JOURNAL OF NUTRITION COLLEGE
Volume 15, Nomor 4, Tahun 2026, Halaman 370-387
Received: 26 November 2025, Revised: 19 Juni 2026
Accepted: 17 Juli 2026, Published:30 Oktober 2026
Online di: http://ejournal3.undip.ac.id/index.php/jnc/ , DOI: 10.14710/jnc.v15i4.54318

ASSOCIATION BETWEEN THE *ADRB2* GLN27GLU (rs1042714) VARIANT AND OBESITY: A NARRATIVE REVIEW

Rachmania Anggita Savitri[1]*, Nani Maharani[2], Adriyan Pramono[1]

[1]Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Jawa Tengah, Indonesia
[2]Department of Medicine, Faculty of Medicine, Universitas Diponegoro, Semarang, Jawa Tengah, Indonesia
***Correspondence** : anggitasav@students.undip.ac.id

ABSTRACT

Background: Obesity is a global health crisis underpinned by a complex interplay between genetics and environment. The β2-adrenergic receptor gene (ADRB2), a key regulator of lipolysis and energy expenditure, is a strong candidate for obesity susceptibility. The ADRB2 Gln27Glu (rs1042714) polymorphism has been widely studied, but its association with obesity and metabolic traits remains controversial, with contradictory findings across the literature.
Objectives: This narrative review aims to summarize and critically analyze the scientific literature regarding the ADRB2 rs1042714 variant.
Methods: A narrative literature review was conducted using the Google Scholar, ScienceDirect, Scopus, and PubMed databases. Inclusion criteria selected primary research articles published in English that investigated the association between ADRB2 rs1042714, obesity, body composition, and interactions with diet or physical activity.
Results: The literature review confirms a profound lack of consensus. Some studies associate the Glu27 (G allele) with increased obesity risk, while others associate the Gln27 (C allele) with risk or find the G allele to be protective. These discrepancies are largely explained by three factors: 1) Ethnicity; 2) Gen-diet interaction; and 3) Gene-exercise interaction.
Conclusion: The ADRB2 Gln27Glu polymorphism is not a deterministic factor for obesity. Its association with adiposity is highly context-dependent, critically modulated by genetic ancestry, dietary macronutrient composition, and physical activity levels. The contradictions in the literature highlight the necessity of moving from simple association studies to more nuanced gene-environment interaction models to understand the variant's true clinical relevance.

Keywords: ADRB2; rs1042714; Gln27Glu; obesity; lipolysis

BACKGROUND

Obesity is currently considered a major global health issue due to its increasing prevalence, underpinned by a complex etiology that involves the interplay between genetic predisposition and an increasingly obesogenic environment.[1] The World Health Organization (WHO) reported that in 2022, the number of individuals with obesity worldwide surpassed one billion, comprising approximately 880 million adults and 159 million children and adolescents.[2] Heritability studies have consistently demonstrated this strong genetic contribution to obesity. Understanding the genetic factors that modulate an individual's susceptibility to weight gain and their response to lifestyle interventions is a cornerstone of modern metabolic research. Genetic factors play a significant role in obesity for approximately 40% to 70% of the variability in body weight and fat distribution among individuals.[3] Some forms of obesity are monogenic, meaning they are caused by mutations in single genes, while others are polygenic, involving numerous genes. Over 250 genes have been linked to obesity, many of which are involved in energy metabolism, adipocyte differentiation (the maturation of fat cells), and thermogenesis.[4] Genetic variants can also influence fat distribution, susceptibility to insulin resistance, and the response to environmental factors such as diet and physical activity.[5]

The *ADRB2* gene, located on chromosome 5, encodes a receptor that serves as a critical mediator for the sympathetic nervous system in regulating energy balance. The *ADRB2* gene has been shown to be associated with obesity as a genetic factor. Several studies indicate that specific polymorphisms (genetic variations) within this gene are associated with obesity-related traits and metabolic changes.[6,7] The beta-2 adrenergic receptors (β2-AR) are expressed on the surface of adipocytes and play a crucial role in initiating lipolysis, the catecholamine-induced process of fat breakdown, as well as stimulating thermogenesis.[8] β2-AR signaling also promotes thermogenic activity in brown adipose tissue (BAT) by facilitating sympathetic nervous

