Validation of consistency of Mendelian sampling variance

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ABSTRACT

Experiences from international sire evaluation indicate that the multiple-trait across-country evaluation method is sensitive to changes in genetic variance over time. Top bulls from birth year classes with inflated genetic variance will benefit, hampering reliable ranking of bulls. However, none of the methods available today enable countries to validate their national evaluation models for heterogeneity of genetic variance. We describe a new validation method to fill this gap comprising the following steps: estimating within-year genetic variances using Mendelian sampling and its prediction error variance, fitting a weighted linear regression between the estimates and the years under study, identifying possible outliers, and defining a 95% empirical confidence interval for a possible trend in the estimates. We tested the specificity and sensitivity of the proposed validation method with simulated data using a real data structure. Moderate (M) and small (S) size populations were simulated under 3 scenarios: a control with homogeneous variance and 2 scenarios with yearly increases in phenotypic variance of 2 and 10%, respectively. Results showed that the new method was able to estimate genetic variance accurately enough to detect bias in genetic variance. Under the control scenario, the trend in genetic variance was practically zero in setting M. Testing cows with an average birth year class size of more than 43,000 in setting M showed that tolerance values are needed for both the trend and the outlier tests to detect only cases with a practical effect in larger data sets. Regardless of the magnitude (yearly increases in phenotypic variance of 2 or 10%) of the generated trend, it deviated statistically significantly from zero in all data replicates for both cows and bulls in setting M. In setting S with a mean of 27 bulls in a year class, the sampling error and thus the probability of a false-positive result clearly increased. Still, overall estimated genetic variance was close to the parametric value. Only rather strong trends in genetic variance deviated statistically significantly from zero in setting S. Results also showed that the new method was sensitive to the quality of the approximated reliabilities of breeding values used in calculating the prediction error variance. Thus, we recommend that only animals with a reliability of Mendelian sampling higher than 0.1 be included in the test and that low heritability traits be analyzed using bull data sets only.

Key words: international sire evaluation, validation, trend, genetic variance

INTRODUCTION

Dairy cattle breeding is a global business, and the highest-ranking bulls are sold worldwide. Therefore, reliable estimation of the genetic merit of dairy bulls originating from different populations and production environments is of fundamental importance. International breeding values are currently obtained with a multiple-trait across-country evaluation (**MACE**) method, which uses deregressed breeding values from national genetic evaluations as observations (Schaeffer, 1994). The MACE method considers one biological trait at a time and accounts for genotype × environment interactions by assuming observations from different countries as different but genetically correlated traits.

Experience has shown that the MACE method is sensitive to the quality of the national evaluations. Several studies have demonstrated that biased genetic trends and genetic variance trends in national evaluations affect the MACE evaluations. Top bulls from birth year classes with inflated genetic variances and bulls from countries with overestimated genetic trends in their national evaluation benefit from an upward bias in ranking (Weigel et al., 1996; Van Doormaal et al., 1999; Gengler et al., 2000; Miglior et al., 2002; Ducrocq et al., 2003).

To ensure unbiased international evaluation, all participating countries are required to validate their national evaluations. The validation methods (Boichard et al., 1995) test whether national evaluations give unbiased genetic trend estimates, but the homogeneity of genetic variance across years has so far not been tested. There is an increasing need to test for homogeneity of genetic variance, which is one of the basic assumptions of the evaluation.

The main cause of heterogeneity of variance (**HV**) is a scaling effect: variance changes with a change in the phenotypic mean (Meuwissen et al., 1996; Robert-Granié et al., 1999; Lidauer et al., 2008). This is observed as animal production levels increase over time or because production levels vary among herds, which may be due to factors such as different management practices and geographical conditions, such as smaller herd sizes in mountain areas with harsh environments versus high-input systems in lowlands (e.g., Lidauer et al., 2008). Today, more and more countries are combining their breeding populations and national genetic evaluations. This increases HV due to differences in production environments and management practices among cows included in the same genetic evaluation. Other reasons for HV are related to factors such as selection, use of different breeds and genetic groups in the same evaluation, and different mating practices (Meuwissen et al., 1996). Precorrection for heterogeneous variance may not be sufficient in more complex cases, which require more elaborate methods (Meuwissen et al., 1996; Robert-Granié et al., 1999; Lidauer et al., 2008, 2015). Currently, countries follow varying practices. Yearly standard deviations (**SD**) of EBV offer a simple option for studying trends in genetic variance because any changes in genetic variance are generally reflected in SD. However, restricted maximum likelihood estimation is a more preferable alternative because within-year SD of EBV are sensitive to factors such as temporal fluctuations in the average number of daughters per bull, number of bulls in different age classes, changes in the genetic structure of a population, and reliability of breeding values (e.g., Miglior et al., 1998; Van Doormaal et al., 1999; Miglior et al., 2002).

Sullivan (1999) suggested a restricted maximum likelihood method for estimating within-year genetic variances by deriving an equation based on Mendelian sampling (**MS**) and its prediction error variance (**PEV**). Using Sullivan's method, Miglior et al. (2002) outlined a new validation test for the International Bull Evaluation Service (Interbull). Because the computation of PEV from large data sets is not feasible, Fikse et al. (2003) proposed a procedure that uses approximated reliabilities of EBV of animals and their parents. Later,

Fikse et al. (2005) introduced a framework for obtaining lower and upper bounds of the tolerance interval; the test then boiled down to counting the number of years for which the across-year estimate of genetic variance was outside the tolerance interval. The empirical tolerance interval for a birth year class was obtained by bootstrapping data within that birth year class and finding the 0.025 and 0.975 quantiles for the lower and upper genetic variance estimates. Any inaccuracies in the approximation of PEV values were taken into account in the lower and upper genetic variance estimates by applying a multiplication factor of 0.99 (lower) and 1.02 (upper) to the approximated PEV. The sensitivity and specificity of the test were unknown, calling for further research. When the procedure was tested on field data, some inconclusive results were obtained. Testing with simulated data sets gave reliable results for large cow data sets, but the method failed to detect a generated trend in genetic variance for bulls from small birth year classes (Tyrisevä et al., 2011).

Further, Lidauer et al. (2007) developed a full model sampling method (**FMS**) to estimate within-year genetic variances. Although this FMS method and the method by Fikse et al. (2003) differ in their way of estimating the PEV of MS, they yield relatively similar results (Lidauer et al., 2007). The FMS approach requires simulation of new observations according to the model used in the national evaluation system and therefore is not easy to implement in a scheme with a wide variety of national evaluation models. Based on experiences from earlier studies, our aim was to develop and test a validation method for HV of MS that would be applicable for national evaluations.

MATERIALS AND METHODS

Estimation of Genetic Variance

A univariate animal model can be described as

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Zu} + \mathbf{e},$$

where $\mathbf{y}$ is a vector of records, $\mathbf{b}$ is a vector of fixed effects, $\mathbf{u}$ is a vector of random animal effects, and $\mathbf{e}$ is a vector of random residuals. Incidence matrices $\mathbf{X}$ and $\mathbf{Z}$ relate the records to the appropriate effects. Further, we assumed that $\mathbf{u} \sim MVN\left(\mu_u, \mathbf{A}\sigma_u^2\right)$, with the expected value of breeding values defined as μ_u and covariance among breeding values defined as $\mathbf{A}\sigma_u^2$. The breeding value of animal i can be further expressed as $u_i = 1/2(u_s + u_d) + m_i$, where u_s and u_d are the breeding values of the sire and dam of animal i, and m_i is the MS of animal i. Accordingly, the relationship matrix $\mathbf{A}$ can be