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Original article

A meta-analytic assessment of a Thyroglobulin marker for marbling in beef cattle

Ian A. WOOD[a]*, Gerhard MOSER[b], Daniel L. BURRELL[a], Kerrie L. MENGERSEN[a], D. Jay S. HETZEL[b]

[a] School of Mathematical Sciences, Queensland University of Technology, GPO Box 2434 Brisbane, QLD 4001, Australia
[b] Genetic Solutions Pty. Ltd., 31 Dover St. Albion, QLD 4010, Australia

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Abstract – A meta-analysis was undertaken reporting on the association between a polymorphism in the Thyroglobulin gene (*TG5*) and marbling in beef cattle. A Bayesian hierarchical model was adopted, with alternative representations assessed through sensitivity analysis. Based on the overall posterior means and posterior probabilities, there is substantial support for an additive association between the *TG5* marker and marbling. The marker effect was also assessed across various breed groups, with each group displaying a high probability of positive association between the T allele and marbling. The WinBUGS program code used to simulate the model is included as an Appendix available online at www.edpsciences.org/gse.

Bayesian hierarchical model / meta-analysis / association studies / TG5 marker / beef marbling

1. INTRODUCTION

Marbling is the fat that is deposited between individual muscle fibres of the *M. longissimus dorsi*. Marbling and the distribution of intramuscular fat are economically important factors with respect to beef quality. A polymorphism in the 5' promoter region of the bovine Thyroglobulin gene (*TG5*) has been reported to be associated with variation in marbling [3]. The polymorphism is a C/T transition whereby cattle that are either homozygous or heterozygous for the Thymine (T) allele (*i.e.* TT or CT genotypes) appear to have higher marbling scores than cattle that are homozygous for the Cytosine (C) allele (*i.e.* CC genotypes).

* Corresponding author: i.wood@qut.edu.au

A search of published and available unpublished literature revealed 14 independent studies that provide 19 estimates of the association between *TG5* and marbling. The study-specific results generally support an association, but not all are individually convincing. Each study was based on a relatively small number of animals and four different measurements of marbling were used. It is then of interest to assess whether the accumulation of evidence provides stronger support for this association.

Meta-analysis provides a means of statistically combining study results [8]. A meta-analysis of comparable study estimates was undertaken using a Bayesian hierarchical model. Although meta-analysis has been used in human genetics [1, 6, 7, 17], less attention has been paid to meta-analysis in the context of livestock genomics. Goffinet and Gerber [12] and Khatkar *et al.* [13] have presented methods for combining QTL results from independent studies, based on a modified Akaike criterion.

The dataset used for the meta-analysis is described in Section 2.1 and the statistical model is detailed in Section 2.2. Computational issues are addressed in Section 2.3 and a sensitivity analysis is described in Section 2.4. Results are reported in Section 3 and discussed in Section 5. Studies which could not be included in the meta-analysis are described in Section 4.

2. METHODS

2.1. Dataset for meta-analysis

A literature review and communication with research groups identified 14 studies which provide estimates of the association between *TG5* and marbling. Results in most studies were either directly reported as, or were able to be calculated as contrasts with corresponding standard errors. Therefore this was the measure used in the meta-analysis. Details of the individual studies are summarised in Table I. Three studies reported measures of association which could not be represented as contrasts and so were excluded from the meta-analysis. These studies are discussed separately in Section 4.

Study 1 was undertaken using a subgroup of the Angus cattle of a large dataset described in detail in [19]. The data for Study 6 was first analysed in [4]. The excluded studies were described in [22] and [5]. All other studies were unpublished technical reports provided by Genetic Solutions Pty. Ltd.

Each study assessed the degree of marbling using one of four methods. Three methods (AUS-MEAT, MSA, USDA) involved trained assessors scoring the chilled carcass against specific grading standards [21]. AUS-MEAT marble scores range from 0 to 6 in steps of 1 [2], Meat Standards Australia (MSA)

Table I. Summary of datasets used in the meta-analysis of the association between *TG5* and marbling in beef cattle.

