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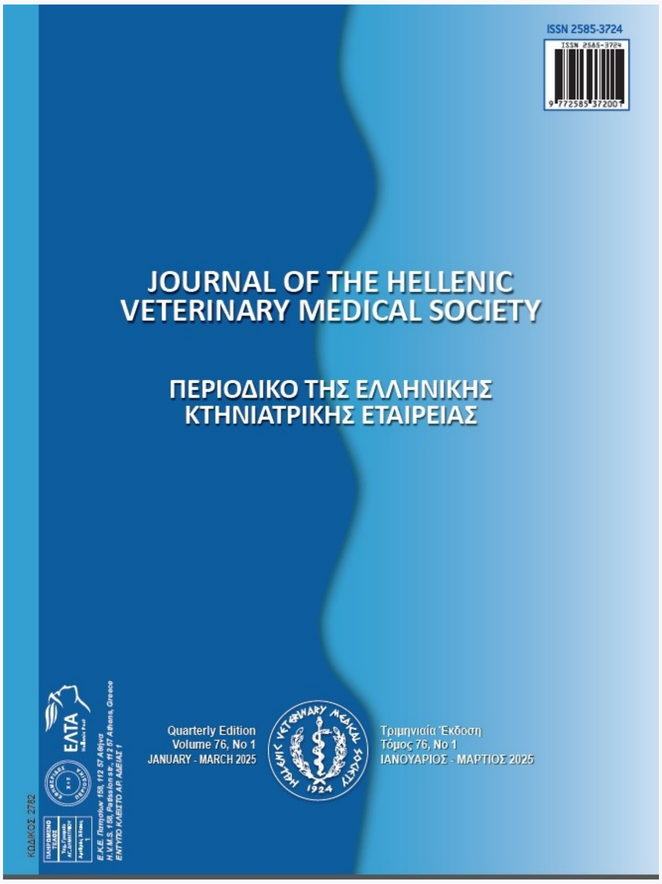

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Research article
Ερευνητικό άρθρο

A meta-analysis on the relationship between *IGF-1* gene polymorphism and milk production traits in cattle

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ABSTRACT: This study aims to investigate by meta-analysis using different genetic models the associations between insulin-like growth factor-1 (*IGF-1/SnaBI*) polymorphism and certain milk production traits, such as total milk yield, fat and protein yield, and content in cattle. The results of this analysis can provide important contributions to breeding programs and animal husbandry practices maximize the genetic potential of cattle and increase efficiency in milk production. The study employed the meta-analysis method and examined four genetic models for each genotype region of the data set: dominant (TT + CT vs. CC), recessive (TT vs. CT + TT), over-dominant (TT + CC vs. CT), and co-dominant (TT vs. CT, TT vs. CC, and CT vs. CC). Standard mean differences (SMD), standard errors, and 95% confidence intervals were calculated to assess the strength of the relationship between the yield trait averages of the gene variants. The fixed model was applied when study results were homogeneous, and the random-effects model was applied when they were heterogeneous. The estimation of heterogeneity was calculated based on the I^2 statistic. For SMD results, Hedges' method was used due to the low number of studies. According to the results of the test applied in the published studies examining the relationship between *IGF-1* polymorphism and milk yield traits, it is seen that there is no publication bias. The results of the evaluation according to genetic models indicate that the associations of the *IGF-1* gene with the other yield traits should generally be examined using a codominant genetic model. The *IGF-1* gene polymorphism appears to have significant effects on fat yield, fat content, protein yield, and protein content in cattle, but not lactation milk yield. Significant differences were observed between TT-CT genotypes for fat yield and fat content, and between TT-CC genotypes for protein yield and between CT-CC genotypes for protein content, while there was no significant overall effect of the *IGF-1* gene polymorphism on lactation milk yield. As a result, the impact of *IGF-1* gene polymorphism on milk production traits may vary according to genotypes, and it is suggested that the *IGF-1* gene can be used as a significant molecular marker in breeding studies, especially for increasing the fat and protein percentage in milk.

Keywords: IGF-1; polymorphism; meta-analysis; milk yield traits; cattle

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INTRODUCTION

Cattle play a critical role in the production of milk and meat products, which are one of the main food sources of humans. Milk yield traits are one of the most interesting and researched areas in cattle breeding. These traits depend on various factors such as milk yield quantity and quality. Milk yield traits result from the complex interaction of genetic variation and environmental factors in a cattle population. In recent years, genetic research has made great progress in identifying and understanding genes associated with milk yield traits. In this framework, the *insulin-like growth factor-1* (*IGF-1*) gene has emerged as a candidate gene thought to play an important role in milk yield traits in cattle (Szewczuk et al., 2013; Wasielewska and Szatkowska, 2019).

Insulin-like growth Factor I (*IGF-1*) is an important growth factor that plays a critical role in the regulation of metabolism, embryonic development, growth, and cell proliferation. The *IGF-1* gene is a polypeptide consisting of 70 amino acids with a molecular weight of 7649 kD located on chromosome 5 (Sönmez et al., 2023). Since the *IGF-1* gene has an important role in the regulation of growth and cell proliferation, it is considered one of the candidate genes for meat and milk yield traits and growth rate in cattle (Siadkowska et al., 2006; Bonakdar et al., 2010; Szewczuk et al., 2013; Putra et al., 2017; Ardıçlı et al., 2018; Gui et al., 2018).

Numerous studies have been conducted to investigate the potential effects of *IGF-1/SnaBI* gene polymorphisms on yield traits in various cattle populations. While some researchers have associated *IGF-1* polymorphism with milk production, milk components (Siadkowska et al., 2006; Bonakdar et al, 2010; Szewczuk et al., 2013; Wasielewska and Szatkowska, 2019), dairy cattle fertility (Nicolini et al., 2013), body weight, carcass, and meat quality (Curi et al., 2005; Putra et al., 2017; Ardıçlı et al, 2018; Gui et al., 2018) and suggested its use in cattle breeding programs, others have stated that this polymorphism does not affect yield traits and more research is needed to confirm its effects (Chung and Kim 2005; Arslan et al., 2016; Putra et al., 2019; Wasielewska and Szatkowska, 2019). However, the findings of these studies have been inconsistent, and a definitive consensus has not yet been reached. Therefore, a comprehensive analysis that combines the results of existing research, known as meta-analysis, can help shed light on the relationship between IGF-1 gene polymorphism and milk yield traits.

Meta-analysis is a statistical method used to reach a general conclusion by combining the quantitative and qualitative results of studies conducted in different places, times, and populations on the same subject. Some researchers argue for the necessity of meta-analysis in terms of increasing the sample size as a result of combining studies, increasing the reliability and power of statistical results, resolving uncertainties and inconsistencies that may arise in individual studies conducted by different researchers, determining the causes of heterogeneity between studies, and helping the analysis questions that were not initially included by the researchers to become ready to be answered at the end of the analysis (Hedges 1992; Egger, 1997; Ozdemir et al., 2018; Ozdemir and Esenbuga, 2020).

This study aimed to comprehensively examine the effects of *Insulin-Like Growth Factor-1* (*IGF-1*) gene polymorphism on milk production traits in cattle and to provide a more powerful and reliable analysis by combining the results of existing research. The results of the analysis can provide important contributions to breeding programs and animal husbandry practices to maximize the genetic potential of cattle and increase efficiency in milk production.

MATERIALS AND METHODS

The search strategy in sources

The research material includes studies published in Google Scholar, Wiley, Springer, Taylor & Francis, PubMed, and Elsevier between 2003 and 2023. In these studies, a joint search was conducted in English and Turkish using the keywords "*IGF-1* polymorphism", "production/yield traits; milk production/yield trait", "relationship; association", and "cattle". PRISMA (The Preferred Report Items for Systematic Reviews and Meta-Analyses) criteria were used for the search criteria.

Publication selection and excluding criteria

In publication selection, studies reporting the effects of *IGF-1*/*SnaB*I gene polymorphism on milk production traits, number of animals per genotype, least squares means for yield traits, and standard deviation/error of the related mean were taken into consideration.

Abstract publications, studies that did not mention the number of animals per genotype, studies that did not show the standard deviation or error of the mean per genotype, and studies published in more than one place were taken into consideration as screening criteria. A total of 46 studies were collected, but 36 were excluded because they did not meet the above-mentioned criteria and 10 were used in the analyses.

Organizing data

The selected studies were recorded by entering the author of each study, year of publication, breed of animal, number of animals used, and mean and standard deviation or error data in separate columns through the Microsoft Excel program.

Statistical analysis

The meta-analysis used data sets organized separately for each genotype region. These were;

a. The analysis of differences between means is performed according to a chance or fixed model. The choice of model is determined based on proportions according to whether the results are homogeneous or heterogeneous (Hintze, 2007). When the study results are homogeneous, the fixed model is applied, and when they are heterogeneous, the chance model is applied. The heterogeneity estimate was calculated based on the I^2 statistic.

b. In the study, inheritance patterns were analyzed with four genetic models: Dominant; TT + CT and CC, recessive; TT and CT+TT, Over-dominant; TT+CC and CT, and Co-dominant; TT and CT, TT and CC, and CT and CC.

c. Standard mean differences (SMD) and standard errors with 95% confidence intervals were calculated to evaluate the strength of the relationship between the means of the relevant yield trait of the gene variants analyzed. This procedure was used for all pairwise comparisons of variants

d. For SMD results, Cohen's method was preferred when the number of studies was large (n>10), and Hedges's method was preferred when the number of studies was small. For standardized mean differences, Cohen's method is better when the number of studies is >10. If you have a small number of studies, it tends to overestimate the effect size. Hedges method for standardized mean differences is better when there are few studies (Ozdemir et al., 2018).

