Table 1. **Continue …**

Gene	Polymorphism	Cohort (sex, sample size)	Population	Favorable allele/ genotype	Type of diet therapy	Outcome	References
UCP2	rs660339 G/A	n= 386, women 100%	East Asian	G	Caloric restriction diet for 4 weeks.	carriers of the G allele had significantly reduced body fat mass (BFM) (-5.0±0.2 kg vs. -3.9±0.3 kg, P=0.016) compared to carriers of the AA genotype	(Cha et al., 2007)
UCP2	rs659366 G/A	n= 458, women 100%	East Asian	G	markedly hypocaloric diet for 4 weeks.	individuals with the G allele showed a significant reduction in BMI (-2.8±0.8 units vs. -2.4±1.0 units, P=0.02) and body fat mass (BFM) (-5.3±3.6 kg vs. -4.2±2.1 kg, P=0.03) compared to those with the AA genotype	(Yoon et al., 2007)
UCP3	rs1800849 rs2075576 rs1800006 rs1685325 rs2734827 rs2075577	n= 214, women 100% the average age is 28.6±9.6 years	East Asian	Haplotype [CGTACC]	extremely hypocaloric diet for 4 weeks	carriers of the haplotype [CGTACC], compared to carriers of the haplotype [TCCGTT], had significantly reduced body mass (BMI: -7.7±2.2 kg vs. -6.5±2.5 kg, P=0.016), body mass index (BMI: -2.98±0.91 vs. -2.54±0.94, P=0.039), and fat mass (FM: -5.5±4.6 kg vs. -4.3±1.8 kg, P=0.028)	(Cha et al., 2006)

n/d- no data; MT- body mass; BMI- body mass index, FM- fat mass; WC- waist circumference

Table 2. **Genetic markers associated with exercise-induced weight loss efficiency.**

Gene	Polymorphism	Cohort (sex, sample size)	Population	Favorable allele/ genotype	Type of exercise	Outcome	References
ACSL1	rs116143768 C/T	n=126, women 100%	European	T	aerobic training for 12 weeks	carriers of the T allele, compared to those with the CC genotype, had significantly reduced relative fat mass (by 31.4% vs. -3.8%, P=1.18×10^{-9})	(Bojarczuk et al., 2022)
ADRA2B *ADRB3* *ADRB2*	rs28365031 I/D rs4994 A/G rs1042714 G/C	n=70, women 78,6%	Mixed (USA)	Haplotype [*ADRA2B II, ADRB3 G]*, Haplotype [*ADRA2B II, ADRB2* G]	aerobic exercises of moderate intensity for 24 weeks	carriers of the haplotype [*ADRA2B* II, *ADRB3* G], compared to non-carriers of this haplotype, had significantly reduced total body fat (-3.8±1.0 vs. -0.8±0.3 kg, P=0.007), relative total body fat (-4.0±0.9%, P=0.009), and relative trunk fat (-4.8±1.1%, P<0.01) carriers of the haplotype [*ADRB3 G*, *ADRB2 G*], compared to non-carriers of this haplotype, significantly reduced total body fat (-3.2 ± 0.8 kg vs. -1.4±0.6 kg, P=0.031) and relative total body fat (-4.2±0.8%, P<0.005)	(Phares et al., 2004)
ADRB2 *ADRB2* *ADRB3* *ADRA2A*	rs1042713 G/A rs1042714 G/C rs4994 A/G rs553668 G/A	n=163, women 100%	European	Alleles rs1042713 A, rs1042714 C, rs553668 A in combination	aerobic training for 12 weeks	carriers of a small number (0–3) of obesity risk alleles [rs1042713 G, rs1042714 G, rs553668 G] had significantly reduced relative total body fat compared to carriers of a high number (5-6) of risk alleles (7.7±9.8% vs. 4.0±9.4%, P = 0.0362)	(Leońska-Duniec et al., 2018)
ADRB2	rs1042714 G/C	n=70, women 78,6%	Mixed (USA)	G	aerobic exercises of moderate intensity for 24 weeks	carriers of the G allele, compared to carriers of the C allele, had significantly reduced relative total body fat (-2.7±0.4% vs. -1.3±0.4%, P=0.015) and relative trunk fat (-3.2±0.5% vs. -1.5±0.5%, P=0.02	(Phares et al., 2004)
ADRB3	rs4994 A/G	n=70, women 78,6%	Mixed (USA)	G	aerobic exercises of moderate intensity for 6 months	carriers of the G allele, compared to individuals with the AA genotype, had significantly reduced relative total body fat (-2.7±0.5% vs. -1.3±0.3%, P=0.027) and relative trunk fat (3.1±0.6% vs. -1.6±0.3%, P=0.03)	(Phares et al., 2004)
ADRB3	rs4994 A/G	n=65, women 72,3%	European	AA	aerobic exercise on the background of a hypocaloric diet for 12 weeks	individuals with the AA genotype, compared to individuals with the AG genotype, had significantly reduced BMI (n/d, P<0.05), body mass (n/d, P<0.05), fat mass (n/d, P<0.05), and waist circumference (WC) (n/d, P<0.05).	(de Luis et al., 2007)