Est. No.	Study[a]	Breed Group[b]	Trait[c]	No. CC	No. CT	No. TT	CC/CT Effect[d]	TT/CT Effect
1	1	BE	AUS	229	172	22	0.14 (0.10)	0.13 (0.23)
7	1	BE	MSA	69	55	5	0.07 (0.18)	0.01 (0.46)
13	1	BE	IMF	438	298	44	–0.01 (0.10)	0.07 (0.21)
2	2	WC	AUS	24	105	40	–0.54 (0.23)	0.15 (0.18)
3	3	WC	AUS	73	80	24	–0.26 (0.16)	0.22 (0.23)
4	4	C1	AUS	123	154	21	–0.10 (0.11)	0.24 (0.21)
8	4	C1	MSA	128	173	24	–0.10 (0.11)	–0.22 (0.20)
9	4	C1	USDA	94	114	17	–0.25 (0.13)	0.06 (0.25)
14	4	C1	IMF	156	205	30	–0.05 (0.10)	–0.02 (0.18)
5	5	WC	AUS	35	128	143	–0.07 (0.20)	0.29 (0.14)
6	6	BE	AUS	1060	511	51	–0.01 (0.05)	0.24 (0.14)
10	7	BE	USDA	242	195	34	–0.25 (0.09)	0.11 (0.18)
11	8	BE	USDA	84	162	33	–0.09 (0.14)	0.18 (0.21)
12	9	C2	USDA	282	30	3	–0.15 (0.19)	–0.95 (0.59)
15	10	WC	AUS	97	156	82	–0.15 (0.12)	0.12 (0.13)
16	11	WC	AUS	371	435	100	–0.08 (0.09)	0.04 (0.07)

[a] See acknowledgements for study sources. Study breed: 1: Angus × Angus, 2,5: Wagyu × Wagyu, 3,10,11: crosses of Wagyu bulls over Angus or Angus cross cows, 4: Alexandria Composite (3/8 Brahman, 1/8 Africander, 1/8 Charolais, 5/16 Shorthorn, 1/16 Hereford) × (Brahman × Shorthorn), 6: Angus × Angus, Shorthorn × Shorthorn, 7: Angus × Angus cross, 8: Simmental × Angus, 9: Santa Gertrudis (3/8 Brahman, 5/8 Shorthorn) × Santa Gertrudis.

[b] British/European (BE); Wagyu Cross (WC); Composite 1 (C1); Composite 2 (C2).

[c] AUS-MEAT (AUS); Meat Standards Australia (MSA); United States Department of Agriculture (USDA); intramuscular fat (IMF).

[d] Number in brackets is the standard error of the effect.

marble scores range from 0.0 to 6.9 in increments of 0.1 [16] and United States Department of Agriculture (USDA) marble scores range from 100 to 1000 in increments of 10 [14]. The fourth method involves physically measuring the percentage of intramuscular fat (IMF) [18]. These four measurements of marbling are hereafter called traits. For each trait, a higher score indicates more marbling.

The studies included a variety of breeds, as listed in Table I. For the purposes of the meta-analysis, four distinct breed groups were defined: British/European, Wagyu Cross, and two Composites. This classification groups breeds with similar genetic origin and *TG5* allele frequencies.

The composites were divided into two breed groups because the Alexandria Composite animals (study 4) were all offspring of heterozygous sires.

Two experimental herds (studies 1 and 4) provided the basis for seven of the 14 estimates, with different subsets of animals used to measure each trait. Because of the lack of specific information about the overlap or composition of these subsets, it was not feasible to incorporate corresponding covariances into the model.

For the purposes of the meta-analysis, phenotypic data were standardized to residual standard deviation units for each study. The reported estimates comprised genotypic (effects and standard error estimates) and phenotypic information (marble scores and IMF). In order to combine the estimates in the meta-analysis, the results were represented as deviations of the observed CC and TT effects from the heterozygous (CT) effect, centred around zero. If the T allele is positively associated with marbling, we would expect to see a negative effect for CC versus CT and a positive effect for TT versus CT and for TT versus CC. The standardised data from all 11 studies used in the meta-analysis is summarised in Table I.

2.2. Meta-analysis model

A Bayesian hierarchical model was adopted for the meta-analysis. Separate models were fit for the effects CC/CT, TT/CT and TT/CC.

The four marbling traits (AUS-MEAT, MSA, USDA, IMF) are denoted by $m = 1, \ldots, 4$ respectively. Similarly, the four breed groups (British/European, Wagyu Cross, Composite 1 and Composite 2) are denoted by $b = 1, \ldots, 4$ respectively. For each of the effects of interest (CC/CT and TT/CT), study s provides n_s estimates of contrasts y_{isb}, $i \in (1, \ldots, n_s); s \in (1, \ldots, 11); b \in (1, \ldots, 4)$. Here $(n_1, \ldots, n_{11}) = (3, 1, 1, 4, 1, 1, 1, 1, 1, 1, 1)$, so the total number of estimates is $n = \sum_{s=1}^{11} n_s = 16$.