All statistical analyses were performed using STATA version 11.2 (Stata Corp. 2001, Stata Statistical Software). A p-value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Meta-analysis results

Publication bias and homogeneity tests were first applied to the data and then Meta Analysis was performed according to the criteria.

Publication bias

Publication bias was subjected to Begg's test and it was aimed to examine whether there was publication bias in published studies that examined the relationships between *IGF-1*/*SnaB*I polymorphism and yield traits (Table 1).

According to the results of the test applied in the published studies examining the relationship between IGF-1 polymorphism and milk yield traits, it is seen that there is no publication bias (P>0.05) (Figure 1, Table 1).

According to the results of the test applied in the published studies examining the relationship between *IGF-1* polymorphism and fat yield, it is seen that there is no publication bias (P>0.05) (Figure 2, Table 1).

According to the results of the test applied to the published studies examining the relationship between *IGF-1* polymorphism and fat percentage trait, it is seen that there is no publication bias (P>0.05) (Figure 3, Table 1).

According to the results of the test applied in the published studies examining the relationship between *IGF-1* polymorphism and protein yield trait, it is seen that there is no publication bias (P>0.05) (Figure 4, Table 1).

According to the results of the test applied to the published studies examining the relationship between *IGF-1* polymorphism and protein percentage, it is seen that there is no publication bias (P>0.05) (Figure 5, Table 1).

Meta-analysis results on associations

Table 2 presents the SMD and 95% confidence interval values for each comparison group, while Figures 6-15 show the forest plots. In the forest plot, the dark squares represent the difference in the standard mean/ratio for the respective trait, while the horizontal lines indicate the 95% confidence interval. The weight each study contributed to the meta-analysis is

Table 1. Publication bias test results according to inheritance patterns

Production Traits/ Inheritance Model	**Begg test**	**Significance (P)**	**Begg test**	**Significance (P)**
	I-Dominant Model TT+CT versus CC		**IV-(a)-Co-dominant Model TT versus CT**	
Milk yield	0.72	0.474	0.72	0.474
Fat yield	0.00	1.000	0.30	0.764
Fat content (%)	1.77	0.076	1.15	0.251
Protein yield	0.90	0.368	0.30	0.764
Protein content (%)	0.73	0.466	0.73	0.466
	II-Recessive Model TT versus CT+CC		**IV-(b)-Co-dominant Model TT versus CC**	
Milk yield	0.36	0.721	1.79	0.074
Fat yield	0.30	0.764	1.20	0.230
Fat content (%)	1.36	0.175	0.52	0.602
Protein yield	1.20	0.230	0.60	0.548
Protein content (%)	1.15	0.251	0.73	0.466
	III-Over-dominant Model TT+CC versus CT		**IV-(c)-Co-dominant Model CT versus CC**	
Milk yield	0.00	1.000	0.36	0.721
Fat yield	0.60	0.548	0.60	0.548
Fat content (%)	0.10	0.917	0.94	0.348
Protein yield	0.60	0.548	0.90	0.368
Protein content (%)	0.52	0.602	0.10	0.917

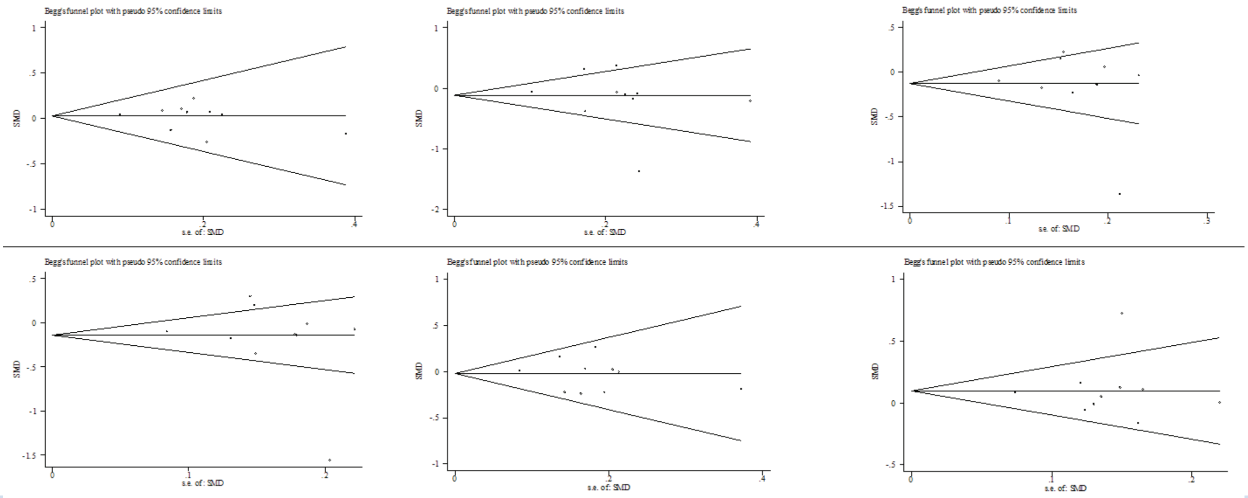

Figure 1. Funnel plots of the publication bias of the studies examining the effect of *IGF-1* polymorphism on milk yield trait (Upper line Co-dominant model, respectively; TT-CT, TT-CC, CT-CC; Lower line, respectively; Dominant, Recessive, and Over-dominant genetic models)

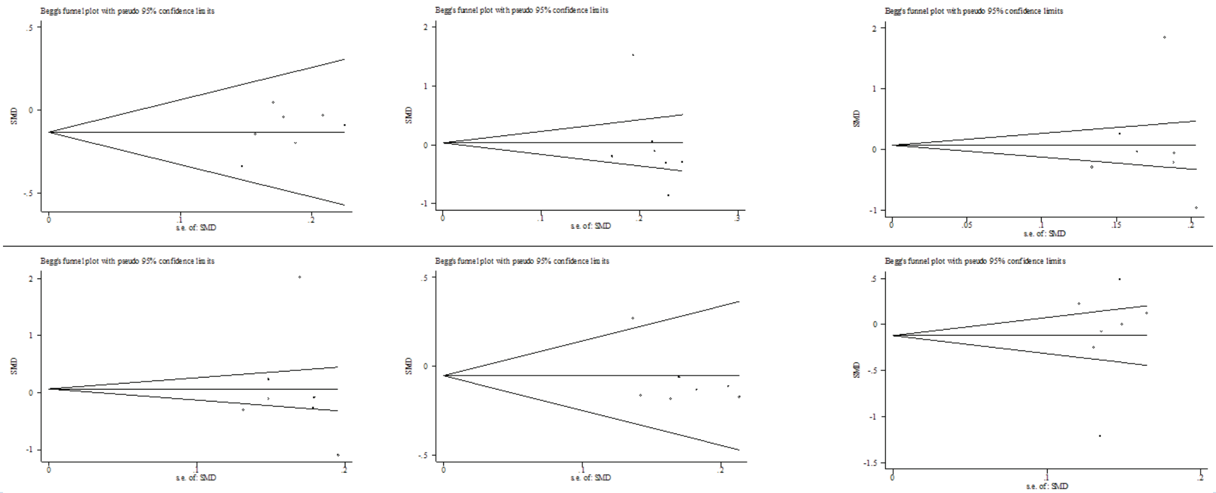

Figure 2. Funnel plots of the publication bias of the studies examining the effect of *IGF-1* polymorphism on fat yield (Upper line Co-dominant model, respectively; TT-CT, TT-CC, CT-CC; Lower line, respectively; Dominant, Recessive, and Over-dominant genetic models)

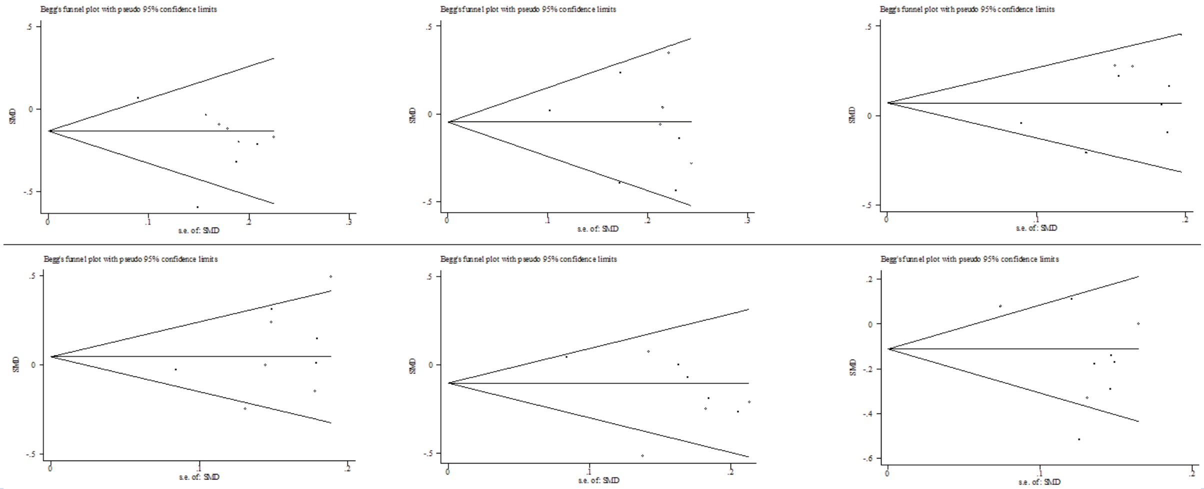

Figure 3. Funnel plots of the publication bias of the studies examining the effect of *IGF-1* polymorphism on fat percentage (Upper line Co-dominant model, respectively; TT-CT, TT-CC, CT-CC; Lower line, respectively; Dominant, Recessive, and Over-dominant genetic models)