n/d- no data; MT- body mass; BMI- body mass index, FM- fat mass; WC- waist circumference

Table 2. Continue ….

Gene	Polymorphism	Cohort (sex, sample size)	Population	Favorable allele/ genotype	Type of exercise	Outcome	References
AHSG	rs4917 T/C	n=105, women 100%	European	TT	high-intensity aerobic exercise on the background of a hypocaloric diet for 10 weeks	carriers of the TT genotype, compared to carriers of the C allele, had significantly reduced trunk fat (-3.7±11.4 kg vs. 1.5±15.1 kg, P<0.005)	(Suchanek et al., 2011)
COMT	rs4680 G/A	n=173, women 100%	Mixed (USA)	GG	aerobic exercise of moderate intensity for 1 year	carriers of the GG genotype, compared to carriers of the AA genotype, had significantly reduced relative total body fat (-1.9% vs. -0.7%, P=0.05)	(Tworoger et al., 2004)
CYP19	(TTTA)n	n=173, women 100%	Mixed (USA)	(TTTA)2-11	aerobic exercise of moderate intensity for 1 year	carriers of the (TTTA)2-11 allele, compared to non-carriers, had significantly reduced total body fat (-3.1 kg vs. -0.5 kg, P = 0.01) and relative total body fat (-2.4% vs. -0.6%, P=0.001)	(Tworoger et al., 2004)
DRD2	rs1800497 C/T	n=127, women 100%	European	C	resistance training with weights on the background of a hypocaloric diet for 6 months	carriers of the C allele, compared to carriers of the T allele, had significantly reduced BMI (-2.3 units vs. -1.4 units, P=0.001), body mass (-7 kg vs. -4.4 kg, P=0.001), and body fat mass (-6.2 kg vs. -4.4 kg, P=0.001)	(Cameron et al., 2013)
FABP2	rs1799883 T/C	n= 69, women 79,7%,	European	C	aerobic exercise in conjunction with a hypocaloric diet for 12 weeks	carriers of the C allele, compared to individuals with the TT genotype, had significantly reduced total body fat (-1.6 kg vs.-1.3 kg, P<0.05)	(de Luis et al., 2006)
FTO	rs8050136 C/A	n= 481, women 51,8%	European	CC	aerobic exercise of low/moderate intensity for 20 weeks	carriers of the CC genotype, compared to individuals with the AA genotype, had significantly reduced total body fat (-0.8±0.1 kg vs. -0.2±0.2 kg, P=0.0065) and relative total body fat (-1.0±0.1% vs. -0.3±0.2%, P=0.0087)	(Rankinen et al., 2010)
IL15	rs1057972 A/T	n= 163, women 100%	European	A	aerobic exercise of moderate intensity for 12 weeks	carriers of the A allele, compared to individuals with the TT genotype, had significantly reduced relative total body fat (n/d, P=0.00002)	(Ficek et al., 2019)
IL15	rs1589241 T/C rs1057972 A/T	n= 163, women 100%	European	Haplotype [TA]	aerobic exercise of moderate intensity for 12 weeks	carriers of the [TA] haplotype, compared to carriers of the [AT] haplotype, had significantly reduced relative visceral fat (n/d, P=0.027)	(Ficek et al., 2019)
INSIG2	rs7566605 C/G	n=752, women 60%	European	GG	resistance training with added weight for 12 weeks	among men, carriers of the GG genotype, compared to carriers of the C allele, had significantly reduced relative subcutaneous fat (-1.0±1.7% vs.6.4±1.8%, P=0.035)	(Orkunoglu-Suer et al., 2008)
NYD-SP18	rs6971091 G/A	n=139, women 100%	European	GG	high-intensity aerobic exercise in conjunction with a hypocaloric diet for 10 weeks	carriers of the GG genotype, compared to carriers of the A allele, significantly reduced fat mass (-5.0±3.3 kg vs. -3.7±3.5 kg, P=0.037)	(Suchánek et al., 2015)
PLIN1	rs1052700 A/T	n=30, women 100%	American	TT	high-Intensity Interval Training (HIIT) alongside a hypocaloric diet for 12 weeks	carriers of the TT genotype, compared to carriers of the AA and AT genotypes, had significantly reduced body fat mass (BFM)(-5.1±1.8 kg vs. -1.8±1.4 kg and vs. -2.1±2.3 kg, respectively, P=0.04)	(Andrade-Mayorga et al., 2021)

