

# Health traits in current dairy cattle breeding: A review

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**Abstract:** The review focuses on breeding practices aimed at improving resistance to diseases and health disorders that are associated with better efficiency, welfare and longevity of cows. It is commonly known that diseases like mastitis, foot and claw disorders, metabolic and reproductive issues seriously violate dairy cows' well-being. The cause of prevailing health and fertility deterioration has been the intensive selection merely based on higher milk production starting after the Second World War. Therefore since the last decades of the 20<sup>th</sup>-century genetic selection programs have been increasingly focused on increasing resistance to diseases and improving fertility traits using several omics techniques, including genomics. The first steps for maintaining the goal of genetic breeding for disease resistance were the introduction of disease data collection at national levels followed by an elaboration of gene evaluation systems. It was proved that diseases exhibit additive genetic variability exploitable in the breeding. For greater breeding efficiency, the indicator traits are used, which were strongly genetically correlated with health traits, have higher heritability, and above all, are usually easily measurable at low cost. Genome-wide association studies have identified several polymorphisms associated with disease liability that could also be used for speeding up of selection efforts.

**Keywords:** cow; clinical mastitis; foot and claw disease; metabolic disease; genomics

## Introduction

Today's dairy cattle breeding has to face several challenges that include sustainability of livestock production and its impact on climate changes, limited sources of feed and water, or growing public interest in animal welfare and quality of animal products. For more than 20 years, the research has focused on functional traits like longevity, fertility and health, which have been deteriorated by long-term selection for high milk production. Our aim was to review breeding practices aimed at improving resistance to diseases and health disorders, which is associated with enhanced efficiency, welfare and longevity of cows.

It is commonly known that dairy cows' life is fairly below the life expectancy given for this species of animals. In fact, a dairy cow as a farm animal will not surely be able to achieve its natural life length even under optimal life conditions due to the farm economy and voluntary culling. Nevertheless, cows are culled much sooner than the economic optimum on dairy farms. De Vries and Marcones (2020) reported that the productive lifespan of average cows is between 2.5 and four years in most developed dairy industries. Unfortunately, this early involuntary removal is very often linked to the impaired health of cows. De Vries and Marcones (2020) suggested that many cows are discharged for culling reasons that imply temporarily poor welfare caused by disease,

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feet and leg disorders (lameness) and mastitis. Also, the high prevalence of lameness on many dairy farms indicate the low welfare of cows (von Keyserlingk et al. 2013). One possible solution is to change breeding practices, which would put the focus on disease resistance rather than production. Breeding cows for better resilience, reproduction and morphology, especially of udder and claws, enables the longer production life of cows and also increases the welfare of animals. Resilience can be defined as the cow's ability to maintain its usual production, fertility and health even under rapid environmental disturbances such as sudden changes in temperature, changes in composition and quantity of feed or exposure to an infectious agent (Poppe et al. 2020).

The reduction in the lifespan of dairy cows occurred after a long intensive selection for milk production (Oltenacu and Broom 2010). Nowadays, the high genetic ability for production in dairy cattle has been achieved, but at the expense of the deteriorating health and reproduction state of cows. Rauw et al. (1998) explained that the increase in milk production had been associated with risks of altering behavioural, physiological and immunological conditions toward the unbalanced state, and this process is sometimes dangerous for the life of the cow. The altered condition burdens the organism of the cow and causes an increased incidence of health disorders and fertility issues. Thus, to prevent culling, cows must get pregnant in time,

avoid udder and claw diseases, maintain appropriate milk production and have functional udders and feet and legs (De Vries and Marcones 2020).

Therefore, genetic selection programs are increasingly focused on reducing diseases and improving fertility traits (Miglior et al. 2017). Osteras et al. (2007) evaluated the results of thirty years of health recordings in the Norwegian dairy cattle population. They found out that for some of the most common diseases, there was a reduction of more than 50% from 1990 to the years after 2000, which reflected the general trend in the population. They listed (a) changes in breeding effect, (b) an impact of preventive work, (c) a result of changes in the therapeutic attitude as the main three reasons for disease occurrence. According to Kelton et al. (1998), disease occurrence in dairy cattle changed thanks to a recording of the most common clinical diseases with economic significance in dairy cattle, which were clinical mastitis, lameness (foot and leg problems), parturient paresis, retained placenta, metritis, ketosis, displaced abomasum and cystic ovarian disease. Papers dealing with the calculation of economic losses related to the occurrence of such diseases in dairy cattle herds published recently are overviewed in Table 1 (clinical mastitis), Table 2 (foot and claw disorders) and Table 3 (reproductive and metabolic diseases).

Information in Tables 1 to 3 accounts mainly for the direct economic impact of a disease consid-

Table 1. Economic aspects of clinical mastitis (CM) in dairy cattle published recently

Value per case	Description (details)	Breed or population	Country	Reference
USD 444	CM: total loss occurring in the first 30 days in milk included direct losses (diagnostics, therapeutics, non-saleable milk, veterinary service, labour, death loss) and indirect losses (future milk production, premature culling and replacement loss, future reproductive loss).	dairy cattle	USA	Rollin et al. (2015)
EUR 365/363	Mastitis: direct loss from incidence considered a cost of veterinary treatments and drugs, additional labour time of farmer, laboratory analyses and reduced milk returns during the withdrawal period after antibiotic application. Chronic and acute mastitis (with 63% and 37% occurrence, respectively) is combined there as one trait.	Fleckvieh/ Brown Swiss	Austria	Fuerst-Waltl et al. (2016)
EUR 70.65	CM: direct economic impact per cow and year for cattle on pasture. It included an additional cost of veterinary treatment, drugs, herdsman time, and discarded milk.	Pinzgau	Slovakia	Krupova et al. (2016)
USD 325.76/ 426.50	Mastitis: total loss per cow in 1 <sup>st</sup> /2 <sup>nd</sup> parity included direct (additional veterinary treatment and producer labour costs, and discarded milk) and indirect loss (extended days open, increased culling and death, decreased milk).	dairy cattle	USA	Liang et al. (2017)
EUR 115.4/ 193.0	CM: direct economic impact per cow and year included an additional cost of veterinary treatment, drugs, herdsman time, and discarded milk, all discounted per bull/cow in the breeding system.	Holstein	Czech Republic	Krupova et al. (2018; 2019)

