Implementation of GPS-MACE accounts for genomic preselection

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Abstract

Genomic pre-selection (GPS) has altered the distributions of breeding values for AI bulls, because genomics made it possible to identify above average bulls within a family prior to progeny testing. Before genomics, it was reasonable to assume within-family pre-selection was random in EBV models, but this assumption is no longer valid. The international MACE model was thus modified to account for non-random within-family GPS of AI bulls. The effects of GPS are estimated and included in the international EBV of sires in the new model: GPS-MACE. The estimates reflect different intensities of GPS across traits, breeds, countries of selection and time, and the accumulation of differential effects of GPS across multiple generations in a bull's ancestry, and across international borders. Estimates of GPS effects, and differences between EBV from GPS-MACE versus MACE were studied for three breeds (Holstein, Brown Swiss, and Jersey) and eight traits (milk fat, milk protein, conformation score, udder score, somatic cell score, fertility interval, cow conception, and milking speed). The effects of GPS were generally largest for countries that have shared genotypes of proven bulls to improve national genomic predictions and the effectiveness of national GPS programs. The countries identified as sharing genotypes were in the Inter-continental and Eurogenomics Holstein consortia, and the Intergenomics Brown Swiss service provided by Interbull. Estimates of GPS effects were largest and almost always favourable across all breeds and countries for the main traits of selection (fat, protein, conformation score, and udder score), and were generally centred on zero for the traits under weaker selection intensities (milking speed). The addition of GPS effects to the international model caused generally higher estimates of Mendelian sampling effects and correspondingly lower EBV for the dams of GPS bulls, when the estimated effects of GPS were positive. The net effects on EBV were small for older GPS bulls with high national EBV reliabilities, but they were notably larger and favourable for the most recent AI bulls from countries with effective GPS programs. The benefits of GPS-MACE over MACE were likely underestimated in the present study because GPS effects are only partially included in the current national EBV. As national EBV models are improved to more fully account for the effects of GPS, benefits of using GPS-MACE are expected to grow.

Key words: international evaluation, MACE, selection bias, genomic preselection, double-counting

Introduction

MACE evaluations use biased input EBV that were generated without genotypes, and therefore ignoring genomic pre-selection (GPS) effects on the distributions of breeding values for most recent AI bulls. Theories and modeling options to better account for GPS effects on these distributions in MACE results have been proposed (e.g. Patry et al, 2013; Fikse, 2014; Sullivan et al, 2019, 2022).

Objectives of the present study were to develop and describe a new model, which accounts for GPS effects in national EBV used as input to MACE and includes the GPS effects in international MACE evaluations published by Interbull. Impacts of GPS effects on MACE results for different traits, breeds, countries of selection and population scales of evaluation were studied.

The new model will be referred to as GPS-MACE to emphasize the addition of new parameters to estimate and include the effects of

GPS in the international EBV of selected AI bulls and their progeny.

Materials and Methods

Input data for eight traits from the MACE evaluations published in April 2022 for each of three breeds (Holstein, Brown Swiss, and Jersey) were re-analyzed using GPS-MACE. The traits were milk fat and milk protein yields (FAT and PRO), overall conformation and udder scores (OCS and OUS), somatic cell score (SCS), cow conception rate one (CC1), fertility interval (INT) and milking speed (MSP). International GPS programs have been in place for these three breeds of varying population size, while intensities of GPS vary among traits generally, and among combinations of trait by breed.

Bulls with national EBV based on progeny phenotypes for the 24 breed-trait combinations studied were born as recently as 2017. Approximately eight completed years of GPS bulls, born between 2009 and 2016, were included in these data.

1 - Estimating GPS effects

Genomic evaluation models can account for GPS effects when the genomic information used for selection is included in the evaluated data (Jibrila, 2022; Jibrila et al, 2023). For MACE, however, it is not possible to include genotypes directly, nor use national GEBV as input data without double-counting the predictive information from genotypes when MACE results are subsequently used as input in national genomic evaluations. Additionally, Interbull does not have access to all genotypes, so the GPS effects must be estimated without genotypes in GPS-MACE.

The effects of GPS are included in true breeding values (TBV) of selected sires and expressed in phenotypes of daughters of the GPS sires. The distributions of TBV for groups of GPS sires have shifted means and reduced variances, and these changes due to selection can be estimated from the EBV input data used currently by Interbull for MACE.

A simulation study confirmed that GPS effects on groups of AI bulls can be estimated without genotypes if the input national EBV include GPS effects on the EBV means for GPS groups of bulls. An analysis of national EBV currently available to Interbull showed a partial correction for GPS effects is possible, because the national EBV presumably include a portion of the true GPS effects (Sullivan et al, 2022). Conclusions from these studies were that MACE evaluations can be improved by updating both the international MACE model and the national EBV models, by:

A. adding GPS trend effects to the MACE model, to improve evaluation of the current input data.
B. adding GPS effects in national EBV models, while excluding the individual genotype effects, to reduce GPS biases and improve future MACE input data.

