Livestock Science 189 (2016) 8–16

Contents lists available at ScienceDirect

Livestock Science

journal homepage: www.elsevier.com/locate/livsci

Causal relationships between clinical mastitis events, milk yields and lactation persistency in US Holsteins

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ARTICLE INFO

Article history:
Received 17 August 2015
Received in revised form
11 April 2016
Accepted 22 April 2016

Keywords:
Causal effects
Mastitis
Milk yield
Structural equation models

ABSTRACT

Complex relationships exist between udder susceptibility to mastitis and milk production traits. Identifying causal association between these traits could help to disentangle these complex relationships. The main objective of the study was to use producer-recorded health data to examine the causal relationship between mastitis events, milk yield and lactation persistency. A total of 48,058 first lactation cows, daughters of 2213 Holstein bulls and raised across 207 herds were analyzed using structural equation models. Traits included in the dataset were mastitis events and average test day milk yields recorded in three different periods: period 1 (5–60 DIM), period 2 (61–120 DIM) and period 3 (121–180 DIM). In addition, lactation persistency was also included. A subset including 28,867 daughters of 1809 Holstein sires having both first and second lactation across 201 herds was further investigated. In these datasets, mastitis events were defined on a lactation basis as binary trait; either a cow was assigned a score of 1 (had a mastitis event in that lactation) or a score of 0 (healthy) for that particular lactation, regardless of the time of occurrence. Total milk yield from first and second lactation were also included in the analyses. We estimated negative structural coefficient (−0.032) between clinical mastitis and test day milk production in early lactation period suggesting that mastitis results in a direct decline in milk production in early lactation. We nonetheless elicited little impact of mastitis on test day milk production of mid and late lactation periods, and on milk yield lactation persistency. Likewise the positive estimate of the structural coefficient (0.123) from mastitis event in first lactation to second lactation suggests an increased risk of mastitis in second lactation if a case of mastitis occurs in the primiparous cow. Heritability estimates obtained from the structural equation models were low for mastitis (ranged 0.04 to 0.07), and negative genetic correlations were found between mastitis events and milk yield. The study illustrates how mastitis events and production are causally linked. Through the use of structural equation models we elicited the causal effect among mastitis and production traits that evolve over the course of cow life.

1. Introduction

Mastitis is a mammary inflammation and is one of the most economically impacting health events in the dairy cattle industry. The losses due to mastitis are costly (Koeck et al., 2012b), mostly due to veterinary and treatment costs (Hinrichs et al., 2005), discarded milk (Shim et al., 2004), and reduced milk production (Bar et al., 2008), but also due to increased risk of culling (Hertl et al., 2011), and increased reproductive problems (Moore et al., 1991). Moreover, replacement costs and increased labor cost due to mastitis directly impact the profitability of dairy enterprises (Huijps et al., 2008). The average cost of a clinical mastitis has been previously estimated at $179 with $115 from milk lost per case, $14 due to increased mortality loss, and $50 from treatment costs (Bar et al., 2008). The antagonistic relationship between health disorders and milk yield in dairy cows is generally accepted (Rauw et al., 1998). In the past 50 years, there has been an intense selection for yield traits. This has resulted in an increased deterioration of dairy health (Miglior et al., 2005). These problems in dairy cattle have pointed towards genetic selection for increased disease resistance and several researchers in the past decade have suggested inclusion of clinical mastitis in the overall breeding goal of Holstein dairy cattle (Kadarmideen and Pryce, 2001; Ødegård et al., 2003). Direct selection for mastitis resistance has been so far fully implemented in Nordic cattle (Heringstad et al., 2003; Philipsson and Lindhé, 2003) and national genetic and genomic

Abbreviations: LP, lactation persistency of milk yield; LMAST, liability to mastitis; MY, milk yield; SEM, structural equation models; TD, test-day; TMY, total milk yield

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http://dx.doi.org/10.1016/j.livsci.2016.04.015
1871-1413/

evaluations for clinical mastitis has been started in Canada (Jamrozik et al., 2013) and France (Govignon-Gion et al., 2012). Similarly, routine genetic evaluation of mastitis is done in Austria (Fuerst et al., 2011; Koeck et al., 2015).

Several researchers in the past have used mixed models to compute genetic correlations between mastitis and milk yield. Recently, Pfeiffer et al. (2015) described genetic relationships between functional longevity and mastitis as well as other direct health traits. Results from those studies mostly revealed the unfavorable genetic correlations between mastitis events and milk yield traits. Yet correlations do not imply causation and there is still a lack of knowledge about the cause and effect between these traits, which could be addressed using structural equation models (SEM). In the context of animal breeding, Gianola and Sorensen (2004) extended multivariate mixed model theory to infer recursive relationships between phenotypes by accounting for possible feedback situations. Several papers that have been published in the realm of animal breeding over the past few years used structural equation models to infer causal relationships between health traits (Wu et al., 2008; Heringstad et al., 2009; Dhakal et al., 2015). Wu et al. (2008) used a dataset of Norwegian Red cows to study the causal effect between mastitis and milk yield. To the best of our knowledge, no study has been conducted to infer causal relationships between mastitis events and milk yield in the US Holstein cattle population. Similarly, there is a knowledge gap regarding the causal effect of mastitis occurring in first lactation and mastitis events occurring in later lactations. Thus, the objective of the current study was to elicit direct causal phenotypic effects and genetic relationships among mastitis events and production traits (milk yield and lactation persistency of milk yield) in US Holsteins using recursive models.

2. Materials and methods

2.1. Data

Health information records were made available from Dairy Records Management Systems (Raleigh, NC) from US dairy farms from 1996 through June 2013. Holstein cows with mastitis records in first and second parity were retained for the analyses which included calving records from 1996 to 2012. Health data quality edits were applied as described in detail in Parker Gaddis et al. (2012) with some slight modifications for herd edits. In order to avoid herds that over or under reported mastitis events, maximum and minimum constraints were applied to the dataset. The maximum constraint was imposed by excluding records when reporting frequency of herds were greater than two standard deviations above the mean reporting frequency of mastitis event. Similarly, minimum constraint was imposed by selecting records from herd with at least one reported incidence of the mastitis event and herds consisting of at least 5 cows. In addition, only records of cows having lactation length less than or equal to 400 days in milk (DIM) were included. After applying data quality edits, a dataset was formed to identify causal effects between mastitis and production measures (test-day milk yields and lactation persistency) in first parity US Holsteins. This dataset included 48,058 first parity daughters of 2213 Holstein sires across 207 herds and will be referred to as First-Lactation dataset.