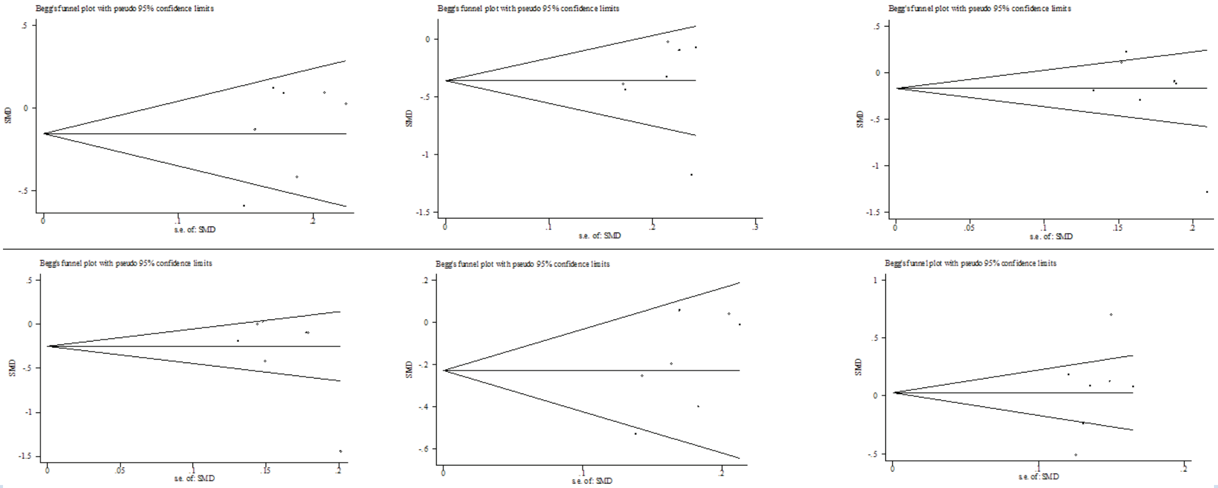

Figure 4. Funnel plots of the publication bias of the studies examining the effect of *IGF-1* polymorphism on protein yield trait (Upper line Co-dominant model, respectively; TT-CT, TT-CC, CT-CC; Lower line, respectively; Dominant, Recessive, and Over-dominant genetic models)

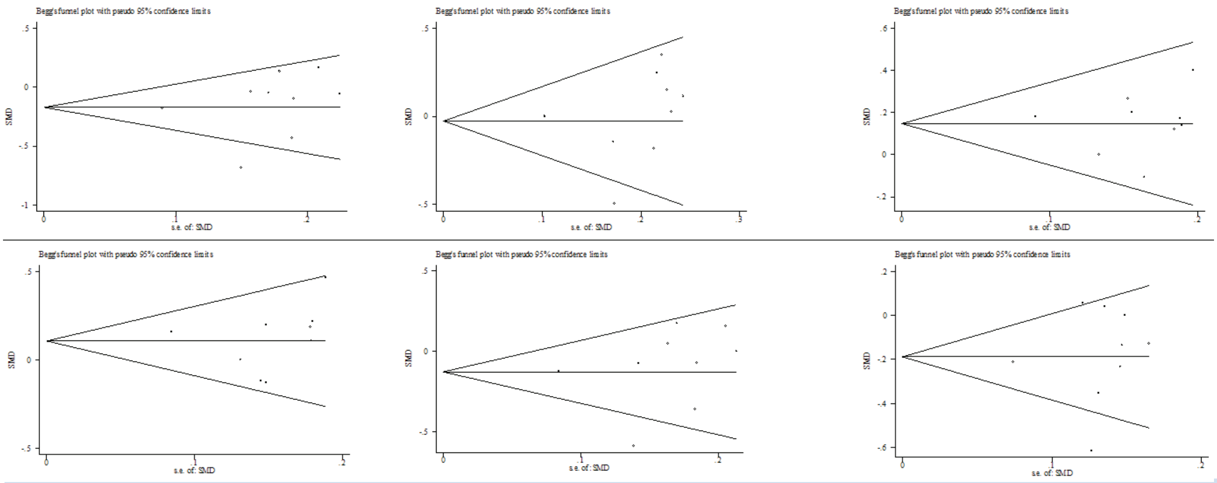

Figure 5. Funnel plots of the publication bias of the studies examining the effect of *IGF-1* polymorphism on protein percentage trait (Upper line Co-dominant model, respectively; TT-CT, TT-CC, CT-CC; Lower line, respectively; Dominant, Recessive, and Over-dominant genetic models)

reflected in the area of the black square. At the bottom of the plot, a diamond shape represents the overall mean/ratio effect from all studies, along with its confidence interval. The diamond shape is assessed based on whether it is to the right or left of the continuous vertical line and the difference is concluded as significant (P<0.05) or not significant (P>0.05). Similarly, each study's confidence interval line is evaluated, and if it touches the uninterrupted vertical line, the difference is statistically insignificant (P>0.05), otherwise, the difference is significant (P<0.05). These results show the statistical significance of the relationships between the comparison groups.

Figure 6 displays forest plots depicting the impact of *IGF-1* polymorphism on milk yield trait, specifically under the Co-dominant model and with respect to CT-CC, TT-CC, and TT-CT genotype combinations. Meta-analysis results reveal that there is no statistically significant relationship between *IGF-1* polymorphism and milk yield trait, as evidenced by the lack of significance (P>0.05) in all subgroup analyses. These findings suggest that genotype combinations do not have a uniform effect on milk yield. However, when comparing mean differences in CT-CC and TT-CC milk yield of cattle across various studies, Bonakdar et al. (2010), Siadkowska et al. (2006), Szewczuk et al. (2013), Wasielewska and Szatkowska (2019), and Czerniawska-Piatkowska et al. (2021), it appears that CT and TT have a slight prevalence over CC. Similarly, when examining mean differences in TT-CT milk yield, it is evident that TT generally outperforms CT, except for the Jersey breed in Czerniawska-Piatkowska et al. (2021) (Figure 6).

Figure 7 shows forest plots of studies that examined the effect of *IGF-1* polymorphism on milk yield traits based on other three different genetic models: Over-dominant, Recessive, and Dominant. According to the meta-analysis results, there is no statistically significant relationship between *IGF-1* polymorphism and milk yield trait according to the Recessive and Dominant models (P>0.05). These findings suggest that the effect of *IGF-1* gene polymorphism on milk yield may be multifaceted and complex since it was not statistically significant when analyzed in different genetic models. Moreover, the similar results of the analyses performed in different genetic models suggest that the relationship between *IGF-1* polymorphism and milk yield is not significant statistically.

Figure 8 displays forest plots of studies that investigate the impact of *IGF-1* polymorphism on fat yield using the Co-dominant model, CT-CC, TT-CC, and TT-CT, respectively. The meta-analysis results indicate that there is an overall advantage in favor of the CT genotype in terms of *IGF-1* polymorphism and fat yield, and there is a statistically significant difference between the TT-CT genotypes (P<0.05). The CT genotype has a general advantage in terms of fat yield, but this superiority was only observed for the CC genotype in the study of Szewczuk et al. (2013), implying that genotype traits and population differences may affect the results.

In Figure 9, you can see forest plots of studies that analyzed the impact of *IGF-1* polymorphism on fat yield, using other three genetic models - Over-dominant, Recessive, and Dominant Models. However, the