Table 2. Economic aspects of foot and claw disorders in dairy cattle published recently

Value per case	Description (details)	Breed or population	Country	Reference
USD 216.07 USD 132.96 USD 120.70	Sole ulcer (1 <sup>st</sup> row), digital dermatitis (2 <sup>nd</sup> row), foot rot (3 <sup>rd</sup> row): total loss per case included a loss in milk, decreased fertility and cost of treatment.	dairy cattle	USA	<a href="#">Cha et al. (2010)</a>
EUR 26.73	Claw disease: direct economic impact per case per cow and year for cattle on pasture. It included additional cost of veterinary treatment, drugs, and herdsman time, all discounted per bull in the breeding system.	Pinzgau	Slovakia	<a href="#">Krupova et al. (2016)</a>
USD 53.0/402.4 USD 232.3/622.3 USD 220.6/590.3	Dermatitis (1 <sup>st</sup> row), sole ulcer (2 <sup>nd</sup> row), and white line disease (3 <sup>rd</sup> row): total economic losses per cow and year from mild/severe lesions. They included direct (additional costs of animal treatment by trimmer and farmer and milk loss) and indirect loss (longer calving interval, increased culling of cows).	Holstein	Spain	<a href="#">Charfeddine and Perez-Cabal (2017)</a>
USD 185.10/ 333.17	Lameness: total loss per cow in 1 <sup>st</sup> /2 <sup>nd</sup> parity included direct (additional veterinary treatment and producer labour costs, and discarded milk) and indirect losses (extended days open, increased culling and death, decreased milk).	dairy cattle	USA	<a href="#">Liang et al. (2017)</a>
EUR 7–14	Lameness: avoided costs by using various systems of automatic detection in comparison with the farmers' visual detection. They included costs of automatic systems (purchase, installation, depreciation, interests, maintenance), costs of lameness treatment and savings due to better detection and earlier treatment of lameness (recalculated per cow and year).	dairy cattle	Belgium	<a href="#">Van De Gucht et al. (2018)</a>
EUR 100.1/168.0	Claw disease: direct economic impact per cow and year. It included additional cost of veterinary treatment, drugs and herdsman time, all discounted per bull/cow in the breeding system.	Holstein	Czech Republic	<a href="#">Krupova et al. (2018; 2019)</a>

ering additional costs needed for animal treatment and medicament application, reduced revenues and indirect effect on increased susceptibility to other diseases.

An economic value expressing the direct impact of a given disease should be known to avoid double counting in the selection when correlated traits are incorporated into the breeding program simultaneously. For example, we can provide milk yield and clinical mastitis ([Koivula et al. 2005](#)) and milk discarded during mastitis treatment not correlated with milk lost in the rest of lactation and/or in the next lactations.

## Udder health

Clinical mastitis (CM) is one of the most frequent and most expensive diseases in dairy cattle ([Heikkilä et al. 2012](#)). The occurrence of CM is higher in early lactation ([Koeck et al. 2010a](#)), but the cow suffers from CM during the entire lactation. [Martin et al. \(2018\)](#) stated that despite improved management practices in dairy cattle production systems, CM still occurs in most

dairy herds. Selective breeding for enhanced mastitis resistance may provide the means to control the disease further. [Heringstad et al. \(2001\)](#) validated a positive genetic response related to CM incidence for bull sires born from 1983 onwards. They stated that the selection pressure on the CM trait was large enough to counteract the expected unfavourable correlated response due to selection for increased milk production. However, the (phenotypic) incidence of CM increased in most dairy breeds at the population level. [Heringstad et al. \(2001\)](#) explained that phenomenon by a more pressing concern of farmers about the udder health. The positive consequences are that higher accuracy in collecting information about the disease allows for a more accurate estimate of the genotype of the animals.

Globally, the need for direct selection for clinical mastitis resistance has raised the necessity of regular nationwide recording. In Norway, recording began on a nationwide level in 1975 ([Solbu 1983](#)). Resistance against clinical mastitis was included in the breeding programme in Norway in 1978; subsequently, the Scandinavian countries started recording CM in the eighties and nineties of the

Table 3. Economic aspects of reproductive and metabolic diseases in dairy cattle published recently

