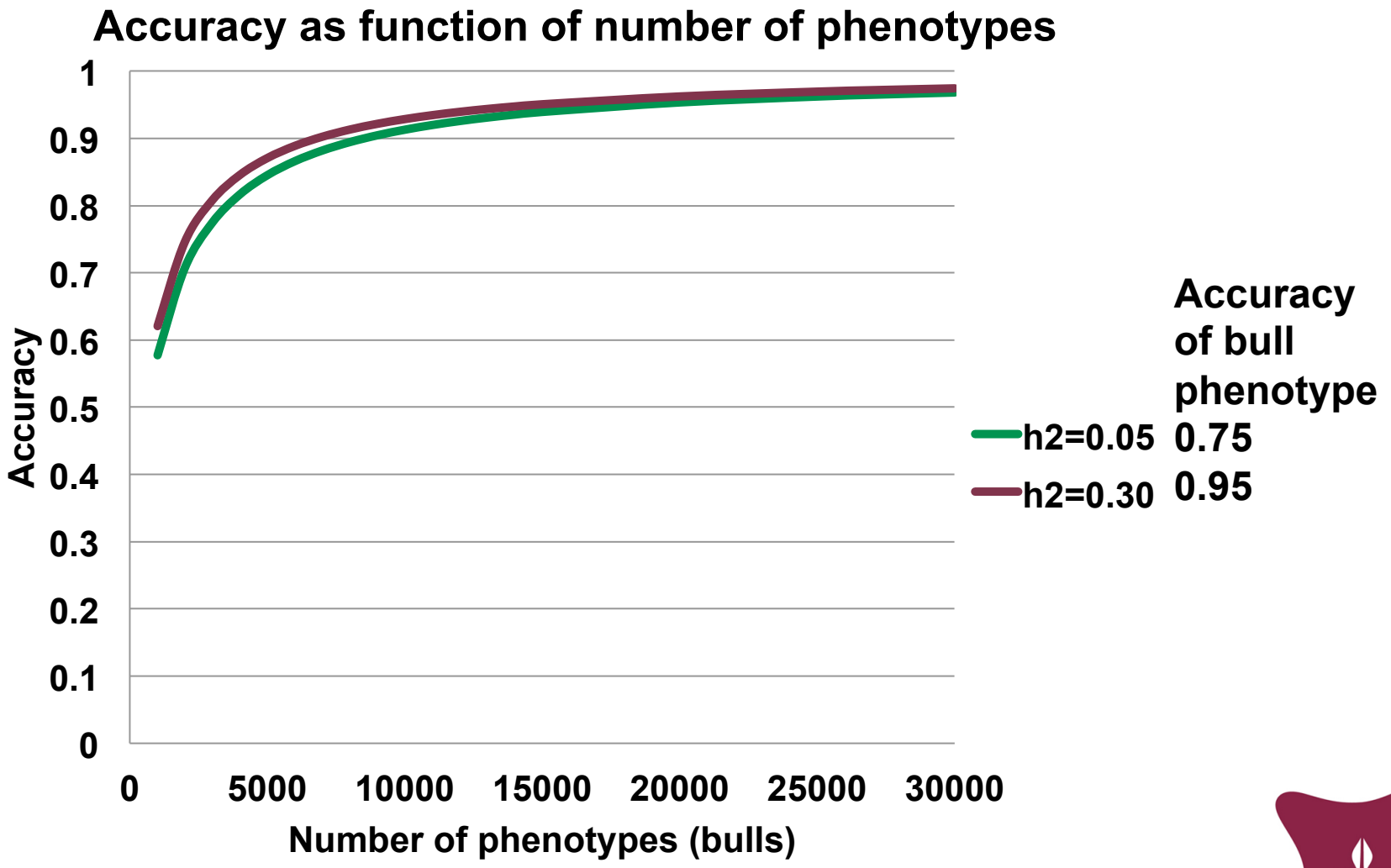
Daetwyler, 2009 thesis

$$where\ M_e = 2N_e L / \ln(4N_e L)$$

Goddard, 2008

Effective number of chromosome segments

Accuracy in Genomic Evaluation



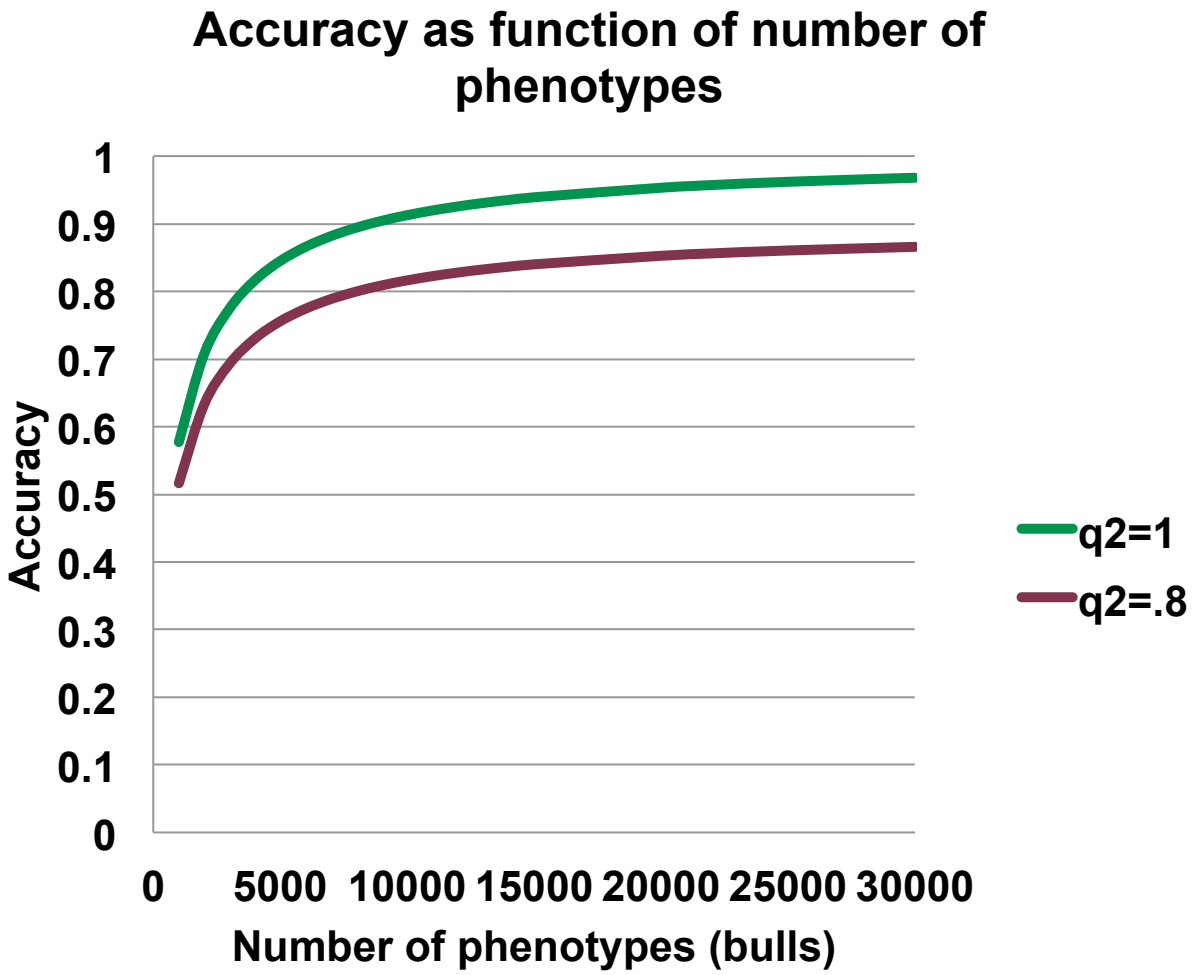
Me =1500, 100 daughters

Accuracy in Genomic Evaluation

- Previous equation not the whole truth
- **Total accuracy** depends on
  - how well the markers predict the QTL
  - how much the SNP-chip actually explains of the total genetic variation
- Current 50k chip approx 80% (Hol)

$$r^2_{obs} = q^2 r^2_{g\hat{g}}$$

Accuracy in Genomic Evaluation



Me =1500, accuracy of EBVs=0.75

Accuracy in Genomic Evaluation

- Still quite good accuracy, **in theory**
- However, requires that traits:
  - can be measured on all daughters of bulls
  - large number of bulls
  - **have been measured for a long time**
    - Also good: for longevity, we can use (almost) actual longevity
    - **problematic for new traits, say, progesterone-based fertility traits**