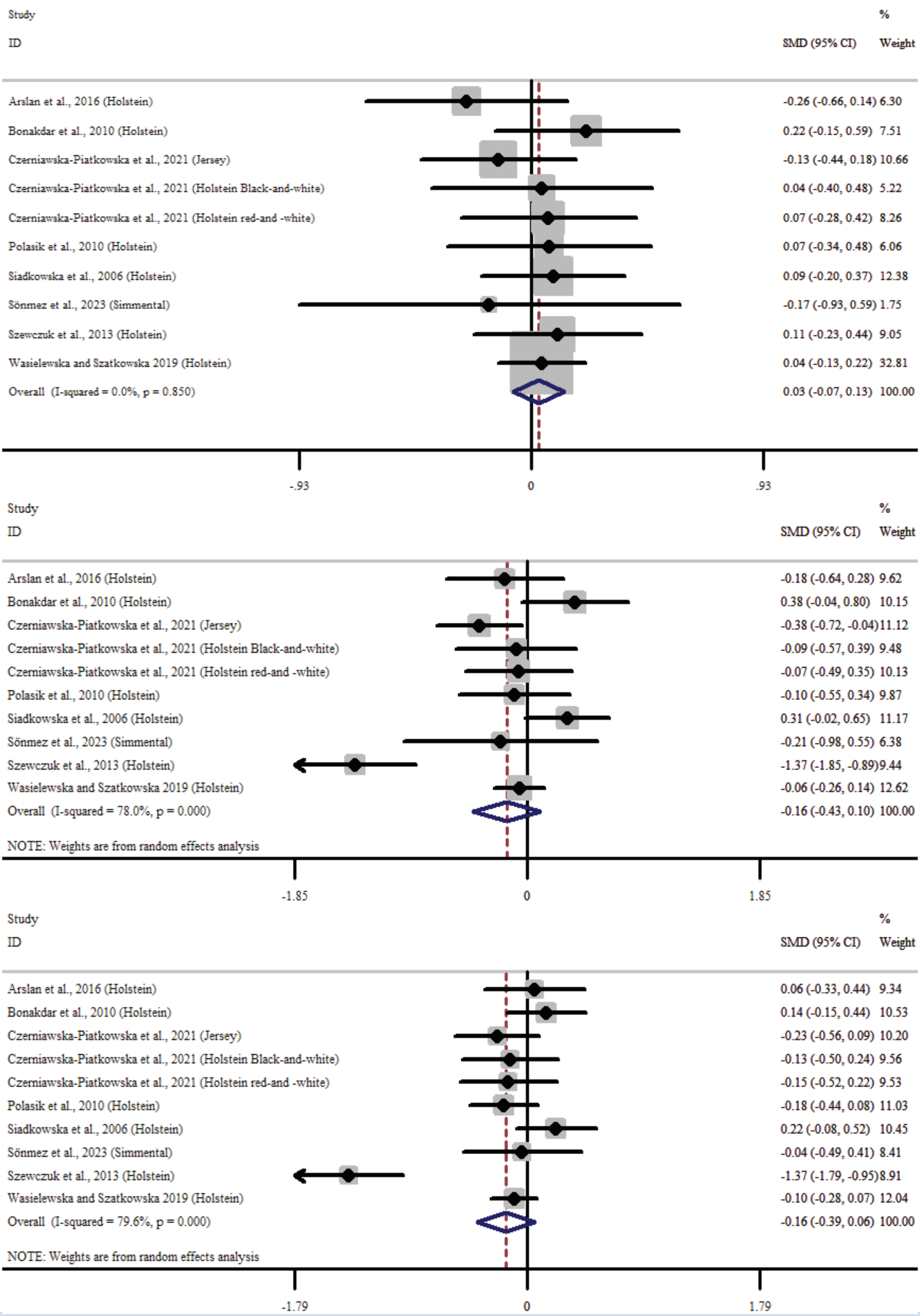

Figure 6. Forest plots of the studies examining the effect of *IGF-1* polymorphism on milk yield trait (Co-dominant model, from left to right; CT-CC, TT-CC, TT-CT, respectively)

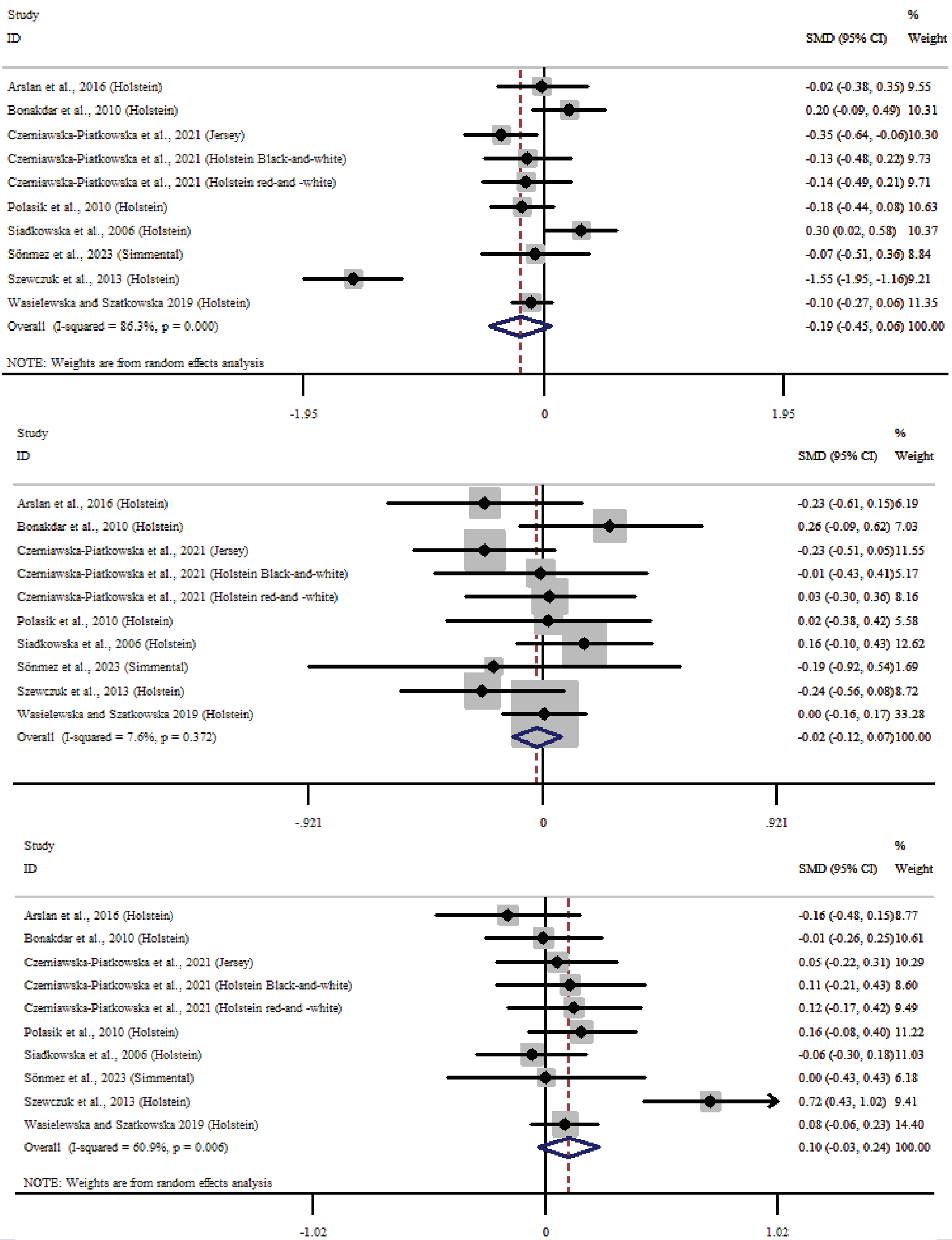

Figure 7. Forest plots of the studies examining the effect of *IGF-1* polymorphism on milk yield trait (Respectively, Over-dominant, Recessive, Dominant Model)

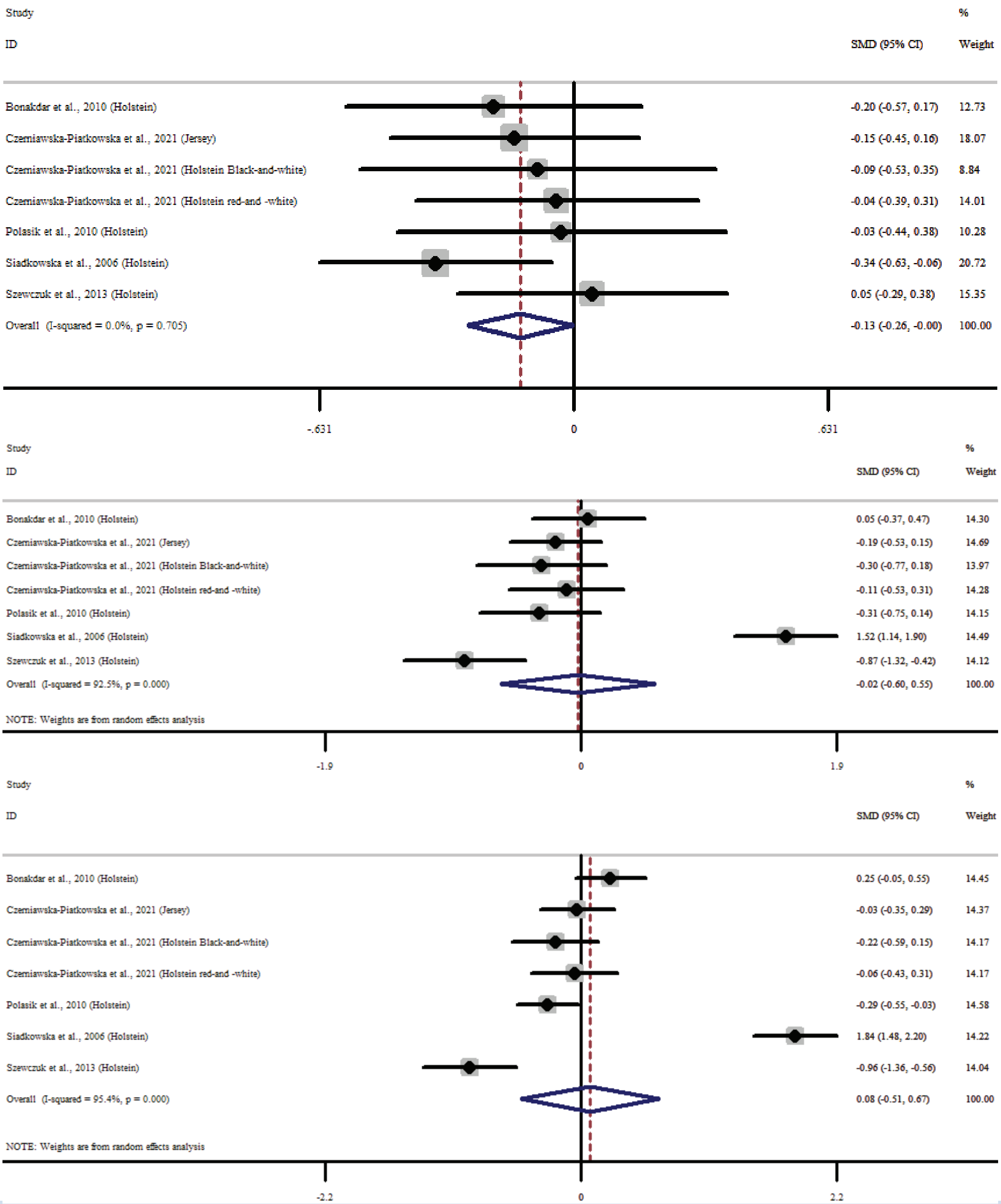

Figure 8. Forest plots of the studies examining the effect of *IGF-1* polymorphism on fat yield (Co-dominant model, CT-CC, TT-CC, TT-CT, respectively)

