Development of genetic and genomic evaluation for wellness traits in US Holstein cows

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ABSTRACT

In March 2016, Zoetis Genetics offered the first commercially available evaluation for wellness traits of Holstein dairy cattle. Phenotypic data on health events, pedigree, and genotypes were collected directly from producers upon obtaining their permission. Among all recorded health events, 6 traits were chosen to be included in the evaluation: mastitis, metritis, retained placenta, displaced abomasum, ketosis, and lameness. Each trait was defined as a binary event, having a value of 1 if a cow has been recorded with a disorder at any point during the lactation and zero otherwise. The number of phenotypic records ranged from 1.8 million for ketosis to 4.1 million for mastitis. Over 14 million pedigree records and 114,216 genotypes were included in the evaluation. All traits were analyzed using univariate threshold animal model with repeated observations, including fixed effect of parity and random effects of herd by year by season of calving, animal, and permanent environment. A total of 45,425 single nucleotide polymorphisms were used in the genomic analyses. Animals genotyped with low-density chips were imputed to the required number of single nucleotide polymorphisms. All analyses were based on the single-step genomic BLUP, a method that combines phenotype, pedigree, and genotype information. Predicted transmitting abilities were expressed in percentage points as a difference from the average estimated probability of a disorder in the base population. Reliabilities of breeding values were obtained by approximation based on partitioning of a function of reliability into contributions from records, pedigree, and genotypes. Reliabilities of genomic predicted transmitting abilities for young genotyped and pedigreed females without recorded health events had average values between 50.2% (displaced abomasum) and 51.9% (mastitis). Genomic predictions for wellness traits can provide new information about an animal's

genetic potential for health and new selection tools for dairy wellness improvement.

Key words: wellness traits, dairy cattle, single-step genomic BLUP, reliability

INTRODUCTION

Interest is growing in the use of genetic improvement strategies as a component to the management of health in dairy cattle. Breeding strategies that incorporate information on health traits have the potential to improve animal well-being and overall effectiveness of dairy operations. Dairy animals that experience health events have a negative effect on herd profitability through increased culling, veterinary expenses, and labor, as well as monetary losses through reduced milk sales (Parker Gaddis et al., 2014). Guard (2009) estimated the expenses related to the common dairy cow diseases to range from \$181 per case of ketosis to \$391 per case of displaced abomasum. Dairy researchers and producers have focused on providing the best environment to reduce health events through nutrition, management, and housing. However, improving functional traits genetically presents a challenge, because health traits have low heritability and may be difficult and expensive to measure and record.

Genetic evaluation of health traits has a long tradition in countries with routine health data recording. In Scandinavian countries, health traits have been included in breeding programs since the mid-1970s (Heringstad and Østerås, 2013); currently, over 97% of Norwegian dairy cows are included in the recording system (Heringstad, 2010; Haugaard et al., 2012). In other countries, the use of direct health data in genetic evaluation is progressing rapidly. Routine data collection and genetic evaluation for health traits in Germany and Austria started in 2006 (Fuerst et al., 2011). In France, clinical mastitis has been included in routine genetic evaluation since 2010 (Govignon-Gion et al., 2012). In 2014, genetic evaluation for mastitis resistance was introduced for Canadian dairy cows; the evaluation is based on clinical mastitis incidence recorded in the first and second lactation and SCS (Koeck

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et al., 2012; Miglior et al., 2014). In Canada, research is currently underway to implement genetic evaluation for ketosis and displaced abomasum in December 2016, followed by metritis and retained placenta, hoof health and lameness, and other functional traits in the following years (Beaver and VanDoormal, 2016).

Currently, genetic evaluation and selection for dairy health traits in the United States is based on indicator traits. Somatic cell score, certain feet and leg traits, and productive life are included in the national genetic evaluation and have shown desirable genetic trends in recent years. However, the availability of predictions for these traits has not resulted in the expected reduction in the incidence of mastitis, lameness, or metabolic diseases in dairy herds (NAHMS, 2007), possibly because of low heritabilities of the indicator traits and the incomplete correlations with the target traits. The most frequently cited reason for not using direct health data in genetic evaluation of dairy cattle is the absence of a national system to collect health record data. Although most dairy producers record health information of their animals, the user-defined nature of health records makes it more difficult to use health data in a genetic evaluation due to insufficient accuracy and inconsistency of recording (Wenz and Giebel, 2012). On the other hand, studies based on large amounts of producer-recorded health events have shown that genetic selection for wellness traits should result in favorable genetic trends for health in dairy cattle as long as the health recording protocol within a herd can be assumed fairly consistent (Zwald et al., 2004; Parker Gaddis et al., 2012, 2014).