2 - The GPS-MACE model

With the currently proposed model changes for MACE, international EBV of GPS sires include Mendelian sampling terms (MS=EBV-PA) that are assumed to be drawn from selection-modified distributions, having altered means and variances due to increasing GPS intensities for AI sires born since 2009. The GPS effects are estimated based on national EBV distributions of males born at a given point in time, relative to parent average (PA) contributions from their male-only ancestors (Jakobsen and Dürr, 2012). Estimated MS-means for proven bulls will deviate farther from zero, and the variance of estimated MS deviations about the means will be less, for groups of GPS bulls from countries with effective GPS programs and high intensities of GPS. For populations with means and variances of estimated MS deviations being similar after 2009 as they were before, the estimated effects of GPS are expected to be close to zero. Efficiency of GPS can be lower for small populations, or if the availability or use of genotyping and genomic evaluation services has been limited in the local AI sire pre-selection programs.

Estimates of GPS effects are cumulative across generations. For example, the evaluation of a GPS bull with a GPS sire will include a first-generation estimate of GPS effects in the sire's EBV contribution to PA, plus a second-generation estimate of GPS effects in the MS of the bull. After many generations of GPS, as is the case for dairy cattle, the EBV of most recent AI bulls are based on PA that include many generations of accumulated GPS effects in the EBV distributions of male ancestors, plus the newest estimates for GPS-modified MS distributions.

2.1 - International GPS effects

Methods to estimate international GPS effects should account for changes in GPS intensities over time, which can vary significantly among the different combinations of trait by population included in MACE.

An input EBV in MACE is from a country or regional population where sire daughter performance was recorded and evaluated. The sire's country of pre-selection (*x*) can differ from the sire's EBV population of daughters (*d*). Although a sire is assumed to be pre-selected by one country, he can have current EBV and future daughters in any of the MACE populations. Predictions of GPS effects for the sire are therefore required for genetic predictions of future daughter performance in all MACE populations.

For the implementation of GPS-MACE, a proven bull's country of pre-selection was assigned based on country of registration, and not the countries where national EBV are available, which is where GPS effects are expressed through daughters of the GPS bulls. The country of registration is mapped to a population evaluation scale (*x*) included in the GPS-MACE model, and a selected MS-distribution is assumed for each group of GPS bulls born in the same birth cohort and preselected by the group of countries linked to a given population *x*. In most cases there is one country per population, but DFS is an example of a population including three countries (Denmark, Finland, and Sweden).

For a proven bull from a GPS group in population *x*, the GPS effect is estimated for his EBV as it would be expressed in population *x* ($\hat{s}_x$) and extended internationally through genetic regressions. For example, the expression of GPS effects in any population *d* of future daughters ($\hat{s}_{x:d}$) is:

$$\hat{s}_{x:d} = \frac{G_{x,d}}{G_{x,x}} \hat{s}_x$$

The genetic regressions used to predict expressions of GPS effects internationally are based on the genetic covariance matrix among MACE populations ($\mathbf{G_t}$) with the assumption that GPS effects follow the same pattern of international genetic expression as is currently assumed for unknown parent group (UPG) effects and for all other genetic partitions of animal EBV in the current MACE model.

2.2 - Trends in GPS effects

To avoid estimation problems with small genetic group classes, year is fitted as a genetic covariable rather than a genetic class effect, for smoothed estimates of trends in GPS effects over time. Separate GPS trends are estimated for each trait and population.

To allow non-linearity of GPS trends, an approach with 3-year knotted linear slopes is used, with the following assumptions for MACE input data from April 2022:

- GPS intensity = 0 for all birth years prior to the start of GPS (1980-2008).
- GPS intensity = X for all birth years in the most recent period (2014-2017).
- GPS effects have non-zero slopes for intermediate periods only (2009-2011 and 2012-2014).

- X = 0 in all years for smallest populations, where the GPS effects would be relatively small and unreliably estimated.

The GPS-MACE model accounts for different timings of GPS implementation, and different yearly changes in intensities of GPS for each combination of trait and population. Different types of trend that can be estimated under this model are demonstrated in Figure 1, with an example of yearly estimates for GPS effects in five countries from one of our previous studies.

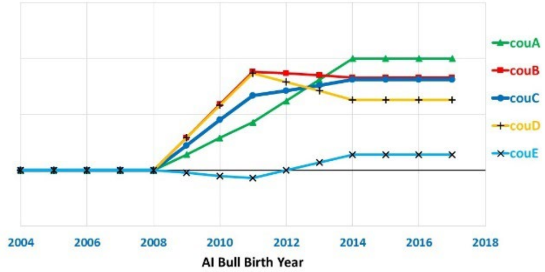


Figure 1. Examples of estimated trends in GPS effects from a previous GPS-MACE research trial.