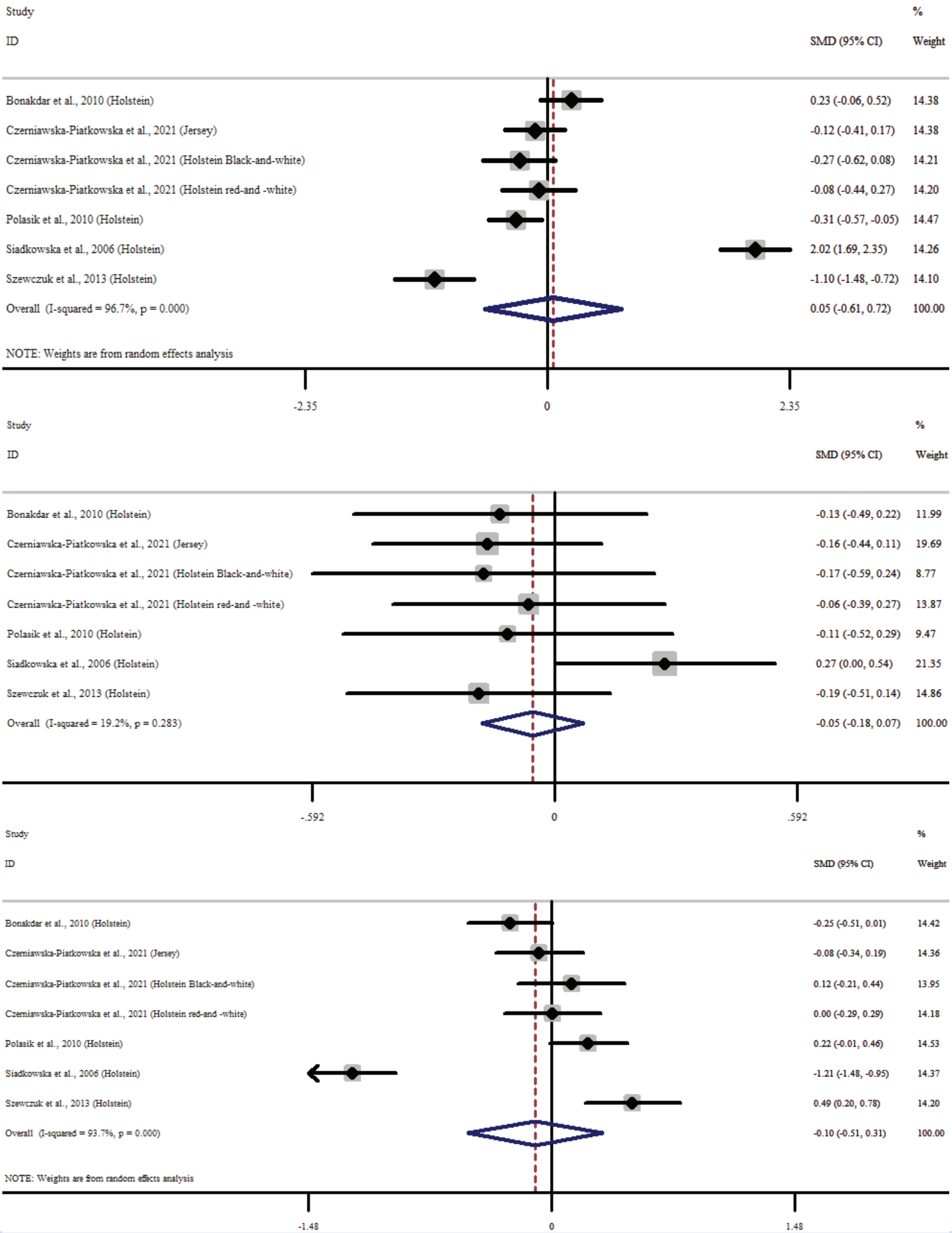

Figure 9 Forest plots of the studies examining the effect of *IGF-1* polymorphism on fat yield (Respectively, Over-dominant, Recessive, and Dominant Models)

meta-analysis results show no significant relationship between *IGF-1* polymorphism and fat yield according to the Over-Dominant, Recessive, and Dominant Models. Therefore, we can conclude that *IGF-1* polymorphism has no significant effect on fat yield, regardless of the genetic model used. However, it is important to note that these studies usually focus on a specific population or sample group.

Figure 10 displays forest plots of studies investigating the impact of *IGF-1* polymorphism on fat percentage traits using Co-dominant models for CT-CC, TT-CC, and TT-CT genotypes. The meta-analysis results indicate a statistically significant association between IGF-1 polymorphism and fat percentage trait for TT-CT genotypes under the co-dominant model (P<0.05). It appears that CT genotypes may be more effective in impacting fat percentage traits.

Figure 11 shows forest plots of studies that examined the impact of *IGF-1* polymorphism on fat percentage traits under other three genetic models - Over-dominant, Recessive, and Dominant. The results of the meta-analysis reveal that there is a significant relationship between *IGF-1* polymorphism and fat percentage trait under the Over-dominant and Recessive Models (P<0.05), while no significant relationship exists under the Dominant Model (P>0.05). These findings suggest that the effect of *IGF-1* polymorphism on fat percentage traits can vary depending on the genetic model used to examine it. Although the analyses conducted under the Dominant genetic model did not find a statistically significant association between *IGF-1* polymorphism and fat percentage, the results suggest that differences between genetic models and the effect of genotype combinations may determine the impact of *IGF-1* polymorphism on fat percentage. Taken together, these findings suggest that the effect of *IGF-1* polymorphism on fat percentage traits is complex and may yield different results epending on the genetic model used.

Figure 12 shows forest plots of studies that examined the impact of *IGF-1* polymorphism on protein yield, using the Co-dominant model. The meta-analysis results reveal a statistically highly significant relationship between *IGF-1* polymorphism and protein yield between TT-CC genotypes (P<0.01). However, there was no significant association between IGF-1 polymorphism and protein yield in the TT-CT and CT-CC genotypes.

Forest plots in Figure 13 display the results of studies examining the effect of *IGF-1* polymorphism on protein yield according to other three different genetic models - Over-dominant, Recessive, and Dominant Models, respectively. The meta-analysis results indicate that there is no statistically significant relationship between *IGF-1* polymorphism and protein yield according to the Over-Dominant and Dominant models (P>0.05). However, there is a statistically significant relationship between the two according to the Recessive model (P<0.05). The results suggest that the effect of *IGF-1* polymorphism on protein yield may vary when examined in different genetic models. The analyses conducted according to the Over-Dominant and Dominant models reveal no statistically significant relationship between *IGF-1* polymorphism and protein yield. On the other hand, according to the Recessive genetic model, there is a statistically significant relationship between IGF-1 polymorphism and protein yield. These results may indicate that *IGF-1* polymorphism has a significant effect on protein yield in this specific genetic model.

Figure 14 shows forest plots of studies that investigate the impact of *IGF-1* polymorphism on protein percentage traits through different genotype combinations, including CT-CC, TT-CC, and TT-CT, under the Co-dominant model. Meta-analysis results indicate a strong correlation between *IGF-1* polymorphism and protein percentage trait in the co-dominant genetic model (P<0.05). Therefore, the effect of *IGF-1* polymorphism on protein percentage trait is statistically significant when analyzed in the co-dominant genetic model. These results suggest that IGF-1 polymorphism has a significant impact on protein percentage traits. Our analyses further reveal that the association between *IGF-1* polymorphism and protein percentage trait is statistically significant across CT-CC and TT-CT genotype combinations. This indicates that genotype combinations play a crucial role as an advantage in favor of CT genotype in determining protein percentage, and *IGF-1/SnaB*I CT genotype can be used for breeding purposes on the milk protein content.

Forest plots in Figure 15 display the results of studies that examined the impact of *IGF-1* polymorphism on protein percentage trait, based on other three genetic models: over-dominant, recessive, and dominant. Meta-analysis indicates a statistically significant relationship between *IGF-1* polymorphism and protein percentage trait under the Over-Dominant and Dominant model (P<0.05), but not under the Recessive models (P>0.05). These results suggest that the effect of *IGF-1* polymorphism on protein percentage traits may vary depending on the genetic model used for examination. In analyses conducted based on the Over-Dominant and Dominant models, a statistically significant relationship was observed between *IGF-1* polymorphism and protein percentage yield. However, in the analysis under the Recessive model, no statistically significant relationship between *IGF-1* polymorphism and protein percentage was found.

