

International Genetic Evaluations for Udder Health Traits in Dairy Cattle

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Abstract

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The aim of this thesis was to investigate different approaches for international genetic evaluations of dairy sires for udder health traits. For this purpose, deregressed national genetic evaluations were used of Holstein milk somatic cell (SC) from 12 countries, clinical mastitis (CM) from 3 of these countries as well as Ayrshire fore udder attachment from 9 weakly linked countries.

Deregression and multiple-trait across-country genetic evaluations (MACE) worked satisfactorily for a lowly heritable trait ($h^2=0.02$) such as CM. The across-country genetic correlations ranged from 0.47 to 0.97 (median = 0.88) for SC and from 0.59 to 0.89 for CM. International genetic udder health evaluations enable more efficient global selection than selection based on national evaluations.

The predictive ability and reliability of international genetic evaluations were improved by including multiple traits per country (CM and SC) in international genetic evaluations. The advantage of analysing SC and CM simultaneously was most noticeable for young bulls with daughters in countries not using the within-country correlation structure in their national genetic evaluation and for prediction of CM. The average reliability of international breeding values for young bulls with most daughters in Sweden increased from 18 to 25% on Nordic CM scales.

Estimates of the same genetic correlation differed considerably (up to 1.03 units) depending on estimation strategy when genetic ties between the respective pairs of countries were weak. The use of prior genetic parameters improved the predictive ability of international breeding values for weakly linked populations, especially when the uncertainty of the (co)variances was considered, i.e. in fully Bayesian MACE. For young bulls on foreign scales, the predictive ability of such analyses was 11 to 15% higher than for traditional MACE.

The recommendations are that deregressed national genetic evaluations should be used as dependent variables in MACE, that multiple-trait MACE should be used for international genetic udder health evaluations, and that prior genetic correlations should be considered. The implication is that global selection against CM will be more effective, which can reduce the use of antibiotics globally.

Keywords: MACE, multiple traits, genetic correlation, clinical mastitis, milk somatic cell, deregression, connectedness, prior, Bayesian, Interbull

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Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

- I. Mark, T., W.F. Fikse, U. Emanuelson and J. Philipsson, 2002. Short Communication: Effect of Phantom Parent Grouping and Properties of Deregression for a Low Heritability Trait. *J. Dairy Sci.* 85:2393-2395
- II. Mark, T., W.F. Fikse, U. Emanuelson and J. Philipsson, 2002. International Genetic Evaluations of Holstein Sires for Milk Somatic Cell and Clinical Mastitis. *J. Dairy Sci.* 85:2384-2392.
- III. Mark, T. and P. G. Sullivan, 2005. Multiple-Trait-Multiple-Country Genetic Evaluations for Udder Health traits. *J. Dairy Sci.* (submitted).
- IV. Mark, T., P. Madsen, J. Jensen and W. F. Fikse, 2005. Short Communication: Difficulties in Estimating Across-Country Genetic Correlations for Weakly Linked Bull Populations. *J. Dairy Sci.* 88:3303-3305.
- V. Mark, T., P. Madsen, J. Jensen and W. F. Fikse, 2005. Prior (Co)Variances can Improve Multiple-trait Across-Country Evaluations of Weakly Linked Bull Populations. *J. Dairy Sci.* 88:3290-3302.

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Abbreviations

CM = clinical mastitis
DER = deregressed national genetic evaluations
DYD = daughter yield deviations
EDC = effective daughter contributions (Fikse and Banos, 2001)
MACE = multiple-trait across-country genetic evaluations
n = effective independent daughter contributions
MT-MACE = multiple-trait-multiple-country genetic evaluations
RI = relative importance (in percentage)
SC = milk somatic cell
SCC = somatic cell count
SCS = somatic cell score
ST-MACE = single-trait-multiple-country genetic evaluations

Introduction

Identification of superior animals is needed to better select parents for breeding the next generation of animals and thereby achieve genetic progress and improve animal production. Dairy cattle breeding has become an increasingly international business over the past decades. An optimal worldwide use of semen from a limited number of elite sires requires that the genetic merit of bulls can be objectively compared across countries. International genetic evaluations for all, or at least the most important, breeding goal traits are needed to accurately identify bulls with superior total genetic merit.

Interbull at present conducts international genetic evaluations for an array of the most important production and functional traits in dairy cattle breeding (Interbull, 2005; Mark, 2004). The genetic exchange between countries is primarily through semen and accurate international evaluations of bulls are of main interest. Thus, this thesis focuses on bull comparisons.

Udder health is generally considered as one of the most important traits in dairy cattle production (Miglior et al., 2005). Several countries conduct national genetic evaluations for milk somatic cell (SC)¹, whereas national genetic evaluations for clinical mastitis (CM) are only available in the Nordic countries (Mark et al., 2005). CM exhibits considerable genetic variance (Rupp and Boichard, 2003), but it also has low heritability. That is, the heritability ranged from 0.02 to 0.05 for the national genetic evaluations considered in this thesis.

International genetic evaluations for udder health are possible because a (small) proportion of bulls have daughters in multiple countries and because national genetic udder health evaluations exist. As a result, international genetic evaluation for udder health has been investigated for a decade. The development of such evaluations are, however, challenging due to the low heritabilities for CM, and the fact that almost all bulls generally have daughters in only one country.

Rogers et al. (1998) obtained promising across-country genetic correlation estimates among somatic cell score, productive life and selected conformation traits from the United States, and CM and milk somatic cell (SC) from Denmark and Sweden. These researchers used a simple method, which adjusts product-moment correlations between two independent sets of breeding values by the reliability of each breeding value (Calo et al., 1973). The bulls considered were limited to those that had evaluations for both traits.

The statistical model used by Interbull for routine international genetic evaluations is based on national genetic evaluations. The national genetic evaluations must be deregressed to avoid double counting information in the national and international genetic evaluation. The first deregression procedures proposed for the dependent variable in international genetic evaluations were simple and accounted for the number of daughters of each bull and the heritability

¹ Milk somatic cell (SC) is used throughout the thesis to denote any logarithmic transformation of the somatic cell count regardless of which logarithmic base is used for the transformation and regardless of whether the sign of the variable is reversed or not. Hence, SC includes both what is commonly referred to as 'somatic cell score' by some national genetic evaluation units and what is referred to as 'somatic cell count' by other units.

(Goddard, 1985; Schaeffer, 1985). Later pedigree information was also included by considering a subset of the MACE equations associated with the genetic effects within country (Banos et al., 1990; Sigurdsson and Banos, 1995).

Problems associated with low heritabilities and few daughters were observed by Rogers (pers. comm.) and Rozzi and Schaeffer (1996) for a deregression procedure not accounting for the equations pertaining to the country mean (Sigurdsson and Banos, 1995). The problem was that deregressed evaluations deviated more from national evaluations when the country mean was not considered in the deregression procedure, compared with when the mean was considered, especially for traits with low heritability and for bulls with few daughters. This prevented MACE and REML estimation of across-country genetic correlations for low heritability traits such as CM.

Modifying the deregression procedure to account for country means seemed to alleviate the problems associated with low heritabilities and few daughters (Rozzi and Schaeffer, 1996). Based on the modified deregression procedure, international genetic evaluations for CM and SC using MACE were developed (Mark et al., 2000, 2001) and have been implemented routinely from May 2001. The purpose of this thesis was to describe and investigate international genetic evaluations of dairy sires for udder health traits for current and improved methods.

Background

Multiple-trait genetic evaluations

Multiple-trait genetic evaluations can be used to analyse two or more traits simultaneously to take advantage of genetic and residual correlations among the traits. Thus the information from one trait is allowed to contribute to the precision and unbiasedness of the evaluations of the other traits. The predictions can be improved both due to increased precision because of correlated information and by eliminating or reducing bias from selection on the other traits.

Mixed model equations can be expanded or augmented to include animals without records (Henderson, 1977). Information about a correlated trait can dominate a trait of interest, when the information about the correlated trait is much more than for the trait of interest. While this can potentially both increase and reduce bias compared with single-trait genetic evaluations, the precision of breeding values for the trait of interest typically increases. For animals with no own and no offspring records for the trait of interest, the predicted genetic merit is equal to the average breeding value of the parents for the trait of interest unless correlated information from other traits are considered.

The genetic and residual correlations among traits partly determine the degree to which traits can affect the evaluations of each other. In general, multiple-trait analyses are most useful when genetic correlations differ considerably from residual correlations, when heritabilities differ considerably, or when fewer records are available for one trait than for other traits. When the residual correlation is equal to the genetic correlation, it is not possible to determine which part of the phenotypic deviation is due to genetic or environmental effects. Hence,

multiple-trait evaluations are not more accurate than single-trait evaluations in such situations.

Multiple-trait models can be used to simultaneously analyse both the performance of different biological traits (e.g., production and health) and the performance of the same biological trait as expressed in different discrete environments (e.g., countries). The multiple-trait model is sometimes referred to as a 'character state model' when applied to the latter scenario (e.g., Via et al., 1995). Multiple biological traits expressed in multiple discrete environments can also be accommodated for in multiple-trait models.

