

Feasibility of a genomic selection approach for gastro-intestinal nematodes resistance based on single-step evaluation and a female informative population in Sarda breed sheep

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INTRODUCTION

Gastrointestinal nematodes:

- infections determine **important yield reductions and increased production costs** in Sardinian grazing sheep
- **99.4%** of sheep farms in the island administrate **anti-helminthics treatments** (on average 1.54/year)
- **Not well planned protocols** in terms of individual diagnosis, doses and frequency of treatments
- **Anti-helminthics resistance** has already been reported in several countries and there are some evidence of its appearance also in Sardinia

INTRODUCTION

Gastrointestinal nematodes:

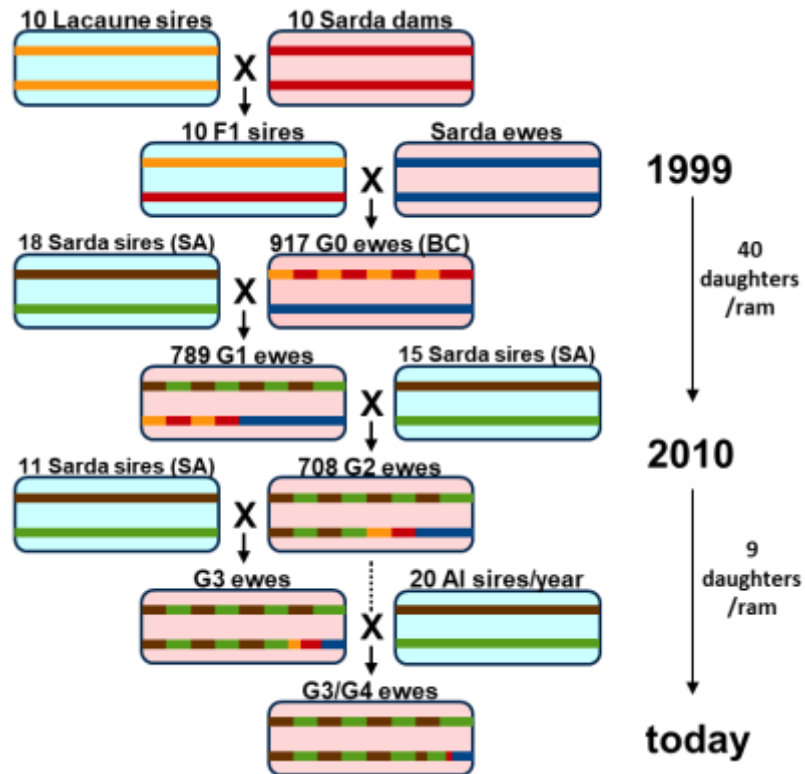
- **Fecal egg count (FEC)**, i.e. the number of parasite eggs per gram of faeces has been largely used as proxy trait to measure resistance
- **FEC genetic variation** between individuals and breeds has been documented in sheep
- **But including** nematodes resistance in current **breeding schemes is hampered** by the difficulty to record FEC at Herd Book scale.

AIM

To assess the feasibility of a **genomic selection approach** based on a **female nucleus (FRP) as reference population** and young herd book (HB) rams as selection candidates by:

- a) using **single-step GBLUP** to improve the genomic predictions accuracy of HB rams by **exploiting pedigree information**
- b) detecting the **optimal weights of A and G matrices into H matrix** using **heritability** and **predictive ability** as indicators
- c) evaluating the **expected accuracies of selection candidates**

NUCLEUS FLOCK: Female Reference population



- 800 milking ewes raised with the typical Sardinian dairy sheep farming system
- 25% yearly replacement with AI or NM rams HB
- All genotyped with the Illumina OVINE50bEADCHIP
- All recorded for the most important economic traits

Finally, until now 20 generations were produced for a total of 5,386 ewes from 10 F1 and 208 Sarda HB rams

