Comparison of genomic predictions for lowly heritable traits using multi-step and single-step genomic best linear unbiased predictor in Holstein cattle

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ABSTRACT

The success and sustainability of a breeding program incorporating genomic information is largely dependent on the accuracy of predictions. For low heritability traits, large training populations are required to achieve high accuracies of genomic estimated breeding values (GEBV). By including genotyped and nongenotyped animals simultaneously in the evaluation, the single-step genomic BLUP (ssGBLUP) approach has the potential to deliver more accurate and less biased genomic evaluations. The aim of this study was to compare the accuracy and bias of genomic predictions for various traits in Canadian Holstein cattle using ssGBLUP and multi-step genomic BLUP (msGBLUP) under different strategies, such as (1) adding genomic information of cows in the analysis, (2) testing different adjustments of the genomic relationship matrix, and (3) using a blending approach to obtain GEBV from msGBLUP. The following genomic predictions were evaluated regarding accuracy and bias: (1) GEBV estimated by ssGBLUP; (2) direct genomic value estimated by msGBLUP with polygenic effects of 5 and 20%; and (3) GEBV calculated by a blending approach of direct genomic value with estimated breeding values using polygenic effects of 5 and 20%. The effect of adding genomic information of cows in the evaluation was also assessed for each approach. When genomic information was included in the analyses, the average improvement in observed reliability of predictions was observed to be 7 and 13 percentage points for reproductive and workability traits, respectively, compared with traditional BLUP. Absolute deviation from 1 of the regression coefficient of the linear regression of de-regressed estimated breeding values on genomic predictions went from 0.19 when using

traditional BLUP to 0.22 when using the msGBLUP method, and to 0.14 when using the ssGBLUP method. The use of polygenic weight of 20% in the msGBLUP slightly improved the reliability of predictions, while reducing the bias. A similar trend was observed when a blending approach was used. Adding genomic information of cows increased reliabilities, while decreasing bias of genomic predictions when using the ssGBLUP method. Differences between using a training population with cows and bulls or with only bulls for the msGBLUP method were small, likely due to the small number of cows included in the analysis. Predictions for lowly heritable traits benefit greatly from genomic information, especially when all phenotypes, pedigrees, and genotypes are used in a single-step approach.

Key words: genomic evaluation, dairy cattle, reference population, reliability, single-step model

INTRODUCTION

In Canada, genomic evaluation for a series of traits has been successfully implemented in Holstein cattle since 2009 through a multi-step genomic BLUP method (**msGBLUP**; Van Doormaal et al., 2009). This procedure consists of (1) running a traditional genetic evaluation based solely on pedigree and phenotypic information, (2) calculation of pseudo-phenotypes such as de-regressed estimated breeding values (**DEBV**) using results obtained from the previous step, (3) estimation of SNP effects to obtain direct genomic values (**DGV**) for genotyped animals, and (4) blending of genomic predictions with EBV or parent averages (**PA**). Loss of information during the de-regression step can introduce bias and errors into the evaluation (Legarra et al., 2014), thus reducing the contribution of genomic information. Moreover, in msGBLUP, only information on genotyped animals is directly used. Given that only a small portion of the animals are genotyped, bias can also be introduced by the fact that not all information used for selection decisions is accounted for.

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To overcome potential problems, Misztal et al. (2009), Aguilar et al. (2010), and Christensen and Lund (2010) developed single-step genomic BLUP (**ssGBLUP**), a methodology that combines genotypic, pedigree, and phenotypic information into a single evaluation. It consists of augmenting the pedigree relationship matrix with contributions from genomic relationships into a matrix of realized (observed or imputed) relationships, the inverse of which is used in the BLUP mixed model equations. In this way, genotyped and nongenotyped animals can be included simultaneously in the evaluation. As several steps are avoided, ssGBLUP is, in many instances, simpler to use and has the potential to deliver more accurate and less biased genomic evaluations. The main advantage of ssGBLUP, especially for dairy cattle, is its ability to account for genomic preselection (Legarra et al., 2014). Accuracy of ssGBLUP is usually as high as, if not greater than, other methods of genetic merit evaluation (Christensen et al., 2012; Baloché et al., 2014; Lourenco et al., 2014a).

Accuracy of genomic predictions is critical for the expected genetic gains resulting from genomic selection and is dependent on many factors, such as heritability of the trait, the statistical method used to estimate SNP effects in the training population, and most importantly, the size of the training population (Goddard, 2009; Hayes et al., 2009; Hozé et al., 2014). For the latter, the number of genotyped progeny-tested bulls could be a limitation, especially for lowly heritable traits or those traits that are difficult or expensive to measure. One way of overcoming this problem is by incorporating genomic information of cows into the evaluation (Calus et al., 2013; Tsuruta et al., 2013; Uemoto et al., 2017). However, it is important that cow and bull traditional evaluations are comparable to avoid a decrease in reliability of genomic predictions, especially due to preferential treatment. Wiggans et al. (2011) reported a decrease in reliability of genomic predictions with the inclusion of cows in the training population. The authors hypothesized that many cows were subject to preferential treatment for having higher genetic merit. A pre-adjustment was then developed to reduce the mean and variance of cows' EBV so they would be comparable to those of bulls (Wiggans et al., 2012). Tsuruta et al. (2013) suggested that by using ssGBLUP, the inclusion of cows in the training population would be possible without any pre-adjustments.

