Selection against Metabolic Diseases

B. Heringstad[1], J.E. Pryce[2], K.L. Parker Gaddis[3], A. Koeck[4], C. Bastin[5], M. Abdelsayed[6], N. Gengler[5], F. Miglior[4,7], C. Egger-Danner[8], K.F. Stock[9], A.J. Bradley[10] & J.B. Cole[11]

[1]Norwegian University of Life Sciences, Ås, Norway
[2]La Trobe University, VIC, Australia
[3]University of Florida, USA
[4]University of Guelph, Guelph, Canada
[5]University of Liège, Gembloux, Belgium
[6]Holstein Australia, VIC, Australia
[7]Canadian Dairy Network, Guelph, Canada
[8]ZuchtData, Vienna, Austria
[9] VIT, Verden, Germany
[10]University of Nottingham, UK
[11]USDA, Beltsville MD, USA

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Metabolic diseases

- Disturbances or dysfunction of metabolic processes
- Can be improved by genetic selection.
  - Direct selection based on clinically observed traits
  - Indirect selection using indicators or predictors

Aim:

- Review of genetic parameters for metabolic diseases
- Give a status of genetic evaluation of metabolic diseases
- Discuss possible indicator traits

Metabolic diseases

The health key in "*ICAR guidelines for recording, evaluation and genetic improvement of health traits in dairy cattle*" **72** metabolic conditions

The most prevalent:

- Ketosis
- Displaced abomasum
- Milk fever
- Tetany

Published genetic parameters

Ketosis

- Negative energy balance and mobilization of body fat
- Accumulation of ketone bodies in blood, milk and other body fluids
- Reduced appetite leads to a vicious cycle of worsening negative energy balance and ketosis

Displaced abomasum

- Stretching of the abomasal attachments during gestation and increased space in the abdominal cavity after calving.
- Due to reduced motility of the abomasum, it fills with gas and then displaces
- Accompanied by torsion, gas accumulation increases and drives displacement further.

Milk fever / hypocalcemia

- Characterized by very low blood calcium.
- Clinical signs: lower-than-normal body temperature, partial or complete paralysis,
- Subclinical milk fever is diagnosed by decreased serum calcium.

Tetany / hypomagnesemia

- The amount of magnesium is insufficient for maintenance of regular muscle function.
- Clinical signs: changes in behavior, muscle spasms, convulsions, and paralysis.
- Can lead to sudden death.

Heritability

Heritability estimates of clinical metabolic diseases (review by Pryce et al., 2016)

	Threshold model	Linear model
Ketosis	0.02-0.16	0.01-0.39
Displaced abomasum	0.12-0.35	0.00-0.08
Milk fever	0.07-0.18	0.01-0.08
Tetany	0.02	0.004

Breed: HF, NR, FL
Data: Veterinary treatment, farmer recorded
No of cows: 2000 – 370,000
No of lactations

Genetic correlations among metabolic diseases

	Ketosis	Reference
Displaced abomasum	0.45 – 0.79	Zwald et al., 2004; Parker Gaddis et al., 2014; Jamrozik et al., 2016
Milk fever	0.19 – 0.45	Heringstad et al., 2005; Ederer, 2014

Positive genetic correlations – possible favorable correlated selection response

Genetic correlations to other diseases

	Ketosis	Displaced abomasum	Milk fever
Retained placenta	-0.21 – 0.26	-0.07 – 0.42	-0.04 – 0.18
Cystic ovaries	-0.19 – 0.42	-0.11 – 0.26	
Lameness	-0.10 – 0.25	-0.13 – 0.31	
Mastitis	-0.20 – 0.36	0.02 – 0.20	0.12 – 0.64
Metritis	0.17 – 0,32	0.08 – 0.44	0.08

(Pryce et al., 2016)

Wide range of estimates
Mostly positive correlations
Limited number of studies

Genetic correlations with milk production

Wide range of estimates
Lack of consistency
Limited number of studies
Small datasets
Large SE