Advances in methodology used in genomic evaluation have resulted in improved accuracy of selection for traits with low heritabilities and incomplete information. The single-step genomic BLUP (ssGBLUP) method (Misztal et al., 2009; Aguilar et al., 2010) is being widely adopted as the method of choice in genomic evaluation. The method uses joint information on pedigree, phenotype, and genomic data in a single analysis. The ssGBLUP works in the same way as traditional BLUP, except that it modifies the additive relationship matrix by incorporating relationships estimated from genotyped animals. The ssGBLUP method is rapidly gaining popularity in both research and commercial communities due to its simplicity and applicability to most evaluation models and data structures. The method is considered free of double counting and pre-selection bias (Misztal et al., 2013a). Parker Gaddis et al. (2014) applied ssGBLUP methodology to approximately 300,000 records of health events and concluded that the inclusion of genomic data would substantially improve accuracy of selection for health traits.

Although several research projects have shown the value and feasibility of selection for wellness traits, na-

tional evaluation based on direct health records in the United States seems unlikely in the near term (Chesnaïs et al., 2016). In response to market needs for genetic improvement of dairy wellness traits, and in collaboration with the Holstein Association USA (Brattleboro, VT), University of Georgia in Athens, and customers, Zoetis Genetics launched a project to develop genetic and genomic evaluation for wellness traits in dairy cattle. In particular, this project focuses on creating genomic tools that would allow commercial dairy farmers to make management and selection decisions based on genetic predisposition of their heifer calves for wellness traits that will be expressed later in life. The objective of our study was to develop foundations for commercially viable genetic and genomic evaluation for wellness traits in Holstein dairy cattle based on producer-recorded data and ssGBLUP methodology.

MATERIALS AND METHODS

Data Sources

Phenotypic data were obtained directly from producers upon obtaining their signed permissions. Data were obtained from approximately 240 herds located in 29 different states in all regions of the United States. Each herd provided information on 13,720 animals, on average. As of January 2016, over 3 million health events from approximately 14.5 million lactation records have been collected for the analysis. For some herds, the records dated back to the 1990s.

Data from on-farm software was extracted and processed using internally written scripts. Pedigree information, lactation data, and health events were extracted from the backup files and converted into standard USDA-defined data-exchange formats (<https://www.cdcb.us/formats/formats.html>). Phenotypic records on about 25,000 animals collected from past research projects conducted by Zoetis (Vukasinovic et al., 2013) or obtained from collaborators were also added to the data set.

Pedigree information was supplied by Holstein Association USA for all registered bulls born between 1950 and 2014 and cows born between 2005 and 2014. Pedigree information for nonregistered animals was obtained from farm software backup files. For animals with owner permissions and genomically tested at Zoetis, pedigree information was initially supplied by the customer on the order form and later updated based on reports received from the Council of Dairy Cattle Breeding (CDCB, Bowie, MD). Bulls of foreign origin were manually queried using publicly available queries.

Animals from commercial herds, originally submitted to Zoetis for genomic testing, were genotyped with vari-

Figure 1. Contribution of various sources to the phenotype and genotype data. Genotype data are shown by the type of chip used for genotyping [3K, 50K+, and LD are standard Illumina (San Diego, CA) chips; ZL2 and ZLD are chips with Zoetis proprietary content].

ous versions of low-density chips: Illumina Bovine3K (Illumina Inc., 2011b), Illumina BovineLD (Boichard et al., 2012), or Zoetis customized low-density chips (proprietary information). Animals from research projects, as well as bull DNA samples purchased by Zoetis for research purposes, were genotyped with the Illumina Infinium BovineSNP50 BeadChip (Illumina Inc., 2011a). Figure 1 shows the contribution of various sources to the phenotype and genotype data used in the project.

Data Editing

Animal identification (**ID**) was checked for accuracy using similar criteria as described in Norman et al. (1994). Animals with incorrect ID were removed from analysis. Animals with incorrect sire or dam ID were filtered and incorrect parental information was deleted. Animals were excluded if the parental age or sex were incorrect. If an animal was found to have the same parents and date of birth as another animal already present in the pedigree file, the new animal was excluded unless specifically declared as a twin or a product of embryo transfer. Samples of animals were occasionally run through the CDCB's genotype query (https://www.cdeb.us/CF-queries/GT_q.cfm) to ensure high compatibility with the national database.

Health events were reduced to traits of interest: mastitis (**MAST**), metritis (**METR**), retained placenta (**RETP**), displaced abomasum (**DA**), ketosis (**KETO**), and lameness (**LAME**). These traits were selected based on the presence of records across the

herds and the average incidence in the population. Each trait was defined as a binary event—having a value of 1 if a cow has been recorded with the problem at any point during the lactation and zero otherwise—regardless of how many times disease incidence or treatment was actually recorded during the lactation. Each animal was required to have a lactation record with a valid calving date and a lactation number as well as a calving interval between 250 and 999 d. No minimum or maximum values were set for the number of DIM to include animals culled soon after calving due to postpartum disorders as well as those recorded with a health problem in late lactations. Phenotype records were checked against the pedigree and all animals found to be male in the pedigree file or having a calving date preceding their birth date were removed. Lactations of a cow without recorded disorders, as well as lactations of all herdmates without records on a particular disorder, were added as healthy records.

