The use of herd management data for development of genetic evaluations to enhance disease resistance in dairy cattle: Preliminary Analysis

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Abstract

Enhancing disease resistance in dairy cattle has economic and welfare benefits and can contribute positively to societal acceptance of agriculture. There are several diseases, including enzootic bovine leukosis (**EBL**), Johne's disease (**JD**), calf respiratory problems, and calf diarrhea, that impact dairy farm profitability for which no genetic evaluations are currently available in Canada. The overall goal of this project is to assess the potential for genetic selection for EBL, JD, and calf respiratory problems and diarrhea, and ultimately incorporate them into a novel resilience index.

EBL and JD are contagious diseases caused by single pathogens, bovine leukemia virus (**BLV**) and *Mycobacterium avium* ssp. *Paratuberculosis* (**MAP**), respectively, while respiratory problems and diarrhea are caused by various pathogens. Diseases like EBL and JD have a clear impact on cow productivity, health, and longevity. Unfortunately, these diseases are untreatable, and a commercially available vaccine has yet to be developed. Respiratory problems and diarrhea are the main causes of morbidity and mortality in calves. Not only are these calfhood diseases a major welfare concern, but they also impact the profitability of the farm due to costs of treatment and long-term effects on performance.

Animal level data related to EBL (n=84 653 cows), JD (n=223 475 cows), and calf diseases (n=69,385 calves) were provided by Lactanet Canada (Guelph, ON, Canada). For EBL, individual cow milk ELISA test data from 988 herds were analyzed. Eighty-seven percent of herds had at least one test-positive animal for BLV, and an average of 39% of animals in those herds were test-positive. Heritability for EBL was estimated to be 0.09 (SE=0.01). Cows test-positive for MAP were present in 40% of the 2 679 herds in the JD dataset, and those infected herds had an average test-positive prevalence of 3%. Genetic parameter estimation for JD is currently being performed. Respiratory problem records were available for 644 herds, where an average of 15% of calves had at least one recorded case. Records from 425 herds were analyzed for diarrhea, with an average of 12% of calves having at least one case recorded. Heritability estimates for respiratory problems and diarrhea were 0.03 (SE=0.003) and 0.01 (SE=0.001), respectively.

While preliminary, these results provide the groundwork for further development of genetic evaluations for disease resistance in Canadian dairy cattle. Incorporating these traits into the Canadian dairy genetic evaluations may allow for the opportunity to select animals with enhanced disease resistance.

Key words: calf health, diarrhea, Johne's disease, enzootic bovine leukosis, resilience, respiratory problems

Introduction

Animal health and welfare are priorities in the Canadian dairy industry, and although it has been traditionally more difficult to make genetic improvements in fitness traits compared to production or conformation traits, advancements in genomic technologies have made it more achievable. In 2007, a national system to collect 8 specific dairy cow disease traits was launched in Canada and led to genetic evaluations for Mastitis Resistance, Metabolic Disease Resistance, Hoof Health, and Fertility Disorders. These evaluations provide options to producers to select for healthier, more productive cows. However, there is still a lack of genetic evaluations for several other major health traits, such as enzootic bovine leukosis (**EBL**), Johne's disease (**JD**), and calf health traits such as diarrhea and respiratory problems. Performing genetic evaluations for these additional traits can strongly contribute to the profitability and successes of the Canadian dairy industry.

Enzootic bovine leukosis is a chronic, contagious disease caused by the bovine leukemia virus (**BLV**) which spreads through the transmission of infected lymphocytes (Bartlett et al., 2014; Berg et al., 2015; Kuczewski et al., 2021). Infection with EBL can lead to decreased fertility and production, a lower immune response to vaccinations, higher susceptibility to other diseases, and consequently, premature culling. Johne's disease is an enteric infection caused by *Mycobacterium avium* ssp. *paratuberculosis* (**MAP**). Infection with MAP causes chronic intestinal inflammation leading to diarrhea and malnutrition, and ultimately death. In both EBL and JD, it can take years before signs develop (Tiwari et al., 2006; Frie and Coussens, 2015). Furthermore, infection by either pathogen is not preventable through commercially available vaccines, has no treatment, and the immune system generally lacks defences against infection (Berg et al., 2015; Tiwari et al., 2006). Although a vaccine for JD does exist, it is rarely used as it interferes with testing for Tuberculosis (Coad et al., 2013). Producers can test milk or blood samples for antibodies to BLV and MAP through enzyme-linked immunosorbent assay (**ELISA**) tests, but in the case of JD the test lacks sensitivity, making identification of positive animals difficult (Nekouei et al., 2015a; Tiwari et al., 2006). Overall, these challenges mean that breeding for resistance to EBL or JD may be a promising alternative control strategy (Abdalla et al., 2013; Brito et al., 2018).