Multiple-trait across-country genetic evaluations (MACE)

Schaeffer (1994) proposed a multiple-trait sire model with random genetic groups for the purpose of international genetic evaluation of dairy bulls. This model is a character state model and it considers daughter performance in different countries as different, but genetically correlated traits. The daughter performance (dependent variable) in this meta-model was assumed to be independent of all non-genetic and non-additive genetic effects affecting the recorded phenotypes at national level. This greatly simplified the model in the sense that the only necessary fixed effect was a country mean effect.

The residual variances were heterogeneous in MACE to accommodate for a variable effective number of daughters per bull for different traits (=countries). Residual correlations were zero because an individual cow is assumed to have performance records in only one country. The heritabilities for each trait and genetic correlations between traits were assumed to be known.

The current international bull evaluation service by Interbull

Interbull applies the MACE model to perform international genetic evaluations of dairy bulls. Such evaluations are routinely conducted four times per year for 6 different dairy breeds and up to 5 different trait groups per breed. These trait groups are production (milk, fat and protein yield), conformation (19 to 21 traits), udder health (CM and SC), direct longevity, and calving traits (calving ease and stillbirth; both direct and maternal effects).

Test evaluations are performed biannually during which across-country genetic correlations are estimated using an EM-REML (Klei and Weigel, 1998) applied to a well-connected subset of bulls (Sigurdsson et al., 1996). Countries also have the opportunity to submit traits from new or modified genetic evaluations provided that the genetic trends are unbiased (Boichard et al., 1995).

The consistency of current and previous genetic evaluation results is verified for each trait and bull (Klei et al., 2002) at all test and routine evaluations. Another major task in preparing data for MACE is to assign a unique identification number to each bull and its ancestors and to prepare pedigree files by merging information from all participating countries. After data edits, the international genetic evaluations are obtained after performing the following steps:

- Trace pedigree and define genetic groups for missing ancestors within country
- Deregress national genetic evaluations within country (Jairath et al., 1998)
- Estimate sire variances within country (Sullivan, 1999)
- Trace pedigree and define genetic groups for missing ancestors across countries
- Compute MACE solutions (Schaeffer, 1994; Klei, 1998)

The results of MACE are sets of international genetic evaluations for all bulls on each country specific scale. The bulls can rank differently for different countries due to genetic correlations less than unity. These breeding values are distributed together with their approximate reliabilities (Harris and Johnson, 1998) to member countries, which are responsible for publishing the results for their own country scale and breeding objectives.

Trait definitions and predictors of udder health

Accurate genetic evaluations for traits of economic importance are crucial in order to achieve genetic progress. It is important to recognise the breeding goal and to assess to what extent the recorded traits measure the breeding goal trait. Resistance to CM is the trait of main interest regarding udder health because of reduced milk production, high veterinary costs and reduced cow welfare associated with a clinical mastitis incidence (e.g., Nielsen et al., 2005).

Resistance to sub-clinical mastitis is also important. Milk somatic cell is widely used as an indicator of both clinical and sub-clinical mastitis, whereas CM is currently recorded in only the Nordic countries. High levels of SCC can cause decreased milk production in cows without CM (e.g., de los Campos et al., 2005; Hortet et al., 1999). Thus SC is valuable in addition to being an indicator of CM.

Heritabilities for lactation SC ranged between 0.08 and 0.43 for traits considered in the Interbull August 2005 routine evaluation and tend to be higher for countries that use a random regression test-day model. Information about SC is available at about the same time as CM records depending on the exact definition of both traits. Breeding values for SC tend to be available sooner for countries using a test-day model, but CM records can occur before calving (trait definition for CM include 7 to 10 days before calving). The genetic correlation between CM and SC is about 0.7, but varies between different investigations depending on trait definitions, estimation method and population (Mark, 1999).

In addition to SC, some countries also consider correlated information from conformation traits and milking ease in their udder health indexes. This further emphasises that several sources of information should preferably be considered simultaneously for an optimal genetic evaluation of udder health. In a review, Rupp and Boichard (2003) concluded that milking ease is genetically correlated to SC (0.4), but not genetically correlated with CM. The reason for a zero genetic correlation with CM may be that several factors associated with fast milking, such as easier entry of pathogens through the teat duct and rapid draining of the udder, neutralise each other.

Udder conformation traits are useful indicators of udder health; because information is available early in first parity, they have moderate to high heritabilities (median = 0.25 for both Ayrshire and Holstein; Interbull, 2005) and moderate genetic correlations (0.2 to 0.7) with CM (e.g. Lund et al., 1999; Van Dorp et al., 1998; Nielsen et al., 2000; Rupp and Boichard, 2003). Angularity is an indicator of poor resistance to CM (e.g., Hansen et al., 2002; Lassen et al., 2003).

Table 1 summarises across-country genetic correlations estimated from data considered in the March 2004 Interbull test evaluation. Udder depth, fore udder attachment and angularity had the strongest genetic correlations with CM and SC in Denmark and Sweden. Cows that are less angular, that have strong attachment of fore udder with abdominal wall, and have a short distance between the hock and the bottom of fore udder also tend to have a healthier udder. That is, such cows tend to have less clinical mastitis and lower SCC.

Table 1. Summary of Holstein across-country genetic correlation estimates¹ between either clinical mastitis (CM) or milk somatic cell (SC) evaluated in Denmark and Sweden and different conformation traits evaluated in Canada, Germany, France and the United States.

	CM	SC
Angularity	0.36 _{0.12}	0.26 _{0.05}
Fore udder attachment	-0.36 _{0.11}	-0.26 _{0.13}
Udder depth	-0.58 _{0.04}	-0.41 _{0.03}
Overall udder	-0.33 _{0.10}	-0.25 _{0.04}
Other traits	-0.2 to 0.2	-0.2 to 0.3

¹Average estimate of correlation between trait x and y, where x={CM or SC in Denmark, Sweden} and y={conformation trait in CAN, DEU, FRA, USA} from 36 separate 6-variate ST-MACE EM-REML analyses. Standard deviations across non-Nordic countries of average estimates for DNK and SWE are given in subscript. Data as used in Interbull March 2004 test evaluations.

Electrical conductivity of milk is currently not considered for genetic evaluation, but is a promising trait for improving udder health (Goodling et al., 2000; Norberg, 2004). This is because much data could become available on a daily basis from automated milking systems (de Mol, 2000) and because of the genetic association between electrical conductivity and udder health. Norberg (2004) found that electrical conductivity is highly correlated with CM (0.7) and also with SC (0.9). The heritability of electrical conductivity is within the range of heritabilities used in SC genetic evaluations (0.2 to 0.4; Norberg, 2004). However, electrical conductivity can potentially be measured more frequently than SCC. Currently information about electrical conductivity is not systematically made available for routine genetic evaluations.

Dairy production traits have moderate to high heritability (0.10 to 0.58; Interbull, August 2005) and are the traits that are subject to most selection emphasis (Miglior et al., 2005). Dairy production traits are unfavourably correlated with CM. The estimated genetic correlation between production (milk or protein) and CM was 0.33 for Danish Holsteins (Hansen et al., 2002), 0.01 to 0.45 for Swedish Holstein (Carlén et al., 2004B), -0.10 to 0.32 for Swedish Ayrshire (Emanuelson et al., 1988), 0.43 for Norwegian Ayrshire (Heringstad et

al., 2005), and 0.31 to 0.61 for Finnish Holstein and Ayrshire (Luttinen and Juga, 1997; Pösö and Mäntysaari, 1996). In a review, Rupp and Boichard (2003) concluded that the genetic correlation was unfavourable and about 0.4.

These unfavourable genetic correlations underline the importance of considering udder health simultaneously with production traits in selection of dairy cattle. The high selection emphasis on production traits and the non-zero genetic correlation between production traits and udder health also make it useful to analyse production and CM simultaneously to reduce selection bias of CM evaluations, but also to improve precision of CM breeding values. This is, however, not done in practise. The correlation between production and SC is lower (0.1; Rupp and Boichard, 2003), but a few countries analyse production traits and SC simultaneously (e.g., Canada, Italy and Switzerland).

National genetic evaluation procedures for udder health

An increasing number of countries have implemented national genetic evaluations for CM and SC in recent years. Most of these countries consider information from the first three parities, but a few countries consider SC in the first five parities. Table 2 shows that CM is analysed with sire models in all cases, and in two out of three cases with a multiple-trait model including SC as a correlated trait. CM, SC and selected conformation traits are analysed simultaneously in Denmark, CM and SC are analysed simultaneously in Sweden, whereas CM is analysed univariately in Finland.

Table 2. Summary (frequency) of national genetic Holstein evaluations considered in Interbull August 2005 udder health routine evaluation.

	CM	SC
Participating countries ¹	3	21
Animal Models	0	19
Sire Model	3	2
Test-day models	0	13
Multiple-trait models ²	2	5
Multiple-lactation models ³	1	14
Repeatability models	2	5
Genetic groups	2	20
At least 3 parities considered	3	19
Only first half of lactation considered ⁴	2	2

¹Countries participating in joint genetic evaluations (i.e. Germany and Austria) each count once; Red Holsteins from Denmark, France and Switzerland are not considered although included in the international Holstein evaluation.