The First-Lactation dataset included test-day (TD) records for milk yield (MY) and lactation persistency of MY in addition to mastitis events. Test Day records from 5 to 180 days after calving were included and cows with missing TD records were removed from the original dataset in the process of forming the First-Lactation dataset. Days in milk up to 180 days after calving were divided into 3 lactation periods such that period 1 included 5–60 days, period 2 included 61–120 days, and period 3 included 121–180 days similarly to the procedure adopted by Wu et al. (2008). Single MY TD records were assigned to each period as the closest in time to the midpoint of each segment and will be hereafter referred to as MY1, MY2, and MY3, respectively. Cows were assigned a value of 0 (healthy) or 1 (mastitis) in each period. Only mastitis records that were prior and temporally closer to the assigned TD for each period were considered. This definition implies that pre-existing mastitis events would affect the MY of the following TD. Lactation persistency of MY (LP), a measure describing the shape of the lactation curve after peak milk yield, was calculated for each cow using BESTPRED software (Cole and VanRaden, 2007).

A subset (First & Second-Lactation) dataset was formed to identify causal effects from mastitis in first lactation to second lactation and from mastitis to total milk yield for first and second lactation. The First & Second-Lactation dataset included 28,867 daughters from 1809 sires having first and second lactation across 201 herds. Only cows showing records for both lactations were included in the dataset. To reduce complexity and improve the interpretation of the results mastitis events were in this case defined on a lactation basis as binary trait; a cow was assigned either a score of 1 (had a mastitis event in that lactation) or a 0 (healthy) for that particular lactation, regardless of the time of occurrence. Total milk yield (305-day milk yield) from first and second lactation were also included in the analysis as calculated from the BESTPRED software (Cole and VanRaden, 2007).

2.2. Statistical analysis

Recursive Gaussian-threshold sire models were used for the statistical analyses. The threshold model assumed an underlying continuous variable, liability (l_i), for binary mastitis events that defines the observed binary variable into a value of 1 if liability is larger than a fixed threshold and 0 otherwise. Two different series of analysis (Lactation first (LAC1) and Lactation first and second (LAC12)) were defined for the purpose of identifying causal relationships between mastitis events and production measures. The LAC1 series of analyses employed a SEM to find recursive relationships between mastitis events, TD milk yields, and LP in first lactation. Four analyses were performed, which are as follows:

- LAC1. A: This analysis included two traits: liability to mastitis in the first period (LMAST1) and MY1. The direct recursive effect was assumed from LMAST1 to MY1.
- LAC1. B: This analysis included MY1, liability to mastitis in the second period (LMAST2) and MY2. The direct recursive effect was assumed from MY1 to LMAST2 and from LMAST2 to MY2.
- LAC1. C: This analysis included MY2, liability to mastitis in the third period (LMAST3) and MY3. The direct recursive effect was assumed from MY2 to LMAST3 and from LMAST3 to MY3.
- LAC1. D: Liability to mastitis of each period and LP were included in this analysis. The direct recursive effects were assumed from mastitis of each period (LMAST1, LMAST2, and LMAST3) to lactation persistency of milk yield.

Lastly, the LAC12 analysis (using First & Second-Lactation dataset) assumed direct recursive effects from liability to first lactation mastitis (LM1) to liability to second lactation mastitis (LM2). Direct recursive effects were also considered from LM1 to total milk yield of first parity (TMY1) and also to total milk yield of second parity (TMY2). An indirect recursive effect was also assumed from LM1 to LM2 and TMY2. A direct recursive effect measures how much TMY1, LM2, and TMY2 would be affected by changes in LM1. An indirect recursive effect measures how much LM2, and TMY2 would be affected by changes in LM1 through the

mediating effect of TMY1. For instance, the indirect recursive effect from LM1 to LM2 can be calculated as the product of structural coefficients (LM1→LM2)=(LM1→TMY1)×(TMY1→LM2). The overall causal effect on LM2 can be calculated as (LM1→LM2)+(LM1→TMY1)×(TMY1→LM2) (Lopez de Maturana et al., 2009; Shipley, 2002).

The models used in LAC1 and LAC12 analyses can be summarized as follows:

$$LAC1.\ A:\begin{cases} y_1 = Xb_1 + Z_h h_1 + Z_s s_1 + e_1 \\ y_2 = \lambda_{21} y_1 + Xb_2 + Z_h h_2 + Z_s s_2 + e_2 \end{cases}$$

$$LAC1.\ B/LAC1.\ C:\begin{cases} y_1 = Xb_1 + Z_h h_1 + Z_s s_1 + e_1 \\ y_2 = \lambda_{21} y_1 + Xb_2 + Z_h h_2 + Z_s s_2 + e_2 \\ y_3 = \lambda_{32} y_2 + Xb_3 + Z_h h_3 + Z_s s_3 + e_3 \end{cases}$$

$$LAC1.\ D:\begin{cases} y_1 = Xb_1 + Z_h h_1 + Z_s s_1 + e_1 \\ y_2 = Xb_2 + Z_h h_2 + Z_s s_2 + e_2 \\ y_3 = Xb_3 + Z_h h_3 + Z_s s_3 + e_3 \\ y_4 = \lambda_{41} y_1 + \lambda_{42} y_2 + \lambda_{43} y_3 + Xb_4 + Z_h h_4 + Z_s s_4 + e_4 \end{cases}$$

$$LAC12:\begin{cases} y_1 = Xb_1 + Z_h h_1 + Z_s s_1 + e_1 \\ y_2 = \lambda_{21} y_1 + Xb_2 + Z_h h_2 + Z_s s_2 + e_2 \\ y_3 = \lambda_{31} y_1 + \lambda_{32} y_2 + Xb_3 + Z_h h_3 + Z_s s_3 + e_3 \\ y_4 = \lambda_{41} y_1 + \lambda_{42} y_2 + \lambda_{43} y_3 + Xb_4 + Z_h h_4 + Z_s s_4 + e_4 \end{cases}$$