In Canada, genomic evaluations are currently based solely on bulls' genomic information and there is still a lack of studies investigating the feasibility of ssGBLUP in Canadian dairy cattle. The incorporation of genomic information into breeding programs using alternative approaches to improve genomic predictions for lowly heritable traits is needed. In addition, the importance

of workability and reproduction traits have increased over time in the dairy cattle industry. Advantages of incorporating genomics into a breeding program are the greatest for lowly heritable traits, especially due to the higher relative increase in reliabilities of predictions achieved for these traits by using genomic information (García-Ruiz et al., 2016; Wiggans et al., 2017). Therefore, the objective of this study was to compare the accuracy and bias (spread) of genomic predictions for various workability and reproductive traits in Canadian Holstein cattle using multi-step and single-step GBLUP methods under different strategies, such as adding genomic information of cows in the analysis, testing different adjustments of the genomic relationship matrix, and using a blending approach to obtain GEBV from the multi-step method.

MATERIALS AND METHODS

Data

Genotypic data consisted of 10,590 bulls born between 1960 and 2012 genotyped with the Illumina Bovine SNP50 BeadChip (**50K**, Illumina Inc., San Diego, CA) or a higher density panel. The SNP present in the higher density panel that overlapped with the 50K panel were imputed to the 50K panel using the FImpute software (Sargolzaei et al., 2014). In addition, 6,842 cows born between 1997 and 2015 genotyped either with the 50K SNP panel or a low-density panel (6K) were imputed to the 50K panel by also using the FImpute software. Thus, all animals had information on the same SNP set. Genotypes were coded as 0, 1, or 2 for calculation of the genomic relationship matrix (**G**). Genotype quality control excluded monomorphic SNP, SNP and individuals with call rate lower than 90%, SNP that were out of Hardy-Weinberg equilibrium with very low probability ($P < 10^{-6}$) or with minor allele frequency less than 0.05, and individuals with parent-progeny Mendelian conflicts. After quality control, the number of genotyped animals retained was 17,430 and the final genotype data set included 40,635 informative SNP. The PREGSF90 software was used for SNP and sample quality control (Misztal et al., 2002).

Data on Holstein reproductive and workability traits were extracted from the April 2017 genetic evaluation carried out by the Canadian Dairy Network (Guelph, Ontario, Canada, www.cdn.ca). The traits selected for this study were milking speed (**MS**), milking temperament (**MT**), age at first insemination (**AFS**), days from calving to first insemination (**CTFS**), number of services (**NS**), 56-d nonreturn rate (**NRR**), days from first service to conception (**FSTC**), calving ease (**CE**), stillbirth (**SB**), gestation length (**GL**), and calf size

(CZ). Traits that were recorded during or before first calving were considered as heifer traits and were coded as parity 0. Traits measured in first-lactation cows were coded as parity 1 and the same approach was applied to subsequent lactations (parity >1). Single-trait analyses were carried out for all heifer and cow traits. The animal models used for genetic evaluation can be found in Jamrozik and Kistemaker (2016). Descriptive statistics for each trait are shown in Table 1.

De-regressed EBV were used as response variables for genomic prediction in the msGBLUP approach. De-regression was computed following VanRaden et al. (2009):

$$ERC_P = \left[\lambda \frac{EBV_{rel}}{(1 - EBV_{rel})} \right] - ERC_{PA},$$

$$ERC_{PA} = \lambda \frac{PA_{rel}}{(1 - PA_{rel})},$$

$$DEBV = PA + \left[\frac{EBV - PA}{ERC_P / (ERC_P + ERC_{PA} + 1)} \right],$$

where DEBV are de-regressed breeding values, ERC_{PA} is the effective record contribution from PA, ERC_P

is the effective record contribution from own record/progeny information, PA_{rel} is reliability of parent average, λ is equal to $(1 - h^2)/h^2$, and EBV_{rel} is reliability of EBV. For computational ease, de-regressed EBV of bulls were not adjusted for the potential contributions from daughters in the training population because the average number of daughters per bull in the training set was very small ($n \sim 0.10$) compared with the minimum number of daughters required for a bull to be included in the training set ($n = 10$). Therefore, most of the bull information came from daughters not included in the training set, making the double counting of information very small. In scenarios with a much larger number of cows included in the training population relative to the number of bulls, where bulls would be expected to have several daughters in the training population, an adjustment to prevent double counting would be necessary, such as the iterative procedure proposed by Calus et al. (2016).

Lourenco et al. (2014b) have shown that by retaining only 4 to 5 generations of pedigree records decreased computing costs when using ssGBLUP approach and did not significantly decrease the accuracy of genomic evaluations. Therefore, the pedigree file used here for the analysis was generated by tracing the pedigree of animals with records for each trait to 4 generations back and its size ranged from 2,343,158 animals for CTFS to 5,070,448 for MS.