Each estimate y_{isb} is considered to be drawn from a normal distribution with mean μ_{sb} given by the sth study-level effect in breed group b. For each breed group, these μ_{sb} are in turn considered to be drawn from an overall breed group effect μ_b, which are in turn drawn from an overall effect μ_0.

The effects are each taken to be normally distributed with corresponding parameters (μ_c, ξ_c), where the subscript c can be sb, b or 0, meaning that the parameter describes the study within breed, breed or overall distribution respectively. $\xi = 1/\sigma^2$ denotes the precision. Estimates s_{isb} of the standard error σ_{isb} are given in Table I.

In the absence of information about the covariance structure between study- and breed-specific estimates, the observed and prior precision matrices at each level of the hierarchy were assumed to be diagonal. The consequences of this assumption are discussed in Section 5. Each ξ_c is assumed to have a chi-square distribution with degrees of freedom ν broadly set in line with the corresponding sample sizes. So for the effects CC/CT, TT/CT and TT/CC, the respective values are $\nu_{sb} = (200, 100, 130)$, $\nu_b = 10$, $\nu_0 = 3$.

The study-specific priors were adjusted to account for the informativeness of each study population. Assuming an additive gene action (no dominance), prior weights ω_s were computed for each study as the ratio of the genetic variance to that of a maximally informative population (one in which the C and T alleles have the same frequency, *i.e.* $p_T = 0.5$) [9]. Each study population was assumed to be in Hardy-Weinberg equilibrium. This yielded a study-specific weight vector $\omega_s = (0.751, 0.991, 0.923, 0.891, 0.875, 0.613, 0.805, 0.967, 0.216, 0.998, 0.911)'$. In principle, similar weights could be used with the priors for the breed group effects, but in the absence of additional information on the breed groups, all breed group weights ω_b were set to 1. To preserve scale at each level of the hierarchical model, the weights at the study and breed levels were multiplied by $\alpha = 100$.

Thaller *et al.* [22] and Barendse *et al.* [4] suggested that the T allele may have a recessive gene effect on marbling, so we re-analysed the data using this assumption. Recessivity alters the maximum genetic variance and places it at $p_T = 1/\sqrt{2}$. Prior weights were recalculated for this analysis, giving a study-specific weight vector $\omega_s = (0.235, 0.839, 0.455, 0.398, 0.993, 0.134, 0.288, 0.556, 0.013, 0.704, 0.431)'$.

The full model is thus represented as follows:

$$y_{isb} \sim N(\mu_{sb}, \xi_{isb}) \; ; \qquad \mu_{sb} \sim N(\mu_b, \xi_{sb}); \qquad \mu_b \sim N(\mu_0, \xi_b) \; ; \qquad \mu_0 \sim N(0, D \to 0)$$

where $\xi_{isb} = \tau_{sb}/s^2_{isb}$, $\xi_{sb} = \alpha\omega_s\tau_b$ and $\xi_b = \alpha\omega_b\tau_0$, and

$$\tau_{sb} \sim \chi^2_{\nu_{sb}}/\nu_{sb} \; ; \qquad \tau_b \sim \chi^2_{\nu_b}/\nu_b \; ; \qquad \tau_0 \sim \chi^2_{\nu_0}/\nu_0 \; .$$

Figure 1 illustrates the structure of this hierarchical model.

2.3. Computation

The analysis was performed using Markov chain Monte Carlo (MCMC) through the Bayesian computation software WinBUGS [15, 20]. The model

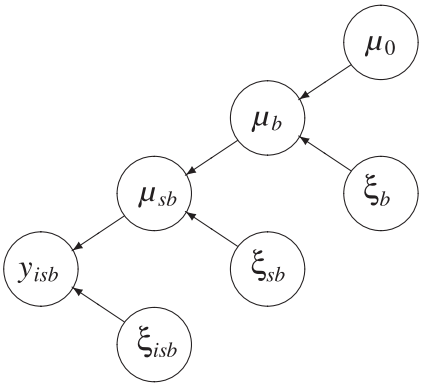

Figure 1. Graphical model representation of the Bayesian hierarchical model used in the meta-analysis, where *b* indicates breed, *sb* indicates study within breed and *isb* indicates estimate within study within breed.

code is listed in the Appendix for the main model which assumes additive gene action (this code is available online at www.edpsciences.org/gse). One hundred thousand iterations were dismissed as burn-in and the following two hundred thousand iterations were used for parameter estimation. Satisfactory convergence of the simulated Markov chains to the target posterior distributions was assessed using the diagnostics in WinBUGS.

