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Reaction-norm analysis of neonatal lamb mortality suggests heritability varies with cold-stress: an example in the Elsenburg Merino selection lines

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ABSTRACT

Context. Coping with high levels of cold stress should be beneficial to survival of lambs, given the high mortality rate associated with severe winter storms. The Elsenburg Merino selection experiment involved divergent selection for reproduction. Phenotypic results comparing the positively selected H-Lines and negatively selected L-Lines suggested that cold-stress adaption could have contributed to the favourable genetic trends for survival of H-Line lambs. However, observing the genetic merit of better adapted animals depends on the presence of cold stress at the time of recording. A genotype by environment component (G × E) could, thus, be important when assessing survival/mortality phenotypes. **Aim.** This study proposed the genetic analysis of this possible G × E component and compared the H- and L-Lines in this regard. **Methods.** The sire model allowed the use of progeny phenotypes for neonatal mortality recorded during different levels of cold stress, and the possible G × E could be investigated through the reaction-norm approach. Genetic parameters were evaluated as random regression components by implementing a Gibbs sampling approach. A data set of 5723 individual lamb records was analysed as the progeny of 213 sires. **Results.** A modelled G × E component played an important role in mortality outcomes, with the mean estimate (and 95% confidence interval) for the slope ($\sigma^2_{s_b} = 0.113[0.0019\text{–}0.28]$) only marginally smaller than the corresponding estimate for the intercept ($\sigma^2_{s_a} = 0.124[0.003\text{–}0.26]$). The reaction-norm model showed a higher heritability ($h^2 \pm$ posterior standard deviation) for mortality at 3 days of age during high cold-stress (0.22 ± 0.16 at ~1100 $\text{KJm}^{-2}\text{h}^{-1}$) than during mild (0.13 ± 0.10 at ~960 $\text{KJm}^{-2}\text{h}^{-1}$) conditions, suggesting a greater ability to discriminate between sires at increasing stress levels. **Conclusions.** Failure to account for this G × E component putatively contributes to the low h^2 commonly reported for survival traits. The higher h^2 at increased levels of cold stress could have played an important part in the higher survival of the H-Line progeny, who were better at coping with cold, wet and windy conditions. **Implications.** Larger studies representing a wider environmental trajectory are recommended. This should be very feasible since cold stress can be derived from commonly available weather-station data.

Keywords: chill index, early mortality, genotype by environment interaction, Gibbs sampling, lamb survival, random regression, sheep, welfare.

Introduction

The incidence of lamb mortality is of great importance from both an economical and welfare point of view (Brien *et al.* 2014; Hinch and Brien 2014). There has thus been considerable interest in improving lamb survival by targeting additive genetic effects. However, this approach has been discouraged by the low heritability (h^2) for survival traits reported for Merinos (Brien *et al.* 2009*a*; Hatcher *et al.* 2010) and other breeds (Lopez-villalobos and Garrick 1999; Morris *et al.* 2000; Riggio *et al.* 2008; Vanderick *et al.* 2015). The first days after birth have been identified as particularly critical having the highest mortality rates (Hatcher *et al.* 2009), and a possibly higher level of genetic variation (Sawalha *et al.* 2007; Riggio *et al.* 2008; Hatcher *et al.* 2010). The neonatal period delivers a stringent test to the adaptive capacity of lambs, including a dramatic change in temperature on leaving the uterine environment. The ability of the lamb to quickly respond with its own mechanisms of thermoregulation has been emphasised as a key factor contributing to lamb viability (Plush *et al.* 2016). In extensive production systems, this period can be particularly challenging when lambs are born into cold, wet and windy conditions, which interact to exacerbate the level of cold stress. Exposure to a high rate of heat loss slows lamb progress by a group of inter-related factors, such as poor feeding, behaviour and thermoregulation. Lambs who succumb to cold stress are typically identified by aetiology named the 'starvation–mismothering–exposure' complex at autopsy (Haughey 1991; Cloete and Scholtz 1998). The expected rate of heat loss has been quantified as a function of ambient temperature, rainfall and windspeed as an environmental stress variable termed the 'chill index' (Nixon-Smith 1972; Donnelly 1984). Cold stress represented by increasing values of the chill index has been linked to high mortality rates in new-born lambs (Donnelly 1984; Gudex *et al.* 2005; Oldham *et al.* 2011; Geenty *et al.* 2014), extending on earlier reports of 'bad weather' (Alexander *et al.* 1980) or the interaction among cold, wet and windy conditions (Obst and Day 1968).

An opportunity to mitigate these effects is presented by the fact that individuals vary in their ability to tolerate high rates of heat loss. Differences in the ability to resist cold stress have been reported across breeds (Dwyer and Morgan 2006), selection lines (Slee and Stott 1986), sire lines (Gudex *et al.* 2005), and individuals (Slee *et al.* 1991). It could be expected that genotypes better adapted to high levels of cold stress should incur lower incidences of mortality under conditions of severe cold exposure. However, the favourable merit of these genotypes would not be observed in environments where cold stress is absent or limited. A genotype by environment interaction (G × E) could thus be an important component of neonatal lamb survival, particularly in extensive conditions where there is often little protection against environmental elements.

The presence of a significant G × E effect means that the observed merit of genotypes depends on the environment they are evaluated in (Falconer and Mackay 1996), and implies that the estimated breeding value (EBV) varies according to environmental factors. This variation has often been described as the 'environmental sensitivity' (ES) or 'phenotypic plasticity' of the genotype. A high ES is generally not desirable, since a breeding objective would target 'robust' genotypes capable of expressing their potential despite varying environments (Knap 2005). If the environment at recording can be reliably quantified, the presence of G × E can be investigated by the 'reaction-norm' (RN) approach (de Jong 1995; de Jong and Bijma 2002). Reaction-norm models define breeding values as continuous functions of an environmental descriptor by random regression of genetic effects across the environmental trajectory, such as the gradient of cold stress. Random regression models has been proposed for survival analysis (Veerkamp *et al.* 1998) and could contribute to better understanding of the role of G × E in neonatal lamb mortality, but this has not been investigated.

The Elsenburg Merino selection lines have been divergently selected for reproductive fitness (lambs weaned per ewe joined) from 1986 to 2020. Despite the low h^2, worthwhile and divergent genetic trends for lamb survival were reported for the H-Lines (positive selection) and L-Lines (negative selection; Cloete *et al.* 2009; Nel *et al.* 2021*a*). In a phenotypic comparison between H- and L-Line lambs, H-Line lambs coped better with stressful levels of cold exposure (Nel *et al.* 2021*b*), suggesting that the relative fitness of H-Line lambs could be linked with better cold-stress adaption. Since the start of the experiment, the incidence of lamb mortality has been recorded in close proximity to weather stations, providing data to quantify cold stress on a daily basis. The influence of G × E can thus be investigated by linking phenotypes of mortality to the variable gradients of cold stress during the neonatal period. The first aim of this study was thus to use the RN approach to investigate the potential contribution of G × E to genetic parameters of neonatal mortality across an environmental trajectory defined by cold stress. Second, the study aimed to determine whether the favourable fitness of the H-Line (Cloete and Scholtz 1998; Cloete *et al.* 2009; Nel *et al.* 2021*b*) can be linked to cold-stress resistance on the genetic level by comparing RN components of H- and L-Line sires during selected periods of the selection experiment. The within-flock analysis was constrained by the fact that the edited data set was small, but was aided by the historic divergence of the flock, as discussed by the above references.