Table 1. Descriptive statistics and h^2 of reproductive and workability traits in first and later parities

Parity	Trait ¹	h^2	No. of records	Mean	SD	Minimum	Maximum
Reproductive trait							
First	AFS	0.09	1,217,701	478.97	55.81	274	639
	NRR	0.03	1,404,619	0.72	0.45	0	1
	NS	0.02	1,420,060	1.62	1.04	1	10
	FSTC	0.03	1,086,405	18.25	33.64	0	206
	GL	0.19	1,000,420	278.78	6.41	240	300
	CE	0.12	1,075,704	1.57	0.68	1	4
	SB	0.11	1,068,520	0.89	0.31	0	1
	CZ	0.11	1,040,971	2.01	0.57	0	3
	NRR	0.04	3,771,204	0.55	0.50	0	1
	NS	0.06	3,815,035	2.31	1.62	1	10
Later	CTFS	0.07	3,803,907	86.95	31.54	14	244
	FSTC	0.08	2,545,203	37.34	47.98	0	206
	GL	0.16	2,359,727	279.88	6.54	240	300
	CE	0.08	2,747,813	1.40	0.59	1	4
	SB	0.01	2,733,684	0.95	0.22	0	1
	CZ	0.09	2,704,295	2.19	0.58	0	3
Workability trait							
First ²	MT	0.13	2,921,775	3.29	0.75	1	5
	MS	0.14	3,573,346	3.12	0.70	1	5

¹Age at first service (AFS) in days, calf size (CZ), calving ease (CE), days from calving to first service (CTFS), days from first service to conception (FSTC), gestation length (GL) in days, milking speed (MS), milking temperament (MT), 56-d nonreturn rate (NRR), number of services (NS), stillbirth (SB).

²For both MS and MT, scoring is made only once during the first 6 mo of first lactation.

Statistical Models

The statistical models used for the analysis in different scenarios are described below.

Multi-Step GBLUP Model. This approach consisted of 4 steps:

- (1) Estimation of breeding values using traditional BLUP;
- (2) De-regression of EBV;
- (3) Prediction of DGV; and
- (4) Blending of DGV with PA/EBV.

Consider the following model:

$$\mathbf{y} = \mathbf{1}\mu + \mathbf{Z}\mathbf{g} + \mathbf{e},$$

where $\mathbf{y}$ is a vector of de-regressed evaluations of genotyped animals, $\mathbf{1}$ is a vector of ones, μ is the overall mean, $\mathbf{Z}$ is a design matrix that allocates records to breeding values, $\mathbf{g}$ is a vector of DGV to be estimated, and $\mathbf{e}$ is a vector of random residual effects. It was assumed that $\mathbf{g} \sim N(\mathbf{0}, \mathbf{G}\sigma_g^2)$, where $\mathbf{G}$ is the genomic relationship matrix based on SNP markers, and σ_g^2 is the additive genetic variance; $\mathbf{e} \sim N(\mathbf{0}, \mathbf{R}\sigma_e^2)$, where $\mathbf{R}$ is a diagonal matrix containing weights based on the reliability of the breeding values and σ_e^2 is the residual variance.

Here, DGV were estimated with either 5 or 20% weight (δ) for the expected additive relationship matrix when combined with the genomic relationship matrix. Thus, the model becomes

$$\mathbf{y} = \mathbf{1}\mu + \mathbf{Z}\mathbf{g}_\delta + \mathbf{e},$$

where $\mathbf{g}_\delta \sim N(\mathbf{0}, \mathbf{G}_\delta\sigma_{g_\delta}^2)$, where $\mathbf{G}_\delta$ is a combined relationship matrix, $\mathbf{G}_\delta = \delta\mathbf{A}_{22} + (1 - \delta)\mathbf{G}$.

Blending. The blending approach used to generate GEBV was as follows:

$$\text{GEBV} = w_1\text{DGV} + w_2\text{EST},$$

$$w_1 = \frac{\text{Rel}_{\text{DGV}}}{\text{Rel}_{\text{DGV}} + \text{Rel}_{\text{EST}}},$$

$$w_2 = \frac{\text{Rel}_{\text{EST}}}{\text{Rel}_{\text{EST}} + \text{Rel}_{\text{DGV}}},$$

where EST is either EBV (for training population animals) or PA (for validation population animals) from traditional BLUP, and Rel is the reliability of estimates.

Single-Step GBLUP Model. This method uses information from both genotyped and nongenotyped animals simultaneously. The mixed model equations then become

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{Z} \\ \mathbf{Z}'\mathbf{X} & \mathbf{Z}'\mathbf{Z} + \mathbf{H}^{-1}\alpha \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{Z}'\mathbf{y} \end{bmatrix},$$

where $\mathbf{y}$ is the vector of observations, $\mathbf{b}$ is the vector of fixed effects, $\mathbf{u}$ is the vector of random additive genetic effects, $\mathbf{X}$ and $\mathbf{Z}$ are the corresponding design matrices, α is the variance ratio, and $\mathbf{H}^{-1}$ is derived as in Aguilar et al. (2010) and Christensen and Lund (2010):

