



Effect of transgenerational environmental condition on genetics parameters of Italian Brown Swiss

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ABSTRACT

The aim of this study was to infer the effects of heat stress (HS) of dams during late gestation on direct and maternal genetic parameters for traits related to milk production and milk quality parameters (90,558 records) in Italian Brown Swiss cattle (12,072 cows in 617 herds). Daily average temperature-humidity indices (THI) during the last 56 d of pregnancy were calculated, using the climate data from the nearest public weather station for each herd. Heat load effects were considered as the average across the entire periods considering a thermoneutrality condition for data below the THI 60. For parameter estimation a random regression model using the second-order Legendre polynomial regression coefficient for THI considering both animal and maternal effect for heat load. Direct heritability increased sharply from THI 60 to 65, then decreased gradually up to THI ~72, and sharply thereafter. Maternal heritability showed a different trend, with values close to 0 up until to THI 65 and slightly increasing toward extreme THI values. The study suggests a lower threshold of THI 60 for the onset of HS. Higher heritability values indicate greater selective efficiency in the THI range of 65 to 70, even if a higher standard deviation value have been detected. The effects of high THI during intrauterine life varied among traits with different heritability levels. Genetic correlations for milk, fat, and protein content at 60 THI with increasing value of environmental variable, remained constant (~0.90) until THI >75, where they slightly decreased (~0.85). Fat and protein yields, as well as milk and energy-corrected milk, showed correlations dropping to 0.80 around THI 67 to 68 and stabilizing between 0.75 and 0.85 at extreme THI values. Maternal component correlations dropped close to zero, with negative values for

protein content at THI 65 to 70. Antagonism between direct and maternal components was stronger for intermediate THI values but less divergent for extremes. Genotype by environment interaction was observed, indicating the selection of resilient animals would be theoretically possible. In the future, the application of climate variables in selection schemes first should take into account the dimensions of the genetic correlations to be able to decide between the simple inclusion of the environmental effect in the statistical models, rather than a real parallel genetic evaluation.

Key words: heat stress, across-generation, Brown Swiss, genetic parameters

INTRODUCTION

In dairy cows, environmental conditions strongly affect production efficiency but also reproduction (Oseni et al., 2003; Brügemann et al., 2011; Gernand et al., 2019). In many studies, the effect of heat stress (HS; often expressed by the bioclimatic index based on temperature and humidity) on performance of numerous cattle breeds has been assessed, which has resulted in the identification of genetic parameters useful for the selection of resilient animals (Misztal et al., 2000; Carabaño et al., 2016). Random regression models (RRM) or reaction norm models can be used to infer genetic (co)variances on a continuous temperature-humidity index (THI) scale, with possible genetic correlation estimates for a broad grid of THI combinations (Aguilar et al., 2009; Santana et al., 2016). The most direct implication is the possibility of obtaining EBV along the scale of the environmental descriptor, allowing the quantification of the bulls re-ranking at different points.

Including bioclimatic variables in the EBV prediction is also useful for management decisions. For instance, considering the EBVs decline after a certain HS threshold value is helpful in choosing the most suitable bull in certain circumstances. The analysis of the additive genetic component of thermal stress in dairy cattle

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has been proposed in several studies by associating the meteorological conditions at the test day with different productive (Carabaño et al., 2014; Cheruiyot et al., 2020; Kipp et al., 2021a) and reproductive (Sigdel et al., 2020) traits, allowing the calculation of genetic estimates. These studies, however, highlighted that HS has a delayed effect on traits and that environmental conditions several days before rather than on the test day affect the trait of interest (Ravagnolo et al., 2000; Bernabucci et al., 2014; Maggiolino et al., 2020). The number of consecutive days above the upper critical THI (i.e., threshold beyond which animals experience HS) is also important because HS is additive; hence, the greater the number of days of exposure to HS, the more detrimental its effect on performance (Maggiolino et al., 2022). In addition, Negri et al. (2021) demonstrated that the magnitude of temperature variations is also important, as wider temperature ranges have a greater impact.

Cattle breed and genotype may also play a role on the response to HS. Landi et al. (2023) demonstrated that the interaction between genotype and environment affected ranking of daughters of Brown Swiss sires, suggesting that genetic differences may explain differences in HS thresholds and resistance to HS. The effect of prolonged and time-lagged HS on dairy cow performance is known, as well as the possible carryover along future generations (Davidson et al., 2021). In an experimental trial, Laporta et al. (2020) showed the negative effect of a THI greater than 68 during the 46 d before calving on daughter and granddaughter milk yield (MY). In utero HS reduces birth weight, growth, and passive immune transfer in newborns (Fabris et al., 2020; Carabaño et al., 2022). Traits related to longevity, fertility, and disease resistance seem to be affected by the thermal comfort conditions experienced by cows during the gestation (Kipp et al., 2021a; Yin et al., 2022). This study aimed to estimate genetic parameters for production traits as a function of THI from the last 8 wk (56 d) of gestation (dry periods), targeting the detection of possible genotype by environment interactions ($G \times E$) based on genetic correlation estimates from RRM between the same traits across different THI value during the late-gestation period.

MATERIALS AND METHODS

Ethics Statement

Animal welfare and use committee approval was not needed for this study because datasets were obtained from pre-existing databases based on routine animal recording procedures.

