UNIVERSIDADE FEDERAL DE VIÇOSA

Genetic parameters estimation for novel traits

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Doctor Scientiae

VIÇOSA - MINAS GERAIS
2025

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Thesis submitted to the Animal Science Graduate Program of the Universidade Federal de Viçosa in partial fulfillment of the requirements for the degree of *Doctor Scientiae*.

Adviser: Simone E. F. Guimaraes

Co-adviser: Daniela A. Lino Lourenço

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Ficha catalográfica elaborada pela Biblioteca Central da Universidade Federal de Viçosa - Campus Viçosa

T
G216g
2025

Garcia, Arielly Oliveira, 1994-
Genetic parameters estimation for novel traits / Arielly Oliveira Garcia. – Viçosa, MG, 2025.
1 tese eletrônica (77 f.): il. (algumas color.).

Inclui apêndice.
Orientador: Simone Eliza Facioni Guimarães.
Tese (doutorado) - Universidade Federal de Viçosa, Departamento de Zootecnia, 2025.
Inclui bibliografia.
DOI: https://doi.org/10.47328/ufvbbt.2025.519
Modo de acesso: World Wide Web.

1. Bovinos de corte - Melhoramento genético. 2. Bovinos de leite - Melhoramento genético. 3. Suínos - Melhoramento genético. 4. Análise de variância. 5. Suínos - Doenças. 6. Padrões de herança. I. Guimarães, Simone Eliza Facioni, 1966-. II. Universidade Federal de Viçosa. Departamento de Zootecnia. Programa de Pós-Graduação em Zootecnia. III. Título.

CDD 22. ed. 636.0821

Bibliotecário(a) responsável: Bruna Silva CRB-6/2552

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APPROVED: July 31, 2025.

Assent:

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ACKNOWLEDGMENTS

To my mother, Antonia Garcia, and my father, Adriano Garcia, who did and do everything to make my dreams come true. To my sister Arianny Garcia, who inspires me and taught me about sharing, partnership, and dedication without judgment since she was born. To my grandparents (*in memoriam*).

To all my family (and chosen family) for the moments of joy.

To my advisor, Dra. Simone Eliza Facioni Guimarães, and my co-advisor, Dra. Daniela Lourenco, for all your support, lessons, and patience. Without your guidance, my life would be much harder. I admire the strong women you both are. You both inspire me in life.

To all my friends, whom I consider an essential part of my personal and professional success. You have given, and still give me, strength and support in the face of any challenge. Thank you for your support and for making me feel seen, accepted, and valued. Here are some, because the list is HUGE. Thank you, Luane, Wesley, Eula, Arícia, Layla, Mateus, Pedro, Letícia, and Renata Rocha. I love you all.

To the Federal University of Viçosa for the opportunity to complete the postgraduate course.

To the Department of Animal Science and all my professors. Thank you, Simone (again), Renata Veroneze, Fabyano (in memoriam), Delvan, Daniele, and Paulo Sávio. I admire all your effort and dedication.

To the University of Georgia (UGA), especially the Animal Breeding and Genetics team. Professors Daniela (again), Jorge, Misztal, Matias, Rekaya, and our newly minted researcher, Dr. Fernando Bussiman. At UGA, I met people I will cherish for the rest of my life. Thank you, Sergio, Zuleica, Marisol, Zuri, Narjice, Joe, and Heegun. I love you all.

To all the brilliant professionals who supervised me throughout my projects. Thank you, Fabio Toral, John Cole, Natalia Leite, and Roos Vogelzang. All of your advice, tips, and feedback have been truly helpful in my development as a geneticist, researcher, and scientist.

To the Grupo de Discussão em Genética e Melhoramento Animal (GDMA) and the Animal Biotechnology Laboratory (LABTEC) for all learning and knowledge exchange.

This work has been sponsored by the following Brazilian research agencies: Coordination for the Improvement of Higher Education Personnel (CAPES; Financing code 001), Minas Gerais State Foundation for Research Aid (FAPEMIG) and National Council of Scientific and Technological

Development (CNPq).

“Two roads diverged in a wood, and I — I took the one less traveled by, and that has made all the difference”.

Robert Frost

ABSTRACT

GARCIA, Arielly Oliveira, D.Sc., Universidade Federal de Viçosa, July, 2025. **Genetic parameters estimation for novel traits**. Adviser: Simone Eliza Facioni Guimaraes. Co-adviser: Daniela Andressa Lino Lourenço.

Genetic improvement is a cornerstone of animal production systems, potentially enhancing productivity, health, and welfare across livestock species. The success of breeding programs relies on the accurate estimation of genetic parameters, which guide selection decisions and enable the prediction of breeding values. The parameters, heritability, genetic correlation, and repeatability, are informative, as they quantify the extent to which phenotypic variation is attributable to genetic causes and help to define the expected response to selection. Genetic parameters are derived from the decomposition of phenotypic variance into its underlying components, including additive genetic, maternal, environmental, and permanent environmental variances. Estimating these components typically involves linear mixed models and relies on appropriately structured data sets. Understanding the magnitude and structure of these components is essential for the design and implementation of effective breeding strategies. Different categories of traits tend to exhibit distinct patterns of genetic variability. Production traits, such as milk yield and composition, are typically characterized by moderate to high heritability and repeatability. Reproductive traits, in contrast, often show low heritabilities due to their complex physiological nature and strong environmental influence. Welfare-related traits and health indicators usually present low to intermediate values, reflecting both genetic and environmental contributions to their expression. These expected ranges provide important context when interpreting estimated genetic parameters and inform selection strategies across trait types. This thesis aimed to estimate variance components and genetic parameters across different countries, animal populations, and trait categories, providing a comprehensive evaluation of the genetic architecture of production, reproductive, and welfare traits. Despite the biological and species-specific differences, a unified analytical approach was applied, with each study focusing on genetic (direct and maternal) variances and covariances and repeatability when applicable. The first study focused on dairy Gir cattle in Brazil, aiming to estimate heritability, genetic correlations, and repeatability for milk quality traits, namely fat percentage, protein percentage, and somatic cell count. The second study evaluated calving ease in a beef-on-dairy system in the United States, involving Jersey and Holstein cows inseminated with Angus, Charolais, and Simmental bulls, intending to estimate direct and maternal heritabilities for this reproductive trait. The third study, conducted in the Netherlands, involved a pig population and focused on the estimation of genetic parameters for two welfare-related traits: swine inflammation and necrosis syndrome and skin damage. The analysis included direct and maternal heritability estimates, genetic correlations between the traits, and repeatability estimates for skin damage. Across studies, the results aligned with established expectations for the trait categories: reproductive traits exhibited the lowest heritabilities, welfare traits also showed low estimations, and production traits demonstrated higher heritabilities and repeatabilities. These findings reinforce the importance of tailoring breeding strategies to the genetic characteristics of each trait and contribute to the broader understanding of trait-specific genetic variability across livestock species.

Keywords: Beef-on-Dairy. Gir cattle. Livestock. Pigs. Variance components. SINS.

RESUMO

GARCIA, Arielly Oliveira, D.Sc., Universidade Federal de Viçosa, julho de 2025. **Estimativa de parâmetros genéticos para novas características**. Orientadora: Simone Eliza Facioni Guimaraes. Coorientador: Daniela Andressa Lino Lourenço.

O melhoramento genético é um pilar fundamental na produção animal, aumentando potencialmente a produtividade, reprodução e o bem-estar independente da espécie. O sucesso dos programas de melhoramento depende da estimativa acurada dos parâmetros genéticos, que orientam as decisões de seleção e permitem a previsão dos valores genéticos. Os parâmetros (herdabilidade, correlação genética e repetibilidade) são particularmente informativos, pois quantificam a extensão em que a variação fenotípica é atribuível a causas genéticas e ajudam a definir a resposta esperada à seleção. Os parâmetros genéticos são derivados da decomposição da variância fenotípica, incluindo variâncias genéticas aditivas, maternas, ambientais e ambientais permanentes. A estimativa desses componentes normalmente envolve modelos lineares mistos e depende de conjuntos de dados adequadamente estruturados. Compreender a magnitude e a estrutura desses componentes é essencial para a implementação de estratégias de melhoramento genético eficazes. Diferentes categorias de características tendem a exibir padrões distintos de variabilidade genética. Características de produção, como produção e composição do leite, são tipicamente caracterizadas por herdabilidade e repetibilidade de moderadas a altas. Características reprodutivas, por outro lado, frequentemente apresentam baixa herdabilidade devido à sua natureza fisiológica complexa e forte influência ambiental. Características relacionadas ao bem-estar e indicadores de saúde geralmente apresentam valores baixos a intermediários, refletindo contribuições genéticas e ambientais para sua expressão. Essas faixas esperadas fornecem contexto importante ao interpretar parâmetros genéticos estimados e informam estratégias de seleção entre os tipos de características. Esta tese teve como objetivo estimar componentes de variância e parâmetros genéticos em diferentes países, populações animais e categorias de características, fornecendo uma avaliação abrangente da arquitetura genética de características de produção, reprodução e bem-estar. Apesar das diferenças biológicas e específicas das espécies, uma abordagem analítica unificada foi aplicada, com cada estudo focando em variâncias e covariâncias genéticas (diretas e maternas) e repetibilidade quando aplicável. O primeiro estudo se concentrou em gado Gir leiteiro no Brasil, com o objetivo de estimar herdabilidade, correlações genéticas e repetibilidade para características de qualidade do leite, analisou-se porcentagem de gordura e proteína, e contagem de células somáticas. O segundo estudo avaliou a facilidade de parto em um sistema de Beef-on-Dairy nos Estados Unidos, envolvendo vacas Jersey e Holandesas inseminadas com touros Angus, Charolês e Simental, com o objetivo de estimar as herdabilidades direta e materna para essa característica reprodutiva. O terceiro estudo envolveu uma população de suínos na Holanda, e se concentrou na estimativa de parâmetros genéticos para duas características relacionadas a saúde e bem-estar, síndrome de inflamação e necrose suína e danos à pele. A análise incluiu estimativas de herdabilidade direta e materna, correlações genéticas entre as características e estimativas de repetibilidade para danos à pele. Entre os estudos, os resultados se alinharam às expectativas para as categorias de características. As características reprodutivas e de bem-estar exibiram baixas herdabilidades, enquanto as características de produção demonstraram maiores herdabilidades e repetibilidades. Essas descobertas reforçam a importância de investigar e adaptar as estratégias de melhoramento para cada característica, contribuindo para uma compreensão mais ampla da variabilidade genética específica da característica entre as espécies de animais de produção.

Palavras-chave: Bovino de corte. Bovino de leite. Estimação de componentes de variância. Gir Leiteiro. Suínos. SINS.

SUMMARY

CHAPTER 1

1.1. General introduction

Genetic improvement has long been fundamental for increasing productivity and efficiency in animal production systems. The success of any breeding program depends on identifying animals with superior genetic merit and strategically using this information to accelerate genetic gain across generations. Estimating and interpreting genetic parameters are essential components of quantitative genetic analysis to support these goals.

Genetic parameters such as heritability, genetic correlations, and repeatability are used to describe the proportion of phenotypic variation that is attributable to genetic causes, the degree of association between traits at the genetic level, and the consistency of an individual's performance across repeated measurements or environments (Mrode, 2014). These parameters directly inform the selection efficiency and the design of breeding schemes. Traits with higher heritability respond faster to selection, while genetic correlations are key to understanding the magnitude and direction of correlated responses and managing trade-offs between traits (Falconer and Mackay, 1996).

Milk composition and health-related traits in dairy cattle are key indicators of milk quality and processing yield, particularly in cheese-producing regions. In Brazil, Gir dairy cattle play a central role in tropical dairy systems, valued for their heat tolerance and parasite resistance (Otto et al., 2021). In recent decades, emphasis has shifted from volume-based payment systems to those rewarding milk quality, motivating genetic studies of both milk composition and udder health-related traits (Botaro, Gameiro & Santos, 2013; Paixão et al., 2017). Somatic cell count, often log-transformed for statistical analysis, is widely used as an indicator of udder health and subclinical mastitis. Joint genetic evaluations of these traits can support selection strategies that balance profit, productivity, and health (Prata et al., 2015; Carmo et al., 2023).

In beef-on-dairy systems, calving ease is a critical trait due to its direct impact on cow production and calf survival. The increasing use of beef sires on dairy cows, a common practice in the United States to enhance calf value, has raised concerns about dystocia (Berry et al., 2019). Some studies have already shown that dystocia rates increase in dairy cows crossed to certain breeds of beef sires, but the prevalence of easy calving increases with the dam's age, regardless of the service-sire breed (Fouz et al., 2012; Eriksson et al., 2020). Differences in dystocia rate according to bull breed seem to be associated with genetic factors, however, pedigree limitations and the complex nature of calving ease, affected by both direct and maternal genetic effects, make it a challenging trait to evaluate. Accurate modeling and proper trait and score definitions are essential to incorporate calving ease into selection programs that aim to optimize productivity in beef-on-dairy scenarios (Saad et al. 2020; Miller, 2021).

In Europe, animal welfare has emerged as a priority trait alongside productive and reproductive performance. The Swine Inflammation and Necrosis Syndrome (SINS) is a recently described condition associated with inflammation in the extremity body regions of suckling piglets, weaners, and fattening pigs (Reiner et al., 2019; Reiner et al., 2020). These lesions not only compromise animal welfare but may also reduce performance and increase culling rates. Genetic studies have started to explore the heritable nature of these traits and identify associated genomic regions, contributing to the development of selection tools to reduce the prevalence of SINS and improve overall pig health (Kuehling et al., 2021; Reiner et al., 2022; Leite et al., 2023). Furthermore, studies have shown that SINS in suckling piglets is associated with future skin damage, and that skin lesions in animals at slaughter result in economic losses (Niemi et al. 2021; Leite et al., 2023).

An important aspect of interpreting genetic parameters is recognizing that they vary depending on the biological nature of the trait. Production traits are typically moderately to highly heritable, reflecting strong genetic control (Kőrösi et al., 2025; Otwinowska-Mindur, 2025). In contrast, reproductive traits often exhibit low heritability due to their complex physiological underpinnings and sensitivity to environmental influences (Ye et al., 2018; Ogawa et al., 2019; Chen et al., 2025). Health and welfare traits tend to present low to intermediate heritabilities, depending on the precision of trait definition and measurement, as well as the genetic diversity within the population (Leite et al., 2023; Fan et al., 2025; Otwinowska-Mindur, 2025). Understanding these expected ranges is critical for the correct interpretation of estimates and for setting realistic expectations regarding selection response.

Furthermore, knowledge of the typical genetic parameters' behavior across trait categories contributes to optimizing breeding goals and integrating new traits. As animal breeding continues to evolve to address societal concerns such as animal welfare and environmental sustainability, the accurate estimation and understanding of genetic variability across a wide spectrum of traits remain central to genetic improvement efforts.

1.2. Objectives

1.2.1. Main objective

This thesis aimed to estimate variance components and genetic parameters across different countries, animal populations, and trait categories, providing a comprehensive evaluation of the genetic architecture of production, reproductive, and welfare traits.

1.2.2. Specific objectives

1. To perform a multi-trait analysis to simultaneously estimate heritability, repeatability, genetic correlations, and breeding values for fat and protein percentage, and the logarithm of somatic cell count in Gir cattle;
2. To estimate variance components and direct and maternal heritabilities for calving ease in beef-on-dairy crosses, considering the first and first three lactations, comparing linear and threshold models;
3. To estimate variance components and direct and maternal genetic heritabilities for Swine Inflammation and Necrosis Syndrome (SINS) in suckling piglets, to estimate variance components, direct heritability, and repeatability for skin damage in gilts, to investigate whether there is a genetic correlation between SINS and skin damage, and to investigate whether there are genetic variants and candidate genes associated with SINS and skin damage.

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CHAPTER 2

GENETIC PARAMETERS ESTIMATION FOR MILK QUALITY TRAITS IN DAIRY GIR CATTLE

Arielly O. Garcia,[1,2] Daniela Lourenco,[2] Simone E. F. Guimarães,[1] and Fabio L. B. Toral[3]

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2.1. Abstract

Milk and cheese production is a hallmark of the Minas Gerais state in Brazil. As necessary to produce higher-quality milk, understanding the genetic and phenotypic relationships among milk composition and milk hygienic quality becomes increasingly critical. We aimed to perform a multi-trait analysis to simultaneously estimate heritability, repeatability, genetic correlations, and breeding values for fat and protein percentage, and the logarithmic somatic cell count (logSCC). Data included 182 test-day records of 531 Gir cows from two farms in Minas Gerais, Brazil. Each animal has an average of six records per lactation, and an average of two lactations evaluated. Variance components for additive genetic and permanent environment effects, heritabilities, genetic correlations, repeatabilities, and breeding values were estimated using a multi-trait model including all traits simultaneously. Heritability estimates were equal to 0.15 ± 0.03 for fat percentage, 0.34 ± 0.05 for protein percentage, and 0.10 ± 0.04 for logSCC, which reinforces that production-related traits tend to have higher genetic influence, and therefore higher heritability, while health-related traits, such as logSCC, are more influenced by environmental factors, resulting in lower heritability. The genetic correlation between fat and protein percentages was positive and high (0.69 ± 0.10), which is expected, as both traits contribute to total milk solids production. The genetic correlation between logSCC and fat percentage was negative (-0.45 ± 0.34), while the correlation between logSCC and protein percentage was not significantly different from zero. A negative genetic correlation between logSCC and milk composition traits is expected, as genes that contribute to lower logSCC are often associated with improved milk composition. Repeatabilities ranged from low to moderate (0.17 to 0.42), indicating inconsistency in the performance of the same individual across different measurements, suggesting a substantial influence of temporary environmental factors on these traits. In closing, it was possible to use a multi-trait model that simultaneously considers fat and protein percentages, as well as logarithmic somatic cell count (logSCC), three key traits related to milk quality. All results presented will be used for animal selection decisions within the two farms evaluated.