Accuracy in Genomic Evaluation
Results from practice

- In practice often measured as difference between r^2(GBV,DYD) and r^2(PI,DYD)
  - Extra gain in REL due to genomic information
- Often the largest gain for traits with highest heritability (VanRaden et al., 2009)
- Extra gain in accuracy of 19-33 %-units for production but only 2-22 %-units for functional traits (Wiggans et al., 2010)

Accuracy in Genomic Evaluation
Results from practice

- In practice often measured as difference between r^2(GBV,DYD) and r^2(PI,DYD)
  - Extra gain in REL due to genomic information
- NZ results (calculated from MME): 14-30 %-units increase
- Australian results:

ASI "Milk"	APR Milk+FT +LWT	Prot	Prot %	Fertility
+6-10%	+18-20%	+17-20%	+9-16%	-2-+2%

Accuracy in Genomic Evaluation
Results from practice

- In practice often measured as difference between r^2(GBV,DYD) and r^2(PI,DYD)
  - Extra gain in REL due to genomic information
- UK results: about +20 %-units, less for longevity (Mrode et al.)
- Dutch results:

Fat%	Protein	FeetLegs	Udder, SCS	Fertility
+33%	+19%	+15%	+13%	+9%

Accuracy in Genomic Evaluation
Results from practice

- Results from Nordic Red populations:
  - REL of GBV lower than for PI in for several traits
  - However, generally an increase when combining GBV with PI, ca 5 %-units
  - Larger N_e and admixed population compared with HOL

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Accuracy in Genomic Evaluation Conclusions

- Practical accuracies not as high as originally theoretically expected
- **Especially for functional traits**
- Varies across populations/breeds
  - More problem for Red than for Holstein

What affects accuracy?

1. Reference population size
2. LD between markers and QTL
3. (Heritability/Reliability of “phenotypes”)
4. ~~Distribution of QTL effects~~

e.g. Goddard, 2008; Hayes et al. 2009

How to increase accuracy?

1. Expand the reference population

- Eurogenomics example Holstein
  - From 4000 to 16,000 bulls
  - Increase in reliability of 8-11 %-units (6-8%-units in accuracy)
  - Where extra gain was lower – often for functional traits (longevity, fertility, calving ease)

Lund et al., 2010, WCGALP

How to increase accuracy?

1. Expand the reference population

- Nordic Red breeds
  - Danish, Finnish and Swedish populations
  - For Sweden (Finland) average accuracy:
    - 0.44 with only Swedish (Finnish) ref pop
    - 0.50 (0.52) with Swedish-Finnish ref pop
    - 0.51 (0.51) with all 3 countries

Bröndum et al., 2011, JDS

How to increase accuracy?

1. Expand the reference population

- Possible drawbacks:
  - Traits may not be recorded in the same way
    - More likely for functional traits, production more standardized recording
  - True GxE might exist
    - Also seems more likely for functional traits, quite high across-country correlations for production
  - The populations may be genetically different
    - QTL might have different effects (epistasis)
    - SNPs might be in other linkage phase