Further, each herd by year and season of calving (**HYS**) group with a minimum of 20 lactation records was required to have at least 1 recording of a particular disorder. Lacking this, the entire group was discarded, as it was assumed that the herd did not record that disorder at all or did not record it during that period. Smaller HYS groups were assumed to have no incidence of a disorder if no records of that disorder were found. Due to large herd sizes, the number of small HYS groups included in the genetic evaluation without the minimum incidence requirement was very low.

Raw genotypes were edited following the criteria described in Wiggans et al. (2011). After removing ani-

imals with low call rates, Hardy-Weinberg equilibrium errors, sex or breed conflicts, and duplicated genotypes of nontwins, the remaining genotyped animals were run through the parentage check. The parentage check procedure compared pairs of genotypes present in both the offspring and its parent using a subset of 1,000 markers provided to Zoetis (George Wiggans, Animal Genomics and Improvement Laboratory, Beltsville, MD, personal communication). Parentage check was performed only if at least 900 markers were present in both offspring and its parent. A parentage conflict was declared if the animal and its parent showed more than 2% mismatches. For such animals, as well as animals without a parent in the pedigree, a search for the most likely parent was performed. The most likely alternative parent was declared if at least 98% matches between the animal and the potential parent were found. If the alternative parent could not be found, the conflicting parent was considered unknown.

All animals genotyped with lower-density chips (fewer than 40,000 markers) were imputed to 45,425 markers using the program FImpute (Sargolzaei et al., 2011).

Statistical Model

Each trait was analyzed separately using a univariate threshold animal model with repeated observations:

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}_h\mathbf{h} + \mathbf{Z}_a\mathbf{a} + \mathbf{Z}_p\mathbf{p} + \mathbf{e},$$

where $\mathbf{y}$ represents a vector of the animals' unobserved liabilities to the given disorder; $\boldsymbol{\beta}$ is the vector of fixed parity effects, with parities 1, 2, 3, 4, and 5 and higher were considered; $\mathbf{h}$ is the random herd-year-season effect, where $\mathbf{h} \sim N(0, \mathbf{I}\sigma_h^2)$, with the variance σ_h^2 , where $\mathbf{I}$ is the identity matrix; 4 seasons were defined within each calving year [winter (December-February), spring (March-May), summer (June-August), and fall (September-November)]; $\mathbf{a}$ is the random animal effect, with $\mathbf{a} \sim N(0, \mathbf{H}\sigma_a^2)$, where σ_a^2 is the additive genetic variance and $\mathbf{H}$ is the pedigree relationship matrix augmented using genotypes; $\mathbf{p}$ is the random effect of permanent environment with $\mathbf{p} \sim N(0, \mathbf{I}\sigma_{pe}^2)$, and $\mathbf{e}$ is the residual, where $\mathbf{e} \sim N(0, 1)$; and $\mathbf{X}$, $\mathbf{Z}_h$, $\mathbf{Z}_a$, and $\mathbf{Z}_p$ are incidence matrices corresponding to the fixed effects in $\boldsymbol{\beta}$ and the random effects of HYS, animal, and permanent environment, respectively.

Variance components for all wellness traits were estimated with the same model but without genomic information. The THRGIBBS1F90 program from the BLUPF90 family (Misztal et al., 2002) was used to estimate variance components.

Genetic Evaluation Process

In ssGBLUP, the inverse of the traditional pedigree relationship matrix, $\mathbf{A}^{-1}$ is replaced by the inverse of $\mathbf{H}$ matrix that combines pedigree and genomic relationships (Legarra et al., 2009; Aguilar et al., 2010):

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

where $\mathbf{G}^{-1}$ is an inverse of the genomic relationship matrix and $\mathbf{A}_{22}^{-1}$ is an inverse of the pedigree-relationship matrix for genotyped animals only. Programs from the BLUPF90 family (Misztal et al., 2014) were used for data analyses. Program preGSf90 was used to create the matrices and their inverses. Once the $\mathbf{H}^{-1}$ matrix was created, the program cblup90iod with a genomic option was used to obtain genomic breeding values based on a threshold model. The program cblup90iod was chosen due to its ability to handle very large models using iteration on data. Because the current version of the cblup90iod program cannot include more than 1 threshold trait, a decision was made to perform univariate analyses. Each trait was run in a separate process, but with the same model and $\mathbf{H}^{-1}$ matrix. The reliabilities of estimated breeding values were approximated using the program accf90GS that implements an algorithm that combines contributions of genotypes, pedigree, and phenotypes (Misztal et al., 2013b).

