Genetic analysis of fetal loss in Holstein cattle

Anil Sigdel,1 Rafael S. Bisinotto,2 and Francisco Peñagaricano1*

1Department of Animal and Dairy Sciences, University of Wisconsin-Madison 53706
2Department of Large Animal Clinical Sciences, University of Florida, Gainesville 32611

ABSTRACT

Pregnancy loss is recognized as one of the major factors contributing to poor reproductive performance in dairy cattle. Here, we performed a comprehensive genetic analysis of fetal loss, defined as a pregnancy loss that occurs after detection of a viable embryo around 42 d of gestation. The objectives of this study were to reveal (1) whether fetal loss is heritable and, hence, whether it will respond to selection, and (2) to what extent current fertility traits, such as daughter pregnancy rate, are associated with fetal loss. Data consisted of 59,308 confirmed pregnancy or fetal loss records distributed across nulliparous heifers and primiparous and multiparous cows. We defined fetal loss as a binary trait (yes vs. no) or as an ordinal trait (pregnancy maintenance, early fetal loss ≤150 d of gestation, and late fetal loss >150 d of gestation), and we assessed both linear and threshold models. Heritability estimates for fetal loss ranged from 1 to 18%, depending upon parity, trait definition, and statistical model used. Heritability estimates were greater for lactating cows than for nonlactating nulliparous heifers. Threshold models were able to capture more additive genetic variance and, thus, yielded higher heritability estimates than linear models. Notably, fetal loss traits were highly genetically correlated with each other but only weakly correlated with current fertility traits included in the national genetic evaluation. Overall, our study provides evidence that fetal loss is heritable enough to make genetic selection for reducing fetal loss and improving pregnancy maintenance feasible. In addition, our results suggest that fetal loss is largely independent from current traits used to select for cow fertility, and thus current breeding efforts have unfortunately little effect on reducing the incidence of fetal loss.

Key words: abortion, genetic parameter, pregnancy loss, threshold model

INTRODUCTION

Pregnancy loss is one of the major factors contributing to poor reproductive performance in dairy cattle. Although fertilization is observed in 70 to 75% of dairy cows subjected to insemination, pregnancy losses result in calving rates that range between 30 and 35% (Santos et al., 2004; Diskin et al., 2011). Pregnancy loss severely limits herd viability and production efficiency, as it is associated with longer calving interval, reduced availability of potential herd replacements, decreased milk production, increased insemination, veterinary, and labor costs, and premature culling (De Vries, 2006). Cabrera (2012) estimated the cost of losing a 90-d-old fetus at 210 DIM at US$323 for an average dairy cow. It should be noted that pregnancy loss is expensive, and its cost increases rapidly as the gestation progresses.

Pregnancy losses in dairy cattle during the first 41 d of gestation are typically referred to as embryonic losses, whereas pregnancy losses after 41 d of gestation are referred to as fetal losses. Reports of embryonic losses range from 25 to 40%, whereas fetal losses range between 8 and 10%, potentially exceeding 14% in some herds (Wiltbank et al., 2016). Although embryonic losses are more frequent, fetal losses have a much greater economic impact. Embryonic losses result in increased days open, whereas fetal losses often result in early culling of productive cows, extended calving intervals, and reduced milk production (Cabrera, 2014). Fetal losses may also result in the retention of fetal membranes and the development of endometritis, which further reduces reproductive performance and increases veterinary costs (Lee and Kim, 2007). Numerous factors may cause fetal losses, including infectious diseases, toxic agents, heat stress, and genetic factors. Known genetic factors include lethal recessive alleles, such as CVM and DUMPS, and an increasing list of recessive haplotypes (VanRaden et al., 2011). Despite the use of vaccines, improvements in management, and the use of genetic markers and haplotype tests to identify carriers of major genetic defects, fetal loss continues to be a critical problem for the dairy industry. Hence, a clear need exists to develop novel
strategies for reducing fetal loss and improving cows’ ability to maintain pregnancy.

