

1 Running head: Evaluation of GeneMax Advantage

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3 **Evaluation of Zoetis GeneMax Advantage genomic predictions in commercial *Bos taurus***

4 **Angus cattle**

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21

22 **ABSTRACT:** The GeneMax (GMX) Advantage test, developed by Zoetis, uses approximately
23 50,000 single nucleotide polymorphisms (SNP) to predict the genomic potential of a commercial
24 Angus heifer. Genetic predictions are provided for Calving Ease Maternal, Weaning Weight,
25 Heifer Pregnancy, Milk, Mature Weight, Dry Matter Intake, Carcass Weight, Marbling, Yield,
26 and three economic selection indices. Test results can inform selection and culling decisions
27 made by commercial beef cattle producers. To measure the accuracy of the trait predictions, data
28 from commercial Angus females and their progeny at the University of Missouri Thompson
29 Research Center were utilized to analyze weaning weight, milk, marbling, fat, ribeye area, and
30 carcass weight. Progeny phenotypic data were matched to the respective dam, then the cow's
31 genomic predictions were compared to the calf's age-adjusted phenotypes using correlation and
32 linear model effect sizes. All tested GeneMax scores of the dam were significantly correlated
33 with and predicted calf performance. Our predicted effect sizes, except for fat thickness, were
34 similar to those reported by Zoetis. In conclusion, the GeneMax Advantage test accurately ranks
35 animals based on their genetic merit and is an effective selection tool in commercial cowherds.

36

37 **Key words:** genomic prediction, validation, *Bos taurus*, growth, carcass

38

39 **Abbreviations:**

40 GMX, GeneMax

41 SNP, single nucleotide polymorphisms

42 BIR, Beef Improvement Records

43 WW, Weaning Weight

44 MBV, molecular breeding value

45 BLUP, best linear unbiased prediction

- 46 CW, carcass weight
- 47 Marb, marbling
- 48 RE, ribeye area
- 49 Fat, fat thickness

50

INTRODUCTION

51

52 Prediction of quantitative traits using DNA markers in beef cattle was first commercialized in the
53 1990s. However, many of these tests relied on a small number of markers and failed validation
54 trials (Van Eenennaam et al., 2007). Genomic prediction, the use of thousands of genome-wide
55 DNA markers (Nejati-Javaremi et al., 1997; Meuwissen et al., 2001), has proven to be a much
56 more efficacious strategy in driving genetic improvement (García-Ruiz et al., 2016; Taylor et al.,
57 2016). Still, many farmers, ranchers (Weaber et al., 2014), extension professionals, and even
58 academics question the effectiveness of genomic prediction in commercial beef cattle.
59 Demonstrations of the ability of genomic tests to accurately predict genetic merit may encourage
60 farmers and ranchers to adopt this technology and accelerate genetic progress in commercial
61 herds. Our objective is to evaluate the effectiveness of the Zoetis GeneMax Advantage (genomic
62 predictions designed for commercial heifers) in predicting the genetic merit of Angus cattle. We
63 hypothesize that, because this test was built using principles of genomic prediction, the dam's
64 GeneMax scores will significantly predict her calves' performance.

65

66

MATERIALS AND METHODS

67 An Animal Care and Use Committee protocol is not necessary for this project as DNA samples
68 were collected as part of routine animal production practices. However, the University of
69 Missouri has a demonstration ACUC protocol, number 7491, which covers the procedures used
70 in this research.

71 Cows were commercial Angus that were from a crossbred base that were straightbred Angus

72 since 1995. Phenotypic and pedigree data were collected for commercial animals at the

73 University of Missouri's Thompson Research Center and entered into Angus Genetics Inc. Beef
74 Improvement Records (BIR) program through AngusOnline.org. Pedigree, phenotype, and
75 GeneMax Advantage score information were retrieved as Excel files from AngusOnline.org in
76 June of 2018. Phenotypic records were collected from 1995 to 2018, however only calves born
77 from 2003 to 2011 and from 2014 to 2018 had data reported to BIR and genotyped dams (**Figure**
78 **1**). Summary statistics are presented in **Table 1**. Excel files were read into R (Team, 2018) and
79 similar files from different years were combined. Packages utilized included readr (Wickham et
80 al., 2018b), ggplot2 (Wickham, 2016), tidyr (Wickham and Henry, 2018), dplyr (Wickham et al.,
81 2018a), and stringr (Wickham, 2018).