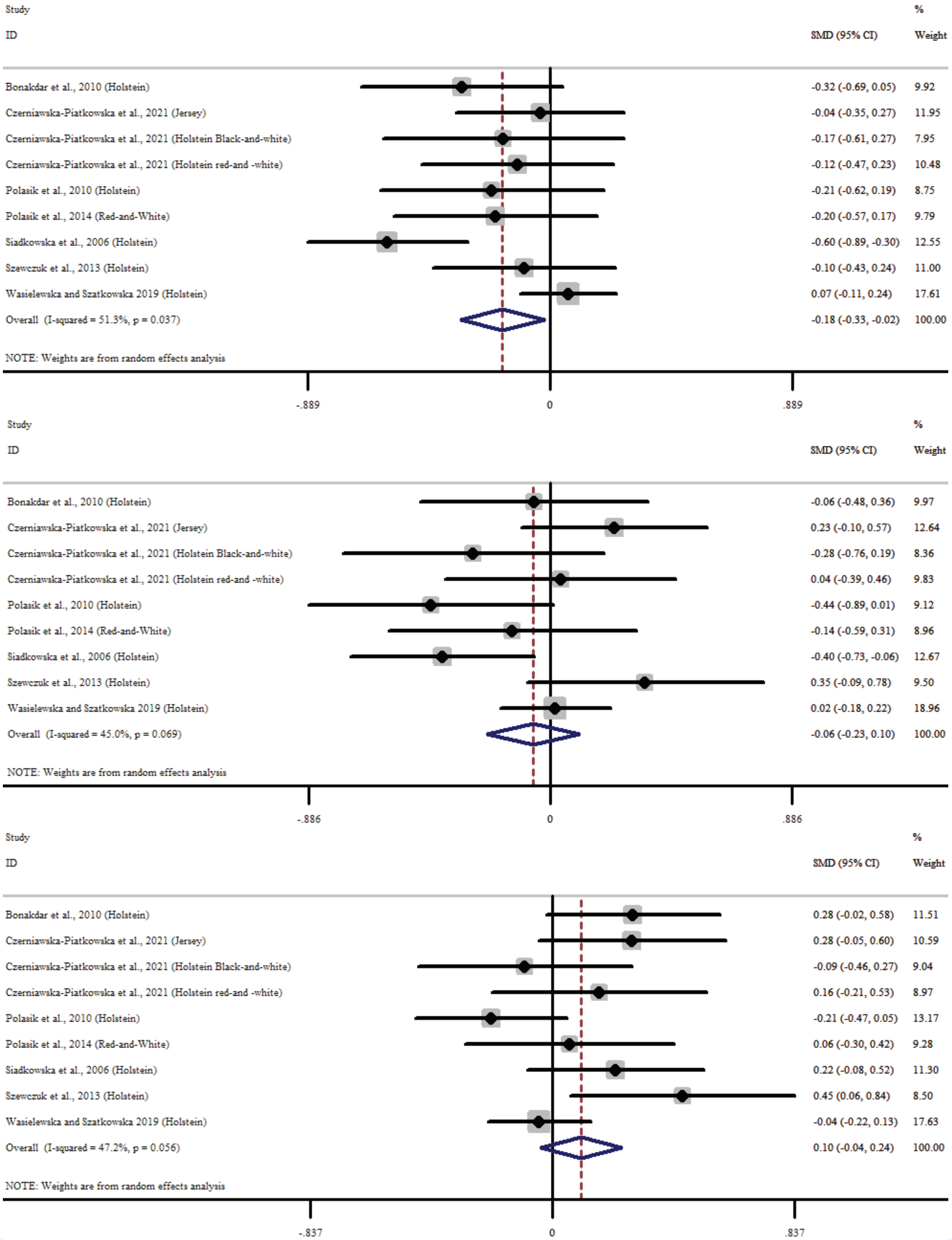

Figure 10 Forest plots of the studies examining the effect of *IGF-1* polymorphism on fat percentage trait (Co-dominant model, respectively; CT-CC, TT-CC, TT-CT)

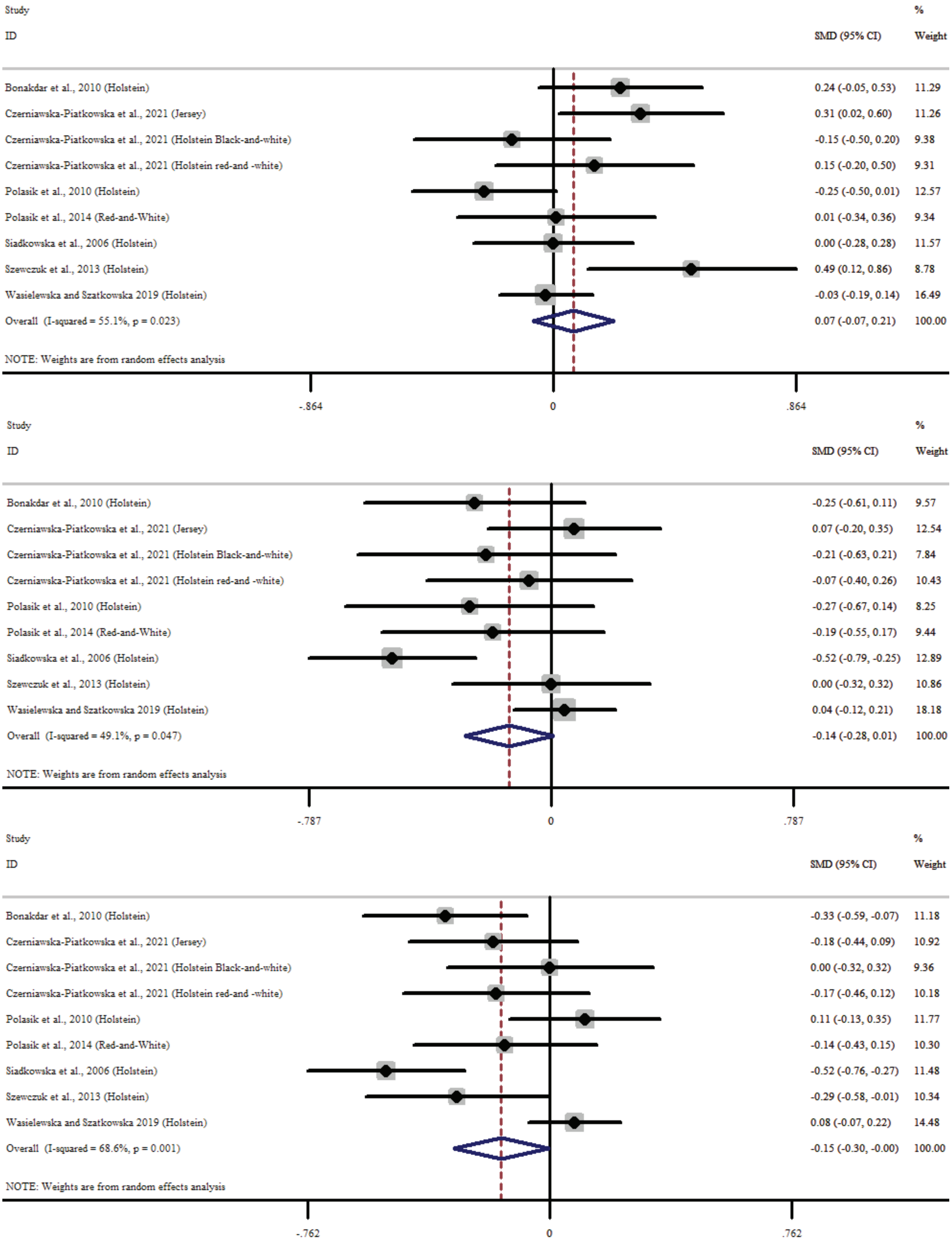

Figure 11 Forest plots of the studies examining the effect of *IGF-1* polymorphism on fat percentage trait (Respectively, Over dominant, Recessive, Dominant Model)

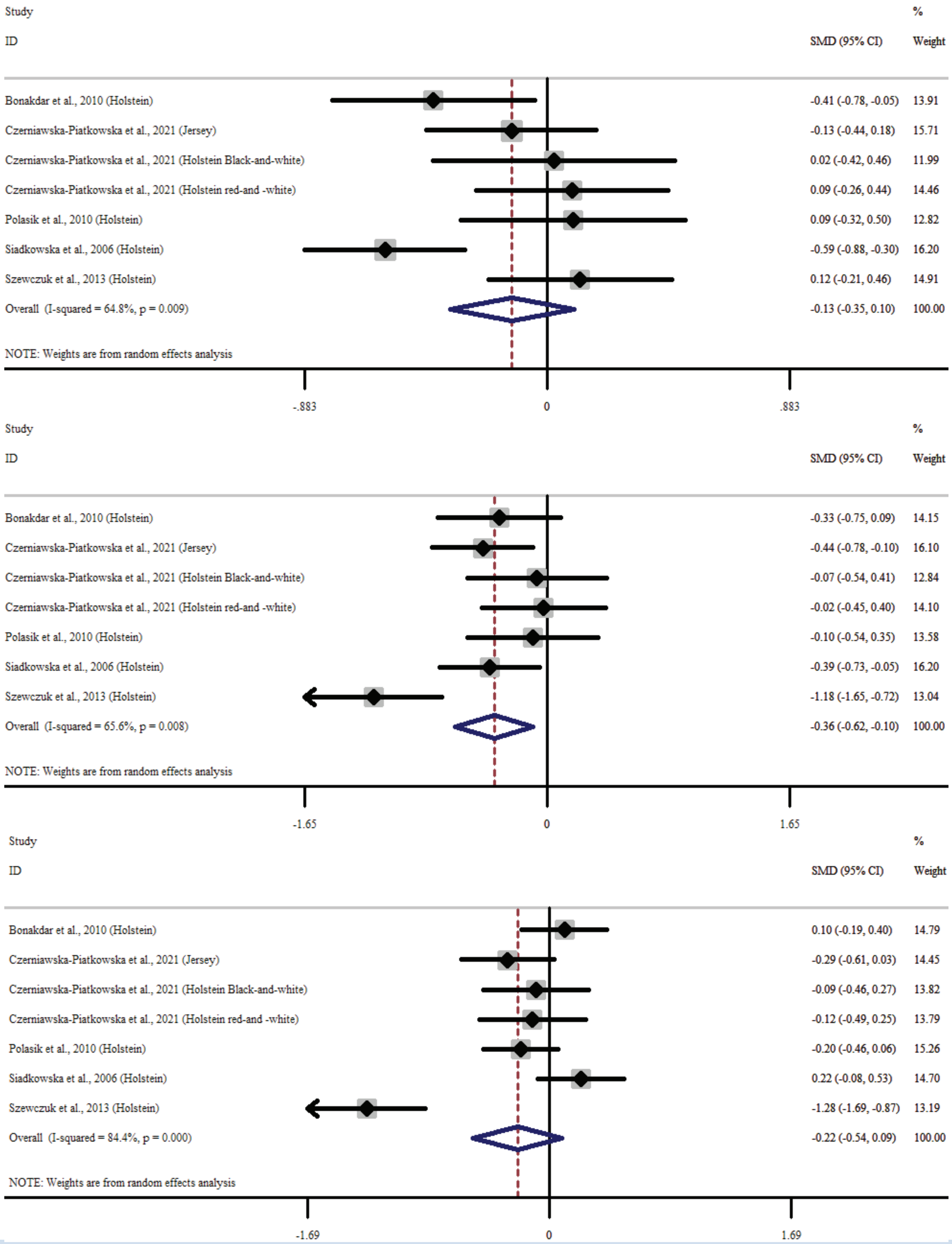

Figure 12 Forest plots of the studies examining the effect of *IGF-1* polymorphism on Protein yield (Co-dominant model, CT-CC, TT-CC, TT-CT, respectively)

