Genomic Evaluation for Resistance to Fertility Disorders in Canadian Dairy Breeds

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Abstract

Genomic evaluation was developed for resistance to fertility disorders in Canadian Ayrshire, Holstein and Jersey breeds, with the first official release in December 2020. The evaluation model includes the following traits: CO = Cystic Ovaries, MET = Metritis, and RP = Retained Placenta. All traits are scored as 0 (no case) or 1 (at least one case) in the period from calving to 305 d, 150 d, and 14 d after calving, for CO, MET and RP, respectively. First and later lactation traits are treated as different but correlated traits. Observations from lactations >2 are repeated records of lactation 2. The model is a multiple-trait (6 traits) linear animal model. Genomic information is utilized in additive relationships among animals via single-step method implemented in the MiX99 software. Genetic parameters were estimated using a subset (N= 76,082) of Holstein data. Heritability for fertility disorders ranged from 0.02 to 0.03. Genetic correlation between fertility disorders expressed in first and later lactation cows were between 0.55 (CO) and 0.70 (MET). This confirmed that disease resistance to fertility disorders are genetically different traits in first and later parities. Resistance to CO was genetically uncorrelated with resistance to 2 other disorders within and across parities (correlations did not statistically differ from 0). MET and RP were moderately genetically correlated (0.44 to 0.54). Estimated genomic breeding values for all traits are reversed in sign. Three additional evaluations are created by combining proofs for first and later lactation for a given disorder with equal weights. All proofs are expressed as RBV (mean = 100 and SD = 5, for base bulls).

Key words: fertility disorders, genetic parameters, genomic evaluation

Introduction

A national dairy cattle health data collection system in Canada was introduced in 2007. Eight diseases (mastitis, displaced abomasum, ketosis, milk fever, retained placenta, metritis, cystic ovaries and lameness) are recorded by producers on a voluntary basis. Producers are provided with disease definitions, adapted from Kelton et al. (1998), as a guide for identification and recording. Data is collected by milk recording technicians at each test day herd visit and forwarded to the DHI database. Additionally, health data from Quebec producers participating in the "Dossier Santé Animale/Animal Health Record" (DS@HR) program is collected and forwarded to DHI by their veterinarians. All data is stored in the national database at Lactanet, Canada. About 40% of all herds enrolled on milk recording participate in the health recording system (Koeck et al., 2012).

In 2014, national genetic and genomic evaluation for mastitis was introduced in Canada (Jamrozik et al., 2013), followed by national evaluation for metabolic disease resistance traits (Jamrozik et al., 2016b).

Fertility disorders (cystic ovaries, metritis and retained placenta) is the next group of health traits genetically evaluated in Canadian dairy breeds. The focus of this paper is to present a routine genomic evaluation system for resistance to fertility disorders, implemented in Canada in Canada in December 2020.

Materials and Methods

Traits

The new genetic evaluation system for resistance to fertility disorders includes the following traits :

- Cystic Ovaries (**CO**): scored as 0 (no case) or 1 (at least one case) in the period from calving to 305d after calving,
- Metritis (**MET**): Scored as 0 (no case) or 1 (at least one case) in the period from calving to 150d after calving, and
- Retained Placenta (**RP**): scored as 0 (no case) or 1 (at least one case) in the period from calving to 14d after calving.

First and later lactations (up to the 5th) traits are considered as different but correlated traits. Data on lactations >2 is treated as repeated observations for a trait in lactation 2, giving 6 traits in total.

No indicator traits for fertility disorders were considered. Earlier studies showed a limited degree of genetic relationships between this group of traits and their potential indicators (Jamrozik et al., 2016a; Koeck et al., 2014).

Data

The time threshold for inclusion of the data is April 1, 2007 (the beginning of health data collection in Canada) for all data sources. A minimum disease frequency (reported cases per herd and year) of 1% was applied for CO, MET and RP, to ensure continuous data recording within individual herds.

The final data sets (after edits) for the August 2020 test-run ranged from 24,653 records on 14,085 cows for the Jersey breed, to 1,968,876 records on 1,004,586 Holstein cows. Table 1 gives a detailed characteristic of the phenotypic data, pedigree (4 generations) and genotypes used for the within-breed evaluation. The reference population for the single-step method was defined as genotyped (50K or imputed) bulls and cows that were present in the pedigree for fertility disorders data. The size of reference population in August 2021 ranged from 2,602 (Ayrshire) to 81,886 animals (Holstein). Table 2 shows descriptive statistics of the phenotypes.