n/d- no data; MT- body mass; BMI- body mass index, FM- fat mass; WC- waist circumference

Table 2. **Continue ….**

Gene	Polymorphism	Cohort (sex, sample size)	Population	Favorable allele/ genotype	Type of exercise	Outcome	References
PPARG	rs1801282 C/G	n=201, women 100%	European	CC	aerobic training for 12 weeks	carriers of the CC genotype had significantly reduced fat mass (not specified, P=0.0002) and relative fat mass (not specified, P=0.00003) compared to carriers of the G allele	(Zarebska et al., 2014)
PPARG	rs1801282 C/G	n=79, women 45,6%	European	G	aerobic exercises for 10 weeks	carriers of the G allele, compared to individuals with the CC genotype, had significantly reduced body mass (-1.8±1.8 kg vs. -0.3±1.4 kg, P<0.05	(Østergård et al., 2005)
PPARG	rs1801282 C/G	n = 1004, women n/d	Mixed	G	moderate-intensity physical activity for one year (e.g., walking)	carriers of the G allele, compared to individuals with the CC genotype, significantly reduced body mass (n/d, P = 0.04) and subcutaneous fat mass (n/d, P=0.03)	(Franks et al., 2007)
PPARGC 1A	rs17650401 C/T	n=39, women 100%	European	T	high-intensity aerobic exercise alongside a hypocaloric diet for 12 weeks	carriers of the T allele, compared to individuals with the CC genotype, had significantly reduced relative body fat mass (BFM) by 2.5 times (P = 0.00013)	(Mazur et al., 2020)
TCF7L2	rs7903146 C/T	n=309, women 62,8%	European	CC	moderate-intensity physical activity over the course of 2 years	carriers of the CC genotype, compared to carriers of the T allele, significantly reduced BMI (-1.2±1.6 units vs. -0.7±1.5 units, P=0.0034), non-visceral fat mass (-2.7±3.6 kg vs. -1.3±2.9 kg, P=0.0022), and visceral fat mass (-0.5±0.6 kg vs. -0.3±0.6 kg, P=0.0165)	(Haupt et al., 2010)
UCP2	I/D	n=42, women 100%	East Asian	D	moderate-intensity aerobic exercise for 6 months	carriers of the DD and ID genotypes, compared to carriers of the II genotype, had significantly reduced body mass (-1.57 kg, P=0.001 for DD; -2.03 kg, P=0.003 for ID), body mass index (BMI) (-0.64 units, P=0.001 for DD; -0.83 units, P=0.003 for ID), relative fat mass (-1.24%, P=0.014 for DD), and waist circumference (WC) (-5.56 cm, P<0.001 for DD; -5.63 cm, P<0.001 for ID)	(Lim and Shin, 2014)
UCP3	rs1800849 C/T	n=107, women 74,7%	European	CC	low-intensity aerobic exercise alongside a hypocaloric diet for 12 weeks	carriers of the CC genotype, compared to carriers of the T allele, had significantly reduced fat mass (-2.9 kg, P<0.05) and waist circumference (WC) (-3.5 cm, P<0.05)	(de Luis et al., 2008)

n/d- no data; MT- body mass; BMI- body mass index, FM- fat mass; WC- waist circumference.