²Analysed with biologically different traits (e.g. production, conformation); not different parities treated as different traits.

³Different parities treated as different traits.

⁴Records only considered when days in milk <181.

In the previous section it was concluded that several useful indicators of udder health are available for CM and SC. These traits should preferably be analysed simultaneously with the trait of interest to increase precision and reduce selection bias of inferences. This is especially important for CM because of the relatively

low heritability for CM compared with SC and other predictor traits. The importance of including more predictor traits in a multiple-trait evaluation relative to accounting for preferential mating is higher for CM compared with other traits such as production. This is because more precision can be gained from correlated information for CM, because CM is subject to less selection (Mark et al., 2005; Miglior et al., 2005) and because the genetic merit of females is of less interest for CM due to low precision compared with production.

CM in the national genetic evaluations of the Nordic countries is defined as a binary trait, but the genetic evaluation models assume normally distributed observations. Current trait definitions for CM do not distinguish between one or multiple CM incidences during the given time interval. However, CM in four different time periods is treated as different, but correlated traits, in Denmark.

It has been suggested that improved genetic inferences can be achieved by analysing CM with threshold (e.g. Gianola, 1982; Mäntysaari et al., 1993), longitudinal threshold (Rekaya et al., 2003), survival (Carlén et al., 2004B), mixture (Detilleux and Leroy, 2000; Ødegård et al., 2003) or negative binomial models (Tempelman and Gianola, 1996) instead of traditional linear models with constant genetic value over time. Some of these methods are, however, currently too computationally demanding to be considered for genetic evaluations based on large-scale field data and can be difficult to extend to multiple-trait analyses compared with traditional linear models.

SC was analysed using a test-day animal model in more than half of the countries participating in the Interbull August 2005 routine evaluation (Table 2). Most of these countries applied a random regression model for the genetic effects. Random regression test-day models offer potential advantages for analysing SC over traditional linear models with constant genetic effects over time. With a random regression test-day model it is possible to simultaneously account for the environmental and genetic effects associated with each test-day. This typically yields higher heritabilities for SC on a lactation basis and increases the genetic correlation between SC and CM (e.g., Mark, 2004).

Gengler and Mayers (2003) found that increasing the weight on observations for SC associated with high residuals can increase the genetic correlation with CM. This is because the SC usually increases dramatically in connection with mastitis infections. Hence, the liability of CM is expected to be greater at a test-day where the SC deviates considerably from a standard function used to describe the lactation SC curve.

Data structures for international dairy populations

Large amounts of data are available for international dairy populations, but national populations are often weakly connected with each other. While this data structure makes international genetic evaluations a possibility, it also makes such evaluations a special challenge compared with national genetic evaluations. The special data structure must be considered in the development of international genetic evaluations since the optimal genetic evaluation methods, models and algorithms dependent on the available data. Hence, experience gained with national evaluations procedures cannot always be generalised to international evaluations procedures, and vice versa. It is, however, of interest to compare data

structures within and across countries because most research regarding genetic evaluations focuses on national comparisons and because utilisation of the information about correlated traits within countries may be used to improve international genetic evaluations.

Most bulls considered in international genetic evaluations have daughters in only one country. For example, in the August 2005 Interbull udder health evaluation, 96 and 93% of the bulls had a national evaluation in only one country (Table 3) and no bull had evaluations in all countries for Ayrshire and Holstein, respectively. The degree of connectedness varies substantially between breeds and across different country pairs within breed. Holstein and Ayrshire are the populations with most countries participating in Interbull evaluations, and they represent the two extremes with respect to the average number of common bulls.

Table 3. Population statistics from August 2005 Interbull udder health routine evaluation¹.

	Ayrshire	Holstein
No. populations	12	23
No. bulls	10144	79374
No. national genetic evaluations	10728	90578
Percent bulls with evaluation in only one country	96	93
Average no. common bulls ²	15	132
Coefficient of Variation of no. common bulls (%)	122	116

¹Bulls included in a run, which includes CM evaluations from Nordic countries and SC evaluations from other countries.

²Bulls with a national evaluation in both countries for a given country pair.

The distribution of bulls with evaluations for both of two traits measured either in the same or a different country is illustrated by the data considered in Paper III (Table 4). Here each of the three Nordic countries had two traits included in an international genetic evaluation. In Finland and Sweden all bulls with a CM breeding value also had an SC breeding value, whereas 99% of the Danish bulls with a CM breeding value also had an SC breeding value. Similarly 87, 94 and 93% of the bulls with an SC breeding value also had a CM breeding value for Denmark, Finland and Sweden, respectively. The reason why fewer bulls had CM breeding values compared with SC breeding values with the Nordic countries was partly because a stricter requirement (i.e. minimum 50 daughters) was imposed for CM, but not for SC in Paper III. These high proportions are in contrast to the low proportion of bulls with evaluations for two traits measured in different countries. For example, only 158 of the bulls with Danish CM evaluations also have an SC evaluation in the United States (<1%).

In national genetic evaluations, most bulls typically have daughter records for all traits considered in a multiple-trait model. This is because most bulls with records for one trait typically also have records for most other evaluated traits nationally, and because genotype by environment interaction is usually not considered in national genetic evaluations. Poor connectedness for national genetic evaluations is mainly an issue of lacking genetic ties between contemporary groups such as herd or herd-year-seasons, e.g. when most bulls have all their daughters in a specific region.

Table 4. Total number of bulls (diagonal) and number of common Holstein bulls (above diagonal) in data considered for correlation estimation in Paper III¹.

	Clinical mastitis				Milk somatic cell							
	DNK	FIN	SWE		DNK	FIN	SWE	CAN	DEA	EST	FRA	USA
DNK	4767	35	178		4721	40	186	126	224	10	159	158
FIN		855	43		36	855	44	16	43	0	44	36
SWE			2411		206	47	2411	218	301	13	275	322
DNK					5423	41	219	170	284	11	206	215
FIN						911	49	17	47	0	49	41
SWE							2580	248	337	13	297	372
CAN								6851	520	21	593	1259
DEA									14393	48	730	931
EST										344	16	24
FRA											11317	990
USA												23051

¹ISO codes are used as country codes, except for DEA (Germany-Austria).

Challenge to make best use of all available information

Incomplete or inaccurate information about genetic merits for breeding goal traits of some selection candidates can lead to decreased efficiency in selection decisions. Furthermore, to record information is often associated with considerable costs. Therefore it is important that the information available for genetic evaluation is fully used, both within and across country.

The ideal situation might be to analyse raw performance data from all animals, traits, times and places simultaneously. This is, however, not feasible in practice, at least not with a statistical model in which all assumptions are satisfied. Progress is usually a stepwise process. First national genetic evaluations are developed. When national genetic evaluations from a number of different countries are in place for the trait of interest and across-country genetic correlations among similar traits are sufficiently high, international genetic evaluations based on MACE can be developed in order to share information across countries. In principle, international genetic evaluations can be useful when across-country genetic correlations are different from zero, but their usefulness increases with increasing across-country genetic correlations (Smith and Banos, 1991).

Once a genetic evaluation model is in operation, ways to fine-tune and develop the evaluation can be sought and improved methods can be pursued. Initially, international genetic evaluation for udder health has been implemented using the same MACE model that was applied for production trait evaluations. This model allows one trait per country to be considered and does not incorporate information from separate breeds. By considering multiple traits per country, instead of only one trait per country, more efficient use of data measured for all considered traits within and across countries can be made. Sharing information for all traits within and across countries takes advantage of the within-country correlation structures and the many genetic ties among traits within country. This may help to bridge the CM information in the Nordic countries with SC information in the non-Nordic countries.

Information can also be used across breeds, either by analysing the data from different breeds simultaneously, or perhaps better, when genetic ties across breeds are weak, by including information from one breed as prior information for the analysis of the other breed. MACE inferences for weakly linked populations such as Ayrshire might be improved by including prior (co)variance components from breeds such as Holstein. The Holstein parameters are useful priors for Ayrshire because Holstein cattle are found in almost all countries with Ayrshire cattle, trait definitions are similar for Ayrshire and Holstein, and for Holstein it is possible to obtain more precise estimates of (co)variance components than for most corresponding Ayrshire populations.

Bayesian methodology provides an elegant framework to include prior information, but approximate methods that require less computer capacity may be able to achieve some of the expected gain in predictive performance from fully Bayesian methods. However, inferences of genetic merit in a fully Bayesian setting can be useful because they allow evaluating the impact of ignoring uncertainty of (co)variances on predicted genetic merit. This is especially of interest in international genetic evaluations due to the weak genetic ties across certain populations since the weak ties result in high standard errors of across-

country genetic correlations. Such uncertainty is ignored in traditional MACE approaches, but not in a fully Bayesian MACE.