2.4. Sensitivity analysis

A sensitivity analysis was performed to investigate the impact of the assumptions made in developing the model described in Section 2.2.

The first issue was the choice of prior distributions. In the absence of other distributional information, the adoption of normal prior distributions for the location parameters appears satisfactory. However, the use of chi-squared or more general gamma distributions to describe scale parameters has recently been called into question [10]. A suggested alternative is to use uniform priors on the standard deviations. In order to assess the impact of this particular choice, the model was re-analysed, replacing the chi-squared priors on the precisions with over-dispersed but proper uniform distributions on the standard deviations.

Another issue in prior modelling was the effect of using prior weights on studies which depend on the animals' genetic variance. To assess the effect of ignoring the genetic variance within studies, these weights were all made equal to unity.

In addition to the additive and recessive models, a third model was considered that assumes the T allele is dominant in its effect on marbling.

This yielded a study-specific weight vector ω_s = (0.985, 0.652, 0.966, 0.987, 0.375, 0.9, 0.999, 0.901, 0.395, 0.794, 0.976)′.

As described above, the AUS-MEAT, MSA and USDA marbling scores are all based on visual judgement of the amount of marbling present in the carcass, whereas the IMF score is based on a physical analysis. For this reason, the meta-analysis was repeated without the IMF-based estimates (numbered 13 and 14 in Tab. I). The study prior weights were consequently adjusted to account for the changed allele frequencies and became ω_s = (0.759, 0.991, 0.923, 0.889, 0.875, 0.613, 0.805, 0.967, 0.216, 0.998, 0.911)′.

The impact of small numbers of TT animals in some studies was also considered. Estimates 7 and 12 (see Tab. I) are based on just five and three TT animals, respectively. The meta-analysis was repeated without these two estimates. Estimate 12 was the only estimate from study 9 and the Composite 2 breed group, so these were omitted from the analysis. The study-specific weight vector was consequently recalculated as ω_s = (0.75, 0.991, 0.923, 0.891, 0.875, 0.613, 0.805, 0.967, 0.998, 0.911)′.

Finally, the goodness of fit of the meta-analysis model was assessed using posterior predictive checks. Following Gelman *et al.* [11], the minimum, maximum, mean and standard deviation of the 16 effect estimates were compared against the model posterior densities of the same statistics. The model is asserted to be adequate if the observed statistic is included in the body of the corresponding posterior predictive distribution.

3. RESULTS

As described in Section 2, for the purposes of comparability the CC/CT and TT/CT estimates are represented as zero-centred deviations of the homozygous (CC and TT) effects from the heterozygous (CT) effect. The posterior distributions of these effects for the additive case are depicted in Figure 2.

Posterior means, standard deviations and 95% credible intervals for the breed-specific and overall effects are shown in Table II for the additive case. The posterior means (s.d.) for the overall CC/CT, TT/CT and TT/CC effects were –0.117 (0.079), 0.091 (0.093) and 0.198 (0.100), respectively. The posterior probability that the overall CC/CT effect is less than zero was 0.935, and that the overall TT/CT and TT/CC effects are greater than zero were 0.854 and 0.973, respectively.

The Wagyu cross (WC) breed group shows the greatest association between *TG5* and marbling, giving a posterior probability of association of 0.998 for the TT/CC effect. A high degree of association was also found for the

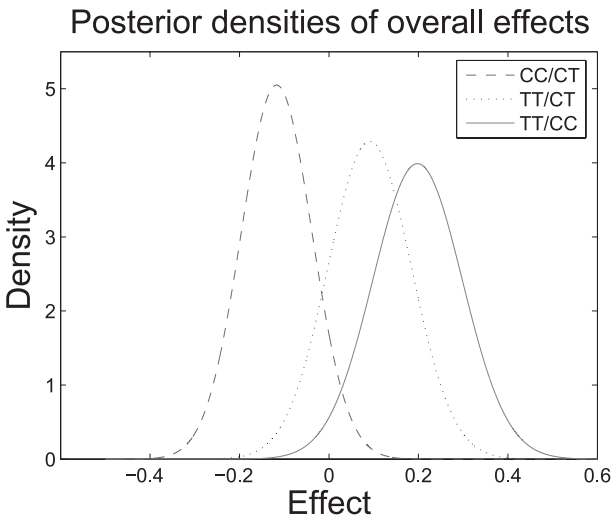

Figure 2. Posterior densities of the overall CC/CT, TT/CT and TT/CC effects.