2.3 - GPS effects across generations

The current MACE model for an observed deregressed EBV of a bull (Schaeffer et al., 1996; Jakobsen and Dürr, 2012) is:

$$y = \mu + \mathbf{Q_1 g} + \mathrm{A} + \mathrm{e}$$

Defining and parenthesizing the between (PA) and within family (MS) contributions in A:

$$y = (\mu^* + \mathbf{Q_1 g}^* + \mathrm{P}^*) + (\mathrm{m}^*) + \mathrm{e}^*$$

$$\mathrm{A} = \mathrm{P}^* + \mathrm{m}^*$$
$$\mathrm{PA} = (\mu^* + \mathbf{Q_1 g}^* + \mathrm{P}^*)$$
$$\mathrm{MS} = (\mathrm{m}^*)$$

The GPS-MACE model expands MS with new parameters ($\mathbf{Q_2 s}$) for the effects of GPS:

$$y = (\mu + \mathbf{Q_1 g} + \mathrm{P}) + (\mathbf{Q_2 s} + \mathrm{m}) + \mathrm{e}$$

$$\mathrm{A} = \mathrm{P} + (\mathbf{Q_2 s} + \mathrm{m})$$
$$\mathrm{PA} = (\mu + \mathbf{Q_1 g} + \mathrm{P})$$
$$\mathrm{MS} = (\mathbf{Q_2 s} + \mathrm{m})$$

The genetic group class effects for UPG, as expressed in the PA through $\mathbf{Q_1 g}$, account for selected base generations, while analogously the genetic group covariable effects, as expressed in the MS through $\mathbf{Q_2 s}$, account for selection effects in the most recent generations.

2.4 - Selection-modified distributions

Under current MACE, the vector of international, within-family genetic deviations ($\mathbf{MS}^*$) for an individual (a) with known parents has a multivariate normal distribution:

$$\mathbf{MS}_{\boldsymbol{a}}^* \sim \mathbf{N}(\,\mathbf{0}, 0.5 * \mathbf{G_t}\,)$$

where $\mathbf{G_t}$ is the genetic covariance matrix among trait expressions by population, and all $\mathbf{MS}_{\boldsymbol{a}}^*$ deviations are independent between different animals ***a*** and ***a'***.

Under GPS-MACE, $\mathbf{MS} = \mathbf{Q_2 s} + \mathbf{m}$, and if treating $\mathbf{s}$ as fixed, then:

$$\mathbf{MS}_{\boldsymbol{a}} \sim \mathbf{N}(\,\mathbf{Q}_{\mathbf{2}\boldsymbol{a}}\mathbf{s}, \mathbf{k}_{\boldsymbol{a}} * 0.5 * \mathbf{G_t}\,)$$
$$\mathbf{m}_{\boldsymbol{a}} \sim \mathbf{N}(\,\mathbf{0}, \mathbf{k}_{\boldsymbol{a}} * 0.5 * \mathbf{G_t}\,)$$

where $\mathbf{k}_{\boldsymbol{a}}$ is a diagonal matrix of variance reduction factors corresponding with the effects of GPS on variance for the selection group of bull a. Under this model, the $\mathbf{m}_{\boldsymbol{a}}$ are independent between animals ***a*** and ***a'***. The variance reduction factors can be approximated by considering $\mathbf{Q}_{\mathbf{2}\boldsymbol{a}}\hat{\mathbf{s}}$ as changes in MS-means caused by truncation selection (Tyrisevä et al, 2018).

If treating $\mathbf{s}$ as random, then:

$$\mathbf{MS}_{\boldsymbol{a}} \sim \mathbf{N}(\mathbf{0}, (\,\mathbf{V}(\mathbf{Q}_{\mathbf{2}\boldsymbol{a}}\mathbf{s}) \;+\; \mathbf{k}_{\boldsymbol{a}} * 0.5 * \mathbf{G_t}\,)$$
$$\mathbf{m}_{\boldsymbol{a}} \sim \mathbf{N}(\,\mathbf{0}, \mathbf{k}_{\boldsymbol{a}} * 0.5 * \mathbf{G_t}\,)$$

The $\mathbf{m}_{\boldsymbol{a}}$ are still independent between animals, but there are non-zero covariances between $\mathbf{MS}_{\boldsymbol{a}}$ and $\mathbf{MS}_{\boldsymbol{a'}}$ whenever $\mathbf{Q}_{\mathbf{2}\boldsymbol{a}}\hat{\mathbf{s}}$ and $\mathbf{Q}_{\mathbf{2}\boldsymbol{a'}}\hat{\mathbf{s}}$ are correlated, for example between animals in the same selection cohort, or between selection groups with similar GPS effects. The expectation of MS estimates is zero, but this does not force MS averages to equal zero. All MS estimates are regressed to some degree towards zero, and with a corresponding non-zero covariance imposed among the MS solutions of animals with similar GPS effects.