Value per case	Description (details)	Breed or population	Country	Reference
EUR 303/302 EUR 260/259	Early reproductive disorders (1 <sup>st</sup> row) and ketosis (2 <sup>nd</sup> row): direct loss included veterinary treatments and drugs, additional labour time of farmer, laboratory analyses and reduced milk returns during the withdrawal period after antibiotic application.	Fleckvieh/ Brown Swiss	Austria	Fuerst-Waltl et al. (2016)
EUR 72/71 EUR 219/218	Ovarian cysts (1 <sup>st</sup> row) and milk fever (2 <sup>nd</sup> row): direct loss included costs of veterinary treatment, drugs, laboratory analyses and additional labour time of farmer.	Fleckvieh/ Brown Swiss	Austria	Fuerst-Waltl et al. (2016)
USD 203	Subclinical ketosis: indirect economic loss per case included costs of increased risk of other clinical diseases (displaced abomasum, clinical ketosis and metritis) treatment, impact on longer time to pregnancy, on culling and death ratio, and milk production loss.	dairy cattle	Canada	Gohary et al. (2016)
USD 171.69/262.65	Metritis: total loss per cow in 1 <sup>st</sup> /2 <sup>nd</sup> parity included direct (additional veterinary treatment and producer labour costs, and discarded milk) and indirect loss (extended days open, increased culling and death, decreased milk).	dairy cattle	USA	Liang et al. (2017)
USD 150.41/ 313.49	Retained placenta: total loss per cow in 1 <sup>st</sup> /2 <sup>nd</sup> parity included direct (additional veterinary treatment and producer labour costs) and indirect loss (extended days open, decreased milk).	dairy cattle	USA	Liang et al. (2017)
USD 432.48/ 639.51 USD 77.00/180.91 USD –/246.23	Left displaced abomasum (1 <sup>st</sup> row), ketosis (2 <sup>nd</sup> row) and hypocalcaemia (3 <sup>rd</sup> row): total loss per cow in 1 <sup>st</sup> /2 <sup>nd</sup> parity included direct (additional veterinary treatment and producer labour costs) and indirect loss (extended days open, increased culling and death, decreased milk).	dairy cattle	USA	Liang et al. (2017)
EUR 150.41	Subclinical ketosis: total loss from incidence during the first 30 days in milk included direct loss (treatment costs of medicaments, additional labour of farmer and veterinarian consultation; discarded milk; reduced milk yield and change in feed costs). Indirect accounted losses in milk yield, discarded milk, prolonged calving interval and removal of cows, all associated with diseases related to subclinical ketoses (mastitis, metritis, displaced abomasum, lameness, clinical ketosis).	dairy cattle	Netherlands	Mostert et al. (2018)

last century. In the same years, recording of health and disease data including CM began in the USA, Canada, Germany and Austria, France, Spain and Czech Republic (Zwald et al. 2004; Koeck et al. 2012; Zavadilova et al. 2017; Kasna et al. 2018).

Generally, CM is a trait with low heritability ( $h^2$ ) of around 0.10 (Martin et al. 2018) regardless of the type of statistical model, CM trait definition, part and length of lactation observed, parity or breed of cattle (see Table 4). For the genetic evaluation, breeders very often define CM as a binary trait, i.e. 1 – diseased or 0 – healthy. Although for binary traits threshold models are the more appropriate solution from the statistical point of view because of the non-normal distribution of the trait, linear models are commonly used to estimate breeding values for clinical mastitis resistance (Koeck et al. 2010a; Zavadilova et al. 2017; Martin et al. 2018; Costa et al. 2019). Threshold models usually lead to higher  $h^2$  estimates than linear models but they

do not increase the predictive ability when compared with the results of linear models (Koeck et al. 2010a). Vazquez et al. (2009) found the highly correlated predictions of sire effects from Poisson, logit, and linear models, but the larger differences between the estimates of sire occurred due to differences in the definition of CM traits (binary or the number of cases). Negussie et al. (2008) obtained higher breeding value accuracy of sires by threshold models in comparison with univariate models. Nevertheless, they found more significant improvements in accuracy when instead of the univariate linear models the bivariate linear models were employed than when threshold models substituted the linear ones.

Genetic evaluation for mastitis resistance is applied in several countries, for example in Australia, USA, UK and in Germany, Austria and Luxembourg mostly for Holstein breeds. An overall index for mastitis resistance is applied in Canada. It is

Table 4. Heritabilities of clinical mastitis (CM) in dairy cattle breeds

Trait	Range of lactation in days	Citation	Breed	No. of animals	Parity/incidence (%)	Model	Heritability
CM	–15–120	Heringstad et al. (2005)	Norwegian Red	372 227	1/15.8	MT-TM	0.08 ± 0.005
				247 692	2/19.8		0.07 ± 0.005
				147 051	3/24.2		0.07 ± 0.006
CM	–7–150	Negussie et al. (2008)	Finnish Ayrshire	119 915	1/10.1	TM	0.06
						LM	0.02
CM	–30–300	Vazquez et al. (2009)	Norwegian Red	36 178	1/23	LM	0.07
						logistic	0.11
						Poisson	0.06
CM	–10–50	Koeck et al. (2010b)	Austrian Fleckvieh	41 793	all/5.6	TM	0.063 ± 0.020
						TM	0.060 ± 0.018
						TM	0.084 ± 0.024
						LM	0.019 ± 0.005
CM	0–305	Koeck et al. (2012)	Canadian Holstein	61 800	1/12.6	LM	0.02 ± 0.004
CM	0–210	Neuenschwander et al. (2012)	Canadian Holstein	143 657	all/9.7	TM	0.05 ± 0.010
CM	0–305	Zavadilova et al. (2017)	Czech Holstein	16 497	1/29.56	LM	0.05 ± 0.007
					2/37.36		
					3/43.36		
					4/47.57		
					5/62.30		
CM	0–100	Kasna et al. (2018)	Czech Holstein	12 793	all/38.69	LM	0.08
CM	101–200				1/30.93	LM 1 <sup>st</sup> parity	0.09
CM	21–305				2/38.61	LM 2 <sup>nd</sup> parity	0.10
NCM					3/45.18	LM	0.09
NCM					4 <sup>th</sup> and later/55.26		
NCM	0–150					LM 1 <sup>st</sup> parity	0.12
	0–305					LM 2 <sup>nd</sup> parity	0.11
CM	0–150	Costa et al. (2019)	Austrian Fleckvieh	175 154	1/4.60	LM	0.017 ± 0.005
					2/5.12		
					3/6.18		
					4/7.87		
					5/8.61		
CM	0–305	Shabalina et al. (2020)	German Holstein	129 386	1/28.06	ST-LM	0.05–0.08*
					2/35.69		0.05–0.07
					3/40.33		0.05–0.06

CM = clinical mastitis; LM = linear model; MT = multitrait model; NCM = number of CM cases; ST = single trait model; TM = threshold model

\*Standard errors ranged from 0.007 to 0.017 for udder diseases

based on the multiple trait linear model where several clinical mastitis traits, together with somatic cell score and type traits, are included. The index itself is an even combination of relative breeding values for the occurrence of CM in the first par-

ity cows, CM for cows in the later lactations and somatic cell score evaluated across the first three lactations.

