INTERNATIONAL GENETIC AND GENOMIC EVALUATIONS OF BEEF CATTLE

RENZO BONIFAZI

Propositions

1. International genetic evaluations are not only important for small breeding programs but also for large ones.
   (this thesis)

2. Future international genetic evaluations for beef cattle are inadequate without the use of individual genotypes.
   (this thesis)

3. Fulfilment of society-driven goals in research limits scientific progress in animal science.

4. Proactivity and communication are the most important factors to make international cooperation in research successful.

5. COVID-19 demonstrated the lack of knowledge in society about the level of hygiene in farming systems.

6. Full transition to veganism is not a solution to the climate crisis.

Propositions belonging to the thesis entitled

International genetic and genomic evaluations of beef cattle

Renzo Bonifazi

Wageningen, 16 September 2022

International genetic and genomic evaluations of beef cattle

Renzo Bonifazi

Thesis Committee

Promotor

Prof. Dr R.F. Veerkamp
Special Professor Numerical Genetics
Wageningen University & Research

Dr M.P.L. Calus
Associate Professor, Animal Breeding and Genomics Group
Wageningen University & Research

Co-promotors

Dr J. Vandenplas
Researcher, Animal Breeding and Genomics Group
Wageningen University & Research

Other members

Prof. Dr F.A. van Eeuwijk, Plant Science Group, Wageningen University & Research
Prof. Dr N. Gengler, University of Liège, Belgium
Dr G. Gorjanc, the Roslin Institute, Scotland, United Kingdom
Prof. Dr D.P. Berry, Teagasc, Cork, Ireland

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International genetic and genomic evaluations of beef cattle

Renzo Bonifazi

Thesis

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Renzo Bonifazi
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Abstract

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In cattle, advancements in reproductive technologies such as artificial insemination allowed breeders to access the genetic material of superior bulls from foreign countries. However, animals' estimated breeding values (EBV) computed from different national evaluations are not directly comparable across countries due to differences in scales and genetic bases, trait and model definitions, and the possible presence of genotype-by-environment interactions. International evaluations account for such differences by jointly analysing all national data and modelling the same trait recorded in different countries as different correlated traits. The resulting international EBV (EBV_{INT}) facilitate the comparison of domestic and foreign sires and worldwide trading of their genetic material. This thesis aimed to improve and further develop methodologies for international beef cattle evaluations (Interbeef) by addressing various challenges, mainly related to: i) the estimation of across-country genetic correlations (r_g) and their impact on the EBV_{INT}; ii) the inclusion of national genomic information; and iii) the development of an official procedure for participating countries to integrate the distributed EBV_{INT} back into their national evaluations. First, I showed that both large and small participating countries benefit from current Interbeef pedigree-based evaluations. Second, I showed the feasibility of estimating across-country r_g using a multi-trait approach that simultaneously fits data from all countries and proposed data sub-setting strategies to improve computational time. Third, I showed that the current practice of assuming across-country direct-maternal r_g to be 0 has limited impact on the EBV_{INT} of animals of interest such as publishable sires, i.e., sires that meet Interbeef publications rules. On the other hand, assuming zero within-country direct-maternal r_g impacts the EBV_{INT} of such animals. Fourth, I developed international genomic evaluations for beef cattle using a single-step SNPBLUP approach (ssSNPBLUP). International ssSNPBLUP evaluations lead to higher accuracies compared to both current international pedigree evaluations and either national pedigree or genomic evaluations, while keeping similar or slightly reduced level and dispersion bias. Finally, I developed a generalized procedure to integrate pedigree-based or single-step EBV_{INT} of publishable sires into national evaluations. The procedure can be easily implemented with current software. Compared to national evaluations without integration, the integration reduces level bias, gives similar dispersion, and increases accuracies of publishable sires' EBV_{INT}. Overall, this thesis contributes to the development of international evaluations of beef cattle.

Contents


CHAPTER
1

General introduction

The main goal of animal breeding is to improve a population for specific characteristics by selecting the best animals from the current generation to be the parents of the next generation. In livestock, to help farmers make this selection decision, national breeding organizations rank the animals in a population according to their genetic values for a series of traits of interest. These traits usually have economic and societal relevance, such as, the animal's carcass weight, its feed efficiency or its methane emissions. Thanks to the usage of reproductive technologies, top bulls that carry desired genetic characteristics can have thousands of offspring, leading to major genetic improvements in cattle populations. Such reproductive technologies also allow exchanging genetic material of top bulls across countries, mainly through frozen semen next to exchanging live animals. However, differences in environmental characteristics and trait definitions between different countries make the ranking of top bulls in one country different from that of another country. Therefore, evaluations that combine data from different countries, also called *international evaluations*, have been developed to help breeders to rank top bulls across different countries accurately. The international evaluations for beef cattle face several challenges that will be addressed in this thesis, with the overall aim to improve and develop the current evaluations further.

1.1 Genetic evaluations of quantitative traits

In livestock populations, breeders aim to improve animals for a group of desired characteristics, also called *traits*; for example, weight at one year of age, milk production, or feed intake. Most of these traits of interest are *quantitative traits*, i.e. they are affected in their observed measurable expression, called *phenotype*, by many genes and by environmental effects such as the season of the year. Quantitative traits are analysed assuming the so-called *infinitesimal model*, i.e. each gene is assumed to have a small (infinitesimal) additive effect on the trait. During genetic evaluations of quantitative traits, the phenotype of an individual is dissected using statistical models into environmental effects, genetic effects, and a residual effect. For an individual, the additive genetic effect for a specific trait represents its *true breeding value* (TBV). In an ideal situation, breeders would use the TBV to rank and select animals in a population. However, the TBV is an unknown quantity and must be estimated using statistical models and different data sources recorded either on the animal itself or its relatives. The resulting predicted genetic merit for an individual is its *estimated breeding value* (EBV). The weighted sum of EBV for a series of traits to be improved composes the individual's *(total merit) index*, which is used for selection decisions. The weight of each trait on the aggregated EBV is defined in the breeding program and reflects the aim and direction in which the

population will be improved, i.e. the *breeding goal* or *selection objective*. For example, heavier animals at one year of age with lower feed intake.

In quantitative traits, even though each gene has a small effect on the trait, the many underlying loci obey Mendelian inheritance rules. Thus, the underlying genetic variation of a quantitative trait is heritable. The additive genetic proportion of the total variance is also defined as *heritability* (h^2). To compute EBV for one or more quantitative traits, statistical models require knowledge of the sources of random variation within the same trait, i.e. *variances*, and similarities between traits, i.e. *covariances*. However, such (co)variance components are unknown and need to be estimated via a process called *variance component estimation* (VCE) either using experimental designs or from the available data collected at the population level. Different methods and algorithms have been developed to perform VCE on data in animal breeding. The methods usually used can be grouped into two main classes (Misztal 2008): Residual Maximum Likelihood (REML) methods, developed from Patterson and Thompson (1971), and Bayesian methods, commonly using Gibbs sampling (Sorensen and Gianola 2002). Different VCE methods present pros and cons in terms of accuracy of the estimated parameters, computational time, and flexibility for complex statistical models (Thompson and Mantysaari 2004; Thompson *et al.* 2005; Misztal 2008).

Starting with the so-called *daughter-dam comparison* at the beginning of the 20th century, statistical methods for the computation of EBV in animal breeding have been improving continuously to be more accurate, more efficient (in computation time and memory), and to include multiple sources of data at once (Brotherstone and Goddard 2005; Weigel *et al.* 2017). During the second half of the 20th century, Henderson (1949, 1975) developed the Best Linear Unbiased Prediction methodology (BLUP), which still represents the most commonly used statistical approach in cattle genetic evaluations. Since then, the implementation of BLUP with more complex models have been improving: from the sire and sire-maternal grand-sire model to the animal model and its later developments to account for multiple traits and longitudinal traits, e.g. test-day and random regression models. Next to BLUP models, Bayesian approaches are also used for genetic evaluations (Weigel *et al.* 2017). Traditionally, the most common sources of information used in statistical models to compute EBV are: phenotypes (collected on the individual itself, on its relatives such as its offspring, or both), environmental factors that affect the observed phenotypes (e.g. the contemporary group or the season of the year when the phenotype was recorded), and the pedigree relationships between the evaluated animals. These evaluations are referred to as *pedigree-based evaluations*.

In the last two decades, the availability of individual-level molecular information has started a new era in animal breeding (Meuwissen *et al.* 2016). Nejati-Javaremi *et al.* (1997) and Meuwissen *et al.* (2001) proposed to use the mixed model theory to estimate the effect of single nucleotide polymorphisms (SNP) at the individuals' genome level to obtain a Direct Genomic Value (DGV), laying the foundations of so-called *genomic predictions*. Genomic predictions use a training dataset called the *reference population* to estimate SNP' effects for traits of interest. The training dataset comprises animals genotyped for thousands of SNP with associated phenotype or pseudo-phenotype like de-regressed EBV (Garrick *et al.* 2009). For a selection candidate, knowing the SNP' effects and its genotype at those SNP, a prediction equation is used to obtain a DGV without having information on its phenotype or that of its offspring (Meuwissen *et al.* 2001; Goddard and Hayes 2009). This selection process is called *genomic selection*. Given the high accuracies that could be obtained for young selection candidates, it was soon recognized that applying genomic selection would have a profound impact on national cattle evaluations leading to major genetic improvements and reduced costs compared to traditional breeding schemes (Schaeffer 2006). As soon as genotyping in the form of panels at about 50,000 SNP was available at a low cost, genomic predictions became widely used at the national level in so-called *genomic-based evaluations*, initially using *multi-step* approaches (VanRaden 2008; Loberg and Dürr 2009; Eggen 2012). In multi-step approaches, a first evaluation is performed to estimate DGV, which is then combined with the EBV from traditional evaluations without genomic information into a Genomic EBV (GEBV) (VanRaden 2008). The main advantage of multi-step approaches is that no changes are required to the existing traditional genetic evaluation, and only the additional DGV estimation step has to be performed. However, DGV are obtained only for genotyped animals without direct propagation of genomic information to ungenotyped individuals. Moreover, the approximation steps involved, such as calculating de-regressed EBV, may introduce bias and loss of accuracy (Legarra *et al.* 2014; Lourenco *et al.* 2017). These issues were overcome with the development of *single-step* approaches, which jointly combine into a single evaluation information on phenotypes, pedigree, and genotypes (Misztal *et al.* 2009; Christensen and Lund 2010; Aguilar *et al.* 2010). In single-step approaches, genomic information is propagated to all animals in the evaluation, resulting in an estimated GEBV for all individuals. Nowadays, genomic selection has become largely adopted in dairy cattle breeding (Interbull Centre 2022) and is being implemented in many beef cattle breeding programs (Van Eenennaam *et al.* 2014; Lourenco *et al.* 2015; Venot *et al.* 2016; Berry *et al.* 2016; Johnston *et al.*

2018), but only a few national evaluations use single-step approaches (Berry *et al.* 2016; Mäntysaari *et al.* 2020).

Genetic evaluations in cattle are usually established at the national level connected to a national breeding goal. National organizations are usually involved in collecting data such as pedigree, phenotypes, and genotypes, centralized genetic evaluations, and final distribution to breeders of an "official" national EBV and its associated measure of accuracy, usually its reliability. Advancements in animal breeding and the role of national breeding organizations have considerably contributed to the improvements of many traits such as growth rate, beef quality, and milk production and quality, among others. For instance, in Angus, Abdollahi-Arpanahi *et al.* (2021a) reported annual genetic gains for weaning weight between 4.06 kg and 4.96 kg from 2006 to 2018. In US Holstein, fat yield increased by about 300 kg between 1957 and 2015, 50% of which was due to genetic progress (Cole and VanRaden 2018). Similarly, milk yield improved from 6,619 kg to 12,662 kg over 50 years (1963-2013), with 56% of such increase attributed to genetics (García-Ruiz *et al.* 2016). Genetic improvements in health, fertility and longevity traits have also been reported in more recent years, thanks to their inclusion in the selection objective (e.g. García-Ruiz *et al.* 2016; Cole and VanRaden 2018; Berry 2021). Furthermore, alongside the increases in production traits, the efficiency and sustainability of cattle production systems have also increased (Gerber *et al.* 2011; Hayes *et al.* 2013). Thus, national breeding organisations have a major role in sustainable food production.

1.2 International evaluations in cattle: from conversion equations to genomic models

The introduction of reproductive technologies such as Artificial Insemination (AI) and embryo transfer have profoundly impacted cattle breeding programs (Brotherstone and Goddard 2005; Moore and Hasler 2017). With access to semen from superior proven bulls, breeders increased the number of offspring from elite sires and the selection intensity of national cattle breeding schemes (Vishwanath 2003; Moore and Hasler 2017). Thus, elite sires started having offspring among different herds and environmental conditions, increasing their EBV's reliability in national evaluations. Moreover, AI enabled breeders to access the semen of superior bulls from all over the world rather than just from the national breeding program. The *Holsteinization* process of Black and White dairy cattle populations (Philipsson 2011) represents a clear example of how exchanges of genetic material can impact a cattle breed and national breeding programs worldwide. In the '70s, the results of

an FAO experiment highlighted the significant superiority in milk production of North-American Holstein-Friesians sires over European ancestral Black and White dairy populations (Stolzman *et al.* 1988; Zarnecki *et al.* 1991). The results of this experiment led to increased trade of sires' frozen semen among countries, mainly from North America to the rest of the world. Exchanges of genetic material at different levels also involved other cattle dairy breeds like Brown Swiss, Red Dairy Cattle group, Jersey, Guernsey, and Simmental (Fikse and Philipsson 2007). Exchanges of genetic material across countries also occurred in beef cattle breeds such as Limousin and Charolais (Renand *et al.* 2003; Bouquet *et al.* 2011). As a consequence of these exchanges across countries, sires started to have offspring recorded in two or more countries. Additionally, both the importers and the exporters of frozen semen needed methods to express sires' EBV on the scale of the importing countries to compare fairly foreign sires with domestic ones (Philipsson 1982, 2011; Durr and Philipsson 2012).

Animals' EBV from different national evaluations are not directly comparable across countries. For instance, national evaluations may express their EBV on different genetic bases or scales (Philipsson 1987). Moreover, the ranking of sires in one country may differ from that of another country due to different factors. First, countries may have different trait and model definitions. Second, *genotype-by-environment interaction* (GxE) may occur between countries due to different environmental conditions (Philipsson 1987; Jakobsen *et al.* 2009). GxE can be defined as the different performances of the same genotype in different environments (Falconer and Mackay 1996). Figure 1.1 shows a simplified example of how GxE affects the ranking of sires exchanged and used in two countries. At the national level, each country has its own ranking of national sires according to their respective national evaluations (panel A in Figure 1.1). When sires are exchanged and ranked in each country, their ranking may differ due to GxE (panel B in Figure 1.1). For instance, sire A performs better than sire B in country 1 but worse than sire B in country 2. Non-parallel lines in Figure 1.1 show the re-ranking of sires, and it illustrates how the best sire in one environment, or country in this case, may not be the best in another environment. A solution to make sires' EBV comparable across countries is to have an *international evaluation* that jointly analyses all national data. International evaluations allow taking into account the presence of GxE, and differences in model and trait definitions across countries. This is done by modelling the same trait recorded in different countries as different correlated traits and allowing across-country genetic correlations (r_g) to be different from unity (Schaeffer 1994; Falconer and Mackay 1996). The EBV computed from international evaluations can be

expressed on the same scale and base as those computed from national evaluations, facilitating the comparison of foreign sires with domestic ones.

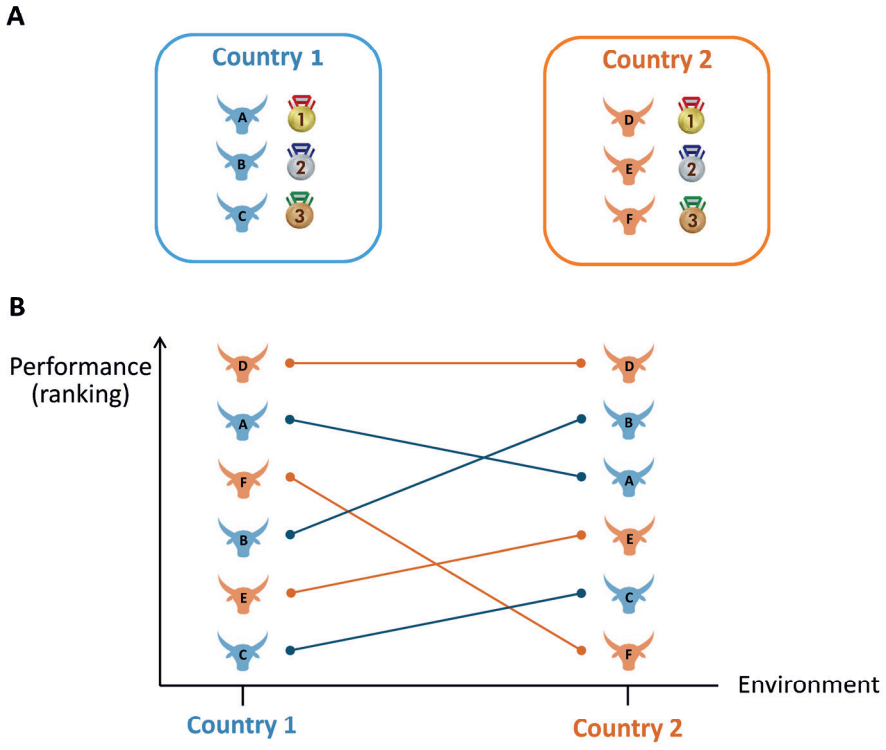


Figure 1.1 Schematic example of genotype-by-environment interaction (GxE) between two countries.

1.2.1 International evaluations for dairy cattle

Following the more intensive usage of AI, the developments of international evaluations started in dairy cattle. In 1975, the International Dairy Federation and the European Association for Animal Production established a working group to investigate methods for standardising the expression of sires' EBV. Later, in 1983, together with the International Committee for Animal Recording (ICAR 2022), the International Bull Evaluation Service (Interbull 1983) was founded (Philipsson 2005). The first approach developed for comparing EBV across countries was that of conversion equations which used a regression model to convert national sires' EBV

between two countries (IDF 1981; Gravert 1983). This approach was straightforward but did not account for the genetic relationships between sires and assumed across-country r_g equal to 1 (Banos and Sigurdsson 1996; Vandenplas and Gengler 2015). While further improvements were made (e.g. Goddard 1985; Wilmink *et al.* 1986), introducing the Multiple Across-Country Evaluation (MACE) methodology (Schaeffer 1994) was the major breakthrough development. MACE is still in use nowadays and accounts for GxE via non-unit across-country r_g, relationships between sires, and different heritabilities and trait definitions between countries. Moreover, MACE provides sires' EBV in the country-base of participating countries for all bulls included in the evaluation (Fikse and Philipsson 2007). In MACE, de-regressed EBV (DRP) from national EBV are used as dependent variables, avoiding sharing raw phenotypic data between countries and overcoming political or privacy limitations (Sigurdsson and Banos 1995). Later, the MACE methodology was further developed to simultaneously analyse multiple traits for each participating country, although this approach has not been officially implemented in Interbull evaluations (Schaeffer 2001; Nilforooshan *et al.* 2010; Nilforooshan and Jorjani 2022).

With genomic selection being implemented at the national level, international evaluations for dairy cattle were also extended to include genomic information. There are currently two different international genomic evaluations for dairy cattle which differ in the type of data and model used. The Genomic MACE (GMACE) evaluation for Holstein breed computes international GEBV for young bulls (Sullivan and VanRaden 2010; VanRaden and Sullivan 2010). GMACE uses DRP from national GEBV, avoiding the need to exchange genomic data at the international level. Instead, the InterGenomics evaluation for Brown Swiss and Holstein breeds uses a genomic BLUP model at the international level (Jorjani *et al.* 2011). InterGenomics combines DRP from MACE EBV as dependent variables and genotypes from a joint international reference population (VanRaden and Sullivan 2010; Durr and Philipsson 2012). Nowadays, Interbull provides genetic and genomic evaluations for 33 countries worldwide, 6 breeds and 7 trait groups, for a total of 50 different traits (Palucci *et al.* 2022). Other international collaboration projects exist in dairy cattle, such as the North America Consortium (Muir *et al.* 2010) and EuroGenomics (Lund *et al.* 2011). One of the aims of these collaboration projects is to facilitate the exchange of genotypes between countries to enlarge existing national reference populations.

1.3 International evaluations for beef cattle

The developments of international evaluations for beef cattle followed another path compared to that of dairy. As in dairy cattle, the need to compare sires' EBV across countries also arose for beef cattle breeders, driven by the increasing international exchange of genetic material (Baker *et al.* 1976; Renand *et al.* 2003; Journaux *et al.* 2006; Bouquet *et al.* 2011). Most of the developments to establish international evaluations in beef cattle were carried out during the last two decades. Compared to dairy, beef cattle's farming systems and environmental conditions can be very different between countries and sometimes even within regions of the same country (Renand *et al.* 2003; Journaux *et al.* 2006). The first research project for international beef cattle evaluations was the EUBEEVAL project, conducted by the Irish Cattle Breeding Federation (ICBF) in collaboration with the Institut de l'Elevage (France) and the Meat Livestock Commission (United Kingdom) (Renand *et al.* 2003; Journaux *et al.* 2006). In early 2000, the first studies among European countries explored the presence of GxE across countries and underlined the need for an international evaluation (Quintanilla *et al.* 2002a, 2002b; Renand *et al.* 2003). Phocas *et al.* (2005) compared three models for beef cattle international evaluations: i) the Animal Model Accounting for Across Country Interactions (AMACI model), which is based on raw phenotypes, and it accounts for across-country r_g different from unity as well as heterogeneous variances across countries; ii) the same model as i) but using phenotypes pre-corrected for fixed effects; iii) a MACE sire model using DRP, as for dairy cattle. The AMACI model was chosen as it allows obtaining EBV for all animals in the evaluation (dams and calves included) while giving the most consistent ranking between national and international animals and the best estimates of genetic parameters (Phocas *et al.* 2005). The AMACI model is equivalent to a multi-trait animal model in which phenotypes of the same trait but from different countries are modelled as different correlated traits. In 2006, the international beef cattle evaluation service named Interbeef was established as a working group of ICAR, with its genetic evaluations carried out at the Interbull Centre (Uppsala, Sweden) (Interbeef 2006; Venot *et al.* 2014). A year later, Venot *et al.* (2007) implemented the first international genetic evaluation for Limousin. During the last decade, Interbeef has grown rapidly and currently provides international pedigree-based genetic evaluations for 15 countries worldwide (Australia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Ireland, Italy, Latvia, Slovenia, South Africa, Sweden, Switzerland, United Kingdom), five breeds (Limousin, Charolais, Beef Simmental, Angus, and Hereford), and three traits: birth weight and calving ease, grouped as calving traits (Vesela *et al.* 2019), and age-adjusted weaning weight

(Venot *et al.* 2014). Evaluations for fertility and carcass traits (weight, fat, and conformation) are currently under research (Palucci *et al.* 2022).

The AMACI model requires sharing national raw phenotypes and pedigree data at the international level, making the data exchange of Interbeef evaluations different from that of dairy cattle. Figure 1.2 illustrates the current workflow of Interbeef evaluations. At the national level, each country independently collects pedigree, phenotypic, and (some of them) genomic data (Country A and B in Figure 1.2). These three data sources are used in national pedigree-based or genomic-based evaluations resulting in a national (G)EBV with its associated reliability ((G)EBV_{NAT} and REL_{NAT}, respectively). National breeding organizations share with Interbeef phenotypic and pedigree information which are used as input in the AMACI model to compute pedigree-based international EBV and associated reliabilities (EBV_{INT} and REL_{INT}, respectively) (Figure 1.2). Currently, genomic data are not used in Interbeef. National data are also used to estimate across-country r_g used in the AMACI model (long-dash lines in Figure 1.2). The estimation of r_g takes place only when changes at the national or international level may affect the genetic parameters. For instance, when a new country joins the international evaluation, and no estimated r_g are available, or when there are major changes in the (inter)national model. Finally, the main output of Interbeef evaluations is a list of official EBV_{INT} and associated $REL_{INT,}$ which is distributed back to participating countries (Figure 1.2) for: i) all animals that appear in the national pedigree, and ii) publishable sires, i.e. sires that meet Interbeef publication rules. These rules are mainly based on the sires' REL_{INT} and its number of recorded (grand-)progeny. It is then up to each participating country to choose how to use the EBV_{INT} and REL_{INT} at the national level.

It should be mentioned that next to Interbeef other organizations may provide international evaluations for beef cattle. To my knowledge, only Breedplan provides a structured international evaluation like that of Interbeef for, amongst others, Brahman, Hereford, and Angus (Crook *et al.* 2019). Other evaluations may exist between two or more countries by pooling together data in a joint analysis with country-specific agreements, e.g. between USA and Canada (Bullock *et al.* 2003; Berry *et al.* 2016).

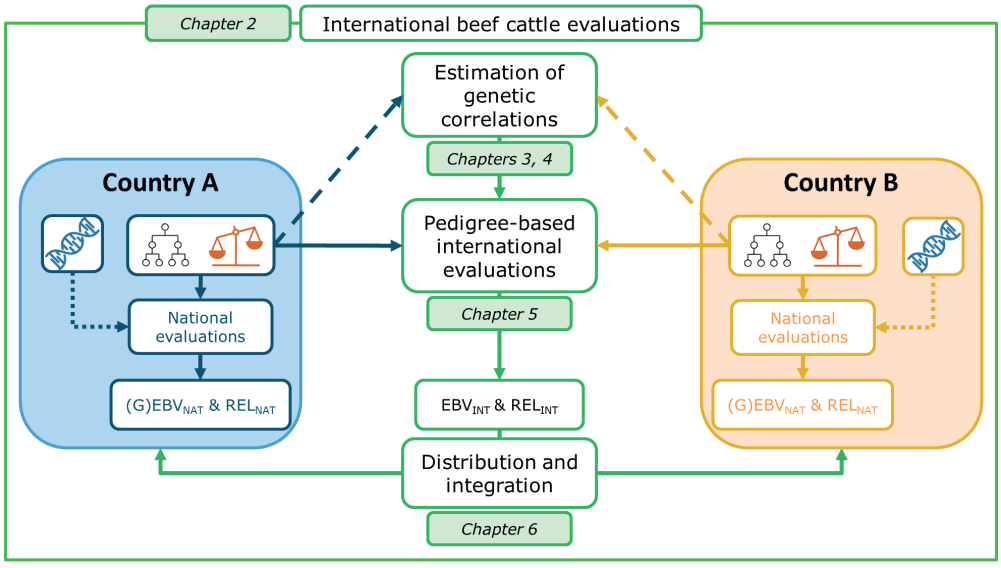


Figure 1.2 Data exchange overview in current international beef cattle evaluations (Interbeef). Green-shaded boxes indicate the aspects of the international evaluations on which *Chapters 2* to *6* of this thesis focus.

1.4 Challenges in beef cattle international evaluations

Various challenges need to be addressed in beef cattle international evaluations. Hereafter I describe the background and highlight the knowledge gaps this thesis aims to address.

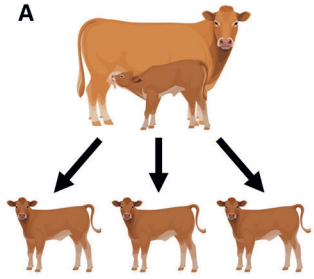
1.4.1 Estimation of across-country genetic correlations

Genetic correlations are key for international evaluations as they determine how much the information of relatives recorded in one country weighs on the animal's international EBV in another country. The r_g between two countries needs to be estimated as it may deviate from unity due to differences in trait and model definitions and the possible presence of GxE (Zwald *et al.* 2003). Genetic connections between populations are needed to estimate across-country r_g accurately. These connections are mainly created by sires with recorded offspring in more than two countries, also called *common bulls* (CB). Other further pedigree links can also establish genetic connections, although CB establish the closest genetic ties between countries. In general, estimating across-country r_g is challenging due to the usually low level of genetic connectedness between populations. In beef cattle breeds, there

is a structural lack of genetic connections between populations due to the lower usage of AI compared to some dairy breeds like Holstein (Berry *et al.* 2016). These low level of connectedness leads to lack of convergence and long computational times in addition to large uncertainty of the estimated r_g reflected in large standard errors (e.g. Mark *et al.* 2005a; Venot *et al.* 2009b; Pabiou *et al.* 2014). Moreover, many traits evaluated in beef cattle such as weaning weight are *maternally affected traits*, i.e. their phenotypic expression is affected by the dam (Box 1.1) (Willham 1963, 1972). Maternal effects make estimating across-country r_g even more challenging as next to direct r_g, maternal r_g between countries needs to be estimated. Useful connections for estimating maternal r_g between countries are provided by maternal grand-sires with grand-offspring recorded in more than one country, also called *common maternal grand-sires* (CMGS).

Box 1.1 Maternally affected traits.

A



B

$$[\text{eq. } 1]\ P_i = \mu + G_i + E_i + e_i$$

$$[\text{eq. } 2]\ P_i = \mu + G_i + maternal\ effects + E_i + e_i$$

$$[\text{eq. } 3]\ P_i = \mu + G_i + G_{dam} + PE_{dam} + E_i + e_i$$

Weaning weight is an example of a maternally affected trait. The calf's weaning weight is influenced in its phenotypic expression by the cows' maternal effects, such as milk production and maternal abilities (panel A). Maternal effects create similarities within the same family and variations between families. For instance, the three calves in panel A will show similar weaning weights as they are offspring of the same cow and have been subject to the same maternal effects. Therefore, maternal effects need to be considered in the statistical model during genetic evaluations of maternally affected traits.

The individual's phenotype (P_i) is usually dissected with statistical models into direct (i.e. due to the individual) genetic effect (G_i), environmental effects (E_i), and a residual effect (e_i) (eq. 1 in panel B). For maternally affected traits, maternal effects are dissected next to the individuals' direct genetic effect (eq. 2 in panel B). Maternal effects are dissected into a maternal (i.e. due to the dam) genetic effect (G_{dam}) and a maternal permanent environmental effect (PE_{dam}) (eq. 3 in panel B). These statistical models allow estimating a *maternal EBV,* which is of interest to animal breeders as it can be used for selection to improve the maternal abilities of heifers and cows.

Given the low level of connectedness in beef populations, using all available data during the VCE process would be preferred to retain all existing connections between countries. However, using all data is computationally demanding, and data subsets are instead commonly used. There are two main data sub-setting strategies that have been considered for estimating across-country r_g (Jorjani *et al.* 2005). A first approach is *country sub-setting* which reduces the number of countries simultaneously analysed and decreases the number of r_g estimated at the same time. An advantage of this approach is that potentially all data of the countries analysed can be used in the estimation process. However, a drawback of country sub-setting is that it could lead to losing connections from sires that have offspring recorded in multiple countries. For example, consider three countries, with a good connectedness level provided by CB and CMGS between countries A and B, and A and C, but poor connectedness between B and C. If a bi-variate country sub-setting is applied, i.e. r_g are estimated for two countries at the time, an accurate estimated r_g would be obtained between A and B as well as between A and C. However, a poor (if any) estimated r_g would be obtained between B and C. Using data from all three countries may lead to a more accurate estimated r_g between countries B and C through genetic connections in A. Moreover, when combining multiple estimates of r_g obtained with a country sub-setting approach, the resulting r_g matrices are often non-positive definite, and bending techniques are required (Hill and Thompson 1978; Jorjani *et al.* 2005). A second approach is *within-country data sub-setting* which aims to reduce the data within each country, allowing the estimation of all r_g simultaneously and potentially avoiding bending techniques. A challenge of within-country data sub-setting approaches is to ensure a high level of genetic connectedness in each retained national subset. Thus, measures of genetic connectedness between populations have been developed to identify the more connected countries or subsets of national data (Jorjani 1999, 2000, 2001; Rekaya *et al.* 1999; Jorjani *et al.* 2005).

Interbeef currently estimates r_g using a bi-variate approach (Pabiou *et al.* 2014; Vesela *et al.* 2019). Moreover, when the combined national datasets are too large for the estimation process, Interbeef applies data sub-setting strategies that try to maximize the retained existing connectedness between two countries. Thus, country sub-setting and within-country data sub-setting are both applied. However, lack of convergence of estimated r_g and non-positive definite matrices are often experienced (Pabiou *et al.* 2014; Vesela *et al.* 2019). Using all available data in a multi-trait approach that fits all countries at the time could overcome such issues, but it is computationally expensive and unfeasible using, for instance, REML algorithms. Recently developed Monte Carlo REML algorithms based on sampling

techniques made it possible to analyse large amounts of data with complex models and are computationally efficient (Lidauer *et al.* 2009; Matilainen *et al.* 2012, 2013, 2019). However, approaches that simultaneously estimate r_g between all countries, combined with strategies to apply within-country data sub-sets, have not been investigated in beef cattle international evaluations.

1.4.2 Modelling of direct-maternal genetic correlations between countries

Genetic evaluations of maternally affected traits require modelling the correlation between direct and maternal genetic effects (r_{dm}) (Willham 1963; Bijma 2006). In international evaluations of maternal traits, r_{dm} needs to be estimated and modelled both within-country (i.e. the genetic correlation between direct and maternal genetic effects of the same country) and between-country (i.e. the genetic correlation of the direct (or maternal) genetic effect of one country with the maternal (or direct) genetic effect of another country). For beef cattle breeds, estimates of within-country r_{dm} are often reported to be negative (e.g. Robinson 1996b; Dodenhoff *et al.* 1999; Phocas and Laloë 2004; Pardo *et al.* 2020). Few studies suggested that such negative estimates could be affected by lack of proper data structure during the estimation process, low connectedness levels between management units, or modelling sire-by-herd interactions (Gerstmayr 1992; Robinson 1996b; Lee and Pollak 1997; Clément *et al.* 2001; Heydarpour *et al.* 2008). Between-country r_{dm} are challenging to estimate and are currently assumed to be 0 in Interbeef evaluations (Pabiou *et al.* 2014; Vesela *et al.* 2019). However, the impact of within-country and between-country r_{dm} on the EBV_{INT} of beef cattle international evaluations is mostly unknown and needs to be investigated.

1.4.3 Inclusion of genomic data in international beef cattle evaluations

Genomic evaluations in beef cattle have shown lower realized accuracies compared to those of dairy cattle, due to differences between beef and dairy populations (Garrick 2011; Berry *et al.* 2016). First, the low usage of AI in beef compared to dairy results in smaller sire families with less connectedness between herds. Second, there is usually less systematic recording of phenotypes in beef compared to dairy, especially for difficult-to-measure traits. These two factors impact the size and the composition of national reference populations, which commonly present a low amount of animals with accurate EBV. Third, many beef cattle traits, such as growth traits, have medium or high heritability and can be measured on the selection candidates. Thus, these traits have smaller gains in

accuracy when moving from pedigree-based to genomic evaluations than sex-limited and low heritability traits (Goddard 2009). Fourth, the extensive use of crossbreeding in some countries together with several different local breeds makes it difficult, if not impossible, to establish a large reference population for each breed (Hayes *et al.* 2013; Van Eenennaam *et al.* 2014; Meuwissen *et al.* 2016).

Two solutions can be explored using nationally available data to increase the benefits of genomic evaluations in beef cattle (Durr and Philipsson 2012; Hayes *et al.* 2013; Van Eenennaam *et al.* 2014). The first approach is to enlarge the national reference population by combining data of multiple breeds, i.e. performing a multi-breed genomic evaluation. However, multi-breed genomic evaluations has shown low increases in accuracy over that of single-breed genomic evaluations, possibly due to differences in linkage disequilibrium phases that do not persist between breeds (Hayes *et al.* 2013; Meuwissen *et al.* 2016). A second approach is to combine national datasets of the same breed across countries to establish a larger common reference population. Larger reference populations can be achieved by exchanging genotypes between countries and using them next to associated pseudo-phenotypes from international evaluations or by performing within-breed international genomic evaluations. Within-breed international genomic evaluations have proven successful in InterGenomics evaluations for dairy cattle. Most Interbeef participating countries have started systematically collecting genomic data at the national level or have already implemented national genomic evaluations (Berry *et al.* 2016; Interbeef 2017). However, genomic data cannot be used in international evaluations as Interbeef evaluations are pedigree-based (Figure 1.2). Given the current Interbeef data exchange (Figure 1.2), participating countries could upload national genomic data, i.e. individuals' genotypes, next to pedigree and phenotypic data, allowing for the implementation of single-step genomic international evaluations. This single-step approach would allow combining the three sources of information into a single international evaluation without approximating national data. However, to date, no studies have investigated the feasibility and potential benefits of including genomic data in international beef cattle evaluations using a single-step approach.

1.4.4 Integration of international EBV into national evaluations

For countries participating in international evaluations, using either EBV_{INT} or EBV_{NAT} (Figure 1.2) would lead to losing the information contained only in the discarded EBV. Indeed, EBV_{INT} and EBV_{NAT} are computed using different sources of information but with partial overlap of the same data, i.e. the part of the national data used in the international evaluation (Figure 1.2). Interbeef evaluations consider recorded relatives in other countries but are performed within-breed and for one

trait group at the time, e.g. weaning weight or calving traits. On the other hand, national evaluations are multi-trait, could be multi-breed, and possibly include crossbred data. Furthermore, national evaluations may include more national data than international evaluations, for example, when not all national data is submitted for the international evaluations or when national evaluations occur between international ones. Due to these differences, animals' EBV_{INT} and EBV_{NAT} may differ. *Integration procedures* can be used to overcome these issues by combining EBV_{INT} and EBV_{NAT} and their associated information into a single *blended EBV* (e.g. Bonaiti and Boichard 1995; Vandenplas *et al.* 2014).

Different ways to integrate external information into national evaluations have been developed and can be summarised into post-evaluation and simultaneous approaches (Vandenplas and Gengler 2015). In the context of Interbeef, post-evaluation approaches would be performed after the Interbeef and the national evaluation are independently carried out and aim to make EBV_{INT} and EBV_{NAT} comparable. Instead, in simultaneous approaches, Interbeef information would be combined with national data into a national *blended* evaluation. Simultaneous approaches are appealing as they integrate the external international information (i.e. EBV_{INT} and its REL_{INT}) back into the national evaluations and propagate it to all animals included in the evaluation. However, an official procedure for integrating publishable sires' international information into national evaluations is lacking. Pabiou *et al.* (2018) tested the integration of pedigree-based international information into Irish national evaluations, showing promising initial results. However, the integration of international information from genomic-based models into national evaluations remains unknown. Furthermore, the method proposed by Pabiou *et al.* (2018) involves algorithms that may not be available at the national level as they are usually implemented in commercial software packages. Therefore, there is the need for further investigation and generalization of an integration procedure that allows countries participating in Interbeef to integrate publishable sires' international information computed from either pedigree-based or genomic-based international evaluations into national ones.

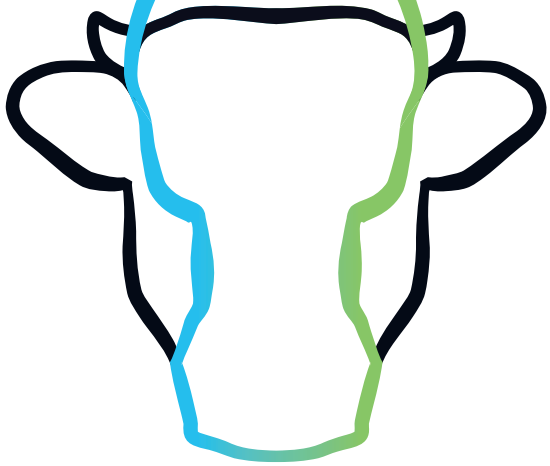
1.5 Aims and outline of this thesis

The overall objective of this thesis was to improve and further develop methodologies for beef cattle international evaluations. The overall thesis objective focused on three aspects of beef cattle international evaluations (Figure 1.2) and addressed the challenges and knowledge gaps outlined in the above section. **Chapters 3** and **4** focus on the estimation of across-country r_g. **Chapter 5** focuses on the current pedigree-based international model and the inclusion of genomic data.

Chapter 6 focuses on the integration of Interbeef EBV_{INT} by participating countries into their national evaluations.

Chapter 2 investigates the benefits of participating in current Interbeef pedigree-based evaluations from a national point of view. In this chapter, we investigated how Interbeef evaluations allow enlarging the panel of available sires at the national level with foreign sires and how including information on relatives recorded in other countries affect domestic animals' reliabilities. In **Chapter 3**, we first explored the existing level of genetic connectedness across 8 Limousin cattle populations representing 10 European countries. We then investigated a multi-trait approach for the estimation of across-country r_g using all available data. Finally, using this evaluation as a reference scenario, we studied how different strategies of within-country data sub-setting based on selecting herds of the largest population may impact the estimated parameters. **Chapter 4** follows from the results of the previous chapter where we observed that data sub-setting strategies impacted mainly the estimation of r_{dm}. In this chapter, we investigated how ignoring, i.e. setting to 0, within-country and between-country estimated r_{dm} in the international model can impact the EBV_{INT} of different groups of animals of interest for Interbeef evaluations. **Chapter 5** focuses on including genomic data in Interbeef evaluations using a single-step approach and Limousin data from 7 European countries. In this chapter, we developed a single-step single nucleotide polymorphism BLUP evaluation (ssSNPBLUP) for beef cattle. We investigated the benefits of adding genomic data over pedigree-based international evaluations through increases in accuracies of EBV_{INT}. Finally, we investigated possible changes in level and dispersion bias of ssSNPBLUP international evaluations compared to national and pedigree-based Interbeef evaluations. In **Chapter 6,** we aimed to develop a generalised approach to integrate publishable sires' EBV_{INT} computed either from pedigree-based or single-step international evaluations into national evaluations. Using the Italian Limousin pedigree-based evaluation as a case study, we investigated the benefits of such an integration procedure for both model adequacy and predictivity compared to national evaluations without integration. The final chapter of this thesis (**Chapter 7**) is divided into three main parts and puts the results of this thesis in a broader context. The first part discusses a general standard procedure for estimating across-country r_g in Interbeef. The second part explores the usage of genomic data to estimate across-country r_g and to measure connectedness between populations. Finally, the last part discusses the modelling of missing parental information in current pedigree-based Interbeef evaluations and future single-step evaluations.

CHAPTER 2



Impact of Interbeef on national beef cattle evaluations

Renzo Bonifazi[1], Jérémie Vandenplas[1], Jan ten Napel[1], Andrew Cromie[2], Roel F. Veerkamp[1], Mario P.L. Calus[1]

[1] Animal Breeding and Genomics, Wageningen University and Research, P.O. Box 338, 6700 AH Wageningen, the Netherlands
[2] Irish Cattle Breeding Federation, Highfield house, Bandon, P72 X050, Co Cork, Ireland

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Abstract

International evaluation models for beef cattle allow to compare animals' estimated breeding values (EBV) across different countries, thanks to sires having offspring in more than one country. In this study we aimed to provide an up-to-date picture of the Interbeef international beef cattle evaluations from a national perspective, considering both large and small populations. Limousin age-adjusted weaning weight (AWW) phenotypes were available for 3,115,598 animals from 10 European countries, born between 1972 and 2017. EBV and reliabilities were obtained using a multi-trait animal model including maternal effects where AWW from different countries are modelled as different traits. We investigated the country of origin of the sires with internationally publishable EBV and, among them, the country of origin of the top 100 sires for each country scale. All countries had 20 to 28,557 domestic sires whose EBV were publishable, according to Interbeef's rules, on the scale of other countries. All countries, except one, had domestic sires that ranked among the top 100 sires on other country scales. Across countries, inclusion of information from relatives recorded in other countries increased the reliability of EBV for domestic animals on average by 9.6 percentage points for direct EBV, and 8.3 percentage points for maternal EBV. In conclusion, international evaluations provide small countries access to a panel of elite foreign sires with EBV on their country scale and a more accurate estimation of EBV of domestic animals, while large countries obtain EBV for their sires on the scale of different countries which helps to better promote them.

Key words: international breeding values, genotype-by-environment interaction, Interbeef, reliabilities, weaning weight.

2.1 Introduction

The introduction of reproductive technologies such as artificial insemination and embryo transfer had a huge impact on both dairy and beef cattle breeding systems (Moore and Hasler 2017). The availability of semen from superior proven bulls allowed breeders to increase the number of offspring of elite sires in their herds and to increase the selection intensity of cattle breeding schemes (Vishwanath 2003). With the availability of such reproductive technologies, bulls started to have recorded offspring in different herds and different environmental conditions. Next to it, with the increased trade of frozen semen across countries, genetic links across populations were established (Fikse and Philipsson 2007; Philipsson 2011). With the exchange of genetic material across countries, both the importers, interested in comparing the genetic level of foreign and domestic bulls, and the exporters, interested in accessing foreign markets, sought for methods to express sires' estimated breeding values (EBV) on the scale of other countries (Philipsson 2011; Durr and Philipsson 2012). Therefore, following up from the initial conversion equations to translate EBV from one country scale to another (Goddard 1985; Wilmink *et al.* 1986), cattle international genetic evaluation models were developed to allow the comparison of animals EBV across different countries (Schaeffer 1994; Venot *et al.* 2006; Wickham and Durr 2011).

In beef cattle, both farming livestock systems and environmental conditions can be very different between countries, and sometimes even within regions of the same country (Renand *et al.* 2003; Journaux *et al.* 2006). In early 2000, the first studies among European countries underlined the need of an international evaluation for beef cattle that would take into account, among others, the presence of genotype-by-environment interaction (Quintanilla *et al.* 2002a, 2002b). In 2005, the AMACI model (Animal Model accounting for Across-Country Interactions) was developed for comparing beef cattle EBV at the international level (Phocas *et al.* 2005), and in 2006 the international beef cattle evaluations service (Interbeef) was established as an ICAR working group, with evaluations carried out at the Interbull Centre (Uppsala, Sweden) (Interbeef 2006; Journaux *et al.* 2006). Currently, Interbeef collaborates with 13 countries worldwide (Australia, Czech Republic, Denmark, Finland, France, Germany, Ireland, Italy, South Africa, Spain, Sweden, Switzerland, United Kindom) providing international genetic evaluations for 5 breeds (Limousin, Charolais, Beef Simmental, Angus and Hereford) and three traits (weaning weight, birth weight, calving ease).

The main advantage of beef cattle international evaluations is that breeders can access a larger international panel of bulls that better meet their selection objectives and have EBV expressed on their own domestic scale, in addition to the original scale

of their country of origin (Renand *et al.* 2003; Venot *et al.* 2007). Moreover, for any sires with foreign recorded progeny, the reliabilities of their EBV will increase (Venot *et al.* 2008, 2009a, 2014). In cattle international evaluations, sires with recorded offspring in more than one country are often referred to as common bulls (CB) (Jorjani *et al.* 2005). These CB provide the genetic connections required to estimate genetic correlations across countries which allow to compare animals' EBV on different country scales during international evaluations (Phocas *et al.* 2005; Bonifazi *et al.* 2020b). So far, few studies looked into international beef cattle evaluations from a national perspective. We provide here an up-to-date picture of the Interbeef international evaluations from a national point of view, considering both large and small populations. To achieve this, we aimed to show how the Interbeef evaluations: 1) enrich the panel of available sires per country with foreign bulls, and 2) affect animals' EBV reliabilities due to the use of foreign phenotypes.

2.2 Material and methods

Data from the 2018 routine Interbeef evaluations for age-adjusted weaning weight (AWW) of Limousin beef cattle were available, including a total of 3,115,598 phenotypes (one phenotype per animal), recorded on males (49%) and females (51%) between 1972 and 2018, distributed across 19,330 herds (Table 2.1).

Table 2.1 Number of age-adjusted weaning weight (AWW), herds and year of birth distribution of recorded animals per country. Table originally reported in Bonifazi *et al.* (2020b).

COU [a]	AWW	%	Herds	Year of Birth
CZE	10,500	0.3	121	1991 – 2017
DFS	90,456	2.9	9,190	1980 – 2017
ESP	33,152	1.1	188	1989 – 2011
GBR	127,840	4.1	745	1972 – 2017
IRL	20,609	0.7	1,304	1975 – 2017
FRA	2,714,368	87.1	6,677	1972 – 2017
DEU	88,628	2.8	881	1981 – 2017
CHE	30,045	1.0	224	1993 – 2017
Total	3,115,598	100	19,330	1972 - 2017

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Phenotypes were recorded in the eight populations that participated in the 2018 evaluation: Switzerland (CHE), Czech Republic (CZE), Germany (DEU), Denmark, Finland and Sweden (DFS), Spain (ESP), France (FRA), Great Britain (GBR), and Ireland (IRL). Note that the DFS population was composed of three countries joining

together as a single population in the international evaluation. Hereafter we will use the term country to refer to each of the eight populations. Pedigree information were extracted from the Interbeef international pedigree database and, after quality control, the final pedigree included 3,431,742 animals. For a more detailed description of the data and quality control see Bonifazi *et al.* (2020b).

AWW phenotypes were analysed using the AMACI model, which is a multi-trait animal model where the AWW information from each country is modelled as a different trait (Phocas *et al.* 2005). All country-specific fixed and random effects were fitted in the AMACI model as:

$$\begin{bmatrix}\mathbf{y}_1\\ \vdots\\ \mathbf{y}_8\end{bmatrix} = \begin{bmatrix}\mathbf{X}_1 & \cdots & 0\\ \vdots & \ddots & \vdots\\ 0 & \cdots & \mathbf{X}_8\end{bmatrix}\begin{bmatrix}\mathbf{b}_1\\ \vdots\\ \mathbf{b}_8\end{bmatrix} + \begin{bmatrix}\mathbf{C}_1 & 0 & 0 & 0\\ 0 & \mathbf{C}_2 & 0 & 0\\ 0 & 0 & \mathbf{C}_3 & 0\\ 0 & 0 & 0 & \mathbf{C}_4\end{bmatrix}\begin{bmatrix}\mathbf{r}_1\\ \mathbf{r}_2\\ \mathbf{r}_3\\ \mathbf{r}_4\end{bmatrix} + \begin{bmatrix}\mathbf{Z}_1 & \cdots & 0\\ \vdots & \ddots & \vdots\\ 0 & \cdots & \mathbf{Z}_8\end{bmatrix}\begin{bmatrix}\mathbf{u}_1\\ \vdots\\ \mathbf{u}_8\end{bmatrix}$$
$$+ \begin{bmatrix}\mathbf{W}_1 & \cdots & 0\\ \vdots & \ddots & \vdots\\ 0 & \cdots & \mathbf{W}_8\end{bmatrix}\begin{bmatrix}\mathbf{m}_1\\ \vdots\\ \mathbf{m}_8\end{bmatrix} + \begin{bmatrix}\mathbf{P}_1 & \cdots & 0\\ \vdots & \ddots & \vdots\\ 0 & \cdots & \mathbf{P}_7\end{bmatrix}\begin{bmatrix}\mathbf{pe}_1\\ \vdots\\ \mathbf{pe}_7\end{bmatrix} + \begin{bmatrix}\mathbf{e}_1\\ \vdots\\ \mathbf{e}_8\end{bmatrix}$$

where, *i* = country; $\mathbf{y}_i$ = vector of AWW; $\mathbf{b}_i$ = vector of fixed effects; $\mathbf{r}_i$ = vector of random environmental effects; $\mathbf{u}_i$ = vector of random additive genetic (direct) effects; $\mathbf{m}_i$ = vector of random maternal (indirect) additive genetic effects; $\mathbf{pe}_i$ = vector of random maternal permanent environmental effects; $\mathbf{e}_i$ = vector of random residual effects. $\mathbf{X}_i$ and $\mathbf{C}_i$ are incidence matrices linking records to fixed, and random environmental effects, respectively. $\mathbf{Z}_i$, $\mathbf{W}_i$, and $\mathbf{P}_i$ are incidence matrices linking records to the animal, maternal genetic and maternal permanent environmental effects, respectively.

For each country, genetic and environmental variances in the international model were fixed at the national estimates (Bonifazi *et al.* 2020b). Across the countries, the heritability for AWW ranged from 0.11 to 0.36 for the direct, and 0.05 to 0.15 for the maternal effect. Covariances among countries are assumed to be null for all random effects, i.e. independent from each other, except for the direct genetic and the maternal genetic covariances between countries, which were estimated in a previous study (Bonifazi *et al.* 2020b). A permanent environmental effect ($\mathbf{pe}$) was fitted for all countries except DEU, assuming null covariances between countries. One or more random environmental effects ($\mathbf{r}$) were fitted in four countries: herd-year-season for CZE, herd-year for DEU and CHE, and sire-herd for CHE. All other countries had a fixed contemporary effect in their model. A more detailed description of the model and of all the fixed and random effects can be found in Bonifazi *et al.* (2020b).

Two scenarios were implemented for comparing national and international evaluations:

1) Scenario INT represents the current Interbeef genetic evaluation for AWW using the AMACI model. Table 2.2 reports the genetic correlations used between countries.
2) Scenario NAT represents a pseudo-national single trait evaluation for AWW. In this scenario, genetic covariances between countries were set to zero in the AMACI model. Thus, information of one country did not contribute to the EBVs of animals in another country, as it would be in a national evaluation. After the evaluation, for each country, EBVs of all animals with phenotypes of their own, or any of their relatives, or both, were retained. Hereafter, we will refer to these animals as the domestic set of animals for each country.

The MiX99 software package (MiX99 Development Team 2017) was used to compute the EBV for both scenarios. Convergence criteria for the preconditioned conjugate gradient (PCG) algorithm, defined as the square root of the relative difference between solutions of the last two PCG iterations rounds, was set to 10^{-7}. From the MiX99 software package, apax99 was used to compute individual approximated reliabilities for both Scenario NAT (REL_{NAT}) and INT (REL_{INT}) using the Tier and Meyer methodology (Tier and Meyer 2004).

As agreed within Interbeef, international EBV (EBV_{INT}) for foreign sires are required to fulfil the following set of rules (in place since 2013) to allow them to be distributed and published in another country. For direct EBV_{INT}, a sire must have: a REL_{INT} greater or equal to 0.5 in at least one country scale for the direct EBV, and at least 25 recorded progeny across all countries. For maternal EBV_{INT}, a sire must have: a publishable direct EBV_{INT}, a REL_{INT} greater or equal to 0.3 in at least one country scale for the maternal EBV, at least 15 daughters with recorded progeny, and at least 25 recorded grand-progeny across all countries. In Interbeef, direct and maternal EBV_{INT} are distributed as two separate sets of EBV_{INT}. Thus, in each country scale, sires can be ranked for either their direct or their maternal EBV_{INT}.

After identifying publishable sires' EBV_{INT} for each country, we ranked and selected the top 100 sires for each country scale, for both direct and maternal EBV_{INT}. To identify the origin of the top 100 sires for each country, we then extracted the sire's country of first registration. Furthermore, to show how the composition of top sires changes between national and international evaluations, we applied the same Interbeef publication rules to national EBV computed under Scenario NAT, with the exception that the required number of recorded offspring and grand-offspring per sire was considering only national phenotypes.

To show the gain in reliability for domestic animals when moving from a national evaluation to an international evaluation, i.e. from Scenario NAT to INT, the difference (Δ_{REL}) between REL_{INT} and REL_{NAT}, both expressed on a scale from 0 to 100, was computed, for both direct and maternal EBV.

Table 2.2 Direct (Dir) and maternal (Mat) genetic correlations [a] within and across countries [b].

		Dir								Mat							
		CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
Dir	CZE																
	DFS	0.87															
	ESP	0.74	0.77														
	GBR	0.71	0.82	0.94													
	IRL	0.83	0.76	0.87	0.91												
	FRA	0.76	0.89	0.77	0.82	0.76											
	DEU	0.76	0.94	0.76	0.77	0.62	0.81										
	CHE	0.85	0.81	0.76	0.71	0.70	0.70	0.70									
Mat	CZE	-0.12	0.04	0.07	0.12	-0.01	-0.10	0.08	0.01								
	DFS	-0.05	-0.14	0.02	-0.01	-0.02	-0.11	-0.07	-0.01	0.68							
	ESP	0.03	0.09	-0.22	-0.08	-0.09	-0.05	0.05	0.02	0.67	0.68						
	GBR	0.14	0.06	-0.03	-0.10	-0.03	-0.14	0.07	0.08	0.79	0.69	0.70					
	IRL	-0.03	0.07	-0.06	-0.05	-0.19	-0.12	0.12	0.11	0.69	0.68	0.81	0.72				
	FRA	-0.02	-0.05	-0.03	-0.06	-0.09	-0.33	-0.01	0.08	0.85	0.69	0.71	0.87	0.82			
	DEU	-0.02	-0.09	-0.03	-0.01	0.06	-0.10	-0.24	0.09	0.68	0.68	0.67	0.69	0.68	0.69		
	CHE	0.12	0.11	0.07	0.08	0.03	-0.05	0.06	0.40	0.73	0.68	0.67	0.66	0.65	0.77	0.66	

[a] Genetic correlations originally reported in Bonifazi *et al.* (2020b).

[b] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR.

2.3 Results and discussion

Domestic sires with at least one recorded offspring were identified from the pseudo-national pedigree (Scenario NAT) and their number ranged from 554 for CZE to 57,784 of FRA (Table 2.3). Among domestic sires with at least one recorded offspring, on average, across all countries, 464 sires were also CB, ranging from 212 for CZE to 1,171 for FRA (Table 2.3). The number of domestic sires in the pedigree for each country under Scenario NAT may be different compared to a real national evaluation for two reasons. First, countries may have a different pedigree depth for national evaluations, for instance when not all national data are also used for international evaluations. Second, the international pedigree of Interbeef may provide connections that allow to track relationships that go further back in the pedigree compared to the national ones.

Table 2.3 Description of the pseudo-national pedigree under Scenario NAT, including numbers of: domestic sires with at least one recorded offspring, and domestic sires that are also common bulls (CB).

	Number of:		
COU [a]	**Pedigree entries**	**Domestic sires with > 1 rec. off** [b]	**Domestic sires that are CB**
CZE	30,843	554	212
DFS	117,623	4,375	227
ESP	63,526	1,188	364
GBR	172,229	5,486	524
IRL	56,694	2,073	321
FRA	2,942,297	57,784	1,171
DEU	121,228	4,366	473
CHE	55,104	1,699	421

[a] COU = country: see Table 2.1.
[b] Domestic sires with at least one recorded offspring in the country.

The total number of sires' EBV_{INT} that were publishable was equal to 32,208 and 13,016 for the direct and the maternal EBV, respectively, and the distribution of their country of first registration is reported in Table 2.4. The majority of the publishable sires' EBV_{INT} were from France (89% and 90% for direct and maternal genetic effect, respectively), followed by Great Britain, DFS and DEU (2-4% for both direct and maternal EBV). 1% or less of the total publishable sires' EBV_{INT} were registered in the remaining participating countries (Table 2.4). The lowest number of publishable sires' EBV_{INT} were for CZE: 66 and 20 for the direct and the maternal EBV,

respectively. Less than 1% of the publishable sires' EBV_{INT} were from sires whose country of first registration was not among the eight participating countries in the evaluation: 102 and 47 for the direct and maternal EBV, respectively.

Table 2.4 Country of origin of sires with publishable international EBV. The number of sires for both direct and maternal EBV are reported [a].

COU [a]	Direct	Maternal
CZE	66	20
DFS	931	333
ESP	166	36
GBR	1,099	480
IRL	93	23
FRA	28,557	11,721
DEU	959	306
CHE	235	50
Others	102	47
Total	32,208	13,016

[a] COU = country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland, Others: country of first registration different from participating countries.

The country of origin of the top 100 publishable sires' EBV_{INT} ranked on each country scale is reported in Table 2.5. For each country scale, the majority of the top 100 sires originated from France. In the top 100 sires of each country, at least one foreign sire appeared, except for FRA for direct EBV (Table 2.5). CZE was the only country with all top 100 sires being foreign, both for direct and maternal EBV. The distribution of the country of origin for the top 100 publishable sires for each country scale based on Scenario NAT is shown in Table 2.6. Comparison of Table 2.6 and Table 2.5 shows the change in the composition of the top 100 publishable sires after the inclusion of international information. As expected, a higher proportion of nationally registered sires was present when sires were ranked based on their national EBV instead of EBV_{INT}. Interbeef publication rules may be more restrictive compared to real national ones; for instance, publishable sires for maternal EBV in CZE and IRL were less than 100, but in practice this number may be higher. Nevertheless, the presence of publishable sires registered in other countries based on Scenario NAT (Table 2.6) underlines the importance of international evaluations for large populations, which allows a more accurate estimation of their sires' EBV on the scale of other countries.

Table 2.5 Country of first registration of the top 100 publishable sires for direct and maternal international EBV for each country scale.

		Country of first registration							
EBV	**COU** [a]	**CZE**	**DFS**	**ESP**	**GBR**	**IRL**	**FRA**	**DEU**	**CHE**
Direct	CZE		2				98		
	DFS		2				98		
	ESP		1		4		95		
	GBR		1		6		93		
	IRL				4		96		
	FRA						100		
	DEU		2				98		
	CHE		2				97		1
Maternal	CZE		1	1	2		95		1
	DFS		12	1	3		84		
	ESP			2	1		97		
	GBR			1	5		94		
	IRL			1			99		
	FRA		1	1	1		97		
	DEU		1	1	2		94	2	
	CHE			1			95	1	3

[a] Country scale of the top 100 publishable sires; COU = country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Table 2.6 Country of first registration of the top 100 [a] publishable sires for direct and maternal national EBV for each country scale.

		Country of first registration								
EBV	**COU** [b]	**CZE**	**DFS**	**ESP**	**GBR**	**IRL**	**FRA**	**DEU**	**CHE**	**Others**
Direct	CZE	44	4				48	4		
	DFS		77				22			1
	ESP			35			65			
	GBR				82	3	15			
	IRL				12	37	51			
	FRA						100			
	DEU		2		1		29	67		1
	CHE						38	8	53	1
Maternal	CZE	19	1				33	3		
	DFS		80		1		17			2
	ESP			23			77			
	GBR				80	1	19			
	IRL				9	14	67			
	FRA						100			
	DEU		2				33	63		2
	CHE						53	4	42	1

[a] Total number of publishable sires for CZE and IRL maternal EBV are 56 and 90.
[b] Country scale of the top 100 publishable sires; COU = country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland, Others = Country not among those participating in the evaluation.

We have used the current set of rules for publication of sires' EBV_{INT} to give a close representation of Interbeef evaluations. Other rules may apply to the international evaluation and they were not considered in this study, for instance, the distinction between AI bulls and natural service bulls, and country-specific restrictions for publishing sires' EBV_{INT} on the scale of other countries. Nevertheless, Table 2.4 shows how each country has sires that fulfil the requirements and that could be publishable on other country scales. FRA was the country with the highest proportion of domestic sires with recorded offspring that were also publishable in other countries: 49% and 20% for direct and maternal EBV, respectively. Moreover, FRA sires were prominent in top 100 publishable sires' EBV_{INT} for each country scale (Table 2.5). Nonetheless, each country besides CZE had one or more sires ranking within the top 100 publishable sires' EBV_{INT} of another country scale (Table 2.5), showing the potential exchange of their superior genetics across participating countries. Exchanging AI bulls across countries allow to create new genetic connections. In a previous study conducted on five Limousin beef cattle populations, Bouquet *et al.* (2011) concluded that despite Limousin European populations were connected to the French one via AI bulls, genetic diversity was still maintained between populations.

The impact of additional information from relatives as provided with the international evaluations can be reflected in the gain in individuals' reliabilities when moving from Scenario NAT to Scenario INT (Venot *et al.* 2014). Hereafter, all mentioned reliabilities are expressed on a 0-100 scale, and any gains in reliability are expressed in percentage points. The distribution of REL_{NAT} is reported in Table 2.7. Average REL_{NAT} ranged from 23.2 of CZE to 52.1 of FRA, and from 15.5 for CZE and CHE to 33.8 for DEU, for the direct and the maternal EBV, respectively. As expected, the average REL_{NAT} for maternal EBV was lower than the average REL_{NAT} for direct EBV for all countries. The distribution of REL_{INT} is reported in Table 2.8. Average REL_{INT} ranged from 38.3 of CHE to 52.1 of FRA, and from 28.0 for GBR to 39.0 for CZE, for the direct and the maternal EBV, respectively. Also for Scenario INT, as expected, for all countries the average REL_{INT} for maternal EBV was lower than the average REL_{INT} for direct EBV. The gain in reliability when moving from Scenario NAT to Scenario INT (Δ_{REL}) for both direct and maternal EBV is shown in Figure 2.1, with the smallest countries having the highest Δ_{REL}. In each country, the highest frequency of Δ_{REL} was observed for the 0 to 5 bin, for both direct and maternal EBV, comprising more than 20% of the domestic animals. The average Δ_{REL} across countries was 9.6 and 8.3 for the direct and the maternal EBV, respectively. FRA was the only country with no increase in average Δ_{REL} for both direct and maternal EBV: this was expected since FRA had relatively the largest amount of data at the national level. Larger countries,

like GBR and DFS, had smaller Δ_{REL} (average direct EBV Δ_{REL} of 3.9 and 4.4, respectively) compared to those of smaller countries like CZE, CHE and IRL (average direct EBV Δ_{REL} of 24.3, 14.5 and 10.7, respectively). The same pattern was observed for the maternal EBV Δ_{REL} being the smallest for DFS (average Δ_{REL} of 2.2) and the largest for CZE (average Δ_{REL} of 23.6). Δ_{REL} for maternal EBV was smaller in all countries compared to the Δ_{REL} for direct EBV (Figure 2.1). There were no large differences between males and females for Δ_{REL} (results not shown). The observation that almost all Δ_{REL} values are greater than 0 shows that the information from foreign phenotypes is propagated to almost all animals in the national pedigree, with the individual Δ_{REL} depending on the relationship with CB and the genetic correlations between countries.

To further illustrate how international data from foreign relatives allows for a more accurate estimation of EBV, we also compared the variance of EBV between Scenario NAT and Scenario INT, for all countries. When more information is used for the estimation of the genetic merit of an animal, EBV are less regressed to the mean, and thus show larger variance (Robinson 1991; Mrode 2014a). The variance of EBV of domestic animals increased on average by 91% and 55% for direct and maternal EBV, respectively, under Scenario INT compared to Scenario NAT (Figure 2.2). These increases in EBV variance ranged from 24% (GBR) to 307% (CZE) for direct EBV, and from 10% (DEU) to 238% (CZE) for maternal EBV (Table 2.6). FRA was the only country without an increase in EBV variance (Figure 2.2). The increase in EBV variance was particularly evident in smaller countries (Figure 2.2), confirming that in those countries more accurate estimates of EBV of domestic animals were obtained under Scenario INT by considering the information of recorded relatives in other countries.

Table 2.7 Distribution of national individuals' reliabilities (REL_{NAT}) for domestic animals direct and maternal EBV per country [a].

Effect	COU [b]	First Quartile	Median	Mean	Third Quartile	Maximum
Direct	CZE	0.8	6.3	23.2	52.8	96.3
	DFS	43.0	47.2	42.1	49.1	98.6
	ESP	8.7	40.6	30.5	45.5	98.3
	GBR	45.6	50.1	45.2	51.9	99.3
	IRL	10.5	32.8	30.3	48.6	98.1
	FRA	50.7	52.4	52.1	53.9	100.0
	DEU	43.9	48.5	42.4	50.1	97.2
	CHE	3.3	31.7	23.8	37.1	96.4
Maternal	CZE	1.0	7.0	15.5	25.4	91.8
	DFS	18.1	24.7	25.8	31.4	96.5
	ESP	9.3	19.7	20.4	28.0	93.7
	GBR	16.3	23.0	23.6	29.1	97.8
	IRL	11.2	22.1	22.3	31.4	96.5
	FRA	23.2	28.3	30.0	34.0	99.9
	DEU	24.0	30.8	33.8	36.8	97.1
	CHE	3.1	16.0	15.3	22.6	92.1

[a] Minimum not shown (all countries had a minimum REL_{NAT} equal to 0).
[b] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Table 2.8 Distribution of international individuals' reliabilities (REL_{INT}) for domestic animals direct and maternal EBV per country [a].

Effect	COU [a]	Min	First Quartile	Median	Mean	Third Quartile	Maximum
Direct	CZE	0.4	41.0	50.3	47.5	55.3	97.4
	DFS	0.0	45.0	47.9	46.1	49.6	99.0
	ESP	0.3	40.5	44.9	43.5	47.3	98.5
	GBR	0.0	48.0	50.6	49.6	52.4	99.3
	IRL	0.0	32.0	44.5	41.0	50.7	98.6
	FRA	0.2	50.7	52.4	52.1	53.9	100.0
	DEU	0.2	47.0	49.2	48.7	50.8	98.0
	CHE	0.6	34.3	37.6	38.3	41.4	97.4
Maternal	CZE	0.1	28.7	39.0	39.0	47.6	97.4
	DFS	0.0	20.2	26.3	28.1	33.3	96.5
	ESP	0.4	22.0	28.3	29.8	35.2	96.2
	GBR	0.0	19.6	26.0	28.0	33.9	97.8
	IRL	0.0	22.1	30.7	31.7	40.2	97.4
	FRA	0.2	23.2	28.4	30.1	34.1	99.9
	DEU	0.3	27.0	32.3	37.4	42.1	97.2
	CHE	0.4	20.5	27.7	29.0	36.5	95.3

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

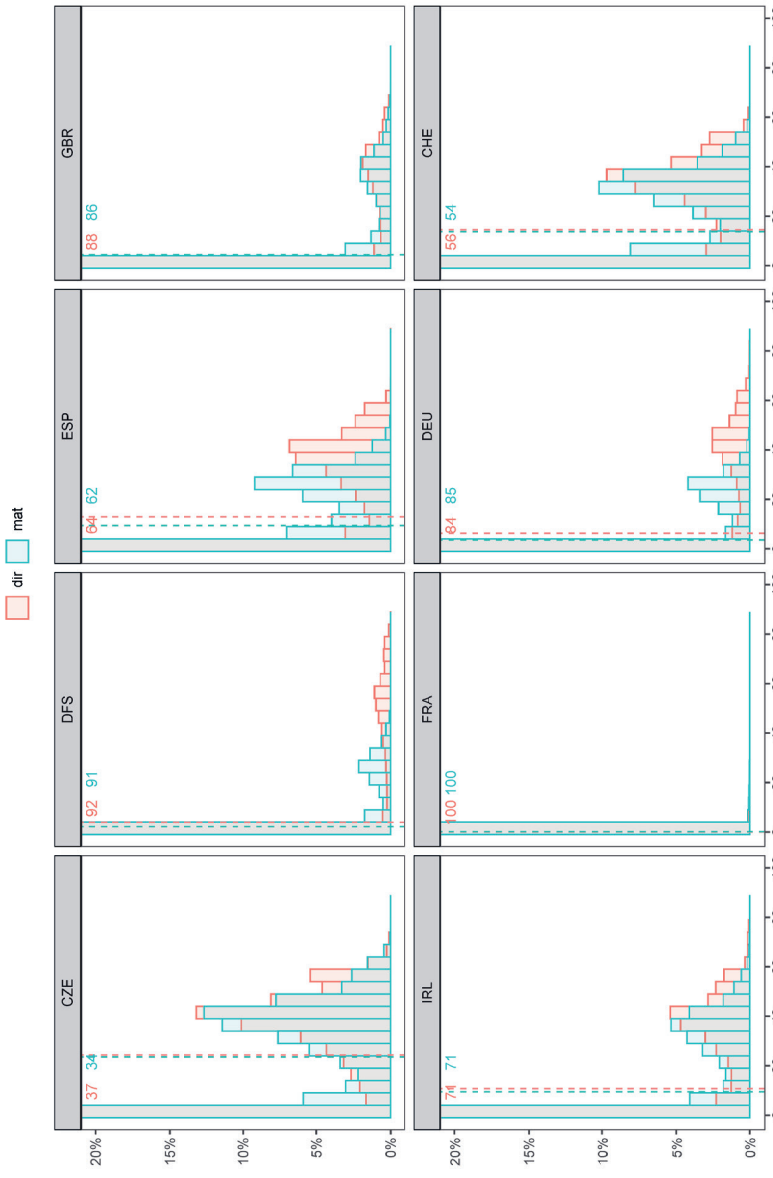

Figure 2.1 Distribution of the gain in individual reliability (Δ_{REL} = REL_{INT} – REL_{NAT}, on a scale from 0 to 100) for domestic animals for the direct (dir) and maternal (mat) EBV in each country. The y-axis is the percentage of domestic animals in each bin (bin size of 5). Dotted lines indicate the average Δ_{REL}. The frequency of Δ_{REL} between 0 and 5 was always greater than 20%; the actual percentage in these bins are reported as text in each plot.

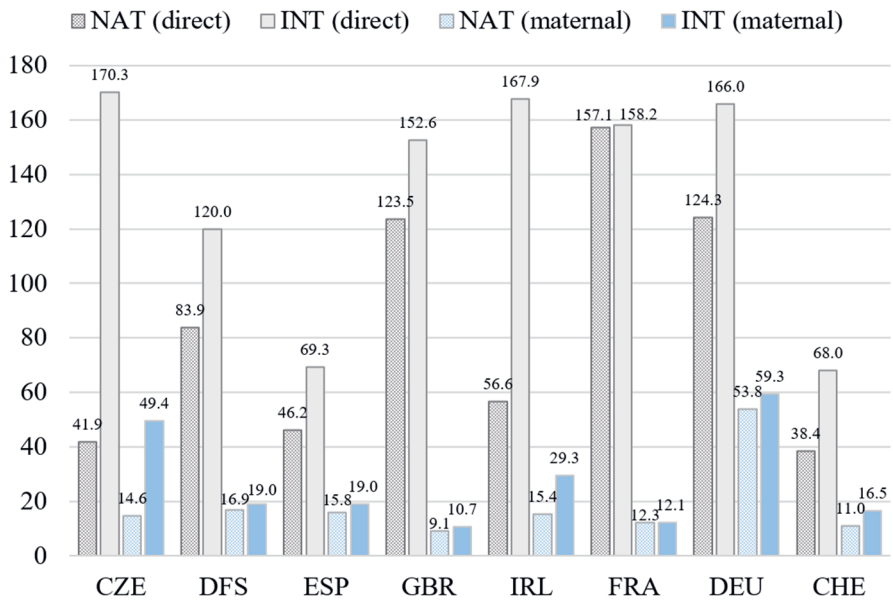

Figure 2.2 Direct and maternal EBV variances across all domestic animals under Scenario NAT and Scenario INT per country. Country = country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

2.4 Conclusions

Our study gives an up-to-date picture of the Interbeef international evaluations from the national perspective, for both large and small countries. On one hand, small countries get access to a panel of elite foreign sires with EBV on their own country scale, as well as more reliable EBV for domestic animals via the international model, which is reflected in the increase of EBV variance and reliabilities. On the other hand, especially elite sires from large countries obtain EBV on different country scales, which facilitates the comparison of sires' EBV, and, in turn, the export of their genetic material across countries.

