

# Genome-wide association study of fertility traits in dairy sheep

Bridge event  
June 2021



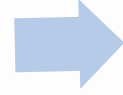
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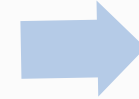
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# Introduction I

Selective animal breeding



desirable trait (e.g. fertility) maximisation



production increase

Traditional breeding techniques



pedigrees, markers & phenotypic data to estimate breeding values



often impractical (they ignore genes with small effects on phenotype)

(Meuwissen et al., 2016)

Genomic selection

Genome - Wide Association Studies (GWAS)

SNPs are analysed to identify association with phenotype

# Introduction II

## Chios sheep



[https://commons.wikimedia.org/wiki/File:Chios\\_Sheep.jpg](https://commons.wikimedia.org/wiki/File:Chios_Sheep.jpg)

first appeared in Chios – then spread to mainland Greece

high milk production

can be further improved to increase annual yield

(Ligda et al., 2000)

### Fertility traits analysed in the current study:

- **total prolificacy:** number of total lambs born
- **lamb survival:** number of living offspring / total number of lambs born
- **age at first lambing**

# Methodology I

## 1) Genotyping

- 538 sheep from 3 farms genotyped with the *Ovine SNP50K Bead Chip*

## 2) Quality Control (*Plink v1.07*)

- SNPs in mitochondrial and sex chromosomes
- SNP call rate
- Minor Allele Frequency (MAF)
- Sample call rate
- Duplicates
- SNPs in “chromosome 0”
- **Result**: 45,937 SNP markers and 528 individuals

(Turner et al., 2011)

## 3) Principal Component Analysis (*GEMMA*)

- genomic relatedness matrix decomposition
- aims to detect population structure

# Methodology II

## 4) Genome Wide Association Analysis (*GEMMA*)

- association between SNPs and phenotypes
- direct linear mixed model

$$\text{Model equation: } \mathbf{y} = \mathbf{W}\boldsymbol{\alpha} + \mathbf{x}\boldsymbol{\beta} + \mathbf{u} + \boldsymbol{\epsilon}$$