Keywords: Fat percentage, logSCC, multi-trait analysis, protein percentage, somatic cell count

2.2. Introduction

Originating from India, Gir dairy cattle have been selectively bred in Brazil for dairy purposes and now contribute meaningfully to both purebred and crossbred dairy systems. Among the Brazilian states, Minas Gerais stands out as the leading dairy producer, responsible for nearly 27% of the country's total milk output (IBGE, 2022), supported by favorable climate conditions, extensive pasturelands, and a strong tradition in dairy production and processing.

Historically, the Gir dairy cattle genetic selection was primarily focused on milk yield, driven by economic incentives tied directly to the volume of milk delivered. As a result, selection programs and breeding decisions emphasized animals with superior lactation performance (Prata et al., 2015). However, over the last decades, there has been growing recognition of the importance of milk quality and composition traits, particularly the solids, such as fat, lactose, and protein content (Botaro, Gameiro & Santos, 2013; Paixão et al., 2017), which are essential for cheese production, a hallmark of the Minas Gerais dairy industry. In addition, hygienic quality and health indicators are also evaluated, such as somatic cell count (SCC) expressed on a logarithmic scale (logSCC), which impacts cheese yield, the lipolysis level in yogurt, the casein hydrolysis through proteases, and even the proteolysis level in pasteurized milk, and reflects udder health (Prata et al., 2015; Carmo et al., 2023).

As necessary to produce higher-quality milk, understanding the genetic and phenotypic relationships between composition, milk quality, and health becomes increasingly critical. These traits are interrelated, while higher fat production also increases protein concentrations, favorable correlations can exist depending on the population and selection context (Riggio et al., 2009). Moreover, improvements in udder health, as indicated by lower logSCC, may have neutral or favorable correlations with milk composition traits. A comprehensive understanding of these relationships is essential to designing balanced breeding goals that optimize milk quality.

Our objective was to perform a multi-trait analysis to simultaneously estimate heritability, repeatability, genetic correlations, and breeding values for fat percentage, protein percentage, and the logarithm of somatic cell count.

2.3. Material and Methods

Animal care and use committee approvals were unnecessary as the data were obtained from preexisting databases.

2.3.1. Dataset

Test-day milk records from 531 Gir dairy cows, with an average of 33 ± 12 cows per test-day, collected between March 2012 and November 2022 as part of routine milk recording, were provided by Fazenda Cachoeira (Ferros, MG, Brazil) and Fazenda Palmeiras (Paraopeba, MG, Brazil). A total of 6,045 records for each trait were evaluated. The cows had between one and five lactations, with an average of two lactations per cow. Within each lactation, an average of 6 ± 2 test-day records was available. Pedigree information was provided by both farms and included cows with phenotypic records and their ancestors, with a total of 3,901 animals.

Phenotypes analyzed from the records were fat percentage, protein percentage, and somatic cell count. Because somatic cell count (SCC) exhibits a highly skewed distribution, a logarithmic transformation was applied for statistical purposes. Therefore, we considered the log-transformed somatic cell count (logSCC) in this study.

2.3.2. Statistics Analyses

A three-trait animal model was used for variance components estimation, heritabilities, repeatabilities, and genetic correlation estimations for fat percentage, protein percentage, and the logarithmic somatic cell count. The model was as follows:

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z_1}\mathbf{u_a} + \mathbf{Z_2}\mathbf{p_e} + \mathbf{e}$$

where $\mathbf{y}$ is the vector of phenotypes (fat percentage, protein percentage, and logSCC), $\boldsymbol{\beta}$ is the vector of fixed effects of farm (2), contemporary group (653), parity (1 to 5), and lactation day (5 to 305) as covariable (linear, quadratic, and cubic), $\mathbf{u_a}$, and $\mathbf{p_e}$ are vectors for the random effects of additive genetic and permanent environment effects, respectively. $\mathbf{X}$, $\mathbf{Z_1}$, and $\mathbf{Z_2}$ are the incidence matrices for $\boldsymbol{\beta}$, $\mathbf{u_a}$, and $\mathbf{p_e}$effects, respectively, and $\mathbf{e}$ is the vector of random residuals. Random effects were assumed to follow $\mathbf{u_a} \sim \mathrm{N}(\mathbf{0}, \mathbf{A} \otimes \boldsymbol{\Sigma}_{\boldsymbol{u}})$, $\mathbf{p_e} \sim \mathrm{N}(\mathbf{0}, \mathbf{I} \otimes \boldsymbol{\Sigma}_{\boldsymbol{p_e}})$, and $\mathbf{e} \sim \mathrm{N}(\mathbf{0}, \mathbf{I} \otimes \boldsymbol{\Sigma}_{\boldsymbol{e}})$, where $\mathbf{A}$ is the pedigree relationship matrix, $\mathbf{I}$ is an identity matrix of proper order, and $\boldsymbol{\Sigma}_{\boldsymbol{u}}$, $\boldsymbol{\Sigma}_{\boldsymbol{p_e}}$ and $\boldsymbol{\Sigma}_{\boldsymbol{e}}$ are the covariance structure matrix to additive genetic, permanent environment and residuals. Because the analysis for the three traits came from the same sample, all covariances between the three random effects were considered.

2.3.2.1. Genetic Parameters

Heritability for each trait was estimated as the ratio of additive genetic variance to the total phenotypic variance ($h_i^2 = \sigma^2_{u\,i}/\sigma^2_{p_i}$). Genetic correlations between traits were calculated by dividing the corresponding covariances by the product of the standard deviations of the involved components, where the genetic correlation between traits i and j was calculated as ($\rho_{u_{ij}} = \sigma_{u_{ij}}/(\sqrt{\sigma^2_{u_i} \times \sigma^2_{u_j}})$). Repeatability was estimated as the ratio of the sum of additive genetic and permanent environmental variances to the total phenotypic variance ($Rep_i = (\sigma^2_{u_i} + \sigma^2_{pe_i})/\sigma^2_{p_i}$), reflecting the consistency of an individual's performance over time or repeated measurements.

2.3.2.2. Breeding Value Estimation and Reliability

Estimated breeding values (EBV) for each animal were obtained from the solutions of the mixed model equations based on the three-trait animal model, as described above. The EBV reflects the additive genetic merit of each individual and is used for selection purposes. The EBV reliability (rel) for each animal i was calculated as a function of the inbreeding (F), prediction error variance (PEV), and the trait j additive genetic variance ($rel_{ij} = 1 - {PEV_{ij}}\big/{(1 - F_i)\sigma^2_{u_j}}$). Higher reliability values indicate more reliable EBV and depend on the amount of information available for each individual, including their own performance, relatives' records, and trait heritability.

All analyses for variance components, genetic parameters, and breeding value estimations were performed using BLUPF90+ (Misztal et al., 2014; Lourenco et al., 2022). For reliability, we used ACCF90 (Misztal et al., 2014).

2.4. Results and Discussion

Distribution and descriptive statistics for the fat percentage, protein percentage, and logarithmic somatic cell count (logSCC) are presented in **Figure 1**. The averages were 4.6% for fat, 3.5% for protein, and 6.8 for logSCC.

Fat percentage showed the highest range among the traits, with a standard deviation of 1.4% and values ranging from 0.5% to 8.8%. In contrast, protein percentage was the trait with the least variation, with a narrow range (2.5% to 4.4%) and a lower standard deviation (0.32%), indicating little variation among animals.

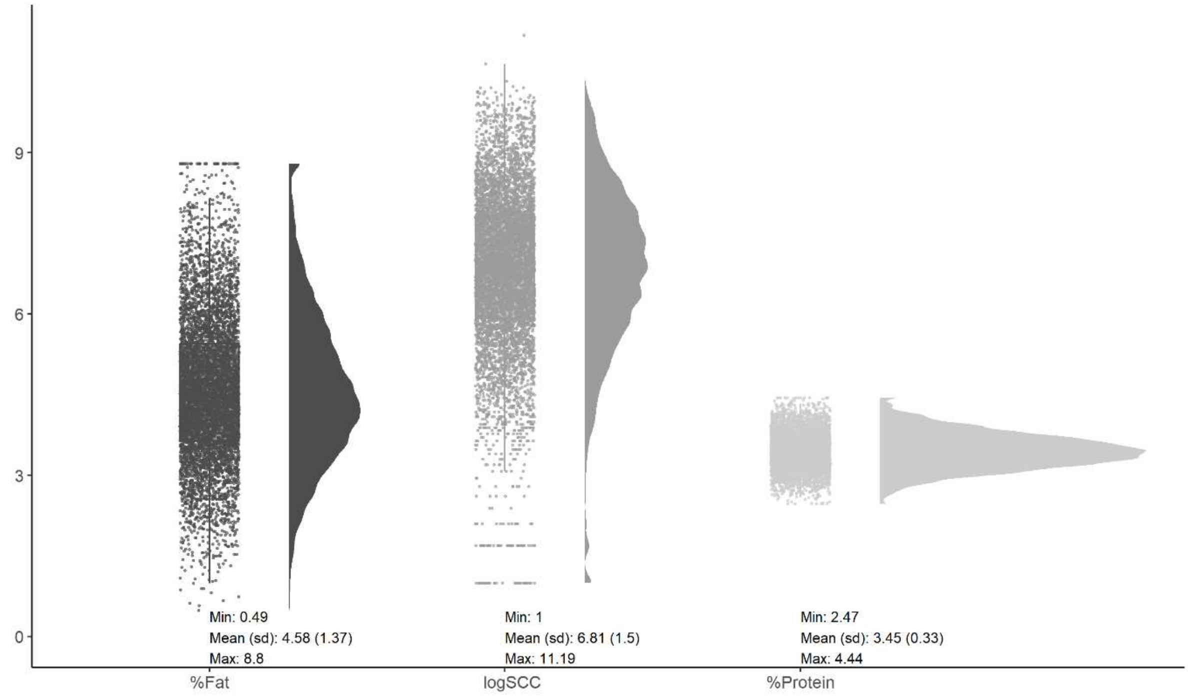

Figure 1. Phenotypic distribution for fat percentage, protein percentage, and the logarithm of somatic cell count (logSCC).

The logSCC had a wide range of values (1.8 to 11.2) and a relatively high standard deviation (1.5), reflecting substantial variation in udder health among samples. Overall, the differences in variability among traits are consistent with the literature. Petrini et al. (2016), working with Holstein cows under tropical conditions, also reported higher variability for fat percentage (SD = 0.75%) compared to protein percentage (SD = 0.30%), and a wide range for the somatic cell score (from –2.64 to 10.11). Chernet et al. (2024), studying multi-breed dairy cows in Ethiopia, observed even greater variability in fat percentage content (2.68 ± 1.71), similar values for protein percentage (3.17 ± 0.24), and similarly high log-transformed somatic cell score values (12.39 ± 1.61), reflecting the impact of mastitis and management differences under tropical and low-resource production systems. Overall, the observed differences in trait variability likely reflect both genetic and environmental influences, and reinforce the importance of separating these effects through proper modeling in genetic evaluations.

2.4.1. Genetic Parameters

Heritabilities, genetic correlations, phenotypic variances, and repeatabilities for the three milk quality traits are shown in **Table 1**. All parameters were estimated using a three-trait animal model.

Heritability estimates ranged from low to moderate. The heritability for fat percentage was 0.15 ± 0.03, indicating a low but existent genetic influence on the trait variation. Protein percentage showed the highest heritability (0.34 ± 0.05), suggesting greater potential for genetic improvement through selection. The heritability for logSCC was the lowest (0.10 ± 0.04), reflecting a stronger influence of environmental factors on udder health. These values are consistent with those found by Panetto et al. (2024) in the most recent Brazilian sire summary for Gir cattle in Brazil, which presented heritabilities of 0.14 for fat percentage and 0.44 for protein percentage.

Petrini et al. (2016) evaluating Holstein cows in a tropical environment, reported heritability estimates equal to 0.19, 0.35, and 0.12 for fat percentage, protein percentage, and somatic cell score, respectively. The slightly higher heritability for protein content observed in both studies suggests this trait has stronger genetic control compared to fat or udder health traits, even under challenging environmental conditions.

Table 1. Direct heritabilities (diagonal), genetic correlations (off-diagonal), phenotypic variance (σ^2_{pheno}), and repeatability (Rep) for fat and protein percentage and log of somatic cell (logSCC) count in Gir cattle. All estimations were obtained using a three-trait model.

	% FAT	**% PROTEIN**	**LOGSCC**	σ^2_{pheno}	**REP**
% FAT	**0.15 ± 0.03**			0.84 ± 0.02	0.17 ± 0.02
% PROTEIN	0.69 ± 0.10	**0.34 ± 0.05**		0.71 ± 0.00	0.42 ± 0.02
LOGSCC	-0.45 ± 0.34	-0.16 ± 0.29	**0.10 ± 0.04**	1.50 ± 0.04	0.28 ± 0.02

Average ± standard deviation

Similarly, Liu et al. (2022), studying a Holstein population in Shanghai, reported heritability estimates obtained from a random regression model ranging from 0.07 to 0.22 for fat percentage and 0.07 to 0.35 for protein percentage, values close to those observed in our Gir cattle population. For somatic cell score, Liu et al. found heritability estimates between 0.04 and 0.14 depending on the stage of lactation, which also agrees with our estimate of 0.10. Despite differences in breed, environment, and methodology, the general pattern remains consistent. Protein percentage tends to have the highest genetic influence among milk traits, while somatic cell traits show low heritability across diverse dairy populations. These findings reinforce that, even in different management and genetic contexts, milk composition traits are generally more responsive to selection than udder health traits.

Genetic correlations between traits revealed interesting relationships. A strong positive genetic correlation (0.7) was observed between fat and protein percentages, indicating that if we genetically select for one of these traits, we consequently increase the other. On the other hand, logSCC showed weak and negative genetic correlations, with a large standard deviation, with fat (–0.45 ± 0.34) and a correlation not different from zero with protein percentage (–0.16 ± 0.29).

Although correlations involving logSCC were close to zero in our study, indicating a weak genetic association between milk composition and udder health in this population, our results were similar to Petrini et al. (2016). These authors found a genetic correlation of 0.6 for fat and protein percentage, and for logSCC, they found genetic correlations equal to 0.00 and –0.04 with fat and protein percentage, respectively. These negative and weak correlations suggest a favorable genetic association between protein percentage and udder health, as we desire a reduction in somatic cells and an increase in protein, although further data may be needed to confirm the strength of these relationships.

In a study using a sire model, Schutz et al. (1990) estimated genetic correlations between milk components and somatic cell score in Holstein using data from first, second, and third or more lactations. They found moderate positive genetic correlations between fat and protein percentages (0.66 to 0.78 across parities) and generally negative or neutral genetic correlations, with high standard deviation, between somatic cell traits and protein percentage (0.07 to 0.09) and fat percentage (-0.15 to 0.09). This aligns with our results, where fat-protein correlation was strong, and logSCC correlations with fat and protein were weak to moderate and negative.

Repeatability estimates were 0.17 for fat percentage, 0.42 for protein percentage, and 0.28 for logSCC. Among the traits, protein percentage showed the highest repeatability, indicating more consistent records across test-day records, likely due to stronger genetic control and lower environmental influence. In contrast, fat percentage had the lowest repeatability, reflecting its greater sensitivity to environmental factors such as management, season, and stage of lactation. Compared to Petrini et al. (2016) results, where repeatabilities were 0.26 for fat percentage, 0.46 for protein percentage, and 0.42 for somatic cell score, our estimates are slightly lower, especially for fat percentage and logSCC. These differences may be attributed to breed and management differences. Nonetheless, the general pattern observed in both studies supports the interpretation that protein content is a more stable trait over time, while temporary environmental conditions influence fat percentage and udder health traits more.

2.4.2. Breeding Value Estimation and Reliability

Descriptive statistics for estimated breeding values (EBV) and their reliabilities are presented in **Figure 2**. As expected, EBV averages for fat and protein percentages and logSCC were close to zero, because EBV are based on deviations of the base population. However, the range of EBV reveals important genetic variability among animals.