where, the $\mathbf{y_1}$ and $\mathbf{y_2}$ are vectors reporting LMAST1 and MY1 respectively in LAC1.A analysis. The $\mathbf{y_1}$, $\mathbf{y_2}$, and $\mathbf{y_3}$ are the vectors reporting MY1, LMAST2, and MY2 respectively in LAC1.B analysis. Similarly, the $\mathbf{y_1}$, $\mathbf{y_2}$, and $\mathbf{y_3}$ are vectors reporting MY2, LMAST3, and MY3 respectively in LAC1.C analysis. In the case of LAC1.D analysis, the $\mathbf{y_1}$, $\mathbf{y_2}$, $\mathbf{y_3}$, and $\mathbf{y_4}$ of are vectors reporting LMAST1, LMAST2, LMAST3, and LP respectively. In equations reported above for LAC12 analysis, the $\mathbf{y_1}$, $\mathbf{y_2}$, $\mathbf{y_3}$, and $\mathbf{y_4}$ are vectors reporting LM1, TMY1, LM2, and TMY2 respectively. The λ_{ij} is the structural coefficients describing the rate of change for trait *i* with respect to trait *j*, **b** is a vector of systematic effects including the effect of year-season of calving, **h** is a vector of herd effects, **s** is a vector of sire of cow effects, and **e** is a vector of residuals; **X**, $\mathbf{Z_h}$, and $\mathbf{Z_s}$ are the corresponding incidence matrices. In matrix form, the general model was:

$$\mathbf{y} = (\Lambda \otimes \mathbf{I})\mathbf{y} + \mathbf{Xb} + \mathbf{Z_h h} + \mathbf{Z_s s} + \mathbf{e}$$

where, $\mathbf{\Lambda}$ are lower triangular matrices with 1 on diagonal, λ_{ij} on off-diagonals representing the recursive effects from *j* to *i*, and 0 everywhere else.

Multivariate normal prior distributions were assigned to structural coefficients as $N(\mathbf{1}\lambda_0, \mathbf{I}\ \tau^2)$, where hyperparameters were $\lambda_0=0$ and $\tau^2=10{,}000$. Elements of **b** were assigned normal prior distributions, with mean 0 and variance 10,000. Sire effects were assigned a multivariate normal prior distribution $\mathbf{s}\sim N(0, \mathbf{G}\otimes\mathbf{A})$, where **G** is the sire covariance matrix for the traits involved and **A** is the matrix of additive genetic relationships among bulls. The prior distribution of herd effects was $\mathbf{h}\sim N(0, \mathbf{H}\otimes\mathbf{I})$, where **H** is the herd (co)variance matrix and **I** is an identity matrix. Independent inverse-Wishart prior distributions were used for **H** and **G**, the covariance matrices of **h** and **s**, respectively. In order to achieve identifiability, residual variances of threshold traits were fixed to 1. Furthermore, all residual covariances were forced to be equal to 0. In this case, the prior distribution of the **R** matrix fixing the residual covariances with unit residual variances was an inverse-Wishart distribution. Transformation of the estimated covariance matrices for the SEM in multiple trait model scale was performed as:

$$\mathbf{G_n^*} = (\mathbf{I}-\mathbf{\Lambda})_\mathbf{n}^{-1}\mathbf{G_n}(\mathbf{I}-\mathbf{\Lambda})_\mathbf{n}^{\prime-1}$$
$$\mathbf{H_n^*} = (\mathbf{I}-\mathbf{\Lambda})_\mathbf{n}^{-1}\mathbf{H_n}(\mathbf{I}-\mathbf{\Lambda})_\mathbf{n}^{\prime-1}$$
$$\mathbf{R_n^*} = (\mathbf{I}-\mathbf{\Lambda})_\mathbf{n}^{-1}\mathbf{R_n}(\mathbf{I}-\mathbf{\Lambda})_\mathbf{n}^{\prime-1}$$

where the index n indicates the models used in first and second series of analyses, and **G**, **H**, **R**, and $\mathbf{\Lambda}$ were as defined above. Heritabilities and genetic correlations were then calculated in the usual manner from (co)variance components in $\mathbf{G^*_n}$, $\mathbf{H^*_n}$, and $\mathbf{R^*_n}$.

Data analyses were conducted in Bayesian framework using the SIR-BAYES package (Wu et al., 2008) in which all Bayesian models were implemented via Markov chain Monte Carlo (MCMC) sampling. For each model, 100,000 iterations were generated and the first 20,000 iterations were discarded as burn-in. Posterior samples from each chain were thinned every 25 iterations after burn-in and retained for analysis. Posterior distributions of parameters of interest were inferred based on posterior samples after burn-in. Markov chain convergence was assessed by visual inspection of trace plots. Additional diagnostic tests such as Geweke's convergence statistic (Geweke, 1992) was obtained to confirm convergence through R (http://cran.r-project.org) with the CODA package (Plummer et al., 2012).

Transformation of lambda coefficients estimates from liability to observable scale was done following Wu et al. (2008). For example, the difference in mean peak milk yield between sick (1) cows due to MAST1 and healthy (0) cows can be calculated as

$$\Delta \approx \lambda(\bar{l}_1 - \bar{l}_0)$$

where $\bar{l}_1$ and $\bar{l}_0$ are averages of augmented liabilities for sick cows due to MAST1 and healthy cows, respectively.

3. Results and discussion

The incidence of mastitis events in First-Lactation dataset were 6.58%, 4.13%, and 3.90% for lactation periods 5–60, 61–120, and 121–180 DIM respectively (Table 1). The TD MYs decreased over the three lactation periods. The mean (standard deviation) of TD MY was 34.66 (7.18) kg, 34.28 (7.92) kg, and 28.55 (7.32) kg at lactation periods 1, 2, and 3, respectively (Table 2). The mean (standard deviation) of LP was 0.38 (0.97) LP units. The mean of LP in our study was lower than that reported by Appuhamy et al. (2009). In their study, they reported a mean (standard deviation) 0.53 (1.19) LP units for first parity cows. Incidences of mastitis events in the First & Second-Lactation dataset were 10.87% and 14.05% for lactations 1 and 2, respectively (Table 1). Incidences of

Table 1
Descriptive statistics for mastitis events.