Phenotyping

- **16,977 individual FEC recorded on 4304 ewes** from 1 to 3 times per year from 2000 to 2020.
- FEC recording for a QTL detection experiment was closed in 2012 and restarted in 2015 for the new cohorts with the perspective of implementing MAS or GS
- FEC were log-transformed using $\ln\text{Fec}=\ln(\text{FEC}+14)$

	Mean	Std.Dev	Min	Max
FEC	332	727	0	21090
lnFec	4.82	1.43	2.64	9.96

Genotyping

- **4304 FRP ewes, their sires (194) and available male ancestors (78 rams) as well as 734 Sarda rams** were genotyped with the Illumina Inc. OvineSNP50 Beadchip.
- SNP editing was performed using call rate and MAF thresholds of 90% and 1%, respectively.
- After quality control, 43,293 SNP across 26 autosomes were retained for the analysis.

Pedigree files

- Pedigree file of FRP traced back to three generations and included 6,242 animals.
- 2,323 animals were added when HB rams were considered

Single-step GBLUP, different weights of A and G into H

H matrix contains the joint relationships of genotyped
and ungenotyped animals

$$\mathbf{H} = \begin{bmatrix} \mathbf{A}_{11} & \mathbf{A}_{12} \\ \mathbf{A}_{21} & \mathbf{G}_w \end{bmatrix} = \mathbf{A} + \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{G}_w - \mathbf{A}_{22} \end{bmatrix}$$

$$\mathbf{G}_w = w\mathbf{G} + (1 - w)\mathbf{A}_{22} \quad (\text{VanRaden, 2008})$$

w assumed values of 0.00, 0.20, 0.40, 0.60, 0.80, 1.00

Repeatability animal model with date of sampling, age of the animal (from 1 to 4 years), and the interaction between number of lambs and distance from lambing as fixed effects

All the analyses were performed using BLUPf90 suite programs (Miształ et al. 2002)

Predictive Ability (PA):

Records of 235 ewes of the last two cohorts were masked in the GEBV estimation model and correlations between genomic predictions and **Yield Deviations** (average InFec adjusted for fixed effects) were calculated

The model with the highest h^2 and predictive ability estimates was used for the GEBV estimation of:

1006 genotyped rams

- 272 sires or ancestors of FRP ewes
- 489 old rams of HB born from 1993 to 2015
- 245 rams born from 2016 and 2020 as **selection candidates**.

The **expected accuracy** of breeding values was calculated as: $r_{BV_i} = \sqrt{1 - \frac{SEP_i^2}{h_{ii} \times \sigma_a^2}}$

Variance components estimates with single-step GBLUP
using different weights (w) when blending G and A into H

	wG = 0.00	wG= 0.20	wG = 0.40	wG = 0.60	wG = 0.80	wG = 1.00
s^2_a	0.416 ± 0.035	0.460 ± 0.035	0.459 ± 0.034	0.438 ± 0.032	0.407 ± 0.030	0.383 ± 0.029
s^2_{pe}	0.067 ± 0.022	0.029 ± 0.021	0.029 ± 0.020	0.045 ± 0.019	0.070 ± 0.018	0.082 ± 0.017
s^2_e	1.189 ± 0.015	1.190 ± 0.015	1.191 ± 0.015	1.192 ± 0.015	1.192 ± 0.015	1.193 ± 0.015
s^2_{tot}	1.672	1.680	1.678	1.675	1.669	1.658

h^2	0.249	0.274	0.273	0.262	0.244	0.231
r	0.289	0.292	0.290	0.288	0.286	0.281

Heritability, Predictive Ability (PA) and expected accuracy (r_{BV})

(comparison with milk yield)

