Genetic Evaluation for Resistance to Metabolic Diseases in Canadian Dairy Breeds

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Abstract

Genetic evaluation was developed for resistance to metabolic disease traits in Canadian Ayrshire, Holstein and Jersey breeds, with the first official release scheduled for December 2016. The model is a 9-trait animal linear model including producer-recorded data on clinical ketosis (**CK**) and displaced abomasum (**DA**), sub-clinical ketosis (**SCK**) defined as a level of milk β-hydroxybutyrate, and 2 indictor traits: fat to protein ratio (**F:P**) and first lactation body condition score (**BCS**) from the conformation classification. First and later (up to the 5th) lactations are considered as different (but correlated) traits. Genetic parameters were estimated using a subset (records on 35,575 cows) of the Holstein data. Heritabilities for CK and DA ranged from 0.02 to 0.06. Higher heritabilities were estimated for SCK and indicator traits, from 0.08 (SCK in later lactations) to 0.30 (BCS). Genetic correlations of clinical disease traits between first and later lactations were strong (0.70 for CK and 0.79 for DA), correlations for SCK and F:P were 0.50 and 0.70, respectively. First lactation CK was strongly correlated with DA (0.77) and SCK (0.68); lower correlations were estimated with BCS (-0.56) and F:P (0.42). Genetic links between DA in first and lactations and indicator traits were weaker. EBVs for CK, DA and SCK are published as relative breeding values, with a mean of 100 and standard deviation of 5, where higher values are desirable. The overall Metabolic Disease Resistance (**MDR**) index includes SCK, CK and DA, with weights of 50%, 25% and 25%, respectively, and the component EBVs are the averages of first and later lactation EBV for each trait. The MDR index is standardized in the same way as EBVs for individual metabolic disease traits.

Key words: metabolic diseases, genetic parameters, genetic evaluation

Introduction

A national dairy cattle health and disease data management system in Canada was started in 2007. Eight diseases are recorded by producers on a voluntary basis, namely mastitis, displaced abomasum, ketosis, milk fever, retained placenta, metritis, cystic ovaries and lameness. Producers are provided with disease definitions, adapted from work by 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 the DHI by their veterinarians. All data is stored in the national database at Canadian Dairy Network (CDN). About 40% of all herds enrolled on milk recording participate in the health recording system (Koeck *et al.*, 2012b).

The feasibility of using producer recorded health data for genetic evaluation of disease resistance in Canada has been shown previously (Neuenschwander *et al.*, 2012; Koeck *et al.*, 2012b). In 2014, national genetic and genomic evaluation for mastitis was introduced in Canada (Jamrozik *et al.*, 2013).

Metabolic disease traits (ketosis and displaced abomasum) is the next group of health traits scheduled for genetic evaluation in Canadian dairy breeds. The focus of this paper is the implementation of a routine genetic evaluation system for metabolic disease traits in Canada.

Materials and Methods

Definition of Traits

A detailed analysis of clinical and sub-clinical ketosis, displaced abomasum and their predictors was given by Koeck *et al.* (2012a, 2012b, 2014, 2015) and Loker *et al.* (2012). Based on this research, the new genetic evaluation system for metabolic disease resistance includes the following traits (9 traits in total):

Metabolic disease traits and milk recording indicators from first and later (up to the 5th) lactations:

- Clinical ketosis (**CK**) and Displaced abomasum (**DA**)
  Scored as 0 (no case) or 1 (at least one case) in the period from calving to 100 d after calving.
- Sub-clinical ketosis (**SCK**)
  Expressed as milk β-hydroxybutyrate (**BHB**) in mmol/L, log(1+x) transformed, recorded at the first test-day from 5 to 45 DIM.
- Fat to protein ratio (**F:P**)
  From the first test-day between 5 to 45 DIM.

First and later lactation disease traits and their indicators are considered as different but correlated traits. Data on lactations >2 is treated as repeated observations for a trait in lactation 2.

Type traits from first lactation cows (from first classifications within 365 DIM):

- Body condition score (**BCS**), measured trait

Data

Three data sources (health, milk recording, conformation) are used to generate phenotypes for genetic evaluation for metabolic disease traits. The time threshold for inclusion of the data is April 1, 2007 (the beginning of health data collection in Canada) for all data sources. For the health data, only herds with CK or DA records are included. A minimum disease frequency (reported cases per herd and year) of 1% is applied for CK and DA to ensure continuous data recording within individual herds. All data on SCK (milk BHB) is included. Data of F:P and BCS is included only from herds that also collect metabolic disease data.