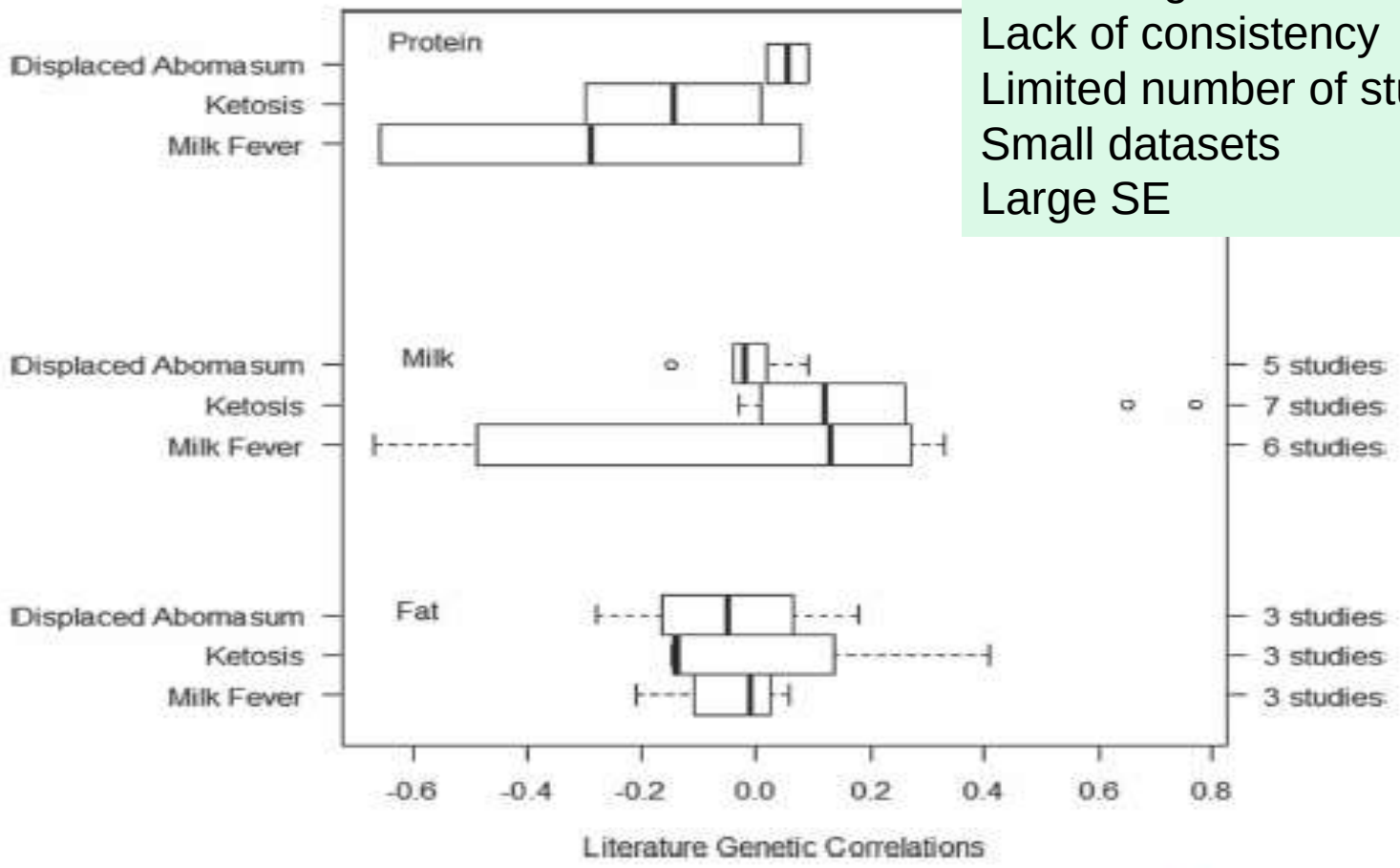


Figure 3. Genetic correlation estimate medians (vertical line), interquartile range (box), and range (whiskers) of genetic correlations with milk, fat, and protein yields of the following metabolic diseases: displaced abomasum, milk fever, and ketosis. Source: Tveit et al. (1991), Uribe et al. (1995), Pryce et al. (1997), Kadarmideen et al. (2000), Zwald et al. (2004b), Koeck et al. (2013), Parker Gaddis et al. (2014).