British/European (BE) breed group, with a posterior probability of association of 0.989 for the same effect. The Composite 1 (C1) breed group, which contains animals with a significant Brahman component, had a posterior probability of association of 0.939 for this effect. The Composite 2 (C2) breed group showed a 0.874 posterior probability of association on the TT/CC effect, but this result was based on just one study which contained very few TT genotype animals.

The shrinkage of estimates at each hierarchy of the model is depicted in Figure 3, for each of the effects CC/CT, TT/CT and TT/CC. Figure 3 also shows the posterior 95% credible interval for the overall effect (μ_0).

The results were very similar when a recessive model was assumed (see Tab. III). Since the overall posterior probability of an association was similar (ranging from 0.85 to 0.94) for both the CC/CT and TT/CT contrasts under both models, we have strong evidence that the gene effect of the T allele is additive.

As described in Section 2.4, the influence of various modelling decisions was assessed by analysing alternative models. Table IV shows the influence of this sensitivity analysis on the overall posterior mean, standard deviation, 95% credible interval and probability of positive association between marbling and the number of copies of the T allele for each breed group and overall. Comparison with the analogous values in Tables II and III shows that

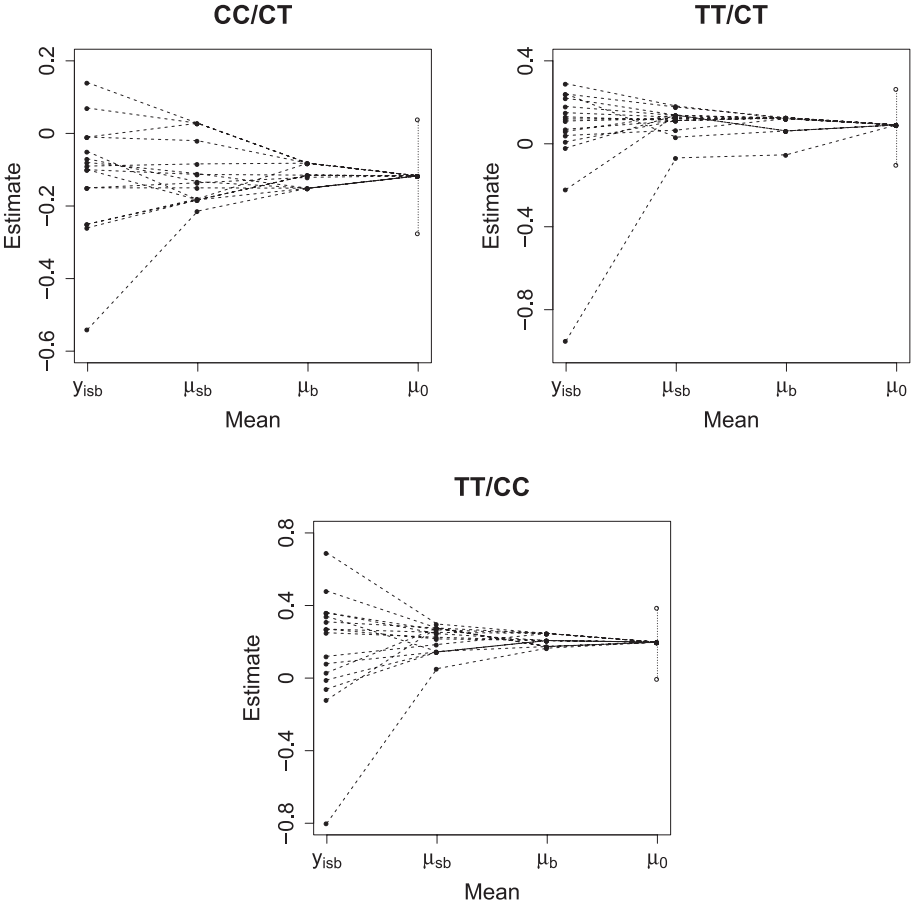

Figure 3. Shrinkage plots for the CC/CT, TT/CT and TT/CC effects showing observed values y_{isb}, posterior mode estimates for μ_{sb} (study within breed), μ_b (breed) and μ_0 (overall) effects and the 95% credible interval for μ_0.

the alternative sensitivity models gave very similar results and that the largest change to any of the overall posterior probabilities of association was 6%.

The choice of distributional form for the priors on the scale parameters was not found to be influential since the alternative uniform priors induced negligible change in the posterior estimates of effects and precisions.