For fat percentage, the EBV ranged from –0.74 to 0.94, with a standard deviation of 0.17. Protein percentage EBV showed less variation (–0.39 to 0.34; SD = 0.08), in line with the smaller phenotypic variance observed for this trait. The logSCC trait had EBV ranging from –0.67 to 0.71, and a standard deviation equal to 0.16.

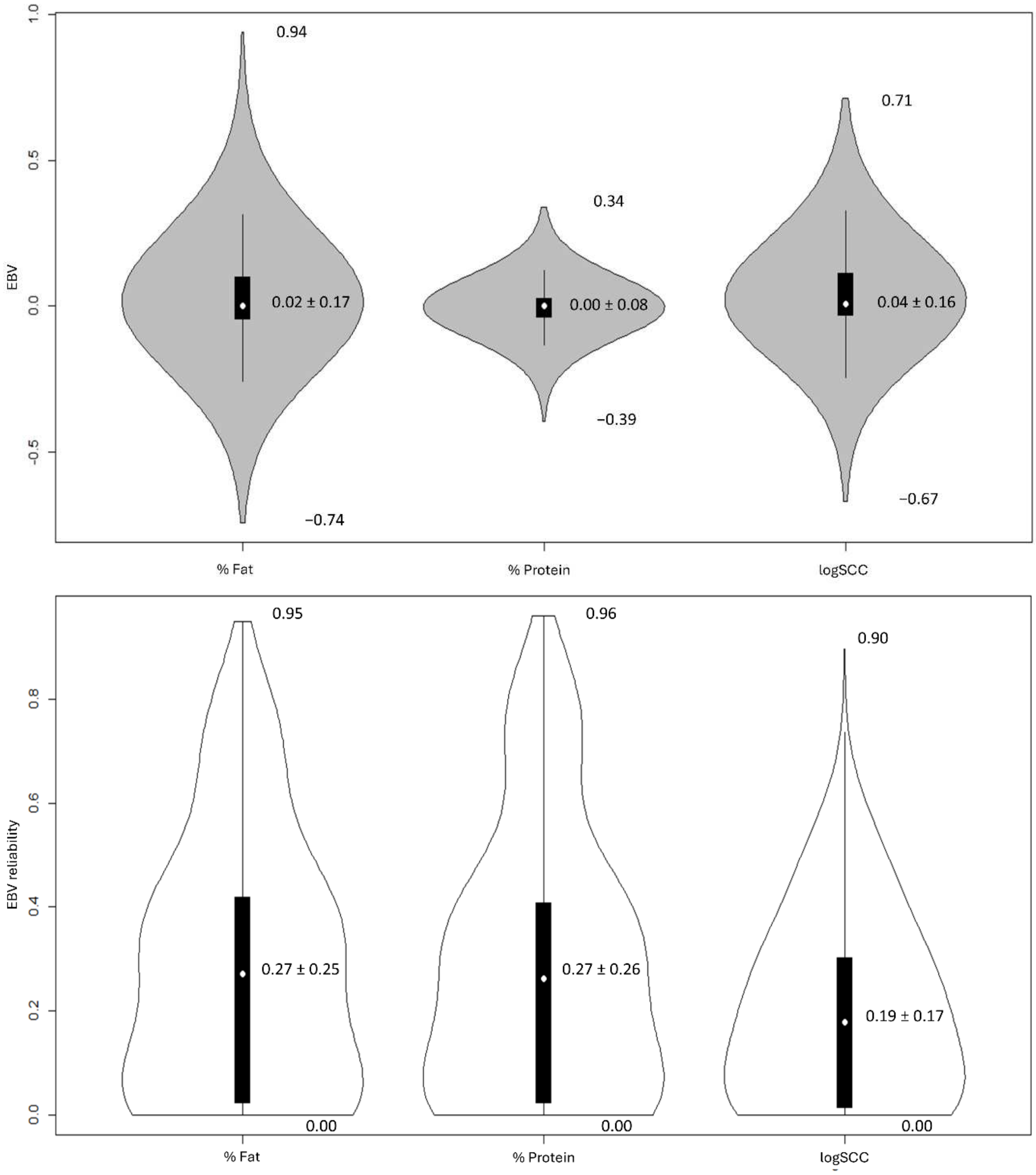

Figure 2. Violin plot with the distribution and descriptive values for estimated breeding value (EBV) (gray) and EBV reliability (white) for fat and protein percentage, and logarithmic somatic cell count (logSCC) in Gir cattle. The values presented are the maximum, average ± standard deviation, and minimum.

The reliability values (**Figure 2**) varied across animals and traits, reflecting differences in the amount of relatives' information available and the genetic architecture of each trait. The mean reliability was similar for fat (0.27) and protein percentage (0.27), with values ranging from 0 to 0.95 and 0 to 0.96, respectively. These distributions indicate that while some animals had highly reliable EBVs, likely due to more records or better-connected pedigrees, many others had low reliability, especially those with limited or no own performance or few relatives with records. For logSCC, the mean reliability was lower (0.19), and values ranged from 0 to 0.90. This result is consistent with the lower proportion of variance explained by genetic factors of this trait and its weak association with the others. High standard deviations for the genetic parameters and the distribution of reliability values for logSCC suggest that greater data depth is needed to achieve accurate genetic evaluations for this trait.

In general, the wide range of reliabilities observed for all traits highlights the importance of pedigree depth, number of records, and trait heritability in influencing the breeding value accuracies.

2.5. Conclusion

Despite the limited number of phenotypic records, it was possible to use a multi-trait model that simultaneously considers fat and protein percentages, as well as logarithmic somatic cell count (logSCC), three key traits related to milk quality. Heritability estimates reinforce the well-established understanding that production-related traits tend to have higher genetic influence, and therefore higher heritability, while health-related traits, such as logSCC, are more influenced by environmental factors, resulting in lower heritability. The genetic correlation between fat and protein percentages was positive and high (0.7), which is expected, as both traits contribute to total milk solids production. In this case, we suggest selecting for milk solids based on fat percentage. Although protein showed the highest heritability, fat had greater genetic and phenotypic variances, indicating a higher potential to identify and select the best animals using this trait. The genetic correlation between logSCC and fat percentage was weak and negative, while the correlation between logSCC and protein percentage was not significantly different from zero. Repeatability estimates ranged from low to moderate (0.17 to 0.42). These repeatability values indicate inconsistency in the performance of the same individual across different measurements, suggesting a substantial influence of temporary environmental factors on these traits, and in this case, repeated measurements are useful to improve reliability. All results presented will be used for animal selection decisions within the two farms evaluated.

2.6. Acknowledgments

This study was in partnership with the Federal University of Minas Gerais (UFMG), Fazenda Cachoeira (Ferros, MG, Brazil), and Fazenda Palmeiras (Paraopeba, MG, Brazil). The availability of data is highly appreciated. Support from Brazilian Federal Agency for Support and Evaluation of Graduate Education CAPES/PROEX 88887.844747/2023-00 (Brasilia, DF, BR) and the Minas Gerais State Agency for Research and Development – FAPEMIG (Belo Horizonte, MG, BR) is appreciated.

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CHAPTER 3

GENETIC BACKGROUND OF CALVING EASE IN BEEF-ON-DAIRY

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3.1. Abstract

A common practice in dairy herds is to breed females not selected as replacement heifers to beef bulls. This increases the market value of the surplus calves sold for beef purposes. Some beef breed associations have built selection indices focusing mainly on carcass traits; however, calving ease (CE) is also an important trait, given that crossbreeding with beef bulls can change gestation patterns (e.g. gestation length) or calf conformation (e.g. weight and size), generating a negative effect on the health, and consequently on the production, of the cows. We used linear and threshold animal models to estimate genetic parameters and breeding values for direct and maternal additive effects for calving ease in beef-on-dairy crosses, considering only the first or the first three lactations. We analyzed 231k CE records in the first lactation and 1.2M in the first three lactations from Holstein and Jersey cows inseminated with Angus, Charolais, or Simmental semen. Although CE was scored in five categories, we reduced this to a binary trait (1=easy and 2, 3, 4, 5=difficult). We compared single-trait linear and threshold models with age of the cow as a covariable, sex of the calf, dam-sire breed interaction, and year-season as fixed effects; and herd-year, animal, and maternal effects as random. The average incidence of difficult calving (scores ≥2) was approximately 15%. Direct and maternal heritabilities for the linear (threshold) model were 0.01 ± 0.002 (0.01 ± 0.001) and 0.02 ± 0.002 (0.04 ± 0.004), respectively, using the first lactation, and equal to 0.01 ± 0.003 (0.03 ± 0.004) and 0.19 ± 0.002 (0.25 ± 0.005), respectively, considering the first three lactations. Maternal heritabilities were always greater than the direct ones. Maternal heritabilities were inflated when we considered more than one lactation, probably because of a confounding with the maternal permanent environmental effect. Linear and threshold models provided similar direct EBV rankings, with a correlation of at least 0.87 when considering all different breeds; for maternal effect, it was high for dairy breeds (> 0.89) and close to zero in beef breeds. Validation metrics were better for the linear model with only first lactation records. Although the small direct heritabilities, the results showed that direct genetic variability exists, with direct genetic variance ranging from 0.002 to 0.214, and that it would be possible to select beef bulls based on their direct EBV for calving ease in beef-on-dairy systems. One of the challenges in beef-on-dairy analyses is the lack of pedigree depth on the sire side. When this is the case, we suggest using linear models considering only the first lactation to evaluate CE, given that EBV are highly correlated with those obtained by the threshold model but are less biased and converge almost 10 times faster, proving to be more efficient for routine genetic evaluations.

Keywords: Calving difficulty, crossbreed, linear and threshold models, variance components

3.2. Introduction

Beef-on-dairy is not a recent practice, but it has been intensified due to a combination of factors, such as exploring heterosis effect and complementarity, increasing the use of dairy-sire X-bearing sexed semen, so that more females not selected as replacement heifers are crossed with beef bulls, resilience to volatile milk prices through the sale of surplus calves and increasing availability of beef bulls with easy calving and short gestation (Berry, 2021). In the United States, beef-on-dairy herds represent 20.5% to 22.7% of beef production (DelCurto et al., 2017). Some studies have shown that dystocia rates increase in dairy cows mated to certain breeds of beef sires (Fouz et al., 2013; Eriksson et al., 2020). Thus, beef-on-dairy may not be profitable if such calves negatively affect the health and production of cows that carry beef-on-dairy calves.

The American Angus Association (St. Joseph, MO) has created an Angus-on-Dairy Index (Miller, 2021). This index is an economic weighting of estimated breeding values for important traits in beef-on-dairy crosses. It shows the expected performance of a future beef-on-dairy progeny of each Angus sire, on average, when compared with a progeny of other Angus sires, if the sires were randomly mated and the calves were exposed to the same environment. So far, indices have been developed for crosses of Angus with Holstein and Jersey cows considering traits of calving ease (CE), growth from birth through the feeding phase, feed intake, dressing percent, yield grade, quality grade, muscling, and height. All these traits have different weights in the indices for Holstein and Jersey, except for height, which is only considered for Holsteins, and CE, which has more weight in the Jersey index.

Calving ease is a categorical trait that indicates the ability of a cow to give birth without difficulty or the degree of assistance required during calving. Dairy cattle producers in the United States use the National Association of Animal Breeders (NAAB) CE scoring system, in which a CE score of 1 indicates no problem, 2 indicates slight problem, 3 indicates needed assistance, 4 indicates considerable force, and 5 indicates extreme difficulty (Berger, 1994). In contrast, beef cattle producers used to use the CE scoring according to Beef Improvement Federation guidelines, where a CE score of 1 indicates no assistance, 2 is some assistance, 3 is mechanical assistance, 4 is a caesarean section, and scores equal to 5 used to be excluded because it indicates abnormal presentation and is not inherited (BIF, 2022). Generally, these scores are combined to form a binary trait indicating either easy or difficult calving. The method of combining these scores depends on the incidence rate. The International Committee for Animal Recording (ICAR) recommends that if a single CE class has a very low incidence (less than 1%), it should be merged with an adjacent class (ICAR, 2022). In the United States, beef cattle genetic evaluations define difficulty as a calving score of ≥ 2 (Patterson, 2005), while dairy cattle genetic evaluations consider scores of ≥ 4 as indicating difficulty (CDCB, 2022).

Calving ease can be affected by two additive genetic components: the direct effect, which is the calf's contribution, and the maternal effect, which is the dam's contribution. In theory, threshold models are preferred over linear models for genetic analysis of categorical traits with a discrete probability distribution (Gianola, 1982). However, it is possible to use linear models and obtain similar results in animal ranking in a faster and more computationally efficient way (Hidalgo et al., 2024). This explains why most of the routine genetic evaluations of categorical calving traits are based on linear models (Interbull, 2013), although such data violates the normality assumption. One notable exception to this trend is the US national genetic evaluation for calving ease, which uses a sire-maternal grandsire threshold model (Van Tassell et al., 2003). We aimed to estimate variance components and direct and maternal heritabilities for calving ease in beef-on-dairy crosses, comparing linear and threshold models. We used phenotypes collected in the first and first three lactations. In addition, we tested two ways of combining the calving ease categories to create a binary trait. The models were compared considering the computational time and the animal ranking correlation based on breeding values.

3.3. Material and methods

Animal care and use committee approvals were unnecessary as data were obtained from preexisting databases.

3.3.1. Dataset

Data from URUS Group LP (Madison, WI) were used in this study. The pedigree included 1.2M Holstein, Jersey, Angus, Charolais, and Simmental animals, born from 1951 to 2021, and 1.3M crossbreds born from 2014 to 2023. The pedigree only had three generations. All phenotyped animals had to have information about the sire and dam breeds to be considered beef-on-dairy. All dams of generation II had information about their sires (29,773 bulls) and unknown dams, but only 401 sires from generation II had pedigree information. A pedigree chart with the number of animals in each generation and breed is shown in **Figure 1**. The phenotypes were assigned to calves. There were about 230k CE records in the first lactation and almost 1.3M total in the first three lactations from Holstein and Jersey cows inseminated with Angus, Charolais, or Simmental semen. Considering only singleton calves, in the first lactation we had 142,175 male and 86,991 female calves; considering the first three lactations, we had 827,263 males and 440,658 females. In the first lactation, the heifers had an average of 24 ± 1.8 months of age; for the first three lactations, the females had an average of 39 ± 9.4 months. The incidence of unassisted calving in the first three lactations was equal to 87.4%, 88.6%, and 87.5%, respectively, and the incidence of all five categories in the first three lactations is presented in **Table 1**.

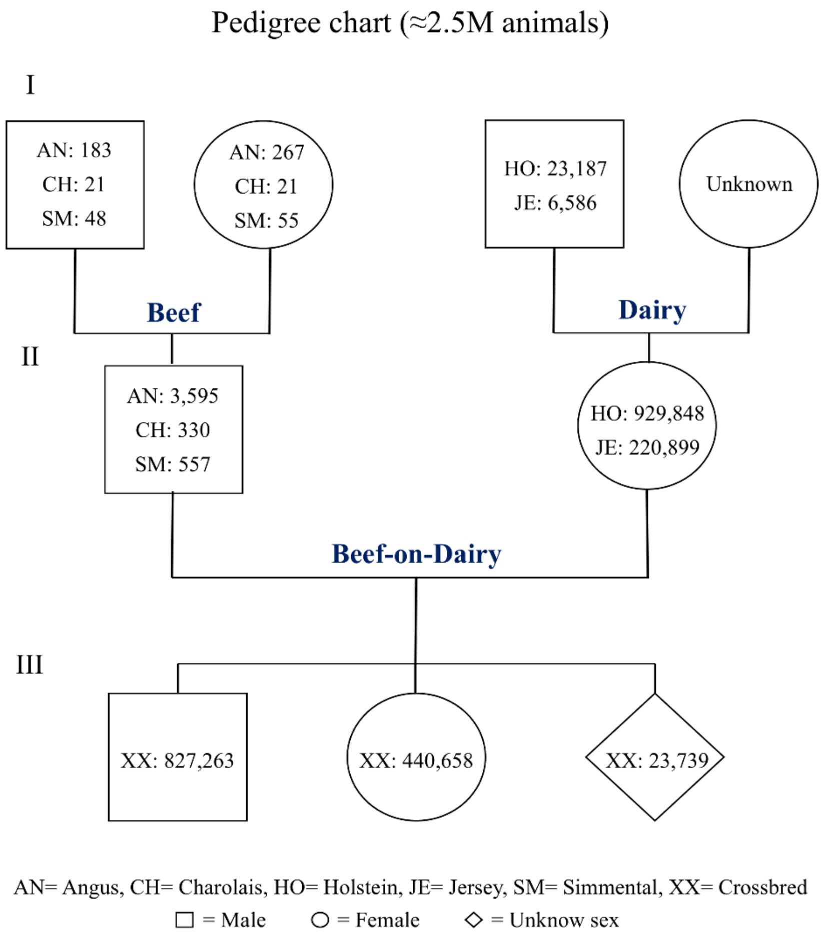

Figure 1. Pedigree chart with the number of animals in each generation and breed.