Breeding cattle to improve udder health depends primarily on the possibilities of collecting data on



mastitis in dairy cows. The essential drawback is the laboriousness and cost of collecting disease data from dairy cows. These costs are present, while the effects of breeding for udder health improvements are manifested only after several generations. Using genomic selection, we can assume the several times earlier positive impact of breeding on udder health (Georges et al. 2019).

### Foot and claw disorders

Foot and claw disorders (FCds) constitute an essential cause for the deterioration in the welfare of dairy cows (Heringstad et al. 2018), since claw lesions are usually long-term and painful (van der Waaij et al. 2005). FCds cause worsening of production and reproduction of dairy cows (Charfeddine and Perez-Cabal 2017), involuntary culling and among others, due to an increase of the antibiotic use they also influence food safety and quality (Koenig et al. 2005; van der Waaij et al. 2005). Horn disorders and claw diseases arise mostly as a result of the hard flooring surfaces and exposure to wet manure, causing the increased spread of contagious diseases and significant horn wear. The painful disorder often manifests as lameness, e.g. impaired locomotion of variable severity and deviation from normal gait or posture (Greenough 2007; Van De Gucht et al. 2018). Von Keyserlingk et al. (2012) showed that around 20% to 55% of indoor-housed dairy cows in North America suffer from lameness. As stated, Vermunt (2006) described lameness as a crucial indicator of the reduced welfare of dairy cows with significant economic losses and reproduction problems (Bicalho et al. 2007). However, unfortunately, there is a trend in farmers to overlook the economic effect as well as the prevalence and severity of lameness in their herds (Van De Gucht et al. 2018). This behaviour has dire consequences for cow productivity and welfare. Nevertheless, early identification of foot and claw disorder is crucial (Krpalkova et al. 2019). Optimally, the sooner a lame cow is identified, the sooner the causes of the dysfunction can be treated and optimal conditions are restored.

Like for CM, genetic selection for the resistance to FCds lowers the incidence of such disorders as lameness in dairy cattle (Heringstad et al. 2018). The genetic component was identified for most of the relevant claw diseases/disorders, but their  $h^2$  is low. Efforts to increase the genetic resistance

to foot and claw diseases/disorders are complicated by the fact that those disorders cover the whole variety of illnesses with different incidences,  $h^2$  (Koenig et al. 2005), aetiology and pathogenesis (Greenough 2007). However, not all this information is available and is routinely used for genetic selection of animals characterised by higher incidence,  $h^2$  and genetic correlation with other claw diseases or lameness. The choice of particular claw disorders and their subsequent employment in genetic selection go hand in hand with the possibilities of monitoring their presence in a given population of cattle. Without regular and consistent recording of phenotypes, accurate genetic evaluations are not possible.

### Classification of foot and claw diseases

Greenough (2007) distinguished foot and claw diseases as infectious and non-infectious disorders according to aetiology and pathogenesis. Infectious diseases like digital or interdigital dermatitis, interdigital phlegmon, and heel horn erosion predominantly affect the skin and are mostly connected to environmental hygiene. On the other hand, non-infectious ones include claw horn disorders and lesions like ulcers, sole haemorrhage, and white line disease, and these are prevalently caused by a combination of metabolic and mechanical factors. Many authors like e.g. Odegard et al. (2013) or Krupova et al. (2018, 2019) differentiate between infectious diseases and non-infectious disorders when genetic evaluation and selection are employed.

Grouping of FCds in purulent and non-purulent diseases was used by Koenig et al. (2005) or Gernand et al. (2013). The purulent disease included mainly digital dermatitis, sole ulcer and phlegmon, and some purulent claw diseases of low incidence such as sepsis or interdigital dermatitis. Among non-purulent claw disorders, laminitis, interdigital hyperplasia and other non-purulent disorders with low prevalence like white line disease stand out.

Harmonisation and description of several claw diseases can be found in ICAR claw health atlas (Egger-Danner et al. 2015a). Digital dermatitis (DD) is the most frequently recorded disease for genetic evaluation. Often used disorders are sole ulcer (SU), white line disease (WL), or interdigital hyperplasia (IH) for their high occurrence in dairy cattle (Manske et al. 2002; Solano et al. 2016). Wall disor-

der (WD) was defined by Koenig et al. (2005) as different types of white line disease and other lesions along the wall of the claw.

As seen for CM, these traits are mostly scored on an all-or-none basis, i.e. 1 – diseased or 0 – healthy, predominantly on rear legs. A cow is considered diseased regardless of one or both rear legs are with the disease (Koenig et al. 2005).

### Lameness

Lameness is a symptom *per se*, not a disease. In fact, it is highly correlated with foot and claw disease and disorders (Bicalho et al. 2007). It occurs in the first three months after calving (Bicalho et al. 2007) and during the dry period (Daros et al. 2019). First-lactation locomotion score and lameness records are suitable indicators for the future claw health (van der Waaij et al. 2005). Visual locomotion score is a worldwide used tool for defining lameness. Usually, a cow with score 0 is healthy; greater scores indicate cows with more severe lameness. For simplicity, these scores are implemented in genetic evaluation systems instead of the specific disease. Heritability of lameness (score) has been estimated in the range from 0.07 to 0.10 (see Table 5).

### Recording of foot and claw diseases

The foot and claw disorder records are carried out by farmers, veterinarians or by trimmers (emergency or preventive visits) (Kock et al. 2019). Koenig et al. (2005) stated that data recorded by hoof trimmers are the most valuable for genetic evaluation, i.e. the systematic effect of primary records from preventive visits where the cohort of trimmed cows arises. The group of together trimmed cows creates the contemporary groups for genetic evaluation, the systematic effect of the herd-date trimmer (Perez-Cabal and Charfeddine 2015).