Cow Traits

Data editing was performed in R software (R Core Team, 2019) using the *tidyverse* package (Wickham et al., 2019). Data were provided by the Italian Brown Swiss Breeders Association (Verona, Italy) and included record from 12,072 Brown Swiss cows in 617 herds. The initial dataset contained 91,075 test-day records (taken from 2008 to 2017) for MY (kg/d), fat yield (FY; kg/d), protein yield (PY; kg/d), fat percentage (FP), and protein percentage (PP). The following equation, reported by the IFCN network (Reincke et al., 2018), was used to compute the ECM yield:

$$\text{ECM, kg/d} = \text{MY} \\ \times [0.25 + (0.122 \times \text{FP}) + (0.077 \times \text{PP})].$$

Environmental Data

Meteorological data (minimum and maximum temperature and humidity) were retrieved using the records from 76 weather stations across the Italian territory. To be included in the final dataset, farms needed to meet several requirements. First, they should have had at least one weather station within a 10-km radius. Additionally, their location had to be less than 700 m above sea level and linked to a weather station situated at a similar altitude, with a difference not surpassing 50 m. Moreover, there should have been no notable orographic or hydrographic features separating the farm from the weather station. Only farms meeting all these conditions were considered for inclusion in the dataset.

Based on daily averages for temperature (°C) and relative humidity (%), the daily THI was calculated as follows (NRC, 1971):

$$\text{THI} = (1.8 \times \text{temperature} + 32) \\ - (0.55 - 0.0055 \times \text{relative humidity}) \\ \times (1.8 \times \text{temperature} - 26).$$

To evaluate the association between intrauterine exposure to HS and the traits of interest, we calculated the average THI of the 56 d before calving (THID). For the intrauterine period, THI values <60 were set to 60 to focus on heat load effects, whereas THI values >75 were set to 75 to avoid THI classes with few observations. The HS threshold of 60 was chosen according to results from previous studies that evaluated time-lagged HS effects for a broad phenotypic trait pattern (Halli et al., 2021; Kipp et al., 2021a). In addition, to control for environmental conditions during the lactation, the average THI of the 5 d before each test day

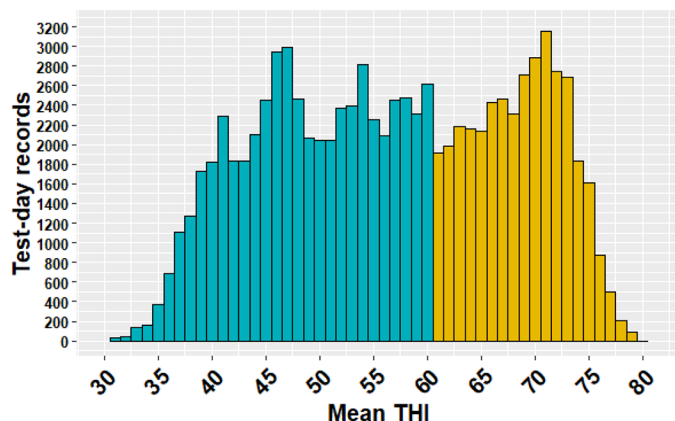


Figure 1. Distribution of records for milk yield by mean temperature-humidity index (THI) during the intrauterine phase (56 d before calving). The colors indicate observations that fall before or after THI = 60, a threshold value identified by previous studies (Halli et al., 2021; Kipp et al., 2021a).

(THIC) was calculated. For lactational period, values <70 were set to 70 to consider the thermoneutrality threshold (Landi et al., 2023) and THI >79 to were set 79 to avoid THI class with few observations. The distribution of MY records by THI registered during the late gestation periods considered is shown in Figure 1.

Statistical Models

The final dataset contained 90,558 test-day records of 12,072 Brown Swiss cows from 617 herds. Test-day records for each trait were analyzed in a single-trait RRM to estimate the effects of intrauterine exposure to HS on additive genetics and maternal effect. The model included the following fixed effects: AP, defined as the combination of age (years) and parity class (level 1 has 42,066 records and 7,243 cows; level 2 has 26,248 records and 3,240 cows; level 3 has 13,855 records and 1,253 cows; and level >4 has 8,876 records and 336 cows), resulting in classes 23 classes with more than 5 observations, DIM class (with 5 levels: 0–30, 31–90, 91–180, 181–270, and 271–365), and the combination of year and season of calving (defined as December to February, March to May, June to September, and October to November) of each cow (with 33 levels). For all dependent variables, THIC (THI = 70 to 79) and THID (THI = 60 to 75), as previously defined, trends were modeled using second-order Legendre polynomials ($k = 2$; i.e., 3 regression coefficients) using *polynom* and *sommer* R package (Covarrubias-Pazaran, 2016; Venables et al., 2022). Fixed regressions were included in the model to capture population means. In the random part the effect of the contemporary group as a

combination of the herd, year, and season of calving (HYS; 4,883 classes with more than 5 records in each level) was considered.

Random regressions were fitted for the direct (a) and maternal (m) genetic effects, animal (p), and maternal (c) permanent environmental effects, using THID Legendre polynomial coefficients.

We considered the random effect of the contemporary group as a combination of the herd, year, and season of calving (HYS = 4,883 classes with more than 5 records in each level). The HYS variance and the residual variances were considered homogeneous across THI levels. The matrix representation of the models is

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{S}\mathbf{d} + \mathbf{Z}_1\mathbf{a} + \mathbf{Z}_2\mathbf{m} + \mathbf{W}_1\mathbf{p} + \mathbf{W}_2\mathbf{c} + \mathbf{e},$$

where $\mathbf{y}$ is the vector of observations, $\mathbf{b}$ is the vector that included the set of systematic effects (including the Legendre polynomials (covariates) to model the average trajectory of the population), $\mathbf{d}$ is the vector of HYS random effects, $\mathbf{a}$ is the vector for additive direct random effects, $\mathbf{m}$ is the vector for additive maternal random effects, $\mathbf{p}$ is the vector for animal permanent environmental random effects, $\mathbf{c}$ is the vector for maternal permanent environmental random effects, $\mathbf{e}$ is the vector of residual random effects, and $\mathbf{X}$, $\mathbf{S}$, $\mathbf{Z}_1$, $\mathbf{Z}_2$, $\mathbf{W}_1$, and $\mathbf{W}_2$ are the corresponding incidence matrices. The (co)variance structure for random effect was