Different statistical approaches can be used for the genetic analysis of fetal loss. For instance, if fetal loss is defined as a binary trait (presence vs. absence), then the use of a binary threshold model, also known as a probit model, is a natural approach. However, defining fetal loss as a binary trait may lead to an important loss of information, because cows’ ability to maintain pregnancy may vary greatly across gestation. In this context, fetal loss can be modeled as an ordinal trait with different levels, such as pregnancy maintenance, early fetal loss, and late fetal loss, and these ordinal responses can be evaluated using a multi-threshold model. Alternatively, despite the binary or ordinal nature of the trait, fetal loss can be analyzed using linear models.

The main goal of this study was to reveal the genetic basis of fetal loss in Holstein cattle. We considered fetal loss as both a binary trait and an ordinal trait. We evaluated whether fetal loss is heritable and, hence, whether it will respond to selection. We fitted alternative linear and nonlinear (threshold) models. We also evaluated to what extent currently available fertility traits, such as daughter pregnancy rate, are associated with fetal loss. In other words, we aimed to answer the question of whether fetal loss may add new information to guide breeding decisions. The findings of this study will contribute to the development of innovative strategies for improving reproductive performance in the Holstein breed.

MATERIALS AND METHODS

Data

Pregnancy records from nonlactating nulliparous heifers (n = 24,476) and lactating primiparous (n = 20,805) and multiparous (second lactation only, n = 14,027) Holstein cows between 2001 and 2019 were compiled from a single US commercial dairy herd located in Florida.

All cows were diagnosed as pregnant at 42 d after breeding, and records of fetal loss were obtained from subsequent veterinary pregnancy examinations. Note that, in this study, fetal loss was recorded after detection of a viable embryo, and, hence, this data set comprised direct records of fetal loss, rather than indirect indicators of fetal loss, such as long insemination intervals. Other relevant variables, such as breeding date, DIM at breeding, types of breeding (AI or embryo transfer), service sire, and presence or absence of postpartum uterine diseases, were collected for all cows. Pedigree was created by tracing the genealogy of all cows back to 5 generations. The pedigree file encompassed 35,006 animals, including 3,478 sires.

Trait Definition

Fetal loss was defined either as a binary trait or as an ordinal trait. Fetal loss was considered as a binary trait; that is, Y = 1 if the heifer or cow diagnosed as pregnant 42 d after breeding was diagnosed as nonpregnant in subsequent examinations, and Y = 0 if the heifer or cow remained pregnant in subsequent examinations. Alternatively, fetal loss was considered as an ordinal trait with 3 levels: pregnancy maintenance, early fetal loss (pregnancy loss ≤150 d of gestation), and late fetal loss (pregnancy loss >150 d of gestation). Note that the ordinal trait was then defined using a temporal sequence; that is, all the cows used in this study were pregnant at 42 d after breeding, most of them remained pregnant, but some experienced early fetal loss and other experienced late fetal loss.

Statistical Framework

Threshold and linear models were used for the analysis of binary or ordinal responses of fetal loss. Records from nulliparous, primiparous, and multiparous females were first evaluated separately. All models included the following linear predictor:

\[ \eta = X\beta + Z_1a + Z_2ss, \]

where \( \eta \) is a function of the expected value of the binary or ordinal response of fetal loss, \( \beta \) is a vector for fixed effects of year-season of breeding (39 levels), DIM at breeding (3 levels: early, mid, and late; only for lactating cows), type of breeding (2 levels: AI or embryo transfer), and occurrence of postpartum uterine diseases (yes vs. no; only for lactating cows), \( a \) is a vector of random additive genetic effects, and \( ss \) is a vector of random service sire effects. The matrices \( X, Z_1, \) and \( Z_2 \) are the incidence matrices relating phenotypic records to fixed, animal, and sire effects, respectively. Random effects were assumed to follow a multivariate normal distribution:

\[
\begin{pmatrix}
a \\
ss
\end{pmatrix} \sim N \left( 0, \begin{pmatrix}
\sigma_a^2 & \sigma_{as}^2 \\
\sigma_{as}^2 & \sigma_{ss}^2
\end{pmatrix} \right),
\]

