

GénoSanté: Improving Productive Health of Dairy Cows by Genomic Selection and Management: A First Step with Ketosis

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Abstract

Started in 2015, GénoSanté is a collaborative project bringing together French companies (AI cooperatives with Evolution, Elitest and Auriva, milk recording organizations and herd support with BCEL-Ouest, Seenergi and EILYPS, and dairy industry with Agrial) and research organizations (INRA, ALLICE, and IDELE). The aim of this project is to provide selection tools on new traits to improve productive health, in order to improve the profitability and sustainability of dairy herds. The first results deal with ketosis, one of the most common disorders in dairy cows due to energy deficit in early lactation. Its prevalence reaches 4% and 12-20% for clinical and subclinical forms, respectively. Data included milk beta-hydroxybutyrate (BHB), acetone and a ketosis indicator (Cetodetect®) from 887,000 Holstein (3 million samples) and 148,000 Normande cows (487,000 samples) collected between 2012 and 2015, from 7 to 120 days in milk. BHB and acetone measurements were predicted from Mid Infra Red spectra and log-transformed to improve normality. Genetic breeding values and permanent environment effects were estimated using a repeatability BLUP animal model applied to multiple lactations. Heritability estimates of BHB were 0.12 and 0.15 in Holstein and Normande breeds, respectively, and 0.10 and 0.16 for acetone. Genetic correlation estimates between the 3 traits ranged from 0.72 to 0.85 in Holstein and from 0.85 to 0.98 in Normande. A genomic evaluation was carried out with a reference population of 31,213 Holstein and 6,870 Normande males and females with both genotype and phenotypes. These new indices are part of a Productive Health synthesis in combination with udder health, fertility, and longevity. As part of the same project, genetic and genomic evaluations for claw disorders are in preparation.

Key words: genetic parameter, genomic evaluation, ketosis, health, dairy cow

Introduction

Genetic selection of dairy cattle, initially based on production traits, has been gradually completed by functional and health trait. Presently, genomic selection development brings new perspectives. Genetic trend is expected to increase, thanks to the reduction in generation interval, particularly for low heritability traits such as those related to animal health. Different strategies can be used to enlarge the panel of traits evaluated in the evaluations: 1/ better use of existing information, such as MIR spectra, or 2/ building a new reference population from scratch, by collecting new phenotypes (eg. claw disorders); this second option is of course much more expensive than the first one.

Genosanté is a French collective achievement initiated by the Evolution breeding company in 2015. It gathers partners representing stakeholders of the whole dairy sector, from upstream (milk recording organizations or MROs and breeding companies) to downstream (milk processing industry) and R&D partners. It aims at improving animal health by proposing new tools both for management and selection. The project should also help the milk industry to better answer consumer's requests for less veterinarian treatments and for animal welfare. This project is based on the complementarity of competences of the partners : new phenotypes recording, herd management and health support with MROs, genotyping and selection with breeding companies, genetic evaluation with

UMT 3G (gathering INRA, idele and Alice). The implementation of a genetic and genomic evaluation for ketosis is the first result of this 4-year program.

Ketosis: the first trait evaluated within the Génosanté program

Ketosis is a metabolic disorder of dairy cows at early stage of lactation. It is due to a lack in energy intake relative to the energy required for milk production. In France, its prevalence is estimated at 3 to 4 % for clinical ketosis and at 12 to 20% for subclinical cases. A main impact of this disorder is a decrease in milk production by 300 to 500 kg milk per lactation. Moreover, it is associated to reproduction disorders (delay in cyclicity, lower conception rate) and to other disorders such as mastitis.

In 2012, the tool Cetodetect[®] was implemented, thanks to the European program Optimir (2011-2015), in order to help farmers and technicians to detect early cases of ketosis (Schwartz *et al.*, 2015). This tool is based on a combination of beta hydroxybutyric acid (BHB) and acetone concentrations estimated from MIR spectra of milk samples. Lactating cows receive a score between 0 and 5, with 0 corresponding to healthy cows; 1 to 2 to subclinical cases, 3 to 5 to clinical ketosis. This indicator helps farmers to prevent ketosis by adapting the feeding or through treatments in case of clinical ketosis. Génosanté aims at completing the panel of tools with a genetic evaluation.

Development of a genetic evaluation

Polygenic evaluation

Phenotypes used for the genetic evaluation are milk BHB and milk acetone contents predicted from MIR spectra. These concentrations were log-transformed in order to obtain a normal distribution, assuming that the risks have a multiplicative effect. Only data from the farms working with the MROs participating to Génosanté were used.

The analysis was based on test days of pure breed Holstein (HOL) and Normande (NMD) cows recorded between 7 and 120 days of lactation and in 1st to 5th parity. Contemporary groups of less than 5 animals per herd x test-day were excluded from the analysis. More than 800 000 HOL cows and 140 000 NMD cows meet all these requirements (table 1).

Table 1. Data used for the estimation of genetic parameters.

Breed	HOL	NMD
Nb Test days	2 688 583	451 808
Nb herds	12 378	2 890
Nb cows	806 039	140 015
Nb lactations	1 097 930	189 798
Nb herds x Test days	183 436	32 803

The model used was a multiple-trait animal model, using each test day as repeated data within and between lactations. It includes fixed effects of herd x year, month x year, stage of lactation x parity (3 classes: 1, 2, 3 to 5), age at 1st calving for nulliparous cows and days dry x parity for multiparous ones, and an effect of the laboratory within year.

The estimated heritabilities (table 2) were 12 and 15% for BHB concentration in HOL and in NMD breeds, respectively, and 10% and 16% for acetone. The estimated repeatabilities were 22 and 26% for BHB, 18 and 24% for acetone.

