INTERBULL: Past, Present and Future

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Introduction

This review of INTERBULL's role considers briefly the history and the current position but then concentrates on some issues that INTERBULL faces today and in the future.

The Past

The widespread international trade in semen, embryos and cattle created a need to compare the genetic merit of bulls and cows from different countries. Unfortunately each country uses a different scale for expressing EBVs and so EBVs from different countries are not comparable.

The first solution to this problem was the use of conversion equations (Goddard, 1985; Wilmink, 1986). These equations predict the breeding value in one country (EBV_1) given an EBV in another country (EBV_2). They have the form:

$EBV_1 = b * EBV_2 + a$

where

$b = b_g$ = $r_g * (\sigma_1/\sigma_2)$ = genetic regression of trait in country 1 on trait in country 2
r_g = genetic correlation between the trait in country 1 and country 2
σ_i = genetic standard deviation in country i.

Goddard and Wilmink proposed slightly different ways of estimates a and b but both were simple empirical methods based on the EBV's of bulls that had daughters in both countries. That is, they did not estimate = r_g , σ_1 and σ_2, but only b.

Conversion equations were a useful and simple way to compare bulls evaluated in different countries but they were not ideal. Schaeffer(1994) proposed a better method. He suggested using daughter yield deviations (DYDs) for each sire in each country as data in a multi-trait BLUP where milk yield (or any other variable) is treated as a different trait in each country. This is conceptually the same model as used for conversions, involving the same a and b, but makes better use of the data. It uses all the relatives of a bull in all countries to estimate breeding values for the bull for production in all countries.

INTERBULL implemented the Multiple Across Country Evaluations (MACE) method of Schaeffer and now more than 25 countries participate.

The Present

Selection of sires should be based on the overall merit of their daughters and this involves many different traits. INTERBULL now calculates EBVs for milk production traits, conformation, udder health, longevity, calving ease and stillbirth. We are nearing the point where a dairy farmer in Australia can obtain an independent evaluation of most of the best AI bulls in the world for the profitability of their daughters in Australia. It is an extraordinary service that is available in few, in any, other industries.

Naturally there are many issues that INTERBULL is facing in providing such an ambitious service.

Genotype x Environment interactions (G x E)

The MACE model allows production in each country to be a different trait. Whenever the genetic correlation between two countries is less than 1.0, this implies a GxE. These genetic correlations are estimated from normal field data that each country analyses in its own way. The true correlation could be less than 1.0 due to a real GxE or because the trait is defined in different ways in different countries. However, the estimated genetic correlation can be less than 1.0 due to sampling error or bias in the estimation method. An approximate method of estimating genetic correlations (Calo *et al.*) is

$r_g = r/\text{sqrt}(R_1 * R_2)$

where

r = the correlation between the EBVs from the two countries
R_i = the reliability of the EBV in country i.

The methods used by INTERBULL to estimate r_g are more accurate than this but the features of the approximate method still apply. For instance, if the accuracy of EBVs is less than the official reliabilities imply, the genetic correlation will be estimated to be less than 1.0, even if the true correlation is 1.0. Almost any imperfections in the data or the statistical model will cause the accuracy of EBVs to be less than the statistical analysis calculates, and so the genetic correlation may the estimated to be less than 1.0 when the true correlation is 1.0.

This implies that estimated genetic correlations may often be less than 1.0 when no GxE exists. We (Hayes *et al.,* 2004) have attempted to test the reality of genetic correlation involving milk production in Australia and other countries. The estimated genetic correlation between Australia and USA is 0.85. If there is a real GxE, it might be because cows in USA receive a higher level of feeding than cows in Australia and consequently have higher average yields. In support of this hypothesis, we found that milk yield in high production herds in Australia was more closely correlated to PTAs from the USA than milk yield in average Australian herds. This suggests that the GxE between USA and Australia is real.

However, not all estimated correlations less than 1.0 may be real. The estimated correlations between many European countries with apparently similar dairying environments is about 0.95. Perhaps some of these correlations could be treated as 1.0?

Genetic correlations between environments within a country can be as low as 0.85 yet typically we treat these as 1.0 and only calculate one EBV for the whole country. Is this inconsistent with allowing for small GxE in international evaluations? In practice the two types of GxE have different effects. Within a country, bulls are likely to be progeny tested in all environments. The genetic correlation between breeding value over all environments and breeding value in any one environment will be approximately 0.95 even if the genetic correlation between two extreme environments is only 0.85. Typically AI studs will also sell into all environments within the country, so bulls are tested across environments and sold across environments. This of course is not the case between countries. Typically a bull is tested in one country and so when it is marketed in another country the genetic correlation between performance in those two countries is relevant. This has large commercial implications because these imported bulls are competing against bulls progeny tested in the importing country.