Traits[a]	Number of records		Mastitis event frequency (%)
	Healthy	Diseased	
MAST1	44,896	3162	6.58
MAST2	46,073	1985	4.13
MAST3	46,184	1874	3.90
M1	25,729	3138	10.87
M2	24,811	4056	14.05

[a] MAST1 is the mastitis event occurring in 5–60 DIM in first lactation; MAST2 is the mastitis event occurring in 61–120 DIM in first lactation; MAST3 is the mastitis event occurring in 121–180 DIM in first lactation; M1 is the mastitis event occurring in first lactation; and M2 is the mastitis event occurring in second lactation.

Table 2
Descriptive statistics of production measures.

Traits[a]	Number of records	Mean	SD	Minimum	Maximum
MY1 (kg)	48,058	34.66	7.18	6.50	81.22
MY2 (kg)	48,058	34.28	7.92	9.64	79.34
MY3 (kg)	48,058	28.55	7.32	8.32	72.09
LP (units)	48,058	0.38	0.97	−3.12	4.86
TMY1 (kg)	28,867	9851.28	2034.32	2938.00	17,944.00
TMY2 (kg)	28,867	10,800.60	1900.98	3094.00	17,470.00

[a] MY1 is the test-day milk yield of first period (5–60 DIM) of first lactation; MY2 is the test-day milk yield of second period (61–120 DIM) of first lactation; MY3 is the test-day milk yield of third period (121–180 DIM) of first lactation; LP is the lactation persistency of milk yield in first lactation; TMY1 is the total milk yield of first lactation; TMY2 is the total milk of second lactation.

mastitis events in this study were slightly higher than those reported by Parker Gaddis et al. (2014) in a similar dataset (9.53% and 10.24% in parities 1 and 2, respectively). The mean (standard deviation) of TMY1 in parity 1 and TMY2 in parity 2 were 9851.28 (2034.32) kg, and 10,800.60 (1900.98) kg respectively (Table 2).

3.1. Recursive effects

Posterior distribution of recursive effects from liability to mastitis to TD milk yields of three lactation periods from the LAC1 series of analyses (LAC1.A, LAC1.B, LAC1.C analysis using First-Lactation dataset) are shown in Fig. 1(A) and that of TD milk yields to liability to mastitis in the following lactation period are shown in Fig. 1(B); the posterior mean, standard deviation (SD) and 95%

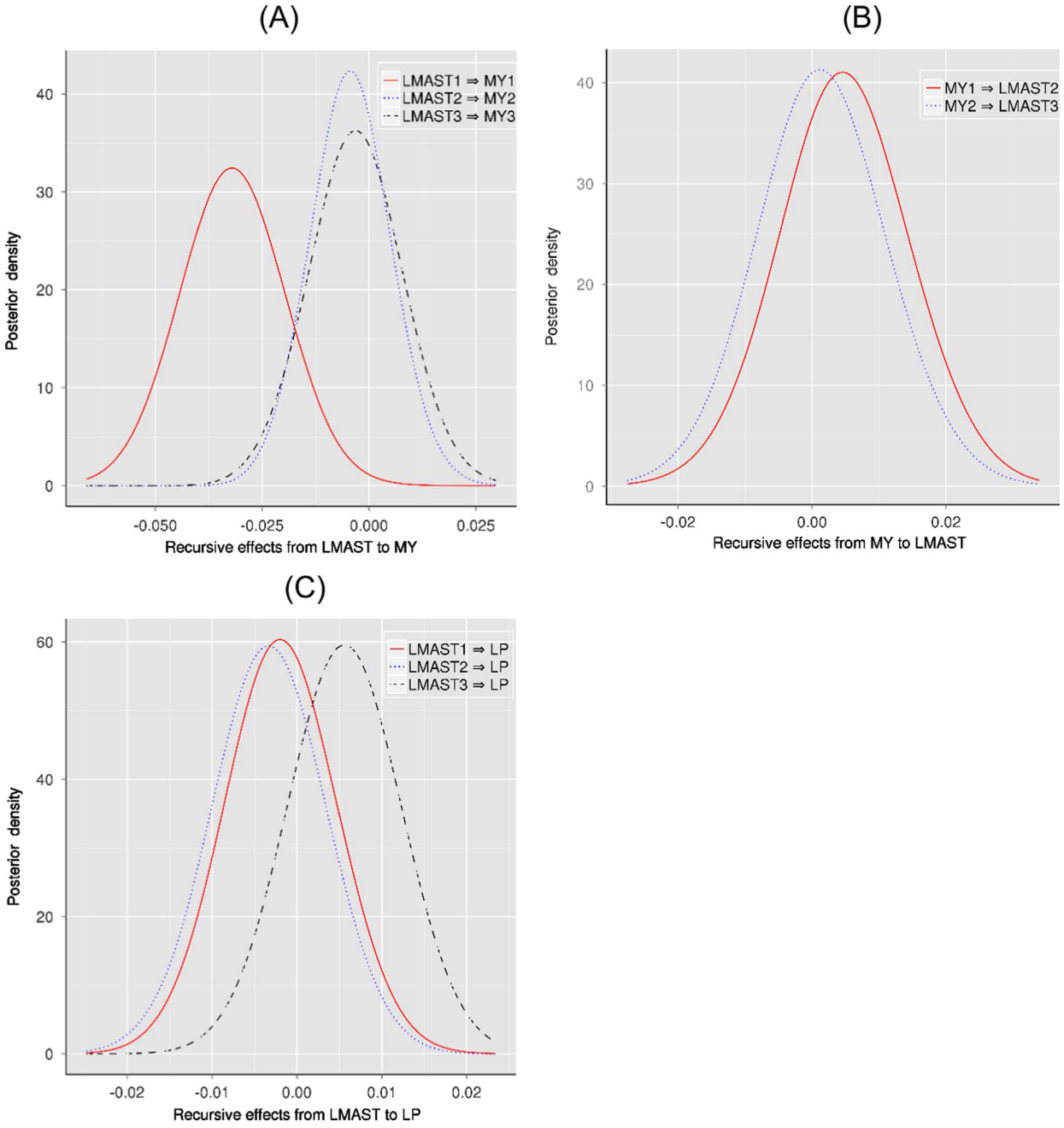

Fig. 1. Recursive effects between milk yields and liability to mastitis in three different periods of First-Lactation (5–60, 61–120, and 121–180 days in milk): (A) Recursive effects from liability to mastitis (LMAST1, LMAST2, LMAST3) to milk yields (MY1, MY2, MY3) of corresponding period of First-Lactation; (B) Recursive effects from milk yields (MY1 and MY2) to liability to mastitis (LMAST2 and LMAST3) of corresponding period of First-Lactation; (C) Recursive effects from liability to mastitis (LMAST1, LMAST2, LMAST3) to lactation persistency of milk yield (LP).

