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# Integration of epidemiology into the genetic analysis of mastitis in Swedish Holstein

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## ABSTRACT

Heritability of mastitis (and diseases in general) tends to be low. One possible cause is that no clear distinction can be made between resistant and nonresistant animals, because healthy animals include animals that have not been exposed to pathogens and resistant animals. To account for this, we quantified the prevalence of clinical mastitis (CM) and subclinical mastitis (SCM) in 2,069 Swedish Holstein herds as a measure of exposure. Herd prevalence averaged 26.5% for SCM and 6.4% for CM; 61% of the first lactations of 177,309 cows were classified as having at least one case of SCM and 10% as having CM. In a reaction norm approach, heritability of (S)CM was quantified as a function of herd prevalence of (S)CM. The best-fitting model was a second-order polynomial of first-lactation cow SCM as a function of herd prevalence SCM, and a first-order (linear) polynomial of first-lactation cow CM as a function of CM herd prevalence. Heritability for SCM ranged from 0.069 to 0.105 and for CM from 0.016 to 0.032. For both, we found no clear effect of herd prevalence on their heritability. Genetic correlations within traits across herd prevalences were all greater than 0.92. Whether relationships among prevalence, exposure, disease, and genetics were as expected is a matter of discussion, but reaction norm analyses may be a valuable tool for epidemiological genetics.
**Key words:** dairy cattle, disease prevalence, reaction norm, somatic cell count

## INTRODUCTION

Mastitis is one of the most frequent and costly diseases in the dairy industry (Halasa et al., 2007; Huijps et al., 2008). Besides management, breeding is an important tool to reduce mastitis incidence. The advantage of reducing mastitis by breeding is that it results in a permanent change in the genetic composition of the dairy herd (Shook, 1989). The heritability of clinical mastitis (**CM**) is low, however, varying from 0.03 to 0.06 (Carlen et al., 2004; de Haas et al., 2008; Koeck et al., 2010). Frequently, SCC or SCC-derived traits, such as subclinical mastitis (**SCM**), are analyzed to facilitate genetic selection for mastitis resistance. Heritabilities of these traits are generally slightly higher than those for CM and vary from 0.05 to 0.16 in different studies (Windig et al., 2010; Martins et al., 2011; Zavadilova et al., 2011; Urioste et al., 2012). Because of these low heritabilities, it is difficult to estimate reliable breeding values and genetic progress can be slow.

Apart from low amounts of genetic diversity in resistance, other factors may cause low heritabilities. Failures in the registration of the disease (e.g., a low specificity or sensitivity of the test used to detect the disease) will lower the heritability. However, even if the registration of the disease is adequate, it can be difficult to distinguish between resistant and nonresistant animals if not all animals have been exposed to the pathogens causing the disease. For example, in a typical study analyzing the genetics of (sub)clinical mastitis [**(S)CM**] using national recording schemes, healthy animals are a mixture of nonresistant animals that have not been exposed and resistant animals that may or may not have been in contact with pathogens. Bishop and Woolliams (2010a) derived formulas showing that incomplete exposure of animals to pathogens can reduce estimated heritabilities considerably, depending on the prevalence of the disease and the exposure probability. One way to account for this is to quantify the exposure probability and estimate heritabilities in environments differing in exposure probability.

Reaction norms are used to describe heritability and other genetic parameters over continuously varying environments. In such an approach, the phenotype is treated as a function of an environmental variable, and genetic variance components are estimated for the parameters describing the function. This enables the estimation of genetic parameters for each value that the environmental variable can take. In dairy cattle

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breeding, reaction norms have been used to analyze, for example, the genetics of production, fertility, and udder health (Calus and Veerkamp, 2003; Carlén et al., 2009; Windig et al., 2011).