Finally, while cow health and wellbeing has been a focus of research for a long time, calf health has been a lower priority. Disease events can affect a calf's ability to reach their full potential when they enter the milking herd (Heinrichs and Heinrichs, 2011). Furthermore, common calfhood diseases like diarrhea and respiratory problems account for 74% of pre-weaning calf mortality (Murray, 2011). Antibiotics and pain relief medications are sometimes used to treat these diseases and are not only costly, but with the growing concern over antimicrobial resistance, the use of antibiotics should be limited whenever possible (Svensson and Hultgren, 2008; Mohd Nor et al., 2013).

This project aims to further extend the health-related trait portfolio and add novel disease traits such as EBL, JD, and calf health related traits to Canadian genetic evaluations. The objective of this study is to evaluate the potential for genetic selection of novel disease traits in Canada by estimating genetic parameters for each disease trait while also identifying barriers and providing recommendations to feeding this data into genetic evaluations. This will ultimately lay the groundwork to incorporate these disease traits into a novel resiliency index.

Materials and Methods

Data structure

Data were provided by Lactanet Canada (Guelph, ON) based on results of ELISA tests performed on individual cow milk samples collected during routine milk recording herd test days at the producer's discretion (EBL and JD) or producer recorded observations of disease occurrence (calf health traits).

A total of 123 021 milk ELISA test records were available for EBL from 86 912 Holstein cows raised in 988 Canadian herds from 2007 to 2021. Similarly, 405 569 milk ELISA test records from 313 005 cows raised on 3 120 Canadian farms from 2007 to 2021 were provided for JD. These records contained herd and animal information as well as EBL or JD test results defined as positive, suspicious, or negative as per test kit instructions. A variety of commercially procured test kits were used depending on the year and location of the testing. EBL ELISA tests had an approximate sensitivity of 100% and specificity of 99% (Kuczewski et al., 2018) (Kuczewski et al., 2018), whereas JD ELISA tests had an approximate sensitivity of 30% and specificity of 99% (Norton et al.; Collins et al., 2006; Laurin et al., 2017).

Calf health data were voluntarily recorded by producers through management software. The dataset contained 69 385 Holstein calf disease records for respiratory problems and diarrhea, from 62 361 calves collected on 1 617 Canadian dairy herds from 2007 to 2020. Detailed herd information and pedigree data were also acquired from Lactanet Canada (Guelph, Ontario).

Data editing

The EBL dataset was edited to contain only one record per cow. For cows with multiple records, the first positive record was used to define them as sick. Cows with only negative test results were considered to be healthy. Suspicious results were excluded from this analysis due to the carryover effect that occurs when sampling with shared milk meters (Nekouei et al., 2015b). Contemporary groups (lactation-age at calving, year-season of calving and herd-year of calving) with fewer than 5 animals were removed.

The JD dataset was edited to contain only herds with a minimum annual 1% prevalence. Cows with multiple records were defined as sick if they had at least one positive test result and as healthy if they had only negative test results.

The calf health dataset was edited to only contain herd years with a minimum of one disease record per year. Repeated records of disease incidence were removed. Disease records must have occurred during the first six months of the calf's life. In addition, herds were required to have at least 3 years of consecutive data available, or to have records from 2019 and 2020. In the final dataset, data from 2007 and 2008 were removed after edits, meaning that data ranged from 2009 to 2020.

The final analyzed dataset for each trait is described in Table 1.

Statistical models and analysis

Preliminary analyses to estimate genetic parameters for EBL and calf health traits have been completed; those for JD are still in progress and will not be discussed further.

For EBL, records from lactations one to nine were included, and placed into classes (lactations 1, 2, 3, 4, 5+). Age at calving in months included nine classes (18-22, 23, 24, 25, 26-27, 28-36, 37-47, 48-58, and >59) and four seasons of calving were defined as January to March, April to June, July to September, and October to December. The animal linear model used to estimate genetic parameters for EBL is defined as follows:

$$y = Xb + Za + e$$

where y is a vector of EBL phenotypes (0= negative, 1= positive), b is a vector of fixed effects of year-season of calving (61 levels) and lactation-age class at calving (17 levels), a is a vector of random effects of herd-year of calving (2,502 herd-years) and additive genetic effects, e is a vector of random residuals, and X and Z are corresponding incidence matrices. Variance component estimation for EBL was performed using the AIREMLF90 program, within the BLUPF90 family of programs (Misztal et al., 2018).