Most publications (n = 22) examine the efficacy of a traditional low-calorie diet. The goal of a hypocaloric diet is to create a calorie deficit, meaning that the energy intake is lower than the energy expenditure. This deficit is believed to prompt the body to use stored energy, typically fat, leading to weight loss. This approach represents the most straightforward and efficient method for weight loss (Koliaki and Katsilambros, 2022), and, for that reason, it is probably most often used in research. Nevertheless, the nutritional composition of a diet can impact diverse physiological aspects. This includes hormonal levels (Ryan and Seeley, 2013; Kim et al., 2021), metabolic pathways (Moszak et al., 2020), gene expression (Mierziak et al., 2021), and the composition of the gut microbiome (Singh et al., 2017). Therefore, this emphasizes the importance of conducting studies that explore the effectiveness of diets with varying macronutrient compositions for weight loss, taking into account the genetic status of individuals.

Individuals exhibit genetic variability, and specific alleles or genotypes might be more advantageous regarding fat loss efficiency in response to specific dietary interventions. Favorable alleles are those genetic variants linked to a more favorable outcome, such as efficient fat loss, in response to particular diets. These alleles might be associated with enhanced metabolism, improved nutrient utilization, or better responses to specific dietary components. Table 1 presents these alleles. Certain alleles or genotypes might also be linked to more efficient utilization of fat as an energy source during physical activity. As in the case of diet-induced fat loss, understanding an individual's genetic profile, including the presence of favorable alleles, can facilitate personalized exercise recommendations. Tailoring exercise routines based on genetic information seems a very attractive way to optimize individuals' fat loss outcomes and overall fitness. The favorable alleles related to exercise-induced fat loss are demonstrated in Table 2. The analyzed publications exhibited different SNPs for the same genes in most cases. However, among the studied genes in the context of diet-induced fat loss, for the *FTO* gene, 2 polymorphisms were identified, with one of them, rs9939609, appearing in 2 publications (de Luis et al., 2015a; 2015b), and the other, rs1558902, in one publication (Zhang et al., 2012).

Interestingly, there is no difference in weight loss outcomes between a high-protein/low-carbohydrate diet and a standard hypocaloric diet. The findings indicate an association between the *FTO* variant rs9939609 and weight loss reduction following hypocaloric diet interventions (de Luis et al., 2015a). In the case of *MTNR1B* and rs1083096, two studies indicated that carriers of the CC genotype, compared to carriers of the G allele, were more effective in fat loss (de Luis et al., 2020a, 2020b). However, inconsistent findings were also observed. For instance, a study by Phares et al. (2004) with 70 individuals carrying the G allele of *ADRB3* rs4994 showed an effective reduction in body fat mass (Phares et al., 2004). In contrast, de Luis et al. (2007) demonstrated the highest efficiency for carriers with the AA genotype (de Luis et al., 2007).

Notably, most of the genetic variants identified in intervention studies were revealed through the candidate-gene approach, constrained by the current understanding researchers possess regarding the biology of obesity. Specifically, in the 27 publications studied in Table 1 and the 20 publications studied in Table 2, genome-wide association studies (GWAS) were used only once in Table 2 and in Bojarczuk et al., (2022). This underscores the existing limitations in our knowledge of genetic markers influencing body weight and the physiological response to physical activity and macronutrient intake. Association studies are the most commonly used in genetic analysis in sports. However, they have two weaknesses - they rely on the analysis of candidate genes (somewhat closing themselves off to other potentially unrelated markers with the examined trait). GWAS, instead, can assess hundreds of thousands of SNPs, and it is not hypothesis-driven (Tam et al., 2019; Loos and Yeo, 2022) To overcome these limitations and gain a more comprehensive understanding, extensive GWAS, replication studies, and meta-analyses are crucial (Egorova and Ahmetov, 2023). To avoid false positive results in association studies, studies of this type should undergo repetition in so-called replication studies (Kraft et al., 2009), either in subgroups of the same population (internal replication) or in additional groups of athletes and non-athletes of diverse ethnic backgrounds (external replication) (Liu et al., 2008).

Furthermore, genetic markers explain the observed differences in how individuals respond to weight-loss interventions. Understanding these markers allows researchers and clinicians to tailor interventions for better outcomes. The ultimate goal is, therefore, to use genetic information to develop personalized strategies for weight loss. This involves recommending specific diets and exercise plans based on an individual's genetic profile.