$\mathbf{y}$  = phenotypes

$\mathbf{W}$  = covariates

$\boldsymbol{\alpha}$  = associated fixed effects

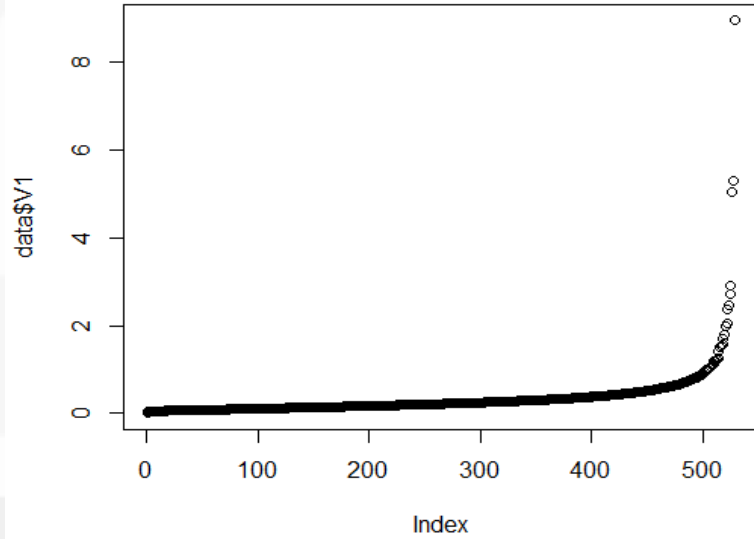
$\mathbf{x}$  = marker genotypes

$\boldsymbol{\beta}$  = regression on the phenotype of the marker genotypes

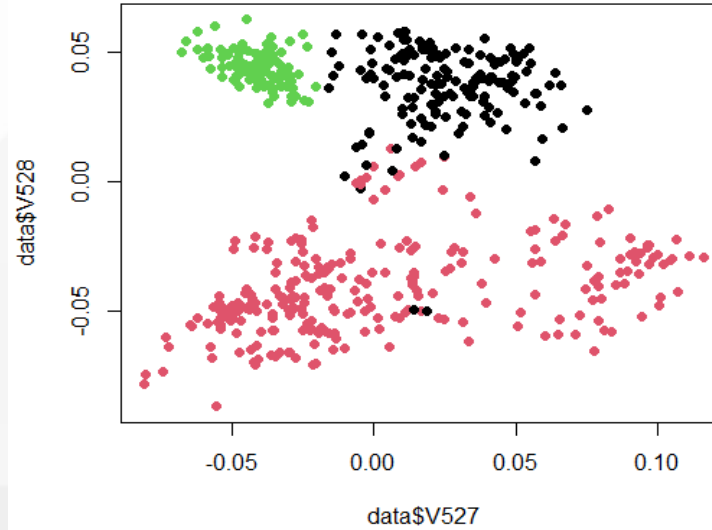
$\mathbf{u}$  = polygenic effects

$\boldsymbol{\epsilon}$  = residual errors

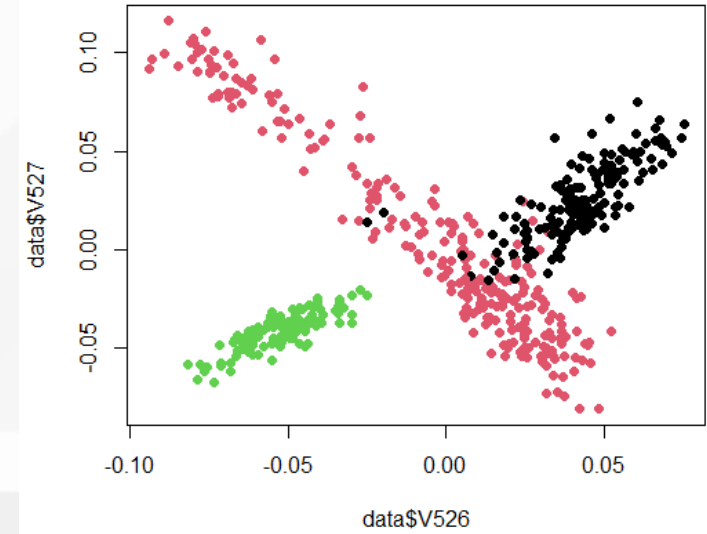
# PCA results



**Figure 1.** Eigenvalues in increasing order. The top three (Principal Components) explain most of the variance and are taken into account to correct for population structure.



**Figure 2.** Score plot of the PCA with PC1 (528) plotted versus PC2 (527). Each dot represents an animal, coloured by their farm of origin.