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

system regulation, enhancing blood perfusion, and increasing energy expenditure through heat production.[9]

Genetic variations in this gene can modulate these processes by affecting receptor function and expression, which influences individual differences in fat metabolism and obesity risk. The Gln27Glu variant (rs1042714) is known to be strongly associated with obesity susceptibility, particularly influencing fat mass, body mass index (BMI), and metabolic traits in certain populations, especially in female subjects.[10,11] Studies regarding the association of this variant with obesity and related metabolic traits have yielded controversial and often contradictory findings. The functional distinction between the Gln27 and Glu27 alleles is central to this discussion. Studies conducted in Caucasian, Japanese, Korean, Brazilian, African, and Pacific Islander populations have reported associations that vary not only in statistical significance but in the direction of effect: some studies link the Gln27 allele to higher adiposity, others link the Glu27 allele to the same outcome, and a number find no significant association at all. [12–14] The conventional biological explanation rests on a functional distinction between alleles, in which Glu27 is hypothesized to favor energy conservation, a trait plausibly advantageous under historical conditions of caloric scarcity, while Gln27 is associated with relatively higher energy expenditure. Framed this way, the variant's relevance to modern obesity becomes a question of gene-environment mismatch, where a once-adaptive thrifty phenotype becomes a liability in calorically abundant, sedentary environment. It suggests a potential gene-environment mismatch in modern society, where a trait once potentially beneficial for survival may now, in an obesogenic environment, become maladaptive.[15] This suggests that the role of this gene variant may be more complex and context-dependent. Most existing reviews and primary studies treat the variant's functional consequences as biologically fixed, without adequately considering how unequal genotype distribution across populations constrains the interpretability and comparability of reported effects. Moreover, the handful of studies examining how nutritional intake or physical activity modifies the relationship between this variant and obesity-related traits have been conducted predominantly in populations where GG carriers are sufficiently common to study, leaving open the question of whether these gene-environment interactions hold in populations where the genotype is rare.

The primary objective of this review is to summarize and critically analyze the scientific literature regarding the *ADRB2* rs1042714 variant. Furthermore, this review aims to construct a more nuanced understanding focused on how this gene-phenotype relationship with obesity is influenced by two key environmental factors: nutritional intake and physical activity.

METHODS

This study was conducted as a narrative literature review. A comprehensive literature search was performed utilizing the Google Scholar, ScienceDirect, Scopus, and PubMed databases to identify relevant articles. The selection process prioritized significant primary research articles (both quantitative and qualitative) pertaining to the *ADRB2* gene and its role in obesity. The inclusion criteria required articles to be: 1) primary research relevant to *ADRB2* variants, obesity/lipolysis, diet, or physical activity; 2) discuss at least one of the primary variables; 3) published in English; and 4) available in full-text for detailed analysis. Exclusion criteria were applied to remove articles that were opinions, editorials, or lacked empirical data, as well as those that did not explicitly discuss the primary variables, failed to establish a connection between them, or were not available in full-text. The search was conducted using combinations of the following keywords and Boolean operators: ("ADRB2" OR "beta-2 adrenergic receptor" OR "β2-adrenoceptor") AND ("Gln27Glu" OR "rs1042714" OR "Glu27" OR "Gln27") AND ("obesity" OR "body mass index" OR "BMI" OR "adiposity" OR "body composition" OR "fat mass" OR "lipolysis"). For articles addressing gene-environment interactions, the search terms were further combined with ("diet" OR "carbohydrate intake" OR "dietary pattern" OR "weight loss intervention") OR ("physical activity" OR "exercise" OR "sedentary" OR "energy expenditure"). No restriction was placed on publication date, as the objective was to capture the full historical trajectory of research on this polymorphism. The search was last conducted in December, 2025 and articles published up to that date were eligible for inclusion.