An alternative to treating each country as a separate environment is to define environments regardless of country based on other criteria (eg climate and herd average milk yield). This has been called ‘borderless evaluations’. The criterion for grouping farms into the same environment should be that the genetic correlations between farms that are collected into the same environment is close to 1.0. In practice it is hard to estimate genetic correlations between individual farms with enough precision. So an alternative has been to group farms according to similarity in mean performance or physical characteristics. However, we need to be careful because two environments, that are similar by the criteria that we use, may still have a genetic correlation < 1.0.

Research in Australia and USA illustrates this problem. Mean level of milk yield appears to be a useful variable to use in defining environments. We found that high yielding herds in Australia had a higher genetic correlation with USA PTAs than low yielding herds in Australia. This supports the use of mean herd milk yield as a criterion. However, milk yield in low yielding herds in USA did not predict performance in Australia any better than performance in high yielding herds in USA. Therefore it would be inappropriate to group low yielding herds in USA together with Australian herds. It appears that the some other environmental factor (eg use of grazing) is important in defining environments. A similar conclusion might be reached by comparing two countries with low average yields such as Poland and New Zealand, which despite this fact have a genetic correlation < 1.0.

Thus before implementing borderless evaluations we need to identify environmental grouping such that herds within a group all have a genetic correlation close to 1.0.

Traits other than production

Although the economic importance of fertility has long been admitted, most countries, with the notable exception of the Scandinavians, were reluctant to evaluate bulls for the fertility of their daughters. One reason for this reluctance was the low heritability of fertility traits but another important reason was the absence, in countries such as Australia, of a mechanism by which to collect the necessary data. Now there is an outcry in many countries that fertility has declined. In Sweden, although some decline has occurred in their Holsteins whose genes trace to America, no decline has occurred in Swedish Red and Whites (Philipsson *et al.,* 2003).

The decline of fertility in the absence of direct selection, should not be surprising since we knew that there was a negative genetic correlation between milk yield and fertility. Are we seeing or will we see a similar decline in other traits?

Unfavourable genetic correlation also exist between mastitis and milk yield. However, here the situation is more complex. In Australia, we estimated the genetic correlation between milk yield and somatic cell count to be unfavourable early in first lactation but zero or even favourable by late in third lactation (Haile-Mariam *et al.,* 2001). In agreement with these estimates, we have not seen a genetic trend upwards in somatic cell count. However, perhaps the genetic trend in mastitis is upwards. We do not know this because we do not record mastitis incidence.

There are other traits that are not systematically recorded. For instance, Gary Rogers (pers comm) reports a phenotypic increase in cow mortality rates in USA. In Australia we do not always know whether a cow left the herd due to death or sale and so we cannot estimate trends in cow mortality or perform genetic evaluations for this trait.

In conclusion, history shows that it is dangerous not to record economically important traits, even those that are hard to record or have low heritabilities. It may be that these traits add little to the accuracy of the selection index, but we should at least monitor them so that we know if they are declining.

Estimating a large number of parameters

If INTERBULL is to estimate EBVs for many countries and many traits there are a large number of genetic correlations that must be estimated. These are affected by sampling error. For instance, in a 25 x 25 matrix of estimated genetic covariances it is unlikely that the matrix will be positive definite. If it is singular this means that there is a linear dependency. For instance, it is possible that the estimated covariance matrix implies that breeding value in country A, $BV_a = 3*BV_b - 2BV_c + 0.5\ BV_d$. By bending the matrix the singularity can be removed but a near dependency may remain, which is difficult to identify by inspection of the covariance matrix. Such a near dependency could lead to unsatisfactory EBVs for certain bulls.

More robust and more accurate EBV might be obtained from a covariance matrix that had less parameters and hence less sampling error. One approach is a factor analysis model. In this model BV in each country is a linear combination of underlying factors plus a component that is unique to that country. Only a small number of factors would probably give a good fit to the 25 x 25 matrix. The factor analysis model increases the number of traits because it includes a separate effect on each country as well as the factors, but the number of parameters is reduced because all these unique country effects are uncorrelated. Vincent Ducroq (pers comm) has investigated a similar model (principle components) and found it explains the observed covariances very well. This method should also improve the estimate of the genetic correlation between any two countries that have few direct links.

Total merit index

Each country may have different economic weights in their profit function. Therefore it is convenient for INTERBULL to calculate EBVs but for each country to combine these into its own selection index.