Finally, the overall goodness of fit of the model was assessed. As demonstrated in Figure 4, the overall goodness of fit of the model was satisfactory. For the CC/CT, TT/CT and TT/CC contrasts, the posterior predictive distributions of the four test statistics all included the observed value of the statistic (indicated by a vertical line) in areas of reasonable probability.

Table II. Summary of posterior distributions of effects at breed level and overall assuming additive effect.

Effect	Breed group[a]	Mean	SD[b]	95% CI[c]	Probability[d]
CC/CT	BE	–0.082	0.064	(–0.209,0.044)	0.901
	WC	–0.151	0.069	(–0.290,–0.017)	0.987
	C1	–0.115	0.087	(–0.289,0.057)	0.910
	C2	–0.121	0.120	(–0.364,0.116)	0.857
	Overall	–0.117	0.079	(–0.275,0.039)	0.935
TT/CT	BE	0.126	0.083	(–0.036,0.290)	0.938
	WC	0.121	0.068	(–0.012,0.255)	0.963
	C1	0.062	0.104	(–0.150,0.261)	0.738
	C2	0.053	0.155	(–0.293,0.323)	0.686
	Overall	0.091	0.093	(–0.101,0.265)	0.854
TT/CC	BE	0.207	0.090	(0.029,0.384)	0.989
	WC	0.246	0.085	(0.081,0.416)	0.998
	C1	0.174	0.112	(–0.053,0.389)	0.939
	C2	0.165	0.160	(–0.185,0.450)	0.874
	Overall	0.198	0.100	(–0.004,0.388)	0.973

[a] British/European (BE), Wagyu Cross (WC), Composite 1 (C1), Composite 2 (C2).
[b] Standard deviation (SD).
[c] 95% credible interval (CI) for effect size.
[d] Posterior probability of positive association between marbling and the number of copies of the T allele, *i.e.* CC/CT: $P(\mu < 0)$, TT/CT: $P(\mu > 0)$, TT/CC: $P(\mu > 0)$.

4. OTHER STUDIES

Three studies reported the association between *TG5* and marbling as least squares means. For reasons of comparability these were not included in this meta-analysis and are instead summarised and discussed below.

Thaller *et al.* [22] investigated the association between *TG5* and IMF in 28 German Holsteins and separately in 27 Charolais animals. They reported significantly higher IMF values for TT genotypes against CC genotypes in German Holsteins. Their results suggested a recessive effect of the T allele on marbling, also found by Barendse *et al.* [4], but were based on small studies with just three German Holsteins and one Charolais having TT genotype.

Casas *et al.* [5] investigated the association between the *TG5* marker and USDA marble score in a sample of 467 Brahman (*Bos indicus*) cattle. They found no association, but the sample included only 18 CT and 7 TT animals.

Table III. Summary of posterior distribution of effects at breed level and overall assuming recessive effect.

Effect	Breed group[a]	Mean	SD[b]	95% CI[c]	Probability[d]
CC/CT	BE	–0.106	0.084	(–0.272,0.060)	0.898
	WC	–0.161	0.076	(–0.312,–0.014)	0.984
	C1	–0.125	0.105	(–0.332,0.082)	0.890
	C2	–0.131	0.147	(–0.423,0.161)	0.838
	Overall	–0.131	0.093	(–0.313,0.053)	0.927
TT/CT	BE	0.129	0.097	(–0.062,0.321)	0.911
	WC	0.138	0.074	(–0.006,0.283)	0.970
	C1	0.083	0.117	(–0.156,0.307)	0.774
	C2	0.096	0.157	(–0.235,0.389)	0.766
	Overall	0.111	0.099	(–0.090,0.303)	0.881
TT/CC	BE	0.226	0.106	(0.017,0.436)	0.983
	WC	0.269	0.093	(0.090,0.454)	0.998
	C1	0.201	0.126	(–0.055,0.444)	0.943
	C2	0.213	0.166	(–0.133,0.525)	0.914
	Overall	0.227	0.109	(0.010,0.440)	0.979

[a] British/European (BE), Wagyu Cross (WC), Composite 1 (C1), Composite 2 (C2).
[b] Standard deviation (SD).
[c] 95% credible interval (CI) for effect size.
[d] Posterior probability of positive association between marbling and the number of copies of the T allele, *i.e.* CC/CT: $P(\mu < 0)$, TT/CT: $P(\mu > 0)$, TT/CC: $P(\mu > 0)$.