2.5 Acknowledgements

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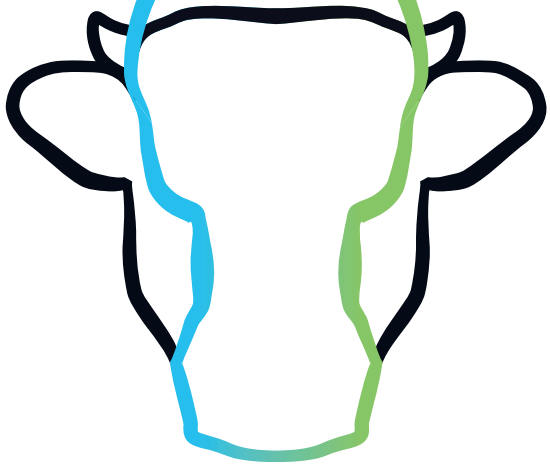
CHAPTER 3



Impact of sub-setting the data of the main Limousin beef cattle population on the estimates of across-country genetic correlations

Renzo Bonifazi[1], Jérémie Vandenplas[1], Jan ten Napel[1], Kaarina Matilainen[2], Roel F. Veerkamp[1], Mario P.L. Calus[1]

[1] Animal Breeding and Genomics, Wageningen University and Research, P.O. Box 338, 6700 AH Wageningen, the Netherlands
[2] Production Systems, Animal Genetics, Natural Resources Institute Finland (Luke), 31600 Jokioinen, Finland

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Abstract

Background: Cattle international genetic evaluations allow the comparison of estimated breeding values (EBV) across different environments, i.e. countries. For international evaluations, across-country genetic correlations (r_g) need to be estimated. However, lack of convergence of the estimated parameters and high standard errors of the r_g are often experienced for beef cattle populations due to limited across-country genetic connections. Furthermore, using all available genetic connections to estimate r_g is prohibitive due to computational constraints, thus sub-setting the data is necessary. Our objective was to investigate and compare the impact of strategies of data sub-setting on estimated across-country r_g and their computational requirements.

Methods: Phenotype and pedigree information for age-adjusted weaning weight was available for ten European countries and 3,128,338 Limousin beef cattle males and females. Using a Monte Carlo based expectation–maximization restricted maximum likelihood (MC EM REML) methodology, we estimated across-country r_g by using a multi-trait animal model where countries are modelled as different correlated traits. Values of r_g were estimated using the full data and four different sub-setting strategies that aimed at selecting the most connected herds from the largest population.

Results: Using all available data, direct and maternal r_g (standard errors in parentheses) were on average equal to 0.79 (0.14) and 0.71 (0.19), respectively. Direct-maternal within-country and between-country r_g were on average equal to −0.12 (0.09) and 0.00 (0.14), respectively. Data sub-setting scenarios gave similar results: on average, estimated r_g were smaller compared to using all data for direct (0.02) and maternal (0.05) genetic effects. The largest differences were obtained for the direct-maternal within-country and between-country r_g, which were, on average 0.13 and 0.12 smaller compared to values obtained by using all data. Standard errors always increased when reducing the data, by 0.02 to 0.06, on average. The proposed sub-setting strategies reduced the required computing time up to 22% compared to using all data.

Conclusions: Estimating all 120 across-country r_g that are required for beef cattle international evaluations, using a multi-trait MC EM REML approach, is feasible but involves long computing time. We propose four strategies to reduce computational requirements while keeping a multi-trait estimation approach. In all scenarios with data sub-setting, the estimated r_g were consistently smaller (mainly for direct-maternal r_g) and had larger standard errors.

3.1 Background

International genetic evaluations of beef cattle performed by Interbeef allow the comparison of estimated breeding values (EBV) across countries. Current Interbeef evaluations involve up to ten countries, five breeds (Limousin, Charolais, Beef Simmental, Angus, and Hereford), and two trait groups: animal weaning weight (composed of age-adjusted weaning weight) and calving (composed of birth weight and calving ease) (Cromie, personal communication). To estimate international EBV (IEBV), across-country estimated genetic correlations (r_g) are necessary (Phocas *et al.* 2005), which in turn require sufficient genetic connections between countries that are usually provided by sires with recorded offspring in more than one country. However, there are two main challenges for the estimation of across-country r_g in beef cattle international evaluations: the small number of genetic connections available for the estimation process and the long computing time necessary to obtain them. In beef cattle, although many phenotypes are recorded in both sexes, the number of genetic connections between populations is small due to the limited use of artificial insemination (Berry *et al.* 2016). Such small numbers of genetic connections between populations have been reported since the first Interbeef pilot study (Renand *et al.* 2003) and in international evaluations of small dairy breeds (Jorjani 2000; Mark *et al.* 2005a). This lack of genetic connections between beef cattle populations makes the estimation of across-country r_g more difficult. Furthermore, estimating across-country r_g is even more challenging in Interbeef evaluations than in dairy breeds because, in addition to the direct genetic effect, and permanent environment effects are usually included in the model (Renand *et al.* 2003; Phocas *et al.* 2005).

Estimating across-country r_g using all the available data from participating countries would allow the use of all the available genetic connections. However, this has been prohibitive due to computational constraints, and thus, most often, subsets of data are used. To overcome these computational constraints, two main approaches have been used: (1) reduction of the number of populations analysed simultaneously, i.e. country sub-setting, or (2) use of subsets of national submitted data, i.e. within-country data sub-setting (Jorjani *et al.* 2005).

Strategies for country sub-setting reduce the amount of data, but also results in not using all the genetic connections provided by sires with offspring recorded in more than two countries. In turn, not using all the genetic connections may lead to inaccurate estimates of r_g and impair the convergence of estimated parameters, resulting in long computing times (Jorjani *et al.* 2005). Moreover, the resulting across-country r_g matrices are very often non-positive definite, as expected for large variance–covariance matrices (Hill and Thompson 1978), and require a bending

approach (e.g. Jorjani *et al.* 2003). The most extreme approach of country sub-setting is the current estimation procedure of Interbeef, which is based on a series of bivariate estimations (Pabiou *et al.* 2014), i.e. by analysing two countries at a time. However, in theory, some of the described shortcomings by Pabiou *et al.* (2014), such as lack of convergence and use of bending, could be overcome by using a multivariate model including all the countries simultaneously.

To date, the application of a within-country data sub-setting approach for a multivariate estimation of r_g in Interbeef evaluations has not been fully investigated, mainly because of computational constraints. With such multivariate models and large datasets, traditional restricted maximum likelihood (REML) algorithms are not suitable, which is one of the reasons why Bayesian Gibbs sampling algorithms have been developed and used (Cantet *et al.* 2004; Misztal 2008). Based on García-Cortés *et al.* (1992), Matilainen *et al.* (2012) developed a Monte Carlo based expectation–maximization restricted maximum likelihood (MC EM REML) algorithm that gives the possibility to compute variance components (VC) from a large amount of data using a multi-trait approach, while being more efficient than Gibbs sampling (Lidauer *et al.* 2009).

Thus, our objectives were: (1) to estimate across-country r_g for the Limousin Interbeef genetic evaluations by using a multiple trait approach, and (2) to investigate the impact of possible within-country data sub-setting strategies on the estimated r_g and associated standard error, and on the required computing time, by taking the low across-country genetic connectedness into account. The within-country data sub-setting strategies aimed at selecting the most connected herds across countries, based on genetic connectedness measures and, for comparison, one strategy used a random selection of herds.

3.2 Methods

3.2.1 Limousin data and pedigree

Interbeef January 2018 routine evaluation data for age-adjusted weaning weight (AWW) were available for eight Limousin populations, representing ten European countries: Switzerland (CHE), Czech Republic (CZE), Germany (DEU), Denmark, Finland and Sweden (DFS), Spain (ESP), France (FRA), Great Britain (GBR) and Ireland (IRL). The following data edits were applied to the submitted national datasets: (1) animals belonging to contemporary groups (CG) smaller than the defined national minimum size (Table 3.1), and (2) embryo transfer animals, were removed. The presence of outliers can affect the procedure to estimate variance components both in terms of accuracy of the across-country estimated r_g (i.e. standard errors) and of

computing time, thus, data that were below or above three phenotypic standard deviations from the phenotypic mean of each population-sex combination were removed. After these edits, individual phenotype records were available for 3,115,598 Limousin males and females, distributed across 19,330 herds.

The numbers of observations available for each population are in Table 3.1. The FRA population alone represents 87.1% of the observations, followed by the GBR population with 4.1%. DFS and DEU populations represented 2.9 and 2.8% of the observations, respectively. ESP, CHE, IRL and CZE were the smallest populations, each representing 1% or less of the data. Recorded animals were born between 1972 and 2017. FRA and GBR were the only two populations with animals recorded since 1972, whereas submitted records for Spain stopped in 2011 (Table 3.1). Furthermore, each country adopted different national models for AWW, both in terms of fixed and random effects. National environmental effects for each population are in Supplementary Table S3.1.

Pedigree information for the available data was extracted from the Interbeef international pedigree database using the Interbeef routine workflow, and the following quality controls were performed: all recorded animals without a corresponding record in the pedigree, involved in duplicates and pedigree cycles (i.e. an animal being its own ancestor) were removed. Furthermore, using the RelaX2 software (Strandén 2014), the available pedigree data were pruned to include animals with phenotypes and their ancestors (i.e. using the option "prediction" in RelaX2), without a limit on generation. The final pedigree included 3,431,742 animals, born between 1927 and 2017, and a maximum depth of 19 generations.

Table 3.1 Number of age-adjusted weaning weight phenotypes, number of herds, year of birth of recorded animals, and minimum contemporary group size by population.

POP [a]	N	%	Herds	YoB [b]	Min CG [c]
CZE	10,500	0.3	121	1991–2017	1
DFS	90,456	2.9	9190	1980–2017	1
ESP	33,152	1.1	188	1989–2011	5
GBR	127,840	4.1	745	1972–2017	5
IRL	20,609	0.7	1304	1975–2017	3
FRA	2,714,368	87.1	6677	1972–2017	2
DEU	88,628	2.8	881	1981–2017	3
CHE	30,045	1.0	224	1993–2017	5
Total	3,115,598	100	19,330	1972–2017	-

[a] POP, populations; CZE, Czech Republic; DFS, Denmark, Finland and Sweden; ESP, Spain; GBR, Great Britain; IRL, Ireland; FRA, France; DEU, Germany; CHE, Switzerland.
[b] Year of birth.
[c] Minimum contemporary group.

3.2.2 Measure of connectedness

Genetic connections across countries are provided by animals having recorded offspring across two or more populations. First, an analysis was conducted to investigate and quantify the existing common bulls (CB), common dams and common maternal grandsires (CMGS) across-populations. Then, this information was used to compute the following measures of connectedness: coefficients of genetic similarity, coefficient of adjusted number of populations for sires, and the harmonic mean of a sire's progeny size. Finally, these measures were used to identify the best-connected subsets of data for the estimation of across-country r_g.

3.2.2.1 Genetic similarity

The concept of genetic similarity between two populations initially proposed by Rekaya *et al.* (1999, 2003) has been applied in dairy cattle studies (Jorjani 1999, 2000) as a measure of connectedness between two countries. We adapted the formula slightly to include sires' offspring of both sexes to account for the structure of beef cattle data, such that the coefficient of genetic similarity between two populations a and b (GS_{ab}) is defined as:

$$GS_{ab} = \frac{\sum_{k=1}^{2}\sum_{i=1}^{CB_{ab}} NO_{ik}}{\sum_{k=1}^{2}\sum_{i=1}^{TB_{ab}} NO_{ik}},$$

where CB_{ab} is the number of common bulls between populations a and b, TB_{ab} is the total number of bulls in populations a and b, NO_{ik} is the number of offspring (male and females) of sire i in country k (k = 1, 2).

The coefficient of genetic similarity ranges from 0 to 1 and can be interpreted as the proportion of offspring between two populations that originate from CB. Therefore, the closer the coefficient of genetic similarity between two populations is to 1, the larger is the number of genetic connections between two populations.

3.2.2.2 Balanced offspring distribution (BOD) and adjusted number of populations (AN_POP)

The concept of genetic similarity was extended by Jorjani *et al.* (2005) to take the across-country balanced number of daughters for dairy sires into account by using the coefficient of balanced daughter distribution. We extend this concept to include both male and female offspring, hereafter referred to as the balanced offspring distribution, which is computed for sire i (BOD_i) as:

$$BOD_i = 1 - \frac{\sum_{j=1}^{N_P}|n_{ij} - \overline{n}_{i.}|}{2 \cdot \sum_{j=1}^{N_P} n_{ij}},$$

where N_P is the number of populations in the international genetic evaluation, n_{ij} is the number of offspring of sire i in population j, $\overline{n}_{i.}$ is the average number of offspring of sire i across all populations.

Following Jorjani *et al.* (2005) the adjusted number of populations (AN_POP) of sire i was computed for an easier interpretation of the BOD coefficient as:

$$AN\_POP_i = N_P \cdot BOD_i.$$

The BOD coefficient ranges from 0 to 1 and the AN_POP coefficient ranges from 1 to N_P. For example, a CB with a balanced distribution of recorded offspring across N countries would have an AN_POP coefficient equal to N. If the distribution of offspring of CB is not balanced across all N countries, the AN_POP coefficient would be between 1 and N.

3.2.2.3 Harmonic mean of a sire's progeny size

The harmonic mean of a sire's progeny size across two countries can be used as a measure to identify an unbalanced distribution of offspring. The harmonic mean of the progeny size for sire i (HM_i) with recorded offspring in two countries can be calculated as:

$$HM_i = 2 / (\frac{1}{N_1} + \frac{1}{N_2}),$$

where N_1 and N_2 are the progeny sizes of sire i in countries 1 and 2, respectively.

The use of the harmonic mean to measure the unbalanced distribution of offspring can be extended to the herd level as follows:

$$HM_h = \sum_{j=1}^{N_P} \sum_{i=1}^{CB_{jh}} HM_{ijh},$$

where HM_h is the harmonic mean coefficient for herd h, N_P is the number of populations in the international genetic evaluation, CB_{jh} is the number of common bulls between population j and herd h, HM_{ijh} is the harmonic mean of the CB_i progeny size for a common bull i between population j and herd h.

3.2.3 Scenarios

The data sub-setting strategies were focused only on the French Limousin population, since it was the largest national dataset and, therefore, it has a large impact on computing time. Data sub-setting was not applied to the other Limousin populations since it could lead to a relatively large reduction in the number of observations for any of those populations (especially for the smallest ones). In order to minimize variation in data size across different scenarios, and allow a meaningful

comparison of computational requirements, the FRA population was reduced in all sub-setting strategies such that the selected amount of data was close to the number of phenotypes for the GBR population, which is the second largest dataset. As a result, the total number of records retained across all populations in any of the data subsets was approximately 0.5 million.

For the subsequent estimation of variance components, we considered different scenarios depending on which FRA records were selected for the analysis, whereas all the records of all other countries were included in all scenarios:

1. Scenario ALL: using the complete dataset, i.e. 3,115,598 AWW records and 3,431,742 animals in the pedigree.
2. Scenario RND: selection of randomly composed groups of FRA herds. FRA herds were randomly divided into 20 subsets. For each subset, the coefficients of genetic similarity with all participating countries were computed. The three subsets with the highest coefficients of genetic similarity were analysed separately. In these subsets of data, 533,816, 521,077 and 556,100 phenotypes were retained, with 706,717, 692,205 and 729,778 animals in the pedigree, respectively.
3. Scenario GSCB: selection of FRA herds based on herd-level coefficients of genetic similarity, defined as the average of the coefficients of genetic similarity computed between herd h and each population b (GS_{hb}), with $GS_{hb} = \frac{\sum_j \sum_{i=1}^{CB_{hb}} NO_{ij}}{\sum_j \sum_{i=1}^{TB_{hb}} NO_{ij}}$, where CB_{hb} is the number of common bulls between herd h and population b, TB_{hb} is the total number of bulls in herd h and population b, NO_{ij} is the number of offspring (male and females) of sire i in j, with $j = h, b$ (i.e. in herd *h* or population *b*).
   The final dataset included 506,080 phenotypes and the pruned pedigree included 654,841 animals across all involved countries. The amount of retained data for the FRA population corresponded to 1% of the FRA herds.
4. Scenario GSTOT: selection of FRA herds based on the herd-level coefficient of genetic similarity that includes information from both CB and CMGS (common maternal grand-sires, i.e. maternal grand-sires with grand-offspring in more than one country). Genetic similarity at the herd level was defined as the average of the coefficients of genetic similarity computed between herd h and each population b, as $GS_{TOT_{hb}} = (GS_{CB_{hb}} + GS_{CMGS_{hb}})/2$. $GS_{CB_{hb}}$ was the coefficient of genetic similarity computed at the herd level considering CB as defined in Scenario GSCB, and $GS_{CMGS_{hb}}$ was the coefficient of genetic similarity computed at the herd level

considering CMGS defined as $GS_{CMGS_{hb}} = \frac{\sum_j \sum_{i=1}^{CMGS_{hb}} NO_{ij}}{\sum_j \sum_{i=1}^{TMGS_{hb}} NO_{ij}}$, where $CMGS_{hb}$ is the number of CMGS between herd h and population b, $TMGS_{hb}$ is the number of total maternal grand-sires in herd h and population b, NO_{ij} is the number of grand-offspring (male and females) of maternal grand-sire i in j, with $j = h, b$ (i.e. in herd *h* or population *b*).

The final dataset included 513,969 phenotypes and the pruned pedigree included 663,127 animals across all involved countries. The amount of retained data for the FRA population corresponded to the top 1% of the FRA herds ranked on their GS_{TOT} coefficient.

5. Scenario HM: selection of FRA herds based on the harmonic mean of sires' progeny size. Based on the harmonic means computed at the herd level, FRA herds were selected until the FRA population was reduced to about 0.5 million records. The final dataset included 502,716 phenotypes, with a pruned pedigree of 649,081 animals across all involved countries.

When data reduction was applied to the FRA population (i.e. all scenarios except Scenario ALL), the RelaX2 software was used for pedigree pruning with the following options: "prediction" pruning method and no generation limit.

3.2.4 Model and software

In all scenarios, variance component estimation (VCE) was performed using an animal model accounting for across-country interaction (AMACI) (Phocas *et al.* 2005). The AMACI model accounts for country-specific fixed and random effects by fitting for each country their national model. The AMACI model, currently used for Interbeef routine evaluations, is equivalent to a multi-trait animal model with maternal effects, where each population is modelled as a different trait:

$$\begin{bmatrix} \mathbf{y}_1 \\ \mathbf{y}_2 \\ \vdots \\ \mathbf{y}_8 \end{bmatrix} = \begin{bmatrix} \mathbf{X}_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \mathbf{X}_8 \end{bmatrix} \begin{bmatrix} \mathbf{b}_1 \\ \vdots \\ \mathbf{b}_8 \end{bmatrix} + \begin{bmatrix} \mathbf{C}_1 & 0 & 0 & 0 \\ 0 & \mathbf{C}_2 & 0 & 0 \\ 0 & 0 & \mathbf{C}_3 & 0 \\ 0 & 0 & 0 & \mathbf{C}_4 \end{bmatrix} \begin{bmatrix} \mathbf{r}_1 \\ \mathbf{r}_2 \\ \mathbf{r}_3 \\ \mathbf{r}_4 \end{bmatrix} +$$

$$\begin{bmatrix} \mathbf{Z}_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \mathbf{Z}_8 \end{bmatrix} \begin{bmatrix} \mathbf{u}_1 \\ \vdots \\ \mathbf{u}_8 \end{bmatrix} + \begin{bmatrix} \mathbf{W}_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \mathbf{W}_8 \end{bmatrix} \begin{bmatrix} \mathbf{m}_1 \\ \vdots \\ \mathbf{m}_8 \end{bmatrix} + \begin{bmatrix} \mathbf{P}_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \mathbf{P}_7 \end{bmatrix} \begin{bmatrix} \mathbf{pe}_1 \\ \vdots \\ \mathbf{pe}_7 \end{bmatrix} + \begin{bmatrix} \mathbf{e}_1 \\ \vdots \\ \mathbf{e}_8 \end{bmatrix},$$

where $\mathbf{y}_i$ is the vector of observations for population i; $\mathbf{b}_i$ is the vector of fixed effects for population i; $\mathbf{r}_i$ is the vector of random environmental effects for population i; $\mathbf{u}_i$ is the vector of random additive genetic (direct) effects; $\mathbf{m}_i$ is the vector of

random maternal (indirect) additive genetic effects; $\mathbf{pe}_i$ is the vector of random maternal permanent environmental effects (provided by the dam); $\mathbf{e}_i$ is the vector of random residual effects. $\mathbf{X}$ and $\mathbf{C}$ are incidence matrices linking records to fixed and random environmental effects, respectively. $\mathbf{Z}$, $\mathbf{W}$, and $\mathbf{P}$ are incidence matrices linking records to the animal, maternal genetic and maternal permanent environmental effects, respectively.

The four random environmental effects refer to the national effects of herd-year-season in CZE, herd-year in DEU and CHE, and sire-herd in CHE (see Supplementary Table S3.1). Furthermore, a maternal permanent environmental effect was not fit for the DEU population in the national evaluation (Ruten, personal communication). Because the international model follows the national evaluation models, DEU was the only population without a maternal permanent environmental effect in the AMACI model (see Supplementary Table S3.1).

It is assumed that:

$$var\begin{bmatrix}\mathbf{u}_1\\ \mathbf{u}_2\\ \vdots\\ \mathbf{u}_8\\ \mathbf{m}_1\\ \mathbf{m}_2\\ \vdots\\ \mathbf{m}_8\end{bmatrix} = \begin{bmatrix} \sigma^2_{u_1} & & & & & & & \\ \sigma_{u_2,u_1} & \sigma^2_{u_2} & & & & Sym & & \\ \vdots & \vdots & \ddots & & & & & \\ \sigma_{u_8,u_1} & \sigma_{u_8,u_2,} & \cdots & \sigma^2_{u_8} & & & & \\ \sigma_{m_1,u_1} & \sigma_{m_1,u_2} & \cdots & \sigma_{m_1,u_8} & \sigma^2_{m_1} & & & \\ \sigma_{m_2,u_1} & \sigma_{m_2,u_2} & \cdots & \sigma_{m_2,u_8} & \sigma_{m_2,m_1} & \sigma^2_{m_2} & & \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \\ \sigma_{m_8,u_1} & \sigma_{m_8,u_2} & \cdots & \sigma_{m_8,u_8} & \sigma_{m_8,m_1} & \sigma_{m_8,m_2} & \cdots & \sigma^2_{m_8}\end{bmatrix} \otimes \mathbf{A},$$

$$var(\mathbf{r}) = \bigoplus_{i=1}^{4} \mathbf{I}_{n_i} \cdot \sigma^2_{r_i}, \quad var(\mathbf{pe}) = \bigoplus_{i=1}^{7} \mathbf{I}_{n_i} \cdot \sigma^2_{pe_i}, \quad var(\mathbf{e}) = \bigoplus_{i=1}^{8} \mathbf{I}_{n_i} \cdot \sigma^2_{e_i},$$

where, $\sigma^2_{u_i}$ is the direct additive genetic variance for population i, $\sigma^2_{m_i}$ is the maternal additive genetic variance for population i, σ_{u_i,m_i} is the additive genetic covariance between direct and maternal effect for population i, σ_{u_i,u_j} is the additive genetic covariance between populations i and j, σ_{u_i,m_j} is the additive genetic covariance between the direct effect for population i and the maternal effect for population j, $\sigma^2_{r_i}$ is the random environmental variance for population i, $\sigma^2_{pe_i}$ is the permanent environmental variance for population i, $\sigma^2_{e_i}$ is the residual error variance for population i, $\mathbf{A}$ is the numerator relationship matrix, $\mathbf{I}$ is the identity matrix, $\oplus$ indicates the matrix direct sum of i diagonal matrices, and $\otimes$ indicates the Kronecker

product. Permanent environmental covariances between countries were fixed to 0 since only 697 dams had offspring in more than one country.

All analyses for VCE were conducted using the MC EM REML algorithm as implemented in the MiX99 software (MiX99 Development Team 2017). The MC EM REML algorithm performs two main steps within each REML round. In the first step, best linear unbiased prediction (BLUP) estimates of random effects are obtained from the real data. In the second step, BLUP estimates of random effects are obtained from repeatedly simulated data based on the model and a given set of VC. Successively, via MC EM REML, VC are estimated using the sum of the squares of estimated random effects obtained from the real data, and the prediction error variances obtained from the simulated data. For both the real and simulated data, the preconditioned conjugate gradient (PCG) algorithm is used to obtain solutions of the mixed model equations. The PCG convergence criterion is defined as the square root of the relative difference between solutions of consecutive PCG iteration rounds. In the REML round step, the convergence criterion for VCE is defined by using a linear regression of the estimated VC over the last REML rounds. When the linear regression slope is smaller than a given value, convergence is reached (for more details see Matilainen *et al.* 2012).

The VCE estimated via MC EM REML was standardized for all scenarios using: (1) a maximum of 1000 PCG iterations, (2) a convergence criterion for PCG iterations equal to 10^{-5}, (3) one simulated dataset for each REML round, and (4) a convergence criterion of 10^{-9} for the VCE. In all scenarios, the provided set of starting values were the most recent estimates available and currently in use for the 2018 Limousin Interbeef routine evaluations.

Approximated standard errors (SE) of the estimated VC can be obtained in an additional MC EM REML round (Matilainen *et al.* 2014). This additional MC EM REML round was performed using the same setting as described above for VCE, but with 500 simulated datasets and no limit for the maximum number of PCG iterations. The same settings were used in all scenarios. Approximated standard errors of across-country r_g were calculated from the obtained information matrix as described by Klei and Tsuruta (2008).

3.3 Results

First, we present the results for the assessment of the available genetic connections in the whole dataset, followed by the estimated r_g in each scenario and their computational requirements.

3.3.1 Measures of connectedness

3.3.1.1 Common bulls and common maternal grand sires

We assessed the available genetic connections between countries by quantifying the number of recorded offspring of CB. The number of CB varied with the country combination, with a minimum of 44 CB between ESP-CZE and a maximum of 396 for FRA-GBR (Table 3.2). The average number of CB between two populations was 143.6. The number of sires used within a country varied considerably, with a minimum of 554 bulls for CZE, and a maximum of 57,784 bulls for FRA, which reflects the differences in the population sizes of participating countries.

Since CB can have recorded offspring in more than one bivariate country-combination, hereafter we will use the term "unique CB" to indicate an individual CB. The total number of unique CB in the available dataset was equal to 1436. Of these unique CB, 1053 (73.4%) had offspring in two populations, while 12.4, 5.2, 4.4, 2.2, 1.7 and 1.2% had offspring in three up to all eight populations, respectively. Moreover, the distribution of CB by number of connecting populations and by country of origin (Table 3.3) showed that the majority of CB were from France (82.5%), followed by Germany (6.3%), Great Britain (5.7%), Denmark (2.0%) and Ireland (1.81%). Finally, sires that connected four or more populations were mostly French bulls (Table 3.3).

The distribution of the number of CB per year of birth and country of first registration reflects the exchange of genetic material across the analysed populations (Figure 3.1). Figure 3.1 indicates that consistent genetic connections between countries started with the use of CB born during the 1970s and 1980s. In addition, the use of sires born in more recent years reflects the use of more recent genetic material, with the majority of the CB born after the 1990s, and with the highest frequency of year of birth of CB being in 2001 (Figure 3.1). Furthermore, French sires represented a large proportion of CB in each year, with sires from Germany, Ireland and Great Britain becoming more frequently used at the international level during the last decade.

Table 3.2 Total number of bulls used within population (diagonal), number of common bulls (above diagonal) and genetic similarity coefficients (below diagonal) between populations.

POP [a]	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
CZE	554	65	44	67	64	157	101	63
DFS	0.06	4375	76	109	94	171	143	73
ESP	0.07	0.06	1188	97	78	358	105	71
GBR	0.04	0.05	0.04	5486	239	396	125	72
IRL	0.14	0.07	0.12	0.15	2073	200	120	65
FRA	0.11	0.13	0.13	0.13	0.12	57,784	339	342
DEU	0.06	0.06	0.06	0.04	0.07	0.15	4366	188
CHE	0.12	0.06	0.08	0.04	0.10	0.13	0.11	1699

[a] POP, population; CZE, Czech Republic; DFS, Denmark, Finland and Sweden; ESP, Spain; GBR, Great Britain; IRL, Ireland; FRA, France; DEU, Germany; CHE, Switzerland.

Table 3.3 Distribution of common bulls per country of first registration and across different numbers of connected populations.

COU [a]	Number of connected populations							
	2	3	4	5	6	7	8	Sum
CAN	5	1	1					7
CHE	4							4
CZE	3							3
DEU	71	11	4	3	2			91
DNK	25	2	1	1				29
ESP	1	1						2
FRA	861	139	61	58	29	20	17	1185
GBR	57	19	5	1				82
IRL	21	4	1					26
LUX	3							3
NOR	1							1
SWE		1						1
USA	1		1					2
Sum	1053	178	74	63	31	20	17	1436

[a] COU, country of first registration; CAN, Canada; CHE, Switzerland; CZE, Czech Republic; DEU, Germany; DNK, Denmark; ESP, Spain; FRA, France; GBR, Great Britain; IRL, Ireland; LUX, Luxemburg; NOR, Norway; SWE, Sweden; USA, United States of America.

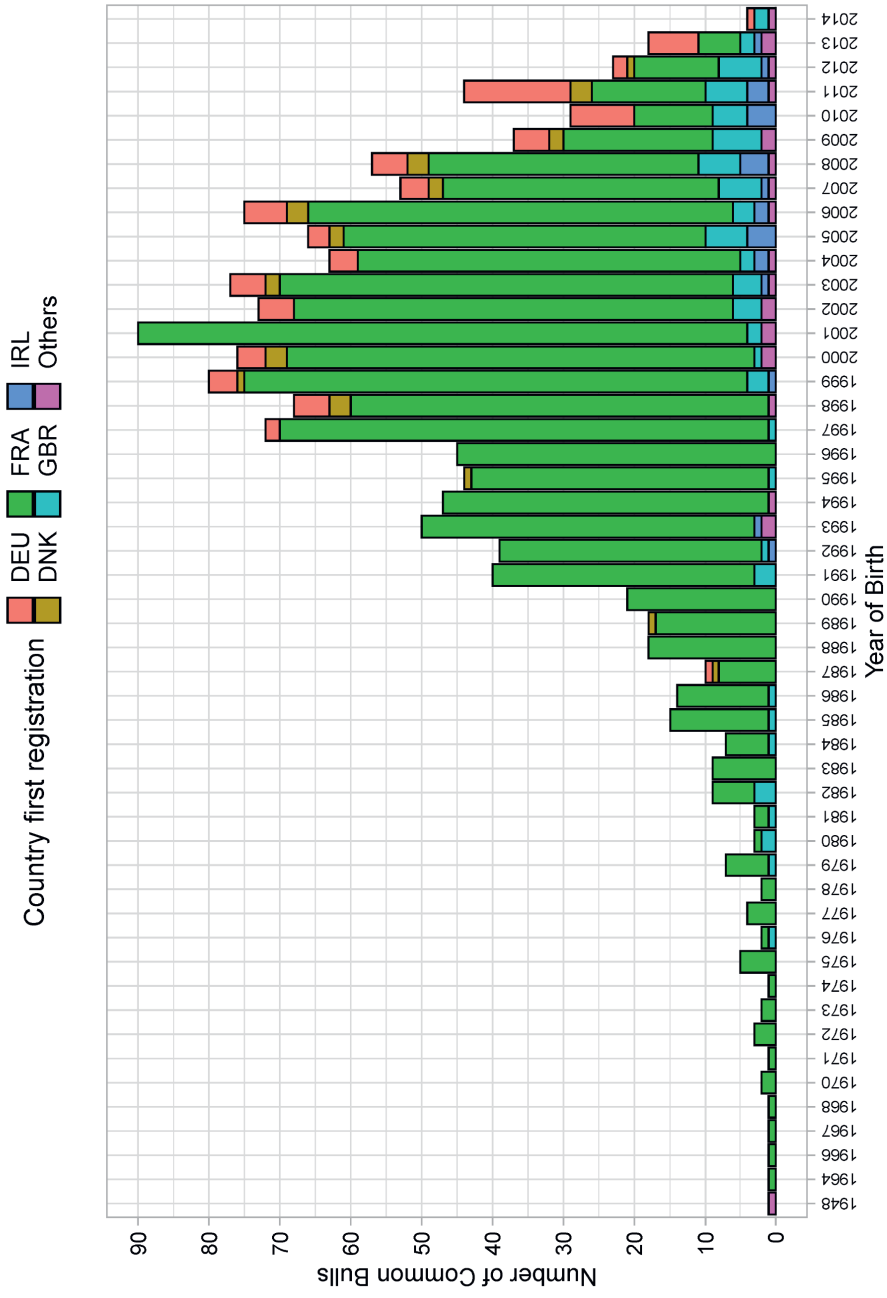

Figure 3.1 Distribution of year of birth of common bulls and their country of first registration. DEU, Germany; DNK, Denmark; FRA, France; GBR, Great Britain; IRL, Ireland.

Common maternal grand-sires can also provide valuable genetic connections (Renand *et al.* 2003; Phocas *et al.* 2005), particularly for the estimation of the maternal and direct-maternal across-country r_g. Table 3.4 shows the distribution of CMGS per number of connected populations. Of the total 3828 unique CMGS, 79.4% had recorded grand-offspring in only two populations, whereas there is an inversely proportional relationship between number of CMGS and number of connected populations with 13.2, 3.1, 1.9, 1.2, 0.7 and 0.5% of CMGS connecting three up to all eight populations, respectively. Furthermore, 25.5% of the CMGS are also CB (Table 3.4).

Table 3.4 Distribution of common maternal grand-sires (CMGS) with grand-offspring in two or more populations and number of CMGS that are also common bulls (CB).

Connected POP	CMGS	CMGS also CB	
		Yes	No
2	3040	552	2488
3	507	204	303
4	119	76	43
5	72	57	15
6	46	42	4
7	25	24	1
8	19	19	0
Sum	3828	974	2854

3.3.1.2 Genetic similarity

Coefficients of genetic similarity between populations are in Table 3.2. Jorjani (1999) used a coefficient of genetic similarity of 0.06 as a threshold to divide Ayrshire bull populations into two country groups. However, in the literature, we found no other clear thresholds for the coefficient of genetic similarity to define the level of connectedness between two populations. Therefore, we defined three arbitrary thresholds for the coefficient of genetic similarity: a low, medium and high level of connectedness for coefficients of genetic similarity lower than 0.05, between 0.05 and 0.10, and higher than 0.10, respectively.

Overall, we observed a medium level of across-country connections when all the data were considered, with an average coefficient of genetic similarity of 0.09 across populations. All the populations showed a high level of connectedness with FRA (> 0.10), which reflects the high proportion of French CB. Moreover, the IRL population had a high level of connections with all countries except with DFS and DEU. As a result, IRL and FRA were the two populations with the highest average coefficient of

genetic similarity with other countries (0.11 and 0.13, respectively). GBR showed the lowest bivariate connections (GS < 0.05) with CZE, ESP, DEU, and CHE.

3.3.1.3 Balanced offspring distribution (BOD) and adjusted number of populations (AN_POP)

The balanced offspring distribution and the adjusted number of population coefficients can be considered as two quantitative measures of the same quantity, i.e. balance in sires' offspring records across country. Table 3.5 reports the AN_POP and BOD distribution for CB. Among all CB, none had a balanced distribution across all eight populations, resulting in all sires having an AN_POP smaller than 8 and a maximum AN_POP of 5 for a single CB. The majority of the CB (> 65%) had an AN_POP smaller than 2. In addition, 23.1% of the CB had an AN_POP of 2 and only 11.9% of the total CB had AN_POP larger than 2. Since the AN_POP coefficients are computed as a function of the BOD coefficients, their distributions are similar.

Table 3.5 Average number of populations (AN_POP) and balanced offspring distribution (BOD) coefficients for common bulls (CB).

AN_POP	BOD	Number of CB
Balanced		
= 2	= 0.25	332
= 3	= 0.375	18
= 4	= 0.5	0
= 5	= 0.625	1
Unbalanced		
> 1 – 1.999	> 0.125 – 0.25	933
> 2 – 2.999	> 0.25 – 0.375	104
> 3 – 3.999	> 0.375 – 0.5	43
> 4 – 4.999	> 0.5 – 0.625	5
Sum (all CB)		
> 1	> 0.125	1436

3.3.2 Estimated genetic correlations in different scenarios

Modelling the countries as different traits in international evaluations, as in the AMACI model, allows the genetic correlations between countries to be lower than 1, which accounts for genotype-by-environment interactions and possible differences in phenotypic distribution, trait and national model definition of the AWW. Descriptive statistics for each population-sex combination highlight differences in phenotypic mean for AWW across populations (see Supplementary Table S3.2). These differences may be associated with a variation in trait definition across

countries and, in particular, with the adjustment criteria applied (see Supplementary Table S3.3). Although an improved harmonization of traits across countries is desirable, it does not remove the need to model each country as a separate trait.

Using different approaches to select the data leads to different subsets of data for the FRA population. First, we present the estimated r_g for Scenario ALL, and second, we provide a description of the data selected and the result yielded in each sub-setting scenario.

Results of the across-country estimated r_g and approximated standard errors (SE) when using all the data (Scenario ALL) are in Table 3.6. The average across-country r_g for the direct genetic effect was equal to 0.79 and ranged from 0.62 (DEU-IRL) to 0.94 (DEU-DFS). The average across-country r_g for the maternal effect was equal to 0.71 and ranged from 0.65 (CHE-IRL) to 0.87 (FRA-GBR). The average estimated direct-maternal within-country r_g was equal to -0.12 and ranged from -0.33 for FRA to 0.40 for CHE. Direct-maternal between-country r_g were on average equal to 0 and ranged from -0.14 (GBR-FRA) to 0.14 (GBR-CZE). For the CHE population, most of the direct-maternal between-country r_g were positive (average of 0.06), whereas for the FRA population most of the direct-maternal r_g were negative (average of -0.06). SE of the estimated r_g in Scenario ALL were on average equal to 0.14 for the direct r_g (ranging from 0.06 to 0.22), and 0.19 for the maternal r_g (ranging from 0.07 to 0.33). SE of direct-maternal within-country and between-country r_g were on average equal to 0.09 (ranging from 0.02 to 0.16), and 0.14 (ranging from 0.06 to 0.23), respectively. The DEU-FRA combination always had the largest SE of estimated r_g and the ESP-CHE combination had the smallest.

Table 3.7 provides a summary of the comparison between each sub-setting scenario (RND, GSCB, GSTOT and HM) and Scenario ALL, for the across-country estimated r_g and SE. Complete comparisons are in Supplementary Tables S3.4, S3.5, S3.6, and S3.7.

In Scenario RND, random subsets of FRA herd data were used to provide an easy-to-implement approach for data sub-setting. By chance, some of the 20 subsets could include better-connected herds, which would result in slightly different average coefficients of genetic similarity across the 20 random samples of Scenario RND (see Supplementary Table S3.8). The three subsets that we analysed had the closest coefficients of genetic similarity to those calculated in Scenario ALL with average differences of -0.008, -0.0007 and -0.012, respectively (see Supplementary Table S3.8).

Table 3.6 Scenario ALL—heritabilities (italic characters on the diagonal), estimated genetic correlations (below diagonal) and standard errors of estimated correlations (above diagonal), for direct and maternal genetic effects [a].

	Direct								Maternal							
	CZE	**DFS**	**ESP**	**GBR**	**IRL**	**FRA**	**DEU**	**CHE**	**CZE**	**DFS**	**ESP**	**GBR**	**IRL**	**FRA**	**DEU**	**CHE**
Direct																
CZE	*0.24*	0.16	0.21	0.15	0.19	0.12	0.14	0.22	0.10	0.15	0.20	0.16	0.16	0.10	0.12	0.19
DFS	0.87	*0.30*	0.16	0.10	0.13	0.07	0.10	0.15	0.13	0.06	0.14	0.11	0.12	0.06	0.09	0.16
ESP	0.74	0.77	*0.13*	0.17	0.20	0.14	0.17	0.22	0.20	0.18	0.16	0.16	0.16	0.10	0.15	0.22
GBR	0.71	0.82	0.94	*0.29*	0.14	0.06	0.10	0.18	0.15	0.12	0.15	0.06	0.11	0.06	0.11	0.18
IRL	0.83	0.76	0.87	0.91	*0.35*	0.11	0.13	0.21	0.16	0.15	0.18	0.11	0.14	0.09	0.12	0.20
FRA	0.76	0.89	0.77	0.82	0.76	*0.29*	0.06	0.13	0.09	0.08	0.10	0.08	0.10	0.02	0.06	0.12
DEU	0.76	0.94	0.76	0.77	0.62	0.81	*0.24*	0.14	0.13	0.11	0.16	0.13	0.13	0.06	0.05	0.15
CHE	0.85	0.81	0.76	0.71	0.70	0.70	0.70	*0.12*	0.19	0.18	0.23	0.20	0.19	0.11	0.14	0.10
Maternal																
CZE	-0.12	0.04	0.07	0.12	-0.01	-0.10	0.08	0.01	*0.18*	0.20	0.26	0.21	0.22	0.14	0.16	0.27
DFS	-0.05	-0.14	0.02	-0.01	-0.02	-0.11	-0.07	-0.01	0.68	*0.14*	0.23	0.18	0.19	0.11	0.14	0.24
ESP	0.03	0.09	-0.22	-0.08	-0.09	-0.05	0.05	0.02	0.67	0.68	*0.07*	0.24	0.25	0.15	0.21	0.33
GBR	0.14	0.06	-0.03	-0.10	-0.03	-0.14	0.07	0.08	0.79	0.69	0.70	*0.07*	0.18	0.12	0.16	0.26
IRL	-0.03	0.07	-0.06	-0.05	-0.19	-0.12	0.12	0.11	0.69	0.68	0.81	0.72	*0.17*	0.16	0.16	0.24
FRA	-0.02	-0.05	-0.03	-0.06	-0.09	-0.33	-0.01	0.08	0.85	0.69	0.71	0.87	0.82	*0.09*	0.07	0.17
DEU	-0.02	-0.09	-0.03	-0.01	0.06	-0.10	-0.24	0.09	0.68	0.68	0.67	0.69	0.68	0.69	*0.20*	0.20
CHE	0.12	0.11	0.07	0.08	0.03	-0.05	0.06	0.40	0.73	0.68	0.67	0.66	0.65	0.77	0.66	*0.05*

[a] Population: CZE, Czech Republic; DFS, Denmark, Finland and Sweden; ESP, Spain; GBR, Great Britain; IRL, Ireland; FRA, France; DEU, Germany; CHE, Switzerland.

Table 3.7 Summary statistics for estimated across-country genetic correlations (r_g) and their standard errors (SE), for the direct, maternal and direct-maternal effect (within and between-country) in ALL versus each sub-setting scenario (RND, GSCB, GSTOT, HM).

Scenario [a]	Direct			Maternal			Direct-maternal					
							Within-country			Between-country		
	average	min	max	average	min	max	average	min	max	average	min	max
Genetic correlations												
ALL	0.79	0.62	0.94	0.71	0.65	0.87	-0.12	-0.33	0.40	0.00	-0.14	0.14
Difference [b] in r_g												
RND	-0.02	-0.04	-0.01	-0.04	-0.07	-0.02	-0.12	-0.17	-0.04	-0.11	-0.16	-0.06
GSCB	-0.02	-0.03	0.00	-0.05	-0.08	-0.03	-0.13	-0.17	-0.04	-0.11	-0.17	-0.03
GSTOT	-0.02	-0.03	0.00	-0.05	-0.08	-0.03	-0.13	-0.18	-0.05	-0.12	-0.17	-0.04
HM	-0.02	-0.04	0.00	-0.06	-0.09	-0.03	-0.11	-0.17	-0.03	-0.10	-0.17	-0.02
Standard errors												
ALL	0.14	0.06	0.22	0.19	0.07	0.33	0.09	0.02	0.16	0.14	0.06	0.23
Difference [b] in SE												
RND	0.03	0.01	0.06	0.06	0.02	0.10	0.03	0.01	0.07	0.05	0.01	0.09
GSCB	0.03	0.00	0.06	0.05	0.01	0.10	0.03	0.01	0.08	0.04	0.01	0.09
GSTOT	0.02	0.00	0.05	0.05	0.02	0.09	0.03	0.01	0.07	0.04	0.01	0.08
HM	0.03	0.00	0.06	0.06	0.02	0.11	0.03	0.01	0.07	0.04	0.01	0.09

[a] ALL, all data; RND, herds selected randomly; GSCB, herds selected based on genetic similarity considering common bulls; GSTOT, herds selected based on genetic similarity considering common bulls and common maternal grandsires; HM, herds selected based on harmonic mean of sire's progeny size.

[b] Results for the sub-setting scenarios are expressed as a deviation from ALL, i.e. after subtracting the results of ALL.

The estimated r_g, averaged across the three analysed samples of Scenario RND, were lower than those obtained with Scenario ALL (see Supplementary Table S3.4). In particular, r_g were slightly lower in Scenario RND for the direct effect (average difference of -0.02) and lower for the maternal effect (average difference of -0.04) (Table 3.7). However, the largest differences in r_g between Scenarios RND and ALL were observed for the direct-maternal effect with average differences of -0.12 and -0.11 for within-country and between-country r_g, respectively. On average, the SE of estimated r_g were 0.03 greater for the direct effect in Scenario RND than in ALL, and 0.06 greater for the maternal effect (Table 3.7). The SE were on average 0.03 and 0.05 greater for the direct-maternal within-country and between-country r_g, respectively.

In Scenario GSCB, r_g were estimated based on the top FRA herds that were ranked based on their coefficient of genetic similarity, including connections provided by CB. The coefficients of genetic similarity of selected FRA herds ranged from 0.07 to 0.11. In total, 36% of the FRA herds had a coefficient of genetic similarity lower than 0.001,

which indicates a low use of international semen and that their contribution to the estimation of across-country r_g is small. The Scenario GSCB resulted, across the selected FRA herds, in an average increase of genetic similarity of 0.15 with other populations compared to Scenario ALL.

Across-country estimated r_g from Scenario GSCB were on average lower than from Scenario ALL by 0.02 for the direct and 0.05 for the maternal effect (Table 3.7). Direct-maternal r_g from Scenario GSCB were also on average smaller than from Scenario ALL, by 0.11 within-country and 0.13 between-country. On average, the SE of estimated r_g were 0.03 and 0.05 larger for the direct and maternal r_g respectively, in Scenario GSCB than in Scenario ALL (Table 3.7). The SE of the direct-maternal within-country and between-country r_g were on average also 0.03 and 0.04 larger in Scenario GSCB than in Scenario ALL.

In Scenario GSTOT, r_g were estimated based on the top FRA herds that were ranked based on their coefficient of genetic similarity, including connections provided by both CB and CMGS. The coefficients of genetic similarity of selected FRA herds ranged from 0.08 to 0.12. The coefficient of genetic similarity was lower than 0.001 for many FRA herds (33%). In Scenario GSTOT, selection of the most connected herds resulted, across FRA herds, in a higher coefficient of genetic similarity (considering only CB) with other populations, with an average increase of 0.14 compared to Scenario ALL.

Direct and maternal r_g were on average smaller, by 0.02 and 0.05, respectively, in Scenario GSTOT than in Scenario ALL (Table 3.7), and the largest differences were related to the direct-maternal within-country and between-country r_g: on average -0.13 and -0.12, respectively. On average, the SE of the estimated direct and maternal r_g were 0.02 and 0.05 larger in Scenario GSTOT than in Scenario ALL (Table 3.7) and the SE of the direct-maternal r_g were also on average 0.03 and 0.04 larger in Scenario GSTOT than in Scenario ALL, within-country and between-country, respectively.

The aim of Scenario HM was to select FRA herds based on their harmonic mean coefficient (HM). The average HM coefficient of all FRA herds was 965.7 but large variations were observed across herds, with HM coefficients ranging from 0 (small herds with recorded offspring from unknown sires) up to 15,116. For Scenario HM, the 37 selected herds had an average HM coefficient of 8942. Selecting FRA herds on their HM resulted in an average increase of 0.08 of the coefficient of genetic similarity at the population level for FRA compared to Scenario ALL.

Across-country estimated r_g from Scenario HM were on average lower than from Scenario ALL by 0.02 for the direct and 0.06 for the maternal effect (Table 3.7). The direct-maternal r_g in Scenario HM were also smaller on average than in Scenario ALL

by 0.11 within-country and 0.10 between-country. On average, the SE of the estimated r_g were 0.03 and 0.06 larger for the direct and maternal r_g, respectively (Table 3.7). Similarly, the SE of the direct-maternal r_g from Scenario HM were on average, 0.03 and 0.04 larger than from Scenario ALL, within-country and between-country, respectively.

3.3.3 Computational requirements

Using all the data, Scenario ALL took 43 days and 23 h to estimate across-country r_g (Table 3.8). The data sub-setting scenarios (RND, GSCB, GSTOT, HM) that were aimed at reducing the number of phenotypes to 0.5 million, decreased the total computing time by 9 to 16 days (Table 3.8), corresponding to 22% up to 36% of the time required for Scenario ALL. Differences in computational requirements between data sub-setting scenarios can be due to differences in CPU frequency, but also to external factors, such as the server's load. Considering this, the total computing time was similar across the different data sub-setting scenarios. Random access memory (RAM) requirements were low for all scenarios and ranged from 2.39 gigabytes when using all the data to about 0.5 gigabytes with reduced data (Table 3.8). Sub-setting scenarios decreased the required time per REML round to ~17% of that for Scenario ALL (Table 3.8). Compared to Scenario ALL, sub-setting the data led to an increase of the number of REML rounds, which ranged from 22% (Scenario RND sample 15) to 43% (Scenario HM).

Table 3.8 Computational requirements across scenarios based on single-core analyses.

Scenario [a]	Phenotypic records	Pedigree records	CPU (GHz) [b]	RAM peak usage (GB) [c]	REML rounds (number)	Average time per REML round (min)	Total time (days:hours) [d]
ALL	3,115,598	3,431,742	4.0	2.39	1173	53	43:23
RND sample 15	533,816	706,717	4.0	0.49	1432	11	11:12
RND sample 20	521,077	692,205	3.7	0.48	1543	14	15:21
RND sample 2	556,100	729,778	3.7	0.51	1462	15	16:00
GSCB	506,080	654,841	4.0	0.46	1496	9	9:21
GSTOT	513,969	663,127	4.0	0.45	1530	9	10:06
HM	502,716	649,081	4.0	0.46	1675	9	11:06

[a] ALL, all data; RND, herds selected randomly; GSCB, herds selected based on genetic similarity considering common bulls; GSTOT, herds selected based on genetic similarity considering common bulls and common maternal grandsires; HM, herds selected based on harmonic mean of sire's progeny size.
[b] Central Processing Unit (CPU) frequency.
[c] Random access memory (RAM) peak usage.
[d] Total elapsed time.

3.4 Discussion

In this study, we applied a multi-trait approach to estimate a 16 × 16 across-country r_g matrix for Limousin beef cattle international evaluation in a single analysis. Furthermore, we investigated the application of within-country sub-setting strategies to reduce the amount of data required for estimating r_g. We applied these sub-setting strategies only to the FRA herds, because this is the largest population in the evaluation. Sub-setting the data from the other countries would yield only relatively small reductions in overall data size but could cause loss of valuable information and genetic connections. Our approach could be applied to international beef cattle evaluations of other breeds with population structures similar to that of the Limousin breed, e.g. for country that has a much larger population than the others. An example is the Charolais breed in Interbeef evaluations, with the French population representing more than 90% of the overall data (Venot *et al.* 2009a, 2014).

Hereafter, first we discuss the genetic level of the connections available in the dataset used, then the impact of the sub-setting strategies on the estimated r_g and the required computing time. Finally, we describe possible implications of this study in the context of beef cattle international evaluations.

3.4.1 Genetic connections across-country

Direct connections varied greatly across countries as indicated by the number of CB (Table 3.2). Most of the CB in this study connected only two populations, but a good proportion of CB connected more than two populations at the same time, most of which were born after 1980 (see Supplementary Figure S3.1). Across-country genetic connections also occurred through CMGS, most of them connecting only two or three populations. However, CMGS that connected more than four populations increasingly appeared as CB (79, 91, 96 and 100% from 5 up to 8 connected populations, respectively). This increased proportion indicates that daughters of popular imported sires are likely to be kept as dams for the next generation and, in turn, will provide grand-offspring's phenotypes for such sires. In this study, the range of the numbers of CB and CMGS that connected Limousin populations were similar to those previously reported (Venot *et al.* 2008, 2009b; Pabiou *et al.* 2014), and only a few populations had a small number of connecting CB, but none had missing connections. Limited across-country connections were reported in previous studies both for the Charolais (Venot *et al.* 2009b; Pabiou *et al.* 2014) and Simmental (Fouilloux *et al.* 2006) breeds. Furthermore, previous studies in dairy cattle breeds, such as Guernsey (Fikse *et al.* 2003b), Ayrshire (Jorjani 1999, 2000), Brown Swiss and

Jersey (Jorjani 2000), also reported low across-country connectedness levels, which suggest that our approach may also be beneficial to low-connected dairy breeds. Nevertheless, the number of available connections in the Limousin populations in our study is still small compared to that of dairy breeds such as the Holstein–Friesian (Jorjani 2000, 2001).

The coefficient of genetic similarity provides a quantification of the number of genetic connections available between two countries. The coefficients of genetic similarity revealed that IRL and FRA are "link-provider" countries, as termed in dairy cattle international evaluations (Jorjani 2000; Jorjani *et al.* 2005; Mark *et al.* 2005b). The inclusion of such link-provider countries, together with the less connected ones, during the estimation of across-country r_g may help to overcome the lack of convergence (Jorjani *et al.* 2005), either when including all the countries together in the model or only a group of them, i.e. when applying a country sub-setting strategy.

The sire's AN_POP coefficient provided further insights on the level of genetic connectedness available in the data. Jorjani *et al.* (2005) showed that selecting sires with a balanced offspring's distribution may be beneficial to estimate across-country r_g in large dairy populations. When applied to international beef evaluations, about 65% of the CB had an AN_POP lower than 2. In addition, all CB with connections in all eight populations were severely penalized for being unbalanced. These results indicate that the majority of the genetic connections are established between two countries and that the number of offspring for CB is unbalanced in beef cattle international evaluations. These unbalanced distributions of sires' offspring imply that implementing a herd sub-setting strategy for the estimation of across-country r_g based on AN_POP was not possible.

3.4.2 Estimated genetic correlations using all data

The across-country estimated r_g and heritabilities obtained in our study are in line with those from previous international beef cattle studies (Venot *et al.* 2009b; Pabiou *et al.* 2014). Estimated direct-maternal within-country r_g were negative and ranged from -0.10 to -0.33, with the exception of CHE. Using national data, CHE reported a direct-maternal within-country r_g of -0.01 (Interbeef 2006); the positive direct-maternal r_g that we obtained for CHE may be related to its sire-by-herd interaction effect (see Supplementary Table S3.1). Berweger Baschnagel *et al.* (1999) also observed that fitting a sire-by-herd interaction effect in the model affected the estimation of direct-maternal r_g in Swiss beef cattle data.

In cattle international evaluations, across-country r_g determine to what extent the information from participating countries contributes to the estimation of International EBV (Weigel *et al.* 2001) and can be lower than 1 for different reasons.

First, countries may differ in terms of environmental conditions (Zwald *et al.* 2003), which can lead to genotype-by-environment (i.e. country) interactions (Falconer and Mackay 1996). Second, national trait definitions may differ, for instance, depending on the country, AWW being adjusted to a different time period and with different approaches (see Supplementary Table S3.3). Third, differences in national evaluation procedures may exist (Mark 2004): an example in beef cattle is the definition of contemporary groups (CG) (see Supplementary Table S3.1).

Submitted AWW were partly modelled differently by each participating country (see Supplementary Table S3.1). Countries adapt their national model to represent in the best way their production system and national evaluations. Thus, effects that explain specific national genetic evaluations should be included in the international evaluation to account for possible non-genetic sources of variation of the submitted data (Mark 2004). Examples of specific national sources of variation are access to alpine grazing, seasonality effects and small CG modelled as random (Visscher and Goddard 1993). In international evaluations, both in dairy and beef cattle, it is common practice to have different effects fitted at the national level between countries. In dairy cattle international evaluations, countries correct for their national fixed and random effects before submitting sires' de-regressed proofs (Schaeffer 1994; Mark 2004). In Interbeef, since phenotypes are shared across countries, the correction for fixed and random national effects is done in one step at the international level with the AMACI model by modelling each country, and its associated national model, as a different trait (Phocas *et al.* 2005; Venot *et al.* 2007).

Large SE of across-country estimated r_g (Table 3.6) are common in studies concerning international evaluations, both in beef (Phocas *et al.* 2005; Venot *et al.* 2009b) and dairy cattle (Weigel *et al.* 2001; Fikse *et al.* 2003a). Large SE may be due to a lack of direct connections across-country that are established through CB, and to the heterogeneous data structure between different countries for the same trait (Weigel *et al.* 2001; Venot *et al.* 2009b). Although in our dataset, there was a medium level of connectedness, in terms of coefficient of genetic similarity, and no population had missing genetic links (i.e. CB = 0), the large SE obtained underline and support the need to increase genetic connections across-country in beef cattle populations.

Estimated variance components depend, to some extent, on the information content of the data. For instance, it is important that the performance of an animal can be compared to contemporaries within herd. In international beef cattle evaluations, the minimum size of the CG is defined by each participating country (Table 3.1). Two populations (CZE and DFS) reported a minimum size of CG of 1. However, in Scenario ALL, the number of animals belonging to a CG of size 1 was

limited to only 0.1% of the total phenotypes. We tested the hypothesis that animals belonging to a CG of size 1 had no impact on the results of this study: the maximum difference in r_g with ALL was 0.009, for a direct-maternal between-country r_g (results not shown).

Removing old data from the process to estimate variance components is an alternative straightforward approach to reduce the amount of data used. We investigated the effect of removing old disconnected Limousin beef cattle data on the across-country estimated r_g. Since most of the across-country genetic connections, established through CB that connected more than two populations, were initiated after 1980 (see Supplementary Figure S3.1), we chose this year as a threshold for the recorded year of birth of an animal. The retained data included 3,019,527 phenotypes, with a pruned pedigree of 3,345,349 animals. Removing old disconnected data had a negligible impact on the estimated r_g compared to all data in Scenario ALL: average differences of 0.00 for direct and maternal r_g, and -0.01 for direct-maternal within-country and between-country r_g (results not shown). This limited impact on across-country estimated r_g is in agreement with the findings of Jorjani (2001) in dairy cattle international evaluations.

3.4.3 Impact of reducing data

In this study, we shifted the focus from the selection of the most connected sires, which is typical of international dairy cattle evaluations (Jorjani *et al.* 2005), to the selection of the management unit, i.e. the most connected herds. Selection of entire herds better accounts for beef cattle data structure and allows retaining all within-herd CG information for those dams and sires with multiple recorded offspring. In turn, selecting herds may be beneficial for the estimation of maternal genetic effects. The coefficient of genetic similarity applied at the herd level as in Scenarios GSCB and GSTOT do not account for the herd size. Nevertheless, we observed a linear relationship between the coefficient of genetic similarity of herd and the herd size. A possible explanation for this positive relationship is that small herds may be more inclined to use natural service bulls, as opposed to large herds, in which the more frequent use of artificial insemination leads to a higher use of international sires' semen. Furthermore, herd coefficients of genetic similarity revealed a large proportion (more than 30%) of FRA herds disconnected from other populations, and in all non-random scenarios (GSCB, GSTOT and HM), larger herds, compared to Scenario ALL, were selected: average number of records per herd of 406.5, 1588.6, 1708.2 and 2742.9 for Scenarios ALL, GSCB, GSTOT and HM, respectively. Likewise, compared to Scenario ALL, larger CG were selected in non-random scenarios:

average number of records per CG of 16.2, 20.9, 21.7 and 30.6 for Scenarios ALL, GSCB, GSTOT and HM, respectively.

Genetic similarity computed at the FRA population level increased in non-random scenarios compared to Scenario ALL, even if some CB between FRA and other populations were removed due to the herd selection process. Nevertheless, estimated r_g are similar across sub-setting scenarios. All sub-setting scenarios resulted in smaller across-country r_g, which ranged from an average of 0.02 for the direct r_g up to 0.13 for the direct-maternal within-country r_g. The SE of estimated r_g always increased when reduced data were used, regardless of the scenario considered, and ranged from an average increment of 0.02 up to 0.06. The average difference in estimated r_g between Scenarios GSCB and GSTOT was 0.00 (regardless of the effect considered), which indicated that there was no benefit in including information from CMGS in the coefficient of genetic similarity. Results from non-random scenarios suggest that given a certain level of genetic connections, as in Scenario GSCB, there is no additional benefit in including information related to CMGS, as in Scenario GSTOT, or to the CB's balanced offspring distribution, as in Scenario HM.

To further understand the impact of reducing FRA data on across-country estimated r_g, we performed an additional scenario (NO_FRA), i.e. by using the same dataset as in Scenario ALL, but the FRA population was excluded from the estimation process. The results showed that the inclusion of FRA data helps to estimate the national genetic variances of other populations (see Supplementary Figures S3.2 and S3.3). For example, smaller maternal genetic variance and larger maternal permanent environmental variance were estimated for IRL in NO_FRA than in Scenario ALL, leading to a lower maternal heritability for IRL in NO_FRA than in Scenario ALL. On the other hand, for the GBR population, the exclusion of FRA data resulted in a larger estimated maternal genetic variance than in Scenario ALL. In addition, compared with Scenario ALL, reducing or removing FRA data resulted in a larger estimated maternal permanent environmental variance for ESP (see Supplementary Figure S3.2). Thus, it seems that differences in across-country estimated r_g across scenarios are related to the amount of FRA data used in the estimation process, rather than to how the subset of FRA data was chosen. Thus, we foresee that the application of other methods for the selection of connected herds, even if they are more sophisticated such as the CD methodology (Fouilloux *et al.* 2008a), would not result in across-country estimated r_g closer to those obtained when using of all data. After all, differences in estimated r_g between Scenario ALL and other scenarios were small.

While Scenario RND reduced the number of FRA herds randomly, Scenarios GSCB, GSTOT and HM reduced the number of observations by selecting the best-connected herds. Therefore, selected data are not "missing-at-random" (Rubin 1976; Im *et al.* 1989). Bayesian algorithms have been suggested to be better suited for dealing with such non-missing-at-random data structures compared to REML algorithms (Rubin 1976). Nevertheless, in our study, scenarios with non-random sub-setting showed small differences in estimated r_g compared to those of Scenario RND.

The total required computing time was similar for all sub-setting scenarios, with the computing time per REML round being directly proportional to the data reduction applied. Indeed, by reducing data to ~16% of the complete dataset (from 3.1 to ~0.5 million phenotypes), the required computing time per REML round was reduced to ~17% (from 53 min in Scenario ALL to 9 min in non-random scenarios). However, the larger required number of REML rounds in sub-setting scenarios resulted in the total computing time not being proportional to the data reduction applied (Table 3.8). A larger number of REML rounds may indicate a more difficult estimation of the parameters during VCE as suggested by Jorjani *et al.* (2005). In this study, selecting herds based on the coefficient of genetic similarity as in Scenarios GSCB and GSTOT, required a smaller number of REML rounds than in Scenario HM, which indicates that herds selected based on genetic similarity could result in an easier estimation of genetic parameters. Although Scenario RND subsets resulted in a similar number of REML rounds compared to Scenarios GSCB and GSTOT, the required computing time was longer due to the larger number of records analysed.

3.4.4 Implications

Estimated within-country genetic and environmental variances may differ from those reported by member countries, both when estimated using all international data (ALL Scenario) and subsets of data (RND, GSCB, GSTOT, HM Scenarios) (see Supplementary Figures S3.2 and S3.3). However, national reported variances are considered more accurate than those obtained from international data, since countries can use a more representative national dataset for VCE, e.g. when not all the data are submitted for international evaluations. Thus, in Interbeef evaluations, changes in across-country r_g are of primary interest, whereas within-country estimated variances are replaced with those reported by member countries. Indeed, it is common practice to use the reported national variances together with the estimated across-country r_g to build the across-country genetic covariance matrix from which IEBV are estimated.

The multi-variate approach proposed in this study is preferable over the current-in-use bi-variate approach for Interbeef evaluations (Pabiou *et al.* 2014): matrices

obtained in different scenarios were positive definite and bending procedures were avoided. This was enabled by the MC EM REML algorithm that allowed the estimation of all 120 across-country r_g at the same time. In comparison, when using the bi-variate method with a similar dataset as in this study, many estimated across-country r_g did not converge, for example, 8 and 17 out of the 28 r_g, for the direct and maternal effects, respectively (Pabiou, personal communication). As a result, across-country r_g are usually set to an arbitrary default value. The use of such arbitrary values may be questionable, especially considering the possible impact on IEBV and, in turn, on establishing future genetic connections across populations. Moreover, under the current bi-variate approach, all 56 direct-maternal between-country r_g are not estimated but are assumed to be 0, which may not be realistic. For instance, using all data, direct-maternal between-country estimated r_g were all negative for FRA (Table 3.6), while for CHE they were almost all positive.

3.5 Conclusions

The MC EM REML algorithm allowed the simultaneous estimation of all across-country r_g using a multi-trait animal model. Reducing the data mainly affected the estimates of direct-maternal within-country and between-country r_g, but had a small impact on the estimated direct and maternal across-country r_g. Estimated r_g were very similar across sub-setting strategies, which means that the way the subset of FRA data was chosen hardly affected the values of r_g. The standard errors of estimated r_g increased when reduced data were used. Using the data sub-setting strategies reduced the amount of data used to about 16% of the complete dataset and the required computing time decreased to 22% of that required when using all data.

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3.8 Supplementary material

3.8.1 Supplementary tables

Table S3.1 List [a] of fixed, random environmental and covariate environmental effects in the national model per each population.

POP [b]	Fixed							Random			Covariates	
CZE		asextwin	aaca	year				PE	HYS			
DFS	HYS	asex	aaca	seas	twin			PE				
ESP	herd_birth	asex	aaca					PE				
GBR	HYS_mgt	asex		month	twin	fostered	wdam_brd	PE			agedam	agedam2
IRL	HYS	asex	pariagedam					PE			agedam2	aawg
FRA	HY-asex-mgt		pariaaca	seas			individual	PE				
DEU		asex	parity	month	twin				HY			
CHE		asex		yearmonth			alpine	PE	HY	SireHerd	agedam	agedam2

[a] *aaca* = age at calving; *aawg* = age at weighting; *agedam* = age of the dam; *agedam*2 = age of the dam fitted as quadratic effect; *alpine* = access to alpine grazing for calves; *asex* = sex of the animal; *asextwin* = interaction between *asex* and *twin*; *fostered* = foster code; *herd_birth* = contemporary group defined based on the herd and birth date; *HY* = Herd-Year; *HY-asex-mgt* = contemporary group defined based on *HY*, *asex* and management group defined as calf-dam couple; *HYS* = Herd-Year-Season; *HYS_mgt* = contemporary group defined by herd, management group and date of birth; *individual* = individual situation, e.g. preferential treatment; *month* = month of birth; *pari* = parity; *pariaaca* = interaction between *pari* and *aaca* effects; *pariagedam* = interaction between *pari* and *agedam*; *PE* = maternal permanent environmental effect; *seas* = season; *SireHerd* = interaction between sire and herd; *twin* = twinning; *wdam_brd* = breed of the weaning dam; *year* = year of birth; *yearmonth* = interaction between *year* and *month*.

[b] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Table S3.2 Number of phenotypes (N), minimum, phenotypic mean, maximum and phenotypic standard deviation (σ_P) of males and females per population.

	MALES					FEMALES				
POP [a]	**N**	**Min**	**Mean**	**Max**	$\boldsymbol{\sigma_P}$	**N**	**Min**	**Mean**	**Max**	$\boldsymbol{\sigma_P}$
CZE	5,119	176	292.84	407	36.71	5,381	155	262.07	366	33.64
DFS	45,191	111	239.60	368	41.55	45,265	106	212.22	316	33.99
ESP	16,416	147	268.01	376	43.70	16,736	147	245.94	361	38.14
GBR	62,980	158	288.85	419	42.57	64,860	145	254.19	363	35.44
IRL	11,370	120	286.24	454	55.20	9,239	118	257.51	397	46.89
FRA	1,324,990	154	277.34	400	40.53	1,389,378	148	250.07	352	33.41
DEU	43,725	135	266.83	398	43.01	44,903	126	239.74	353	36.99
CHE	15,323	112	232.12	351	38.87	14,722	106	207.86	310	32.92

[a] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Table S3.3 Age of adjustment, recording time frame, editing and adjusting criteria for weaning weight records in each population as reported in Interbeef national Genetic Evaluation forms in 2018 (Interbeef).

POP [a]	Adjustment (days)	Recording time (days)	Editing criteria	Adjustment criteria
CZE	210	171-290	Incomplete data removed. Data over 3 standard deviations from breed-sex mean are removed.	-
DFS	200	140-260 (DNK [a]) 150-250 (FIN [a]) 125-275 (SWE [a])	Incomplete data removed.	$200 \cdot \frac{WW^{\,d} - BW^{\,b}}{Weaning\ age - Birth\ age}$
ESP	210	BW [b] – 300 days	Daily weight gain limit: 0.0 - 2.5 Kg. At least 2 weights (one after 60 days).	Individual linear regression
GBR	200	170-300	Max weight: 500 kg.	Interpolation of the two nearest weights before and after 200 days
IRL	200	150-300	-	Average of recorded weights
FRA	210	At least 2 weights recorded within 300 days; each at maximum 2 months apart from the 210 days weight.	If 210 days AWW [c] is not possible to be calculated, a 120-days weight is considered.	Individual intra-extrapolation
DEU	200	90-280	Incomplete data removed.	-
CHE	200	90-320	Daily weight gain limit: 0.3 - 2.5 Kg. Animals without WW [d] and incomplete information are removed.	$200 \cdot \frac{WWW^{\,d} - BW^{\,b}}{Weaning\ age}$

[a] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland, DNK = Denmark, FIN = Finland, SWE = Sweden.
[b] BW = Birth Weight. [c] AWW = Age-adjusted Weaning Weight. [d] WW = weaning weight.

Table S3.4 Differences in estimated genetic correlations for direct and maternal genetic effects (below diagonal) and their standard errors (above diagonal) between RND and ALL [a, b].

		DIRECT								MATERNAL							
		CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
DIRECT	CZE		0.02	**0.05**	0.03	0.02	0.03	0.02	0.03	0.04	0.04	**0.09**	**0.07**	0.05	**0.05**	0.03	**0.06**
	DFS	-0.02		0.03	0.02	0.02	0.03	0.01	0.04	0.03	0.01	**0.06**	**0.05**	0.03	0.05	0.02	0.03
	ESP	-0.03	-0.03		0.04	0.04	0.04	0.03	**0.06**	**0.06**	0.04	**0.07**	**0.06**	0.05	**0.07**	0.03	**0.07**
	GBR	-0.04	-0.02	-0.01		0.02	0.04	0.02	0.03	0.05	0.03	**0.05**	0.02	0.03	**0.06**	0.03	**0.06**
	IRL	-0.02	-0.02	-0.02	-0.01		0.03	0.02	0.03	0.04	0.03	0.04	0.03	0.02	**0.05**	0.03	**0.05**
	FRA	-0.03	-0.01	-0.02	-0.01	-0.02		0.04	0.04	0.05	0.03	**0.08**	**0.06**	0.05	**0.07**	0.04	**0.06**
	DEU	-0.02	-0.01	-0.02	-0.02	-0.03	-0.01		0.04	0.03	0.01	**0.05**	0.05	0.03	0.05	0.01	0.04
	CHE	-0.02	-0.02	-0.02	-0.03	-0.03	-0.03	-0.03		0.03	0.05	**0.06**	**0.06**	0.04	**0.06**	0.03	0.02
MATERNAL	CZE	**-0.11**	**-0.12**	**-0.10**	**-0.10**	**-0.09**	**-0.10**	**-0.11**	**-0.11**		0.04	**0.10**	**0.07**	0.05	**0.06**	0.03	**0.06**
	DFS	**-0.14**	**-0.17**	**-0.14**	**-0.14**	**-0.12**	**-0.13**	**-0.16**	**-0.14**	-0.05		**0.07**	0.05	0.04	**0.07**	0.02	**0.05**
	ESP	**-0.12**	**-0.14**	**-0.16**	**-0.14**	**-0.12**	**-0.12**	**-0.14**	**-0.14**	**-0.05**	-0.04		**0.07**	**0.07**	**0.10**	0.03	0.05
	GBR	**-0.09**	**-0.12**	**-0.12**	**-0.14**	**-0.10**	**-0.12**	**-0.12**	**-0.12**	-0.03	-0.05	**-0.06**		0.04	**0.08**	0.04	**0.10**
	IRL	**-0.12**	**-0.13**	**-0.13**	**-0.13**	**-0.12**	**-0.11**	**-0.12**	**-0.11**	**-0.05**	-0.05	-0.03	**-0.05**		**0.05**	0.02	**0.08**
	FRA	**-0.11**	**-0.14**	**-0.12**	**-0.13**	**-0.11**	**-0.14**	**-0.13**	**-0.11**	-0.03	-0.04	-0.05	-0.02	-0.03		**0.07**	**0.09**
	DEU	**-0.07**	**-0.08**	**-0.08**	**-0.08**	**-0.06**	**-0.06**	**-0.10**	**-0.07**	-0.03	-0.03	-0.03	-0.04	-0.03	-0.04		0.04
	CHE	**-0.07**	**-0.09**	**-0.09**	**-0.09**	**-0.08**	**-0.08**	**-0.10**	-0.04	-0.05	**-0.06**	**-0.06**	**-0.07**	**-0.06**	-0.04	-0.04	

[a] Differences greater than 0.05 are reported in bold.