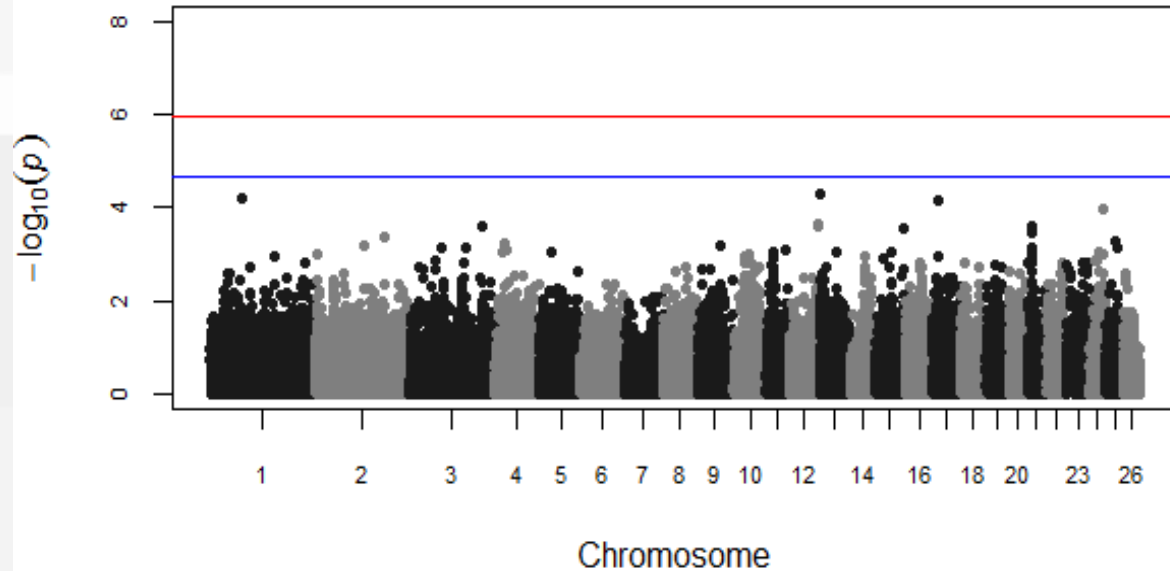


**Figure 3.** Score plot of the PCA with PC2 (527) plotted versus PC3 (526).

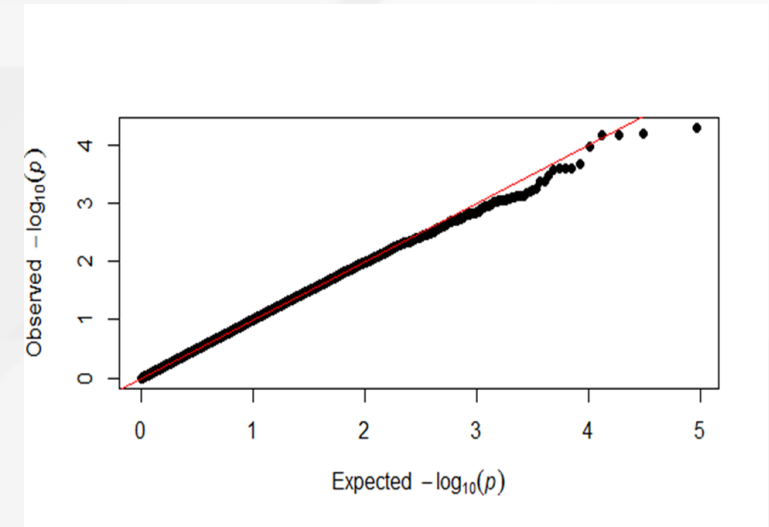
**Clustering** → **population structure** linked to the **farm of origin**

# GWAS results - total prolificacy

- **Phenotype:** total prolificacy
- **covariates & fixed effects:** farm, number of lactations, total days milked, principal components



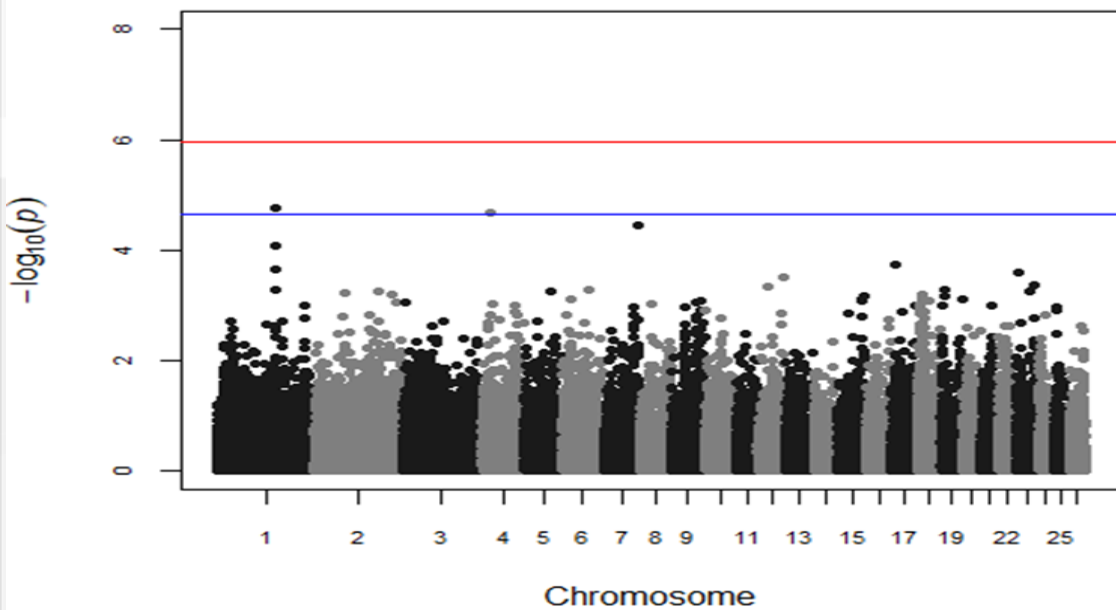
**Figure 4.** Manhattan plot. No SNP reached the genome-wide/suggestive significance level.