Nematodes resistance

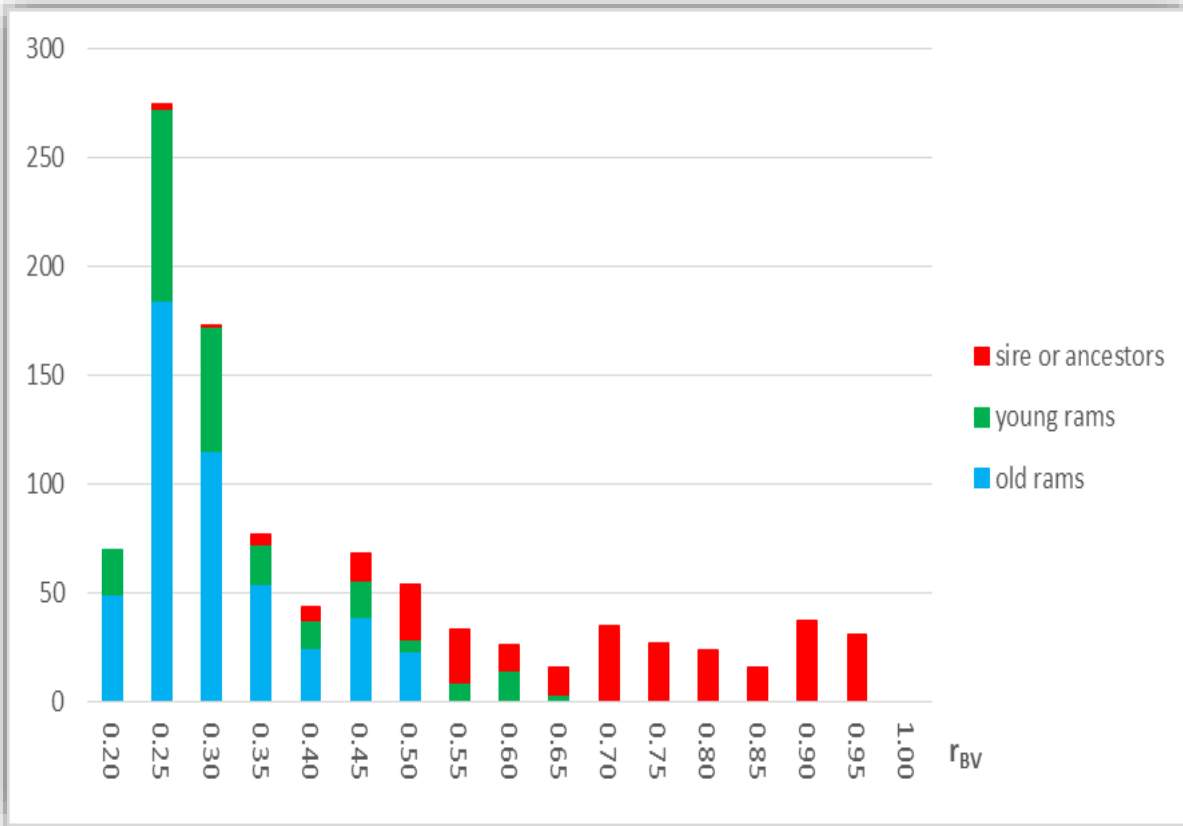
	wG= 0.00	wG = 0.20	wG = 0.40	wG = 0.60	wG = 0.80	wG = 1.00
h^2	0.25	0.27	0.27	0.26	0.24	0.23
PA	0.304	0.317	0.320	0.320	0.319	0.316
r_{BV}	0.450	0.470	0.493	0.519	0.547	0.575