Our methods involved a meticulous approach to ensure the inclusion of studies directly relevant to investigating genetic factors influencing fat loss outcomes. However, we do not exclude the possibility that our systematic review might have limitations, such as potential biases in individual studies (patient selection, performance evaluation, measurement) or publication biases (Yuan and Hunt, 2009; Vrabel, 2015). When assessing the literature, crucial factors include variables such as diet duration. For example, in the study of Hamada et al. (2011), the intervention period was relatively brief, and the dietary method was homogeneous. Thus, it is intriguing to explore whether the genetic effects identified in such a study manifest over the long term and/or with different dietary interventions (Hamada et al., 2011). Another primary source of uncertainty is the nature of the exercise, duration, and intensity. For instance, in (Phares et al., 2004), the participants were subjected to aerobic exercises of moderate intensity for 24 weeks. Similar to the publication (Hamada et al., 2011), the effects of long-term exercise training have not been determined (Phares et al., 2004). The subjects' recruited characteristics are also important considerations. This is because the body composition is determined by, e.g., age, sex, ethnicity, height, and weight. Despite adjustments for variables like age, sex, ethnicity, height, diabetes status, smoking, dietary intake, and physical activity, the heritability of percentage fat mass, whole-body fat mass, and whole-body lean mass (fat-free mass) persist at a notably high level (Bojarczuk et al., 2022). A key aspect of the response to training or diet is the nutritional status (normal, overweight, or obese). Not everyone within a specific weight category will respond the same way to dietary changes. Next, the training status also matters. Changes in traits are always more pronounced in untrained individuals than in their trained counterparts (Bojarczuk et al., 2022). As described, several methodological considerations regarding the response training or diet can significantly affect experimental outcomes. Moreover, systematic reviews have no rules regarding the sample size requirements (Ferrari, 2015). However, we used articles with representative sample sizes.

Conclusion

In conclusion, this comprehensive analysis highlights the intricate interplay between genetic factors and the effectiveness of weight loss strategies, shedding light on potential markers linked to fat loss in dietary and exercise interventions. The approach presented here identified 30 genetic markers associated with the efficiency of fat loss in reaction to dietary interventions and 24 markers in response to physical activity. If advancements are made in this field, a methodology could be developed to tailor the selection of diet and exercise based on genetics to prevent and treat obesity.

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Key points

- Inter-individual differences play a crucial role in determining body weight and shaping the body's response to changes in diet and engagement in physical activity.
- The review identified 30 genetic markers associated with fat-loss efficiency in response to various diets and 24 markers in response to exercise.
- In the future, the focus should be on tailoring the choice of diet and exercise types to individual genetic characteristics to prevent and treat obesity.

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Supplementary Table 1. Assessing the risk of bias for randomized controlled trials using an adapted, validated version of the Cochrane Collaboration's tool (0 – low risk, 1 – unclear risk, 2 – high risk) and final the risk of bias (A, B, C) according to the Cochrane Collaboration's tool.

Article	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Final the risk of bias assessment based on 6 questions	Other bias	Final the risk of bias assessment based on 7 questions
Goni et al., 2018	0	1	2	0	0	0	C	0	A
de Luis et al, 2018b	0	0	1	0	0	0	B	0	A
Zhang et al., 2012	0	0	0	0	0	0	A	0	A
Heianza et al., 2018	0	0	0	0	1	0	B	0	A
de Luis et al., 2020	1	1	1	0	0	0	B	0	A
de Luis et al, 2020	1	1	1	0	0	0	B	0	A
Sun et al., 2018	0	0	0	0	1	0	B	0	A
Lin et al., 2015	0	0	0	0	0	0	A	0	A
Chmurzynska et al, 2019	0	0	0	0	0	0	A	0	A
Grau K et al., 2010	0	1	2	0	0	0	C	0	A
Cameron et al., 2013	1	1	1	1	0	0	B	1	B
Franks et al., 2007	1	1	0	0	0	0	B	0	A
Ramos-Lopez et al., 2019	0	1	2	1	2	0	C	0	A
Heianza et al., 2016	0	0	0	0	0	0	A	0	A

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Supplementary Table 2. Quality assessment of cohort studies by using the Newcastle Ottawa Scale.