$$\text{var} \begin{bmatrix} \mathbf{a} \\ \mathbf{m} \\ \mathbf{p} \\ \mathbf{c} \\ \mathbf{h} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{A} \otimes \mathbf{K}_a & \mathbf{A} \otimes \mathbf{K}_{a,m} & 0 & 0 & 0 & 0 \\ \mathbf{A} \otimes \mathbf{K}_{m,a} & \mathbf{A} \otimes \mathbf{K}_m & 0 & 0 & 0 & 0 \\ 0 & 0 & \mathbf{I} \otimes \mathbf{K}_p & 0 & 0 & 0 \\ 0 & 0 & 0 & \mathbf{I} \otimes \mathbf{K}_c & 0 & 0 \\ 0 & 0 & 0 & 0 & \mathbf{I}\sigma_d^2 & 0 \\ 0 & 0 & 0 & 0 & 0 & \mathbf{I}\sigma_e^2 \end{bmatrix},$$

where $\mathbf{K}_a$, $\mathbf{K}_m$, $\mathbf{K}_{a,m}$, $\mathbf{K}_{m,a}$, $\mathbf{K}_p$, and $\mathbf{K}_c$ are (co)variance matrices between random regression coefficients for additive direct, additive maternal, and animal and maternal permanent environmental effects. $\mathbf{A}$ is the relationship matrix, $\mathbf{I}$ is an identity matrix, $\otimes$ is the Kronecker product between matrices, and σ_d^2 and σ_e^2 are the contemporary group and residual variances.

The THRGIBBS1F90 program (Tsuruta and Misztal, 2006) was used for estimating (co)variance components using Gibbs sampling. Flat priors were assumed for all effects in the statistical model. Uniform prior distributions were assumed for $\mathbf{b}$; $\mathbf{b} \sim p(\mathbf{b})$, where $p(\mathbf{b}) \propto \text{constant}$. Scaled inverted Wishart prior distribu-

tions were assigned to covariance matrices for $\mathbf{a}$, $\mathbf{m}$, $\mathbf{p}$, and $\mathbf{c}$ to represent vague prior knowledge about these parameters; $(\mathbf{A} \otimes \mathbf{K}) \sim \text{IW}(\mathbf{S}, \nu)$, $\mathbf{S} = [0]$ and $\nu = -2$. Similarly, scaled inverted chi-squared prior distributions were assigned to variance components for $\mathbf{h}$ and $\mathbf{e}$; $\sigma^2 \sim S\chi_v^{-2}$, $\mathbf{S} = 0$, and $\nu = -2$.

For each analysis, 500,000 samples, saving every 100 sample and discarding a burn-in of 250,000 iterations, were drawn. Convergence was determined from a visual inspection of trace plots using the POSTGIBBSF90 program (Misztal et al., 2014).

The pedigree used was prepared excluding cow with unknown sire. All record was retained for generics parameter estimation resulting in 116,145 animals.

Parameter Calculations

Using the generated Gibbs samples, the posterior mean was computed as a point estimate of (co)variance components and related genetic parameters at intercept value of 60 THI as defined previously. We also computed lower and upper bounds of the 95% highest posterior probability density regions using the *HDIInterval* package in R.

Using the (co)variance matrices ($\mathbf{K}_i$), as well as the row vector of the Legendre polynomials coefficients (Φ), the (co)variance for effect i ($i = a, m, p, c$, or h) can be estimated along the trajectory of THID, following

$$\sigma_{ij} = \Phi \mathbf{K}_{ij} \Phi'.$$

Genetics parameters, and the standard deviation of their sampling distribution, were then calculated and, specifically, the heritability (h_a^2), maternal heritability (h_m^2), and intraherd heritability (h_{iha}^2) or intraherd maternal heritability (h_{ihm}^2) were calculated as follows:

$$h_a^2 = \frac{\sigma_a^2}{\sigma_a^2 + \sigma_m^2 + \sigma_h^2 + \sigma_p^2 + \sigma_c^2 + \sigma_{am}^2 + \sigma_e^2},$$

$$h_m^2 = \frac{\sigma_m^2}{\sigma_a^2 + \sigma_m^2 + \sigma_h^2 + \sigma_p^2 + \sigma_c^2 + \sigma_{am}^2 + \sigma_e^2},$$

$$h_{iha}^2 = \frac{\sigma_a^2}{\sigma_a^2 + \sigma_m^2 + \sigma_p^2 + \sigma_c^2 + \sigma_{am}^2 + \sigma_e^2},$$

$$h_{ihm}^2 = \frac{\sigma_m^2}{\sigma_a^2 + \sigma_m^2 + \sigma_p^2 + \sigma_c^2 + \sigma_{am}^2 + \sigma_e^2}.$$

RESULTS AND DISCUSSION

Heritability and Genetic Variances

Posterior means for heritabilities and maternal heritabilities and HYS variances for the observed traits are shown in Table 1. The observed heritability values were similar to those found in the same population in other studies conducted with or without the inclusion of the average THI of the 5 d before the test day (Landi et al., 2023), and the general trend among them remained almost unchanged. Intraherd heritability differed from the heritability when there was a high HYS variance. The estimate was always higher than the direct heritability, as is to be expected. The inclusion of a random HYS effect had a double purpose: (1) fitting HYS as a random effect reduces the loss of information due to the small contemporary group size (Visscher and Goddard, 1993), and (2) at the same time allow to account for the nongenetic covariance between individuals within a contemporary group (a season within a herd in a particular calving year). In this way, the model makes it possible to consider changes, even small ones, due to breeding conditions, nutrition, and seasonality (Schaeffer, 2018; Biffani et al., 2020).