Materials and methods

The Elsenburg Merino flock

The history of the selection lines is divided into two periods defined by the location of the flock. From 1986 to 1992, the flock was maintained at the Tygerhoek research farm near to the town of Riviersonderend (34°8′S, 21°11′E), in the Western Cape, South Africa. In 1992, the flock was moved to Elsenburg research farm near the town of Stellenbosch (33°51′S, 18°50′E) in the same province. Weather data were available for both sites used during the selection experiment but lambing at the Tygerhoek site generally commenced during the autumn season. The warmer climate thus confounded year or site effects, and data collected during the Tygerhoek period of this experiment were discarded to avoid a biased presentation of the effects of the environmental descriptor (described below).

Except at joining, the two lines were maintained as a single flock of ~200–260 ewes for most of the year. Pregnant ewes were randomly allocated to 10–20 kikuyu lambing paddocks of approximately 0.3–0.4 ha each, prior to the commencement of lambing. Ewes remained in their lambing paddocks for 3–14 days (depending on year and the research conducted), before being drifted from their lambing paddocks onto larger (1–2 ha) Lucerne paddocks in larger groups of 30–40 (Cloete *et al.* 1998). Other details pertaining to management and nutrition are available elsewhere (Cloete *et al.* 2004).

The H- and L-Lines were formed from the same base population at the commencement of the selection experiment in 1986. After the flocks were generated by random sampling within age groups, selection proceeded by screening subsequent cohorts of ram and ewe replacements according to their rankings for number of lambs weaned per joining (Cloete *et al.* 2004). Except for misadventure and severe health issues, replacement ewes remained in the flock for at least five joinings. At the beginning of the experiment, roughly 120 ewes were assigned into each selection line. The H-line has since grown to 130–200 ewes, while numbers in the L-Line decreased to about 40–80 breeding ewes. Selection of rams was predominantly based on the progeny of dams on the basis of at least three joinings. Five rams were initially used for each line and a ram was used only for a single year until 1992, after which two to three rams per line were used across years to provide sire links. Following the results by Cloete *et al.* (2004), selection from 2003 was also guided by the use of best linear unbiased prediction (BLUP) breeding values derived from a single-trait repeatability model fitted to ewe reproduction records. During this period, the original ranking values were still considered in tandem to BLUP-derived breeding values, but BLUP values have been the only selection criterion since 2010. From 2008 to 2019, 349 H-Line lambs and 151 L-Line lambs were born as the progeny of external sires, selected from other flocks on the same criteria as used in the Elsenburg flock (i.e. national or within-flock breeding values for number of lambs weaned per joining/lambing). These animals were also considered for selection and 740 H-Line, and 118 L-Line lambs were subsequently born as grand-progeny of external sires between 2010 and 2019.

Data and recording

The recording of incidences of mortality (0 = lamb survived, 1 = lamb did not survive) and birth weight (BW) took place during daily lambing rounds from 08:00 am that identified all lambs born within the previous 24-h period with their dams, thus enabling linkage back to the selection line and sire (Cloete *et al.* 2004, 2009). Data for lamb survival were recorded as lambs having succumbed at disjoined intervals starting with mortality at birth (MB) and, subsequently, before 3 days of age (M3), tail-docking (MT) and weaning (MW), which sum to total mortality (TM) at weaning. Birth weight was also recorded to the nearest 0.1 kg. The pedigree file identified the sires ($n = 282$) and dams ($n = 2141$) for the vast majority of animals.

Environmental descriptor

Climatic data were available from a weather station near the lambing paddocks. During the entire history (1986–2020) of the selection experiment, 8446 records of BW and mortality were originally recorded. Owing to discarding the data linked to the Tygerhoek site ($n = 1521$) and random technical errors at the Elsenburg weather station ($n = 1202$) where climate data were missing in a few seasons, a reduced data set of 5723 mortality records of 213 sires could be linked to the environmental descriptor. The weather station (33°51′S, 18°50′E, alt: 171 m) was within an 1800 m radius to the furthest boundary of the lambing paddocks used after 1992. The weather station recorded daily data that included windspeed, rainfall and ambient temperature. These data allowed for the quantification of an environmental-stress variable defined as the chill-index (Nixon-Smith 1972; Donnelly 1984). This index estimates heat loss per unit surface area per hour such that

$$\mathrm{CI} = [11.7 + 3.1V^{0.5}][40 - T] + 481 + 418(1 - \mathrm{e}^{-0.04\,R})$$

where CI is the chill index that depicts colds stress as the estimated heat loss (KJ m^{-2} h^{-1}), V is the mean daily wind velocity (m s^{-1}), T is the mean daily temperature (°C) and R is the total daily rainfall (mm). To define CI as a single measure of cold stress, daily data were used to define the mean values for the first 3 days of age, including the date of birth. This definition of CI has been observed as an important predictor to M3, but with little to no relationship for other periods of mortality (Nel *et al.* 2021*b*). Consequently, only M3 was subject to extended analysis in this study and only summary statistics of MB, MT, and MW are reported.

Statistical analyses

Given the discrete expression of the mortality phenotype as either alive (0) or dead (1), it could be beneficial to analyse M3 as a threshold character (Falconer 1989) that considers a hypothetical normal distribution on the underlying liability scale. This issue justifies some comment. Theoretically, linear models are not ideal for the analysis of threshold or binary phenotypes, and the same restrictions would apply to random regression models. However, examples of analysis of survival data on both underlying and observed scale (Matos *et al.* 2000; Everett-Hincks *et al.* 2014; Vanderick *et al.* 2015) have shown that linear models have very similar predictive properties to those of transformed or threshold models. Following this reasoning and leading on from previous examples for survival and/or other binary traits such as fertility (Haile-Mariam *et al.* 2008; Dominik and McWilliams 2014), preliminary analysis evaluated survival data by random regression on the observed scale. However, linear analysis delivered unreasonably high correlation estimates (>0.95) between intercept and slope components of the sire reaction norms (defined below), suggesting that breeding values at a particular point of the environmental trajectory could also have been a function of the mean at that point rather than a true discrimination between sires. Consequently, it was deduced that random regression on a linear scale was unreliable if the incidence (and thus the mean) of the binary variable is very low (e.g. the ~6% incidence observed for M3), likely because the large proportional change in variance across the environmental trajectory is too great a violation of the assumptions of linear models.

Subsequently, analysis commenced on the transformed/underlying scale in two phases. First, fixed effects and the phenotypic relationship between CI and M3 were tested by fitting generalised linear models by using a logit transformation so as to obtain a 'fixed effects' model for downstream analysis. Second, following previous analysis of binary variables by random regressions across time (Tsuruta *et al.* 2009) or across a heat stress index (Brügemann *et al.* 2013), random variance components of M3 were estimated through a threshold model by implementing a Gibbs sampling approach within the Bayesian framework, as outlined below.