Article	1. Representative of exposed cohort	2. Selection of non-exposed cohort	3. Valid ascertainment of exposure	4. Outcome of interest not present at start of study	5. Control for important factors (age, sex, BMI)	6. Control for additional factors (diet, physical activity)	7. Assessment of outcome	8. Adequate duration of follow-up (≥8 weeks)	9. Adequacy of follow-up (no more than 20%)	Score
Hamada et al., 2010	1	1	1	1	1	1	1	1	1	9
Izaola Jáuregui et al., 2020	1	1	1	1	1	1	1	1	1	9
Rajkumar et al., 2016	1	1	1	1	1	1	1	1	1	9
Tchernof et al., 2000	1	1	1	1	1	1	1	1	1	9
de Luis et al, 2018c	1	1	1	1	1	1	1	1	1	9
de Luis et al., 2015b	1	1	1	1	1	0	1	1	1	8
de Luis et al, 2015a	1	1	1	1	1	0	1	1	1	8
Abete et al, 2009	1	1	0	1	1	0	1	1	1	7
Di Renzo et al, 2013	1	1	1	1	1	0	1	1	1	8
de Luis et al, 2018a	1	1	1	1	1	0	1	1	1	8
Thamer et al., 2008	1	1	1	1	1	0	1	1	1	8
Cha et al., 2007	1	1	0	1	1	0	1	1	0	6
Yoon et al., 2007	1	1	1	1	1	0	1	0	0	6
De Luis et al., 2013	1	1	0	1	1	1	1	1	1	8
Cha et al., 2006	1	1	0	1	1	0	1	0	1	6
Bojarczuk et al., 2022	1	1	1	1	1	0	1	1	1	8
Phares et al., 2004	1	1	1	1	1	0	1	1	1	8
Leońska-Duniec et al., 2018	1	1	1	1	1	1	1	1	1	9
de Luis et al., 2007	1	1	0	1	1	1	1	1	1	8
Suchanek et al., 2011	1	1	1	1	1	0	1	1	1	8
Tworoger et al., 2004	1	1	1	1	1	0	1	1	1	8
de Luis et al., 2006	1	1	0	1	1	1	1	1	1	8
Rankinen et al., 2010	1	1	1	1	1	0	1	1	1	8
Ficek et al., 2019	1	1	1	1	1	0	1	1	1	8
Orkunoglu-Suer et al., 2008	1	1	1	1	1	0	1	1	1	8
Suchánek et al., 2015	1	1	1	1	1	0	1	1	1	8
Andrade-Mayorga et al., 2021	1	1	1	1	1	1	1	1	0	8
Zarebska et al., 2014	1	1	1	1	1	0	1	1	1	8
Østergård et al., 2005	1	1	1	1	1	1	1	1	1	9
Mazur et al., 2020	1	1	1	1	1	0	1	1	1	8
Haupt et al., 2010	1	1	1	1	1	0	1	1	1	8
Lim et al., 2014	1	1	1	1	1	0	1	1	1	8
de Luis et al., 2008	1	1	0	1	1	1	1	1	1	8
de Luis et al., 2023	1	1	1	1	1	1	1	1	1	9

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Supplementary Table 3. **Scale for Quality Assessment of genetic association studies.**

Criteria	Low quality	Intermediate quality	High quality
Gene-diet or gene-physical exercise interaction as primary study goal	No = -1	Not known = 0	Yes = 1
Formal test for interaction	No = -1	Not known or stratified analysis = 0	Yes = 1
Correction for multiple testing	No = -1	Not known = 0	Yes or not necessary = 1
Correction for population stratification/ethnicity	No = -1	Not known = 0	Yes or not applicable = 1
Hardy-Weinberg equilibrium	No or not stated = -1	Not known = 0	Yes = 1
Group similarity at baseline tested		Not known = 0	Yes = 1
Power analysis and sample size	≤65= -1	65-322=0	>322 or power analysis is provided (>80%) = 1
Sufficient details of study procedure stated	No = -1	-	Yes = 1

*the cut offs used to define low, intermediate and high sufficiency of sample size were based on the 15th (n=65) and 75th percentile (n=322) of the sample size of the studies included.