82

83 For statistical analyses, the calf phenotype was compared with the dam's GeneMax score (1 to
84 100 scale). For each of the traits, Pearson and Spearman correlations were calculated.

85

86 To adjust for additional factors, mixed models were used to evaluate the relationship between
87 calf phenotype and dam's GeneMax Score. We used the model:

$$y = X\beta + Zu + e$$

88 where, y is the phenotype of the calf; β are fixed effects of contemporary group, sex, and dam
89 GMX Score; u is the random effect of sire, and e is the residual. Both u and e are $\sim N(0, I)$. For
90 growth traits, the birth year of the calf was considered the contemporary group. For carcass traits,
91 contemporary group was defined by the harvest date. There were 47 bulls who sired calves with
92 weaning weight records, 37 bulls who sired calves with hot carcass weight, marbling, and ribeye
93 area records, and 23 bulls who sired calves with fat thickness records. For each of the traits, four
94 models were compared: a full model including dam GMX Score and the random effect of sire, a

95 reduced model that did not include the effect of sire, a reduced model that did not include the
96 effect of dam GMX Score, and a model with effect of sire and maternal grandsire (MGS). For
97 each trait, a χ^2 test was also run between the first and third models to determine the significance
98 of the inclusion of the cow's GeneMax Advantage score. A χ^2 test was run between the third
99 and fourth models to determine if the inclusion of the random effect of maternal grandsire was
100 significant. Pseudo- R^2 values were calculated using the 'r.squaredLR' function from the MuMIn
101 package (Bartoń, 2022). Calf birth weights were not analyzed because GeneMax does not report
102 a birth weight score or a calving ease direct score (only calving ease maternal). For weaning
103 weight, phenotypes were pre-adjusted to 205-day weights and adjusted for age-of-dam effects by
104 Angus Genetics Inc. Further, a model was also executed that included both Weaning Weight
105 (WW) GMX Score and Milk GMX Score. Models containing 1) WW GMX Score, 2) Milk
106 GMX Score, and 3) WW and Milk GMX Scores were compared to see which best fit the data.
107 Because there is a trend over time for weaning weight phenotypes and we do not have a random
108 sample of DNA tested cows, calves born in the early 2000s may have low weaning weights
109 compared to calves born in later years (**Figure 1d**) but ranked high in their own contemporary
110 group (weaning weight ratio, **Figure 1e**). In other words, entire contemporary groups were not
111 analyzed, only calves of genotyped dams. Thus, some contemporary groups only had a small
112 number of calves represented and the data have inherent selection bias. Therefore, we also
113 measured the association between the dam's GMX WW scores and GMX Milk scores with the
114 calf's weaning weight ratio (no contemporary group effect was included in these models).

115

116 Estimates of GeneMax Advantage score effects were retrieved from Zoetis technical bulletin
117 GMX-00116 (Zoetis Genetics and Angus Genetics Inc., 2018). Effects were converted from

118 Imperial to metric units, divided by 10 to represent a 1-point GeneMax score increase, and
119 divided by 2 to change from molecular breeding values to expected progeny differences
120 (transmitting abilities). Our GeneMax score effect estimates were compared to Zoetis' published
121 estimates using a two-tailed Z-test.