Fixed effects

Estimation of fixed effects commenced using the ASREML® program (Gilmour *et al.* 2015). The factors that were considered as fixed included selection line (H-Line or L-Line), sex (male or female), age of dam (2–7+ years), and birth type (singles vs pooled multiples), and BW was also considered as a linear and quadratic covariate. In a preliminary analysis on the phenotypic level, CI was treated as a standard covariate to test for significance and predict mortality rates overall and for comparing selection lines across the cold-stress trajectory. For these phenotypic predictions of selection lines as fixed effects, pedigree information was not included in the model. The least-square means for selection line predictions were estimated on the logit scale and back-transformed to the observed scale by the inverse link function $\pi = \exp(\boldsymbol{x\beta})/[1+\exp(\boldsymbol{x\beta})]$ where $\boldsymbol{x}$ represents the matrix of fixed effects and $\boldsymbol{\beta}$ the vector of solutions for fixed effects. Generally, factors and covariates observed as significant ($P < 0.05$) in this first phase of the analysis were retained in the 'fixed effects model' that provided the basis for estimating random variance components. However, there were some notes pertaining to the 'fixed effects model' applied in estimating genetic parameters, and subsequently used to compare breeding values of the H- and L-Lines. First, since the H- and L-Lines displayed divergent genetic trends for early survival (Nel *et al.* 2021*a*), the effect of selection line was retained as a fixed term to report genetic parameters better aligning to what could be expected from a traditional flock. Subsequently, the selection line term was removed from analysis for comparing H- and L-Line breeding values, and these results are reported separately and retaining 'selection line' as a fixed effect would adjust breeding values accordingly (Cloete *et al.* 2004). Furthermore, to represent the 'population norm' that defines the mean relationship in RN analysis, the relationship between CI and M3 was included only as first-order Legendre coefficients as fixed terms.

The reaction-norm model

For M3 data, RNs were derived by building the genetic relationship matrix according to a sire model. Of the 213 sires with records in the data file, the average sire had ~26–27 progeny and, with variable climatic conditions, sire genotypes could be evaluated by progeny performance at varying levels of the environmental trajectory described by the CI. Subsequently, the RN model was structured as a random regression by fitting a first degree Legendre polynomial nesting-sire genetic effects within the trajectory of the cold-stress gradient, CI. In Legendre polynomials, the values observed for the environmental trajectory (CI) were first standardised to an interval between −1 and 1, aligning with the minimum and maximum values of CI respectively. The standardised value, m, at the ith environmental level was obtained as: $m_i = -1 + 2\left(\frac{\mathrm{CI}_i - \mathrm{CI}_{\min}}{\mathrm{CI}_{\max} - \mathrm{CI}_{\min}}\right)$. The elements m_i are presented in matrix $\boldsymbol{M}$, with dimensions ($t \times n$) dependent on the t environmental levels and n the order of the polynomial. The elements of $\boldsymbol{M}$ are then scaled to the appropriate Legendre coefficients by matrix $\boldsymbol{\Lambda}$. For a first-order polynomial, the resulting Legendre coefficients for three environmental levels (min, intercept, max) can be defined in matrix $\boldsymbol{\phi}$ as follows:

$$\boldsymbol{\phi} = \begin{bmatrix} 0.7071 & -1.2247 \\ 0.7071 & 0 \\ 0.7071 & 1.2247 \end{bmatrix} = \boldsymbol{M\Lambda} \quad \text{where} \quad \boldsymbol{M} = \begin{bmatrix} 1 & -1 \\ 1 & 0 \\ 1 & 1 \end{bmatrix}$$

$$\text{and } \boldsymbol{\Lambda}' = \begin{bmatrix} 0.7071 & 0 \\ 0 & 1.2247 \end{bmatrix}$$

Genetic parameters of the RN model are thus represented as sire variances at the intercept ($\sigma^2_{s_a}$), the slope ($\sigma^2_{s_b}$), and their covariance ($\sigma_{s_{ab}}$). The single-trait threshold model with a random regression on CI was defined as follows (in matrix notation):

$$\boldsymbol{l} = \boldsymbol{X}_1\boldsymbol{b} + \boldsymbol{Z}_1\boldsymbol{m} + \boldsymbol{Z}_2\boldsymbol{s_a} + \boldsymbol{Z}_3\boldsymbol{s_b} + \boldsymbol{e}$$

where $\boldsymbol{l}$ is the vector of unobserved liabilities for observations, $\boldsymbol{b}$ is a vector of fixed effects including the fixed coefficients of the population norm, $\boldsymbol{m}$ the vector of maternal effects, $\boldsymbol{s_a}$ and $\boldsymbol{s_b}$ the sire genetic effects for the intercept and slope respectively, and $\boldsymbol{e}$ is the vector of residual effects. $\boldsymbol{X}_1$ is a design matrix relating $\boldsymbol{l}$ to the appropriate coefficients for fixed effects. $\boldsymbol{Z}_1$ related $\boldsymbol{l}$ to the appropriate random solutions for maternal genetic effects, $\boldsymbol{Z}_2$ and $\boldsymbol{Z}_3$ were design matrices relating $\boldsymbol{l}$ to the sire EBVs for the intercept ($\boldsymbol{s_a}$) and slope ($\boldsymbol{s_b}$), with $\boldsymbol{Z}_2$ containing the Legendre regression coefficients for the intercept on the diagonal (i.e. 0.7071) and $\boldsymbol{Z}_3$ containing the Legendre regression coefficients for the slope corresponding to each record in $\boldsymbol{l}$ on the diagonal.

The variance–covariance structure of random variance components was assumed as

$$\mathrm{Var}\begin{bmatrix}\boldsymbol{s_a}\\ \boldsymbol{s_b}\\ \boldsymbol{m}\\ \boldsymbol{e}\end{bmatrix}=\begin{bmatrix}\boldsymbol{A}\sigma^2_{s_a} & \boldsymbol{A}\sigma_{s_{ab}} & & \\ \boldsymbol{A}\sigma_{s_{ab}} & \boldsymbol{A}\sigma^2_{s_b} & & \\ & & \boldsymbol{I}\sigma^2_m & \\ & & & \boldsymbol{I}\sigma^2_e\end{bmatrix}$$

where $\sigma^2_{s_a}$ and $\sigma^2_{s_b}$ are sire genetic variances for the intercept and slope respectively, σ^2_m is the maternal effect, and σ^2_e is the residual variance. $\boldsymbol{A}$ is the numerator relationship matrix containing sire relationships, and $\boldsymbol{I}$ an identity matrix of the appropriate order. The permanent maternal environmental component (σ^2_c) was determined by subtracting $\sigma^2_{s_a}$ from the total maternal variance (σ^2_m).