Table 3
Posterior mean, standard deviation (SD), and 95% highest posterior density interval (95% HPD) of causal relationships between liability to mastitis, milk yields, and lactation persistency.

Traits[a]	Recursive effects			
	Liability scale			Observable scale
	Mean	SD	95% HPD	Mean
LAC1.A				
LMAST1 → MY1	−0.032	0.010	[−0.051; −0.013]	−0.24 kg
LAC1.B				
MY1 → LMAST2	0.005	0.008	[−0.011; 0.021]	
LMAST2 → MY2	−0.004	0.008	[−0.021; 0.010]	−0.09 kg
LAC1.C				
MY2 → LMAST3	0.001	0.008	[−0.015; 0.017]	
LMAST3 → MY3	−0.003	0.009	[−0.020; 0.016]	−0.08 kg
LAC1.D				
LMAST1 → LP	−0.002	0.005	[−0.013; 0.008]	−0.01 LP units
LMAST2 → LP	−0.003	0.005	[−0.015; 0.007]	−0.01 LP units
LMAST3 → LP	0.006	0.005	[−0.005; 0.016]	0.02 LP units
LAC12				
LM1 → TMY1	−0.031	0.021	[−0.087; 0.028]	−0.24 kg
LM1 → LM2	0.123	0.033	[0.058; 0.186]	
LM1 → TMY2	0.018	0.039	[−0.056; 0.096]	0.09 kg
TMY1 → LM2	−0.005	0.015	[−0.035; 0.022]	
TMY1 → TMY2	0.740	0.009	[0.722; 0.755]	
LM2 → TMY2	−0.119	0.04	[0.038; −0.195]	−0.83 kg

[a] Liability to mastitis in first parity divided into three periods (LMAST1, LMAST2, LMAST3); test-day milk yields (MY1, MY2, MY3); Lactation persistency of milk yield denoted as LP; liability to mastitis in lactation 1 and 2 denoted as LM1 and LM2. Total amount of milk yield in first and second lactation denoted as TMY1 and TMY2.

posterior density interval (95% HPD) are shown in Table 3. The graphical representation of causal structure assumed and the posterior means obtained for LAC1 series are shown in Fig. 3.

The recursive effects from liability to mastitis to milk yields were between −0.032 and −0.003. Among the recursive effects from liability from mastitis to milk yields, only the recursive effect from LMAST1 to MY1 did not include zero in 95% HPD credible interval. Posterior means of structural coefficients indicate a negative recursive effect of liability to mastitis to TD milk yields. An increase in 1-unit of liability to mastitis decreased TD milk yields by 0.032, 0.004, and 0.003 kg per day, in lactation period 1, 2, and 3, respectively. The decrease in TD milk yield was higher in period 1 but similar for period 2 and 3. This may be interpreted as cows affected by mastitis during the early lactation period might have acquired some immunity against mastitis causing pathogens, thereby reducing the effect of mastitis in milk yields during successive lactation periods. Wu et al. (2008) reported similar decrease in TD milk yields in Norwegian Red cows with clinical mastitis. In the observable scale, the difference in mean MY1, MY2 and MY3 between the sick cows due to mastitis and healthy cows in our study were −0.24 kg, −0.09 kg and −0.08 kg per day for lactation periods 1, 2, and 3, respectively. Based on results, an increased liability to mastitis slightly reduces milk yield at the following TD. This result is in agreement with a study by Wu et al. (2008), in which they reported the presence of a causal relationship between mastitis incidence and milk yield production. Estimates of structural coefficients obtained were also similar. Several other authors have reported the causal relationship between somatic cell score (SCS) and milk yield (de los Campos et al., 2006; Jamrozik et al., 2010; Wu et al., 2007) and found that increases in SCS decreased the milk yield production. These results were also reflected in our study because SCS can be considered as an indicator of udder infection (Jamrozik et al., 2010) and high SCS is often associated with clinical mastitis cases (Shook and Schutz, 1994). High genetic correlations between SCS and mastitis ranging from 0.63 to 0.85 (Heringstad et al., 2006; Koeck et al., 2012a, 2012b) have been reported in literature.

Based on the recursive effects from TD milk yields to liability to mastitis in the following lactation period (e.g. MY1 → LMAST2), it was concluded that a weak positive relationship might exist, nonetheless zero was included in the 95% HPD credible region (Table 3). This may be an indication of the fact that the increase in TD milk production in lactation period 1 and 2 had no effect on occurrence of mastitis events. It is otherwise possible that our data were insufficient to estimate the true recursive effects between TD milk yields and liability to mastitis.

Posterior distribution of recursive effects from liability to mastitis of lactation periods 1, 2 and, 3 to LP are shown in Fig. 1(C); the posterior mean, standard deviation (SD) and 95% HPD are shown in Table 3. All the 95% HPD for the structural coefficients obtained in this analysis included zero in the credible interval. Posterior means of structural coefficients indicate a weak effect of liability to mastitis of each period to LP. An increase of 1-unit of liability to mastitis decreased LP by 0.002 (LMAST1 → LP) and 0.003 (LMAST2 → LP) LP units and increased LP by 0.006 (LMAST3 → LP) LP units, thus indicating that a mastitis event (LMAST1 and LMAST2) happening in a cow's early lactation period would marginally affect persistency while late mastitis (LMAST3) would slightly increase persistency. Mastitis events occurring at the beginning of the lactation might compromise later production more than those occurring possibly in part because in late lactation cows may have enough energy reserves to utilize slowly and efficiently to maintain their production (Ferris et al., 1985).