Aims of the thesis

The overall aims of this thesis were to investigate current and improved methods for international genetic evaluations of dairy sires for udder health traits. More specifically, the aims were to first determine the suitability and genetic consequences of applying MACE to milk somatic cell and clinical mastitis, and secondly to investigate possible improvements of MACE by extending the method to:

- Accommodate for multiple-traits per country
- Incorporate prior knowledge of (co)variance components
- Account for the uncertainty of dispersion parameters

Overview of the investigations

Materials

Holstein field data used in Interbull evaluations for udder health traits (i.e. CM and SC) collected from Interbull member countries were used in all investigations, except for the studies specifically dealing with weakly linked populations (Table 5). Holstein data were used because Holstein is the largest international dairy population, covers most different population structures and has the highest number of bulls with evaluations in multiple countries. The countries considered in Paper III were a subset of the data considered in both Paper I and II.

Table 5. Summary of materials considered in Paper I to V.

Paper	Traits ¹	Breed ²	Countries ³
I, II	CM, SC	HOL	CAN, CHE, DEU, DNK, EST, FIN, FRA, GBR, ISR, NLD, SWE, USA
III	CM, SC	HOL	CAN, DEA, DNK, EST, FIN, FRA, SWE, USA
IV, V	Fore udder attachment	AYS	AUS, CAN, DNK, FIN, GBR, NOR, NZL, SWE, USA

¹CM = clinical mastitis; SC = milk somatic cell

²HOL = Holstein; AYS = Ayrshire.

³ISO codes are used as country codes, except for DEA (Germany-Austria).

Ayrshire conformation data was used for the studies about uncertainty of (co)variances since application of standard international genetic evaluation methods was not feasible for this group of traits due to extremely poor connectedness (Klei and Lawlor, 2001). Fore udder attachment was the udder conformation trait evaluated by most Ayrshire countries.

Methods

All analyses were based on the MACE model (Schaeffer, 1994) or extensions of this model. The MACE model accommodated multiple-traits per country in Paper III. This multiple-trait-multiple-country model considered effective independent weighting factors (Sullivan and Wilton, 2001) and multivariately deregressed evaluations (Schaeffer, 2001) for countries having a multiple-trait CM and SC evaluation. Single-trait deregressed national genetic evaluations were considered in all other studies.

The MACE model was conditional on known genetic parameters in Paper I to III and in the traditional MACE approach in Paper V. The necessary across-country genetic correlations were estimated with an EM-REML procedure (Klei and Weigel, 1998) applied to a reduced set of MACE equations. Sire variances were estimated within country and trait using an EM-REML procedure (Sullivan, 1999).

Prior (co)variances were included and uncertainty of location and dispersion parameters was considered in Paper V. A fully Bayesian MACE using Gibbs sampling was considered for this purpose and compared to traditional MACE assuming different sets of fixed parameters. These sets included the posterior means from the fully Bayesian MACE. An approximate method was also used to combine prior genetic correlations with REML estimates in Paper V. In the fully Bayesian MACE, prior and posterior (co)variance matrices followed inverse-Wishart distributions. Further details of the statistical models are given in the respective papers. The pedigrees and parameters used in different analyses are summarised in Table 6.

Reliabilities for predicted international genetic merits were approximated with an information source method based on selection index theory (Harris and Johnson, 1998) in Paper II and V. In Paper III, reliabilities for MT-MACE were approximated with a multivariate extension of the Harris-Johnson information source method (Sullivan and Mark, 2005). In Paper V, posterior standard deviations of breeding values were calculated and compared with reliabilities approximated according to the Harris-Johnson information source method.

Table 6. Description of the use of pedigrees, genetic group definitions and parameters used for creation of weighting factors (EDC)¹, deregression (DER) and MACE in Paper I to V, where N = provided from national genetic evaluation units, S = defined or estimated at international level based on information from given country only, I = compiled, defined or estimated based on information from multiple countries.

	Paper I and II (Current Interbull practice)		Paper III (MT-MACE)		Paper V (Bayesian MACE)	
	EDC ¹	DER MACE	EDC ¹	DER MACE	EDC ¹	DER MACE
Pedigree ²	N	I I	N	I I	N	I I
Groups (d) ³	N	S S	N	S S	N	S S
Groups (f) ³	N	S I	N	I I	N	S I
Heritability	N	N N	N	N N	N	N I
F^2_{sire}	-	- S	-	S S	-	- I
r_G within ⁴	-	- -	N	N N	-	- -
r_G across ⁵	-	- I	-	- I	-	- I
r_e within ⁶	-	- -	N	- -	-	- -

¹EDCs were provided by countries and used as is, except in Paper III where they were transformed to effective independent weighting factors.

²Pedigree information for known ancestors; tracing for bulls with daughter records only (i.e., different relationship matrices for different steps)

³Genetic group definition for bulls first registered in given country (d) or in another country (f).

⁴Genetic correlation between two traits measured in same country.

⁵Genetic correlation between two traits measured in different countries.

⁶Residual correlation between two traits measured in same country.

Main findings

This thesis has demonstrated the suitability of deregression and MACE for SC and CM (Paper I and II) and has helped to establish the foundation for other low heritability traits to be considered in international genetic evaluations. The procedure to deregress national genetic evaluation results was found to work satisfactorily for a low heritability trait (0.02) and MACE predictions agreed well with national predictions (Paper I, III, V). For example, the product-moment correlation between national and international genetic CM evaluations on the Swedish scale was 1.00 when only local information was considered and 0.97 when correlated information from other countries was considered (Paper I).

SC and CM evaluated in different countries were highly correlated (Paper II). The across-country genetic correlation ranged from 0.47 to 0.97 for SC with a median of 0.88, and ranged from 0.59 to 0.89 for CM. This made possible a substantially higher genetic progress, when selection is based on international genetic evaluations rather than national genetic merits alone (Paper II). The highest selection differential for CM for non-Nordic countries could be achieved when selecting for resistance to CM on the Danish scale rather than for SC on domestic country scale. As regards genetic trends, the average genetic levels of CM and SC on the Swedish scale have been constant for bulls from all countries during the past decade, but deteriorated slightly for bulls born in the last two years (Paper II).

A multiple-trait-multiple-country (MT-MACE) model uses the available information better than separate ST-MACE models that only allow one trait per country (Paper III). As a result, MT-MACE yields more reliable international breeding values and is associated with higher predictive ability than ST-MACE. Predictions for all traits and groups of bulls were improved by changing from ST-MACE to MT-MACE, but to a different degree. Bulls receive evaluations with a given reliability earlier with MT-MACE than with ST-MACE. This was especially so for traits with low heritability and in situations where the within-country residual and genetic correlations were not used in the national evaluation (Paper III).

Young bulls with daughters in countries, which did not use the within-country correlation structure in their national genetic evaluation, benefited most from changing from ST-MACE to MT-MACE. This was true both on domestic and on foreign country-trait scales. For example, the average reliabilities of international breeding values for young bulls with most daughters in Sweden increased 18, 25 and 20% on the Danish, Finnish and Swedish CM scales, respectively. The impacts of MT-MACE versus ST-MACE on predictions and their reliabilities were smaller for SC and especially for countries not recording CM and for countries with a national multiple-trait model for CM and SC (Paper III).

Estimates of the same genetic correlation differed considerably (up to 1.03 units) depending on the data, the assumptions of the model and the method used for the estimation when genetic ties were weak between the two involved countries. The differences in estimates of the same genetic correlation decreased with an increasing number of genetic ties between countries. There was essentially no difference between estimated genetic correlations for the country combination with the most (61) common bulls regardless of the estimation strategy used. The

variation of the differences in correlations estimated with different strategies was closely related to the asymptotic standard error of the correlation estimate, and 88% of differences were less than one standard error unit. These results underlined the potential gain in precision of estimated correlations that may be achieved by considering prior correlations.

A fully Bayesian method to predict international genetic merit and a simple approximate Bayesian method to combine prior genetic correlations with genetic correlations estimated from data were presented and compared in Paper V. The overall predictive performance of fully Bayesian analyses was superior to traditional MACE assuming different sets of genetic parameters. This was true regardless of whether only genetic correlations obtained with the approximate Bayesian method or posterior means of all dispersion parameters from the fully Bayesian MACE were considered in traditional MACE.

The differences in predicted international genetic merits between fully Bayesian MACE and traditional MACE increased as the reliability of the breeding values decreased (Paper V). The predictive superiority of fully Bayesian MACE was most clear for the 5% youngest and 5% randomly chosen bulls, whereas results were inconclusive for a small subset containing the 25% youngest import bulls. For the young bulls on foreign scales, the average product-moment correlation between evaluations based on the reduced and full data was 0.97 for Bayesian MACE, whereas it was 0.84 to 0.87 for traditional MACE, depending on the parameters assumed. Similar results were found for randomly chosen bulls.

Regressions of predicted genetic merit from full analysis on predicted genetic merit in reduced analysis indicated that all MACE models yielded predictions that were nearly unbiased, except for the youngest import bulls, where regression coefficients ranged from 0.93 to 1.12. Varying prior degree of belief only slightly affected predicted genetic merits (Paper V).

The computational requirements for a fully Bayesian MACE was much higher than that of traditional MACE (Paper V). This was partly due to poor mixing of the Markov chain. The present implementation of the fully Bayesian MACE was therefore considered unfeasible for routine international genetic evaluations given current computational capacity.

