Application of various models for the genomic evaluation of bovine tuberculosis in dairy cattle

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Introduction

- Bovine tuberculosis (bTB) is a chronic bacterial disease of cattle caused *by Mycobacterium bovis*
- It presents a significant challenge to the UK cattle sector incurring annual costs of about £175 million
- Routine genetic evaluation for resistance to bTB has been implemented in the UK since January 2016.
- Trait was defined as positive skin test plus no positive skin test but having positive post–mortem examination results with infection rate of 8.29%
- bTB has a low heritability of about 0.09 and with bulls having an average reliability of 0.45

Objectives

- Study investigated whether inclusion of genotypic data might help increase accuracy.
- Some peculiar issues
  - Rate of infection is different for older vs younger bulls due to exposure time of their progeny to the disease.
  - With an all-or-none trait this can result in quite big shifts from one run to the next when progeny groups are still small.
  - Therefore validation candidates based on year of birth might not be optimum

- The study therefore looked at various models in addition to different methods of creating validation data sets
  - SNPBLUP, BayesCpi, Single-Step (SS)
  - Different levels of polygenic effects

Objectives

- Generally, polygenic effects are fitted to capture genetic variance not accounted by SNPs.
- Questions is; does including polygenic effects a uniform effect on SNPs of different allele frequencies?

- Therefore the impact of different levels of polygenic effects on SNP solutions for SNPs of different alleles is also examined.

Data for SNP-BLUP and BayesCpi

- Data consisted of 2232 Holstein-Friesian bulls
  - with deregressed proofs with at least 10 daughters and 40% reliability
  - Genotypes equivalent to the 50K chip were used - low density chips were all imputed to 50K chip and relevant SNPs extracted from HD chips
  - 43143 SNPs were analysed after edits
  - 1695 reference bulls were those born before 2007
  - 537 validation bulls born 2007 and onwards

Distribution of REF bulls and VAL by reliabilities

	REF	VAL
<=45	0	17
46-50	14	38
51-55	55	88
56-60	103	105
61-65	164	108
66-70	146	82
71-75	158	47
76-80	126	14
81-85	161	17
86-90	206	13
91-95	248	7
94-99	314	1

Different Validation sets

- Two additional different validation bulls were created
  - Random sample of first 30 bulls with reliability >=89 in the reference set plus all validation bulls with the same level of reliability (1888 bulls in REF & 344 in VAL)
  - Random sample of first 30 bulls with reliability >=93 in the reference set plus all validation bulls with the same level of reliability (2018 bulls in REF & 214 in VAL)

SNP-BLUP -Model and Analysis

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- Linear model consisting of
  - mean effect
  - random residual polygenic effect (0, 10, 20 and 30%)
  - random SNP effects

- Y- variable de-regressed sire proofs
- The number of daughters used as weights

- Accuracy were computed from correlations between DGVs and de-regressed proofs in validation set.

- BayesCpi - same model but with no polygenic effect

- Chain length was 80,000 with 24,000 regarded as burn-in period

Single step Analysis

- Analysis based on 607,929 cows with 934,987 records and a pedigree of 7,486034 animals
- Model of described in detail in Banos et al 2016 was fitted.
- Briefly an animal model
  - Fixed effects: mean, breakdown, year by month of breakdown, parity
  - Covariates: duration, age, %Holstein genes