The above described criteria for including phenotypes for metabolic disease resistance model were applied to obtain the data for genetic evaluation using August 2016 official extracts of health, test-day and conformation data. This resulted in generating data on 20,697 Ayrshire, 985,762 Holstein, and 21,745 Jersey cows. Numbers of cow-lactation records were 36,765, 1,621,630 and 34,088 for Ayrshire, Holstein and Jersey breeds, respectively. The same procedure was applied to other coloured breeds in Canada (Canadienne, Brows Swiss, Guernsey and Milking Shorthorn). The amount of usable data that was obtained was too small to justify routine genetic evaluation for these breeds.

Summary statistics of the Holstein data extracted in August 2016 is given in Table 1.

Genetic Evaluation Model

The model is a multiple-trait (9 traits) linear animal model. Single-trait models are the same for CK and DA, and for SCK and F:P in first or later lactations. Models for metabolic diseases, SCK and F:P 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. Additionally, the effect of days in milk is included in models for milk recording collected traits (SCK and F:P). Example models for CK in later lactations, SCK in the first lactation and BCS, in a simplified scalar notation, can be presented as:

$$CK = H + YS + ASP + HY + A + PE + E$$
$$SCK = H + YS + ASP + HY + DIM + A + PE + E$$
$$BCS = HRC + AST + A + E,$$

where the fixed effects are:

H: herd, YS: year-season, DIM: days in milk, ASP: age-season-parity, HRC: herd-round-classifier, AST: age-stage-time of classification,

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,.., 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

$\mathbf{V}_1 = \mathbf{I} \otimes \mathbf{H}$, **I** is an identity matrix, **H** is a covariance (8x8) matrix for HY effects;
$\mathbf{V}_2 = \mathbf{A} \otimes \mathbf{G}$, **A** is an additive relationship matrix, **G** is a genetic covariance (9x9) matrix;
$\mathbf{V}_3 = \mathbf{I} \otimes \mathbf{P}$, **P** is a covariance (4x4) matrix for PE effect;
$\mathbf{V}_4 = \sum_{i=1}^{N} \mathbf{E}_i$, $\mathbf{E}_i$ is a residual covariance matrix (of order up to 5x5, depending on how many traits were missing) for either first or later lactations, N is the total number of records. Residuals for clinical diseases and milk recording indicator traits are assumed correlated within each lactation and uncorrelated across lactations. All other residual correlations are equal to 0.

Genetic Parameters

Co-variance components and genetic parameters of the model were estimated using Bayesian methods with Gibbs sampling. A subset of Holstein data with 52,996 records on 35,575 cows was used with the same model as intended for genetic evaluation purposes. 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 due to insufficient amount of the data. Holstein parameters, therefore, will be used for genetic evaluation for these 2 breeds.

*Metabolic Disease Resistance (**MDR**) index*

The genetic evaluation for resistance to metabolic diseases produces 6 EBV that are the components of the MDR index: SCK, CK and DA, for first and later lactations. The weighting for the MDR index are: 50% on SCK, 25% on CK, and 25% on DA; where the included EBV are the averages of the first and later lactations EBVs for each trait.

The overall strong influence of ketosis on MDR is advised because of the higher frequency and costs associated with ketosis compared to DA. Sub-clinical ketosis is more common that CK, and the cost of SCK at the herd level is much greater than cost of CK (McArta *et al.*, 2014; Gohary *et al.*, 2016). Sub-clinical ketosis (determined by BHB level between 5 and 45 DIM) is a strong indicator of CK in both first and later lactations, and a moderate indicator of DA in the first lactation. Furthermore, the quantity and quality of BHB records may be superior to the producer recorded CK and DA data.

The MDR index was validated by examining expected responses for individual traits in scenarios with different weights. Results are in Figure 1 (different weights for combined SCK, CK and DA) and in Figure 2 (different weights for first versus later lactation traits). Overall, the proposed weights in the MDR index seem to generate close to optimal responses when compared with other scenarios.