This approach could be extended to other cases. If overall type is different in different countries because some countries place more emphasis on some type traits than other countries, it might be advantageous for countries to combine individual type traits calculated by INTERBULL into an overall type EBV for their country. This is already possible for longevity with INTERBULL calculating EBVs for direct longevity and many countries including this in a their longevity index. Could this approach also be applied to fertility assuming that fertility in each country depends on slightly different underlying traits?

Effective population size and inbreeding

The worldwide spread of Holstein cattle from USA has caused concern that the effective population size of the breed may be lower than is desirable. Estimates from the USA find that the rate of inbreeding is about 0.002 per year (Thompson *et al.,* 2000). Assuming a generation length of 5 years, this is equivalent to an effective population size Ne = 50. Many people feel that this is dangerously low although the inbreeding coefficient is only about 0.03 among current cattle assuming a base about 1960.

The optimum rate of inbreeding is a compromise between the benefit of intense selection using only the best cattle as parents, and the disadvantages of inbreeding. Goddard and Smith (1990) found that the optimum number of sires of sons to select each year for a single population was between 1 and 4. Two sires of sons selected per year corresponds roughly to a rate of inbreeding of 0.0025. Therefore the current rate the inbreeding may not be far from optimal. Goddard (1992) considered a world population and found that the optimum rate was lower when different countries had different selection objectives or when the gains in breeding value were discounted at a faster rate than the losses from inbreeding depression. (Breeding objectives that change gradually over time mean that an increased rate of discounting should be applied to the gains from selection but not to the loss from inbreeding because decreased fitness is always a cost).

Studies of inbreeding traditionally focus on past inbreeding while there might be more concern that, in the future, inbreeding will be higher. Haile-Mariam and Goddard (unpub) have used semen sales and the pedigrees of young bulls to predict the composition of the future Australian herd including the inbreeding. This analysis predicts that the rate of inbreeding from 2005-2008 will be 0.0016.

Selection methods have been proposed that maximize gains in breeding value minus losses from inbreeding (Wray and Goddard, 1994) or equivalently, that maximize gains in breeding value at a fixed rate of inbreeding (Meuwissen, 1997). However, these methods are appropriate for a decision maker controlling the whole Holstein breeding program in the long term interests of the world dairy industry. In practice, the decision makers, such as AI studs, control only part of the world breeding program and wish to maximize their own profits. What selection method is appropriate for these real decision makers and how does this selection method affect long term inbreeding?

A dairy farmer buying semen should maximize the estimated breeding value of the calf minus the inbreeding depression predicted from the inbreeding coefficient of that calf. Therefore AI studs should select bulls whose semen such farmers will buy. We can assess the value of any individual bull or a team of bulls by calculating the average breeding value minus inbreeding depression of the calves they would sire if selected and used. We have tested a variety of selection methods in the Australian

Holstein herd. If the best bull is selected for each cow, based on calf EBV minus inbreeding depression, then the average inbreeding of the calves is reduced much below that which occurs if bulls are mated randomly. More surprisingly, the average relationship among the bulls, which controls long term inbreeding, is nearly as low as achieved by the method of Wray and Goddard. This occurs because cows with quite different pedigrees exist in the population and the new method selects relatively unrelated bulls to mate to these different cows. Thus, AI studs could use this method to select a team of bulls that maximized their own profit and which achieved a reasonable outcome in long term inbreeding.

Some selection decisions made by AI studs result in bulls whose semen will be sold many years in the future (eg choice of young bulls to progeny test). Using the future cow herd predicted by Haile-Mariam and Goddard, we can predict the inbreeding of their calves even if they are mated 5 years from now. Thus a team of bulls can be selected that will maximise the breeding value minus inbreeding depression of their calves born in 6 years time.

In conclusion, although breeding decisions are controlled by many decision makers each maximising their own profit, the rate of inbreeding can be close to optimal if their decisions are made correctly.

The number of sires of sons selected world wide depends on the genetic correlations assumed between the breeding objectives of different countries. Even correlations between countries of 0.9 increase the number of sires selected greatly (Goddard, 1992).

Models used by INTERBULL

National evaluations are moving towards the use of test-day models that allow genetic variation in the shape of the lactation curve but INTERBULL uses a lactation model. In Australia we import the INTERBULL EBVs into our national EBV calculation , so the use of different traits in national and international evaluations will cause some problems. Would it be desirable for INTERBULL to use the same traits as national evaluations (eg a mean and a slope for the lactation curve) although they do not analyse test-day data?