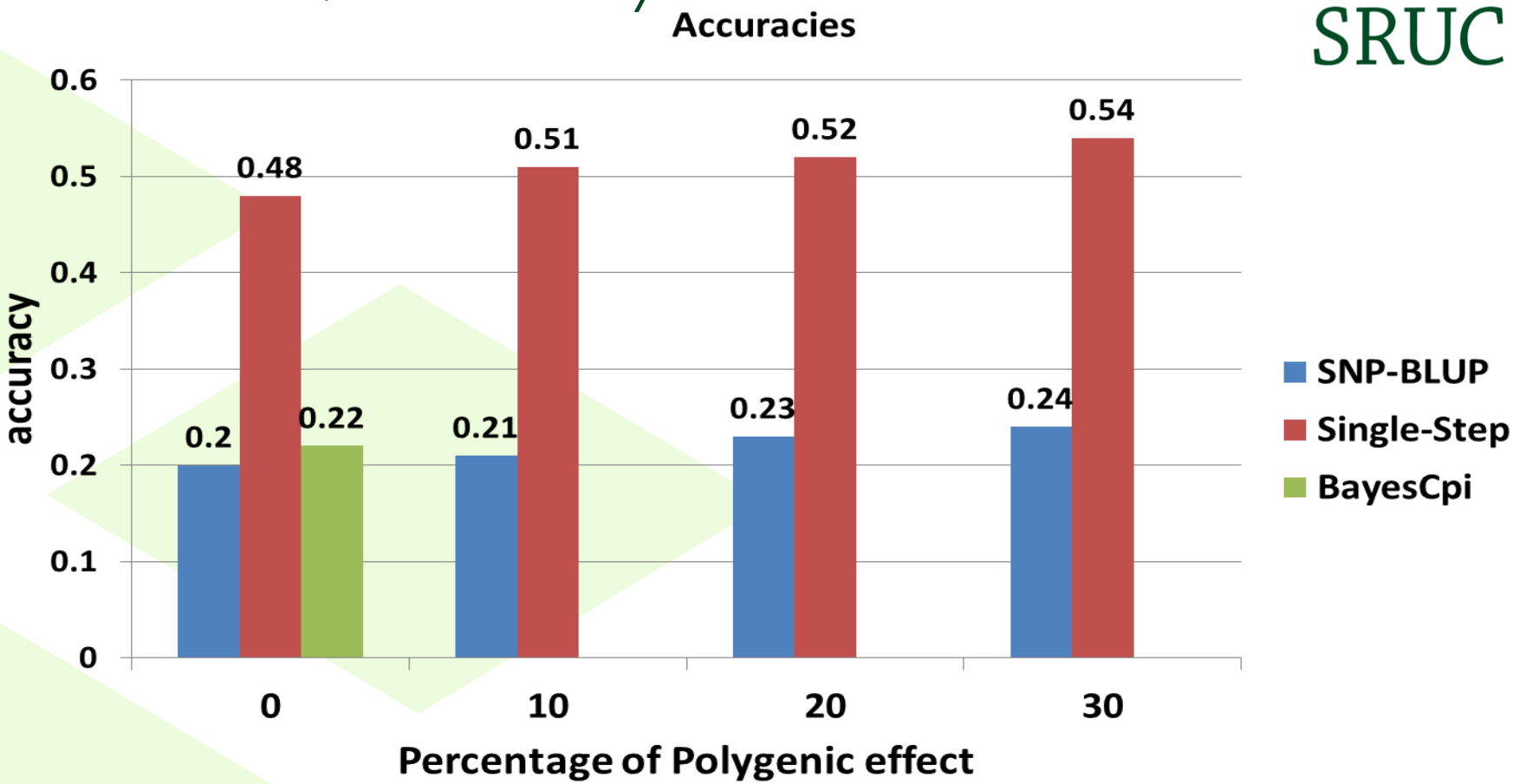
Single step Analysis

- 5435 sires of cows with records had genotypes
- **G** was computed for these sires
- The G_{22} matrix was then computed as
  $G_{22} = (1-w)G + wA_{22}$, with w set at 0, 10, 20 and 30%.

- The H^{-1} was then computed for all animals incorporating the G_{22} for the genotype animals.