(Figure from Pryce et al., 2016)

Example of correlated selection response for ketosis in selection lines of Norwegian Red selected for high milk production and low clinical mastitis (from Heringstad et al., 2007)

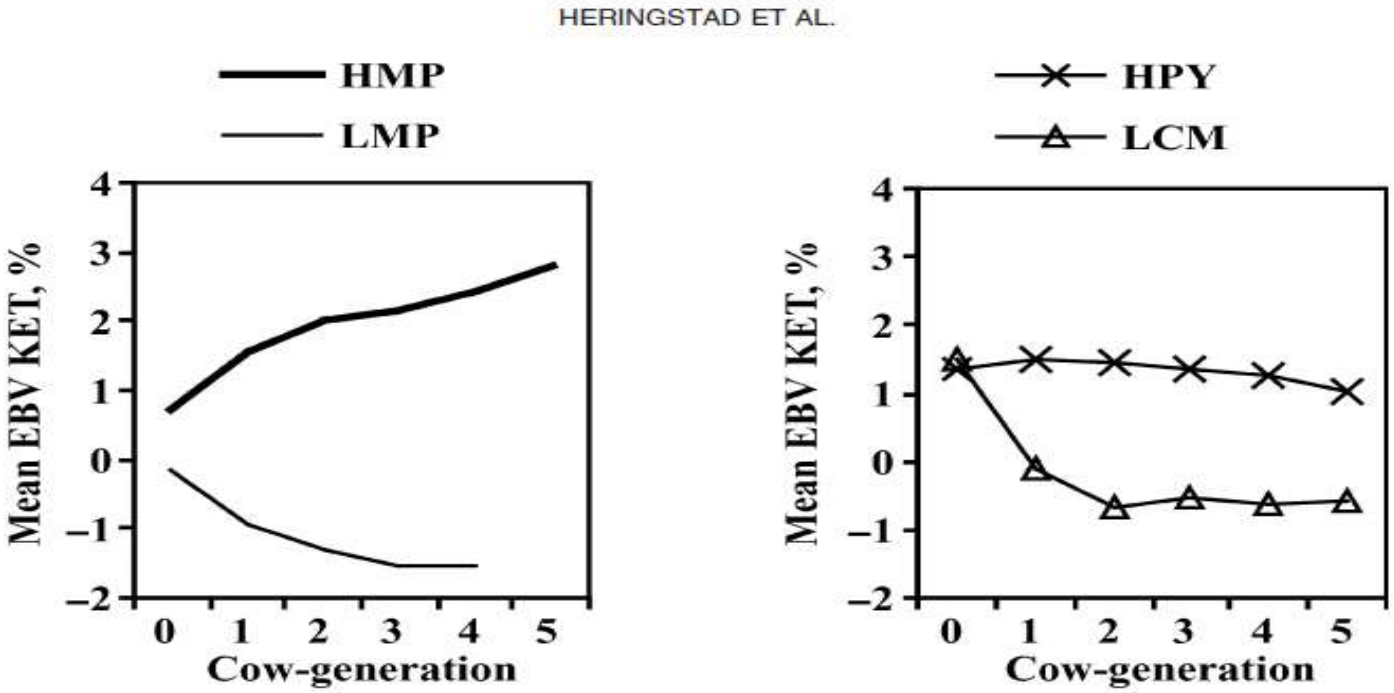
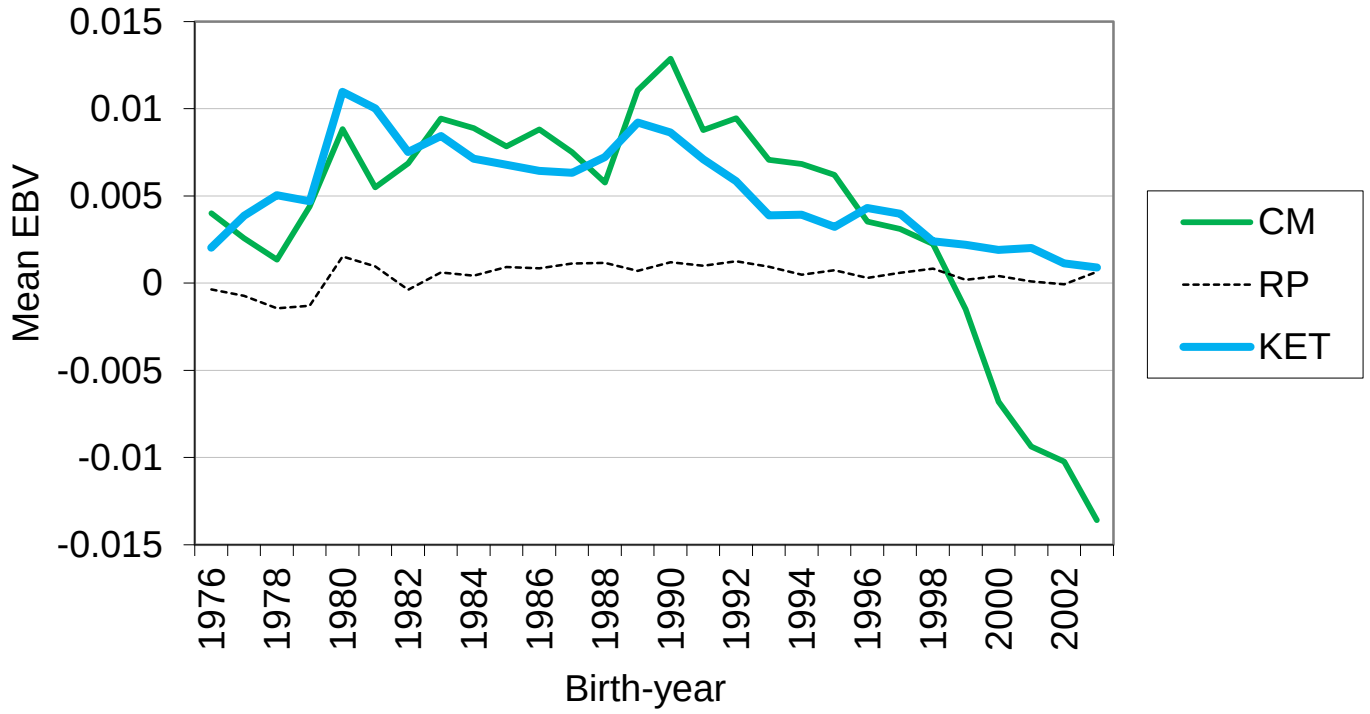