$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & (\mathbf{G}^{-1} - \omega\mathbf{A}_{22}^{-1}) \end{bmatrix},$$

where $\mathbf{A}$ is the pedigree relationship matrix, $\mathbf{G}$ is the genomic relationship matrix, as $0.95\mathbf{G}^* + 0.05\mathbf{A}_{22}$ (to avoid singularity problems), and $\mathbf{G}^*$ is constructed as in VanRaden (2008); $\mathbf{A}_{22}$ is the pedigree relationship matrix among genotyped animals. Inbreeding was considered in the construction of all the relationship matrices. Differences between $\mathbf{A}_{22}$ and $\mathbf{G}$ may occur for several reasons that should be taken into account. For instance, incompleteness and shortness of pedigree, pedigree mistakes, incorrect assignment of genotypes, and poor quality of genotypes can cause such differences resulting in upward bias of genomic EBV for young animals and poor convergence when iteratively solving the mixed model equations for ssGBLUP (Misztal et al., 2013). Previous studies have investigated the use of a scaling factor or weight (ω) on $\mathbf{A}_{22}^{-1}$ to avoid convergence problems and bias, and it has been reported that values lower than 1 usually contribute to reduce the bias of GEBV for various traits in dairy cattle (Misztal et al., 2010; Tsuruta et al., 2011). Therefore, a weight (ω) ranging from 1.0 to 0.6 for different traits was also applied to $\mathbf{A}_{22}^{-1}$ in this study ($\omega = 1$ for FSTC_h, SB_h, NRR_c, and FSTC_c, where subscript h refers to heifer traits and c refers to cow traits; $\omega = 0.8$ for CZ; $\omega = 0.7$ for NS_c, GL_c, and MS; and $\omega = 0.6$ for AFS, NRR_h, NS_h, GL_h, CE_h, CTFS, CE_c, SB_c, CZ_c, and MT). All models described above were also used for analyses including (or not including) cows' genomic information.

Genomic Predictions

The following genomic predictions were evaluated with regarding accuracy and bias: GEBV estimated by ssGBLUP (ssGEBV); DGV estimated by msGB-

LUP (hereafter called the **GBLUP_D**) with either 5% weight for the expected additive relationship matrix of genotyped individuals (**A₂₂**) when combined with the genomic relationship matrix (**DGV-5%A**) or 20% weight (**DGV-20%A**); and GEBV calculated by blending traditional EBV/PA with DGV with either 5% (**GEBV-5%A**) or 20% (**GEBV-20%A**) weight for **A₂₂** (hereafter called the **GBLUP_B** method). In addition, all analyses were carried out including or not including the genomic information of cows. Only cows with DEBV reliabilities equivalent to the reliability due to the contribution of at least 10 daughters were considered in the training population. The weights of 5 and 20% for expected additive relationship matrix were chosen because in the Canadian dairy cattle official genomic evaluations a weight of 20% has been defined and is used (Van Doormaal et al., 2009), whereas in other countries the weight usually ranges between 5 and 20%. Genomic predictions using the GBLUP method were computed using the *gebv* software (Sar-

golzaei et al., 2009) for the msGBLUP method and BLUP90IOD2 program (Tsuruta et al., 2001) for the ssGBLUP method.

For this study, different data sets were prepared to assess prediction performance for the traits of interest: (1) a full data set containing all records of cows from which EBV were calculated and de-regressed to be used as benchmark; and (2) a reduced data set that included records of cows after deleting the last 4 yr of observations. These 2 data sets were used for genomic predictions as previously described. Subsequently, animals from the reduced data set were split into training and validation populations according to year of birth. The validation set (used to assess GEBV prediction reliability and bias) included only genotyped bulls with no daughters in the reduced data set, but with at least 50 daughters in the full data set. Table 2 summarizes the number of bulls and cows in each data set, as well as the average reliability of DEBV for the msGBLUP method for each trait.

Table 2. Structure of training and validation data sets for multi-step genomic BLUP (msGBLUP) and single-step genomic BLUP (ssGBLUP) methods

		Validation population		Training population					
				msGBLUP				ssGBLUP	
				Bulls		Cows		Phenotype ⁵	Phenotype and genotype ⁵
				N ³	Rel _{DEBV} ⁴ (%)	N	Rel _{DEBV} (%)		
Parity	Trait ¹	N ²	Birth year	N ³	Rel _{DEBV} ⁴ (%)	N	Rel _{DEBV} (%)	Phenotype ⁵	Phenotype and genotype ⁵
Reproductive trait									
First	AFS	508	2009–2011	5,365	59	735	12	924,141	5,752
	NRR	317	2009–2011	4,785	22	669	04	1,004,755	5,796
	NS	241	2009–2011	5,146	29	743	03	1,035,548	5,818
	FSTC	209	2008–2010	4,126	17	305	04	774,808	5,551
	GL	418	2009–2011	5,111	68	723	18	761,889	5,018
	CE	438	2009–2011	5,359	65	788	16	825,001	5,119
	SB	438	2009–2011	5,330	44	660	07	817,817	5,118
	CZ	420	2009–2011	5,316	58	711	12	801,544	5,024
Later	NRR	489	2009–2011	5,917	38	779	07	3,361,860	6,444
	NS	570	2008–2010	5,568	66	404	25	3,225,929	6,463
	CTFS	568	2008–2010	5,568	70	404	30	3,230,244	6,464
	FSTC	406	2007–2009	5,060	44	203	15	2,115,685	5,872
	GL	342	2008–2010	5,416	76	396	45	2,054,483	5,757
	CE	363	2008–2010	6,089	65	407	29	2,422,682	5,886
	SB	285	2008–2010	6,040	28	399	06	2,408,553	5,886
	CZ	350	2008–2010	6,060	67	405	32	2,387,080	5,872
Workability trait									
First ⁶	MT	554	2009–2011	7,047	74	772	13	2,485,983	6,184
	MS	554	2009–2011	7,369	76	779	15	3,136,478	6,150