Table 1. Data characteristics

Breed[1]	Records	Cows	Sires	Pedigree	Genotyped		
					Cows	Sires	Pedigree
AY	35,854	17,783	844	36,027	1,500	523	2,602
HO	1,968,876	1,004,586	21,750	1,725,630	59,186	10,609	81,886
JE	24,653	14,085	1,109	33,337	1,039	779	2,812

[1]AY = Ayrshire, HO = Holstein, JE = Jersey

Table 2. Descriptive statistics of the data, by breed[1]

Lactation	Disorder[2]	% 1st lactation data			Frequency (%)		
		AY	HO	JE	AY	HO	JE
First	CO				4.3	6.0	8.1
	MET				5.4	6.7	3.8
	RP				6.2	3.9	1.8
		33.8	36.1	33.2			
Later	CO				10.1	11.2	13.6
	MET				5.5	6.3	5.9
	RP				10.3	5.7	3.4

[1]AY = Ayrshire, HO = Holstein, JE = Jersey
[2]CO = Cystic Ovaries, MET = Metritis, RP = Retained Placenta

Genetic Evaluation Model

The model is a multiple-trait (6 traits) linear animal model. Single-trait models are the same for all disorders. Models for traits in later lactations are the same as for the first lactation data but the permanent environmental effect (**PE**) is included for later lactation traits to account for repeated observations on a cow. An example models for CO in later lactations can be presented as:

$$CO = H + YS + ASP + HY + A + PE + E,$$

where the fixed effects are:
H: herd, YS: year-season, ASP: age-season-parity,
and the random effects are:
HY: herd-year, A: animal additive genetic, PE: permanent environmental, E: residual.
In matrix notation, the model can be written as

$$\mathbf{y} = \mathbf{X}\,\mathbf{b} + \mathbf{Z}_1\,\mathbf{h} + \mathbf{Z}_2\,\mathbf{a} + \mathbf{Z}_3\,\mathbf{p} + \mathbf{e}$$

where **y** is a vector of observations (traits within parities within cows), **b** is a vector of all fixed effects, **h** is a vector of HY effects, **a** is a vector of animal additive genetic effects (A), **p** is a vector of PE effects, **e** is a vector of residuals, **X** and $\mathbf{Z}_i$ (i =1, 2, 3) are respective incidence matrices.

Model assumptions are that

$[\mathbf{h}'\ \mathbf{a}'\ \mathbf{p}'\ \mathbf{e}']' \sim N[\mathbf{0}, \mathbf{V}]$ with $\mathbf{V} = \sum_{i=1}^{4} \mathbf{V}_i$,

where

$\mathbf{V}_1 = \mathbf{I} \otimes \mathbf{HY}$, **I** is an identity matrix, **HY** is the covariance (6x6) matrix for HY effects;
$\mathbf{V}_2 = \mathbf{H} \otimes \mathbf{G}_A$, **H** is a pedigree-genotypes relationship matrix, $\mathbf{G}_A$ is the additive genetic covariance (6x6) matrix;
$\mathbf{V}_3 = \mathbf{I} \otimes \mathbf{P}$, **P** is the covariance (3x3) matrix for PE effect;
$\mathbf{V}_4 = \sum_{i=1}^{N} \mathbf{E}_i$, $\mathbf{E}_i$ is the residual covariance matrix (of order up to 3x3, depending on how many traits were missing) for either first or later lactations, N is the total number of records. Residuals for clinical diseases are assumed correlated within each lactation and uncorrelated across lactations.

Genetic Parameters

Co-variance components and genetic parameters were estimated using Bayesian methods with Gibbs sampling. A subset of Holstein data with 119,917 records on 76,082 cows was used with the same model as intended for genetic evaluation purposes. Combined pedigree-genomic relationship matrix **H** was replaced by an additive relationship matrix **A**. Estimates were calculated as posterior means (SD) of 200,000 samples after the burn-in of 50,000 iterations. No attempts were made to estimate Ayrshire and Jersey specific co-variance components. Holstein parameters, therefore, are used for genetic evaluation for these 2 breeds.