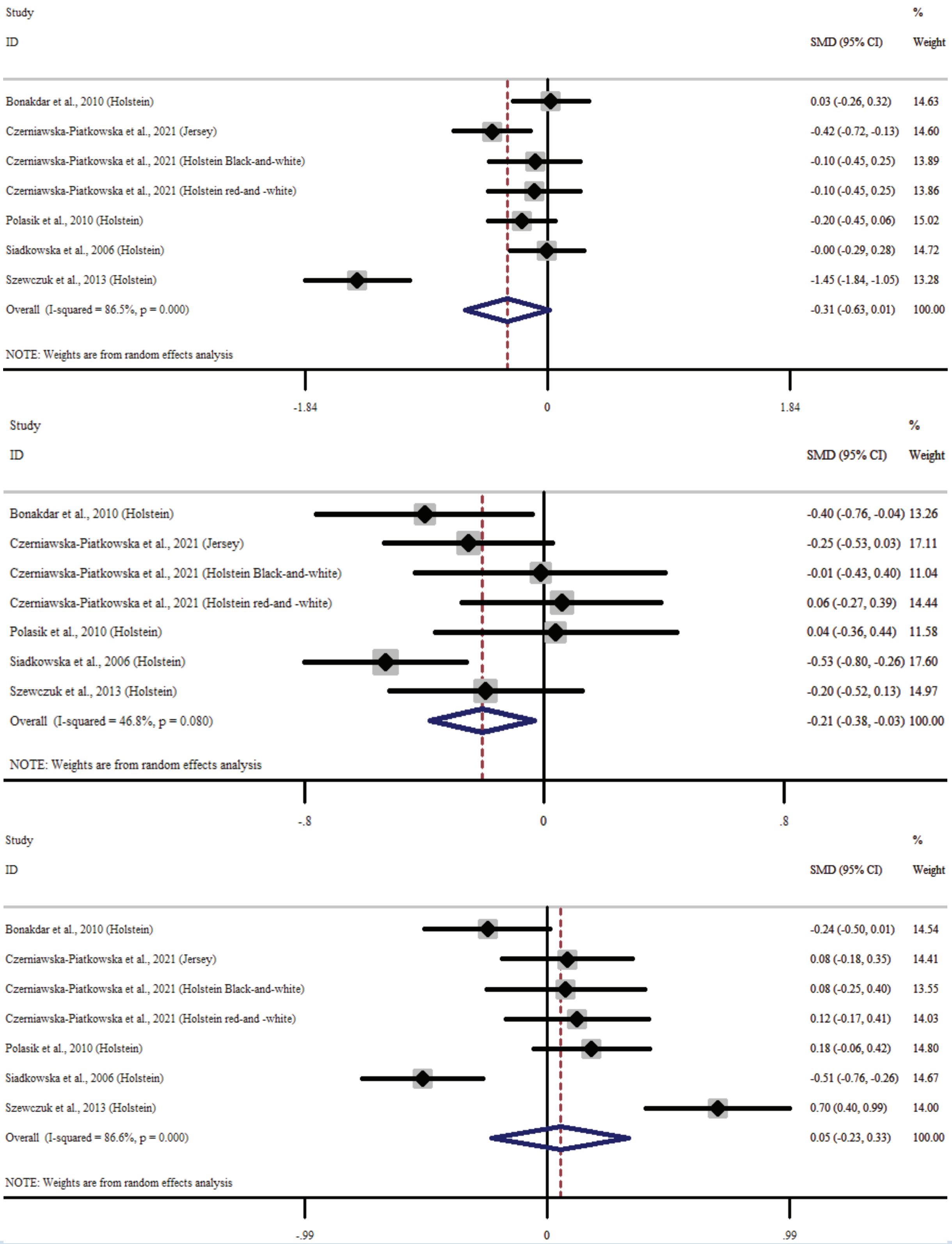

Figure 13 Forest plots of the studies examining the effect of *IGF-1* polymorphism on Protein yield (Respectively, Over-dominant, Recessive, Dominant Model)

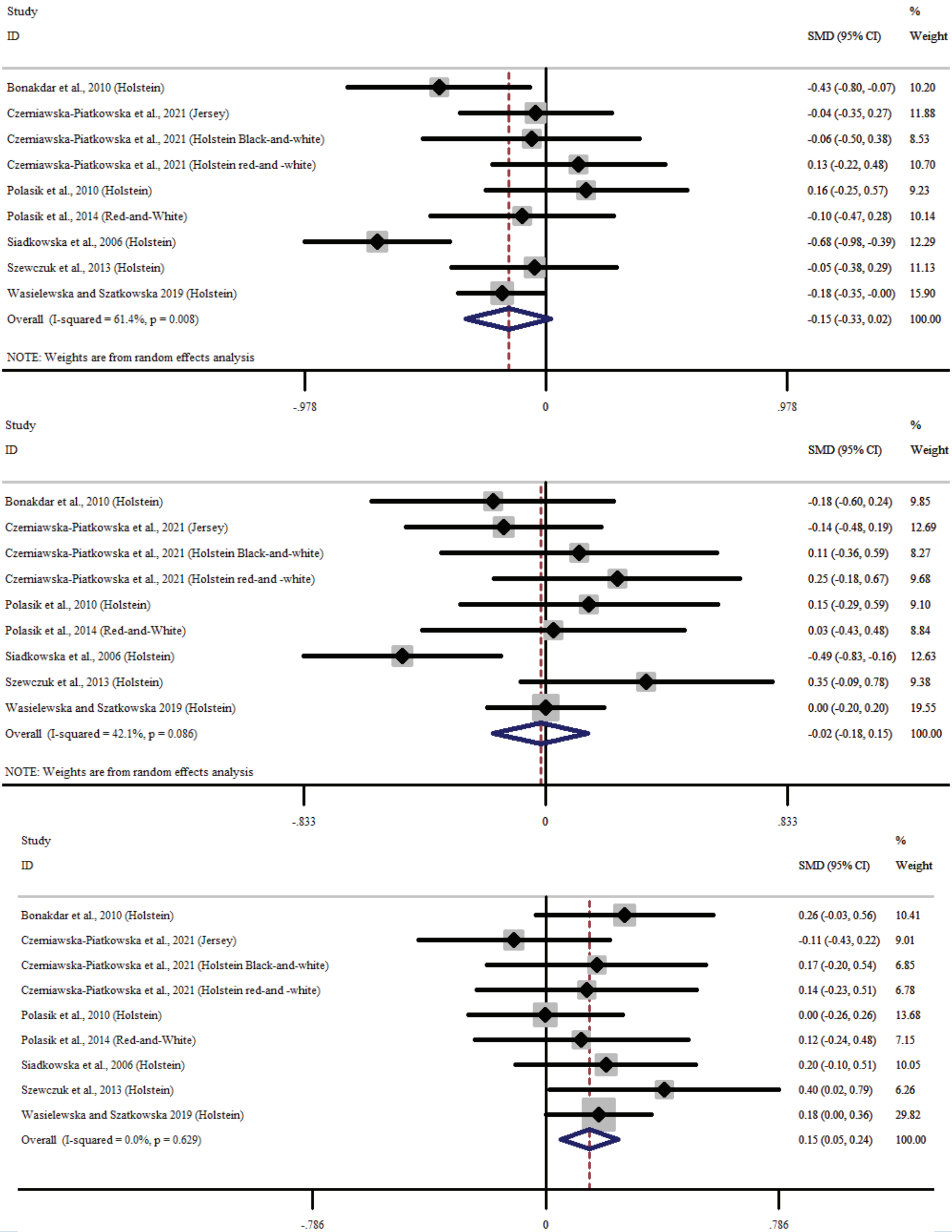

Figure 14 Forest plots of the studies examining the effect of *IGF-1* polymorphism on protein percentage trait (Co-dominant model, CT-CC, TT-CC, TT-CT, respectively)