Using information about trimmers brings an advantage but puts higher demands on the completeness of the database; for example, it demands a unique ID for each trimmer (Heringstad et al. 2018). Advantages are a possibility to determine the lactation stage at trimming, a new group of cows, repeated cases of disease or different trimmer.

Malchiodi et al. (2017) found that if only trimmed cows were included in the analysis, then the preva-

lence of claw diseases could be overestimated with high probability but with no effect on the estimates of genetic parameters.

### Monitoring and genetic evaluation of foot and claw diseases

In Spanish Holstein, digital and interdigital dermatitis (DE), SU, WL, IH, interdigital phlegmon (IP) and chronic laminitis (CL) are included in the list of the most common diseases (Perez-Cabal and Charfeddine 2015) and are combined to define the overall claw disorder (OCD) group based on these six selected diseases to indicate the absence or presence of at least one of them. In the study, 78 257 records of 76 103 Holstein cows collected between July 2012 and June 2013 by 21 trimmers in 834 dairy herds during 5 979 visits were included. Average herd incidence rates were in the range from 0.57% (IH) to 16.18% (SU); 21.44% of cows showed OCD. Linear model provides  $h^2$  in the range from 0.02 (DE) to 0.05 (OCD), while threshold models from 0.06 (IP) to 0.15 (SU). For genetic evaluation, the linear model was chosen because it showed higher accuracy for all traits.

In Canada, breeders' interest in the welfare of dairy cows led to the start of regular monitoring of 19 FCds through the Hoof Supervisor System<sup>TM</sup> to the national database. Digital dermatitis was classified as the most critical disease, with 16.9% incidence and  $h^2$  equal to 0.08. In the new Canadian Hoof Health Index, eight disorders are included: ID, HHE (heel horn erosion), SU, toe ulcer (TU), WL, sole haemorrhage (SH) and IH complement digital dermatitis. Heritabilities of those diseases and lesions were in the range from 0.03 (SH) to 0.08 (DD, HHE) and frequency from 1.3% (TU) to 16.9% (DDs). Heel depth, feet and legs and rear legs are also an essential part of the index with correlation with the index from 21% to 47%.

### Reproductive and metabolic diseases

The occurrence of the most common reproductive disorders differs according to breed and population (Table 6), with frequencies of 3–10% for the retained placenta (RP), 8–10% for metritis (MET) and 7–17% for cystic ovarian disease (CYS). Heritabilities of these traits are low, mostly < 0.10

Table 5. Heritabilities for the foot and claw disorders and lameness in dairy cattle breeds

Trait/range of lactation in days	Citation	Breed	No. of animals	Parity/incidence (%)	Model	Heritability
CL*	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 4.1	TM	0.01 ± 0.01
CL*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	0.80	LM	0.04 ± 0.003
CL*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	0.80	TM	0.11 ± 0.007
DD*	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 21.7	TM	0.10 ± 0.02
DD*	Koenig et al. (2005)	German Holstein	5 634	all/13.2	TM	0.073 ± 0.009
DD, ID*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	all 8.58	LM	0.02 ± 0.004
DD, ID*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	all 8.58	TM	0.14 ± 0.031
HYP*	Koenig et al. (2005)	German Holstein	5 634	all 6.3	TM	0.115 ± 0.002 1
HYP*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	0.57	LM	0.01 ± 0.002
HYP*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	0.57	TM	0.69 ± 0.155
HYP*	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 5.9	TM	0.10 ± 0.02
IDHE	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 38.7	TM	0.05 ± 0.01
IP*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	all/3.94	LM	0.01 ± 0.002
IP*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	all/3.94	TM	0.06 ± 0.019
SH*	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 39.9	TM	0.08 ± 0.02
SU*	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 5.4	TM	0.01 ± 0.01
SU*	Koenig et al. (2005)	German Holstein	5 634	all/16.1	TM	0.086 ± 0.006
SU*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	16.18	LM	0.04 ± 0.004
SU*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	16.18	TM	0.15 ± 0.024
WD*	Koenig et al. (2005)	German Holstein	5 634	all/9.6	TM	0.104 ± 0.001 4
WLD*	van der Waaij et al. (2005)	Dutch Holstein	29 198	1/12, 9.6	TM	0.02 ± 0.01
WLD*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	all/7.20	LM	0.02 ± 0.003
WLD*	Perez-Cabal and Charfeddine (2015)	Spanish Holstein	78 257	all/7.20	TM	0.09 ± 0.021
LAME/0–305	Koeck et al. (2012)	Canadian Holstein	36 353	1/9.2	LM	0.01 ± 0.004
LAME/0–210	Neuenschwander et al. (2012)	Canadian Holstein	70 165	all/6.0	TM	0.05 ± 0.017
LAME*	Zwald et al. (2004)	Dairy cattle	50 611	all/10	TM	0.06 ± 0.003

CL = chronic laminitis; DD = digital dermatitis; HYP = interdigital hyperplasia; ID = interdigital dermatitis; IDHE = interdigital dermatitis/heel horn erosion; IP = interdigital phlegmon; LAME = lameness; SH = sole haemorrhage; SU = sole ulcer; WD = wall disorder; WLD = white line disease

\*Undefined range of lactation in days

(Egger-Danner et al. 2015b; Pryce et al. 2016), though estimates from threshold models are usually slightly higher compared to linear models, as observed in other health traits. In particular,  $h^2$  ranges from 0.03 to 0.10 for RP, from 0.02 to 0.03 for MET and from 0.03 to 0.07 for CYS (Heringstad 2010; Koeck et al. 2012; Neuenschwander et al. 2012; Jamrozik et al. 2016; Gernand and Koenig 2017).