DISCUSSION

The β2-Adrenergic Receptor: A Central Mediator of Lipolysis and Energy Expenditure

The *ADRB2* gene, a quintessential member of the G protein-coupled receptor (GPCR) superfamily which encodes the beta-2 adrenergic receptor, is located on the long arm of chromosome 5, specifically at the cytogenetic band 5q31-q32. According to the latest genomic data, the gene spans the region from base pairs 148,826,611 to 148,828,623 on chromosome 5 (GRCh38 assembly).

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

The gene is intronless and encodes a protein involved in multiple physiological processes including lipolysis and thermogenesis.[14,16] The β2-adrenergic receptor (β2-AR) is a key effector of the sympathetic nervous system and is activated by the binding of endogenous catecholamines, primarily epinephrine and norepinephrine. Upon binding these ligands, β2-AR undergoes a conformational change that allows it to interact with and activate the heterotrimeric G protein Gs. This activation stimulates adenylyl cyclase, leading to increased production of cyclic AMP (cAMP), which then activates protein kinase A (PKA). The downstream signaling cascade results in physiological effects such as smooth muscle relaxation, bronchodilation, lipolysis in adipocytes, and thermogenesis.[17,18]

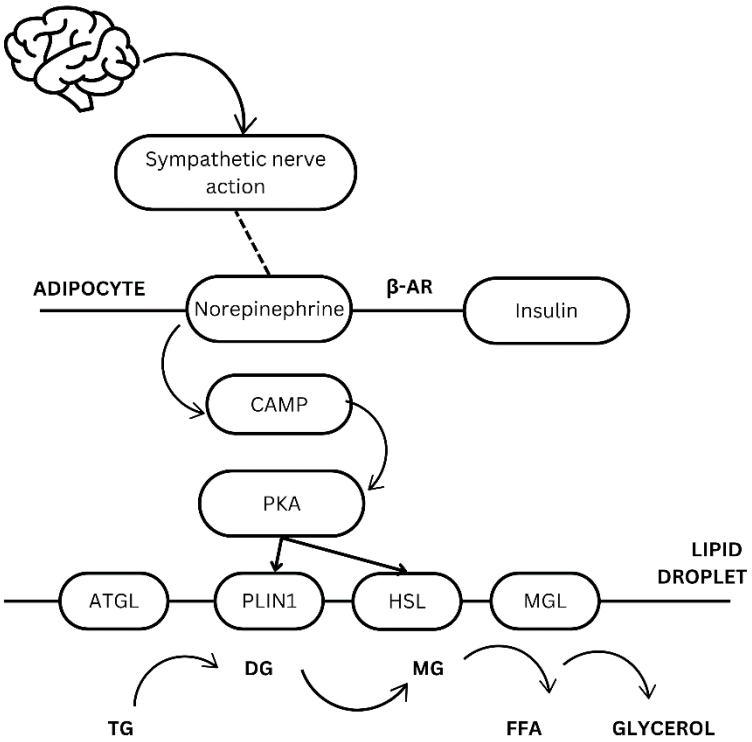


Figure 1. Lipolisis regulation

Within the adipocyte, this PKA-driven signaling cascade initiated by β2-AR activation has clear targets to initiate lipolysis. PKA acts as the central kinase that orchestrates the subsequent lipolytic events. PKA phosphorylates two key target proteins: 1) Perilipin 1 (PLIN1), the protein that coats the lipid droplet, and 2) Hormone-Sensitive Lipase (HSL). The phosphorylation of PLIN1 is a crucial gatekeep step, altering its structure to allow HSL and other lipases, like Adipose Triglyceride Lipase (ATGL), to access the triglyceride core. Concurrently, PKA-mediated phosphorylation activates HSL, which then efficiently hydrolyzes these triglycerides into free fatty acids and glycerol, allowing their release from the adipocyte.[17] This β2-AR-mediated lipolytic pathway is, however, tightly regulated within the cell's hormonal context. This lipolytic pathway exists in a state of dynamic opposition to the anti-lipolytic signaling pathway, which is primarily driven by insulin. This establishes a fundamental hormonal balance at the fat cell membrane: insulin promotes energy storage and suppresses fat breakdown, while catecholamine activation of the β2-AR must overcome this storage signal to successfully mobilize the stored triglycerides.[19]

