



# Next-Level Genomic Selection: Mitigating Inbreeding

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# Topics

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**Lyon:**

**“Inbreeding becomes a serious issue”**

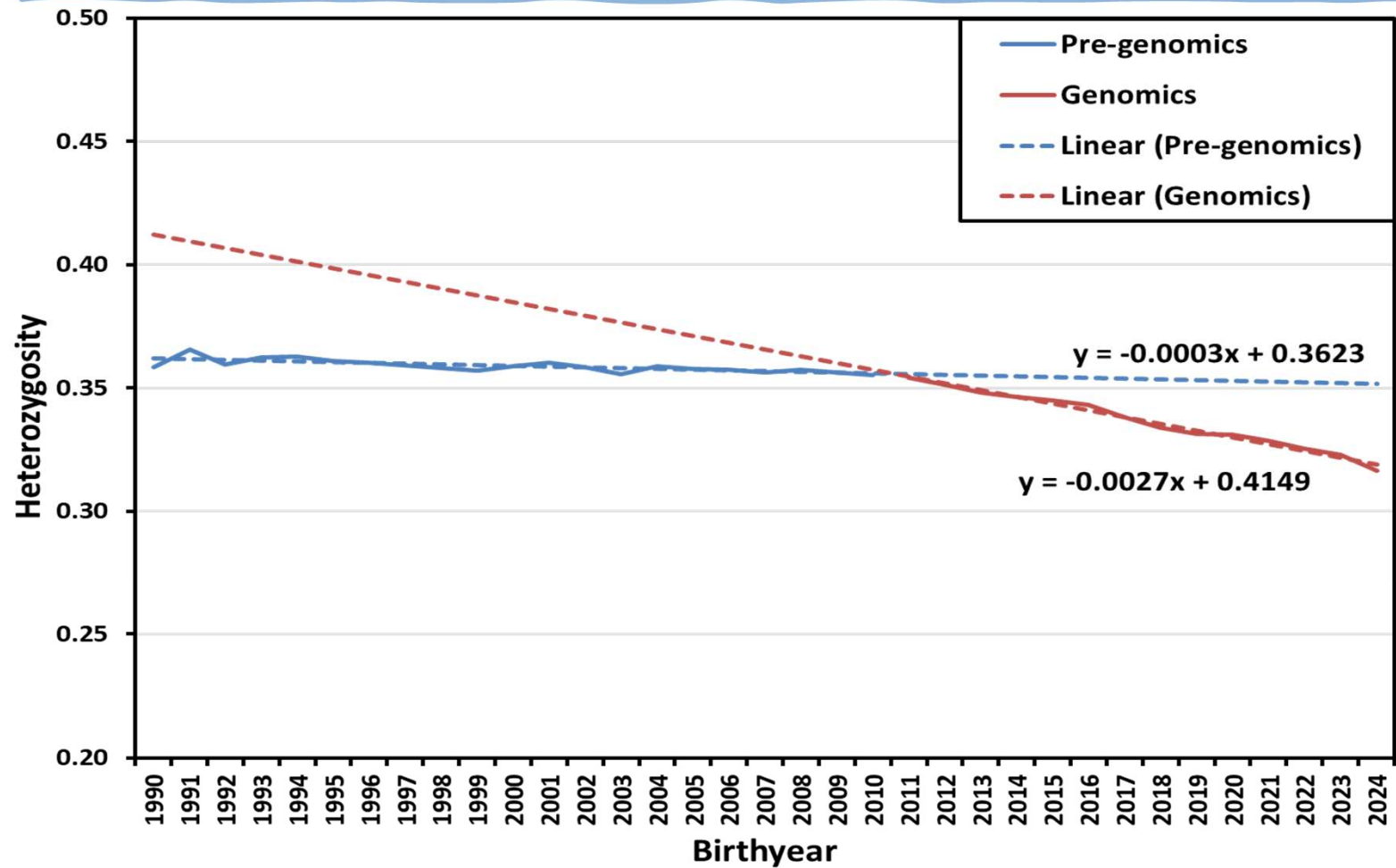
**Bled:**

**“Next-Level Genomic Selection: Mitigating Inbreeding”**

1. Issue of declining genetic variation
2. Genomic inbreeding coefficients from imputed data
3. Correlation between  $F_{ROH}$  and  $F_{GRM0.5}$
4. Inbreeding depression standardized effect size across traits