Figure 4. Mean EBV for ketosis (KET) per cow-generation for groups of cows selected for high milk production (HMP) and low milk production (LMP) in experiment 1, and for high protein yield (HPY) and low clinical mastitis (LCM) groups in experiment 2.

Genetic Evaluation - status

- **Norway**: ketosis and milk fever included in “other diseases”, a sub-index of the Total Merit Index of Norwegian Red since 1978.
- **Denmark, Finland and Sweden** (joint evaluation): metabolic diseases included in “other diseases”, a sub-index of the Nordic Total Merit.
- **Austria (and Germany**): Routine genetic evaluation of milk fever and preliminary evaluation for other metabolic diseases in Fleckvieh since 2010, Brown Swiss since 2013. For German Holsteins, the prototype includes ketosis, milk fever and left-displaced abomasum.
- **Canada**: genetic evaluations for metabolic diseases (clinical and subclinical ketosis and displaced abomasum) for Holstein, Ayrshire and Jersey will be implemented in December 2016

Correlated selection response for ketosis in the Norwegian Red population (from Heringstad et al., 2007)



Genetic improvement of clinical mastitis

Positive genetic correlation CM-KET

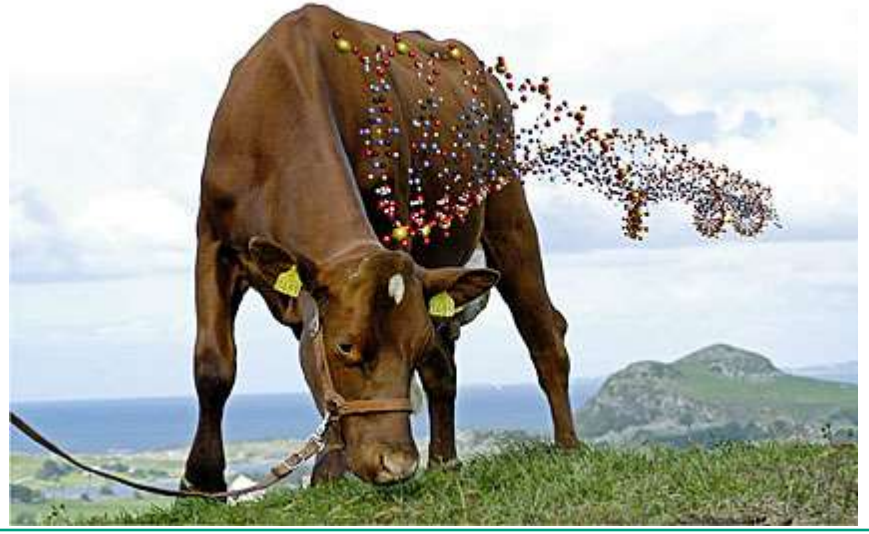
Correlated response in ketosis

Genetic Evaluation

- Direct selection requires large-scale recording of disease traits
- Alternatively, indicators of metabolic diseases can provide information to be used in genetic evaluation

Genomic selection:

- Use information from later lactations (e.g. milk fever)
- Genotyping cows + high resolution phenotyping in selected herds



Possible indicator traits

Challenges related to

- Disease recording
- Under-reporting
- Diagnosis of subclinical cases

→ Increased interest in predictors

Predictors can be used for genetic evaluation, diagnosis of subclinical cases, risk assessment and herd management.

Possible indicator traits

- Sensor data
- Milk or blood tests, such as ß-Hydroxybutyrate (**BHB**), other biomarkers
- Changes in body condition score (**BCS**)
- Changes in body weight
- Predictors based on data from routine milk recording (e.g., milk mid-infrared spectral data, **MIR,** fat: protein ratio)

Automation and Sensor data

- Increased automation and use of advanced sensors
  - ➡ new opportunities and solutions
- Advanced management systems
  - – combine data from multiple sources
  - – predict risk and detect possible health problems
  - – reliabilities not always convincing
- Monitoring rumination pattens – early predictor
- Association to negative energy balance
  - – Automated weighing and automated scoring of BCS (camera)
    - frequent and objective measures of new phenotypes
    - assessment of energy balance
- Moderate genetic correlations between metabolic diseases and both BCS and body weight change (Dechow et al.2004; Jamrozik et al.2016; Frigo et al., 2010).

MIR of milk samples

- Evaluate subclinical disease
- Potential for large scale recording - established and used in routine milk recording
- Useful for screening purposes (healthy cows vs. cows at risk)
- Prediction accuracy insufficient for ketosis parameters (e.g., de Roos et al., 2007; Grelet et al., 2016b).
- Used to predict energy balance (Mc Parland et al., 2014).

Indicators of ketosis

- Ketosis (clinical and subclinical) affects 40-60 % of dairy cows, average cost of $289 per case in USA (AgSource, 2016)
- BHB in blood – standard diagnosis of ketosis
  - Expensive, not practical for large scale
- BHB and acetone in milk
  - Prediction from milk MIR
- Genetic correlation 0.37-0.75 between clinical ketosis and milk BHB 1st testday (Koeck et al 2014; 2015; Jamrozik et al, 2016)
- Combine information from different sources to increase accuracy
- Indicators of subclinical ketosis useful for genetic evaluation

Conclusion

- Direct selection to reduce metabolic diseases is possible
- Lack of recording of direct disease traits is a challenge.
- Several potential indicator traits have been suggested
- New phenotypes, including better tools for diagnosis of subclinical cases, may support more efficient selection against metabolic diseases.

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