122

123 **Results**

124 For each trait evaluated, the Pearson's correlation and Spearman's correlation between the calf's
125 phenotype and the dam's corresponding GMX Score were statistically different from zero (**Table**
126 **2**). Further, from the six regression models, the dam's GMX Score had a significant effect on the
127 calf's phenotype (**Table 3**). Except for fat thickness, our estimated effect sizes were not
128 statistically different compared with those published by Zoetis (**Table 3**). When weaning weight
129 ratio was the dependent variable to more accurately account for an animal's rank in its
130 contemporary group, WW GMX score was significantly predictive in the simple model with sex
131 and random sire (0.08944 ± 0.02057 , $p\text{-value} = 1.8e-05$). When Milk GMX Score was compared
132 to weaning weight ratio, the effect was not significant ($p\text{-value} = 0.16$). A model containing both
133 GMX WW Score and GMX Milk Score provided a better fit to the data and estimated larger
134 effects for the GMX Scores compared with the models using one GMX Score (**Table 4**). Calf
135 phenotypes were plotted against dam's GMX Score in **Figure 2**.

136 Tables 5 through 10 report additional model statistics. Models that included GeneMax score and
137 sire fit the data better (lower AIC, lower BIC, higher pseudo- R^2 , better log likelihoods) than
138 models that included maternal grandsire (MGS) and sire. Further, GeneMax scores were more
139 significantly associated with progeny performance (smaller P -values) than the random effect of
140 maternal grandsire.

141 **Discussion**

142 In the last ten years, the use of DNA information to produce genomic predictions has changed
143 substantially. For example, when first launched in 2010, the IGENITY MBVs (molecular
144 breeding values) were only based on 384 DNA markers (Weber et al., 2012). However, even the
145 initial genomic predictions (which were use as indicator traits in a multi-step genomic-enhanced
146 EPD analysis) trained with a couple thousand animals accurately predicted genetic merit (Weber
147 et al., 2012). In the last ten years, hundreds of thousands of beef cattle have been genotyped from
148 multiple breeds, increasing the power of these datasets not just for genetic prediction, but also for
149 basic research (Decker, 2015). Since 2015, breed associations have switched to single-step
150 methods, in which pedigree and genomic data are combined in a single analysis (Lourenco et al.,
151 2015). Pedigree information is not typically known for commercial cattle, so a DNA marker
152 effects model is typically used to predict genetic merit for commercial cattle. However, the
153 estimated breeding values produced by a genomic relationship model and a marker effects model
154 are equivalent (Hayes et al., 2009). The marker effects used to calculate GMX scores in the
155 Zoetis GeneMax Advantage test are based on the American Angus Association single-step
156 BLUP analysis (Zoetis Genetics and Angus Genetics Inc., 2018).

157
158 All traits had relatively weak correlations between the calf's phenotype and the dam's GMX
159 Score. However, this is to be expected as this analysis does not account for Mendelian sampling
160 (random shuffle of genes between generations), contemporary group effects (management and
161 environment effects), sire effects, or the heritability of the trait. Nevertheless, as all correlations
162 were significantly different from zero, it does demonstrate the predictive ability of the GeneMax
163 Advantage test.

164

165 Regression analysis allowed a more sophisticated evaluation of the relationship between a dam's
166 GMX Score and her calf's phenotype. These models accounted for variation due to sex, year of
167 birth or slaughter date, and sire effects. However, this model still did not account for Mendelian
168 sampling or other non-additive genetic effects, including genotype-by-environment effects. The
169 amount of variation due to Mendelian sampling is large and theoretically equal to half of the
170 additive genetic variance. These sources of variation are likely why we still observe substantial
171 spread around the regression lines in **Figure 2**. Genetic predictions are not designed to predict
172 performance of individual animals, but rather the average performance of a large group of
173 progeny out of a parent compared to the progeny average of a different parent or population
174 average. Our results show that the GeneMax Advantage test accurately predicts the average
175 progeny performance for weaning weight, milk, marbling, carcass weight, ribeye area and fat
176 thickness. Further, GeneMax scores provided more information than simply knowing the sire of
177 the dam.