The posterior distribution of direct recursive effects from LM1 to TMY1, LM2, and TMY2 are shown in Fig. 2(A); from TMY1 to LM2 and TMY2 are shown in Fig. 2(B); from LM2 to TMY2 is shown in Fig. 2(C), and the posterior mean, SD, and 95% HPD are shown in Table 3 (Fig. 3). The causal structure assumed and the posterior means obtained for LAC12 series are shown in Fig. 4. The results show how the direct recursive effect from LM1 to TMY1 is negligible. The direct recursive effect from LM1 to LM2 had a positive posterior mean of approximately 0.123 liability unit increase of LM2 for a 1-unit increase of LM1. The indirect effect of LM1 to LM2 through the mediating effect of TMY1 was likewise weak. The overall causal effect of LM1 to LM2 was positive (0.124 liability unity increase of LM2 for a 1-unit increase of LM1). A cow with a mastitis infection in first parity would have an increased risk of incurring in mastitis in second parity due to the direct causal effect of the first event on the second. The direct recursive effect of LM1 to TMY2 was positive with approximately 0.018 kg per day increase of TMY2 for a 1-unit increase of LM1. The indirect recursive effect of LM1 to TMY2 was negligible. Thus cows with mastitis events in first lactation would produce a slightly higher amount of milk in second lactation compared to cows which were assumed healthy in this analysis. It should be noted here that an increase in milk yield in second lactation for the cows having mastitis problem in first lactation could be due to other unidentified management effects in second lactation such as additional care or better nutrition, or the cows that were assumed healthy (no mastitis event) in second lactation may have other health events affecting milk yield not accounted in the current analysis. The direct recursive effect of LM2 to TMY2 was negative with approximately 0.119 kg per day decrease of TMY2 for a 1-unit increase of LM2.

The direct causal effect of TMY1 on LM2 had negligible effect. The direct recursive effect of TMY1 on TMY2 had a positive

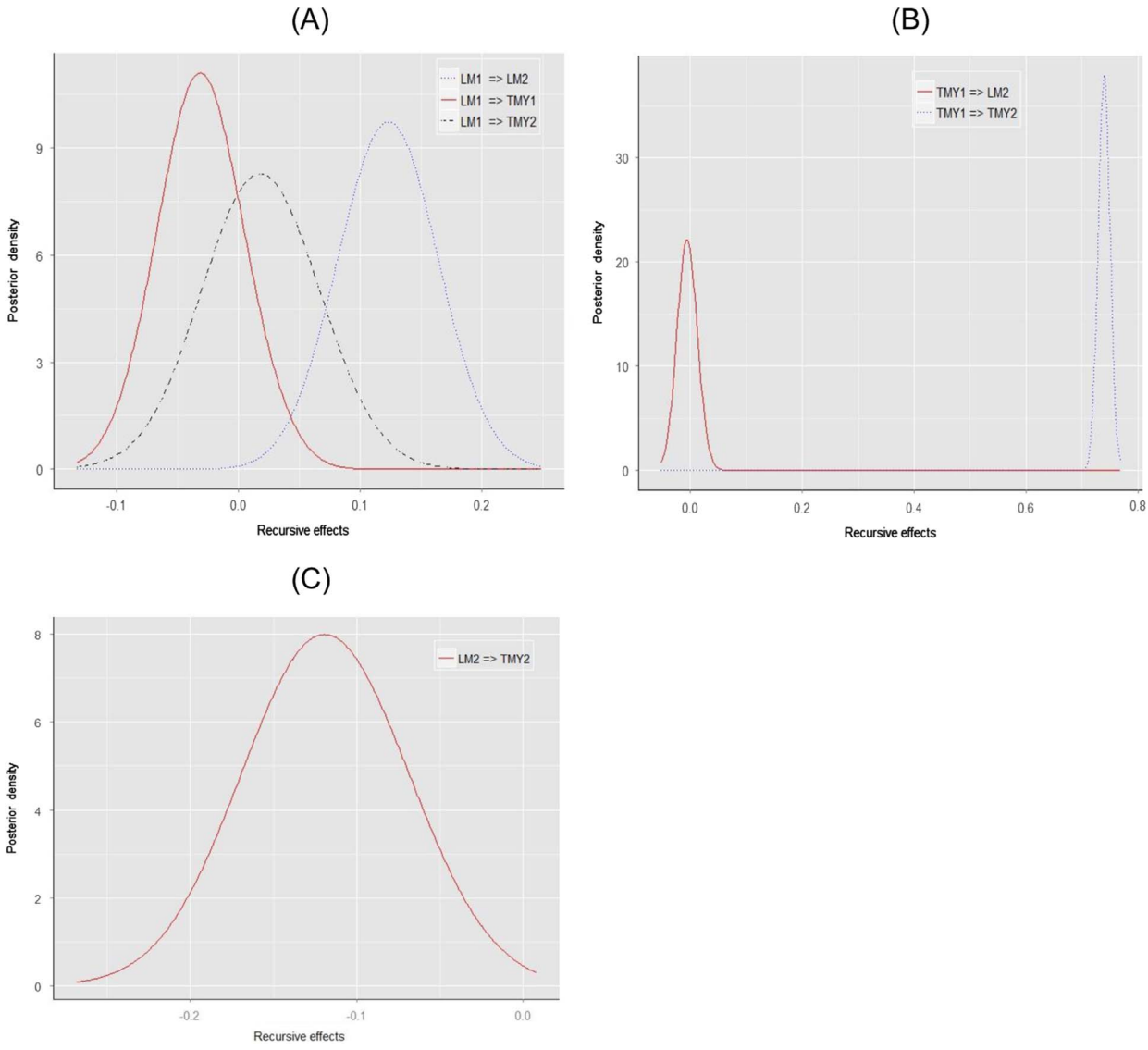

Fig. 2. Recursive effects between liability to mastitis events between parity 1, 2, total milk yield of first parity (TMY1) and second parity (TMY2): (A) Recursive effects from liability to mastitis in parity 1 (LM1) to liability to mastitis in parity 2 (LM2), LM1 to TMY1 and LM1 to TMY2; (B) Recursive effects from TMY1 to LM2, TMY1 to TMY2; (C) Recursive effects from LM2 to TMY2.

recursive effect of approximately 0.74 kg per day increase of TMY2 for a 1-unit increase of TMY1.

