Genomic data:

Insights into breed histories, population structures and genetic background of traits

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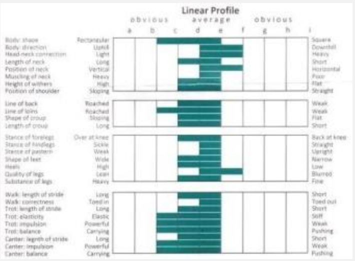
CAG
Center for Animal Genetics

Establishing a Linear Profile

- Define specific traits of value for breeding program
- Describe horses precisely, accurately, reproducibly
- Ultimate - full description of a horse’s phenotype
- Along with performance data from self and relatives, can derive Estimated Breeding Values (EBV) and other metrics.



Limitations of EBV

- Precision and reproducibly of measurements
- Number of traits of interest in breeding program
- Incidence of traits of interest in population

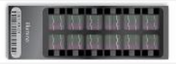
Mating two animals with high EBV will only on AVERAGE result in offspring with higher EBV

- Complex inheritance
  - Multiple genetic variants with small effects
  - Environmental effects
  - Slow genetic progress if selection for one trait is deleterious for other, harder to measure traits

Need to combine phenotype and genotype data

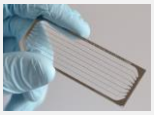
Genomic Profiling

- Illumina Equine SNP70 beadchip
  - 70 k SNP



- Affymetrix Axiom Equine HD chip
  - 670 k SNP

- Next generation sequencing (NGS)
  - Whole genome or exome sequencing (WGS/WES)
  - All variants, huge amount of data

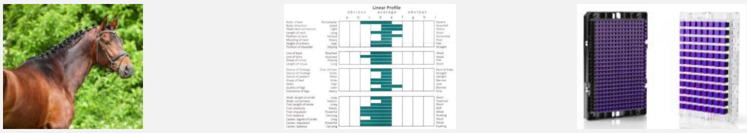


Once this “profile” exists, the genetic variants can be analyzed for association with any trait that has been recorded.

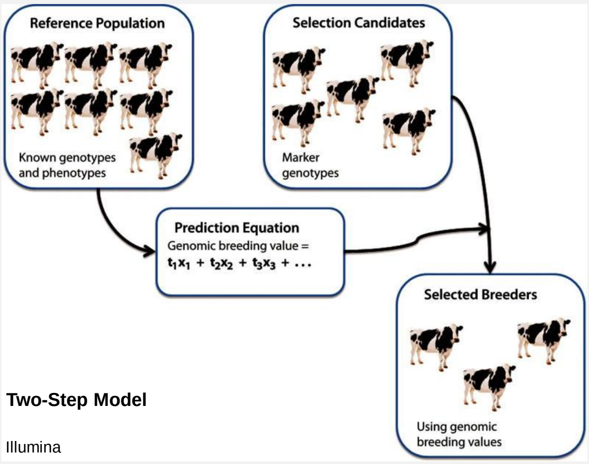
Genomic Selection

- Identifying genetic variants positively associated with traits and selecting for them in a breeding program
- (Requires: precise definition of traits of interest, consistent measurement)

