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- CO:** Confidential, only for members of the consortium (including the Commission Services)
- CI:** Classified, as referred to in Commission Decision 2001/844/EC



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1. Summary

This paper corresponds to deliverable D4.6 of GenTORE workpackage 4 (*Genomic management tools to optimise resilience and efficiency*). It is an INRAE contribution which follows a presentation at an online GenTORE meeting by Vincent Ducrocq on May 11, 2021 describing the overall ambition of the study and another one by Roberta Rostellato at the 4th GenTORE annual meeting in Padova on November 15, 2021, detailing the steps required to reach actual genomic evaluation of functional longevity (FL), which is used as an indicator of long-term resilience.

2. Introduction

Functional longevity is defined as the time during which the cows stay productive in their herd, independently from their level of production. In the study performed in workpackage 2.2, we found that FL is affected by factors that are known to reflect resilience, such as fertility problems and diseases, suggesting that this trait can be used as an overall measure of resilience integrated over the whole life.

Hence, it should be possible to genetically improve resilience through genetic / genomic evaluation of FL. However, statistical evaluations of longevity require special tools (“**survival models**”) to account for specificities such as nonlinear distributions, i.e., the existence of censored data -only a lower bound of true longevity is known for animals still alive- and the influence of time-dependent effects (continuous changes in herd size, in level of production, pregnancy status, etc.). WP2.2 confirmed the influence on FL of traits such as milk production (to be corrected for to reach functional longevity), udder health, reproduction traits, some morphological traits, etc. Due to the relatively low accuracy of FL and of some of its correlated traits, especially in young cows, it was proposed to improve genetic evaluation accuracies of bulls and cows on FL by combining genetic and genomic information into a multivariate Single-Step approach, i.e., including actual FL together with traits predicting functional longevity.

Such an approach faces several challenges: 1) survival models must be extended to include all animals (and not only sires of cows) in Single-Step models (including genetic and genomic information); 2) FL and its predictor traits are described by management effects that are so different that it may be not possible to build a special software to analyse them together directly; 3) to get minimum accuracy it is necessary to analyse all traits together (multiple traits approach), which in turn requires an accurate estimation of genetic correlations between them; 4) only then, a “combined” Single-Step approach based on a unique statistical model can provide Single-Step genetic/genomic breeding values on all traits and all animals, to be used to improve FL and resilience.

3. Results

The following paper covers the first 3 points in the case of the Montbéliarde breed in France, considering 7 traits together: functional longevity, conception rate of heifers, conception rate of lactating cows, somatic cell score, clinical mastitis, udder depth and udder balance. In this study, genetic correlations among the aforementioned traits were estimated by means of bivariate sire models using a pedigree relationship matrix or a genomic relationship matrix.

We found that fertility, udder health and udder type traits are genetically correlated with FL, confirming that they can be used as predictors of this trait in a “combined” Single-Step evaluation. In addition, the comparison of estimates obtained using a pedigree relationship matrix or a genomic relationship matrix revealed that the use of genomic information tended to slightly increase genetic correlation between traits.

The model for genomic evaluation is similar to the one used for genetic parameter estimation, but at the animal level. The multiple trait model applies to preadjusted records, making the computations feasible even with many traits and very large numbers of genotyped and/or phenotyped individuals.

4. Partners involved in the work

INRAE, AU

5. Annex

These results are presented in a communication by Rostellato et al (2022) at the World Congress of Genetics Applied to Livestock Production (Rotterdam, NL). The paper is in Annex 1.

5.1. Annex1

Genetic correlations among longevity, fertility, udder health and type traits including or not genomic information

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Abstract

The aim of the study was to estimate genetic correlations among functional longevity, conception rate of heifers and of lactating cows, somatic cell score, clinical mastitis, udder depth and udder balance in Montbéliarde breed. Bivariate random regression sire models including a pedigree or a genomic relationship matrix were used to compute (co)variance components. Genetic correlations obtained including genomic information were consistent with those estimated using the pedigree relationship matrix. Conception rate, somatic cell score, clinical mastitis and udder depth showed moderate to high genetic correlations with functional longevity, suggesting that they can be good indirect predictors of the length of productive life when included in a combined genomic evaluation. In addition, the large genetic correlations among the two udder health traits and udder depth indicate that they can improve the prediction of the other traits in a multi-trait single-step model.