Regarding maternal heritability, the estimates were lower, as expected, and the difference between the maternal and intraherd maternal heritability was low or absent. We have no references in the literature for these traits, but Gudex et al. (2014) reported that the prenatal environment of the mother and grandmother can influence milk production in daughters and granddaughters, although they reported small effects. However, it is important to note that our study focuses on assessing immediate, nontransgenerational effects rather than transgenerational influences. In summary, while maternal heritability focuses on additive genetic effects from the mother, nonadditive variance could still have a notable effect on the traits of interest. Investigating these nonadditive genetic influences can enhance our breeding strategies and lead to more successful selection decisions when choosing breeding animals. (Vitezica et al., 2018).

The use of random regressions and Legendre polynomials allowed us to estimate the trend of genetic parameters of production traits according to the THI scale in Brown Swiss dairy cattle assuming that the relative daily production of a cow is unaffected over a range of low and medium temperatures during the late gestation periods of its mother, to estimate the change in response as suggested by Ravagnolo et al. (2000). Figures 2 and 3 show the trend of direct and maternal heritability for the considered traits along the increasing

Table 1. Posterior means (at intercept value, i.e., temperature-humidity index = 60) of direct and maternal heritability and intra-herd heritability (lower and upper bounds of the 95% highest posterior density region in parentheses), and herd-year-season of calving (HYS) and residual (Res) variance for yields of protein, fat, milk, and ECM, and percentage of fat and protein

Trait	HYS variance	Heritability	Intra-herd heritability		Intra-herd maternal heritability		Res variance
			Intra-herd heritability	Maternal heritability	maternal heritability	Res variance	
Protein, %	0.011 (0.01–0.012)	0.247 (0.196–0.301)	0.269 (0.215–0.329)	0.083 (0.042–0.133)	0.084 (0.039–0.134)	0.065 (0.064–0.066)	
Protein, kg/d	0.02 (0.019–0.021)	0.126 (0.078–0.2)	0.176 (0.113–0.28)	0.064 (0.029–0.093)	0.068 (0.029–0.107)	0.023 (0.023–0.023)	
Fat, %	0.052 (0.047–0.057)	0.111 (0.076–0.143)	0.12 (0.082–0.155)	0.081 (0.037–0.124)	0.088 (0.047–0.128)	0.444 (0.439–0.448)	
Fat, kg/d	0.026 (0.024–0.028)	0.099 (0.059–0.139)	0.127 (0.078–0.179)	0.066 (0.04–0.102)	0.066 (0.025–0.11)	0.055 (0.054–0.055)	
Milk, kg/d	12.525 (11.72–13.42)	0.17 (0.123–0.219)	0.223 (0.161–0.285)	0.043 (0.006–0.099)	0.052 (0.019–0.092)	17.379 (17.21–17.54)	
ECM, kg/d	15.319 (14.33–16.39)	0.135 (0.096–0.172)	0.181 (0.132–0.232)	0.035 (0.002–0.078)	0.049 (0.022–0.082)	21.314 (21.11–21.52)	

values of THI derived from the variance values reported in Supplemental Figures S1 and S2 (<https://doi.org/10.6084/m9.figshare.24901464.v1>; Landi, 2024). All the traits showed the same behavior: the estimates of heritability increased sharply from THI 60 to 65 (between 0.1 and 0.2), decreased gradually up to THI ~72, and then descended sharply thereafter. Kipp et al. (2021a) reported a similar behavior for MY, whereas they observed an increasing trend for milk content of FP when THI increased above 58. In the latter work, the authors observed a slightly lower critical THI threshold (59). It is important to note that Kipp et al. (2021a) used Holstein-Friesian cows and only evaluated the first test day after calving of the first lactation. Previous studies in Brown Swiss have reported that primiparous cows may exhibit higher susceptibility to HS due to various factors, including their lower production levels compared with multiparous cows and the metabolic load associated with ongoing growth processes (Maggiolino et al., 2020). Considering these factors, it is possible that the negative carryover effect of intrauterine exposure to HS becomes more evident during early adult life. In our study, we fixed the presence of a thermal neutral zone with no effect of THID (plateau) until THID 60 that is followed by a decay, which agrees with previous studies that found a decrease in production when THID >60 (Halli et al., 2021; Kipp et al., 2021a) and a different threshold for fixed regression for direct effect of THI on production (THIC). The distinction arises from the nature of the datasets and the specific traits examined. The THID primarily involves genetic parameters during the prenatal phase, whereas THIC pertains to the lactational period. The choice of HS thresholds for these 2 stages is influenced by the respective literature and the observed patterns in our dataset. In line with this, we will provide a more comprehensive explanation in the manuscript to elucidate the rationale behind the distinct thermoneutral zones for THID and THIC, considering the temporal dynamics and trait-specific variations associated with each phase.