3.2. Heritabilities and genetic correlations

Posterior mean, SD, and 95% HPD heritabilities of mastitis events and milk yields of all three lactation periods of first lactation and LP are shown in Table 4. The posterior mean of heritabilities for LMAST1 (0.04), LMAST2 (0.07) and LMAST3 (0.04) were slightly lower than the study done by Wu et al. (2008) using recursive Gaussian threshold model for Norwegian Red cows. Heritabilities in that study of liability to clinical mastitis (LCM) for three periods of lactation were 0.067 (LCM1), 0.094 (LCM2) and 0.079 (LCM3), respectively. The lower heritabilities of mastitis in this study could be due to the fact that no selection was performed in respect to health-related traits in the US Holstein population, and also may be due to the use of farmer recorded data in estimating heritability. Lower estimate of heritability of mastitis (0.003) was also reported in the study of farmer observed health data of Austrian Fleckvieh cows by Koeck et al. (2015). The posterior mean of heritabilities for MYs ranged from 0.12 to 0.24. These estimates of heritabilities for MYs were similar to those estimated by Wu et al. (2008). The posterior mean of heritability for LP was approximately 0.14 and fell within the range of previous estimates of heritability for LP. Gengler (1996) reported heritability for LP of 0.14 for Holstein cows. Cole and VanRaden (2006) estimated the heritability of LP equal to 0.10. Posterior mean, SD, and 95% HPD of heritabilities for mastitis events in first and second lactation and TMY are shown in Table 4. The posterior mean of heritabilities for LM1 and LM2 were 0.04. These estimates of heritabilities were lower than that reported by Zwald et al. (2006) using producer-recorded data where heritability of liability to mastitis for first parity was 0.12 and for second parity was 0.10. Heritability estimates of liability to mastitis in the present study were in agreement with Parker Gaddis et al. (2014) where they reported a heritability of 0.06 for mastitis in first parity cows and 0.03 for mastitis in later parity cows using producer-recorded dataset. The posterior mean of heritability for TMY1 and TMY2 were 0.22 and 0.18 respectively. Carlen et al. (2004) reported heritability estimate of 305-day milk yield of first and second lactation of 0.34 and 0.25 respectively, in the study done in Swedish Holstein cows. Similar heritability estimates ranging from 0.19 to 0.25 of 305-day milk yield across three parities in small and large herds of

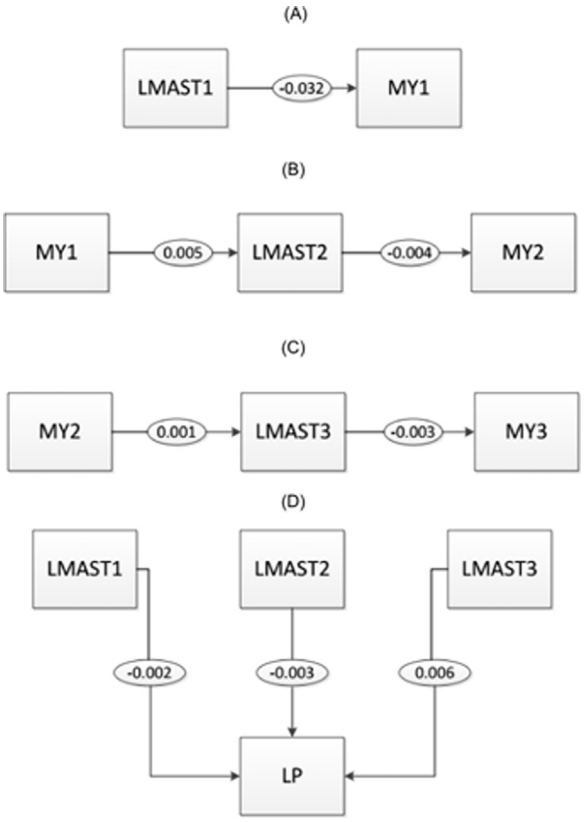

Fig. 3. Acyclic graphical representation of causal structure assumed and posterior means obtained for causal effects between milk yields and liability to mastitis in three different periods of First–Lactation (5–60, 61–120, and 121–180 days in milk): (A) Causal structure assumed in first period between liability to mastitis (LMAST1) and milk yield (MY1); (B) Causal structure assumed between milk yield (MY1) of first period, liability to mastitis (LMAST2) and milk yield (MY2) of second period; (C) Causal structure assumed between milk yield (MY2) of second period, liability to mastitis (LMAST3) and milk yield (MY3) of third period; (D) Causal structure assumed between liability to mastitis (LMAST1, LMAST2, LMAST3) to lactation persistency of milk yield (LP).

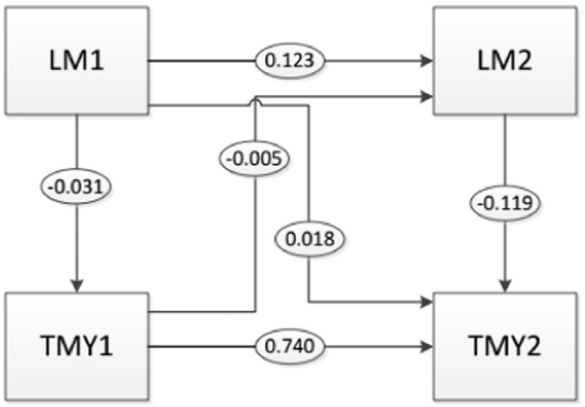

Fig. 4. Acyclic graphical representation of causal structure assumed and posterior means obtained between liability to mastitis events between parity 1 (LM1), parity 2 (LM2), total milk yield of first parity (TMY1) and second parity (TMY2).

Holstein cows in US was reported by Tsuruta et al. (2015).