In genomic models, a covariance among selected cohorts is imposed in a similar way, when matrix A fitting covariances before selection is replaced by a genotype-based covariance matrix G, which has higher realized covariances after selection of only the similarly superior sibs within a family (VanRaden, 2008; Hayes et al, 2009). Analogously, only the similarly superior bulls are represented within a GPS group. The degree of regression towards zero is much smaller, and the non-zero covariance higher in GPS-MACE than in MACE with no **s** effects at all. The degree of regression can be minimized by a small ridge factor, or equivalently assuming large V(**s**).

While drafting the paper, we realized that when treating **s** as random instead of fixed, we did not add any fixed regressions across countries to the model. In the present study, the random regressions for GPS effects in every country were thus regressed towards zero, instead of regressing towards an overall fixed regression line, or towards a fixed regression that could be some function of population size. Although we have not explored this alternative approach yet, it could be considered in future research as a potential improvement to the GPS-MACE model.

The implementation of GPS-MACE in the present study was simplified by assuming $\mathbf{k}_a = \mathbf{I}$ for all bulls, as we continue to explore options for a practical application fitting heterogeneous genetic variances, with $\mathbf{k}_a \neq \mathbf{I}$ (Mäntysaari and Strandén, 2023). The covariances among selection cohorts are already included in EBV predictions from the currently simplified model, because $\mathbf{Q}_{2a}\hat{\mathbf{s}}$ is part of the predicted EBV definition for each animal, as shown below.

2.5 - The mixed model equations

After QP transformation of the **g** effects for UPG, the mixed model equations for GPS-MACE, with a ridge factor *c*>0 when treating **s** effects as random, or with fixed regressions in **s** if setting *c*=0 are:

$$\begin{bmatrix} \mathbf{X}'\mathbf{DX} & \mathbf{X}'\mathbf{DZ} & \mathbf{X}'\mathbf{DZQ}_2 \\ \mathbf{Z}'\mathbf{DX} & \mathbf{Z}'\mathbf{DZ} + \mathbf{W} \otimes \mathbf{G}_t^{-1} & \mathbf{Z}'\mathbf{DZQ}_2 \\ \mathbf{Q}_2{}'\mathbf{Z}'\mathbf{DX} & \mathbf{Q}_2{}'\mathbf{ZDZ} & \mathbf{Q}_2{}'\mathbf{Z}'\mathbf{DZQ}_2 + c\mathbf{I} \end{bmatrix} \begin{bmatrix} \boldsymbol{\mu} \\ \mathbf{Q}_1\mathbf{g} + \mathbf{a} \\ \mathbf{s} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{Dy} \\ \mathbf{Z}'\mathbf{Dy} \\ \mathbf{Q}_2{}'\mathbf{Z}'\mathbf{Dy} \end{bmatrix}$$

Matrix **D** is a diagonal matrix of EDC divided by residual variances, **W** in the inverted matrix of additive relationships among sires and UPG (Westell et al, 1988), modified to treat groups as random effects (Sullivan and Schaeffer, 1994), $\mathbf{G}_t$ is the matrix of genetic covariances among countries, and **X** and **Z** are incidence matrices connecting deregressed national EBV in **y** to the countries and AI bulls respectively.

The incidence matrix for **s** is $\mathbf{ZQ}_2$, and the use of ridge regression for **s**, with *c>0* is optional. Adding a ridge factor can reduce the risk of over-fitting current data and improve future predictions, especially for estimated GPS effects in smaller populations. If a ridge factor is too large, however, the expressions of GPS effects in future daughters might be under-predicted. Ridge regression can increase the stability of estimated covariable effects in **s** as new data are added to the evaluation each year, and it also reduces the chance of extreme individual changes from the current MACE results. The GPS-MACE model with a ridge factor *c>0* is relatively closer to current MACE than it would be if treating **s** as fixed.

The command instructions and input file descriptions to implement GPS-MACE using MiX99 software (Pitkänen et al, 2022) are provided in the appendix.

3 - Genetic predictions from GPS-MACE

The vector of international estimated breeding values is defined as:

$$\mathbf{EBV} = \hat{\boldsymbol{\mu}} + \mathbf{Q_1}\hat{\mathbf{g}} + \hat{\mathbf{a}} + \mathbf{Q_2}\hat{\mathbf{s}}$$

The GPS portion of EBV for an individual a can be written as:

$$\hat{\mathbf{s}}_a = \mathbf{Q}_{2:a}\hat{\mathbf{s}}$$

and partitioned as the sum of accumulated GPS effects on ancestor evaluations ($\hat{\mathbf{s}}_{\mathbf{PA}}$) plus the GPS effects on MS of the individual ($\hat{\mathbf{s}}_{\mathbf{MS}}$):

$$\hat{\mathbf{s}}_a = \hat{\mathbf{s}}_{\mathbf{PA}:a} + \hat{\mathbf{s}}_{\mathbf{MS}:a} = \left[\mathbf{Q}_{2,\mathbf{PA}:a} + \mathbf{Q}_{2,\mathbf{MS}:a}\right]\hat{\mathbf{s}}$$