Table 2. Estimated genetic parameters (heritabilities on the diagonal, genetic correlations above and correlations between permanent environment effects below the diagonal).

Breed	Trait	BHB	Acetone
HOL	BHB	0,12	0,85
	Acetone	0,88	0,10
NMD	BHB	0,15	0,89
	Acetone	0,91	0,16

The heritabilities of these traits are moderate, as for other functional traits such as somatic cell score (Rupp and Boichard, 1997). They are consistent with those estimated in other countries, such as in the Netherlands (Van

der Drift *et al.*, 2012), slightly lower than those obtained with models using different lactations as different traits (around 20%, Koeck *et al.*, 2014; Vosman *et al.*, 2015).

Genomic evaluation

A genomic evaluation was performed using a reference population including all females and males with performances and genotyped by one of the breeding companies Génosanté partners. Performances of females were Yield Deviations, those of males were DYDs computed from YDs of ungenotyped daughters. The size of the reference population was quite large in HOL, with more than 31,000 animals, and moderate in NMD, with 6,870 animals.

Table 3. Reference population used for the August 2016 genomic evaluation.

Breed	HOL	NMD
Nb cows	26 899	5 832
Nb bulls	4 314	1 038

The model of genomic evaluation was similar to the one used for the French official genomic evaluations. It is based on a Marker-Assisted BLUP, using from 250 to 3000 QTL according to the breed and the trait. These QTLs were first pre-selected with the BayesC π methodology and then traced with 4-SNP haplotypes. The model also included a residual polygenic effect estimated thanks to 9,000 SNPs of the EuroG10k chip.

Use of genetic and genomic evaluations

The first evaluation for ketosis was published in August 2016. It was based on more than 7 million test-day records of HOL cows and 1.36 million in NMD breed. Table 4 indicates the number of EBVs and GEBVs published with the Genosanté label.

Table 4. Number of EBVs and GEBVs per sex and per breed published with the Génosanté label (August 2016).

Type of evaluation	Sex	HOL	NMD
EBV	Females	1 394 951	257 785
	Males	6 069	1 077
GEBV	Females	137 367	28 980
	Males	26 200	4 811

For ungenotyped animals, the reliability reaches 0.30 for a pedigree index, 0.50 - 0.60 for cows with performances, 0.90 for a bull with 100 daughters with performances. These high reliabilities result from the large number of performances per cow, since a female may have 4-5 test days per lactation, and to the relatively low repeatability of the trait, when compared to other traits such as somatic cell (35% in the French HOL evaluation).

The reliability of GEBVs of young animals without performance reaches 0.66 for HOL and 0.58 for NOR. It is comparable with the reliabilities of other similar traits. This can be explained by the large size of reference population and by the good accuracy of the EBVs.

For each animal with EBVs or GEBVs for BHB and acetone, a ketosis index was computed, with a 50% weight for each trait. In order to facilitate the use of this new information by the breeders, a new synthetic index for productive health was defined, with a weight of 30% for ketosis, udder health and fertility and a weight of 10% for functional longevity. This new synthetic index will evolve in the future, to include health traits newly evaluated in the next steps of the Génosanté program.

GEBVs of females were interpreted according to their indicator Cetodetect[®] obtained at each test day (figure 1). As expected, a reduction of the risk of clinical and

subclinical ketosis was observed for cows with a higher GEBV. For instance, the average percentage of test days corresponding to ketosis cases was 9% for cows with a GEBV between +1 and +2, while it reached 33% for cows with a GEBV between -1 and -2.

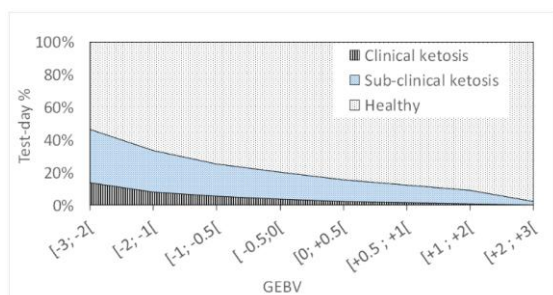


Figure 1. Incidence of ketosis (assessed at each test day by the Cetodetect® indicator) as a function of female genomic index

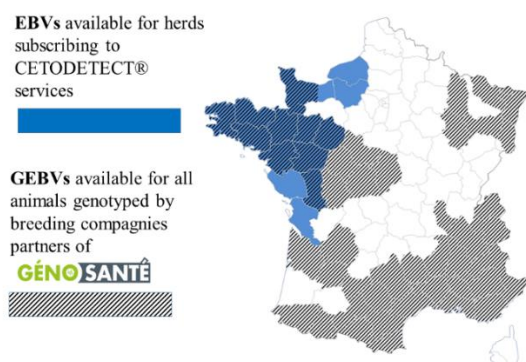


Figure 2. Geographic areas where ketosis EBVs or GEBVs are available for females. All the breeders subscribing to the Cetodetect® service can receive EBVs for their cows, while GEBVs are available for all the females genotyped by the 3 breeding companies partners of Génosanté. Figure 2 shows the French regions where EBVs and GEBVs of females are available.

Conclusions

Génosanté is a collective achievement of partners sharing a common goal, improving the productive health of dairy cows. Evaluations of other new traits are expected over the coming years, especially claw disorders.

The benefit is shared by all the partners of the program. Breeders and AI companies will be able to account for these traits in their breeding process. Genetic evaluations brings also useful information for MROs, which can better understand the major risks for disorders through the estimated environmental effects (eg. herd x year).

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