For each trait, the reliabilities were rescaled to avoid overestimation. The rescaling factors were obtained empirically by comparing exact reliabilities computed from prediction error variances on a sample data set with approximated reliabilities. For each trait, the scaling factor was varied until the correlation between the exact and approximated reliabilities was maximized and differences were minimized. The sampling and estimation process were repeated several times and the best scaling factors from each sample were averaged over all samples.

Expression of Evaluation Results

For each trait, the solutions from the cblup90iod program (raw EBV) were transformed into probabilities of exceeding the threshold value. The threshold represents the transition value between the 2 stages of the categorical variable (healthy and sick). Threshold values for all traits were obtained from the current data. For each animal solution, we calculated the probability that a standard normal variable having a mean equal to that solution and a variance of 1 exceeds the threshold. The probabilities were then multiplied by 100 (to represent

percentages), divided by 2 (to obtain PTA) and expressed as the differences from the average probability of all females born in 2010 with at least 1 phenotypic record for that trait, with higher values representing higher risk of a disorder. For example, if an animal has a PTA for mastitis of 3.5 and the estimated probability of mastitis in the base population is 20%, the offspring of that animal will have 23.5% chance of getting mastitis during a lactation.

For comparison purposes, traditional PTA and reliabilities obtained from pedigree and phenotype information were calculated using the same data, methods, and programs, but without genotypes. All calculations were performed on a computer running Linux (x86_64) RedHat release 7.3 with Intel Xeon E5-4620 CPU (2.6 GHz) processors with 1 TB of memory and 64 computing cores.

Correlations of Wellness Traits with Traits in the National Genetic Evaluation

To check the alignment of the genomic results for wellness traits for young heifers without phenotypic records with the official genomic (g)PTA for traits in the national evaluation, genetic correlations were approximated using all official results generated for animals from 2010 until February 2016. The official evaluation data set comprised close to 495,000 animals; depending on the trait, subsets of 56,000 to 67,000 animals having both official evaluations and wellness trait predictions with reliabilities of at least 40% were used to approximate genetic correlations. Genetic correlations between each wellness trait and the official traits—net merit (\$NM), milk yield, SCS, daughter pregnancy rate (DPR), and productive life—were approximated using the formula by Calo et al. (1973), as described in Parker Gaddis et al. (2014):

Table 1. Number of records (after editing), phenotypic means (average incidence per lactation), and SD of the wellness traits used in genetic and genomic evaluation (GE)

Trait ¹	No. of records in GE	Mean	SD
MAST	4,102,518	0.25	0.43
METR	2,966,946	0.10	0.30
RETP	3,330,123	0.05	0.23
DA	3,015,132	0.02	0.15
KETO	1,841,446	0.05	0.22
LAME	3,400,015	0.12	0.33
Pedigree	14,339,576		
Genotypes	114,216		

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

$$\hat{r}_{g1,2} = \frac{\sqrt{\left(\sum_{i=1}^n REL_{1i}\right)\left(\sum_{i=1}^n REL_{2i}\right)}}{\sum_{i=1}^n (REL_{1i} \times REL_{2i})} \times r_{1,2},$$

where $\hat{r}_{g1,2}$ is the approximated genetic correlation between traits 1 and 2; REL_{1i} and REL_{2i} are reliabilities of (g)PTA for trait 1 and 2, respectively, for animal i ; and $r_{1,2}$ is the Pearson (product-moment) correlation between (g)PTA for traits 1 and 2.

RESULTS AND DISCUSSION

Overall

Table 1 shows the total number of records and phenotypic means and standard deviations for the traits included in the genetic and genomic evaluation. Although the same sources were used to acquire data on all wellness traits, the number of records varied by trait. The greatest numbers of records were available for MAST and LAME, with more than 4 million and about 3.4 million lactation records, respectively. A comparatively lower number of records, about 1.8 million, was obtained for KETO. This difference in number of records by trait exists because not all herds recorded all traits or provided quality data for each trait. The total number of animals with phenotypic records for at least 1 trait was 2,061,511. The total number of pedigree records collected was over 14 million; however, the number of pedigree records included in the evaluation was reduced to 2,662,490 because of pedigree pruning procedure implemented in the BLUPF90 programs that includes in the pedigree only individuals directly related to the animals having phenotype or genotype. Up to 20 generations of ancestors were allowed in the pedigree, although the actual number of generations was much smaller for majority of the animals. The number of genotyped animals in the analysis was 114,216, 65% of which were young animals without own records or progeny. The average incidence per lactation ranged from 0.02 for DA to 0.25 for MAST. The values were comparable with previously published results (e.g., Parker Gaddis et al., 2012).