In national milk recording schemes, SCC is generally recorded next to production traits across a large number of herds. In some Scandinavian countries, data on treatments for mastitis are recorded as well. Both SCC data and treatment data provide an opportunity to develop an indicator for exposure to mastitis pathogens. The idea is that when all animals in a herd are recorded, the fraction of animals with elevated SCC or animals treated at a given time (i.e., prevalence) will be closely related to the exposure probability of animals in the herd. Next, genetic parameters can be estimated as a function of the prevalence, using a reaction norm approach. By using polynomials for the functions describing the relationship between the genetic parameters and the herd prevalence, nonlinear relationships may be accounted for. The hypothesis is that, following Bishop and Woolliams (2010a), the heritability of mastitis increases with increasing prevalence.

In this study, mastitis in Swedish dairy herds was studied to determine whether the genetics of mastitis resistance is influenced by its prevalence. Data on mastitis treatments and SCC were available, so that both CM and SCM could be analyzed, either as a trait or as an environmental variable in the form of prevalence. In particular, the following questions were addressed: (1) Does the heritability of (S)CM increase with increasing prevalence? (2) Is the response different for prevalence of clinical mastitis compared with subclinical mastitis? (3) What is the genetic correlation between (S)CM at different prevalences?

## MATERIALS AND METHODS

### Data Set

The data set was extracted from the Swedish milk recording scheme and included data on mastitis treatments and SCC. First lactations of all cows belonging to the Holstein breed that entered milk recording between 2002 and 2010 were included. Before edits, the number of animals was 178,613. Test-days outside 5 to 366 DIM were excluded as well as test-days without recorded SCC. Only animals with age at calving between 19 and 38 mo were included. Offspring of bulls with fewer than 40 daughters or with offspring in fewer than 20 different herds were excluded. Finally, animals in herds with fewer than 10 animals after the edits were removed. The final data set included 2,069 herds with 177,309 first-lactation cows. These cows were sired by 762 sires and 5,581 maternal grandsires. The pedigree contained a total of 466,720 individuals.

### Definition of SCM and CM

Recorded veterinary treatments for mastitis were used to analyze clinical mastitis per first-lactation cow. The trait CM was scored as a 0/1 trait, with 1 indicating at least one case of treatment of clinical mastitis between 15 d before calving to 366 d after calving, and 0 indicating no treatment. The trait SCM was defined as 1 if the cow had at least one test-day during the lactation with a SCC >150,000 cells/mL, and otherwise as 0. Although CM and SCM were recorded as 0/1 traits, they were treated as continuous traits in subsequent analyses.

### Prevalence

To quantify the prevalence of either CM or SCM, data of all animals present in the herds were used. These included not only the Holstein first-lactation cows for which the genetics were studied, but also animals in later lactations and animals of other breeds (mainly Swedish Red). The prevalence of SCM on a single test-day was defined as the fraction of all animals in the herd >15 DIM that had an SCC >150,000 cells/mL (following de Haas et al., 2008). Animals before 15 DIM were excluded because healthy cows may have SCC levels >150,000 cells/mL just after calving (de Haas et al., 2008).

Prevalence was used as the environmental variable in the reaction norm analysis as a proxy for exposure probability. Ideally, the prevalence should be measured over the period in which infection takes place. Because the traits (S)CM were defined on a whole-lactation basis, it was not clear over which period the prevalence should be defined. For SCM, 2 periods were used. First, the prevalence at the test-day at calving or at the first test-day before calving was used as the environmental value in the reaction norm analysis (**SCMPREVday0**). This may be the best period if we assume that most infections take place at the start or just before the start of the lactation. Second, the prevalence was averaged over all test-days that fell within the lactation period (**SCMPREVday1–305**). This may be the best period if infections are equally likely to occur over the whole lactation.

Similar to SCM, prevalence for CM was defined over 2 periods, 1 around the start of the lactation and 1 over the whole lactation. Prevalence of CM at the start of the lactation was defined as the fraction of animals in the herd that were treated for mastitis between 15 d be-