where \( a \) and \( ss \) are the vectors of animal and service sire effects respectively; \( \sigma_a^2 \) and \( \sigma_{ss}^2 \) are animal and service sire variances respectively; \( \mathbf{A} \) is the additive gen-
The binary threshold model, also known as probit model, was used to evaluate the binary response of fetal loss in each of the 3 parities. This model describes the variation observed at a binary response variable \( Y \), either 0 or 1, using an underlying random variable \( z \), known as liability, \( z = \eta + \varepsilon \), where \( \eta \) is a vector of linear predictors and \( \varepsilon \) is a vector of independent and identically distributed standard normal random variables [i.e., \( \varepsilon \sim N(0,1) \)]. Here, fetal loss is \( Y = 1 \) if the underlying liability \( (z) \) is greater than zero [i.e., \( Y = (1 \text{ if } z > 0; 0 \text{ otherwise}) \)]. Therefore, the conditional probability of observing a fetal loss event, given the linear predictor, is \( P(Y = 1|\eta) = \Phi(\eta) \), where \( \Phi(.) \) is the standard normal cumulative distribution.

The ordinal threshold model was used to evaluate the ordinal response of fetal loss. The ordinal threshold model is in fact an extension of the binary threshold model. The model postulates that the observed ordinal response of fetal loss is in fact an extension of the binary threshold model, was used to evaluate the binary response of fetal loss in the pedi-

gree, and \( I \) is an identity matrix.

**Binary Threshold Model**

The binary threshold model, also known as probit model, was used to evaluate the binary response of fetal loss in each of the 3 parities. This model describes the variation observed at a binary response variable \( Y \), either 0 or 1, using an underlying random variable \( z \), known as liability, \( z = \eta + \varepsilon \), where \( \eta \) is a vector of linear predictors and \( \varepsilon \) is a vector of independent and identically distributed standard normal random variables [i.e., \( \varepsilon \sim N(0,1) \)]. Here, fetal loss is \( Y = 1 \) if the underlying liability \( (z) \) is greater than zero [i.e., \( Y = (1 \text{ if } z > 0; 0 \text{ otherwise}) \)]. Therefore, the conditional probability of observing a fetal loss event, given the linear predictor, is \( P(Y = 1|\eta) = \Phi(\eta) \), where \( \Phi(.) \) is the standard normal cumulative distribution.

**Ordinal Threshold Model**

The ordinal threshold model was used to evaluate the ordinal response of fetal loss. The ordinal threshold model is in fact an extension of the binary threshold model. The model postulates that the observed ordinal response takes value equal to \( m \) (either 1 = pregnant, 2 = early loss, or 3 = late loss) only if \( T_{m-1} \leq z < T_m \), where \( z \) is the unobserved underlying liability and \( T_{m-1} \) and \( T_m \) are thresholds. Here, thresholds must satisfy \( -\infty = T_0 \leq T_1 \leq T_2 \leq T_3 = +\infty \). The conditional probability of observing an event that falls in category \( m \), given the linear predictor, is \( P(Y = m|\eta) = \Phi(T_m - \eta) - \Phi(T_{m-1} - \eta) \), where \( m \) is vector of ordinal responses, \( \Phi(.) \) is the standard normal cumulative distribution function, and \( T_{m-1} \) and \( T_m \) are vectors with threshold values.

**Linear Models**

Linear models were fitted to both binary and ordinal responses of fetal loss. Linear models were obtained by adding a random residual to the linear predictor \( \eta \); that is, \( y = \eta + \varepsilon \), where \( y \) is a vector of either binary or ordinal responses of fetal loss, and \( \varepsilon \) is a vector of independent and identically distributed Gaussian random residual with mean 0 and variance \( \sigma^2 \varepsilon \).

**Implementation**

Both linear and threshold models were implemented in a Bayesian framework via the Gibbs sampler using the R package MCMCglmm (Hadfield, 2010). Inference for each of the models were based on 100,000 samples obtained after discarding 10,000 samples as burn-in. A thinning interval of 100 was used for computing features of the posterior distribution. Convergence diagnostics and graphical analysis of Markov chain Monte Carlo sampling output were carried out by visual inspection of trace plots of key parameters such as variance components.