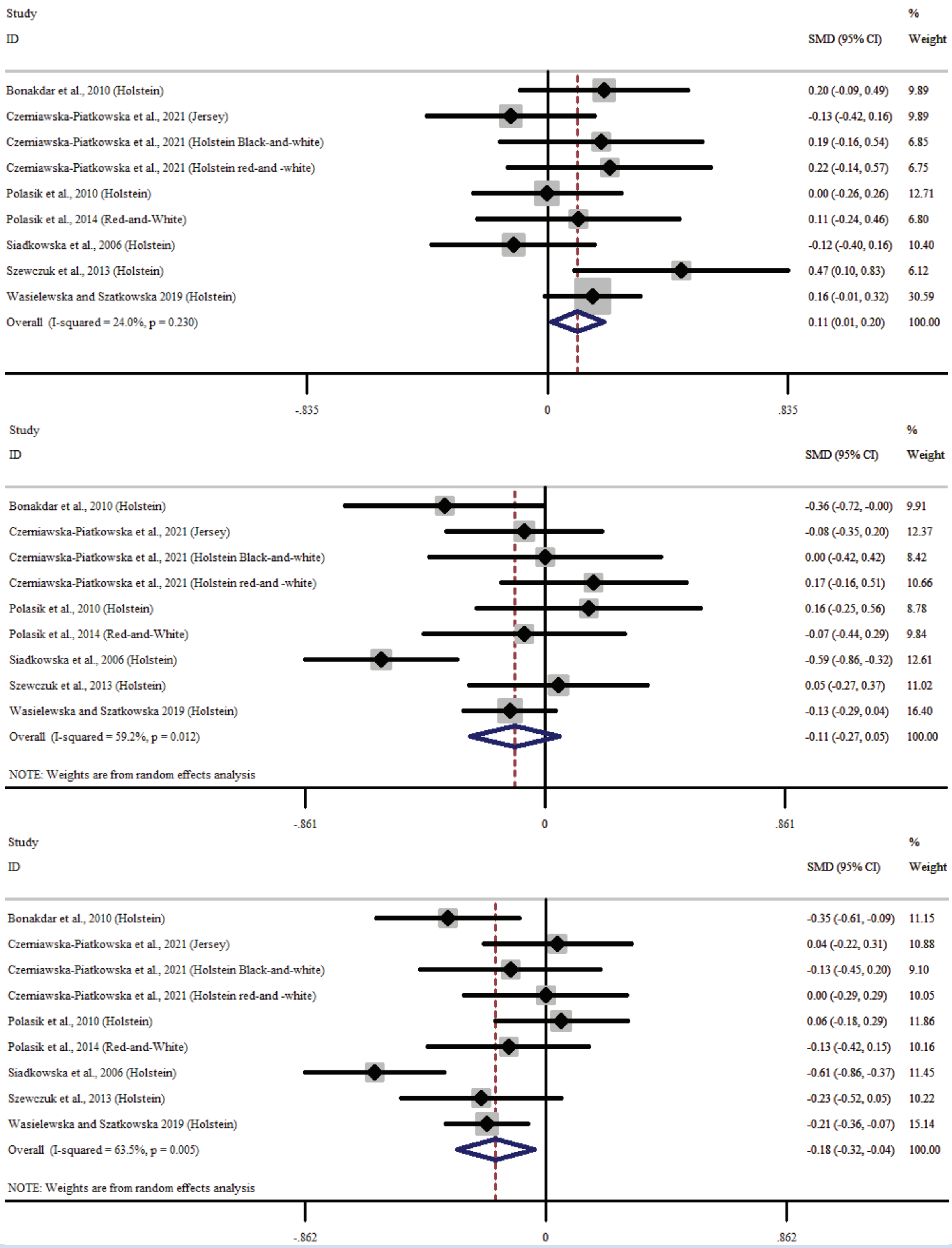

Figure 15 Forest plots of the studies examining the effect of *IGF-1* polymorphism on Protein percentage trait (Respectively, Over-dominant, Recessive, Dominant Model)

Homogeneity-heterogeneity of studies

The homogeneity-heterogeneity status of the studies, the analysis model applied, and the results of meta-analysis (SMD values, confidence intervals, and significance levels) according to the tests applied separately according to the inheritance patterns on the studies examining the relationships between *IGF-1* polymorphism and yield traits are presented in Table 2.

The results of the I^2 heterogeneity test show that there is high heterogeneity between studies generally. The reason for this difference could be due to the small number of studies analyzed, high sampling error, and population differences. Therefore, meta-analyses in heterogeneous groups were conducted based on the random model.

In a meta-analysis of ten studies on lactation milk yield, there was no significant association between the mean lactation milk yields of *IGF-1/SnaB*I genotypes (TT, CT, and CC) in cattle. The mean differences according to the other genetic models examined were also not significant. However, some individual stud-

Table 2. Results of I^2 heterogeneity test, Model selection, and Meta-analysis of yield traits according to four genetic models

Production Traits	N	I^2 (%)	Model	SMD	Confidence Interval 95% Lower-Upper		Significance (P)
I-Dominant Model; TT+CT versus CC							
Milk yield	10	86.3***	R	-0.193	-0.447	0.061	0.136
Fat yield	7	96.7***	R	0.054	-0.608	0.716	0.873
Fat content (%)	9	55.1**	R	0.071	-0.072	0.215	0.330
Protein yield	7	86.5***	R	-0.308	-0.628	0.013	0.060
Protein content (%)	9	24.0	F	0.106	0.014	0.197	0.023*
II-Recessive Model; TT versus CT+CC							
Milk yield	10	7.6	F	-0.021	-0.116	0.074	0.663
Fat yield	7	19.2	F	-0.053	-0.177	0.071	0.403
Fat content (%)	9	49.1**	R	-0.138	-0.281	0.005	0.059
Protein yield	7	46.8*	R	-0.207	-0.380	-0.034	**0.019***
Protein content (%)	9	59.2**	R	-0.110	-0.269	0.050	0.177
III-Over-dominant Model; TT+CC versus CT							
Milk yield	10	60.9**	R	0.102	-0.031	0.236	0.0133
Fat yield	7	93.7***	R	-0.103	-0.512	0.307	0.622
Fat content (%)	9	68.6***	R	-0.153	-0.302	-0.005	**0.043***
Protein yield	7	86.6***	R	0.053	-0.226	0.333	0.707
Protein content (%)	9	63.5***	R	-0.179	-0.317	-0.041	**0.011***
IV-(a)-Co-dominant Model; TT versus CT							
Milk yield	10	0.0	F	0.029	-0.072	0.130	0.572
Fat yield	7	0.0	F	-0.133	-0.265	-0.002	**0.046***
Fat content (%)	9	51.3**	R	-0.175	-0.329	-0.021	**0.026***
Protein yield	7	64.8***	R	-0.128	-0.352	0.096	0.263
Protein content (%)	9	61.4***	R	-0.153	-0.326	0.021	0.084
IV-(b)-Co-dominant Model; TT versus CC							
Milk yield	10	78.0***	R	-0.164	-0.430	0.102	0.227
Fat yield	7	92.5***	R	-0.024	-0.595	0.548	0.935
Fat content (%)	9	45.0*	R	-0.063	-0.231	0.104	0.460
Protein yield	7	65.6***	R	-0.360	-0.624	-0.097	**0.007****
Protein content (%)	9	42.1*	R	-0.017	-0.180	0.146	0.839
IV-(c)-Co-dominant Model; CT versus CC							
Milk yield	10	79.6***	R	-0.165	-0.385	0.056	0.144
Fat yield	7	95.4***	R	-0.076	-0.513	0.666	0.799
Fat content (%)	9	47.2*	R	0.101	-0.039	0.240	0.156
Protein yield	7	84.4***	R	-0.223	-0.536	0.090	0.163
Protein content (%)	9	0.0	F	0.147	0.050	0.243	**0.003****

N: Number of publications, F: Fixed Model, R: Rondom-effects Model.
For I^2; *:p<0.10, **:p<0.05, ***:p<0.01, For SMD; *:p<0.05, **:p<0.01, ***:p<0.001.

ies reported significant mean differences in lactation milk yield between *IGF-1* genotypes according to the co-dominant model (Bonakdar et al., 2010; Szewczuk et al., 2013), while others did not.

A meta-analysis of 7 studies found a significant association between the mean lactation fat yields of cattle with *IGF-1* gene TT and CT genotypes (P<0.05), but not with CC genotype. However, the mean differences in lactation fat yields of TT-CC and CT-CC genotypes and mean differences according to other genetic models examined were not significant (P>0.05).

Similarly, in the meta-analysis of 9 studies, a significant association was found between the mean lactation fat content (%) of cattle with TT and CT genotypes of the IGF-1 gene (P<0.05), while a significant association was not found between the mean lactation fat content (%) of TT-CC and CT-CC genotypes (P>0.05) and the mean differences according to the other genetic models analyzed.

The analysis of 7 studies found a significant association between lactation protein yield and the IGF-1 gene in cattle, with a highly significant association between the TT and CC genotypes (P<0.001). However, mean differences between TT-CT and CT-CC genotypes and other genetic models examined were not significant statistically (P>0.05).

In the meta-analysis of 9 studies, a highly significant association was found between the mean lactation protein content (%) and the *IGF-1* gene in cattle, particularly with the CT and CC genotypes (P<0.01). A significant association was not found between the mean lactation protein content (%) and the TT-CT and TT-CC genotypes (P<0.001). In the Over-Dominant and Dominant models, a statistically significant relationship was observed between *IGF-1* polymorphism and protein percentage trait but not in the recessive model.

CONCLUSION

After conducting a meta-analysis study, it was found that *IGF-1/SnaB*I gene polymorphism has a significant effect on the fat and protein yield and content in the milk of cows. The Meta-analysis shows that the association of the *IGF-1* gene must generally be investigated under the co-dominant genetic model. Although the milk yield was not significantly affected, there were significant mean differences in favor of the CT genotype between TT-CT genotypes for fat yield and fat content, and in favor of the CC genotype between TT-CC genotypes for protein yield and in favor of the CT genotype between CT-CC genotypes for protein content. These results show that *IGF-1* gene polymorphism can be utilized in the breeding of certain milk production traits in cattle breeding.

CONFLICT OF INTEREST

The authors declare no competing interests.

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