→ Leverage Linear Profiling Data for the phenotyping



Genomic Selection

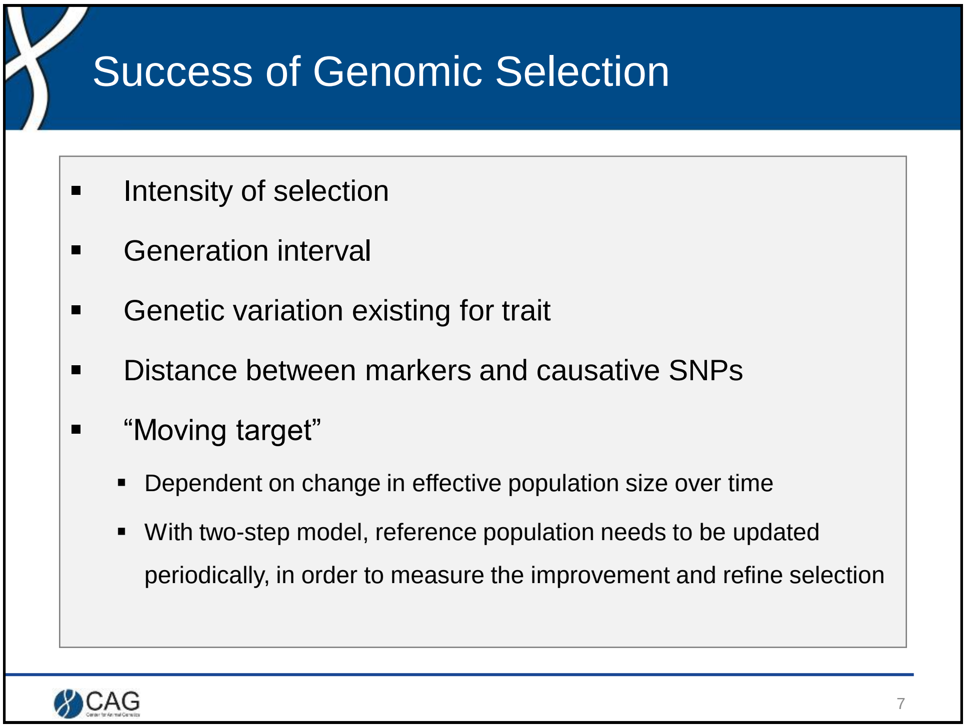


Two-Step Model

Illumina

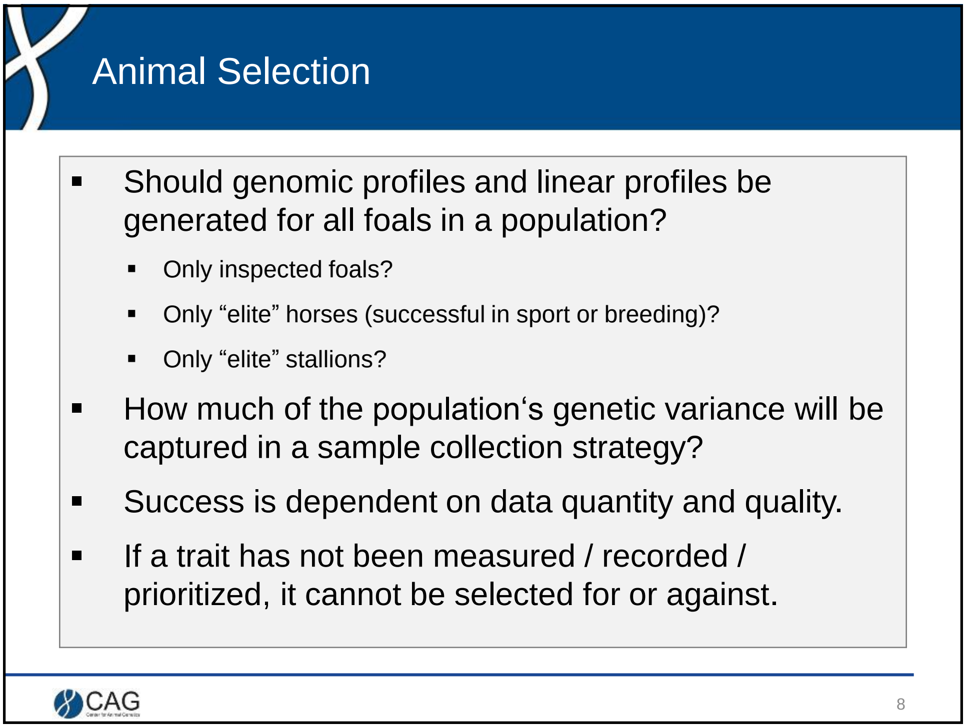
Single-Step Models also being considered in livestock

- Could include different trait groups (conformation, performance, etc.) and different breeds/populations
- Extremely computationally intensive
- Still in early development.



Success of Genomic Selection

- Intensity of selection
- Generation interval
- Genetic variation existing for trait
- Distance between markers and causative SNPs
- “Moving target”
    - Dependent on change in effective population size over time
    - With two-step model, reference population needs to be updated periodically, in order to measure the improvement and refine selection



Animal Selection

- Should genomic profiles and linear profiles be generated for all foals in a population?
    - Only inspected foals?
    - Only “elite” horses (successful in sport or breeding)?
    - Only “elite” stallions?
- How much of the population‘s genetic variance will be captured in a sample collection strategy?
- Success is dependent on data quantity and quality.
- If a trait has not been measured / recorded / prioritized, it cannot be selected for or against.

Trait Selection

If not under selection, a trait may be negatively affected by selection for other traits.