**Heritability Estimates**

In linear models, heritability (\( h^2 \)) can be evaluated in the observed scale using the standard formula \( h^2 = \sigma_a^2/\left(\sigma_s^2 + \sigma^2_a + \sigma^2_e\right) \), where \( \sigma_a^2 \), \( \sigma_s^2 \), and \( \sigma^2_e \) are animal, service sire, and residual variances, respectively. By contrast, in threshold models, heritability can be evaluated at the liability scale using the same formula with \( \sigma^2_e = 1 \). Note that following Dempster and Lerner (1950), the heritability obtained with the binary threshold model (probit model) can be back-transformed to the observed scale using the following formula: \( h^2 = h^2_o z^2 / K (1 - K) \), where \( h^2_o \) and \( h^2 \) are the heritability estimates in the observed and liability scale, respectively, \( z \) is the height of the standard normal probability density function at the truncation threshold, and \( K \) is the proportion of cases in the population.

**Model Comparison**

Goodness of fit of each of the models was assessed by computing the mean squared error statistic, \( \text{MSE} = \text{n}^{-1} \cdot \sum (y - \hat{y})^2 \), where \( \hat{y} \) is the conditional expectation function evaluated at the posterior mean of model unknowns, \( y \) is the corresponding value of the response, and \( n \) is the number of observations. The conditional expectation functions of the linear and threshold models are \( \hat{y} = \eta \) and \( \hat{y} = \Phi(\eta) \), respectively. In addition, Pearson correlation between \( \hat{y} \) and \( y \) was calculated for each model under evaluation.

Predictive ability was evaluated using a 5-fold cross-validation. The entire data set was split randomly into 5 disjoint folds. Four of the 5 folds were combined to become a training set to estimate the solutions of fixed and random effects, and the remaining set was used as training set to evaluate model predictive ability. Each of the 5 folds was used as a testing set one time. The ability to predict yet-to-be observed fetal loss values was assessed using the Pearson product-moment correlation coefficient and the mean squared error of prediction. The correlation between observed fetal loss records \( (y) \) and predicted fetal loss records \( (\hat{y}_{test}) \) and the mean squared error of prediction, defined as the average of
the squared differences between \( y \) and \( \hat{y} \) were calculated in each cross-validation testing fold. The entire 5-fold cross-validation procedure was repeated 5 times, and, hence, each analysis resulted in 25 estimates.

**Correlations Between Fetal Loss Across Parities**

An important question is whether fetal loss in nulliparous heifers, primiparous cows, and lactating multiparous cows, can be considered as the same trait. To answer this question, genetic correlations among fetal loss traits were estimated between parities using bivariate analyses. All models included the following linear predictor, \( \eta = X\beta + Z_1a + Z_2ss \), which included the same effects as in the univariate analyses. The effect \( a \) was assumed to follow the multivariate normal distribution with mean zero and \( \text{Var}(a) = K \otimes A \), where \( A \) is the numerator relationship matrix, \( K \) is the additive genetic covariance matrix, and \( \otimes \) is the Kronecker product.

**Correlations Between Fetal Loss and Current Fertility Traits**

Three female fertility traits are routinely evaluated in US Holstein cattle, namely heifer conception rate (HCR), cow conception rate (CCR), and daughter pregnancy rate (DPR). The traits HCR and CCR are defined as the percentages of inseminated heifers or cows that become pregnant at each service. The trait DPR is defined as the percentage of nonpregnant cows that become pregnant during a given 21-d period. A key question is to what extent currently available fertility traits are associated with fetal loss. To answer this question, sires’ genetic merit for fetal loss were estimated for both binary and ordinal responses using linear and threshold models. Then, sires’ genetic merit for current fertility traits were obtained from the Council on Dairy Cattle Breeding (August 2021). Finally, genetic correlations were estimated from the correlations between the genetic merits and the reliability of the genetic merits using Calo’s method (Calo et al., 1973):

\[
\hat{r}_{1,2} = \sqrt{\frac{\sum_{i=1}^{n} REL_i \times REL_2}{\sum_{i=1}^{n} (REL_i \times REL_2) \times \eta_{1,2}},}
\]

where \( REL_1 \) and \( REL_2 \) are the reliabilities of the genetic merits of trait 1 and trait 2, and \( \eta_{1,2} \) represents the correlation between the genetic merits for traits 1 and 2.