Supplementary Table 4. **Risk of bias assessment outcomes for all studies reviewed according to Scale for Quality Assessment of genetic association studies.**

Article	Gene-diet or gene-physical exercise interaction as primary study goal	Formal test for interaction	Correction for multiple testing	Correction for population stratification/ ethnicity	Hardy-Weinberg equilibrium	Group similarity at baseline tested	Power analysis and sample size	Sufficient details of study procedure stated	Score
Goni et al., 2018	1	1	0	1	1	1	1	1	7
de Luis et al, 2018b	1	1	1	1	1	1	1	1	8
Zhang et al., 2012	1	1	-1	1	1	1	1	1	6
Heianza et al., 2018	1	1	0	1	1	1	1	1	7
de Luis et al., 2020	1	1	0	0	1	1	1	1	6
de Luis et al, 2020	1	1	1	0	1	1	1	1	7
Sun et al., 2018	1	1	1	0	0	1	1	1	6
Lin et al., 2015	1	1	1	1	1	1	1	1	8
Chmurzynska et al, 2019	1	1	-1	1	0	1	0	1	4
Grau K et al., 2010	1	1	1	1	1	1	1	1	8
Cameron et al., 2013	1	1	-1	0	1	1	0	1	4
Franks et al., 2007	1	1	1	1	1	1	1	1	8
Ramos-Lopez et al., 2019	1	1	1	1	1	1	1	1	8
Heianza et al., 2016	1	1	0	1	1	1	1	1	7
Hamada et al., 2010	1	1	0	0	1	1	0	1	5
Izaola Jáuregui et al., 2020	1	1	0	0	1	1	1	1	6
Rajkumar et al., 2016	1	1	0	1	1	1	0	1	6
Tchernof et al., 2000	1	1	1	0	0	1	0	1	5
de Luis et al, 2018c	1	1	0	1	1	1	1	1	7
de Luis et al., 2015b	1	1	0	1	1	1	1	1	7
de Luis et al, 2015a	1	1	0	0	1	1	1	1	6
Abete et al, 2009	1	1	1	0	1	1	1	1	7
Di Renzo et al, 2013	1	1	1	0	0	1	0	1	4
de Luis et al, 2018a	1	1	1	0	1	1	1	1	7
Thamer et al., 2008	1	1	1	1	0	0	0	1	5

Supplementary Table 4. Continue …

Article	Gene-diet or gene-physical exercise interaction as primary study goal	Formal test for interaction	Correction for multiple testing	Correction for population stratification/ ethnicity	Hardy-Weinberg equilibrium	Group similarity at baseline tested	Power analysis and sample size	Sufficient details of study procedure stated	Score
Cha et al., 2007	1	1	1	1	1	0	1	1	7
Yoon et al., 2007	1	1	1	1	1	0	1	1	7
De Luis et al., 2013	1	1	1	0	0	0	1	1	5
Cha et al., 2006	1	1	0	1	1	0	0	1	5
Bojarczuk et al., 2022	1	1	1	1	1	0	0	1	6
Phares et al., 2004	1	1	0	1	1	1	0	1	6
Leońska-Duniec et al., 2018	1	1	0	0	1	0	1	1	5
de Luis et al., 2007	1	1	1	0	0	1	1	1	6
Suchanek et al., 2011	1	1	1	0	0	1	0	1	5
Tworoger et al., 2004	1	1	1	1	1	1	0	1	7
de Luis et al., 2006	1	1	1	0	0	1	0	1	5
Rankinen et al., 2010	1	1	1	1	1	0	1	1	7
Ficek et al., 2019	1	1	1	0	1	0	0	1	5
Orkunoglu-Suer et al., 2008	1	1	-1	1	1	1	1	1	6
Suchánek et al., 2015	1	1	1	0	1	0	0	1	5
Andrade-Mayorga et al., 2021	1	1	0	0	1	1	-1	1	4
Zarebska et al., 2014	1	1	1	0	1	0	0	1	5
Østergård et al., 2005	1	1	0	0	1	1	0	1	5
Mazur et al., 2020	1	1	1	0	0	0	-1	1	3
Haupt et al., 2010	1	1	0	1	1	0	1	1	6
Lim et al., 2014	1	1	1	0	1	0	-1	1	4
de Luis et al., 2008	1	1	1	0	0	1	1	1	6
de Luis et al., 2023	1	1	1	1	1	1	1	1	8