General discussion

Deregression

It is important to assure that all information, which is accounted for in national genetic evaluations, is also accounted for, implicitly or explicitly, in international genetic evaluations. Furthermore, it is important to assure that the information is not double counted. One way to verify this is by comparing national and international evaluations for bulls with information in only one country. However, the international breeding values of these bulls are in practice potentially affected by correlated information from foreign countries. By ignoring correlated information from foreign countries in the international genetic evaluation, it is

possible to evaluate the reversibility of MACE and deregression for a specific trait.

Paper I investigated whether MACE predictions agreed with national breeding values, when disregarding information from foreign national genetic evaluations. This was only done for the Swedish CM scale and only for bulls with daughters in Sweden. While this was sufficient to test the deregression procedure as well as the reversibility of MACE for domestic bulls for the concerned low heritability trait, the following five questions were not answered in Paper I:

- Does the use of deregressed national genetic evaluations cause underestimation of genetic correlations?
- Do the conclusions hold for production traits, which are subject to stronger selection than CM?
- Are daughter yield deviations (DYD; VanRaden and Wiggans, 1991) better as dependent variables for across-country genetic evaluation?
- To which extent are predicted international genetic merits for foreign bulls affected by differences in genetic group definitions between deregression and MACE?
- Do the conclusions for the univariate deregression procedure apply to the multivariate deregression procedure?

Correlation estimation

Madsen and Mark (2002) touched upon the first three questions. They considered milk production data from the United Kingdom, Hungary, Italy, the Netherlands and the United States, and they observed that the use of deregressed national genetic evaluations appears to be appropriate for correlation estimation. Estimated genetic correlations ranged between 0.84 and 0.97 (median = 0.92), when based on deregressed national genetic evaluations. Hence, there is little margin for underestimation. These estimates were on average 0.07 units higher compared with estimates based on the DYDs provided by the respective countries. A reason for this could be that DYD is not calculated in a standardised way among different countries. In comparison, the deregression procedure is tailored specifically to MACE and is applied in a standardised way for all countries by Interbull.

MACE for milk yield

Madsen and Mark (2002) also studied the reversibility of deregression and MACE for production traits and compared these results with MACE predictions based on DYD. The analyses were conceptually similar to those conducted in Paper I and the results are summarised in Table 7. The deregression procedure and MACE were completely reversible for domestic bulls, whereas the product-moment correlation between national predictions for milk production in the USA and univariate MACE predictions based on DYD was 0.995. A possible reason for the deviation from unity is that MACE does not consider as elaborate within-country pedigree information as the national genetic evaluation and that DYD ignores information from granddaughters and -sons. Similar results were found for the four other countries (unpublished).

Table 7. Correlation (r) and standard deviation (SD) of differences between national genetic evaluations (NGE) for milk production in the USA and X, which is either deregressed NGE (DER) or daughter yield deviations (DYD), univariate MACE applied to only milk production in USA (I_1), 5-variate MACE using zero genetic correlations (I_2), or 5-variate MACE using estimated genetic correlations (I_3) and based on either DER or DYD. 17,269 bulls with milk NGE for milk production in the USA was considered (some of the results were published by Madsen and Mark, 2002).

X	DER		DYD	
	SD_{X-NGE}	$r_{X,NGE}$	SD_{X-NGE}	$r_{X,NGE}$
DER/DYD	179.7	0.903	117.0	0.991
I_1	0.0	1.000	81.5	0.995
I_2	3.6	1.000	81.4	0.995
I_3	50.3	0.998	94.3	0.993

Daughter yield deviations versus deregressed national genetic evaluations

The deregressed evaluations are intermediate products and should only be interpreted in conjunction with the meta-analysis in which they are used as dependent variables. The deregressed evaluations do not have the same well-defined statistical properties as DYD. However, the required normality assumptions for MACE should be satisfied for both DER and DYD according to the Central Limit Theorem.

The deregression procedure should in theory account for all information which is used in the national genetic evaluation and subsequently in MACE based on deregressed national genetic evaluations. Double counting of information will thus be avoided. In practice, pedigree information compiled from all countries is sometimes more complete (i.e. more generations of known ancestors) than the pedigree that has been used in the national evaluation, thereby violating the concept of only deregressing information considered in the concerned national evaluation (Paper III). This could affect especially import bulls for which the pedigree information available at international level is more complete than that used in the national genetic evaluation of the importing country.

The deregression procedure should not and does not remove information from the national genetic evaluations which is not modelled in MACE. The pedigree information for domestic bulls is often more complete in the sense that national genetic evaluations commonly use animal models, contrarily to MACE which is a sire model. This means that the deregressed national genetic evaluations often contain information, which is not specifically modelled in MACE, but is allowed to influence the international breeding values from MACE. Such information is not included in DYD, and therefore ignored in MACE when DYDs are used as dependent variable.

The above mismatch between the completeness of pedigree information for domestic bulls in MACE and national genetic evaluations may explain the observations by Sigurdsson and Banos (1995). They observed that MACE predictions based on deregressed national evaluations were closer to the true simulated breeding values compared with MACE predictions based on DYD. This

was true irrespective of whether the initial genetic levels and the genetic trends of the two simulated populations differed or not.

The superiority of deregressed evaluations over DYD as dependent variable in MACE is expected to be reduced if more complete pedigrees are considered in MACE. However, granddaughters, great-granddaughters etc are typically ignored when computing DYD (e.g. VanRaden and Wiggans, 1991), so this information would not be considered in MACE when using DYD as dependent variable.

Sigurdsson and Banos (1995) considered a deregression procedure, which did not account for the country means. However, the superiority of the deregressed evaluations compared with DYD as dependent variable in MACE are not expected to be less for the procedure accounting for the country mean. An improved deregression procedure should rather increase the superiority of deregressed national genetic evaluations. The analyses based on field data (Paper I; Madsen and Mark, 2002) support the conclusion of Sigurdsson and Banos (1995): deregressed national genetic evaluations are superior to DYD as dependent variable in MACE, even for low heritability traits.

Impact of different genetic group definitions in MACE and deregression

Differences in the definition of genetic groups in the deregression compared with MACE are expected to affect predictions for bulls without daughter information in the concerned country (foreign bulls) and other bulls first registered in another country (import bulls) most. This is because less pedigree information is available about these bulls for the deregression step, and because the genetic groups related to such bulls are directly affected by differences in genetic group definitions between deregression and MACE. This was not investigated in Paper I. The effect of the different genetic group definitions was, however, found to be negligible for the data considered in Paper III. That is, Pearson product-moment correlations between MACE predictions using either the same genetic groups in deregression and MACE or a grouping strategy according to Paper I were >0.999 for all country scales, when both bulls with and without a national genetic evaluation in the given country were considered.

Multivariate deregression

The multivariate deregression procedure used in Paper III is an extension of the single-trait deregression procedure considered in the other studies. The concept behind the multivariate procedure is the same as for the single-trait procedure. Both procedures are expected to have similar properties as those specified in Paper I. The single-trait deregression is affected by the ratio between sire and residual variances, but not by the magnitude of the variances. The lower the heritability, the more deregressed evaluations differ from national evaluations. This is also the case for the multivariate deregression procedure, which is also affected by the sire variances for each trait within country and the correlation among them.

The Danish CM and SC data in Paper III was used to confirm that the multivariate deregression procedure has the same reversibility properties as the single trait procedure. These two traits were analysed simultaneously in the national evaluation, deregressed simultaneously and analysed simultaneously by MT-MACE. The correlation between national and bi-variate MT-MACE

predictions was 1.000 and the standard deviation of the difference between national and bi-variate MT-MACE predictions was 0.000 for the two Danish traits. The residual and genetic correlations, which were used in the multivariate deregression and in MT-MACE, were equal to those used in the national multiple-trait evaluation. Furthermore, the variances, which were used as inputs to the multivariate deregression, were the same as those used in MT-MACE.

Genetic groups

Genetic groups are included in MACE to account for unequal genetic level of unknown ancestors. Genetic group effects were included in the genetic models considered in all investigations, but the assumptions about these effects and the rules to define genetic groups differed between the studies included in the thesis. Bayesian MACE was implemented with fixed genetic group effects, whereas the other MACE approaches were implemented assuming random genetic group effects. Although the impact on predicted genetic merits of the assumption about genetic group effects was expected to be minor in Paper V due to large genetic group sizes, random genetic groups are preferred for MACE.

Random genetic groups are preferred because of many poorly connected country-pairs and the potential differences in genetic levels of missing ancestors of bulls of varying national origin. Often there is only limited information available to infer certain genetic group effects on certain country scales. For example, maternal grand-dam group effects for the youngest bulls are typically difficult to infer precisely on foreign country scales because progeny group testing of young bulls is primarily performed within country. Genetic group effects cannot be estimated when they are assumed fixed and there is no information available about them. Treating the genetic groups as random instead of fixed effects makes the resulting MACE mixed model equations non-singular, but regresses the genetic group solutions towards zero.

The implied constraint on random genetic group effects in MACE is that all genetic group solutions must sum to zero. This may not be appropriate when base populations are selected (Sullivan, 2002). Thus, Sullivan (2002) investigated an alternative MACE approach in which only the genetic group solutions for the base populations were constrained to sum to zero in order to remove bias due to selected base populations. This selection-modified MACE approach reduced the bias and prediction error variance compared with the traditional approach in which all genetic group solutions were required to sum to zero, but had poorer convergence properties (Sullivan, 2002). Convergence was especially time consuming when three traits per country were considered (Sullivan, pers. comm.).