Furthermore, assuming identical thresholds that mark the onset of HS implies disregarding individual variability, which could potentially introduce bias in the slopes of individual production loss (Carabaño et al., 2017). Our goal was to describe the trend of the phenomenon and the calculation of the genetic parameters, and considering that the definition of individual thresholds is in any case a complex process (Sánchez et al., 2009), we believe that the threshold value of THI 60 is a good assumption according literature and our dataset. Moreover, although RRM with polynomials are generally suitable and widely used for these applications, they do have some drawbacks. For example, border effects often occur at the beginning and end of

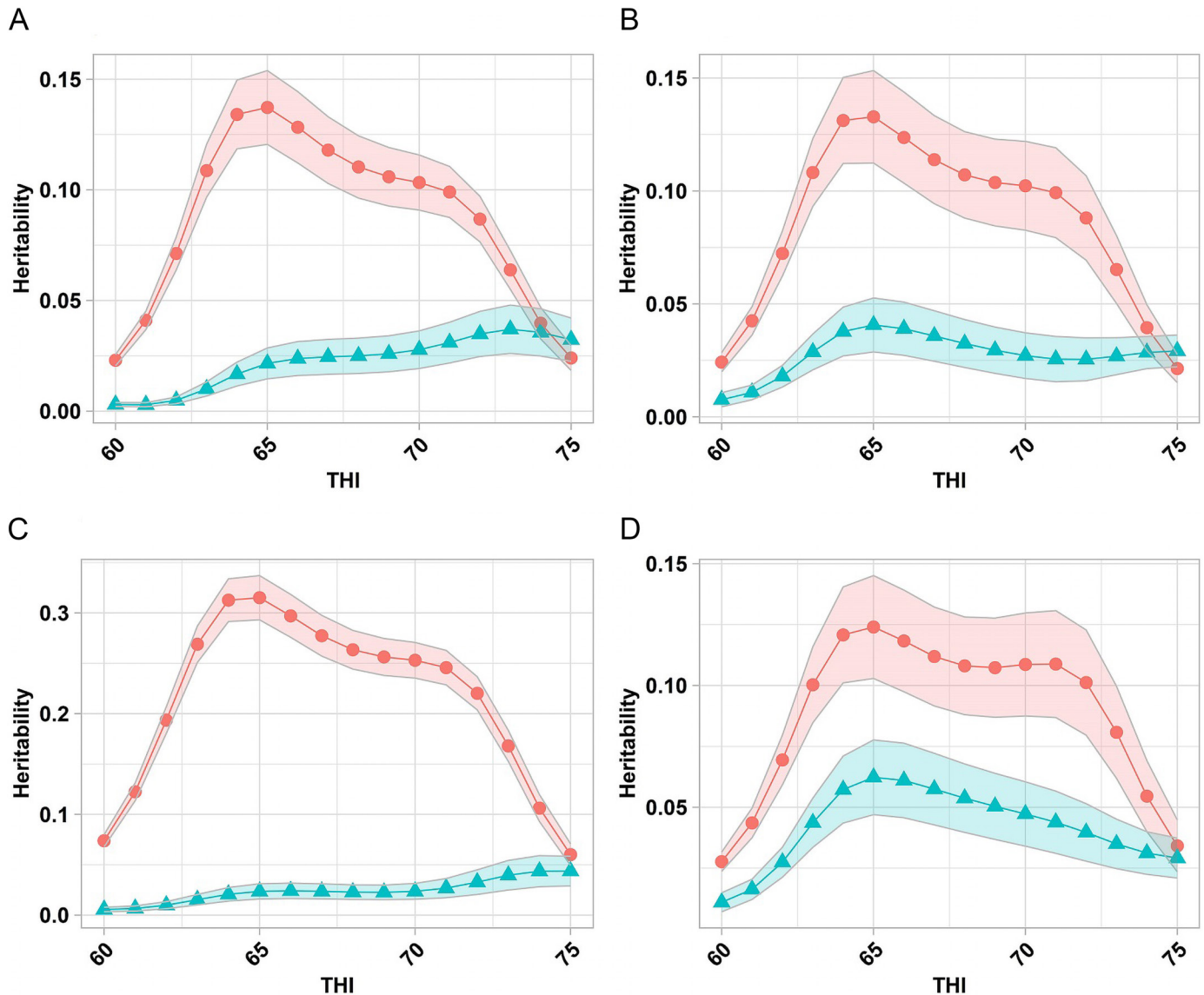


Figure 2. Posterior means for direct (red lines) and maternal (blue lines) heritabilities for fat percentage (A), fat yield (B), protein percentage (C), and protein yield (D), according to temperature-humidity index (THI) during the intrauterine phase (56 d before calving). The shaded areas around the lines indicate SD.

a curve, and waves can form when there is little data to draw upon (Druet et al., 2003; Strabel et al., 2003). For these reasons, we decided to maintain a simpler structure of the model also considering the limitations of the dataset in relation to the classes of the environmental variable.

In Supplemental Figure S2, different patterns can be observed depending on the character of the maternal genetic variance, contrasting with what is observed in the additive genetic variance. For all traits, an increase is noticeable from THI 60 to THI 65, followed by a gradual decrease. The curves, in all cases, tend to rise toward extreme THI values (>72). However, this trend

is not evident for the PP trait, where the maternal variance (along with all other variances, except for the additive genetic variance) remains consistently low across the entire range of the climatic variable.

Maternal heritability instead follows a different trend respect to additive genetic heritability, with values almost close to 0 up to THI 65, which become slightly increasing toward extreme THI values, except for MY and PY. Yin et al. (2022) observed a similar trend in traits related to resistance to some calf diseases in the Holstein breed. In our results, THI = 65 seems to be the break point after which environmental conditions affect the expression of additive and maternal genetic