Genomic evaluation

The single-step method was implemented via MiX99 and related software (MiX99 Development Team, 2017). The genomic relationship matrix (**G**) is constructed by Van Raden Method I (i.e. centered and scaled **Z**) (Van Raden, 2008), and **G** is blended with the additive relationship matrix (**A**) assuming that 80% of the total genetic variance was explained by the SNP effects. Scaling of **G** and **A** is performed using Christensen (2014) method. The APY algorithm for Proven and Young (Misztal et al., 2014) is applied in Holsteins for inversion of **G**, with the core population of 20,000 (the oldest genotyped animals in the Lactanet data-base) and groups for unknown parents are not included in the model. SNP effects, to be used for calculating Genomic Estimated Breeding Values (**GEBV**) for genotyped animals not included in the single-step core analysis, are estimated from the GEBV of reference animals (as in Lourenco et al., 2015).

Reliability of GEBV is approximated by a weighted (80:20) average of Direct Genomic

Value (**DGV**) and animal model reliabilities (Sullivan et al., 2005). DGV reliabilities are calculated using SNP prediction error co-variances with the SNP-BLUP-REL software (Luke, Finland). Animal model reliabilities are calculated based on Effective Daughter Contributions (**EDC**). The EDC software of Sullivan (2010) is used.

Relative Breeding Values

Estimated genomic breeding values for all traits are reversed in sign. Three additional evaluations are created by combining proofs for 1st and later lactation for a given disorder with equal weights. All proofs are then expressed as Relative Breeding Values (RBV), with mean = 100 and SD = 5, for base bulls (for August 2020 run: born 2005 – 2015 and with the 'Official' status). Sire evaluation for a combined trait is defined as 'Official' when it has daughter records in at least 5 herds and reliability for that trait at least 50% (Ayrshire and Jersey), or 70% (Holstein). Finally, a sire receives an 'Official' status when his proof for any combined trait is official.

Results and Discussion

Genetic Parameters

Estimates of heritability for fertility disorders ranged from 0.018 (CO in first lactation) to 0.029 (RP in later lactations) (Table 3).

Metritis in first lactation was the only disease trait with the largest contribution of the herd-year to the total (phenotypic) variance (2.7%). The PE effect captured between 1.9% to 2.6% of the total variance for the disease traits of later lactation cows.

Genetic correlation between fertility disorders expressed in first and later lactations were between 0.55 (CO) and 0.70 (MET) (Table 3). This confirmed that disease resistance to fertility disorders are genetically different traits in first and later parities. Resistance to CO was genetically uncorrelated with resistance to 2 other disorders across all comparisons (correlations did not statistically differ from 0). MET and RP were moderately genetically correlated.

Table 3. Estimates (posterior means*100) of heritabilities (diagonal) and genetic correlations (above diagonal) (posterior standard deviations in brackets).

Lactation/Trait[1]		First			Later		
		CO	MET	RP	CO	MET	RP
First	CO	1.8 (0.24)	27 (11)	16 (11)	55 (9)	18 (12)	12 (11)
	MET		2.7 (0.41)	54 (8)	21 (11)	70 (6)	44 (9)
	RP			3.0 (0.47)	10 (11)	53 (8)	62 (9)
Later	CO				2.8 (0.50)	9 (12)	0 (11)
	MET					2.3 (0.37)	51 (7)
	RP						2.9 (0.40)

[1] CO = Cystic Ovaries, MET = Metritis, RP = Retained Placenta

All the within-cow environmental correlations (PE) among disease traits were statistically non-significant.

Estimates of heritability for fertility disorders were generally in agreement with previous estimates for the Canadian Holsten data (Jamrozik et al., 2016a). Genetic and non-genetic associations among fertility disorders confirmed earlier results; in particular the lack of genetic correlations between CO and other reproductive disorders (Koeck et al., 2012).

Genomic Evaluations

There were 6,604 Holstein sires with official status for fertility disorders in the test-run using August 2020 data. The corresponding number of official Ayrshire and Jersey sires were 261 and 124, respectively.

Summary statistics for RBVs and for official sires are presented in Table 4. Average of RBV for individual and combined traits were close to 100, with SD fluctuating around 5. Average reliabilities were higher for Holsteins (78 – 82%) compared with Ayrshire (53 – 62%) and Jersey (54 – 65%).

Correlations among RBV for individual disorders followed trends observed earlier for genetic correlations (results not shown). Correlations for a given disorder in first and later lactations were high and positive for all breeds and traits. Proofs for CO were weakly correlated with RBV for other traits. Proofs for combined traits were very strongly correlated with RBVs for individual traits, for all breeds and disorders (correlations ranged from 0.93 to 0.98). Combined CO was uncorrelated (AY and JE) or slightly (0.12 and 0.23) correlated with proofs for other combined traits. Correlations between combined MET and combined RP ranged from 0.74 (AY and JE) to 0.91 (HO).