Milk yield

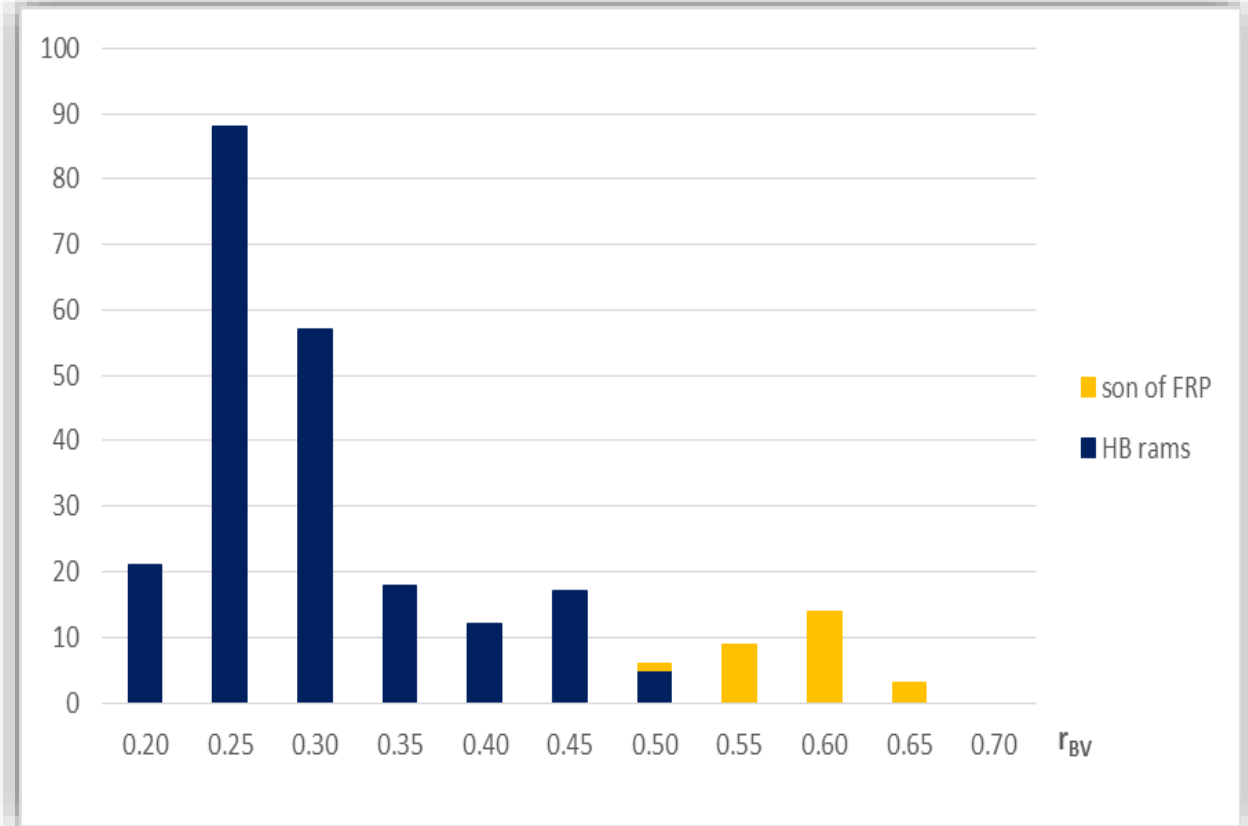
	wG= 0.00	wG = 0.20	wG = 0.40	wG = 0.60	wG = 0.80	wG = 1.00
h^2	0.41	0.44	0.42	0.39	0.35	0.33
PA	0.244	0.262	0.260	0.251	0.238	0.221
r_{BV}	0.479	0.496	0.514	0.535	0.557	0.582

Expected accuracy (r_{BV}) of HB rams obtained using the best model (0.40 weight of G)