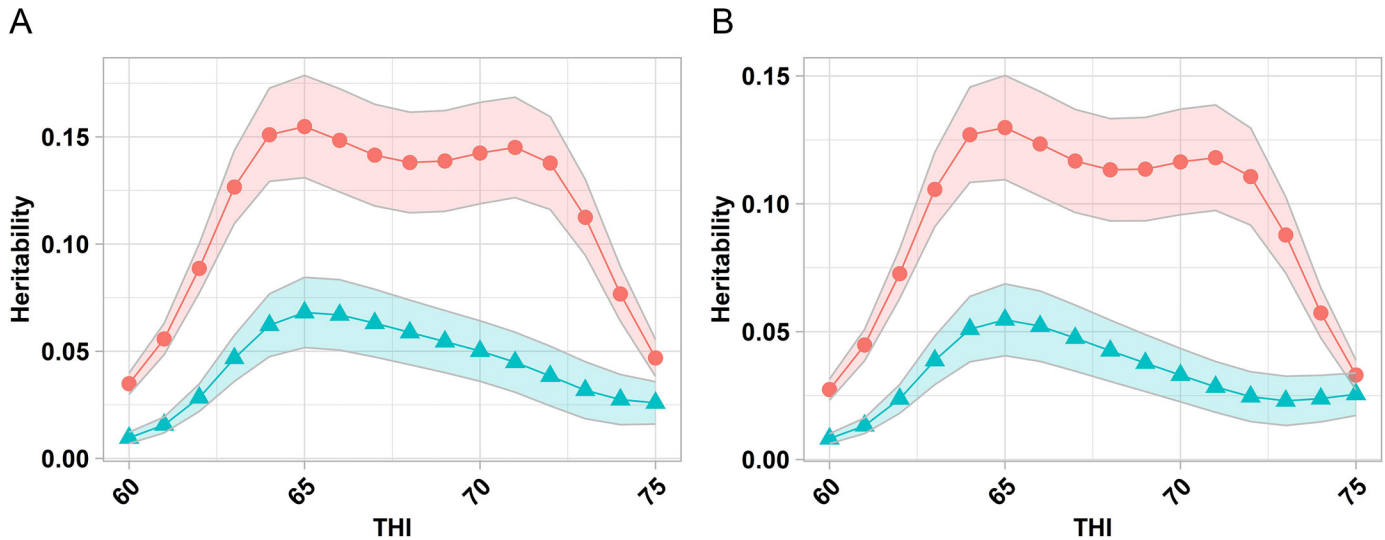


Figure 3. Posterior means for direct (red lines) and maternal (blue lines) heritability for milk yield (A) and ECM (B), according to temperature-humidity index (THI) during the intrauterine phase (56 d before calving). The shaded areas around the lines indicate SD.

components for all traits, except for PP and FP. This is a lower value compared with the average breakpoint reported by Maggiolino et al. (2020), who considered the effect of maximum average of THI over 15 d before the test day on the production. Using the same dataset, we computed genetic parameters by considering the maximum average of THI over 5 d before the test day and defining a thermoneutrality breaking point at THI 70. These considerations resulted in distinct patterns of the curves for the additive genetic variances, varying according to the specific trait under investigation. Generally, all variances, initially high, exhibit a decline toward THI 75 to 80, followed by a subsequent increase toward extreme THI values. However, PP stands as an exception, demonstrating a consistent and continuous decreasing trend throughout the THID range (Landi et al., 2023). High values of heritability suggest a greater additive genetic variance and a greater variability (Rahayu et al., 2015), supposing that in our case, a greater selective efficiency and accuracy would be observed when THID is between 65 and 70 (Kipp et al., 2021a). The decrease in heritability toward increasing values of THI has already been described in numerous studies that investigated the inclusion of the environmental variable in the calculation of the genetic parameters in dairy cows. This phenomenon would be explained by the suppression of the potential additive genetics merit of animals under adverse conditions (Brügemann et al., 2011) and a lower response to selection (Kipp et al., 2021a). In the current study, PP, the traits with higher average heritability values had a relatively lower SD values than other traits, confirming that the high THID during intrauterine life would have a more het-

erogeneous effect on characters with lower heritability (Yin and König, 2018).

Genetic Correlation

Figures 4 and 5 show the genetic correlations of the traits of interest and the intrauterine (56 d before calving) THI compared with THI = 60, the thermoneutrality threshold used in this study. The genetic correlations of milk content of FP and PP were relatively constant (~ 0.90) at THID approximating to 75, when it slightly decreased (~ 0.85). Our results are consistent with those reported by Kipp et al. (2021a) for MY and FP. These results suggest a small $G \times E$ interaction for these traits, likely a consequence of the time-lagged effect of THI intrauterus. The additive genetic correlations for yields of fat, protein, milk, and ECM show the drop to lower values (~ 0.80) until THI values around 70, then reach a plateau, except for the FY. Yield of fat reached minimum values of 0.60 when THI was ≥ 74 . Conversely, the maternal genetic correlations resulted in values close to zero, except for milk content of PP that reached negative values (-0.30) when THI ranged from 65 to 70. When THI > 70 , the trend singly increases toward positive values for of FY and PY. The values of the correlation, in the same range of THI, between the additive genetic and maternal component (Supplemental Figure S3, <https://doi.org/10.6084/m9.figshare.24901464.v1>; Landi, 2024), reaches minimum values between THI 60 and 70, while rising toward higher values (0.40–0.70) between THI 70 and 75. This would indicate a higher antagonism between the 2 components for intermediate THI values and less divergent