The definition of genetic groups often involves a dilemma. Large genetic group sizes are needed to obtain precise predicted genetic group effects, but dense genetic group definitions are required to avoid that missing ancestors with considerably different genetic levels are treated as contemporaries. A fuzzy assignment of each missing ancestor to several adjacent birth year groups can result in smoother trends in genetic group effects over time (Fikse, 2003) and may improve predicted international genetic merits. The fuzzy assignment may also be applied between genetic groups for adjacent populations. It may be more difficult to identify adjacent populations. The classification may be based on mean

breeding values for known animals, which are contemporaries to the unknown ancestors, if such breeding values are available.

Relative importance of information sources: an example

The accuracy of international genetic evaluations depends on the heritabilities, effective daughter contributions, genetic correlations, relationships as well as unbiased national genetic evaluations, correct identities and pedigree information. Resistance to CM is characterised by a low heritability, but correlated traits are available. In this small example, the importance of different effective daughter contributions is illustrated to give a more detailed explanation of the mechanics behind the findings in Paper II, V and especially III.

The relative importance (RI) of different information sources can in principle be quantified from the row of the mixed model equations pertaining to the animal of interest. Klei et al. (1999) derived simple formulas for bulls with only daughter and parent information (i.e., no male progeny) to calculate RI for MACE. These formulas are used here to illustrate RI of various information sources for CM in Sweden (Figure 1).

The genetic parameters from Paper III are assumed and two correlated traits (i.e. SC from Sweden and Canada) are considered in addition to CM from Sweden. CM in Sweden and SC from Canada represent the two extremes regarding heritability in Paper III. That is, the heritabilities are assumed to be 0.02, 0.08 and 0.27 for CM in Sweden, SC in Sweden and SC in Canada, respectively. The genetic correlation between CM in Sweden and SC from Sweden or Canada is estimated to be 0.68 and 0.65, respectively. The number of effective independent daughters (n) is assumed to be either the same for CM (n_{CM}) and SC (n_{SC}) in Sweden (MT-MACE) or zero for SC in Sweden (ST-MACE), whereas the number of effective daughters in Canada (n_{CA}) is fixed at 0, 50 or 1000.

Parent information receives relatively high emphasis for low heritability traits unless the bull has several daughters with records for the given trait or some daughters with records for a correlated trait. Two hundred and ninety n_{CM} are required to obtain equal emphasis for the own effective daughter contribution as the parent average (if $n_{SC}=n_{CA}=0$; otherwise less). In comparison, 71 and 20 effective daughters are needed when the heritability is 0.08 and 0.27, respectively, of the trait of interest. The RI from correlated traits decreases as the amount of direct information increases, but a bull with 4009 n_{CM} has a combined RI of 90% for direct daughter and parent information when $n_{CA}=1000$ and $n_{SC}=n_{CM}$.

Information from a correlated trait with high heritability is more important than direct information when the total number of daughters is low. Hence, with a decreasing total number of effective independent daughters, it is advantageous to increase the percentage of daughters tested for the correlated trait with the highest heritability (i.e., increase number of daughters tested in Canada in this example) in order to maximise the total Mendelian sampling contribution relative to parent information. The maximum relative importance of daughter information for a correlated trait is equal to the genetic correlation with the trait of interest. This means that as the total number of daughters increases, the RI of indicator traits with low genetic correlation decreases compared with indicator traits with a higher genetic correlation, but lower heritability.

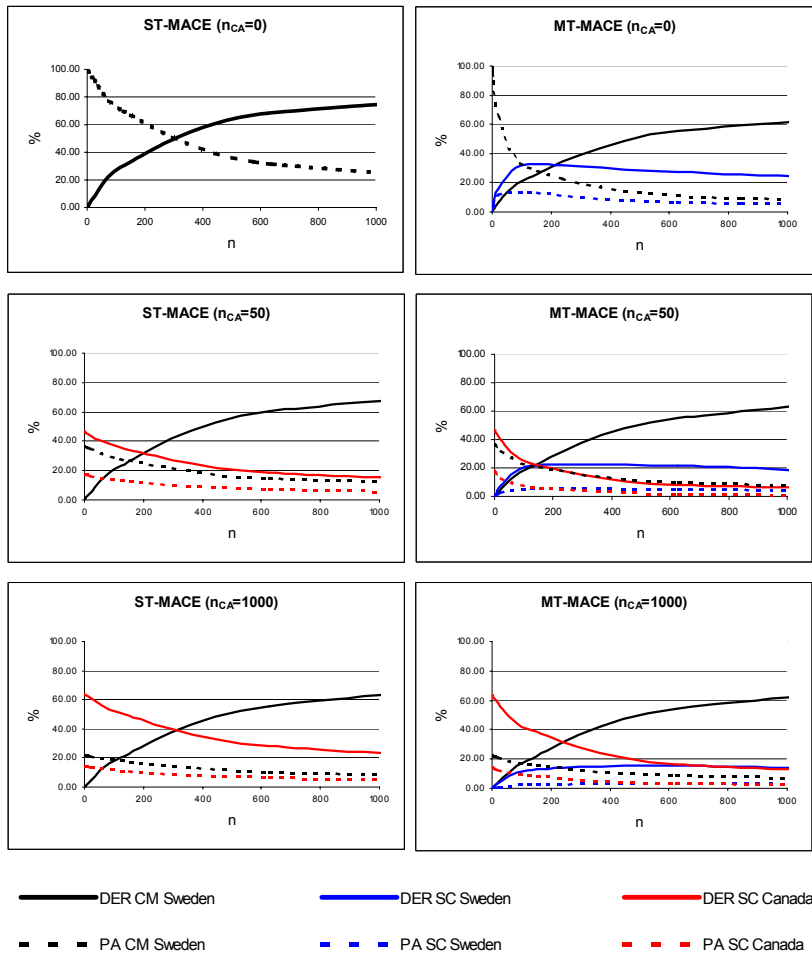


Figure 1. Relative importance (in percentage) of information sources due to effective independent daughters (DER) and parent information (PA) for CM in Sweden, SC in Sweden and SC in Canada on the Swedish CM scale. For MT-MACE, information for all three traits is considered, whereas information for SC in SWE is not considered for ST-MACE. Genetic parameters were as in Paper III.

Selection intensity

It was concluded in Paper II that the best single scale to base selection decisions on for the non-Nordic countries was expected to be the Danish CM scale, if the aim is to maximise the selection differential of the 10 highest ranking bulls for resistance to CM for the concerned non-Nordic country. However, the conclusion may be different when the international genetic evaluation is based on MT-MACE instead of ST-MACE and when the overall selection goal is assumed to be broader than just resistance to CM.

Selection differentials tended to be higher when based on MT-MACE than ST-MACE predictions (MT04 versus ST04; Table 8). This was especially true for the two Swedish traits, which can be explained by higher reliabilities for MT-MACE than ST-MACE predictions. The top 10 bulls based on MT-MACE predictions also had ST-MACE predictions, so in this case, the increased selection differentials were due to differences in predictions rather than more bulls to select among because the population means were consistent for ST-MACE and MT-MACE.

Table 8. Selection differentials for national (N01, N03, N04)¹ and international ST-MACE (ST04) and MT-MACE (MT04) predictions, and number of common bulls (CB) between top 10 ST-MACE and MT-MACE predictions.

	N01	N03	N04	ST04	MT04	CB
Clinical Mastitis:						
DNK	1.22	1.24	1.25	1.29	1.29	8
FIN	0.90	1.00	0.95	1.04	1.06	4
SWE	0.82	0.83	0.84	1.12	1.19	6
Milk Somatic Cell:						
DNK	1.16	1.18	1.16	1.22	1.23	6
FIN	1.04	1.04	1.04	1.21	1.22	7
SWE	1.03	1.02	1.02	1.22	1.27	5
CAN	1.24	1.27	1.26	1.33	1.33	8
DEA	1.26	1.34	1.33	1.33	1.33	9
EST	0.88	0.86	0.89	1.25	1.26	7
FRA	1.19	1.18	1.19	1.29	1.29	5
USA	1.23	1.22	1.22	1.27	1.29	6

¹N01 = evaluations used in Paper II and May 2001 Interbull routine evaluation;

N03 = evaluations used in Paper III and November 2003 Interbull routine evaluation;

N04 = evaluations used in Paper III and February 2004 Interbull routine evaluation.

The conclusions from Paper II still hold for newer data and when MT-MACE is used for international genetic evaluations. That is, selection differentials would be higher when based on international rather than national evaluations for most country-trait combinations, mainly because there are more bulls to select among for international evaluations (Smith and Banos, 1991). Furthermore, the correlated selection differential in CM is expected to range between 0.88 and 0.93 genetic standard deviation units for the non-Nordic countries, when selecting for SC MT-MACE predictions in the same country and when assuming a within-country genetic correlation of 0.7 between CM and SC. In comparison, the expected

correlated selection differential in CM for these countries would be 1.1 genetic standard deviation units if selection were based on the Danish CM MT-MACE predictions (if a genetic correlation of 0.85 is assumed between CM in DNK and a non-Nordic country).