Furthermore, the activation of the β2-AR pathway induces significant metabolic cross-talk, ensuring that the adipocyte's functions are fully coordinated toward energy release. A key secondary effect of this cascade: catecholamine-induced lipolysis actively inhibits glucose uptake into the adipocyte. This suppression of glucose consumption was found to be linked to the dissociation of the mTOR complex, a central hub for sensing nutrients and regulating cellular metabolism. This mechanism functions as a powerful intracellular feedback loop, ensuring that when the adipocyte receives the β2-AR signal to mobilize and release energy (lipolysis), it simultaneously shuts down its own pathways for energy consumption (glucose uptake).[18]

Beyond its established role in lipid mobilization from white adipose tissue (WAT), the β2-AR is also the principal mediator of energy

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

expenditure via thermogenesis. This function is specifically localized to brown adipose tissue (BAT), a specialized tissue that dissipates energy as heat. While rodent models historically emphasized the primary role of the β3-adrenergic receptor (β3-AR) in activating BAT, this does not translate accurately to human physiology. Literature provided definitive in vivo evidence that thermogenesis in human brown adipocytes is driven primarily by β2-AR stimulation, not β3-AR. This study identified the β2-AR as the dominant functional receptor for activating human BAT, placing it as a central regulator of whole-body energy expenditure.[20] Taken together, these findings establish that the β2-AR is not a peripheral or redundant component of energy metabolism, but a central node linking sympathetic nervous system activity to both lipid mobilization in white adipose tissue[21,22] and thermogenesis in brown adipose tissue.[9,20,23] This dual role provides the essential physiological rationale for why a functional variant of ADRB2, such as Gln27Glu, would be biologically plausible as a modulator of obesity risk, setting the stage for the genotype-specific effects discussed in the following sections.

Functional Consequences of the Gln27Glu (rs1042714) Polymorphism

The rs1042714 polymorphism is a common non-synonymous SNP characterized by a cytosine (C) to guanine (G) substitution in the coding region of the *ADRB2* gene.[1] This nucleotide change translates to an amino acid substitution at codon 27 in the extracellular N-terminus of the receptor protein, replacing glutamine (Gln), encoded by the C allele, with glutamic acid (Glu), encoded by the G allele.[24] The functional impact of this Gln27Glu substitution has been a subject of intense research and debate. The leading hypothesis posits that the polymorphism alters the receptor's susceptibility to agonist-induced downregulation and desensitization, a process by which the receptor becomes less responsive after prolonged stimulation.[25] Specifically, the Glu27 variant (G allele) has been proposed to be more resistant to downregulation compared to the Gln27 variant. In theory, this could lead to a more sustained signaling response upon initial stimulation but might also render the receptor more prone to long-term desensitization under conditions of chronic agonist exposure, such as in obesity. This altered sensitivity could, in turn, impact the efficiency of the lipolytic response to catecholamines.[26] However, the evidence is not definitive. Some functional studies have yielded conflicting results, and an alternative hypothesis suggests that rs1042714 may not directly alter receptor function itself but could be in linkage disequilibrium with another, truly functional, variant elsewhere in the gene.[27]