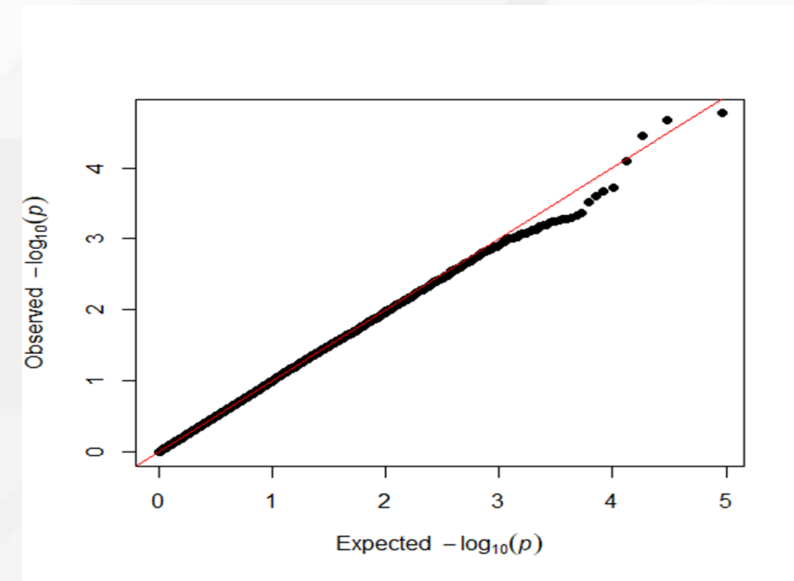
**Figure 5.** QQ plot of the data shown in the Manhattan plot.

# GWAS results - lamb survival

- **Phenotype:** lamb survival
- **covariates & fixed effects:** farm, total prolificacy, first lambing year, total number of lactations, age at first lambing, principal components