5. DISCUSSION

The meta-analysis of eleven independent association studies provides increased support for an association between the *TG5* marker and marbling in beef cattle. The posterior means (s.d.) for the overall CC/CT, TT/CT and TT/CC effects were –0.117 (0.079), 0.091 (0.093) and 0.198 (0.100), respectively. The consistency of the sign of these effects under various assumptions further supports an association between *TG5* and marbling.

Moreover, the corresponding probabilities that the effects are real (*i.e.* that the CC/CT effect is less than zero and the TT/CT and TT/CC effects are greater than zero) were 0.935, 0.854 and 0.973, respectively. These are sufficiently large to propose selecting animals based on their *TG5* genotype to improve marbling in beef cattle. This association warrants further analysis, particularly of large samples of *Bos indicus* breeds, such as Brahman, which have low frequencies of the favourable T allele.

The sensitivity analysis showed that the posterior estimates were consistent despite changes in the assumptions underlying the model. The removal of

Table IV. Summary of posterior distributions of overall effects: sensitivity analysis.

Analysis[a]	Effect	Mean	SD[b]	95% CI[c]	Prob[d]	Breed probs[e]
equal	CC/CT	–0.114	0.076	(–0.267, 0.035)	0.938	0.896, 0.987, 0.911, 0.872
dom. T	CC/CT	–0.114	0.078	(–0.269, 0.039)	0.934	0.895, 0.984, 0.911, 0.861
w/o IMF	CC/CT	–0.121	0.081	(–0.282, 0.038)	0.938	0.883, 0.987, 0.924, 0.860
w/o small	CC/CT	–0.116	0.086	(–0.285, 0.051)	0.924	0.899, 0.985, 0.903
equal	TT/CT	0.089	0.092	(–0.101, 0.261)	0.854	0.946, 0.965, 0.735, 0.675
dom. T	TT/CT	0.085	0.092	(–0.106, 0.258)	0.841	0.942, 0.945, 0.726, 0.668
w/o IMF	TT/CT	0.098	0.095	(–0.098, 0.278)	0.866	0.939, 0.965, 0.764, 0.701
w/o small	TT/CT	0.113	0.092	(–0.068, 0.292)	0.904	0.952, 0.971, 0.780
equal	TT/CC	0.195	0.098	(–0.004, 0.381)	0.973	0.990, 0.998, 0.939, 0.869
dom. T	TT/CC	0.193	0.099	(–0.008, 0.381)	0.971	0.989, 0.997, 0.937, 0.868
w/o IMF	TT/CC	0.214	0.102	(0.008, 0.408)	0.978	0.989, 0.998, 0.953, 0.890
w/o small	TT/CC	0.222	0.100	(0.026, 0.417)	0.984	0.992, 0.999, 0.952

[a] Equal study and breed group weights (equal), assuming T allele is dominant (dom. T), without IMF-based estimates (w/o IMF), without small studies-based estimates (w/o small).
[b] Standard deviation (SD).
[c] 95% credible interval (CI) for effect size.
[d] Overall posterior probability of positive association between marbling and the number of copies of the T allele, *i.e.* CC/CT: $P(\mu_0 < 0)$, TT/CT: $P(\mu_0 > 0)$, TT/CC: $P(\mu_0 > 0)$.
[e] Overall posterior probability of positive association between marbling and the number of copies of the T allele for each of the four breed groups in the following order: British/European, Wagyu Cross, Composite 1, Composite 2. The Composite 2 breed group was only represented by a study with a small sample, so is not present in the results without small studies (w/o small).

estimates based on small numbers of animals of one genotype or those measured on the IMF trait tended to increase the posterior probability of association. For example, the posterior probability of association for the TT/CC effect with the Composite 1 breed group rose from 0.939 to 0.953 without the IMF estimates and to 0.952 without the small-sample estimates.

The graphical posterior predictive checks provided further confidence that the data do not contradict the model. The limitations of these checks in confirming the model are acknowledged, in that other reasonable models may also provide equally good fits and lead to different conclusions. Similarly, other representations of the data might be considered, such as vector descriptions of the four traits for each study. The corresponding multivariate analysis would require the estimation of substantial missing data; although this is straightforward in a Bayesian MCMC approach, the gain in interpretation is not immediately clear.