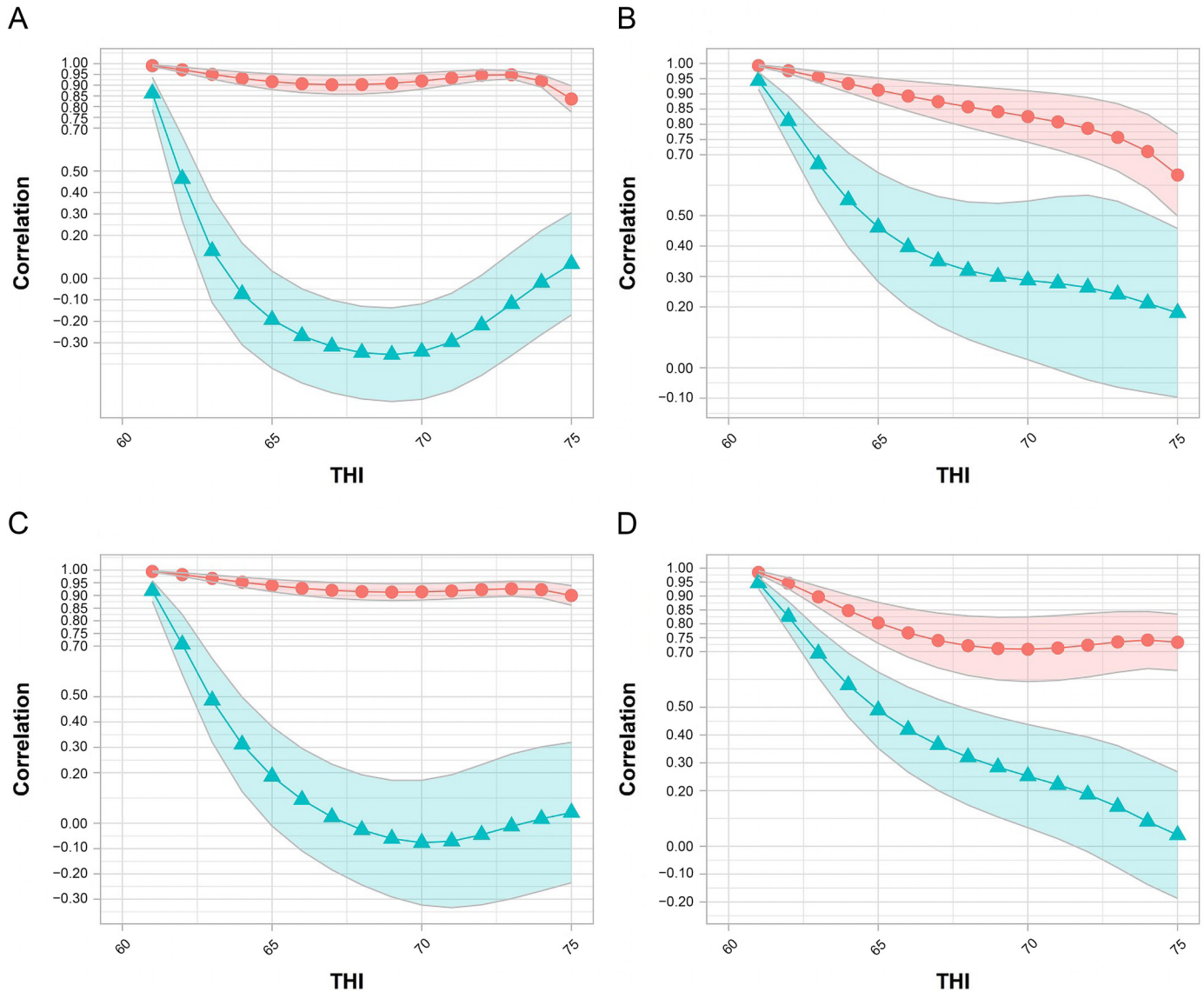


Figure 4. Posterior means for direct (red lines) and maternal (blue lines) genetic correlations for fat percentage (A), fat yield (B), protein percentage, (C), and protein yield (D), according to temperature-humidity index (THI) during the intrauterine phase (56 d before calving). The shaded areas around the lines indicate SD.

for extreme values, in contrast with what was observed for live weight traits in relation to THI from before birth until weaning in Spanish sheep breed lambs (Molina et al., 2022). It should be noted that the correlation for the maternal component shows higher standard deviation values throughout the THI scale similar to what was found by Yin et al. (2022) in characters relating to calf disease resistance and by Kipp et al. (2021a) for production traits in dairy cows. Higher posterior standard deviation values can certainly affect low correlation values; Yin et al. (2022) and Kipp et al. (2021a) found small genetic correlations values at extreme THI, associated with higher standard deviation values. How-

ever, we can conclude that there is a strong tendency to low values, always lower than 0.80. According to what was observed by other authors, this is an indication of a strong $G \times E$. The presence for many characters of a $G \times E$ effect both for the direct and maternal components for the time-lagged thermal stress in the dry period of the dam, highlights the possibility of various considerations on the selection of resilient bulls or cows (Robertson, 1959). It is difficult to discuss the results in the face of other authors' evidence because the study of genetic parameters for the intragenerational effect of HS in dairy cows or other ruminants has only recently been taken into consideration by other authors (Kipp