Posterior means, SD and 95% HPD genetic correlations between mastitis and between mastitis event and milk yields and between mastitis event and LP are shown in Table 5. Posterior means of genetic correlations among mastitis events in three lactation periods of first lactation were all positive. Genetic correlations between LMAST1 and LMAST2, LMAST1 and LMAST3, and LMAST2 and LMAST3 were 0.58, 0.45, and 0.59, respectively. These

Table 4
Posterior mean, standard deviation (SD), and 95% highest posterior density interval (95% HPD) of heritability of liability to mastitis, milk yields (MY), and lactation persistency, and total milk yield of first lactation (TMY1) and second lactation (TMY2).

Traits[b]	Heritability[a]		
	Mean	SD	95% HPD
LMAST1[c]	0.04	0.01	[0.020; 0.070]
LMAST2[c]	0.07	0.02	[0.034; 0.104]
LMAST3[d]	0.04	0.01	[0.017; 0.058]
MY1	0.12	0.01	[0.091; 0.141]
MY2[b]	0.13	0.02	[0.104; 0.161]
MY3	0.24	0.02	[0.203; 0.281]
LP	0.14	0.02	[0.114; 0.172]
LM1	0.04	0.01	[0.018; 0.065]
LM2	0.04	0.02	[0.013; 0.075]
TMY1	0.22	0.01	[0.198; 0.242]
TMY2	0.18	0.01	[0.145; 0.204]

[a] Heritability computed as $h^2=\frac{4\sigma_s^2}{\sigma_s^2+\sigma_h^2+\sigma_e^2}$, where σ_s^2 is the sire additive genetic variance, σ_h^2 is the herd environmental variance, σ_e^2 is residual variance.

[b] Liability to mastitis in first lactation divided into three periods (LMAST1, LMAST2, LMAST3); test-day milk yields (MY1, MY2, MY3); Lactation persistency of milk yield denoted as LP; liability to mastitis in lactation 1 and 2 denoted as LM1 and LM2. Total amount of milk yield in first and second lactation denoted as TMY1 and TMY2 respectively.

[c] Heritability of liabilities of mastitis were reported from LAC1.D analysis.

[d] Heritability of MY2 was reported from LAC 1.B analysis.

Table 5
Posterior mean, standard deviation (SD), and 95% highest posterior density interval (95% HPD) of genetic correlation between liability to mastitis, milk yields, and lactation persistency.

Traits[a]	Genetic Correlation		
	Mean	SD	95% HPD
LMAST1 and MY1	0.21	0.20	[−0.191; 0.612]
LMAST2 and MY1	−0.14	0.20	[−0.517; 0.260]
LMAST2 and MY2	−0.15	0.19	[−0.532; 0.237]
LMAST3 and MY2	0.44	0.20	[0.084; 0.816]
LMAST3 and MY3	0.43	0.20	[0.046; 0.780]
LMAST1 and LMAST2	0.58	0.15	[0.268; 0.814]
LMAST1 and LMAST3	0.45	0.16	[0.134; 0.745]
LMAST2 and LMAST3	0.59	0.13	[0.342; 0.820]
LMAST1 and LP	0.008	0.17	[−0.316; 0.355]
LMAST2 and LP	0.003	0.15	[−0.291; 0.289]
LMAST3 and LP	0.20	0.15	[−0.068; 0.502]
LM1 and LM2	0.48	0.23	[−0.149; 0.526]
LM1 and TMY1	−0.004	0.20	[−0.042; 0.036]
LM1 and TMY2	−0.01	0.02	[−0.060; 0.035]
TMY1 and LM2	0.006	0.02	[−0.031; 0.043]
TMY1 and TMY2	0.59	0.10	[0.286; 0.785]
LM2 and TMY2	−0.001	0.02	[−0.038; 0.041]

[a] Liability to mastitis in first lactation divided into three periods (LMAST1, LMAST2, LMAST3); test-day milk yields (MY1, MY2, MY3); Lactation persistency of milk yield denoted as LP; liability to mastitis in lactation 1 and 2 denoted as LM1 and LM2. Total amount of milk yield in first and second lactation denoted as TMY1 and TMY2 respectively.

estimates of genetic correlations are moderate and were lower than those obtained by Wu et al. (2008). The genetic correlations between LMAST1 and MY1, LMAST2 and MY1, LMAST2 and MY2, LMAST3 and MY2, and LMAST3 and MY3 were 0.21, −0.14, −0.15, 0.44, and 0.43, respectively. Among these posterior means only genetic correlations between LMAST3 and MY2 and LMAST3 and MY3 were well defined and others include zero in their 95% HPD credible interval. The genetic correlations between LMAST1 and LP, LMAST2 and LP, and LMAST3 and LP were 0.008, 0.003, and 0.20, respectively, and included zero in the 95% HPD credible interval.

Posterior mean, SD, and 95% HPD genetic correlations between mastitis events of first and second lactation, TMY1 and TMY2 were shown in Table 5. The genetic correlation between LM1 and LM2 was 0.48. The genetic correlation between TMY1 and TMY2 was 0.59. The genetic correlations of mastitis events with total milk yields were negligible.

4. Conclusion

Causal relationships between mastitis events along with production traits such as milk yields and lactation persistency can help us to identify the real biological pathway of disease process and its consequences in production traits. The causal relationship between mastitis events and milk yields showed that with an increase in mastitis events there would be a decline in milk production. There is little to no impact of mastitis events on lactation persistency of milk yield. The causal relationship among mastitis events in first and second lactation found in this study indicate that having a mastitis event in first lactation is likely to increase the risk of a mastitis event in second lactation. Based on the causal relationships between clinical mastitis events and production traits, economic loss from clinical mastitis events can be mitigated by addressing proper disease management strategies such as providing proper vaccination to boost immunity, proper treatment of infected cows, feeding improved feed stuffs, having better nutritional standards to cope with disease, etc. Greater insight into relationships between mastitis and production traits could be achieved by incorporating other factors in a recursive model such as risk factors of mastitis, herd demographics, housing conditions, and feeding procedures.

Conflict of interest statement

The authors declare that there is no conflict of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Author's contribution

C. Maltecca, F. Tiezzi, and K. Dhakal designed the research. J.S. Clay provided the data for research. K.Dhakal performed the statistical analyses and wrote the first draft of the manuscript. F. Tiezzi contributed in statistical analyses. C. Maltecca, F. Tiezzi, and K. Dhakal contributed to the interpretation and discussion of the results. All authors approve the final draft of manuscript for publication.

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