**RESULTS**

**Descriptive Statistics**

Table 1 provides a summary of fetal loss records by parity and trait definition. Fetal loss records from a total of 24,476 nulliparous heifers, 20,805 primiparous cows, and 14,027 multiparous cows were evaluated in this study. All animals were diagnosed as pregnant at 42 d after breeding; most remained pregnant, but some were diagnosed as nonpregnant in subsequent examinations and were classified as having undergone fetal loss. The incidence of fetal loss ranged from 4.7% to 14.1% depending on the year. Roughly 11% of the animals had at least one event of fetal loss. The largest incidence of fetal loss was observed in multiparous cows (13.6%), followed by primiparous cows (13.3%) and finally nulliparous heifers (8.1%). Moreover, the incidence of early fetal loss was greater than the incidence of late fetal loss, representing between 85% and 93% of total fetal losses.

**Heritability Estimates**

Figure 1 shows the estimates of heritability for fetal loss according to parity, trait definition, and statistical model. Heritability estimates ranged between 1 and 2% for nulliparous heifers, between 1 and 8% for primiparous cows, and between 3 and 18% for multiparous cows. Threshold models were able to capture more additive genetic variance, and thus yielded higher heritability estimates, than linear models. In fact, Figure 1 clearly shows that for a given parity and trait definition, the threshold model always returned a higher heritability than the linear model. It should be noted that the heritability estimates from threshold and linear models are on 2 different scales, and to facilitate the direct comparison, the heritability estimates obtained with the binary threshold model were back-transformed to the observed scale. The back-transformed heritability estimates were equal to 1% for nulliparous heifers, 3.4% for primiparous cows, and 7.4% for multiparous cows. As expected, these estimates are slightly smaller than

<table>
<thead>
<tr>
<th>Trait</th>
<th>Nulliparous</th>
<th>Primiparous</th>
<th>Multiparous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of records</td>
<td>24,476</td>
<td>20,805</td>
<td>14,027</td>
</tr>
<tr>
<td>Fetal loss events</td>
<td>1,990</td>
<td>2,778</td>
<td>1,909</td>
</tr>
<tr>
<td>Fetal loss frequency</td>
<td>8.1%</td>
<td>13.3%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Ordinal response</td>
<td>22,486</td>
<td>18,027</td>
<td>12,118</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1,850</td>
<td>2,371</td>
<td>1,698</td>
</tr>
<tr>
<td>Early loss</td>
<td>140</td>
<td>407</td>
<td>211</td>
</tr>
</tbody>
</table>

Table 1. Descriptive statistics: summary of fetal loss records by parity and trait definition
those on the liability scale due to the loss of information by grouping into 2 categories.

**Model Comparison**

Goodness of fit of the different models was evaluated using mean squared error and the correlation between observed and fitted values. For both trait definitions, threshold and linear models showed very similar mean squared error values and correlations between observed and fitted values. Moreover, regardless of trait definition, models fitting data from nulliparous heifers showed slightly better goodness of fit than models fitting data from lactating cows, showing lower mean squared error values and high correlation values.

It should be noted that predictive power is more important than goodness of fit. As such, in this study, model predictive ability was evaluated in cross-validation. Figure 2 shows predictive correlations and mean squared error of predictions according to parity, trait definition and statistical model. Interestingly, regardless of trait definition, threshold models exhibited better predicted abilities than linear models, especially for lactating cows. In fact, threshold models yielded an increase in predictive correlations of around 10 to 15% and a decrease in prediction bias of around 5 to 10%. Moreover, regardless of parity, the models yielded similar predictive correlations across trait definitions.