To determine the CE categories (easy or difficult) in our work, we considered the score combinations most commonly used for pure breeds of beef and dairy cattle. For beef cattle, we classified score 1 as easy and combined scores 2, 3, 4, and 5 as difficult. For dairy cattle, we followed the coding used by the Council on Dairy Cattle Breeding (CDCB, 2022), where scores 1, 2, and 3 are considered easy calving, and scores 4 and 5 are considered difficult calving, but this did not reach convergence and therefore does not appear in the results.

Table 1. Number of observations and (**incidence**) of calving ease scores in the first three lactations.

Lac[1]	**Calving ease scores**[2]					**Total**
	1	**2**	**3**	**4**	**5**	
1	202528 (**87%**)	15839 (**7%**)	10518 (**5%**)	1719 (**.5%**)	1238 (**.5%**)	231842
2	467972 (**88%**)	34819 (**7%**)	19807 (**4%**)	3046 (**.5%**)	2591 (**.5%**)	528235
3	465347 (**88%**)	38964 (**7%**)	21182 (**4%**)	3399 (**.5%**)	2691 (**.5%**)	531583
Total	1135847	89622	51507	8164	6520	1291660

[1] Lac is the lactation number.

[2] Calving ease score equal to 1 indicates no problem, 2 indicates slight problem, 3 indicates needed assistance, 4 indicates considerable force, and 5 indicates extreme difficulty.

3.3.2. Variance Components and Breeding Value Estimation

Variance components were estimated using single-trait, linear or threshold models, based on pedigree:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Z_1h} + \mathbf{Z_2a} + \mathbf{Z_3m} + \mathbf{e}$$

in which $\mathbf{y}$ is a vector with calving ease scores; $\mathbf{b}$ is a vector of fixed effects of sex, dam-sire breed interaction, year-season, and age of the cow (covariable); $\mathbf{h}$, $\mathbf{a}$, $\mathbf{m}$, and $\mathbf{e}$ are vectors for herd-year interaction, direct genetic, maternal genetic, and residual as random effects; $\mathbf{X}$, $\mathbf{Z_1}$, $\mathbf{Z_2}$, and $\mathbf{Z_3}$ are the respective incidence matrices.

In the model considering the first three lactations, the effect of lactation order was not included because preliminary analyses, using a tri-trait analysis (each lactation as a different trait), showed high genetic correlations between lactations (> 0.97). Additionally, including lactation order as a fixed effect did not result in different variance component estimates. Based on these results, the simpler model was preferred.

The assumed covariance structures were:

$$\mathbf{h} \sim \mathrm{N}(\mathbf{0}, \mathbf{I}\sigma_h^2)$$

$$\begin{bmatrix} \mathbf{a} \\ \mathbf{m} \end{bmatrix} \sim \mathrm{N}\left(\mathbf{0}, \begin{matrix} \mathbf{A}\sigma_a^2 & \mathbf{A}\sigma_{a,m} \\ \mathbf{A}\sigma_{m,a} & \mathbf{A}\sigma_m^2 \end{matrix}\right)$$

$$\mathbf{e} \sim \mathrm{N}(\mathbf{0}, \mathbf{I}\sigma_e^2)$$

where $\mathbf{A}$ is the pedigree relationship matrix, $\mathbf{I}$ is an identity matrix of proper order, σ_h^2, σ_a^2, σ_m^2, $\sigma_{a,m}$, and σ_e^2 are the variances for the herd-year interaction, direct genetic, maternal genetic, covariance between direct and maternal, and residual. After initial investigation, we assumed the covariances between direct and maternal genetic effects equal to zero ($\mathbf{A}\sigma_{a,m} = \mathbf{A}\sigma_{m,a} = \mathbf{0}$).

In the threshold model, it was assumed that CE is the expression of an underlying continuous random variable, the liability (l_{ce_i}) of individual i. If l_{ce_i} exceeds an unknown fixed threshold (t), then $y_{ce_i} = 2$ (difficult calving), and $y_{ce_i} = 1$ (easy calving) otherwise. We assumed that liability was normally distributed with mean vector $\boldsymbol{\theta}$ and unit variance:

$$\mathbf{l}_{\mathrm{ce}} \sim \mathrm{N}(\mathbf{s}\boldsymbol{\theta}, \mathbf{1})$$

where $\boldsymbol{\theta}' = (\mathbf{b}', \mathbf{h}', \mathbf{a}', \mathbf{m}')$ is a vector of fixed and random effects, and $\mathbf{s}$ is an incidence vector linking $\boldsymbol{\theta}$ to the phenotypic records.

The conditional response of CE, given the liability and the threshold, was modeled with the following distribution:

$$p(\mathbf{y}|\mathbf{l}_{\mathrm{ce}}, \boldsymbol{\theta}, t) = \prod_{i=1}^{n} \begin{matrix}[I(l_{ce_i} \leq t)I(y_{ce_i} = 1) \\ + I(l_{ce_i} > t)I(y_{ce_i} = 2)]\end{matrix}$$

where I is an indicator function that takes the value of 1 if the specified condition is true, otherwise, it takes the value of 2.

Variance components were estimated on the observed and liability scales using linear and threshold models respectively, under a Bayesian approach using the Gibbs sampling methodology implemented in the GIBBSF90+ v3.23 software (Misztal et al., 2014; Lourenco et al., 2022). First, a Gibbs chain of 100k samples was generated. Then, after discarding the initial 20k samples, one in every 10 samples was stored to compute the means and standard deviations of the posterior distributions. Estimated breeding values (EBV) were obtained via the best linear unbiased predictor (BLUP) under the linear and threshold models described above. Computations were done using the BLUP90IOD3 v3.139 and CBLUP90IOD2 v3.39 software (Misztal et al., 2014) for linear and threshold models, respectively. Both programs implement the preconditioned conjugate gradient algorithm with iteration on data (Tsuruta et al., 2001) for optimal computing performance.

3.3.3. Model Comparison

For model comparison, we used the LR method. This method, derived from linear regression, compares genetic evaluations using partial and whole data based on differences in means, covariance, and correlation (Legarra and Reverter, 2018). Data after 2022 was used as a validation set, allowing us to estimate dispersion, bias, and correlation for estimated breeding values. Additionally, we assessed the accuracy of the partial data set using the equation provided by Legarra and Reverter (2018). For the first lactation, the complete and partial data sets had 231,842 and 220,520 phenotypes, respectively. Considering the first three lactations, the complete and partial data sets had 1,291,660 and 1,223,583 phenotypes, respectively.

Spearman rank correlation, considering only purebred animals and bulls with reliabilities greater than or equal to 0.5, was used to investigate the concordance between EBV from linear and threshold models. Computing time and the number of iterations to reach convergence were also evaluated as model feasibility indicators.

3.4. Results and discussion

Table 2 presents the calving ease incidence for all crosses in the first and first three lactations and the number of records in each case. It is possible to see that there is a preference in the choice of animals to be crossed. Regarding breeds, there are about four times more Holstein than Jersey cows, and there is a preference for Angus and Simmental bulls. Crossbreeding with Charolais represents only 4% and 7% of the records for the first and first three lactations, respectively. This preference seems to come from the fact that both breeds, dairy and beef, are known for their success in reducing calving ease and birth weight, a factor that impacts calving ease (Miller, 2021; Saad et al., 2020). Another factor that seems to be preferred, based on the number of records, is the parity of the cows. The number of records in the second and third parity is twice as high as the number of records in the first parity. Depending on the dam-sire breed combination, CE scores equal to 1, indicating "easy" births free from dystocia, were more frequent in the first three lactations than in the first lactation alone (Table 2).

Table 2. Incidence of calving ease score and number of observations (N_{CE}) per crossing considering the first and (first three) lactations.

Breeds[1]		**Calving ease incidence (%)**					N_{CE}[2]
Dam	**Sire**	**1**	**2**	**3**	**4**	**5**	Lac_1 (Lac_3)
	AN	88 (88)	6 (7)	5 (4)	.5 (.5)	.5 (.5)	161572 (824589)
HO	CH	73 (88)	10 (5)	12 (5)	3 (1)	2 (1)	3421 (32949)
	SM	88 (87)	7 (8)	4 (4)	1 (1)	0 (0)	24479 (188336)
	AN	91 (92)	5 (4)	3 (3)	1 (.5)	0 (.5)	20394 (85144)
JE	CH	90 (94)	5 (3)	3 (1)	1 (1)	1 (1)	6665 (55113)
	SM	78 (84)	16 (12)	5 (3)	.5 (.5)	.5 (.5)	15311 (105529)

[1] The abbreviations for the breeds are: HO = Holstein, AN = Angus, CH = Charolais, SM = Simmental, JE = Jersey.

[2] Lac_1 = first lactation, and Lac_3 = first three lactations.

In this study, approximately 88% and 7% of the scores were equal to one (no problem) and two (slight problem), respectively, independently of lactation order (**Table 1**), showing that calving difficulty is not frequent in these beef-on-dairy data. The high rate of easy calvings indicates low variability of the trait, which could result in low genetic variability and genetic parameters of small magnitude. On the other hand, the low incidences of difficult calving are probably because beef breed associations focus on obtaining lighter calves at birth (Bourdon and Brinks, 1982; Togashi et al., 2024). Smaller, lighter calves are less likely to have birth issues. Basiel et al. (2024) investigated the impact of several beef bull breeds on dystocia when they were used to inseminate cows in US dairy herds. The authors initially considered dystocia as CE scores ≥ 4 and found an incidence of less than 1%. Due to the low incidence, the authors decided to consider dystocia scores ≥ 3, which increased the incidence to 3%. Although the change in coding increased the average probability of dystocia incidence by calf sire breed, the authors did not find statistically significant differences among breeds in both scenarios.

As in Basiel et al. (2024), our initial idea was to use different thresholds to define easy or difficult calving, as described in material and methods. However, due to the low incidence of difficult calvings when using the coding proposed by CDCB (2022), we could not achieve model convergence. Therefore, we considered only the first coding (easy = score equal to 1, difficult = scores from 2 to 5) to estimate the variance components and breeding values.

3.4.1. Estimation of Variance Components and Genetic Parameters

Variance components and genetic parameters were different from zero, except for the covariance between direct and maternal effects, which was disregarded. Variance components estimated by threshold models are usually greater than those estimated by linear models, despite the proportion of genetic variance being close (Vanderick et al., 2014). Direct and maternal heritabilities from the linear (threshold) model were respectively equal to 0.014 ± 0.002 (0.002 ± 0.001) and 0.016 ± 0.002 (0.040 ± 0.004) for the first lactation, and equal to 0.014 ± 0.003 (0.030 ± 0.004) and 0.186 ± 0.002 (0.251 ± 0.005) considering the first three lactations. The variance components and genetic parameters for the first and first three lactations can be seen in **Table 3**.

Table 3. Posterior mean ± posterior standard deviation of variance components and genetic parameters for calving ease in beef-on-dairy using linear (LIN) and threshold (THR) models considering only the first ($_1$) and first three ($_3$) lactations.

PARAMETERS[1]	**LIN$_1$**	**THR$_1$**	**LIN$_3$**	**THR$_3$**

$\boldsymbol{\sigma_h^2}$	0.061 ± 0.002	1.683 ± 0.063	0.066 ± 0.001	4.134 ± 0.121
$\boldsymbol{\sigma_a^2}$	0.002 ± 0.000	0.005 ± 0.004	0.002 ± 0.000	0.214 ± 0.030
$\boldsymbol{\sigma_m^2}$	0.002 ± 0.000	0.113 ± 0.011	0.024 ± 0.000	1.788 ± 0.051
$\boldsymbol{\sigma_e^2}$	0.062 ± 0.000	1.00 ± 0.004	0.038 ± 0.001	0.999 ± 0.002
$\boldsymbol{h_a^2}$	0.014 ± 0.002	0.002 ± 0.001	0.014 ± 0.003	0.030 ± 0.004
$\boldsymbol{h_m^2}$	0.016 ± 0.002	0.040 ± 0.004	0.186 ± 0.002	0.251 ± 0.005

[1] Where: σ^2 are the variance components for herd-year (h), direct genetic (a), maternal genetic (m), and residual (e) effects; h^2 are the heritabilities for direct (a) and maternal (m) effects.

Herd-year interaction presented the highest variances in all models. This effect represents differences in phenotypes due to births occurring in different herds and years, so the high variances may be partly due to differences in subjective scoring of calving ease within each herd. Vanderick et al. (2014) found the same behavior using linear and threshold models for CE in Holsteins. In their work, the authors highlight the importance of considering herd-year as random to avoid statistical and convergence problems. We can have such problems when considering the contemporary group as a fixed effect in threshold models because they contain groups of small size or without variation in scores, i.e., with an extreme category problem (Misztal et al., 1989; Lourenco et al., 2022).

The heritabilities of calving performance traits are generally low (ICAR, 2022). In our study, the direct genetic heritability was low and identical in all scenarios ($\mathrm{h}_{\mathrm{a}}^2 = 0.01$), except for the threshold model using three lactations, when it was equal to 0.03. In general, higher heritabilities are usually expected with threshold models than linear models (Vanderick et al., 2014; Weller and Gianola, 1989). McGuirk et al. (1998) estimated genetic parameters for calving traits in beef × dairy crosses in the United Kingdom, considering three categories of CE in observed and liability scale using a sire model. These authors found a sire heritability equal to 0.09 and 0.16 for observed and liability scale, respectively. Although we have results with small direct heritabilities and the same behavior regarding linear and threshold models, in which the threshold model obtained greater heritability, the results are not comparable, as the models and the categories for CE used were different. Due to the lack of studies evaluating genetic parameters in beef-on-dairy, we compared our results with previous studies that used purebred beef or dairy cattle breeds. Direct CE heritabilities previously published ranged between 0.02 and 0.29, in which dairy breeds usually present lower values than beef breeds (Ahlberg et al., 2016; ICAR, 2022). In Holsteins, heritabilities ranged from 0.03 to 0.12 (Weller and Gianola, 1989; Wiggans et al., 2003; López de Maturana, 2007; Eaglen et al., 2012). Jeyaruban et al. (2016) estimated genetic parameters for calving difficulty in five beef breeds in Australia and found direct heritabilities equal to 0.24, 0.22, and 0.17 for Angus, Charolais, and Simmental breeds, respectively. Eaglen et al. (2012) compared primiparous and multiparous Holstein cows and found that the percentage of easy calving increased by eleven percentage points for multiparous cows and that direct and maternal heritabilities reduced by at least half in analyses using data from multiparous cows. In our case, the incidences did not differ when we considered the first three lactations, so there were no drastic changes in direct heritability values.

Maternal heritabilities were greater than direct in all models. When considering only the first lactation, the slight difference observed comes from potential confounding between direct and maternal genetic effects. They were much larger when we considered the first three lactations than when we used only the first lactation. This may have been partly due to the lack of maternal permanent environmental effect in the model, as cows did not have enough data to ensure convergence for this effect. Therefore, the maternal permanent environmental effect seems to have been captured by the maternal effect, as Vanderick et al. (2014) found in their preliminary analyses of CE in Holstein. Maternal heritabilities were within the range found in the literature, which was between 0.02 and 0.20 (Wiggans et al., 2003; Eaglen et al., 2012; Jeyaruban et al., 2016; ICAR, 2022; American Angus Association, 2024). Maternal heritabilities from models considering three lactations were more like those found in beef breeds, such as Charolais and Angus, than those found in dairy breeds (Jeyaruban et al., 2016; American Angus Association, 2024). These estimates are not directly comparable because the authors consider purebreds and use different models, such as sire and maternal grand-sire, and multiple-trait models, and different effects, e.g. some of them did not consider maternal or consider maternal permanent environment effect.

To investigate the maternal heritability inflation, we randomly omitted data from cows with more than one scored calving. Using the same model, with the first three lactations and only one record per dam, considering 1.1M CE records, we found that the maternal heritability was equal to 0.03 ± 0.003 for the linear model and 0.02 ± 0.002 for the threshold model. The direct heritabilities remained the same as when using data with cows with repeated data, equal to 0.01 ± 0.001 and 0.03 ± 0.002 for the linear and threshold models, respectively. These results suggest that when more than one lactation is considered, and there is not enough repeated data to include the maternal permanent environmental effect, more attention must be paid to the maternal component.

We also tested the same model by considering the two different dairy breeds, Holstein and Jersey, separately. Most of the variance components and genetic parameters were different from zero. However, when we used threshold models under Gibbs Sampling, the Gibbs chains showed very large fluctuation due to the limited and unbalanced number of phenotypes in each combination with beef breeds (Angus, Charolais, or Simmental). The number of observations in each breed combination is in **Table 2**. For the direct effect, we found heritabilities ranging from 0 to 0.08, and for the maternal effect, this ranged from 0.01 to 0.25 (**Appendix 1**).

The direct heritabilities in our study were low, which can indicate that the pedigree is shallow and unconnected. In the future, more information about relatives or the use of genomic information can help capture more genetic variation.