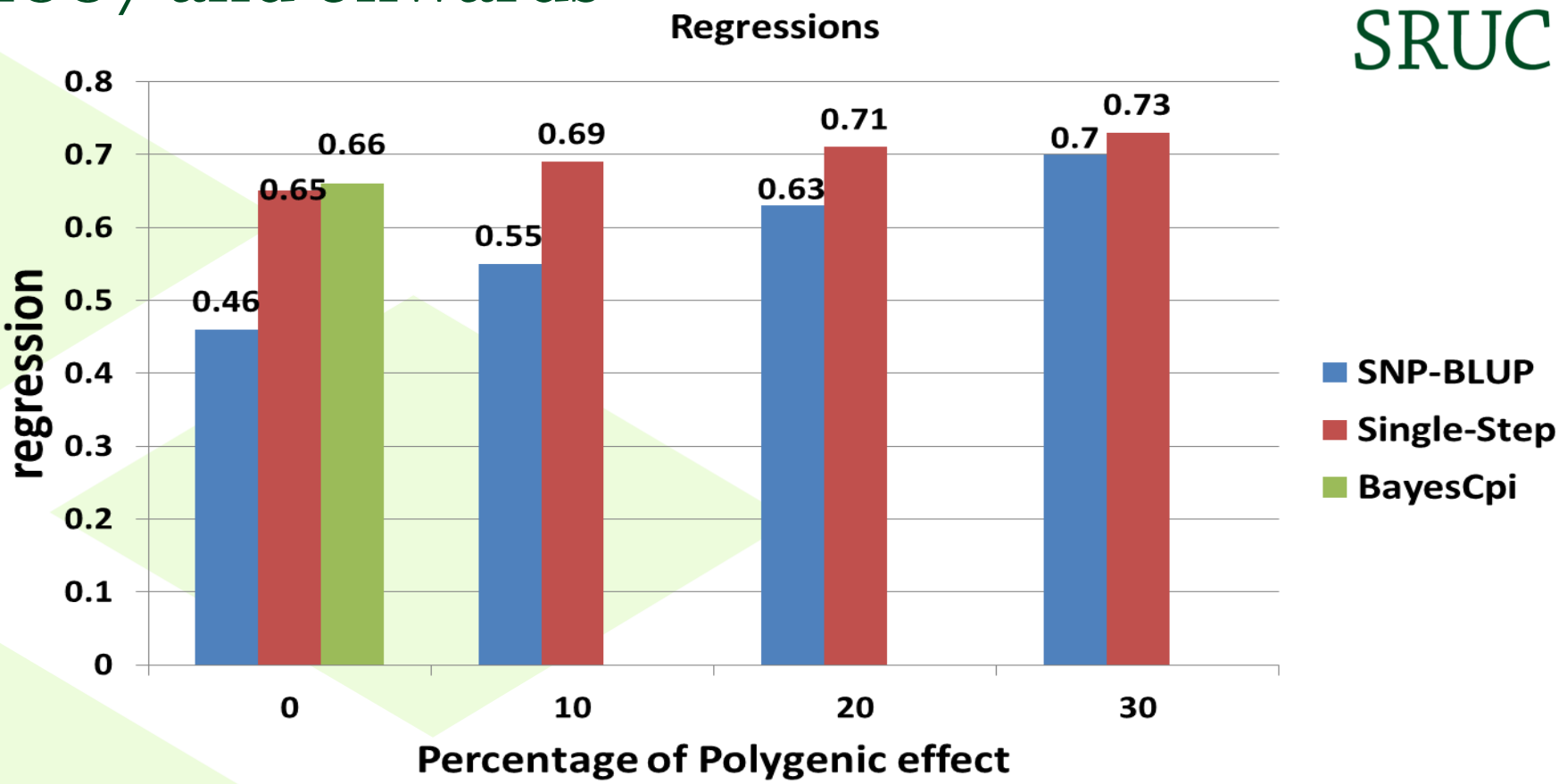
- The same set of validation bulls were also with records for their daughters set missing
- Accuracy were computed from correlations between GEBVs and
  - mean of the bull's individual daughter deviations
  - or de-regressed proofs in validation set

Accuracies of genomic prediction from validation bulls 2007 and onwards



- Corrections based on de-regressed proofs for Single-Step varied from 0.56 to 0.62

