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ACCOMMODATING VARIABLE DISEASE CHALLENGE ON BREEDING VALUE PREDICTION FOR SIRES – USING FOOTROT AS AN EXAMPLE

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SUMMARY

Footrot is a highly contagious hoof disease of sheep, the expression of which depends on environmental conditions and the presence of infective strains of bacteria. Footrot scored from field exposure is, therefore, a potentially difficult trait to analyse across time and production environments. This study explores the use of pre-analysis transformation techniques to account for the disease incidence and pattern of scores obtained, using footrot as an example. A biological transformation, where the phenotypes were transformed to a similar incidence level based on a non-linear transition of scores over time produced the highest rank correlation of the sire's breeding values across challenges compared to more traditional statistical transformation techniques. The results suggest that using a transformation based on biological information is likely to improve the estimation of breeding values for footrot.

INTRODUCTION

Footrot is a highly contagious and difficult to manage hoof disease in sheep that begins with interdigital dermatitis and progresses to separation of the hard horn from the foot (Mulvaney 2013). Infection and progression of footrot within the flock is heavily influenced by the prevailing weather conditions and the presence of the infective bacteria *Dichelobacter nodosus*, with onset occurring approximately 5 days after exposure in susceptible animals (Nieuwhof *et al.* 2009).

Footrot records from field data are collected as a result of uncontrolled natural footrot challenges. Consequently, the incidence of footrot (affected vs unaffected) and the distribution of scores for affected animals, affecting means and variances, will vary within the data used for genetic evaluation. These factors result in sire breeding values (SBV) that may not accurately predict progeny performance when faced with a subsequent footrot challenge under different environmental conditions. To overcome the heterogeneity across challenges there are multiple options including: arithmetic transformations, scaling observations with the phenotypic standard deviation, or fitting multiplicative mixed model equations (Huisman *et al.* 2016). There is an assumption associated with many of these transformation techniques that the data are normally distributed and that the standard deviation decreases as the mean nears the extremes of the categorical scores. However, these assumptions are not valid for disease traits such as footrot, where variation in the animal's susceptibility means that the phenotypic variation within a challenge is unlikely to be normally distributed and can become heavily dominated by a single score.

This paper explores the use of pre-analysis transformations to adjust for differences in disease incidence and the distribution of scores between footrot challenges, using New Zealand Merino central progeny test data from 2013 and 2014.

MATERIALS AND METHODS

In each of 2013 and 2014, approximately 2,000 commercial fine wool NZ Merino ewes were artificially inseminated to 40 Merino type rams (one link ram). Rams were perceived as trait leaders for footrot or other key production traits and considered to be widely used and linked to the NZ

[1]AGBU is a joint venture of the NSW Department of Primary Industries and University of New England

Merino industry. The commercial ewe flock (no pedigree available) were aged between 2 and 6 years and were declared free of footrot at the start of the trial. The ewes and resulting progeny were managed in Waipara, New Zealand. The 2014 progeny were not mothered up and thus dam, birth type and rear type were unknown for these animals.

The project was designed to move the yearling wether progeny (n= 1,300) in the spring-summer period to a footrot-infected property where they would be run with infected sheep on waterlogged paddocks. Each foot was scored on a 5 point scale, with 0 being not affected and 1 to 5 representing different degrees of severity of foot damage, from water maceration (1) to chronic footrot (5) (Mulvaney 2013). The footrot challenge was deemed to have occurred when 20 to 30% of a weekly subsample were considered underrun. The 2014 progeny were recorded twice (20 day difference) during the challenge period (Table 1). An unexpected footrot outbreak occurred in the 2013 progeny in autumn at Waipara, animals were scored and subsequently treated. The trait analysed in this study was the average footrot score ($\overline{x}_{fs}$) of all four feet (0-5).