¹Age at first service (AFS), calf size (CZ), calving ease (CE), days from calving to first service (CTFS), days from first service to conception (FSTC), gestation length (GL), milking speed (MS), milking temperament (MT), 56-d nonreturn rate (NRR), number of services (NS), stillbirth (SB).

²Only bulls with at least 50 daughters were considered in the validation population.

³Only bulls with at least 10 daughters were considered in the training population.

⁴Average reliability of de-regressed EBV in the training population.

⁵Number of animals with phenotypes and number of animals with both phenotypes and genotypes.

⁶For both MS and MT, scoring is made only once during the first 6 mo of first lactation.

Validation

The reliability of genomic predictions for the studied traits were measured as squared correlation between the predicted breeding values (obtained with the reduced data set) and de-regressed EBV (from the full data set) in the validation data sets. To access the bias (spread) of genomic predictions for each method, the following regression model was used:

$$\text{DEBV}_C = b_0 + b_1 X_P + e,$$

where DEBV_C are de-regressed EBV, obtained from the complete data set, of genotyped bulls with no daughters in the reduced data set, but with at least 50 daughters in the complete data set; b_0 is the intercept; b_1 is the linear regression coefficient indicating bias of the predictions; X_P is the bull's PA or GEBV obtained with the reduced data set; and e is the residual.

RESULTS AND DISCUSSION

In the present study, when genomic information was included in the analyses, the average improvement in observed reliability of predictions was 7 and 13 percentage points for reproductive traits and workability traits, respectively, compared with traditional BLUP (Table 3). Moreover, averaged over the 18 traits, the absolute deviation from 1 of the regression coefficient of the linear regression of de-regressed EBV on genomic predictions went from 0.19 when using traditional BLUP to 0.22 when using msGBLUP, and to 0.14 when using ssGBLUP (Table 4). Regression coefficients ranged from 0.51 to 1.35 for msGBLUP, whereas for ssGBLUP, the coefficients ranged from 0.66 to 1.04 (Table 4).

Regression coefficient values close to 1 suggest that 1-unit difference in the genomic evaluation results in a 1-unit change in the trait, and therefore, they are considered to be on the same scale (Sullivan, 2009; Wiggins et al., 2011). A regression coefficient less than 1 indicates inflation of the variance of genomic predictions, whereas deflation occurs when the coefficient is larger than 1. Traditional BLUP models consider all information available in the evaluation (i.e., phenotypes and pedigree), and therefore, less bias derived from selection is observed (Sorensen and Kennedy, 1984). Bias on multi-step genomic predictions may arise from the fact that genomic prediction models do not simultaneously fit all data used for selection decisions, and therefore, it is assumed that the populations being evaluated have not undergone selection. Yet, in dairy cattle, a large number of genotyped populations usually consist of progeny-tested bulls, which are highly selected animals (Hayes et al., 2009; Vitezica et al., 2011).

By including all information available in the evaluation simultaneously (i.e., phenotypes, genotypes, and pedigree), ssGBLUP is able to partially account for pre-selection, thus minimizing possible selection bias on the predictions (Legarra et al., 2014). In addition, there are various specificities in msGBLUP regarding PA information (VanRaden et al., 2009), whereas in the ssGBLUP PA are automatically included in the genomic predictions. Gao et al. (2012) applied 3 multi-step GBLUP and 2 single-step blending methods for genomic prediction in Nordic Holsteins. In their study, the 2 single-step methods led to less bias than the other GBLUP methods. Similarly, Ma et al. (2015) showed that regression coefficients went from 0.69 when using a multi-step GBLUP to 0.78 for the single-step GBLUP method. In the present study, averaged over all traits, ssGBLUP resulted in regression coefficients with the smallest absolute deviation from 1. For reproductive and workability traits, the deviation of the regression coefficient from 1 for ssGBLUP was equal to 0.11 and 0.19, respectively, whereas for msGBLUP, this deviation was 0.21 and 0.25, respectively. The single-step approach also resulted in a slight increase in reliability of genomic predictions compared with those of msGBLUP.