3.4.2. Model Comparison

Considering all animals in the pedigree, the EBV ranking correlations from the linear and threshold models for direct and maternal effects were 0.96 and 0.98, respectively, when we analyzed the first lactation and 0.90 and 0.92, respectively, when we analyzed the first three lactations. Since we are working with five different breeds, it is important to note that there may be differences in these correlations within some breeds. The Spearman ranking correlation values between the EBV from the linear and threshold models for direct and maternal effects within each breed are presented in **Table 4**. The number of purebred animals used in the correlation can be seen in **Figure 1**.

Table 4. Spearman rank correlations between EBVs from threshold and linear models for the first (LAC$_1$) and first three (LAC$_3$) lactations, considering only purebred animals.

	FEMALE				**MALE**			
	HOLSTEIN		JERSEY		HOLSTEIN		JERSEY	
	LAC$_1$	**LAC$_3$**	**LAC$_1$**	**LAC$_3$**	**LAC$_1$**	**LAC$_3$**	**LAC$_1$**	**LAC$_3$**
DIRECT	0.97	0.90	0.97	0.87	0.98	0.97	0.98	0.95
MATERNAL	0.98	0.91	0.98	0.89	0.98	0.98	0.98	0.96
NANIMALS	189,472	929,848	42,370	220,899	10,838	23,187	2,858	6,586

	MALE					
	ANGUS		CHAROLAIS		SIMMENTAL	
	LAC$_1$	**LAC$_3$**	**LAC$_1$**	**LAC$_3$**	**LAC$_1$**	**LAC$_3$**
DIRECT	0.95	0.98	0.94	0.97	0.93	0.96

MATERNAL	-0.02	0.11	0.07	0.01	-0.11	0.16
NANIMALS	1,921	3,595	132	330	257	557

For the dairy breeds, Holstein and Jersey, distinguishing between the cows (female) and the cows' sires (male), we can see that the correlations were high, where for direct EBV, this ranged from 0.87 to 0.98, and for maternal EBV, it ranged from 0.89 to 0.98. When we look at the bulls of the beef breeds, Angus, Charolais, and Simmental, for the direct effect the EBV ranking correlations were high and ranged from 0.93 to 0.98, but the EBV correlations for the maternal effect were very close to zero and even negative for Simmental and Angus considering the first lactation. These distinct correlations, when compared with the dairy breeds, probably occurred because we have almost no female animals in these breeds. Only about 400 bulls have information on at least one known parent, with only 343 known dams (for the number within each breed, see **Figure 1**). Due to the lack of dam information in the beef pedigree and the fact that we do not have phenotyped beef females, the estimation of the maternal genetic value for this effect proved to be inconsistent between the two evaluations. Fortunately, in a beef-on-dairy system scenario in the United States, the maternal EBV of beef bulls, which tells us about the ability of the daughter of that animal to have an easy calving, is useless since the calf resulting from the cross is the final product and will be harvested. For all breeds, the ranking correlations between direct EBV estimated in the two models, linear and threshold, were at least 0.87. These high correlation values between direct EBV suggest that selection decisions will not be substantially affected using linear instead of threshold models.

The intensity with which we use an animal for breeding is determined by the confidence we have in its EBV. This confidence is called reliability, which ranges from 0 to 1, and the closer to 1, the more likely it is that the EBV is close to the animal's true breeding value. Animals with high reliability are preferentially selected, and because of this, we also investigated the EBVs' rank correlation, estimated by the linear and threshold models, using only bulls with reliabilities greater than 0.5 in each breed (**Table 5**). As expected, with the filter applied to reliability, the number of animals decreases considerably, but the behavior does not change. The correlations for direct EBV remain close to 1 for all breeds, and for the beef breeds, the maternal correlations were very close to zero.

Table 5. Spearman rank correlations between EBVs from threshold and linear models for the first (LAC_1) and first three (LAC_3) lactations, considering only purebred bulls with reliabilities ≥ 0.5.

	DAIRY BULLS				BEEF BULLS					
	HOLSTEIN		JERSEY		ANGUS		CHAROLAIS		SIMMENTAL	
	LAC$_1$	**LAC$_3$**	**LAC$_1$**	**LAC$_3$**	**LAC1**	**LAC3**	**LAC1**	**LAC3**	**LAC1**	**LAC3**
DIRECT	0.97	0.96	0.97	0.94	0.89	0.96	0.97	0.95	0.86	0.94
MATERNAL	0.97	0.96	0.97	0.96	0.24	-0.07	0.09	-0.05	-0.08	-0.04
Nanimals	222	877	33	193	63	1043	4	103	20	141

Alongside the rank correlations, we used the LR validation metrics to compare models. Within the metrics, bias and b_0 equal to or close to zero, and b_1 equal to or close to one are ideal. Where b_0 and b_1 are the regression parameters of the mean of the EBV in the complete data on the mean of the EBV in the partial data. When b_1 values are lower than one, EBV from partial data are overdispersed, and values greater than one indicate that EBV from partial data are underdispersed. Correlation and accuracy values, where accuracy is the accuracy of the partial EBV as described in Legarra and Reverter (2018), as close to one as possible are desirable. Pearson's correlation between the EBV obtained from total and partial data shows the consistency between the estimations, while the partial data accuracy shows the accuracy of the EBV from partial data as a function of the EBVs from whole data (Legarra and Reverter, 2018). **Table 6** shows the LR parameters for linear and threshold models considering only the first and the first three lactations. The b_0 and bias values were considered ideal in all scenarios. Both values were close to zero, indicating that there was no bias. As previously mentioned, the slope (b_1) shows the breeding values dispersion. The linear model using only the first lactation presented the least dispersion, with a slope close to 1. Nevertheless, the threshold model, also considering only the first lactation, was shown to be largely underestimated, with a slope twice as large as expected. This indicates that the EBV of the partial data in this scenario were much smaller than the EBV obtained when using the complete data. This is reasonable since we have much less phenotypes when considering only the first lactation and the animals do not have a connected pedigree to be able to estimate these EBV. In addition, threshold models are generally more complex, since they have more variables to be estimated (thresholds) than linear models. The high correlation in this model supports that all EBVs in this scenario had the same behavior (underestimated). The models using the first three lactations were overdispersed but more stable.

Table 6. Parameters for linear (LIN) and threshold (THR) models considering the first ($_1$) and the first three ($_3$) lactations using the LR method.

PARAMETERS[1]	**LIN$_1$**	**THR$_1$**	**LIN$_3$**	**THR$_3$**
$\boldsymbol{b_0}$	-0.0001	0.0001	0.0002	-0.0003
$\boldsymbol{b_1}$	0.98	2.11	0.76	0.88
$\boldsymbol{bias}$	0.0001	0.0009	0.0005	-0.0035
$\boldsymbol{corr}$	0.89	0.95	0.88	0.90
$\boldsymbol{acc}$	0.31	0.14	0.36	0.24

[1] Where: b_0 and b_1 are the linear regression parameters, $bias = \overline{\widehat{\mathbf{u}}_{\mathrm{p}}} - \overline{\widehat{\mathbf{u}}_{\mathrm{w}}}$, $corr$ = Pearson's correlation, acc = accuracy.

Accuracies ranged from 0.14 to 0.36. Models using the first three lactations showed higher accuracies when compared to equivalent models using only the first lactation. Since they have more data over time and more data per animal, it is expected that excluding recent data will have less impact on the accuracy of breeding values than when having a small amount of data. The threshold model, considering only the first lactation, had the lowest accuracy, reinforcing the underestimation of EBV in the partial data of this model. In general, linear models perform better than threshold models and are less computationally expensive. Misztal et al. (1989) showed that threshold models require 3 to 5 times more computing time than linear models. The computational cost is a function of the number of iterations and the time per iteration. In addition to the number of iterations being greater when using the threshold model, the time per iteration when using the threshold model was at least 2.5 times greater than when using the linear model, reflecting the computational complexity of this non-linear statistical method. As expected, linear models and models that included only the first lactation were faster. It took at least 9-fold less time when we used linear instead of threshold models, and models with only the first lactation took at least half the time of models using the first three lactations. Considering only the first lactation, the linear model took 5 min and the threshold 45 min to converge (75 and 4,510 iterations, respectively). When we added the phenotypes from the other two lactations, the linear model took 10 min, and the threshold took 270 min to converge (289 and 5,011 interactions, respectively).

Working with genetic parameters in a beef-on-dairy scenario is challenging, and the biggest challenge is in the structure of the dataset and pedigree. The phenotype must always be attributed to the calf, as it is the only link between the two breeds. If the phenotype is attributed to the cow, the beef bulls would be left without breeding value predictions. Additionally, accurate separation of direct and maternal effects requires CE records for the dams at birth, a large number of progenies with CE phenotypes per dam, and deep pedigree information. In beef-on-dairy, however, phenotypes are typically available only for a single progeny generation, as crossbred animals are not retained for breeding, although some collateral information may be available. Furthermore, the primary selection objective is to improve the performance of purebred parents. When cows are selected for CE based on their progeny performance (i.e., when progeny phenotypes are included in the evaluation), genetic progress can occur in both direct and maternal effects.

Regarding the pedigree, as the sire and dam are of different breeds, the pedigrees are disconnected and collected with different focuses. For dairy cattle, greater attention is given only to the sires of the cows, and for beef cattle, the bulls' pedigree used in this scenario is often full of gaps. Some bulls have a large number of phenotyped progeny, which increases their EBV reliability, but since most bulls have no known ancestry, this large amount of information does not help the reliability of the others. Moreover, we know that the heritability for this trait is usually higher than that found here, especially for beef cattle. This leads us to believe that a better and more connected data structure, as well as a more complete and connected pedigree inside each breed, will help us find higher and more accurate heritabilities for this trait in the beef-on-dairy scenario. One point that we think would be valuable for this to happen would be the use of pedigree records from the Associations of the breeds involved.

3.5. Conclusion

We evaluated the computational aspects and the genetic background of calving ease in beef-on-dairy crosses. Overall, working with beef-on-dairy data is still challenging. The data structure and lack of pedigree depth and connection can make variance components estimation an ambitious task. Low incidences of extremely difficult calving (scores 4 and 5) make it hard to apply the definition of easy and difficult calving proposed for the dairy cattle industry. Adopting the definition used in beef cattle (1=easy; 2 to 5=difficult) is attainable. Although the direct heritabilities in our study were low, there is genetic variability for calving ease, and accounting for this trait when selecting beef bulls can help reduce the incidence of difficult calving in beef-on-dairy crosses. For that, we suggest using linear models considering only the first lactation, given that EBV are highly correlated with those obtained by the threshold model but are less biased and almost 10 times faster, proving to be more efficient for routine genetic evaluations. Analyses using more than one lactation or repeated data should be investigated for the influence of parity and the effect of the maternal permanent environment. Replicating this study with large, more connected beef and dairy datasets will help to validate our results.

3.6. Acknowledgments

This study was partially supported by PEAK (URUS Group LP, Madison, WI, USA); the availability of data and feedback is highly appreciated. Support from Brazilian Federal Agency for Support and Evaluation of Graduate Education CAPES/PROEX 88887.844747/2023-00 (Brasilia, DF, BR) and Minas Gerais State Agency for Research and Development – FAPEMIG (Belo Horizonte, MG, BR) are appreciated. Discussions with Renata Veroneze, Fernando Bussiman, and Jorge Hidalgo are valued. We gratefully acknowledge the valuable comments of the anonymous reviewers.

3.7. Appendix

Appendix 1. Posterior mean ± posterior standard deviation of variance components and genetic parameters for calving ease (CE) in beef-on-dairy and linear (LIN) and threshold (THR) models considering only the first (1) and first three (3) lactations for Holstein and Jersey breeds separately.

HOLSTEIN[1]	**LIN$_1$**	**THR$_1$**	**LIN$_3$**	**THR$_3$**
σ_h^2	0.03±0.001	1.29±0.063	0.03±0.000	1.57±0.412
σ_a^2	0.00±0.000	0.11±0.018	0.00±0.000	0.18±0.050
σ_m^2	0.00±0.000	0.07±0.026	0.01±0.000	0.46±0.520
σ_e^2	0.03±0.000	1.00±0.005	0.02±0.000	0.99±0.002
h_a^2	0.02±0.002	0.04±0.007	0.01±0.000	0.06±0.027
h_m^2	0.01±0.001	0.03±0.010	0.20±0.000	0.11±0.116
JERSEY*	**LIN$_1$**	**THR$_1$**	**LIN$_3$**	**THR$_3$**
σ_h^2	0.01±0.001	0.64±0.089	0.02±0.001	1.15±0.142
σ_a^2	0.00±0.000	0.16±0.043	0.00±0.000	0.19±0.029
σ_m^2	0.00±0.000	0.08±0.030	0.00±0.000	0.89±0.112
σ_e^2	0.04±0.000	1.00±0.001	0.02±0.000	1.00±0.004
h_a^2	0.03±0.004	0.08±0.020	0.00±0.001	0.05±0.007
h_m^2	0.02±0.005	0.04±0.014	0.18±0.006	0.25±0.020

[1] Where: σ^2 are the variance components for herd-year (h), direct genetic (a), maternal genetic (m), and residual effects; h^2 are the heritabilities for direct (a) and maternal (m) effects.

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CHAPTER 4

GENETIC ARCHITECTURE OF SWINE INFLAMMATION AND NECROSIS SYNDROME AND ITS GENETIC CORRELATION WITH REPEATED SKIN DAMAGE SCORES

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4.1. Abstract

Lesions and injuries to the extremities of the pig's body parts, like the tail and ears, are commonly associated with biting. Lesion signs identified at birth and in 3-d-old piglets suggest that injuries might be caused not only by biting but also by Swine Inflammation and Necrosis Syndrome (SINS), which can occur without any interaction between animals. We aimed to investigate whether 1. there is a direct and maternal genetic effect on swine inflammation and necrosis syndrome; 2. we can use a proxy for different body parts for SINS and skin damage; 3. there is a genetic correlation between SINS and skin damage recorded in multiple time points; 4. there are genetic variants and important genes associated with both traits. We analyzed about 7k female pigs born from February 2022 to June 2023 on three farms in the Netherlands. At birth, we scored SINS (no SINS=1, and SINS=2) on the ears, tail, and teats. Tail docking occurred after SINS phenotyping. We defined the Total_sins as the number of affected parts by SINS. The same animals were scored for skin damage (DMG on the ears, tail, and flank on average three times during the rearing phase (no DMG=4, slight DMG=5, severe DMG=6, and very severe DMG=7), resulting in around 20k DMG records. We defined Sum_dmg as the sum of scores for DMG in the three body parts. Single and two-trait animal models were used to estimate heritabilities and genetic correlations. Direct (maternal) heritabilities for SINS were equal to 0.03±0.02 (0.05±0.04) for the ear, 0.03±0.01 (0.01±0.00) for the tail, 0.07±0.03 (0.06±0.05) for teats, and 0.08±0.01 (0.04±0.05) for the Total_sins score. Direct heritability for DMG was equal to 0.08±0.01, 0.05±0.01, 0.04±0.01, and 0.09±0.01 for ear, tail, flank, and Sum_dmg, respectively. Total_sins and Sum_dmg were highly genetically correlated (0.76). The genetic correlations between Total_sins and DMG in the ear, tail, and flank were 0.78±0.00, 0.20±0.05, and 0.22±0.05, respectively. Overall, our study suggests that selection for reduced skin damage may be initiated earlier in life, based on SINS, and that piglets genetically less susceptible to SINS are more likely to experience improved welfare throughout the production system. At a genomic level, SINS was genetically associated with the genes *DLL1*, *PHF10*, *WDR27*, and *THBS2*, which are mainly related to embryonic and tissue formation, and warrant further investigation.

Keywords: Genetic parameters, GWAS, SINS, target genes

4.2. Introduction

Skin damage and biting behavior in pigs are significant economic and welfare concerns in modern swine production. In the European Union, strict animal welfare and food safety regulations, particularly under Regulations (EU) No 2019/627 and No 853/2004, mandate that animals exhibiting signs of systemic disease, extensive inflammation, or necrosis are deemed unfit for human consumption. Even localized lesions may result in partial condemnation if they compromise tissue integrity or present signs of infection. This implies that producers may face significant economic losses. Niemi et al. (2021) calculated economic losses in a simulation study ranging from approximately €2 to €12 per slaughtered pig when the tail biting lesion prevalence ranges from 10% to 50%. Therefore, minimizing skin damage through preventive strategies is critical for maintaining economic viability in swine systems. While skin damage is widely recognized as a welfare and economic concern, Swine Inflammation and Necrosis Syndrome (SINS) represents a novel challenge, requiring further research into its economic impact, pathophysiology, and potential genetic or environmental risk factors.

Swine Inflammation and Necrosis Syndrome is a condition recently described in piglets by Reiner et al. (2019). It manifests as inflammatory and necrotic lesions affecting multiple body parts, including the tail, ears, teats, coronary bands, heels, and claws. Studies have shown that the prevalence of SINS in piglets in at least one body part exceeds 50%, and that every evaluated herd was affected (Reiner et al., 2019; Kuehling et al., 2021; Leite et al., 2023a). In most cases, SINS is non-severe and can be observed throughout the animal's life, as long as there are signs of inflammation or necrosis without evidence of lesions resulting from trauma or infection (Ringseis et al., 2021). Given this premise, SINS is more easily characterized in the first week of life, when piglets have not yet been exposed to social interaction and environmental pathogens. Moreover, its identification can be non-invasive, as newborn piglets are already routinely handled for standard neonatal procedures such as airway clearance, umbilical cord care, colostrum administration, iron injection, and tail docking when applicable.