Table 1: Summary of footrot records for the 2013 and 2014 progeny

					Proportion of feet in category					
Drop	**Challenge**	**Records**	**Mean**	**SD**	**0**	**1**	**2**	**3**	**4**	**5**
2013	Autumn	725	2.75	1.40	0.01	0.32	0.10	0.07	0.49	0.01
	Spring	715	1.99	1.59	0.09	0.48	0.18	0.05	0.04	0.17
2014	Summer	621	2.92	1.07	0.03	0.12	0.07	0.45	0.33	0.00
	+20 days	621	3.37	1.39	0.08	0.11	0.00	0.03	0.72	0.05

The heritability and sire breeding values were estimated from a sire model using ASReml (Gilmour *et al.* 2009). The fixed effects model fitted included birth type (1,2,3,4+), rearing type (1,2,3+), age of dam (linear and quadratic covariates), age (linear) and year of birth effect (YOB) (2). To account for genetic diversity between sires, sire breed and strain (Dohne, Corriedale, Polworth, South African Meat Merino, Merino and Poll Merino) were fitted as a random term and the genetic group proportions (10 groups) (Brown and Swan 2016) of the sire were fitted as fixed effects. The analysis was undertaken using a single record for each animal, with the 2013 progeny records coming from the spring challenge and the 2014 progeny records coming from the summer challenge (Table 1), except when noted.

To account for the incidence of footrot within each challenge several pre-analysis transformation techniques were explored. These include (1) no adjustment (transformed observation $y^* = \overline{x}_{fs}$), (2) fitting a mixed model allowing for a heterogeneous residual applied to each challenge, (3) transformation to a mean score of 2.5 ($y^* = (\overline{x}_{fs} / \overline{x}_{year}$ of year cohort) × 2.5), (4) standardised to a mean of 0 and a SD of 1 ($y^* = ((\overline{x}_{fs} / \overline{x}_{year})$ / SD of year cohort)), (5) standardised to a mean of 0 and a weighted SD that accounts for the decline in variation as the mean nears the extremes ($y^* = ((\overline{x}_{fs} / \overline{x}_{year}) / SD_{year}) \times$ weighted SD_{year}), and (6) transformation based on a biological model for the progression of scores over time. Under the assumption that the rate of progression between scores is not equal and that simple linear transformations of average values are therefore inaccurate, we developed a biologically based transformation. Data from the 2014 challenge provided 2 scoring events 20 days apart. From the two time points recorded, a transition matrix based on probability of change could be estimated (Table 2). Using this transition matrix the challenge data for each foot could be progressed forward to the n^{th} day to achieve a common incidence (affected vs unaffected) across challenges, based on the weighted probability of change from each score. This generated for each foot a transformed score (rounded to an integer) that was then averaged to produce y*. Based on the very high genetic correlation between the two time points (0.99 ± 0.23) and the very low heritability for change in score (0.08 ± 0.09), it was assumed that the genetic merit of the sires was

constant and differences in incidence between scoring events were predominantly due to the prevailing production environment. To test the biological transformation, the 2013 data from both spring and autumn events was transformed based on the biological model (developed from 2014 data) to a similar incidence to 2014 challenge (approximately 15% of feet were scored 0 or 1).

Table 2: Probability of a foot transitioning from one score to another score for the front and back feet (parentheses) after 20 days during the 2014 challenge.

	Front footrot score 20 days later						Back footrot score 20 days later					
Footrot score	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
0	0.51	0.46	0.01	0.00	0.01	0.00	0.20	0.80	0.00	0.00	0.00	0.00
1	0.42	0.49	0.00	0.01	0.07	0.00	0.26	0.37	0.00	0.11	0.26	0.00
2	0.05	0.23	0.03	0.08	0.60	0.02	0.04	0.19	0.03	0.09	0.65	0.00
3	0.00	0.00	0.00	0.11	0.84	0.05	0.00	0.00	0.00	0.12	0.84	0.04
4	0.00	0.00	0.00	0.00	0.82	0.18	0.00	0.00	0.00	0.00	0.93	0.07
5	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00

RESULTS AND DISCUSSION

The impact of alternative models or transformations on parameter estimates are presented in Table 3. The heritability of footrot ranged from 0.11 to 0.35 across challenges with an average of 0.19 and were found to not be significantly different across transformation models. The additive variance was relatively similar across all models and transformations. It should be noted that the additive variance was greatest when the data was transformed to a common mean or standardised to a common SD, as in all cases the manipulation of raw data values lead to an increase in the phenotypic variation of the 2013 and 2014 challenges, respectively. Allowing for heterogeneous residuals highlighted that the variation in the 2013 spring challenge had almost 4 times the variation of the 2014 summer challenge. In contrast, the biological transformation of the 2013 data to a common incidence resulted in no significant change to the variation in scores. Adjusting to a common incidence and not a common mean implies that the original distribution of the raw data remains informative and is reflected after the biological adjustment.