Each row in $\mathbf{Q}_{2,\mathbf{PA}}$ is equal to the average of corresponding parental rows in $\mathbf{Q_2}$, which include the sums of PA and MS contributions to $\mathbf{Q_2}$ of the sire and dam respectively:

$$\mathbf{Q}_{2:sire} = \mathbf{Q}_{2,\mathbf{PA}:sire} + \mathbf{Q}_{2,\mathbf{MS}:sire}$$
$$\mathbf{Q}_{2:dam} = \mathbf{Q}_{2,\mathbf{PA}:dam} + \mathbf{Q}_{2,\mathbf{MS}:dam}$$

$$\mathbf{Q}_{2,\mathbf{PA}:a} = 0.5 * [\mathbf{Q}_{2:sire} + \mathbf{Q}_{2:dam}]$$
$$\hat{\mathbf{s}}_{\mathbf{PA}:a} = 0.5 * [\hat{\mathbf{s}}_{sire} + \hat{\mathbf{s}}_{dam}]$$

As with $\mathbf{Q_1}$ (Quaas, 1988) the matrix $\mathbf{Q_2}$ is generated chronologically, building the rows of parents before progeny. For each animal there is a row in $\mathbf{Q_2}$ for each country trait (i.e. MACE population) included in the model.

The definitions for rows of $\mathbf{Q}_{2,\mathbf{MS}:a}$ are based on the proven bull's (individual a) year of birth (BYR) and pre-selecting population (x). The only non-zero values are in columns for population trait x, and for bulls born since 2009 who were preselected by a population with GPS effects being estimated. The non-zero values for these bulls in the row for population d are defined as:

$$\mathrm{Q}_{2,\mathrm{MS}:ad,xk} = W_k * \frac{G_{d,x}}{G_{x,x}}$$

where W_k is the number of years within the k^{th} intermediate 3-year interval that has a non-zero slope (2009-2011 or 2012-2014). For April 2022 data in the present study, W_k were defined as follows, with values as in Table 1:

$$\begin{matrix} W_1 \\ W_2 \end{matrix}\Bigg\} = \begin{cases} BYR - 2008, min = 0, max = 3 \\ BYR - 2011, min = 0, max = 3 \end{cases}$$

Table 1. Number of year contributions from each knotted regression line in the estimated GPS effects of bulls born in different years.

	Bull's birth year - 2000								
	8	9	10	11	12	13	14	15	16
W_1	0	1	2	3	3	3	3	3	3
W_2	0	0	0	0	1	2	3	3	3

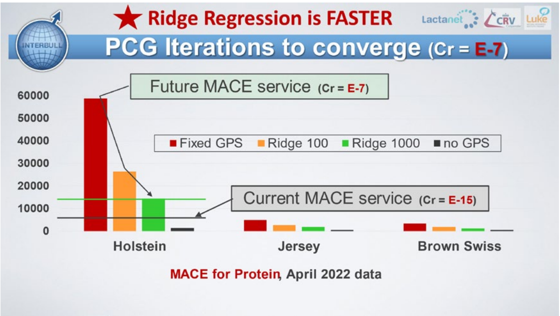
Strategies to add intervals as new years of GPS bulls that are progeny proven were presented previously (Sullivan et al, 2022).

While the columns for all populations other than x are zero in $\mathbf{Q}_{2,\mathbf{MS}:a}$, any column can be non-zero in $\mathbf{Q}_{2,\mathbf{PA}:a}$ because ancestors of bull a can be pre-selected by different countries, as is often the case due to the prevalence of international breeding of dairy cattle. Matrix $\mathbf{Q_2}$ captures details of the international GPS across historical generations, tracing back through each animal's history of GPS in all international ancestors.

Results and Discussion

1 - Solving GPS-MACE equations

Solving the equations took much longer with GPS-MACE than MACE. Using protein yield of Holsteins as an example, the number of PCG iterations to reach a typically acceptable convergence criterion, Cr=E-7, to decide differences are negligible between left and right sides of the equations, was 58,855 iterations for a fixed-regressions GPS-MACE application, compared with only 1,366 iterations for MACE (Figure 2; Fixed GPS vs. no GPS). In the current Interbull MACE service, iterations are extended further, increasing from 1,366 to 5,456 iterations to reach a more stringent convergence criterion, Cr=E-15. However, even after these added iterations, MACE is still solved with less than 10% as many iterations as were needed to reach Cr=E-7 for fixed-regressions GPS-MACE. A GPS-MACE model requiring more than 10 times as long to run as the current MACE service of Interbull might be difficult to implement in practice.


Ridge Regression is FASTER

PCG Iterations to converge (Cr = E-7)

Figure 2. Iterations required to reach convergence of the GPS-MACE system of equations for protein yield, compared with Interbull MACE equations.

In GPS-MACE, selection effects are estimated for both the oldest (through $\mathbf{Q}_1\hat{\mathbf{g}}$) and newest generations (through $\mathbf{Q}_2\hat{\mathbf{s}}$) of pedigreed individuals after many generations of breeding, and with different patterns of data recording and population sizes among the international countries included in the model. International breeding has been used to upgrade different breeds and national populations at different times, to periodically change directions of selection, and to expand local gene pools and reduce inbreeding with the use of foreign out-cross sires. Under the simpler MACE model, selection effects were only being estimated at one end of the pedigree (the base generation) rather than at both ends.