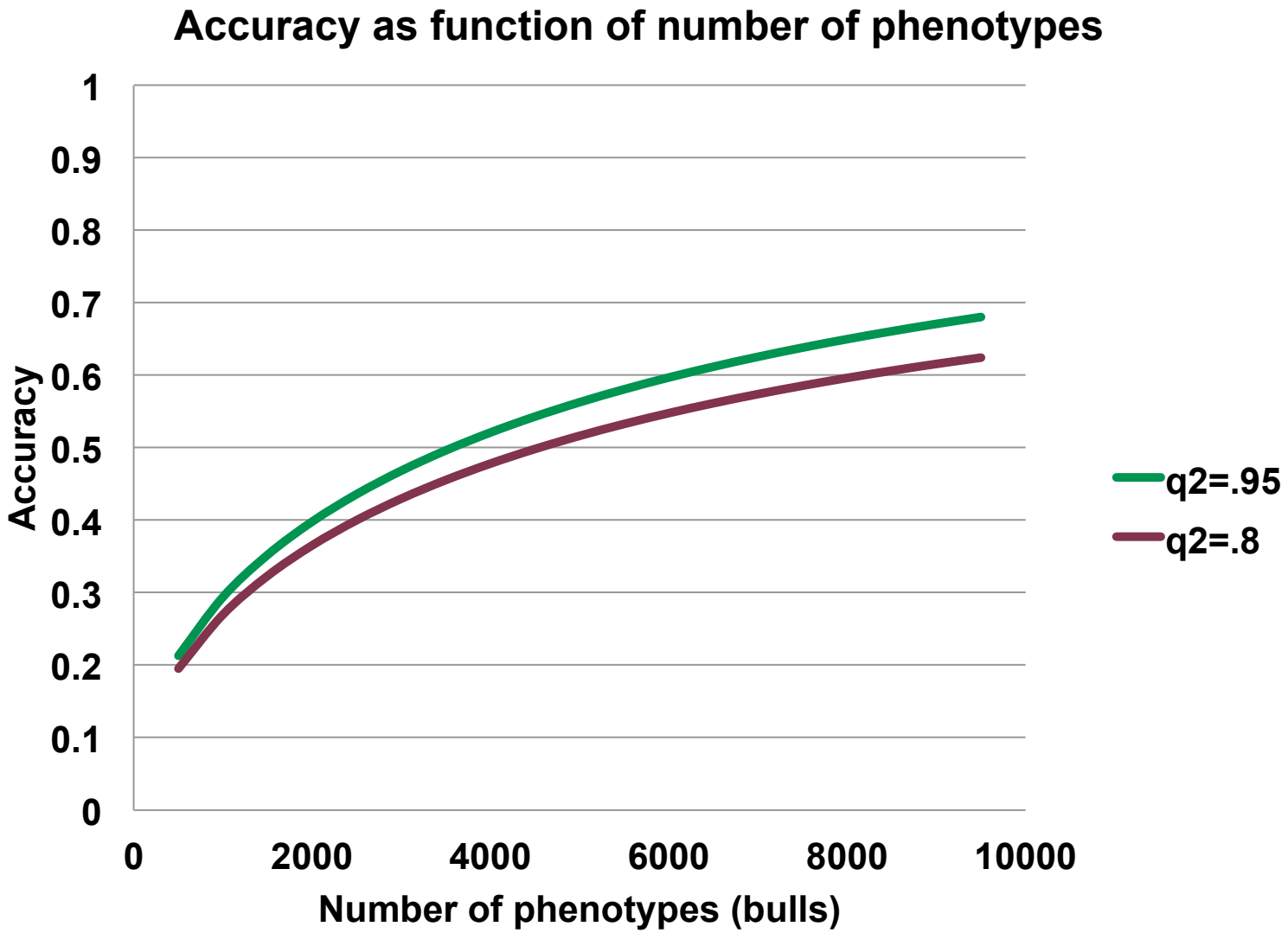
How to increase accuracy?
2. Increase LD

- Keep more SNPs, also with low MAF
  - Capture more rare QTL-alleles
    - a marker with intermediate frequency cannot be in high LD with a QTL with low frequency
  - Opens up for selecting more on (favorable) rare alleles: expected to result in higher long term genetic response
  - But hard to estimate their effects unless large data sets

How to increase accuracy?
2. Increase LD

- Keeping more SNPs might only have a small effect?
- Increase **density** of chip more effective?
  - Stronger LD between SNP and QTL
  - Increases the variation explained by the chip
  - Highly polymorphic traits not marked by low density chips, e.g., MHC
    - Use haplotypes instead?

HD increases accuracy but not by much, perhaps overestimated anyway



How to increase accuracy?
2. Increase LD

- Keeping more SNPs might only have a small effect?
- Increase **density** of chip more effective?
  - Stronger LD between SNP and QTL
  - Increases the variation explained by the chip
  - **However, not very promising results presented at Interbull meeting**
  - Maybe more phenotypes are needed because more effects are estimated
    - Not accounted for in equation for accuracy

How to increase accuracy? Conclusions

1. **Reference population size**
2. LD between markers and QTL

Increasing reference population size works but less well for functional traits

How to increase accuracy? Conclusions

1. Reference population size
2. **LD between markers and QTL**

Increasing chip density does not seem to increase accuracy very much (at least not with current methods)

Accuracy in Genomic Evaluation

- Still quite good accuracy, in theory
- However, requires that traits:
  - can be measured on all daughters of bulls
  - large number of bulls
  - **have been measured for a long time**
    - Also good: for longevity, we can use (almost) actual longevity
    - **problematic for new traits, say, progesterone-based fertility traits**