Table 3: Impact of transformation of footrot records on parameter estimation

	2013 Progeny		2014 progeny		Residual	Additive	
Model/Transformation	**Mean**	**SD**	**Mean**	**SD**	**Variance**	**Variance**	**Heritability**
(1) No adjustment	1.99	1.09	2.92	0.60	0.744	0.150	0.19 +/- 0.07
(2) Heterogeneous Residual	1.99	1.09	2.92	0.60	(2013) 1.116	0.126	0.11 +/- 0.04
					(2014) 0.327		0.35 +/- 0.12
(3) Transformed	2.50	1.36	2.50	0.51	1.057	0.194	0.18 +/- 0.07
(4) Standardised	0.00	1.00	0.00	1.00	0.930	0.228	0.23 +/- 0.07
(5) Weighted Standardisation	0.00	1.09	0.00	0.61	0.767	0.155	0.19 +/- 0.07
(6) Biological Transformation	2.83	1.09	2.92	0.60	0.778	0.138	0.17+/- 0.07

*standard errors ranged from 0.04 to 0.07 for the variance estimates and for heritability from 0.07 to 0.12

Pre-analysis transformations are generally used to lessen the impact of the variation in the outcomes from uncontrolled challenge or scoring events on the spread and rank of sire breeding values. Therefore, under the assumption that the genetic correlation between two separate challenge events should also be high, the appropriate pre-analysis transformation should result in similar SBVs for the 2013 sires, regardless of whether the progeny's performance was recorded in the autumn or spring challenge data. The rank correlation for the 2013 sires estimated from the autumn vs spring

challenge was 0.56 when the data was untransformed (Figure 1a). Rank correlations between the two challenges were not improved by fitting a heterogeneous residual (model 2) (0.51), or when the data were transformed to a common mean (3) (0.49), standardised (4) (0.48), or weighted standardisation (5) (0.49). However, when the challenges were transformed to the same incidence of footrot (~15% uninfected) based on the transition matrix (biological transformation) the rank correlation increased (0.81) (Figure 1b). These results suggest that the biological transformation, which adjusted the challenges to a similar disease incidence, resulted in SBVs which were a truer representation of the sires' merit, both in rank and relative superiority.

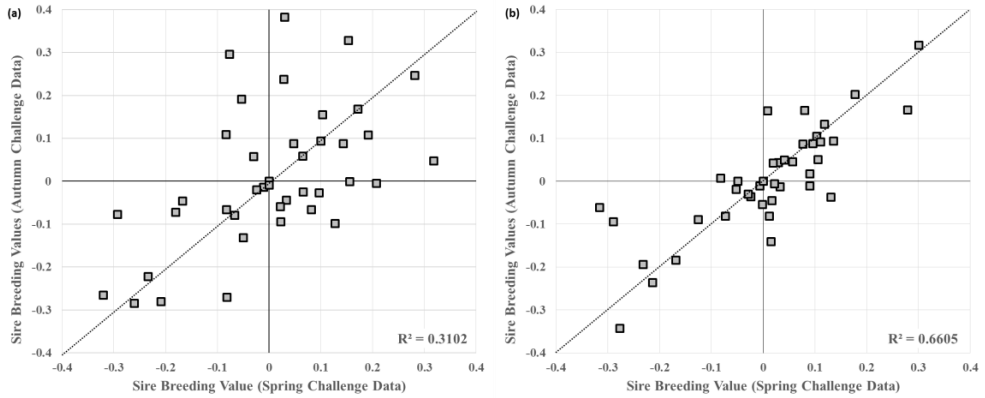

Figure 1: Breeding values for the sires of the 2013 progeny estimated from the autumn and spring challenges from the raw footrot data (a) and when biologically transformed to a similar disease incidence (15% of feet uninfected) (b)

CONCLUSION

These results suggest that pre-analysis transformations based on a non-linear disease progression improved comparison across sires when data from progeny are from uncontrolled challenges, differing both in incidence at scoring and the distribution of scores. Whilst the proposed biological transformation can be used to transform data to similar incidence levels, the analysis of footrot is still dependent on the challenge being strong enough for the variation in sires to be expressed. The bounded nature of the scoring system means that, at both ends of the challenge, the phenotypic variation will compress, which cannot be overcome by the biological transformation. Further research into the use of a transition matrix to develop suitable data transformations and the influence of genetics on the progression of footrot needs to occur as more data becomes available.

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