Although SINS and skin damage involve visible inflammation and lesions on the body surface of pigs, they differ in origin, timing, and management implications. Skin damage typically results from external factors due to social interaction, such as fighting or biting behavior, exposure to pathogens, secondary toxic metabolites such as mycotoxins, and injuries caused by trauma (Reiner et al., 2020; Ringseis et al., 2021; Leite et al., 2023a; Leite et al., 2023b). In contrast, SINS, especially when measured in the first week of life, is believed to originate from endogenous processes, potentially linked to hepatic inflammatory processes accompanied by lipid metabolic derangement, and with evidence of an associated genetic factor (Ringseis et al., 2021; Leite et al., 2023a).

Despite this, Leite et al. (2023a) found evidence of a genetic correlation between SINS and skin damage. They hypothesized that animals affected by SINS are more prone to accepting bites from other individuals since the inflammation causes itching in the affected region (Reiner et al., 2019; Leite et al., 2023a). The existence of a genetic correlation between SINS and skin damage would carry substantial implications for genetic selection and animal welfare in swine breeding programs. Such correlation would indicate that both traits may share common biological pathways, potentially involving immune regulation, systemic inflammatory responses, or stress susceptibility. This association could enable the utilization of SINS phenotypes, recorded early in life, as an indicator trait in genetic evaluation for skin damage. Consequently, understanding the genetic architecture and covariance structure between SINS and skin damage is essential for developing balanced breeding strategies that optimize profitability and increase animal welfare outcomes.

Recent studies have begun to unravel the genetic and physiological drivers underlying SINS in piglets, supporting the hypothesis that metabolic influence and a heritable component contribute to its expression (Reiner et al., 2020; Ringseis et al., 2021; Leite et al., 2023a). These findings reinforce that SINS is not merely environmental but may be influenced by systemic predispositions that are genetically mediated. Understanding the genetic basis of SINS is essential for developing genetic selection tools against the syndrome and for identifying biomarkers that may allow early detection or risk stratification in breeding populations. Given that, in this study we aimed to investigate whether 1. there is a direct and maternal genetic effect on Swine Inflammation and Necrosis Syndrome (SINS), 2. we can use a proxy for different body parts for SINS and skin damage, 3. there is a genetic correlation between SINS and skin damage, 4. there are genetic variants and important genes associated with both traits.

4.3. Material and methods

Animal care and use committee approvals were unnecessary as the data were obtained from preexisting databases.

4.3.1. Dataset

We analyzed phenotypes from 6,955 purebred and two-way crossbred female piglets born from February 2022 to June 2023 on three farms in the Netherlands. Piglets were born from 958 litters produced by 718 purebred sows (Landrace and Large-white) and 172 purebred boars (Hampshire, Large-white, and Landrace). SINS was scored as a binary trait defined as the presence (score 1) or absence (score 0) of inflamed, swelled, or necrotic outer skin tissue on three body parts at birth. An illustration of the scoring protocol is shown in **Figure 1**. Scores for SINS were collected on the ears (Ear_sins), tail (Tail_sins), and teats (Teats_sins). Despite SINS scores being recorded on individual body parts, they were also combined into a single score, defined as SINS total (Total_sins), where Total_sins is the number of affected parts plus one. The tail was docked after SINS phenotyping.

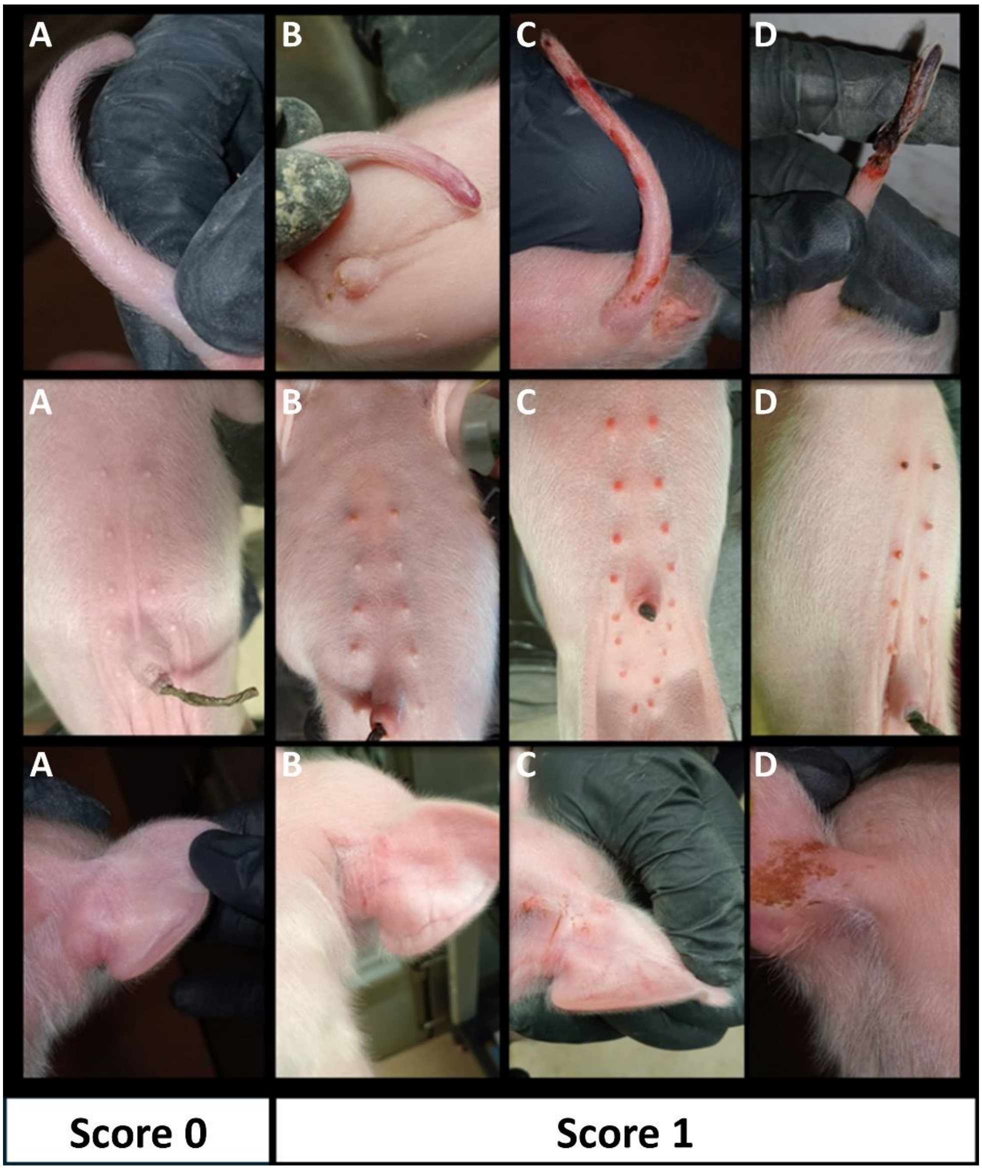


Figure 1. Scoring protocol for Swine Inflammation and Necrosis Syndrome (SINS) in the tail (first line), teats (second line), and ears (third line). The first column (**A**) shows the reference of a healthy skin. From the second to fourth columns (**B**, **C**, and **D**), there are different levels of SINS. (**B**) Redness and subtle signs of inflammation; (**C**) Redness, different levels of exudative inflammation, and bristle loss; (**D**) Necrosis signs and tissue loss. All photos were provided by Topigs Norsvin.

Piglets phenotyped for SINS at birth were subsequently evaluated for skin damage (DMG) during the rearing phase. On average, each animal was assessed for DMG three times, resulting in approximately 20k phenotypic records. Skin damage (DMG) was defined as any visible wound signs on the gilt's skin, which could result from damaging behavior (e.g., fighting), biting behavior (e.g., tail or ear biting), or swine inflammation and necrosis syndrome. Data were collected on the ears (Ear_dmg), tail (Tail_dmg), and flanks (Flank_dmg). DMG scores for each body part ranged from 0 to 3, where 0 indicated no DMG, 1 slight DMG, 2 severe DMG, and 3 very severe DMG. Additionally, similar to SINS, we created a combined score by summing the individual scores from the three body parts, referred to as Sum_dmg. The prevalence and number of records for SINS and DMG are shown in **Figure 2**.

We genotyped 4,949 animals. Quality control was performed for this dataset with 50k SNPs, where sex chromosomes, monomorphic SNPs, SNPs with minor allele frequency $\leq$ 0.02, and maximum difference between observed and expected allele frequency for Hardy-Weinberg Equilibrium of 0.15 were discarded. After quality control analysis, we analyzed approximately 23k SNPs from 4947 animals, of which 41.62% had their phenotypes collected.

4.3.2. Statistics Analyses

4.3.2.1. Swine Inflammation and Necrosis Syndrome

Single- and two-trait animal models were used to estimate variance components, heritability, and genetic correlation between different body parts. The model was as follows:

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z_1 u_a} + \mathbf{Z_2 u_m} + \mathbf{Z_3 c} + \mathbf{e}$$

where $\mathbf{y}$ is the vector of phenotypes for SINS on the *ith* body part (ear, tail, or teats) or the total of affected parts, $\boldsymbol{\beta}$ is the vector of fixed effects of line and technician interaction, herd-year-month at birth, and birth weight and birth weight square as covariable, $\mathbf{u_a}$, $\mathbf{u_m}$, and $\mathbf{c}$ are vectors for the random effects of direct and maternal genetic effects and common litter environment, respectively. The $\mathbf{X}$, $\mathbf{Z_1}$, $\mathbf{Z_2}$, and $\mathbf{Z_3}$ are incidence matrices for the effects in $\mathbf{u_a}$, $\mathbf{u_m}$, and $\mathbf{c}$, respectively, and $\mathbf{e}$ is the vector of random residuals. Random effects were assumed to follow $\begin{bmatrix}\mathbf{u_a}\\ \mathbf{u_m}\end{bmatrix} \sim \mathrm{N}(\mathbf{0}, \mathbf{A} \otimes \Sigma_{\mathbf{u}})$, $\mathbf{c} \sim \mathrm{N}(\mathbf{0}, \mathbf{I}\sigma_c^2)$, and $\mathbf{e} \sim \mathrm{N}(\mathbf{0}, \mathbf{I}\sigma_e^2)$, where $\mathbf{A}$ is the pedigree relationship matrix, σ_c^2 and σ_e^2 are variance components related to common litter environment and residual effects, $\mathbf{I}$ is an identity matrix of proper order, $\Sigma_{\mathbf{u}}$ is a covariance matrix between direct and maternal genetic effects, and $\otimes$ is the Kronecker product.

The covariance structure for the two-trait models was:

$$
\mathrm{V}\begin{bmatrix}\mathbf{u_{a1}}\\ \mathbf{u_{a2}}\\ \mathbf{u_{m1}}\\ \mathbf{u_{m2}}\\ \mathbf{c_1}\\ \mathbf{c_2}\\ \mathbf{e_1}\\ \mathbf{e_2}\end{bmatrix}=\begin{bmatrix}\mathbf{A}\sigma^2_{u_{a1}} & \mathbf{A}\sigma_{u_{a1},u_{a2}} & \mathbf{A}\sigma_{u_{a1},u_{m1}} & \mathbf{A}\sigma_{u_{a1},u_{m2}} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & \mathbf{A}\sigma^2_{u_{a2}} & \mathbf{A}\sigma_{u_{a2},u_{m1}} & \mathbf{A}\sigma_{u_{a2},u_{m2}} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & & \mathbf{A}\sigma^2_{u_{m1}} & \mathbf{A}\sigma_{u_{m1},u_{m2}} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & & & \mathbf{A}\sigma^2_{u_{m2}} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & & & & \mathbf{I}\sigma^2_{c_1} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & \mathit{Symm.} & & & & \mathbf{I}\sigma^2_{c_2} & \mathbf{0} & \mathbf{0}\\ & & & & & & \mathbf{I}\sigma^2_{e_1} & \mathbf{I}\sigma_{e_1,e_2}\\ & & & & & & & \mathbf{I}\sigma^2_{e_2}\end{bmatrix}
$$

where subscripts 1 and 2 indicate the first and second body parts in the model, and other parameters are as defined above.

4.3.2.2. Skin Damage

Single- and two-trait animal models were used for variance components and heritabilities estimation, and genetic correlation between the different body parts, respectively. The model was as follows:

$$\mathbf{y} = \mathbf{X\beta} + \mathbf{Z_1 g} + \mathbf{Z_2 u_a} + \mathbf{Z_3 p_e} + \mathbf{e}$$

where $\mathbf{y}$ is the vector of phenotypes for DMG on the *ith* body part (ear, tail, or flank) or the sum of scores in the three parts, $\boldsymbol{\beta}$ is the vector of fixed effects of line and technician interaction, herd-year-month at birth, and age at scoring as covariable, $\mathbf{g}$, $\mathbf{u_a}$, and $\mathbf{p_e}$ are vectors for the random effects of pen-year-season at scoring, genetic direct and permanent environment effects, respectively. The $\mathbf{X}$, $\mathbf{Z_1}$, $\mathbf{Z_2}$, and $\mathbf{Z_3}$ are incidence matrices for the effects in $\boldsymbol{\beta}$, $\mathbf{g}$, $\mathbf{u_a}$, and $\mathbf{p_e}$, respectively, and $\mathbf{e}$ is the vector of random residuals. Random effects were assumed to follow $\mathbf{g}\sim\mathrm{N}(\mathbf{0},\mathbf{I}\sigma^2_g)$, $\mathbf{u_a}\sim\mathrm{N}(\mathbf{0},\mathbf{A}\sigma^2_u)$, $\mathbf{p_e}\sim\mathrm{N}(\mathbf{0},\mathbf{I}\sigma^2_{p_e})$, and $\mathbf{e}\sim\mathrm{N}(\mathbf{0},\mathbf{I}\sigma^2_e)$, where $\mathbf{A}$ is the pedigree relationship matrix, σ^2_g, σ^2_u, $\sigma^2_{p_e}$, and σ^2_e are variance components related to pen-year-season at scoring, genetic direct, permanent environment and residuals, and $\mathbf{I}$ is an identity matrix of proper order.

The covariance structure for the two-trait models was:

$$
\mathrm{V}\begin{bmatrix}\mathbf{g_1}\\ \mathbf{g_2}\\ \mathbf{u_{a_1}}\\ \mathbf{u_{a_2}}\\ \mathbf{p_{e_1}}\\ \mathbf{p_{e_2}}\\ \mathbf{e_1}\\ \mathbf{e_2}\end{bmatrix}=\begin{bmatrix}\mathbf{I}\sigma^2_{g_1} & \mathbf{I}\sigma_{g_1,g_2} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & \mathbf{I}\sigma^2_{g_2} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & & \mathbf{A}\sigma^2_{u_{a1}} & \mathbf{A}\sigma_{u_{a1},u_{a2}} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & & & \mathbf{A}\sigma^2_{u_{a2}} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & & & & \mathbf{I}\sigma^2_{p_{e_1}} & \mathbf{0} & \mathbf{0} & \mathbf{0}\\ & \mathit{Symm.} & & & & \mathbf{I}\sigma^2_{p_{e_2}} & \mathbf{0} & \mathbf{0}\\ & & & & & & \mathbf{I}\sigma^2_{e_1} & \mathbf{I}\sigma_{e_1,e_2}\\ & & & & & & & \mathbf{I}\sigma^2_{e_2}\end{bmatrix}
$$

where subscripts 1 and 2 indicate the first and second body parts in the model, and other parameters are as defined above.

4.3.2.3. Genetic Correlation between SINS and skin damage

Two-trait animal models were used for genetic correlation estimations between Total_sins and DMG in each part and Sum_dmg. Models in these two-trait analyses follow the same structure used for the single-trait analysis, as described above. The covariance structure between traits only considers the covariance between direct genetic effects.

It is known that threshold models may be more appropriate for categorical traits, as they present more suitable assumptions about distribution. However, these models, being more complex, also require a larger amount of data to reach convergence (Ramirez-Valverde, Misztal, and Bertrand, 2001). Due to this, we employed linear models for all the analyses. All analyses for variance components and genetic parameters estimation were performed using BLUPF90+ (Misztal et al., 2014; Lourenco et al., 2022).