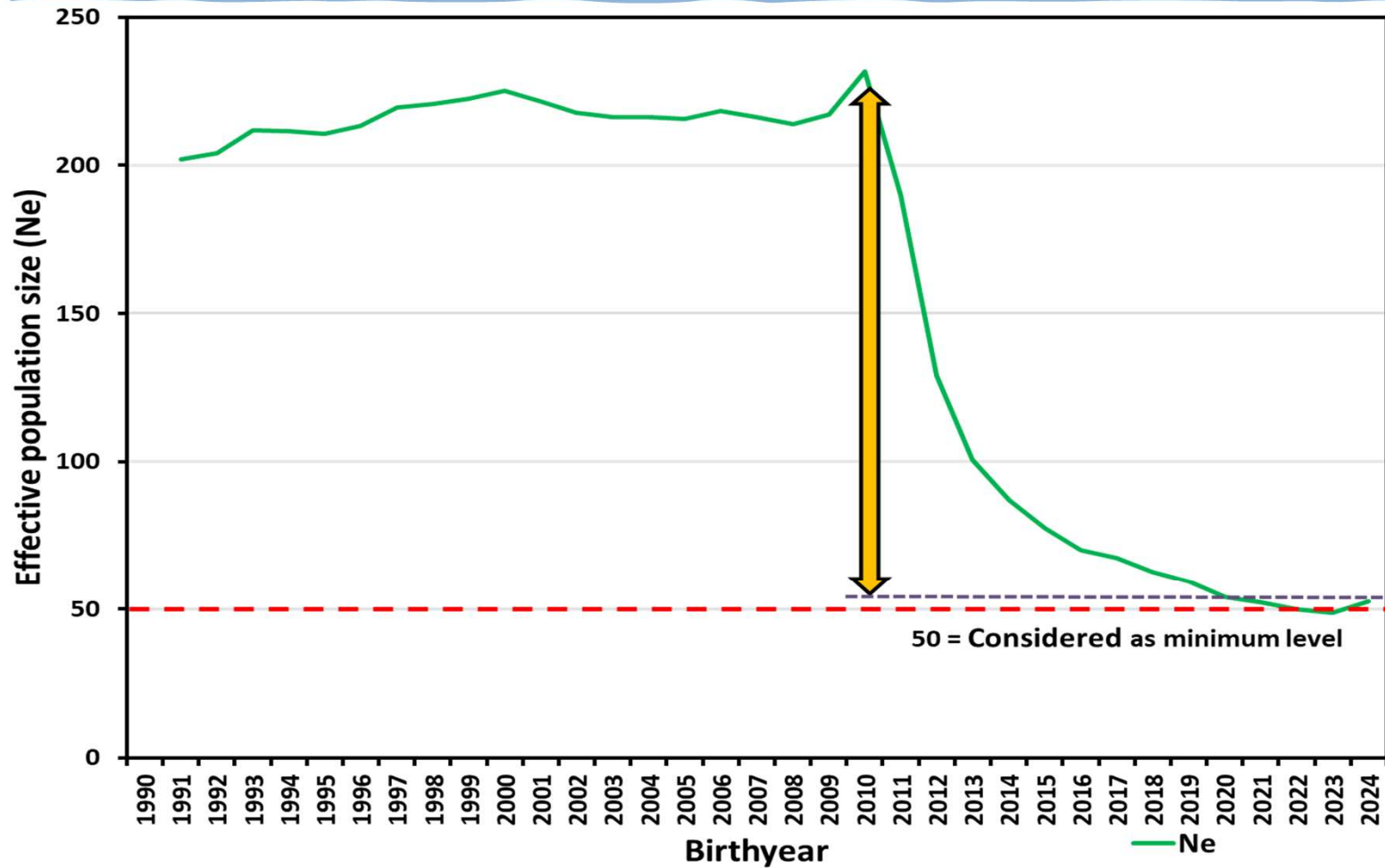
# Trend of SNP heterozygosity



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# Effective population size near minimum level





## Why Runs-Of-Homozygosity (ROH)?

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- SNP-segment based measure:
  - Accounts for **realized** Mendelian sampling
  - Does not depend on pedigree completeness and correctness
  - **IBD**-style: Closer to true inbreeding
  - **Probability**: No negative values
  - Fast computation



# How decent are inbreeding coefficients from imputed genotypes?

Paper:

- Dadousis et al 2024. Genomic inbreeding coefficients using imputation genotypes: assessing the effect of ancestral genotyping in Holstein-Friesian dairy cows. J. Dairy Sci. (In press)

## Check how good are 'imputed' genomic inbreeding coefficients:

- 329 HD (139K/777K) cow genotypes were downgraded by keeping only the SNPs present in one of:
  - GeneSeek Genomic Profiler 3 (26K)
  - Labogena MD (62K)
- Then they were imputed to the full imputation autosomal SNP-set (84K).
- Correlations of  $F_{GRM_{0.5}}$  and  $F_{ROH}$  between each of the 2 imputed downgraded MD datasets (GeneSeek Genomic Profiler 3 and Labogena MD) and the initial 84K SNP-data were estimated.
- $F_{ROH}$  based here on segments of 27 SNPs / 0.95 Mb or 80 SNPs / 2.8 Mb.