Table 1. - Number of records and herds for each trait, in the final datasets.

Trait	Diseased	Healthy	Total Records	Herds
Enzootic bovine leukosis	31 420	53 233	84 653	926
Johne's disease	4 578	218 897	223 475	2 679
Calf diarrhea	18 887	101 857	120 744	425
Calf respiratory problems	43 281	212 502	255 783	664

Univariate threshold animal models with a probit link function were used for both calf traits. Bayesian analyses via Gibbs sampling algorithm with 1,000,000 iterations, 100,000 burn-in and 50 thinning interval were carried out. Analysis was performed using the THRGIBBS1F90 software from the BLUPF90 family of programs (Misztal et al., 2018). Convergence of all chains was achieved, based on the Heidelberger and Welch, and Geweke convergence diagnostic tests (Smith, 2007). The general form of the univariate model used for diarrhea and respiratory problems was defined as:

$$l = Xb + Za + e$$

where l is a vector of underlying liabilities corresponding to the binary observation (0= healthy, 1= diseased), b is a vector of systematic fixed effects of year-month born and herd, a is a vector of random additive genetic effects, e is a vector of random residuals, and X and Z are corresponding incidence matrices.

Results & Discussion

In this study, EBL was found in 87% of herds, defined by having at least one cow test positive in that year. The breakdown of number of herds testing for EBL per year can be seen in Figure 1. In general, there was an increasing occurrence of testing for EBL over time, with the exception of 2021, for which only two months of data were available. BLV positive herds had an average of 39% of animals test positive at any given time (Figure 2). This is consistent with literature values from across North America, reporting an average of 90% herd level prevalence and 40% within herd prevalence (Bartlett et al., 2013; Nekouei et al., 2015a; Norby et al., 2016). The ability to control and/or eradicate EBL from a herd would be of great benefit to producers. In Europe, test-and-cull strategies were effectively used in a concentrated effort to eradicate EBL over the course of several decades, though they generally started with much lower within herd prevalence than is currently seen in North America (Berg et al., 2015). Given the high prevalence of EBL found in this study, it is not economically feasible for producers to cull all infected cows fast enough to control the spread of EBL. Alternative control measure such as genetic selection may be a viable option for the Canadian dairy industry.

Heritability for EBL was estimated to be 0.09 (SE = 0.01), which is consistent with the heritability of 0.08 (SE = 0.01) previously estimated by Abdalla et al. (2013). Disease traits tend to have a low heritability due to a large environmental impact (Abdalla et al., 2013), but the 9% heritability estimated in this study shows that there is genetic variance which could be exploited to reduce incidence of EBL via genetic selection.

Though the EBL prevalence estimates evaluated in this study are consistent with literature values from North America, there is still a general lack of knowledge of when and how this infection is happening. Repeated records on the same animal could provide detailed insights such as when a cow becomes infected and their overall susceptibility. Overall, greater awareness of EBL in Canada could improve the number of producers testing for it and improve the overall data availability. Next steps for studying EBL involve exploring the relationship between EBL and other traits already evaluated in the Canadian national genetic evaluation system.