Metabolic disorders (including displaced abomasum) generally have a low occurrence. Ketosis (KET) is the most frequent of them, with a median incidence of 3.3% of clinical form and the frequency of subclinical KET up to 34% (Pryce et al. 2016). The  $h^2$  value of KET usually ranged from 0.02 to 0.16 (Heringstad et al. 2005; Koeck et al. 2014; Jamrozik et al. 2016). Displaced abomasum (DA)



Table 6. Heritabilities for the metabolic and reproductive disorders in dairy cattle breeds

Trait	Range of lactation in days	Citation	Breed	No. of animals	Parity/incidence (%)	Model	Heritability
CYS	0–300	<a href="#">Heringstad (2010)</a>	Norwegian Red	503 683	1/0.50	TM	0.07 ± 0.01
CYS	0–305	<a href="#">Koeck et al. (2012)</a>	Canadian Holstein	46 341	1/8.2	LM	0.03 ± 0.005
CYS	0–180	<a href="#">Neuenschwander et al. (2012)</a>	Canadian Holstein	85 603	all/7.9	TM	0.05 ± 0.012
					1/4.38		
					2/6.27		
CYS	–10–150	<a href="#">Costa et al. (2019)</a>	Austrian Fleckvieh	175 154	3/7.20	LM	0.005 ± 0.001
					4/7.75		
					5/8.10		
					1/6.24		0.06**
CYS*		<a href="#">Shabalina et al. (2020)</a>	German Holstein	129 386	2/8.20	ST-LM	0.05
					3/8.79		0.05
DA	0–305	<a href="#">Koeck et al. (2012)</a>	Canadian Holstein	43 833	1/3.7	LM	0.06 ± 0.008
DA	0–60	<a href="#">Neuenschwander et al. (2012)</a>	Canadian Holstein	80 882	all/4.0	TM	0.21 ± 0.034
DA*		<a href="#">Dhakar et al. (2015)</a>	US Holstein	77 004	1/0.24	TM	0.10 ± 0.03
				372 227	1/7.5		0.14 ± 0.008
KET	–15–120	<a href="#">Heringstad et al. (2005)</a>	Norwegian Red	247 692	2/13.0	MT-TM	0.16 ± 0.009
				147 051	3/17.2		0.15 ± 0.010
KET	1–100	<a href="#">Koeck et al. (2012)</a>	Canadian Holstein	26 802	1/4.5	LM	0.03 ± 0.008
KET	0–100	<a href="#">Neuenschwander et al. (2012)</a>	Canadian Holstein	80 882	all/2.6	TM	0.09 ± 0.026
KET		<a href="#">Dhakar et al. (2015)</a>	US Holstein	77 004	1/1.67	TM	0.05 ± 0.02
					1/0.62		
					2/0.49		
KET	–10–150	<a href="#">Costa et al. (2019)</a>	Austrian Fleckvieh	175 154	3/0.81	LM	0.006 ± 0.002
					4/0.93		
					5/1.00		
					1/0.77		0.13**
KET*		<a href="#">Shabalina et al. (2020)</a>	German Holstein	129 386	2/1.80	ST-LM	0.08
					3/3.31		0.13
MET	0–300	<a href="#">Heringstad (2010)</a>	Norwegian Red	503 683	1/0.90	TM	0.03 ± 0.01
MET	1–150	<a href="#">Koeck et al. (2012)</a>	Canadian Holstein	59 575	1/10.8	LM	0.02 ± 0.004
MET	0–150	<a href="#">Neuenschwander et al. (2012)</a>	Canadian Holstein	93 573	all	TM	0.03 ± 0.014
MET*		<a href="#">Dhakar et al. (2015)</a>	US Holstein	77 004	1/4.45	TM	0.02 ± 0.01
				372 227	1/0.1		0.09 ± 0.021
PAR (MF)	–15–30	<a href="#">Heringstad et al. (2005)</a>	Norwegian Red	247 692	2/1.9	MT-TM	0.11 ± 0.013
				147 051	3/7.9		0.13 ± 0.011
PAR (MF)	0–5	<a href="#">Neuenschwander et al. (2012)</a>	Canadian Holstein	93 573	all/2.3	TM	0.18 ± 0.038
					1/0.20		
					2/0.76		
PAR (MF)	–10–150	<a href="#">Costa et al. (2019)</a>	Austrian Fleckvieh	175 154	3/2.21	LM	0.015 ± 0.002
					4/4.54		
					5/6.00		
					2/1.17		0.08
PAR (MF)*		<a href="#">Shabalina et al. (2020)</a>	German Holstein	129 286	3/4.46	ST-LM	0.13

Table 6 to be continued

Trait	Range of lactation in days	Citation	Breed	No. of animals	Parity/incidence (%)	Model	Heritability
RP	0–5	Heringstad et al. (2005)	Norwegian Red	372 227	1/2.6	MT-TM	0.08 ± 0.008
				247 692	2/3.4		0.08 ± 0.009
				147 051	3/4.3		0.08 ± 0.010
RP	0–5	Heringstad (2010)	Norwegian Red	503 683	1/1.50	TM	0.06 ± 0.01
RP	0–14	Koeck et al. (2012)	Canadian Holstein	86 005	1/4.6	LM	0.03 ± 0.005
RP	0–10	Neuenschwander et al. (2012)	Canadian Holstein	93 573	all/5.9	TM	0.08 ± 0.016
RP*		Dhakai et al. (2015)	US Holstein	77 004	1/2.28	TM	0.05 ± 0.02
RP	0–7	Costa et al. (2019)	Austrian Fleckvieh	175 154	1/1.08	LM	0.037 ± 0.004
					2/1.74		
					3/2.09		
					4/2.23		
					5/2.37		
RP*		Shabalina et al. (2020)	German Holstein	129 386	1/6.52	ST-LM	0.10**
					2/8.38		0.07
					3/10.60		0.07