Additionally, the added partition for GPS effects within an animal's EBV is partially confounded with PA. This confounding can cause numerical instabilities and slow convergence when iterating on GPS-MACE equations. Ridge regression, or equivalently treating the regressions on GPS effects as random, is guaranteed to break linear dependencies that might otherwise occur in practice, while also increasing the rate of convergence. Similar benefits were shown previously for models that include UPG to account for selected base populations, if the UPG effects are treated as random instead of fixed (Sullivan and Schaeffer, 1994).

A sensitivity analysis was used to assess potential benefits of ridge regression for GPS effects in GPS-MACE, using ridge factors (c) equal to 1, 10, 100 or 1000. Using ridge regression significantly improved the rates of convergence for GPS-MACE (Figure 2). In all comparisons, applications with relatively larger ridge factors consistently required fewer iterations to converge. Relative to the fixed regressions model ($c=0$), which required more than ten times as long, ridge regression with $c=1000$ required only twice as long as the current Interbull MACE service. If ridge factors larger than 1000 could be used, then solving times for GPS-MACE would be reduced even further.

2 - Estimates of GPS effects

All results for GPS effects and EBV are on standardized scales, due to the use of standardized national EBV as input data. The full set of national EBV used in GPS-MACE for a given trait and population, which included progeny-proven bulls born since 1980, were re-scaled to the standard normal (~N(0,1)), and when necessary the scale was also reversed with a multiplication by -1, so that positive normalized EBV were desirable for all traits and populations. Aggregate results were thus easily interpreted across traits, population scales of evaluation, and breeds, because of these standardizations.

The estimated GPS effects were pooled across countries in five breed groups, among which important differences were expected in GPS intensities across and/or within traits:

A. HOA: Holstein populations with shared genotypes of reference animals in the Inter-Continental consortium: CAN, CHE, GBR, ITA, JPN, USA.
B. HOB: Holstein populations with shared genotypes of reference animals in the

Eurogenomics consortium: DEU, DFS, ESP, FRA, NLD, POL.

C. HOC: Holstein populations not in HOA or HOB but included in MACE for any of the eight traits in the present study: AUS, BEL, CZE, EST, HRV, HUN, IRL, ISR, KOR, LTU, LVA, NZL, PRT, SVN, SVK, URY, ZAF.
D. BSW: Brown Swiss populations in MACE for any of the eight traits in the present study: AUS, CAN, CHE, DEA, GBR, FRA, ITA, NLD, NZL, SVN, USA.
E. JER: Jersey populations in MACE for any of the eight traits in the present study: AUS, CAN, CHE, DEU, DFS, GBR, IRL, ITA, NLD, NZL, USA, ZAF.

All populations in HOA and HOB have well-established GPS programs and large numbers of national EBV across all traits for GPS bulls. Data were thus sufficient to estimate GPS effects for all traits in these populations. In contrast, the HOC, BSW and JER groups included many smaller populations, the smallest of which had fewer than 20 GPS bulls with a national EBV for one or more of the traits. The GPS effects were assumed equal to zero if there were fewer than 20 national EBV in total for a given trait from GPS bulls selected in a population, which was the case for 33%, 40% and 38% of the trait-by-population combinations in these three breed groups. The GPS effects were thus estimated for only 67%, 60% and 62% of all population traits in HOC, BSW and JER respectively.

For breed groups with well-established GPS programs and large international reference populations (HOA and HOB), the use of ridge regression had very little impact on the estimated effects of GPS. While the largest notable impacts of using higher ridge factors were decreases in variability of GPS estimates among populations, the SD of estimates within HOA and HOB were nearly the same with fixed versus ridge regressions (*c=0* versus *c=1000*). In contrast, SD of estimates decreased substantially with larger ridge factors for HOC, BSW and JER (Table 2). With *c=1000*, the SD of estimates were still relatively smaller for HOA and HOB than the other groups, but this could reflect true differences in SD if GPS intensities have been relatively more homogeneous among the countries in HOA and HOB.

Table 2. Standard deviations (SD) of estimated GPS effects for bulls born 2014-2017, across *n* country-traits within Breed Group^z.

Ridge Factor	Breed Group HOA *n*=45	HOB *n*=47	HOC *n*=55	BSW *n*=43	JER *n*=43
c=0	0.09	0.11	0.23	0.19	0.22
c=100	0.09	0.10	0.20	0.21	0.15
c=1000	0.09	0.10	0.14	0.15	0.13

^{z}HOA, HOB, HOC = Holstein groups A, B, C; BSW = Brown Swiss; JER = Jersey.