[b] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland. RND = herds selected randomly, ALL = all data.

Table S3.5 Differences in estimated genetic correlations for direct and maternal genetic effects (below diagonal) and their standard errors (above diagonal) between GSCB and ALL [a, b].

		DIRECT								MATERNAL							
		CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
DIRECT	CZE		0.01	**0.05**	0.04	0.02	0.04	0.02	0.01	0.03	0.03	**0.09**	**0.06**	0.02	0.04	0.03	0.03
	DFS	-0.01		0.03	0.01	0.02	0.04	0.00	0.04	0.03	0.01	**0.06**	0.04	0.03	0.04	0.02	0.03
	ESP	-0.03	-0.02		0.03	0.02	0.04	0.02	**0.06**	0.05	0.02	**0.06**	**0.06**	0.03	**0.07**	0.02	0.04
	GBR	-0.03	-0.02	-0.01		0.01	0.04	0.01	0.02	0.05	0.02	**0.06**	0.01	0.02	**0.05**	0.03	0.04
	IRL	-0.01	-0.01	-0.01	-0.01		0.04	0.02	0.00	**0.05**	0.02	0.04	0.03	0.02	0.04	0.04	**0.06**
	FRA	-0.02	0.00	-0.01	-0.01	-0.01		0.04	0.04	**0.05**	0.04	**0.07**	**0.05**	0.05	**0.08**	0.03	**0.05**
	DEU	-0.02	-0.01	-0.02	-0.02	-0.02	-0.01		0.02	0.03	0.01	**0.06**	0.03	0.03	0.05	0.01	0.04
	CHE	-0.02	-0.02	-0.02	-0.02	-0.02	-0.01	-0.02		0.02	0.02	**0.06**	**0.05**	0.02	0.04	0.01	0.02
MATERNAL	CZE	**-0.12**	**-0.12**	**-0.11**	**-0.10**	**-0.09**	**-0.09**	**-0.12**	**-0.12**		0.01	**0.07**	**0.06**	0.05	**0.05**	0.02	0.04
	DFS	**-0.14**	**-0.17**	**-0.14**	**-0.15**	**-0.12**	**-0.13**	**-0.17**	**-0.15**	**-0.06**		0.05	0.05	0.05	**0.06**	0.02	0.05
	ESP	**-0.13**	**-0.14**	**-0.17**	**-0.15**	**-0.12**	**-0.11**	**-0.15**	**-0.15**	**-0.06**	-0.05		**0.07**	**0.07**	**0.10**	0.04	0.04
	GBR	**-0.09**	**-0.13**	**-0.13**	**-0.15**	**-0.10**	**-0.10**	**-0.13**	**-0.13**	-0.04	**-0.06**	**-0.07**		0.03	**0.07**	0.03	**0.09**
	IRL	**-0.12**	**-0.13**	**-0.14**	**-0.14**	**-0.13**	**-0.10**	**-0.13**	**-0.12**	**-0.07**	**-0.05**	-0.04	**-0.07**		**0.05**	0.04	**0.09**
	FRA	**-0.12**	**-0.15**	**-0.14**	**-0.15**	**-0.12**	**-0.13**	**-0.15**	**-0.13**	-0.03	-0.05	**-0.05**	-0.03	-0.04		**0.07**	**0.08**
	DEU	**-0.06**	**-0.07**	**-0.07**	**-0.07**	-0.05	-0.03	**-0.10**	**-0.06**	-0.04	-0.04	-0.04	-0.04	-0.04	-0.05		0.03
	CHE	**-0.07**	**-0.09**	**-0.09**	**-0.09**	**-0.07**	**-0.06**	**-0.10**	-0.04	**-0.06**	**-0.07**	**-0.07**	**-0.08**	**-0.08**	**-0.06**	**-0.05**	

[a] Differences greater than 0.05 are reported in bold.

[b] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland. GSCB = herds selected based on genetic similarity considering common bulls, ALL = all data.

Table S3.6 Differences in estimated genetic correlations for direct and maternal genetic effects (below diagonal) and their standard errors (above diagonal) between GSTOT and ALL [a, b].

		DIRECT								MATERNAL							
		CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
DIRECT	CZE		0.01	0.04	0.03	0.02	0.03	0.01	0.01	0.04	0.05	**0.08**	**0.07**	0.05	0.04	0.02	**0.05**
	DFS	-0.01		0.02	0.02	0.02	0.03	0.00	0.03	0.02	0.01	0.05	**0.06**	0.03	0.03	0.01	0.04
	ESP	-0.03	-0.02		0.03	0.03	0.03	0.02	**0.05**	0.04	0.02	**0.07**	0.04	**0.05**	**0.06**	0.01	0.03
	GBR	-0.03	-0.02	-0.01		0.01	0.04	0.01	0.02	0.03	0.02	0.04	0.02	0.02	**0.05**	0.01	**0.06**
	IRL	-0.01	-0.01	-0.01	-0.01		0.04	0.03	0.02	0.04	0.03	0.04	0.03	0.03	0.05	0.02	**0.05**
	FRA	-0.02	0.00	-0.01	-0.01	-0.01		0.03	0.03	**0.05**	0.04	**0.08**	**0.07**	**0.05**	**0.07**	0.03	**0.06**
	DEU	-0.02	-0.01	-0.02	-0.02	-0.02	-0.01		0.03	0.04	0.02	0.05	0.03	0.04	0.04	0.01	0.04
	CHE	-0.02	-0.02	-0.02	-0.02	-0.03	-0.01	-0.03		0.03	0.04	**0.07**	**0.06**	0.03	0.03	0.01	0.02
MATERNAL	CZE	**-0.12**	**-0.12**	**-0.11**	**-0.11**	**-0.10**	**-0.09**	**-0.12**	**-0.12**		0.04	**0.06**	**0.06**	0.03	**0.07**	0.03	**0.06**
	DFS	**-0.14**	**-0.18**	**-0.14**	**-0.15**	**-0.12**	**-0.13**	**-0.17**	**-0.15**	**-0.06**		0.04	0.04	0.04	**0.06**	0.02	0.05
	ESP	**-0.13**	**-0.14**	**-0.17**	**-0.15**	**-0.12**	**-0.11**	**-0.16**	**-0.15**	**-0.06**	-0.05		**0.07**	**0.07**	**0.09**	0.04	0.02
	GBR	**-0.09**	**-0.13**	**-0.13**	**-0.15**	**-0.10**	**-0.11**	**-0.13**	**-0.13**	-0.04	**-0.06**	**-0.07**		0.04	**0.07**	0.03	**0.08**
	IRL	**-0.12**	**-0.14**	**-0.14**	**-0.14**	**-0.13**	**-0.11**	**-0.13**	**-0.12**	**-0.07**	**-0.05**	-0.04	**-0.07**		**0.06**	0.03	**0.08**
	FRA	**-0.13**	**-0.16**	**-0.14**	**-0.15**	**-0.13**	**-0.14**	**-0.15**	**-0.13**	-0.03	-0.05	**-0.05**	-0.03	-0.04		**0.06**	**0.08**
	DEU	**-0.06**	**-0.07**	**-0.07**	**-0.07**	-0.05	-0.04	**-0.10**	**-0.06**	-0.04	-0.04	-0.04	-0.04	-0.04	-0.05		0.03
	CHE	**-0.07**	**-0.09**	**-0.09**	**-0.09**	**-0.08**	**-0.07**	**-0.10**	-0.05	**-0.06**	**-0.07**	**-0.07**	**-0.08**	**-0.08**	**-0.06**	**-0.05**	

[a] Differences greater than 0.05 are reported in bold.

[b] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland. GSTOT = herds selected based on genetic similarity considering common bulls and common maternal grandsires, ALL = all data.

Table S3.7 Differences in estimated genetic correlations for direct and maternal genetic effects (below diagonal) and their standard errors (above diagonal) between HM and ALL [a, b].

		DIRECT								MATERNAL							
		CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
DIRECT	CZE		0.00	0.05	0.03	0.03	0.02	0.01	0.02	0.03	0.04	**0.09**	0.04	0.04	0.04	0.03	0.05
	DFS	-0.02		0.03	0.02	0.03	0.03	0.01	0.05	0.04	0.02	**0.06**	0.04	0.04	0.03	0.02	0.02
	ESP	-0.03	-0.03		0.03	**0.06**	0.03	0.02	**0.06**	0.05	0.02	**0.07**	**0.06**	0.04	**0.06**	0.02	0.04
	GBR	-0.04	-0.02	-0.01		0.02	0.04	0.02	0.02	**0.05**	0.02	**0.06**	0.02	0.02	**0.06**	0.02	**0.06**
	IRL	-0.02	-0.02	-0.02	-0.01		0.04	0.01	0.02	0.05	0.02	**0.07**	0.04	0.04	**0.05**	0.03	**0.06**
	FRA	-0.03	0.00	-0.02	-0.01	-0.02		0.04	0.04	**0.05**	0.04	**0.08**	0.05	0.05	**0.07**	0.04	**0.06**
	DEU	-0.03	-0.01	-0.02	-0.02	-0.03	-0.01		0.04	0.03	0.01	0.05	0.04	0.03	0.04	0.01	0.03
	CHE	-0.02	-0.02	-0.02	-0.03	-0.03	-0.02	-0.03		0.04	0.03	**0.06**	**0.06**	0.04	**0.06**	0.03	0.01
MATERNAL	CZE	**-0.10**	**-0.09**	**-0.08**	**-0.08**	**-0.07**	**-0.05**	**-0.09**	**-0.09**		0.05	**0.07**	**0.06**	0.05	**0.07**	0.03	**0.06**
	DFS	**-0.14**	**-0.17**	**-0.14**	**-0.15**	**-0.12**	**-0.12**	**-0.17**	**-0.15**	**-0.06**		**0.06**	0.04	0.05	**0.06**	0.02	0.04
	ESP	**-0.12**	**-0.13**	**-0.17**	**-0.14**	**-0.12**	**-0.09**	**-0.14**	**-0.14**	**-0.07**	**-0.05**		**0.08**	**0.08**	**0.11**	0.05	0.04
	GBR	**-0.07**	**-0.11**	**-0.11**	**-0.13**	**-0.09**	**-0.08**	**-0.11**	**-0.11**	-0.04	**-0.06**	**-0.07**		0.03	**0.07**	0.04	**0.09**
	IRL	**-0.11**	**-0.11**	**-0.12**	**-0.12**	**-0.12**	**-0.08**	**-0.11**	**-0.10**	**-0.07**	**-0.06**	-0.04	**-0.07**		**0.07**	0.04	**0.07**
	FRA	**-0.10**	**-0.12**	**-0.11**	**-0.12**	**-0.10**	**-0.11**	**-0.12**	**-0.10**	-0.04	-0.05	**-0.06**	-0.03	-0.04		**0.07**	**0.09**
	DEU	**-0.05**	**-0.06**	**-0.07**	**-0.06**	-0.04	-0.02	**-0.09**	**-0.06**	-0.04	-0.04	-0.04	-0.05	-0.04	**-0.05**		0.02
	CHE	**-0.05**	**-0.07**	**-0.07**	**-0.07**	**-0.06**	-0.04	**-0.08**	-0.03	**-0.06**	**-0.07**	**-0.08**	**-0.09**	**-0.08**	**-0.05**	**-0.05**	

[a] Differences greater than 0.05 are reported in bold.

[b] Population: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland. HM = herds selected based on harmonic mean of sire's progeny size, ALL = all data.

Table S3.8 Average differences in GS between each random subset of FRA-herds of RND and ALL [a].

Subset n.	Average GS difference
1	-0.0044
2	*-0.0012*
3	-0.0050
4	-0.0035
5	-0.0020
6	-0.0028
7	-0.0030
8	-0.0019
9	-0.0023
10	-0.0021
11	-0.0038
12	-0.0032
13	-0.0018
14	-0.0045
15	*-0.0007*
16	-0.0027
17	-0.0036
18	-0.0052
19	-0.0037
20	*-0.0008*

[a] The 3 analysed subsets are reported in italic.

3.8.2 Supplementary figures

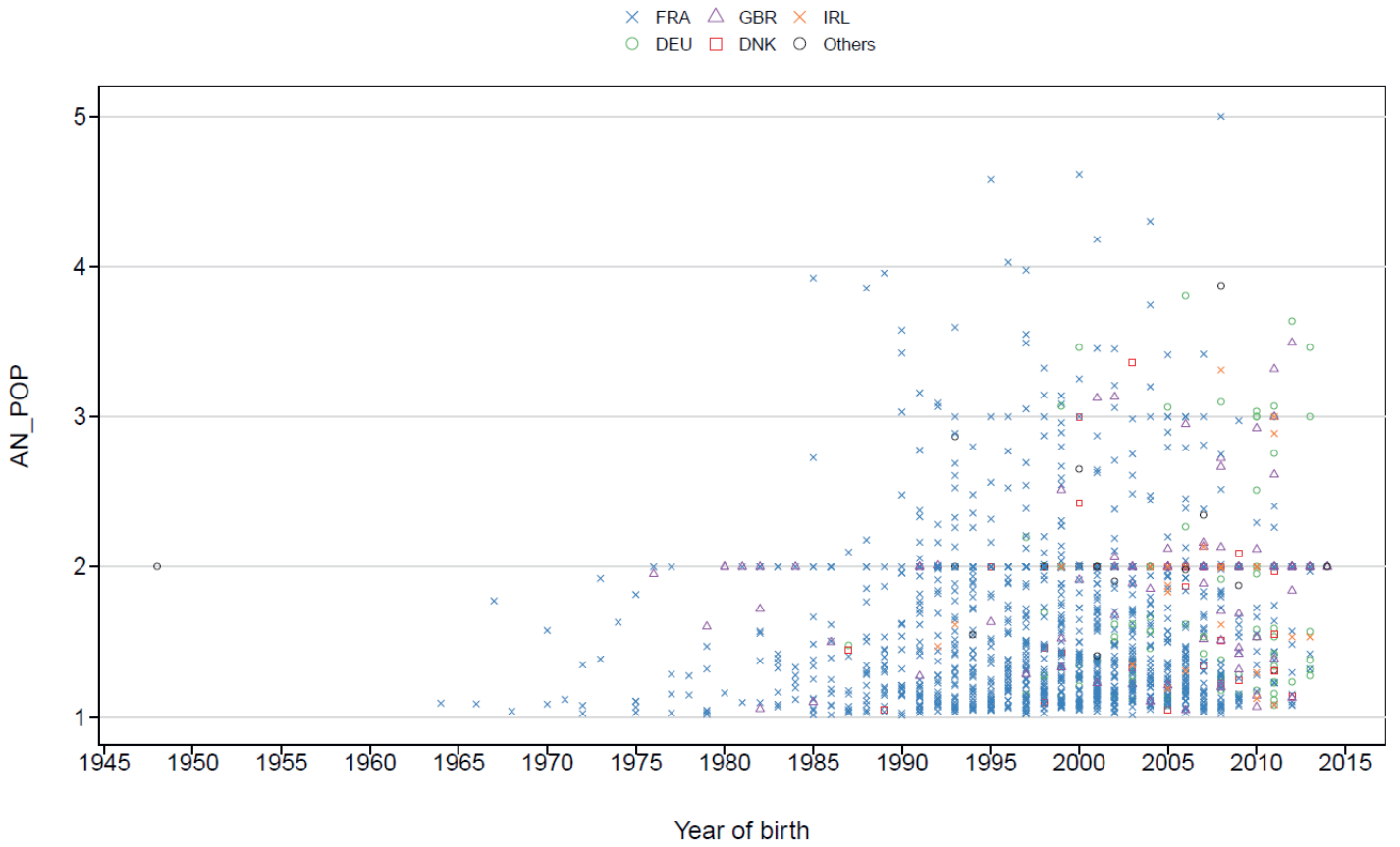


Figure S3.1 Adjusted Number of Populations (AN_POP) for all common bulls in function of their year of birth and country of first registration. DEU = Germany, DNK = Denmark, FRA = France, GBR = Great Britain, IRL = Ireland.

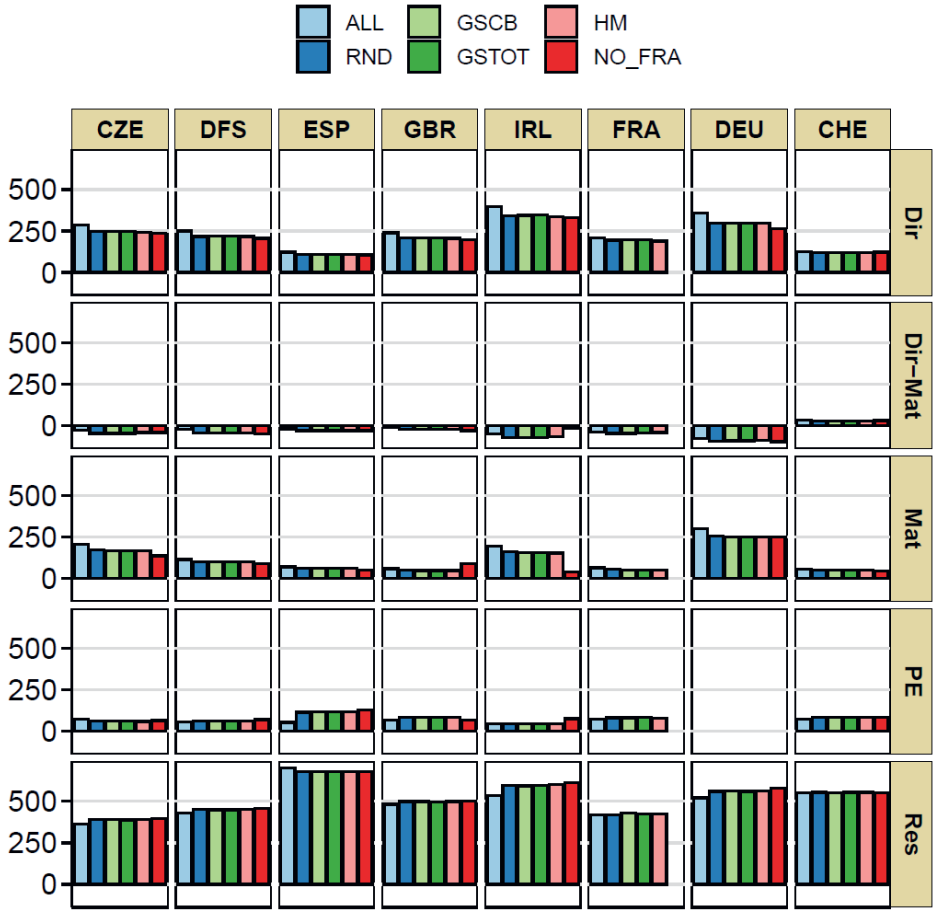


Figure S3.2 Estimated (co)variance components per population across different scenarios. ALL = all data, RND = herds selected randomly, GSCB = herds selected based on genetic similarity considering common bulls, GSTOT = herds selected based on genetic similarity considering common bulls and common maternal grandsires, HM = herds selected based on harmonic mean of sire's progeny size, NO_FRA = FRA population not included in the analysis, CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland, Dir = direct genetic variance, Mat = maternal genetic variance, Dir-Mat = direct-maternal genetic covariance, PE = maternal permanent environmental variance, Res = residual variance.

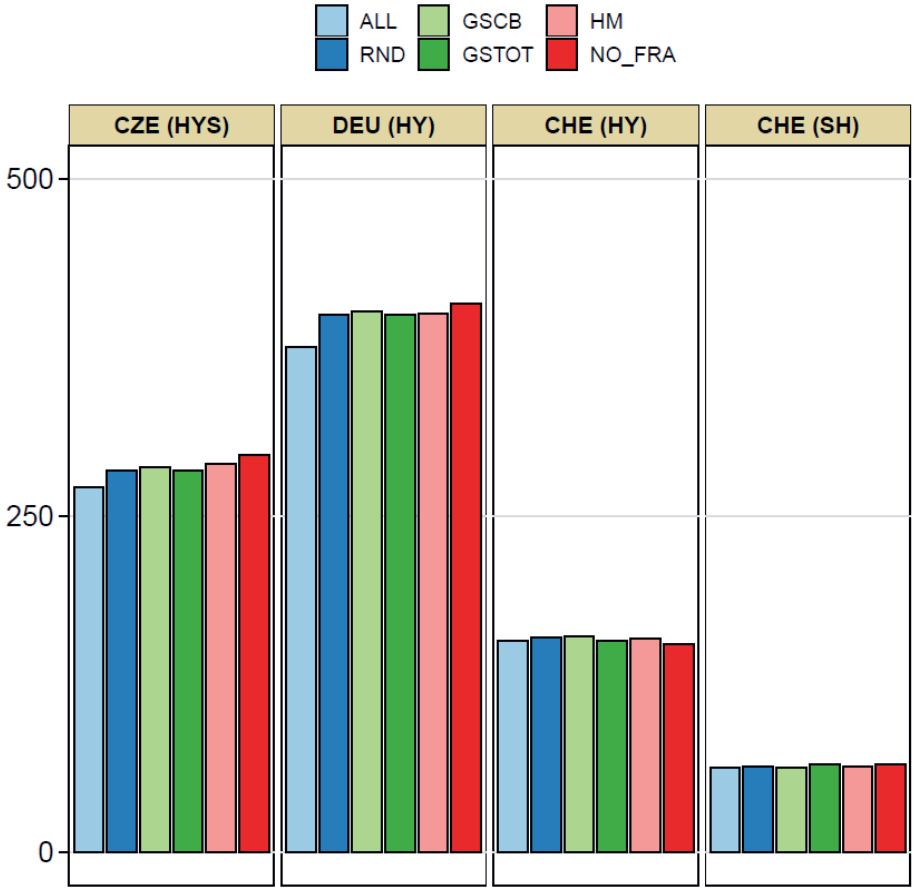
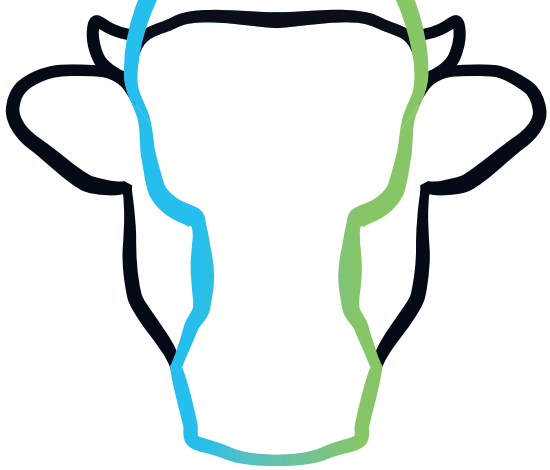


Figure S3.3 Estimated random contemporary group and sire by herd interaction variances across different scenarios. ALL = all data, RND = herds selected randomly, GSCB = herds selected based on genetic similarity considering common bulls, GSTOT = herds selected based on genetic similarity considering common bulls and common maternal grandsires, HM = herds selected based on harmonic mean of sire's progeny size, NO_FRA = FRA population not included in the analysis, CHE = Switzerland, CZE = Czech Republic, DEU = Germany, HYS = Herd-Year-Season, HY = Herd-Year, SH = Sire by Herd interaction.

CHAPTER 4



The impact of direct-maternal genetic correlations on international beef cattle evaluations for Limousin weaning weight

Renzo Bonifazi[1], Jérémie Vandenplas[1], Jan ten Napel[1], Roel F. Veerkamp[1], Mario P.L. Calus[1]

[1] Animal Breeding and Genomics, Wageningen University and Research, P.O. Box 338, 6700 AH Wageningen, the Netherlands

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Abstract

In beef cattle maternally influenced traits, estimates of direct-maternal genetic correlations (r_{dm}) are usually reported to be negative. In international evaluations, r_{dm} can differ both within countries (r_{dm_WC}) and between countries (r_{dm_BC}). The r_{dm_BC} are difficult to estimate and are assumed to be zero in the current model for international beef cattle evaluations (Interbeef). Our objective was to investigate re-ranking of international estimated breeding values (IEBVs) in international beef cattle evaluations between models that either used estimated values for r_{dm} or assumed them to be 0. Age-adjusted weaning weights and pedigree data were available for Limousin beef cattle from ten European countries. International EBVs were obtained using a multi-trait animal model with countries modeled as different traits. We compared IEBVs from a model that uses estimated r_{dm_BC} (ranging between -0.14 and +0.14) and r_{dm_WC} (between -0.33 and +0.40) with IEBVs obtained either from the current model that assumes r_{dm_BC} to be 0, or from an alternative model that assumes both r_{dm_BC} and r_{dm_WC} to be 0. Direct and maternal IEBVs were compared across those three scenarios for different groups of animals. The ratio of population accuracies from the linear regression method was used to further investigate the impact of r_{dm} on international evaluations, for both the whole set of animals in the evaluation and the domestic ones. Ignoring r_{dm_BC}, i.e., replacing estimated values with 0, resulted in no (rank correlations > 0.99) or limited (between 0.98 and 0.99) re-ranking for direct and maternal IEBVs, respectively. Both r_{dm_BC} and r_{dm_WC} had less impact on direct IEBVs than on maternal IEBVs. Re-ranking of maternal IEBVs decreased with increasing reliability. Ignoring r_{dm_BC} resulted in no re-ranking for sires with IEBVs that might be exchanged across countries and limited re-ranking for the top 100 sires. Using estimated r_{dm_BC} values instead of considering them to be 0 resulted in null to limited increases in population accuracy. Ignoring both r_{dm_BC} and r_{dm_WC} resulted in considerable re-ranking of animals' IEBVs in all groups of animals evaluated. This study showed the limited impact of the current practice of ignoring r_{dm_BC} in international evaluations for Limousin weaning weight, most likely because the estimated r_{dm_BC} were close to 0. We expect that these conclusions can be extended to other traits that have reported r_{dm} values in the range of r_{dm_WC} values for weaning weight in Limousin.

Key words: beef cattle, direct-maternal genetic correlation, international genetic evaluations, interbeef, international estimated breeding values, weaning weight.

Abbreviations

CB – Common Bulls; EBV – Estimated Breeding Value; IEBV – International Estimated Breeding Value; LR – Linear Regression; REL – approximated reliability; r_g – genetic correlations, r_{dm} – direct-maternal genetic correlations; r_{dm_WC} – within-country direct-maternal genetic correlations; r_{dm_BC} – between-country direct-maternal genetic correlations; SD – Standard Deviation.

4.1 Introduction

In livestock, recorded traits can be influenced in their expression by the mother, i.e., they are influenced by maternal effects (Falconer and Mackay 1996). Examples of such traits are growth and survival during the early stage of an animal's life (Meyer 2001; Knol *et al.* 2002; Hartmann *et al.* 2003; Eaglen and Bijma 2009). Maternal effects reflect the mothers' role in providing the environment to survive as well as nourishment for the offspring, starting from uterine development and continuing after birth until weaning (Meyer 2001; Eaglen and Bijma 2009), and have both a genetic and an environmental component (Falconer and Mackay 1996). Therefore, in genetic evaluations of maternally influenced traits, the observed phenotypes are often dissected into a direct genetic effect, a maternal genetic effect, a maternal permanent environment effect, and into environmental effects common to siblings (Bijma 2006; Mrode 2014b; Schaeffer 2019a). Maternal effects can contribute to phenotypic similarity in multiple offspring of the same dam, e.g., full-sibs and half-sibs, either arising from the same litter or different parities, and variability between families (Falconer and Mackay 1996).

Models that account for direct and maternal genetic effects allow animal breeders to better estimate breeding values (EBVs) for these components, which are important for selection decisions and genetic progress of maternally influenced traits (Van Vleck *et al.* 1977; Gerstmayr 1992; Mrode 2014b). Maternal effects are therefore usually included in the total merit indices for beef cattle (e.g., ICBF 2020; Institut de l'Élevage 2020) to reflect the maternal abilities of heifers and cows. Many studies have estimated the co-variance components of direct and maternal genetic effects in chickens, cattle, pigs, sheep, and rabbits (e.g., Koch 1972; Krogmeier *et al.* 1994; Knol *et al.* 2002; Hartmann *et al.* 2003; Abbasi *et al.* 2012). The estimation of the magnitude of the genetic covariance and correlation between direct and maternal effects has been the object of study of animal breeders for a long time (Koch 1972; Baker 1980; Robinson 1996a, 1996b). In beef cattle, estimates of direct-maternal genetic correlations (r_{dm}) are usually reported to be negative (Robinson 1996b; Meyer 1997). Estimates of r_{dm} could be subject to possible different sources

of bias (Meyer 1997; Clément *et al.* 2001; Bijma 2006), and Meyer (1992) showed that large datasets are required for accurate estimation of genetic parameters of maternally affected traits. Later, Schaeffer (2019) suggested that three generations of female data are required to have a proper data structure for accurate estimations of r_{dm}, and when this pedigree depth is not present, to set r_{dm} equal to 0 instead. Given the difficulties associated with the estimation of r_{dm}, David *et al.* (2015) investigated the impact of ignoring r_{dm}, on direct, maternal, and total EBVs (defined as the sum of direct and maternal EBVs) in sheep, pigs, and rabbits genetic evaluations. The authors showed that r_{dm} had a small influence on the total EBV, recommending, therefore, to set r_{dm} to 0 when their values are uncertain.

In the context of international evaluations, international EBVs (IEBVs) are computed across different environments (i.e., countries) for a series of traits (Durr and Philipsson 2012; Crook *et al.* 2019). Some of the traits evaluated in beef international evaluations are influenced by maternal effects, e.g., birth weight, weaning weight, and calving ease (Phocas *et al.* 2005; Venot *et al.* 2006, 2007, 2008; Pabiou *et al.* 2014; Crook *et al.* 2019; Vesela *et al.* 2019). Due to the presence of genotype by environment interaction (i.e., genotype by country interaction), and differences in trait and model definition, genetic correlations (r_g) for direct genetic effects, maternal genetic effects, and r_{dm} can differ between countries (De Mattos *et al.* 2000; Mark *et al.* 2005a; Pabiou *et al.* 2014; Bonifazi *et al.* 2020b).

International genetic evaluations require estimates of across-country r_g (Phocas *et al.* 2005). However, the estimation process can be challenging (Mark *et al.* 2005a; Venot *et al.* 2007), especially in beef cattle due to the low number of existing genetic connections between countries (Berry *et al.* 2016). These connections are established through animals having recorded offspring in more than one country, i.e., mainly international bulls (Jorjani *et al.* 2005; Bonifazi *et al.* 2020b). Moreover, this process is even more challenging for maternally influenced traits. Using large national datasets during this process allows to consider all existing genetic connections between countries at the expense of long, or even prohibitive, computational times (Bonifazi *et al.* 2020b). Therefore, data are usually reduced based on criteria that aim to maximize retained genetic connections across countries (Jorjani *et al.* 2005; Mark *et al.* 2005a; Bonifazi *et al.* 2020b). Using a multi-country dataset, (Bonifazi *et al.* 2020b) investigated the impact of data sub-setting on across-country r_g in beef cattle international evaluations led by Interbeef (2006) for Limousin weaning weight. While reducing data did not significantly affect across-country direct and maternal r_g, within-country direct-maternal genetic correlations (r_{dm_WC}) and between-country direct-maternal genetic correlations (r_{dm_BC}) were more negative and were consistently affected by data reduction (-0.12 and -0.11 on

average, respectively). When using all data, estimates of r_{dm_BC} were on average 0 and ranged from -0.14 to +0.14. However, they were most often not significantly different from zero, with standard errors being on average 0.14. France, however, had negative r_{dm_BC} (between -0.14 and -0.01) with all other countries except Switzerland which was the only country with a positive r_{dm_WC}. Moreover, France represented 87% of the data and had the strongest connectedness with other countries. Four out of the 8 countries, including France, had an r_{dm_WC} that was significantly different from 0. These r_{dm_WC} being significantly different from 0 suggest that these estimates may be negative. Based on the estimates involving FRA, it seems that r_{dm_BC} do also have a tendency to be negative, albeit with relatively small deviations from zero.

In international evaluations, r_{dm_BC} are assumed to be zero since estimating them can be difficult (Venot *et al.* 2007; Vesela *et al.* 2019; Bonifazi *et al.* 2020b). However, little is known about the impact in international evaluations of assuming r_{dm_BC} and r_{dm_WC} to be zero. Therefore, our objective was, using previously estimated parameters, to investigate the impact on EBVs of using 0 instead of non-zero estimates for r_{dm} in the current international beef cattle evaluations model using Limousin weaning weight data. We studied the potential impact of this assumption on selection decisions by evaluating the re-ranking of different groups of animals, and the change in population accuracies and dispersion through the linear regression (LR) method (Legarra and Reverter 2018).

4.2 Materials and Methods

Animal Care and Use Committee approval was not requested for this study because commercial data were obtained from existing databases.

4.2.1 Data and model

Age-adjusted weaning weight (AWW) phenotypes were available for 3,115,598 Limousin males and females, representing 8 Limousin populations and 10 European countries in the 2018 January Interbeef evaluation: Switzerland (CHE), Czech Republic (CZE), Germany (DEU), Denmark, Finland and Sweden (DFS, modeled as one population), Spain (ESP), France (FRA), Great Britain (GBR), and Ireland (IRL). Weaning weight was adjusted to an age of 210 days in CZE, ESP, and FRA and of 200 days in the remaining countries. Individual phenotypic records were distributed across 19,330 herds (Table 4.1). The majority (87%) of the observations available for AWW were from FRA, followed by GBR (4%), DFS, and DEU (about 3% each), whereas 1% or less of the total amount of records was from ESP, CHE, IRL, and CZE. Pedigree

information were available for 3,431,742 animals, born between 1927 and 2017, with a maximum pedigree depth of 19 generations. A more detailed description of the data and pedigree editing criteria applied is provided in Bonifazi *et al.* (2020b). The number of direct and maternal genetic connections available in the pedigree was quantified in Bonifazi *et al.* (2020b). In total, 1,436 sires (also called "Common Bulls"—CB) and 3,828 maternal grand-sires (also called "Common MGS"—CMGS) had recorded offspring and grand-offspring in one or more countries, respectively. The number of CB ranged from 1,053 connecting 2 populations to 17 connecting 8 populations. The number of CMGS ranged from 3,040 connecting 2 populations to 19 connecting 8 populations. About 25% of the CMGS were also CB. Hereafter, for simplicity, we will refer to populations as countries, even though the DFS population is composed of more than one country.

Table 4.1 Summary of available age-adjusted weaning weights per country.

COU [a]	AWW [b]	% [c]	Herds	YoB [d]	Pedigree [e]
CZE	10,500	0.3	121	1991–2017	30,843
DFS	90,456	2.9	9,190	1980–2017	117,623
ESP	33,152	1.1	188	1989–2011	63,526
GBR	127,840	4.1	745	1972–2017	172,229
IRL	20,609	0.7	1,304	1975–2017	56,694
FRA	2,714,368	87.1	6,677	1972–2017	2,942,297
DEU	88,628	2.8	881	1981–2017	121,228
CHE	30,045	1.0	224	1993–2017	55,104
Total	3,115,598	100	19,330	1972–2017	3,559,544

[a] COU, Country: CZE, Czech Republic, DFS, Denmark, Finland and Sweden, ESP, Spain, GBR, Great Britain, IRL, Ireland, FRA, France, DEU, Germany, CHE, Switzerland.
[b] AWW, Age-adjusted weaning weight.
[c] %, Percentage of AWW records per country.
[d] YoB, Year of birth of animals with records for AWW.
[e] Pedigree: number of animals retained in scenario NAT (national single-trait evaluations).

The AMACI model (Animal Model accounting for Across-Country Interaction) (Phocas *et al.* 2005) was used for the estimation of an animal's breeding value, which accounts for country-specific fixed and random effects by fitting the national model of each country. The AMACI model is a multi-trait animal model with maternal effects, in which each country is modeled as a different trait:

$$\mathbf{y}_i = \mathbf{X}_i\mathbf{b}_i + \mathbf{C}_i\mathbf{r}_i + \mathbf{Z}_i\mathbf{u}_i + \mathbf{W}_i\mathbf{m}_i + \mathbf{P}_i\mathbf{pe}_i + \mathbf{e}_i$$

where *i* is the country; $\mathbf{y}_i$ is the vector of observations for country *i*; $\mathbf{b}_i$ and $\mathbf{r}_i$ are the vectors of fixed and random environmental effects, respectively, for country *i* (as

detailed below); $\mathbf{u}_i$ and $\mathbf{m}_i$ are the vectors of direct and maternal random additive genetic effects, respectively, for country *i* (i.e. corresponding to the vectors of IEBV for each individual on each of the 8 country scales); $\mathbf{pe}_i$ is the vector of random maternal permanent environmental effects (provided by the dam) for country *i*; $\mathbf{e}_i$ is the vector of random residual effects for country *i*. $\mathbf{X}_i$ and $\mathbf{C}_i$ are incidence matrices linking records to fixed, and random environmental effects, respectively. $\mathbf{Z}_i$, $\mathbf{W}_i$, and $\mathbf{P}_i$ are incidence matrices linking records to the animal, maternal genetic and maternal permanent environmental effects, respectively. Fixed and random effects for each country are reported in Supplementary Table S4.1. In particular, random environmental effects were modelled for only three countries: CZE (herd-year-season), DEU (herd-year), and CHE (herd-year, and sire-herd). The maternal permanent environmental effect was not fitted for the DEU population. It is assumed that:

$$var\begin{bmatrix}\mathbf{u}\\ \mathbf{m}\end{bmatrix} = \mathbf{G} \otimes \mathbf{A} = \begin{bmatrix}\mathbf{G}_{d,d} & \mathbf{G}_{d,m}\\ \mathbf{G}_{m,d} & \mathbf{G}_{m,m}\end{bmatrix} \otimes \mathbf{A}$$

where $\mathbf{u}$ is the vector of random direct additive genetic effects for all countries; $\mathbf{m}$ is the vector of random maternal additive genetic effects for all countries; $\mathbf{G}$ is the across-country genetic (co)variance matrix of order 16 by 16 in which $\mathbf{G}_{d,d}$ is the across-country direct additive genetic (co)variance matrix, $\mathbf{G}_{m,m}$ is the across-country maternal additive genetic (co)variance matrix, and $\mathbf{G}_{d,m}$ ($\mathbf{G}_{m,d}$) contains additive genetic covariances between direct and maternal effect within-country (diagonal elements) and additive genetic covariances between direct and maternal effect between-country (off-diagonal elements); $\mathbf{A}$ is the numerator relationship matrix; $\otimes$ indicates the Kronecker product. Random environmental effects, random maternal permanent environmental effects, and residuals were fitted using block-diagonal variance matrices.

To closely represent current Interbeef evaluations, the genetic variance-covariance matrix with additive direct and maternal genetic effects ($\mathbf{G}$) was built as:

$$\mathbf{G} = \mathbf{S}\,\mathbf{\Phi}\,\mathbf{S}$$

where, $\mathbf{S}$ is the diagonal matrix with national genetic standard deviations for direct and maternal genetic effects, and $\mathbf{\Phi}$ is the across-country estimated genetic correlation matrix (of order 16x16 with diagonal values of 1). The genetic correlation matrix $\mathbf{\Phi}$ was previously estimated in Bonifazi *et al.* (2020b) (Scenario ALL) and was used for all scenarios implemented in this study. Both $\mathbf{\Phi}$ and the obtained $\mathbf{G}$ (co)variance matrix are reported in Table 4.2. Both genetic and environmental variances were the same as those used in the national genetic evaluations of participating countries (Supplementary Table S4.2). Interbeef uses this procedure to

Table 4.2 Direct and maternal genetic correlations [a] (below diagonal), genetic variances (diagonal), and covariances (above diagonal) within and across countries [b].

		DIRECT								MATERNAL							
		CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
DIRECT	CZE	*310*	251.94	152.87	204.79	311.51	208.82	261.23	171.23	-28.53	-10.54	4.37	17.70	-7.52	-3.21	-6.45	14.89
	DFS	0.87	*269*	147.29	220.99	264.72	227.34	300.42	151.69	9.56	-24.69	12.65	7.85	14.99	-6.42	-25.95	12.76
	ESP	0.74	0.77	*136*	180.07	216.46	138.92	172.35	100.86	11.67	2.25	-21.18	-2.52	-10.30	-3.13	-5.53	5.77
	GBR	0.71	0.82	0.94	*268*	314.46	208.76	247.87	133.39	27.80	-2.47	-10.31	-11.63	-12.25	-7.68	-3.71	10.02
	IRL	0.83	0.76	0.87	0.91	*450*	252.19	257.72	169.97	-1.95	-5.61	-15.15	-4.68	-55.13	-14.71	24.25	4.72
	FRA	0.76	0.89	0.77	0.82	0.76	*242*	245.78	123.50	-22.60	-18.28	-6.22	-16.64	-25.56	-40.56	-27.93	-5.70
	DEU	0.76	0.94	0.76	0.77	0.62	0.81	*383*	157.07	20.83	-15.46	8.64	10.00	33.06	-1.72	-86.43	9.15
	CHE	0.85	0.81	0.76	0.71	0.70	0.70	0.70	*130*	1.87	-0.89	2.17	6.96	17.38	7.04	17.99	33.52
MATERNAL	CZE	-0.12	0.04	0.07	0.12	-0.01	-0.10	0.08	0.01	*197*	104.59	77.28	81.82	135.06	93.62	173.11	75.33
	DFS	-0.05	-0.14	0.02	-0.01	-0.02	-0.11	-0.07	-0.01	0.68	*120*	61.60	55.68	104.23	59.81	135.22	54.55
	ESP	0.03	0.09	-0.22	-0.08	-0.09	-0.05	0.05	0.02	0.67	0.68	*68*	42.66	93.59	46.17	100.20	40.46
	GBR	0.14	0.06	-0.03	-0.10	-0.03	-0.14	0.07	0.08	0.79	0.69	0.70	*55*	73.90	51.00	91.90	35.84
	IRL	-0.03	0.07	-0.06	-0.05	-0.19	-0.12	0.12	0.11	0.69	0.68	0.81	0.72	*194*	89.86	171.16	66.66
	FRA	-0.02	-0.05	-0.03	-0.06	-0.09	-0.33	-0.01	0.08	0.85	0.69	0.71	0.87	0.82	*62*	98.75	44.44
	DEU	-0.02	-0.09	-0.03	-0.01	0.06	-0.10	-0.24	0.09	0.68	0.68	0.67	0.69	0.68	0.69	*326*	87.49
	CHE	0.12	0.11	0.07	0.08	0.03	-0.05	0.06	0.40	0.73	0.68	0.67	0.66	0.65	0.77	0.66	*54*

[a] Genetic correlations originally reported in Bonifazi *et al.* (2020b).

[b] Country: CZE, Czech Republic, DFS, Denmark, Finland and Sweden, ESP, Spain, GBR, Great Britain, IRL, Ireland, FRA, France, DEU, Germany, CHE, Switzerland.

compute the genetic variance-covariance matrix under the assumption that the national estimates of genetic variances are more accurate (e.g. when not all national data are submitted for international evaluations) (Michenet, Interbull Centre, personal communication). The presence of genotype-by-country interactions due to differences in production systems and management conditions, as well as differences in trait and model definitions between countries, is accounted in the AMACI model by modelling AWW of different countries as different correlated traits. These factors are reflected in estimated genetic correlations between countries lower than unity (Mark 2004; Bonifazi *et al.* 2020b).

4.2.2 Scenarios

Breeding values were estimated for the following scenarios, where r_{dm} within and between countries were either used or replaced by zero, while between-country direct and maternal r_g were used in all scenarios. This led to the following three scenarios, hereafter referred to as "international scenarios" (Table 4.3 summarizes the implemented (co)variance structure in each scenario):

- Scenario REF: both r_{dm_WC} and r_{dm_BC} are used in the evaluation, i.e., the covariance structure across countries is as shown in Table 4.2. In this scenario, the information between direct and maternal breeding values is exchanged at the national level, through r_{dm_WC}, and at an international level through r_{dm_BC}. We considered this scenario as the reference scenario.
- Scenario CUR: r_{dm_WC} are used in the evaluation, but r_{dm_BC} are set to zero. This scenario represents the current-in-use methodology for Interbeef evaluations (Bonifazi *et al.* 2020b), where r_{dm} information is used at its minimum since information between direct and maternal breeding values is exchanged only at a national level through r_{dm_WC}.
- Scenario NONE: both r_{dm_WC} and r_{dm_BC} are set to 0. In this scenario, there is no usage of r_{dm} and it was used as an extreme case to understand the effects of completely ignoring r_{dm}.

Next to the international scenarios, breeding values were estimated with the following scenario aiming to represent pseudo-national single-trait evaluations:

- Scenario NAT: the AMACI model was run with all between-country r_g set to 0 (i.e., for direct r_g, maternal r_g, and r_{dm_BC}), while r_{dm_WC} were used. With this setting, the AMACI model is equivalent to run eight separate single-trait national evaluations. Once the model was run, for each country, EBVs were retained for all animals with phenotypes on their own, or any of their ancestors, or both. Hereafter, we will refer to those animals as the domestic set of animals. The number of retained domestic animals per country is reported in Table 4.1.

It should be noted that the resulting genetic correlation matrix in scenario CUR was non-positive definite, and therefore, it was bended using the unweighted bending approach of Jorjani *et al.* (2003) (using the R package "mbend" (Nilforooshan 2020) with a threshold of 10^{-3}). Initial analyses showed that the effects of bending on all the estimated r_g were minimal with an unweighted bending approach and allowed to keep the r_{dm_BC} close to 0. Moreover, bending the genetic correlation matrix allows to keep the same national genetic variances between international scenarios, which is often desired in international evaluations (Jorjani *et al.* 2003; Bonifazi *et al.* 2020b). Due to the bending process, some r_{dm_BC} showed small deviations from the fixed value of zero: ranging from -0.03 to 0.02. Changes due to bending in direct r_g, maternal r_g and r_{dm_WC} ranged between -0.03 and 0.02, -0.03 and 0.01, and -0.04 and 0.09, respectively.

Table 4.3 Fitted (●) variances and non-zero genetic correlations (r_g) within and between countries per scenario [a, b].

	Scenario [b]			
(co)variance structure	REF	CUR	NONE	NAT
Within-country direct and maternal variance	●	●	●	●
Between-country direct r_g	●	●	●	
Between-country maternal r_g	●	●	●	
Within-country direct-maternal r_g	●	●		●
Between-country direct-maternal r_g	●			

[a] Not used r_g were replaced by 0.
[b] Scenario: NAT = national single-trait evaluations, NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations, and r_{dm_BC} = between-country direct-maternal genetic correlations.

4.2.3 Groups of animals evaluated

Changes in across-country r_g may result in re-ranking of animals, e.g., top bulls. We computed Spearman rank correlations of direct and maternal IEBVs for different groups of animals between the tested international scenarios that all used the full international pedigree:

1. All (3,431,742) animals included in the international evaluation.
2. Reliability (REL) class. Three groups of animals were formed based on their direct and maternal IEBV REL: REL ≤ 0.3, 0.3 < REL ≤ 0.6, and REL > 0.6.

Approximated REL were computed using Tier and Meyer (2004) methodology under scenario REF.

3. Common Bulls (CB). In the analyzed dataset, 1,436 CB, i.e., sires with recorded offspring in more than one country, were present. Re-ranking of CB is an indicator of the r_{dm_BC} effect on the IEBV of animals having recorded offspring in two or more countries.
4. Sires with publishable IEBVs. In order to be published across countries, sire's IEBV should fulfil several conditions (Michenet, Interbull Centre, personal communication). Sire's direct IEBV should be associated with the following: 1) a REL ≥ 0.5 on at least one country scale and 2) ≥ 25 recorded progeny across all countries. Sire's maternal IEBV should fulfil the following conditions: 1) have a publishable direct IEBV; 2) an associated REL ≥ 0.3 on at least one country scale; and 3) ≥ 15 daughters with recorded progeny and ≥ 25 recorded grand-progeny from daughters across all countries. Sires with IEBVs that fulfil the above requirements under the scenario REF were selected.
5. Young sires. Sires that fulfil the following conditions under the scenario REF were selected: 1) a publishable direct IEBV (following the same rules as described in group 4) and 2) a REL associated with a maternal IEBV < 0.3 on all country scales.

For each of the above groups of animals, we considered that no re-ranking was present between scenarios REF and CUR, and scenarios REF and NONE when the rank correlation was equal to or greater than 0.990. When the rank correlation was between 0.980 and 0.990, we considered that small re-ranking was present. Furthermore, for each scenario, we selected the top 100 sires on each country scale from those with a publishable IEBV (following the same rules as described in group 4) and calculated the number of commonly selected top 100 sires between scenarios.

4.2.4 Increases in population accuracies and dispersion

To investigate the impact of modelling across-country r_{dm} on the population accuracies (acc), we used the Linear Regression method (Legarra and Reverter 2018). Population accuracy is defined as the correlation between the true breeding values (TBVs) and the estimated breeding values (EBVs) across individuals in a population (Legarra and Reverter 2018). Following Legarra and Reverter (2018), the ratio of population accuracies of two evaluations, evaluation *p* with partial information, and evaluation *w* with all (i.e., whole) information, is defined as $\rho_{p,w} =$

$\frac{acc_p}{acc_w}$, and is computed as the Pearson correlation between EBVs from evaluations *p* and *w*:

$$\rho_{p,w} = \frac{\left(\hat{\mathbf{u}}_p - \bar{\hat{\mathbf{u}}}_p\right)' \left(\hat{\mathbf{u}}_w - \bar{\hat{\mathbf{u}}}_w\right)}{\sqrt{\left(\hat{\mathbf{u}}_w - \bar{\hat{\mathbf{u}}}_w\right)' \left(\hat{\mathbf{u}}_w - \bar{\hat{\mathbf{u}}}_w\right) \left(\hat{\mathbf{u}}_p - \bar{\hat{\mathbf{u}}}_p\right)' \left(\hat{\mathbf{u}}_p - \bar{\hat{\mathbf{u}}}_p\right)}}$$

where $\hat{\mathbf{u}}_p$ is the vector of animals' EBVs from the partial evaluation and $\hat{\mathbf{u}}_w$ is the vector of animals' EBVs from the whole evaluation. Thus, $\rho_{p,w}$ is a direct estimator of the increase in population accuracy of EBVs from an evaluation with partial data to an evaluation with whole data (Legarra and Reverter 2018).

In the context of international evaluations, national evaluations can be seen as evaluations with partial information, where recorded phenotypes are available only at the country level. International evaluations provide a new source of information through related animals being recorded in other countries and, therefore, represent evaluation *w*. Thus, the relative increases in population accuracy when moving from the partial (i.e. national; NAT) to the whole (i.e. international; INT) evaluations were calculated for each country and for international scenarios CUR and REF as the reciprocal of ρ_{NAT_d,INT_d} (Macedo *et al.* 2020a), i.e. $1/\rho_{NAT_d,INT_d}$, with $\rho_{NAT_d,INT_d} = \frac{acc_{NAT_d}}{acc_{INT_d}}$, by using only domestic animals' EBVs (denoted by *d*) of each country from Scenario NAT, i.e. national animals. For example, when ρ_{NAT_d,INT_d} is 0.8, the additional information from the international evaluation increased the accuracy by 25% relative to the national evaluation ($1/\rho_{NAT_d,INT_d}$ = 1.25).

The change in the r_{dm} structure implemented in the international scenarios can also be viewed as increasingly adding data to a "partial" international evaluation when moving from Scenario NONE to CUR or REF, since non-zero values for the r_{dm} effectively changes the amount of information contributing to the domestic direct and maternal animal's IEBVs in a specific country. Thus, using all 3,431,742 IEBVs expressed on each country scale, we computed $1/\rho_{NONE,REF}$ and $1/\rho_{NONE,CUR}$. For instance, the latter represents the increase in population accuracy when fitting r_{dm_WC}.

Using the LR method, we also evaluated any changes in dispersion of the EBVs between partial and whole evaluations. The estimator for dispersion ($\hat{b}_{w,p}$) is defined as the slope of the regression of $\hat{\mathbf{u}}_w$ on $\hat{\mathbf{u}}_p$, computed as: $\hat{b}_{w,p} = \frac{cov(\hat{\mathbf{u}}_w, \hat{\mathbf{u}}_p)}{var(\hat{\mathbf{u}}_p)}$ (Legarra and Reverter 2018). The expectation of $\hat{b}_{w,p}$ is 1 if $\hat{\mathbf{u}}_w$ and $\hat{\mathbf{u}}_p$ have the same dispersion, while $\hat{b}_{w,p} > 1$ indicates less dispersion in $\hat{\mathbf{u}}_p$ compared to $\hat{\mathbf{u}}_w$, and $\hat{b}_{w,p} < 1$ indicates more dispersion in $\hat{\mathbf{u}}_p$ compared to $\hat{\mathbf{u}}_w$. We computed $\hat{b}_{w,p}$ between CUR

or REF (whole evaluations) and NAT (partial evaluation) using only domestic animals' EBV, and between REF (whole evaluation) and NONE or CUR (partial evaluations) using all IEBVs.

4.2.5 Software and settings

In all scenarios, estimated breeding values and approximated reliabilities were obtained using MiX99 software (MiX99 Development Team 2017). The convergence criterion of the preconditioned conjugate gradient (PCG) algorithm for the mixed-model equation solutions was defined as the square root of the relative difference between solutions of two consecutive PCG iterations and was set to 10^{-7}. Convergence was also monitored for two other criteria, i.e., the relative difference between two consecutive solutions for the additive genetic animal effects and the relative residual of the mixed model equations.

4.3 Results

First, we present the distribution of the EBV for the implemented scenarios, followed by the results on rank correlations for the different groups of animals evaluated and for the LR method.

4.3.1 Distribution of EBV

We computed the standard deviation (SD) across the EBV for the group of domestic animals for each country and scenario (Figure 4.1). The SD of domestic animals' direct and maternal EBVs remained equal or increased when moving from national (NAT) to international evaluations (i.e., NONE, CUR, and REF) for all countries (Figure 4.1). The increase in EBV SD when comparing national with international evaluations was larger for smaller countries in terms of phenotypes (CZE, IRL, and CHE). CZE had the largest increase of EBV SD when moving from scenario NAT to REF, being 102% for direct EBV and 84% for maternal EBV. The SD of FRA domestic animals' direct EBV remained almost the same under NAT and international scenarios, while slightly increased (5%) for maternal EBV under scenario NONE. In general, there were no large differences in terms of EBV SD between international scenarios.

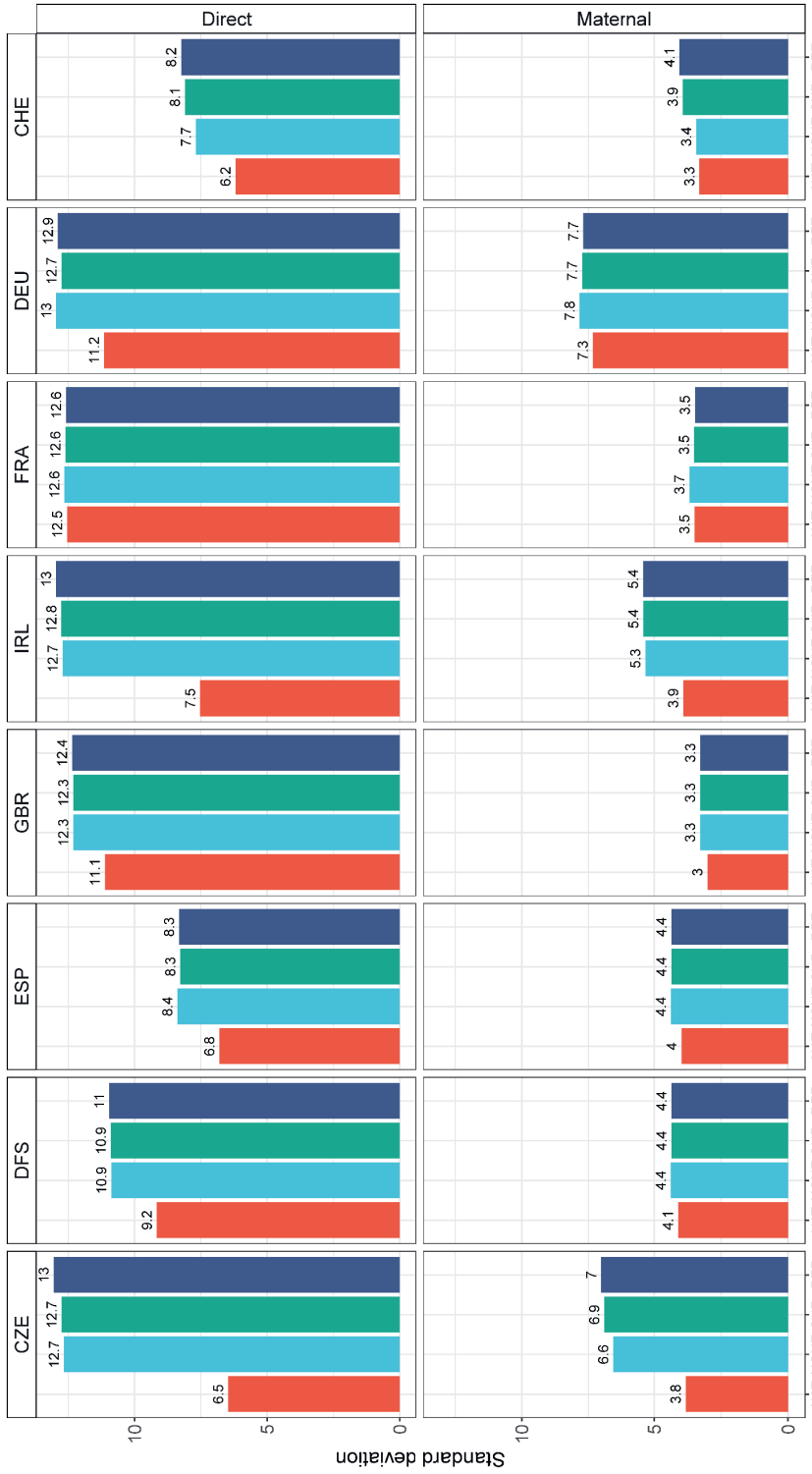

Figure 4.1 Direct and maternal estimated breeding value standard deviations of domestic animals per scenario on each country scale. Domestic: animals retained in scenario NAT. Scenario: NAT = national single-trait evaluations, NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations and r_{dm_BC} = between-country direct-maternal genetic correlations. Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, and CHE = Switzerland.

4.3.2 Impact on re-ranking of animals' IEBV

Regarding the direct IEBV, no re-ranking was observed when considering all animals for all international evaluations in any country (rank correlations > 0.990). The only exceptions were for DEU and CHE for which small re-ranking was observed for the scenario NONE (i.e., rank correlations between REF and NONE ranged between 0.980 and 0.990; Table 4.4). Regarding the maternal IEBV, large re-ranking (i.e., rank correlations smaller than 0.980) could be observed across the different international scenarios. For example, the rank correlations between scenarios REF and NONE for maternal IEBVs of all animals were on average 0.965 across countries, with a minimum rank correlation of 0.917 for FRA (Table 4.4). The comparison between scenarios REF and CUR showed small re-ranking for maternal IEBVs, with an average rank correlation of 0.988 across countries, and a minimum rank correlation of 0.980 for DFS (Table 4.4).

For common bulls, re-ranking was more severe for maternal IEBVs than for direct IEBVs (Table 4.4). The comparison between scenarios REF and NONE showed re-ranking: rank correlations were on average 0.979 for direct IEBVs and 0.965 for maternal IEBVs, across countries. The comparison between scenarios REF and CUR showed no re-ranking for CB's direct IEBV on any country scale (rank correlations > 0.990), and small re-ranking for maternal IEBV (rank correlations between 0.980 and 0.990) for CZE, DFS, GBR, IRL, and DEU (Table 4.4).

When grouped by their individual approximated reliabilities, the majority of the animals (> 78%) had a direct IEBV REL between 0.3 and 0.6, with the exception for CHE, where 64% of the animals had direct IEBV REL ≤ 0.3 (Supplementary Table S4.3). When grouped by maternal IEBV REL, almost all animals had a REL ≤ 0.6 and the majority of them had REL ≤ 0.3. FRA was the only country that had about 1% of the animals with maternal IEBV REL > 0.6 (Supplementary Table S4.3). Rank correlations between scenarios REF and NONE for direct IEBVs were 0.990, 0.990, and 0.985, for the three REL classes, respectively (Table 4.5). There was more variation in rank correlations between countries in the class of REL > 0.6 compared to the other two classes, with the smallest direct IEBV rank correlations for CHE (0.973) and DEU (0.975) (Table 4.5). There was no re-ranking between scenarios REF and CUR for direct IEBVs for any REL class on any country scale (all rank correlations > 0.997). Rank correlations between scenarios REF and NONE for maternal IEBVs increased with the REL class: average rank correlations across countries were 0.962, 0.968, and 0.980, respectively. Similarly, rank correlations between scenarios REF and CUR for maternal IEBVs increased with the REL class: average rank correlations across countries were 0.987, 0.991, and 0.995, respectively (Table 4.5).

Table 4.4 Spearman rank correlations of international estimated breeding values (IEBVs) between scenarios for different group of animals, and number of top 100 sires selected in common between scenarios.

			All [c]		CB [d]		Sires with publishable IEBVs [e]		Young sires [f]		Top 100 sires	
Scenario [a]		**COU** [b]	Direct	Maternal	Direct	Maternal	Direct	Maternal	Direct	Maternal	Direct	Maternal
REF	CUR	CZE	0.998	0.986	0.994	0.980	0.997	0.990	0.998	0.979	94	89
		DFS	0.998	0.980	0.993	0.988	0.997	0.990	0.999	0.968	92	84
		ESP	0.999	0.994	0.998	0.992	0.999	0.997	1.000	0.989	93	93
		GBR	0.999	0.984	0.997	0.985	0.999	0.992	0.999	0.973	93	88
		IRL	0.999	0.988	0.998	0.984	0.999	0.994	1.000	0.980	95	91
		FRA	1.000	0.992	0.999	0.996	1.000	0.997	1.000	0.985	99	94
		DEU	0.997	0.982	0.993	0.986	0.996	0.991	0.998	0.970	93	87
		CHE	0.997	0.995	0.993	0.994	0.995	0.997	0.997	0.992	91	91
REF	NONE	CZE	0.991	0.971	0.977	0.968	0.984	0.982	0.993	0.967	78	77
		DFS	0.991	0.976	0.978	0.978	0.986	0.987	0.994	0.962	82	80
		ESP	0.990	0.965	0.980	0.951	0.984	0.969	0.994	0.963	80	71
		GBR	0.994	0.973	0.987	0.973	0.989	0.987	0.996	0.956	85	84
		IRL	0.995	0.975	0.990	0.966	0.992	0.985	0.996	0.968	81	84
		FRA	0.998	0.917	0.998	0.952	0.999	0.971	0.999	0.831	97	78
		DEU	0.983	0.971	0.961	0.965	0.976	0.983	0.991	0.956	75	79
		CHE	0.982	0.972	0.966	0.967	0.971	0.977	0.986	0.975	73	75

[a] Scenario: NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations, and r_{dm_BC} = between-country direct-maternal genetic correlations. [b] COU, Country: CZE, Czech Republic, DFS, Denmark, Finland and Sweden, ESP, Spain, GBR, Great Britain, IRL, Ireland, FRA, France, DEU, Germany, CHE, Switzerland. [c] All, All animals included in the international evaluation (i.e., 3,431,742). [d] CB, Common bulls (1,436). [e] Sires with publishable IEBVs: 32,208 direct IEBVs and 13,016 maternal IEBVs obtained under scenario REF. [f] Young sires: 1,561 sires obtained under scenario REF.

Table 4.5 Spearman rank correlations of animals direct (Dir) and maternal (Mat) international estimated breeding values (IEBVs) between scenarios [a] per class of reliability (REL) [c], per country, and averaged across countries.

Scenario [a]		COU [b]	Rank correlations					
			REL ≤ 0.3		0.3 < REL ≤ 0.6		0.6 < REL	
			Dir	Mat	Dir	Mat	Dir	Mat
REF	CUR	CZE	0.997	0.985	0.998	0.990	0.996	0.990
		DFS	0.996	0.980	0.998	0.987	0.997	0.998
		ESP	0.999	0.994	0.999	0.995	0.999	0.997
		GBR	0.999	0.983	0.999	0.990	0.999	0.993
		IRL	0.999	0.988	0.999	0.992	0.999	0.992
		FRA	0.999	0.989	1.000	0.995	1.000	0.998
		DEU	0.997	0.982	0.997	0.985	0.996	0.999
		CHE	0.997	0.995	0.997	0.997	0.995	0.996
		Average	0.998	0.987	0.998	0.991	0.997	0.995
REF	NONE	CZE	0.992	0.971	0.990	0.971	0.982	0.981
		DFS	0.993	0.976	0.991	0.978	0.986	0.993
		ESP	0.992	0.966	0.989	0.953	0.982	0.966
		GBR	0.995	0.972	0.994	0.979	0.990	0.988
		IRL	0.995	0.975	0.995	0.980	0.992	0.979
		FRA	0.993	0.892	0.998	0.947	0.996	0.974
		DEU	0.983	0.971	0.984	0.962	0.975	0.993
		CHE	0.981	0.973	0.981	0.971	0.973	0.967
		Average	0.990	0.962	0.990	0.968	0.985	0.980

[a] Scenario: NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations, and r_{dm_BC} = between-country direct-maternal genetic correlations.
[b] COU, Country: CZE, Czech Republic, DFS, Denmark, Finland and Sweden, ESP, Spain, GBR, Great Britain, IRL, Ireland, FRA, France, DEU, Germany, CHE, Switzerland.
[c] REL computed under scenario REF.

The number of sires with publishable IEBVs was 32,208 and 13,016 for direct and maternal IEBVs, respectively. These sires were mainly recorded in FRA (89% and 90% of the total, for both direct and maternal IEBVs, respectively), followed by GBR, DFS, and DEU (each accounting for 2% to 4% of the total sires) and less than 1% in other countries (results not shown). The mean REL of sires with publishable IEBVs was 0.64 and 0.50 on average across countries for direct and maternal IEBVs, respectively (Supplementary Table S4.4). Re-ranking was present for sires with publishable IEBVs between scenarios REF and NONE for direct IEBVs on all country scales except for FRA and IRL: average rank correlation across countries of 0.985 and minimum rank correlation of 0.971 for CHE (Table 4.4). Similarly, re-ranking was present between

scenarios REF and NONE for sires' maternal IEBVs on all country scales: average rank correlation across countries of 0.980 and minimum rank correlation of 0.969 for ESP (Table 4.4). No re-ranking was observed, on any country scale, for sires with publishable IEBVs between scenarios REF and CUR, for both direct and maternal IEBVs (rank correlations > 0.995 and > 0.990, respectively; Table 4.4).

There were in total 1,561 young sires, the majority of which were recorded in FRA (78%), followed by GBR (9%), DFS (6%), DEU and CHE (2%), and other countries (1% or less) (results not shown). Young sires showed no re-ranking between scenarios REF and NONE for direct IEBVs, with the only rank correlations below 0.99 for CHE (0.986) (Table 4.4). Young sires showed re-ranking between scenarios REF and NONE for maternal IEBVs, with average rank correlations of 0.947 and minimum rank correlation of 0.831 for FRA. No re-ranking was observed for young sires between scenarios REF and CUR for direct IEBVs in any country (rank correlations > 0.997), while re-ranking was present for maternal IEBVs (average rank correlation of 0.979 and minimum rank correlation of 0.968 for DFS), with the exception of CHE (rank correlation of 0.992).

The number of commonly selected top 100 publishable sires between scenarios REF and NONE was 81 and 79 on average across countries for direct and maternal IEBVs, respectively (Table 4.4). The minimum number of commonly selected top 100 sires was 73 for CHE for direct IEBVs and 71 for ESP for maternal IEBVs. We further quantified the re-ranking between these scenarios using the absolute mean of the change in position of the list of top 100 sires selected under scenario REF when ranked based on their IEBVs under scenario NONE. Across countries, the top 100 sires moved on average by 16 and 23 positions, for direct and maternal IEBVs, respectively (Supplementary Table S4.5). The number of commonly selected top 100 publishable sires between scenarios REF and CUR was 94 and 90 on average across countries for direct and maternal IEBVs, respectively (Table 4.4). The minimum number of commonly selected top 100 sires was 91 for CHE for direct IEBV and 84 for DFS for maternal IEBV. Across countries, the top 100 sires, comparing scenario REF to CUR, moved on average by 2 and 5 positions, for direct and maternal IEBVs, respectively (Supplementary Table S4.5).

4.3.3 Increases in population accuracies and dispersion

The increases in population accuracy when moving from scenario NONE to CUR or to REF, measured using $1/\hat{\rho}_{NONE,CUR}$ and $1/\hat{\rho}_{NONE,REF}$, respectively, are reported in Table 4.6. When comparing scenarios NONE and CUR, for direct IEBVs, $1/\hat{\rho}_{NONE,CUR}$ ranged from 0% (for CZE, DFS, GBR, IRL, and FRA) to 1% (for ESP, DEU, and CHE), while for maternal IEBVs, it was on average 2%, ranging from 1% (for DFS,

IRL, and DEU) to 4% (for FRA) (Table 4.6). When comparing scenarios NONE and REF, $1/\hat{\rho}_{NONE,REF}$ was on average 1% for direct IEBVs across all countries, ranging from 0% (for FRA and IRL) to 2% (for CHE and DEU), while for maternal IEBVs, it was on average 3% across all counties, ranging from 2% (for GBR, IRL, and DFS) to 8% (for FRA) (Table 4.6). Comparison of $1/\hat{\rho}_{NONE,REF}$ with $1/\hat{\rho}_{NONE,CUR}$ shows similar gains of population accuracy when moving from scenario NONE to REF instead of moving to CUR, i.e., on average 0% for direct IEBVs and 1% for maternal IEBVs across countries. Only FRA benefits from using all correlations in the scenario REF in comparison to CUR (increase of 4%).

The increases in population accuracy for domestic animals obtained when moving from scenario NAT to CUR or REF are reported in Table 4.6. When comparing scenarios NAT and CUR, the increases in population accuracy for direct EBVs were on average 19% across countries, ranging from 0% of FRA to 59% of CZE. For maternal EBVs, the increases in population accuracy were on average 27% across countries, ranging from 1% of FRA to 101% of CZE. When comparing scenarios NAT and REF, the increases in population accuracy for direct EBVs were on average 21% across countries, ranging from 0% of FRA to 63% of CZE. For maternal EBVs, the increases in population accuracy were on average 29% across all countries, ranging from 0% of FRA to 106% of CZE. Comparison of $1/\hat{\rho}_{NAT_d,REF_d}$ with $1/\hat{\rho}_{NAT_d,CUR_d}$ shows the increase in population accuracy for domestic animals when moving from scenario NAT to REF instead of moving to CUR. For direct EBVs, differences of $1/\hat{\rho}_{NAT_d,REF_d}$ with $1/\hat{\rho}_{NAT_d,CUR_d}$ were on average 2%, ranging from 0% of FRA to 5% of CZE, while for maternal EBVs, differences were on average 2%, ranging from -1% for FRA to 5% of IRL.

Regression coefficients of IEBVs of whole on partial evaluations for all animals in the international evaluation are reported in Table 4.7. The regression coefficients $\hat{b}_{w,p}$ for direct IEBVs of REF-NONE were close to 1 in all countries, ranging from 0.99 of FRA to 1.06 of CHE. Direct IEBVs $\hat{b}_{w,p}$ of REF-CUR were also close to 1 in all countries, ranging from 1.00 of FRA to 1.04 of DFS and DEU. For maternal IEBVs, the $\hat{b}_{w,p}$ of REF-NONE were close to 1 in most of the countries, except for FRA and CHE for which $\hat{b}_{w,p}$ were 0.88 and 1.15, respectively. Maternal IEBVs $\hat{b}_{w,p}$ of REF-CUR were close to 1 in all countries, ranging from 0.96 of DFS to 1.06 of CHE.

Regression coefficients of EBVs of whole on partial evaluations for domestic animals are also reported in Table 4.7. The regression coefficients $\hat{b}_{w,p}$ for direct and maternal EBVs of NAT-CUR and NAT-REF were similar across countries. In NAT-CUR, direct EBVs $\hat{b}_{w,p}$ were close to 1 in almost all countries, ranging between 1.01 of FRA and 1.12 of DFS, except for CZE (1.24) and IRL (1.25). Similarly, direct EBVs $\hat{b}_{w,p}$ of

NAT-REF ranged between 1.00 of FRA and 1.12 of DFS, except for CZE (1.23) and IRL (1.25). Maternal EBVs $\hat{b}_{w,p}$ of NAT-CUR were close to 1 in all countries, ranging between 0.90 of CZE and 0.99 of FRA. Similarly, maternal EBVs $\hat{b}_{w,p}$ of NAT-REF were close to 1 in all countries, ranging between 0.89 of CZE and 0.99 of FRA.

Table 4.6 Increase in population accuracy [a] of moving from partial evaluation (*p)* to whole evaluation (*w*) [b] for all animals included in the international evaluations (All) and domestic animals [c].

Effect	**Scenario** [d]		**Country** [e]							
All	Evaluation *p*	Evaluation *w*	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
Direct	NONE	CUR	0	0	1	0	0	0	1	1
	NONE	REF	1	1	1	1	0	0	2	2
Maternal	NONE	CUR	2	1	3	2	1	4	1	3
	NONE	REF	3	2	3	2	2	8	3	3
Domestic [c]	Evaluation *p*	Evaluation *w*								
Direct	NAT	CUR	59	6	19	4	35	0	9	21
	NAT	REF	63	7	20	4	38	0	10	23
Maternal	NAT	CUR	101	7	20	12	45	1	10	21
	NAT	REF	106	7	21	13	50	0	10	23

[a] Expressed as the relative % increase of evaluation *p*, i.e., $(1/\hat{\rho}_{p,w} - 1) \cdot 100$.