CYS = cystic ovarian disease; DA = displaced abomasum; KET = clinical ketosis; LM = linear model; MET = metritis; MT = multitrait model; PAR = parturient paresis (milk fever); RP = retained placenta; ST = single trait model; TM = threshold model

\*Undefined range of lactation in days; \*\*standard errors ranged from 0.023 to 0.105 for metabolic disorders and from 0.006 to 0.025 for reproductive disorders

has a median incidence of 2.7% (Pryce et al. 2016), but as it requires veterinarian intervention, it is accurately recorded. The  $h^2$  value of DA ranged from 0.04 to 0.21 (Neuenschwander et al. 2012; Koeck et al. 2014; Jamrozik et al. 2016). Parturient paresis (PAR), also called milk fever, is more common in older cows, while primiparous cows are at a lower risk (Kelton et al. 1998; Heringstad et al. 2005). The median incidence of clinical form was 2.8%, with a much higher incidence of subclinical form up to 54% (Pryce et al. 2016). The  $h^2$  value of PAR ranged from 0.01 to 0.13 (Heringstad et al. 2005).

Genetic relationships between discussed diseases are usually positive, which indicates that selection for one trait will lead to a favourable response in others. The strongest genetic correlations were detected between RP and MET (0.55–0.79; Heringstad 2010; Koeck et al. 2012; Neuenschwander et al. 2012), or between DA and KET (0.58–0.79; Koeck et al. 2012; Neuenschwander et al. 2012; Jamrozik et al. 2016). Koeck et al. (2012) found a moderate genetic correlation between MET and KET (0.32) and between MET and DA (0.44). Other genetic correlations, mainly between both groups of diseases (metabolic,

reproductive) were found to be low or negligible (Heringstad et al. 2005; Heringstad 2010; Koeck et al. 2012; Neuenschwander et al. 2012; Gernand and Koenig 2017). Genetic correlations between RP and CYS varied from –0.26 in Norwegian Red cattle (Heringstad 2010) to 0.55 in Holstein cattle (Gernand and Koenig 2017). Gernand and Koenig (2017) explained that this broad spectrum of genetic associations might be due to the breed differences, due to the effects of selection or due to the environmental effects on gene expressions – however, further in-depth analysis is suggested. Neuenschwander et al. (2012) supposed that CYS, mastitis and lameness had no apparent relationship with each other or with other mentioned health traits, and therefore they analysed them separately. However, Costa et al. (2019) found a moderate genetic correlation between CM and PAR (0.46). Heringstad et al. (2005) reported a lower correlation between CM and PAR (0.12–0.22), and also a weak correlation between CM and KET (0.08–0.26).

Genetic relationships between health traits and milk production traits are supposed to be unfavourable. This trend was supported by moderate genetic

correlations that ranged from 0.23 to 0.45 between CM and milk yield, as [Martin et al. \(2018\)](#) summed up in their review. The relationship of milk production traits with other disorders is less clear, as the estimates of genetic correlations between reproductive and metabolic diseases broadly differ, and the results of different studies lack consistency. According to comprehensive reviews, the genetic correlations ranged from –0.60 to 0.77 between milk yield and metabolic diseases ([Pryce et al. 2016](#)) and from –0.28 to 0.70 between milk yield and reproductive disorders ([Berry et al. 2011](#)). Some studies ([Koeck et al. 2010b](#); [Dhakal et al. 2015](#); [Gernand and Koenig 2017](#)) evaluated the genetic relationship between health and milk production traits as weak or negligible. [Dhakal et al. \(2015\)](#) offered some possible explanations: (1) cows affected by health disorder in early lactation could have been culled or recovered by the time production traits were recorded and thus estimations may be biased or (2) both traits (health vs production) might be regulated by the third trait such as negative energy balance, which may not produce a direct link between health disorder and milk yield. [Pryce et al. \(2016\)](#) supposed that lack of consistency and large standard errors of genetic correlation estimates might be due to the very low frequencies of diseases, size of data sets and therefore sampling errors. Also, the relationship between lameness (or claw health) and milk production traits is generally described as antagonistic, though genetic correlations are low ([Heringstad et al. 2018](#)).

[Benzaquen et al. \(2007\)](#) found that metritis had no significant effect on the reproductive performance of cows in terms of conception at first service or accumulated pregnancy. Contrary to that, [Vacek et al. \(2007\)](#) found a significant effect of RP and MET on the evaluated reproductive parameters (days from calving to the first insemination, open days, number of inseminations per conception). [Gernand and Koenig \(2017\)](#) found genetic correlations ranging from 0.19 between RP and interval from calving to pregnancy and 0.20 between RP and interval from calving to the first service, but according to them, the occurrence of CYS was strongly correlated with the interval from calving to the first service (0.70) and interval from the first service to pregnancy (0.83).

[Shabalina et al. \(2020\)](#) identified strong phenotypic detrimental effects of CM and metabolic disorders from early lactation stages on longevity

traits in German Holstein cows. They estimated strong genetic correlations (up to –0.77) between longevity traits and CM, and between longevity and KET (–0.76). Genetic correlations between claw disorders and length of productive life or stability were also mostly negative, indicating that selection for improved claw health is associated with favourable indirect selection response in longevity traits. [Pfeiffer et al. \(2015\)](#) suggested that selection for disease resistance in cows is closely connected with increased functional longevity because of the moderate to high genetic correlation between functional longevity and resistance to CM (0.63) and early fertility disorders (0.29), cystic ovaries (0.20), and milk fever (0.20).