**Correlations Between Fetal Loss Traits Across Parities**

Table 2 shows the genetic correlations between fetal loss traits across parities. Here, fetal loss was defined as a binary trait and evaluated using linear and threshold models. Genetic correlations ranged between 0.22 to 0.31, denoting that fetal loss traits across parities should be considered as different traits.

**Correlations Between Fetal Loss and Fertility Traits**

Figure 3 shows the genetic correlations between fetal loss traits and other fertility traits, namely DPR, CCR, and HCR, by parity. We calculated the genetic correlations using Calo’s method, which considers both the correlation between PTA and the reliabilities of the
PTA. Notably, fetal loss traits are highly correlated with each other, suggesting that trait definition (binary vs. ordinal) or statistical model (linear vs. threshold) has little influence on animal rankings. Even more important, fetal loss traits are only weakly correlated with current fertility traits, especially among lactating cows.

**DISCUSSION**

Pregnancy loss, and in particular, pregnancy loss during the fetal period, is a major welfare issue that directly affects herd reproductive efficiency and farm profitability. This study was specifically conducted to...
investigate the genetic basis of fetal loss in Holstein cattle. We considered fetal loss as either a binary or an ordinal trait, and we used both linear and nonlinear (threshold) models. We aimed to reveal whether fetal loss is a heritable trait and which trait definition and statistical model should be preferred. We also evaluated whether currently available fertility traits, such as DPR and cow and heifer conception rates, are associated with fetal loss.

**Fetal Loss Is a Heritable Trait**

The estimates of heritability ranged from 1 to 18% depending on the parity, the definition of the trait, and the statistical model. Fetal loss as a (1) binary trait, (2) measured in lactating cows, and (3) analyzed using threshold models, showed the largest heritability estimates: 8% and 18% in the liability scale, which correspond to 3.4% and 7.4% in the observable scale, for primiparous and multiparous cows, respectively. These findings agree with those of Gershoni et al. (2020), who reported heritability estimates between 3 and 10% for long insemination interval in Israeli dairy cattle as an indicator of fetal loss. Recently, Ask-Gullstrand et al. (2021) reported a heritability of 2% for fetal loss in Swedish Holstein cattle, using fetal loss records derived from in-line milk progesterone profiles. Note that heifer and cow conception rates, 2 of the female fertility traits currently included in the US national evaluation, have heritability estimates around 1 and 2% in the observed scale (Ma et al., 2019). Similarly, the heritability of DPR, which is considered the primary trait for improving cow fertility in the United States, has been estimated at around 4% (VanRaden et al., 2004). Therefore, our study provides evidence that fetal loss is equal to or more heritable than the female fertility traits currently included in the national genetic evaluation. It should be noted that heritability estimates for fetal loss were obtained with a reasonable precision, and reliable estimates of heritability are needed for defining a breeding strategy for fetal loss. Overall, our findings suggest that genetic selection for reducing fetal loss and improving pregnancy maintenance is feasible in Holstein cattle.

**Fetal Loss Is Largely Independent of Current Fertility Traits**

An important question is to what extent fetal loss would add new information to current dairy cattle selection programs. To answer this question, we calculated the genetic correlations between fetal loss traits and currently available fertility traits, namely DPR, HCR, and CCR. Notably, fetal loss traits, especially in lactating cows, are largely independent of current fertility traits. Note that HCR and CCR reflect a heifer or cow’s genetic ability to conceive, and therefore it is not surprising that conception and pregnancy maintenance are poorly correlated traits. The trait DPR reflects a cow’s genetic ability to conceive sooner after

![Fig 3](image.png)

**Table 2.** Genetic correlations between fetal loss across parities; fetal loss was defined as a binary trait and analyzed using linear and threshold models.

