

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 cattle¹**

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6 Brian. C. Arisman* †, Troy N. Rowan † ‡, Jordan M. Thomas†, Harly J. Durbin† ‡, David J.

7 Patterson †, Jared E. Decker † ‡ § ²

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9 * Agricultural and Medical Biotechnology, University of Kentucky, Lexington, Kentucky, 40506

10 †Division of Animal Sciences, University of Missouri, Columbia, Missouri, 65211

11 ‡Genetics Area Program, University of Missouri, Columbia, Missouri, 65211

12 §Informatics Institute, University of Missouri, Columbia, Missouri, 65211

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21 ²Corresponding author: DeckerJE@missouri.edu

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24 **ABSTRACT:** The GeneMax (GMX) Advantage test, developed by Zoetis, uses approximately
25 50,000 single nucleotide polymorphisms (SNP) to predict the genomic potential of a commercial
26 Angus heifer. Genetic predictions are provided for Calving Ease Maternal, Weaning Weight,
27 Heifer Pregnancy, Milk, Mature Weight, Dry Matter Intake, Carcass Weight, Marbling, and
28 Yield. Indices of economically important traits are estimated on an index score (1-100 scale) and
29 are divided into three indices; Cow Advantage index, Feeder Advantage index, and Total
30 Advantage index. The indices provide a genomic prediction of the profitability of the cow's
31 calves. Therefore, test results can inform selection and culling decisions made by commercial
32 beef cattle producers. To measure the accuracy of the trait predictions, data from commercial
33 Angus females and their progeny at the University of Missouri Thompson Research Center was
34 utilized to analyze weaning weight, milk, marbling, fat, ribeye area, and carcass weight. Progeny
35 phenotypic data was matched to the respective dam, then the cow's genomic predictions were
36 compared to the calf's age-adjusted phenotypes using correlation and linear models. All tested
37 GeneMax scores of the dam were significantly correlated with and predicted calf performance.
38 Our predicted effect sizes, except for fat thickness, were similar to those reported by Zoetis. In
39 conclusion, the GeneMax Advantage test accurately ranks animals based on their genetic merit
40 and is an effective selection tool in commercial cowherds.

41

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

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INTRODUCTION

45

46 Prediction of quantitative traits using DNA markers in beef cattle was first commercialized in the
47 1990s. However, many of these tests relied on a small number of markers and failed validation
48 trials (Van Eenennaam et al., 2007). Genomic prediction, the use of thousands of genome-wide
49 DNA markers (Nejati-Javaremi et al., 1997; Meuwissen et al., 2001), has proven to be a much
50 more efficacious strategy in driving genetic improvement (García-Ruiz et al., 2016; Taylor et al.,
51 2016). Still, many farmers, ranchers (Weaber et al., 2014), extension professionals, and even
52 academics question the effectiveness of genomic prediction in commercial beef cattle.
53 Demonstrations of the ability of genomic tests to accurately predict genetic merit may encourage
54 farmers and ranchers to adopt this technology and accelerate genetic progress in commercial
55 herds. Our objective is to evaluate the effectiveness of the Zoetis GeneMax Advantage (genomic
56 predictions designed for commercial heifers) in predicting the genetic merit of Angus cattle. We
57 hypothesize that, because this test was built using principles of genomic prediction, the dam's
58 GeneMax scores will significantly predict her calves' performance.

59

60

MATERIALS AND METHODS

61 An Animal Care and Use Committee protocol is not necessary for this project as DNA samples
62 were collected as part of routine animal production practices. However, the University of
63 Missouri has a demonstration ACUC protocol, number 7491, which covers the procedures used
64 in this research.
65 Phenotypic and pedigree data were collected at the University of Missouri's Thompson Research
66 Center and entered into Angus Genetics Inc. Beef Improvement Records (BIR) program through

67 AngusOnline.org. Pedigree, phenotype, and GeneMax Advantage score information were
68 retrieved as Excel files from AngusOnline.org in June of 2018. Phenotypic records were
69 collected from 1995 to 2018, however only calves born from 2003 to 2011 and from 2014 to
70 2018 had data reported to BIR and genotyped dams (**Figure 1**). Summary statistics are presented
71 in **Table 1**. Excel files were read into R (Team, 2018) and similar files from different years were
72 combined. Packages utilized included readr (Wickham et al., 2018b), ggplot2 (Wickham, 2016),
73 tidyr (Wickham and Henry, 2018), dplyr (Wickham et al., 2018a), and stringr (Wickham, 2018).