Random fluctuations can cause some differences in the average of the highest 10 predictions, and hence also in the presented selection differentials as illustrated by some of the differences between the 2003 and 2004 national evaluations. This was best illustrated by Estonia, which had the lowest number of bulls evaluated. Finland, Canada, and Germany (Germany-Austria) changed their model for national genetic evaluation of udder health between May 2001 and November 2003. This may explain the differences in selection differentials based on these two sets of evaluations for each of these countries.

The selection goal is broader than CM alone for all countries. Production traits generally receive the highest selection emphasis (Miglior et al., 2005) and young bulls are typically the most interesting selection candidates. Hence, it is not only top ranking bulls for udder health that are of interest for selection purposes. To base the choice of best scale on the selection differentials for the top 10 ranking bulls can therefore be misleading. The genetic evaluation model for CM should therefore predict breeding values well for young bulls in particular, and regardless of whether the bull has a superior genetic merit for CM.

Combining information from different MACE scales

The discussion in the previous section focused on which international udder health scale is the best to base selection decisions on for the non-Nordic countries. These countries only use international genetic udder health evaluations on their own SC scale. However, more than one udder health scale could be used to better capture the additive genetic variation for CM in the Nordic countries. The vector of MACE solutions ($\mathbf{u}_i = \mathbf{Q}\mathbf{g}_i + \mathbf{s}_i$) for each country-trait scale i can be combined into one or several phantom MACE scales (\mathbf{u}_j) for country j by using the following formula:

$$\mathbf{u}_j = \mathbf{g}'\mathbf{V}^{-1}\mathbf{u}_i,$$

where \mathbf{g} is a vector containing the expected genetic correlations between the phantom scale and the traits included in MACE, and \mathbf{V} is the (co)variance matrix among the estimated international breeding values from MACE. This formula is a generalisation of the equation derived by Klei (1995) for a situation in which a bull has daughter information in only one country for a total of two countries. The elements in \mathbf{V}^{-1} and \mathbf{u}_i are computed during routine international genetic evaluations and are therefore readily available. The benefit of this approach is that genetic correlations are modelled directly between predictor traits (e.g., Nordic CM) and CM in a non-Nordic country. If CM in a Nordic country is first converted to SC in a non-Nordic country most information is lost.

The challenge is to find appropriate genetic correlations (\mathbf{g}) and sire variances for the phantom traits. The latter is required for interpreting and deriving economic weights in the country of interest. The sire variances may be estimated based on data from research herds. Alternatively, estimates from a similar trait

measured in a country with similar production circumstances may be used, or economic values may be assigned ad hoc.

The genetic correlations between a phantom scale and the country-trait scales for which data is available and included in MACE are obviously not known, but some guidance may be given by the genetic correlations between traits that are included in MACE. Thus, the genetic correlation between CM measured in a Nordic and a non-Nordic country may be assumed equal to 0.85 based on available across-country genetic correlation estimates for CM (Paper II). Alternatively, estimated genetic correlations between SC measured in different countries might to some extent be an indication of the genetic correlations for CM between the same countries. For example, the across-country genetic correlation between Denmark and Sweden is 10% higher for SC than CM (Paper III). Thus, the genetic correlation between CM in a Nordic and a non-Nordic country could be assumed to equal 0.9 times the genetic correlation between SC in the same two countries. Likewise a genetic correlation of 0.7 may be assumed between CM and SC within a non-Nordic country, and a correlation between CM and SC measured in two different non-Nordic countries may be assumed equal to 0.7 times the genetic correlation between SC measured in the same two countries.

Arbitrary differences in trait definitions may cause across-country genetic correlations estimated for MACE to be lower than the genetic correlation between true traits of interest. Hence, regression techniques may instead be used to estimate prediction formulas based on estimated genetic correlations among similar traits measured in other countries and different indicators of the average production system in these countries. Such formulas would be most reliable when data are available from several countries representing a broad range of different production systems and useful descriptors of the environmental factors causing genotype by country (environment) interaction are available. Such techniques may also be used to predict international breeding values for countries not contributing any data to international genetic evaluation.

The phantom scale for CM in a non-Nordic country would be dominated by SC measured in the home country for most local bulls. This is especially true because parents do not have direct local information for CM in the non-Nordic country. However, for bulls with daughters in multiple countries including one or more of the Nordic countries, the trait with the highest genetic correlation with the trait of interest would contribute significant information as illustrated in the previous section. Sires with daughters in multiple countries are typically elite sires, which further instigates capturing the Nordic CM information in a more optimal way.

The different sets of international breeding values pertaining to a particular country can be combined into super traits using selection index methodology. For example, CM and SC breeding values can be combined into an udder health index by weighting each set of breeding values by the economic weights associated with each trait. The construction of such an index is easiest when the individual breeding values are inferred simultaneously. In such cases exact selection index weights can be obtained since the correlation structure and possible differences in pedigrees and in environmental effects have already been accounted for in the multiple-trait breeding values (Schneeberger et al., 1991). The economic value for SC should then reflect the value of low SCC alone and not include the value of lower mastitis liability.

An optimal combination of separate ST-MACE evaluations (e.g. use of both CM and SC evaluations for the same country) requires the knowledge of covariances between evaluations, which do not only depend on the correlation structures, but also the pedigree information used for the separate genetic evaluations. The latter is ignored in practice when combining evaluations from separate models. The ease of combining evaluations for different traits is another practical advantage of MT-MACE over ST-MACE.

Multiple-trait MACE

MT-MACE is expected to be advantageous compared with ST-MACE, even if all countries perform multiple-trait national genetic evaluations for all the traits they include in international genetic evaluations. This is because correlations are modelled among each individual (pure) trait rather than among combined traits (Figure 2). In a simulation study, Sullivan et al. (2005) showed that MT-MACE predictions of lactation specific production traits were closer to true breeding values compared with both ST-MACE of the combined lactation traits and with separate ST-MACE of the single lactation traits. This was for a situation where all countries had the same type of national genetic evaluation model.

In practise national genetic evaluation models differ. In more than half of the national genetic evaluations considered in the August 2005 Interbull udder health routine evaluation different parities were considered as different, but correlated traits (Table 2). MT-MACE allows different national evaluation practices, but can to some degree force a harmonization on traits from various countries through the multivariate deregression. The harmonisation is forced in the sense that it is less important whether the national evaluation were single- or multiple-trait. The multivariate deregression separates the information due to each trait and thereby ensures comparisons of “cleaner” traits at the correlation estimation and MT-MACE level compared with the univariate deregression procedure as illustrated in Paper III. This is illustrated for CM in Denmark and Sweden in Figure 2. A higher genetic correlation between CM in Denmark and Sweden could probably have been obtained if the udder conformation information considered in the Danish national genetic evaluation model was also considered in the multivariate deregression procedure.

Although the same genetic correlations were used for ST-MACE and MT-MACE in Paper III, the predictive ability for bulls with most daughters in Denmark still benefited from changing from ST-MACE to MT-MACE. Denmark utilised the within-country correlation structure between CM and SC in their national multiple-trait model. The correlation between consecutive evaluations for the bulls with most daughters in Denmark was 0.01 higher for MT-MACE than ST-MACE on the Swedish and Finnish CM scale, but essentially the same for ST-MACE and MT-MACE for other country-trait scales. Thus, the advantage of changing from ST-MACE to MT-MACE was largest for countries not considering the within-country correlation structure in their national genetic evaluation. Pearson product-moment correlations between MT-MACE and ST-MACE predictions for bulls with most daughters in Denmark was 0.97 and 0.98 for CM in Finland and Sweden, respectively, and ranged between 0.98 and 0.99 for SC in countries other than Denmark.

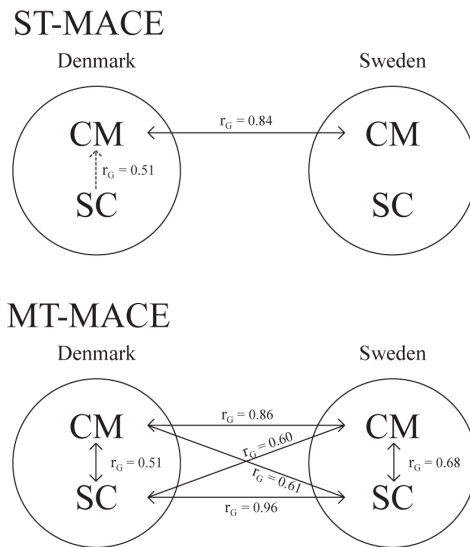


Figure 2. Illustration of correlated information used to predict international genetic merits for clinical mastitis (CM) for two countries (i.e. Denmark and Sweden). Solid lines represent correlation structures modelled in MACE, whereas broken lines represent correlation structures modelled in the national model and indirectly accounted for in MACE.

Next steps toward better international genetic udder health evaluations

Two different methods were implemented and compared with the international genetic evaluation procedure currently applied for routine international genetic evaluations. Both methods enable more information to be considered in the international genetic evaluation, either by accommodating for multiple traits per country or for prior information. Both methods had better overall predictive ability compared with the current method. A fully Bayesian Mace applied to multiple traits and countries is expected to be a better approach than the current MACE model extended only to either multiple-traits per country or to a fully Bayesian setting but allowing only one trait per country, if computational requirements were not a concern.