The estimation of random variance components was performed within the Bayesian framework, using the THRGIBBS1F90 software package (Misztal *et al.* 2014). In total, 200 000 samples were generated in a single cycle, of which the first 50 000 were discarded as the burn-in period, and the remaining samples were plotted against iterations for visual inspection. A stable convergence of all random variance components was observed within this chain length, and longer cycles were not investigated. Following the burn-in period, every 10th sample was stored, which delivered 15 000 samples for the calculation of posterior statistics such as the posterior means, standard deviation (PSD) and 95% highest posterior density (HPD) confidence intervals. Point estimates reported were based on the posterior mean of the respective variance components.

Covariance functions (CF)

To estimate sire genetic variance at t levels of the environmental descriptor, the matrix $\hat{\boldsymbol{G}}$ of dimensions $t \times t$ was derived as

$$\hat{\boldsymbol{G}}=\boldsymbol{\phi}\boldsymbol{K}\boldsymbol{\phi}' \text{ where } \boldsymbol{K}=\mathrm{Var}[\boldsymbol{s}]=\begin{bmatrix}\sigma^2_{s_a} & \sigma_{s_{ab}}\\ \sigma_{s_{ab}} & \sigma^2_{s_b}\end{bmatrix}$$

where ϕ is a $t \times n$ matrix that contains the n Legendre polynomial coefficients for each of t environmental levels. The ith diagonals of $\hat{\boldsymbol{G}}$ were the estimates of sire genetic variances when $t = i$. In the case of first-degree polynomials, a diagonal element of $\hat{\boldsymbol{G}}$ can be defined as

$$\{g_{ii}\}=c^2\sigma^2_a+2x_i c\sigma_{ab}+x_i^2\sigma^2_b$$

where c is the constant coefficient for the intercept, and x is the appropriate coefficient for the slope at the ith environmental level. The phenotypic (co)variance matrix $\hat{\boldsymbol{P}}$ was determined by summing the variance components where the permanent maternal environmental and residual variances were homogenously added to all elements of $\hat{\boldsymbol{G}}$, as follows:

$$\hat{\boldsymbol{P}}=\hat{\boldsymbol{G}}+\boldsymbol{J_t}\sigma^2_c+\boldsymbol{J_t}\sigma^2_e$$

The heritability (h^2) across t environments are then

$$\mathrm{vec}(h^2)=4\times\mathrm{diag}(\hat{\boldsymbol{G}})/\mathrm{diag}(\hat{\boldsymbol{P}})$$

For threshold models, the mean residual variance is ±1 for a convergent chain of samples. All estimates of h^2 in this study are reported on the underlying scale.

Sire EBVs and selection-line comparisons

The RN of sires with five or more progeny were represented by plotting $\boldsymbol{\phi S}'$ where the first to nth column of $\boldsymbol{S}$ contained the sire genetic solutions and $\boldsymbol{\phi}$ contained the appropriate Legendre coefficients corresponding to the environmental levels for which a particular sire had progeny. This was first reported for sire solutions from the first analysis where selection line was maintained in fixed-model terms. Subsequently, for the RNs of H- and L-Line sires to be compared, sire solutions were derived from the second analysis where selection line was excluded from the fixed terms. The RNs of H- and L-Line sires with progeny in the latter period (born after 2003) of the selection experiment were plotted as previously described but identified by selection line of origin. The timeframe was chosen since genetic trends for perinatal survival reported elsewhere (Nel *et al.* 2021*a*) reported differences between the lines to be more or less manifested by the mid-2010s (following 18–22 years of selection). So as to represent the general trend of H- and L-Line RNs over the duration of the experiment, the intercept and slope solutions of 'pure' H- or L-Line (>75% of line-specific genetic background) sires were plotted for all sires with progeny in the dataset. Simple linear regression lines were fitted to within-line intercept and slope solutions and tested for significant coefficients and divergence using individual standard errors and pooled standard errors respectively. These regression lines were forced through the origin according to the initial start of the experiment in 1985 (year zero).

Results

Summary statistics

In total, 22% of lambs succumbed before weaning. According to partitioned time periods, 4% were recorded dead at birth, 6% died before 3 days of age (M3), 6% before tail-docking and the remaining 7% before weaning. Lambs were thus particularly susceptible in the 3-day period defined by M3, since this narrow timeframe contributed a large proportion (27%) of the total incidence of mortality within only the first three days of age. The mean rate of heat loss (CI) of the three days following birth across all observations of M3 was 963.5 KJ m^{-2} h^{-1}. The dataset was adjusted for 40 erratic records by deleting values of CI outside of the interval between 800 and 1250 KJ m^{-2} h^{-1} to better fit a normal distribution (Fig. 1). However, the dataset remained skewed slightly right with a longer tail of higher CI values. This was considered acceptable for downstream analysis, but had implications for the interpretation of the 'intercept' component of regression equations. According to Legendre polynomials, the intercept (as the midpoint between $t_{\max}$ and $t_{\min}$) was represented by 1025 KJ m^{-2} h^{-1}, which was higher than the aforementioned arithmetic mean.

Fixed effects

The outcome of M3 was affected by birth type ($P < 0.01$) but not sex ($P > 0.05$), with multiples being more likely to succumb. However, the inclusion of BW as a linear covariate eliminated these effects, indicating that BW was the primary driver of these differences between singles and multiples. According to the retransformed values from the logit scale, selection lines differed ($P < 0.01$) substantially in their incidence of neonatal mortality, with M3 for the L-Line (0.051 ± 0.007) about 46% higher than the predicted rate for H-Line lambs (0.035 ± 0.004).

On the phenotypic level, the CI was an important ($P < 0.01$) predictor for M3, and Fig. 2 shows the predicted M3 with an increasing cold stress for the whole population, as well as for individual selection lines. When cold stress was absent, M3 was below 2%, but could increase to nearly 15% when levels of cold stress were extreme (~1200 KJ m^{-2} h^{-1}). The L-Line lambs appeared particularly susceptible when subjected to these conditions (Fig. 2), but the wide standard errors surrounding these predictions point to limited statistical power at the extreme upper levels of the environmental trajectory.

Posterior distributions

The posterior distributions for the random variance components can be seen in Fig. 3. Skewed distributions of the intercept ($\sigma^2_{s_a}$) and slope components ($\sigma^2_{s_b}$) attributable to sires were visible, but this could be expected given that the low estimates of M3 were approaching the lower theoretical boundary. A modelled G × E component played an important role in mortality outcomes, with the mean estimate (and 95% confidence interval) for the slope ($\sigma^2_{s_b} = 0.113[0.0019\text{–}0.28]$) only marginally smaller than the corresponding estimate for the intercept ($\sigma^2_{s_a} = 0.124[0.003\text{–}0.26]$), suggesting a strong influence of the environmental trajectory on sire breeding values. The mean estimate of the covariance between the intercept and slope components was positive in absolute direction ($\sigma_{s_{ab}} = 0.064$), but included some negative values, with a 95% HPD confidence interval between −0.074 and 0.22 (Fig. 3). The correlation was positive and moderately high ($r_{ab} = 0.541$), suggesting that sires favoured at the intercept tended to retain their ranking as the CI increased. The posterior distribution for the total maternal component was normal (Fig. 3) and with a comparatively large mean estimate ($\sigma^2_m = 0.42[0.24 - 0.61]$). An estimate of the dam permanent environmental variance ratio (σ^2_c) was derived ($\sigma^2_m - \sigma^2_{s_a}$) as 0.30, which was thus the largest random variance component affecting M3 after excluding the residual variance ($\sigma^2_e = 1.0025[0.95 - 1.06]$).