The MDR index is assumed to be an official sire evaluation when a bull has at least 20 daughters in at least 10 herds, with a minimum reliability of 45% (Holstein) or 35% (other breeds) for 1st lactation SCK.

Relative Breeding Values

Estimated breeding values for CK, DA, SCK and MDR index are standardized to relative breeding values (**RBV**) with a mean of 100 and a standard deviation of 5 and reversed in sign. Thus, higher RBVs indicate sires with daughters more resistant to a given disease.

Reliabilities of sire RBVs for all traits and MDR are calculated based on effective daughter contribution (EDC). The EDC software of Sullivan (2010) is used.

Results and Discussion

The overall August 2016 data characteristics is shown in Table 1 for the Holstein breed. The frequency of CK (DA) in Holsteins increased with parity and it was 4 (3) and 7 (4) % in first and later lactation cows, respectively. Similar frequencies of clinical cases were estimated for two other breeds.

Genetic Parameters

Estimates of heritability for metabolic clinical disease traits ranged from 0.02 (CK and DA in later lactations) to 0.06 (DA in the first lactation). Heritabilities of SCK and F:P were relatively higher; and ranged from 0.08 (SCK in later lactations) to 0.16 (F:P in first lactation). Genetic correlations between disease traits expressed in first and later lactations were 0.70, 0.79, and 0.50 for CK, DA and SCK, respectively. Resistance to CK was genetically strongly correlated (0.77) with resistance to DA in first lactation. Weaker genetic correlations were estimated between these traits in later lactations (0.53). Resistance to CK was genetically related to resistance to SCK; correlations of 0.68 and 0.51 for first and later lactations, respectively. Weaker genetic correlation were estimated between DA and SCK in both first and later lactations, with a non-significant level in lactations greater than 1. Fat to protein ratio (F:P) and BCS were relatively good genetic indicators for disease traits in first lactation. Genetic relationships between indicator and disease traits in later lactations were weak and generally non-significant.

Genetic Evaluations

The current data (August 2016) available for genetic evaluation yielded 108, 1720 and 99 sires with an official evaluation for MDR for Ayrshire, Holstein and Jersey breeds, respectively. Breed specific summary statistics related to MDR and its reliability for official sires are given in Table 3. Top 10 Holstein sires for MDR had on average 6% and 3% more first lactation daughters in the data that were free of CK and DA, respectively, compared with the bottom 10% sires. Similarly, top MDR sires had 7% and 3% more healthy daughters for respective traits in later lactations.

Relationships with Other Traits

Correlations of sire RBV for MDR with other routinely evaluated traits for 1520 bulls with official MDR and Lifetime Profit Index (**LPI**) are shown in Figure 3. Routinely evaluated traits in Canada, with the exception of SCS, are scored to have a higher breeding value being favorable. Desirable, positive associations were found between MDR with both fertility and longevity. This means that selection for metabolic disease resistance would lead to selection for cattle with improved fertility and longer herd life.

Genomic Evaluation Method

SNP-BLUP methodology as used officially by CDN will be applied to estimate genomic evaluations for metabolic disease resistance traits for the Holstein breed. Progeny proven sires reaching the minimum requirements for publication of an official RBV for metabolic disease traits will be used as the reference population for estimation of SNP effects. Direct Genomic Values (DGV) will be blended with RBV (or Parent Average), weighted by the relative Reliability of each value, to produce published genomic RBV for bulls.

Conclusions

- Routine genetic evaluation for metabolic disease resistance will be officially implemented in December 2016 for Holstein, Ayrshire and Jersey breeds.
- Due to insufficient data on CK and DA for breeds other than Holstein, genetic parameters estimated for Holstein will be used for the other breeds.

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Table 1. Holstein data characteristics (August 2016 extract).

Lactation	Trait[1]	No. of records	Mean	SD
	CK	116,672	0.04	
	DA	264,489	0.03	
First	F:P	243,805	1.33	0.27
	SCK	342,431	0.10	0.07
	CK	210,605	0.07	
Later	DA	47,679	0.04	
	F:P	313,530	1.32	0.27
	SCK	609,432	0.11	0.08
BCS		246,491	2.82	0.34

[1] CK = Clinical Ketosis , DA = Displaced abomasum, F:P = Fat to protein ratio, SCK = Sub-clinical ketosis (Milk ß-hydroxybutyrate, mmol/L) , BCS = Body Condition Score

Table 2. Estimates (posterior means*100) of heritabilities (diagonal) and genetic correlations (above diagonal) (posterior standard deviations in brackets).