Regressions based validation bulls 2007 and onwards



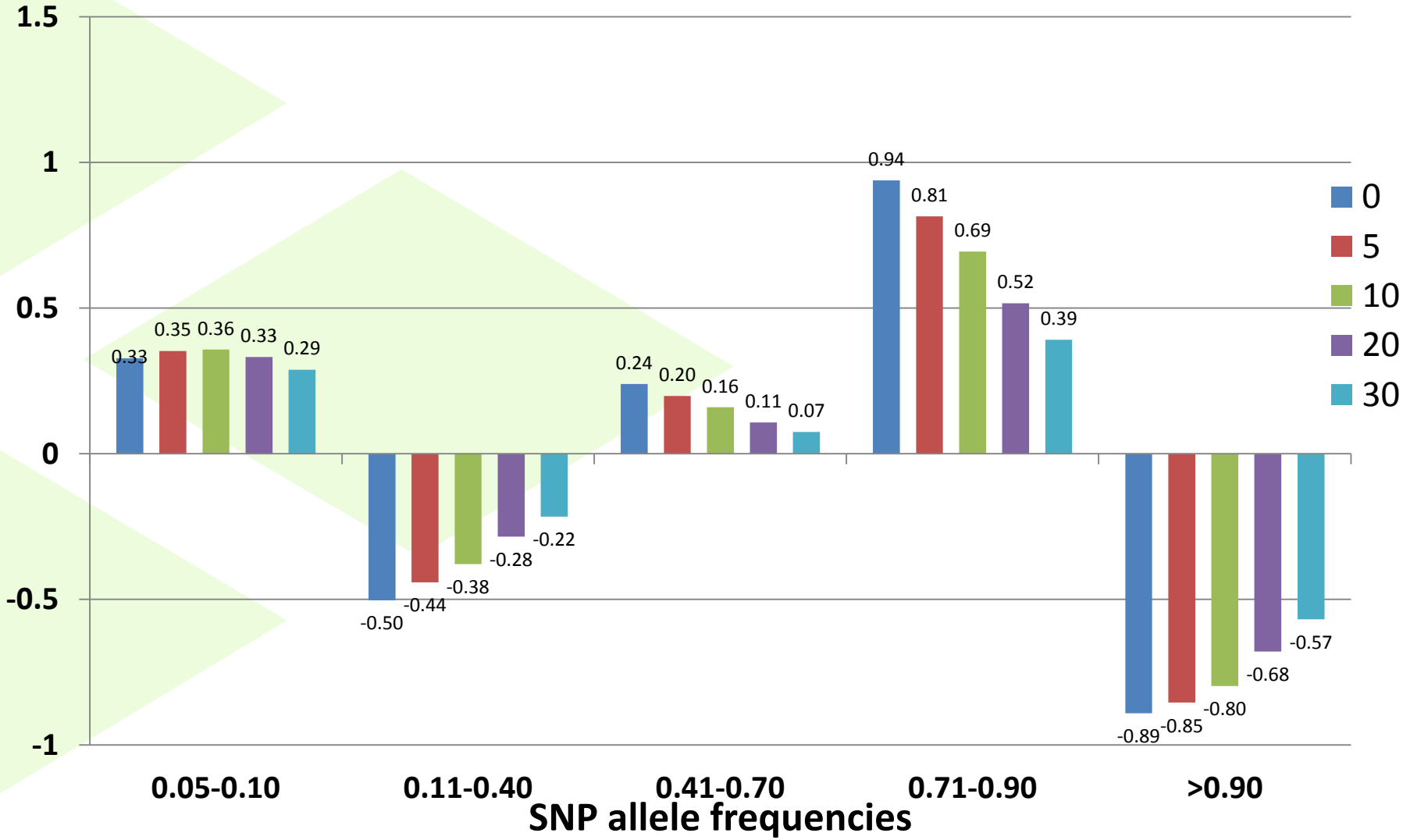
- Regression based on de-regressed proofs for Single-Step varied from 0.75 to 0.83