The level of reliability of young animals, that are not included in the single-step and their proofs are derived from SNP estimates using genotypes, is of a major concern for breeders. Such reliabilities, corresponding to December 2019 data, will be briefly discussed in the following paragraph.

There was an increase in the data volume between 11% (AY) to 17% (HO) between December 2019 and August 2020. More importantly, the size of the reference population (used for SNP estimates) increased by 6% (AY) to 9% (JE) within this ~6 months period. Consequently, average reliabilities for the single-step sires in August 2020 were larger than corresponding values for the December 2019 run. The largest increase was observed for JE, followed by AY and HO breeds. Average reliability in December 2019 run for young bulls (born in 2019) are in Tables 5a and 5b for first and later lactation traits. There were not significant differences between reliabilities of first lactation traits compared with later lactations for both, single-step and young, bulls. Sires included in the single-step model had much larger level of reliability compared with young bulls. Young bulls, on average, had slightly lower reliabilities compared with a group of all genotyped sires (results not shown). Smaller breeds (AY and JE) had much lower level of reliability compared with Holsteins (15 - 20 vs. 60) for a group of young bulls. This illustrated a strong impact of the size of the reference population and the amount of phenotypic data on the accuracy of genomic evaluation.

Table 4. RBV statistics across all individual traits for official sires, by breed[1]

Breed	N	Mean	SD	Min	Max
AY	261	100	5.1 ÷ 5.7	79 ÷ 84	111 ÷ 115
HO	6,604	99 ÷ 101	5.0 ÷ 5.3	73 ÷ 80	114 ÷ 120
JE	124	100	4.8 ÷ 5.4	79 ÷ 89	110 ÷ 116

[1]AY = Ayrshire, HO = Holstein, JE = Jersey

Table 5a. Reliability of young, genotyped bulls (born in 2019) – first lactation

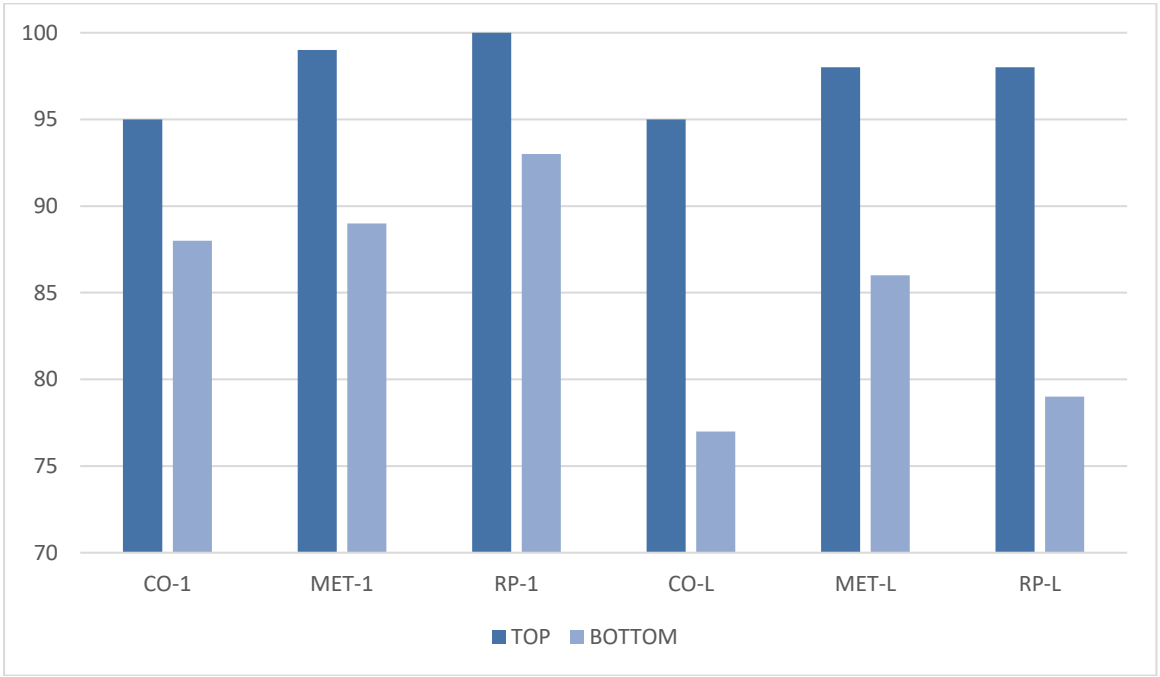
Breed[1]	Size of Reference Population	# Animals	Trait[2]					
			CO		MET		RP	
			Mean	SD	Mean	SD	Mean	SD
AY	2,336	84	18	5	20	5	20	5
HO	70,027	24,942	61	2	62	2	62	2
JE	2,497	3,031	13	3	15	3	15	3