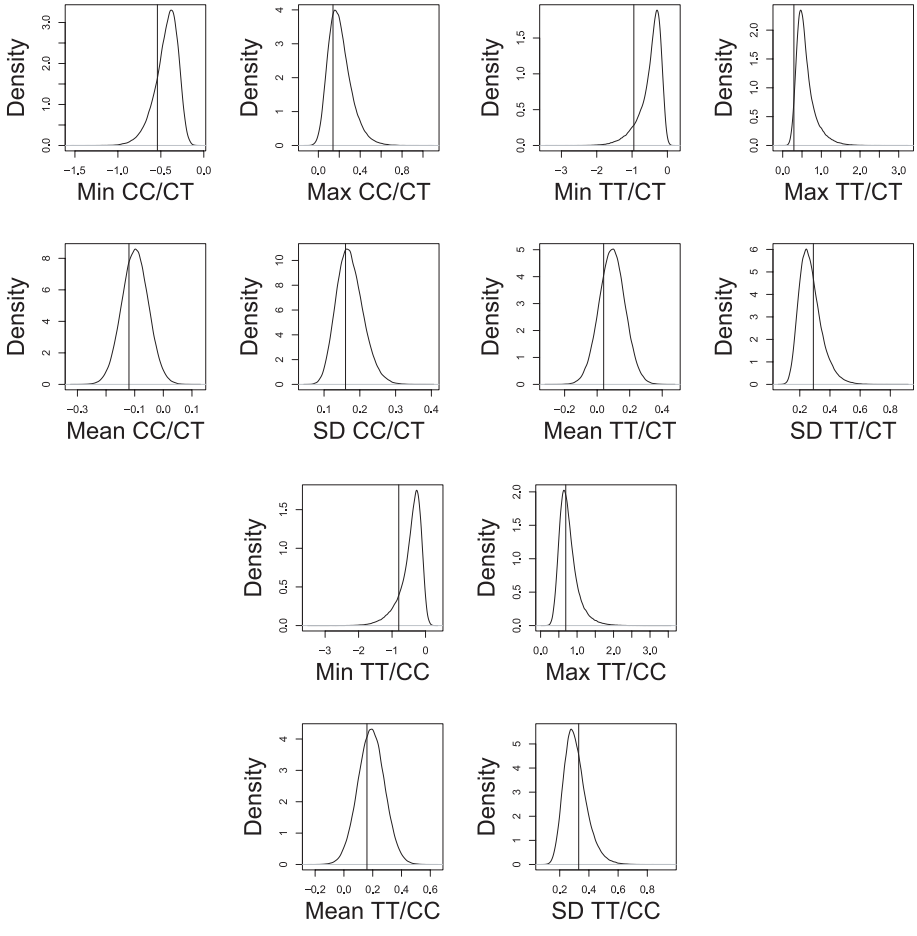

Figure 4. Comparison of minimum, maximum, mean and standard deviation across study effect estimates (vertical lines) against posterior predictive distributions from the meta-analysis model.

A Bayesian analysis allows one to make a variety of probabilistic statements. For example, a threshold value could be set for the overall effect below which there is no practical effect. The posterior probability of the effect being below this threshold can then be calculated. It is also easy to check the other posterior functions of interest, such as the probability distribution of the study means, ranking and comparison of studies and breed groups or the distribution of breed group ranks. See [20] for examples of these types of posterior summaries computed using WinBUGS.

The model presented here is sufficiently flexible to allow structural changes such as non-normal distributional assumptions, proportional representation of breed groups, and additional subgroups. Such changes can be accommodated through the distribution of the likelihood or priors, weights ω_s and ω_b and the hierarchical structure, respectively. In the present analysis, there was insufficient information available to allow the pursuit of these features.

The breed groups were formed on the basis of average frequency of the T allele but the breeds could be grouped in other ways. Similar groups could also be formed by considering typical time on feed for these breeds, which also affects marbling. Wagyu crosses are typically long-fed, British and European breeds are fed for less time and the Santa Gertrudis and Alexandria composite breeds are fed very briefly. Breed group weights could also be derived from factors such as the typical environment or finishing system (*e.g.* grass or grain-fed) for the breeds included.

Although the model described in Section 2.1 conceptually allows for correlation between estimates within studies and breeds, in light of the lack of information about the size or strength of these, the estimates were taken to be independent. A positive correlation structure would lead to an overstatement of the observed effects, but the degree of overstatement is difficult to assess without further data.

One could consider a fixed effects analysis rather than the random effects approach described here. In the context of the present study, the random effects model seemed appropriate from both genetic and statistical perspectives. Alternatively, as discussed above, different models could be contemplated. For example, one could explicitly describe the probability of no effect via a mixture distribution, with one component being a Dirac delta function placed on the origin and the other a normal distribution.

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