Historically, ssGBLUP could not converge or had a large bias in some cases, and one measure to improve on both counts was a weight parameter (ω) given to $\mathbf{A}_{22}^{-1}$. Such a parameter was shown to account for missing inbreeding, especially when some pedigrees were missing (Misztal et al., 2017). When inbreeding was accounted for in $\mathbf{A}$ including in phantom parent groups, the b_1 parameter improved from 0.75 to 0.90. Accounting for reduced heritability due to genetic selection improved the parameter b_1 to 0.96 and slightly increased accuracy. These measures indicated that special modeling is required to account for selection practices under genomic selection (Misztal et al., 2017).

Obtaining unbiased predictions is of fundamental importance for an accurate ranking and fair comparison of animals across generations (Patri and Ducrocq, 2009; Aguilar et al., 2010). Gao et al. (2012) showed that absolute deviations of the regression coefficients from 1 tended to decrease with increasing polygenic weights in a GBLUP model, which is consistent with the literature (Aguilar et al., 2010; Liu et al., 2011). This could be explained by the fact that genetic markers are not able to explain the total genetic variance of a given trait. Thus, the polygenic effect would account for the residual genetic variance, which is not accounted for by using only genetic markers. In the present study, the polygenic weight of 20% in the msGBLUP slightly improved the observed reliability of predictions while reducing the bias. Averaged over all traits, the deviation of the regression coefficient from 1 for GBLUP_D

Table 3. Observed reliabilities of genomic predictions obtained using different methods¹

Parity	Trait ²	Average reliability of DEBV _c ³	Observed reliability									
			DGV-5%A		GEBV-5%A		DGV-20%A		GEBV-20%A		ssGEBV	
			Bulls	and cows	Bulls	and cows	Bulls	and cows	Bulls	and cows	Bulls	and cows
Reproductive trait	First											
	AFS	0.712	0.153	0.155	0.153	0.174	0.161	0.162	0.161	0.179	0.159	0.157
	NRR	0.389	0.045	0.038	0.045	0.044	0.041	0.040	0.047	0.046	0.050	0.053
	NS	0.516	0.103	0.089	0.104	0.099	0.094	0.090	0.108	0.104	0.112	0.127
	FSTC	0.331	0.038	0.122	0.116	0.104	0.114	0.109	0.098	0.094	0.120	0.110
	GL	0.797	0.280	0.355	0.352	0.376	0.365	0.363	0.381	0.379	0.367	0.373
	CE	0.758	0.155	0.237	0.242	0.339	0.242	0.247	0.244	0.349	0.250	0.254
	SB	0.575	0.131	0.302	0.300	0.289	0.300	0.298	0.279	0.278	0.293	0.302
	CZ	0.718	0.149	0.243	0.244	0.250	0.250	0.253	0.252	0.255	0.268	0.286
	Average ⁵	0.599	0.129	0.192	0.191	0.196	0.196	0.195	0.196	0.210	0.202	0.208
Later	NRR	0.326	0.021	0.039	0.039	0.042	0.040	0.040	0.042	0.042	0.030	0.034
	NS	0.681	0.161	0.237	0.237	0.261	0.250	0.251	0.267	0.267	0.271	0.284
	CTFS	0.731	0.138	0.187	0.190	0.208	0.192	0.194	0.206	0.208	0.206	0.207
	FSTC	0.474	0.093	0.155	0.158	0.165	0.159	0.161	0.161	0.164	0.164	0.169
	GL	0.808	0.315	0.454	0.450	0.464	0.464	0.460	0.463	0.462	0.459	0.465
	CE	0.695	0.092	0.126	0.127	0.144	0.133	0.133	0.149	0.149	0.133	0.138
	SB	0.328	0.067	0.075	0.075	0.083	0.079	0.080	0.085	0.085	0.086	0.089
	CZ	0.722	0.180	0.325	0.326	0.332	0.330	0.331	0.330	0.331	0.337	0.350
	Average ⁵	0.596	0.133	0.200	0.200	0.212	0.206	0.206	0.213	0.214	0.211	0.217
Workability trait	First ⁶											
	MT	0.797	0.106	0.184	0.184	0.188	0.192	0.192	0.191	0.191	0.200	0.207
Average ⁵	MS	0.815	0.219	0.385	0.383	0.399	0.392	0.390	0.401	0.400	0.412	0.418
	Average ⁵	0.806	0.163	0.285	0.284	0.294	0.292	0.291	0.296	0.296	0.306	0.312

¹GBLUP using a blending approach with a polygenic effect with a weight of 0.05 (GEBV-5%A); GBLUP using a blending approach with a polygenic effect with a weight of 0.2 (GEBV-20%A); GBLUP with a polygenic effect with a weight of 0.05 (DGV-5%A); GBLUP with a polygenic effect with a weight of 0.2 (DGV-20%A); single-step GBLUP (ss-GBLUP).

²Age at first service (AFS), calf size (CZ), calving ease (CE), days from calving to first service (CTFS), days from first service to conception (FSTC), gestation length (GL), milking speed (MS), milking temperament (MT), 56-d nonreturn rate (NRR), number of services (NS), stillbirth (SB).

³Average reliability of de-regressed EBV obtained from complete data set for validation population.

⁴PA = parent average.

⁵Average reliability across traits is shown in these rows.