Two ways to measure new traits

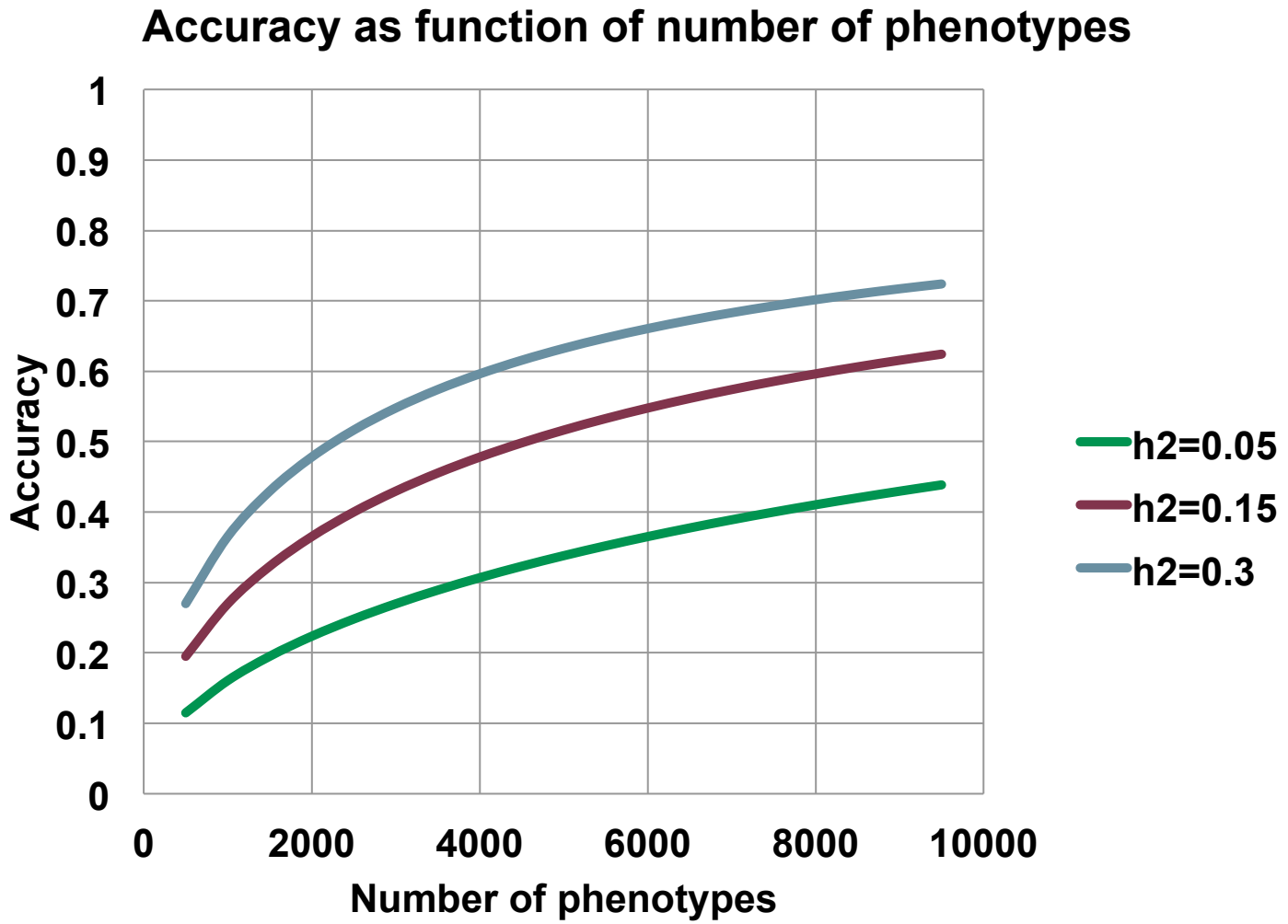
- 1. **Current approach of GS**: large number of observations on daus of sires
- Routine measurements from automatic recording etc,
  - Gives high accuracy/heritability for recent bulls but on too few bulls for a new trait
  - Works better for progeny testing, possible to select within batch of young bulls
- Not possible approach for direct measurements of traits that are very expensive or difficult to record, like feed efficiency