[1]AY = Ayrshire, HO = Holstein, JE = Jersey
[2]CO = Cystic Ovaries, MET = Metritis, RP = Retained Placenta

Table 5b. Reliability of young, genotyped bulls (born in 2019) – later lactations

Breed[1]	Size of Reference Population	# Animals	Trait[2]					
			CO		MET		RP	
			Mean	SD	Mean	SD	Mean	SD
AY	2,336	84	20	5	21	5	21	5
HO	70,027	24,942	62	2	62	2	62	2
JE	2,497	3,031	15	3	16	3	16	3

[1]AY = Ayrshire, HO = Holstein, JE = Jersey
[2]CO = Cystic Ovaries, MET = Metritis, RP = Retained Placenta



[1]CO = Cystic Ovaries, MET = Metritis, RP = Retained Placenta

Figure 1. Proportion of lactations (1 = first, L = later) free of fertility disorders in top 10 vs. bottom 10 official Holstein sires for a combined trait[1] RBV

Relationships between sire RBV and daughter phenotypes

Proportions (%) of 'healthy' lactations, that is lactations free of any incidence of a given disorder, for the 10 Top and 10 Bottom sires ranked by RBV for combined disorders, are presented in Figure 1. The difference in averages of 'healthy' lactations between Top and Bottom sires ranged from 7% for CO in the 1st lactation, to 19% for RP in later lactations. This confirmed a good relationship between sire's proof and the phenotypic performance of his daughters.

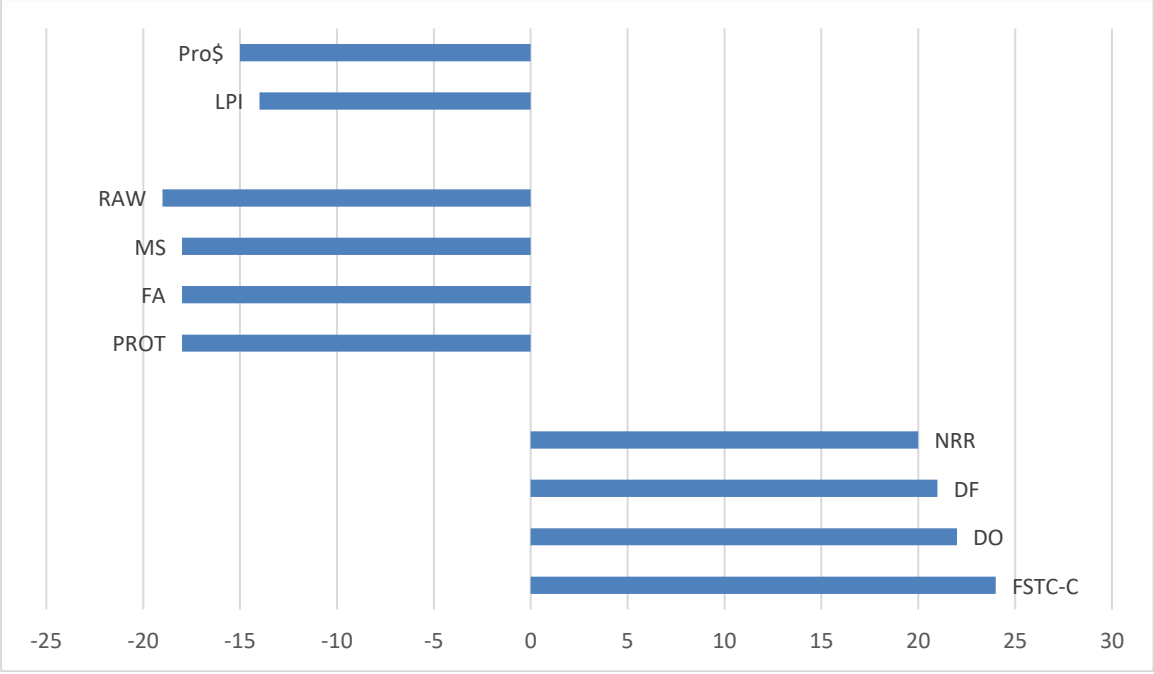
Relationships with Other Traits

To estimate proof correlations between fertility disorders and other routinely evaluated traits in Canada, 9,816 genotyped Holstein bulls with official LPI were selected. Correlations for the two selection indices (LPI and Pro$), and selected trait (with the extreme values + or - of these correlations) are in Figures 2a and 2b for CO and MET, respectively. Combined CO proofs were slightly unfavorably correlated with LPI and Pro$, correlations with other traits were all in the interval between -0.25 to +0.25. In particular, CO was favorably correlated with fertility and calving performance traits, and unfavorably correlated with protein yield and several conformation traits.