4.3.2.4. Genome-Wide Association Study

Models and assumptions used in the Genome-Wide Association Study (GWAS) are the same as those mentioned above for the Total_sins and Sum_dmg traits. Genotypes were used to estimate genomic breeding values (GEBV) using the single-step GBLUP (ssGBLUP) methodology, as implemented in BLUPF90+ (Misztal et al., 2014; Lourenco et al., 2022). The SNP effects were obtained from backsolving GEBV using the following linear transformation (VanRaden, 2008):

$$\hat{\mathbf{a}} = (1-\alpha)b\frac{\sigma_u^2}{\sigma_a^2}\mathbf{Z}'\mathbf{G}^{-1}\hat{\mathbf{u}}$$

where $\hat{\mathbf{a}}$ is the vector of SNP effects, α is the blending parameter (0.05) to avoid singularity problems in $\mathbf{G}$, b is a tuning parameter (Vitezica et al., 2011), σ_u^2 is the total genetic variance, σ_a^2 is the SNP variance, $\mathbf{Z}$ is a matrix of SNP content centered by two times the allele frequency (p_i), $\hat{\mathbf{u}}$ is the vector of GEBV, and $\mathbf{G}^{-1}$ is the inverse of the genomic relationship matrix, with $\mathbf{G}$ constructed as the method one of VanRaden (VanRaden, 2008).

We used the sliding window approach to calculate the percentage of genetic variance explained by 30 adjacent SNPs ($Var(\sum_{i=1}^{30}\mathbf{z}_i\hat{\mathbf{a}}_i)/\sigma_u^2 \times 100$) (Wang et al., 2014). To calculate the effects of the SNPs and the variance explained by the window, we used the POSTGSF90 program (Misztal et al., 2014; Lourenco et al., 2022).

4.3.3. Gene Search and Gene Ontology Analysis

All windows with 30 adjacent SNPs that explained more than 1% of the genetic variance explained for Total_sins and Sum_dmg were considered for gene searching. Putative genes were identified based on initial and final coordinates of each selected window on the *Sscrofa* 11.1 assembly of the swine genome, using the Ensembl Release 113 (Harrison et al., 2024). Then, all identified protein-coding genes were used to perform biological processes enrichment analysis using the ClueGO application (Bindea et al., 2009) in Cytoscape (Shannon et al., 2003), with a Bonferroni correction test applied. Additionally, all annotated genes were further investigated through a comprehensive literature review.

4.4. Results and discussion

The number of records and the prevalence of SINS and DMG scores in each body part, as well as the total number of affected body parts for SINS and the sum of scores for DMG, are shown in **Figure 2**. All 6,955 animals had their phenotypes collected for SINS in all three body parts. Of these 25.8%, 61.6%, and 32.5% of the animals presented SINS signs in the ear, tail, and teats, respectively (**Figure 2A**). Regarding the total affected parts, 78.1% of the animals presented signs of SINS in at least one body part. About 44.0% (N = 3,059) had SINS signs in only one part, 26.4% (N = 1,834) had two affected parts, and 7.7% (N = 537) presented SINS signs in all three parts. From a total of 958 evaluated litters, with on average 7.3 ± 2.5 females phenotyped per litter, only 7 litters did not have any affected piglets, 599 litters (62.5%) had at least one piglet presenting SINS signs, whereas, in 352 litters (36.7%), all piglets were affected. The raw average BW of piglets presenting all three body parts affected was not significantly different from piglets with no SINS signs (1.5 ± 0.3 kg vs. 1.3 ± 0.3 kg).

Of the 6,955 animals phenotyped for SINS, 5,768 were also phenotyped for DMG at least once during the rearing phase. The number of records for DMG per animal ranged from 1 to 4, with an average of 3 observations per animal. At scoring, the animals' average age, considering the entire phase, ranged from 35 to 247 days, with an average of 110.6 ± 39.4 days. The prevalence of skin damage scores in each body part, as well as the sum of the scores, is shown in **Figure 2B**. Specifically, DMG was present in at least one body part (Sum_dmg > 0) in 62.1% of cases, with 12,842 records exhibiting some level of DMG. We evaluated about 20,700 records for each body part, and the prevalence of records with no DMG signs in these areas was 50.6%, 78.8%, and 83.2% for ear, tail, and flank, respectively.

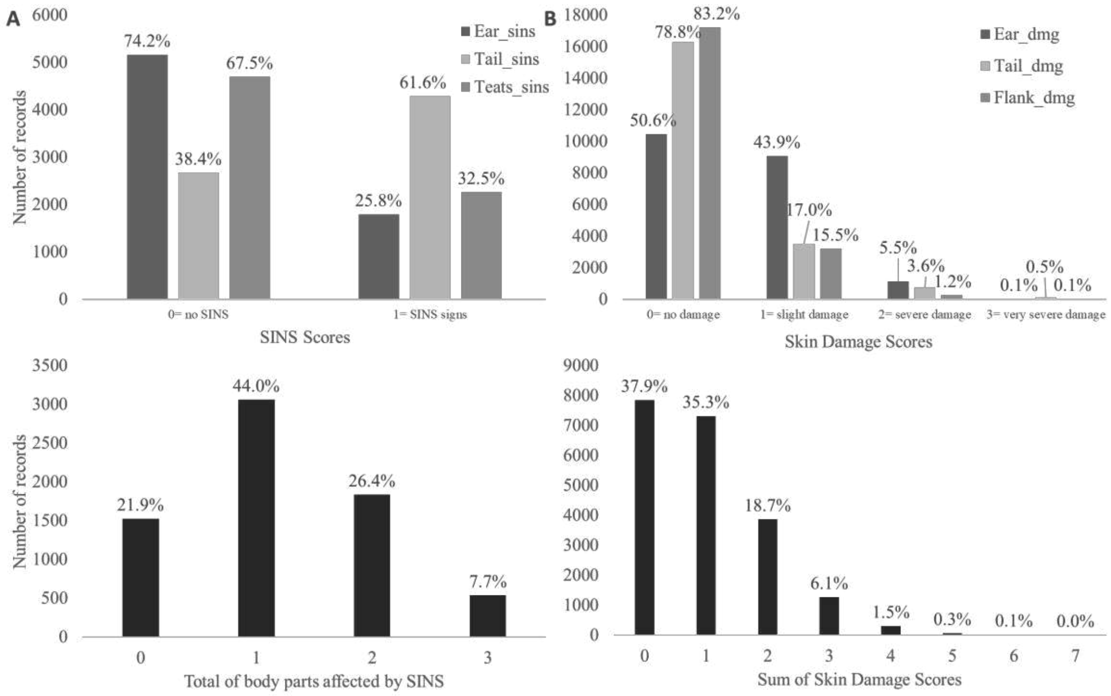


Figure 2. (**Column A**) Number of records and prevalences for Swine Inflammation and Necrosis Syndrome (SINS) score in the ears (Ear_sins), tail (Tail_sins), teats (Teats_sins), and the total of affected body parts (Total_sins). SINS scores were collected in around 7k piglets at birth; (**Column B**) Number of records and prevalences for Skin Damage (DMG) score in the ears (Ear_dmg), tail (Tail_dmg), flanks (Flank_dmg), and the sum of scores (Sum_dmg). DMG scores were collected on average three times in around 6k gilts during the rearing phase.

As DMG and SINS were recorded on the ears and tail, when we compare these body parts in both traits, the ears were the part that showed the least SINS signs (25.8%), but it was the part with the highest percentage of DMG, in which 49.4% of the records showed some level of DMG. This low prevalence of SINS in the ears can be related to a failure in the visual identification of inflammation in this area, since Reiner et al. (2023) have already found that SINS is better identified in the ear in piglets from three days of age. Our study considered piglets 0.4±0.6 days old, whereas the available studies evaluated SINS in animals 3 days old or older (Reiner et al., 2019; Leite et al., 2023a). In contrast, the tail was the area most affected by SINS, with approximately 61.6% of the piglets showing signs of SINS in this part. However, the prevalence of DMG in the tail was much lower, with 21.2% of the records showing different levels of DMG. This was expected, as the animals underwent tail docking after birth, and studies have shown that this practice, although it does not entirely solve the problem, reduces the prevalence of DMG in this area (Lahrmann et al., 2017; Niemi et al., 2021). Furthermore, it is interesting to note that although almost 80% of the records did not show DMG in the tail, the highest prevalence of very severe DMG (DMG score = 3) was observed in this area.

4.4.1. Genetic Parameters

Direct and maternal heritabilities for SINS, as well as genetic correlations between individual body parts and the sum of the affected body parts (Total_sins), are presented in **Table 1**. Direct heritability estimates ranged from 0.03 to 0.08. When the affected body parts were analyzed separately, the heritabilities were lower. This is likely due to the binary nature of the trait, which limits the linear model's ability to detect and differentiate existing variation. When a combined score was created by summing the scores of the affected body parts, the number of categories increased, making the results more informative. Consequently, the linear model was better able to capture the variation among animals.

Table 1. Direct heritabilities (diagonal), maternal heritabilities (h_m^2), and genetic correlations (off-diagonal) for Swine Inflammation and Necrosis Syndrome (SINS) in three body parts and the sum of affected parts (Total_sins). Heritabilities were estimated using a single-trait model, and genetic correlations were estimated using two-trait models.

	Ear_sins	**Tail_sins**	**Teats_sins**	**Total_sins**	h_m^2
Ear_sins	0.03 ± 0.02	0.29 ± 0.12	0.88 ± 0.04	0.92 ± 0.02	0.05 ± 0.04
Tail_sins		0.03 ± 0.01	0.44 ± 0.13	0.75 ± 0.12	0.01 ± 0.00
Teats_sins			0.07 ± 0.03	0.97 ± 0.01	0.06 ± 0.05
Total_sins				0.08 ± 0.01	0.04 ± 0.05

Average ± standard deviation

Leite et al. (2023a) reported direct heritabilities for four body parts (ears, tail, teats, and claws) in piglets from F1 dams and 17 different boar lines, ranging from 0.08 to 0.34. For a combined SINS score including all body parts, the heritability was 0.26. Although their study involved a similar number of piglets over a comparable time, the results are not directly comparable to ours due to differences in the pedigree structure and the genetic lines involved. It is also important to note that estimates of genetic parameters and the prevalence of SINS in different body parts may vary depending on the age at which measurements are taken. Reiner et al. (2019) have already shown that SINS is more easily identifiable in certain body parts depending on the piglets' age.

Maternal heritabilities ranged from 0.01 to 0.06. However, considering the standard deviations, these estimates were close to zero. This is likely due to limitations in our data structure, which includes only one generation of phenotyped females and an average of four daughters per boar. Even though our estimates of maternal heritability appear negligible, it is important to consider that SINS, when manifested at birth, occurs before piglets are exposed to pathogens or social interactions within the litter or pen, suggesting that maternal genetic effects may still play a role. In addition, there is evidence that both maternal genetic and environmental factors influence SINS expression. Leite et al. (2023a) found maternal heritabilities significantly different from zero, ranging from 0.07 to 0.12 for combined SINS scores. Reiner et al. (2019) evaluated SINS in eight body parts in a population with approximately 5k piglets aged 5.5 ± 2.7 days, born to sows from four commercial lines. They found that the effect of sow line on SINS in the claw coronary bands, tail, and ears was significant, explaining between 3% and 14% of the phenotypic variance of the trait. Only SINS in the teats showed a smaller and non-significant sow line effect (2%).

Genetic correlations between the different body parts showed that the Tail_sins was only weakly to moderately associated with other parts, with genetic correlations of 0.29 and 0.44 with ears and teats, respectively. A high genetic correlation was observed between ears and teats (0.88). The combined SINS score (Total_sins), representing the total number of affected parts, was developed to reduce the number of analyses, increase trait informativeness, and facilitate its evaluation and association with other traits. Genetic correlations between individual body parts and Total_sins ranged from high to very high, with the lowest correlation observed for the tail (0.75) and the highest for the teats (0.97). These high correlations suggest that Total_sins can reliably serve as a single, representative measure of SINS severity across all affected body parts. Leite et al. (2023a) reached a similar conclusion by combining information from four body parts into a single binary score for SINS. They found that this combined score effectively summarized all individual parts, maintained high genetic correlations with them, and presented lower standard deviations and higher heritabilities. Consequently, they used this combined score to estimate genetic correlations between SINS and the combined skin damage score, as well as pre- and post-weaning production traits.

Direct heritabilities, repeatabilities, and genetic correlations between the individual body parts and the sum of the scores for skin damage (Sum_dmg), as well as their genetic correlations with Total_sins, are shown in **Table 2**. Heritabilities for DMG ranged from 0.04 to 0.09. In which flanks presented the lowest heritability and Sum_dmg the highest one. Ears and tail presented heritabilities equal to 0.08 and 0.05, respectively. Some studies have investigated the heritability of skin lesions in pigs, often associated with damaging behaviors such as tail and ear biting or aggression during social interactions. Breuer et al. (2005)

estimated the heritability of tail biting in Landrace pigs, finding values of 0.05 on a binary scale and 0.27 on an underlying continuous scale, suggesting a genetic component to this behavior. The heritability was not statistically different from zero in Large White pigs (Breuer et al., 2005). Turner et al. (2009) reported heritability estimates for skin lesions resulting from aggressive encounters post-mixing, with values ranging from 0.08 to 0.43, indicating that both the propensity to initiate and receive aggression have a genetic basis. Additionally, Canario and Flatres-Grall (2019), working with a composite Sino-European line, observed a heritability of 0.06 for tail-biting receipt, measured by the presence of tail injuries in gilts. These findings highlight the genetic factors in skin lesions in pigs, suggesting that selective breeding could be a viable strategy to mitigate such welfare issues.

When animals are housed in groups, pen mates can have both direct and indirect genetic impacts on one another (Canario et al., 2007; Turner et al., 2009; Leite et al., 2023b). Leite et al. (2023b) evaluated a combined skin damage score in gilts on five multiplier farms in the Netherlands. They compared two models, one that included social genetic effects and the other that did not. Using the model without a social genetic effect, the authors found a heritability of 0.03, which is similar to the heritability found in our work when evaluating flanks and tails. When they considered the social genetic effect, the total heritable variance increased to 0.10, a value similar to what we found here for Sum_dmg. Although the model with a social genetic effect had a higher total heritable variance, the correlation between the direct genetic and social effects was close to zero (-0.05), indicating that classical selection based only on direct effects for skin damage should not be detrimental in that population (Leite et al., 2023b).

Table 2. Direct heritabilities (diagonal) and genetic correlations (off-diagonal) for Skin Damage (DMG) in three body parts and the sum of the scores for the three parts (Sum_dmg). Genetic correlations between DMG in different body parts and Swine Inflammation and Necrosis Syndrome (SINS), and repeatability (Rep) for DMG. Heritabilities were obtained using a single-trait model, and two-trait models were used for genetic correlations.

	Ear_dmg	**Tail_dmg**	**Flank_dmg**	**Sum_dmg**	**Total_sins**[1]	**Rep**
Ear_dmg	0.08 ± 0.01	0.40 ± 0.09	0.26 ± 0.11	0.91 ± 0.02	0.78 ± 0.00	0.20 ± 0.01
Tail_dmg		0.05 ± 0.01	0.28 ± 0.10	0.87 ± 0.03	0.20 ± 0.05	0.14 ± 0.01
Flank_dmg			0.04 ± 0.01	0.66 ± 0.06	0.22 ± 0.05	0.08 ± 0.01
Sum_dmg				0.09 ± 0.01	0.76 ± 0.00	0.16 ± 0.01

Average ± standard deviation; [1] Total_sins is the sum of affected body parts (ear, tail, and teats) for SINS.

Even when accounting for social genetic effects, Leite et al. (2023b) emphasized that including the group environmental effect also contributes substantially to explaining the phenotypic variation in skin damage. The authors found that the group effect, which captures differences inherent to each pen and non-heritable social interactions, explained a larger proportion of the phenotypic variance than the heritable components; this was equal to 17% and 18% in the models with and without social genetic effect, respectively. A similar result was observed in our study, while genetic variance accounted for at most approximately 10% of the phenotypic variance, the group (pen) effect explained 18%, 19%, 27%, and 28% of the phenotypic variance for flanks, ears, tail, and Sum_dmg, respectively. It reinforces that environmental social interaction factors largely influence skin lesion variation.

Genetic correlations for DMG in individual body parts were low to moderate (0.26 to 0.40), and the combined score for DMG, in which we sum the scores of the body parts (Sum_dmg), was highly correlated with all individual parts (≥0.70; **Table 2**). These results indicate that, as for SINS, a combined score can be effectively used to evaluate skin damage, given its high correlation with all individual body parts, higher heritability, and lower standard deviation. This finding leads us to investigate the base hypotheses of our study: the genetic association between SINS and DMG. To explore this, we compared Total_sins with the individual body parts and the Sum_dmg (**Table 2**).

The ears were phenotyped for SINS and DMG, and the genetic correlation between these two traits in this body part was high (0.80). Genetic correlations between SINS and DMG in the tail and flanks were low (0.20). This low genetic correlation for the tail is due to the tail docking after scoring for SINS, which later reduced the prevalence of SINS and later DMG in this body part (see **Figure 2**). This behavior is expected, as there is literature proving the reduction of biting and tail damage due to the tail docking practice (Li et al., 2017; Teixeira et al., 2024). Nevertheless, the low genetic correlation between Total_sins and Flank_dmg comes from the non-recording of the SINS phenotype in this same body part.