Lactation/Trait[1]		First				Later				
		CK	DA	F:P	SCK	CK	DA	F:P	SCK	BCS
First	CK	4.1 (0.64)	77 (4)	42 (9)	68 (15)	70 (8)	59 (10)	7 (10)	34 (12)	-56 (7)
	DA		6.3 (0.88)	31 (8)	34 (11)	58 (7)	79 (7)	5 (10)	8 (14)	-39 (8)
	F:P			16.5 (1.69)	47 (10)	40 (10)	13 (11)	70 (5)	10 (14)	-41 (6)
	SCK				15.0 (2.59)	49 (14)	10 (14)	13 (11)	50 (12)	-61 (6)
Later	CK					2.0 (0.33)	53 (10)	31 (12)	51 (12)	-19 (12)
	DA						1.9 (0.31)	4 (12)	5 (15)	-9 (10)
	F:P							10.0 (1.19)	18 (13)	8 (7)
	SCK								7.8 (1.99)	3 (13)
BCS										29.1 (2.23)

[1] CK = Clinical Ketosis , DA = Displaced abomasum, F:P = Fat to protein ratio, SCK = Sub-clinical ketosis (Milk ß-hydroxybutyrate) , BCS = Body Condition Score

Table 3. Summary of MDR index evaluation for sires with official proofs, by breed.

Breed	N	RBV				Reliability			
		Mean	SD	Min	Max	Mean	SD	Mean	Max
Ayrshire	108	100	5	87	120	65	12	49	96
Holstein	1720	100	5	81	115	74	11	43	99
Jersey	99	100	5	86	110	62	13	41	93

Figure 1. Expected responses (on the RBV scale) for MDR index with different weights on traits.