Metritis showed a slightly different picture. Combined proofs for this disorder were favorably correlated with both LPI and Pro$. Again, favorable correlations with fertility and calving traits but also with survival. A similar pattern of correlations, but with slightly smaller values, was generated for RP (results not shown).

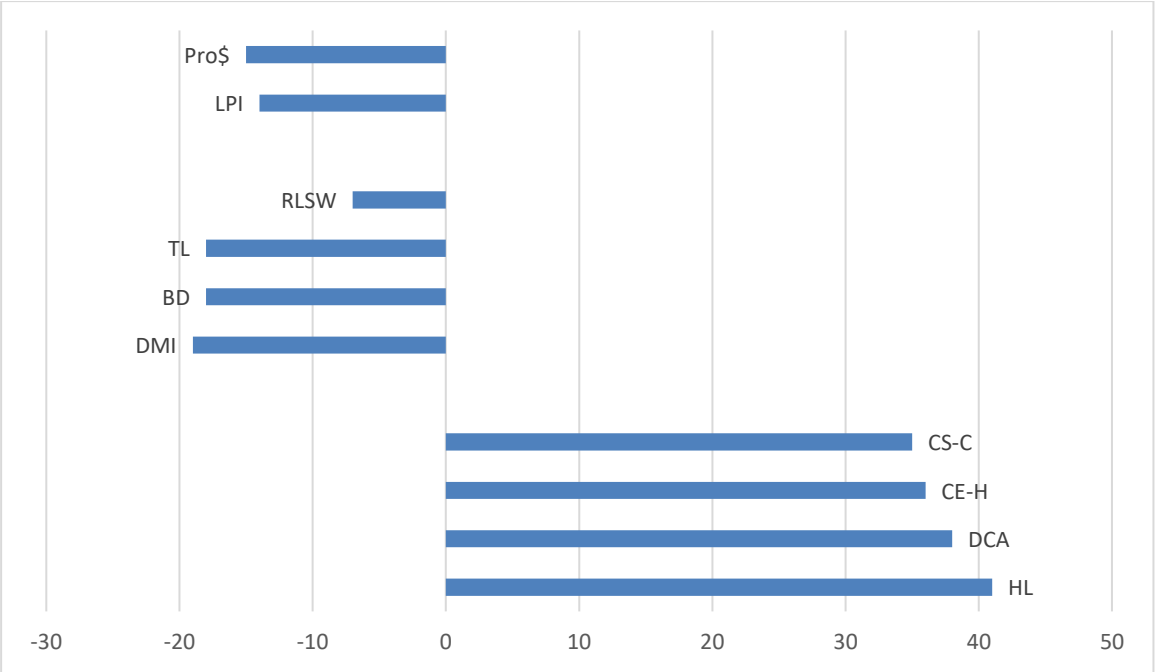
Conclusions

- Routine genomic evaluation for resistance to fertility disorders was officially implemented in December 2020 for Holstein, Ayrshire and Jersey breeds.
- Due to insufficient data on fertility disorders for breeds other than Holstein, genetic parameters estimated for Holstein are used for the other breeds



[1] Pro$ = Pro$ Index, LPI = Lifetime Profit Index, RAW = Rear Attachment Width, MS = Mammary System, FA = Fore Attachment, PROT = Protein Yield, NRR = Non-Return Rate, DF = Daughter Fertility, DO = Days Open, FSTC-C = First Service to Conception in Cows

Figure 2a. Correlations (x100) between RBV for combined Cystic Ovaries and GEBV for other traits[1] for Holstein genotyped and LPI sires



[1] Pro$ = Pro$ Index, LPI = Lifetime Profit Index, RLSW = Rear Leg Side View, TL = Teat Length, BD = Body Depth, DMI = Dry Matter Intake, CS-C = Calf Survival in Cows, CE-H = Calving Ease in Heifers, DCA = Daughter Calving Ability, HL = Herd Life

Figure 2b. Correlations (x100) between RBV for combined Metritis and GEBV for other traits[1] for Holstein genotyped and LPI sires

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