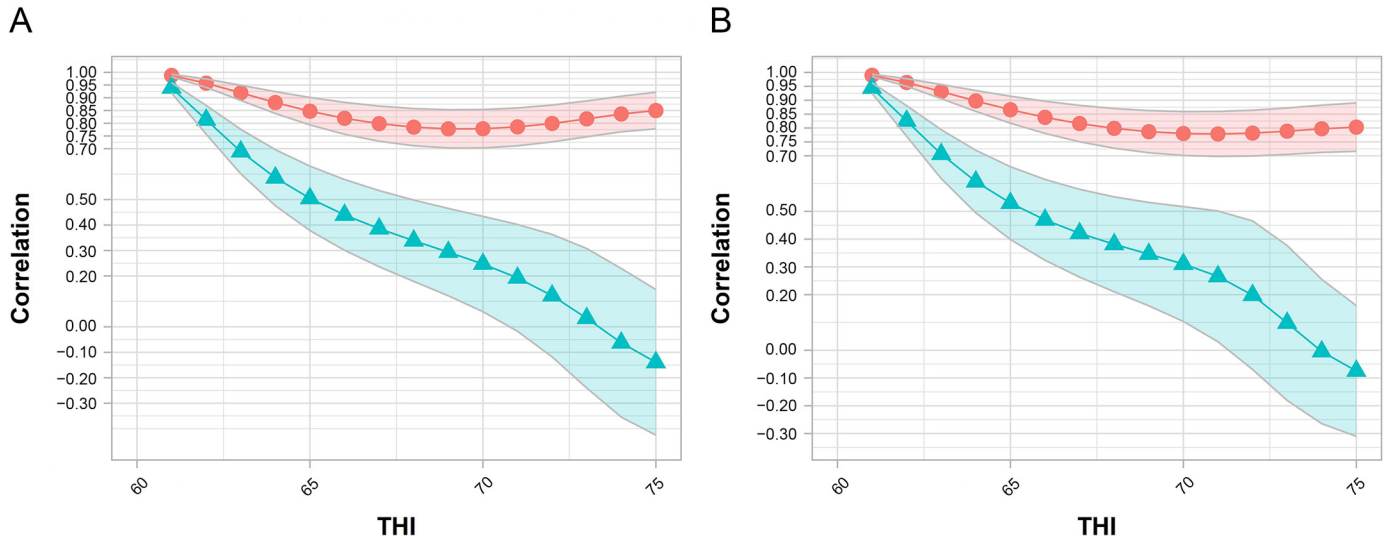


Figure 5. Posterior means for direct (red lines) and maternal (blue lines) genetic correlations for milk yield (A) and ECM (B), according to the temperature-humidity index (THI) during the intrauterine phase (56 d before calving). The shaded areas around the lines indicate SD.

et al., 2021a; Molina et al., 2022). Still, it should be emphasized that there are now numerous studies that associate time-lagged HS with physiological, productive, and reproductive performance in dairy cows (Tao and Dahl, 2013; Kipp et al., 2021b).

Biological and Genetics Implications

Transgenerational HS is a phenomenon through which the effects of exposure to high temperatures are carried over multiple generations of a species (Deng et al., 2021). Some studies showed that exposure to HS could affect reproduction, growth, and survival rate in a variety of organisms, including plants, insects, and mammals (Frésard et al., 2013). Maternal HS during late pregnancy affects the dam but also the fetus, and the effects of intrauterine stress seem to carry over into the offspring's postnatal life (Tao and Dahl, 2013). Although research on this topic in dairy cattle is limited, studies on other farm animals and humans can provide valuable insight and information (Lucy and Safranski, 2017; Rashid et al., 2017). From a genetic perspective, the impact of time-lagged thermal stress on future cow production can lead to various hypotheses. First, the initial rise in the dam's body temperature might influence fetal growth, resulting in offspring exhibiting permanent physiological changes. This could potentially cause a disparity between these offspring and their peers of similar genetic quality but conceived under optimal thermal conditions (Laporta et al., 2020). Furthermore, the individual's performance can be affected by the genetic traits inherited from the mother, introducing indirect genetic effects (Kruuk

and Hadfield, 2007; Wolf and Wade, 2016). Dams with superior maternal characteristics, especially under specific climatic conditions like higher average THI values, exhibit exceptional maternal abilities. Consequently, they produce offspring with outstanding performance, even in similar environmental conditions (Marshall and Uller, 2007). Efficiently measuring the dimensions of the dam $\times$ environment ($M \times E$) interaction, however, is complex and would require focusing on changes in the offspring's environment once maternal care has ceased (Vega-Trejo et al., 2018). In this study we have shown how maternal genetic variability or heritability are limited in absolute value but that there is a high variability toward the extremes of the environmental values, which would suggest the possibility of selecting more resilient mothers toward this phenomenon (González-Recio et al., 2012; McAdam et al., 2014). Regarding at least in 4 out of 6 traits (FY, PY, MY, and ECM), the highest maternal heritability values were not concentrated at the extremely high THID end. Instead, these values were more prominent around the THID value of 65.

Alterations in the intrauterine environment, ranging from maternal malnutrition and stress to elevated body temperature during pregnancy, have the potential to cause lasting structural and functional modifications in the developing fetus, which may endure into adulthood (Fowden et al., 2006). These changes may not be immediately observable but can have long-term effects on the organism's growth, development, and reproduction (Skibieli et al., 2018). Epigenetic changes involve 3 main mechanisms: DNA methylation, histone modifications, and RNA-mediated gene silencing (Strahl and Allis, 2000; Goldberg et al., 2007; Guttman et al., 2009;

Pikaard and Mittelsten Scheid, 2014). Epigenetic regulation through DNA methylation is a well-understood mechanism, having been one of the first discoveries in the field of epigenetics. It is recognized as a persistent and inheritable modification, affecting various biological processes including gene expression, transposable element behavior, and genomic imprinting across generations (Bartels et al., 2018; Sun et al., 2022). Therefore, it is logical to assume that the effect of time-lagged HS on the genetic parameters of lactating cows is due, at least in part, to these modifications but as suggested in previous studies this should be verified through genomic tools (Kipp et al., 2021a). Future investigation should also focus on the difference of immediate response of epigenetic modification (Del Corvo et al., 2021) and “inherited response” or “transgenerational epigenetic plasticity” (Ng et al., 2010; Weyrich et al., 2016).

CONCLUSIONS

To the best of our knowledge, this is the first study analyzing the association of intrauterine exposure to HS and genetic parameters of milk production traits from an across-generation perspective in Brown Swiss cows. As demonstrated in this study, the HS condition resulting from exposure to elevated temperature and humidity during the last 56 d of gestation alters the expression of both direct and indirect genetic components starting from an approximate THI threshold of 60. Not all traits respond to the same intensity, but in general a $G \times E$ interaction is present and should be taken into consideration for future selection decisions. In a breed such as Brown Swiss, present in different environments (both for intensity of thermal stress and for distribution) and often used in outdoor systems, the time-lagged effect of HS may add precision to the genetic evaluation of sire (particularly those used internationally) and be more easily addressed than a separate genetic evaluation.

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