74

75 For statistical analyses, the calf phenotype was compared with the dam's GeneMax score. For
76 each of the traits, Pearson and Spearman correlations were calculated.

77

78 To control for potential confounding factors, mixed models were used to evaluate the
79 relationship between calf phenotype and dam's GeneMax Score. We used the model:

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

80 where, y is the phenotype of the calf; β are fixed effects of year of birth, sex, and dam GMX
81 Score; u is the random effect of sire, and e is the residual. Both u and e are $\sim N(0, I)$. There were
82 47 bulls who sired calves with weaning weight records, 37 bulls who sired calves with hot
83 carcass weight, marbling, and ribeye area records, and 23 bulls who sired calves with fat
84 thickness records. For each of the traits, three models were compared: a full model including
85 dam GMX Score and the random effect of sire, a reduced model that did not include the effect of
86 sire, and a reduced model that did not include the effect of dam GMX Score. For growth traits,
87 the birth year of the calf was considered the contemporary group. For carcass traits,
88 contemporary group was defined by the harvest date. For each trait, a χ^2 test was run between

89 the first and second models to determine if the inclusion of the random effect of sire was
90 significant. A χ^2 test was also run between the first and third models to determine the
91 significance of the inclusion of the cow's GeneMax Advantage score. For weaning weight, we
92 also fit models that included age-of-dam as a fixed effect factor and dam as a random effect.
93 Further, a model was also executed that included both Weaning Weight (WW) GMX Score and
94 Milk GMX Score. Models containing 1) WW GMX Score, 2) Milk GMX Score, and 3) WW and
95 Milk GMX Scores were compared to see which best fit the data. Because there is a trend over
96 time for weaning weight phenotypes and we do not have a random sample of DNA tested cows,
97 calves born in the early 2000s may have low weaning weights compared to calves born in later
98 years (**Figure 1d**) but ranked high in their own contemporary group (weaning weight ratio,
99 **Figure 1e**). Thus, we also measured the association between the dam's GMX WW scores and
100 GMX Milk scores with the calf's weaning weight ratio (no contemporary group effect was
101 included in these models).

102
103 Estimates of GeneMax Advantage score effects were retrieved from Zoetis technical bulletin
104 GMX-00116 (Zoetis Genetics and Angus Genetics Inc., 2018). Effects were converted from
105 Imperial to scientific units, divided by 10 to represent a 1-point GeneMax score increase, and
106 divided by 2 to change from molecular breeding values to expected progeny differences
107 (transmitting abilities). Our GeneMax score effect estimates were compared to Zoetis' published
108 estimates using a two-tailed Z-test.

109

110 **Results**

111 For each trait evaluated, the Pearson's correlation and Spearman's correlation between the calf's
112 phenotype and the dam's GMX Score were statistically different from zero (**Table 2**). Further,
113 from the six regression models, the dam's GMX Score had a significant effect on the calf's
114 phenotype (**Table 3**). Except for fat thickness, our estimated effect sizes were not statistically
115 different compared with those published by Zoetis (**Table 3**). When weaning weight was
116 adjusted for age-of-dam as a factor and a random effect of dam, the estimated effect of a 1-point
117 change in WW GMX Score increased to 0.29 ± 0.08 kg (p-value = $6.4e-4$). Conversely, when
118 Milk GMX Score was evaluated in a model containing age-of-dam, random dam effect, or both,
119 the estimated effect of Milk GMX Score was not different from zero (p-value > 0.9). When
120 weaning weight ratio was the dependent variable to more accurately account for an animal's rank
121 in its contemporary group, WW GMX score was significantly predictive in the simple model
122 with sex and random sire (0.08944 ± 0.02057 , p-value = $1.8e-05$) and in the more complicated
123 model with age-of-dam and random dam effect (0.1011 ± 0.0321 , p-value = 0.002). When Milk
124 GMX Score was compared to weaning weight ratio, the effect was not significant (p-value =
125 0.16). A model containing both GMX WW Score and GMX Milk Score provided a better fit to
126 the data and estimated larger effects for the GMX Scores compared with the models using one
127 GMX Score (**Table 4**). Calf phenotypes were plotted against dam's GMX Score in **Figure 2**.