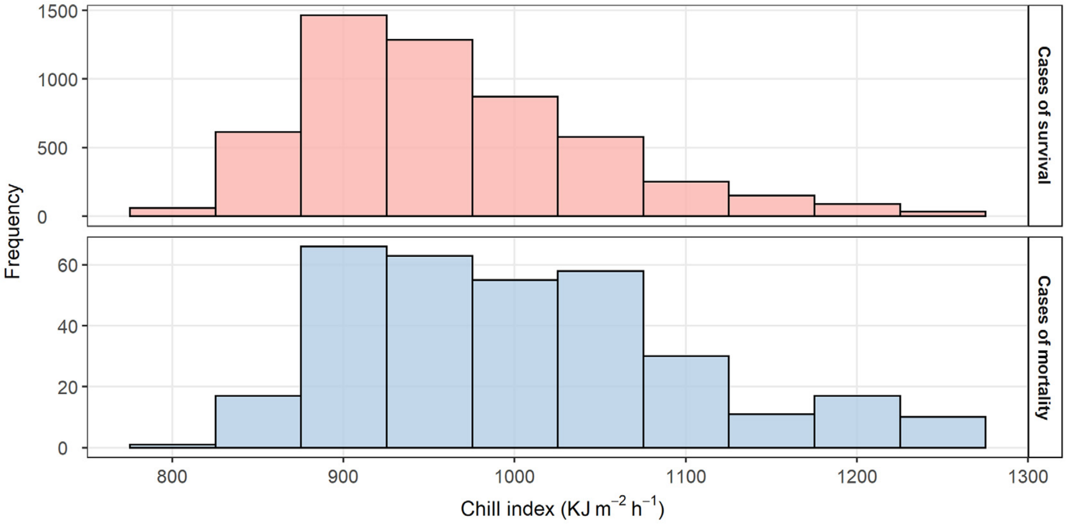

Fig. 1. Observed frequencies of observations of lamb survival or neonatal moratlity (to 3 days of age; M3) across levels of the chill index (CI) for the period of 1993–2020.

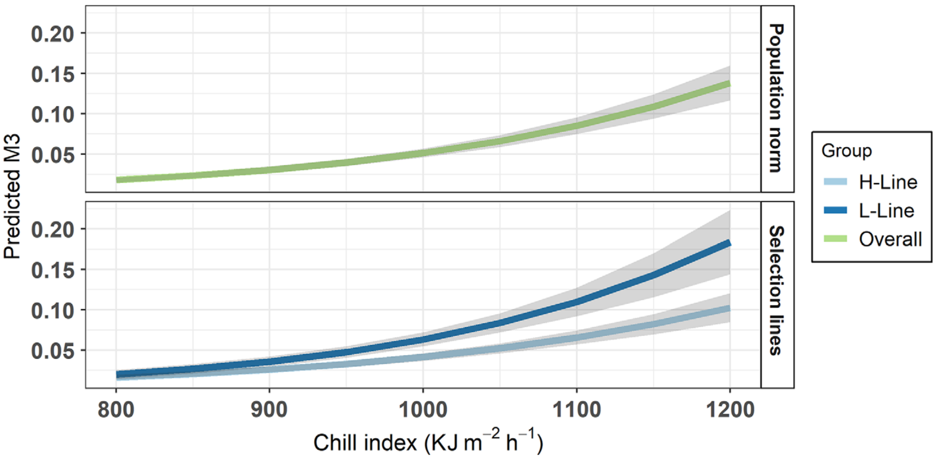

Fig. 2. Predicted neonatal mortality (M3) across the cold-stress gradient (CI) for the whole population, as well as within individual H- and L- selection lines. For these predictions, selection lines were compared as fixed effects, without considering information in the pedigree.

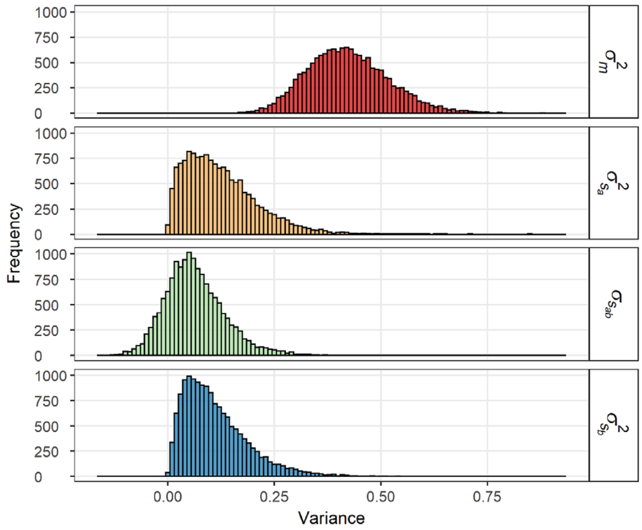

Fig. 3. Posterior density distributions for the sire reaction-norm intercept $\sigma^2_{s_a}$, slope ($\sigma^2_{s_b}$) and covariance ($\sigma_{s_{ab}}$) and total maternal variance (σ^2_m) components of neonatal mortality (M3).

Heritability of M3 across the cold-stress trajectory

The magnitude of the h^2 of M3 varied considerably according to the intensity of cold stress during the neonatal period (Fig. 4). Surrounding the environment of the mean (~960 KJ m^{-2} h^{-1}) or that of the intercept (1025 KJ m^{-2} h^{-1}), h^2 (mean ±PSD) was moderately low (h^2 = 0.13 ± 0.10 to 0.15 ± 0.11). Following an increasing gradient of CI, absolute h^2 accordingly increased markedly with the intensity of cold stress. At ~1100 KJ m^{-2} h^{-1}, absolute h^2 was moderate (0.22 ± 0.16), but tended towards values as high as 0.40 at levels of extreme cold stress where the CI was 1150 KJ m^{-2} h^{-1} or larger. Along with the marked changes in absolute h^2, it was clear that the reliability of h^2 estimates also continuously decreased for estimates extending further away from the mean, with the largest PSD being observed at either end of the environmental trajectory. Following the curvilinear trend of the resulting parabola, a slight increase in absolute h^2 was also observed for lower values of the CI gradient, an estimate of 0.22 ± 0.17 when CI was ~850 KJ m^{-2} h^{-1}. The wide PSD margins are arguably a function of the small data set and complicate comparisons among h^2 estimates.