## Inbreeding coefficients entire downgraded set

Downgrade	N	Correlation	$F_{GRM_{0.5}}$	$F_{ROH}$ 27 SNP	$F_{ROH}$ 80 SNP
GGP <sub>3</sub> (26 K)	329	Spearman rank	0.85	0.85	0.90
	329	Pearson	0.43	0.48	0.89
	329	Concordance	0.26	0.39	0.87
Labogena MD (62 K)	329	Spearman rank	0.93	0.96	0.96
	329	Pearson	0.65	0.97	0.98
	329	Concordance	0.55	0.97	0.96



## Influence of parental information

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- Split the downgraded set in **2** subsets:
  - Subset **1** of animals **with** information on **both** parental sides i.e. **S+D** or **S+MGS** or **S+D+MGS**
  - Subset **2** of animals **without** information on **one or both** parental sides





# Inbreeding coefficients downgraded subset **1**: **With** info on **both** parental sides

Downgrade subset 1	N	Correlation	$F_{GRM_{0.5}}$	$F_{ROH}$ 27 SNP	$F_{ROH}$ 80 SNP
GGP3 (26 K)	266	Spearman rank	0.93	0.96	0.96
	266	Pearson	0.89	0.96	0.96
	266	Concordance	0.82	0.96	0.94
Labogena MD (62 K)	266	Spearman rank	0.98	0.99	0.98
	266	Pearson	0.97	0.99	0.98
	266	Concordance	0.95	0.99	0.97



## Inbreeding coefficients downgraded subset **2**: **Without** info on **one or both** parental sides

Downgrade subset 2	N	Correlation	$F_{GRM_{0.5}}$	$F_{ROH}$ 27 SNP	$F_{ROH}$ 80 SNP
GGP3 (26 K)	63	Spearman rank	0.68	0.54	0.67
	63	Pearson	0.65	0.34	0.65
	63	Concordance	0.14	0.10	0.55
Labogena MD (62 K)	63	Spearman rank	0.83	0.77	0.83
	63	Pearson	0.72	0.82	0.90
	63	Concordance	0.27	0.79	0.84

Shows importance of phasing



## Conclusions on imputed inbreeding coefficients

- 62K chip does better than 26K chip.
- $F_{ROH}$  shows better correlations than  $F_{GRM0.5}$ .
- Longer  $F_{ROH}$  shows better correlations than shorter  $F_{ROH}$ .
- Spearman rank correlations > Pearson correlations > Concordance correlations
- When **both** parental sides have genotypes results are fine.
- In 2023 **>97.3%** of animals has parental genotypes on both sides... so for recent animals results should be fine.



## GEFI: Genomic Expected Future Inbreeding

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- Genomics: More accurate relationship with future population
- **Expected Future Inbreeding... NOT own inbreeding**
- Expected future inbreeding coefficient: The probability in an autosomal segment that the haplotype transmitted from a future random mate is identical in descent to the transmitted haplotype of this individual.
- Fast check for expected fraction of autosomal segments that would be homozygous. This is ROH expected future inbreeding.



## Comparison Anafibj GEFI – CDCB GFI (1)

- **GEFI:**

- **ROH** based (~2.8 Mb), requires phasing, **IBD**-style, probability-style [0,1],
- Corresponds better with pedigree coefficients, genetic load and inbreeding depression,
- 2 years of reference, reference ~60.000 animals

- **GFI:**

- **GRM** based, does not require phasing, **IBS**-style, correlation-style [-1,1] (outcross can be -),
- Corresponds with covariance matrices/relationship matrices, MME,
- 4 years of reference, reference 2.000 animals



## Comparison Anafibj GEFI – CDCB GFI (2)

- 38.280 animals
- Correlation GEFI – GFI: **0,959**

	GEFI	GFI
Average	6,9	7,2
Std deviation	2,6	2,6
Maximum	15,3	13,5
Minimum	0,1	<b>-3,1</b>



## Standardized effect size $b \cdot SD(F)/SD(y)$ per trait type

Average across trait standardized effect sizes based on  $F_{ROH}$ :

- Yields: -0,072%
  - Contents: -0,014%
  - SCS: 0,014%
  - Fertility: -0,019% (in undesirable direction)
  - Type: Negligible
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- Ablondi et al 2023/2024, Doekes et al 2019, Makanjuola et al 2020, Mugambe et al 2023, Bjelland et al 2013



## Take home messages

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- Fast increase of inbreeding since genomic selection.
- Inbreeding negatively impacts nearly all traits, but the biggest impact is on **yield** traits.
- Anafibj intends to introduce a premium/penalty for expected future inbreeding later this year.
- We will use genomic estimates when possible and otherwise pedigree-based estimates on a comparable scale.
- Important to give a signal.





Thanks for your attention!!!

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