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## Invited review: Opportunities for genetic improvement of metabolic diseases

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### ABSTRACT

Metabolic disorders are disturbances to one or more of the metabolic processes in dairy cattle. Dysfunction of any of these processes is associated with the manifestation of metabolic diseases or disorders. In this review, data recording, incidences, genetic parameters, predictors, and status of genetic evaluations were examined for (1) ketosis, (2) displaced abomasum, (3) milk fever, and (4) tetany, as these are the most prevalent metabolic diseases where published genetic parameters are available. The reported incidences of clinical cases of metabolic disorders are generally low (less than 10% of cows are recorded as having a metabolic disease per herd per year or parity/lactation). Heritability estimates are also low and are typically less than 5%. Genetic correlations between metabolic traits are mainly positive, indicating that selection to improve one of these diseases is likely to have a positive effect on the others. Furthermore, there may also be opportunities to select for general disease resistance in terms of metabolic stability. Although there is inconsistency in published genetic correlation estimates between milk yield and metabolic traits, selection for milk yield may be expected to lead to a deterioration in metabolic disorders. Under-recording and difficulty in diagnosing subclinical cases are among the reasons why

interest is growing in using easily measurable predictors of metabolic diseases, either recorded on-farm by using sensors and milk tests or off-farm using data collected from routine milk recording. Some countries have already initiated genetic evaluations of metabolic disease traits and currently most of these use clinical observations of disease. However, there are opportunities to use clinical diseases in addition to predictor traits and genomic information to strengthen genetic evaluations for metabolic health in the future.

**Key words:** metabolic disease, ketosis, displaced abomasum, milk fever

### INTRODUCTION

In dairy cattle management, data recording, and genetic evaluation, interest has been growing in reducing the manifestation of dairy production diseases to improve animal welfare, production efficiency, and farm profitability. The image of the dairy industry is also of great importance, as consumer awareness and interest in animal welfare and consequent societal effects have become more prominent (Boichard and Brochard, 2012). Common dairy cattle health disorders, such as mastitis and lameness-causing claw diseases, have received a large amount of attention, as the relative economic effect of these diseases is substantial (e.g., Kelton et al., 1998; Cha et al., 2010, 2011). In comparison, the literature pertaining to selection and data recording focusing on metabolic diseases has received less attention, but is nevertheless an important issue for breeding goals today and in the future (Boichard and Brochard, 2012).

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Metabolic disorders are disturbances to one or more of the metabolic processes. Metabolic processes are the release and conversion of metabolites that are either used in production processes or excreted as waste (Ametaj et al., 2010). Dysfunction, or physiological imbalance, of any of these processes are associated with the manifestation of metabolic diseases or disorders (Ingvartsen and Friggens, 2005). In a veterinary context, the terms diseases and disorders can be used interchangeably. In total, 72 metabolic conditions (mostly causal, some descriptive diagnoses) have been considered in the central health key included in the recommendations for recording health disorders in dairy cattle of the International Committee for Animal Recording (ICAR; <http://www.icar.org/index.php/publications-technical-materials/recording-guidelines/>, Section 7, appendix). As the occurrence of many of these diseases is likely to be too low for genetic parameter estimation, the focus of this review will be on the most prevalent diseases, in clinical or subclinical form, in addition to those for which potential indicator traits have already been reported: (1) ketosis, (2) displaced abomasum, (3) milk fever, and (4) tetany.

There are multiple and complex associations between metabolic diseases and other diseases, affecting, for example, feet and legs and reproductive function (Curtis et al., 1985). Intermediate traits, such as energy balance, could be defined to capture such relationships (e.g., Suthar et al., 2013). However, secondary conditions and feeding and management interventions will not be included in this review. Our focus is on data recording and subsequent use of these data for genetic parameter estimation and genetic evaluation.

Intense selection for production has led to a reliance on body reserves to support early lactation. Consequently, the commencement of lactation and some of the remainder of lactation are often in negative energy balance. This leads to an imbalance in hormones and metabolites giving rise to metabolic diseases (White, 2015). Dysfunction or imbalance in metabolic processes leads to disease, so it is not surprising that genetic correlations between many dairy cow production diseases and milk production traits are mostly unfavorable (e.g., Uribe et al., 1995; Pryce et al., 1997; Van Dorp et al., 1998; Zwald et al., 2004b; Koeck et al., 2013). Usable genetic variation in metabolic stability implies that breeding should be considered as a way to achieve improvements.

In 1988, the first major review of data recording opportunities and consequently breeding strategies to improve production diseases was published (Emanuelson, 1988). Since then, several countries have implemented routine genetic evaluations for health traits using predominantly producer-recorded data (Egger-Danner et

al., 2015). Disease resistance breeding values are also available commercially from several breeding companies and commercial genotyping service providers. Additionally, a large amount of effort has gone into genetic analysis of subclinical disease, measured either in blood, which is often the gold standard for diagnosis of subclinical diseases, or alternatively, using other predictors from automated systems (e.g., based on routine milk analysis, on-farm sensors, or both). This is especially valuable if the predictor can be measured objectively and in a repeated manner, as it reduces the risk of bias and generally means that the genetic variation is easier to disentangle from residual variation. Furthermore, genomic selection has become a powerful enabling tool for generating breeding values where the data are only collected in a relatively small population of genotyped individuals, but the prediction equations are available for entire genotyped populations (Egger-Danner et al., 2015). Therefore, several new strategies could be used for the genetic improvement of metabolic diseases.

The aims of this review were to describe (1) large-scale (national) data recording for metabolic diseases; (2) incidences of metabolic diseases from large (national) data sets; (3) issues associated with the quality of data recording; (4) heritability estimates of metabolic diseases; (5) genetic correlations with other traits; (6) overview of genetic evaluations for metabolic diseases (by country of selected countries); and (7) alternative measures and assays that can be used as predictors of metabolic diseases.

## NATIONAL DATA RECORDING OF DIRECT METABOLIC DISEASE TRAITS

Consistent standards for the definition of metabolic diseases are a prerequisite in any program designed to quantify and monitor incidences, develop management practices, and estimate breeding values (Kelton et al., 1998). The first necessity is defining the disease and the basis of its clinical and subclinical diagnosis (Table 1), and second, provided the disease is measured consistently, assessing the frequency of the disease. This can either be the incidence (rate of new cases per unit of time), or prevalence, which is the proportion of animals affected at a single point in time (ICAR, 2014).

Recording programs differ between countries, due to many factors such as the reporting requirements of the country (e.g., drug usage audits) and the detail of recording in farm (herd management) software programs. The health data collected may also be collected by a variety of people including veterinarians, producers, para-professionals (e.g., hoof trimmer, nutritionist), or others.

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