# Genetic and non-genetic factors of disease and fertility problems in dairy cattle

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**Summary:** Genetic selection in dairy cattle have been successfully applied to increase milk production. Further understanding of the genetic and non-genetic factors related to disease and reproduction will support progress in these traits. In this study, two response variables were evaluated: a) disease problems encompassing diseases typically caused by pathogens such as metritis, clinical endometritis, mastitis, and respiratory disorders; and b) fertility problems identified indicators of reproductive performance. The models used to describe disease and fertility problems included the fixed effects of season, U.S. region, body condition score at 35 days in milk, calving problems, and metabolic problems. These variables were significant with disease and fertility problems. Results showed that disease-related explanatory variables were associated with fertility problems in cows. Heritability estimates were 0.05 and 0.07 for fertility and disease problems, respectively. The genetic parameter estimates can be used in selection programs.

*Keywords: reproduction, disorder, Holstein, selection*

## Introduction

Health management of dairy cattle is challenging because of the multifactorial nature of many diseases (LeBlanc *et al.*, 2016). Prevention and treatment for mastitis and infertility in dairy cattle have been explored (LeBlanc *et al.*, 2016). Programs that consider multiple diseases that affect dairy cows are necessary. A broad range of health considerations should be evaluated, including diseases that are caused by pathogens because their contagious classification decreases productivity (LeBlanc *et al.*, 2016).

In efficient reproductive herds, cows become pregnant shortly after calving and produce one calf per year (Morton, 2010). Adequate reproductive performance would require high pregnancy rates per artificial insemination (AI) and low numbers of anovular cows as they prevent successful AI (Morton, 2010; Ribeiro *et al.*, 2013). Health problems postpartum and low body condition score (BCS) could cause anovulation, decrease pregnancy rates per AI, and increase the risk for pregnancy loss which highly affects overall pregnancy result (Ribeiro *et al.*, 2013; Santos *et al.*, 2011). Over time, general consequences for low reproductive performance is the decrease in milk production, the delay of calving events, the increase in costs with treatment, and premature culling from the system.

Some diseases can affect reproductive performance of cows. Ribeiro *et al*. (2013) showed that

metritis, respiratory disorders, and digestive problems reduced estrous cyclicity, while calving problems, metritis, clinical endometritis, and digestive problems decreased pregnancy rate per AI. Metritis and clinical endometritis are both characterized by abnormal uterine discharge. Metritis occurs during the first three weeks after calving, while in clinical endometritis purulent vaginal discharge is detected after 21 days postpartum (Sheldon *et al.*, 2009). Respiratory disease diagnostic can be attributed to multiple causes like a viral or bacterial infection (Gaeta *et al.*, 2017; Tuncer & Yesilbag, 2015). Mastitis is characterized by mammary gland infection, abnormal milk presenting elevated somatic cell count and changes in organoleptic characteristics, and inflammatory reaction of the tissue (Ribeiro *et al*., 2013).

The study of large datasets including disease and fertility measurements in dairy cattle can help understand the causes of poor health and fertility performance and aid in the development of genetic improvement, prevention programs, and treatments. In this study, a large dataset that encompasses dairy cattle fertility and disease information was evaluated. Two new traits, one identifying disease problems and the other identifying fertility problems were analysed. The genetic variation of these type of traits has been successfully introduced in other studies involving dairy health and reproduction (Weller *et al*., 2017). The combination of fertility and disease measurements reflects that both fertility and infectious diseases are associated with many factors. The non-genetic and genetic factors associated with both traits were assessed and genetic parameters were estimated.

## Materials and Methods

### Animals

Fertility and disease records were collected on 6,283 Holstein cows across four U.S. regions: the U.S Pacific (California), Southeast (Florida), Midwest (Minnesota) and, Southwest (Texas). Cows were the offspring of 2,029 Holstein sires and raised on nine farms (3 in Midwest; 1 in Southeast; 3 in Pacific; 2 in Southwest). Cows were inseminated (using timed AI or estrous detection practices) and information on one calving event spanning two years (2013 and 2014) was recorded.

### Response variables

Two binary traits were evaluated using a mixed effects logistic model. The response variable fertility problems were coded 1 when at least one of the following events was recorded: no estrous cycling, days open higher than 100 days in milk (DIM), early loss of embryo between 32 and 60 days after second AI, no pregnancy 32 days after first insemination or no pregnancy 60 days after second artificial insemination. Otherwise, fertility problems was coded 0 for no problem. The variable disease status was coded 1 when at least one of the following events was recorded: metritis, clinical endometritis, mastitis at 60 DIM, or respiratory diseases at 60 DIM. Otherwise, disease status was coded 0. Metritis and clinical endometritis were evaluated according to vaginal mucous score at 7 DIM and 35 DIM, respectively. Mucous score varied in a range from 1 to 5 score: 0 = no mucous; 1 = crystalline; 2 = flecks of pus; 3 = mucopurulent < 50% pus; 4 = purulent, > 50% pus; 5 = watery, reddish/brownish fetid discharge. The cow was considerate metritic at 7 DIM with mucous score = 5 and at 35 DIM, mucous score = 1 and 2 was considerate clinical endometritis and metritic with a mucous score > 2.