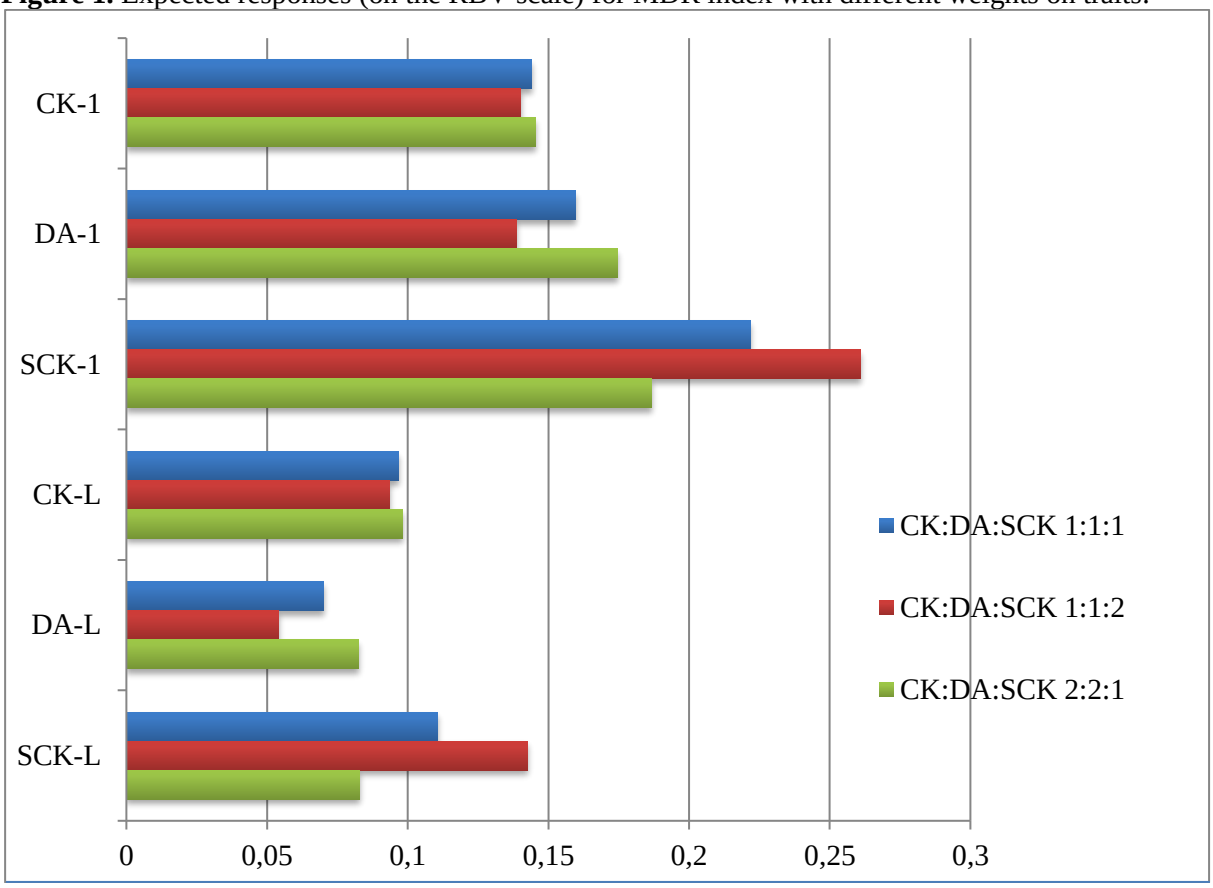


Figure 2. Expected responses (on the RBV scale) for MDR index with different weights on first (1) and later (L) lactation traits.