The variance components for the traits included in genetic evaluation are shown in Table 2. The heritabilities for all wellness traits were relatively low, ranging from 0.059 for METR and KETO to 0.081 for DA. These values were in agreement with several previous studies reporting heritabilities under 10% for most health traits (e.g., Zwald et al., 2004; Parker Gaddis et al., 2014). Including genomic information in the model for estimating variance components did not have effect

Table 2. Genetic parameters and variance components with their SD (in parentheses) for the traits used in genetic evaluation¹

Trait ²	h^2	r_p	σ_a^2	σ_{pe}^2	σ_h^2	σ_e^2
MAST	0.069	0.167	0.141 (0.019)	0.201 (0.012)	0.701 (0.033)	1.000 (0.003)
METR	0.059	0.126	0.099 (0.025)	0.109 (0.017)	0.444 (0.023)	1.000 (0.003)
RETP	0.073	0.124	0.100 (0.038)	0.070 (0.024)	0.201 (0.012)	1.000 (0.008)
DA	0.081	0.115	0.110 (0.051)	0.046 (0.047)	0.210 (0.019)	1.000 (0.003)
KETO	0.059	0.103	0.104 (0.066)	0.077 (0.045)	0.580 (0.051)	1.000 (0.003)
LAME	0.063	0.149	0.140 (0.028)	0.189 (0.017)	0.875 (0.046)	1.000 (0.003)

¹ h^2 = heritability; r_p = repeatability; σ_a^2 = additive genetic variance; σ_{pe}^2 = variance of permanent environment effect; σ_h^2 = variance of herd by year by season effect; σ_e^2 = residual variance. Heritabilities were calculated as $\frac{\sigma_a^2}{\sigma_a^2 + \sigma_{pe}^2 + \sigma_h^2 + \sigma_e^2}$. Repeatabilities were calculated as $\frac{\sigma_a^2 + \sigma_{pe}^2}{\sigma_a^2 + \sigma_{pe}^2 + \sigma_h^2 + \sigma_e^2}$.

²MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

on the estimated heritabilities of wellness traits (results not shown).

The preGSf90 program took approximately 14.5 h to complete. This step was the longest and the most computationally demanding part of the genetic evaluation process. Each of the cblupf90iod runs required between 7 and 15 h, depending on the number of iterations needed to reach convergence and availability of resources. The accf90GS programs needed between 2.5 and 3 h to complete.

PTA and Reliabilities

Table 3 shows average gPTA and traditional PTAs for young genotyped heifers obtained from ssGBLUP and traditional evaluation. Young females with only pedigree and genotype information were the primary subpopulation for evaluation in our analyses. With almost 64,000 animals, they also represented the largest category of genotyped individuals in the data. Genomic and traditional PTA for young heifers with no phenotypic records had similar means, but gPTA showed larger variability and wider range across all traits, as would be expected. Table 4 shows average reliabilities for young genotyped females without phenotypic re-

cords obtained from genomic and traditional evaluation. The genomic reliabilities for all 6 traits were very similar, ranging from 50.2% for DA to 51.9% for MAST. The corresponding average traditional reliabilities were below 20% for all traits. The gain in reliability achieved by using ssGBLUP compared with the traditional parent average was 34%, on average. The increase in reliabilities above parent averages was lower than average gains of about 44% observed by Di Croce et al. (2014) for production traits in a similar population of commercial heifers, but comparable to the gains obtained for calving ease in the national genetic evaluation (https://www.cdc.us/eval/summary/comparexml_menu.cfm).

Tables 5 and 6 show genomic and traditional PTA and reliabilities, respectively, for non-progeny-tested bulls. These bulls had no daughters in the data, regardless of their actual age. Both genomic and traditional PTA for these bulls were similar to those of young females with no phenotypes. The reliabilities for these bulls were somewhat lower, on average, and more variable than those for heifers. This occurred because this category also contained several foreign bulls that were not well connected genetically with the rest of the population, but were kept in the data set for the purpose of parentage check, should some customers

Table 3. Averages, SD, minima and maxima for genomic and traditional PTA¹ for young genotyped Holstein heifers (n = 63,845) without phenotypic records

Trait ²	Genomic PTA				Traditional PTA (PA)			
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum
MAST	-2.03	3.13	-11.0	15.3	-1.30	1.81	-7.7	9.1
METR	-0.14	2.61	-8.2	13.4	-0.32	1.35	-4.8	7.5
RETP	-0.16	2.23	-7.0	11.5	-0.10	1.28	-4.9	7.1
DA	-1.28	2.64	-6.8	16.9	-0.87	1.43	-5.6	11.0
KETO	-0.90	2.16	-6.4	10.0	-0.72	1.18	-4.9	5.9
LAME	-0.05	2.91	-8.5	16.1	-0.08	1.61	-6.9	12.2

¹Values of PTA are given in percentage points as a difference from the estimated average risk in the base population.

²MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 4. Averages, SD, minima and maxima for genomic and traditional reliabilities (%) for young genotyped Holstein heifers (n = 63,845) without phenotypic records

Trait ¹	Genomic reliability				Traditional reliability				Difference, genomic – traditional
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum	
MAST	51.9	5.4	16	67	18.3	8.0	0	44	33.6
METR	50.5	5.5	15	66	16.2	7.5	0	42	34.3
RETP	50.8	5.4	15	66	16.4	7.6	0	42	34.4
DA	50.2	5.3	15	66	15.5	7.7	0	43	34.7
KETO	50.7	5.4	14	66	15.3	7.5	0	40	35.4
LAME	51.5	5.5	15	67	17.8	7.9	0	43	33.7

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

submit samples of foreign bulls' daughters for genotyping. The gain in reliability contributed by genomic information compared with parent average was about 29%. The amount of increase in reliability was almost twice the value obtained by Parker Gaddis et al. (2014) in a similar study for the same 6 wellness traits in a population of bulls with less than 10 daughters per bull. The gains in reliability contributed by genomics were similar to those observed by VanRaden et al. (2009) for production and type traits in young genomic bulls.

Tables 7 and 8 contain genomic and traditional PTA and reliabilities, respectively, for progeny-tested bulls. Progeny-tested bulls were defined as bulls having at least 100 offspring in the genetic evaluation, including sons and daughters with genotypes, phenotypes, and own progeny. As expected, the PTA and reliabilities for progeny-tested bulls did not vary substantially between genomic and traditional analyses. Regarding reliabilities, genotypes provided little benefit to high-reliability bulls; for all traits except KETO, the gain in reliability resulting from genomics was less than 10%. However, progeny-tested bulls with genotypes will remain an important part of the genetic evaluation program because the accuracy of estimates for their offspring depends on availability of high-reliability genotyped sires (Lourenco et al., 2015).

Tables 9 and 10 show PTA and reliabilities, respectively, for females with 1 or more phenotypic records

or progeny in the data. This group of animals was very heterogeneous because of differences in the available information for each animal. Therefore, the PTA and reliabilities showed more variation, and the gain in reliability achieved through the use of genomics was different for each animal depending on the amount of phenotypic or pedigree information available. However, ssGBLUP showed superior results for all traits, with average gain in reliability approaching 29% compared with traditional evaluation.

Table 11 illustrates the effect of having a known sire or a genotyped sire on the reliabilities of genomic predictions for young genotyped females without their own phenotypes. The highest reliabilities for all traits were achieved when the animal had a known sire, and this sire was genotyped. Such animals showed the greatest increase in reliability of gPTA compared with the reliability of parent average (Table 6). Having a known sire in the pedigree that was not genotyped reduced the genomic reliability by about 2%, on average; additionally, the range between the minimum and the maximum reliability was much narrower than for animals with known and genotyped sires. Reliabilities were most affected when the sire of a heifer was unknown. The average reliability of such animals was decreased by over 13% for all traits compared with animals with known and genotyped sires. Many of those animals also had unknown dams and, therefore, their pedigree

Table 5. Averages, SD, minima and maxima for genomic and traditional PTA¹ for non-progeny-tested bulls (n = 3,365)

Trait ²	Genomic PTA				Traditional PTA (PA)			
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum
MAST	-2.52	3.42	-10.4	12.1	-1.91	2.51	-8.9	8.7
METR	0.48	2.80	-7.5	16.9	0.30	1.55	-4.7	7.3
RETP	-0.26	2.16	-5.9	13.8	-0.16	1.20	-4.8	6.7
DA	-0.18	3.08	-6.2	14.9	0.09	1.79	-4.8	10.6
KETO	-0.45	2.34	-6.0	11.6	-0.43	1.36	-4.7	5.6
LAME	0.24	3.10	-7.8	19.2	0.09	1.93	-4.6	14.2

¹Values of PTA are given in percentage points as a difference from the estimated average risk in the base population.

²MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 6. Averages, SD, minima and maxima for genomic and traditional reliabilities (%) for non-progeny-tested bulls (n = 3,365)

Trait ¹	Genomic reliability				Traditional reliability				Difference, genomic – traditional
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum	
MAST	48.7	10.7	17	67	20.1	11.5	0	44	28.6
METR	47.5	10.7	16	66	18.5	11.2	0	42	29.0
RETP	47.9	10.7	16	67	19.1	11.3	0	43	28.8
DA	47.4	10.8	16	67	18.5	11.5	0	44	28.9
KETO	47.5	10.8	16	66	17.4	11.3	0	41	30.1
LAME	48.3	10.7	16	67	19.5	11.4	0	44	28.8

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 7. Averages, SD, minima and maxima for genomic and traditional PTA¹ for progeny-tested bulls (n = 1,154)

Trait ²	Genomic PTA				Traditional PTA			
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum
MAST	–1.00	4.18	–11.4	17.5	–1.07	4.28	–12.5	17.7
METR	0.85	3.24	–6.8	12.2	0.76	3.14	–6.5	11.8
RETP	0.03	2.71	–6.5	12.9	–0.05	2.56	–6.0	11.9
DA	0.35	4.13	–6.6	19.5	0.35	3.70	–6.4	19.0
KETO	0.11	2.96	–6.9	14.2	–0.05	2.73	–6.2	15.0
LAME	0.84	3.68	–9.2	19.3	0.78	3.66	–9.5	19.9

¹Values of PTA are given in percentage points as a difference from the estimated average risk in the base population.

²MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 8. Averages, SD, minima and maxima for genomic and traditional reliabilities (%) for progeny-tested bulls (n = 1,154)

Trait ¹	Genomic reliability				Traditional reliability				Difference, genomic – traditional
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum	
MAST	92.5	5.6	29	100	86.4	12.9	23	100	6.1
METR	89.7	7.4	27	99	80.3	15.1	21	99	9.4
RETP	90.8	6.8	27	99	82.3	15.0	21	99	8.5
DA	90.2	7.8	23	99	80.8	17.0	17	99	9.4
KETO	87.5	9.6	22	99	75.4	18.0	16	99	12.1
LAME	91.5	6.3	29	99	84.4	13.5	22	99	7.1

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 9. Averages, SD, minima and maxima for genomic and traditional PTA¹ for females with recorded health traits or progeny (n = 30,518)

Trait ²	Genomic PTA				Traditional PTA			
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum
MAST	–1.68	3.23	–10.9	12.9	–1.17	2.26	–7.4	11.4
METR	0.21	2.74	–7.4	14.3	–0.09	1.73	–4.9	10.9
RETP	–0.32	2.28	–7.2	13.2	–0.22	1.54	–5.5	8.0
DA	–1.01	2.81	–7.0	18.6	–0.82	1.80	–5.3	11.8
KETO	–0.48	2.27	–6.5	11.2	–0.56	1.47	–4.7	7.0
LAME	0.05	2.94	–8.2	14.7	0.01	2.00	–6.9	12.5

¹Values of PTA are given in percent points as a difference from the estimated average risk in the base population.

²MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 10. Averages, SD, minima and maxima for genomic and traditional reliabilities (%) for females with recorded health traits or progeny (n = 30,518)

Trait ¹	Genomic reliability				Traditional reliability				Difference genomic - traditional
	Mean	SD	Minimum	Maximum	Mean	SD	Minimum	Maximum	
MAST	57.4	6.0	18	88	30.2	8.5	0	68	27.2
METR	55.4	6.5	18	88	26.5	9.0	0	62	28.9
RETP	55.9	6.5	18	88	27.0	9.2	0	63	28.9
DA	54.6	6.5	18	87	24.5	9.1	0	58	30.1
KETO	54.8	6.7	17	87	23.7	9.0	0	55	31.1
LAME	56.9	6.2	18	89	29.3	8.8	0	70	27.6

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

contribution to reliability was zero. In practice, some commercial producers do not keep accurate pedigree records and submit samples without sire and dam information. One may argue that animals with incomplete pedigree reduce the quality of the data and should be excluded. However, in a commercial setting, all animals submitted by paying customers must be included in the genetic evaluation and have their results reported. Our genetic evaluation system is set up to determine the most likely sire in cases where the animal does not have a sire in the pedigree, or has an incorrectly assigned sire based on genotype exclusions. However, at the time of this study, we did not have enough sire genotypes in our database to address every missing sire case. Fortunately, the number of animals with unknown sires in the data was relatively small and is expected to further decrease as we continue to increase the number of bull genotypes.

Correlations with Official Results for Traits in the National Genetic Evaluation

Table 12 shows approximated genetic correlations as well as Pearson (product-moment) correlations between wellness trait predictions and official gPTA for traits in the national genetic evaluation: \$NM, milk yield, SCS, DPR, and productive life. Almost all wellness traits were negatively correlated with \$NM, ranging from -0.23 (MAST) to -0.54 (DA); only RETP was not correlated with \$NM, whereas it was very lowly correlated

with all other traits. Similar correlations were obtained between wellness traits and DPR and productive life. Low correlations were obtained between most wellness traits and milk yield, possibly suggesting that high milk production may not necessarily be genetically strongly associated with poor health. The highest correlation in magnitude of milk yield with the wellness traits was obtained between milk yield and MAST: MAST and milk yield showed a positive correlation of 0.25, indicating that animals with higher genetic potential for yield were more susceptible to MAST. Mastitis was also highly correlated with SCS, having an approximated genetic correlation of 0.72; an identical result was reported by Boichard and Rupp (2000). Overall, the results were comparable with the correlations presented by Parker Gaddis et al. (2014) obtained from a similar study focusing on bulls; however, the magnitude of the correlations in our analysis was greater, indicating possible overestimation due to comparably lower reliabilities of females used in Calo's formula (Calo et al., 1973). The Pearson correlations between wellness traits and official predictions for traits in the national evaluation obtained from the same data had the same direction but significantly lower magnitude than approximated genetic correlations.