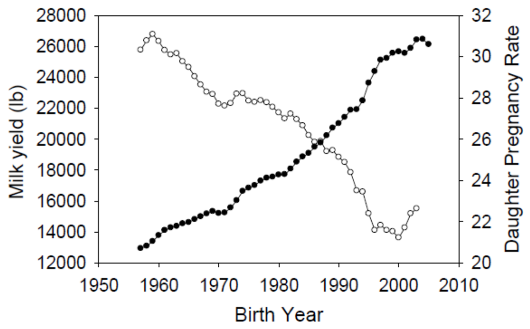


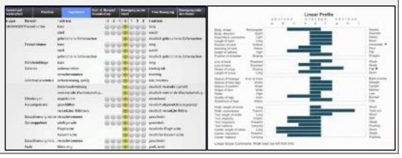
Figure 1. Trends in milk yield (●) and Daughter Pregnancy Rate (○) for US Holsteins. Data are from USDA-ARS Animal Improvement Programs Laboratory, February 2007 (available at http://aipl.arsusda.gov/ARSWeb/eval/summary/trend.cfm).

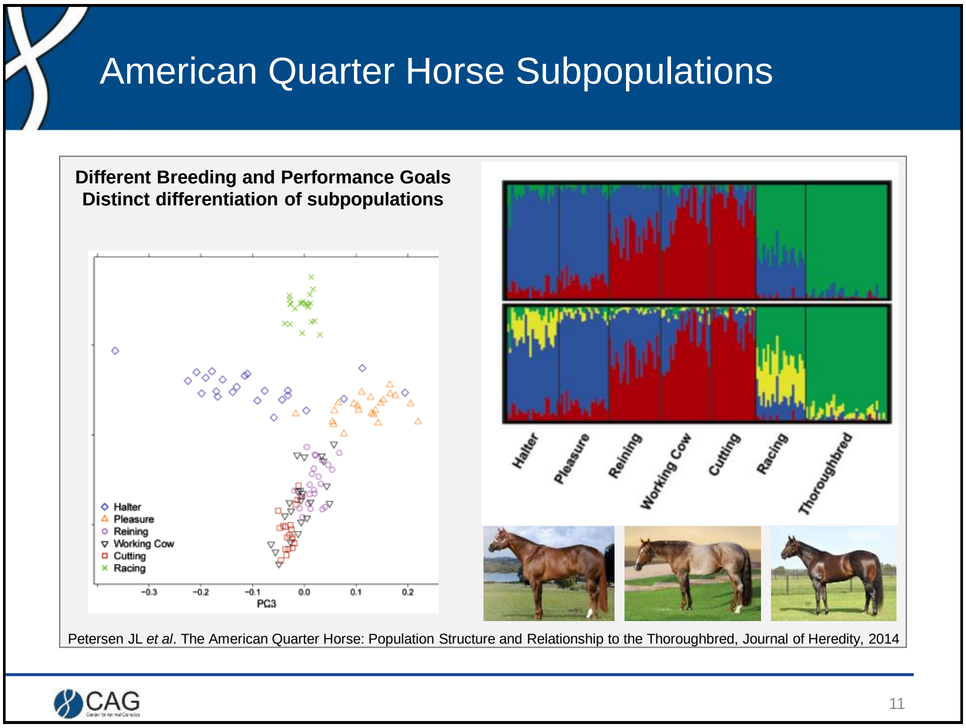
Selection for milk production in Holstein cattle led to reduced fertility.

Linear Profiling Considerations

- Each horse is compared to the average for that breed
- Average of the “elite” population may be very different than the average population of all horses in the breed, or of another breed
- Even if the trait definitions are standardized, genomic selection based on linear profiling of one population may not be appropriate for a different population.

→ Genomic profiling can help evaluate differentiation between (sub)populations.