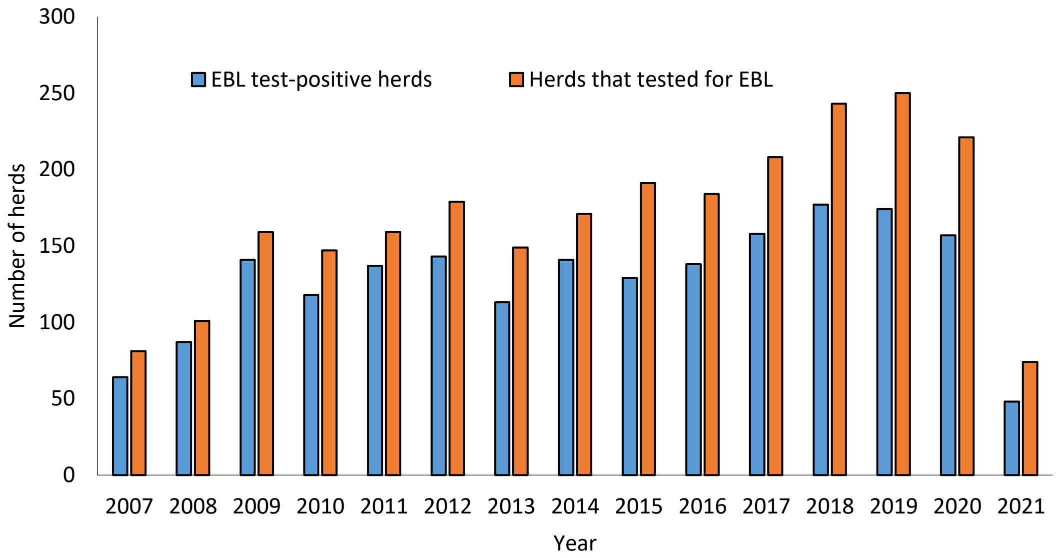

Figure 1. - Number of dairy herds in Canada with positive enzootic bovine leukosis (EBL) milk ELISA tests as indicated by at least one cow having a positive milk sample compared to the number of herds that test for EBL within each year.

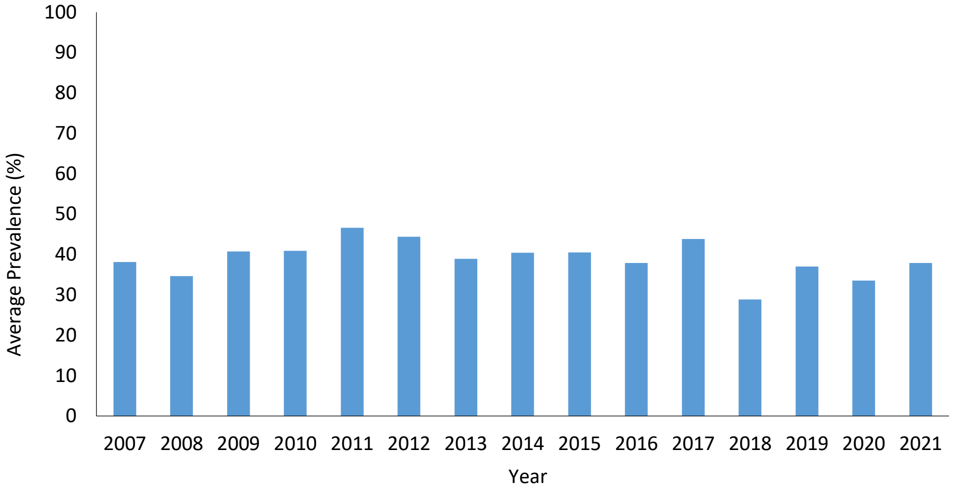

Figure 2. Prevalence of enzootic bovine leukosis within test-positive dairy herds in Canada

JD poses a similar challenge to EBL in regard to the long incubation period, with the added difficulty of testing for the disease. Unlike EBL, tests for JD have a high proportion of false-negatives due to the intermittent shedding of the MAP bacteria (Tiwari et al., 2006). In this study, 40% of herds which elected to test for JD had at least one positive test result. Within those herds, there was an average prevalence of 3%, but that is likely an artificially deflated value due to the low sensitivity of the test. More records on each animal over a longer time span could help identify disease despite intermittent shedding. Due to test and data limitations, true prevalence of JD in Canada was difficult to estimate. Next steps for studying JD include genetic parameter estimation and an exploration of the correlation between JD and other economically important traits.

In regard to calf health, on average, 12% and 15% of calves within a herd had at least one case of diarrhea and respiratory problems, respectively. Figure 3 shows the number of herds recording the data per year, and the trend in mean incidence rate across years, which was defined as the proportion of animals born in a specific herd year that became sick.

Studies generally estimate the incidence rate for diarrhea to be between 23-44% (Urie et al., 2018; Haagen et al., 2021; USDA 2010, 2018). This is higher than the range found in the current study, in which the highest mean incidence was 16% (2009; 54 herds), and the lowest was 12% (2020; 145 herds). In contrast, mean incidence rates for respiratory problems varied from 13% to 17%, which is slightly higher than that reported in the literature where the average incidence was around 12% (USDA 2010, 2018; Urie et al., 2018; Haagen et al., 2021).