178

179 Our estimates of the effects of GeneMax scores did not differ from those published by Zoetis
180 with respect to Milk ($P = 0.88$), Marb ($P = 0.21$), CW ($P = 0.19$), or RE ($P = 0.58$). However, our
181 estimate of the effect of GeneMax score did differ from that published by Zoetis with respect to
182 Fat ($P < 1.0e-22$) and tended to differ with respect to WW ($P = 0.08$). However, for all traits, our
183 estimated effect sizes were smaller than those reported by Zoetis. These smaller effect sizes
184 could be for many reasons, including data from a single environment in northwest Missouri, the
185 size of the dataset, or that this was an external validation.

186

187 Regardless of whether we expressed weaning growth as a weight or as a ratio within
188 contemporary group, WW GMX Score significantly predicted variation in weaning growth.
189 However, Milk GMX scores were not predictive of weaning weight ratio. This likely reflects the
190 well-known difficulty of predicting maternal effects (Willham, 1980). For example, in the 2014
191 Angus genomic-enhanced EPD calibration based on 57,550 animals, the correlation between
192 weaning weight and Milk EPD was 0.36. The average of the other traits was 0.66 (range of 0.45
193 to 0.78). In 2016, when 108,211 animals were used to estimate molecular breeding values, the
194 correlation between weaning weight and Milk EPD was 0.37, range of 0.56 to 0.80 for other
195 traits (Albers, 2016). Further, only 491 observations were available when analyzing weaning
196 weight ratio, compared to 781 observations for the models that only fit contemporary group, sex,
197 and sire. Thus, the difficulty of predicting maternal effects and the smaller sample sizes affected
198 the more complicated Milk GMX models.

199
200 We note that the Zoetis GeneMax Advantage prediction is designed to work in high-percentage
201 Angus animals and is not designed for cattle with substantial ancestry from other breeds.
202 However, other similar genomic predictions for crossbred cattle should be equally accurate
203 provided they contain the appropriate breeds in a large, multi-breed training population
204 (Kachman et al., 2013).

205
206 Genetic predictions, whether based on pedigree or genomic relationships, work when trained
207 using ample and appropriately structured data. Models using contemporary group effects and
208 random effects to account for covariance between relatives appropriately separate additive
209 genetic variation from other sources of variation, including management and environment. While

210 genetic predictions were never intended to predict the performance of a single individual, the
211 average progeny performance is accurately predicted by the additive genetic merit of the parent.
212 However, biological variation remains, including non-additive genetic effects and interactions
213 (Smith et al., 2019; Braz et al., 2020) and especially Mendelian sampling (Cole and VanRaden,
214 2011) between full- or half-siblings. The increased adoption of genomic technologies in
215 commercial cattle production has the opportunity to significantly increase long-term genetic gain
216 through more accurate replacement animal selection.

217

218 **Conclusions**

219 Genomic predictions, including the Zoetis GeneMax Advantage, accurately predict a
220 straightbred, commercial Angus animal's genetic merit and the average performance of their
221 offspring. Academics and extension professionals can confidently state to farmers and ranchers
222 that genomic predictions in commercial animals are accurate and effective.

223

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235 at the University of Missouri in 1997 based on analysis of field records of Angus cattle. He was
236 lead author of *Biostatistics for Animal Science*, a widely used reference text that was published in
237 multiple editions and languages.

238

239 **Author Statement**

240 **Brian. C. Arisman:** Formal analysis, Writing - Original Draft **Troy N. Rowan:** Formal analysis,
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245 Supervision, Funding acquisition

246 **Disclosures**

247 Jared Decker is a member of the scientific advisory board of Vytelle, LLC.

248

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327

328 **Tables and Figures**

329 **Table 1.** Summary statistics of data used for GeneMax Advantage evaluation. For GeneMax

330 scores, we report the number of animals with test results (Number) and the number of cows with

331 calves with phenotypes (Number with matched calves).