Individual-sire reaction norms

Sire RNs suggested a highly variable ES across sire genotypes (Fig. 5). With an increasing cold stress, there was more discrimination across sire breeding values, especially when the CI exceeded ~1000 KJ m^{-2} h^{-1}. Some evidence of re-ranking was also visible at CI gradients between 850 and 900 KJ m^{-2} h^{-1}, but in these cases sire RNs tended to intersect below the environment of the intercept of ~1025 KJ m^{-2} h^{-1}. This is also expected from the positive correlation (0.54) between the intercept and slope components, which suggested that sires tended to maintain their ranking at the intercept across increasing values of the CI trajectory.

From a separate analysis where selection line was excluded as fixed effect, the patterns of RN generally resembled the same patterns as for Fig. 5, but the RNs of H-Line sires were generally associated with favourable rankings predicting a greater resistance to mortality as cold stress progressively increased (Fig. 6). It was also clear that the scale separating the RNs was influenced by the removal of the selection line fixed effect, with considerably larger differences between sire RNs in Fig. 6 than in Fig. 5. Similar to Fig. 5, sire reaction norms tended to intersect below ~900 KJ m^{-2} h^{-1}, but any evidence of re-ranking would apply only to very low values of CI not rigorously tested in this dataset.

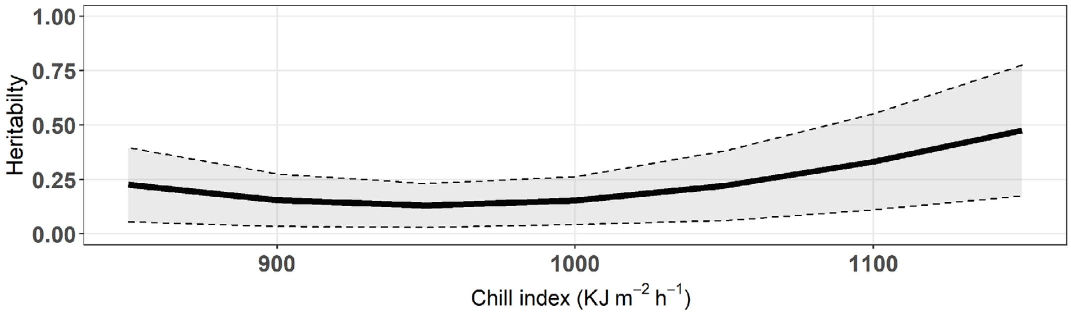

Fig. 4. The heritability (h^2) of neonatal mortality (M3) across a cold-stress gradient represented by the chill index (CI). Estimates are presented on the underlying scale. Dotted lines represent the posterior standard deviation of the estimates.

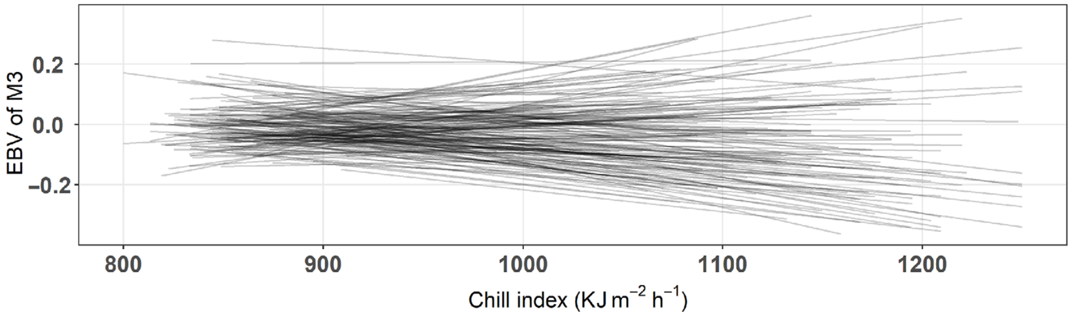

Fig. 5. Estimated breeding values for neonatal mortality M3 as sire reaction norms across the cold-stress gradient (CI). Lines are plotted only for the range in which the specific sire had progeny. M3 is neonatal mortality at 3 days of age.

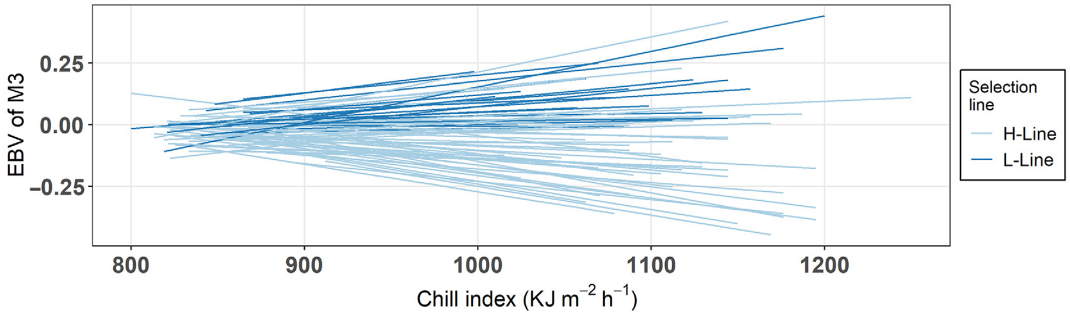

Fig. 6. Estimated breeding values for neonatal mortality (M3) as H- and L-Line sire reaction norms across the cold-stress gradient (CI) for sires born 2004 or later. Lines are plotted only for the range in which the specific sire had progeny. M3 is neonatal mortality at 3 days of age.

Individual intercept and slope components of H- and L-Line sires can be seen in Fig. 7, which shows that the selection line solutions trend in favour of the H-Line sires from the year 1994 onward. The coefficients of the linear regressions fit within line for both intercept and slope components of sire RNs were significant ($P < 0.01$) as the H-Line trended downward for the intercept (−0.0046 ± 0.0008) and slope (−0.0024 ± 0.0005) components. These trends were divergent ($P < 0.01$) from L-Line trends that were upward for the corresponding intercept (0.0047 ± 0.0008) and slope (0.0028 ± 0.0006) components (Fig. 7).

Discussion

Genetic parameters for neonatal lamb mortality according to the RN model

This study has shown that a G × E component could play an important role in the genetic basis for neonatal mortality. The

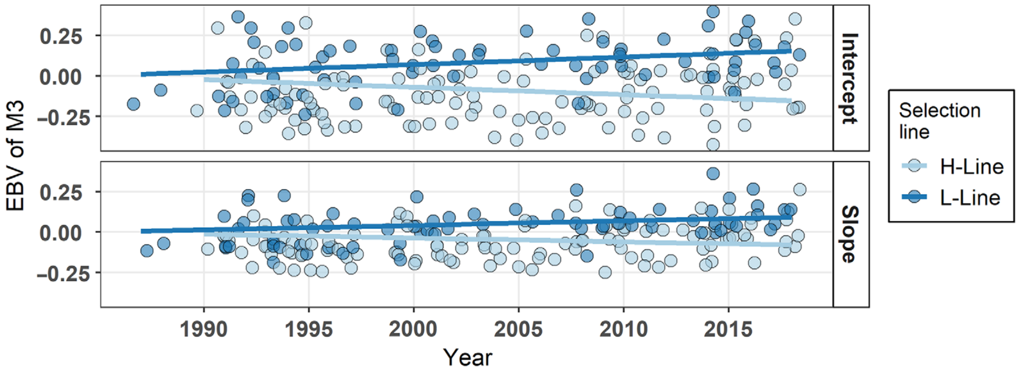

Fig. 7. Linear regression lines fitted to individual intercept and slope components of H- and L-Line sires with progeny born at the Elsenburg site (>1993). M3 is neonatal mortality at 3 days of age.

magnitude of the $\sigma_{s_b}^2$ component and the variable h^2 (Fig. 4) suggested that genetic merit of M3 depended considerably on the environment during the first days after birth. To our knowledge, this is the first study to model the genetic merit of neonatal mortality (or survival) as a function of cold exposure, and no directly comparable results were found in the literature. The influence of fixed effects in the Elsenburg Merino dataset has been discussed elsewhere (Nel *et al.* 2021*a*, 2021*b*; Nel 2022) and are not repeated here. Instead, only genetic parameters will be highlighted, with the additional treatment of the H- and L-Lines.