### Explanatory variables

Explanatory variables included: calving problems and metabolic problems. Calving problems were coded 1 if at least one of the following events was recorded: dystocia, twins, stillbirth, or retained placenta. Metabolic problems were coded 1 if at least one of the following events was recorded: lameness at 60 DIM, subclinical ketosis at 30 DIM (BHBA concentration >1.0 mM), or displacement abomasum at 60 DIM. Otherwise, calving and metabolic problems were coded 0. Other fixed effects

evaluated included: lactation number (1, 2, 3, and 4+), season (summer and winter), U.S. region, and body condition score at 35 DIM (BCS35). The binary variable disease problems was also used as an explanatory variable for fertility problems. The sire of the cow measured was included as random effect. The analysis was performed using PROC Glimmix in SAS software (Saxton & Institute, 2004).

## Results and Discussion

Understanding the factors that influence dairy cattle health can help to elucidate methods for prevention of diseases such as metritis, endometritis, and mastitis that remain elusive. In this study, approximately 65% of the cows presented at least one fertility problem, and 46% presented at least one disease problem. Region, season, BCS35, calving problems, and metabolic problems were associated (P-value < 0.05) with fertility and disease problems (Table 1). The odds of fertility problems increased with the odds of disease problems. This result is in agreement with a study that associated respiratory diseases with reproductive problems (Gagnon *et al*., 2017). Another study proposed that non-uterine diseases responsible for inflammatory-like changes in dairy cows could cause pregnancy loss, lower conception, or problematic calving events (Ribeiro *et al*., 2016).

Lactation number was not associated with fertility problems and was excluded from the model. Cows in the Midwest and Southeast regions had higher fertility problems whereas cows in the U.S. Pacific had lower fertility problems relative to cows in the Southwest (Table 1). The incidence of fertility problems was higher in summer than in winter. Almost 32% of the cows presenting fertility problems also presented a disease problem. Calving and metabolic problems were associated with both fertility and disease problems. The probability of fertility and disease problems decreased with higher BCS35 levels.

The lactation number was significant and positively associated with disease problems (Table 1). Cows in the Southeast region had significantly higher probability of disease problems whereas cows in the Midwest and U.S. Pacific had lower probability of disease problems relative to cows in the Southwest. The incidence of disease problems was higher in winter than summer.

*Table 1. Estimates of the odds of disease and fertility problems by explanatory variable.*

| Variables | Fertility problems | | Disease problems | |
|---|---|---|---|---|
| Level | Estimate | P-value[1] | Estimate | P-value |
| [2]Lactation 1 | - | - | 0.7341 | S |
| [3]Region - Midwest | 0.0857 | NS | -1.2232 | S |
| Region - Southeast | 0.0793 | NS | 0.2056 | S |
| Region - U.S. Pacific | -0.2846 | S | -0.7715 | S |
| [4]Season Sum-Win | 0.2893 | S | -0.2553 | S |
| [5]BCS35 | -0.2554 | S | -0.6220 | S |
| [6]Calving problems | -0.1491 | S | -0.9838 | S |
| [7]Metabolic problems | -0.1880 | S | -0.2660 | S |
| [8]Disease problems | -0.2628 | S | - | - |
| Heritability | 0.0419 | 0.05 | 0.0625 | 0.07 |

[1]S is significant at P-value <0.05.
[2]Lactation 1: lactation 1 relative to 4+.
[3]Region: the estimate provided is from Midwest, Southeast, and U.S. Pacific relative to Southwest.
[4]Season Sum-Win: summer relative to winter.
[5]BCS35: body condition score at 35 DIM.
[6]Calving problems (no): no problem relative to problems.
[7]Metabolic problems (no): no problem relative to problems.
[8]Disease problems (no): no problem relative to problems

Large dairy dataset can be efficiently used to study complex traits like disease and fertility

problems to improve management (LeBlanc *et al*., 2006). In previous studies on this data, heritability estimate for the individual diseases analyzed individually was on average 0.27. Heritability estimates for fertility and disease problems were 0.05 and 0.07, respectively. These results are consistent with another study that reported low heritability (0.001-0.05) estimates for reproductive traits (Carthy *et al*., 2015). The heritability for disease problems found in the present study is also in agreement with previously reported estimates ranging from 0.03 to 0.14 for metritis, lameness, displaced abomasum, ketosis, and mastitis (Zwald *et al*., 2004).

Studies of genetic markers and genetic selection for health and disease resistance have already shown an association between immune response and postpartum issues in dairy cattle (LeBlanc *et al*., 2006). The immune system is especially important to sustain mammary and uterine health, consequently affecting the reproductive system. These studies have the advantage of including more traits in the selection indices and help to elucidate genes that are involved with disease and fertility processes.

The genetic parameter estimates for reproductive and disease problems offer insights to develop an effective approach to lower the incidence of overall diseases through selection. In conclusion, these traits can be incorporated into selection indices, and genetic estimates will be supplemented with genomic information in the future.

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