Results from alternative validation sets

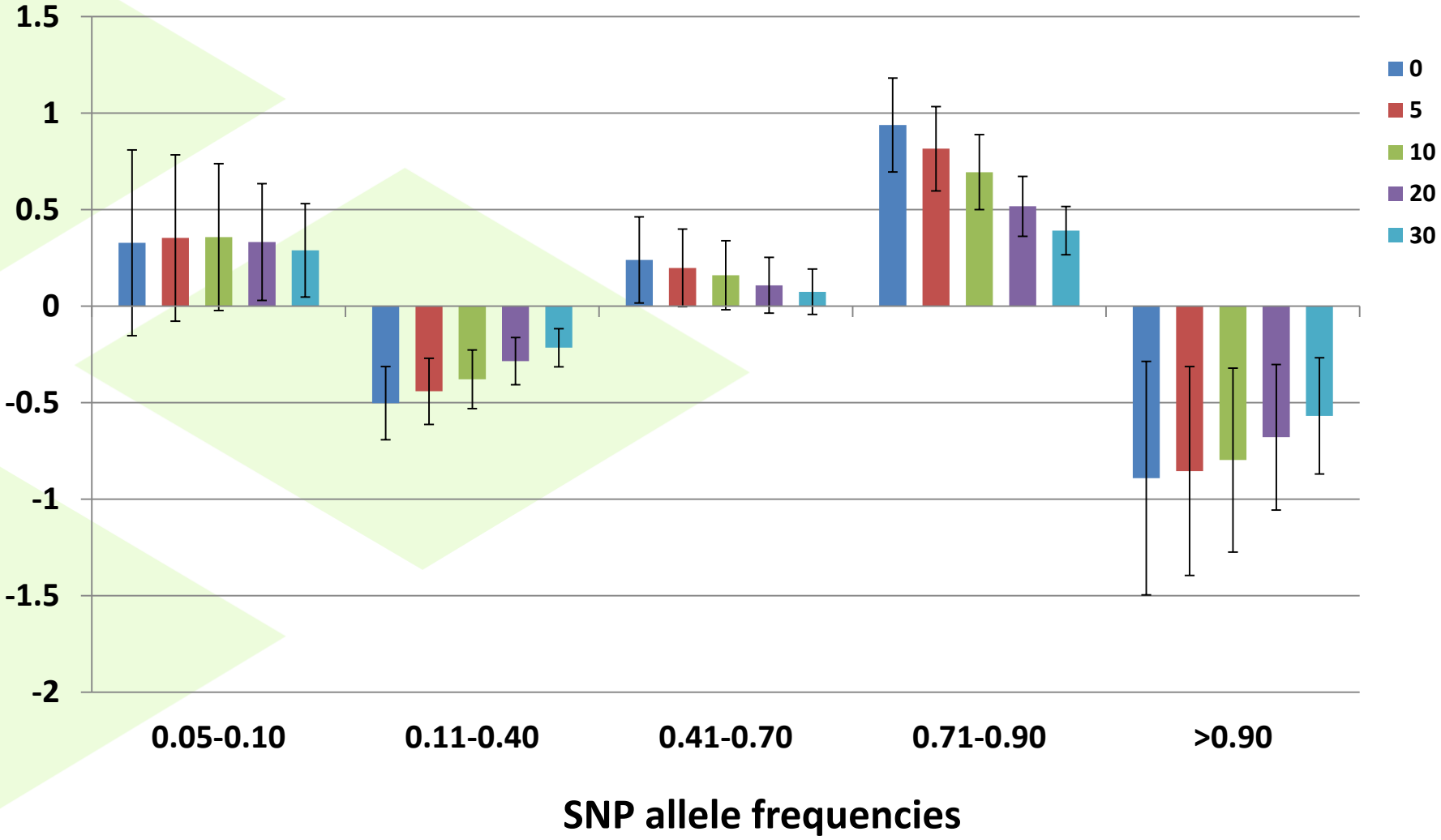
	SNP-BLUP (30% polygenic)		BayesCpi		Single-Step	
	Corr.	Reg.	Corr.	Reg.	Corr.	Reg.
>=89 Rel bulls	0.32	0.65	0.34	0.70	0.51	0.53
>=93 Rel Bulls	0.41	0.77	0.42	0.83	0.56	0.54

- Average accuracy for young animal from Animal model evaluations = 0.37

Mean SNPs effects at different levels of polygenic effects from SNP-BLUP



Mean SNPs effects with SEs at different levels of polygenic effects from SNP-BLUP



Conclusions

- Given the data structure and size
  - Single-Step evaluations seems the most appropriate to apply in this study
- Definition of validation data sets to capture similar rate of infection as in the reference sets seems crucial for SNP-BLUP & BayesCpi
- Incorporating genotypes information resulted in increased accuracies
- Fitting a polygenic effect does not have a uniform impact on the estimates of SNP effects
  - Its influence is dependent on the allele frequency of the SNP

Acknowlegements

- Funding by AHDB Dairy gratefully acknowledged

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