Two ways to measure new traits

- 2. **Measurements on genotyped cows**
  - measure whole cooperating herds
  - university research herds are a possible resource, publically funded, should be publically available
  - more cows need to be genotyped (than bulls) but fewer cows measured for the trait than if using bull EBVs

	h^2 0.05	h^2 0.15	h^2 0.3
Bull with 100 daughters	11 cows	5 cows	3 cows

Accuracy when measuring on cows



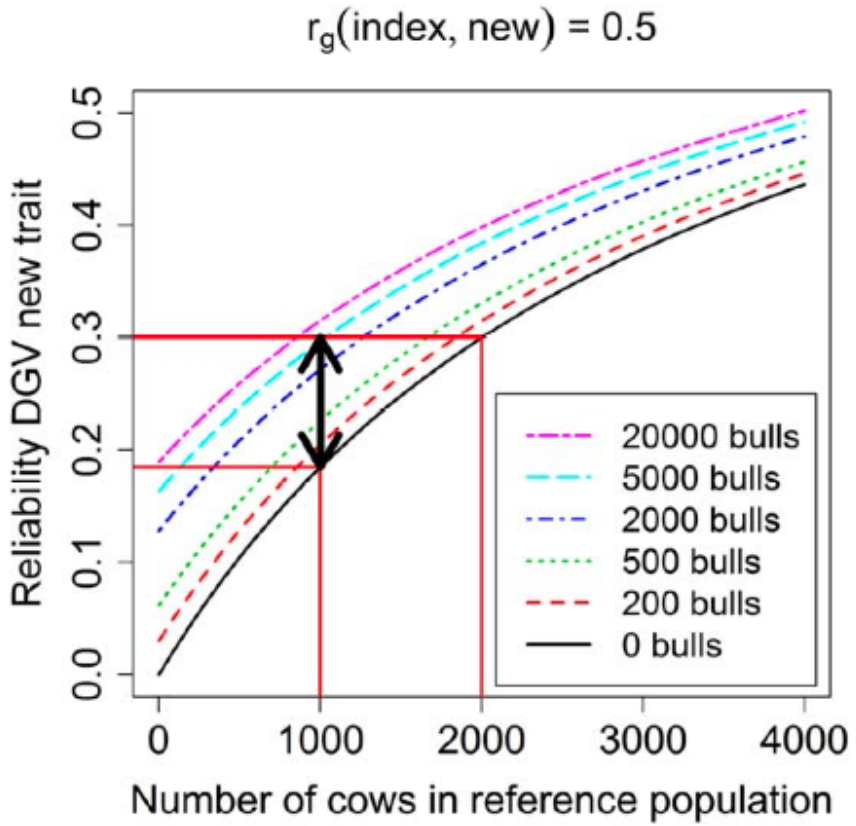
q^2=0.8

Measuring and genotyping cows

- Even if low accuracy still higher than nothing
  - Learn to accept low accuracy
- More likely that we measure the true traits rather than a proxy
  - CLA vs calving to first insemination interval,
  - therefore no loss of information due to rg<1 with goal trait

Measuring and genotyping cows

- Need to combine (new) traits measured in cow populations with old traits measured in bull reference population
- (Calus et al., 2011 (yesterday))



Measuring and genotyping cows

- Use of contract herds
- Which herds should be selected?
  - Top genetic herds but with genetic diversity
- Recording can be more standardized and therefore higher h^2
- GxE?
- Cost of recording might not go down in price as much as cost of genotyping

Merging herds – Example: RobustMilk

- Merging of phenotypes and genotypes from 4 countries' experimental stations
  - About 1650 records for milk production traits
  - Accuracy 0.7-0.8 for percentages, 0.23-0.48 for yields
  - Only about 1150 genotypes for progesterone, calving to first luteal activity CLA h^2=0.15-0.2, accuracy only expected to be around 0.3
  - More cows needed (but some of these probably exist already)

Veerkamp et al., 2011

Measuring and genotyping cows

- Might be only option for small breeds
- Run out of bulls to genotype
- Benefit from measuring new good traits and genotype cows

Conclusions

- Relative genetic response in functional traits most likely lower than the relative economic weights indicate also with genomic selection
- More work needed on how accuracy can be increased for functional traits
- GS gives possibilities to select for new traits closer to true physiological traits
  - Measuring and genotyping cows necessary
  - Combine with old traits from bull reference populations