[b] Partial: national evaluations (scenario NAT) where recorded phenotypes are available only at the country level. Whole: international evaluations (scenario CUR and REF) providing new information from other countries. Similarly, NONE is a partial evaluation relative to scenarios CUR and REF.

[c] Domestic: animals retained in the national evaluations for scenario NAT.

[d] Scenario: NAT = national single-trait evaluations, NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations, and r_{dm_BC} = between-country direct-maternal genetic correlations.

[e] Country: CZE, Czech Republic, DFS, Denmark, Finland and Sweden, ESP, Spain, GBR, Great Britain, IRL, Ireland, FRA, France, DEU, Germany, CHE, Switzerland.

Table 4.7 Direct and maternal regression coefficients of EBV of whole evaluation (w) on partial evaluation (p) [a] ($\hat{b}_{w,p}$) for all animals included in the international evaluation (All) and domestic [b] animals.

Effect	Scenario [c]		Country [d]							
All	Evaluation p	Evaluation w	CZE	DFS	ESP	GBR	IRL	FRA	DEU	CHE
Direct	NONE	REF	1.04	1.05	1.03	1.04	1.04	0.99	1.03	1.06
	CUR	REF	1.03	1.04	1.02	1.03	1.02	1.00	1.04	1.03
Maternal	NONE	REF	1.08	1.01	1.04	1.00	1.04	0.88	1.01	1.15
	CUR	REF	1.02	0.96	1.00	0.97	1.00	0.99	0.97	1.06
Domestic [b]	Evaluation p	Evaluation w								
Direct	NAT	CUR	1.24	1.12	1.02	1.06	1.25	1.01	1.05	1.08
	NAT	REF	1.23	1.12	1.02	1.06	1.25	1.00	1.05	1.08
Maternal	NAT	CUR	0.90	0.99	0.91	0.97	0.95	0.99	0.96	0.98
	NAT	REF	0.89	0.99	0.91	0.97	0.92	0.99	0.95	0.99

[a] Partial: national evaluations (scenario NAT) where recorded phenotypes are available only at the country level. Whole: international evaluations (scenario CUR and REF) providing new information from other countries. Similarly, NONE is a partial evaluation relative to scenarios CUR and REF.
[b] Domestic: animals retained in the national evaluations for scenario NAT.
[c] Scenario: NAT = national single-trait evaluations, NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations, and r_{dm_BC} = between-country direct-maternal genetic correlations.
[d] Country: CZE, Czech Republic, DFS, Denmark, Finland and Sweden, ESP, Spain, GBR, Great Britain, IRL, Ireland, FRA, France, DEU, Germany, CHE, Switzerland.

4.4 Discussion

In this study, we investigated the impact of three different definitions of across countries r_{dm} on the ranking of international beef cattle IEBVs. We further explored the impact of r_{dm} on population accuracies and dispersion in international evaluations using the LR method. To the best of our knowledge, this is the first study that investigates the impact of the r_{dm} structure in the context of beef cattle international evaluations. Hereafter, we first discuss the impact of r_{dm_BC} and r_{dm_WC}, followed by the possible implications of this study for beef cattle international evaluations.

4.4.1 Impact of r_{dm_BC} on international evaluations

Ignoring r_{dm_BC} had a small impact on international evaluations. Ignoring r_{dm_BC} did not result in direct IEBV re-ranking for any country when considering all animals, while it did result in limited maternal IEBV re-ranking. This re-ranking was not

associated with particular countries, but it was mainly related to animals with low maternal IEBV REL (REL ≤ 0.3). Ignoring r_{dm_BC} had also a small impact on all country scales for CB, with rank correlations between 0.980 and 0.990, while publishable sires showed no re-ranking on any country scale. In the latter group, Interbeef publication rules may have mitigated the impact of r_{dm_BC} by requiring sires to have records across two or three generations. As expected, young sires with low maternal IEBV REL (< 0.3) showed re-ranking for maternal IEBV on all country scales when r_{dm_BC} were ignored. Similarly, the impact of r_{dm_BC} on the re-ranking of the top 100 sires, assessed as the absolute mean change in ranking of the sires, was mostly limited to the maternal IEBV. Ignoring r_{dm_BC} had limited impact on domestic animals EBV SD: on average, the increase in EBV SD for scenario REF compared to CUR was 1% and 0% for direct and maternal EBVs, respectively, and mostly related to countries with smaller national populations (CZE, CHE, and IRL). These results are supported by the increases in population accuracy, when considering the whole set of IEBVs on each country scale, which hardly increased from using r_{dm_BC}. Similar results were obtained for domestic animals: increases in population accuracy from modeling r_{dm_BC} were on average 2% for both direct and maternal EBVs, and at maximum 5% (associated with smaller countries such as CZE and IRL). These results were further confirmed by computing $1/\hat{\rho}_{CUR,REF}$ (results not shown) where no gain (0% for all countries) and maximum gains of 2% were obtained for direct and maternal EBVs, respectively. Similarly, regression coefficients $\hat{b}_{w,p}$ of REF-CUR were close to 1 in all countries for both direct and maternal IEBVs, indicating that IEBVs were not largely over- or under-dispersed, in comparison to REF, when ignoring r_{dm_BC}. For domestic animals, corresponding regression coefficients $\hat{b}_{w,p}$ of REF-NAT and CUR-NAT were similar for both direct and maternal EBVs. Moreover, FRA had regression coefficients $\hat{b}_{w,p}$ close to 1 for both direct and maternal EBVs, while CZE and IRL showed the largest under-dispersion ($\hat{b}_{w,p}$ > 1.23) of domestic animals' national direct EBV compared to either CUR or REF. These results suggest that national EBVs in NAT may be under-dispersed compared to either CUR or REF international evaluations for smaller countries such as CZE and IRL. On the other hand, large countries like FRA showed no under- or over-dispersion ($\hat{b}_{w,p}$ close to 1) of national EBVs relative to the international evaluations when data from other countries are considered. Thus, results from the LR method suggest that modeling r_{dm_BC} would not lead to large increases in population accuracy or dispersion in IEBV compared to ignoring them.

4.4.2 Impact of r_{dm_WC} on international evaluations

Our results suggest that ignoring r_{dm_WC} affects international evaluations. Ignoring r_{dm_WC} resulted in re-ranking for both direct and maternal IEBVs. As expected, the largest impact on IEBVs re-ranking was observed for those countries with strong negative estimated r_{dm_WC}, i.e., ESP and FRA. For example, FRA showed the lowest rank correlation for maternal IEBVs (0.917) when considering all animals, but grouping animals by their REL revealed that this re-ranking of FRA was mainly related to animals with REL ≤ 0.3. In general, when animals were grouped by REL, re-ranking within each group of REL was more severe in those countries with absolute values of r_{dm_WC} greater than 0.2 (i.e., FRA, ESP, DEU, and CHE). These results are in agreement with those of Phocas *et al.* (2004) which also observed an increased re-ranking for maternal IEBVs when ignoring r_{dm_WC} in international evaluations. Ignoring r_{dm_WC}, in addition to r_{dm_BC}, also gave more severe re-ranking for publishable sires and CB than ignoring only r_{dm_BC}. Re-ranking in the latter group may be due to the majority of the CB originating from FRA (82.5%) (Bonifazi *et al.* 2020b). These FRA CB may have mainly recorded domestic offspring and, ignoring r_{dm_WC} for FRA, would lead to a different ranking for this group of animals on all country scales. Similarly, ignoring r_{dm_WC} led to high re-ranking of maternal IEBVs on all country scales for young sires, with the lowest rank correlation being for FRA. Re-ranking in this group may be related to the majority of young sires originating from FRA (78%). Ignoring r_{dm_WC} also affected the top 100 sires with publishable IEBVs, both for direct and maternal IEBVs. This was also confirmed by the results for the absolute mean change in position of top 100 sires. FRA contributes with the largest amount of data in the Limousin Interbeef evaluation (87% of all phenotypes) and has the strongest pedigree connections with other countries. Thus, ignoring r_{dm_WC} in FRA may have contributed to generating re-ranking for the categories of publishable sires, young sires, and CB not only on the FRA scale, but also on other countries scales since the majority of the animals in these categories originates from FRA. Ignoring r_{dm_WC} affected the increases of domestic animals EBV SD, for both small countries like CHE and CZE (increases in EBV SD of CUR compared to NONE higher than 5%), and large countries like FRA (maternal EBV SD 5% smaller in scenario NONE compared to CUR). The importance of using r_{dm_WC} in international evaluations was also reflected in the increases in population accuracy for the whole set of IEBVs. Similarly, regression coefficients $\hat{b}_{w,p}$ of REF-NONE show that ignoring r_{dm_WC}, in addition to r_{dm_BC}, led to over- or under-dispersion of maternal IEBVs compared to REF, especially in countries such as FRA and CHE where r_{dm_WC} were the strongest (absolute values > 0.3). On the other hand, when r_{dm_WC} were considered in the international evaluation, the difference in dispersion in comparison to REF reduced for almost all countries with

values for regression coefficients $\hat{b}_{w,p}$ closer to 1. Van Vleck *et al.* (1977) showed that when r_{dm} are negative, these correlation need to be considered for selection decisions. Thus, the results of our study support the suggestion of Phocas *et al.* (2004) that when estimates of r_{dm_WC} are considerably different from 0, as was the case for most countries, they should be used in international evaluations and not ignored.

4.4.3 Implications

Both r_{dm_BC} and r_{dm_WC} had less impact on the re-ranking of animals for direct IEBVs than for maternal IEBVs. For a young sire, the AWW record is available at an early stage of his life, while data recorded on his daughters and daughters' progeny, necessary to make an accurate estimate of the maternal EBV, are available only later in his life (Willham 1980; Gerstmayr 1992). The maternal EBV of young sires is mainly based on its direct EBV through r_{dm_WC}, while later in life it will be increasingly more based on daughters' progeny records, and thus will be less affected by the r_{dm_WC}. In international evaluations, the maternal IEBV of a domestic young sire with mostly recorded foreign offspring will heavily depend on its foreign direct IEBV through the r_{dm_BC}. Therefore, re-ranking in maternal IEBV of young sires is expected as they become older and, considering both the large standard error of estimated r_{dm_BC} and the associated difficulties in estimating them (Bonifazi *et al.* 2020b), a ranking based on progeny' record may be desired. These expected re-rankings were confirmed by the low rank correlations observed for maternal IEBVs for the group of young sires. Results of this study are in line with the findings of David *et al.* (2015) in other species who suggested that r_{dm} have a greater impact on maternal EBV since they are derived from offspring performance, as opposed to direct EBV. Our results showed that re-ranking of maternal IEBV decreased with increasing reliability, regardless of the r_{dm} structure used, suggesting that when more information is available at the animal level, the r_{dm} become less important for the estimation of maternal IEBVs. Another possible explanation for r_{dm} having a greater impact on maternal IEBV, as suggested by David *et al.* (2015), may be that national direct genetic variances were larger than maternal ones. On the other hand, our results confirmed that little or no re-ranking is expected when ignoring r_{dm_BC} for top 100 sires and sires with publishable IEBVs, respectively, because these sires have both recorded progeny and daughters' offspring available. Thus, the results of this study provide support that fixing r_{dm_BC} to 0 has limited impact on IEBV for Limousin weaning weight.

Estimated values used for r_{dm_BC} tended to be negative, similarly to r_{dm_WC}. The different r_{dm_BC} of FRA were consistently negative and, given the amount of phenotypes provided by FRA to the Limousin international evaluation, ignoring r_{dm_BC}

potentially could affect international evaluations. However, our results show that the impact of ignoring r_{dm_BC} in international evaluations was limited, most likely because the absolute values of r_{dm_BC} were close to 0. Absolute values of r_{dm_BC} were smaller compared to absolute values of r_{dm_WC}; this difference is expected, as relative to r_{dm_WC}, the magnitude of r_{dm_BC} may be reduced due to genotype-by-country interactions. With stronger genotype-by-country interactions, we expect estimates of r_{dm_BC} to be closer to 0, reducing the impact of ignoring r_{dm_BC} on international evaluations. On the other hand, the presence of stronger genotype-by-country interactions should not result in different estimates for r_{dm_WC} as these are estimated within the same country. We used Limousin breed and weaning weight data, but similar estimates of r_{dm_WC} for weaning weight are reported in other breeds already included in international evaluations, e.g., Charolais (Pabiou *et al.* 2014). Reported r_{dm} values for birth and weaning weight in popular beef cattle breeds (Trus and Wilton 1988; Waldron *et al.* 1993; Meyer *et al.* 1993; Meyer 1994; Dodenhoff *et al.* 1999; Phocas and Laloë 2004), on average, are close to the r_{dm_WC} values observed for weaning weight in Limousin, albeit there are large differences between estimates across studies. Nevertheless, assuming that the absolute r_{dm_BC} for such breeds is smaller than r_{dm_WC} as it was in this study suggests that in international evaluations of weight traits for several other beef breeds it may also be valid to assume that r_{dm_BC} are zero. For a trait like yearling weight, however, reported r_{dm} values are typically stronger (over ±0.55) (Waldron *et al.* 1993; Meyer 1994; Robinson 1996a), suggesting that both r_{dm_WC} and r_{dm_BC} may be stronger than for weaning weight, possibly to the extent that in those cases it would be needed to use estimated r_{dm_BC} in international evaluations. r_{dm_WC} estimated at a national level may be biased due to data structure or modeling issues as reported in the literature (Meyer 1997; Clément *et al.* 2001; Bijma 2006). This could potentially also affect Interbeef evaluations as the current Interbeef AMACI model adopts each participating countries' national model. The results of this study show that r_{dm_WC} have an impact on the re-ranking of IEBVs, underlining the importance of validation procedures of participating countries' national models.

Domestic animals' EBV are expected to re-rank when data from relatives recorded in other countries are accounted for through international evaluations (Venot *et al.* 2014). In popular breeds such as Limousin, including information from countries as France where most connections and founders can be traced (Bouquet *et al.* 2011; Bonifazi *et al.* 2020b) is beneficial for two reasons as shown in previous studies (Venot *et al.* 2014; Bonifazi *et al.* 2020a). First, accounting for information from relatives recorded in other countries leads to higher EBV's reliabilities of domestic animals, especially for smaller countries. Second, breeders get access to

elite foreign bulls IEBV expressed on their own country scale and that rank similar or higher than domestic ones, giving breeders the opportunity to achieve higher genetic gains and better meet their selection objectives (Bonifazi *et al.* 2020a).

The LR method has been applied in evaluations with multiple traits, maternally affected traits, and traits where phenotypes are not available on all individuals for all environments (Chu *et al.* 2019; Macedo *et al.* 2020a; Picard Druet *et al.* 2020). As such, the LR method appears to be a useful choice to evaluate the increase in population accuracy when ignoring r_{dm} in the context of beef cattle international evaluations. The LR statistics $\rho_{p,w}$ relies on two assumptions (Legarra and Reverter 2018). The first assumption, which does not affect $\rho_{p,w}$, is that the regression of $\widehat{\mathbf{u}}_p$ and of $\widehat{\mathbf{u}}_w$ on the TBV is equal to one. The second assumption is that the regression of $\widehat{\mathbf{u}}_w$ on $\widehat{\mathbf{u}}_p$ is also equal to one, i.e., $cov(\widehat{\mathbf{u}}_w, \widehat{\mathbf{u}}_p) = var(\widehat{\mathbf{u}}_p)$. When the LR method was applied, this latter assumption did hold for most of the comparisons between scenarios as shown by the regression coefficients $\hat{b}_{w,p}$ being mostly between 0.9 and 1.1. We further noticed that the assumption of the LR method was met very closely, especially for domestic animals with reliable EBVs under the evaluation *p* (i.e., with country recorded phenotypes and with direct or maternal REL for evaluation $p > 0.6$; results not shown). Recently, Macedo *et al.* (2020) reported that some of the LR method statistics may be sensitive to incorrectly estimated genetic parameters; nonetheless, the same authors reported that the ratio of population accuracies $\rho_{p,w}$ performed well in their study. Results of the reported $\hat{\rho}_{p,w}$ statistic should be treated with caution since estimates of r_g between countries are prone to sampling error during the estimation process and often reported with high SE (Bonifazi *et al.* 2020b). Nevertheless, we expect that the observed trends in increases of population accuracy across the scenarios are not affected by departures of the underlying assumptions of the LR method or inaccuracy of estimated variance components.

4.5 Conclusions

Results of this study, based on Limousin weaning weight data, provide support that the current practice of ignoring r_{dm_BC} in international beef cattle evaluations results in limited decreases in population accuracies, negligible impact on dispersion of EBVs, and no or limited re-ranking of animals' direct and maternal IEBVs, respectively. Re-ranking for maternal IEBVs was mainly related to animals with REL ≤ 0.3. No re-ranking was present for sires with publishable IEBVs. Moreover, results show that fixing r_{dm_WC} to 0 would result in considerable re-ranking of animals.

4.6 Funding

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4.7 Supplementary material

4.7.1 Supplementary tables

Table S4.1 List of fixed, random and covariate environmental effects in the national model per each country [b].

COU [a]	Fixed							Random			Covariates	
CZE		asextwin	aaca	year				PE	HYS			
DFS	HYS	asex	aaca	seas	twin			PE				
ESP	herd_birth	asex	aaca					PE				
GBR	HYS_mgt	asex		month	twin	fostered	wdam_brd	PE			agedam	agedam2
IRL	HYS	asex	pariagedam					PE			agedam2	aawg
FRA	HY-asex-mgt		pariaaca	seas			individual	PE				
DEU		asex	parity	month	twin				HY			
CHE		asex		yearmonth			alpine	PE	HY	SireHerd	agedam	agedam2

[a] COU, Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

[b] *aaca* = age at calving; *aawg* = age at weighting; *agedam* = age of the dam; *agedam*2 = age of the dam fitted as quadratic effect; *alpine* = access to alpine grazing for calves; *asex* = sex of the animal; *asextwin* = interaction between *asex* and *twin*; *fostered* = foster code; *herd_birth* = contemporary group defined based on the herd and birth date; *HY* = Herd-Year; *HY-asex-mgt* = contemporary group defined based on *HY*, *asex* and management group defined as calf-dam couple; *HYS* = Herd-Year-Season; *HYS_mgt* = contemporary group defined by herd, management group and date of birth; *individual* = individual situation, e.g. preferential treatment; *month* = month of birth; *pari* = parity; *pariaaca* = interaction between *pari* and *aaca* effects; *pariagedam* = interaction between *pari* and *agedam*; *PE* = maternal permanent environmental effect; *seas* = season; *SireHerd* = interaction between sire and herd; *twin* = twinning; *wdam_brd* = breed of the weaning dam; *year* = year of birth; *yearmonth* = interaction between *year* and *month*.

List originally reported in Bonifazi *et al.* (2020b).

Table S4.2 National genetic, environmental and residual (co)variances [b].

COU [a]	σ^2_{HYS}	σ^2_{HY}	$\sigma^2_{Sire\text{-}Herd}$	σ^2_{PE}	σ^2_{dir}	σ^2_{mat}	$\sigma_{dir\text{-}mat}$	σ^2_{res}	h^2_{dir}	h^2_{mat}
CZE	1,782			81	310	197	-28.53	374	0.11	0.07
DFS				90	269	120	-24.69	547	0.27	0.12
ESP				43	136	68	-21.18	294	0.26	0.13
GBR				63	268	55	-11.63	421	0.34	0.07
IRL				45	450	194	-55.13	647	0.35	0.15
FRA				63	242	62	-40.56	354	0.36	0.09
DEU		477			383	326	-86.43	719	0.21	0.18
CHE		142	86	69	130	54	33.52	565	0.12	0.05

[a] COU, Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.
[b] σ^2 = variance, HYS = Herd-Year-Season, HY = Herd-Year, Sire-Herd = interaction between Sire and Herd, PE = maternal permanent environment, h^2 = heritability, dir = direct genetic effect, mat = maternal genetic effect, $\sigma_{dir\text{-}mat}$ = direct-maternal genetic covariance, res = residual.

Table S4.3 Number of animals in each class of reliability (REL) [a, b] per country for direct (Dir) and maternal (Mat) international estimated breeding values (IEBV).

	Number of animals					
COU [b]	REL ≤ 0.3		0.3 < REL ≤ 0.6		0.6 < REL	
	Dir	Mat	Dir	Mat	Dir	Mat
CZE	720,516	2,943,083	2,702,478	485,017	8,748	3,642
DFS	228,329	3,277,750	3,144,370	152,181	59,043	1,811
ESP	598,794	3,247,000	2,820,177	183,977	12,771	765
GBR	313,252	2,857,086	3,084,474	570,358	34,016	4,298
IRL	724,382	3,001,151	2,699,170	428,715	8,190	1,876
FRA	195,449	2,121,322	2,932,768	1,284,177	303,525	26,243
DEU	363,291	3,230,289	3,038,454	185,189	29,997	16,264
CHE	2,184,863	3,164,338	1,244,741	266,977	2,138	427

[a] REL computed under Scenario REF: both r_{dm_WC} (within-country direct-maternal genetic correlations) and r_{dm_BC} (between-country direct-maternal genetic correlations) used in the evaluation.
[b] COU, Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Table S4.4 Distribution of publishable sires' individual reliabilities (REL) [a] per country.

Effect	COU [b]	Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
Direct	CZE	0.38	0.53	0.56	0.57	0.60	0.97
	DFS	0.43	0.70	0.74	0.74	0.78	0.99
	ESP	0.38	0.54	0.57	0.59	0.61	0.98
	GBR	0.34	0.60	0.64	0.65	0.68	0.99
	IRL	0.30	0.52	0.56	0.56	0.59	0.99
	FRA	0.33	0.82	0.87	0.85	0.91	1.00
	DEU	0.33	0.59	0.63	0.64	0.67	0.98
	CHE	0.35	0.47	0.51	0.51	0.54	0.97
Maternal	CZE	0.25	0.48	0.53	0.53	0.58	0.97
	DFS	0.20	0.34	0.38	0.40	0.43	0.97
	ESP	0.21	0.37	0.41	0.42	0.46	0.96
	GBR	0.20	0.50	0.56	0.56	0.62	0.98
	IRL	0.20	0.45	0.50	0.50	0.55	0.97
	FRA	0.26	0.64	0.70	0.70	0.77	1.00
	DEU	0.20	0.35	0.39	0.41	0.44	0.97
	CHE	0.21	0.41	0.45	0.45	0.50	0.95

[a] REL computed under Scenario REF: both r_{dm_WC} (within-country direct-maternal genetic correlations) and r_{dm_BC} (between-country direct-maternal genetic correlations) used in the evaluation.

[b] COU, Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.

Table S4.5 Top 100 sires [a] absolute mean rank position change between scenarios [b] for direct and maternal international estimated breeding values (IEBV).

			Absolute mean rank position change	
Scenario [b]		**COU** [c]	Direct	Maternal
REF	CUR	CZE	1.7	5.8
		DFS	2.2	10.1
		ESP	1.4	2.1
		GBR	1.5	4.8
		IRL	1.0	3.4
		FRA	0.0	1.4
		DEU	2.7	8.3
		CHE	4.7	3.0
REF	NONE	CZE	16.1	30.7
		DFS	13.0	13.1
		ESP	14.3	37.7
		GBR	9.5	8.6
		IRL	11.7	13.0
		FRA	0.4	23.2
		DEU	22.1	22.8
		CHE	42.2	34.7

[a] Top 100 publishable sires obtained under Scenario REF.
[b] Scenario: NONE = both r_{dm_WC} and r_{dm_BC} set to 0, CUR = r_{dm_WC} used in the evaluation, and r_{dm_BC} set to 0, REF = both r_{dm_WC} and r_{dm_BC} used in the evaluation. With r_{dm_WC} = within-country direct-maternal genetic correlations, and r_{dm_BC} = between-country direct-maternal genetic correlations.
[c] COU, Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, ESP = Spain, GBR = Great Britain, IRL = Ireland, FRA = France, DEU = Germany, CHE = Switzerland.


CHAPTER
5

International single-step SNPBLUP beef cattle evaluations for Limousin weaning weight

Renzo Bonifazi[1], Mario P.L. Calus[1], Jan ten Napel[1], Roel F. Veerkamp[1], Alexis Michenet[2], Simone Savoia[2], Andrew Cromie[3], Jérémie Vandenplas[1]

[1] Animal Breeding and Genomics, Wageningen University and Research, P.O. Box 338, 6700 AH Wageningen, the Netherlands
[2] Interbull Centre - Department of Animal Breeding and Genetics, SLU - Box 7023, S-75007 Uppsala, Sweden
[3] Irish Cattle Breeding Federation, Link Road, Ballincollig, P31 D452, Co Cork, Ireland

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Abstract

Background: International collaboration projects further improve accuracies of estimated breeding values (EBV) compared to that of national evaluations by building larger reference populations or performing a joint evaluation using data (or proxy of them) from different countries. Genomic selection is increasingly adopted in beef cattle, but the benefits of including genomic information in international evaluations are not explored yet. Our objective was to develop an international beef cattle single-step genomic evaluation and investigate its impact on the accuracy and bias of genomic evaluations over current pedigree-based evaluations.

Methods: Weaning weight records were available for 331,593 animals from 7 European countries. The pedigree included 519,740 animals. After imputation and quality control, 17,607 genotypes at a density of 57,899 SNP from 4 countries were available. We implemented two international scenarios where countries were modelled as different correlated traits: an international genomic single-step Single Nucleotide Polymorphism Best Linear Unbiased Prediction (SNPBLUP) evaluation ($ssSNPBLUP_{INT}$) and an international pedigree-based BLUP evaluation ($PBLUP_{INT}$). Two national scenarios were implemented for pedigree and genomic evaluations using only nationally submitted phenotypes and genotypes. Accuracies, level and dispersion bias of EBV of animals born from 2014 onwards, and increases in population accuracies were estimated using the Linear Regression method.

Results: On average across countries, 39% and 17% of sires and maternal-grand-sires with recorded (grand-)offspring across two countries were genotyped. $ssSNPBLUP_{INT}$ showed the highest accuracies of EBV and led to increases in population accuracy compared to $PBLUP_{INT}$ of 13.7% for direct EBV, and 25.8% for maternal EBV, on average across countries. Increases in population accuracies when moving from national scenarios to $ssSNPBLUP_{INT}$ were observed in all countries. Overall, $ssSNPBLUP_{INT}$ level and dispersion bias remained similar or slightly reduced compared to $PBLUP_{INT}$ and national scenarios.

Conclusions: International single-step SNPBLUP evaluations are feasible and lead to higher population accuracies for both large and small countries compared to current international pedigree-based evaluations and national evaluations. These results are likely related to the larger multi-country reference population and the inclusion of phenotypes from relatives recorded in other countries via single-step international evaluations. The proposed international single-step approach can be applied to other traits and breeds.

5.1 Background

In livestock species, genomic selection (Meuwissen *et al.* 2001) has become increasingly important for driving selection decisions of both economically and socially relevant traits (Goddard and Hayes 2009; Hayes *et al.* 2013; Meuwissen *et al.* 2016). In animal breeding programs, the inclusion of genomic data in addition to conventional sources of information (pedigree and phenotypes) leads to an increase in prediction accuracy of estimated breeding values (EBV) and to reduced generation intervals which, in turn, allows to achieve higher genetic gains (Schaeffer 2006). National genomic evaluations make use of phenotypic, genomic and pedigree information either based on multi-step approaches (VanRaden 2008) or single-step approaches (Christensen and Lund 2010; Aguilar *et al.* 2010). Even though genotyping is becoming cheaper and the availability of individual genomic data is increasing (Meuwissen *et al.* 2016), accurate genomic predictions often require large and representative reference populations (Goddard and Hayes 2009; Goddard 2009; Habier *et al.* 2010; Pszczola *et al.* 2012), which can be expensive and time-consuming to build and maintain, especially for difficult-to-measure traits (de Haas *et al.* 2012; Berry *et al.* 2014). Moreover, with small livestock populations, building a reference population using only national resources can be challenging or even unfeasible. For such small national populations, a combined international genomic evaluation is appealing, especially when genomic predictions are performed within-breed (VanRaden *et al.* 2009; Lund *et al.* 2016).

In cattle, international collaborations projects aim to pull together genomic data from different countries and build large reference populations within the same breed (Durr and Philipsson 2012). These projects allow to either 1) share genotypes and breeding values as pseudo-phenotypes among national breeding organizations and, in turn, enlarge existing national reference populations, or 2) have an international genomic evaluation where raw national data or a proxy of them (e.g. de-regressed proofs; Liu 2011) are used. Examples of international collaboration projects in dairy cattle are the “North America Consortium” (Muir *et al.* 2010), “EuroGenomics” (Lund *et al.* 2011), and “InterGenomics” (Jorjani *et al.* 2011).

Genomic selection has also been increasingly adopted in beef cattle national evaluations (Van Eenennaam *et al.* 2014; Gunia *et al.* 2014; Lourenco *et al.* 2015; Berry *et al.* 2016), however, some additional difficulties exist in comparison with dairy cattle (Garrick 2011; Berry *et al.* 2016). In particular, the lower use of artificial insemination (which results in lower connectedness between herds and smaller sire families) and the lower systematic recording of phenotypes compared to dairy breeding programs contribute to smaller benefits of genomic selection in beef cattle. These difficulties also make international evaluations more challenging in beef cattle

compared to dairy, especially due to low pedigree connectedness between countries (Venot *et al.* 2009b; Berry *et al.* 2016). International genomic evaluations may contribute to increase connectedness among countries by using genomic data next to pedigree and phenotypic data (Yu *et al.* 2017). Moreover, genomic data would help to combine (small) national reference populations into an international one and, in turn, result in an increase in the accuracies of genetic evaluations. However, the current international beef cattle evaluations led by Interbeef (Interbeef 2006) do not yet consider genomic information.

When properly parametrized, it is expected that the optimal approach for international genomic evaluations would be to implement a single-step evaluation because it allows combining phenotypic, genomic and pedigree national information at once (Legarra *et al.* 2014), using raw national phenotypes and genotypes without the need to approximate them. Moreover, such a model would need to be easily scalable to efficiently handle a large amount of traits and (genomic) data. To date, the feasibility and the benefits of joint single-step beef cattle international evaluations are not explored yet. Therefore, the aim of our study is to develop a joint international single-step genomic evaluation for beef cattle using Limousin weaning weight data, and to investigate its benefits for both the increase in accuracies of EBV and genetic connectedness among countries over the current pedigree-based Interbeef evaluations. Moreover, we evaluated whether moving towards international single-step genomic evaluations would affect level and dispersion bias of EBV compared to both current international pedigree-based evaluations and national evaluations.

5.2 Methods

Hereafter we first describe the available data and its preparations steps, followed by the implemented scenarios and a description of the international models used. Finally, we describe the assessment of connections among countries and the validation methodology implemented.

5.2.1 Phenotypes

A total of 333,333 Limousin male and female age-adjusted weaning weight (AWW) phenotypes were available. Phenotypes were available from 5 Limousin populations, representing 7 European countries joining the 2020 January Interbeef evaluation. These countries were: Czech Republic (CZE), Denmark, Finland and Sweden (DFS, modelled as one population), Ireland (IRL), Germany (DEU), and Switzerland (CHE). Weaning weight was age-adjusted to 210 days in CZE and to 200

days in the remaining countries. For further details on data recording and adjustment factors at the national level see Bonifazi *et al.* (2020b, Additional file 1, Table S3), and Interbeef National Genetic Evaluations forms (Interbeef). Phenotypes above or below three phenotypic standard deviations from the phenotypic mean of each population-sex combination were discarded to remove possible outliers. A total of 331,593 individual phenotypic records remained and were distributed across 19,051 herds. The number of phenotypes available in each population is reported in Table 5.1. DEU represented the largest population with 35% of the observations, followed by DFS (29%), IRL (21%), CHE (11%), and CZE (4%). Recorded animals were born between 1975 and 2019. Descriptive statistics per population of the available phenotypes are reported in Supplementary Table S5.1. Hereafter, even though the DFS population is composed of more than one country, for simplicity, we will refer to populations as "countries".

5.2.2 Pedigree

The pedigree was extracted from the Interbeef international pedigree database and the following quality controls were performed. The pedigree was checked for absence of pedigree loops (an animal being its own ancestor), duplicates, and conflicts between the sex reported in the international identification number and its sex as a parent (e.g. a female reported in the pedigree as a sire). Finally, using the RelaX2 software v1.73 (Strandén and Vuori 2006), the checked pedigree was pruned to include animals with phenotypes, genotypes, or both, and all their ancestors, without any limit on the number of generations retained. The final pedigree included 519,740 animals, born between 1927 and 2019, with a maximum depth of 17 generations.

Table 5.1 Summary of available data per country.

COU [a]	AWW [b]	AWW %	Herds	Year of birth (min-max)	Genotypes	% Genotypes	Genotypes with phenotypes [c]	% Genotypes with phenotypes [c]
CZE	13,892	4	172	1991-2019	1,625	9	1,207	74
DFS	96,671	29	9,548	1980-2019	-	-	-	-
IRL	68,086	21	8,218	1975-2019	11,300	64	5,237	46
DEU	117,249	35	866	1981-2019	742	4	640 [d]	86
CHE	35,695	11	247	1992-2018	3,940	22	3,516	89
Total	331,593	100	19,051	1975-2019	17,607	100	10,600	60

[a] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.
[b] AWW: Age-adjusted weaning weight.
[c] Genotypes with an associated phenotype in COU.
[d] 49 and 1 genotypes with associated phenotypes in DEU were sent from CHE and IRL, respectively.

5.2.3 Genotypes

Genotypes were available for 17,733 animals from 4 countries: CZE, DEU, IRL, and CHE. Genotypes were available from single nucleotide polymorphism (SNP) panels with different SNP densities: 467 DEU animals at 41,913 SNP (42K), 11,354 IRL animals at 52,690 SNP (52K), 1,004 CZE animals at 53,218 SNP (53K), 278 DEU animals at 54,609 SNP (55K), and 648 CZE and 3,982 CHE animals at 139,480 SNP (139K). SNP were coded as 0 and 2 for the two homozygotes, and as 1 for the heterozygote. Genotypes originating from different sources were merged using the unambiguous A/B Illumina allele coding (Illumina 2006).

5.2.3.1 Imputation to a selected panel of SNP

Genotypes sent by various countries were imputed to a selected panel of SNP as described in the following sections.

Pre-imputation genomic data edits. Only autosomal SNP with a known name and chromosome position for the *Bos Taurus* UMD 3.1 bovine genome assembly (Zimin *et al.* 2009) were retained from each SNP panel. Duplicated SNP that were in the same physical position within a genotype SNP panel were discarded. The selected panel of SNPs consisted of 147,511 autosomal SNP. Before imputation, a total of 22 genotypes (8 sent by CHE and 14 sent by IRL) were removed due to duplication, and the following edits were applied to the available genotypes.

1. SNP in common with the selected panel were retained from each country genotype; the remaining SNP were discarded. Table 5.2 reports the amount of retained SNP from each panel, together with the number of SNP in common between panels.
2. SNP with too many Mendelian conflicts were removed. A SNP was removed from the selected panel if the amount of parent-offspring genotype conflicts exceeded 1% of the parent-offspring pairs that both have their genotype called for this SNP. A total of 1,411 SNP were removed.
3. Detection of parent-offspring conflicts. A parent-offspring conflict was detected when the number of conflicting autosomal SNP between the parent-offspring pair exceeded 1% of the amount of SNP shared between the SNP panel used for the parent and the offspring (as in Table 5.2). For each parent-offspring conflict detected, the pedigree link between the parent and the offspring was removed by setting the offspring's parent to missing. 19 parent-offspring pedigree links were removed.

After the above edits, 146,100 SNP and 17,711 genotypes (out of the initial 17,733) were used for imputation.

Table 5.2 Number of autosomal SNP retained in each panel [a] (diagonal), across panels (off-diagonal), and between each panel and the selected panel of SNP (i.e. 147,511 SNP) (diagonal).

Panel [a]	42K	52K	53K	55K	139K
42K	40,367				
52K	36,519	44,181			
53K	39,907	40,283	51,250		
55K	39,465	39,779	48,744	52,352	
139K	36,270	37,665	40,550	39,990	131,584

[a] 42K = 41,913 SNP, 52K = 52,690 SNP, 53K = 53,218 SNP, 55K = 54,609 SNP, 139K = 139,480 SNP.

Imputation and quality control. All the genotypes were imputed to the selected panel using Findhap v3 (VanRaden 2013) (see Supplementary File S5.1 for applied settings). After imputation, the following quality controls were performed using Plink v1.9 (Chang *et al.* 2015): 1) call rates per SNP across animals ≥ 95%; 2) SNP with *p-value* for Hardy-Weinberg equilibrium Chi-square test higher than 10^{-15}; 3) SNP with minor allele frequency higher than 0.01; 4) call rates per animal across SNP ≥ 90%. SNP and genotypes that did not match these criteria were removed: a total of 17,688 genotypes and 57,899 SNP remained. The percentage of autosomal SNP retained after quality control relative to the original panels were 89%, 94%, 77%, 74%, and 40%, for the 42K, 52K, 53K, 55K, and 139K panel, respectively. Additionally, genotypes with < 87.5% pedigree-based breed composition for Limousin breed were removed (32 genotypes excluded), and genotypes with pedigree incompatibilities (observed from plotting genomic against pedigree-based relationships, Supplementary Figure S5.1) were also removed (41 genotypes excluded). Finally, genotypes of animals without phenotypic records, progeny and known parents were removed (8 genotypes excluded). The final number of genotypes was 17,607 and their distribution per country is reported in Table 5.1; the majority were from IRL (64% of the total), followed by CHE (22%), CZE (9%) and DEU (4%). Principal component analysis (PCA) was performed on the genomic relationship matrix of all genotypes to further investigate connectedness between countries for genotyped animals. The program calc_grm (Calus and Vandenplas 2016) was used to build the genomic relationship matrix following VanRaden (2008) method 2and to perform the PCA following Patterson *et al.* (2006).

5.2.4 Scenarios

To investigate the benefits of including genomic information in international evaluations compared to the current international pedigree-based evaluation, we implemented the following two scenarios, hereafter referred to as "international scenarios".

- Scenario $PBLUP_{INT}$: international pedigree-based Best Linear Unbiased Prediction BLUP evaluation (as described below) using all available phenotypes. This scenario represents the current Interbeef international evaluations.
- Scenario $ssSNPBLUP_{INT}$: international single-step SNPBLUP evaluation (as described below) using all available phenotypes and genotypes.

In both international scenarios, the complete international pedigree was used.

To investigate the benefits of international evaluations compared to national ones, we additionally implemented the following two scenarios, hereafter referred to as "national scenarios", which aim to represent national single trait evaluations.

- Scenario $PBLUP_{NAT}$: national pedigree-based BLUP evaluation, performed separately for each country using only national submitted phenotypes (as reported in Table 5.1).
- Scenario $ssSNPBLUP_{NAT}$: national single-step SNPBLUP evaluation, performed separately for each country using only national submitted phenotypes and genotypes (as reported in Table 5.1). DFS was excluded for this scenario as no genotypes were available.

In both national scenarios, the complete international pedigree was used for the estimation of both pedigree and single-step EBV. In each national scenario, the EBV of animals that appear in a pseudo-national pedigree were used. Pseudo-national pedigrees were obtained by pruning the international pedigree to include all national animals with phenotypes, genotypes, or both, and all their ancestors, without any limit on the number of generations retained. National scenarios used the same within-country variance components as the international scenarios. Table 5.3 presents a summary of the source of information included in both international and national scenarios, while Table 5.4 reports the number of phenotypes, genotypes and size of the pedigree in each scenario.

Table 5.3 Sources of information included (●) in implemented scenarios [a].

	National scenarios		International scenarios	
Sources of information	$PBLUP_{NAT}$	$ssSNPBLUP_{NAT}$	$PBLUP_{INT}$	$ssSNPBLUP_{INT}$
Within-country national pedigree [b]	●	●	●	●
Within-country national phenotypes	●	●	●	●
Within-country national genotypes		●		●
Across-country International pedigree			●	●
Across-country International phenotypes			●	●
Across-country International genotypes				●

[a] Scenarios: $PBLUP_{NAT}$ = Pedigree-based BLUP national, $ssSNPBLUP_{NAT}$ = single-step SNP-BLUP national, $PBLUP_{INT}$ = Pedigree-based BLUP international, $ssSNPBLUP_{INT}$ = single-step SNP-BLUP international.
[b] Within-country national pedigree: this is a pseudo-national pedigree obtained by pruning the international pedigree to include all national animals with phenotypes, genotypes, or both, and all their ancestors, without any limit on the number of generations retained.

Table 5.4 Number of phenotypes, genotypes, and size of the pedigree in whole and partial [a] evaluations of international and national scenarios [b], and number of animals in the focal group [c] for each country [d].

Evaluation	**Scenarios [b]**					
	International	**National**				
		CZE	DFS	IRL	DEU	CHE
whole						
pedigree	519,740	44,130	125,743	186,080	165,318	67,567
genotypes	17,607	1,625	-	11,300	742	3,940
phenotypes	331,593	13,892	96,671	68,086	117,249	35,695
partial [a]						
phenotypes	243,109	7,104	78,730	49,579	82,876	24,820
Focal group [c]	-	1,057	-	3,869	407	1,191

[a] *partial*: as *whole* but with phenotypes of animals born from 2014 onwards excluded.
[b] International scenarios: $PBLUP_{INT}$ (Pedigree-based BLUP international) and $ssSNPBLUP_{INT}$ (single-step SNP-BLUP international). National scenarios: $PBLUP_{NAT}$ (Pedigree-based BLUP national) and $ssSNPBLUP_{NAT}$ (single-step SNP-BLUP international).
[c] focal group: animals with phenotypes and genotypes born from 2014 onwards.
[d] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

5.2.5 Models

5.2.5.1 International pedigree-based BLUP

The current Interbeef model for breeding value estimation without genomic information is the AMACI model (Animal Model accounting for Across-Country Interaction) (Phocas *et al.* 2005), which accounts for country-specific fixed and random effects by fitting the national model of each country. The AMACI model is a multi-trait animal model with maternal effects, in which each country is modelled as a different trait:

$$\mathbf{y}_i = \mathbf{X}_i\mathbf{b}_i + \mathbf{C}_i\mathbf{r}_i + \mathbf{Z}_i\mathbf{u}_i + \mathbf{W}_i\mathbf{m}_i + \mathbf{P}_i\mathbf{p}_i + \mathbf{e}_i$$

where *i* is the country; $\mathbf{y}_i$ is the vector of observations for country *i*; $\mathbf{b}_i$ is the vector of fixed effects for country *i*; $\mathbf{r}_i$ is the vector of random environmental effects for country *i*; $\mathbf{u}_i$ is the vector of random additive genetic (direct) effects for country *i*; $\mathbf{m}_i$ is the vector of random maternal additive genetic effects for country *i*; $\mathbf{p}_i$ is the vector of random maternal permanent environmental effects (provided by the dam) for country *i*; $\mathbf{e}_i$ is the vector of random residual effects for country *i*. $\mathbf{X}_i$ and $\mathbf{C}_i$ are incidence matrices linking records to fixed, and random environmental effects, respectively. $\mathbf{Z}_i$, $\mathbf{W}_i$, and $\mathbf{P}_i$ are incidence matrices linking records to the animal, maternal genetic and maternal permanent environmental effects, respectively. National fixed and random effects for each country are reported in Supplementary Table S5.2. Random environmental effects were modelled for three countries: CZE (herd-year-season), DEU (herd-year), and CHE (herd-year). Following the national model, the maternal permanent environmental effect was not fitted for the DEU population. It was assumed that:

$$Var\begin{bmatrix}\mathbf{u}\\ \mathbf{m}\end{bmatrix} = \mathbf{G}\otimes\mathbf{A} = \begin{bmatrix}\mathbf{G}_{d,d} & \mathbf{G}_{d,m}\\ \mathbf{G}_{m,d} & \mathbf{G}_{m,m}\end{bmatrix}\otimes\mathbf{A}$$

where **u** is the vector of random direct additive genetic effects for all countries; **m** is the vector of random maternal additive genetic effects for all countries; $\mathbf{G}$ is the across-country genetic co-variance matrix of order 10x10, in which $\mathbf{G}_{d,d}$ is the across-country direct additive genetic co-variance matrix; $\mathbf{G}_{m,m}$ is the across-country maternal additive genetic co-variance matrix; and $\mathbf{G}_{d,m}$ ($\mathbf{G}_{m,d}$) contains additive genetic covariances between direct and maternal effect within countries (diagonal elements) and additive genetic covariances between direct and maternal effect across countries (off-diagonal elements); **A** is the numerator relationship matrix; $\otimes$ indicates the Kronecker product. Random environmental effects, random maternal permanent environmental effects, and residuals were fitted using block-diagonal variance matrices.

The genetic co-variance matrix with additive direct and maternal genetic effects ($\mathbf{G}$) was built as:

$$\mathbf{G} = \mathbf{S}\,\mathbf{\Phi}\,\mathbf{S}$$

where, $\mathbf{S}$ is the diagonal matrix with national genetic standard deviations for direct and maternal genetic effects, and $\mathbf{\Phi}$ is the across-country estimated genetic correlation matrix (of order 10x10 with diagonal values of 1). The across-country $\mathbf{\Phi}$ matrix was composed by combining the pairwise genetic correlations between countries used in the Interbeef January 2020 evaluation. The combined across-country $\mathbf{\Phi}$ matrix was not positive definite and a bending procedure was applied using the R package "mbend" (Nilforooshan 2020) (method "hj" (Jorjani *et al.* 2003), unweighted, with a threshold value of 10^{-4}). The resulting across-country genetic correlation matrix $\mathbf{\Phi}$ and the final $\mathbf{G}$ co-variance matrix are reported in Supplementary Table S5.3. Both within-country genetic and environmental variances were the same as those used in the national genetic evaluations of participating countries and are reported in Supplementary Table S5.4. Interbeef uses this procedure to compute the genetic co-variance matrix under the assumption that the national estimates of genetic variances are more accurate (e.g. when not all national data are submitted for international evaluations) (Bonifazi *et al.* 2021). Possible differences in trait and model definition between countries, as well as genotype-by-environment interactions, are accounted for in the AMACI model by modelling each country as a different correlated trait and with genetic correlations between countries lower than 1 (Mark 2004; Bonifazi *et al.* 2020b).

5.2.5.2 International single-step SNPBLUP

Genomic data was included in the AMACI model using a single-step Single Nucleotide Polymorphism BLUP (ssSNPBLUP) approach as proposed by Liu *et al.* (2014) and later applied by Vandenplas *et al.* (2020) to multi-trait models with maternal genetic effects. Following Vandenplas *et al.* (2020), observed allele frequencies were used to center the SNP genotypes. The estimated co-variance components used for the ssSNPBLUP evaluation were the same as the estimated co-variance components used for the pedigree-based BLUP evaluation. The proportion of variance (due to additive genetic effects) considered as due to residual polygenetic effects was assumed to be 5%. For further details on the ssSNPBLUP evaluation applied to a multi-trait model with a maternal effect, see Vandenplas *et al.* (2020).

The compatibility between pedigree and genomic information was guaranteed by fitting two $\mathbf{J}$ covariates (corresponding to the additive and maternal genetic

effects) as fixed effects in the model (Hsu *et al.* 2017). Such compatibility is required to account for allele frequencies being computed from the observed genotypes rather than from the unknown base population (Vitezica *et al.* 2011; Hsu *et al.* 2017). In short, **J** covariates model the genetic level of genotyped animals ensuring the compatibility of genomic information with that of animals without genotypes in single-step approaches. **J** covariates are computed as follows (Tribout *et al.* 2019). First, entries of **J** corresponding to genotyped animals (*g*) are set to -1, i.e. $\mathbf{J}_g = -\mathbf{1}$. Second, covariate values for non-genotyped ancestors of genotyped individuals (*anc*) are computed as $\mathbf{J}_{anc} = \mathbf{A}_{anc,g}\left(\mathbf{A}_{g,g}\right)^{-1}\mathbf{J}_g$, where $\mathbf{A}_{anc,g}$ and $\mathbf{A}_{g,g}$ are the partitions of the pedigree-relationship matrix **A** relating non-genotyped ancestors of genotyped animals and genotyped animals, and among genotyped animals, respectively. Finally, using $\mathbf{J}_g$ and $\mathbf{J}_{anc}$, ungenotyped animals that are not ancestors of genotyped animals receive a covariate value corresponding to the average of their parents' covariate. After computing the covariates for all animals, the **J** covariates were fitted in the model as follows. The **J** covariate for the additive genetic effect corresponded to that of the animal itself, while the **J** covariate for the maternal genetic effect corresponded to that of its dam. Following Fernando *et al.* (2014) and Hsu *et al.* (2017), the product of an animal's **J** covariate and the estimated regression coefficient was added to its estimated genetic value to compute the animal's genomic EBV.

5.2.6 Genetic and genomic connections among countries

In international evaluations, genetic connections among countries are mainly provided by common bulls (CB), i.e. sires having recorded offspring in two or more countries. Therefore, we quantified the number of CB and common maternal grand-sires (CMGS, i.e. maternal grand-sires with recorded grand-offspring in two or more countries). Furthermore, we quantified the number of sires and dams with recorded offspring in each national pedigree. Then, for all these groups of animals, we also quantified whether a genotype was provided by the same country or provided by other countries. This shows the potential increases in genetic connectedness among countries over national evaluations and pedigree-based international evaluation due to the inclusion of genotypes provided by other countries in a ssSNPBLUP$_{INT}$ evaluation.

5.2.7 Validation

We used the Linear Regression (LR) method (Legarra and Reverter 2018) to evaluate level and dispersion bias, as well as the population accuracy of the EBV to

investigate the benefits of using genomic and international data over current international pedigree-based evaluations and national evaluations. Hereafter, we describe the LR method and its estimators that we used, and how these were applied in the above scenarios.

5.2.7.1 Linear Regression method and estimators

The LR method (Legarra and Reverter 2018) compares EBV for a group of individuals (called "focal group") obtained in two evaluations: a partial evaluation (hereafter denoted by subscript *p*) and a whole evaluation (hereafter denoted by subscript *w*). In the partial evaluation, EBV ($\hat{\mathbf{u}}_p$) are estimated using less information, while in the whole evaluation, EBV ($\hat{\mathbf{u}}_w$) are estimated using more information. The following estimators from the LR method were calculated:

- Level bias ($\hat{\Delta}_p$): defined as the difference between the mean EBV under the evaluation *p* and *w* ($\hat{\Delta}_p = \bar{\hat{\mathbf{u}}}_p - \bar{\hat{\mathbf{u}}}_w$). The expectation of $\hat{\Delta}_p$ is 0 in absence of level bias. Level bias was expressed in national genetic standard deviations ($\hat{\sigma}_u$) for easier interpretation, i.e. as $\widehat{\Delta_p}/\hat{\sigma}_u$.
- Dispersion bias ($\hat{b}_p$): defined as the slope of the regression of $\hat{\mathbf{u}}_w$ on $\hat{\mathbf{u}}_p$ and computed as $\hat{b}_p = \frac{cov(\hat{\mathbf{u}}_w, \hat{\mathbf{u}}_p)}{var(\hat{\mathbf{u}}_p)}$. The expectation of $\hat{b}_p$ is 1 in the absence of dispersion bias, while deviations from 1 indicate dispersion bias. We considered that under-dispersion was present when $\hat{b}_p$ > 1.15 while over-dispersion was present when $\hat{b}_p$ < 0.85. We assumed that values within 15% from the optimal value of 1 were acceptable, similarly to Tsuruta *et al.* (2011) and the Interbull genomic validation test (Mäntysaari *et al.* 2010).
- Accuracy of partial EBV ($\widehat{acc}_p$): based on the covariance of $\hat{\mathbf{u}}_w$ and $\hat{\mathbf{u}}_p$ and computed as $\widehat{acc}_p = \sqrt{\frac{cov(\hat{\mathbf{u}}_w, \hat{\mathbf{u}}_p)}{(1-\bar{F})\,\hat{\sigma}_u^2}}$, where $\bar{F}$ is the mean inbreeding coefficient of the focal group computed from the international pedigree. $\widehat{acc}_p$ is an estimator of the accuracy of the partial EBV ($\hat{\mathbf{u}}_p$).
- Increases in population accuracies ($inc\_acc_{p,w}$): the ratio of accuracy $\hat{\rho}_{p,w}$ is defined as the Pearson correlation between $\hat{\mathbf{u}}_p$ and $\hat{\mathbf{u}}_w$ and computed as $\hat{\rho}_{p,w} = \frac{cov(\hat{\mathbf{u}}_w, \hat{\mathbf{u}}_p)}{\sqrt{var(\hat{\mathbf{u}}_p)var(\hat{\mathbf{u}}_w)}}$. $\hat{\rho}_{p,w}$ has expectation equal to the ratio of the accuracies in the two evaluations ($\frac{acc_p}{acc_w}$), where acc is defined as the correlation between the true breeding values (TBV) and the EBV across individuals in a population (Legarra and Reverter 2018). Consequently, $1/\hat{\rho}_{p,w}$ represents the increase in accuracy obtained with evaluation *w*

(Macedo *et al.* 2020a). We expressed the increase in accuracy relative to evaluation *p* in percentage, i.e. $inc\_acc_{p,w} = (1/\hat{\rho}_{p,w} - 1) \cdot 100\%$. For example, if $\hat{\rho}_{p,w}$ is 0.80, the relative increase in population accuracy when moving from evaluation *p* to *w* is 25%.

The LR estimates were obtained using R statistical software (R Core Team 2020) and their standard errors (SE) were obtained using bootstrapping (R "boot" package; Canty and Ripley 2020) of individuals within each focal group. A total of 10,000 bootstrap samples were generated, where each sample was obtained by randomly drawing with replacement *N* animals from the focal group, with *N* being the number of animals in the focal group.

5.2.7.2 Application of the LR method

Focal group. The LR method can be applied to any focal group, defined as a homogenous group of individuals in a population, i.e. with prediction at the time of selection based on the same sources and amount of information (Macedo *et al.* 2020b). For each country, we defined the focal group as the group of animals with both phenotype and genotypes (irrespectively of which country provided the genotype) born from 2014 onwards. Animals born from 2014 onwards are assumed to be part of the last generation of the pedigree (up to 2019), with the generation interval estimated to be $\frac{L_m+L_f}{2}$ = 4.6 years, where L_m and L_f is the average generation interval for males and females, respectively. Table 5.4 reports the number of animals in each focal group for each country.

Figure 5.1 shows a schematic overview of the application of the LR method within-scenario and between scenarios.

Within-scenario level and dispersion bias, and accuracy of partial EBV. LR estimators of level bias, dispersion bias, and accuracy of partial EBV were computed within-scenario for both the international and national scenarios. These estimators were computed by carrying out a whole and a partial evaluation for each scenario (Figure 5.1). In the whole evaluation of each scenario all available data was used, whereas in the partial evaluation phenotypes of animals born from 2014 onwards were set to missing (Figure 5.1). Pedigree and genomic data remained the same in both whole and partial evaluations. Thus, in both whole and partial evaluations, the same observed allele frequencies were used in the single-step models. Table 5.4 presents the number of phenotypes in the whole and partial evaluations of each scenario. Knowing the expected unbiased values described above, level and dispersion bias can be compared in each scenario to evaluate whether any changes

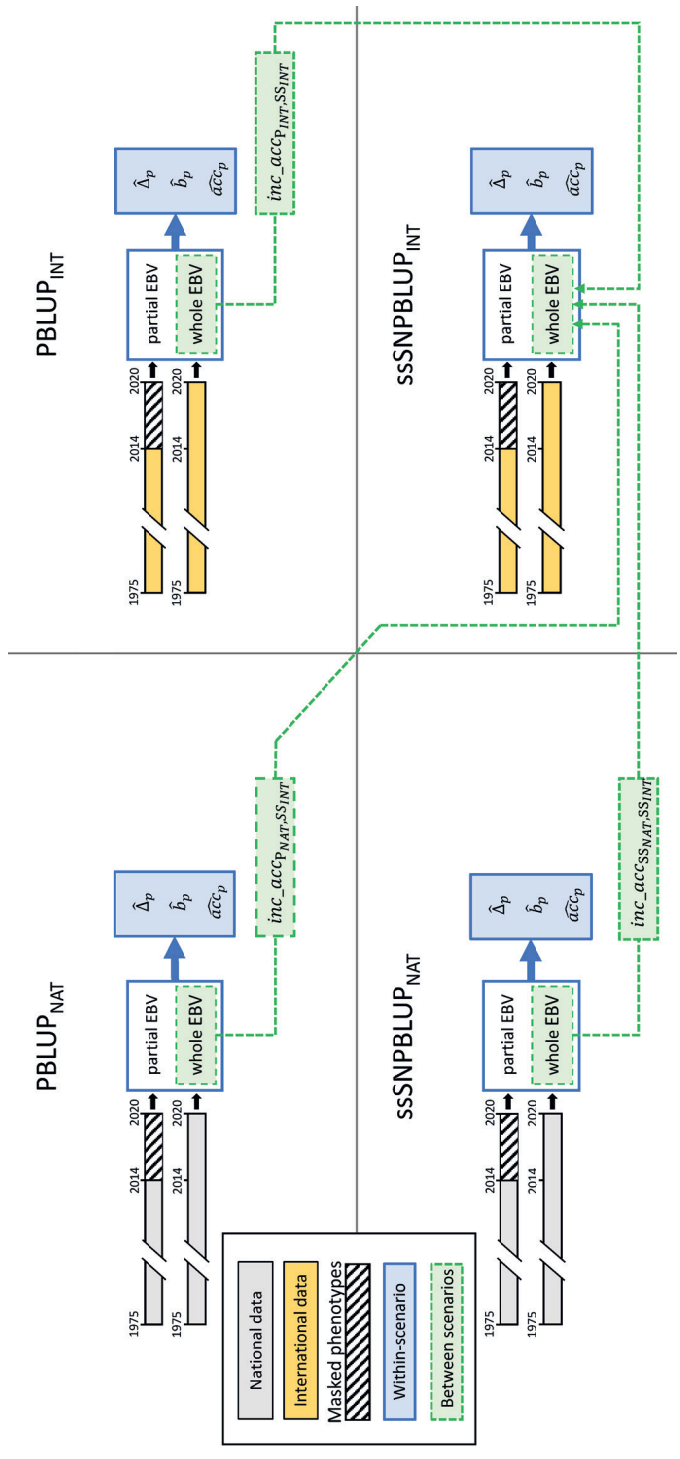

Figure 5.1 Schematic overview of the validation. Scenarios: $PBLUP_{NAT}$ = Pedigree BLUP national, $ssSNPBLUP_{NAT}$ = single-step SNP-BLUP national, $PBLUP_{INT}$ = Pedigree BLUP international, $ssSNPBLUP_{INT}$ = single-step SNP-BLUP international. For each scenario, a partial and a whole evaluation was carried out (timelines). National scenarios used only national data (grey timelines), while international scenarios used data from all countries (yellow timelines). In the partial evaluation, partial EBV were obtained by masking the phenotypes of animals born from 2014 onwards (striped timeline). In the whole evaluation, whole EBV were obtained using all phenotypes. Within-scenario estimators of level bias ($\hat{\Delta}_p$), dispersion bias ($\hat{b}_p$), and accuracy of partial EBV ($\widehat{acc}_p$) were obtained from the partial and whole EBV of each scenario (blue solid lines and boxes). Between scenarios increases in population accuracies (inc_acc) of moving towards $ssSNPBLUP_{INT}$ scenario were computed using the whole EBV of each scenario (green dotted lines and boxes).

in bias were introduced when moving from the current $PBLUP_{INT}$ scenario to $ssSNPBLUP_{INT}$ scenario and, in a similar way, whether the observed level and dispersion bias of international scenarios were already present in the national ones. Finally, the $\widehat{acc}_p$ provides an estimate of the changes of the accuracy of partial EBV in each scenario given the different sources of information used.

Increases in population accuracies between scenarios. To evaluate the benefits of using genomic information at the international level we compared the increases in population accuracies ($inc\_acc_{p,w}$) obtained when moving from either $PBLUP_{NAT}$, $ssSNPBLUP_{NAT}$, or $PBLUP_{INT}$ scenarios to $ssSNPBLUP_{INT}$ scenario (Figure 5.1). Following Legarra and Reverter (2018), adding genotypes to pedigree-based models can be considered as additional information. Similarly, national scenarios can be viewed as evaluations with partial information, and international scenarios as evaluations with additional information which is represented by phenotypes and genotypes of relatives recorded in another country. The $inc\_acc_{p,w}$ when moving towards $ssSNPBLUP_{INT}$ were computed using the EBV from the whole evaluations ($\hat{\mathbf{u}}_w$) of each scenario (Figure 5.1). Thus, $inc\_acc_{\mathrm{P}_{NAT},\mathrm{SS}_{INT}}$ estimates the increase in population accuracy from $PBLUP_{NAT}$ towards $ssSNPBLUP_{INT}$; $inc\_acc_{\mathrm{SS}_{NAT},\mathrm{SS}_{INT}}$ estimates the increase from $ssSNPBLUP_{NAT}$ to $ssSNPBLUP_{INT}$; and $inc\_acc_{\mathrm{P}_{INT},\mathrm{SS}_{INT}}$ estimates the increase from $PBLUP_{INT}$ to $ssSNPBLUP_{INT}$. Differences in observed allele frequencies that could be present between $ssSNPBLUP_{NAT}$ and $ssSNPBLUP_{INT}$ whole evaluations are accounted for by modelling the $\mathbf{J}$ covariates (Hsu *et al.* 2017).

5.2.8 Software and settings

EBV were computed using MiXBLUP software (ten Napel *et al.* 2020) (instruction files for $PBLUP_{INT}$ and $ssSNPBLUP_{INT}$ are reported in Supplementary File S5.2 and Supplementary File S5.3, respectively). The convergence criterion for the Preconditioned Conjugate Gradient (PCG) algorithm for iteratively solving the mixed model equations was defined as the square root of the relative difference between solutions of two consecutive PCG iterations and was set to 10^{-5}. To ensure that all EBV were expressed against the same base, EBV were scaled relative to a base generation common to all scenarios, which was defined in each country as the group of national animals born in the year 2002 with an available AWW phenotype. All validation results were computed using these scaled EBV.

5.3 Results

Hereafter we first present the results on genetic and genomic connections among countries, followed by the LR estimates computed within-scenario for ssSNPBLUP$_{INT}$, and the differences with those estimates computed for the other scenarios implemented. Finally, we present the results on the increases in population accuracies between scenarios.

5.3.1 Genetic and genomic connections among countries

The distribution of genotyped animals varied between countries. Most of the genotyped animals were born after the year 2000, with an overall increasing genotyping trend during more recent years (Figure 5.2). In particular, in CZE and DEU, 88% and 60% of the genotyped animals were born from 2014 onwards. Overall, genotyped animals were 51.5% males and 48.5% females. The sex ratio of the genotyped animals differed between countries, with 45%, 31%, 77%, and 95% of the genotypes being males in CZE, IRL, DEU, and CHE, respectively. Finally, PCA shows that the populations were genetically close and no specific population clusters were observed (Figure 5.3).

The number of genotyped sires ranged from 57 for DFS to 1,166 for IRL, and the number of genotyped dams from 68 for DEU to 4,190 for IRL with DFS having no genotyped dams (Table 5.5). In IRL, DEU and CHE the majority of genotyped sires in the national pedigree were genotyped by the country itself. Nonetheless, the number of sires with a genotype provided by another country ranged from 24 of IRL to 110 of CZE (equal to 83% of the total genotyped sires in CZE). Interestingly, DFS, which did not provide genotypes, was associated with 57 genotyped sires, thanks to genotypes provided by other countries. The proportion of genotyped sires that had recorded offspring was 57% for CZE, 79% for DFS and >90% for IRL, DEU and CHE. Except for IRL, genotyped sires had a higher average number of recorded offspring compared to that of all sires with records. The number of genotyped sires with over 100 recorded offspring in at least 5 herds (which provides an indication of sires that may be used in artificial insemination) was small in all countries (< 15 sires). Finally, almost all genotyped dams in the national pedigree were genotyped by the country itself and only a small number was genotyped by another country (2, 8 and 3 for CZE, DEU and CHE, respectively).

We quantified the total number of CB and CMGS that had recorded offspring in two or more countries. In total, there were 422 CB, of which 106 were genotyped, and 642 CMGS of which 72 were genotyped. The average number of CB between countries was 95, ranging between 38 of CZE-CHE to 155 of DFS-DEU (Table 5.6). On

average across pairs of countries, 33 CB were also genotyped, ranging from 20 of CZE-CHE to 49 of IRL-DEU. The average number of CMGS between countries was 124 ranging from 58 of DFS-CHE and IRL-CHE to 235 of DEU-CHE (Table 5.6). On average across pairs of countries, 19 CMGS were genotyped, ranging from 11 of CZE-CHE to 36 of DEU-CHE.

Table 5.5 Overview of recorded offspring per sires and dams, and number of genotyped sires and dams in each national pedigree [a].

	CZE	DFS	IRL	DEU	CHE
Sires					
with recorded offspring	720	4,591	9,341	5,283	1,892
average recorded offspring	19.3	21.1	7.3	22.2	18.9
≥ 20 recorded offspring	220	1,399	600	1,855	518
≥ 100 recorded offspring	15	162	59	163	63
≥ 100 recorded offspring (in at least 5 herds)	11	157	57	43	38
Sires with genotype					
amount	132	57	1,166	368	956
genotyped by the country itself	22	-	1,142	273	863
genotyped by another country	110	57	24	95	93
with recorded offspring	75	45	1,100	350	856
average recorded offspring	28.1	30.7	6.3	48.0	22.1
≥ 20 recorded offspring	34	23	51	273	295
≥ 100 recorded offspring	4	4	7	35	32
≥ 100 recorded offspring (in at least 5 herds)	4	4	7	10	14
Dams					
with recorded offspring	4,457	30,212	47,334	35,340	9,785
average recorded offspring	3.1	3.2	1.4	3.3	3.6
Dams with genotype					
amount	375	-	4,190	68	185
with recorded offspring	355	-	3,311	58	181
average recorded offspring	2.9	-	1.4	2.9	6.5

[a] CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

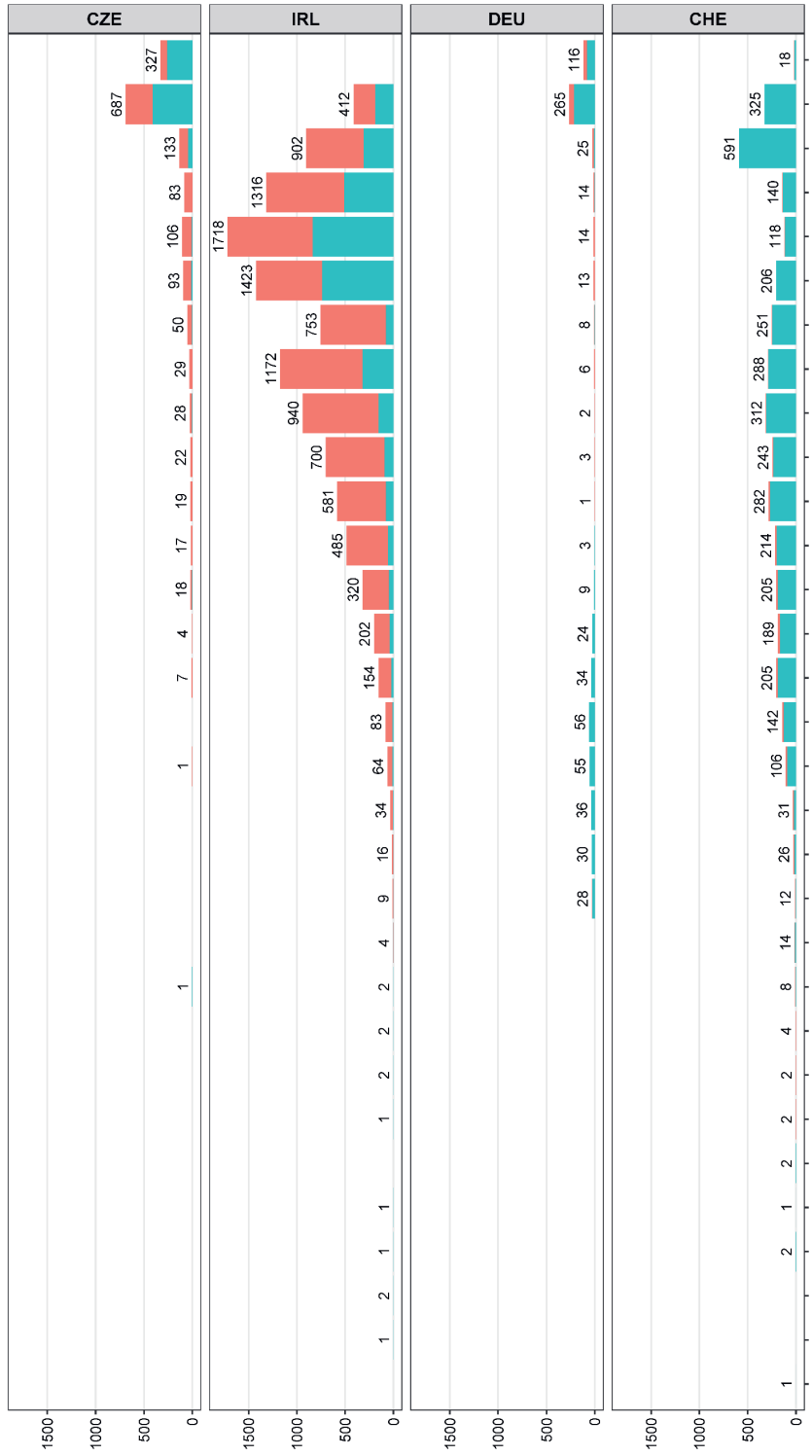

Figure 5.2 Number of genotyped animals (on the y-axis) per year of birth (on the x-axis) and sex (red = females, blue = males) in each country. Country: CZE = Czech Republic, IRL = Ireland, DEU = Germany, CHE = Switzerland.

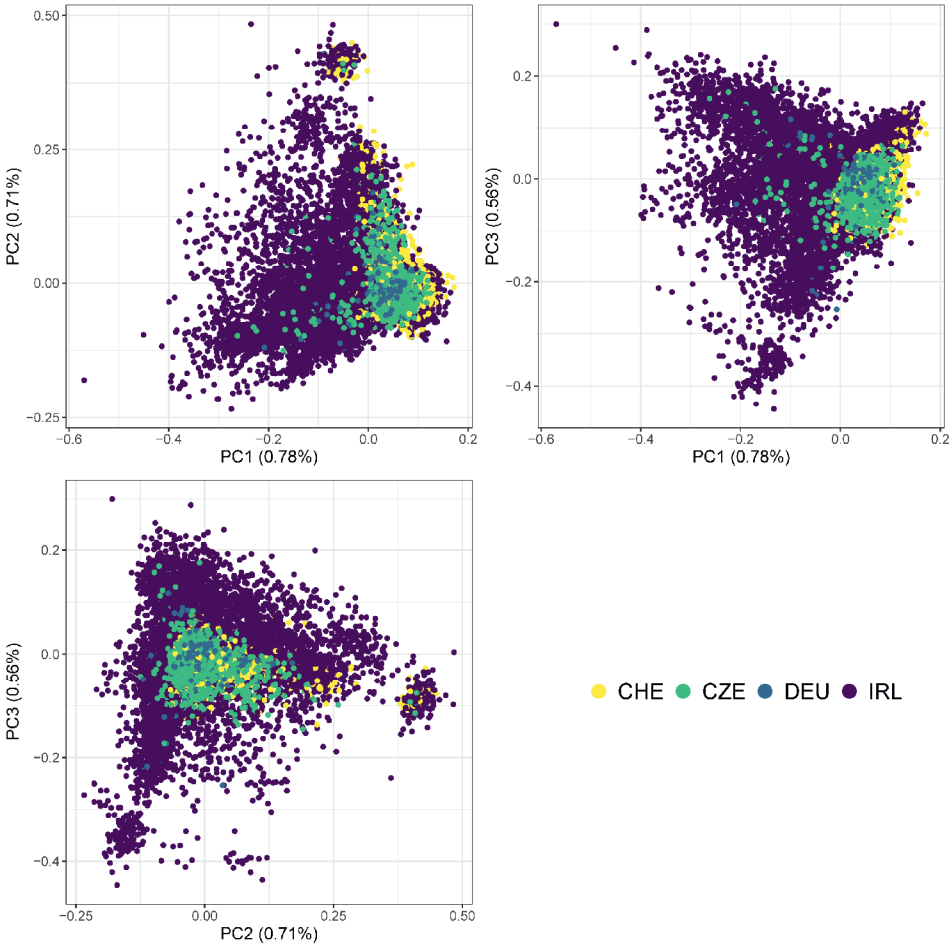

Figure 5.3 Plot of first three principal components (PC) and percentage of explained variance (within brackets) of the genomic relationship matrix. Colours indicate the country sending the genotype. Country: CHE = Switzerland, CZE = Czech Republic, DEU = Germany, IRL = Ireland.

Table 5.6 Number of (genotyped) Common Bulls (CB) and (genotyped) Common Maternal Grand-Sires (CMGS) connecting each pair of countries [a].

Pair of countries [a]		CB		CMGS	
		n	with genotype	n	with genotype
CZE	DFS	77	24	92	17
CZE	IRL	87	43	82	16
CZE	DEU	133	38	189	30
CZE	CHE	38	20	72	11
DFS	IRL	102	32	114	15
DFS	DEU	155	37	190	21
DFS	CHE	40	21	58	13
IRL	DEU	142	49	149	22
IRL	CHE	41	22	58	12
DEU	CHE	131	47	235	36

[a] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland. Details on countries sending the genotype for CB or CMGS are reported in Supplementary Table S5.8.