128

129 **Discussion**

130 In the last ten years, the use of DNA information to produce genomic predictions has changed
131 substantially. For example, when first launched in 2010, the IGENITY MBVs (molecular
132 breeding values) were only based on 384 DNA markers (Weber et al., 2012). However, even the
133 initial genomic predictions (which were use as indicator traits in a multi-step genomic-enhanced

134 EPD analysis) trained with a couple thousand animals accurately predicted genetic merit (Weber
135 et al., 2012). In the last ten years, hundreds of thousands of beef cattle have been genotyped from
136 multiple breeds, increasing the power of these datasets not just for genetic prediction, but also for
137 basic research (Decker, 2015). Since 2015, breed associations have switched to single-step
138 methods, in which pedigree and genomic data are combined in a single analysis (Lourenco et al.,
139 2015). Pedigree information is not typically known for commercial cattle, so a DNA marker
140 effects model is typically used to predict genetic merit for commercial cattle. However, the
141 estimated breeding values produced by a genomic relationship model and a marker effects model
142 are equivalent (Hayes et al., 2009). The marker effects used to calculate GMX scores in the
143 Zoetis GeneMax Advantage test are based off of the American Angus Association single-step
144 BLUP analysis (Zoetis Genetics and Angus Genetics Inc., 2018).

145
146 All traits had relatively weak correlations between the calf's phenotype and the dam's GMX
147 Score. However, this is to be expected as this analysis does not account for Mendelian sampling
148 (random shuffle of genes between generations), contemporary group effects (management and
149 environment effects), sire effects, or the heritability of the trait. Nevertheless, as all correlations
150 were significantly different from zero, it does demonstrate the predictive ability of the GeneMax
151 Advantage test.

152
153 Regression analysis allowed a more sophisticated evaluation of the relationship between a dam's
154 GMX Score and her calf's phenotype. These models accounted for variation due to sex, year of
155 birth or slaughter date, and sire effects. However, this model still did not account for Mendelian
156 sampling or other non-additive genetic effects, including genotype-by-environment effects. The

157 amount of variation due to Mendelian sampling is large and theoretically equal to half of the
158 additive genetic variance. These sources of variation are likely why we still observe substantial
159 spread around the regression lines in **Figure 2**. Genetic predictions are not designed to predict
160 performance of individual animals, but rather the average performance of a large group of
161 progeny out of a parent compared to the progeny average of a different parent or population
162 average. Our results show that the GeneMax Advantage test accurately predicts the average
163 progeny performance for weaning weight, milk, marbling, carcass weight, ribeye area and fat
164 thickness. Our estimates of the effects of GeneMax scores, except for fat thickness, in a
165 validation population were not significantly different from those published by Zoetis.
166
167 Regardless of whether we expressed weaning growth as a weight or as a ratio within
168 contemporary group, WW GMX Score accurately predicted variation in weaning growth.
169 Further, when we adjusted for age-of-dam and accounted for dependency between data with a
170 random dam effect, the magnitude the WW GMX effect increased from 0.18 to 0.29. This larger
171 estimate is closer to that published by Zoetis. However, Milk GMX scores were not predictive of
172 weaning weight ratio or when more complicated models were used. This likely reflects the well-
173 known difficulty of predicting maternal effects (Willham, 1980). For example, in the 2014
174 Angus genomic-enhanced EPD calibration based on 57,550 animals, the correlation between
175 weaning weight and Milk EPD was 0.36. The average of the other traits was 0.66 (range of 0.45
176 to 0.78). In 2016, when 108,211 animals were used to estimate molecular breeding values, the
177 correlation between weaning weight and Milk EPD was 0.37, range of 0.56 to 0.80 for other
178 traits (Albers, 2016). Further, only 491 observations were available when analyzing weaning
179 weight ratio or age-of-dam effects, compared to 781 observations for the models that only fit

180 contemporary group, sex, and sire. Thus, the difficulty of predicting maternal effects and the
181 smaller sample sizes affected the more complicated Milk GMX models.