Similarly some countries might use multi-trait analyses to calculate EBVs while INTERBULL uses single trait. The distinction is not important for traits such as milk and protein yield but it could be important for, for instance, milk yield and fertility. It is not possible to carry out a proper multi-trait analysis using only bull DYDs or EBVs: you need to use individual cow data. An approximation based on DYDs will work well if all cows are recorded for all traits but less well if cows are measured for different subsets of traits. Would it be possible for INTERBULL to use a multi-trait animal model? Vincent Ducroq has proposed an approximate method that corrects phenotypic records for fixed effects and then carries out the multi-trait animal model which makes the method much less computationly demanding than a full multi-trait BLUP.

Why do we go to so much trouble to compare sires from different countries but not compare sires from different breeds? In a few countries (eg NZ) crossbreeding is used widely. These countries create links between the breeds as does the use of Holstein bulls in red breeds. Should INTERBULL analyse all breeds together and hence compare breeds and generate EBVs on crossbred bulls that are progeny tested in , for instance, NZ?

The Future

An international breeding program

Economic weights in many countries are similar implying selection for similar objectives. However, subtle differences in economic weights and GxE mean that breeding objectives vary from one country to another. Should we maintain one interbreeding Holstein population serving all or most temperate countries or should each country or group of countries develop a separate strain of Holstein?

If a single large population is maintained the advantage is that the larger size allows more intense selection. If this is the case, it is more efficient for all bulls to be progeny tested for the objectives of all countries. This is easy to do if countries differ in economic weights but there are no GxE. However, if there are GxE, then progeny testing each bull in only one country is inefficient. It would lead to greater progress and less inbreeding if all bulls were tested in a range of environments. It is not necessary to test all bulls in all countries. The fact that a few factors or principle components can explain the observed genetic correlations means that daughters in only a few countries are necessary to estimate breeding value in any country. As the AI industry is rationalised world wide perhaps multiple country progeny testing will increase.

DNA data

Publication of the bovine genome sequence combined with new, cheap genotyping methods will lead to a great increase in the use of DNA tests for quantitative traits in the next few years. How should INTERBULL respond to this?

We propose that there will be two phases in the use of DNA tests. In the first phase, which may last till 2008, DNA data will be used within AI studs and not made public. In this phase, there will be no need or opportunity for INTERBULL to use this data. In phase two, DNA tests will be for specific genes and will be patented as already occurs for single gene abnormalities such as CVM. In this phase, knowledge of the alleles that a bull carries at each gene will be part of the public description of the bull's genetic merit. It will undermine EBVs as a basis for selection if they do not include this data. Therefore, INTERBULL should store and use DNA data.

As the number of DNA tests marketed explodes, there will be a great need for impartial information on the effect of these genes on many traits in many countries. INTERBULL could be the ideal organisation to estimate these effects because it could have access to the whole world dataset. In fact, estimation of the effect of specific gene variants on phenotype could become a major new role for INTERBULL.

Conclusions

The current INTERBULL EBVs are a remarkable service to the world dairy industry, allowing dairy farmers to select the most suitable bulls for their needs from a world population of AI bulls. However, there are many issues for both INTERBULL and the world breeding program that are still worth consideration.

There may be a tendency to underestimate the genetic correlations between the same traits recorded in different countries, but at least some of these GxE are biologically real and need to be included in INTERBULL evaluations. Estimation of these genetic correlations could perhaps be improved by using a model, such as factor analysis, to explain the correlations. Different environments exist within, as well as between, countries, supporting the idea of 'borderless evaluations', but we need to show that environments that are grouped together have a genetic correlation with each other close to 1.0.

The genetic decline in fertility that has occurred, should act as a warning of the need to record traits that are economically important even if they are lowly heritable and or hard to record.

The domination of Black and White cow populations by Holstein and the intense selection of bull sires that is practiced, has reduced the effective population size of the world Black and White cattle population. However, it is not clear that current selection departs too greatly from an economic optimum. We propose a new method of selection to balance gains in breeding value against inbreeding that is appropriate for competing AI studs and which leads to reasonable levels of inbreeding. Selection among the world population of bulls would be more accurate and effective population size would be greater if bulls were progeny tested in multiple countries.

There are advantages if the models used by INTERBULL are compatible with the models used for national evaluations. This might lead INTERBULL to consider genetic variation in lactation curve, multi-trait and animal models.

In a few years time DNA tests will be common and the public description of each bull's genetic merit will include a list of the alleles he carries at specific genes. INTERBULL should respond to this by integrating DNA data into EBVs. In fact a major new role for INTERBULL could be to store a world wide dataset of DNA results and to provide accurate and unbiased estimates of the effects of many genes on many traits.

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