5.3.2 Within-scenario bias and accuracy of EBV

Bias and accuracy of EBV were calculated comparing partial and whole EBV of each scenario. Overall, ssSNPBLUP$_{INT}$ showed negative level bias ($\hat{\Delta}_p$) for direct EBV and small $\hat{\Delta}_p$ for maternal EBV (Table 5.7). For direct EBV, the average $\hat{\Delta}_p$ across countries was -0.17 genetic standard deviations (GSD), ranging from -0.22 GSD of CZE to -0.10 GSD of IRL. For maternal EBV, the average $\hat{\Delta}_p$ across countries was 0.02 GSD, ranging from -0.02 GSD of DEU to 0.06 GSD of CHE. Overall, direct EBV were over-dispersed in all countries except for IRL: $\hat{b}_p$ was 0.83 on average across countries, ranging from 0.79 of CZE to 0.87 of IRL. For maternal EBV, $\hat{b}_p$ was 0.88 on average across countries and showed over-dispersion only for DEU, while other countries showed over-dispersion but remained within the 0.85-1.15 interval. The average $\widehat{acc}_p$ across countries for ssSNPBLUP$_{INT}$ was 0.36 (ranging from 0.35 of CZE, IRL and DEU to 0.40 of CHE) and 0.25 (ranging from 0.23 of CZE and DEU to 0.29 of CHE), for direct and maternal EBV, respectively.

Overall, ssSNPBLUP$_{INT}$ performed better than PBLUP$_{NAT}$ based on level bias, dispersion bias, and accuracy. Indeed, for direct EBV, ssSNPBLUP$_{INT}$ showed less level bias and less over-dispersion (albeit not statistically significant) compared to PBLUP$_{NAT,}$ with values of $\hat{\Delta}_p$ improving by 0.03 GSD on average across countries, and $\hat{b}_p$ being closer to 1 in all countries (except for IRL) (Table 5.7). For maternal EBV,

ssSNPBLUP$_{INT}$ showed similar level bias compared to PBLUP$_{NAT}$: difference in $\hat{\Delta}_p$ of 0.00 GSD on average across countries. However, maternal EBV were more over-dispersed in ssSNPBLUP$_{INT}$ compared to PBLUP$_{NAT}$: average difference in $\hat{b}_p$ of -0.07. In CZE and CHE $\hat{b}_p$ went from small under-dispersion of PBLUP$_{NAT}$ to small over-dispersion of ssSNPBLUP$_{INT}$. Finally, in all countries the accuracy of partial EBV was greater in ssSNPBLUP$_{INT}$ than in PBLUP$_{NAT}$: on average across countries, the difference in $\widehat{acc}_p$ between scenarios was 0.10 and 0.06 for direct and maternal EBV, respectively.

Overall, on average across countries, ssSNPBLUP$_{INT}$ showed similar level bias and dispersion bias for both direct and maternal EBV compared to ssSNPBLUP$_{NAT}$, but ssSNPBLUP$_{INT}$ did have a larger accuracy (Table 5.7). In all countries, the accuracy of partial EBV was greater with ssSNPBLUP$_{INT}$ compared to ssSNPBLUP$_{NAT}$: on average across countries, the difference in $\widehat{acc}_p$ between scenarios was 0.06 and 0.03 for direct and maternal EBV, respectively.

Overall, on average across countries, ssSNPBLUP$_{INT}$ resulted in similar or less level bias, similar dispersion bias, and greater accuracy than PBLUP$_{INT}$. Indeed, for direct EBV, ssSNPBLUP$_{INT}$ showed similar or less level bias compared to PBLUP$_{INT}$: $\hat{\Delta}_p$ improved by 0.02 GSD on average across countries, with the largest improvement observed for DEU (0.06 GSD) (Table 5.7). For maternal EBV, ssSNPBLUP$_{INT}$ showed similar level bias as PBLUP$_{INT}$. In all countries except for IRL, direct EBV showed less over-dispersion in ssSNPBLUP$_{INT}$ compared to PBLUP$_{INT}$ with values of $\hat{b}_p$ being closer to 1. In IRL more over-dispersion of direct EBV was observed in ssSNPBLUP$_{INT}$ compared to PBLUP$_{INT}$ although $\hat{b}_p$ remained within the 0.85-1.15 interval. Maternal EBV showed similar or more over-dispersion in ssSNPBLUP$_{INT}$ compared to PBLUP$_{INT}$. In CZE, $\hat{b}_p$ for maternal EBV went from small under-dispersion of PBLUP$_{INT}$ to small over-dispersion of ssSNPBLUP$_{INT}$. Finally, in all countries, the accuracy of partial EBV was greater with ssSNPBLUP$_{INT}$ compared to PBLUP$_{INT}$: on average across countries, the difference in $\widehat{acc}_p$ between scenarios was 0.08 and 0.05 for direct and maternal EBV, respectively.

5.3.3 Increases in population accuracies between scenarios

Increases in population accuracies (inc_acc) were observed in all countries when moving from any scenario towards ssSNPBLUP$_{INT}$ scenario (Table 5.8). When moving from PBLUP$_{NAT}$ to ssSNPBLUP$_{INT}$, $inc\_acc_{P_{NAT},SS_{INT}}$ was 14.9% (ranging from 9.2% of CZE to 27.2% of IRL) and 33.0% (ranging from 19.0% of DEU to 47.8% of IRL) on average across countries for direct and maternal EBV, respectively. When moving from ssSNPBLUP$_{NAT}$ to ssSNPBLUP$_{INT}$, $inc\_acc_{SS_{NAT},SS_{INT}}$ was 6.2% (ranging from

Table 5.7 Level bias ($\hat{\Delta}_p$) [a], dispersion bias ($\hat{b}_p$) and accuracy of partial EBV ($\widehat{acc}_p$) of direct and maternal EBV for the focal group [b], in each scenario [c] and for each country [d].

COU [d]	Direct				Maternal			
	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	ssSNPBLUP INT	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	ssSNPBLUP INT
$\hat{\Delta}_p$ (GSD) [a]								
CZE	-0.25	-0.23	-0.23	-0.22	-0.01	-0.03	0.00	0.01
IRL	-0.08	-0.10	-0.10	-0.10	-0.02	0.01	-0.01	0.02
DEU	-0.19	-0.10	-0.21	-0.15	-0.06	-0.02	-0.05	-0.02
CHE	-0.28	-0.27	-0.23	-0.21	0.04	0.03	0.04	0.06
Range of SE [e]	0.01-0.02	0.01-0.02	0.01-0.02	0.01-0.02	0.00-0.01	0.00-0.01	0.00-0.01	0.00-0.01
$\hat{b}_p$								
CZE	0.72	0.76	0.65	0.79	1.04	0.94	1.06	0.96
IRL	0.96	0.87	1.00	0.87	0.92	0.87	0.91	0.85
DEU	0.79	0.85	0.77	0.82	0.78	0.79	0.79	0.79
CHE	0.80	0.79	0.80	0.82	1.06	0.98	0.99	0.93
Range of SE [e]	0.02-0.07	0.02-0.06	0.02-0.06	0.02-0.04	0.02-0.07	0.02-0.07	0.02-0.07	0.02-0.05
$\widehat{acc}_p$								
CZE	0.23	0.25	0.25	0.35	0.17	0.17	0.19	0.23
IRL	0.23	0.29	0.26	0.35	0.17	0.22	0.18	0.24
DEU	0.26	0.31	0.27	0.35	0.18	0.20	0.18	0.23
CHE	0.34	0.38	0.35	0.40	0.22	0.27	0.24	0.29
Range of SE [e]	0.00-0.02	0.00-0.02	0.00-0.02	0.01-0.02	0.00-0.01	0.00-0.01	0.00-0.01	0.00-0.01

[a] Level bias is expressed in genetic standard deviations (GSD). [b] focal group: animals with phenotypes and genotypes born from 2014 onwards. [c] Scenario: $PBLUP_{NAT}$ = Pedigree-based BLUP national, $ssSNPBLUP_{NAT}$ = single-step SNP-BLUP national, $PBLUP_{INT}$ = Pedigree-based BLUP international, $ssSNPBLUP_{INT}$ = single-step SNP-BLUP international. [d] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland. [e] Range of SE: minimum and maximum Standard Error across countries in each scenario (all standard errors are reported in Supplementary Table S5.7).

Table 5.8 Increases in population accuracy (inc_acc) of moving from each scenario to ssSNPBLUP$_{INT}$ [a, b] for direct and maternal EBV in the focal group [c] for each country [d].

COU [d]	Direct			Maternal		
	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT
CZE	9.2	5.6	8.5	32.8	25.6	19.5
IRL	27.2	6.8	25.0	47.8	14.1	41.8
DEU	13.1	9.3	11.4	19.0	12.4	16.5
CHE	10.3	3.4	9.8	32.3	14.9	25.3
Range of SE [e]	0.6-1.5	0.2-1.0	0.6-1.3	2.0-2.8	0.6-2.1	1.5-2.1

[a] Increases in population accuracies are expressed in % relative to each scenario whole EBV.
[b] Scenarios: PBLUP$_{NAT}$ = Pedigree-based BLUP national, ssSNPBLUP$_{NAT}$ = single-step SNP-BLUP national, PBLUP$_{INT}$ = Pedigree-based BLUP international, ssSNPBLUP$_{INT}$ = single-step SNP-BLUP international.
[c] focal group: animals with phenotypes and genotypes born from 2014 onwards.
[d] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.
[e] Range of SE: minimum and maximum Standard Error across countries in each scenario.

3.4% of CHE to 9.3% of DEU) and 16.8% (ranging from 12.4% of DEU to 25.6% of CZE) on average across countries for direct and maternal EBV, respectively. Finally, when moving from the current PBLUP$_{INT}$ to ssSNPBLUP$_{INT}$, $inc\_acc_{P_{INT},SS_{INT}}$ was 13.7% (ranging from 8.5% of CZE to 25.0% of IRL) and 25.8% (ranging from 16.5% of DEU to 41.8% of IRL) on average across countries for direct and maternal EBV, respectively.

5.4 Discussion

In this study, we developed an international single-step SNPBLUP genomic evaluation for beef cattle and investigated the benefits of including genomic data in the current pedigree-based international evaluations. Hereafter, we first discuss the possible benefits of single-step evaluations to increase the existing pedigree genetic connectedness among countries. Then, we discuss the increases in accuracies of EBV due to the inclusion of genomic data in international evaluations, followed by its impact on level and dispersion bias compared to both current pedigree-based international evaluations and national evaluations. Finally, we discuss the possible implications of this study for beef cattle international evaluations.

5.4.1 Connectedness among countries

In international evaluations straightforward measures are used to quantify genetic connectedness between countries, such as the number of CB and CMGS (Jorjani 1999; Pabiou *et al.* 2014; Bonifazi *et al.* 2020b). Table 5.6 shows that an average of 39% and 17% of CB and CMGS among country pairs were also genotyped. Additionally, Table 5.5 shows an increase of genotyped sires within each country when combining genomic data in international genomic evaluations, especially for DFS and CZE that have no or small amount of genotyped sires at the national level. Genomic data can help to reveal existing relationships between animals that would otherwise appear as disconnected according to pedigree data, but also by refining relationships that are observed in the pedigree based on the captured Mendelian sampling (Pszczola *et al.* 2012; Yu *et al.* 2017). Supplementary Figure S5.1 shows that genomic data help to differentiate existing pedigree relationships among genotyped animals, which are also extended to ungenotyped animals in single-step approaches (Legarra *et al.* 2014). Sophisticated measures of genetic connectedness require the inverse of the left-hand side of mixed models equations, making them computationally very demanding and not applicable to large pedigrees. Nonetheless, it is expected that genotyping CB and CMGS and using genomic data in international evaluations would increase connectedness between countries. For instance, Yu *et al.* (2017) showed that genomic data increase connectedness between management units (e.g. herds) compared to pedigree data.

5.4.2 Benefits of international single-step genomic evaluations

We used the LR method to validate results within and between scenarios as it presents several advantages compared to other validation methods. The LR method can be applied to multi-trait models and traits where the animals' phenotype is not available for all environments (Legarra and Reverter 2018; Chu *et al.* 2019; Macedo *et al.* 2020a). One of the main advantages of the LR method is that it does not require pre-correction of phenotypes, which are particularly difficult to define for maternally affected traits (Lourenco *et al.* 2015), allowing for validation of both direct and maternal effects (Legarra and Reverter 2018; Macedo *et al.* 2020a).

Our results showed that $ssSNPBLUP_{INT}$ improved accuracies relative to $PBLUP_{INT}$, in line with the results of VanRaden and Sullivan (2010) and Jorjani *et al.* (2011), and also relative to $ssSNPBLUP_{NAT}$, in line with the results of Lund *et al.* (2011). Even for countries with the largest amount of genotyped animals with phenotypes at the national level, such as IRL and CHE in this study, we observed increases in population accuracies (Table 5.8). Increases in population accuracies for IRL and CHE may be related to two factors: 1) a larger multi-country reference population compared to

national ones (e.g. in international single-step evaluations the number of genotyped animals with phenotypes for IRL increased by 102% relative to national evaluations; Table 5.1), and 2) the inclusion via single-step international evaluations of phenotypic information on relatives recorded in other countries and connected via sires, CB and CMGS (Table 5.5 and Table 5.6). The observed benefits of sharing genotypes across countries were also confirmed by the accuracy of partial EBV (which, unlike inc_acc, does not consider the phenotypes of animals in the focal group) with values of $\widehat{acc}_p$ being the highest under ssSNPBLUP$_{INT}$: on average across countries 0.36 and 0.25, for direct and maternal EBV, respectively (Table 5.7). Overall, $\widehat{acc}_p$ of ssSNPBLUP$_{INT}$ were closer to those of ssSNPBLUP$_{NAT}$ than to those of PBLUP$_{INT}$, showing that genomic information should be considered in international evaluations.

Genomic information is expected to increase the accuracy for genotyped animals due to increases in the variation in relationships between animals and by better capturing variation in Mendelian sampling. Using a single-step approach, the benefits of genomic information are also propagated to ungenotyped animals (Legarra *et al.* 2014). This was reflected in higher $\widehat{acc}_p$ under ssSNPBLUP$_{INT}$ compared to other scenarios, and in increases in population accuracies (albeit small) when moving towards ssSNPBLUP$_{INT}$ also for animals with phenotypes but no genotypes born from 2014 onwards (Supplementary Table S5.5 and Supplementary Table S5.6). The increases in accuracies for DFS, which did not provide genotypes, shows the potential benefits of international single-step evaluations for countries with no genomic data available yet at the national level.

To our knowledge, this is the first published study that investigates bias in Interbeef evaluations. We evaluated whether moving towards genomic international models may introduce any level and dispersion bias compared to either international pedigree-based evaluation or national evaluations. Overall, ssSNPBLUP$_{INT}$ had a similar level and dispersion bias compared to either PBLUP$_{INT}$ or national scenarios. Across countries and scenarios, direct EBV showed negative level bias and over-dispersion ($\hat{b}_p$ < 0.85) (except for IRL), while maternal EBV showed level bias close to 0 GSD and dispersion within the 0.85-1.15 interval (except for DEU). As expected, the largest SE of the LR estimates were observed for DEU having the smallest number of animals for the focal group among countries (Supplementary Table S5.7). Across scenarios, IRL showed the smallest level and dispersion bias compared to other countries; this result could be related to IRL having the highest amount of genotypes among countries. These results also underline the importance of formal validation procedures for current Interbeef international evaluations. We further investigated possible genetic level differences between ssSNPBLUP$_{INT}$ and PBLUP$_{INT}$ using genetic

trends of sires with at least 10 recorded offspring in a country (Supplementary Figure S5.2). If selective genotyping is present, genetic trends between ssSNPBLUP$_{INT}$ and PBLUP$_{INT}$ can differ (Abdollahi-Arpanahi *et al.* 2021b). Overall, genetic trends overlapped between ssSNPBLUP$_{INT}$ and PBLUP$_{INT}$ for all countries except for a systematic difference in DEU for direct effects, and in CHE for both direct and maternal effects. CHE had almost 55% of the sires with at least 10 recorded offspring genotyped, while other countries ranged from about 1% (DFS) to 15% (CZE). Differences for DEU and CHE could be related to selective genotyping. The slightly lower trend in ssSNPBLUP$_{INT}$ compared to PBLUP$_{INT}$ in the last year for countries like IRL is most likely related to the low number of sires and their low amount of information. We expect that with more data becoming available genetic trends will overlap as observed in the previous years. Differences in genetic trends between pedigree-based and single-step evaluations were already present for national scenarios and reduced for international scenarios (results not shown). Overall, the results of this study suggest that national evaluations' level and dispersion bias will remain similar or slightly reduce with international single-step genomic evaluations.

So far, only few national studies reported LR estimates in beef cattle, in particular for weaning weight. Overall, we observed improvements in $\widehat{acc}_p$ when including genomic information in national scenarios. On average across countries, the $\widehat{acc}_p$ of PBLUP$_{NAT}$ scenarios was 0.26 (ranging from 0.23 of CZE to 0.34 of CHE) for direct EBV and 0.19 for maternal EBV (ranging from 0.17 of CZE to 0.22 of CHE). In ssSNPBLUP$_{NAT}$, $\widehat{acc}_p$ was on average 0.31 for direct EBV (ranging from 0.25 of CZE to 0.38 of CHE) and 0.21 for maternal EBV (ranging from 0.17 of CZE to 0.27 of CHE) (Table 5.7). In Brazilian Angus, Campos *et al.* (2022) conducted pedigree and genomic evaluations for growth traits using ssGBLUP (Christensen and Lund 2010; Aguilar *et al.* 2010) with about 1,600 genotyped animals. For weaning weight gain, the average $\widehat{acc}_p$ across validation groups was 0.39 for direct effect and 0.30 for total maternal (weaning weight and tick count) for PBLUP, and 0.45 for direct effect and 0.37 for total maternal for ssGBLUP. Our values are in agreement to those of these authors for countries like CHE and smaller for other countries like CZE. Differences with our study could be due to the usage of a multi-variate model in combination with other growth traits (birth weight and post-weaning weight) in Campos *et al.* (2022) as well as differences in population structure and trait definition. Recently, Jang *et al.* (2022) reported LR estimates for genomic predictions of weaning weight in American Angus using a large reference population of about 180,000 genotyped animals and over 2,4 million weaning weight phenotypes. Using ssGBLUP with similar modelling as the one we used ("M1" in their study), they found high values of $\widehat{acc}_p$ of 0.72 for direct EBV and 0.62 for maternal EBV. These results confirm that using large reference

populations enables to achieve high weaning weight accuracies for both direct and maternal EBV in young animals. In contrast with the results of our study, both Jang *et al.* (2022) and Campos *et al.* (2022) reported values of dispersion for weaning weight mostly within the 0.85-1.15 interval, except for pedigree evaluations of total maternal in Campos *et al.* (2022).

The negative level bias for direct EBV and its associated over-dispersion may be related to selective genotyping for animals composing the focal group (Vitezica *et al.* 2011; Hsu *et al.* 2017). Negative values of $\hat{\Delta}_p$ indicate a higher mean EBV under whole evaluations compared to partial evaluations. This could be related to the small genotyping rate of animals born from 2014 onwards, being 15%, 17%, 1% and 10% in CZE, IRL, DEU and CHE, respectively. Thus, genotyped animals used in the focal group could be a group of selected individuals with higher EBV for weaning weight compared to those born in the same generation and with no genotype. When the focal group was composed of animals born from 2014 onwards with phenotypes but no genotypes, level and dispersion bias were on average closer to the unbiased values of 0 and 1, respectively (Supplementary Table S5.5). We further investigated the possible presence of selective genotyping using countries' realized Mendelian sampling (RMS) trends under both $PBLUP_{INT}$ and $ssSNPBLUP_{INT}$ scenarios (Supplementary File S5.4) for genotyped animals (with or without phenotypes) and ungenotyped animals (animals with phenotype in the country). Overall, the RMS trends of genotyped and ungenotyped animals of $ssSNPBLUP_{INT}$ followed those of $PBLUP_{INT}$ (Supplementary File S5.4). Following Abdollahi-Arpanahi *et al.* (2021b), the expectation of RMS is 0 when genotyped animals are a random sample of the population. Instead, RMS deviates from 0 with selective genotyping, i.e. when genotyped animals are selected based on information collected on the animal itself or its progeny. In this study, the RMS trends showed that genotyped animals had non-zero and often positive RMS compared to ungenotyped animals generally having zero RMS, except for IRL trends (Supplementary, File S5.4). Overall, in IRL, genotyped animals showed almost no deviation in RMS trends, which suggests absence of selective genotyping. This could be explained by IRL having a large amount of genotyped animals and that the majority of them were females. Thus, results on the RMS trends seem to confirm the presence of selective genotyping in all countries except for IRL, and indeed suggest that the observed level and dispersion bias is due to selective genotyping.

5.4.3 Implications

All countries in this study, except for IRL, do not have a national genomic evaluation in place for Limousin AWW and therefore scenario $PBLUP_{NAT}$ represents their current national evaluations. Pseudo-national scenarios used a subset of the international pedigree, which likely is more complete than the pedigree used in national evaluations. Using this more complete pedigree, our accuracies for national scenarios may slightly overestimate accuracies for equivalent current single-trait national evaluations. Another possible difference between pseudo-national scenarios and national evaluations is that the latter may use genetic groups to model missing pedigree information by fitting unknown parent groups (UPG; Quaas 1988; Westell *et al.* 1988). Similarly to the current Interbeef pedigree-based international evaluations, both international and national scenarios in this study did not use genetic groups. Further research could investigate how UPG or metafounders (Legarra *et al.* 2015) should optimally be defined to be used in (inter)national evaluations and whether or not fitting them in PBLUP or ssSNPBLUP helps to reduce the observed level and dispersion bias (Masuda *et al.* 2022).

The increasing genotyping trend observed at the national level (Figure 5.2) implies the need for the current Interbeef evaluation to consider also genomic data in the near future. In this study, we showed the feasibility of implementing a single-step evaluation at the international level using Limousin weaning weight data. The proposed international single-step evaluation approach is feasible also for other traits and breeds currently evaluated, i.e. Limousin, Charolais, Angus, Hereford and Simmental, provided that genotypes are available. The AWW is a representative trait for those currently evaluated traits in Interbeef, which are all maternally affected traits, i.e. weight traits (composed by AWW; Pabiou *et al.* 2014) and calving traits (composed by calving ease and birth weight; Vesela *et al.* 2019). Thus, we expect that similar benefits of implementing a single-step international evaluation could be observed for other breeds and traits, with larger benefits expected for traits with low heritability (Goddard 2009; Durr and Philipsson 2012). Moreover, we expect that increases in accuracies for $ssSNPBLUP_{INT}$ could be further improved by including more genomic data, e.g. by increasing the number of participating countries. The ssSNPBLUP approach used in this study showed to be applicable to large amounts of data while being computationally attractive (Vandenplas *et al.* 2019a, 2020). In this study, $ssSNPBLUP_{INT}$ took 568 iterations and 23 minutes to converge using 10 CPUs Intel Xeon E5-1650v4 (3.60 GHz) and 4 GB of RAM, and an appropriate two-level PCG method (Vandenplas *et al.* 2019b).

The proposed international single-step approach requires sharing genotypes and phenotypes at the international level, which is subject to some limitations. For

instance, in the Genomic MACE Service released by Interbull Centre for the Holstein breed, the international genomic EBV of young bulls are computed from national genomic EBV provided by participating countries (VanRaden and Sullivan 2010) to avoid sharing raw data. To overcome such limitations and sensitivities around genotype data exchange, platforms have been developed to efficiently and safely share genotypes at the international level, e.g. GenoEX (Durr *et al.* 2014). When sharing genotypes is not possible due to political or privacy limitations, an approximate single-step method could be used in which SNP-effects and summary statistics are shared across countries and used jointly with raw pedigree and phenotype. Similar approaches have been proposed for international dairy cattle evaluations (e.g. Vandenplas *et al.* 2018; Goddard *et al.* 2019; Fragomeni *et al.* 2019).

5.5 Conclusions

We developed an international single-step SNPBLUP genomic evaluation for beef cattle using Limousin weaning weight data and investigated the benefits of using genomic data compared to current pedigree-based evaluations. Combining multi-country genomic data in a single-step approach has the potential to increase existing pedigree-based genetic connectedness among countries via genotyped animals. Single-step international evaluations showed to increase accuracies of EBV compared to current pedigree-based international evaluations for both large and small countries as well as for countries with different amounts of genotypes at the national level. In this study, the increase in population accuracy when moving from current pedigree-based international evaluations to single-step genomic evaluation was on average across countries 13.7% and 25.8% for direct and maternal EBV, respectively. Moreover, increases in accuracies were observed for non-genotyped animals and countries without genotypes at the national level. Level and dispersion bias of international single-step genomic evaluations were similar or slightly reduced compared to current pedigree-based international and national (genomic) evaluations. The proposed international single-step approach can be applied to other traits and breeds allowing countries to improve the accuracies of their genetic evaluations.

5.6 Acknowledgements

The authors thank Interbeef Working Group, the countries and their national representatives participating in this study for providing the data, and the Interbull Centre (Uppsala, Sweden) for providing the infrastructure to perform the analyses. We thank Toine Roozen and the Interbull Centre for helping with the data call, Thierry Pabiou and the Interbull Centre for providing the estimated genetic parameters between countries, and Enrico Mancin and Ibrahim Jibrila for useful discussions.

5.7 Funding

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5.8 Supplementary material

5.8.1 Supplementary tables

Table S5.1 Number of phenotypes (N), minimum, mean, maximum, and phenotypic standard deviation (σ_P) of males and females per country [a].

COU [a]	Males					Females				
	N	Min	Mean	Max	σ_P	N	Min	Mean	Max	σ_P
CZE	6,816	173	293.2	411	37.8	7,076	157	262.8	366	33.5
DFS	48,340	112	240.6	369	41.5	48,331	107	213.3	319	34.1
IRL	40,873	134	297.2	460	53.9	27,213	127	264.4	402	45.2
DEU	58,716	137	269.9	402	43.3	58,533	128	242.3	356	37.0
CHE	18,197	112	233.4	354	39.2	17,498	107	209.7	312	33.2

[a] Country: Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

Table S5.2 List of environmental effects in the national model of each country [a, b].

COU [a]	Fixed						Random		Covariates	
CZE		asextwin		year			PE	HYS	aaca	aaca2
DFS	HYS	asex	aaca	seas	twin		PE			
IRL	HYS	asex	pariagedam				PE		agedam2	aawg
DEU		asex	pari	month	twin			HY		
CHE		asex		yearmonth		alpine	PE	HY	agedam	agedam2

[a] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.
[b] aaca = age at calving; aaca2 = age at calving fitted as quadratic effect; aawg = age at weighting; agedam = age of the dam; agedam2 = age of the dam fitted as quadratic effect; alpine = access to alpine grazing for calves; asex = sex of the animal; asextwin = interaction between asex and twin; HY = Herd-Year; HYS = Herd-Year-Season; month = month of birth; pari = parity; pariagedam = interaction between pari and agedam; PE = maternal permanent environmental effect; seas = season; twin = twinning; year = year of birth; yearmonth = interaction between year and month.

Table S5.3 Direct and maternal genetic covariances (below diagonal), genetic variances (diagonal) and genetic correlations (above diagonal) within and across countries [a].

		Direct					Maternal				
		CZE	DFS	IRL	DEU	CHE	CZE	DFS	IRL	DEU	CHE
Direct	CZE	686	0.86	0.82	0.76	0.83	-0.27	0.00	-0.01	0.00	-0.02
	DFS	368.13	269	0.79	0.89	0.83	0.00	-0.13	0.00	-0.03	0.00
	IRL	452.95	274.16	450	0.66	0.75	-0.01	0.00	-0.20	0.01	0.01
	DEU	387.46	286.45	274.70	383	0.72	-0.01	-0.02	0.00	-0.27	0.00
	CHE	424.10	264.64	309.17	276.30	380	-0.02	0.00	0.00	0.00	-0.24
Maternal	CZE	-99.12	0.61	-2.87	-1.64	-5.15	197	0.59	0.61	0.61	0.65
	DFS	0.74	-22.66	-0.97	-4.75	-0.59	91.10	120	0.69	0.68	0.67
	IRL	-2.68	0.17	-58.46	0.05	1.22	118.64	105.20	194	0.69	0.65
	DEU	-1.25	-9.19	2.00	-95.86	1.10	153.86	134.76	172.61	326	0.66
	CHE	-5.32	0.26	1.27	0.18	-44.79	87.97	71.14	87.34	114.94	94

[a] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

Table S5.4 National genetic, environmental and residual (co)variances [a].

COU [b]	σ^2_{HY}	σ^2_{HYS}	σ^2_{PE}	σ^2_{dir}	σ^2_{mat}	$\sigma_{dir\text{-}mat}$	σ^2_{res}	h^2_{dir}	h^2_{mat}
CZE		294	208	686	197	-110.28	377	0.42	0.12
DFS			90	269	120	-26.95	547	0.27	0.12
IRL			45	450	194	-59.09	647	0.35	0.15
DEU	477			383	326	-106.01	719	0.21	0.18
CHE	203		76	380	94	-47.25	587	0.29	0.07

[a] σ^2 = variance, HY = Herd-Year, HYS = Herd-Year-Season, PE = maternal permanent environment, dir = direct genetic effect, mat = maternal genetic effect, $\sigma_{dir\text{-}mat}$ = direct-maternal genetic covariance, res = residual, h^2_{dir} = direct heritability, h^2_{mat} = maternal heritability.
[b] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

Table S5.5 Level bias ($\hat{\Delta}_p$) [a], dispersion bias ($\hat{b}_p$) and accuracy of partial EBV ($\widehat{acc}_p$) of direct and maternal EBV for animals with phenotypes and no genotypes born from 2014 onwards [b], in each scenario [c] and for each country [d].

COU [d]	Direct				Maternal			
	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	ssSNPBLUP INT	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	ssSNPBLUP INT
$\hat{\Delta}_p$ (GSD) [a]								
CZE	-0.08	-0.08	-0.07	-0.07	0.01	0.00	0.02	0.03
DFS	-0.07	-	-0.08	-0.07	-0.04	-	-0.03	-0.03
IRL	-0.03	-0.07	-0.04	-0.07	-0.02	0.01	-0.02	0.02
DEU	0.08	0.10	0.07	0.08	-0.02	0.01	-0.01	0.01
CHE	-0.04	-0.05	-0.02	-0.02	0.05	0.05	0.05	0.07
Range of SE [e]	0.00-0.01	0.00-0.01	0.00-0.01	0.00-0.01	0.00-0.00	0.00-0.00	0.00-0.00	0.00-0.00
$\hat{b}_p$								
CZE	0.77	0.81	0.74	0.77	0.75	0.78	0.90	0.85
DFS	0.83	-	0.84	0.87	0.95	-	0.98	0.98
IRL	0.94	0.89	0.96	0.89	0.90	0.86	0.88	0.81
DEU	0.90	0.90	0.91	0.92	0.85	0.86	0.84	0.84
CHE	0.95	0.95	0.95	0.95	1.04	1.04	0.98	1.02
Range of SE [e]	0.01-0.02	0.01-0.02	0.01-0.02	0.01-0.02	0.01-0.02	0.01-0.02	0.01-0.02	0.01-0.02
$\widehat{acc}_p$								
CZE	0.27	0.29	0.29	0.30	0.16	0.16	0.18	0.19
DFS	0.33	-	0.33	0.36	0.29	-	0.29	0.30
IRL	0.20	0.23	0.22	0.26	0.15	0.17	0.15	0.18
DEU	0.36	0.39	0.36	0.39	0.24	0.24	0.24	0.24
CHE	0.45	0.49	0.46	0.49	0.22	0.34	0.23	0.33
Range of SE [e]	0.00-0.00	0.00-0.00	0.00-0.00	0.00-0.00	0.00-0.00	0.00-0.00	0.00-0.00	0.00-0.00

[a] Level bias is expressed in genetic standard deviations (GSD). [b] Number of animals in each country: CZE = 5,731, DFS = 17,941, IRL = 14,638, DEU = 33,966, CHE = 9,684. [c] Scenario: $PBLUP_{NAT}$ = Pedigree-based BLUP national, $ssSNPBLUP_{NAT}$ = single-step SNP-BLUP national, $PBLUP_{INT}$ = Pedigree-based BLUP international, $ssSNPBLUP_{INT}$ = single-step SNP-BLUP international. [d] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland. [e] Range of SE: minimum and maximum Standard Error across countries in each scenario.

Table S5.6 Increases in population accuracy (inc_acc) of moving from each scenario to $ssSNPBLUP_{INT}$ [a, b] for direct and maternal EBV for animals with phenotypes and no genotypes born from 2014 onwards [c] for each country [d].

COU [d]	Direct			Maternal		
	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT
CZE	1.4	0.9	0.6	14.0	13.4	3.3
DFS	1.4	-	0.4	1.2	-	0.7
IRL	8.8	2.2	5.1	17.0	6.5	13.9
DEU	0.8	0.5	0.6	1.2	0.9	0.6
CHE	3.8	0.4	2.9	22.4	4.7	25.7
Range of SE [e]	0.0-0.6	0.0-0.0	0.0-0.1	0.0-0.6	0.0-0.4	0.0-0.7

[a] Increases in population accuracies are expressed in % relative to each scenario whole EBV.
[b] Scenario: $PBLUP_{NAT}$ = Pedigree-based BLUP national, $ssSNPBLUP_{NAT}$ = single-step SNP-BLUP national, $PBLUP_{INT}$ = Pedigree-based BLUP international, $ssSNPBLUP_{INT}$ = single-step SNP-BLUP international.
[c] Number of animals in each country: CZE = 5,731, DFS = 17,941, IRL = 14,638, DEU = 33,966, CHE = 9,684.
[d] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.
[e] Range of SE: minimum and maximum Standard Error across countries in each scenario.

Table S5.7 Level bias ($\hat{\Delta}_p$) [a], dispersion bias ($\hat{b}_p$) and accuracy of partial EBV ($\widehat{acc}_p$) of direct and maternal EBV for the focal group [b], in each scenario [c] and for each country [d]. Standard errors reported within parenthesis.

COU [d]	Direct				Maternal			
	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	ssSNPBLUP INT	PBLUP NAT	ssSNPBLUP NAT	PBLUP INT	ssSNPBLUP INT
$\hat{\Delta}_p$ (GSD) [a]								
CZE	-0.25 (0.01)	-0.23 (0.01)	-0.23 (0.01)	-0.22 (0.01)	-0.01 (0.01)	-0.03 (0.01)	0.00 (0.01)	0.01 (0.01)
IRL	-0.08 (0.01)	-0.10 (0.01)	-0.10 (0.01)	-0.10 (0.01)	-0.02 (0.00)	0.01 (0.00)	-0.01 (0.00)	0.02 (0.00)
DEU	-0.19 (0.02)	-0.10 (0.02)	-0.21 (0.02)	-0.15 (0.02)	-0.06 (0.01)	-0.02 (0.01)	-0.05 (0.01)	-0.02 (0.01)
CHE	-0.28 (0.01)	-0.27 (0.01)	-0.23 (0.01)	-0.21 (0.01)	0.04 (0.01)	0.03 (0.01)	0.04 (0.01)	0.06 (0.01)
$\hat{b}_p$								
CZE	0.72 (0.05)	0.76 (0.05)	0.65 (0.05)	0.79 (0.03)	1.04 (0.05)	0.94 (0.05)	1.06 (0.05)	0.96 (0.04)
IRL	0.96 (0.02)	0.87 (0.02)	1.00 (0.02)	0.87 (0.02)	0.92 (0.02)	0.87 (0.02)	0.91 (0.02)	0.85 (0.02)
DEU	0.79 (0.07)	0.85 (0.06)	0.77 (0.06)	0.82 (0.04)	0.78 (0.07)	0.79 (0.07)	0.79 (0.07)	0.79 (0.05)
CHE	0.80 (0.03)	0.79 (0.03)	0.80 (0.03)	0.82 (0.03)	1.06 (0.04)	0.98 (0.04)	0.99 (0.03)	0.93 (0.03)
$\widehat{acc}_p$								
CZE	0.23 (0.01)	0.25 (0.01)	0.25 (0.01)	0.35 (0.01)	0.17 (0.01)	0.17 (0.01)	0.19 (0.01)	0.23 (0.01)
IRL	0.23 (0.00)	0.29 (0.00)	0.26 (0.00)	0.35 (0.01)	0.17 (0.00)	0.22 (0.00)	0.18 (0.00)	0.24 (0.00)
DEU	0.26 (0.02)	0.31 (0.02)	0.27 (0.02)	0.35 (0.02)	0.18 (0.01)	0.20 (0.01)	0.18 (0.01)	0.23 (0.01)
CHE	0.34 (0.01)	0.38 (0.01)	0.35 (0.01)	0.40 (0.01)	0.22 (0.01)	0.27 (0.01)	0.24 (0.01)	0.29 (0.01)

[a] Level bias is expressed in genetic standard deviations (GSD).
[b] focal group: animals with phenotypes and genotypes born from 2014 onwards.
[c] Scenario: $PBLUP_{NAT}$ = Pedigree-based BLUP national, $ssSNPBLUP_{NAT}$ = single-step SNP-BLUP national, $PBLUP_{INT}$ = Pedigree-based BLUP international, $ssSNPBLUP_{INT}$ = single-step SNP-BLUP international.
[d] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

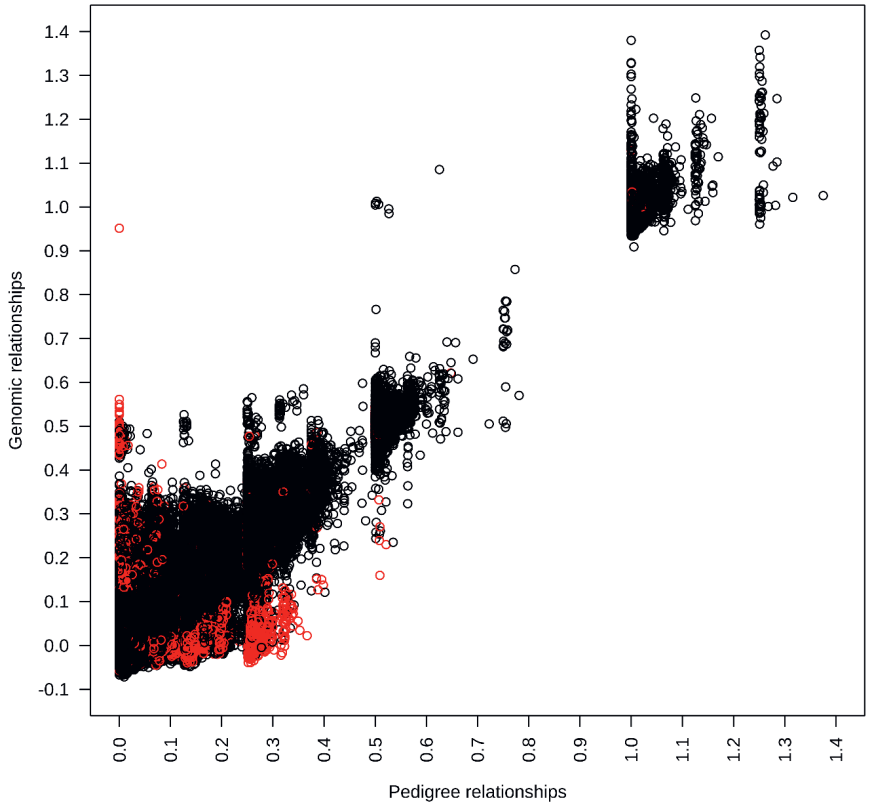
Table S5.8 Countries [a] sending the genotypes for Common Bulls (CB) and Common Maternal Grand-Sires (CMGS).

Pair of countries [a]		Sending genotype for CB			Sending genotype for CMGS		
		IRL	DEU	CHE	IRL	DEU	CHE
CZE	DFS	15	1	8	14	1	2
CZE	IRL	33	2	8	13	1	2
CZE	DEU	22	4	12	15	13	2
CZE	CHE	9	1	10	7	2	2
DFS	IRL	22	1	9	12	0	3
DFS	DEU	21	3	13	16	2	3
DFS	CHE	8	0	13	9	1	3
IRL	DEU	39	2	8	18	1	3
IRL	CHE	10	1	11	9	1	2
DEU	CHE	13	4	30	9	15	12

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

5.8.2 Supplementary figures

Figure S5.1 Plot of pedigree-based (x-axis) and genomic-based (y-axis) relationships between genotyped animals. The red dots indicate the relationships of the 41 genotypes removed due to pedigree incompatibilities.



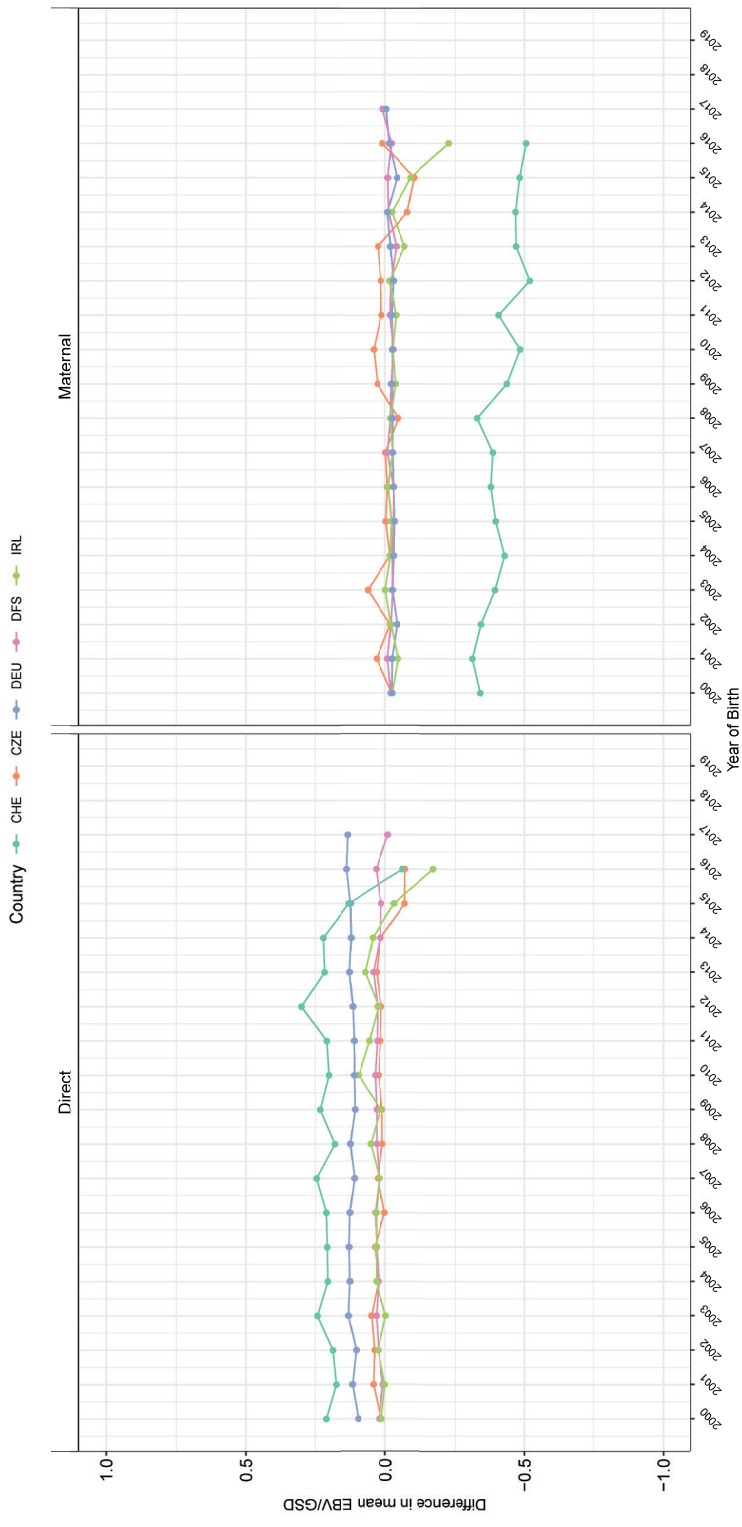


Figure S5.2 Differences in genetic trends between ssSNPBLUP$_{INT}$ and PBLUP$_{INT}$ per country for sires with at least 10 recorded offspring in the country. Differences in genetic trends: differences between the mean EBV in ssSNPBLUP$_{INT}$ and the mean EBV in PBLUP$_{INT}$ for the period 2000-2019 in each country expressed in genetic standard deviations (GSD). CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.

5.8.3 Supplementary files

File S5.1 Findhap instruction file.

```
   4        0      600       75        3    50000          1        5          0        1      .004
iters   Xchrom   maxlen   minlen    steps   maxhap   hapout   genout   damout   listout   errrate
```

File S5.2 International pedigree-based BLUP MiXBLUP instruction file.

```
TITLE International pedigree-based BLUP

DATAFILE data.dat !MISSING 0
ANIM     I
DAM      I
DAMPE    I
R1CZE    I
F1CZE    I
F2CZE    I
F1DFS    I
F2DFS    I
F3DFS    I
F4DFS    I
F5DFS    I
F1IRL    I
F2IRL    I
F3IRL    I
R1DEU    I
F1DEU    I
F2DEU    I
F3DEU    I
F4DEU    I
R1CHE    I
F1CHE    I
F2CHE    I
F3CHE    I
HERD     I
X1CZE    R
X2CZE    R
X1IRL    R
X2IRL    R
X1CHE    R
X2CHE    R
YCZE     T
YDFS     T
YIRL     T
YDEU     T
YCHE     T
POPCODE A

PEDFILE pedigree.ped !CalcInbr
```

```
ANIM  I
SIRE   I
DAM   I
HERD  I

PARFILE parfile.par

MODEL
YCZE ~ X1CZE  X2CZE  F1CZE  F2CZE              !random  R1CZE  DAMPE  G(ANIM, DAM)
YDFS ~ F1DFS  F2DFS  F3DFS  F4DFS  F5DFS       !random             DAMPE  G(ANIM, DAM)
YIRL  ~ X1IRL  X2IRL  F1IRL  F2IRL  F3IRL       !random             DAMPE  G(ANIM, DAM)
YDEU ~ F1DEU  F2DEU  F3DEU  F4DEU               !random  R1DEU              G(ANIM, DAM)
YCHE ~ X1CHE  X2CHE  F1CHE  F2CHE  F3CHE  !random  R1CHE  DAMPE  G(ANIM, DAM)

SOLVING
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!numproc 3
!KEEPTMP
```

File S5.3 International single-step SNPBLUP MiXBLUP instruction file.

```
TITLE International single-step SNPBLUP

DATAFILE data.dat !MISSING 0
ANIM      I
DAM       I
DAMPE   I
R1CZE    I
F1CZE     I
F2CZE     I
F1DFS     I
F2DFS     I
F3DFS     I
F4DFS     I
F5DFS     I
F1IRL     I
F2IRL     I
F3IRL     I
R1DEU    I
F1DEU     I
F2DEU     I
F3DEU     I
```

```
F4DEU    I
R1CHE    I
F1CHE    I
F2CHE    I
F3CHE    I
HERD     I
X1CZE    R
X2CZE    R
X1IRL    R
X2IRL    R
X1CHE    R
X2CHE    R
YCZE     T
YDFS     T
YIRL     T
YDEU     T
YCHE     T
POPCODE  A

PEDFILE pedigree.ped !CalcInbr !makeJcov
ANIM     I
SIRE     I
DAM      I
HERD     I

PARFILE parfile.par

SNPFILE !NoCheck !CalcSNPvar !PREDICT !PLINK
ANIM I
SNP01 Plink_geno.bed !REGTYPE r

REGFILE
 ANIM I
 REG01  !REGTYPE F !Jcov

MODEL
YCZE ~ X1CZE X2CZE F1CZE F2CZE hpReg(01,ANIM) hpReg(01,DAM) !random R1CZE DAMPE hpSNP(01,ANIM) hpSNP(01,DAM) G(ANIM, DAM)
YDFS ~ F1DFS F2DFS F3DFS F4DFS F5DFS hpReg(01,ANIM) hpReg(01,DAM) !random DAMPE hpSNP(01,ANIM) hpSNP(01,DAM) G(ANIM, DAM)
YIRL ~ X1IRL X2IRL F1IRL F2IRL F3IRL hpReg(01,ANIM) hpReg(01,DAM) !random DAMPE hpSNP(01,ANIM) hpSNP(01,DAM) G(ANIM, DAM)
YDEU ~ F1DEU F2DEU F3DEU F4DEU hpReg(01,ANIM) hpReg(01,DAM) !random R1DEU hpSNP(01,ANIM) hpSNP(01,DAM) G(ANIM, DAM)
YCHE ~ X1CHE X2CHE F1CHE F2CHE F3CHE hpReg(01,ANIM) hpReg(01,DAM) !random R1CHE DAMPE hpSNP(01,ANIM) hpSNP(01,DAM) G(ANIM, DAM)

SOLVING
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!hpblup
!hpSNPmodel liu
!numproc 3
!KEEPTMP
```
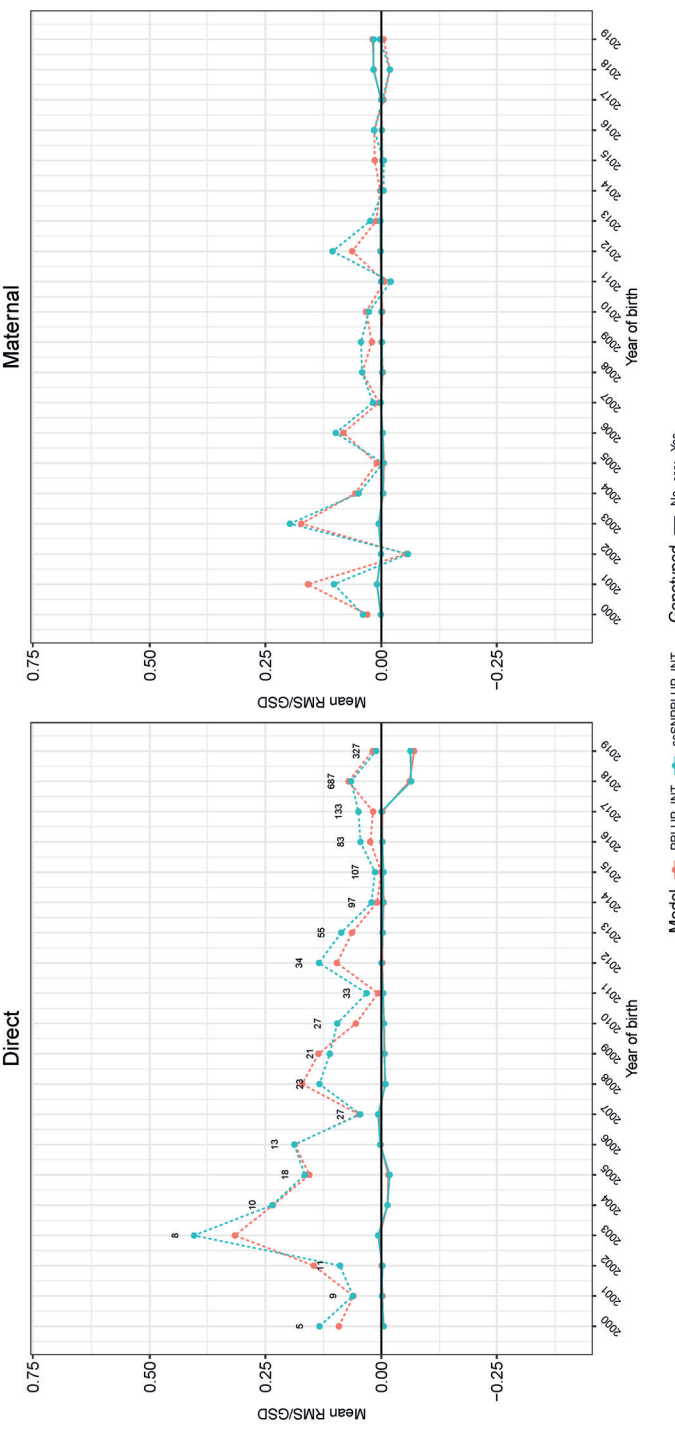
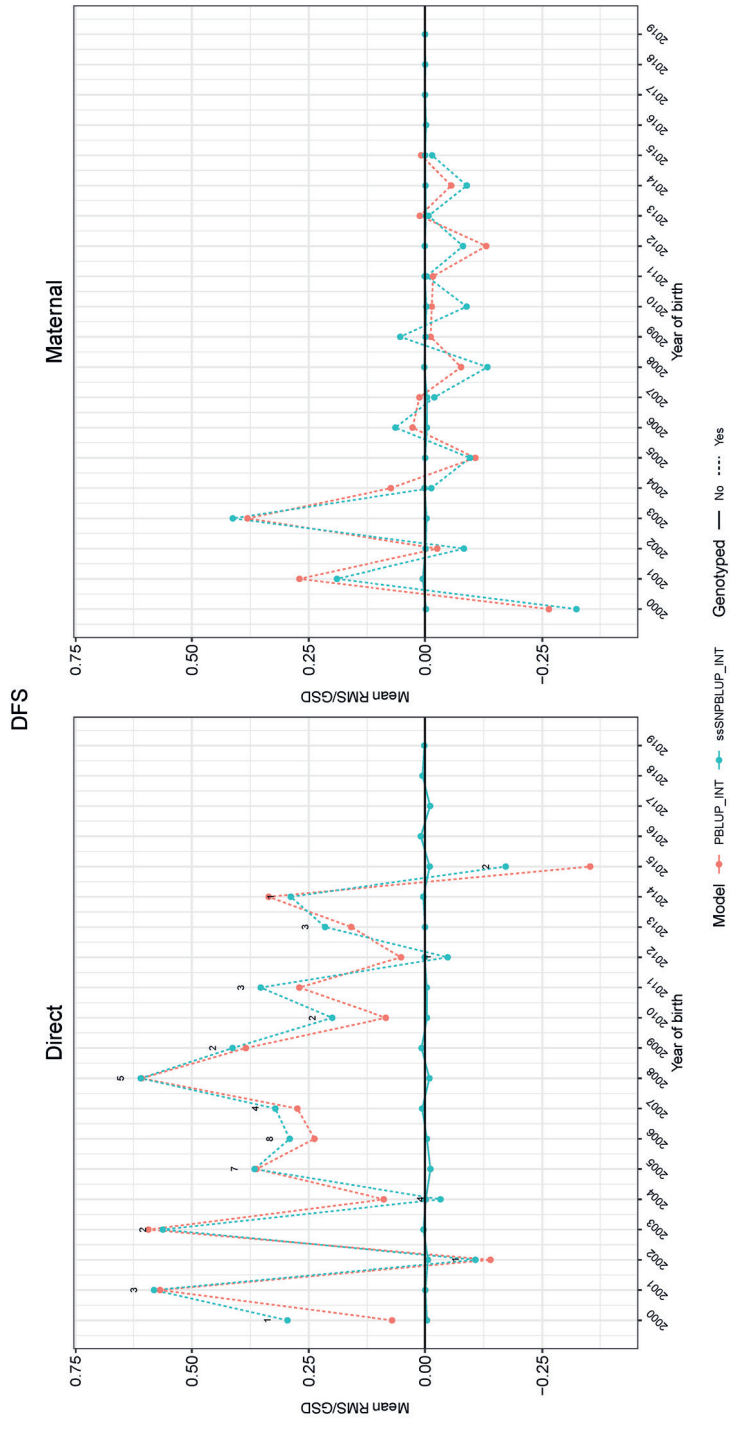



File S5.4 (1 of 5) Direct and maternal EBV realized Mendelian sampling (RMS) trends in each country expressed in genetic standard deviation (GSD) for genotyped and non-genotyped animals computed with Pedigree-based BLUP international ($PBLUP_{INT}$) and single-step SNP-BLUP international ($ssSNPBLUP_{INT}$) models. The numbers reported in the direct panel are the number of genotyped animals in that year (same numbers for the maternal panel). Genotyped animals: animals with genotype that appear in the pseudo-national pedigree (with or without phenotype in the country). Non-genotyped animals: animals that appear in the pseudo-national pedigree without genotype and with phenotype in the country. CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.



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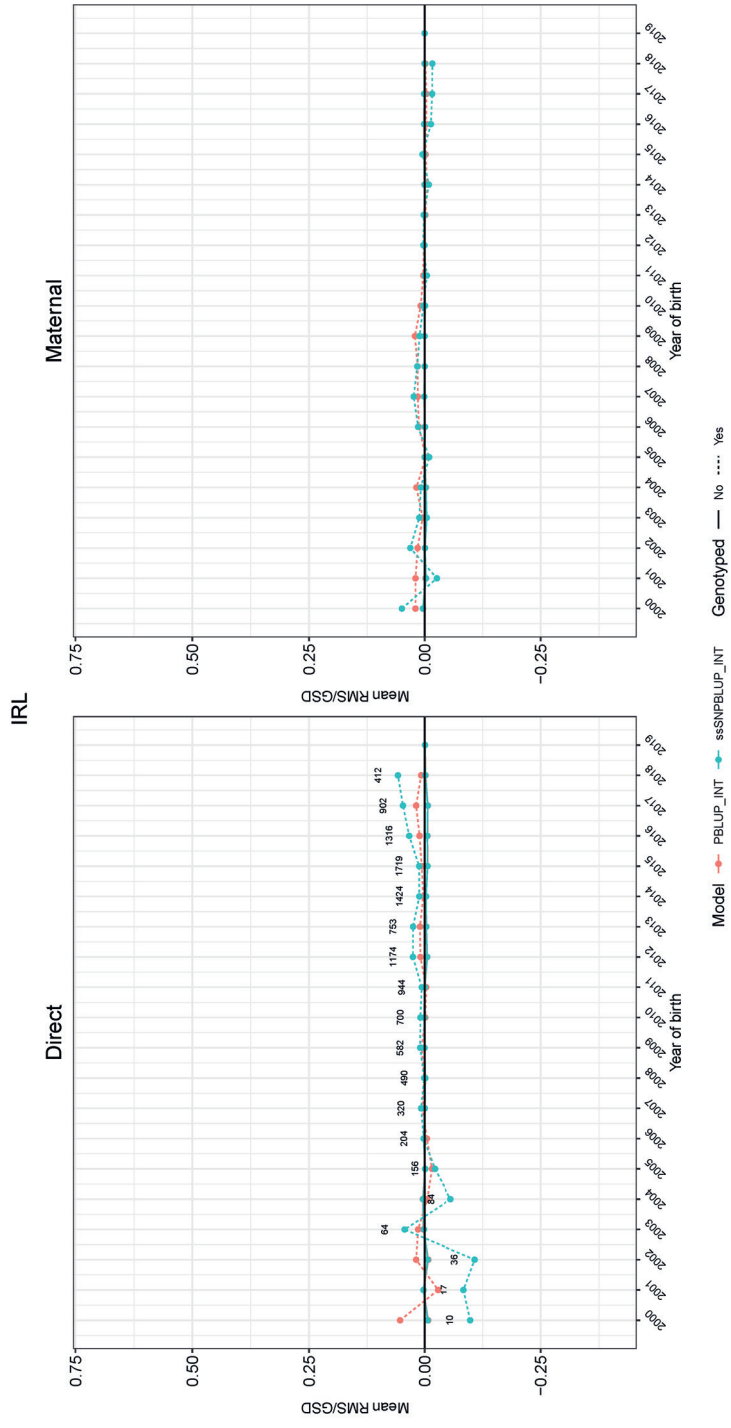

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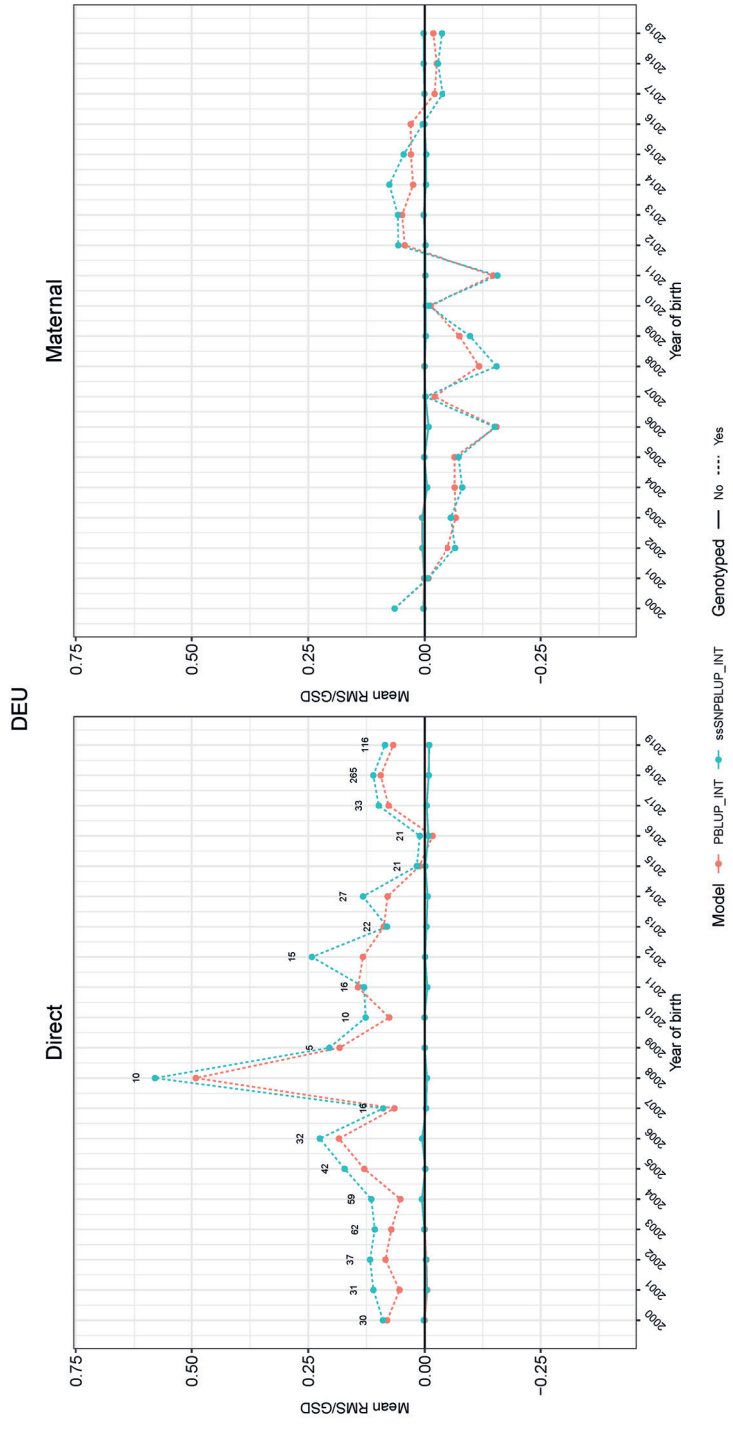

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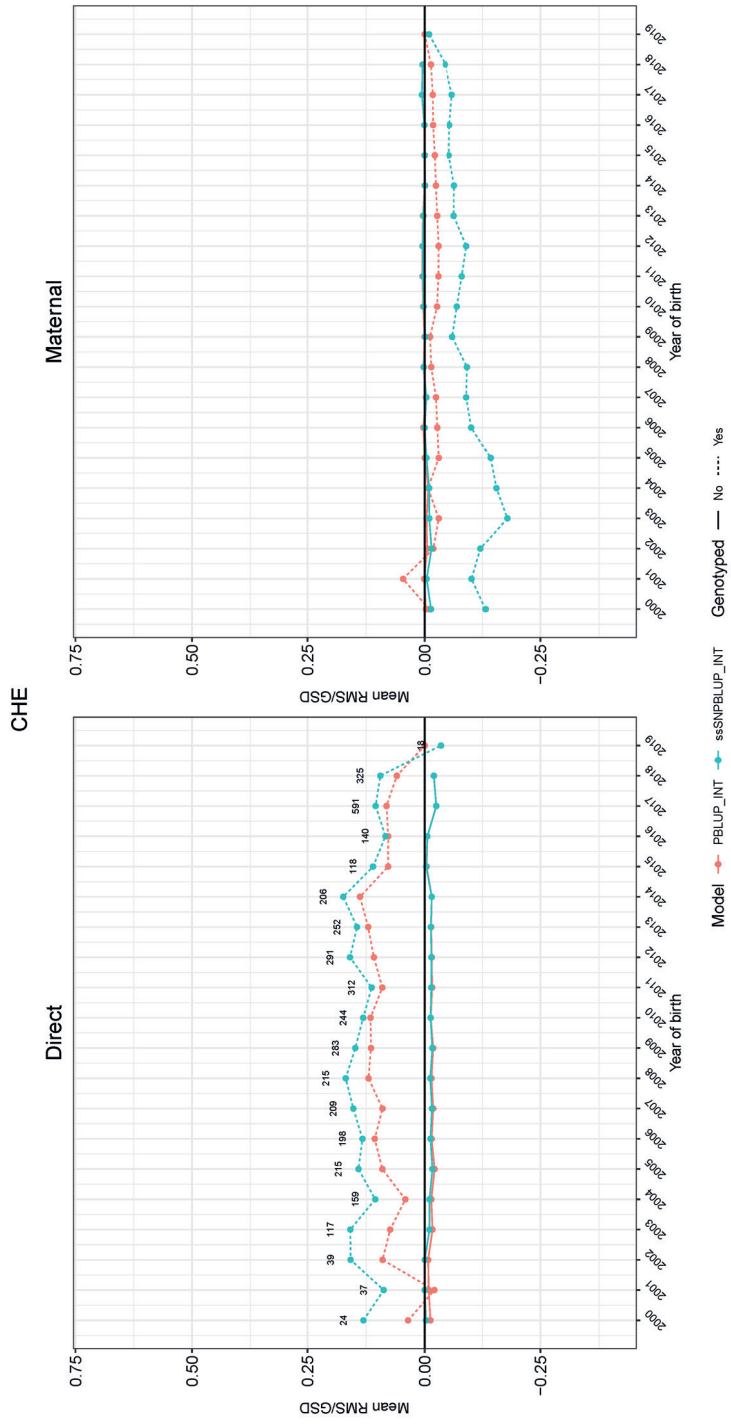
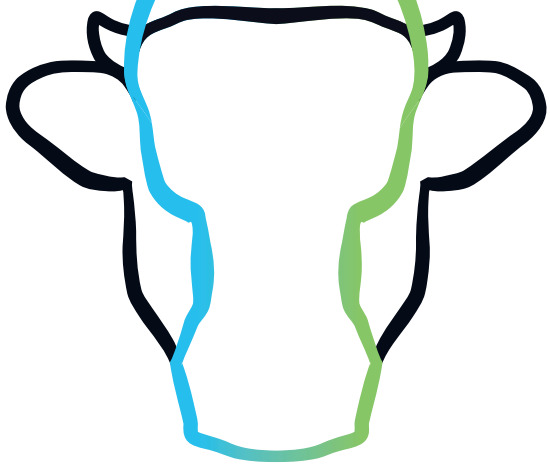


File S5.4 (continues, 5 of 5).

CHAPTER 6



Integration of beef cattle international pedigree and genomic estimated breeding values into national evaluations, with an application to the Italian Limousin population

Renzo Bonifazi[1], Mario P.L. Calus[1], Jan ten Napel[1], Roel F. Veerkamp[1], Stefano Biffani[2], Martino Cassandro[3,4], Simone Savoia[5], Jérémie Vandenplas[1]

[1] Animal Breeding and Genomics, Wageningen University and Research, P.O. Box 338, 6700 AH Wageningen, the Netherlands
[2] Istituto Di Biologia E Biotecnologia Agraria, Consiglio Nazionale Delle Ricerche, Via Edoardo Bassini 15, 20133, Milano, Italy
[3] Department of Agronomy, Food, Natural resources, Animals and Environment (DAFNAE), University of Padova, Viale dell'Università 16, 35020, Legnaro, PD, Italy
[4] National Federation of National Breeders Associations (FedANA), XXIV Maggio 43, 00187, Roma, Italy
[5] Interbull Centre - Department of Animal Breeding and Genetics, SLU - Box 7023, S-75007 Uppsala, Sweden

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Abstract

Background: International evaluations combine data from different countries allowing breeders to access larger panels of elite bulls and increasing estimated breeding values' (EBV) accuracy. However, international and national evaluations can use different sources of information to compute EBV (EBV_{INT} and EBV_{NAT}, respectively), leading to differences between them. Choosing between EBV_{INT} and EBV_{NAT} leads to loss of information that are only contained in the discarded EBV. Our objectives were to define and validate a procedure to integrate publishable sires' EBV_{INT} and associated reliability computed from either pedigree-based or single-step international beef cattle evaluations into national evaluations to obtain a "blended" EBV. The Italian (ITA) pedigree-based national evaluation was used as a case study to validate the integration procedure.

Methods: Publishable sires' international information, i.e. EBV_{INT} and associated reliability, was included in the national evaluation as pseudo-records. Limousin data was available for 444,199 individual age-adjusted weaning weights from eight countries and 17,607 genotypes from four countries (ITA excluded). To mimic differences between international and national evaluations, international evaluations included phenotypes (and genotypes) of animals born up to January 2019, while national evaluations included ITA phenotypes of animals born up to May 2019. International evaluations using all available information were considered as reference scenarios. Publishable sires were divided into three groups: sires with ≥ 15, < 15 and no recorded offspring in ITA.

Results: Overall, for all three groups of publishable sires, integrating either pedigree-based or single-step international information into national pedigree-based evaluations improved the similarity of the blended EBV with the reference EBV compared to national evaluations without integration. For instance, the correlation with the reference EBV for direct (maternal) EBV went from 0.61 (0.79) for a national evaluation without integration to 0.97 (0.88) when integrating single-step international information, on average across the three groups of sires.

Conclusions: The proposed integration procedure yields blended EBV that are in close agreement with full international EBV for all groups of animals analysed. The procedure can be directly applied by countries and allows the straightforward integration of publishable sires' EBV_{INT} from pedigree-based or single-step based international beef cattle evaluations into national evaluations.

6.1 Background

International evaluations allow to compare estimated breeding values (EBV) across countries such that breeders can choose from a larger panel of elite bulls that better meet their selection objectives (Venot *et al.* 2014; Nilforooshan and Jorjani 2022). Moreover, by considering relatives recorded in other countries, international evaluations increase the accuracy of bulls' EBV (VanRaden and Sullivan 2010; Nicolazzi *et al.* 2011; Bonifazi *et al.* 2020a; Nilforooshan and Jorjani 2022) and reduce the potential bias of national EBV for foreign bulls (Bonaiti and Boichard 1995). In beef cattle international evaluations led by Interbeef (Interbeef 2006), national phenotypic and pedigree data from participating countries are analysed simultaneously in a multi-trait animal model in which data in each country is modelled as a separate trait (Phocas *et al.* 2005; Bonifazi *et al.* 2020b). The main output of international evaluations is an international EBV (EBV_{INT}) which usually has higher reliability (REL) than national EBV (EBV_{NAT}) (Venot *et al.* 2014; Bonifazi *et al.* 2020a). In Interbeef, EBV_{INT} are officially distributed to each participating country on their corresponding country scale for: 1) all animals that appear in the national pedigree, and 2) "publishable sires", i.e. sires that meet Interbeef publication rules (based on EBV_{INT} reliabilities and the number of recorded (grand-)progeny; Bonifazi *et al.* 2021). Thus, an individual could have two breeding values at the country level: the EBV_{INT}, and the EBV_{NAT} computed from a national evaluation.

The EBV_{INT} and EBV_{NAT} can differ due to differences between national and international evaluations. For example, on the one hand, international evaluations consider information from relatives recorded in other countries but are performed within-breed and for one trait group at the time (e.g. weaning weight, (Venot *et al.* 2014), or calving traits, (Vesela *et al.* 2019)). On the other hand, national evaluations are mostly multi-trait, can be multi-breed with data of crossbreds included, and usually include more data than those submitted for the international evaluations. One additional reason for having more data included in some national evaluations is that they usually take place according to a country-specific calendar such that national evaluations can be later in time and have more data compared to international ones.

Since national and international evaluations use partly different sources of information, choosing either the EBV_{INT} or the EBV_{NAT} for an individual could lead to losing the information associated with the discarded EBV. To overcome this issue and use all available information, an integration procedure can be used to integrate the EBV_{INT} and its associated measure of precision (e.g. REL) into the national evaluation, resulting in a "blended" EBV (Vandenplas and Gengler 2015). The EBV_{INT} and associated REL can be integrated as pseudo-phenotypes (e.g. DRP – de-

regressed proofs) and weighted by its associated effective records contributions (ERC) into a national evaluation. This procedure allows for the propagation of the international information to all animals and data included in the national evaluation; also those excluded from the international evaluation in the first place (Vandenplas *et al.* 2017). When blending EBV_{INT} and EBV_{NAT}, national information needs to be removed to avoid double-counting, which otherwise may bias national evaluations (Vandenplas *et al.* 2014).

To our knowledge, an official generalized integration procedure for integrating beef cattle publishable sires' EBV_{INT} into national evaluations is currently lacking. In dairy cattle, integration of pedigree-based and genomic-based EBV_{INT} (e.g. from MACE (Schaeffer 1994) or InterGenomics (Jorjani *et al.* 2011) international evaluations, respectively) in national evaluations is common practice, for instance, to increase the size of the national training population for genomic predictions (e.g. Vandenplas *et al.* 2014, 2017; Guarini *et al.* 2019; Luštrek *et al.* 2021). Nonetheless, beef cattle international evaluations differ from those of dairy cattle. First, national phenotypes are directly used as input in the beef cattle international evaluation rather than using EBV as in dairy cattle international evaluations. Second, the structure of beef cattle national breeding programs is usually different from that of dairy cattle, e.g. lower usage of artificial insemination and smaller family sizes in beef compared to dairy (Berry *et al.* 2016). However, little research has been conducted on integrating EBV_{INT} at the national level for beef cattle. Pabiou *et al.* (2018) initially tested a procedure to integrate Interbeef pedigree-based international evaluations into the Irish national evaluations. To date, no study has investigated the integration into national evaluations of genomic EBV_{INT} in beef cattle. Moreover, Pabiou *et al.* (2018) used algorithms to approximate EBV and REL into DRP and ERC which are implemented only in some commercial software packages and that may not be available at the national level, potentially limiting the application of the integration procedure by countries participating in international evaluations. Further testing and generalization of the integration procedure is therefore needed.