<table>
<thead>
<tr>
<th>Parity</th>
<th>Nulliparous</th>
<th>Primiparous</th>
<th>Multiparous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nulliparous</td>
<td>0.281 (0.018)</td>
<td>0.230 (0.090)</td>
<td></td>
</tr>
<tr>
<td>Primiparous</td>
<td>0.314 (0.021)</td>
<td>0.240 (0.010)</td>
<td></td>
</tr>
<tr>
<td>Multiparous</td>
<td>0.224 (0.070)</td>
<td>0.299 (0.028)</td>
<td></td>
</tr>
</tbody>
</table>

1Genetic correlations (SD) obtained with linear models are above the diagonal, and genetic correlations (SD) obtained with threshold models are below the diagonal.
calving, and it possibly captures various components of female fertility, including resuming ovarian cyclicity postpartum, expressing estrus, ovulating, conceiving, and establishing pregnancy (Lucy, 2019). We estimated low genetic correlations, especially for lactating cows, between DPR and fetal loss traits, denoting that the establishment of pregnancy is a component of female fertility largely not captured by DPR. Overall, our findings suggest that selection for female fertility using current fertility traits has little influence on fetal loss, and, hence, it is critical to include this novel trait into selection programs, given its importance.

**Fetal Loss Across Parities**

Lactating cows showed a larger incidence of fetal loss than nulliparous heifers (13.5% versus 8.1%). Lactation is generally associated with increased feed intake and subsequently higher metabolism of progesterone in the liver, and because progesterone is important for pregnancy maintenance, a lesser blood concentration of progesterone may increase the risk of fetal loss in high-producing dairy cows (Martins et al., 2018). Interestingly, we found that fetal loss traits are weakly correlated across parities, with genetic correlations up to 31%. These correlations suggest that genetic control of fetal loss in nulliparous heifers and lactating cows differs somewhat. We recently reported similar results but estimating the genetic correlations as the correlations between SNP effects (Sigdel et al., 2021). Our findings suggest that fetal loss across parities should not be considered as the same trait, and, hence, multitrait models instead of repeatability models should be used for genetic analyses. This result is not surprising for fertility traits, as most national genetic evaluations consider heifer and cow fertility as separate traits (Muttutoranta et al., 2019).

**Trait Definition and Model**

From a breeder’s perspective, an important question is whether predictions of genetic values from the different trait definitions and models yield different breeding decisions. In this study, threshold models showed better predictive performance than linear models, but the PTA values obtained from different models (and trait definitions) were highly correlated, denoting very similar animal rankings. Although threshold models have a theoretical advantage for analyzing discrete traits, our findings suggest that both threshold and linear models could be useful for genetic selection purposes. The genetic analysis of fetal loss as a binary trait using a linear model is probably the most practical approach.

**Phenotyping of Fetal Loss**

In this study we evaluated direct records of fetal loss rather than indirect indicators of pregnancy loss such as long insemination intervals. It is a very valuable and precise phenotype, but difficult to record because it requires multiple pregnancy checks, well-prepared farm personnel, staff veterinarians, and an exceptional recording system. Accurately phenotyping fetal loss nationwide is challenging. One option is to perform high-intensity data collection on a limited number of large farms and use these farms as a reference population to predict genomic breeding values for fetal loss for the entire population, including young selection candidates. One current and successful example of this approach is the national evaluation of dairy cow feed efficiency. Now, direct observations of fetal loss can also be combined with correlated low-cost, high-volume data, such as long insemination intervals, to increase the accuracy of genomic breeding values. It is also possible to improve the national recording system to better capture fetal loss events.

**CONCLUSIONS**

Fetal loss is a major issue that affects animal welfare and longevity, as well as dairy farm profitability through extended calving intervals, increased veterinary costs, and early culling of productive cows. This study provides evidence that genetic selection could be a feasible approach to reduce the incidence of fetal loss in dairy cattle. Changes achieved through genetic selection are incremental, permanent, and cumulative, which makes genetic selection to reduce fetal loss an attractive and cost-effective strategy. Note that current selection efforts to improve cow fertility have unfortunately little or no effect on reducing the incidence of fetal loss. Overall, this study is the foundation for the development of novel strategies for improving cow fertility through breeding for reduced fetal loss and improved pregnancy maintenance.

**ACKNOWLEDGMENTS**

This study received no external funding. The authors have not stated any conflicts of interest.

**REFERENCES**


ORCIDS

Rafael S. Bisinotto  https://orcid.org/0000-0001-6144-2919

Francisco Peñaagaricano  https://orcid.org/0000-0001-6661-3991