	Number (Number with matched calves)	Mean	Standard Deviation	Median	Minimum	Maximum	Skew	Kurtosis
Weaning Weight, kg	781	263.0	26.3	264.4	178.3	347.5	-0.17	3.05
Weaning Weight Ratio	491	100.1	9.0	100	67	130	-0.08	3.53
Marbling Score	374	6.5	1.1	6.6	3.2	9.2	-0.22	3.1
Hot Carcass Weight, kg	376	398.7	40.3	401.9	249.5	504.9	-0.62	3.93
Fat Thickness, cm	290	1.8	0.5	1.7	0.5	4.1	1.1	6.33
Ribeye Area, cm²	374	84.8	9.3	84.5	57.4	112.9	0.12	2.87
WW GMX Score	554 (231)	45.6	20.4	45.0	3	97	0.19	2.27
Milk GMX Score	554 (231)	51.6	21.2	53.0	3	97	-0.14	2.18
CW GMX Score	554 (196)	49.2	19.4	48	7	95	0.11	2.27
Marb GMX Score	555 (196)	64.3	21.2	67	7	98	-0.44	2.25

RE GMX Score	556 (196)	50.5	20.1	49	7	97	0.19	2.06
Fat GMX Score	557 (188)	43.3	19.9	42	3	93	0.26	2.18

332

333

334 **Table 2.** Pearson and Spearman correlation tests between the dam's Zoetis GeneMax Advantage
335 Score (Kalamazoo, MI) and the calf's phenotype (not adjusted for contemporary group or sire
336 effects).

GeneMax Trait	Pearson Correlation (95% Confidence Interval)	Pearson Correlation P-value	Spearman Correlation	Spearman Correlation P-value
Weaning Weight	0.18 (0.11 to 0.25)	5.4e-07	0.18	3.0e-07
Maternal Milk	0.18 (0.11 to 0.25)	2.5e-07	0.16	5.3e-06
Marbling	0.27 (0.18 to 0.36)	8.4e-08	0.25	1.3e-06
Carcass Weight	0.13 (0.02 to 0.22)	1.5e-02	0.15	4.8e-03
Fat Thickness	-0.18 (-0.29 to -0.07)	1.9e-03	-0.19	1.1e-03
Ribeye Area	0.12 (0.02 to 0.22)	2.0e-02	0.11	3.0e-02

337

338 **Table 3.** Estimated effects of GMX Scores on production traits. Each row represents a different
 339 linear mixed model. Models contained contemporary group and sex as fixed effects and sire as a
 340 random effect. Difference from zero *P*-values and MGS *P*-values are from χ^2 test comparing full
 341 and reduced model. Difference from Zoetis effects estimated from a Z-test.

GMX Score	Estimate	Std. Error	GMX effect difference from zero <i>P</i> -value	Zoetis effect	Difference from Zoetis <i>P</i> -value	MGS effect <i>P</i> -value
WW	0.18 kg	0.04 kg	1.1e-05	0.25 kg	0.08	1.1e-03
Milk	0.13 kg	0.04 kg	3.2e-04	0.14 kg	0.88	1.1e-03
Marb	0.01	0.002	1.1e-06	0.01	0.21	3.2e-03
CW	0.20 kg	0.09 kg	3.3e-02	0.32 kg	0.19	1.0*
RE	0.06 cm ²	0.02 cm ²	2.2e-03	0.07 cm ²	0.58	9.5e-03
Fat	-0.003 cm	0.001 cm	2.0e-02	-0.03 cm	<1.0e-22	1.0*

342 *The estimated maternal grandsire variance for these models was zero.

343 **Table 4.** Estimated effects of dam's WW and Milk GMX Scores on calf's weaning weight. *P*-
344 values from χ^2 test comparing full model with both traits versus reduced models with single trait.

GMX Score	Estimate	Std. Error	<i>P</i>-value
WW	0.20 kg	0.04 kg	1.0e-06
Milk	0.15 kg	0.04 kg	3.0e-05

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348 **Table 5.** Summary of weaning weight models.