Introduction

Functional longevity (FL) is defined as the ability of a cow to avoid being culled for other reasons (e.g. illness or infertility) than low milk production (Ducrocq *et al.*, 1988). Dairy cow's longevity can be expressed as the length of productive life, that is the time between the date of the first calving and the culling or death date. Similarly to other functional traits, FL is increasingly considered in breeding programs because of growing concerns about animal welfare. As reported in Rostellato *et al.* (2021), it is affected by factors that are known to reflect resilience, such as fertility problems and diseases, suggesting that FL can be used as an indicator of long-term resilience.

In French dairy cattle, FL is analysed using a Weibull proportional hazard model. The heritability estimated for the trait using such model is small and accuracy of estimated breeding values (EBVs) of young bulls is low given that the majority of their daughters are censored (Ducrocq and Sölkner, 1998). To overcome those drawbacks and to include EBVs for FL in total merit index, a combined polygenic evaluation was developed (Ducrocq *et al.*, 2001). This methodology consists in an approximate multi-trait animal model, where several genetically correlated traits are included and used as predictors of the other traits. In addition to FL, the traits considered are female fertility, udder health and type traits (GenEval, 2021).

Variance and covariance components used in the current combined polygenic evaluation have been estimated ignoring genomic information. Hence, the objective of the present study was to estimate genetic correlations (r_g) among FL, reproductive, udder health and udder type traits using a pedigree (**A**) relationship matrix or a genomic (**G**) relationship matrix.

Materials & Methods

Data. The data were extracted from the French bovine national database. The dataset included 1,308,066 Montbéliarde cows, born between 2000 and 2018, from 2,345 sires with a minimum of 30 daughters. The investigated traits were FL, conception rate of heifers (CR_h) and of lactating dairy cows (CR_c), somatic cell score (SCS), clinical mastitis (CM), udder depth (UDE), and udder balance (UDB).

Sires of cows were genotyped using the BovineSNP50 BeadChip (Illumina Inc., San Diego, CA). Markers exhibiting call rate < 0.9 or minor allele frequency < 5% and monomorphic single nucleotide polymorphisms (SNPs) were discarded. After quality control, 37,133 SNPs remained.

The sire's pedigree was traced back for 3 generations and it included 5,946 animals.

Estimation of genetic correlations. The investigated traits are described by very different statistical models (e.g. FL is analysed using a survival model). It makes the use of a multiple trait animal model not feasible to compute r_g among traits. Hence, pre-adjusted performances (i.e. phenotypes corrected for all non-genetic effects) adjusted for the dam's EBV and their associated weight were computed for each cow and each of the investigated traits by means of an accurate model as described in GenEval (2021). Then, these corrected records were used as pseudo-phenotypes in a simple and unique model for all traits, whatever the complexity of the original univariate model of analysis, as proposed by Ducrocq *et al.* (2001).

Variance and covariance components were estimated using bivariate random regression sire models. To take into account heterogeneous residual variance for each pre-adjusted performance due to the different amounts of information (weight), the statistical model was as follows:

$$y_{i,m}^{\#} = v_{i,m} y_{i,m}^* = v_{i,m} * by_m + v_{i,m} * a_{i,m} + \varepsilon_{i,m} \quad (1)$$

where $v_{i,m}$ is the square root of weight for the trait i and animal m , $y_{i,m}^*$ is the pre-adjusted performance corrected for the dam's EBV of trait i and animal m , by_m is the birth year of cow m , $a_{i,m}$ is the additive genetic value of animal m for trait i , and $\varepsilon_{i,m}$ is a residual. The fixed effect of birth year is to take into account changes in genetic due to selection on correlated traits. Two distinct analyses were carried out in order to estimate (co)variance components using **A** matrix or **G** matrix, respectively.

Variance and covariance components were estimated using the average information REML algorithm implemented in AIREMLF90 program (Misztal *et al.*, 2014).

Results

Genetic correlations among the investigated traits including or not genomic information are presented in Table 1.

Comparison of estimates including or not genomic information. Genetic correlations estimated using the **A** matrix were consistent to those estimated with **G** matrix. The inclusion of genomic information gave higher r_g among FL, SCS and CM, as well as between the two fertility traits. Only r_g estimated using **G** matrix are presented and discussed hereinafter.

Genetic correlations between FL and the other investigated traits. Genetic correlations between FL and the two fertility traits were favourable. Conception rate of heifers exhibited a lower r_g compared to CR_c. High and favourable (i.e. lower culling risk when lower SCS or CM) r_g were found between FL and the two udder health traits. Udder depth and UDB exhibited

a moderate and favourable r_g with FL (i.e, lower culling risk when shallow and/or balanced udder).