Estimates of h^2 at the intercept ($h^2 \sim 0.13$–0.15) could be considered high compared with the very low values common for lamb survival/mortality traits (see review Brien *et al.* 2014), but the differences in data and approach of analysis complicate direct comparisons. First of all, the intercept point on the environmental trajectory (~1025 KJ m^{-2} h^{-1} in the current study) is sensitive to the distribution of CI in a particular dataset. Currently, it was also slightly higher than the arithmetic mean (~960 KJ m^{-2} h^{-1}) and arguably represents a significant level of cold stress. An interpretation of the intercept component ($\sigma_{s_a}^2$) as an estimate directly comparable to the 'average environment' assumed by standard genetic analysis is thus not entirely appropriate.

Furthermore, the magnitude of variance components also tends to vary according to the framework used for the analysis of binary survival/mortality phenotypes. A very low h^2 of 0.03 ± 0.01 (±standard error, or s.e.) for perinatal survival (up to 3 days of age, but also including survival at birth) was derived from the animal model from the same flock, but reported on the observed scale from linear model analyses (Nel *et al.* 2021*a*). Other estimates derived for Merinos by linear models yielded similarly low h^2-values of 0.04 (Brien *et al.* 2009*b*) for survival up to 3 days of age and 0.02 (Hatcher *et al.* 2010) for survival up to 7 days of age. However, on the underlying scale, Cloete *et al.* (2009) reported a h^2 (±s.e.) of 0.12 ± 0.06 for lamb survival from birth to tail docking (~3–4 weeks), and 0.39 ± 0.23 for tail docking to weaning from the same dataset (only including records up to 2007). A h^2 estimate of 0.11 was also reported for total survival (to weaning) from a threshold analysis by Welsh *et al.* (2006). Accordingly, Matos *et al.* (2000) reported that the threshold model h^2 of total survival was about three-fold the magnitude of that derived by linear models in the same study. In other species, Weller *et al.* (1988) reported h^2 estimates for calf mortality from sire threshold models (0.084) also between three- and four-fold of that derived by linear analysis (0.027). A pattern of differences in h^2 is thus visible across analyses, but is expected given the loss of information when treating binary traits on the observed scale.

Regardless of the approach in analysing survival/mortality datasets, the low h^2 of survival traits have led to the suggestion that genetic selection for improved outcomes would not be worth-while (Everett-Hincks *et al.* 2005; Everett-Hincks and Cullen 2009). However, it stands to reason that a variable h^2 as observed in Fig. 4 is plausible when a phenotype is directly linked to an environmental covariate such as mortality and cold stress. In addition to the current results (Fig. 2), the moderate to severe impact of cold exposure on early lamb mortality has been well documented (Alexander 1962; Obst and Day 1968; Alexander *et al.* 1980; Mccutcheon *et al.* 1981), including studies that quantified cold stress by the same or a similar chill index (Donnelly 1984; Gudex *et al.* 2005; Oldham *et al.* 2011; Geenty *et al.* 2014). A base level of mortality can always be expected (Alexander 1984). In some cases, the genetic make-up of the lamb will have little to no influence (e.g. misadventure) on mortality outcome, and the phenotypes will be of little value as indicators of stress resilience. In turn, if M3 is recorded during events characterised by significant levels of cold stress (e.g. 950–1000 KJ m^{-2} h^{-1} or higher), these phenotypes arguably reflect an ability to cope with the stress variable. Assuming that this resilience is significantly influenced by genetic variation, it is plausible to expect an increase in h^2 (Fig. 4), as well as an increased scope to discriminate between sires (Fig. 5) in higher cold-stress conditions. The contention for such genetic components is supported by considering that cold-stress resistance is affected by sire lines (Gudex *et al.* 2005) as well as short-term (4 year) selection experiments (Slee and Stott 1986). The few estimates of the h^2 of cold-stress resistance were estimated with a suboptimal accuracy and from outdated parent–offspring regression methods, but has been reported as moderate (0.44 ± 0.18; Wolff *et al.* 1987) to high (0.52 ± 0.23; Slee *et al.* 1991) after also adjusting for BW.

A high dependence of genetic parameters on the environmental trajectory has important implications for traditional selection programs where the weighted merit of performance in mild and stressful environments is considered equal. This describes the general issue of G × E, which reduces the response to selection when breeding programs do not account for such effects (Mulder and Bijma 2005).

The increase in h^2 estimates suggested that greater genetic gains are possible if selection is focused on cases of survival/mortality known to be recorded in stressful environments. Fig. 4 delivers the first formal presentation of the much earlier suggestion by Haughey (1991) that selection targets genotypes 'born during, and surviving severe weather conditions'. However, the h^2 estimates at the ends of the trajectory could be judged unrealistic also from the perspective of the underlying scale. The limitation of only few data points outside of ~850–1200 KJ m^{-2} h^{-1} (Fig. 1) is also clearly reflected by the higher PSD of h^2 (Fig. 4). Even in large or uniformly distributed datasets, the reliability of Legendre polynomials has been a concern when approaching the extremes of the trajectory in random regression analysis (Van Der Werf *et al.* 1998; Meyer 2001; Fischer *et al.* 2004), and should be treated with caution beyond the bulk of the data.

The evidence for re-ranking of genotypes (Figs 5, 6) and the apparent increase in h^2 at low levels of CI (Fig. 4) also deserves some comment. This was an interesting observation, but most likely a mathematical consequence of considering only first-order Legendre polynomials. With only limited flexibility to model breeding values over the entire range of the cold-stress trajectory, the resulting parabola would inevitably be symmetrical around the vertex (~950 KJ m^{-2} h^{-1}), which would explain the slight increase in h^2 below 900 KJ m^{-2} h^{-1} (Fig. 4). Since there were few records with CI < 850 KJ m^{-2} h^{-1}, this is thus likely to be an artefact of the model reflecting the increase in h^2 at high CI, rather than a genuine result when CI is low. Higher-order models could improve on these results, but we maintain that the restriction to linear RNs was a worth-while trade-off for the benefit of simplicity when analysing a binary trait of low incidence.