⁶For both MS and MT, scoring is made only once during the first 6 mo of first lactation.

Table 4. Regression coefficient of the linear regression of de-regressed EBV (DEBVc) on genomic predictions (GEBV) or on standard BLUP evaluations (PA) obtained using different methods¹

Parity	Trait ²	Average reliability of DEBVc ³	Regression coefficient									
			DGV-5%A		GEBV-5%A		DGV-20%A		GEBV-20%A		ssGEBV	
			Bulls	Bulls and cows	Bulls	Bulls and cows	Bulls	Bulls and cows	Bulls	Bulls and cows	Bulls	Bulls and cows
Reproductive trait First	AFS	0.71	0.79	0.63	0.63	0.63	0.69	0.69	0.69	0.85	0.76	0.82
	NRR	0.39	0.85	0.64	0.63	0.79	0.69	0.68	0.84	0.83	0.92	0.97
	NS	0.61	0.76	0.53	0.51	0.66	0.57	0.56	0.70	0.69	0.79	0.91
	FSTC	0.33	0.76	1.25	1.21	1.35	1.29	1.25	1.32	1.28	0.95	0.87
	GL	0.80	0.95	0.85	0.84	1.00	0.91	0.90	1.04	1.04	0.97	1.01
	CE	0.76	0.84	0.71	0.72	0.71	0.76	0.77	0.77	1.09	0.87	0.93
	SB	0.66	0.96	1.09	1.09	1.25	1.14	1.13	1.27	1.26	0.95	0.97
	CZ	0.72	0.96	0.91	0.90	1.10	0.97	0.96	1.15	1.14	0.97	1.04
		0.62	0.14	0.26	0.26	0.24	0.23	0.23	0.22	0.18	0.10	0.07
	NRR	0.33	0.97	1.05	1.04	1.30	1.13	1.13	1.35	1.35	0.81	0.84
Mean deviation from 1 ⁴ Later	NS	0.68	0.83	0.78	0.78	0.97	0.85	0.85	1.03	1.03	0.94	1.01
	CTFS	0.77	0.61	0.56	0.56	0.68	0.59	0.59	0.70	0.71	0.69	0.72
	FSTC	0.47	1.00	0.92	0.92	1.12	0.99	0.99	1.17	1.18	0.83	0.80
	GL	0.83	0.88	0.89	0.89	1.00	0.94	0.93	1.03	1.03	0.95	0.99
	CE	0.69	0.74	0.57	0.56	0.76	0.63	0.62	0.82	0.81	0.72	0.78
	SB	0.50	0.79	0.69	0.68	0.81	0.74	0.74	0.85	0.84	0.92	1.00
	CZ	0.72	0.78	0.73	0.73	0.86	0.78	0.78	0.90	0.91	0.88	0.96
		0.62	0.18	0.24	0.24	0.17	0.20	0.20	0.16	0.17	0.16	0.12
	MT	0.80	0.54	0.54	0.54	0.63	0.58	0.58	0.67	0.67	0.66	0.71
	MS	0.81	0.97	0.79	0.79	0.99	0.84	0.84	1.04	1.04	0.92	0.97
Mean deviation from 1 Workability trait First ⁵		0.81	0.25	0.34	0.34	0.19	0.29	0.29	0.19	0.19	0.21	0.16

¹GBLUP using a blending approach with a polygenic effect with a weight of 0.05 (GEBV-5%A); GBLUP using a blending approach with a polygenic effect with a weight of 0.2 (GEBV-20%A); GBLUP with a polygenic effect with a weight of 0.05 (DGV-5%A); GBLUP with a polygenic effect with a weight of 0.2 (DGV-20%A); single-step GBLUP (ss-GBLUP).

²Age at first service (AFS), calf size (CZ), calving ease (CE), days from calving to first service (CTFS), days from first service to conception (FSTC), gestation length (GL), milking speed (MS), milking temperament (MT), 56-d nonreturn rate (NRR), number of services (NS), stillbirth (SB).

³Average reliability of de-regressed EBV in the validation population.

⁴Mean of absolute deviation of the regression coefficient from 1.

⁵For both MS and MT, scoring is made only once during the first 6 mo of first lactation.

went from 0.28 when using a 5% polygenic weight to 0.24 with a 20% polygenic weight.

Alternatively, one way to account for the residual genetic variance and ensure that all polygenes are considered is by adopting a blending approach (Sullivan, 2009). In Canada, when using this blending approach, GEV are calculated by combining EBV obtained from traditional pedigree-based (BLUP) evaluations with DGV from GBLUP evaluations through a selection index, weighted by their reliabilities (Van Doormaal et al., 2009). Predictions obtained with GBLUP_B were, on average, less biased and slightly more reliable than those obtained with GBLUP_D. When a polygenic weight of 5% was used, reliabilities ranged from 0.037 to 0.454 (average: 0.206) and from 0.042 to 0.464 (average: 0.217), for GBLUP_D and GBLUP_B, respectively, whereas the range went from 0.040 to 0.464 (average: 0.21) and from 0.042 to 0.463 (average: 0.218), for GBLUP_D and GBLUP_B, respectively, when using 20% polygenic weight (Table 3). These results are in agreement with Lourenco et al. (2014). The authors reported higher reliabilities for GEV compared with DGV for milk yield, fat, and protein percentages. Conversely, Su et al. (2012) reported higher reliabilities for DGV compared with ssGEV for various traits of Nordic Red Cattle. However, according to the authors the reliability of DGV could be overestimated, given the fact that different scaling factors were used as weights for the genomic relationship matrices in each method.