Distribution of the expected accuracies of 1006 HB rams



Distribution of the expected accuracies of 245 selection candidates



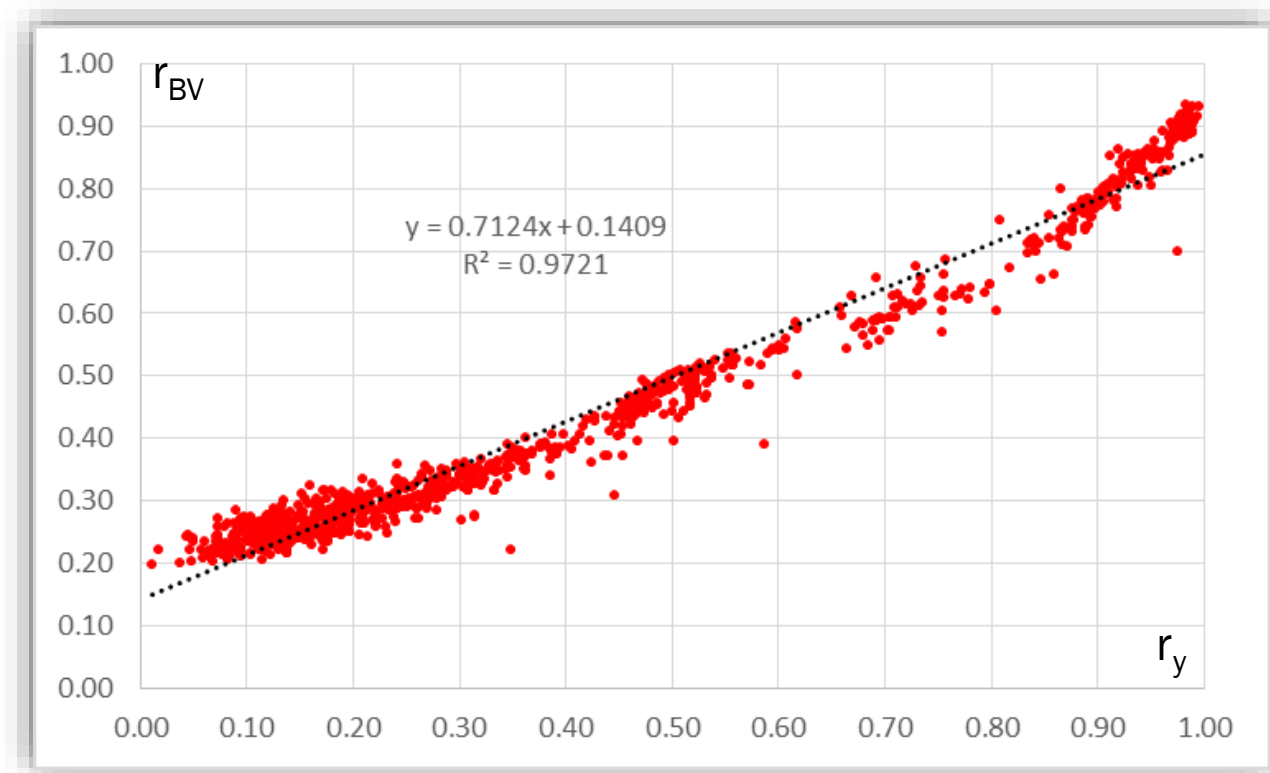
Expected accuracies (r_{BV}) of HB rams depend on the amount of information on relatives (r_y) in FRP and can be predicted by A

Multiple correlation method

$$r_y = \sqrt{a_{yx}^T A_{xx}^{-1} a_{yx}}$$

a_{yx} = vector of relationships between ram y and all ewes of FRP

A_{xx}^{-1} = matrix of relationships between ewes of FRP



Regression of expected accuracy (r_{BV}) on the amount of information on relatives (r_y)

CONCLUSIONS

- ✓ Single-step GBLUP is essential to manage genomic selection based on female reference populations.
- ✓ In our population high **weights** of **A** are needed when building **H** to improve h^2 and predictive ability. It is likely that **A** adjusts for genomic relationships in **G** which are partly due to IBS rather than IBD genome sharing.
- ✓ **Recording pedigree** information in HB is then crucial either to build **H** or calculate information on relatives in FRP and predict expected accuracies.
- ✓ A better understanding of **genomic predictions accuracies** is needed to optimize the flow of animals from and toward the nucleus in order to achieve good accuracies for most selection candidates

Perspectives

- ✓ Accuracy of genomic predictions may be improved including in the evaluation model 10 highly significant SNP identified in QTL detection analysis (Casu et al., submitted)
- ✓ In the short term, **genomic predictions for resistance to gastro-intestinal nematodes will be delivered just for the HB selection candidates** well genetically connected with the nucleus