**Figure 6.** Manhattan plot. 2 SNPs on chromosome 1 and 4 respectively reached the suggestive significance level.

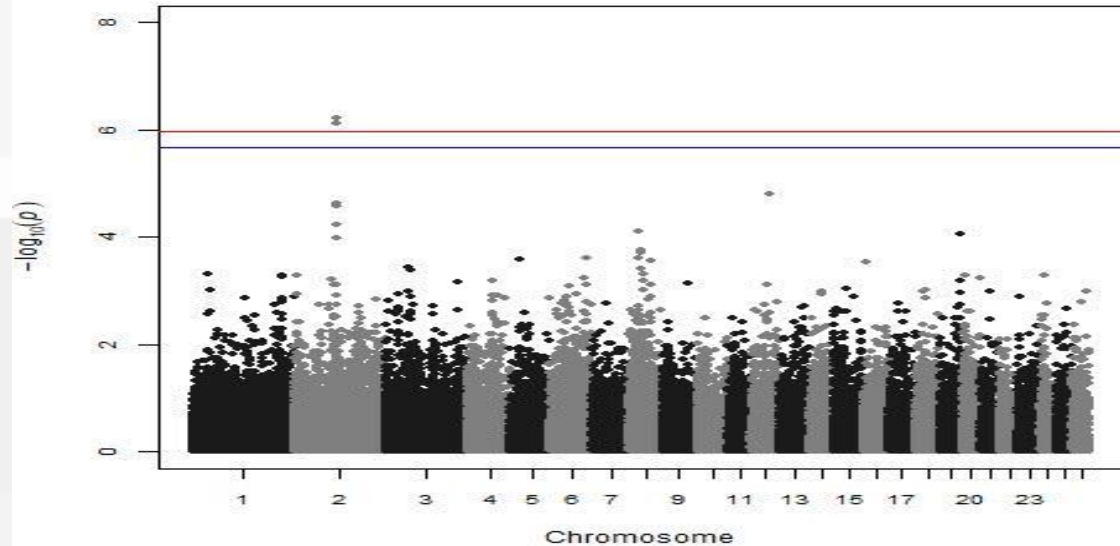


**Figure 7.** QQ plot.

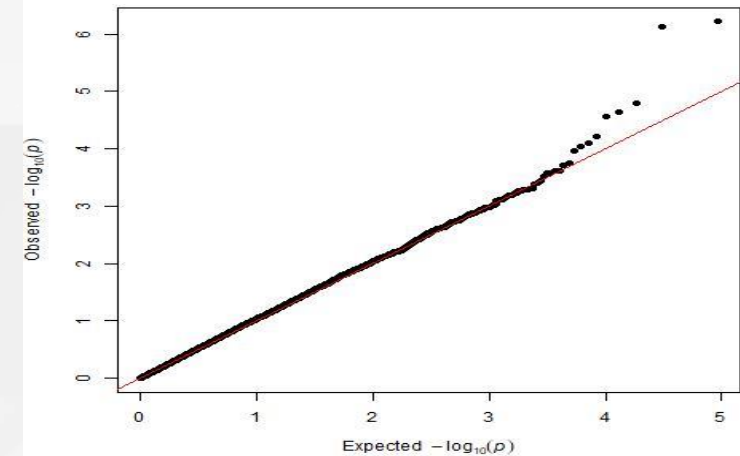


# GWAS results - age at first lambing

- **Phenotype:** age at first lambing
- **covariates & fixed effects:** farm, first lambing year, first lambing month, birth-year, birth-month



**Figure 8.** Manhattan plot. 2 SNPs on chromosome 2 reached the genome-wide significance level.

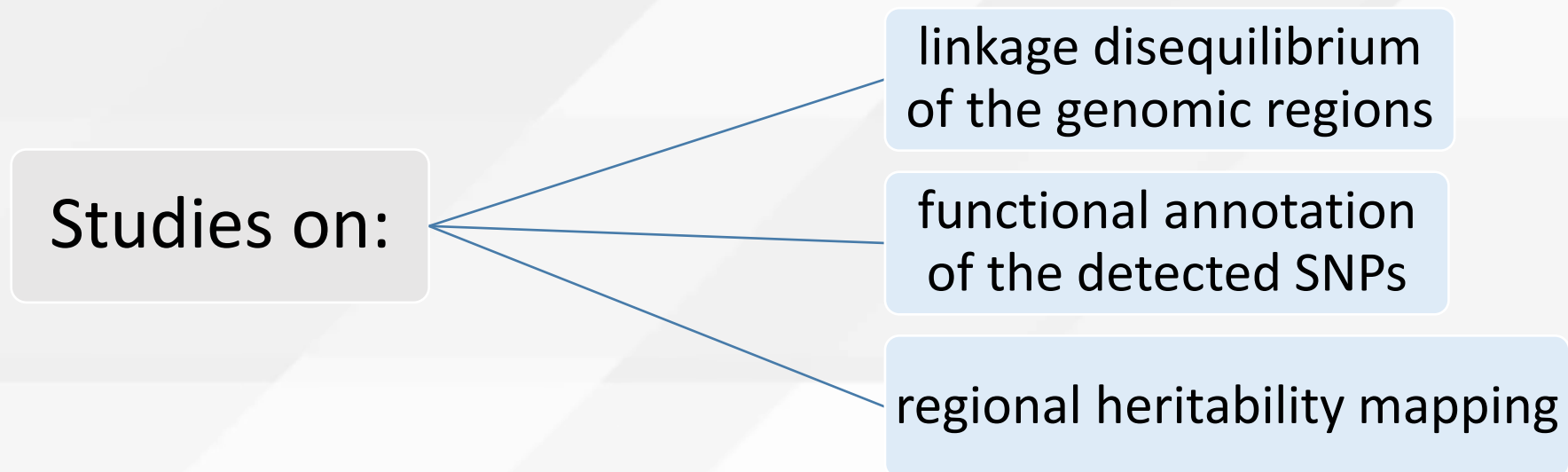


**Figure 9.** Lambda – corrected QQ plot. Lambda factor was calculated at 1.061 ( $> 1.05$ ) indicating inflation, therefore correction for population structure was performed.

# Conclusions

- Overall results imply a **polygenic mode of inheritance** for these traits with specific genomic regions of interest.
- **Two suggestive significant SNPs**, located on chromosome 1 and 4 in the Chios sheep genome, were associated with lamb survival.
- **Two genome – wide significant SNPs** located in chromosome 2 were associated with age at first lambing.

# Future Steps



# Acknowledgements

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Thank you for your attention!!!