Thus, the objectives of our study were to define and validate a procedure that enables participating countries to integrate publishable sires' international EBV, computed either using a pedigree-based or a single-step international evaluation, into a national evaluation to obtain a blended EBV. We used data for Limousin weaning weight from countries participating in Interbeef evaluations and the Italian national dataset as a case study to validate the adequacy of the integration procedure and the predictivity of the resulting blended EBV.

6.2 Methods

6.2.1 Phenotypes, genotypes and pedigree

Individual phenotypes for age-adjusted weaning weights (AWW) were available for 446,493 males and females Limousin animals. Phenotypes were available from six populations, representing eight European countries joining the Interbeef evaluations: Czech Republic (CZE), Denmark, Finland and Sweden (DFS, modelled as one population), Ireland (IRL), Germany (DEU), Switzerland (CHE), and Italy (ITA). Hereafter, for simplicity, we will refer to populations as "countries" even though the DFS population is composed of more than one country. Phenotypes from ITA came from the February 2020 Interbeef pilot evaluation, while phenotypes of other countries came from the January 2020 Interbeef routine evaluation. Phenotypes above or below three standard deviations from the phenotypic mean of each country-sex combination were identified as outliers and discarded. The number of phenotypes available in each country is reported in Table 6.1. After these edits, a total of 444,199 AWW records remained, distributed across 20,559 herds and born between 1975 and 2019. DEU represented the largest country with 26% of the observations, followed by ITA (25%), DFS (22%), IRL (15%), CHE (8%), and CZE (3%). Supplementary Table S6.1 shows a summary of the phenotypic distribution summary per country and sex. A total of 17,607 genotypes imputed at a density of 57,899 single nucleotide polymorphism markers were available and sent by 4 countries (Table 6.1). For a description of the genotypes' preparation, imputation, and distribution per birth year see Bonifazi *et al.* (2022). Hereafter, for simplicity, we will refer to phenotypes from Italy as "national" and to phenotypes and genotypes sent by other countries as "foreign".

Pedigree information was extracted from the Interbeef international database. The following edits were performed: absence of pedigree loops (i.e. an animal being its ancestor), duplicated animals, and conflicts between the sex reported in the international identification number and the animal sex as a parent (e.g. a female reported in the pedigree as a sire). Finally, the pedigree was pruned using the RelaX2 software v1.73 (Strandén and Vuori 2006) to include animals with phenotypes, genotypes, or both, and all their ancestors, without any limit on the number of generations retained. The final pedigree included 683,317 animals, born between 1927 and 2019, with a maximum depth of 18 generations.

Table 6.1 Distribution of age-adjusted weaning weights (AWW), number of herds, year of birth of recoded animals, number of genotyped animals, and number of genotypes with associated phenotype for AWW in each county [a].

COU [a]	AWW	AWW %	Herds	Year of birth (min-max)	Genotypes	% Genotypes	Genotypes with phenotypes [b]	% Genotypes with phenotypes [b]
CZE	13,892	3	172	1991-2019	1,625	9	1,207	74
DFS	96,671	22	9,548	1980-2019	-	-	-	-
IRL	68,086	15	8,218	1975-2019	11,300	64	5,237	46
DEU	117,249	26	866	1981-2019	742	4	640 [c]	86
CHE	35,695	8	247	1992-2018	3,940	22	3,516	89
ITA	112,606	25	1,508	1990-2019	-	-	-	-
Total	444,199	100	20,559	1975-2019	17,607	100	10,600	60

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland, ITA = Italy.
[b] Genotypes with an associated phenotype in COU.
[c] 50 animals with phenotypes in DEU with genotypes sent from CHE (49) and IRL (1).

6.2.2 Models

6.2.2.1 Pedigree-based international evaluations

Pedigree-based international evaluations were implemented using the animal model accounting for across-country interaction (AMACI) (Phocas *et al.* 2005) currently used in Interbeef. The AMACI model is equivalent to a multi-trait animal model with maternal effects in which each country is modelled as a different correlated trait:

$$\mathbf{y}_i = \mathbf{X}_i\,\mathbf{b}_i + \mathbf{C}_i\,\mathbf{r}_i + \mathbf{Z}_i\,\mathbf{u}_i + \mathbf{W}_i\,\mathbf{m}_i + \mathbf{P}_i\,\mathbf{pe}_i + \mathbf{e}_i$$

where *i* is the country; $\mathbf{y}$ is the vector of observations; $\mathbf{b}$ and $\mathbf{r}$ are the vectors of fixed and random environmental effects, respectively; $\mathbf{u}$ and $\mathbf{m}$ are the vectors of direct (animal) and maternal random additive genetic effects, respectively; $\mathbf{pe}$ is the vector of random maternal permanent environmental effects provided by the dam; $\mathbf{e}$ is the vector of random residual effects. $\mathbf{X}$, $\mathbf{C}$, $\mathbf{Z}$, $\mathbf{W}$, and $\mathbf{P}$ are incidence matrices linking records to fixed environmental, random environmental, direct genetic, maternal genetic and maternal permanent environmental effects, respectively. Supplementary Table S6.2 reports the fixed and random effects for each country. As the international model follows the national ones, random environmental effects were modelled for CZE (herd-year-season), DEU and CHE (herd-year). Similarly, the maternal permanent environmental effect was not fitted for the DEU. It is assumed that:

$$var\begin{bmatrix}\mathbf{u}\\ \mathbf{m}\end{bmatrix} = \mathbf{G}\otimes\mathbf{A} = \begin{bmatrix}\mathbf{G}_{d,d} & \mathbf{G}_{d,m}\\ \mathbf{G}_{m,d} & \mathbf{G}_{m,m}\end{bmatrix}\otimes\mathbf{A}$$

where **u** is the vector of random direct additive genetic effects for all countries; **m** is the vector of random maternal additive genetic effects for all countries; $\mathbf{G}$ is the across-country genetic (co)variance matrix of order 12 by 12 in which $\mathbf{G}_{d,d}$ is the across-country direct additive genetic (co)variance matrix, $\mathbf{G}_{m,m}$ is the across-country maternal additive genetic (co)variance matrix, and $\mathbf{G}_{d,m}$ ($\mathbf{G}_{m,d}$) contains additive genetic covariances between direct and maternal effect within-country (diagonal elements) and additive genetic covariances between direct and maternal effect between countries (off-diagonal elements); **A** is the numerator relationship matrix; ⊗ indicates the Kronecker product. Random environmental effects, random maternal permanent environmental effects, and residuals were fitted using block-diagonal variance matrices. The genetic variance-covariance matrix with additive direct and maternal genetic effects ($\mathbf{G}$) was built following the Interbeef procedure outlined in Bonifazi *et al.* (2021) as:

$$\mathbf{G} = \mathbf{S}\,\mathbf{\Phi}\,\mathbf{S}$$

where, $\mathbf{S}$ is the diagonal matrix with national genetic standard deviations for direct and maternal genetic effects, and $\mathbf{\Phi}$ is the across-country estimated genetic correlation matrix (of order 12x12 with diagonal values of 1). The genetic correlation matrix $\mathbf{\Phi}$ was estimated using the MC EM REML algorithm implemented in MiX99 software (MiX99 Development Team 2019) and following the method and settings used in Bonifazi *et al.* (2020b, "scenario ALL"). Both the estimated $\mathbf{\Phi}$ and the final $\mathbf{G}$ (co)variance matrix are reported in Supplementary Table S6.3. Both genetic and environmental variances were the same as those used in the national genetic evaluations of participating countries and are reported in Supplementary Table S6.4.

6.2.2.2 Single-step international evaluations

Genomic data were integrated into the AMACI model using the international single-step Single Nucleotide Polymorphism Best Linear Unbiased Prediction (ssSNPBLUP) model following Bonifazi *et al.* (2022). The estimated (co)variance components used in ssSNPBLUP were the same as in the AMACI model. The proportion of variance not explained by markers and due to residual polygenic effects was assumed to be 5%. Two $\mathbf{J}$ covariates (one for additive genetic and one for maternal genetic effects) were fitted to ensure the compatibility of pedigree and genomic information (Hsu *et al.* 2017). For more details on how $\mathbf{J}$ covariates are calculated see Bonifazi *et al.* (2022).

6.2.2.3 National evaluations

National evaluations for ITA were always pedigree-based as no genomic data were sent by ITA. National evaluations were obtained by running a single-trait evaluation using only ITA submitted phenotypes and the same national model as the one used for the international evaluations.

6.2.2.4 Reliabilities

All reliabilities were computed using MiXBLUP (ten Napel *et al.* 2020) and were expressed on a 0 to 1 scale. For pedigree-based national and international evaluations, REL were computed using the Tier and Meyer (2004) algorithm. As there is no method to approximate REL from ssSNPBLUP models easily, REL were obtained from an equivalent ssGBLUP model (Christensen and Lund 2010; Aguilar *et al.* 2010) using 5% residual polygenic effect. When the same parametrization is used, ssGBLUP and ssSNPBLUP are equivalent (Vandenplas *et al.* 2021b). For single-step international evaluations, the additional REL brought by genomic data was computed using Misztal *et al.* (2013) "approx2" algorithm.

6.2.3 Integration procedure

Figure 6.1 summarizes the exchange of data of Interbeef international evaluations and the steps of the integration procedure outlined hereafter. The direct and maternal EBV from national (EBV_{NAT}) and international (EBV_{INT}) evaluations and its associated reliabilities (REL_{NAT} and REL_{INT}, respectively) for all individuals in the evaluations are computed following the models outlined above. The integration procedure of international information (i.e. EBV_{INT} and associated REL_{INT}) (either pedigree-based or from single-step) into national evaluations consists of four steps.

1) For all publishable sires, direct and maternal effective record contributions (ERC) associated with REL_{NAT} and REL_{INT} (ERC_{NAT} and ERC_{INT}, respectively) are computed as:

$$ERC_i = \lambda \frac{REL_i}{1 - REL_i}$$

where, REL_i is the REL of the individual *i* (either REL_{NAT} or REL_{INT}), and $\lambda = \sigma_e^2/\sigma_a^2$, with σ_e^2 being the national residual variance, and σ_a^2 being either the national direct or maternal genetic variance for the direct and maternal EBV, respectively.

2) For all publishable sires, direct and maternal de-regressed proofs for both national and international EBV (DRP_{NAT} and DRP_{INT}, respectively) are computed following Garrick *et al.* (2009) and Calus *et al.* (2016):

$$DRP_i = PA_i + \frac{(EBV_i - PA_i)}{REL_{i_{(o+p)}}}$$

where, PA_i is the parent average EBV of the individual *i* computed as $(EBV_{sire} + EBV_{dam})/2$, and $REL_{i_{(o+p)}}$ is the reliability due to the individual own performance and its progeny computed as $dERC_i/(dERC_i + \lambda)$. $dERC_i$ is the individual de-regressed ERC computed as $ERC_i - ERC_{PA}$, with ERC_{PA} being the ERC calculated from parent average reliability defined as $(REL_{sire} + REL_{dam})/4$. If either the national or the international $dERC_i \leq 0$, both the $dERC_i$ and its associated DRP_i are set to 0.

3) For all publishable sires, the direct and maternal adjusted DRP (DRP*) and its associated weight (dERC*) adjusted for national data to avoid its double-counting are computed following Vandenplas *et al.* (2014) as:

$$DRP_i^* = \frac{(dERC_{INT_i} \cdot DRP_{INT_i}) - (dERC_{NAT_i} \cdot DRP_{NAT_i})}{dERC_i^*}$$

where, $dERC_i^* = dERC_{INT_i} - dERC_{NAT_i}$. If $dERC_i^* \leq 0$ or if the gain in reliability (defined as the difference between REL_{INT} and REL_{NAT}) is smaller than 0.01, both $dERC_i^*$ and its associated DRP_i^* are set to 0.

4) The direct and maternal blended EBV (EBV_{BLEND}) are then computed with a national evaluation using national phenotypes and direct and maternal DRP* as pseudo-phenotypes. In this blended evaluation, dERC* are used as weights for the DRP*, and the maternal DRP* are associated with the maternal effect of the animal itself and not of its dam. The direct and maternal DRP* were modelled as the same trait (i.e. AWW) and fitting one general mean for each.

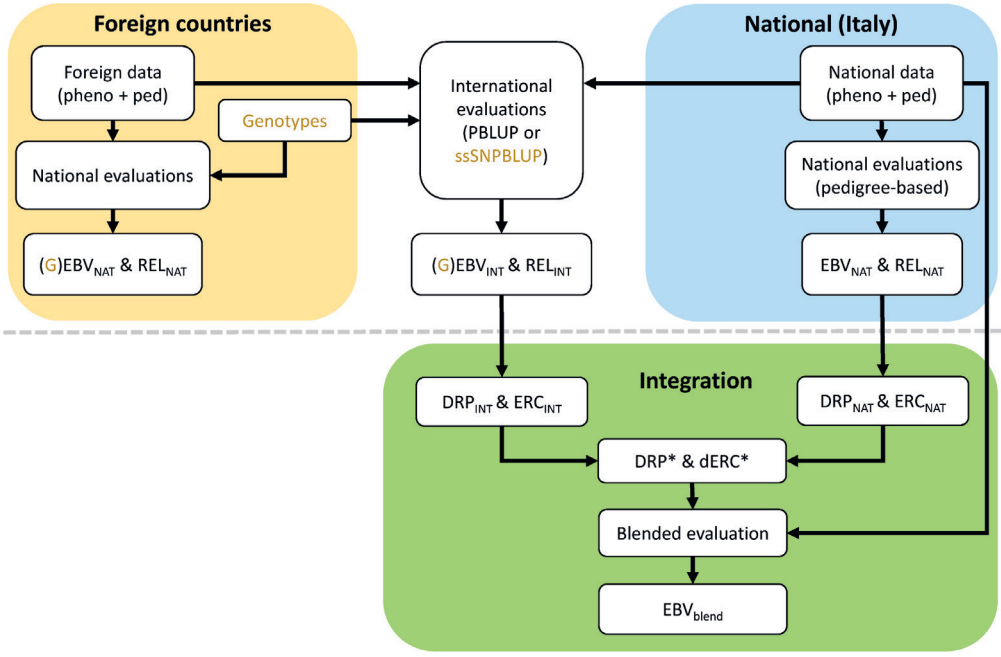

Figure 6.1 Data exchange of Interbeef international evaluations (above the dotted line) and integration procedure (green area). Italy and foreign countries each run independent national evaluations using nationally available information: pedigree (ped), phenotypes (pheno) and genotypes (in yellow). National phenotypic and pedigree information are used in pedigree-based international evaluations to compute international EBV (EBV_{INT}). If available, genotypes can be used in ssSNPBLUP international evaluations (in yellow) to compute international genomic EBV ($GEBV_{INT}$). ssSNPBLUP evaluations are not yet part of routine Interbeef evaluations. PBLUP: pedigree-based BLUP, ssSNPBLUP: single-step SNPBLUP, (G)EBV: (genomic) estimated breeding value, REL: reliability, INT: international, NAT: national, EBV_{blend}: blended EBV, DRP: De-regressed proofs, ERC: Effective Record Contribution, DRP*: adjusted DRP, dERC*: adjusted de-regressed ERC.

6.2.4 Scenarios

The integration procedure was applied on a real-case scenario with Interbeef publishable sires' international information integrated into the Italian evaluation. Italian evaluations are performed by ANACLI ("Associazione Nazionale Allevatori delle razze bovine Charolaise e Limousine Italiane"; ANACLI 2022) and currently take place in January, April, August, and December. Interbeef evaluations currently take place in January and October. To mimic differences between evaluations calendars, Italian national evaluations were assumed to be four months later than the international ones resulting in a larger amount of national phenotypes at the national level. Therefore, we integrated publishable sires' international information from an Interbeef January 2019 evaluation into the ITA national evaluation of May 2019. Phenotypes and genotypes of animals born after April 30th 2019 were discarded. We used the animal's year of birth to include or exclude phenotypes in different scenarios since the animal weighing date for AWW was not available. Publishable sires' international information with and without including genomic data in the international evaluations were integrated into the pedigree-based ITA evaluation. In both cases, the following scenarios were implemented to perform the integration.

Table 6.2 summarizes the different sources of information and the purpose of each scenario. The first two scenarios implemented are needed as inputs during the integration procedure and are defined as:

- **Scenario NAT$_{JAN}$.** A national Italian evaluation using only national phenotypes of animals born up to January 2019. The purpose of this scenario is to obtain national information (i.e. EBV$_{NAT}$ and associated REL$_{NAT}$) included in the international evaluation to avoid its double-counting during the integration procedure.
- **Scenario INT$_{JAN}$.** An international evaluation using both national and foreign phenotypes (and genotypes for single-step evaluation) of animals born up to January 2019. From this scenario, publishable sires and their international information for the integration are obtained. Publishable sires were selected separately for direct and maternal EBV$_{INT}$ based on Interbeef publication rules as follows. Sire's direct EBV$_{INT}$ should have: 1) a REL$_{INT}$ ≥ 0.5 on at least one country scale, and 2) ≥ 25 recorded progeny across all countries. Sire's maternal EBV$_{INT}$ should have: 1) an accompanying publishable direct EBV$_{INT}$, 2) an associated REL$_{INT}$ ≥ 0.3 on at least one country scale, and 3) ≥ 15 daughters with

Table 6.2 Overview of implemented scenarios: names, data and purpose [a].

Scenario	Scenario type [c]	Data [a, b]			Purpose
		Origin [d]	Up to January 2019	January 2019 to May 2019	
NAT_{JAN}	Input	National	●		Used to avoid double-counting in $BLEND_{MAY}$
		Foreign			
INT_{JAN}	Input	National	●		Publishable sires' information to be integrated into $BLEND_{MAY}$
		Foreign	●		
NAT_{MAY}	Validation	National	●	●	A national evaluation without integration. Used for comparison with $BLEND_{MAY}$
		Foreign			
$BLEND_{MAY}$	Validation	National	●	●	A blended national evaluation that integrates publishable sires' information of INT_{JAN} (corrected for NAT_{JAN}) into NAT_{MAY}
		Foreign	●		
INT_{JAN_red}	Input	National			Publishable sires' information to be integrated into GOLD
		Foreign	●		
GOLD	Validation	National	●	●	A national evaluation that integrates publishable sires' information of INT_{JAN_red} into NAT_{MAY}. Used for comparison with $BLEND_{MAY}$
		Foreign	●		
REF_{MAY_trunc}	Reference	National	●	●	Reference scenario to validate scenarios' adequacy
		Foreign	●		
REF_{MAY}	Reference	National	●	●	Reference scenario to validate scenarios' predictivity
		Foreign	●	●	

[a] The integration procedure was tested either with or without genotypes in international evaluations. National evaluations were always pedigree-based.

[b] All scenarios used the full international pedigree.

[c] Scenario type: Input = scenarios whose output is used as input in validated scenarios. Validation = scenarios validated and compared. Reference = scenarios used as reference.

[d] Origin: National = Italian phenotypes. Foreign = phenotypes and genotypes from other countries but Italy.

recorded progeny and ≥ 25 recorded grand-progeny from daughters across all countries. The total number of publishable sires were 4,946 and 1,707 for direct and maternal EBV_{INT}, respectively. The number of publishable sires was the same when INT_{JAN} used a pedigree-based or a single-step international evaluation.

The next two scenarios implemented are a national evaluation without integration and a national blended evaluation with integration, and are defined as:

- **Scenario NAT_{MAY}.** As NAT_{JAN}, but using national phenotypes of animals born up to May 2019. This scenario represents a national evaluation without integration and it is used for comparison with $BLEND_{MAY}$.
- **Scenario $BLEND_{MAY}$.** A blended national evaluation using national phenotypes as in NAT_{MAY} and integrating information of publishable sires from scenario INT_{JAN} using the procedure described in the above section. We observed that few publishable sires (2 and 38 for direct and maternal EBV, respectively) had a dERC* = 0 in INT_{JAN} when using a single-step evaluation but dERC* > 0 when using a pedigree-based evaluation. These differences were related to higher ERC_{PA} values when using a single-step evaluation compared to a pedigree-based one. The dERC* of these few publishable sires were set to 0 in INT_{JAN} when using a pedigree-based evaluation.

The scenarios implemented to this point mimic what would be observed and needed in real-case applications. Finally, we implemented the following scenarios (also summarised in Table 6.2) with the purpose of comparing and validating different aspects of the integration procedure as described in the validation section below. These four scenarios include three international evaluations using various levels of phenotypes, pedigree and possibly genotypes of all involved countries, and one blended evaluation for ITA.

- **Scenario INT_{JAN_red}.** As INT_{JAN}, but without ITA national phenotypes. The purpose of this scenario is to obtain international information of publishable sires free of ITA national information and to be integrated into scenario GOLD.
- **Scenario GOLD**. A blended evaluation using national phenotypes as in NAT_{MAY} and integrating information of publishable sires from scenario INT_{JAN_red}. Scenario GOLD represents a "gold standard" blended evaluation since no double-counting of national information is present because the integrated information are computed from an international evaluation without national ITA phenotypes. Thus, the adjustment in step 3 of the integration procedure is not applied in GOLD as no double-counting of national information has to be removed. Scenario GOLD is used for comparison with scenario $BLEND_{MAY}$ to evaluate the removal of double-counting in this latter. The more accurate the

correction for double-counting of national information in $BLEND_{MAY}$, the closer the results obtained for $BLEND_{MAY}$ will be to those obtained for GOLD.

- **Scenario REF_{MAY_trunc}.** An international evaluation using national phenotypes of animals born up to May 2019, and foreign phenotypes and genotypes of animals born up to January 2019. REF_{MAY_trunc} is used as a reference scenario to validate the adequacy of the integration procedure as described below.
- **Scenario REF_{MAY}.** An international evaluation using both national and foreign phenotypes and genotypes of animals born up to May 2019. REF_{MAY} is used as a reference scenario to validate the increase in predictivity due to the integration procedure as described below.

In all implemented scenarios, the full international pedigree was used. Supplementary Table S6.5 reports the number of phenotypes and genotypes of animals born up to January 2019 and between January 2019 and May 2019 for each country.

6.2.5 Validation

We validated the integration procedure for its adequacy and for the increase in predictivity as described below by regressing the EBV of the references scenarios (i.e. REF_{MAY_trunc} and REF_{MAY}) on the EBV of three validation scenarios (Table 6.2): NAT_{MAY}, $BLEND_{MAY}$ and GOLD. We computed the following validation metrics: Pearson's correlation between EBV (ρ), level bias (LB – defined as the difference between the mean EBV of the validated scenario and the mean EBV of the REF scenario, and expressed in genetic standard deviations), slope (b_1), adjusted coefficient of determination (R^2_{adj}), and Root Mean Square Error (RMSE).

- **Adequacy**. To evaluate the adequacy of the integration procedure, EBV of publishable sires from the validated scenarios were compared with the EBV obtained under scenario REF_{MAY_trunc}. REF_{MAY_trunc} uses the same sources of information as in $BLEND_{MAY}$, but without approximating raw foreign phenotypic (and genomic) information into DRP and ERC. Thus, the more accurate the integration procedure the closer the EBV will be to those of REF_{MAY_trunc}. Publishable sires were divided into three different groups based on having or not recorded offspring in ITA (hereafter referred to as "domestic" and "foreign" publishable sires, respectively), and the amount of recorded offspring in ITA up to January 2019. The three groups defined were: A) domestic publishable sires with ≥ 15 recorded offspring in ITA, B) domestic publishable sires with < 15 recorded offspring in ITA, and C) foreign publishable sires with no recorded offspring in ITA. The number of sires with publishable direct EBV in groups A, B

and C were 1,382, 94 and 3,470, respectively. The number of sires with publishable maternal EBV in groups A, B and C were 491, 51 and 1,165, respectively.

- **Predictivity**. Predictivity is defined as the ability to predict an individual's future EBV before data (phenotypes and/or genotypes) on the animal itself or its relatives becomes available. To evaluate the increase in predictivity due to the integration procedure, EBV of offspring of publishable sires born between January 2019 and May 2019 and with records in ITA from the validated scenarios were compared with those of REF_{MAY}, which included 4 additional months (from January to May 2019) of foreign data. Offspring of publishable sires were divided into two groups: offspring of publishable sires with only direct EBV_{INT} integrated (n = 1,016) and offspring of publishable sires with both direct and maternal EBV_{INT} integrated (n = 60).

Domestic sires with ≥ 15 recorded offspring at the national level are expected to have reliable EBV_{NAT} with small changes in their EBV_{NAT} when integrating international information. However, the effect of double-counting of national information is expected to be higher in this group of sires compared to others. Domestic sires with < 15 recorded offspring are expected to have changes in their EBV_{NAT} and to benefit from the integration of international information from relatives recorded in other countries as only a few recorded offspring are available at the national level. Moreover, in this study, all domestic sires with < 15 recorded offspring had also recorded offspring in other countries. Finally, foreign sires are expected to have the largest differences between EBV_{INT} and EBV_{NAT} as little to no information is present at the national level.

To gain insights on the connectedness level between ITA and other countries we also quantified the number of sires and dams with recorded offspring in ITA, followed by the number of common bulls (CB – sires with recorded offspring in ITA and other countries), and common maternal grand-sires (CMGS – maternal grand-sires with recorded grand-offspring in ITA and other countries). For each of these groups, we also quantified the number of genotyped animals provided by other countries that were present in the Italian pseudo-national pedigree to evaluate the potential increase in connectedness due to genomic data. The pseudo-national pedigree was obtained by pruning the international pedigree to include all animals with ITA phenotypes and all their ancestors.

6.2.6 Software and settings

In all scenarios both EBV and corresponding approximated REL were computed using MiXBLUP software (ten Napel *et al.* 2020). The convergence criterion of the

preconditioned conjugate gradient (PCG) algorithm for the mixed model equation solutions was defined as the square root of the relative difference between solutions of two consecutive PCG iterations, and iteration was stopped when this dropped below 10^{-5}. Finally, custom R (R Core Team 2021) functions were used to compute ERC, DRP, dERC* and DRP* and are available at https://github.com/bonifazi/Integration_EBV_and_GEBV.

6.3 Results

In total, 4,307 sires and 43,321 dams had recorded offspring in ITA. The average number of recorded offspring was 27.9 and 2.6 for sires and dams, respectively. In total, 217 sires had ≥ 100 recorded offspring. Even though no genotypes were sent by ITA, 116 sires and 3 dams in the Italian pseudo-national pedigree had an associated genotype that was provided by other countries. Out of these 116 sires with genotype, 76 also had recorded offspring in ITA. In total, 513 CB and 955 CMGS had recorded offspring in two or more countries. Table 6.3 reports the number of CB and CMGS connecting ITA with any other country: on average across pairs of countries 122 and 192, respectively. Among them, 44 CB and 24 CMGS were also genotyped, with most of the genotypes provided by IRL and CHE (Table 6.3).

Table 6.3 Number (n) of (genotyped) Common Bulls (CB) and (genotyped) Common Maternal Grand-Sires (CMGS) connecting Italy with other countries [a], and country sending the genotype [b].

	CB		**sending genotype** [b]				**CMGS**		**sending genotype** [b]		
COU [a]	n	with genotype	CZE	IRL	DEU	CHE	n	with genotype	IRL	DEU	CHE
CZE	101	39	1	24	2	12	192	21	17	1	3
DFS	128	38	0	24	1	13	152	20	17	0	3
IRL	132	56	0	40	2	14	171	24	20	1	3
DEU	174	53	0	35	2	16	261	31	22	3	6
CHE	74	32	0	10	1	21	182	24	10	1	13

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland.
[b] sending genotype: country sending the genotype for CB or CMGS.

6.3.1 Publishable sires

Comparing REL_{INT} from pedigree-based international evaluations to REL_{NAT} for the three groups of publishable sires shows the increase in REL obtained from international evaluations (Figure 6.2). Domestic sires with ≥ 15 recorded offspring in ITA were associated with $REL_{NAT} \geq 0.50$ for direct EBV and $REL_{NAT} \geq 0.27$ for maternal EBV. In this group of sires, the pedigree-based international evaluation provided almost no increase in REL for direct EBV (0.01 points on average) and no increase in REL for the maternal EBV on average. As expected, compared to the group of sires with ≥ 15 recorded offspring in ITA, publishable sires with < 15 recorded offspring in ITA were associated with lower REL_{NAT}, and obtained an average increase in REL from the pedigree-based international evaluation of 0.27 points for direct EBV and of 0.06 points for maternal EBV. Finally, for both direct and maternal EBV, foreign publishable sires showed the lowest REL_{NAT} among the three groups and the highest increases in REL with the pedigree-based international evaluation: average increase in REL of 0.45 points for direct EBV and 0.14 for maternal EBV.

Figure 6.3 compares REL_{INT} from the single-step international evaluation to REL_{NAT} for the three groups of publishable sires. When using a single-step international evaluation, for all groups of publishable sires, genotyped sires showed a higher REL_{INT} for both direct and maternal EBV compared to non-genotyped sires (Figure 6.3). Moreover, non-genotyped publishable sires showed no changes in REL_{INT} under single-step compared to pedigree-based international evaluations for both direct and maternal EBV (Figure 6.2 and Figure 6.3).

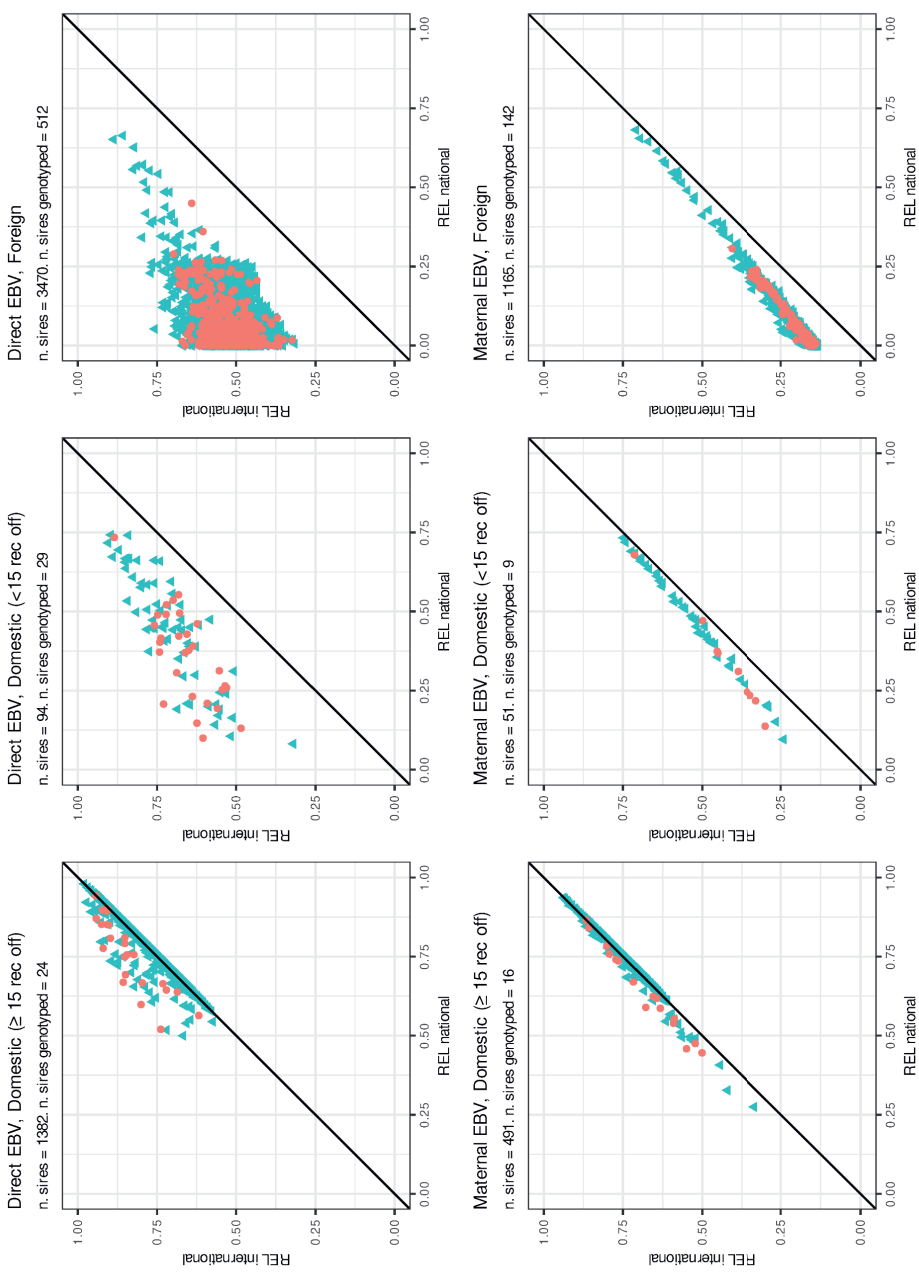

Figure 6.2 Direct EBV (top row) and maternal EBV (bottom row) reliabilities (REL) per group of publishable sires obtained from the national January evaluation (x-axis) versus the international January pedigree-based evaluation (y-axis). Red dots indicate genotyped sires. Publishable sires group = Domestic (≥ 15 rec off): publishable sires with ≥ 15 recorded offspring in Italy, Domestic (< 15 rec off): publishable sires with < 15 recorded offspring in Italy, and Foreign: publishable sires with no recorded offspring in Italy.

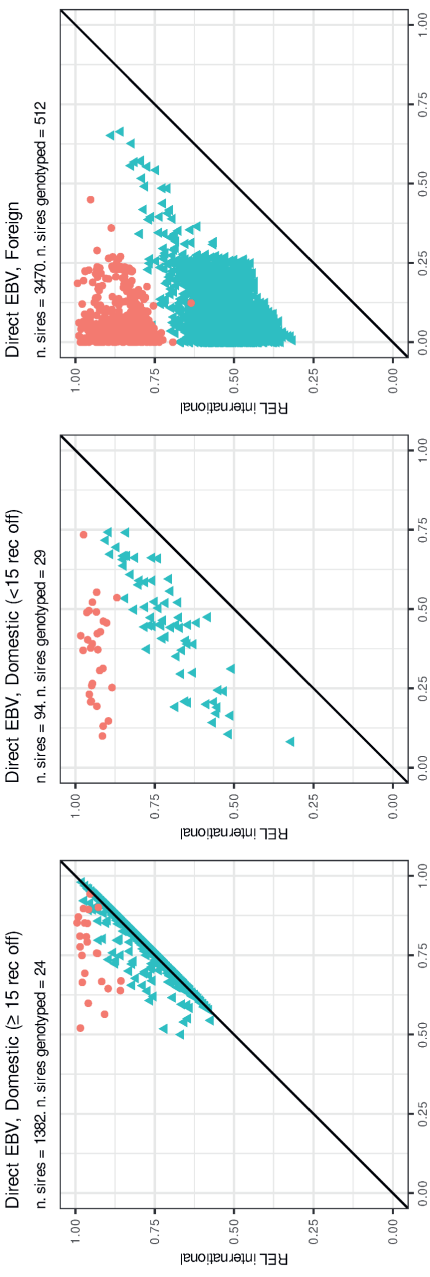

Figure 6.3 Direct EBV (top row) and maternal EBV (bottom row) reliabilities (REL) per group of publishable sires obtained from the national January evaluation (x-axis) versus the international January single-step evaluation (y-axis). Red dots indicate genotyped sires. Publishable sires group = Domestic (≥ 15 rec off): publishable sires with ≥ 15 recorded offspring in Italy, Domestic (< 15 rec off): publishable sires with < 15 recorded offspring in Italy, and Foreign: publishable sires with no recorded offspring in Italy.

6.3.2 Validation

The dERC* express in effective records contributions how much information the international evaluation added through the integration procedure on top of the Italian national information. The dERC* in $BLEND_{MAY}$ reflected the higher amount of international information integrated for the groups of domestic sires with < 15 recorded offspring and foreign sires compared to that of domestic sires with ≥ 15 recorded offspring in ITA. When integrating international information from the pedigree-based evaluation, domestic sires with ≥ 15 recorded offspring had an average dERC* of 0.5 and 0.1 additional effective records integrated for direct and maternal EBV, respectively (Table 6.4). Instead, domestic sires with < 15 recorded offspring and foreign sires had a mean dERC* of 5.2 and 2.5 additional effective records integrated for direct EBV, respectively, and a mean of 0.7 and 0.5 additional effective records integrated for maternal EBV (Table 6.4). The same pattern across groups of sires was also observed when integrating information from the single-step international evaluation, but with a higher number of effective records compared to the pedigree-based international evaluation, reflecting the additional genomic information in the single-step international evaluation. On average across groups of sires, integrating information from the single-step international evaluation resulted in 6.5 and 3.9 additional effective records for direct and maternal EBV, respectively, compared to the pedigree international evaluation (Table 6.6).

Comparing the dERC* distribution in $BLEND_{MAY}$ with the one of GOLD provides an indication of the corrected removal of double-counting of national information in $BLEND_{MAY}$. Overall, dERC* in $BLEND_{MAY}$ showed good agreement with dERC* in GOLD (Table 6.4 and Table 6.6). Compared to the mean dERC* in GOLD, the mean dERC* in $BLEND_{MAY}$ was, on average across the three groups of sires, 0.5 effective records higher for direct EBV or equal for maternal EBV, either when integrating pedigree-based (Table 6.4) or single-step international information (Table 6.6).

6.3.2.1 Integration of pedigree-based international information into national evaluations: adequacy and predictivity

Overall, compared to NAT_{MAY}, both $BLEND_{MAY}$ and GOLD had higher ρ and R^2_{adj}, b_1 closer to 1, LB closer to 0, and smaller RMSE (Table 6.4). As expected, for domestic sires with ≥ 15 recorded offspring, NAT_{MAY} (i.e. a national evaluation without integration of international information) showed high model adequacy for both direct and maternal EBV (ρ ≥ 0.95, $b_1 > 0.90$ and $R^2_{adj} > 0.90$) (Table 6.4). In contrast, for domestic sires with < 15 recorded offspring and for foreign sires, the model adequacy of NAT_{MAY} for both direct and maternal EBV was lower, with the group of foreign sires showing the lowest model adequacy (e.g. ρ = 0.24, $b_1 = 0.69$, and R^2_{adj} =

0.06 for direct EBV). Overall, for direct EBV and for all groups of sires, $BLEND_{MAY}$ and GOLD showed similar results and high model adequacy (values of $\rho \geq 0.97$ and b_1 between 0.96 and 1.14) (Table 6.4). Overall, for maternal EBV and for both groups of domestic sires, $BLEND_{MAY}$ and GOLD showed close or slightly lower model adequacy for maternal EBV to that of NAT_{MAY} (difference in ρ between 0.01 and 0.02). For maternal EBV of foreign sires, both $BLEND_{MAY}$ and GOLD had ρ closer to 1 and b_1 values further below 1 compared to NAT_{MAY}. Nonetheless, the smaller RMSE values for $BLEND_{MAY}$ and GOLD suggest better model adequacy of blended evaluations compared to NAT_{MAY} (Table 6.4). Finally, for direct and maternal EBV of all groups of sires, $BLEND_{MAY}$ performed close or slightly worse than GOLD except for maternal EBV of foreign sires for which $BLEND_{MAY}$ showed slightly higher ρ values (difference of 0.02) and smaller RMSE compared to GOLD (Table 6.4).

Overall, $BLEND_{MAY}$ and GOLD showed similar or higher predictivity than NAT_{MAY} based on ρ, R^2_{adj}, b_1, LB and RMSE (Table 6.5). NAT_{MAY} showed high predictivity for both groups of offspring of publishable sires ($\rho \geq 0.94$ and b_1 between 0.94 and 1.01) with offspring's direct EBV having lower ρ and b_1 further from 1 compared to offspring's maternal EBV (Table 6.5). Overall, predictivity results for $BLEND_{MAY}$ and GOLD were in close agreement, and showed similar or higher predictivity than NAT_{MAY} for both offspring's direct and maternal EBV (ρ, R^2_{adj}, and b_1 closer to 1, LB closer to 0, and smaller RMSE) (Table 6.5). Only maternal EBV of offspring of sires with both publishable direct and maternal EBV had lower predictivity in both $BLEND_{MAY}$ and GOLD compared to NAT_{MAY}, with slightly lower values of ρ (difference of 0.01) and values of b_1 further from 1.

Table 6.4 Validation of scenarios' adequacy for direct and maternal EBV when EBV_{INT} are computed using pedigree-based international evaluations [a].

	Validation group [b]	Scenario [c]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE	Summary dERC*						
								min	1st Q	median	mean	3rd Q	max	n > 0
Direct EBV	Domestic (≥ 15 off)	NAT_{MAY}	0.95	-0.14	0.96	0.90	1.73	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.99	0.01	0.96	0.97	0.94	0.0	0.0	0.0	0.5	0.0	71.1	97
		GOLD	0.99	-0.03	1.01	0.98	0.69	0.0	0.0	0.0	0.3	0.0	11.6	121
	Domestic (< 15 off)	NAT_{MAY}	0.63	-0.52	0.66	0.39	4.78	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.97	-0.10	0.96	0.94	1.43	0.9	2.9	4.0	5.2	6.5	20.3	94
		GOLD	0.97	-0.13	1.03	0.93	1.60	0.9	2.5	3.5	4.0	5.1	10.0	94
	Foreign	NAT_{MAY}	0.24	-0.22	0.69	0.06	6.01	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.97	-0.17	1.13	0.94	1.49	0.0	1.8	2.3	2.5	3.0	17.4	3,469
		GOLD	0.97	-0.14	1.14	0.94	1.56	0.9	1.8	2.2	2.4	2.9	9.3	3,470
Maternal EBV	Domestic (≥ 15 off)	NAT_{MAY}	0.99	0.05	1.01	0.98	0.65	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.98	-0.04	0.96	0.95	0.98	0.0	0.0	0.0	0.1	0.0	3.6	52
		GOLD	0.98	-0.01	1.02	0.97	0.79	0.0	0.0	0.0	0.1	0.0	1.2	70
	Domestic (< 15 off)	NAT_{MAY}	0.86	0.13	0.80	0.73	1.96	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.84	-0.05	0.72	0.71	2.04	0.3	0.6	0.7	0.7	0.9	1.3	51
		GOLD	0.86	-0.03	0.87	0.74	1.94	0.4	0.5	0.7	0.7	0.8	1.1	51
	Foreign	NAT_{MAY}	0.51	0.06	0.98	0.26	2.37	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.83	0.06	0.57	0.69	1.53	0.0	0.4	0.5	0.5	0.5	1.3	1,127
		GOLD	0.81	0.03	0.58	0.65	1.62	0.3	0.4	0.4	0.4	0.5	1.1	1,165

[a] Scenario's EBV are compared with pedigree-based EBV of scenario REF_{MAY_trunc} (international evaluation including national data up to May 2019 and foreign data up to January 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error, dERC*: adjusted de-regressed effective record contribution (representing additional information added on top of NAT_{MAY}), min: minimum, 1st Q: first quartile, 3rd Q: third quartile, max: maximum, n > 0: number of dERC* greater than 0.

[b] Validation group = Domestic (≥ 15 off): publishable sires with ≥ 15 recorded offspring in Italy, Domestic (< 15 off): publishable sires with < 15 recorded offspring in Italy, and Foreign: publishable sires with no recorded offspring in Italy.

[c] Scenario = NAT_{MAY}: national evaluation without integration, $BLEND_{MAY}$: blended national evaluation with integration of publishable sires' international information and correction for double-counting, GOLD: as $BLEND_{MAY}$, but integrating publishable sires' international information that did not include national data.

Table 6.5 Validation of scenarios' predictivity for direct and maternal EBV when EBV_{INT} are computed using pedigree-based international evaluations [a].

Validation group [b]	Offspring' EBV	Scenario [c]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE
Offspring of sires with publishable direct EBV	Direct EBV	NAT_{MAY}	0.96	-0.16	0.94	0.93	1.19
		$BLEND_{MAY}$	0.99	-0.01	0.99	0.99	0.48
		GOLD	0.99	-0.05	1.01	0.99	0.47
	Maternal EBV	NAT_{MAY}	0.99	0.07	1.01	0.97	0.51
		$BLEND_{MAY}$	0.99	-0.02	1.01	0.97	0.53
		GOLD	0.99	0.00	1.04	0.98	0.50
Offspring of sires with publishable direct and maternal EBV	Direct EBV	NAT_{MAY}	0.94	-0.19	0.98	0.89	1.49
		$BLEND_{MAY}$	1.00	-0.01	0.99	0.99	0.43
		GOLD	1.00	-0.05	1.02	0.99	0.45
	Maternal EBV	NAT_{MAY}	0.99	0.07	1.01	0.98	0.42
		$BLEND_{MAY}$	0.98	-0.04	0.94	0.96	0.63
		GOLD	0.98	-0.02	0.97	0.97	0.58

[a] Scenario's EBV are compared with pedigree-based EBV of scenario REF_{MAY} (international evaluation including national data up to May 2019 and foreign data up to May 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error.

[b] Validation group = Offspring of publishable sires for direct EBV (n = 1,016) and for direct and maternal EBV (n = 60) with records in Italy born between January 2019 and May 2019.

[c] Scenario: NAT_{MAY}: national evaluation without integration, $BLEND_{MAY}$: blended national evaluation with integration of publishable sires' international information and correction for double-counting, GOLD: as $BLEND_{MAY}$, but integrating publishable sires' international information that did not include national data.

6.3.2.2 Integration of single-step international information into national evaluations: adequacy and predictivity

Overall, based on ρ, R^2_{adj}, b_1, LB and RMSE, the model adequacy of $BLEND_{MAY}$ and GOLD compared to NAT_{MAY} was higher for direct EBV, and similar or lower for maternal EBV (Table 6.6). The model adequacy of NAT_{MAY} with the international single-step evaluation was similar to the model adequacy of NAT_{MAY} with the pedigree-based international evaluation. NAT_{MAY} had a good model adequacy for domestic sires with ≥ 15 recorded offspring (ρ = 0.95 and b_1 = 0.96 for direct EBV, and ρ = 0.99 and b_1 = 1.01 for maternal EBV) and a low model adequacy for both domestic sires with < 15 recorded offspring and foreign sires (ρ ≤ 0.63) (Table 6.6). For direct EBV and for all groups of sires, $BLEND_{MAY}$ and GOLD showed similar results and had higher model adequacy than NAT_{MAY} (ρ ≥ 0.90 and b_1 between 0.96 and 1.12). For maternal EBV of domestic sires with ≥ 15 recorded offspring, $BLEND_{MAY}$ and GOLD had slightly lower model adequacy than $NAT_{MAY,}$ albeit with ρ = 0.97 and b_1 close to 1. For maternal EBV of domestic sires with < 15 recorded offspring, $BLEND_{MAY}$ and GOLD had similar and lower model adequacy than NAT_{MAY}, respectively. For maternal EBV of foreign sires, $BLEND_{MAY}$ and GOLD showed higher ρ than NAT_{MAY} and b_1 further from 1, albeit R^2_{adj} and RMSE values suggest a better model fit of blended evaluations compared to NAT_{MAY}. For both direct and maternal EBV of domestic sires with < 15 recorded offspring and foreign sires, $BLEND_{MAY}$ showed higher model adequacy than GOLD (Table 6.6).

Overall, $BLEND_{MAY}$ and GOLD showed better or similar predictivity compared to NAT_{MAY} for offspring' direct EBV, and similar or slightly lower predictivity for maternal EBV, as indicated by ρ, R^2_{adj}, b_1, LB and RMSE (Table 6.7). Model predictivity of NAT_{MAY} was similar to that observed for the pedigree-based international evaluation. Overall, NAT_{MAY} showed high predictivity for both groups of offspring of publishable sires, but predictivity was lower for direct EBV compared to maternal EBV: average ρ of 0.95 and average b_1 of 0.96, and average ρ of 0.99 and average b_1 of 1.01, respectively (Table 6.7). Overall, $BLEND_{MAY}$ had better predictivity than NAT_{MAY} with values of ρ, R^2_{adj} and b_1 closer to 1, and values of LB and RMSE closer to 0. $BLEND_{MAY}$ showed lower predictivity only for maternal EBV of offspring of sires with both direct and maternal EBV publishable: lower values of ρ (difference of 0.02) and b_1 (difference of 0.06) (Table 6.7). Overall, for both groups of offspring of publishable sires, GOLD had better predictivity compared to NAT_{MAY} for direct EBV, but similar or slightly worse predictivity for maternal EBV (Table 6.7). Overall, $BLEND_{MAY}$ had similar or slightly better predictivity than GOLD for both direct and maternal EBV of both groups of offspring (except for maternal EBV of offspring of sires with both direct and maternal publishable EBV).

Table 6.6 Validation of scenarios' adequacy for direct and maternal EBV when EBV_{INT} are computed using single-step international evaluations [a].

	Validation group [b]	Scenario [c]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE	Summary dERC*						
								min	1st Q	median	mean	3rd Q	max	n > 0
Direct EBV	Domestic (≥ 15 off)	NAT_{MAY}	0.95	-0.17	0.96	0.90	1.76	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.98	-0.05	0.96	0.96	1.16	0.0	0.0	0.0	2.1	0.0	571.4	99
		GOLD	0.98	-0.14	1.01	0.96	1.09	0.0	0.0	0.0	1.9	0.0	560.9	120
	Domestic (< 15 off)	NAT_{MAY}	0.63	-0.55	0.66	0.39	4.79	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.96	-0.21	0.97	0.93	1.62	0.9	3.3	6.8	19.9	29.3	173.3	94
		GOLD	0.92	-0.24	1.00	0.84	2.46	0.9	2.8	5.1	18.7	29.2	173.2	94
	Foreign	NAT_{MAY}	0.24	-0.26	0.71	0.06	5.98	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.97	-0.26	1.12	0.94	1.47	0.0	1.8	2.5	5.6	3.6	455.7	3,469
		GOLD	0.90	-0.20	1.04	0.81	2.66	0.0	1.8	2.4	5.5	3.4	455.5	3,469
Maternal EBV	Domestic (≥ 15 off)	NAT_{MAY}	0.99	0.06	1.01	0.98	0.63	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.97	-0.01	0.96	0.95	1.02	0.0	0.0	0.0	4.2	0.0	666.7	53
		GOLD	0.97	0.05	1.02	0.93	1.13	0.0	0.0	0.0	4.2	0.0	666.2	69
	Domestic (< 15 off)	NAT_{MAY}	0.86	0.12	0.80	0.73	1.96	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.85	0.00	0.72	0.71	2.03	0.2	0.7	0.7	10.2	1.0	110.3	51
		GOLD	0.77	0.06	0.82	0.59	2.42	0.0	0.6	0.8	10.2	0.9	109.9	50
	Foreign	NAT_{MAY}	0.52	0.06	1.00	0.27	2.35	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.83	0.07	0.59	0.69	1.54	0.0	0.4	0.5	4.3	0.6	544.2	1,127
		GOLD	0.74	0.00	0.53	0.54	1.86	0.0	0.4	0.4	4.3	0.5	544.5	1,111

[a] Scenario's EBV are compared with single-step EBV of scenario REF_{MAY_trunc} (international evaluation including national data up to May 2019 and foreign data up to January 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error, dERC*: adjusted de-regressed effective record contribution (representing additional information added on top of NAT_{MAY}), min: minimum, 1st Q: first quartile, 3rd Q: third quartile, max: maximum, n > 0: number of dERC* greater than 0.

[b] Validation group = Domestic (≥ 15 off): publishable sires with ≥ 15 recorded offspring in Italy, Domestic (< 15 off): publishable sires with < 15 recorded offspring in Italy, and Foreign: publishable sires with no recorded offspring in Italy.

[c] Scenario: NAT_{MAY}: national evaluation without integration, $BLEND_{MAY}$: blended national evaluation with integration of publishable sires' international information and correction for double-counting, GOLD: as $BLEND_{MAY}$, but integrating publishable sires' international information that did not include national data.

Table 6.7 Validation of scenarios' predictivity for direct and maternal EBV when EBV_{INT} are computed using single-step international evaluations [a].

Validation group [b]	Offspring' EBV	Scenario [c]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE
Offspring of sires with publishable direct EBV	Direct EBV	NAT_{MAY}	0.96	-0.17	0.94	0.91	1.30
		$BLEND_{MAY}$	0.99	-0.05	1.01	0.98	0.63
		GOLD	0.97	-0.11	1.02	0.94	1.11
	Maternal EBV	NAT_{MAY}	0.99	0.07	1.01	0.97	0.52
		$BLEND_{MAY}$	0.99	0.00	1.02	0.98	0.46
		GOLD	0.96	0.05	1.06	0.91	0.93
Offspring of sires with publishable direct and maternal EBV	Direct EBV	NAT_{MAY}	0.94	-0.20	0.98	0.88	1.59
		$BLEND_{MAY}$	0.98	-0.07	1.01	0.97	0.81
		GOLD	0.97	-0.11	1.04	0.94	1.07
	Maternal EBV	NAT_{MAY}	0.99	0.07	1.00	0.98	0.45
		$BLEND_{MAY}$	0.97	0.01	0.94	0.94	0.75
		GOLD	0.98	0.03	1.01	0.96	0.67

[a] Scenario's EBV are compared with single-step EBV of scenario REF_{MAY} (international evaluation including national data up to May 2019 and foreign data up to May 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error.

[b] Validation group = Offspring of publishable sires for direct EBV (n = 1,016) and for direct and maternal EBV (n = 60) with records in Italy born between January 2019 and May 2019.

[c] Scenario: NAT_{MAY}: national evaluation without integration, $BLEND_{MAY}$: blended national evaluation with integration of publishable sires' international information and correction for double-counting, GOLD: as $BLEND_{MAY}$, but integrating publishable sires' international information that did not include national data.

6.4 Discussion

National evaluations use pedigree-based or genomic-based BLUP models to estimate breeding values. A requirement of BLUP models to obtain unbiased predictions is that all information used for selection decisions is taken into account in the current evaluation (Henderson 1975; Patry and Ducrocq 2011; Jibrila *et al.* 2021). In practice, this requirement is not always met. For example, foreign sires that have been selected based on foreign recorded offspring may have biased national EBV since foreign records are unavailable during national evaluations (Bonaiti and Boichard 1995; Vandenplas and Gengler 2012). International evaluations allow to take into account data available in other countries, but differences between EBV_{NAT} and EBV_{INT} may arise. In this study, we defined and validated a procedure that allows straightforward integration of beef cattle pedigree-based and single-step EBV_{INT} into

national evaluations by participating countries. Hereafter we first discuss the results of the integration procedure applied to the Italian pedigree-based national evaluations using Limousin weaning weight data, followed by a discussion on the integration procedure itself. Finally, we discuss the possible implications of this study for participating countries in the context of beef cattle international evaluations.

6.4.1 Integration of pedigree-based and single-step international information

Overall, the integration of information of publishable sires into the national pedigree-based Italian evaluation improved the model adequacy while keeping similar model predictivity (Table 6.4 to Table 6.7). Compared to EBV_{NAT}, the blended EBV for publishable sires were in closer agreement with the international EBV of the reference scenarios. Moreover, the blended EBV showed less level bias compared to EBV_{NAT}. Overall, the integration procedure had greater impact for direct EBV than for maternal EBV, especially for sires with < 15 recorded offspring and foreign sires. This was likely due to the lower REL associated with the integrated maternal EBV_{INT} for these two groups of sires compared to their REL of direct EBV_{INT} and the REL of maternal EBV_{INT} for domestic sires with ≥ 15 recorded offspring (Figure 6.2 and Figure 6.3). The lower REL of maternal EBV_{INT} compared to direct EBV_{INT} in these two groups of sires is likely due to the low or null number of offspring recorded in ITA, and the low genetic correlations between ITA and other countries for maternal effects (Supplementary Table S6.3). These results show that due to the lower associated REL the added benefit of integration of publishable sires' maternal EBV_{INT} is lower than for direct EBV_{INT}. Nonetheless, the integration procedure increased the model adequacy of national evaluations for all groups of publishable sires for both direct EBV_{INT} and maternal EBV_{INT}.

The integration procedure improved pedigree-based national evaluations both when integrating pedigree-based and single-step international information, with slightly larger improvements in model adequacy and predictivity for the former compared to the latter. Results for model adequacy are in line with those obtained by Pabiou *et al.* (2018) who integrated pedigree-based international information into the Irish pedigree-based national evaluation. To our knowledge, our study is the first that investigates the integration of EBV_{INT} from single-step beef cattle international evaluations into pedigree-based national evaluations. The main difference in integrating single-step compared to pedigree-based international information is that publishable sires may have genotypes available in the international models resulting in higher REL_{INT} (Figure 6.3). We further investigated possible differences in model adequacy between genotyped and non-genotyped foreign sires, being the only

group with a large number of genotyped publishable sires: 512 for direct EBV and 142 for maternal EBV (Supplementary Table S6.6). Model adequacy was higher for foreign genotyped compared to non-genotyped sires for both direct and maternal EBV. This is likely due to the higher dERC* for genotyped sires which gives more weight to the international information compared to the national one, resulting in blended EBV closer to the reference EBV.

National evaluations without integration showed already high predictivity of offspring' EBV with $\rho > 0.94$ for direct EBV and $\rho > 0.99$ for maternal EBV (Table 6.5 and Table 6.7). The high predictivity of national evaluations is likely due to the offspring of publishable sires having both own phenotypes and phenotypes of national relatives (e.g. half-sibs) available at the national level, leaving little room for improvement to be made by the integration procedure. We tested whether the advantage of the integration procedure would be more pronounced when the phenotypes of offspring of publishable sires (and that of their national and foreign contemporaries) are not yet available by integrating pedigree-based and single-step international information into NAT_{JAN} instead of NAT_{MAY} (Supplementary Table S6.7 and Supplementary Table S6.8, respectively). The integration procedure into NAT_{JAN} was performed both using the integration procedure as in $BLEND_{MAY}$ (here called $BLEND_{JAN}$) and as in GOLD (here called $GOLD_{JAN}$). Overall, model predictivity of NAT_{JAN} was lower than for $NAT_{MAY,}$ and the increases in predictivity due to the integration procedure were more evident, with values of ρ and b_1 for both $BLEND_{JAN}$ and $GOLD_{JAN}$ in most cases closer to 1 than those of NAT_{JAN}. These results suggest that the integration procedure can increase the predictivity of national evaluations for offspring of publishable sires especially when no phenotypes are yet available on the offspring, i.e. through a more accurate parent average EBV.

6.4.2 Integration procedure

Our procedure allows integrating pedigree-based or single-step international information (EBV_{INT} and REL_{INT}) into national evaluations. The proposed procedure is a simplified and generalized version of the one tested by Pabiou *et al.* (2018) in beef cattle which is similar to the one proposed by Pitkänen *et al.* (2018, 2020) for dairy cattle. Our procedure relies on simplified calculation of weights (i.e. ERC) and of de-regressed EBV (i.e. DRP), using the one-animal-at-the-time formulas in steps 1 and 2 (similarly to VanRaden *et al.* 2014). This makes the application of the integration procedure straightforward and computationally inexpensive. More complex algorithms, like those applied in Pabiou *et al.* (2018) and Pitkänen *et al.* (2018), requires availability of dedicated software packages. Since the beginning of international exchange of sires, several methods to integrate different sources of

information into national evaluations have been proposed (Vandenplas and Gengler 2015). However, some of these approaches, e.g. the Bayesian approaches (Vandenplas and Gengler 2012; Vandenplas *et al.* 2014, 2017), may require adapting the software used for national genetic evaluations. Instead, by including external information as additional pseudo-phenotypes, the integration approach proposed in this study allows keeping the same national model and the same software used for national routine evaluations.

In our study, we noticed that the filter for the gain in REL (defined as the difference between REL_{INT} and REL_{NAT}) was key to avoiding double-counting of national information for domestic sires. This filter, similar to the one used by Pitkänen *et al.* (2020), avoids the erroneous integration of publishable sires' information due to approximations in REL. In particular, we noticed that such filter improves the results for publishable sires that have no recorded offspring in other countries than ITA, by avoiding double-counting of national information. For these sires, changes in REL_{INT} compared to REL_{NAT} were due to small changes in their parent average reliability which may be due to approximations involved in the computations of REL_{INT} and REL_{NAT}. It should be noted that, in practice, the REL for a publishable sire' EBV from routine national multi-trait evaluations may be higher than both REL_{INT} and REL_{NAT} which was computed from a single-trait evaluation in this study. Indeed although foreign offspring records for a sire could be available for a trait evaluated in Interbeef, resulting in an associated REL_{INT} greater than the corresponding REL_{NAT}, national information may be available for traits that are not yet included in Interbeef. Therefore, it is advisable to compare the REL_{INT} of publishable sires against a national REL based on the same source of information and model as the international evaluation to determine its integration. These comparable national REL have to be used as input in our integration procedure.

Scenario GOLD avoids double-counting of national information by integrating information from an international evaluation without national phenotypes. Instead, scenario $BLEND_{MAY}$ avoids double-counting through the adjustment of DRP and dERC in step 3 of the integration procedure. Overall, when integrating pedigree-based international information, as expected, GOLD performed slightly better than $BLEND_{MAY}$ based on model adequacy. However, $BLEND_{MAY}$ performed slightly better than GOLD for maternal EBV of foreign sires when integrating pedigree-based international information, and for both direct and maternal EBV of both domestic sires with < 15 recorded offspring and foreign sires when integrating single-step international information. These results could be explained by the possible over-estimation of dERC* in $BLEND_{MAY}$ in comparison to dERC* in GOLD. Step 3 of the integration procedure removes double-counting due to national records

(Vandenplas *et al.* 2014, 2017). However, double-counting due to national records could still be present in $BLEND_{MAY}$ due to the different approximations. In GOLD possible double-counting of national records are absent as the input international evaluation (INT_{JAN_red}) excluded national phenotypes (Table 6.2). The effect on the blended EBV due to the possible remaining double-counting of national information in $BLEND_{MAY}$ was further investigated by regressing the blended EBV of GOLD on those of $BLEND_{MAY.}$ Overall, when integrating pedigree-based international information, EBV correlations between GOLD and $BLEND_{MAY}$ were ≥ 0.98 for all groups of sires. When integrating single-step international information, EBV correlations between GOLD and $BLEND_{MAY}$ were equal to 0.97 for domestic sires with ≥ 15 recorded offspring in ITA, and ≥ 0.89 for domestic sires with < 15 recorded offspring and foreign sires. Overall, these results suggest that the effect of double-counting of remaining national information becomes more important when integrating sires' EBV_{INT} with lower REL compared to EBV_{INT} with high REL, in agreement with Vandenplas *et al.* (2017). These results also suggest that there is more double-counting when integrating single-step international information compared to pedigree-based information. This could be explained by the fact that genomic relationships are not considered when deregressing the international information, resulting in double-counting genomic information in the blended EBV. More sophisticated and computationally demanding algorithms like the TSA by Vandenplas and Gengler (2012), or the algorithm by Calus *et al.* (2016) could be applied to estimate potentially more accurate weights that are free of contributions due to pedigree and genomic relationships, avoiding its double-counting and possibly further improve the results. Similarly, the de-regression step of EBV of sires could potentially be improved by using matrix de-regression procedures (Jairath *et al.* 1998; Garrick *et al.* 2009; Calus *et al.* 2016) which is theoretically expected to be better than the one-animal-at-the-time de-regression proposed here (Calus *et al.* 2016). However, the latter approach can be more easily applied, while it achieves sound results as shown in our study.

6.4.3 Implications

Two assumptions that applied to this study should be acknowledged for the application of the integration procedure by countries participating in Interbeef. First, the same algorithm to compute REL was used for national and international evaluations. If REL_{NAT} and REL_{INT} are approximated with different algorithms, this may cause differences between them and, in turn, differences in their corresponding ERC, which could impact the integration procedure. Thus, having accurate and possibly the same reliability algorithm for national and international evaluations is desirable.

Alternatively, when this is not possible, REL_{NAT} (or the corresponding dERC, similarly to what is done in MACE evaluations; Guarini *et al.* 2018; Luštrek *et al.* 2021) could be computed and distributed at the international level after performing pseudo-national evaluations using the same reliability algorithm as the one used for international evaluations. These pseudo-national evaluations can be obtained by running a pedigree-based or single-step evaluation for each country and using only national data. The second assumption was that EBV_{INT} were already expressed on the same scale as EBV_{NAT}. If the EBV_{INT} or the EBV_{NAT} are expressed on different scales or genetic bases, such differences could impact the integration (Garrick *et al.* 2009) and need to be taken into account (e.g. Guarini *et al.* 2019) before starting the integration procedure.

The proposed integration procedure can be applied by countries participating in Interbeef evaluations to integrate publishable sires' EBV_{INT} at the national level. Integrating information as in scenario GOLD would be optimal because it completely avoids double-counting of national information. However, this integration requires to compute and distribute for each country EBV and REL from an international evaluation with the country's national data removed. Instead, integrating information as in scenario $BLEND_{MAY}$ can be directly applied at the country level using information already available. Applying the integration as in $BLEND_{MAY}$ implies that a pseudo-national evaluation with the same information as provided to Interbeef should be performed to remove possible double-counting during the integration. This pseudo-national evaluation can be performed at the country level or at the international level as explained above. In the latter case, the resulting EBV_{NAT} and REL_{NAT} could be distributed next to the EBV_{INT} and REL_{INT}.

Results of this study suggest that the integration of single-step international information is able to adequately make use of external genomic information. As ITA national evaluations were pedigree-based, no double-counting due to domestic genotypes was present when performing the integration. When integrating single-step international information into single-step national evaluations, a similar procedure as the one proposed here can be used. However, double-counting of national genomic information should be removed from the international single-step evaluation prior to the integration (Vandenplas *et al.* 2017). Our proposed method should therefore be adapted to avoid double-counting of national genomic information, and further research is needed.

Finally, we expect that the integration procedure would give similar results when applied to other traits and breeds evaluated in Interbeef since similar rules for publication of sires' EBV_{INT} apply. The proposed integration procedure could be applied to any animal with an available EBV_{INT} (and associated REL_{INT}). However, the

adequacy of the integration procedure to integrate international information for animals with low associated REL (e.g. cows) is currently unknown and should be further investigated.

6.5 Conclusions

We propose a general integration procedure to integrate beef cattle international EBV of publishable sires into national evaluations. Using Limousin weaning weight from countries participating in Interbeef evaluations and the Italian pedigree-based national evaluations as a case study, we showed that the proposed integration procedure increased the model adequacy for EBV of publishable sires, while giving similar or higher predictivity for EBV of their domestic offspring. The procedure worked well both when integrating information either from pedigree-based international evaluations or from single-step international evaluations. The proposed integration procedure is computationally inexpensive and its application to existing national evaluations is straightforward.

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6.8 Supplementary material

6.8.1 Supplementary tables

Table S6.1 Phenotypic distribution of AWW per country for male and females [a].

COU [b]	Males					Females				
	N	Min	Mean	Max	σ_P	N	Min	Mean	Max	σ_P
CZE	6,816	173	293.2	411	37.8	7,076	157	262.8	366	33.5
DFS	48,340	112	240.6	369	41.5	48,331	107	213.3	319	34.1
IRL	40,873	134	297.2	460	53.9	27,213	127	264.4	402	45.2
DEU	58,716	137	269.9	402	43.3	58,533	128	242.3	356	37.0
CHE	18,197	112	233.4	354	39.2	17,498	107	209.7	312	33.2
ITA	49,100	75	206.1	339	42.8	63,506	75	196.9	320	39.8

[a] AWW = age-adjusted weaning weights, N = number of phenotypes, Min = minimum, Max = maximum, σ_P = phenotypic standard deviation.
[b] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland, ITA = Italy.

Table S6.2 List of environmental effects in each national model [a, b].

COU [a]	Fixed						Random		Covariates		
CZE		asextwin		year			PE	HYS	aaca	aaca2	
DFS	HYS	asex	aaca	seas	twin		PE				
IRL	HYS	asex	pariagedam				PE		agedam2	aawg	
DEU		asex	pari	month	twin			HY			
CHE		asex		yearmonth		alpine	PE	HY	agedam	agedam2	
ITA	HYS	asex			twin		PE		aawg	aaca	aaca2

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland, ITA = Italy.
[b] aaca = age at calving; aaca2 = age at calving as quadratic effect; aawg = age at weighting; agedam = age of the dam; agedam2 = age of the dam fitted as quadratic effect; alpine = access to alpine grazing for calves; asex = sex of the animal; asextwin = interaction between asex and twin; HY = Herd-Year; HYS = Herd-Year-Season; month = month of birth; pari = parity; pariagedam = interaction between pari and agedam; PE = maternal permanent environmental effect; seas = season; twin = twinning; year = year of birth; yearmonth = interaction between year and month.

Table S6.3 Direct and maternal genetic covariances (below diagonal), genetic variances (diagonal) and genetic correlations (above diagonal) within and across countries [a].

		Direct						Maternal					
		CZE	DFS	IRL	DEU	CHE	ITA	CZE	DFS	IRL	DEU	CHE	ITA
Direct	CZE	686	0.73	0.64	0.64	0.72	0.69	-0.39	-0.14	-0.05	-0.04	-0.13	-0.39
	DFS	313.97	269	0.56	0.86	0.72	0.73	0.01	-0.39	-0.08	-0.07	-0.16	-0.39
	IRL	354.93	194.97	450	0.45	0.56	0.63	-0.02	-0.19	-0.41	-0.09	-0.12	-0.39
	DEU	326.74	275.66	184.92	383	0.62	0.68	-0.01	-0.22	-0.07	-0.38	-0.14	-0.38
	CHE	369.97	229.16	232.38	235.53	380	0.70	-0.02	-0.19	-0.07	-0.06	-0.47	-0.40
	ITA	175.75	116.63	130.45	128.58	132.86	94	0.22	0.05	0.16	0.15	0.09	-0.66
Maternal	CZE	-144.99	2.37	-5.11	-1.95	-4.39	29.98	197	0.37	0.42	0.46	0.48	0.22
	DFS	-40.89	-69.68	-43.09	-46.61	-39.94	5.35	56.75	120	0.54	0.56	0.53	0.31
	IRL	-19.59	-18.23	-119.87	-19.09	-19.70	21.29	82.03	81.80	194	0.57	0.49	0.23
	DEU	-19.02	-21.30	-32.76	-132.86	-21.20	27.13	117.18	110.61	143.68	326	0.54	0.25
	CHE	-33.30	-25.32	-25.53	-26.50	-89.26	8.86	65.06	56.00	66.73	94.08	94	0.28
	ITA	-89.19	-56.68	-72.20	-66.45	-68.20	-56.44	27.05	29.79	28.84	40.62	23.69	78

[a] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland, ITA = Italy.

Table S6.4 National genetic, environmental, and residual variances [b].

COU [a]	σ^2_{HY}	σ^2_{HYS}	σ^2_{PE}	σ^2_{dir}	σ^2_{mat}	σ^2_{res}
CZE		294	208	686	197	377
DFS			90	269	120	547
IRL			45	450	194	647
DEU	477			383	326	719
CHE	203		76	380	94	587
ITA			69	94	78	278

[a] Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland, ITA = Italy.
[b] σ^2 = variance, HY = Herd-Year, HYS = Herd-Year-Season, PE = maternal permanent environment, dir = direct genetic effect, mat = maternal genetic effect, res = residual.

Table S6.5 Number of phenotypes and genotypes per country [a] used in the implemented scenarios.

	Phenotypes			Genotypes		
COU [a]	Up to January 2019	January 2019 to May 2019	Total	Up to January 2019	January 2019 to May 2019	Total
CZE	13,741	151	13,892	1,298	286	1,584
DFS	94,852	1,495	96,347	-	-	-
IRL	66,621	1,422	68,043	11,300	-	11,300
DEU	113,993	2,137	116,130	626	90	716
CHE	35,695	-	35,695	3,922	15	3,937
ITA	109,283	2,301	111,584	-	-	-
Total	434,185	7,506	441,691	17,146	391	17,537

[a] COU = Country: CZE = Czech Republic, DFS = Denmark, Finland and Sweden, IRL = Ireland, DEU = Germany, CHE = Switzerland, ITA = Italy.

Table S6.6 Validation of scenarios' adequacy for direct and maternal EBV of foreign publishable sires when EBV_{INT} are computed using single-step international evaluations [a].

	Foreign sires	Scenario [b]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE	Summary dERC*						
								min	1st Q	median	mean	3rd Q	max	number dERC > 0
Direct EBV	Genotyped (n = 512)	NAT_{MAY}	0.18	-0.37	0.61	0.03	6.00	-	-	-	-	-	-	-
		$BLEND_{MAY}$	1.00	-0.33	1.06	0.99	0.51	3.6	10.4	13.7	23.7	25.0	455.7	512
		GOLD	0.94	-0.31	0.97	0.89	2.01	3.3	10.3	13.6	23.6	25.0	455.5	512
	Ungenotyped (n = 2,958)	NAT_{MAY}	0.25	-0.25	0.72	0.06	5.96	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.97	-0.25	1.13	0.94	1.55	0.0	1.7	2.3	2.5	3.0	17.4	2957
		GOLD	0.90	-0.18	1.05	0.81	2.71	0.0	1.7	2.2	2.4	2.9	9.3	2957
Maternal EBV	Genotyped (n = 142)	NAT_{MAY}	0.55	0.07	1.18	0.30	2.49	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.98	0.23	0.93	0.96	0.62	0.0	10.2	12.5	32.3	27.2	544.2	141
		GOLD	0.87	0.14	0.85	0.76	1.46	0.0	10.2	12.5	32.3	27.1	544.5	141
	Ungenotyped (n = 1,023)	NAT_{MAY}	0.52	0.06	0.98	0.27	2.33	-	-	-	-	-	-	-
		$BLEND_{MAY}$	0.82	0.05	0.57	0.68	1.54	0.0	0.4	0.5	0.5	0.5	1.3	986
		GOLD	0.73	-0.02	0.51	0.53	1.85	0.0	0.4	0.4	0.4	0.5	1.1	970

[a] Scenario's EBV are compared with single-step EBV of scenario REF_{MAY_trunc} (international evaluation including national data up to May 2019 and foreign data up to January 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error, dERC*: adjusted de-regressed effective record contribution (representing additional information added on top of NAT_{MAY}), min: minimum, 1st Q: first quartile, 3rd Q: third quartile, max: maximum, n > 0: number of dERC* greater than 0.

[b] Scenario: NAT_{MAY}: national evaluation without integration, $BLEND_{MAY}$: blended national evaluation with integration of publishable sires' international information and correction for double-counting, GOLD: as $BLEND_{MAY}$, but integrating publishable sires' international information that did not include national data.