In the present study, in addition to the increase in reliability caused by blending (GBLUP_B), the GEV bias was reduced. For a polygenic weight of 5%, the deviation of the regression coefficient from 1 was 0.28 and 0.19 for GBLUP_D and GBLUP_B, respectively, whereas for predictions obtained with a 20% polygenic weight, this deviation was 0.24 for GBLUP_D and 0.18 for GBLUP_B (Table 4). Commonly, only animals selected based on their GEV will have their progeny's phenotypes recorded. However, such information is not included in the evaluation, and therefore, pre-selection is not properly accounted for; this will lead to biased pedigree-based predictions (i.e., EBV; Patry and Ducrocq, 2011) and, consequently, affect the blending approach. The use of all information available simultaneously to predict GEV could potentially help avoid such bias.

In dairy cattle genomic evaluation, training populations are usually composed of progeny-tested bulls, as those have more reliable information. However, for lowly heritable traits, such as health and fertility, a very large training population is required to achieve high accuracies of predictions (Hayes et al., 2009), which could be a challenge given the fact that progeny-tested bulls are limited for those traits. Moreover,

progeny-tested bulls are intensively selected, which could potentially lead to loss of genetic variability. The inclusion of cows in training populations is appealing, as they can contribute to increase the size of a training population and are also of major importance during the selection decision process (Wiggans et al., 2011; Buch et al., 2012; Tsuruta et al., 2013; Ma et al., 2015). In this study, the method used for de-regression of EBV was the one proposed by VanRaden et al. (2009), due to its easy and efficient implementation. To our best knowledge, there is no consensus on the best method to use for the traits analyzed here. However, other more computationally demanding alternatives have also been proposed, as for instance in Jairath et al. (1998) and Garrick et al. (2009).

The benefits of adding cows' genomic information into the training populations may depend on the strategy adopted (Tsuruta et al., 2013; Gao et al., 2015). When using a multi-step approach, accuracies of genomic predictions are contingent on the accuracies of de-regressed EBV used and for the cows' EBV lower accuracies are expected compared with those of bulls. In the present study, differences between using a training population with cows and bulls or with bulls only for the msGBLUP methods were small (Tables 3 and 4). This is likely due to the small number of cows included in the analyses and their low reliabilities (Table 2). However, for ssGBLUP the inclusion of cows' information had a positive effect on genomic predictions. Across all traits, the single-step approach including bulls and cows' genomic information led to the highest reliability of genomic predictions, followed by ssGBLUP with bulls only in the training population, and msGBLUP methods. On average, reliabilities of ssGBLUP including bulls and cows' genomic information were 1.21% higher than those of msGBLUP methods with a bulls-only training population, which is the method currently used for Canadian genomic evaluations. Tsuruta et al. (2013) also reported an increase in reliability of 1.9 to 2.7% when cow genotypes were added in the evaluation using ssGBLUP.

The inclusion of cows' genomic information can also help reduce the bias of genomic predictions under a single-step approach. In the present study, the average deviation of the regression coefficient from 1 was 0.18 and 0.19 for GBLUP_B for bulls and cows, and bulls only in the training population, respectively. However, when using the single-step approach this deviation decreased to 0.12 when bulls and cows' genomic information was used for the analysis and when only bulls' genomic information was used, the average deviation across all traits was 0.16. The use of a single-step approach also resulted in a slightly increased mean reliability (0.221) compared with GBLUP_B (0.217).

The average deviation from 1 for msGBLUP was 0.22 and 0.25 for reproductive and workability traits, respectively, when only bulls were included in the training, whereas for ssGBLUP the deviation from 1 was 0.13 and 0.21 for reproductive and workability traits, respectively. When both cows and bulls were included in the training population the average deviation for msGBLUP was 0.20 and 0.25 for reproductive and workability traits, respectively, and was 0.09 and 0.16 for ssGBLUP, respectively. The results obtained for regression coefficients are in agreement with those of previous findings (Tsuruta et al., 2013; Ma et al., 2015; Uemoto et al., 2017).

CONCLUSIONS

Single-step genomic BLUP can reduce bias while slightly increasing observed reliability of genomic predictions. Predictions obtained with the single-step approach by adding cows' genomic information showed a small gain in reliability and a reduction in bias compared with those obtained by only including bulls' genomic information. For the multi-step GBLUP method, no effects on reliability or bias of predictions were observed when genomic information of cows was considered. This may be explained by the fact that only a small number of cows were included in the analyses. The inclusion of a polygenic effect in the multi-step analysis as well as the use of a blending approach had a small effect on reliabilities of predictions, but an important effect on bias. However, the improvements obtained with different strategies adopted in the multi-step method were smaller compared with the use of the single-step approach.

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