182
183 We note that the Zoetis GeneMax Advantage prediction is designed to work in high-percentage
184 Angus animals and is not designed for cattle with substantial ancestry from other breeds
185 (Kachman et al., 2013). However, other similar genomic predictions for crossbred cattle should
186 be equally accurate provided they contain the appropriate breeds in a large, multi-breed training
187 population.

188
189 Genetic predictions, whether based on pedigree or genomic relationships, work when trained
190 using ample and appropriately structured data. Models using contemporary group effects and
191 random effects to account for covariance between relatives appropriately separate additive
192 genetic variation from other sources of variation, including management and environment. While
193 genetic predictions were never intended to predict the performance of a single individual, the
194 average progeny performance is accurately predicted by the additive genetic merit of the parent.
195 However, biological variation remains, including non-additive genetic effects and interactions
196 (Smith et al., 2019; Braz et al., 2020) and especially Mendelian sampling (Cole and VanRaden,
197 2011) between full- or half-siblings. The increased adoption of genomic technologies in
198 commercial cattle production has the opportunity to significantly increase long-term genetic gain
199 through more accurate replacement animal selection.

200

201 **Conclusions**

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

206

207 **Disclosures**

208 The authors declare no competing interests.

209

210 **Literature Cited**

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286

287 *Tables and Figures*

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

	Number (Number with matched calves)	Mean	Standard Deviation	Median	Minimum	Maximum	Range	Skew	Kurtosis
Weaning Weight, kg	781	263.01	26.3	264.44	178.26	347.45	169.19	-0.17	3.05
Weaning Weight Ratio	491	100.05	9.04	100	67	130	63	-0.08	3.53
Marbling Score	374	6.53	1.14	6.55	3.2	9.2	6	-0.22	3.1
Hot Carcass Weight, kg	376	398.65	40.31	401.88	249.48	504.85	255.37	-0.62	3.93
Fat Thickness, cm	290	1.77	0.48	1.7	0.53	4.14	3.61	1.1	6.33
Ribeye Area, cm²	374	84.79	9.31	84.52	57.42	112.9	55.48	0.12	2.87
WW GMX Score	554 (231)	45.59	20.39	45	3	97	94	0.19	2.27
Milk GMX Score	554 (231)	51.57	21.17	53	3	97	94	-0.14	2.18
CW GMX Score	554 (196)	49.18	19.41	48	7	95	88	0.11	2.27
Marb GMX Score	555 (196)	64.33	21.2	67	7	98	91	-0.44	2.25
RE GMX Score	556 (196)	50.54	20.07	49	7	97	90	0.19	2.06

Fat GMX Score	557 (188)	43.28	19.85	42	3	93	90	0.26	2.18
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291 **Table 2.** Pearson and Spearman correlation tests between the dam's Zoetis GeneMax Advantage
292 Score (Kalamazoo, MI) and the calf's phenotype.

GeneMax Trait	Pearson Correlation (95% Confidence Interval)	Pearson Correlation P-value	Spearman Correlation	Spearman Correlation P-value
Weaning Weight	0.178 (0.109 to 0.245)	5.4e-07	0.182	3.0e-07
Maternal Milk	0.183 (0.114 to 0.250)	2.5e-07	0.162	5.3e-06
Marbling	0.273 (0.176 to 0.364)	8.4e-08	0.247	1.3e-06
Carcass Weight	0.125 (0.024 to 0.223)	1.5e-02	0.145	4.8e-03
Fat Thickness	-0.181 (-0.291 to -0.068)	1.9e-03	-0.191	1.1e-03
Ribeye Area	0.120 (0.019 to 0.219)	2.0e-02	0.112	3.0e-02