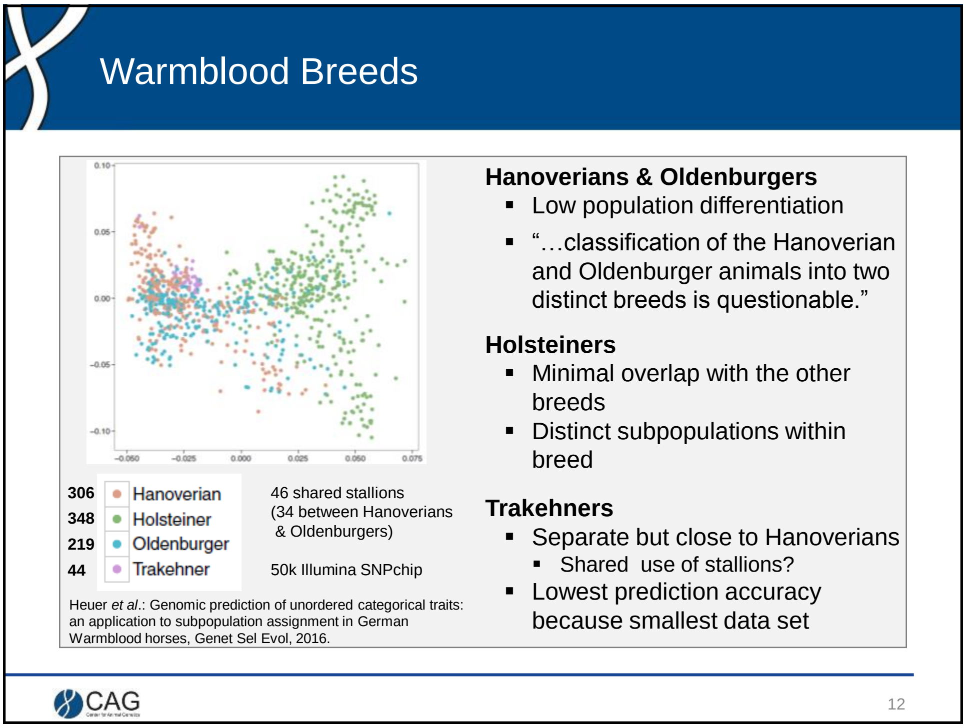




American Quarter Horse Subpopulations

Different Breeding and Performance Goals
Distinct differentiation of subpopulations

Petersen JL *et al*. The American Quarter Horse: Population Structure and Relationship to the Thoroughbred, Journal of Heredity, 2014



Warmblood Breeds

306 Hanoverian
348 Holsteiner
219 Oldenburger
44 Trakehner

46 shared stallions
(34 between Hanoverians & Oldenburgers)

50k Illumina SNPchip

Heuer *et al*.: Genomic prediction of unordered categorical traits: an application to subpopulation assignment in German Warmblood horses, Genet Sel Evol, 2016.

Hanoverians & Oldenburgers

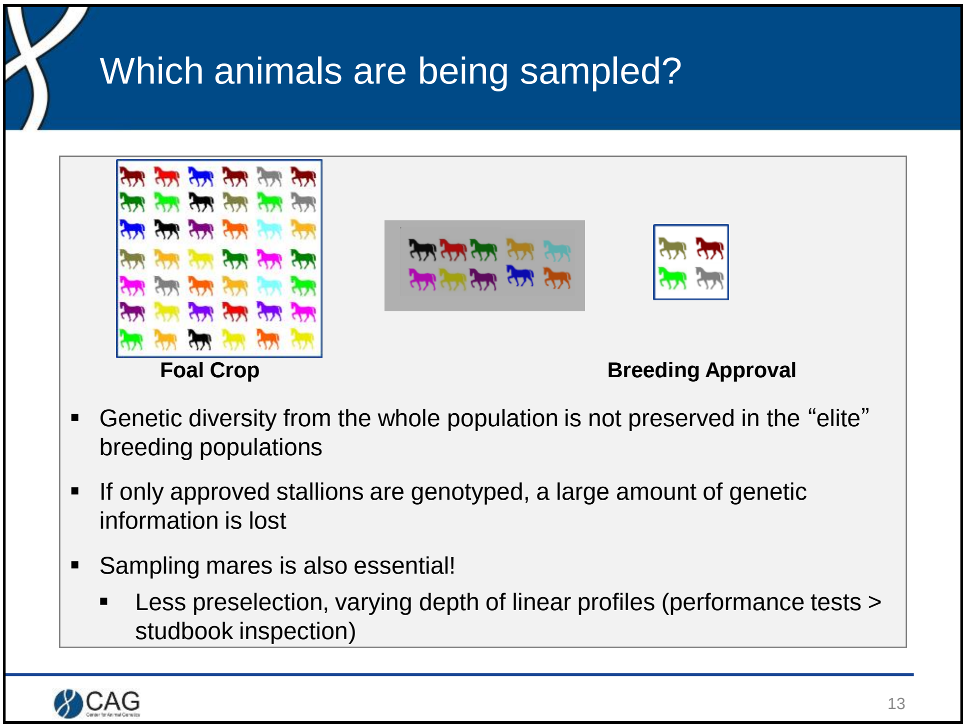
- Low population differentiation
- “…classification of the Hanoverian and Oldenburger animals into two distinct breeds is questionable.”