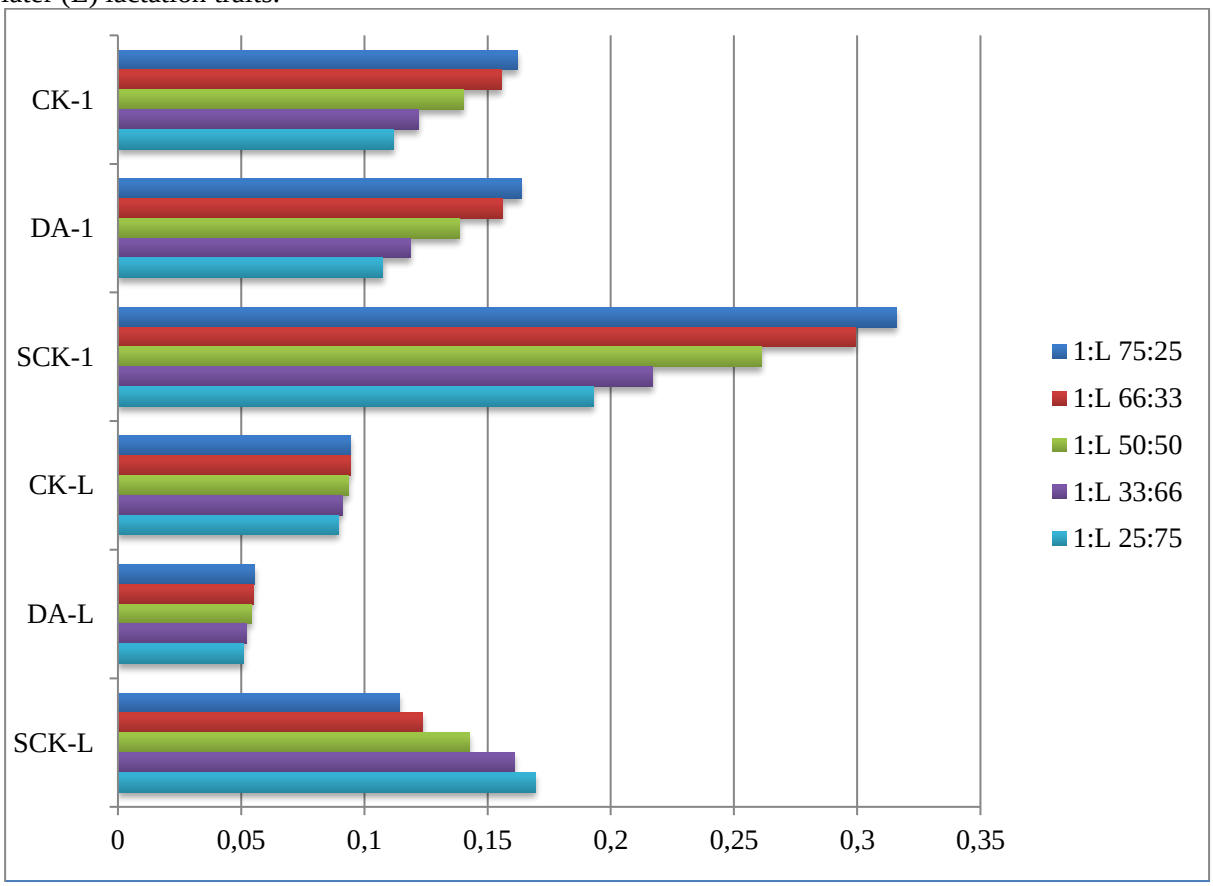
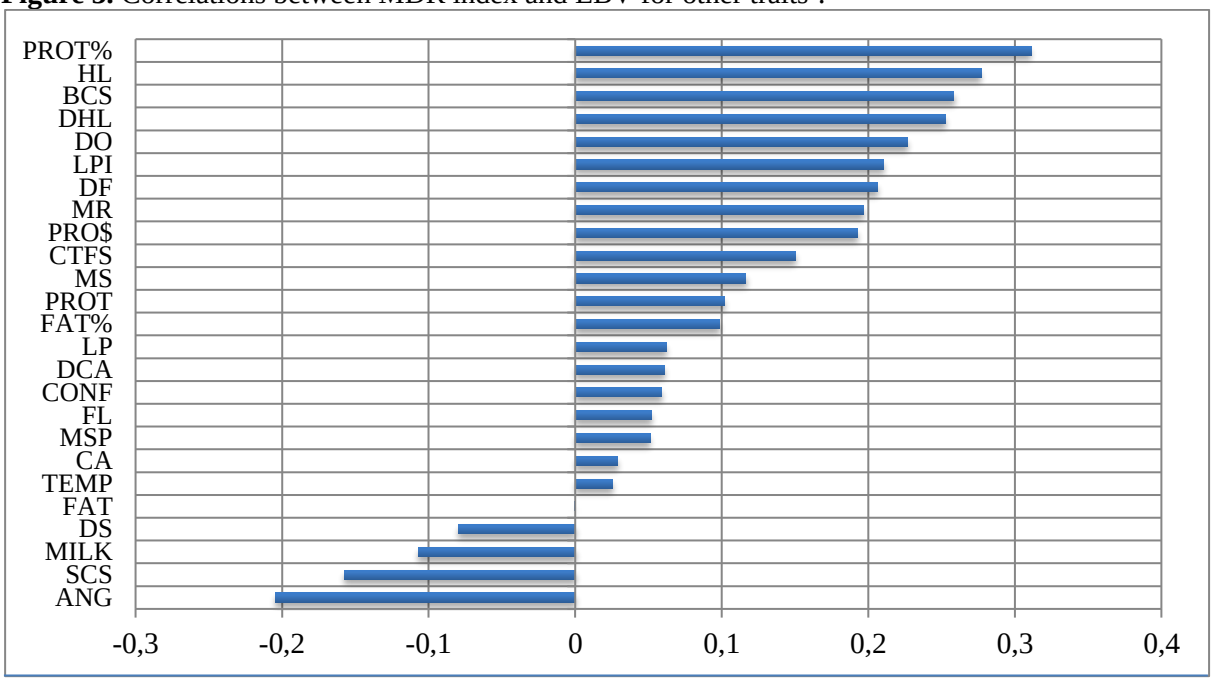


Figure 3. Correlations between MDR index and EBV for other traits[1].



[1]PROT% = Protein Content, HL = Herd Life, BCS = Body Condition Score, DHL = Direct Herd Life, DO = Days Open, LPI = Lifetime Profit Index, DF = Daughter Fertility, MR = Mastitis Resistance, PRO$ = Pro$ Index, FAT% = Fat Content, LP = Lactation Persistency, DCA = Daughter Calving Ability, CONF = Conformation, FL = Feet and Legs, MSP = Milking Speed, CA = Calving Ability, TEMP = Milking Temperament, FAT = Fat Yield, DS = Dairy Strength, MILK = Milk Yield, SCS = Somatic Cell Score, ANG = Angularity