Table S6.7 Validation of scenarios' predictivity for direct and maternal EBV when international information are integrated on Scenario NAT_{JAN} and EBV_{INT} are computed using pedigree-based international evaluations [a].

Validation group [b]	Offspring' EBV	Scenario [c]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE
Offspring of sires with publishable direct EBV	Direct EBV	NAT_{JAN}	0.86	-0.11	0.89	0.73	2.29
		$BLEND_{JAN}$	0.88	-0.02	0.93	0.78	2.06
		$GOLD_{JAN}$	0.89	-0.06	0.96	0.79	2.04
	Maternal EBV	NAT_{JAN}	0.95	0.05	1.02	0.90	1.01
		$BLEND_{JAN}$	0.94	-0.01	1.01	0.88	1.08
		$GOLD_{JAN}$	0.95	0.02	1.06	0.89	1.03
Offspring of sires with publishable direct and maternal EBV	Direct EBV	NAT_{JAN}	0.53	-0.20	0.63	0.27	3.81
		$BLEND_{JAN}$	0.67	-0.07	0.81	0.44	3.35
		$GOLD_{JAN}$	0.66	-0.10	0.83	0.42	3.39
	Maternal EBV	NAT_{JAN}	0.87	0.07	0.95	0.76	1.58
		$BLEND_{JAN}$	0.89	-0.01	0.92	0.79	1.49
		$GOLD_{JAN}$	0.89	0.01	0.96	0.80	1.44

[a] Scenario's EBV are compared with pedigree-based EBV of scenario REF_{MAY} (international evaluation including national data up to May 2019 and foreign data up to May 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error.

[b] Validation group = Offspring of publishable sires for direct EBV (n = 1,016) and for direct and maternal EBV (n = 60) with records in Italy born between January 2019 and May 2019.

[c] Scenario: NAT_{JAN} = National evaluation using only national phenotypes up to January 2019. $BLEND_{JAN}$ = A blended national evaluation using national phenotypes as in NAT_{JAN} and integrating information of publishable sires from scenario INT_{JAN} (INT_{JAN} = international evaluation including national data up to January 2019 and foreign data up to January 2019). $GOLD_{JAN}$ = A blended evaluation using national phenotypes as in NAT_{JAN} and integrating information of publishable sires from scenario INT_{JAN_red} (INT_{JAN_red} = international evaluation including only foreign data up to January 2019).

Table S6.8 Validation of scenarios' predictivity for direct and maternal EBV when international information are integrated on Scenario NAT_{JAN} and EBV_{INT} are computed using single-step international evaluations [a].

Validation group [b]	Offspring' EBV	Scenario [c]	ρ	LB (GSD)	b_1	R^2_{adj}	RMSE
Offspring of sires with publishable direct EBV	Direct EBV	NAT_{JAN}	0.85	-0.12	0.89	0.73	2.32
		$BLEND_{JAN}$	0.89	-0.06	0.96	0.78	2.06
		$GOLD_{JAN}$	0.87	-0.12	0.99	0.75	2.20
	Maternal EBV	NAT_{JAN}	0.95	0.05	1.02	0.90	1.01
		$BLEND_{JAN}$	0.95	0.01	1.02	0.90	1.02
		$GOLD_{JAN}$	0.92	0.06	1.09	0.84	1.25
Offspring of sires with publishable direct and maternal EBV	Direct EBV	NAT_{JAN}	0.53	-0.21	0.63	0.27	3.87
		$BLEND_{JAN}$	0.64	-0.12	0.80	0.40	3.49
		$GOLD_{JAN}$	0.61	-0.16	0.81	0.37	3.59
	Maternal EBV	NAT_{JAN}	0.87	0.07	0.95	0.76	1.58
		$BLEND_{JAN}$	0.89	0.03	0.95	0.79	1.46
		$GOLD_{JAN}$	0.90	0.05	1.04	0.80	1.43

[a] Scenario's EBV are compared with single-step EBV of scenario REF_{MAY} (international evaluation including national data up to May 2019 and foreign data up to May 2019). ρ: Pearson correlation of EBV, LB (GSD): level bias (in genetic standard deviations), b_1: slope, R^2_{adj}: adjusted R^2, RMSE: Root Mean Square Error.

[b] Validation group = Offspring of publishable sires for direct EBV (n = 1,016) and for direct and maternal EBV (n = 60) with records in Italy born between January 2019 and May 2019.

[c] Scenario: NAT_{JAN} = National evaluation using only national phenotypes up to January 2019. $BLEND_{JAN}$ = A blended national evaluation using national phenotypes as in NAT_{JAN} and integrating information of publishable sires from scenario INT_{JAN} (INT_{JAN} = international evaluation including national data up to January 2019 and foreign data up to January 2019). $GOLD_{JAN}$ = A blended evaluation using national phenotypes as in NAT_{JAN} and integrating information of publishable sires from scenario INT_{JAN_red} (INT_{JAN_red} = international evaluation including only foreign data up to January 2019).


CHAPTER
7

General discussion

7.1 Introduction

Reproductive technologies such as artificial insemination allow exchanging top bulls' genetic material within and between countries (Fikse and Philipsson 2007; Moore and Hasler 2017). Thanks to such technologies, major genetic improvements have been achieved in cattle populations (Brotherstone and Goddard 2005; Philipsson 2011). Furthermore, cattle populations became genetically more connected through sires with recorded offspring in more than one country (Fikse and Philipsson 2007). However, bulls' estimated breeding value (EBV) from different national evaluations are not directly comparable due to differences in scales and genetic bases, trait and model definitions, and environmental differences between countries (Nilforooshan and Jorjani 2022). Therefore, international evaluations aim to account for such differences by combining data between countries in a single evaluation. The resulting international EBV makes foreign sires comparable with domestic ones, which facilitates their ranking and helps breeders to make selection decisions. International evaluations also allow breeders to access a larger panel of sires that could better meet their selection objectives. Finally, international evaluations consider recorded relatives in other countries, which improves the accuracy of bulls' EBV.

Beef cattle international evaluations led by Interbeef have grown fast in the last two decades, from its establishment in 2006 until the first official evaluations in 2014 (Venot *et al.* 2007, 2014). Current genetic evaluations involve up to 15 countries, five breeds and three traits. However, there are challenges and knowledge gaps that still need to be addressed in the context of current beef cattle international evaluations. These challenges are mainly related to: i) the estimation of across-country genetic correlations (r_g), which are key for international evaluations, ii) the lack of inclusion of genomic data that are already (or soon will be) included in national breeding programs, and iii) the lack of an official procedure that allows participating countries to integrate the distributed pedigree and genomic international EBV back into their national evaluations. The overall aim of this thesis was to improve and further develop methodologies for beef cattle international genetic evaluations by addressing such challenges and knowledge gaps.

In **Chapter 2,** we provided up-to-date insights on the impact of international evaluations for both large and small countries participating in Interbeef pedigree-based evaluations. We showed that international evaluations are beneficial for small countries as they enlarge the number of elite sires that can be used at the national level by providing international EBV for foreign sires on the same scale as national ones. Moreover, by including information from foreign recorded offspring, the reliability (REL) of the international EBV for domestic animals increases compared to

that of national EBV. Large countries benefit from international evaluations by obtaining international EBV for their elite sires on the scale of other participating countries. This helps to promote and export domestic elite sires' genetic material across countries by facilitating their ranking with other foreign sires. In **Chapter 3,** we showed that estimating across-country r_g using multi-trait approaches that simultaneously fit data from all countries is feasible, even when large datasets are used. The Monte Carlo EM REML algorithm handled the large amount of data and genetic parameters but required a long computational time when using the full dataset. Thus, we used different strategies of data sub-setting based on herd selection of the largest population while keeping a multi-trait estimation approach. Overall, the estimated r_g from scenarios with data sub-setting were close to the r_g estimated using all data. Depending on the scenario, the computational time was reduced up to five-fold of that required using the full dataset. The largest impact on estimated r_g from applying data sub-setting was observed for both within-country and between-country direct-maternal r_g (r_{dm}). **Chapter 4** showed that ignoring, i.e. replacing estimated values with 0, between-country r_{dm} as in current Interbeef evaluations, had a limited impact on international EBV. These results could be due to the estimated between-country r_{dm} being close to 0 on average. We also showed that ignoring within-country r_{dm} to be 0 gave considerable re-ranking for different groups of animals, among which publishable sires, i.e. sires with international EBV publishable in other countries' scales. Thus, within-country r_{dm} should not be ignored in international evaluations. In **Chapter 5,** we developed and showed the feasibility of international genomic evaluations for beef cattle using a single-step SNPBLUP approach (ssSNPBLUP). We showed that ssSNPBLUP international evaluations lead to higher accuracies compared to current pedigree-based international evaluations, and compared to either pedigree-based or genomic-based national evaluations. Moreover, international ssSNPBLUP evaluations showed similar or slightly reduced level and dispersion bias compared to either pedigree-based international evaluations or national evaluations. These results highlighted that international single-step genomic evaluations are beneficial for both large and small countries irrespectively of the number of genotypes available at the national level. Finally, **Chapter 6** presents a generalized procedure to integrate pedigree-based and single-step international EBV of publishable sires into national evaluations. The de-regression procedure is performed one-bull-at-the-time, and the international information (i.e. the international EBV and associated REL) is included in national evaluations as additional phenotypes. The procedure has low computational costs and can be easily implemented at the national level without relying on specific software. Using the Italian Limousin pedigree-based evaluations as a case study, we

showed that, compared to national EBV without integration, the EBV with integration are closer to those of international evaluations that use all available national and foreign information. Moreover, compared to national EBV without integration, the EBV with integration showed similar or higher predictivity for domestic offspring of publishable sires. Finally, the integration procedure performed well both when integrating pedigree-based or single-step international information into pedigree-based national evaluations.

Although this thesis focused on within-breed international evaluations using Limousin and age-adjusted weaning weight data, the results of Chapters 2 to 6 can be extended to other traits and breeds. For instance, in Interbeef evaluations, Limousin has a similar population structure and connectedness level as Charolais (Venot *et al.* 2009a, 2009b; Bouquet *et al.* 2011). Moreover, the insights generated from this thesis can be useful for small dairy cattle populations such as Ayrshire, Guernsey and Jersey. These breeds have connectedness levels more similar to beef cattle breeds than other dairy breeds like Holstein (Jorjani 1999, 2000). Similarly, the single-step genomic international evaluations developed in Chapter 5 will be beneficial for other traits and breeds. Compared to weaning weight, I expect larger benefits of single-step over pedigree-based international evaluations for traits with low heritability such as fertility traits, traits where selection candidates do not have a record such as carcass traits, as well as difficult-to-measure and socially relevant traits such as methane emissions or proxy of them, e.g. feed efficiency (de Haas *et al.* 2012; Berry *et al.* 2014; Negussie *et al.* 2022) or age at slaughter (Berry *et al.* 2017). Moreover, building large reference populations at the national level for such traits is challenging or even unfeasible. Thus, single-step international evaluations will provide an efficient way to obtain large common reference populations and will allow participating countries to either obtain genomic predictions on such traits or to increase the accuracy of their existing national genomic evaluations.

This final chapter is divided into three parts. In the first part, I outline and discuss a procedure for the estimation of across-country r_g in Interbeef evaluations based on the results from Chapters 3 and 4. In the second part, I show how genomic data from participating countries available for single-step international evaluations (Chapter 5) could also be used to aid the estimation of across-country r_g. Furthermore, I show that genomic data increases connectedness between populations and discuss connectedness measures that can capture such increases. Finally, in the third part, I discuss an initial approach for a model improvement in current Interbeef evaluations by modelling missing parental information using genetic groups. Moreover, I discuss the definition of genetic groups for Interbeef

pedigree-based evaluations and its extension to single-step international evaluations.

7.2 Procedures for the estimation of across-country r_g

Various factors can affect the ranking of bulls between countries, including differences in model and trait definition and genotype-by-environment interaction. All these factors will result in a r_g between countries lower than unity (Mark 2004). Therefore, it would be beneficial to harmonize model and trait definitions such that countries could be joined in one population when the r_g between them is close to 1, similarly to Denmark, Finland and Sweden in this thesis. This harmonization could also be beneficial for future international genomic evaluations since low r_g could reduce the benefits of using a common reference population (David *et al.* 2010; Wientjes *et al.* 2015). An advantage of joining countries into a single population is that the number of estimated genetic parameters in the international evaluation reduces. However, such joining could still be unfeasible due to political or privacy constraints such as data ownership. Thus, it is safe to assume that for n countries participating in Interbeef evaluations for a maternally affected trait, there will be up to $n(2n-1)$ r_g to estimate. However, due to the large number of participating countries which is currently up to 15 in Interbeef evaluations and the low level of connectedness between beef cattle populations, the estimation of across-country r_g is challenging (Chapter 3; Pabiou *et al.* 2014).

Standard procedures can be defined at the international level to guide the process of estimating across-country r_g. These procedures can make the estimated parameters across subsequent evaluations more stable by minimizing unwanted changes unless properly justified, e.g. due to changes in (inter)national models. Procedures are in place in Interbull evaluations with guidelines for both the estimation of r_g and their post-processing; for instance, how to apply country and data sub-setting or the minimum and maximum values that an estimated r_g can take (Interbull 2021). Similar procedures are in place for Breedplan evaluations, and a general outline of the steps performed during the estimation of r_g is described in Crook *et al.* (2019). The estimation of r_g in Interbeef takes place during so-called "test runs" and uses a bi-variate approach with within-country data sub-setting (Chapter 1; Pabiou *et al.* 2014). Test runs are performed when changes applied to the (inter)national models may impact either between-country or within-country genetic parameters and when new countries join the international evaluations for a specific trait. However, a procedure to estimate r_g in Interbeef is still under development, although it will soon be needed given the rapid growth in the number of participating countries and traits evaluated. Thus, based on the findings from this

thesis, I hereafter outline and discuss a general procedure to estimate across-country r_g in current Interbeef evaluations using a multi-trait approach to potentially analyse all countries together.

7.2.1 A general procedure to estimate across-country r_g in Interbeef

In Interbeef, the data available for the estimation of across-country r_g consists of national phenotypes and the international pedigree (Figure 7.1). Incoming data are usually filtered to achieve a data structure that fits the trait-specific estimation process. Removing outliers is advised as they may increase the standard errors of the estimated r_g. Next to it, removing animals in small contemporary groups (CG) is advised as they will not help in the estimation process. Similarly to Chapter 3, the minimum CG size reported by national evaluations can be used as a threshold while ensuring at least two animals per CG. Finally, additional data filters such as the minimum number of (grand-)offspring per sires and dams should be applied based on trait-specific requirements.

Given the low level of connectedness between beef cattle populations, a multi-trait approach that simultaneously fits data from all countries, as in Chapter 3, should be preferred when estimating r_g compared to the current bi-variate approach. Chapters 3 and 6 showed the feasibility of estimating r_g in Interbeef using an efficient multi-trait MC EM REML algorithm, with or without applying within-country data sub-setting. The advantage of the multi-trait approach was that all r_g were estimated simultaneously, all available existing connections across countries were retained, and the resulting matrix was positive definite. The latter avoided the need for a separate bending procedure or to set default correlations for parameters that did not converge. However, a multi-trait approach using all available data may be computationally too demanding to fit within the time frame of Interbeef test runs, which is currently about one month. At the national level, a common approach to reduce the computational time of the estimation process is to truncate and remove data. At the international level, removing old and disconnected data does not affect the estimation of across-country r_g; for example, in Chapter 3 we removed data before 1980. However, when truncating data in more recent generations there could be a trade-off between the amount of data removed and the number of retained genetic connections across countries. Future studies should investigate how to remove data from the estimation process with this approach while retaining relationships between animals and connections across countries.

For a general estimation procedure, I outline two possibilities to reduce computational time while maintaining a multi-trait approach that simultaneously fits data from multiple countries (Figure 7.1). First, within-country data sub-setting of

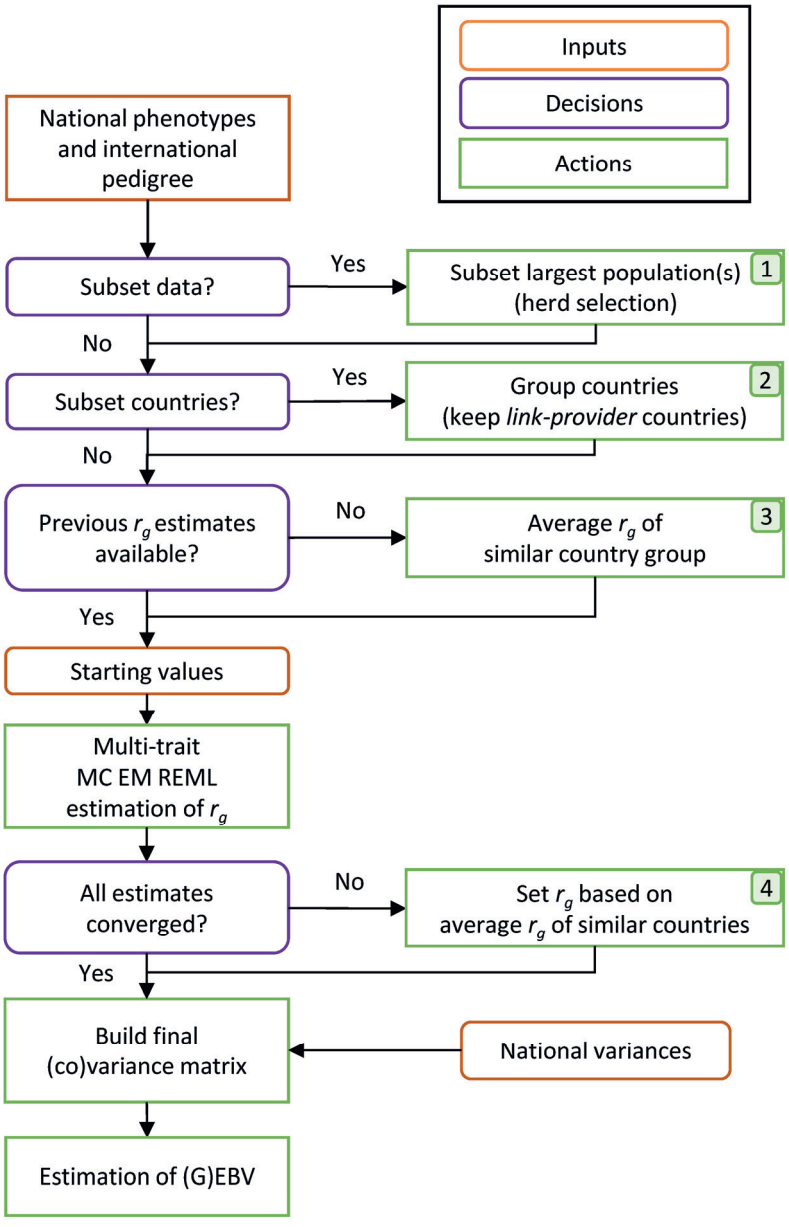


Figure 7.1 Outline of a general procedure to estimate across-country r_g in Interbeef using a multi-trait approach.

the largest populations can be performed using herd selection (Box 1 in Figure 7.1) which is an efficient approach to implement and allows retaining all CG information (Chapter 3). In Chapter 3, I used 0.5 million phenotypes from all eight countries as a threshold for data sub-setting. For large populations like France, I showed that there were no large differences in estimated r_g between sub-setting strategies, even when herds were randomly sampled. However, these results may change depending on the connectedness level of the populations to which data sub-setting is applied. Thus, for large but lowly-connected populations, I recommend using herd sub-setting strategies based on Genetic Similarity (Chapter 3) as they are expected to retain data from more connected herds (Box 1 in Figure 7.1). Second, when a large number of countries are included in the model, the computational time of the estimation process may be too long due to the large number of r_g to estimate. In such a scenario, applying herd sub-setting to each population to remain within a defined maximum dataset size may be too restrictive. In this case, a country sub-setting approach can be used by performing a series of multi-trait analyses with groups of four or five countries (Box 2 in Figure 7.1), following a process similar to the Interbull procedure (Jorjani *et al.* 2005; Interbull 2021; Nilforooshan and Jorjani 2022). This procedure groups countries based on their level of connectedness, for example, using the measures applied in Chapter 3, and always includes in each subset the country (or countries) that provides the majority of genetic connections, i.e. so-called "link-provider" countries. The inclusion of link-provider countries in each group aids the estimation process (Schaeffer 2001; Jorjani *et al.* 2005).

Starting values have to be provided for the estimation process (Figure 7.1). If available, previous estimates of across-country r_g should be used as starting values as they will likely help to reduce the computational time of the estimation process (Figure 7.1). When no previous estimates are available for a country, the average r_g values by "country groups" can be used as starting values (Box 3 in Figure 7.1). That is, the r_g starting value should be the average of the r_g available for a group of countries with similar environmental conditions and similar trait and model definitions. Another possibility is to compute an "estimate" of the r_g to then use as starting values, e.g. using the Calo *et al.* (1973) method. In brief, "Calo correlations" are obtained as the correlation between the EBV of sires used in two countries while adjusting for their EBV's reliabilities.

After the estimation process, the estimated r_g may not be converged, be out of parameter space, or be unreasonable, e.g. estimates of r_g close to 0 between European countries with similar trait and model definitions (Figure 7.1). In these situations, these r_g are usually set to an arbitrary value (Chapter 3; Pabiou *et al.* 2014). The current practice to define such arbitrary values is to use an averaged value

for all countries, irrespective of their location (Vesela *et al.* 2019). To include information on the location of the country, I recommend that this arbitrary value should be defined as the average of the estimated r_g of a group of countries with similar environmental, trait and model definitions to that of the country with an un-estimated value (Box 4 in Figure 7.1). The Interbull (2021) procedure uses this concept as well. When estimated r_g are set to arbitrary values or when a series of r_g estimated using multi-trait models are combined together, bending may be required to ensure that the final r_g matrix across all countries is positive definite (Hill and Thompson 1978). In this thesis, I always used unweighted bending, but weighted bending can also be used (Jorjani *et al.* 2003; Nilforooshan 2020). Weighted bending uses the measure of uncertainty of an estimated r_g, such as the associated standard errors, as weights during the bending process: parameters with low weights change less at each bending iteration compared to those with high weights. When no standard errors are available because no r_g were estimated, arbitrarily defined weights could be used (e.g. Vesela *et al.* 2019). However, such arbitrarily defined weights should be considered carefully as they may introduce undesired and possibly large changes between specific country combinations. In particular, changes larger than for example ±0.20-0.30 introduced with arbitrary weights in within-country and between-country r_{dm} should be carefully considered as Chapter 3 shows that changes on r_{dm} may impact the international EBV for both young and publishable sires. Thus, when arbitrary weights are used, I recommend evaluating the magnitude of changes introduced by the bending process in the across-country r_g matrix, and reconsidering the bending process if large changes are observed. Finally, once the final positive-definite r_g matrix across all countries is obtained, the final genetic (co)variance matrix to use for the estimation of pedigree or genomic EBV is computed using the r_g matrix and national variances as described in Chapter 4 (Figure 7.1).

7.2.2 Concluding remarks

Standard procedures at the international level are needed to estimate across-country r_g consistently. In this section, based on the findings of this thesis, I discuss an Interbeef procedure to use a multi-trait estimation approach where all countries are potentially analysed together. Further testing of this procedure on other traits and breeds is advised. Although genomic evaluations are becoming more common at the national level, genetic parameter estimates from pedigree and phenotypic data are usually used in national genomic models. Similarly, I here assumed that the procedure uses only phenotypes and pedigree information.

7.3 Estimating r_g and connectedness between countries using genomic data

Genomic data already available in most national evaluations could be used for the estimation of r_g between countries. When poor connectedness between countries is structural in the data due to the low number of common bulls, the estimation of r_g is challenging using conventional sources of data, i.e. pedigree and phenotypes. In the extreme case of completely disconnected populations, estimating r_g using conventional sources of data can be impossible. In Chapter 5, we proposed to use national genomic data in the form of genome-wide panels of SNP markers for international single-step genomic evaluations. Another benefit of having individuals' genotypes at the international level is to use this genomic data as an additional source of information for the estimation of r_g between countries. This potential usage of genomic data was not explored in the previous chapters of this thesis and, to my knowledge, is also still unexplored in the context of beef and dairy cattle international evaluations. Populations that appear as (completely) disconnected through pedigree information could be, in theory, connected through genomic data, as shown by Wientjes *et al.* (2015, 2018). Compared to conventional sources of genetic relationship information, genomic data allow to capture connectedness that was lost in pedigree recordings.

In the first part of this section, I will illustrate using simulation that genomic data aids the estimation of r_g between countries compared to only using conventional sources of data. In the second part, I will illustrate and discuss different measures that could capture the increase in connectedness between countries due to genomic data and discuss possible approaches to apply them in Interbeef.

7.3.1 Using genomic data to estimate r_g between countries

I will use a simulation approach instead of real data because it allows comparing estimated and true parameters, e.g. r_g. I will build my discussion on the simulated dataset developed within the work of Neufeld (2021) [1]. In short, two beef cattle populations (POP1 and POP2) originating from the same breed were simulated, mimicking data from two different countries (Figure 7.2). Each population had data on a maternally affected trait simulating weaning weight as a representative trait in Interbeef (Figure 7.2).

[1] MSc thesis carried out at Wageningen University & Research (Animal Breeding and Genomics, Department of Animal Sciences) under the supervision of dr. ir. Mario Calus and myself.

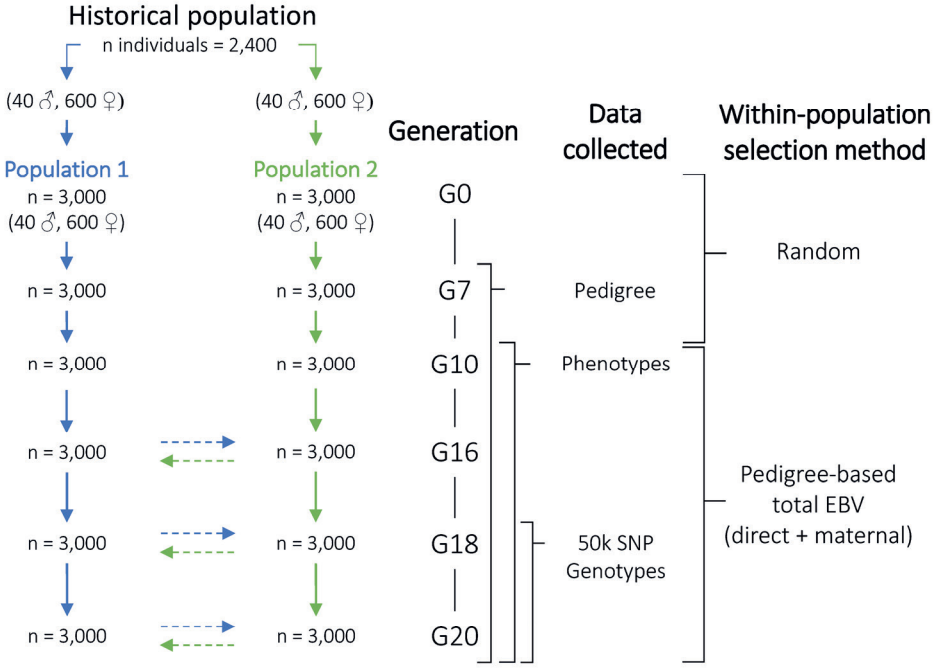


Figure 7.2 Schematic overview of the two simulated populations, data collected, and selection method (each scenario was replicated 10 times). Each population was independently selected for 20 generations (G). Horizontal arrows indicate exchange of top sires between populations to simulate different connectedness levels between populations in different scenarios. The simulated trait direct h^2 was 0.30, the maternal h^2 was 0.15, and the direct-maternal r_g was -0.20. The simulated r_g between populations were (following estimates from Chapter 3): 0.80 for direct r_g, 0.70 for maternal r_g, and 0 for between-country r_{dm}.

To simulate different levels of connectedness between populations, top sires from each population were exchanged throughout the last five generations (G16 to G20), therefore becoming common bulls (CB), mimicking the observations from Chapter 3. In this chapter, I observed that most of the genetic connections between countries were established by CB born after the '90s, i.e. about 5-6 generations from the current population. The four scenarios simulated are named after the exchanged proportions of top sires that were 0% (completely disconnected scenario), 2.5%, 5%, and 20% (Scenarios S0, S0.025, S0.05, and S0.2, respectively); this corresponded to exchanging respectively 0, 1, 2, and 8 sires out of the 40 selected in each population and generation. Preferential treatment was simulated to ensure that daughters of

CB were used as dams in the next generation. This preferential treatment ensured the presence of common maternal grand-sires (CMGS) and, therefore, sufficient connections between populations to estimate maternal r_g between populations. This also follows what I observed with real data in Chapter 3, where large proportions of CB were also CMGS. Finally, coefficients of Genetic Similarity (GS) for CB and CMGS across scenarios agree with those I observed in Chapter 3, where GS between countries ranged between 0.04 and 0.15 (Table 7.1).

The r_g between populations were estimated using a bi-variate model with each population's trait modelled as a different correlated trait (similar to the Interbeef AMACI model used in Interbeef and Chapters 3 and 6) and using three different relationship matrices: i) a pedigree-based relationship matrix (**A**) for all phenotyped animals from G13 to G20; ii) a genomic relationship matrix (**G**) following VanRaden (2008) method 1 for all phenotyped and genotyped animals from G18 to G20, and iii) a combined pedigree and genomic relationship matrix (**H**) following Legarra *et al.* (2009) for all phenotyped and genotyped animals from G13 to G20. With disconnected populations, using genomic data through **G** or **H** matrices gave estimated direct and maternal r_g close to the simulated values, albeit with some variation across replicates (S0 and S0.025 in Figure 7.3). With lowly connected populations, using the **A** matrix gave estimated direct r_g close to the simulated values but large variation for the estimated maternal r_g (S0.025 in Figure 7.3). With more connected populations (S0.05 and S0.20), estimates of **A**, **G** and **H** matrices were similar, except for maternal r_g in S0.05 where **G** and **H** gave somewhat underestimated r_g compared to **A**. In all scenarios, the standard errors associated with direct and maternal r_g were smaller when using an **H** matrix compared to an **A** matrix (not shown). When using the **G** matrix, standard errors of estimated r_g were between those of **H** and **A**. Thus, estimates of r_g between populations became more accurate when genomic information was included in the estimation process.

The more accurate estimation of r_g between populations when the number of CB and CMGS increased (Figure 7.3) highlights the importance of establishing genetic links across countries for estimating r_g. This result is in agreement with Mark *et al.* (2005a) and confirms that the exchange of frozen semen between populations is key to accurately estimate r_g, especially when only conventional data is available. However, building such genetic links takes time as sires need to have recorded offspring in both populations. In Chapter 3, we defined thresholds levels for connectedness based on GS coefficients: low (GS < 0.05), medium (GS between 0.05 and 0.10) and high (GS > 0.10). Low to medium levels of connectedness are common in beef cattle populations. For instance, for Limousin, GS between countries ranged

Table 7.1 Connectedness between populations in different scenarios [1, 2].

Scenarios [1]	Number CB	n. offspring from CB	GS	Mean n. CMGS [3]	Mean number grand-offspring from CMGS [3]	Mean GS_{CMGS} [3]
S0	0	0	0	0	0	0
S0.025	10	1,500	0.02	8	2,322	0.04
S0.05	20	3,000	0.05	16	4,544	0.07
S0.2	80	12,000	0.18	63	15,364	0.23

[1] S = Scenario: numbers indicates the exchanged proportion of sires between populations.
[2] Connectedness computed from G10 to G20. CB = Common Bulls, CGMS = Common Maternal Grand-Sires. GS = genetic similarity coefficient computed from CB. GS_{CMGS} = genetic similarity coefficient computed from CMGS. GS coefficients for CB (and CMGS) were defined as the proportion of recorded offspring (grand-offspring) from CB (CMGS) over the total number of recorded offspring (grand-offspring) in the two populations (Rekaya *et al.* 2010; Chapter 3).
[3] Mean number of CMGS, number of grand-offspring and GS_{CMGS} across the 10 replicates. Underlining results from Neufeld (2021).

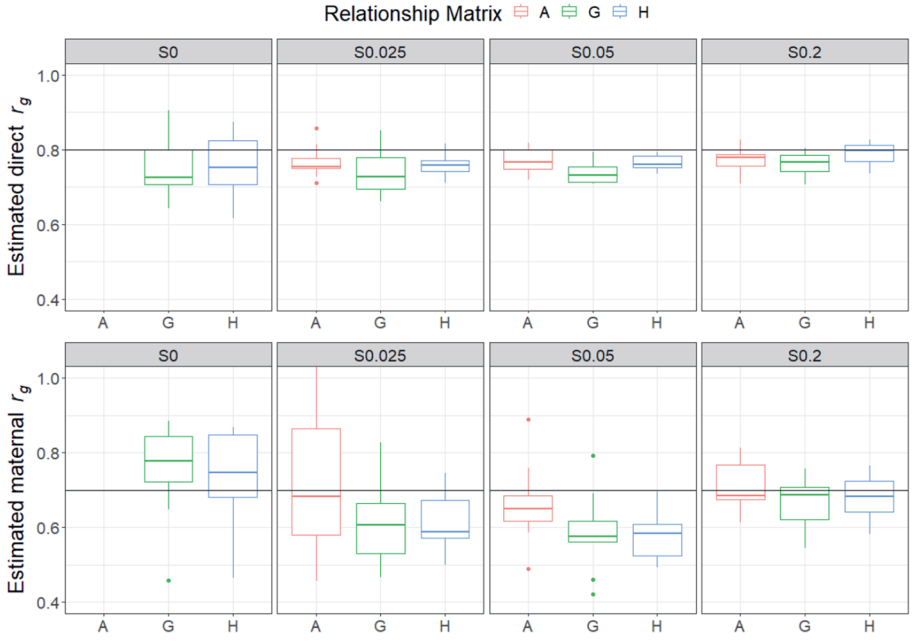


Figure 7.3 Estimated direct (top row) and maternal (bottom row) genetic correlations (r_g) across scenarios (S0 to S0.2) using different relationship matrices (**A**, **G**, and **H**). Horizontal lines represent the simulated values for direct and maternal r_g (0.8 and 0.7, respectively). **A** in S0 did not move from the starting values of 0 (results not shown). Boxplots report estimated values of 10 replicates. Underlining results of **A** and **H** from Neufeld (2021).

between 0.02 and 0.08 in Chapter 6 and was equal to 0.04 in Phocas *et al.* (2005). For both Limousin and Charolais, Venot *et al.* (2009b) reported values of GS as low as 0.01 between countries. A low level of connectedness also leads to large standard errors of the estimated r_g (Chapter 3; Venot *et al.* 2009b). Using genomic data could help the estimation of r_g for beef cattle populations with a low exchange of CB and low GS (Figure 7.3) and could reduce the uncertainty of the estimated r_g, i.e. the associated standard errors. For large dairy cattle international evaluations such as those of Holstein-Friesian, it is unlikely that using genomic data will improve the estimation of r_g between countries as connectedness levels between populations are high (Jorjani 2000). On the other hand, I expect similar benefits as those observed here when using genomic data to estimate r_g for small and weakly linked dairy cattle populations, e.g. Ayrshire, Guernsey, and Jersey (Jorjani 1999, 2000; Mark *et al.* 2005b).

Genotyping levels of countries participating in Interbeef evaluations are still low compared to dairy cattle. Nonetheless, based on the genotyping trends observed in Chapter 5, I expect that the availability of beef cattle genotypes will rapidly increase in the next 5 to 10 years. Thus, the proposed approach could be helpful to estimate across-country r_g in Interbeef. The **G** matrix used three generations of data and gave estimated r_g similar to **A** and **H**, which both used eight generations of data. These results suggest that three complete generations of phenotypes and genotypes could be sufficient to estimate r_g between countries. However, not all animals have both phenotypes and genotypes available in real datasets, and missing records and incomplete pedigrees are also expected. Additionally, the average number of offspring per dam in Chapter 5 ranged from 1.4 to 3.6, depending on the country. Instead, each dam had 5 recorded offspring in this simulation, providing a good data structure to estimate maternal genetic effects (Gerstmayr 1992; Heydarpour *et al.* 2008). A poor data structure for the estimation of maternal genetic effects will affect the estimation of maternal r_g between countries also when using genomic data. This was indirectly confirmed when the above simulation was repeated for traits at lower h^2 to mimic calving ease and birth weight in Interbeef (Vesela *et al.* 2019), i.e. direct h^2 of 0.15 and maternal h^2 of 0.07. Although the results aligned with those presented here, estimated direct r_g and particularly estimated maternal r_g showed larger variation across replicates and larger associated standard errors for all scenarios, regardless of the relationship matrix used. This variation was even more evident when using a **G** matrix compared to **A** and **H** matrices, likely due to **G** including fewer phenotypes and genetic connections via CB and CMGS. Indeed, at lower h^2, a larger amount of phenotypes is needed to better disentangle genetic and non-genetic variances and accurately estimate genetic covariances (Robertson 1959; Bijma and

Bastiaansen 2014). Thus, regardless of the inclusion of genomic data in the estimation process, traits with low h^2 such as calving ease will require more phenotypes and genetic connections to accurately estimate r_g between countries compared to traits with moderate h^2 like weaning weight, especially for maternal r_g.

The approach used to estimate r_g between populations using genomic information is a bi-variate genomic REML (GREML) (Lee *et al.* 2012; Zhou *et al.* 2020). This approach requires individuals' genotypes to be available at the international level to calculate the genomic relationship matrices, e.g. **G** or **H**. An alternative approach to estimate r_g between populations is to use a bi-variate "linkage disequilibrium score regression analysis" (LDSC) which is commonly used in human genetics as sharing data is often a limitation (Bulik-Sullivan *et al.* 2015; van Rheenen *et al.* 2019). This method uses summary statistics from single-population genome-wide association studies (GWAS) and would avoid sharing genotypes at the international level. In short, LDSC combines summary statistics from GWAS analyses by weighting marker effects using linkage-disequilibrium scores and makers' measures of accuracies, e.g. *z* scores (Bulik-Sullivan *et al.* 2015). Even though LDSC is computationally efficient, it is less accurate than GREML and requires larger sample sizes (i.e. number of genotypes) to achieve the same accuracy (Ni *et al.* 2018; van Rheenen *et al.* 2019). Thus, given the availability of platforms to safely collect genotypes at the international level (Durr *et al.* 2014), I recommend using individuals' genotypes with a GREML approach as proposed here to estimate across-country r_g in Interbeef.

7.3.2 Measures of connectedness between countries using genomic data

In the previous section, I showed that genomic data can help to estimate r_g in disconnected and weakly connected populations. This is indirect evidence that genomic data helps to improve connectedness across populations. Connectedness can be measured as genetic relatedness at different levels: between populations, herds, or groups of animals (Yu *et al.* 2018). In beef cattle, genetic connectedness both within and between populations is usually low due to the low usage of AI (Berry *et al.* 2016). Measures of connectedness are usually defined as functions of the inverse of the coefficient matrix. These measures are computationally expensive to apply to large datasets due to the required direct inversion of the coefficient matrix, limiting their application to international evaluations (Fouilloux *et al.* 2008b). For this reason, straightforward approaches are preferred to measure connectedness in international evaluations as they can be computed ahead of the estimation process, have almost no computational cost, and can be adapted to the herd level (Chapter 3; Jorjani 1999; Pabiou *et al.* 2014). However, measures like the GS coefficient between populations are defined at the animal level using pedigree information and are not suited to reflect genomic information. In this section, I aim to show how recently proposed connectedness measures could take into account genomic information better.

Following Yu *et al.* (2017), there are three main measures of connectedness based on Prediction Error Variance (PEV): Prediction Error Variance of Difference (PEVD) (Kennedy and Trus 1993), Coefficient of Determination (CD) (Laloë 1993), and prediction error correlation (r) (Lewis *et al.* 1999). PEVD between two animals *i* and *j* is defined as: $PEVD(\hat{u}_i - \hat{u}_j) = PEV(\hat{u}_i) + PEV(\hat{u}_j) - 2PEC(\hat{u}_i, \hat{u}_j)$, with PEC being the prediction error covariance, i.e. the off-diagonal element of the PEV matrix. CD is similar to PEVD, but considers a penalization term when the variability between compared animal(s) is reduced (i.e. when animals are more related) and is computed as: $CD_{i,j} = 1 - \frac{PEVD_{ij}}{\sigma_u^2 \cdot (\boldsymbol{K}_{ii} + \boldsymbol{K}_{jj} - 2\boldsymbol{K}_{ij})}$, with σ_u^2 being the genetic variance and **K** being the relationship matrix, e.g. the pedigree-based matrix **A**. CD can also be defined as the square of the correlation between predicted and true breeding values (Fouilloux and Laloë 2001). Finally, r is defined as: $r_{i,j} = \frac{PEC(\hat{u}_i, \hat{u}_j)}{\sqrt{PEV(\hat{u}_i) \cdot PEV(\hat{u}_j)}}$. PEVD has a lower bound of 0 but no upper bound. The smaller the PEVD coefficient, the higher the connectedness. Instead, both CD and *r* are bounded between 0 and 1, with higher values indicating higher connectedness. Recently, Yu *et al.* (2017) showed that these three connectedness measures could capture connectedness between

management units, such as herds, due to genomic data. In short, the three PEV-based connectedness measures are computed using the relationship matrix **K**, with **K** being, for example, a pedigree-based, genomic-based or combined pedigree and genomic relationship matrix (Christensen and Lund 2010; Aguilar *et al.* 2010). Thus, increases in connectedness due to genomic data are captured through variations in the relationships between animals of different management units that are otherwise unseen from pedigree data.

Even if genomic data can be helpful to estimate r_g between populations, subsetting has to be applied to make the estimation process computationally feasible when using Interbeef data. Measures of connectedness that account for genomic data are therefore needed to reveal which subsets of data or herds are most closely connected between populations. I here illustrate how PEV-based measures can capture increases in connectedness between populations. Among the three PEV-based measures, I will use the CD as it gave the most consistent results in Yu *et al.* (2017). Using simulated data from the previous section, CD coefficients were estimated following Yu and Morota (2021, "CD_IdAve") between management units defined as the combination of generation (from G13 to G20) and population, e.g. between animals in generation 13 of POP1 and animals in generation 13 of POP2. CD was computed for one replicate of each scenario using either the relationship matrix **A** or **H** and considering only direct genetic effects.

Overall, when moving from **A** to **H**, CD coefficients between populations increased due to genomic data in all scenarios (Figure 7.4), especially for animals in G18 to G20: increases of CD in **H** relative to **A** ranged from 25.8% to 40.4% across scenarios. Moreover, when moving from **A** to **H**, CD between populations increased also between animals in G18-G20 and animals in G13-G17 (Figure 7.4) due to **H** better capturing the relationships between genotyped and non-genotyped animals (Legarra *et al.* 2014). The higher the exchange of CB, the more animals between populations became related, and the more evident were the decreases in CD across generations due to the penalization applied in the CD measure (Yu *et al.* 2017; Amorim *et al.* 2020). These results agree with Yu *et al.* (2017) and Amorim *et al.* (2020) and show that CD can capture increases in connectedness between populations due to genomic data. However, the computational costs associated with the computation and inversion of the coefficient matrix may limit its application to large datasets and international evaluations (Fouilloux and Laloë 2001; Fouilloux *et al.* 2006). Moreover, published work has so far focused on single-trait models with only direct genetic effects (Yu *et al.* 2017; Amorim *et al.* 2020).

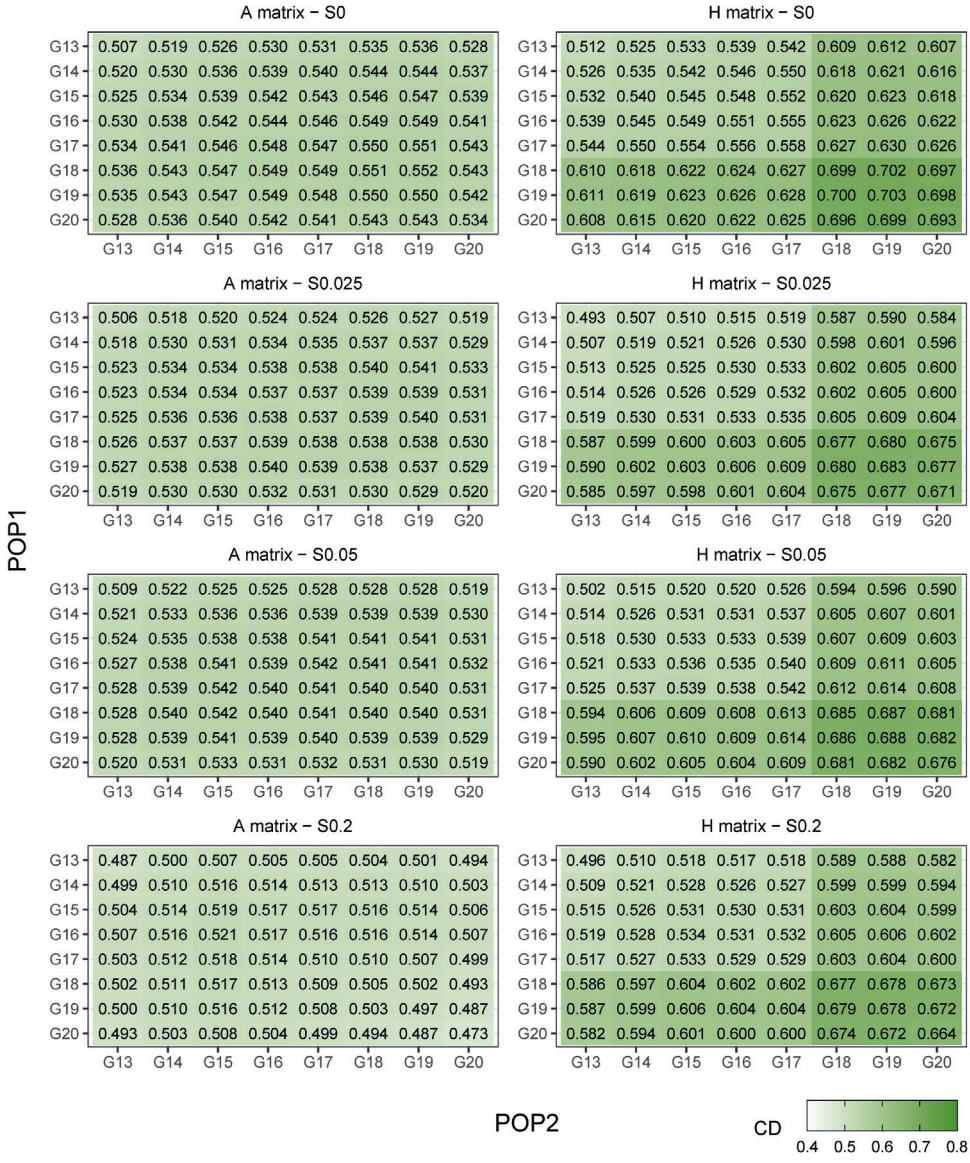


Figure 7.4 CD coefficients between populations and generations for each scenario (S) computed using the pedigree-based relationship matrix **A** or the combined pedigree and genomic relationship matrix **H**. Larger values indicate more connectedness. Underling data is from the previous section using scenarios with trait h^2 of 0.30 for direct effect.

To be used for data sub-setting in the context of beef cattle international evaluations, the PEV-based measures described by Yu *et al.* (2017), with or without considering genomic data, should be extended to models that account for maternal genetic effects and multi-trait models. The extension to maternal genetic effects would better reflect connectedness on the maternal side, as shown by Tarrés *et al.* (2010). The extension to multi-trait models would allow fitting different genetic and residual variances among countries together with r_g between countries lower than unity which is expected to impact the measured connectedness (Tarrés *et al.* 2010). While the extension to such models may be straightforward, the computational costs associated with the coefficient matrix and computation of PEV-based measures would increase, making its application to international evaluations even more challenging. A possible approach to resolve this challenge is to use algorithms that approximate the PEV matrix (Fouilloux and Laloë 2001). For instance, Gibbs sampling methods could be used to obtain both PEV and PEC for either pedigree-based or genomic-based models (Fouilloux and Laloë 2001; Garrick *et al.* 2018). However, their application and efficiency in computing connectedness measures with large datasets are not known yet. Hereafter, I discuss two approaches that have been originally proposed for computing connectedness measures at the (inter)national level without genomic data. These approaches may allow reducing the computational burden of PEV-based measures. Their application and efficiency when including genomic data are still unknown.

A first approach was proposed by Fouilloux *et al.* (2008b) to obtain empirical estimates of CD. This method uses a sampling approach as proposed by García-Cortés *et al.* (1995) and Fouilloux *et al.* (2001) to obtain approximated estimates of the (co)variances between true breeding values (TBV) and EBV. The process consists of three steps. First, individuals' TBV are simulated based on a given genetic variance and data structure, e.g. the pedigree-based relationship matrix. Second, individuals' phenotypes are simulated using the TBV and an error term based on a given residual variance. Finally, EBV are computed from simulated data solving a BLUP model. The process is repeated *n*-times, generating distributions of TBV and EBV that are then used to estimate PEV or CD for individuals or contrasts (Fouilloux and Laloë 2001; Fouilloux *et al.* 2008b). Using this approach, Fouilloux *et al.* (2008b) computed and clustered herds based on their CD connectedness measures in a large Charolais dataset (more than 2.6 million weaning weights) to identify the most-connected subsets. This approach can potentially be used for any of the PEV-based connectedness measures described above, and it can accommodate complex models with maternal genetic effects and multi-trait models (Fouilloux and Laloë 2001; Tarrés *et al.* 2010). With large usage of AI, Tarrés *et al.* (2010) proposed that using a

sire BLUP model may be enough to capture the existing level of connectedness in the population. However, with low usage of AI, an animal model or a sire-MGS model with maternal effects is expected to better capture connectedness between herds as it would also capture connectedness from the dam side (Fouilloux *et al.* 2008b; Tarrés *et al.* 2010). A similar sampling method as that used in this approach (also based on García-Cortés *et al.* 1992, 1995) was applied and extended in Matilainen *et al.* (2012) for variance component estimation of large and complex models resulting in the MC EM REML algorithm I used in Chapter 3. Thus, the applicability of the Fouilloux *et al.* (2008b) approach to beef cattle international evaluations for maternally affected traits should be feasible. To compute coefficients at the herd level, the sampling procedure should be repeated *n*-times. Fouilloux *et al.* (2008b) and Tarrés *et al.* (2010) used *n*=1,000 samples. Therefore, the process could be computationally expensive with large datasets and a large number of samples. To considerably speed up the process, each sample could be analysed independently and in parallel. Nonetheless, I expect that the computational costs will further increase if a genomic relationship matrix **G** (or even a combined matrix **H**) is considered to capture connectedness due to genomic data.

A second approach has been proposed by Fouilloux *et al.* (2006) to obtain estimates of connectedness between countries with low computational costs following the developments on the CD measure by Laloë and Phocas (2003). This approach uses existing known relationships to measure connectedness between different countries, and it has the advantage of being applicable in large datasets as in international evaluations. In short, the process consists of simulating individual performances after introducing a systematic genetic difference (i.e. a level bias in the breeding values) between animals in one country (country *k*) and animals in any other country included in the evaluation (Fouilloux *et al.* 2006, 2008a). Then, a univariate pedigree BLUP sire model is solved using the simulated performances for all countries, with the only fixed effect being the country of recording. Finally, the ratio of the (re-)estimated systematic difference over that originally simulated estimates the connectedness between country *k* and any other country. The whole procedure is repeated *n*-times, where *n* is the number of countries in the evaluation. This method has been applied in beef cattle (Venot *et al.* 2008), dairy cattle (Fouilloux *et al.* 2006, 2008a) and even horses (Ruhlmann *et al.* 2009) international evaluations. Further research should investigate how to extend this approach to compute connectedness at the herd level; a possibility can be to move from simulating the systematic difference in breeding values at the country level to the herd level. Finally, while it seems possible to extend the approach of Fouilloux *et al.* (2006) to consider genomic data by replacing pedigree-based relationships with genomic-based

relationships in both the simulation and estimation steps, the associated computational costs are expected to be considerably larger.

The results described in this section suggest that PEV-based measures of connectedness can be used to capture increases in connectedness between populations due to genomic data and, therefore, can be used for appropriate data sub-setting. Further research should investigate the efficiency of both the above-discussed approaches by Fouilloux *et al.* (2008b) and Fouilloux *et al.* (2006) to compute genetic and genomic connectedness at the international level for large datasets. To my knowledge, Yu *et al.* (2017) is the first study that extended connectedness measures to consider genomic data. Other measures of connectedness have been proposed in the literature (e.g. Kennedy and Trus, 1993), however, it is still unknown whether they can capture increases in connectedness due to genomic data.

7.3.3 Concluding remarks

Genomic data are becoming rapidly available at the national level. I recommend using national genomic information in beef cattle international evaluations as they are expected to be beneficial for participating countries (Chapters 5 and 6). Furthermore, I recommend using a single-step approach to implement genomic evaluations in Interbeef, preferably using the international ssSNPBLUP model proposed in Chapter 5. The SNP effects from the ssSNPBLUP model can be distributed to participating countries next to genomic international EBV and used for genomic predictions of young genotyped animals at the national level. The availability of individuals' genotypes in Interbeef will provide new opportunities to improve beef cattle international evaluations, e.g. correction of parent-offspring conflicts and parent identification. Furthermore, genomic data can help to address the long-standing issue of poor connectedness of beef cattle populations and improve the estimation of across-country r_g. Simulations show that genomic data aids the estimation of r_g for disconnected and weakly connected countries which are commonly observed in beef cattle international evaluations. Moreover, including genomic information in the estimation process can increase the accuracy of the estimated r_g and may reduce the required amount of data. The next step is to confirm these results with real data and investigate the application of GREML approaches in large beef cattle datasets. Finally, further research is needed to improve the efficiency of computing connectedness measures that can capture increases in connectedness due to genomic data in large datasets.

7.4 Modelling missing parental information in pedigree and genomic international beef cattle evaluations

The AMACI model (Phocas *et al.* 2005) implemented in Interbeef evaluations fits participating countries' phenotypes as different correlated traits. The modelling of a given trait at the international level is close to that of the national one: phenotypes are modelled using the same effects and parametrizations (i.e. variances) as that of national models (Venot *et al.* 2006; Chapter 4). Possible differences between international and national evaluations due to using partly different sources of data can be accounted for with an integration procedure (Chapter 6). However, while national evaluations may use genetic groups (Westell *et al.* 1988) to model missing parental information, current Interbeef evaluations do not (Venot *et al.* 2009b; Chapter 4). This could create differences between international and national EBV that may also affect the integration procedure. Moreover, missing parental information could cause bias in international evaluations (Bouquet *et al.* 2011). Thus, modelling missing parental information in international evaluations is highly recommended.

All pedigrees contain some level of missing parental information since we cannot endlessly trace pedigree information back in time. This is also the case in international pedigrees, albeit they are usually expected to be more complete than national ones (Pabiou *et al.* 2018; Chapters 2 and 5). When animals with missing parents are present in the pedigree, their unknown parents are assumed to come from the base population. Animals from the base population are a group of individuals that are assumed to be unselected and unrelated, with mean breeding values equal to zero and variance equal to the genetic variance (Schaeffer 2019b; Masuda *et al.* 2022). Due to selection, these assumptions are violated for unknown parents of animals in recent generations or that originate from different countries. To account for this, genetic groups (also known as unknown-parent groups or phantom-parent groups) are used to model differences in the genetic level of unknown parents across time that are not accounted for by known pedigree relationships (Westell *et al.* 1988; Schaeffer 1994; Masuda *et al.* 2022). In short, phantom parents are assigned to animals with missing parental information and are assumed to be average representatives of similar animals that were selected as parents at the same time (Westell *et al.* 1988). Finally, the effect of the genetic group is the average genetic contribution of the selected unknown parents to the offspring with missing parental information (Westell *et al.* 1988).

Implementing genetic groups in current pedigree-based Interbeef evaluations is a model improvement that should be addressed in the short term. Bouquet *et al.*

(2011) conducted a pedigree analysis on the genetic structure of Limousin and Charolais European populations used in Interbeef. These authors found that individual countries used different founder animals in their populations and suggested that differences in the genetic levels of different countries could lead to bias in international EBV. The same authors recommended taking such differences into account using genetic groups. In Chapter 5, we proposed that using genetic groups could potentially reduce the observed level and dispersion bias. However, implementing genetic groups in beef cattle (inter)national evaluations is not trivial. I foresee two main challenges. First, there is no optimal definition of genetic groups for all evaluations (Robinson 1986). The definition of genetic groups should be tailored to the population evaluated and should take into account the different selection paths (e.g. sires and dams), the origin of the animals with unknown parents (e.g. country, breed, or sub-populations), a time component (e.g. year of birth or generations), and the amount of missing information (Westell *et al.* 1988; Schaeffer 2018; Masuda *et al.* 2022). Second, there is a need to compare models with different definitions of genetic groups to validate whereas they help to reduce bias. However, validation procedures that may be well established in dairy cattle (e.g. Boichard *et al.* 1995) are not always applicable in beef cattle, in particular for maternally affected traits or when the size of the contemporary groups is small (Lourenco *et al.* 2015; Legarra and Reverter 2018). The LR method (Legarra and Reverter 2018) is a recent and promising validation method for complex traits such as maternally affected traits or threshold traits (Chapters 4 and 5; Durbin *et al.* 2020; Cesarani *et al.* 2021a; Campos *et al.* 2022; Jang *et al.* 2022). Thus, the application of the LR method, combined with investigations of genetic trends, opens new possibilities for validating the effect of modelling genetic groups in (inter)national beef cattle evaluations. I hereby discuss an initial approach on using genetic groups to model missing parental information in current pedigree-based Interbeef evaluations validated using the LR method and changes in genetic trends.

7.4.1 Usage of genetic groups in Interbeef evaluations

The approach I will discuss hereafter was investigated within the work of Espinola Alfonso (2021) [2]. The same phenotypes as in Chapter 5 were used and the pedigree was pruned to retain all animals with phenotypes and all their ancestors without any limit on the number of generations. The final pedigree included 516,203 animals

[2] MSc thesis carried out at Wageningen University & Research (Animal Breeding and Genomics, Department of Animal Sciences) under the supervision of dr. ir. Jérémie Vandenplas and myself.

born from 1927 to 2019. In total, 13.2% of the animals had either one or both parents unknown, of which: 30.8% had an unknown dam, 9.5% had an unknown sire, and 59.7% had both parents unknown. Based on the country of first registration, most of the animals with missing parents were from IRL (72.9%), followed by FRA (12.6%), DFS (5.2%), DEU (3.9%), CHE (2.7%), and other countries (2.7%). The higher percentage of animals with missing parents registered in IRL compared to other countries could be explained by the large usage of crossbreeding at the national level: the pedigree of such crossbred animals was not as complete as that of purebred animals. FRA animals with missing parents were mostly born before 1970, possibly indicating that these animals can be considered the founders of the population. Based on country-wise genetic trends, selection for weaning weight did not start until 1985 for both direct and maternal genetic effects. Since genetic groups are used to model differences in the genetic level of animals across time due to selection, animals with missing parental information born before 1985 were grouped into a single genetic group across countries.

For four definitions of genetic groups, the impact on level bias, dispersion bias, and accuracy of partial EBV was evaluated for animals with phenotypes in each country born from 2014 onwards, representing the focal groups of each country. The biggest impact of fitting genetic groups was observed on the estimated level bias (Figure 7.5). Overall, for direct effect, modelling genetic groups defined as the combination of sex, year of birth in groups of five years, and country (Scenario SY5C) gave the lowest average level bias (0.03 GSD on average across countries) compared to other scenarios (ranging on average across countries from 0.08 GSD without genetic groups (CUR) to -0.22 GSD with genetic groups defined as the combination of sex and year of birth (SY)) (Figure 7.5). Reduction in level bias was mainly evident in countries like IRL and DEU. On the other hand, for maternal effect, a larger level bias was present when modelling genetic groups and the best approach was to not fit genetic groups (Scenario CUR; -0.04 GSD on average across countries) (Figure 7.5). These results may be related to the negative direct-maternal genetic correlations so that changes in direct EBV were correlated with those of maternal EBV. Overall, there was similar dispersion bias and accuracy of partial EBV regardless of wheatear or how genetic groups were fitted. A possible explanation for these results is that genetic groups model differences in the genetic level of missing animals and would therefore mostly impact the estimated level bias. Moreover, Interbeef requires that animals with phenotypes have both parents known. Thus, for animals in the focal groups, genetic groups could only affect the missing information of their grand-parents or their missing ancestors further back in the pedigree.

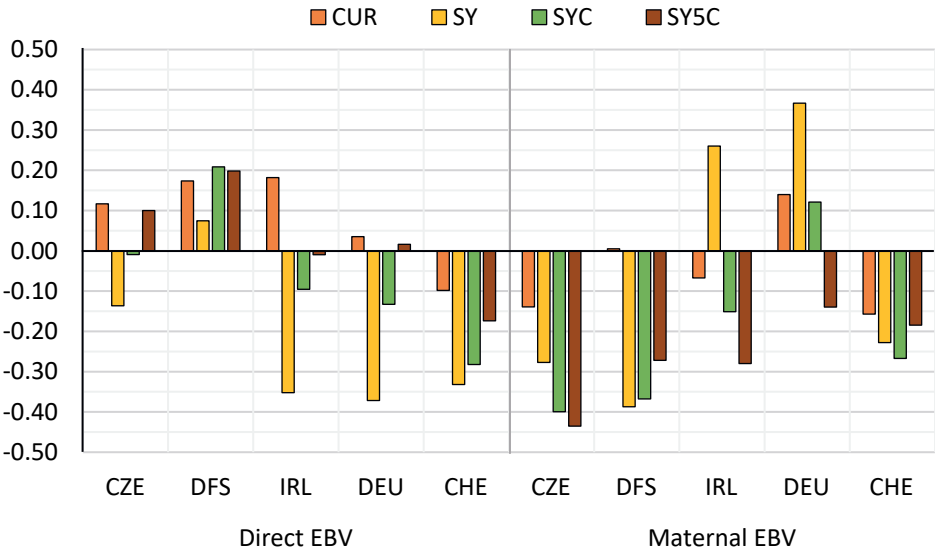


Figure 7.5 Estimated level bias in genetic standard deviations (GSD) for direct and maternal EBV across scenarios using different definitions of genetic groups (underling results from Espinola Alfonso 2021). Genetic groups were defined based on the following criteria: SEX = sex of the missing parent, YOB = year of birth of the animal (from 1985 onwards), YOB5 = as YOB, but grouping intervals of five years, COU = country of first registration (groups were DFS, IRL, DEU, CHE and "other countries"). Scenarios (number of groups in parenthesis): CUR = current Interbeef evaluations with no genetic groups (0), SY = genetic groups based on SEX and YOB (152), SYC: based on SEX, YOB, and COU (346), SY5C = based on SEX, YOB5 and COU (94). Genetic groups were modelled as random (assuming the same variance as the genetic variance).

This initial investigation supports the assumption that using genetic groups in Interbeef could be beneficial. The optimal definition of genetic groups needs to be further investigated, but based on these results it should consider the following criteria defined based on the animals with missing parental information: year of birth, grouped in intervals of five years to reduce the overall number of genetic groups; country of first registration, to account for differences between populations; and sex of the missing parent, to account for selection pathways. These criteria are in agreement with those used in MACE evaluations where genetic groups consider the year of birth, the country of origin of the sires, and four selection pathways (sires of males, sires of females, dams of males, and dams of females) (Nilforooshan and Jorjani 2022). Regardless of their definition, the size of genetic groups should be

taken into account. Indeed, among the different scenarios tested, there were always some small groups that could create convergence issues when genetic groups are treated as fixed. Modelling genetic groups as random is, in general, preferred over modelling them as fixed (Masuda *et al.* 2022). Modelling genetic groups as fixed can create issues in the estimation of their effects because of confounding and dependencies with other genetic groups and fixed effects (Quaas 1988; Schaeffer 2018). Thus, I recommend to model genetic groups in Interbeef as random, similarly to current MACE evaluations (Nilforooshan and Jorjani 2022). Nonetheless, I also suggest using a criteria to merge adjacent small genetic groups into larger groups of, for example, at least 100 animals, based on the expectation that such merged groups have a similar genetic level (Schaeffer 2018). For instance, first, merge groups in adjacent years and of the same sex and country, then merge genetic groups of countries with a similar known history of selection (e.g. Graser *et al.* (2005) merged countries from the same continent), and lastly merge genetic groups of different sex, i.e. by selection pathways.

More research is needed to investigate the impact of genetic groups across different years. The initial investigations on country-wise genetic trends showed that genetic groups introduced changes in the mean EBV across years. As expected, a larger impact was observed in those years with higher proportions of unknown parents. Thus, to validate changes due to the implementation of genetic groups across time using the LR method, I recommend using an approach similar to that of Macedo *et al.* (2020b). In short, it consists in creating several focal groups within the same population and several "whole" and "partial" evaluations from which estimates of bias and accuracies are obtained. In this application, different focal groups with animals of interest could be defined, e.g. using sires or animals with missing parental information. This LR validation approach should better capture changes due to implementing genetic groups throughout the whole pedigree and assess the stability of the model across different years, as suggested by Masuda *et al.* (2022).

Genetic groups should also be implemented in future single-step Interbeef evaluations. For both ssGBLUP and ssSNPBLUP models, multiple methods have been proposed. Masuda *et al.* (2022) grouped them into two main approaches: those that fit unknown parent groups in the mixed models and that aim to make the **G** relationship matrix on the same scale as the **A** relationship matrix, and the metafounder approach. The latter aims to make the **A** relationship matrix on the same scale as the **G** relationship matrix that is computed using allele frequencies of 0.5, i.e. from an ideal base population (Legarra *et al.* 2015). However, fitting genetic groups in single-step evaluations could create convergence issues and may affect

genomic EBV (Masuda *et al.* 2022). In short, these issues arise due to simultaneously modelling in the combined **H** relationship matrix missing parental information for the **A** matrix and the **G** matrix which have different expectations and variances (Masuda *et al.* 2022). While the theory to include genetic groups in pedigree-based evaluations is well developed and widely used, there is not yet consensus on an optimal approach for single-step evaluations. Thus, further research and testing are needed to implement and evaluate the potential impact of genetic groups on bias and accuracies of genomic EBV in the single-step international evaluations proposed in Chapter 5. I suggest starting to implement genetic groups in single-step international evaluations based on the implementations developed for pedigree-based international evaluations. For ssSNPBLUP international evaluations, the Quaas and Pollak transformation as applied by Vandenplas *et al.* (2021a) could be used.

Recent studies suggested that truncating datasets that trace many generations of pedigrees for the estimation of breeding values may help to reduce level and dispersion bias more than fitting genetic groups. In a dairy sheep population, Macedo *et al.* (2022) compared different strategies to model genetic groups and studied the effects on level and dispersion bias. The best strategy to reduce level bias and over-dispersion in their dataset was to truncate old pedigree and phenotypic data. Truncating data yielded better results compared to modelling genetic groups while using the full dataset in either pedigree or single-step genomic evaluations. Macedo *et al.* (2022) suggested that the accumulation across generations of small noises or approximations during the estimation of breeding values could lead to a snowball effect, resulting in bias and dispersion of younger animals' EBV. Truncating the data was an effective solution to alleviate this problem in their study. Similarly, Cesarani *et al.* (2021b) observed a reduction in the over-dispersion of genomic EBV of young selection candidates in Holstein evaluations when old data was truncated. The pedigrees I analysed in the different chapters of this thesis had animals born as far as 1927. In the dataset used in this section, a large proportion of animals with missing parental information were born before 1985. It may not be needed to use such deep pedigrees when computing pedigree and genomic EBV. Indeed, most of the publishable sires with available frozen semen to exchange across countries are probably born in the late 20th century or more recent generations. Then, truncating these deep pedigrees could standardize the base population in the pedigree across animals and could possibly contribute to reduce level and dispersion bias without affecting the accuracies of pedigree and genomic EBV, similarly to Cesarani *et al.* (2021b) and Macedo *et al.* (2022). Thus, I recommend that next to examining the optimal definition of genetic groups, future investigations should also consider the simple, yet possibly effective, strategy of truncating old data.

7.4.2 Concluding remarks

Initial tests on modelling missing parental information in Interbeef pedigree-based evaluations showed the potential of genetic groups to reduce bias. In particular, a reduction in level bias for direct EBV was observed. Dispersion and accuracies of EBV remained similar with or without the inclusion of genetic groups. Further testing and validation are needed to evaluate the optimal definition of genetic groups in pedigree-based beef cattle international evaluations and their impact on animals across different generations. For Interbeef evaluations, the first step is to test the optimal definition under pedigree-based models, then move on to test (and possibly adapt) the same definition in single-step international evaluations. Overall, my recommendation is that genetic groups should be implemented in Interbeef evaluations in the short term as it will ensure that traits in international evaluations are modelled closer to national evaluations. Genetic groups will also make international evaluations more robust as they will correct the violated assumption that all unknown parents come from a single base population.

REFERENCES

References

Abbasi, M. A., R. Abdollahi-Arpanahi, A. Maghsoudi, R. V. Torshizi, and A. Nejati-Javaremi, 2012. Evaluation of models for estimation of genetic parameters and maternal effects for early growth traits of Iranian Baluchi sheep. Small Rumin. Res. 104: 62–69.

Abdollahi-Arpanahi, R., D. Lourenco, and I. Misztal, 2021a. Detecting effective starting point of genomic selection by divergent trends from best linear unbiased prediction and single-step genomic best linear unbiased prediction in pigs, beef cattle, and broilers. J. Anim. Sci. 99: 1–11.

Abdollahi-Arpanahi, R., D. Lourenco, A. Legarra, and I. Misztal, 2021b. Dissecting genetic trends to understand breeding practices in livestock: a maternal pig line example. Genet. Sel. Evol. 53: 89.

Aguilar, I., I. Misztal, D. L. Johnson, A. Legarra, S. Tsuruta, and T. J. Lawlor, 2010. Hot topic: A unified approach to utilize phenotypic, full pedigree, and genomic information for genetic evaluation of Holstein final score. J. Dairy Sci. 93: 743–752.

Amorim, S. T., H. Yu, M. Momen, L. G. de Albuquerque, A. S. Cravo Pereira, F. Baldi, and G. Morota, 2020. An assessment of genomic connectedness measures in Nellore cattle. J. Anim. Sci. 98: 1–12.

ANACLI, 2022. http://www.anacli.it/.

Baker, H. K., B. Bech Andersen, J. Colleau, H. Langholz, G. Legoshin, D. Minkema, and J. Southgate, 1976. Cattle breed comparison and crossbreeding trials in Europe; A survey prepared by a working party of the European association for animal production. Livest. Prod. Sci. 3: 1–11.

Baker, R. L., 1980. The role of maternal effects on the efficiency of selection in beef cattle - A review. Proc. New Zeal. Soc. Anim. Prod. 40: 285–303.

Banos, G., and A. Sigurdsson, 1996. Application of Contemporary Methods for the Use of International Data in National Genetic Evaluations. J. Dairy Sci. 79: 1117–1125.

Berry, D. P., M. P. Coffey, J. E. Pryce, Y. de Haas, P. Løvendahl, N. Krattenmacher, J. J. Crowley, Z. Wang, D. Spurlock, K. Weigel, K. Macdonald, and R. F. Veerkamp, 2014. International genetic evaluations for feed intake in dairy cattle through the collation of data from multiple sources. J. Dairy Sci. 97: 3894–3905.

Berry, D. P., J. F. Garcia, and D. J. Garrick, 2016. Development and implementation of genomic predictions in beef cattle. Anim. Front. 6: 32–38.

Berry, D. P., A. R. Cromie, and M. M. Judge, 2017. Rapid Communication: Large exploitable genetic variability exists to shorten age at slaughter in cattle1. J. Anim. Sci. 95: 4526–4532.

Berry, D. P., 2021. Invited review: Beef-on-dairy—The generation of crossbred beef × dairy cattle. J. Dairy Sci. 104: 3789–3819.

Berweger Baschnagel, M., J. Moll, and N. Künzi, 1999. Comparison of models to estimate maternal effects for weaning weight of Swiss Angus cattle fitting a sire×herd interaction as an additional random effect. Livest. Prod. Sci. 60: 203–

208.
Bijma, P., 2006. Estimating maternal genetic effects in livestock. J. Anim. Sci. 84: 800–806.
Bijma, P., and J. W. Bastiaansen, 2014. Standard error of the genetic correlation: How much data do we need to estimate a purebred-crossbred genetic correlation? Genet. Sel. Evol. 46: 79.
Boichard, D., B. Bonaiti, A. Barbat, and S. Mattalia, 1995. Three Methods to Validate the Estimation of Genetic Trend for Dairy Cattle. J. Dairy Sci. 78: 431–437.
Bonaiti, B., and D. Boichard, 1995. Accounting for foreign information in genetic evaluation. Interbull Bull. 78: 431–437.
Bonifazi, R., J. Vandenplas, J. ten Napel, A. Cromie, R. F. Veerkamp, and M. P. L. Calus, 2020a. Impact of Interbeef on national beef cattle evaluations. Acta Fytotech. Zootech. 23: 144–155.
Bonifazi, R., J. Vandenplas, J. ten Napel, K. Matilainen, R. F. Veerkamp, and M. P. L. Calus, 2020b. Impact of sub-setting the data of the main Limousin beef cattle population on the estimates of across-country genetic correlations. Genet. Sel. Evol. 52: 32.
Bonifazi, R., J. Vandenplas, J. ten Napel, R. F. Veerkamp, and M. P. L. Calus, 2021. The impact of direct-maternal genetic correlations on international beef cattle evaluations for Limousin weaning weight. J. Anim. Sci. 99: 1–14.
Bonifazi, R., M. P. L. Calus, J. ten Napel, R. F. Veerkamp, A. Michenet, S. Savoia, A. Cromie, and J. Vandenplas, 2022. International single-step SNPBLUP beef cattle evaluations for Limousin weaning weight (Under review).
Bouquet, A., E. Venot, D. Laloë, F. Forabosco, A. Fogh, T. Pabiou, K. Moore, J.-Å. Eriksson, G. Renand, and F. Phocas, 2011. Genetic structure of the European Charolais and Limousin cattle metapopulations using pedigree analyses. J. Anim. Sci. 89: 1719–1730.
Brotherstone, S., and M. Goddard, 2005. Artificial selection and maintenance of genetic variance in the global dairy cow population. Philos. Trans. R. Soc. B Biol. Sci. 360: 1479–1488.
Bulik-Sullivan, B., H. K. Finucane, V. Anttila, A. Gusev, F. R. Day, P.-R. Loh, L. Duncan, J. R. B. Perry, N. Patterson, E. B. Robinson, M. J. Daly, A. L. Price, and B. M. Neale, 2015. An atlas of genetic correlations across human diseases and traits. Nat. Genet. 47: 1236–1241.
Bullock, K. D., E. J. Pollak, J. K. Bertrand, D. Garrick, M. Enns, B. Weaber, D. E. Wilson, B. R. Brangus, and S. Gertrudis, 2003. International beef cattle genetic evaluation in the United States and the role of the National Beef Cattle Evaluation Consortium. Interbull Bull. 31: 156.
Calo, L. L., R. E. McDowell, L. D. VanVleck, and P. D. Miller, 1973. Genetic Aspects of Beef Production among Holstein-Friesians Pedigree Selected for Milk Production. J. Anim. Sci. 37: 676–682.
Calus, M. P. L., and J. Vandenplas, 2016. Calc_grm—a program to compute pedigree, genomic, and combined relationship matrices. Wageningen ABGC, Wageningen UR Livest. Res.