### Indicator traits

Low  $h^2$  and difficulties connected with routine collecting of health trait phenotypes ([Egger-Danner et al. 2015b](#); [Pryce et al. 2016](#)) may lower the efficiency of genetic selection for disease resistance. Based on the selection index theory, indicator traits should be strongly genetically correlated with the health traits, are easier and cheap to be measured, and should have exploitable  $h^2$  and genetic variation ([Costa et al. 2020](#)). Type traits from conformation recording and somatic cell score (SCS) are usually evaluated together with mastitis ([Martin et al. 2018](#)). Type traits or traits derived from activity related sensors may be used as indirect traits for genetic evaluation of claw health or lameness ([Heringstad et al. 2018](#)). Mid-infrared (MIR) spectroscopy is another promising tool, as information contained in milk spectra could reflect the physiological status of the cow, milk samples are regularly collected under milk recording scheme, and phenotypes are available at the first test day for all cows in the population. For example, [Koeck et al. \(2014\)](#) and later [Jamrozik et al. \(2016\)](#) proposed a multivariate model which included two direct health traits (ketosis and displaced abomasum) and three indicator traits (body condition score, and MIR-predicted fat-to-protein ratio and  $\beta$ -hydroxybutyrate content in milk), which increased the accuracy of genetic evaluation. Beta-hydroxybutyrate is a ketone body released after body reserve mobilisation, and it can be used to identify cows with negative energy balance ([Benedet et al. 2020](#)). [Bastin et al. \(2016\)](#) showed

how MIR-predicted milk traits ( $\text{Na}^+$ , citrate and acetone) could supplement SCS in the index aimed at decreasing clinical mastitis susceptibility.

### Candidate genes

In general, health traits in dairy cows are usually characterised by a complex genetic architecture (Freebern et al. 2020). Economically important disorders such as ketosis and mastitis, which are the subject of many studies, are largely polygenic traits and are affected by many regions in the genome (Parker Gaddis et al. 2018; Freebern et al. 2020). Complex health traits are influenced not only by a large number of genes and their interactions but also by the environment. Due to the high level of linkage disequilibrium between genomic variants, the exact causal determination of variants is not very simple (Schaid et al. 2018). Great progress in the study of health traits has led to the development of molecular methods for obtaining genomic information. The rapid development of low-cost genotyping strategies has made genomic evaluation for dairy cattle selection and breeding programs globally available. Still, it is difficult to estimate accurate polygenic risk scores for such traits. Genome-wide association studies (GWAS) have identified several polymorphisms associated with disease liability. Tiezzi et al. (2015) found regions associated with CM resistance on *Bos taurus* autosomes (BTA) 2, 14, 20 and 29 that contained genes with known effects in the immune response. Some of the genes in the region of BTA 14 are part of the lymphocyte-antigen-6 complex, which regulates the neutrophil function associated with the major histocompatibility complex (Inlay et al. 2009). The genes found on BTA 2 are also involved in the regulation of the immune response, or they are themselves regulated in the presence of pathogens. Genes annotated on BTA 20 are involved in mammary gland metabolism, antibody production, bacterial cell phagocytosis, mammary gland epithelial development, and cytokine regulation. Another significant single nucleotide polymorphisms (SNPs) were found on BTA 8, 11, 16, 19 and 24, but these regions had no genes annotated. Cai et al. (2018) presented 22 significant and independent quantitative trait loci (QTLs) on BTA 4, 6, 13, 16, 18, 20, which together explained 14% of the total breeding value variability for resistance to clinical mastitis.

The association study for US Jersey cattle showed that ketosis susceptibility was affected by numerous regions across the genome, with the largest peak marker located on BTA 10, and additional peaks on BTA 3, 11 and 25. The putative genes located near those associated regions were involved in insulin secretion or regulation, as well as in the immune system and lipid metabolism (Parker Gaddis et al. 2018). Nayeri et al. (2019) identified several significant regions related to  $\beta$ -hydroxybutyrate concentration (the indicator of subclinical ketosis), with the most significant associations on BTA 6 for primiparous and on BTA 14 for multiparous cows. Nayeri et al. (2019) found highly significant SNP on BTA 14 within the *DGAT1* gene, and a novel region was identified on BTA 20 associated with MIR-predicted milk BHB concentrations in the second and later lactations in Holstein cows. Freebern et al. (2020) reported six significant associations and 20 candidate genes of cattle health, among them *DGAT1* gene for ketosis and *PLXNA4* for displaced abomasum in Holstein cattle. Guarini et al. (2019) performed weighted GWAS and functional analyses to describe the genetic mechanism underlying retained placenta, metritis and cystic ovaries. They identified seven biological pathways related to these diseases, among them “cysteine and methionine metabolism” and “nicotinate and nicotinamide metabolism” that are associated with oxidative stress in mammals. Oxidative stress causes damage to the body’s macromolecules and cells due to unbalanced oxygen production and antioxidant defence (Martinez et al. 2017), and plays an important role in the susceptibility of dairy cows to health disorders. Guarini et al. (2019) also described an association with the “Th1 and Th2 cell differentiation” pathway when T-helper (Th) cells are responsible for modulating immune responses and with the “cyanoamino acid metabolism” pathway, which according to Hailemariam et al. (2014) mediates inflammatory responses, cellular proliferation, cell movement, the cell cycle, and apoptosis in the bovine endometrium.

### Conclusions

Cow health is essential because of its effect on the farm economy, animal welfare, and food safety. Improving dairy cattle health is possible with changes in external environmental condi-

tions and working on management and genetics. Selection schemes attempt to balance production with functional traits, mainly fertility and health traits. However, indicator traits are required because the heritability of health traits is very low. In such a context, the efficiency of indirect selection will be directly proportional to the quality and quantity of phenotypic data used to estimate genetic parameters. The importance of genomic data in the breeding of farm animals has grown in recent years. The genomic data contribute to the refinement of the estimation of breeding values and could improve the effectiveness of the selection response.

### Conflict of interest

The authors declare no conflict of interest.

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