General Discussion

Average reliabilities of about 50% for young genotyped and pedigreed females were achieved using the

Table 11. Influence of genotyping sire on reliability (%) of genotyped daughters without phenotypes

Trait ¹	Sire known, genotyped			Sire known, not genotyped			Sire unknown		
	Average	Minimum	Maximum	Average	Minimum	Maximum	Average	Minimum	Maximum
MAST	52.4	21	67	49.3	16	62	35.6	16	41
METR	50.9	20	66	47.8	15	61	34.7	15	40
RETP	51.3	20	66	48.2	15	61	35.1	15	40
DA	50.6	19	66	47.7	15	60	34.7	15	40
KETO	51.1	20	66	48.0	14	60	35.3	16	40
RETP	52.0	20	67	48.9	15	62	35.4	16	40

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

Table 12. Approximated genetic correlations of wellness trait predictions with Council of Dairy Cattle Breeding's genomic predicted transmitting ability for the traits in the national evaluation

Trait ¹	Approximated genetic correlations					Pearson correlations				
	Net merit	Milk yield	SCS	Daughter pregnancy rate	Productive life	Net merit	Milk yield	SCS	Daughter pregnancy rate	Productive life
MAST	-0.23	0.25	0.72	-0.34	-0.44	-0.15	0.16	0.46	-0.21	-0.28
METR	-0.46	-0.11	0.15	-0.46	-0.47	-0.29	-0.07	0.10	-0.28	-0.29
RETP	0.00	0.06	0.06	-0.12	-0.09	0.00	0.04	-0.08	-0.05	-0.34
DA	-0.54	-0.13	0.25	-0.37	-0.68	-0.34	-0.08	0.16	-0.23	-0.42
KETO	-0.51	0.00	0.25	-0.51	-0.55	-0.32	0.00	0.16	-0.31	-0.34
LAME	-0.31	0.12	0.18	-0.48	-0.43	-0.20	0.08	0.12	-0.30	-0.27

¹MAST = mastitis; METR = metritis; RETP = retained placenta; DA = displaced abomasum; KETO = ketosis; LAME = lameness.

ssGBLUP approach, which was more than a 2-fold improvement over traditional parent average reliability for this population. These relatively high reliabilities for young females are the result of having a large amount of phenotypes in the genetic evaluation and using ssGBLUP method that better describes relationships among the animals and provides better modelling of Mendelian sampling. Although some authors report fairly high reliabilities of gPTA for similar traits for bulls obtained with much smaller phenotypic data (e.g., Parker-Gaddis, 2014), having satisfactory reliabilities of gPTA for commercial females based only on pedigree and genotypes would not be possible without such a large phenotypic database.

Genomic predictions for wellness traits were correlated with \$NM and other traits in the national evaluation. However, the results showed that predictions for wellness traits provide new information about an animal's genetic potential for health.

Our results are based on millions of farm-collected health records. It is necessary, however, to continue collecting data and refreshing the existing database both with new data from existing herds and historical data from new herds. It is also important to increase the number of bulls with genotypes in the database, not only for the purpose of parentage check, but also to increase the accuracy of genomic predictions.

The large computational requirements of ssGBLUP (especially RAM) can be met through the use of powerful computers available in the market. However, as the number of genotypes grows, the computational power offered by the latest hardware may become inadequate. Current algorithms have a soft limit of about 150,000 genotyped animals; after that, the procedure is not feasible on a usual computer. Algorithms are being developed and implemented to alleviate the computational requirements by constructing and inverting the genomic relationship matrix based on the algorithm for proven and young animals (Fragomeni et al., 2015). As demonstrated by Masuda et al. (2016), this algorithm

enables genomic evaluation with any number of animals with affordable computing and memory requirements. In the future, these algorithms will be implemented in the evaluation for wellness traits to accommodate rapidly growing number of genotypes.

CONCLUSIONS

This study showed that farm-collected health data can be successfully used in routine genetic and genomic evaluation for wellness traits. Genomic predictions for wellness traits provide new selection tools for dairy wellness improvement not available to the commercial US dairy producer until now. Genetic selection for improved wellness traits will confer permanent improvement of a herd's health status, as opposed to temporary relief by antibiotics, vaccinations, and other management interventions. Including genomic predictions for wellness traits in an index along with existing predictions for production, fertility, and health could provide dairy producers with a more complete tool for selecting potentially most profitable animals.

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