Model	AIC	BIC	Sire Variance	MGS ^a Variance	Residual Variance	Pseudo-R ²
Linear Model with WW GeneMax score	7075.1	7154.3			491.9	0.3023
Linear Model with Milk GeneMax score	7080.4	7159.7			495.3	0.2975
Mixed Model with WW GeneMax score and sire	7014.0	7097.9	94.02		412.73	0.3564
Mixed Model with Milk GeneMax score and sire	7020.4	7104.3	95.12		416.08	0.3511
Mixed Model with WW GeneMax score, Milk GeneMax score, and sire	6998.6	7087.1	90.71		403.84	0.3706
Mixed model with sire	7031.4	7110.6	98.09		422.81	0.3402
Mixed model with MGS and sire	7022.8	7106.7	99.52	41.77	401.89	0.3491

349 ^a MGS stands for Maternal Grand Sire.

350 **Table 6.** Summary of weaning weight ratio models.

Model	AIC	BIC	Sire Variance	MGS ^a Variance	Residual Variance	Pseudo-R ²
Linear Model with WW GeneMax score	3512.9	3533.8			74.03	0.0997
Linear Model with Milk GeneMax score	3525.2	3546.2			75.92	0.0767
Mixed Model with WW GeneMax score and sire	3496.9	3522.1	8.97		66.37	0.1321
Mixed Model with Milk GeneMax score and sire	3513.4	3538.5	7.365		69.267	0.1025
Mixed model with sire	3513.3	3534.3	8.00		69.33	0.0989
Mixed model with MGS and sire	3509.4	3534.6	8.275	8.337	65.109	0.1097

351 ^a MGS stands for Maternal Grand Sire.

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353 **Table 7.** Summary of marbling models.

Model	AIC	BIC	Sire Variance	MGS ^a Variance	Residual Variance	Pseudo-R ²
Linear Model with GeneMax score	1032.2	1181.3			0.8377	0.4404
Mixed Model with GeneMax score and sire	1002.9	1155.9	0.1050		0.6411	0.4892
Mixed model with sire	1024.7	1173.8	0.0955		0.6887	0.4525
Mixed model with MGS and sire	1018.0	1171.1	0.09282	0.07898	0.63735	0.4661

354 ^a MGS stands for Maternal Grand Sire.

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357 **Table 8.** Summary of carcass weight models.

Model	AIC	BIC	Sire Variance	MGS ^a Variance	Residual Variance	Pseudo-R ²
Linear Model with GeneMax score	3724.2	3873.5			1062.5	0.4089
Mixed Model with GeneMax score and sire	3713.3	3866.6	161.9		848.3	0.4288
Mixed model with sire	3715.8	3865.2	152.1		862.0	0.4220
Mixed model with MGS and sire	3717.8	3871.1	152.1	0.0	862.0	0.4220

358 ^a MGS stands for Maternal Grand Sire.

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360 **Table 9.** Summary of ribeye area models.

Model	AIC	BIC	Sire Variance	MGS ^a Variance	Residual Variance	Pseudo-R ²
Linear Model with GeneMax score	2598.3	2747.4			55.17	0.4256
Mixed Model with GeneMax score and sire	2586.8	2739.9	7.105		44.329	0.4460
Mixed model with sire	2594.2	2743.4	6.418		45.747	0.4318
Mixed model with MGS and sire	2589.5	2742.6	7.952	5.821	41.880	0.4420