293

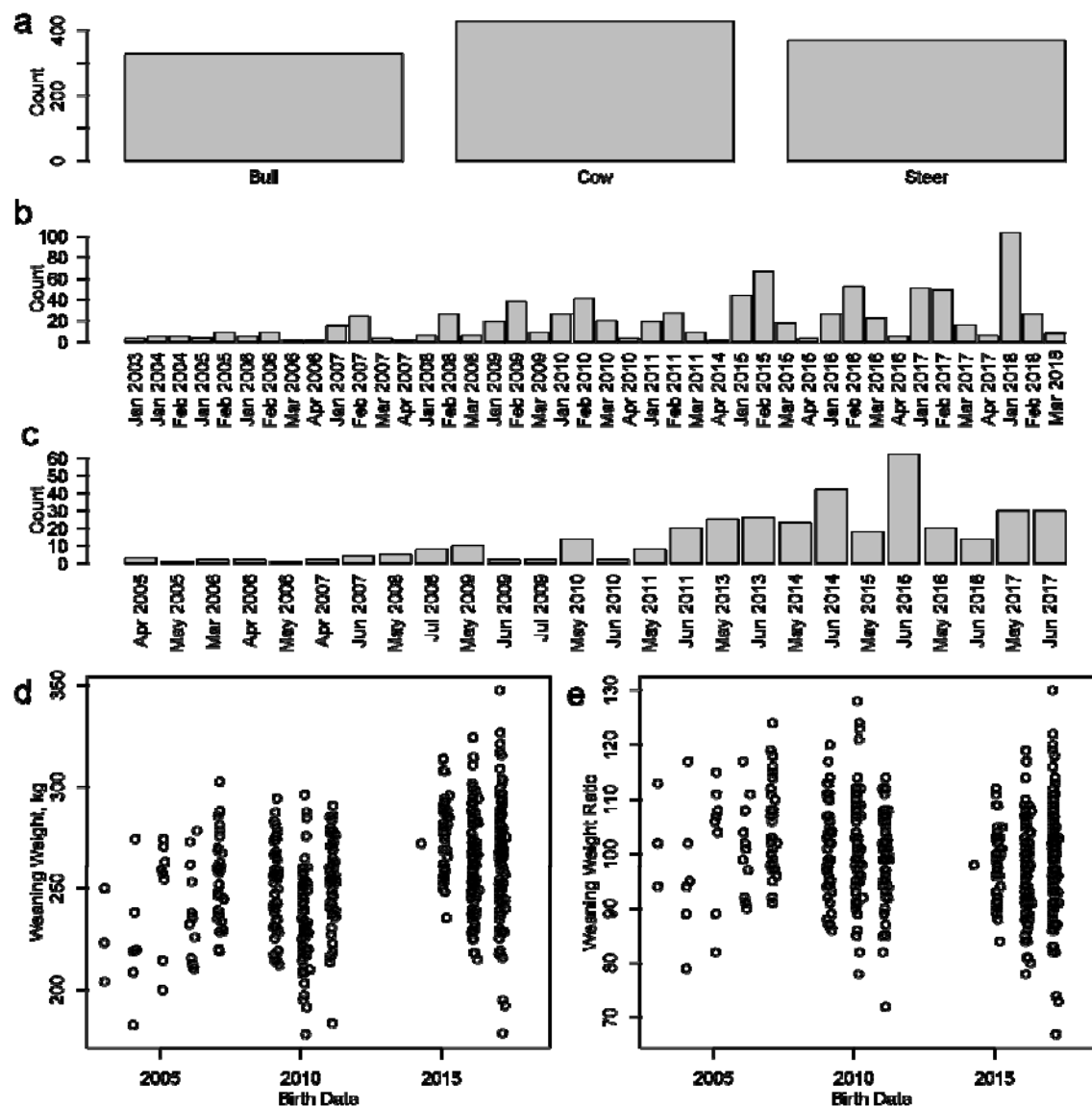
294 **Table 3.** Estimated effects of GMX Scores on production traits. Each row represents a different
295 linear mixed model. Models contained contemporary group and sex as fixed effects and sire as a
296 random effect. Difference from zero P -values from χ^2 test comparing full and reduced model.
297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

GMX Score	Estimate	Std. Error	t-value	Difference from zero P-value	Zoetis effect	Difference from Zoetis P- value
WW	0.18 kg	0.04 kg	4.43	1.1e-05	0.25 kg	0.08
Milk	0.13 kg	0.04 kg	3.62	3.2e-04	0.14 kg	0.88
Marb	0.01	0.002	4.97	1.1e-06	0.01	0.21
CW	0.20 kg	0.09 kg	2.14	3.3e-02	0.32 kg	0.19
RE	0.06 cm ²	0.02 cm ²	3.10	2.2e-03	0.07 cm ²	0.58
Fat	-0.003 cm	0.001 cm	-2.34	2.0e-02	-0.03 cm	<1.0e-22