Holsteiners

- Minimal overlap with the other breeds
- Distinct subpopulations within breed

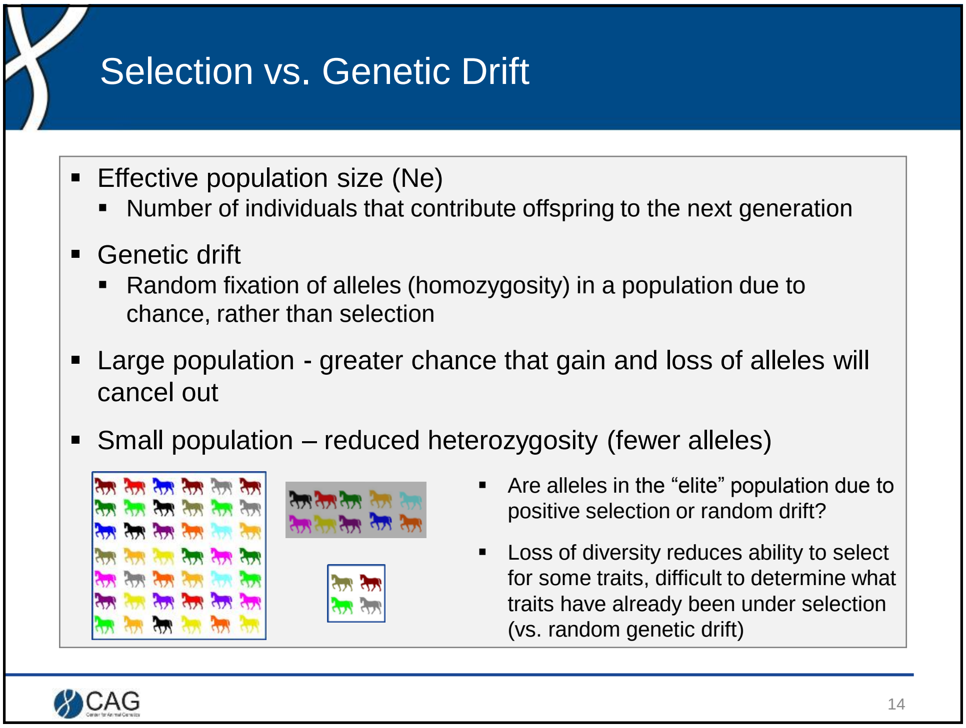
Trakehners

- Separate but close to Hanoverians
    - Shared use of stallions?
- Lowest prediction accuracy because smallest data set



Which animals are being sampled?

- Genetic diversity from the whole population is not preserved in the “elite” breeding populations
- If only approved stallions are genotyped, a large amount of genetic information is lost
- Sampling mares is also essential!
  - Less preselection, varying depth of linear profiles (performance tests > studbook inspection)



Selection vs. Genetic Drift

- Effective population size (Ne)
  - Number of individuals that contribute offspring to the next generation
- Genetic drift
  - Random fixation of alleles (homozygosity) in a population due to chance, rather than selection
- Large population - greater chance that gain and loss of alleles will cancel out
- Small population – reduced heterozygosity (fewer alleles)
  - Are alleles in the “elite” population due to positive selection or random drift?
  - Loss of diversity reduces ability to select for some traits, difficult to determine what traits have already been under selection (vs. random genetic drift)

Maintaining Genetic Diversity

- Inbreeding Depression
  - Lack of diversity decreases fitness
  - Loss of alleles that would allow for selection
- Outbreeding depression
  - Offspring may not be as well adapted / competitive as either parent
- Programs to increase diversity
  - Offspring often fail licensing inspections and are not allowed to breed

  → Intended diversity is therefore lost before entering the population
- Avoid the problem

  → Use genomic profiling to identify animals with high genetic diversity AND favourable genetic variants for traits of interest

Final Thoughts

- It is easier to preserve genetic diversity than to regain it
- Avoid extreme use of a small number of stallions
- Cryopreservation
  - Save sperm/embryos of many horses (not just “elite” stallions) for future use if genetic diversity is high or they have rare alleles
- Design your selection strategy and breeding goals to optimize the full potential of your breed.
- Consider genetic variants associated with traits of interest and overall genetic diversity to allow for sustainable genetic progress.

Thank you!

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