We found a high genetic correlation between Total_sins and Sum_dmg (r = 0.80). Leite et al. (2023b) evaluated the genetic association of SINS and DMG with pre- and post-weaning production traits. They reported the existence of a genetic correlation between SINS and DMG, which ranged from 0.20 to 0.50, depending on the traits analyzed in the model. The genetic correlations found by them were lower and presented larger standard deviations.

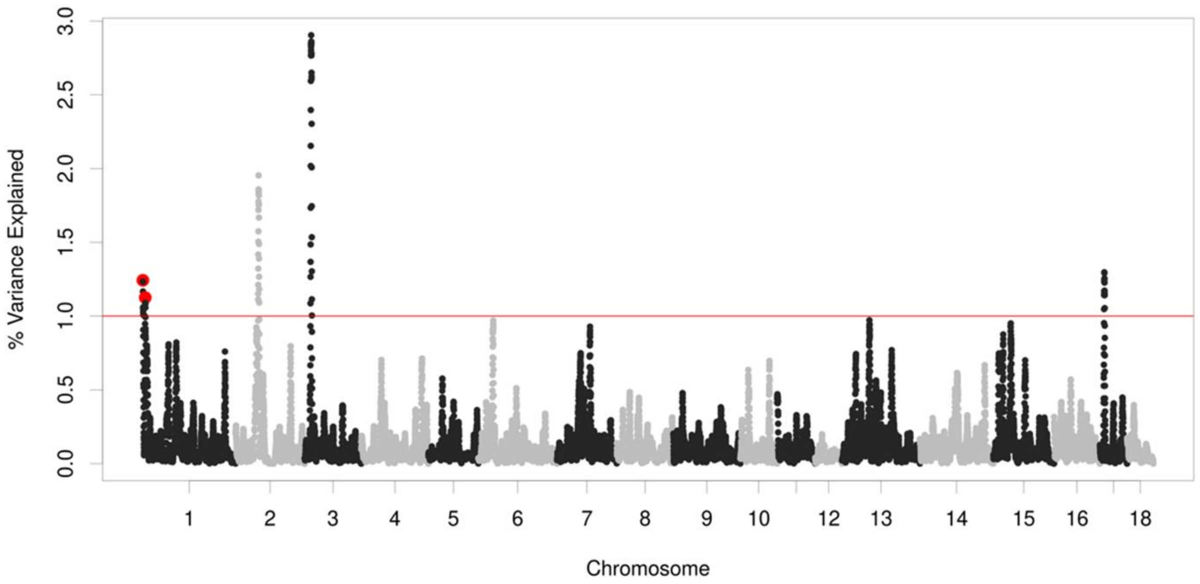
This is likely due to differences in data and pedigree structure, the number of traits analyzed, and differences in the models.

In addition to individual and group heritable factors and non-heritable group effects, an animal's phenotype can also be influenced by permanent and temporary environmental factors. Repeatability, which measures the consistency of phenotypes within the same individual over time and reflects the influence of the permanent environment on trait variation, was low in this study, ranging from 0.08 to 0.20 (**Table 2**). These low repeatability values suggest that DMG in the same individual is strongly affected by temporary environmental conditions. Such conditions may include feeding practices, management, and climatic variations. Consequently, an individual’s DMG score is likely to vary across time points, meaning that animals showing a high DMG score in one assessment do not necessarily present similar scores in subsequent measurements.

4.4.2. GWAS and Gene Ontology Analysis

GWAS detects associations between genetic variants (SNPs) and a trait by analyzing genotype and phenotype data across individuals. In this study, we first performed a single SNP GWAS; however, as in Leite et al. (2023b), no significant single SNPs were found, which reaffirms the polygenic nature of the studied traits. Using the sliding window approach with 30 adjacent SNPs, we identified five non-overlapping windows that explained more than 1% of the direct genetic variance for Total_sins, and seven non-overlapping windows for Sum_dmg (**Figure 3**). Altogether, five protein-coding genes were identified in two windows on SSC 1 for Total_sins (**Figure 3A**). These genes were *DLL1* (delta-like canonical Notch ligand 1), *DYNLT2* (dynein light chain Tctex-type 2), *PHF10* (PHD finger protein 10), *WDR27* (WD repeat domain 27), and *THBS2* (thrombospondin 2).

A Variance explained by 30 adjacent SNPs for SINS (Total_sins, direct effect)



B Variance explained by 30 adjacent SNPs for Skin damage (Sum_dmg)

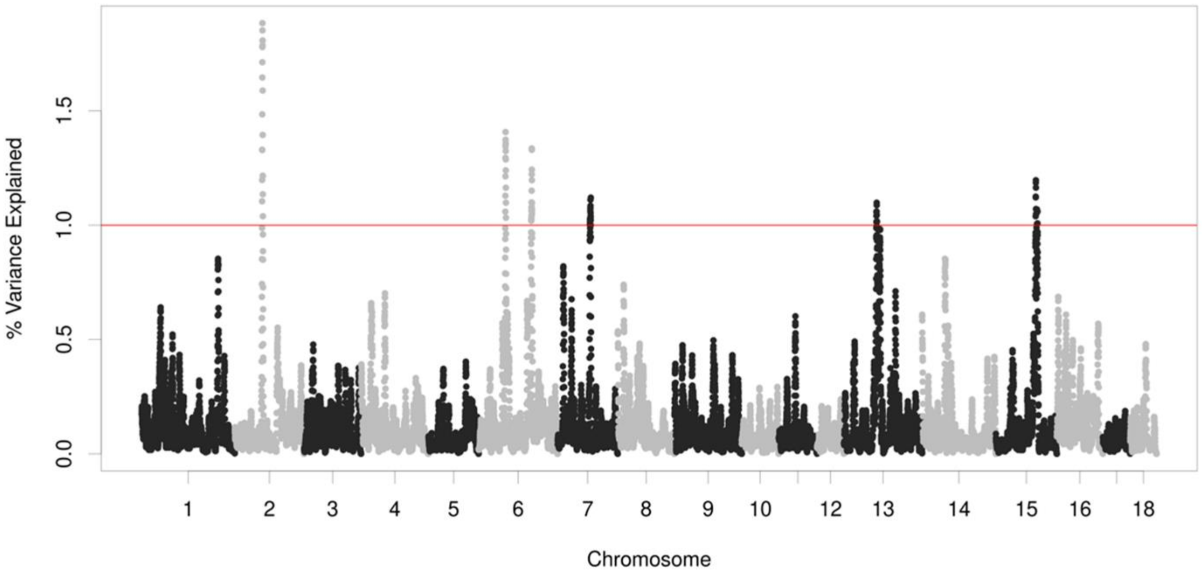


Figure 3. Manhattan plot with the variance explained by 30 adjacent SNPs for the (**A**) sum of affected parts by Swine Inflammation and Necrosis Syndrome (Total_sins), and (**B**) sum of skin damage scores in the three body parts (Sum_dmg), considering only the direct effect. The red line is the threshold for 1% of variance explained by the windows, and the dots highlighted in red represent the two windows in which all five protein-coding genes were identified.

According to GeneCards (2025), *DLL1* is a human homolog of the Notch Delta ligand and plays a role in mediating cell fate decisions (https://www.genecards.org/). The signaling pathway mediated by canonical Notch ligands is essential for proper embryonic development and the maintenance of tissue homeostasis by regulating various cell fate decisions and processes (D'Souza, Meloty-Kapella, and Weinmaster, 2010). According to the Mouse Genome Informatics (https://www.informatics.jax.org/), tissue homeostasis is a process involved in controlling cell proliferation and death in a tissue's internal steady state, including its control of metabolic function. This may imply that the *DLL1* gene plays a role in the formation of tissue in the swine embryonic phase, and its deficiency may result in piglets with visual phenotype related to Swine Inflammation and Necrosis Syndrome at birth. Further exploring the literature, we found that the dysregulation of Notch signaling is linked to numerous developmental anomalies and a range of pathological conditions (Sachan et al., 2024). Endothelial *DLL1* mutant mice presented severe flap necrosis along with enhanced mobilization and expansion of inflammatory cells after flap surgery, a reconstructive treatment for large wounds (Dastagir et al., 2023). The authors suggested that the increased inflammatory response in *DLL1*-deficient mice may be due to the lack of interaction between endothelial cells and monocytes or the large flap necrosis. In pigs, Kiewisz et al. (2014) studied the transcriptomic profile of pig endometrium on Days 12 and 16 between pregnancy and the estrous cycle; they found *DLL1* gene to be highly expressed only on day 12, being associated with several molecular pathways, such as cell death and survival, connective tissue development and function, embryonic and organ development, immune cell trafficking, inflammatory response and cell-mediated immune response, indicating that on the 16th day between the estrous cycle and gestation, the expression of this gene is no longer as necessary as before. This suggests that *DLL1* is a promising target to be explored in future studies in pig endometrium and embryos to investigate whether its expression is associated with inflammation and necrosis syndrome in piglets at birth.

The *THBS2* gene was also highlighted in our ClueGO results for biological processes. Likewise, *THBS2* was shown to be up-regulated activating the Notch signaling pathway, promoting the progression and stemness of gastric cancer in humans (Barani et al., 2023, Wang et al., 2023, Chang et al., 2024). Research in mice indicates that the protein resulting from *THBS2* transcription may influence cell surface traits of mesenchymal cells and play a role in cell adhesion and migration (GeneCards, 2025). Mesenchymal cells are adult stem cells with broad anti-inflammatory and immune-modulatory properties (Pittenger et al., 2019). In swine, the *THBS2* gene was found to be expressed in extracellular vesicles released from mesenchymal stem cells, being associated with angiogenesis, a fundamental process for wound healing (Eirin et al., 2018). This explains the biological processes of negative regulation of angiogenesis, vasculature development, and blood vessel morphogenesis found in our study, which are associated with the *THBS2* gene. It is suggestive that the *THBS2* gene may influence the immunological response at some point in newborn piglets and affect skin inflammation.

Furthermore, the *PHF10* gene presents multiple alternatively spliced transcript variants, but the full-length nature of only two of them is known (GeneCards, 2025). In mammals, specifically humans and mice, it is known that a change in *PHF10* isoform expression affects neural and muscle differentiation (Bayramova et al., 2024). The expression of this isoform prevails in brain tissue, heart tissue, and muscle tissue compared to other isoforms. The Sscrofa11.1 Primary Assembly on National Center for Biotechnology Information (NCBI, 2025) presents seven isoforms for the *PHF10* gene. We may assume that one of the *PHF10* isoforms from the swine genome may affect cell differentiation in embryos, fetuses, or recently born piglets, so its expression could be explored in future studies to verify the influence of this gene on cell death and consequent skin necrosis. As *THBS2*, the *PHF10* gene is part of a signaling cascade that plays an important role in regulating differentiation and stemness in gastric cancer cells (Fan et al., 2024). Stemness, or stem cells, can give rise to differentiated cells and maintain the balance between cell quiescence, proliferation, and regeneration, mostly during embryonic development (Kim and Ramalho-Santos, 2025). Additionally, the transcriptional activity of adult stem and progenitor cells was found to be especially elevated within tissues with rapid cellular turnover (i.e., skin). Quiescent stem cells in muscles exhibit a swift increase in their transcriptional activity in response to injury and regeneration (Kim et al., 2023). To our knowledge, no studies have investigated the association between *PHF10* and any trait in the porcine species. Although the functions of *PHF10* isoforms have not been fully elucidated yet, we suggest that *PHF10* may play a role during embryogenesis related to stem cells, which could affect skin differentiation and regeneration in piglets at birth. This hypothesis should be tested in future studies.

The proteins encoded by *WDR27* contain multiple tryptophan and aspartic acid repeats, which enable these proteins to form scaffolds for protein-protein interactions and play key roles in cell signaling. It is known that certain scaffold proteins participate in pathways that may induce or aggravate necrosis, whereas others are released in the course of necrotic cell death (Pistorio et al., 2022). Considering this role, *WDR27* was already associated with anti-tumor necrosis (Honne et al., 2016), immune responses, and cell movement (Anuraga et al., 2024; Wang et al., 2025) in human diseases. It is suggestive that the *WDR27* gene plays a similar role related to immunity and necrosis in swine, which could be explored further. In humans, *WDR27* splicing results in multiple transcript variants, and its full-length form has not been determined yet (GeneCards, 2025). However, in swine, this gene appears to have only one transcript uncovered so far (NCBI, 2025). Likewise, there is a gap in the literature regarding *WDR27*'s role in swine; therefore, we suggest that this role can be explored in relation to immune response to inflammatory conditions and cell death. Interestingly, Richard Albert et al. (2023) found that *WDR27* expression was maternally imprinted in the rat epiblast, the upper layer of cells in the embryo responsible for giving rise to all tissues, including embryonic stem cells. This is another condition that could be considered when exploring *WDR27* expression in future studies on piglets, as the parent-of-origin effect of a gene may influence the choice of progenitors.

On the other hand, the *DYNLT2* gene appears to be part of the cytoplasmic dynein complex, particularly in the cytosol and the sperm flagellum. This gene may be related to human male infertility (GeneCards, 2025). In The Human Protein Atlas, we found that the *DYNLT2* gene is highly expressed in all brain regions in the pig, from the cerebral cortex to the white matter (https://www.proteinatlas.org/). No studies have investigated this gene's role in skin damage, necrosis, or inflammation in any species. We can argue that this gene was identified because it falls within the established range for gene searching. There is no evidence to suggest that it is a suitable target for testing the effect on phenotype related to visual inflammation and necrosis in swine.

We also suggest searching for single variants around those genes to identify a nucleotide substitution, deletion, or insertion that could be directly related to inflammation or skin damage leading to necrosis.

4.5. Conclusion

The swine necrosis and inflammation syndrome, which is expressed in different body parts of piglets, is directly heritable, with low heritabilities ranging from 0.03 to 0.07. Maternal heritabilities ranged from 0.01 to 0.06, but most estimates showed high standard deviations, which indicate non-significance. The sum of affected parts (Total_sins) and the sum of scores (Sum_dmg) can be used as proxies for SINS and skin damage recorded in different body parts. These combined scores have a high genetic correlation (≥0.70) with all evaluated body parts and still capture greater direct genetic variance when compared with each body part individually, with heritabilities of 0.08 and 0.09 for Total_sins and Sum_dmg, respectively. Total_sins and Sum_dmg are strongly genetically correlated (r=0.80), which suggests that selection decisions for less skin damage may be taken earlier in life, based on SINS, and that piglets genetically less susceptible to SINS are more likely to experience an increase in their welfare throughout the production system. Although SINS is a polygenic trait, using a window-based approach, we identified five linked genes (*DLL1*, *PHF10*, *WDR27*, and *THBS2*) that are primarily related to embryonic and tissue formation, which could be promising targets for future exploration.

4.6. Acknowledgments

This study was supported by Topigs Norsvin ('s-Hertogenbosch, NB, Netherlands), the Brazilian Federal Agency for Support and Evaluation of Graduate Education, CAPES/PROEX 88887.844747/2023-00 (Brasilia, DF, BR), and the Minas Gerais State Agency for Research and Development – FAPEMIG (Belo Horizonte, MG, BR).

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CHAPTER 5

5.1. General conclusions

This thesis addressed genetic parameter estimations of economically relevant traits across different livestock species and production systems, focusing on dairy, beef-on-dairy, and swine. Despite working with data from distinct populations, breeds, and countries, the findings from these projects reinforced the feasibility and importance of incorporating genetic information to make decisions and improve animal performance, welfare, and productivity through selection.

In dairy Gir cattle, the simultaneous evaluation of fat percentage, protein percentage, and logarithmic somatic cell count demonstrated the applicability of multi-trait models even with limited data. Heritability estimates showed that milk composition traits are more heritable than health-related traits. Genetic correlations were consistent with the physiological associations between milk solids and udder health. These results provide valuable parameters and breeding values to support genetic selection decisions in Gir cattle in the evaluated farms.

In beef-on-dairy crossbreeding systems, the study highlighted both the potential and the challenges of performing routine genetic evaluations for calving ease in this context. Although the large amount of data, the data structure is still limiting, mainly due to pedigree connectivity and depth, the trait showed a small genetic variability. The linear model applied to first-lactation records proved to be a practical alternative for large-scale evaluations, providing more reliable breeding values with higher computational efficiency than threshold models and more than one lactation.

In swine, the findings confirmed the presence of low but significant heritabilities for the Swine Inflammation and Necrosis Syndrome (SINS) and skin damage. The strong genetic correlation between both traits supports using SINS as a skin damage predictor. Genomic analyses identified candidate genes involved in tissue development and inflammation, such as *DLL1*, *PHF10*, *WDR27*, and *THBS2*, offering promising targets for future functional validation. These insights highlight the importance of including animal welfare traits in breeding goals and the potential for early-life selection to improve lifetime welfare outcomes.

Altogether, this thesis contributes to advancing the understanding of genetic architecture in diverse livestock systems and proposes practical strategies for enhancing genetic evaluations and animal welfare through selection. The integration of production, reproduction, and health traits in genetic improvement programs is not only feasible but essential for the sustainability of modern animal agriculture.