298

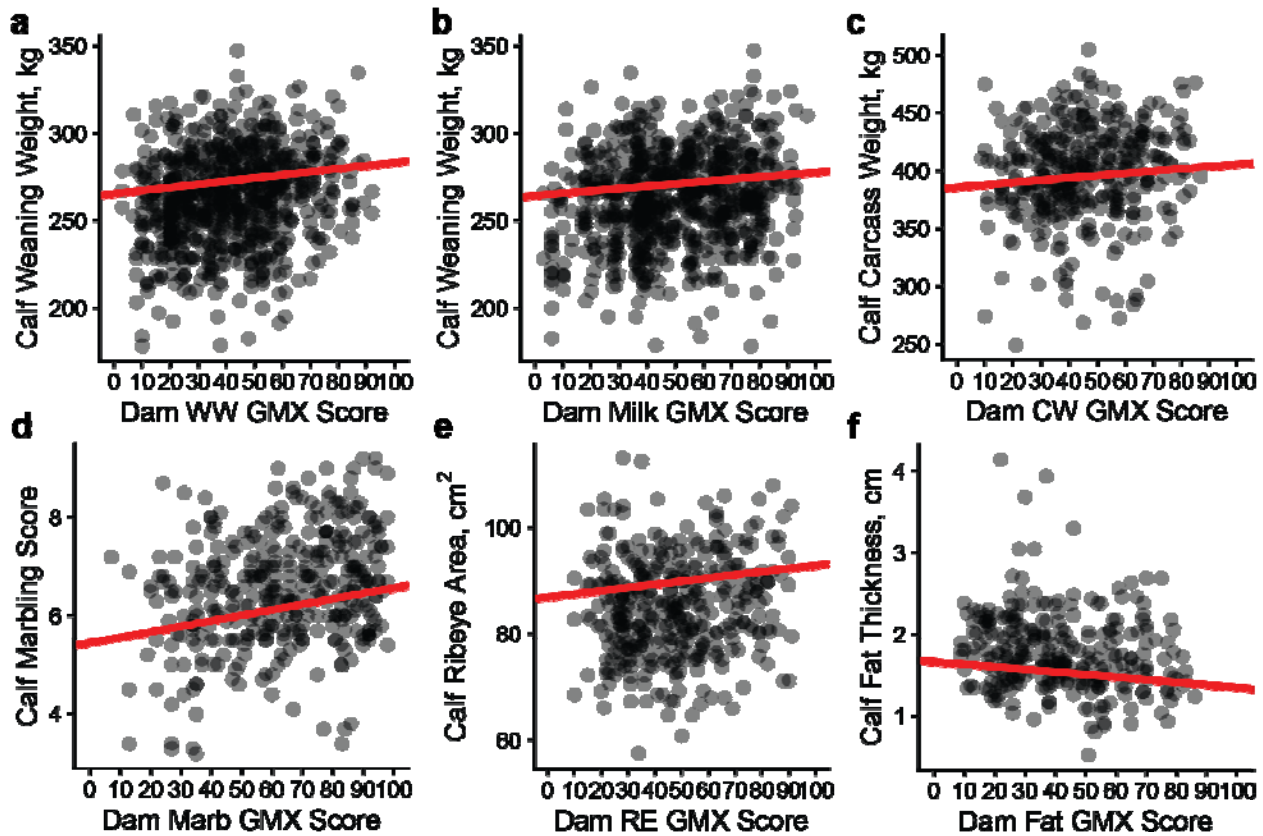
299 **Table 4.** Estimated effects of dam's WW and Milk GMX Scores on calf's weaning weight. *P*-
300 values from χ^2 test comparing full model with both traits versus reduced models with single trait.

GMX Score	Estimate	Std. Error	t-value	<i>P</i>-value
WW	0.20 kg	0.04 kg	4.92	1.0e-06
Milk	0.15 kg	0.04 kg	4.20	3.0e-05



301
 302 **Figure 1.** Graphical summary of data available for analysis. a) Counts of animals by sex. An
 303 animal can be counted as both a bull and a steer, for example if it was a bull at weaning but
 304 castrated prior to entering the feedlot. b) Counts of animals by birth month and year. c) Counts of
 305 animals by slaughter month and year. d) Weaning weight plotted against birth date. e) Weaning
 306 weight ratio plotted against birth date.

307



308

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

314