Observed patterns in the ranges of GPS estimates (Table 3) were consistent with the SD results in Table 2. The minima and maxima for HOA and HOB were almost unaffected by using larger ridge factors, while all minimum estimates moved substantially closer to zero with larger ridge factors for the other three groups, all of which included smaller populations than the smallest ones in HOA and HOB. The maximum estimates were substantially reduced for HOC and JER, but not for BSW. The maxima for BSW were relatively more consistent with HOA and HOB, probably because of the Intergenomics service provided by Interbull, which facilitated an international exchange of all genotypes from participating BSW populations and a large international reference population for the GPS programs used in BSW.

Table 3. Minimum and Maximum GPS effects for bulls born 2014-2017, across *n* country-traits within Breed Group[z], for traits under strong selection (FAT, PRO, OCS, OUS, SCS)

Ridge Factor	Breed Group HOA *n*=30	 HOB *n*=30	 HOC *n*=45	 BSW *n*=30	 JER *n*=30
	Minimum Estimates				
c=0	.09	-.05	-.74	-.32	-.36
c=100	.07	-.05	-.66	-.29	-.33
c=1000	.01	-.07	-.36	-.14	-.11
	Maximum Estimates				
c=0	.40	.41	.56	.37	.94
c=100	.39	.37	.43	.38	.49
c=1000	.37	.36	.27	.39	.41

[z]HOA, HOB, HOC = Holstein groups A, B, C; BSW = Brown Swiss; JER = Jersey.

The maximum estimates of GPS effects within a population were relatively consistent across the five groups when using *c=1000*, while the minimum estimates were still largely negative for HOC and to a lesser extent BSW and JER. The optimum ridge factor might be higher than *c=1000*, the GPS estimates might be unreliable for smallest population(s) with GPS effects being estimated, or the lowest estimates might simply be negative because we did not add an additional set of fixed regressions across countries when treating the within-country regressions as random. Very low minimum estimates could also be explained by larger $\mathbf{\hat{s}_{PA}}$ relative to $\mathbf{\hat{s}_{MS}}$, because sires of the local GPS bulls in small populations can be from larger populations with relatively more effective GPS programs (e.g. HOA and HOB).

Based on the present results, *c=1000* could be a reasonable starting point for practical implementations of GPS-MACE, while future studies involving variance estimation and/or EBV validations could be used to estimate optimal ridge factor(s) more precisely.

Average estimates of current GPS effects are shown in table 4. The highest and lowest averages across groups indicate strongest intensities of GPS have been for FAT and PRO, and lowest intensities for MSP and CC1. Averages for the other traits were variable among breed groups. The patterns of percent positive estimates (Table 5) were like the patterns of averages, and estimates were mainly positive for production and type traits.

Table 4. Average estimates of GPS effects for bulls born 2014-2017, across all countries within each Breed Group[z], using ridge regression *c=1000*.

Trait	Breed Group HOA	 HOB	 HOC	 BSW	 JER
FAT	.27	.20	.11	.21	.24
PRO	.19	.16	.10	.23	.24
OCS	.20	.14	-.02	.14	.20
OUS	.23	.21	.03	.12	.17
SCS	.21	.28	.05	.02	-.02
INT	.02	.18	.11	.04	-.06
CC1	-.06	.12	.03	-.01	.00
MSP	-.06	-.05	.04	.11	.01

[z]HOA, HOB, HOC = Holstein groups A, B, C; BSW = Brown Swiss; JER = Jersey.

Table 5. Percent positive estimates of GPS effects for bulls born 2014-2017, across all countries within each Breed Group[z], using ridge regression *c=1000*.

Trait	Breed Group HOA	 HOB	 HOC	 BSW	 JER
FAT	100	100	70	83	100
PRO	100	100	90	83	100
OCS	100	83	38	83	100
OUS	100	83	57	83	100
SCS	100	100	70	50	33
INT	60	83	80	75	33
CC1	50	80	50	50	75
MSP	40	33	75	100	50

[z]HOA, HOB, HOC = Holstein groups A, B, C; BSW = Brown Swiss; JER = Jersey.

3 - Impacts of GPS effects in EBV

The GPS-MACE model was designed to have minimal impacts on evaluations of OLD bulls born prior to 2009. Across all traits and evaluated populations in all three breeds, correlations between GPS-MACE and MACE proofs of the OLD bulls were 1.000 (Table 6), confirming that GPS-MACE did not re-rank the OLD bulls. The levels of re-ranking were highest among youngest “GPS” bulls, born 2014-2017, although even for this group the degree of re-ranking was extremely small. The minimum correlations within a trait and population were 0.994 for HOL and 0.990 for

BSW+JER. Re-ranking was also minimal across years that included both OLD and GPS bulls, with minimum correlations of 0.999 for HOL and 0.998 for BSW+JER.

Table 6. Minimum trait correlations between GPS-MACE (*c=1000*) versus MACE evaluations (EBV) of progeny-tested bulls, across all (*n*) traits and evaluated populations.