Genetic correlations among fertility, udder health, and udder type traits. Genetic correlation between CR_h and CR_c was moderately positive. Conception rate of heifers did not show significant genetic relationships with udder health and udder type traits. In contrast, conception rate of lactating cows exhibited moderate and favourable r_g with SCS, CM and UDE (higher conception rate when low SCS or CM or UDE). A very high and positive r_g was found between the two udder health traits. Moreover, SCS and CM were positively correlated with UDE. A negative and moderate r_g was estimated between the two udder type traits.

Table 1. Genetic correlations among the investigated traits using a pedigree relationship matrix (above diagonal) or a genomic relationship matrix (below diagonal) ^{1, 2}.

	FL	CR_h	CR_c	SCS	CM	UDE	UDB
FL	-	-0.21 (0.03)	-0.42 (0.03)	0.45 (0.02)	0.47 (0.03)	0.44 (0.02)	-0.29 (0.03)
CR_h	-0.20 (0.04)	-	0.34 (0.04)	-0.08 (0.03)	-0.02 (0.05)	-0.02 (0.03)	-0.1 (0.03)
CR_c	-0.43 (0.03)	0.44 (0.04)	-	-0.23 (0.03)	-0.23 (0.04)	-0.24 (0.03)	0.04 (0.03)
SCS	0.50 (0.02)	-0.08 (0.04)	-0.28 (0.03)	-	0.71 (0.02)	0.33 (0.02)	-0.11 (0.02)
CM	0.53 (0.04)	-0.04 (0.05)	-0.26 (0.05)	0.82 (0.02)	-	0.41 (0.03)	-0.08 (0.02)
UDE	0.42 (0.03)	0.08 (0.04)	-0.26 (0.03)	0.33 (0.02)	0.46 (0.04)	-	-0.39 (0.02)
UDB	-0.29 (0.03)	0.06 (0.04)	-0.05 (0.04)	-0.11 (0.03)	-0.09 (0.04)	-0.36 (0.02)	-

¹ FL : functional longevity (low risk to be culled → high risk to be culled), CR_h : conception rate of heifers (poor conception rate → good conception rate), CR_c : conception rate of lactating dairy cows (poor conception rate → good conception rate), SCS : somatic cell score (low somatic cell score → high somatic cell score), CM : clinical mastitis (few clinical mastitis events → several clinical mastitis events), UDE : udder depth (shallow udder → deep udder), UDB : udder balance (poor udder balance → good udder balance)

² Sample standard deviation within parentheses

Discussion

Comparison of estimates including or not genomic information. The increase of the magnitude of r_g for FL, fertility and udder health traits when genomic information was taken into account was related to higher genetic covariances with respect to the estimates obtained using A matrix (data not shown). Similar results were also found by Gordo *et al.* (2016).

Genetic correlations between FL and the other investigated traits. In our study, we found that FL is genetically correlated with fertility, udder health, and udder type traits, suggesting that they are good indirect predictors of the length of productive life.

The favourable genetic relationships between FL and conception rate indicates that selection for a better fertility can prolong the length of productive life of dairy cows. In addition, it confirms the major importance of reproductive problems in culling-decision making (Olechnowicz *et al.*, 2016). Functional longevity exhibited a quite large relationship with SCS and CM. It suggests that the risk of being culled increased when the cow is more prone to develop sub-clinical or clinical mastitis. Hence, selective breeding for a better udder health improves the length of productive life and animal welfare. The r_g between FL and UDE indicates that a deep udder is associated with poor longevity, as reported in Larroque and Ducrocq (2001). The favourable genetic relationship between FL and UDB suggests that cows with good udder balance have a lower risk to be culled with respect to animals with poor UDB. It is in agreement with the study of Rostellato *et al.* (2021).

Genetic correlations among fertility, udder health, and udder type traits. Conception rate of heifers did not show a significant r_g with the investigated traits, except with CR_c. However, its inclusion in a multi-trait genomic evaluation can improve the prediction of conception rate in multiparous cows. A strong positive genetic relationship between the two udder health traits is reported in many other studies (e.g. Rupp and Boichard, 1999; Govignon-Gion *et al.*, 2016), confirming that SCS can be used as an indicator of CM. In addition, the positive r_g with UDE indicates that deep udders are associated with an increase of the number mastitis events and that this type trait can be used as a predictor of mastitis resistance.

Conclusion. Genetic correlations among functional longevity, conception rate, udder health and udder type traits estimated including genomic information were consistent with those obtained using a pedigree relationship matrix. The analysis presented in this study will be extended to other breeds and the results will be used in the development of a combined single-step evaluation in French dairy cattle.

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