Although the fully Bayesian MACE model presented in Paper V allows non-zero residual correlations and multiple traits per country, the computational requirements for a multiple-trait-multiple-country fully Bayesian genetic evaluation would be too high in the near future, at least for the international Holstein population. Increased computer capacity and more efficient sampling algorithms may, however, help to make such international genetic evaluations feasible for dairy cattle in the foreseeable future. If for example, the processor and memory capacity continues to double approximately every 1.5 years, then fully Bayesian MACE could be applied to breeds other than Holstein in less than 10 years from now if desired. More efficient sampling algorithms could make such an implementation feasible in less time.

Whether a fully Bayesian implementation is desirable, or if instead more traits should be considered per country, depends on the data available. The advantage in terms of predictive ability of inferring international genetic merits simultaneously in a fully Bayesian setting is expected to decrease with increasing strength of genetic ties between populations. Likewise, the advantage of including more traits

per country in a multivariate analysis depends on the availability of useful predictor traits and the ability of national genetic evaluation models in describing all relevant variation associated with the trait of interest (i.e. the size of the heritability). Furthermore, the size of the international population will also to some extent determine what is feasible computationally.

The MT-MACE approach, which was applied in Paper III, can be considered for international genetic udder health evaluations in the near future. The software is available, the procedure has been extensively tested and it has better predictive properties than the currently applied ST-MACE approach. An application of MT-MACE to the current udder health traits considered in routine international genetic evaluation (i.e. only one SC and only one CM trait per country) would not increase the dimension of the mixed model equations dramatically and seems straightforward.

It should, however, be considered to allow each country to submit additional (e.g., up to four) udder health traits for a required research evaluation preceding official implementation to gain experience with large-dimension MACE inferences. Four traits per country would for example allow each country to submit three CM or three SC lactation specific traits plus an additional predictor trait (e.g. udder depth, or SC).

Currently, no experience is available for MACE for more than 30 country-trait combinations and near-singularity of the correlation matrix may pose considerable problems in the computation of international breeding values if the dimensions are extended dramatically beyond this. Estimation of the required genetic correlations will also be a major computational task, but it should be feasible given the current computational capacity and the current country-subsetting procedure practised by Interbull. In this procedure up to seven traits are considered at a time.

Even with country-subsetting and algorithms with better convergence properties such as average-information REML (Madsen et al., 2000), the total number of correlations to be estimated will still be a main practical limitation for MT-MACE. The criteria used for selection of the well-connected subset for correlation estimation may be modified to reduce the number of bulls included from countries with multiple traits and the computational demands. In Paper I to III and in routine Interbull evaluations, the data used for correlation estimation comprise bulls with evaluations for multiple country-trait combinations as well as bulls that belong to 3/4 –sib groups that have members with evaluations for more than one country-trait combination. This means that all or at least most of the bulls from countries with multiple traits will be included in the correlation estimation. It may be desirable to reduce the number of bulls included from such countries for computational convenience (Mark, 1999; Jorjani et al., 2005). However, the risk of underestimating the sire variances increases when the number of bulls in the subset is reduced.

The selection bias may be reduced when all traits per country are analysed simultaneously and the deregression procedure is applied to only the well-connected subset rather than the full data. This idea is similar to the suggestion of Goddard (pers. comm.). He suggested to apply the deregression to only the well-connected subset and to leave out 3/4–sibs from the well-connected subset for minimising selection bias while reducing computational requirements of correlation estimation for ST-MACE.

Conclusions

The main conclusions based on this thesis are:

- Deregression and multiple across country evaluations were feasible and worked satisfactorily for a lowly heritable trait ($h^2=0.02$).
- SC and CM evaluated in different countries were highly correlated. The across-country genetic correlations ranged between 0.47 to 0.97 for SC and 0.59 to 0.89 for CM.
- The high across-country genetic correlations enable more efficient selection of dairy bulls globally compared with selection based on separate national genetic evaluations.
- Direct selection for CM was more advantageous than indirect selection for SC in terms of selection response for CM.
- The use of the Nordic CM evaluations improves the opportunity for selection against CM in non-Nordic countries and especially when MT-MACE is used for international genetic evaluations.
- The predictive ability and reliability of international genetic evaluations can be improved by including multiple traits per country in the international genetic evaluation. This was especially the case for CM and for countries not using the within-country correlation structure between SC and CM in their national genetic evaluation.
- Estimates of the same across-country genetic correlation differed considerably (up to 1.03 units) depending on estimation strategy when genetic ties between the concerned countries were weak. The differences decreased as the number of direct genetic links and hence the precision of the estimates increased.
- The use of prior information about genetic parameters yielded more stable correlations and improved inferences of international genetic merits for weakly linked populations.
- Fully Bayesian MACE yielded better overall predictions of international genetic merits for weakly linked populations compared with MACE inferences, which were conditional on different sets of known genetic parameters.
- An approximate Bayesian method to combine prior genetic correlations with REML estimates gained some of the predictive advantages of fully Bayesian inferences.
- Accounting for the uncertainty of (co)variance components had a large impact, especially for foreign country scales.

Recommendations

The recommendations from this thesis are:

- Deregressed national genetic evaluations are recommended as dependent variables in MACE regardless of the trait considered.
- Immediate improvements of current international genetic evaluations can be achieved by changing to MT-MACE.
- Fully Bayesian international genetic evaluations should be considered as an improvement in the long term when the computational capacity permits such computer intensive analyses to be conducted in a suitably short time period.
- Until fully Bayesian international genetic evaluations become feasible, it is recommended that prior genetic correlations be combined with REML estimates using an approximate Bayesian method.
- Interbull should develop a service in which they provide phantom CM breeding values to non-Nordic countries, which these countries can use to improve their expected selection response for resistance to CM.
- National genetic evaluation units should strive to record CM and evaluate this information using the best possible genetic evaluation models. This would result in better international genetic evaluations and enable increased genetic progress for CM.

Implications

The thesis has helped to establish the foundation for low heritability traits to be considered in international genetic evaluations. This is not only beneficial for clinical mastitis, but also traits such as longevity, calving and fertility traits. The findings have led to the introduction of routine international evaluations for udder health traits for 60 dairy populations representing six different breeds.

Further possibilities for improving current methods in the short and long term have been identified and applied, namely multiple-trait-multiple-country evaluations and Bayesian MACE. Multiple-trait MACE methods are not only useful for international genetic evaluations, but may be used to combine separate national genetic evaluations in a more optimal way than a selection index approach. ST-MACE is already being used for this purpose in a few situations, but residual correlations should preferably be accounted for when different from zero.

The thesis has led to improved genetic correlation estimation procedures including prior information. The use of prior genetic (co)variances enabled international genetic evaluations for weakly linked bull populations, which is useful for populations in their early stages of co-operation. As a result, routine international genetic evaluations for Ayrshire conformation traits have been implemented. The approximate method to weigh prior and REML estimates of genetic correlations has also been applied to other traits and breeds although the sources of prior information and the applied weights vary depending on the concerned trait.

Using the results of this thesis could prevent deterioration of resistance to mastitis globally, which would increase efficiency of dairy cattle production and diminish the needs for antibiotics to treat clinical mastitis.

Future research

Improved ways of using all available information for genetic evaluation will remain an important challenge in the future. Research on the following topics could lead to further improvements in international genetic evaluations for udder health traits:

- Development of methods to obtain prior genetic correlations between CM and various predictor traits measured in the country of interest or a different country.
- Identify and describe environmental factors that cause genotype by country (environment) interaction for CM and SC.
- Test the predictive ability of evaluations for a phantom MACE scale.
- Feasibility and implications of including additional predictor traits per country in MT-MACE (e.g. lactation specific traits, udder conformation).
- Options to reduce the rank of the genetic correlation matrix in MT-MACE and their implications on predictive ability and computational requirements.
- Accuracy of the multivariate method to approximate reliabilities for MT-MACE.
- Field data comparison of the MT-MACE strategy using effective independent weighting factors (Sullivan and Wilton, 2001) and within-country parameters (Paper III) with
 - MT-MACE based on weighting factors and genetic correlations obtained by iterating between creation of effective independent weighting factors and correlation estimation
 - MT-MACE based on multivariate weighting factor blocks (Schaeffer, 2001).
- Optimal strategies to estimate genetic correlations for MT-MACE:
 - More efficient algorithms such as average-information REML (Madsen et al., 2000) or pseudo-REML (Sullivan, 2004)
 - Fixation of within country parameters (heritabilities and correlations), consider priors with variable degree of belief
 - Data to use (e.g. selection of well-connected subset in situations with multiple traits per country)
- Development of more efficient sampling techniques for fully Bayesian MACE (e.g., improved blocking strategies).
- Improved assignment (e.g. fuzzy classification) and constraints for genetic groups (e.g. only solutions for base populations sum to zero).
- Parameters and pedigree information to include in the deregression procedure (e.g. national instead of international pedigree information).

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