Calus, M. P. L., J. Vandenplas, J. ten Napel, and R. F. Veerkamp, 2016. Validation of simultaneous deregression of cow and bull breeding values and derivation of appropriate weights. J. Dairy Sci. 99: 6403–6419.

Campos, G. S., F. F. Cardoso, C. C. G. Gomes, R. Domingues, L. C. de Almeida Regitano, M. C. de Sena Oliveira, H. N. de Oliveira, R. Carvalheiro, L. G. Albuquerque, S. Miller, I. Misztal, and D. Lourenco, 2022. Development of genomic predictions for Angus cattle in Brazil incorporating genotypes from related American sires. J. Anim. Sci. 100: 1–13.

Cantet, R., A. Birchmeier, and J. Steibel, 2004. Full conjugate analysis of normal multiple traits with missing records using a generalized inverted Wishart distribution. Genet. Sel. Evol. 36: 49.

Canty, A., and B. Ripley, 2020. boot: Bootstrap R (S-Plus) Functions.

Cesarani, A., A. Garcia, J. Hidalgo, L. Degano, D. Vicario, N. Macciotta, and D. Lourenco, 2021a. Genomic information allows for more accurate breeding values for milkability in dual-purpose Italian Simmental cattle. J. Dairy Sci. 104: 5719–5727.

Cesarani, A., Y. Masuda, S. Tsuruta, E. L. Nicolazzi, P. M. VanRaden, D. Lourenco, and I. Misztal, 2021b. Genomic predictions for yield traits in US Holsteins with unknown parent groups. J. Dairy Sci. 104: 5843–5853.

Chang, C. C., C. C. Chow, L. C. Tellier, S. Vattikuti, S. M. Purcell, and J. J. Lee, 2015. Second-generation PLINK: rising to the challenge of larger and richer datasets. Gigascience 4: 7.

Christensen, O. F., and M. S. Lund, 2010. Genomic prediction when some animals are not genotyped. Genet. Sel. Evol. 42: 1–8.

Chu, T. T., J. W. M. Bastiaansen, P. Berg, H. Romé, D. Marois, J. Henshall, and J. Jensen, 2019. Use of genomic information to exploit genotype-by-environment interactions for body weight of broiler chicken in bio-secure and production environments. Genet. Sel. Evol. 51: 50.

Clément, V., B. Bibé, É. Verrier, J.-M. Elsen, E. Manfredi, J. Bouix, and É. Hanocq, 2001. Simulation analysis to test the influence of model adequacy and data structure on the estimation of genetic parameters for traits with direct and maternal effects. Genet. Sel. Evol. 33: 369–395.

Cole, J. B., and P. M. VanRaden, 2018. Symposium review: Possibilities in an age of genomics: The future of selection indices. J. Dairy Sci. 101: 3686–3701.

Crook, B. J., S. J. Skinner, and H. P. Nivison, 2019. Developments in multi-source genetic evaluations for beef cattle: a BREEDPLAN perspective, pp. 41–47 in *ICAR Technical Series*, Prague.

David, X., A. de Vries, E. Feddersen, and S. Borchersen, 2010. International genomic cooperation: EuroGenomics significantly improves reliability of genomic evaluations. Interbull Bull. 41: 77–78.

David, I., F. Bouvier, M. Banville, L. Canario, L. Flatres-Grall, E. Balmisse, and H. Garreau, 2015. The direct-maternal genetic correlation has little impact on genetic evaluations. J. Anim. Sci. 93: 5639–5647.

Dodenhoff, J., L. D. Van Vleck, and K. E. Gregory, 1999. Estimation of direct, maternal,

and grandmaternal genetic effects for weaning weight in several breeds of beef cattle. J. Anim. Sci. 77: 840.

Durbin, H. J., D. Lu, H. Yampara-Iquise, S. P. Miller, and J. E. Decker, 2020. Development of a genetic evaluation for hair shedding in American Angus cattle to improve thermotolerance. Genet. Sel. Evol. 52: 63.

Durr, J., and J. Philipsson, 2012. International cooperation: The pathway for cattle genomics. Anim. Front. 2: 16–21.

Durr, J. W., H. Jorjani, and R. Reents, 2014. International Genotype Exchange Platform (GENOEX), pp. 1–10 in *Proc. of the ICAR/Interbull meeting*, Berlin, Germany.

Eaglen, S. A. E., and P. Bijma, 2009. Genetic parameters of direct and maternal effects for calving ease in Dutch Holstein-Friesian cattle. J. Dairy Sci. 92: 2229–2237.

Van Eenennaam, A. L., K. A. Weigel, A. E. Young, M. A. Cleveland, and J. C. M. Dekkers, 2014. Applied Animal Genomics: Results from the Field. Annu. Rev. Anim. Biosci. 2: 105–139.

Eggen, A., 2012. The development and application of genomic selection as a new breeding paradigm. Anim. Front. 2: 10–15.

Espinola Alfonso, R. E., 2021. Definition of phantom parent groups in beef cattle international evaluations, MSc thesis. Wageningen University & Research.

Falconer, D. S., and T. F. C. Mackay, 1996. Introduction to Quantitative Genetics. Harlow Pearson Education Limited.

Fernando, R. L., J. C. Dekkers, and D. J. Garrick, 2014. A class of Bayesian methods to combine large numbers of genotyped and non-genotyped animals for whole-genome analyses. Genet. Sel. Evol. 46: 50.

Fikse, W. F., R. Rekaya, and K. A. Weigel, 2003a. Genotype × Environment Interaction for Milk Production in Guernsey Cattle. J. Dairy Sci. 86: 1821–1827.

Fikse, W. F., R. Rekaya, and K. A. Weigel, 2003b. Assessment of environmental descriptors for studying genotype by environment interaction. Livest. Prod. Sci. 82: 223–231.

Fikse, W. F., and J. Philipsson, 2007. Development of international genetic evaluations of dairy cattle for sustainable breeding programs. Anim. Genet. Resour. 29–43.

Fouilloux, M.-N., and D. Laloë, 2001. A sampling method for estimating the accuracy of predicted breeding values in genetic evaluation. Genet. Sel. Evol. 33: 473.

Fouilloux, M.-N., S. Minery, S. Mattalia, and D. Laloë, 2006. Assessment of Connectedness in the International Genetic Evaluation of Simmental and Montbéliard Breeds. Interbull Bull. 35: 129–135.

Fouilloux, M.-N., R. Dassonneville, S. Minery, S. Mattalia, D. Laloë, and W. F. Fikse, 2008a. To be connected or not? Answers for Dairy Cattle in International Genetic Evaluations. Interbull Bull. 38: 128.

Fouilloux, M.-N., V. Clément, and D. Laloë, 2008b. Measuring connectedness among herds in mixed linear models: From theory to practice in large-sized genetic evaluations. Genet. Sel. Evol. 40: 145–159.

Fragomeni, B., Y. Masuda, H. L. Bradford, D. A. L. Lourenco, and I. Misztal, 2019.

International bull evaluations by genomic BLUP with a prediction population. J. Dairy Sci. 102: 2330–2335.

García-Cortés, L. A., C. Moreno, L. Varona, and J. Altarriba, 1992. Variance component estimation by resampling. J. Anim. Breed. Genet. 109: 358–363.

García-Cortés, L. A., C. Moreno, L. Varona, and J. Altarriba, 1995. Estimation of prediction-error variances by resampling. J. Anim. Breed. Genet. 112: 176–182.

García-Ruiz, A., J. B. Cole, P. M. VanRaden, G. R. Wiggans, F. J. Ruiz-López, and C. P. Van Tassell, 2016. Changes in genetic selection differentials and generation intervals in US Holstein dairy cattle as a result of genomic selection. Proc. Natl. Acad. Sci. 113: E3395–E4004.

Garrick, D. J., J. F. Taylor, and R. L. Fernando, 2009. Deregressing estimated breeding values and weighting information for genomic regression analyses. Genet. Sel. Evol. 41: 55.

Garrick, D. J., 2011. The nature, scope and impact of genomic prediction in beef cattle in the United States. Genet. Sel. Evol. 43: 17.

Garrick, D. P., B. L. Golden, and D. J. Garrick, 2018. Accuracies of contrasts between estimated breeding values of selection candidates from national cattle evaluations using pedigree or single-step genomic methodology, pp. 974 in *11th World Congress of Genetics Applied to Livestock Production*, Auckland, New Zealand.

Gerber, P., T. Vellinga, C. Opio, and H. Steinfeld, 2011. Productivity gains and greenhouse gas emissions intensity in dairy systems. Livest. Sci. 139: 100–108.

Gerstmayr, S., 1992. Impact of the data structure on the reliability of the estimated genetic parameters in an animal model with maternal effects. J. Anim. Breed. Genet. 109: 321–336.

Goddard, M. E., 1985. A method of comparing sires evaluated in different countries. Livest. Prod. Sci. 13: 321–331.

Goddard, M. E., and B. J. Hayes, 2009. Mapping genes for complex traits in domestic animals and their use in breeding programmes. Nat. Rev. Genet. 10: 381–391.

Goddard, M. E., 2009. Genomic selection: prediction of accuracy and maximisation of long term response. Genetica 136: 245–257.

Goddard, M. E., A. Jighly, H. Benhajali, H. Jorjani, and Z. Liu, 2019. SNPMace – A meta-analysis to estimate SNP effects by combining results from multiple countries. Interbull Bull. 54: 1–6.

Graser, H.-U., B. A. Tier, D. J. Johnston, and S. A. Barwick, 2005. Genetic evaluation for the beef industry in Australia. Aust. J. Exp. Agric. 913.

Gravert, H. O., 1983. IDF recommended procedure for international comparison of the merit of dairy cattle. Int. Dairy Fed. Bullettin 165: 3–6.

Guarini, A. R., D. A. L. Lourenco, L. F. Brito, M. Sargolzaei, C. F. Baes, F. Miglior, I. Misztal, and F. S. Schenkel, 2018. Comparison of genomic predictions for lowly heritable traits using multi-step and single-step genomic best linear unbiased predictor in Holstein cattle. J. Dairy Sci. 101: 8076–8086.

Guarini, A. R., D. A. L. Lourenco, L. F. Brito, M. Sargolzaei, C. F. Baes, F. Miglior, S. Tsuruta, I. Misztal, and F. S. Schenkel, 2019. Use of a single-step approach for

integrating foreign information into national genomic evaluation in Holstein cattle. J. Dairy Sci. 102: 8175–8183.

Gunia, M., R. Saintilan, E. Venot, C. Hozé, M. N. Fouilloux, and F. Phocas, 2014. Genomic prediction in French Charolais beef cattle using high-density single nucleotide polymorphism markers1. J. Anim. Sci. 92: 3258–3269.

de Haas, Y., M. P. L. Calus, R. F. Veerkamp, E. Wall, M. P. Coffey, H. D. Daetwyler, B. J. Hayes, and J. E. Pryce, 2012. Improved accuracy of genomic prediction for dry matter intake of dairy cattle from combined European and Australian data sets. J. Dairy Sci. 95: 6103–6112.

Habier, D., J. Tetens, F.-R. Seefried, P. Lichtner, and G. Thaller, 2010. The impact of genetic relationship information on genomic breeding values in German Holstein cattle. Genet. Sel. Evol. 2010 421 42: 5.

Hartmann, C., K. Johansson, E. Strandberg, and L. Rydhmer, 2003. Genetic correlations between the maternal genetic effect on chick weight and the direct genetic effects on egg composition traits in a White Leghorn line. Poult. Sci. 82: 1–8.

Hayes, B. J., H. A. Lewin, and M. E. Goddard, 2013. The future of livestock breeding: Genomic selection for efficiency, reduced emissions intensity, and adaptation. Trends Genet. 29: 206–214.

Henderson, C. R., 1949. Estimation of changes in herd environment. J. Dairy Sci. 32: 706.

Henderson, C. R., 1975. Best Linear Unbiased Estimation and Prediction under a Selection Model. Biometrics 31: 423–447.

Heydarpour, M., L. R. Schaeffer, and M. H. Yazdi, 2008. Influence of population structure on estimates of direct and maternal parameters. J. Anim. Breed. Genet. 125: 89–99.

Hill, W. G., and R. Thompson, 1978. Probabilities of Non-Positive Definite between-Group or Genetic Covariance Matrices. Biometrics 34: 429–439.

Hsu, W.-L., D. J. Garrick, and R. L. Fernando, 2017. The Accuracy and Bias of Single-Step Genomic Prediction for Populations Under Selection. G3 Genes|Genomes|Genetics 7: 2685–2694.

ICAR, 2022. https://www.icar.org/.

ICBF, 2020. Beef evaluations, supporting document. Pages 1, 29. Available from /www.icbf.com/wp-content/uploads/2020/09/Beef-Eval.

IDF, 1981. IDF recommended procedure for international comparison of genetic merit of dairy cattle. Int. Dairy Fed. Doc A-64, Brussels, Belgium.

Illumina, 2006. https://www.illumina.com/documents/products/technotes/technote_topbot.pdf.

Im, S., R. Fernando, and D. Gianola, 1989. Likelihood inferences in animal breeding under selection: a missing-data theory view point. Genet. Sel. Evol. 21: 399.

Institut de l'Élevage, 2020. Methods and results of the genetic evaluation IBOVAL 2020 for the beef cattle breeds. Page 25. Available from https://269ccb85-5bd2-4cb3-bc11-530aba342463.files.

Interbeef. Interbeef Genetic Evaluations Forms. Available from: https://www.icar.org/index.php/technical-bodies/working-groups/interbeef-working-group/genetic-evaluations-in-beef-cattle/.

Interbeef, 2006. https://www.icar.org/index.php/technical-bodies/working-groups/interbeef-working-group/.

Interbeef, 2017. Interbeef Country Feedback. Available from: https://www.icar.org/wp-content/uploads/2017/08/All-Interbeef-Country-Feedback.pdf.

Interbull, 1983. https://interbull.org/index.

Interbull, 2021. https://wiki.interbull.org/public/rG procedure?action=print&rev=32#Genetic_correlation_estimation_procedure.

Interbull Centre, 2022. National genomic evaluation forms. Available from: https://wiki.interbull.org/public/cou_geno_forms.

Jairath, L., J. C. M. Dekkers, L. R. Schaeffer, Z. Liu, E. B. Burnside, and B. Kolstad, 1998. Genetic Evaluation for Herd Life in Canada. J. Dairy Sci. 81: 550–562.

Jakobsen, J. H., J. W. Dürr, H. Jorjani, F. Forabosco, A. Loberg, and J. Philipsson, 2009. Genotype by environment interactions in international genetic evaluations of dairy bulls. Proc. Assoc. Advmt. Anim. Breed. Genet 18: 133–142.

Jang, S., D. Lourenco, and S. Miller, 2022. Inclusion of sire by herd interaction effect in the genomic evaluation for weaning weight of American Angus. J. Anim. Sci. 100: 1–12.

Jibrila, I., J. Vandenplas, J. Napel, R. F. Veerkamp, and M. P. L. Calus, 2021. Avoiding preselection bias in subsequent single-step genomic BLUP evaluations of genomically preselected animals. J. Anim. Breed. Genet. 138: 432–441.

Johnston, D. J., M. H. Ferdosi, N. K. Connors, V. Boerner, J. Cook, C. J. Girard, A. A. Swan, and B. Tier, 2018. Implementation of single-step genomic BREEDPLAN evaluations in Australian beef cattle, pp. 269 in *World Congress on Genetics Applied to Livestock Production*, Auckland, New Zealand.

Jorjani, H., 1999. Connectedness in Dairy Cattle Populations. Interbull Bull. 22: 1–4.

Jorjani, H., 2000. Well-Connected, Informative Sub-Sets of Data. Interbull Bull. 25: 22–25.

Jorjani, H., 2001. Simultaneous Estimation of Genetic Correlations for Milk Yield Among 27 Holstein Populations. Interbull Bull. 27: 80–83.

Jorjani, H., L. Klei, and U. Emanuelson, 2003. A Simple method for weighted bending of genetic (co)variance matrices. J. Dairy Sci. 86: 677–679.

Jorjani, H., U. Emanuelson, and W. F. Fikse, 2005. Data subsetting strategies for estimation of across-country genetic correlations. J. Dairy Sci. 88: 1214–1224.

Jorjani, H., J. Jakobsen, M. A. Nilforooshan, E. Hjerpe, B. Zumbach, and V. Palucci, 2011. Genomic Evaluation of BSW Populations InterGenomics: Results and Deliverables. Interbull Bull. 43: 5–8.

Journaux, L., B. Wickham, E. Venot, and T. Pabiou, 2006. Development of Routine International Genetic Evaluation Services for Beef Cattle as an Extension of Interbull ’s Services. Interbull Bull. 35: 146–152.

Kennedy, B. W., and D. Trus, 1993. Considerations on genetic connectedness

between management units under an animal model. J. Anim. Sci. 71: 2341–2352.

Klei, B., and S. Tsuruta, 2008. Approximate Variance for Heritability Estimates. Available from: http://nce.ads.uga.edu/html/projects/AI_SE_revised.pdf.

Knol, E. F., B. J. Ducro, J. A. M. van Arendonk, and T. Van Der Lende, 2002. Direct, maternal and nurse sow genetic effects on farrowing-, pre-weaning- and total piglet survival. Livest. Prod. Sci. 73: 153–164.

Koch, R. M., 1972. The Role of Maternal Effects in Animal Breeding: VI. Maternal Effects in Beef Cattle. J. Anim. Sci. 35: 1316–1323.

Krogmeier, D., V. Dzapo, and I. L. Mao, 1994. Additive genetic and maternal effects on litter traits in rabbits. J. Anim. Breed. Genet. 111: 420–431.

Laloë, D., 1993. Precision and information in linear models of genetic evaluation. Genet. Sel. Evol. 25: 557.

Laloë, D., and F. Phocas, 2003. A proposal of criteria of robustness analysis in genetic evaluation. Livest. Prod. Sci. 80: 241–256.

Lee, C., and E. J. Pollak, 1997. Relationship between sire x year interactions and direct-maternal genetic correlation for weaning weight of Simmental cattle. J. Anim. Sci. 75: 68.

Lee, S. H., J. Yang, M. E. Goddard, P. M. Visscher, and N. R. Wray, 2012. Estimation of pleiotropy between complex diseases using single-nucleotide polymorphism-derived genomic relationships and restricted maximum likelihood. Bioinformatics 28: 2540–2542.

Legarra, A., I. Aguilar, and I. Misztal, 2009. A relationship matrix including full pedigree and genomic information. J. Dairy Sci. 92: 4656–4663.

Legarra, A., O. F. Christensen, I. Aguilar, and I. Misztal, 2014. Single Step, a general approach for genomic selection. Livest. Sci. 166: 54–65.

Legarra, A., O. F. Christensen, Z. G. Vitezica, I. Aguilar, and I. Misztal, 2015. Ancestral relationships using metafounders: Finite ancestral populations and across population relationships. Genetics 200: 455–468.

Legarra, A., and A. Reverter, 2018. Semi-parametric estimates of population accuracy and bias of predictions of breeding values and future phenotypes using the LR method. Genet. Sel. Evol. 50: 53.

Lewis, R. M., R. E. Crump, G. Simm, and R. Thompson, 1999. Assessing connectedness in across-flock genetic evaluations, pp. 121 in *Proceedings of the British Society of Animal Science*, The British Society of Animal Science, Scarborough, UK.

Lidauer, M. H., P. Madsen, K. Matilainen, E. A. Mäntysaari, I. Strandén, R. Thompson, J. Pösö, J. Pedersen, U. S. Nielsen, J.-Å. Eriksson, K. Johansson, and G. P. Aamand, 2009. Estimation of Variance Components for Nordic Red Cattle Test-Day Model: Bayesian Gibbs Sampler vs. Monte Carlo EM REML. Interbull Bull. 40: 37–41.

Liu, Z., 2011. Use of MACE results as input for genomic models. Interbull Bull. 43: 1–4.

Liu, Z., M. Goddard, F. Reinhardt, and R. Reents, 2014. A single-step genomic model with direct estimation of marker effects. J. Dairy Sci. 97: 5833–5850.

Loberg, A., and J. W. Dürr, 2009. Interbull Survey on the Use of Genomic Information. Interbull Bull. 39: 3–14.

Lourenco, D. A. L., S. Tsuruta, B. O. Fragomeni, Y. Masuda, I. Aguilar, A. Legarra, J. K. Bertrand, T. S. Amen, L. Wang, D. W. Moser, and I. Misztal, 2015. Genetic evaluation using single-step genomic best linear unbiased predictor in American Angus. J. Anim. Sci. 93: 2653–2662.

Lourenco, D., K. Bertrand, H. Bradford, S. Miller, and I. Misztal, 2017. The Promise of Genomics for Beef Improvement, pp. 30–42 in *Proceedings Beef Improvement Federation Conference*, Athens, GA.

Lund, M. S., A. P. De Roos, A. G. De Vries, T. Druet, V. Ducrocq, S. Fritz, F. Guillaume, B. Guldbrandtsen, Z. Liu, R. Reents, C. Schrooten, F. Seefried, and G. Su, 2011. A common reference population from four European Holstein populations increases reliability of genomic predictions. Genet. Sel. Evol. 43: 43.

Lund, M. S., I. van den Berg, P. Ma, R. F. Brøndum, and G. Su, 2016. Review: How to improve genomic predictions in small dairy cattle populations. Animal 10: 1042–1049.

Luštrek, B., J. Vandenplas, G. Gorjanc, and K. Potočnik, 2021. Genomic evaluation of Brown Swiss dairy cattle with limited national genotype data and integrated external information. J. Dairy Sci. 104: 5738–5754.

Macedo, F. L., A. Reverter, and A. Legarra, 2020a. Behavior of the Linear Regression method to estimate bias and accuracies with correct and incorrect genetic evaluation models. J. Dairy Sci. 103: 529–544.

Macedo, F. L., O. F. Christensen, J.-M. Astruc, I. Aguilar, Y. Masuda, and A. Legarra, 2020b. Bias and accuracy of dairy sheep evaluations using BLUP and SSGBLUP with metafounders and unknown parent groups. Genet. Sel. Evol. 52: 47.

Macedo, F. L., J. M. Astruc, T. H. E. Meuwissen, and A. Legarra, 2022. Removing data and using metafounders alleviates biases for all traits in Lacaune dairy sheep predictions. J. Dairy Sci.

Mäntysaari, E., Z. Liu, and P. Vanraden, 2010. Interbull Validation Test for Genomic Evaluations. Interbull Bull. 41: 17–22.

Mäntysaari, E. A., M. Koivula, and I. Strandén, 2020. Symposium review: Single-step genomic evaluations in dairy cattle. J. Dairy Sci. 103: 5314–5326.

Mark, T., 2004. Applied Genetic Evaluations for Production and Functional Traits in Dairy Cattle. J. Dairy Sci. 87: 2641–2652.

Mark, T., P. Madsen, J. Jensen, and W. F. Fikse, 2005a. Short Communication: Difficulties in estimating across-country genetic correlations for weakly linked bull populations. J. Dairy Sci. 88: 3303–3305.

Mark, T., P. Madsen, J. Jensen, and W. F. Fikse, 2005b. Prior (Co)Variances Can Improve Multiple-Trait Across-Country Evaluations of Weakly Linked Bull Populations. J. Dairy Sci. 88: 3290–3302.

Masuda, Y., P. M. VanRaden, S. Tsuruta, D. A. L. Lourenco, and I. Misztal, 2022. Invited review: Unknown-parent groups and metafounders in single-step genomic BLUP. J. Dairy Sci. 105: 923–939.

Matilainen, K., E. A. Mäntysaari, M. H. Lidauer, I. Strandén, and R. Thompson, 2012.

Employing a Monte Carlo algorithm in expectation maximization restricted maximum likelihood estimation of the linear mixed model. J. Anim. Breed. Genet. 129: 457–468.

Matilainen, K., E. A. Mäntysaari, M. H. Lidauer, I. Strandén, and R. Thompson, 2013. Employing a Monte Carlo Algorithm in Newton-Type Methods for Restricted Maximum Likelihood Estimation of Genetic Parameters. PLoS One 8: e80821.

Matilainen, K., I. Strandén, and E. A. Mäntysaari, 2014. Approximation of Standard Errors of Estimates as a By-Product for MC EM REML Analysis, in *10th World Congress of Genetics Applied to Livestock Production Approximation*, Vancouver.

Matilainen, K., E. A. Mäntysaari, and I. Strandén, 2019. Efficient Monte Carlo algorithm for restricted maximum likelihood estimation of genetic parameters. J. Anim. Breed. Genet. 136: 252–261.

De Mattos, D., J. K. Bertrand, and I. Misztal, 2000. Investigation of genotype x environment interactions for weaning weight for Herefords in three countries. J. Anim. Sci. 78: 2121–2126.

Meuwissen, T. H. E., B. J. Hayes, and M. E. Goddard, 2001. Prediction of total genetic value using genome-wide dense marker maps. Genetics 157: 1819–1829.

Meuwissen, T., B. Hayes, and M. Goddard, 2016. Genomic selection: A paradigm shift in animal breeding. Anim. Front. 6: 6–14.

Meyer, K., 1992. Bias and sampling covariances of estimates of variance components due to maternal effects. Genet. Sel. Evol. 24: 487.

Meyer, K., M. J. Carrick, and B. J. P. Donnelly, 1993. Genetic parameters for growth traits of Australian beef cattle from a multibreed selection experiment. J. Anim. Sci. 71: 2614–2622.

Meyer, K., 1994. Estimates of direct and maternal correlations among growth traits in Australian beef cattle. Livest. Prod. Sci. 38: 91–105.

Meyer, K., 1997. Estimates of genetic parameters for weaning weight of beef cattle accounting for direct-maternal environmental covariances. Livest. Prod. Sci. 52: 187–199.

Meyer, K., 2001. Estimates of direct and maternal covariance functions for growth of Australian beef calves from birth to weaning. Genet. Sel. Evol. 33: 487.

Misztal, I., 2008. Reliable computing in estimation of variance components. J. Anim. Breed. Genet. 125: 363–370.

Misztal, I., A. Legarra, and I. Aguilar, 2009. Computing procedures for genetic evaluation including phenotypic, full pedigree, and genomic information. J. Dairy Sci. 92: 4648–4655.

Misztal, I., S. Tsuruta, I. Aguilar, A. Legarra, P. M. VanRaden, and T. J. Lawlor, 2013. Methods to approximate reliabilities in single-step genomic evaluation. J. Dairy Sci. 96: 647–654.

MiX99 Development Team, 2017. MiX99: A software package for solving large mixed model equations. Release XI/2017.

MiX99 Development Team, 2019. MiX99: A software package for solving large mixed model equations. Release XI/2019.

Moore, S. G., and J. F. Hasler, 2017. A 100-Year Review: Reproductive technologies in dairy science. J. Dairy Sci. 100: 10314–10331.

Mrode, R. A., 2014a. Linear models for the prediction of animal breeding values. CABI, 1–360 p.

Mrode, R. A., 2014b. Maternal Trait Models: Animal and Reduced Animal models., pp. 109–120 in *Linear models for the prediction of animal breeding values*, edited by CABI.

Muir, B., B. Van Doormaal, and G. Kistemaker, 2010. International genomic cooperation - North American perspective. Interbull Bull. 41: 71–76.

ten Napel, J., J. Vandenplas, M. Lidauer, I. Stranden, M. Taskinen, E. Mäntysaari, M. P. L. Calus, and R. F. Veerkamp, 2020. MiXBLUP, user-friendly software for large genetic evaluation systems.

Negussie, E., O. González-Recio, M. Battagin, A.-R. Bayat, T. Boland, Y. de Haas, A. Garcia-Rodriguez, P. C. Garnsworthy, N. Gengler, M. Kreuzer, B. Kuhla, J. Lassen, N. Peiren, M. Pszczola, A. Schwarm, H. Soyeurt, A. Vanlierde, T. Yan, and F. Biscarini, 2022. Integrating heterogeneous across-country data for proxy-based random forest prediction of enteric methane in dairy cattle. J. Dairy Sci. 105: 2022.

Nejati-Javaremi, A., C. Smith, and J. P. Gibson, 1997. Effect of total allelic relationship on accuracy of evaluation and response to selection. J. Anim. Sci. 75: 1738.

Neufeld, G. M., 2021. Estimation of genetic correlations across countries in beef cattle using pedigree and genomic information, MSc thesis. Wageningen University and Research.

Ni, G., G. Moser, N. R. Wray, S. H. Lee, S. Ripke, B. M. Neale, A. Corvin, J. T. R. Walters, K.-H. Farh, P. A. Holmans, P. Lee, B. Bulik-Sullivan, D. A. Collier, H. Huang, T. H. Pers, I. Agartz, E. Agerbo, M. Albus, M. Alexander, F. Amin, M. C. O'Donovan *et al.*, 2018. Estimation of Genetic Correlation via Linkage Disequilibrium Score Regression and Genomic Restricted Maximum Likelihood. Am. J. Hum. Genet. 102: 1185–1194.

Nicolazzi, E., F. Forabosco, and W. Fikse, 2011. Assessment of the value of international genetic evaluations for yield in predicting domestic breeding values for foreign Holstein bulls. J. Dairy Sci. 94: 2601–2612.

Nilforooshan, M. A., J. H. Jakobsen, W. F. Fikse, B. Berglund, and H. Jorjani, 2010. Application of a multiple-trait, multiple-country genetic evaluation model for female fertility traits. J. Dairy Sci. 93: 5977–5986.

Nilforooshan, M. A., 2020. mbend: an R package for bending non-positive-definite symmetric matrices to positive-definite. BMC Genet. 21: 97.

Nilforooshan, M. A., and H. Jorjani, 2022. Invited review: A quarter of a century—International genetic evaluation of dairy sires using MACE methodology. J. Dairy Sci. 105: 3–21.

Pabiou, T., M. Nilforooshan, D. Laloë, E. Hjerpe, and E. Venot, 2014. Across-country genetic parameters in beef cattle for Interbeef weaning weight genetic evaluation, in *10th World Congress of Genetics Applied to Livestock Production*, Vancouver, Canada.

Pabiou, T., T. Pitkanen, R. Evans, E. Herpje, and J. Vandenplas, 2018. Using direct and maternal Interbeef information to increase genetic gains in Irish beef, in *11th World Congress of Genetics Applied to Livestock Production Benefits, Interbull Open 2: R&D in (inter)national evaluations: Calving traits and fertility in dairy and beef cattle.*, Auckland, New Zealand.

Palucci, V., J. Sendecka, M. Pedersén, C. Wasserman, H. Persson, J.-E. Strömqvist, S. Savoia, A. Michenet, F. Macedo, K. Haugaard, S. Lennartsson, and T. Roozen, 2022. Interbull Centre activity report 2021. Available from: www.interbull.org.

Pardo, A. M., M. A. Elzo, L. T. Gama, and L. M. Melucci, 2020. Genetic parameters for growth and cow productivity traits in Angus, Hereford and crossbred cattle. Livest. Sci. 233: 103952.

Patry, C., and V. Ducrocq, 2011. Accounting for genomic pre-selection in national BLUP evaluations in dairy cattle. Genet. Sel. Evol. 43: 30.

Patterson, H. D., and R. Thompson, 1971. Recovery of Inter-Block Information when Block Sizes are Unequal. Biometrika 58: 545–554.

Patterson, N., A. L. Price, and D. Reich, 2006. Population structure and eigenanalysis. PLoS Genet. 2: 2074–2093.

Philipsson, J., 1982. International comparison of breeding stock. Second World Congr. Genet. Appl. to Livest. Prod. 8: 119–129.

Philipsson, J., 1987. Standards and Procedures for International Genetic Evaluations of Dairy Cattle. J. Dairy Sci. 70: 418–424.

Philipsson, J., 2005. INTERBULL - How it began and some achievements. Interbull Bull. 33: 131.

Philipsson, J., 2011. Interbull Developments, Global Genetic Trends and Role in the Era of Genomics. Interbull Bull. 44: i–xiii.

Phocas, F., K. Donoghue, and H. Graser, 2004. Comparison of Alternative Strategies for an International Genetic Evaluation of Beef Cattle Breeds. Interbull Bullettin 32: 18–24.

Phocas, F., and D. Laloë, 2004. Genetic parameters for birth and weaning traits in French specialized beef cattle breeds. Livest. Prod. Sci. 89: 121–128.

Phocas, F., K. Donoghue, and H. U. Graser, 2005. Investigation of three strategies for an international genetic evaluation of beef cattle weaning weight. Genet. Sel. Evol. 37: 361–380.

Picard Druet, D., A. Varenne, F. Herry, F. Hérault, S. Allais, T. Burlot, and P. Le Roy, 2020. Reliability of genomic evaluation for egg quality traits in layers. BMC Genet. 21: 17.

Pitkänen, T. J., M. Koivula, I. Strandén, G. P. Aamand, and E. A. Mäntysaari, 2018. Integration of external information into the national multitrait evaluation model, pp. 122 in *Book of Abstracts of the 69th Annual Meeting of the European Federation of Animal Science*, Dubrovnik, Croatia.

Pitkänen, T. J., M. Koivula, I. Strandén, G. P. Aamand, and E. A. Mäntysaari, 2020. Integration of MACE breeding values into domestic multi-trait test-day model evaluations, pp. 582 in *Book of Abstracts of the 71st Annual Meeting of the European Federation of Animal Science*, Virtual Meeting.

Pszczola, M., T. Strabel, H. A. Mulder, and M. P. L. Calus, 2012. Reliability of direct genomic values for animals with different relationships within and to the reference population. J. Dairy Sci. 95: 389–400.

Quaas, R. L., 1988. Additive Genetic Model with Groups and Relationships. J. Dairy Sci. 71: 1338–1345.

Quintanilla, R., D. Laloë, and G. Renand, 2002a. Heteroskedasticity and genotype by environment interaction across European countries for weaning weight in Charolais breed, pp. 147–150 in *Proceedings of the 33rd biennial session of ICAR*, EAAP publication N. 107, 2003, Interlaken, Switzerland.

Quintanilla, R., D. Laloë, and G. Renand, 2002b. Heterogeneity of variances across regions for weaning weight in Charolais breed, pp. 19–23 in *7th World Congress on Genetics Applied to Livestock Production*, Montpellier, France.

R Core Team, 2020. R: A language and environment for statistical computing.

R Core Team, 2021. R: A language and environment for statistical computing.

Rekaya, R., K. A. Weigel, and D. Gianola, 1999. Bayesian estimation of a structural model for genetic covariances for milk yield in five regions of the USA, in *50th annual meeting of the european association for animal production (EAAP)*, Zürich, Switzerland.

Rekaya, R., K. A. Weigel, and D. Gianola, 2003. Bayesian Estimation of Parameters of a Structural Model for Genetic Covariances Between Milk Yield in Five Regions of the United States. J. Dairy Sci. 86: 1837–1844.

Renand, G., D. Laloë, R. Quintanilla, and M. N. Fouilloux, 2003. A first attempt of an international genetic evaluation of beef breeds in europe. Interbull Bull. 31: 151–155.

van Rheenen, W., W. J. Peyrot, A. J. Schork, S. H. Lee, and N. R. Wray, 2019. Genetic correlations of polygenic disease traits: from theory to practice. Nat. Rev. Genet. 20: 567–581.

Robertson, A., 1959. The Sampling Variance of the Genetic Correlation Coefficient. Biometrics 15: 469–485.

Robinson, G. K., 1986. Group Effects and Computing Strategies for Models for Estimating Breeding Values. J. Dairy Sci. 69: 3106–3111.

Robinson, G. K., 1991. That BLUP is a Good Thing: The Estimation of Random Effects. Stat. Sci. 6: 15–32.

Robinson, D. L., 1996a. Estimation and interpretation of direct and maternal genetic parameters for weights of Australian Angus cattle. Livest. Prod. Sci. 45: 1–11.

Robinson, D. L., 1996b. Models which might explain negative correlations between direct and maternal genetic effects. Livest. Prod. Sci. 45: 111–122.

Rubin, D. B., 1976. Inference and missing data. Biometrika 63: 581–592.

Ruhlmann, C., E. Bruns, E. Fraehr, J. Philipsson, S. Janssens, K. Quinn, E. T. Hellsten, and A. Ricard, 2009. Genetic connectedness between seven European countries for performance in jumping competitions of warmblood riding horses. Livest. Sci. 120: 75–86.

Schaeffer, L. R., 1994. Multiple-Country Comparison of Dairy Sires. J. Dairy Sci. 77: 2671–2678.

Schaeffer, L. R., 2001. Multiple trait international bull comparisons. Livest. Prod. Sci. 69: 145–153.

Schaeffer, L. R., 2006. Strategy for applying genome-wide selection in dairy cattle. J. Anim. Breed. Genet. 123: 218–223.

Schaeffer, L. R., 2018. Necessary changes to improve animal models. J. Anim. Breed. Genet. 135: 124–131.

Schaeffer, L. R., 2019a. Maternal Traits, pp. 127–143 in *Animal Models*, Volumes Direct.

Schaeffer, L. R., 2019b. Animal models. Volumes Direct.

Sigurdsson, A., and G. Banos, 1995. Dependent Variables in International Sire Evaluations. Acta Agric. Scand. Sect. A - Anim. Sci. 45: 209–217.

Sorensen, D., and D. Gianola, 2002. Likelihood, Bayesian and MCMC Methods in Quantitative Genetics. Springer Verlag, New York, NY.

Stolzman, M., H. Jasiorowski, Z. Reklewski, A. Zarnecki, and G. Kalinowska, 1988. Comparison of ten Friesian strains in Poland under field conditions. I. Strain comparison for growth rate. Livest. Prod. Sci. 18: 217–237.

Strandén, I., and K. Vuori, 2006. RelaX2: pedigree analysis program, pp. 27–30 in *8th World Congr. Genet. Appl. Livest. Prod.*, Belo Horizonte, MG, Brazil.

Strandén, I., 2014. RelaX2 program for pedigree analysis, version 1.65.

Sullivan, P. G., and P. M. VanRaden, 2010. GMACE implementation. Interbull Bull. 41: 3–7.

Tarrés, J., M. Fina, and J. Piedrafita, 2010. Connectedness among herds of beef cattle bred under natural service. Genet. Sel. Evol.

Thompson, R., and E. Mantysaari, 2004. Prospects for statistical methods in animal breeding. Jour. Ind. Soc. Ag. Stat. 57: 15–25.

Thompson, R., S. Brotherstone, and I. M. S. White, 2005. Estimation of quantitative genetic parameters. Philos. Trans. R. Soc. B Biol. Sci. 360: 1469–1477.

Tier, B., and K. Meyer, 2004. Approximating prediction error covariances among additive genetic effects within animals in multiple-trait and random regression models. J. Anim. Breed. Genet. 121: 77–89.

Tribout, T., D. Boichard, V. Ducrocq, and J. Vandenplas, 2019. A fast method to fit the mean of unselected base animals in single-step SNP-BLUP, pp. 211 in *Book of Abstracts of the 70th Annual Meeting of the European Federation of Animal Science*, Wageningen Academic Publishers, Ghent, Belgium.

Trus, D., and J. W. Wilton, 1988. Genetic parameters for maternal traits in beef cattle. Can. J. Anim. Sci. 68: 119–128.

Tsuruta, S., I. Misztal, I. Aguilar, and T. J. Lawlor, 2011. Multiple-trait genomic evaluation of linear type traits using genomic and phenotypic data in US Holsteins. J. Dairy Sci. 94: 4198–4204.

Vandenplas, J., and N. Gengler, 2012. Comparison and improvements of different Bayesian procedures to integrate external information into genetic evaluations. J. Dairy Sci. 95: 1513–1526.

Vandenplas, J., F. G. Colinet, and N. Gengler, 2014. Unified method to integrate and blend several, potentially related, sources of information for genetic

evaluation. Genet. Sel. Evol. 2014 461 46: 1–15.
Vandenplas, J., and N. Gengler, 2015. Strategies for comparing and combining different genetic and genomic evaluations: A review. Livest. Sci. 181: 121–130.
Vandenplas, J., M. Spehar, K. Potocnik, N. Gengler, and G. Gorjanc, 2017. National single-step genomic method that integrates multi-national genomic information. J. Dairy Sci. 100: 465–478.
Vandenplas, J., M. P. L. Calus, and G. Gorjanc, 2018. Genomic Prediction Using Individual-Level Data and Summary Statistics from Multiple Populations. Genetics 210: 53–69.
Vandenplas, J., R. F. Veerkamp, R. Evans, M. P. L. Calus, and J. Ten Napel, 2019a. Single-step evaluation for calving traits with 1.5 million genotypes: SNP-based approaches, pp. 212 in *Book of Abstracts of the 70th Annual Meeting of the European Federation of Animal Science*, Ghent, Belgium.
Vandenplas, J., M. P. L. Calus, H. Eding, and C. Vuik, 2019b. A second-level diagonal preconditioner for single-step SNPBLUP. Genet. Sel. Evol. 51: 30.
Vandenplas, J., H. Eding, M. Bosmans, and M. P. L. Calus, 2020. Computational strategies for the preconditioned conjugate gradient method applied to ssSNPBLUP, with an application to a multivariate maternal model. Genet. Sel. Evol. 52: 24.
Vandenplas, J., H. Eding, and M. P. L. Calus, 2021a. Technical note: Genetic groups in single-step single nucleotide polymorphism best linear unbiased predictor. J. Dairy Sci. 104: 3298–3303.
Vandenplas, J., M. P. L. Calus, H. Eding, M. van Pelt, R. Bergsma, and C. Vuik, 2021b. Convergence behavior of single-step GBLUP and SNPBLUP for different termination criteria. Genet. Sel. Evol. 53: 34.
VanRaden, P. M., 2008. Efficient methods to compute genomic predictions. J. Dairy Sci. 91: 4414–4423.
VanRaden, P. M., G. R. Wiggans, C. P. Van Tassell, T. S. Sonstegard, and F. Schenkel, 2009. Benefits from Cooperation in Genomics. Interbull Bull. 39: 67–72.
VanRaden, P. M., and P. G. Sullivan, 2010. International genomic evaluation methods for dairy cattle. Genet. Sel. Evol. 42: 7.
VanRaden, P. M., 2013. https://aipl.arsusda.gov/software/findhap/.
VanRaden, P. M., M. E. Tooker, J. R. Wright, C. Sun, and J. L. Hutchison, 2014. Comparison of single-trait to multi-trait national evaluations for yield, health, and fertility. J. Dairy Sci. 97: 7952–7962.
Venot, E., T. Pabiou, B. Wickham, and L. Journaux, 2006. First steps towards a European joint genetic evaluation of the Limousine breed. Interbull Bull. 35: 141–145.
Venot, E., T. Pabiou, J. Guerrier, A. Cromie, L. Journaux, J. Flynn, and B. Wickham, 2007. Interbeef in practice: example of a joint genetic evaluation between France, Ireland and United Kingdom for pure bred Limousine weaning weights. Interbull Bull. 36: 41–47.
Venot, E., M. N. Fouilloux, P. Sullivan, and D. Laloë, 2008. Level of connectedness and reliability in international beef evaluation. Interbull Bull. 38: 3–7.

Venot, E., M. N. Fouilloux, F. Forabosco, A. Fogh, T. Pabiou, K. Moore, J. A. Eriksson, G. Renand, and D. Laloë, 2009a. Interbeef genetic evaluation of Charolais and Limousine weaning weights. Interbull Bull. 40: 61–67.

Venot, E., M. N. Fouilloux, F. Forabosco, A. Fogh, T. Pabiou, K. Moore, J.-A. Eriksson, G. Renand, and D. Laloë, 2009b. Beef without borders: genetic parameters for Charolais and Limousine Interbeef genetic evaluation of weaning weights. Interbull Bull. 40: 55–60.

Venot, E., T. Pabiou, E. Hjerpe, M. A. Nilforooshan, A. Launay, and B. Wickham, 2014. Benefits of Interbeef international genetic evaluations for weaning weight, pp. 17–22 in *10th World Congress of Genetics Applied to Livestock Production Benefits*, Vancouver, Canada.

Venot, E., A. Barbat, D. Boichard, P. Croiseau, V. Ducrocq, R. Lefebvre, F. Phocas, M.-P. Sanchez, T. Tribout, A. Vinet, M. N. Fouilloux, A. Govignon-Gion, A. Launay, J. Promp, M. Barbat, A. Baur, S. Fritz, R. Saintilan, C. Carillier, H. Larroque, A. Legarra, I. Palhière, C. Robert-Granié, R. Rupp, F. Tortereau, J. M. Astruc, V. Clement, V. Loywyck, P. Boulesteix, and S. Mattalia, 2016. French genomic experience: genomics for all ruminant species, in *ICAR - Interbull Meeting*, Puerto Varas, Chile.

Vesela, Z., M. Brzakova, A. Svitakova, L. Vostry, and P. Bucek, 2019. Interbeef international genetic evaluation for calving traits, pp. 49–54 in *ICAR Technical Series*, Prague.

Vishwanath, R., 2003. Artificial insemination: The state of the art. Theriogenology 59: 571–584.

Visscher, P. M., and M. E. Goddard, 1993. Fixed and Random Contemporary Groups. J. Dairy Sci. 76: 1444–1454.

Vitezica, Z. G., I. Aguilar, I. Misztal, and A. Legarra, 2011. Bias in genomic predictions for populations under selection. Genet. Res. (Camb). 93: 357–366.

Van Vleck, L. D., D. St. Louis, and J. I. Miller, 1977. Expected phenotypic response in weaning weight of beef calves from selection for direct and maternal genetic effects. J. Anim. Sci. 44: 360–367.

Waldron, D. F., C. A. Morris, R. L. Baker, and D. L. Johnson, 1993. Maternal effects for growth traits in beef cattle. Livest. Prod. Sci. 34: 57–70.

Weigel, K. A., R. Rekaya, N. R. Zwald, and W. F. Fikse, 2001. International Genetic Evaluation of Dairy Sires Using a Multiple-Trait Model with Individual Animal Performance Records. J. Dairy Sci. 84: 2789–2795.

Weigel, K. A., P. M. VanRaden, H. D. Norman, and H. Grosu, 2017. A 100-Year Review: Methods and impact of genetic selection in dairy cattle—From daughter–dam comparisons to deep learning algorithms. J. Dairy Sci. 100: 10234–10250.

Westell, R. A., R. L. Quaas, and L. D. Van Vleck, 1988. Genetic Groups in an Animal Model. J. Dairy Sci. 71: 1310–1318.

Wickham, B. W., and J. W. Durr, 2011. A new international infrastructure for beef cattle breeding. Anim. Front. 1: 53–59.

Wientjes, Y. C. J., R. F. Veerkamp, P. Bijma, H. Bovenhuis, C. Schrooten, and M. P. L. Calus, 2015. Empirical and deterministic accuracies of across-population

genomic prediction. Genet. Sel. Evol. 47: 5.
Wientjes, Y. C. J., M. P. L. Calus, P. Duenk, and P. Bijma, 2018. Required properties for markers used to calculate unbiased estimates of the genetic correlation between populations. Genet. Sel. Evol. 50: 65.
Willham, R. L., 1963. The Covariance between Relatives for Characters Composed of Components Contributed by Related Individuals. Biometrics 19: 18.
Willham, R. L., 1972. The Role of Maternal Effects in Animal Breeding: III. Biometrical Aspects of Maternal Effects in Animals. J. Anim. Sci. 35: 1288–1293.
Willham, R. L., 1980. Problems in estimating maternal effects. Livest. Prod. Sci. 7: 405–418.
Wilmink, J. B. M., A. Meijering, and B. Engel, 1986. Conversion of breeding values for milk from foreign populations. Livest. Prod. Sci. 14: 223–229.
Yu, H., M. L. Spangler, R. M. Lewis, and G. Morota, 2017. Genomic relatedness strengthens genetic connectedness across management units. G3 Genes, Genomes, Genet. 7: g3-300151.
Yu, H., M. L. Spangler, R. M. Lewis, and G. Morota, 2018. Do stronger measures of genomic connectedness enhance prediction accuracies across management units? J. Anim. Sci. 96: 4490–4500.
Yu, H., and G. Morota, 2021. GCA: an R package for genetic connectedness analysis using pedigree and genomic data. BMC Genomics 22: 119.
Zarnecki, A., J. Jamrozik, and H. D. D. Norman, 1991. Comparison of Ten Friesian Strains in Poland for Yield Traits from First Three Parities. J. Dairy Sci. 74: 2303–2308.
Zhou, X., H. K. Im, and S. H. Lee, 2020. CORE GREML for estimating covariance between random effects in linear mixed models for complex trait analyses. Nat. Commun. 11: 4208.
Zimin, A. V., A. L. Delcher, L. Florea, D. R. Kelley, M. C. Schatz, D. Puiu, F. Hanrahan, G. Pertea, C. P. Van Tassell, T. S. Sonstegard, G. Marçais, M. Roberts, P. Subramanian, J. A. Yorke, and S. L. Salzberg, 2009. A whole-genome assembly of the domestic cow, Bos taurus. Genome Biol. 10: R42.
Zwald, N. R., K. A. Weigel, W. F. Fikse, and R. Rekaya, 2003. Identification of Factors That Cause Genotype by Environment Interaction Between Herds of Holstein Cattle in Seventeen Countries. J. Dairy Sci. 86: 1009–1018.

SUMMARY

Summary

Animal breeding aims to improve a population for a series of economic and societal relevant traits. This goal is achieved by selecting the best animals at such traits from the current generation to be the parents of the next generation. National breeding organizations help farmers to make this selection decision by ranking animals according to their genetic values. In cattle, advancements in reproductive technologies such as artificial insemination led to major genetic improvements by allowing superior bulls with desired genetic characteristics to have thousands of offspring. Thanks to such technologies, breeders could access the genetic material of superior bulls from foreign countries. However, animals' estimated breeding values (EBV) are not directly comparable across countries due to differences in scales and genetic bases, trait and model definitions and the possible presence of genotype-by-environment interactions caused by different environmental conditions between countries. Thus, breeders needed methods to compare and rank domestic sires with foreign ones, leading to the creation of so-called international evaluations.

International evaluations jointly analyse all national data to compute an international EBV (EBV_{INT}) and account for differences across countries by modelling the same trait recorded in different countries as different correlated traits. The resulting EBV_{INT} are expressed on the same country scale as the EBV computed from national evaluations (EBV_{NAT}), facilitating the comparison of domestic and foreign sires and worldwide trading of the genetic material of elite sires. International beef cattle evaluations led by Interbeef (a working group of the International Committee for Animal Recording) currently involve 15 countries worldwide, five breeds and three traits. Current Interbeef evaluations only use national phenotypes and pedigree data. Beef cattle international evaluations face various challenges mainly related to three aspects: i) the estimation of across-country genetic correlations; ii) the inclusion of national genomic information, and iii) the lack of an official procedure for participating countries to integrate the EBV_{INT} back into their national evaluations. By addressing these challenges, this thesis aimed to improve and further develop methodologies for beef cattle international evaluations.

In **Chapter 2**, we provided up-to-date insights on the impact of Interbeef pedigree-based evaluations from a national perspective, considering both small and large participating countries. We evaluated how international evaluations impact the EBV's reliabilities of domestic animals and the number and origin of so-called publishable sires, i.e. sires with EBV_{INT} that are publishable in other countries' scales. On average across countries, international evaluations increased the reliability of

domestic animals' EBV by 9.6 and 8.3 percentage points for direct EBV and maternal EBV, respectively, due to the inclusion of information from relatives recorded in other countries. International evaluations allow small countries to access a larger panel of elite foreign sires with an EBV_{INT} directly expressed on their country scale and increase the EBV's reliabilities of domestic animals. For large countries, international evaluations provide EBV_{INT} for their elite sires on the scale of all participating countries, facilitating their comparison with foreign sires and helping to better promote their genetic material abroad.

Across-country genetic correlations (r_g) are key for international evaluations as they model how the information from animals recorded in foreign countries contributes to the animals' EBV_{INT}. In beef cattle, there is usually a low level of connectedness between populations due to the low usage of artificial insemination. These low levels of connectedness and the presence of maternal effects make the estimation of across-country r_g challenging; lack of convergence of the estimated parameters and high standard errors of r_g are often experienced. Given the low level of connectedness, using simultaneously all data available for the estimation process would be preferred, but it is unfeasible due to computational constraints. In **Chapter 3**, we first quantified the existing level of genetic connectedness in Limousin cattle across eight European populations. We then estimated across-country r_g using a multi-trait approach that simultaneously fits data from all countries. We showed that estimating all 120 across-country r_g required for the Interbeef evaluations is feasible with a multi-trait approach but requires a long computation time. Therefore, we investigated four scenarios that implemented data sub-setting to select the most connected herds from the largest population while keeping a multi-trait estimation approach. These scenarios reduced the computational time up to five-fold of that required using all data. The estimated across-country r_g from scenarios with data sub-setting had larger associated standard errors and were smaller, albeit close, than those obtained when using all data. Data sub-setting mainly impacted within-country and between-country direct-maternal r_g (r_{dm}).

Chapter 4 investigated the impact of ignoring, i.e. replacing estimated values with 0, within-country and between-country estimated r_{dm} on the EBV_{INT} in pedigree-based Interbeef evaluations. Within-country r_{dm} are often reported to be negative in beef cattle. Between-country r_{dm} are currently assumed to be 0 in Interbeef evaluations as they are difficult to estimate. We compared EBV_{INT} from a model that used both within-country and between-country r_{dm} with EBV_{INT} from models that ignored between-country r_{dm} or both within-country and between-country r_{dm}. Results showed that the current practice of ignoring between-country r_{dm} had no or limited impact on the ranking of animals' direct and maternal EBV_{INT}, respectively.

Moreover, there was no re-ranking for publishable sires and the top 100 publishable sires. These results were likely due to the estimated between-country r_{dm} being close to zero on average. On the other hand, ignoring both within-country and between-country r_{dm} gave considerable re-ranking in all groups of animals evaluated, suggesting that within-country r_{dm} should not be ignored in international evaluations.

In **Chapter 5**, we developed and investigated the benefits of single-step international evaluations for beef cattle. At the national level, genomic evaluations are increasingly adopted. However, the feasibility and the benefits of including genomic information in beef cattle international evaluations are unknown. Using Limousin weaning weight data from 7 European countries, we implemented a single-step single nucleotide polymorphism BLUP (ssSNPBLUP) international evaluation that jointly analyses national phenotypes, genotypes and pedigree information. The ssSNPBLUP international evaluations led to higher accuracy than either current pedigree-based international evaluations or national evaluations (both pedigree-based and genomic-based), whilst giving similar or slightly reduced level and dispersion bias. Implementing single-step international evaluations was beneficial for both large and small countries and for countries with different amounts of genotypes available at the national level. On average across countries, moving from pedigree-based international to ssSNPBLUP international evaluations led to increases in population accuracies of 13.7% and 25.8% for direct and maternal EBV, respectively. Moreover, the international single-step approach increased the accuracies for non-genotyped animals and for countries without genotypes at the national level. The developed ssSNPBLUP international evaluation can be applied to other traits and breeds evaluated by Interbeef and will allow participating countries to enlarge existing national reference populations and improve the accuracy of national (genomic) evaluations.

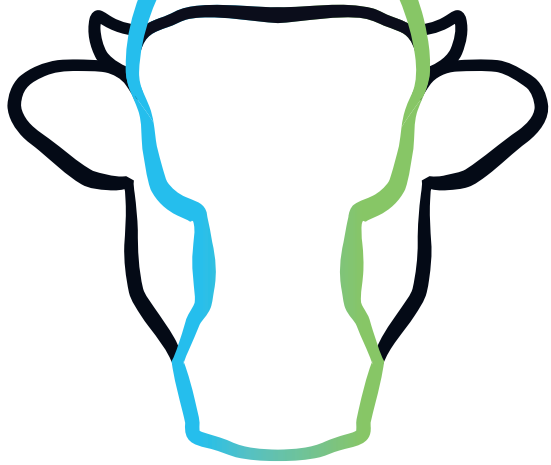
In **Chapter 6**, we developed a generalized procedure to integrate publishable sires' EBV_{INT} computed either from pedigree-based or single-step beef cattle international evaluations into national evaluations. National and international evaluations use different sources of information to compute animals' EBV. Thus, animals' EBV_{NAT} and EBV_{INT} may differ and using only one of the two EBV leads to the loss of information contained only in the discarded EBV. The integration procedure allows combining and propagating international information (i.e. EBV_{INT} and its reliability) to all animals included in the national evaluations, resulting in a blended EBV. In this procedure, publishable sires' information are de-regressed one-bull-at-the-time and included in national evaluations as additional phenotypes next to up-to-date national data. We validated the integration procedure using the Italian

pedigree-based national evaluations for Limousin weaning weight as a case study. The integration procedure increased the model adequacy of national evaluations for publishable sires, while giving similar or higher predictivity for the EBV of publishable sires' domestic offspring. The procedure performed well for integrating either pedigree-based or single-step international information into national evaluations. The integration procedure has low computational costs and can be easily implemented by countries participating in Interbeef evaluations without relying on specific software, making its application to existing national evaluations straightforward.

Chapter 7 is divided into three parts and expands the results of this thesis to a broader context. In the first part, I proposed a general standard procedure to estimate across-country r_g in current Interbeef evaluations using a multi-trait approach that simultaneously fits data from all countries. I discussed the different steps of the procedure and how data could be subset for the estimation process while maintaining a multi-trait approach. In the second part, I discussed how genomic data available from national evaluations can be used to estimate across-country r_g and measure connectedness between populations. Using simulation, I showed that genomic data can aid the estimation of r_g between disconnected and weakly connected countries. Furthermore, genomic data can help to reduce both the standard errors associated with the estimated r_g and the amount of data required for the estimation process. I also discussed measures that can capture increases in connectedness between populations due to genomic data and that can be used to identify connected subsets of herds when estimating across-country r_g. Among these measures, I showed that the coefficient of determination can detect increases in connectedness between populations due to genomic data and I discussed possible approaches to compute them in Interbeef. In the last part of this chapter, I discussed the modelling of missing parental information using genetic groups as a model improvement for Interbeef evaluations. I discussed the definition of genetic groups in current pedigree-based evaluations and its extensions to future single-step evaluations. Based on initial results, I showed that genetic groups can help to reduce level bias in pedigree-based evaluations, mainly for direct EBV_{INT}. Further research should investigate how to implement genetic groups in single-step international evaluations.

APPENDICES

A



Appendices

+ About the author
+ Publications
+ Contribution to conferences
+ Training and Supervision Plan
+ Acknowledgements
+ Colophon

Curriculum vitae

About the author

Renzo Bonifazi was born on the 10th of December 1992 in Recanati (Marche region), a small town in central Italy. Renzo was born and raised in a family of beef cattle farmers of the Marchigiana breed, where his passion for beef cattle started.

Following his interests, Renzo did his BSc in Animal Sciences at the University of Perugia (Italy). He completed his BSc with honours in 2014 with a thesis on investigating selection indices trends in the Marchigiana breed under the supervision of Prof. Emiliano Lasagna. The same year, Renzo enrolled for an MSc in Animal Sciences at the University of Perugia. During his MSc, he did an Erasmus period at the Interbull Centre (Uppsala, Sweden) where he carried out his MSc thesis under the supervision of Prof. Hossein Jorjani. His MSc thesis focused on comparing pedigree and genomic reliabilities of national and international evaluations in dairy cattle. After completing his MSc thesis with honours in 2017, he did another Erasmus traineeship at the Interbull Centre in the same year, followed by a working period as a geneticist. During this period, he became familiar with international beef cattle evaluations (Interbeef).

Finding Interbeef evaluations fascinating, Renzo started his PhD in 2018 at the Animal Breeding and Genomics group at Wageningen (the Netherlands) in a collaboration project between Wageningen University & Research, Interbeef (ICAR working group), the International Bull Evaluation Service (Interbull), the International Committee for Animal Recording (ICAR), and the Irish Cattle Breeding Federation (ICBF). His PhD focused on international genetic and genomic evaluations of beef cattle; the results of his research are described in this thesis. During his PhD research, Renzo spent four months at the Department of Agronomy, Food, Natural Resources, Animals and Environment at the University of Padova (Italy).

Since June 2022, Renzo works as a researcher at Wageningen Livestock Research (Wageningen University & Research).

Publications

Peer-reviewed publications

- **Bonifazi, R.**, M. P. L. Calus, J. ten Napel, R. F. Veerkamp, A. Michenet, S. Savoia, A. Cromie, and J. Vandenplas. *International single-step SNPBLUP beef cattle evaluations for Limousin weaning weight*. Accepted for publication in **Genet. Sel. Evol., 2022**.
- **Bonifazi, R.**, J. Vandenplas, J. ten Napel, R. F. Veerkamp, and M. P. L. Calus. *The impact of direct-maternal genetic correlations on international beef cattle evaluations for Limousin weaning weight*. **J. Anim. Sci., 2021**, 99: 1–14. DOI: https://doi.org/10.1093/jas/skab222
- **Bonifazi, R.**, J. Vandenplas, J. ten Napel, K. Matilainen, R. F. Veerkamp, and M. P. L. Calus. *Impact of sub-setting the data of the main Limousin beef cattle population on the estimates of across-country genetic correlations*. **Genet. Sel. Evol., 2020**, 52: 32. DOI: https://doi.org/10.1186/s12711-020-00551-9
- **Bonifazi, R.**, J. Vandenplas, J. ten Napel, A. Cromie, R. F. Veerkamp, and M. P. L. Calus, 2020. *Impact of Interbeef on national beef cattle evaluations*. **Acta Fytotech. Zootech., 2020**, 23: 144–155. DOI: https://doi.org/10.15414/afz.2020.23.mi-fpap.144-155

Under review

- **Bonifazi, R.**, M. P.L. Calus, J. ten Napel, R. F. Veerkamp, S. Biffani, M. Cassandro, S. Savoia, J. Vandenplas. *Integration of beef cattle international pedigree and genomic estimated breeding values into national evaluations, with an application to the Italian Limousin population*. **Submitted**.

Other publications

- **Bonifazi, R.**, M. P.L. Calus, J. ten Napel, R. F. Veerkamp, S. Biffani, M. Cassandro, S. Savoia, J. Vandenplas. *Integration of beef cattle international estimated breeding values in the Italian evaluation*. In Proceedings of the 12th **World Congress on Genetics Applied to Livestock Production, 2022**.
- **Bonifazi, R.**, J. Vandenplas, J. ten Napel, A. Cromie, R. F. Veerkamp, and M. P. L. Calus. *Re-ranking in International Beef Cattle Evaluations due to ignoring Direct-Maternal Genetic Correlations Between Countries*. **Interbull Bull, 2021**. 70–75. https://journal.interbull.org/index.php/ib/article/view/81

Contribution to conferences and presentations

- **Bonifazi R.**, M.P.L. Calus, J. ten Napel, R.F. Veerkamp, S. Biffani, M. Cassandro, S. Savoia, J. Vandenplas. *Integration of beef cattle international estimated breeding values in the Italian evaluation*. 12th World Congress on Genetics Applied to Livestock Production (Rotterdam, the Netherlands), 3-8 July 2022. *Oral presentation*.
- **Bonifazi R.**, M.P.L. Calus, J. ten Napel, R.F. Veerkamp, S. Biffani, M. Cassandro, S. Savoia, J. Vandenplas. *Integration of pedigree and genomic international EBV into national evaluations*. Interbeef webinar (Online), 11 April 2022. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, R.F. Veerkamp, M.P.L. Calus. *International genetic and genomic evaluations for beef cattle*. Centre for Genetic Improvement of Livestock, University of Guelph (Online), 18 February 2022. *Oral presentation*.
- **Bonifazi R.**, M.P.L. Calus, J. ten Napel, R.F. Veerkamp, A. Michenet, S. Savoia, A. Cromie, J. Vandenplas. *International genomic evaluations for beef cattle*. WIAS Science Days (Wageningen, the Netherlands), 11 February 2022. *Oral presentation*.
- **Bonifazi R.**, M.P.L. Calus, J. ten Napel, R.F. Veerkamp, A. Michenet, S. Savoia, A. Cromie, J. Vandenplas. *International single-step SNPBLUP genomic evaluation for beef cattle*. Interbeef Working Group (Online), 25 November 2021. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, R.F. Veerkamp, M.P.L. Calus. *International genetic and genomic evaluations in beef cattle*. Computational Genetics Discussion Group, The Roslin Institute, The University of Edinburgh (Online), 21 September 2021. *Oral presentation*.
- **Bonifazi R.**, M.P.L. Calus, J. ten Napel, A. Michenet, S. Savoia, A. Cromie, A. Roozen, R.F. Veerkamp, J. Vandenplas. *Evaluation of accuracy and bias of beef cattle international single-step genomic evaluations*. 72th Annual Meeting of the European Federation of Animal Science (Davos, Switzerland), 30 August – 3 September 2021. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Cromie, R.F. Veerkamp, M.P.L. Calus. *Re-ranking in international beef cattle evaluations due to ignoring direct-maternal genetic correlations between countries*. ICAR - Interbull Annual Meeting, 26-30 April 2021 (Online). *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Michenet, A. Cromie, R.F. Veerkamp, M.P.L. Calus. *International single-step genomic evaluations in beef cattle*. 71th

Annual Meeting of the European Federation of Animal Science (Online), 1-4 December 2020. *Oral presentation*.

- **Bonifazi R.**, J. Vandenplas, J. ten Napel, R.F. Veerkamp, A. Michenet, A. Cromie, M.P.L. Calus. *International genetic and genomic evaluations of beef cattle*. Interbeef Working Group (Online), 3 November 2020. *Oral presentation*.
- *Best presentation award in Breeding and Genetics session*: **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Cromie, R.F. Veerkamp, M.P.L. Calus. *Impact of Interbeef on national beef cattle evaluations*. 28th International Symposium Animal Science Days – (Padova, Italy), 23-25 September 2020. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, R.F. Veerkamp, M.P.L. Calus. *International genetic and genomic evaluations of beef cattle*. Interbeef Working Group (Online), 8 July 2020. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Cromie, R.F. Veerkamp, M.P.L. Calus. *Data sub-setting strategies for variance component estimation in Interbeef evaluations*. Interbeef Working Group (Zurich, Switzerland), 4-6 November 2019. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Cromie, R.F. Veerkamp, M.P.L. Calus. *Impact of data-subsetting strategies on variance component estimation for Interbeef evaluations*. 70th Annual Meeting of the European Federation of Animal Science (Ghent, Belgium), 26-30 August 2019. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Cromie, R.F. Veerkamp, M.P.L. Calus. *Data sub-setting strategies for VCE in Interbeef evaluations*. International Animal Recording Committee conference (Prague, Czech Republic), 17-21 June 2019. *Oral presentation*.
- **Bonifazi R.**, J. Vandenplas, J. ten Napel, A. Cromie, R.F. Veerkamp, H. Jorjani, M.P.L. Calus. *System for routine estimation of genetic parameters*. Interbeef working group – (Padova, Italy), 11-12 October 2018. *Oral presentation*.

- **Bonifazi R.**, E. Hjerpe, T. Pabiou, H. Benhajali, H. Jorjani. *Preliminary study of VCE for Limousine and Charolais breeds through Mix99 software*. EAAP - Interbull Annual Meeting (Tallinn, Estonia), 25-27 August 2017. *Oral presentation*.
- **Bonifazi R.**, V. Palucci, E. Hjerpe, F. M. Sarti, E. Lasagna, H. Jorjani, H. Benhajali. *Comparison of genomic reliability in national genomic evaluation of dairy cattle populations*. EAAP - Interbull Annual Meeting (Tallinn, Estonia), 25-27 August 2017. *Oral presentation*.
- **Bonifazi R.**, H. Benhajali, T. Pabiou, E. Hjerpe, M. Lidauer, K. Matilainen, H. Jorjani. *Speed up rG estimation.* EAAP - Interbull Annual Meeting (Tallinn, Estonia), 25-27 August 2017. *Presented by H. Jorjani*.

Training and Supervision Plan

Education and Training	Year(s)	ECTS
A. The Basic Package		**1.8**
WIAS Introduction Day	2018	0.3
Course on philosophy of science and/or ethics	2018	1.5
B. Disciplinary Competences		**33.7**
Writing own research proposal	2018	6.0
Quantitative Genetics Discussion Group (WUR)	2018-2022	2.0
Introduction to Quantitative Genetics - Falconer and Mackay study group (WUR)	2018-2019	2.0
Peer-reviewer of a scientific article	2022	1.0
Genetic Improvement in Livestock (WUR)	2018	6.0
Programming and computer algorithms in animal breeding with a focus on single-step GBLUP and reality of genomic selection (University of Georgia, United States)	2018	4.5
Getting started in ASReml (WUR)	2019	0.3
Application of Genome-Wide SNPs in Single Step Genomic Analysis (NOVA course, Uppsala, Sweden)	2019	1.5
Multivariate Statistics Analysis (University of Sassari, Italy)	2019	0.9
Genotype by environment interaction, uniformity and resilience (WUR)	2020	1.5
Modern Statistics for the Life Sciences (WUR)	2019	6.0
External period at the University of Padova (Italy)	2021	2.0
C. Professional Competences		**6.6**
Project planning and time management (WUR)	2018	1.5
Competence assessment (WUR)	2019	0.3
The essentials for scientific writing and presenting (WUR)	2019	1.2

Scientific Writing (WUR)	2019	1.8
WGS PhD workshop carrousel (WUR)	2019	0.3
Working on your PhD research in times of crisis (WUR)	2020	0.6
WGS PhD workshop carrousel (WUR)	2021	0.3
The Final Touch (WUR)	2021	0.6
D. Societal Relevance		**1.5**
Social impact of research (WUR)	2019	1.5
E. Presentation Skills		**4.0**
Interbeef Working Group (Padova, Italy)†	2018	
International Animal Recording Committee conference (Prague, Czech Republic)†	2019	
70th Annual Meeting of the European Federation of Animal Science (Ghent, Belgium)†	2019	1.0
Interbeef Working Group (Zurich, Switzerland)	2019	
Interbeef Working Group (Online)†	2020	
28th International Symposium Animal Science Days (Padova, Italy), Best presentation award	2020	1.0
Interbeef Working Group (Online)†	2020	
71th Annual Meeting of the European Federation of Animal Science (Online)†	2020	
ICAR - Interbull Annual meeting (Online)†	2021	1.0
72th Annual Meeting of the European Federation of Animal Science (Davos, Switzerland)†	2021	1.0
Computational Genetics Discussion Group, the Roslin Institute (Online)†	2021	
Interbeef Working Group (Online)†	2021	
WIAS Science Day (Wageningen, The Netherlands)†	2022	
Centre for Genetic Improvement of Livestock, University of Guelph (Online)†	2022	
12th World Congress on Genetics Applied to Livestock Production (Rotterdam, the Netherlands) †	2022	

A

F. Teaching competences		**6.0**
Animal Breeding and Genetics (ABG-20306) practicals' supervision	2018 - 2019	2.0
Research Master Class peer-review 2020	2020	0.5
Research Master Class peer-review 2021	2021	
BSc thesis supervision	2020	
MSc thesis supervision	2020-2021	2.0
MSc thesis supervision	2021	1.5
Total		**53.6**

† oral presentation

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representatives for providing the research data and, in particular, the genotypes. Thanks for your trust in this PhD project. A primary driver for me during this thesis was to see how this research could be applied and used in practice. Thank you all for your feedback, valuable comments, support, and encouragement along the way. I want to express a special thank you to **Andrew** for giving me the opportunity to pursue a PhD on Interbeef evaluations. Thanks for your trust since the start and your support along the way.

I then want to thank the extended advisory group accompanying this PhD thesis. Thanks to **Andrew**, **Ross**, **Thierry**, **Martino**, **Emiliano**, **Toine**, **Hossein**, **Eva**, **Alexis**, and **Simone**. Your presence and feedback during our meetings have been greatly valuable to this project. Thanks for your help with organizing the work, asking questions, and for your support along the way. **Emiliano**, thanks for all the valuable suggestions you gave me and for still keeping an eye on me after these many years.

Next, I want to thank the whole **Interbull Centre's group** (present and past), whom I always enjoy visiting. **Toine**, thanks for your support and help with the projects since the start. **Eva**, thanks for helping me to become familiar with Interbeef evaluations and for being supportive. **Marcus** (the best sysadmin), thank you for arranging all the details for remote access to the server and data and for your prompt help when I had issues with it. I lost count of how many cakes I own you, but I hope to have been a good user :) A special thanks go to **Hossein,** who closely supervised me while I was at the Interbull Centre prior to this PhD, and that kickstarted my interest in international evaluations. Thanks for giving me the trust and the encouragement I needed to pursue a PhD.

I also want to thank the **ABG secretary** and the **WIAS secretary**. In particular, I want to thank **Wilma** for all the administrative help throughout these years on the paperwork for courses, conferences, etc. Thanks also for checking on me from time to time.

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Colophon

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