		Evaluated Breeds^z	
Type of Bull	Born^y	HOL (*n=176*)	BSW+JER (*n=143*)
OLD	00-08	1.000	1.000
GPS	09-17	0.997	0.995
GPS	14-17	0.994	0.990
OLD+GPS	00-17	0.999	0.998

^{z}HOL=Holstein, BSW = Brown Swiss; JER = Jersey.
^{y}Birth years – 2000.

The correlations were essentially equal to 1.0, so regressions of GPS-MACE on MACE therefore reflect relative SD of the proofs. Minimum regressions of GPS-MACE on MACE proofs were always closer to 1.0 than were the maximum regressions, so only the maxima are presented in Table 7. For at least one trait on the evaluation scale of one population, the SD of international proofs for youngest GPS bulls (born 2014-2017) increased by approximately 2% for HOL and 5% for BSW and JER, based on these maximum regressions of GPS-MACE on MACE proofs. While the bulls did not re-rank to any notable degree, predicted genetic differences were a bit larger among the youngest GPS bulls for some trait(s) with GPS-MACE. This is indicative of larger estimated superiorities for the highest ranking newly proven bulls in MACE, and where many of the top young bulls would be from populations with most effective GPS programs. These changes could also increase estimates of genetic trends, as would be expected if GPS biases are reduced by adding estimates of GPS effects in the EBV of newest and best young bulls with GPS-MACE.

Table 7. Maximum regression of GPS-MACE (*c=1000*) on MACE evaluations (EBV) for progeny-tested bulls, across all (*n*) traits and evaluated populations.

		Evaluated Breeds^z	
Type of Bull	Born^y	HOL (*n=176*)	BSW+JER (*n=143*)
OLD	00-08	1.004	1.013
GPS	09-17	1.011	1.037
GPS	14-17	1.021	1.050
OLD+GPS	00-17	1.010	1.032

^{z}HOL=Holstein, BSW = Brown Swiss; JER = Jersey.
^{y}Birth years – 2000.

Conclusions

Genomic preselection of AI sires alters the distributions of both true and estimated MS deviations. The MACE model used by Interbull for international genetic evaluations of dairy sires was updated to account for genomic pre-selection effects on the MS-means and MS-variances of GPS bulls. An implementation of GPS-MACE that so far has accounted for selection effects on the MS-means only was applied to three breeds and eight traits. Future developments can additionally include adjustments for selection effects on the MS-variances, as described in the present paper. Accounting for selection effects on the MS-means created larger estimated differences among the international EBV of bulls born in most recent years, where estimated GPS effects have accumulated across generations and are expected to be the most variable among countries. Estimated effects of GPS were largest for the main traits of selection, as expected. The application of GPS-MACE is feasible at Interbull centre if ridge regression is used to accelerate rates of convergence, and with the added benefit of improving stability of the international genetic predictions.

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Appendix – An example GPS-MACE application using MiX99 Software

The MiX99 CLIM instructions below are for a 3-country GPS-MACE model using c=100:

```
INTEGER  An  Cou
REAL  Y  D     #   Y=drp D=edc*R-inv
MISSING -9999.0
DATAFILE  st-am.data
PEDIGREE G am+p 1
PARFILE   st-am.para  # V(reg)=G,  R=1
TABLEFILE identity_matrix
TABLEINDEX Cou
# 2 regressions per country = 6 total
REGMATRIX RANDOM yr_cou FIRST=2 LAST=7
REGFILE  ZQ2_incidence
REGPARFILE  s_ridge_100
MODEL
Y = Cou G(t1 t2 t3| An) ! WEIGHT=D
```

Descriptions for the specified input files above are:

st-am.data:
{an} {Cou} {drp} {edc*R-inv} (NOTE: 1 row per drp across all 3 Cou-populations)

st-am.para:
{i} {j} {G_{ij}} (NOTE: one row for each of the three evaluated populations)
1 1 1.0 (NOTE: only 1 row for the scalar value of R because we fit here a single-trait model)
(NOTE: G covariances are among random regressions of genetic expression in the 3 populations)
(NOTE: Population expressions of EBV weighted by population edc*R-inv have R=1 (scalar))

identity_matrix: (NOTE: for 3 populations in this example, this file links Cou input to covariate=1)
1 0 0
0 1 0
0 0 1

ZQ2_incidence:
(NOTE: 2 estimated regressions per 3 populations = 6 columns)
(NOTE: 1 paired row for each observation row in **st-am.data**)
{an} # # # # # #
{an} # # # # # #
…

s_ridge_100
0.01 (NOTE: this is the scalar value 1/c, where c is the ridge factor for GPS regressions)

A single-trait random-regression (ST-RR) model with regressions using covariate value=1 on the Cou specified in **st-am.data** is equivalent to Schaeffer's multi-trait (MT) MACE model, if matrix G among Cou regressions in ST_RR is the same as G among traits in MT.

An important advantage with ST-RRAM is that regressions for GPS effects can be fit by country of selection only (order of **s** = n), while in MT-MACE the order of **s** = n^2.