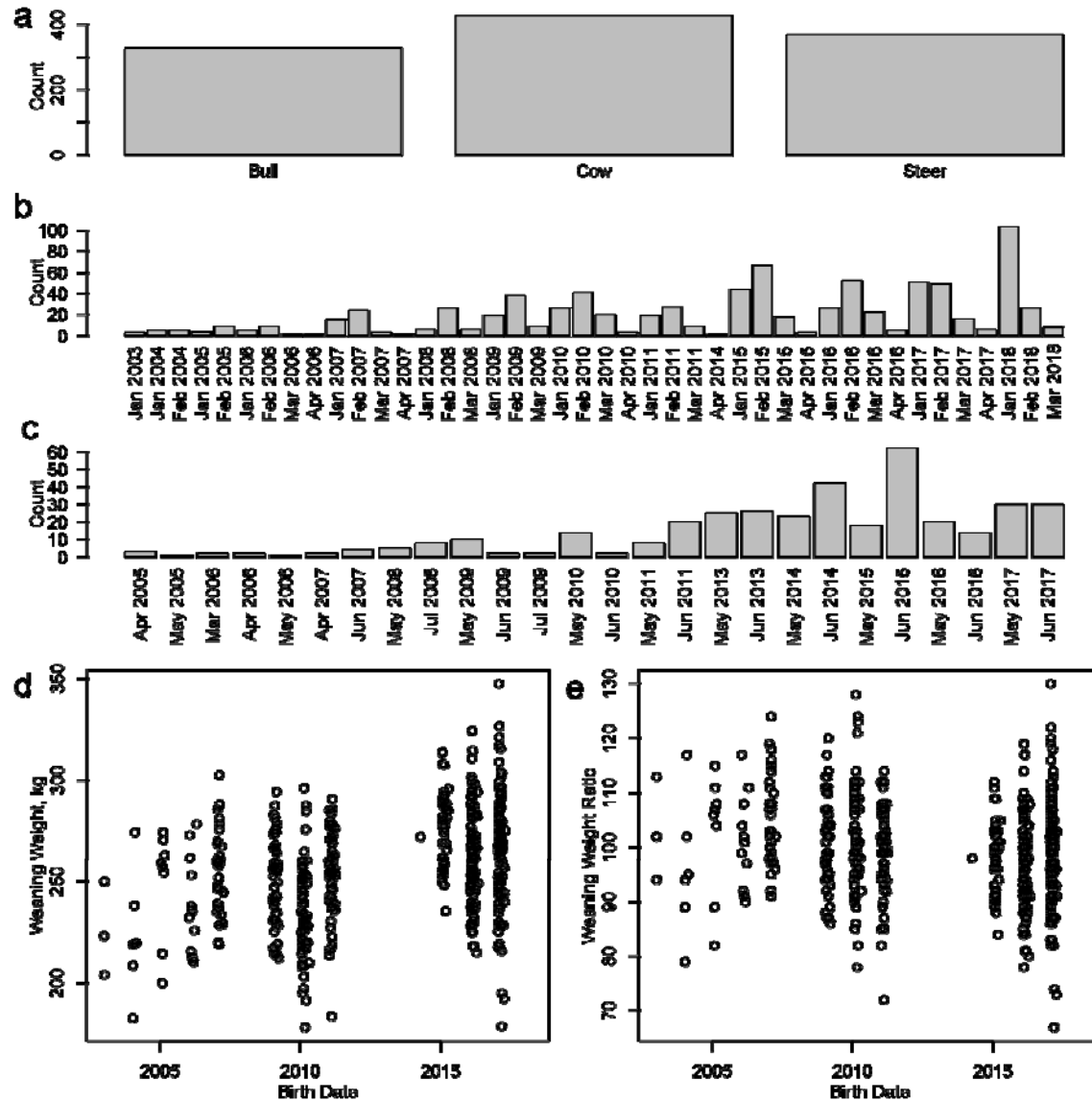
361 ^a MGS stands for Maternal Grand Sire.

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363 **Table 10.** Summary of fat thickness models.