It would be of interest to revisit this issue on a larger dataset recorded across a wider range of climatic variables. At values of CI of <850 KJ m^{-2} h^{-1}, the environment could be approaching a temperature gradient that is too low for animals to dissipate heat at a favourable rate, i.e. resulting in heat stress. If the merit of cold-stress resistance can be supported from future studies, a critical question would be whether the same 'cold-resistant' animals are able to cope well with hot and humid weather. Different breeding programs would be needed if the genetic correlation among points along the environmental descriptor is low, and especially when it is negative (Mulder *et al.* 2006). From this perspective, it is essential to consider that the genetic improvement of M3 depends not only on where the h^2 is highest (e.g. 1000–1100 KJ m^{-2} h^{-1}), but also on the environment where the progeny will be tested (Kolmodin and Bijma 2004), and it is certain that a much wider CI range is possible if a dataset were to include different areas and seasons. For example, at the Tygerhoek site that made use of an autumn lambing season, lambs were sometimes born when CI was ~780 KJ m^{-2} h^{-1} or lower (data not shown). At this level, the mean temperature over 24 h reached 22°C and the maximum temperatures regularly reached 28°C or higher. Excluding the effect of wind or rainfall, this range of CI could putatively have represented a degree of heat stress, since the upper critical range for adult sheep is roughly between 25°C and 32°C (Hahn 1985). However, the effects of high cold exposure are likely to be the biggest constraint to lamb production in an extensive winter lambing season in the H- and L-Lines, suggesting that G × E components could be exploited to improve fitness in a winter-lambing season when CI-values are within the cold-stress range.

Genetic gains in the Elsenburg selection lines

Cold-stress adaption was likely a key mechanism contributing to the favourable outcome of the Elsenburg selection experiment. Theoretically, the RN approach delivers an opportunity to improve 'overall' performance by selecting for an increased performance in the average environment (i.e. the intercept), instead of selecting for genes that are beneficial only in selected environments (i.e. the slope; de Jong and Bijma 2002). However, in the current dataset, the average environment presented at least some level of cold-stress challenge, and it is thus reasonable to assume that adaption to these circumstances would have played a role in the divergent selection responses separating the H- and L-Lines (Fig. 7).

The resulting differences in H- and L-Line RN slopes (Fig. 7) supported previous contentions that a positive correlation between the intercept and slope can lead to favourably exploiting ES when selecting for performance at the intercept (Kolmodin *et al.* 2003; Knap and Su 2008). G × E scenarios where genotypes intersect or cross to the left of the intercept (Figs 5, 6), are beneficial if exploiting G × E is the objective, since favourable changes in the slope are reflected in the same direction at the intercept (see figs 3, 4 of Falconer (1990)). This was supported by the positive and moderately high correlation (r_{ab} = 0.54) between intercept and slope components, although this estimate did not differ from zero with this specific dataset. A more reliable estimate of genetic correlation is needed from larger datasets, but the argument is well supported on the phenotypic level, showing H-Line lambs to be better at maintaining homeothermy under cold-stress conditions (Nel *et al.* 2021*b*). Also, a selection history that successfully exploited G × E components offers at least a partial explanation for the rate of genetic gain (Cloete *et al.* 2009; Nel *et al.* 2021*a*) exceeding expectation for survival traits (Fogarty *et al.* 2006; Brien *et al.* 2009*a*). The mean performance of H-Line lambs, also clear on the phenotypic level (Nel *et al.* 2021*a*, 2021*b*), could thus have benefited from the higher h^2 observed for the upper levels of the CI (Fig. 4). However, considering the RNs of H-Line genotypes as favourable to robustness depends on the assumption that the next generation will be tested within generally similar environmental conditions present during selection of previous generations. More elaborate studies are thus needed, and some suggestions are outlined below.

Future perspectives

The understanding of the G × E components of neonatal mortality would benefit from studies across environments with a larger window of climatic variation. Highly variable environments are a realistic concern in South Africa where sheep production is spatially dispersed over regions with vastly variable climates and marked differences in available resources (Cloete and Olivier 2010; Cloete *et al.* 2014). More comprehensive studies are important, since the results reported here are relevant to the growing interest in selecting animals more resilient to the extreme environments anticipated from climate change (Hayes *et al.* 2013; Misztal 2017; Berghof *et al.* 2019).

Linking cold stress to mortality up to 3 days of age, but excluding birth, has also recently been supported by Horton *et al.* (2019). Since climate data are commonly available, large-scale studies linking climatic stress to neonatal lamb performance (e.g. M3) is possible wherever time of death was recorded reasonably close to weather stations. This approach is also attractive because a reliable and independent covariable circumvents some of the issues of environmental trajectories based on contemporary group means (Strandberg 2006). Good examples of the large-scale implementation of such a system were evident in genetic analyses of heat-stress sensitivity in dairy cattle (e.g. Ravagnolo and Misztal 2000, 2002; Bohmanova *et al.* 2008; Cheruiyot *et al.* 2020).

Improvements on the recording program are also possible. A better phenotyping protocol was proposed by Gudex *et al.* (2005) that eliminates obvious causes of death not typified by an aetiology indicative of starvation–mismothering-exposure. A variation of the survival phenotyping protocol outlined by Vanderick *et al.* (2015) could also be useful. Also, if records from an autumn or early summer lambing season were to be included, the use of the current equation for CI (Nixon-Smith 1972) is not the ideal descriptor of heat stress. In contrast, the temperature–humidity index (Ravagnolo and Misztal 2000) commonly used to model heat stress does not account for the cooling influence of wind or rainfall. An appropriate bilateral stress index is needed to investigate the hypothesised antagonism between climatic extremes. Last, additional recording of phenotypes indicating animal wellbeing (see review Brito *et al.* 2020) will be more expensive than are survival records, but could deliver multiple benefits, including the following: they will be more articulate in indicating resilience; will be simpler to analyse than is M3 (which is binary and of low incidence); and could benefit from the gains in accuracy of including genomic information (Mulder 2016). For example, rectal temperature has been used in field studies of cold-stress resistance (Sykes *et al.* 1976; Nel *et al.* 2021*b*), and can be easily adopted into the lambing rounds, which is standard protocol for breeding flocks that maintain a pedigree (Brien *et al.* 2010).

Conclusions

This study was the first to show that a G × E interaction with cold exposure plays an important role in determining genetic merit for neonatal mortality. The findings support previous notions that G × E is generally largest in fitness traits, which partially explains the low h^2 of such traits recorded across variable environments. Comparing the RNs of selection lines showed that divergent selection for a correlated trait (number of lambs weaned per ewe mated) resulted in worth-while gains in fitness as described by the G × E model fitted. However, this positive result is likely to be linked to perpetual selection of the same population within a relatively stable environmental descriptor. Better gains could be possible if the environment at recording could be quantified and accounted for in genetic evaluation. Re-ranking of genotypes suggests that genetic adaption to cold stress could be detrimental to animal resilience in hot environments, but research across a wider environmental trajectory is needed to confirm or refute this notion.

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