In general, the number of herds recording calf respiratory problems and calf diarrhea increased over time (Figure 3). This is promising because it indicates that producers are starting to see the value of recording these traits and are more likely to record them in their herd management software. However, it should be acknowledged that only approximately 5% of herds in Canada are represented by this calf health data, and results should thus be interpreted with caution. Many farms choose to not record calf health events, or to not put them into the herd management software, or do not record them in a consistent enough manner to be used in genetic analysis. Based on the final datasets, the top 100 herds with the most records for each trait accounted for 88% of diarrhea records and 71% of respiratory problem records. This highlights that although many herds may be collecting this information, most of them are not doing so consistently and intensively, which needs to be improved. Herds without strict recording practices likely have had animals that were assumed healthy in the current study that were in fact sick. For example, some herds may only be collecting information on animals that required treatment and not all cases, impacting model performance and variance component estimation. An effort to encourage producers to record calf disease traits, which would require a collaboration between producers, industry, academia, and veterinarians to provide clear and concise recommendations to collect calf health information, would go a long way to improving data consistency and quality. This limited data and herd representation is a severe limit in this analysis and may explain the lower incidence of diarrhea found in this study compared to literature values.

Heritabilities for calf health traits were estimated on the liability scale and converted to the observed scale. Diarrhea was estimated to have a heritability of 0.01 (SE=0.001) and the estimated heritability for respiratory problems was 0.03 (SE=0.003). These heritabilities are lower than literature values, likely due to differences in data availability and recording practices (Henderson et al., 2011; Haagen et al., 2021). Information on calves was limited and did not include, for example, colostrum intake or birth weight, which are known to have an impact on disease incidence (Henderson et al., 2011). Model performance may be affected by those factors and could explain the lower heritabilities seen in this study. Next steps may include the use of genomic information or splitting the traits into specific time periods to improve model performance and parameter estimation.

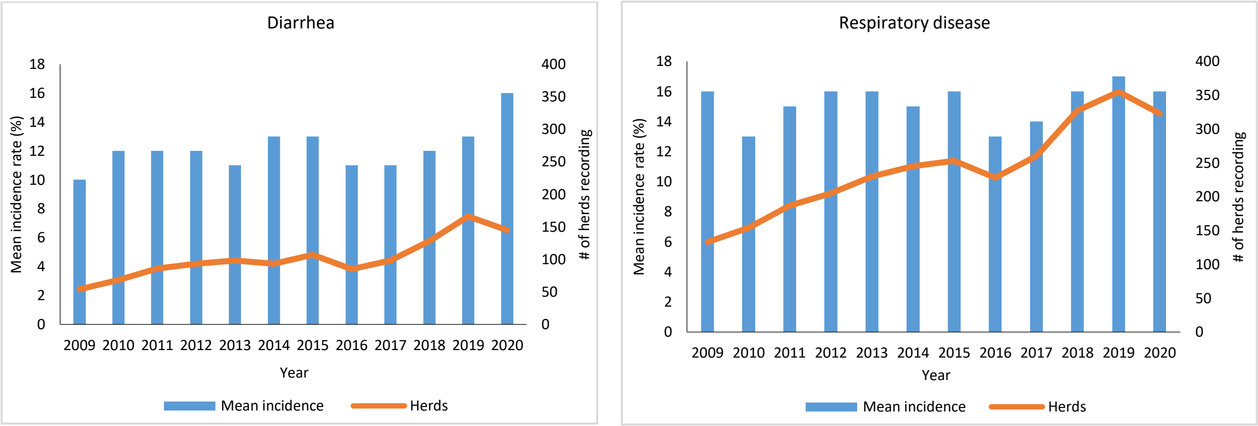

Figure 3. Mean incidence rates of diarrhea and respiratory problems in calves on Canadian farms and number of herds recording those traits.

Conclusions

Emerging issues related to animal welfare and social acceptability in the dairy industry have prompted efforts to improve animal health and welfare through breeding. We showed that calf health related traits (i.e. diarrhea and respiratory problems) and enzootic bovine leukosis are heritable and can be improved through genetic selection. However, increasing awareness and encouraging producers to test for and record health traits (enzootic bovine leukosis, Johne's disease, calf respiratory problems and diarrhea) is paramount. Challenges with data availability and consistency, especially for calf health related traits, will need to be addressed going forward.

This study serves as the groundwork to incorporate novel disease traits such as enzootic bovine leukosis, Johne's disease and calf diseases into Canadian genetic evaluations. Specifically, we showed that there was a genetic component to these novel disease traits and identified barriers that need to be overcome for the successful implementation of selection for enzootic bovine leukosis, Johne's disease, and calf health related traits.

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