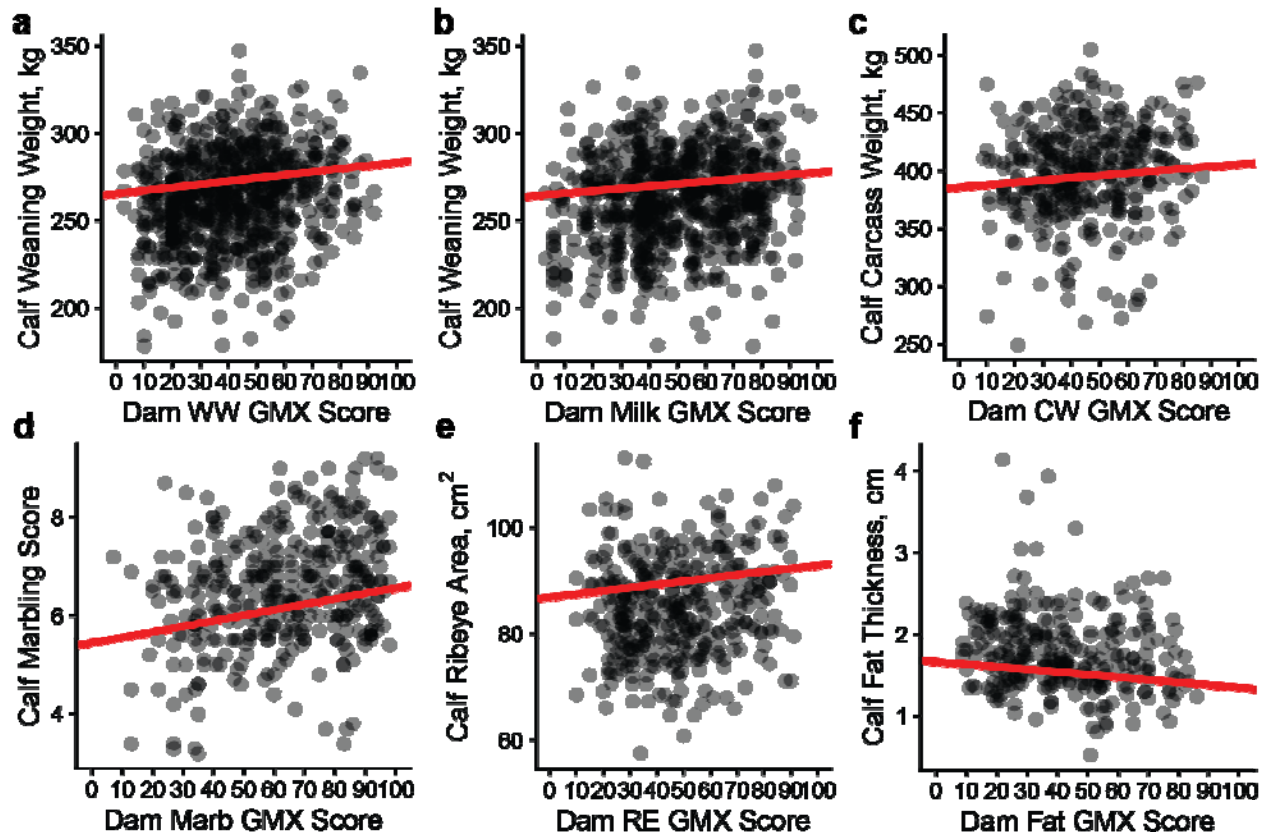
Model	AIC	BIC	Sire Variance	MGS ^a Variance	Residual Variance	Pseudo-R ²
Linear Model with GeneMax score	369.65	432.04			0.1972	0.2527
Mixed Model with GeneMax score and sire	371.0	437.1	0.006747		0.1808	0.2552
Mixed model with sire	374.4	436.8	0.007184		0.1840	0.2347
Mixed model with MGS and sire	376.4	442.5	0.007184	0.00	0.1840	0.2347

364 ^a MGS stands for Maternal Grand Sire.



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 366 **Figure 1.** Graphical summary of data available for analysis. a) Counts of animals by sex. An
 367 animal can be counted as both a bull and a steer, for example if it was a bull at weaning but
 368 castrated prior to entering the feedlot. b) Counts of animals by birth month and year. c) Counts of
 369 animals by slaughter month and year. d) Weaning weight plotted against birth date. e) Weaning
 370 weight ratio plotted against birth date.

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373 **Figure 2.** Calf's phenotype plotted against dam's GMX Score. a) Weaning weight versus WW
374 GMX Score, b) Weaning weight versus Milk GMX Score, c) Carcass weight versus CW GMX
375 Score, d) Marbling score versus Marb GMX Score, e) Ribeye area versus RE GMX Score, and f)
376 Fat Thickness versus Fat GMX Score. Red line represents the intercept and slope estimated from
377 the linear models reported in Table 3.

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