The functional alteration of the β2-AR caused by the Gln27Glu polymorphism is primarily linked to its resistance to downregulation. While the normal receptor (Gln27) is somewhat resistant to degradation, the variant containing Glutamic acid (Glu27) displays a distinctly different behavior. Research indicates that the Glu27 variant is more susceptible to agonist-promoted downregulation. When catecholamines bind to the receptor, the Glu27 variant undergoes a more rapid conformational change that promotes phosphorylation and uncoupling from Gs-proteins. This rapid desensitization means the receptor stops transmitting the fat-burning signal much earlier than the wild-type receptor, even if the stimulating hormones (epinephrine/norepinephrine) are still present. The physiological consequence of this blunted signaling is particularly detrimental in tissues with high β2-AR density, such as visceral white adipose tissue. Under normal conditions, sympathetic nervous system activation triggers these receptors to initiate lipolysis, the hydrolysis of triglycerides into free fatty acids. In carriers of the Glu27 allele, this lipolytic response is dampened. Consequently, during periods of exercise or fasting, the mobilization of energy stores is less efficient. Furthermore, in brown adipose tissue, where β2-AR signaling drives uncoupling protein-1 (UCP1) mediated thermogenesis, the dampened signal may result in reduced obligatory energy expenditure, effectively lowering the basal metabolic rate.

The morphological manifestation of obesity is characterized by the expansion of adipose tissue, a process driven by an increase in both adipocyte number (hyperplasia) and adipocyte size (hypertrophy).[28] This metabolically dynamic organ is not a uniform entity; rather, it is broadly classified into three distinct types: white adipose tissue (WAT), brown adipose tissue (BAT), and beige adipose tissue.[23] A profound functional dichotomy exists between these classifications. WAT is specialized as the body's primary site for storing excess energy in the form of triglycerides, whereas BAT and beige adipose tissue are specialized to catabolize these stored triglycerides to generate heat in a process known as non-shivering thermogenesis.[29] The foundational mechanism governing the release of fatty acids from these stores, basal lipolysis, is not a static process. Instead, lipolytic activity in adipocytes is tightly regulated and systemically influenced by a complex interplay of factors, including sex, age, physical activity levels, the specific anatomical location of the fat depot, and underlying genetic variation.[30]

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

A key early study supporting a direct link investigated the polymorphism in a cohort of 185 non-diabetic Japanese men. Their cross-sectional analysis revealed a significant association between the Gln27Glu variant and the prevalence of obesity. Critically, the study did not just link the variant to an elevated Body Mass Index (BMI), but also to a specific fat distribution phenotype. The researchers observed that the variant was particularly associated with an accumulation of subcutaneous fat rather than visceral fat. This finding was pivotal, as it suggested not only a population-specific effect (Japanese men) but also a tissue-specific impact, implying the β2-AR variant might differentially affect the metabolic behavior of distinct fat depots.[31] This line of inquiry, investigating the variant within specific, well-defined cohorts, has continued to provide nuanced insights. A recent study explored the association between the Gln27Glu polymorphism and obesity risk within a specialized group: patients with both early-onset and late-onset bronchial asthma. The study reported a significant association between the polymorphism and an increased risk of obesity specifically within this patient population. This finding is particularly relevant as it highlights a potential interaction with a comorbidity. Given that the β2-AR is the primary target for asthma therapeutics, it is plausible that the underlying disease state, or even its treatment, unmasks or exacerbates the metabolic consequences of possessing the Glu27 variant, further reinforcing the context-dependent nature of its effect.[32]

Overall, the evidence reviewed here indicates that the functional consequences of the Gln27Glu substitution, while biologically plausible through altered receptor downregulation, are neither uniform nor fully resolved at the molecular level. The conflicting findings on receptor desensitization, together with the possibility that rs1042714 reflects linkage with another functional variant, suggest that the path from genotype to phenotype is not direct. This mechanistic ambiguity foreshadows the inconsistent obesity associations reported in the epidemiological literature, reinforcing that rs1042714's relevance to obesity cannot be assumed from receptor biology alone and must be evaluated empirically across populations and environments.

Overall, the evidence reviewed here indicates that the functional consequences of the Gln27Glu substitution, while biologically plausible through altered receptor downregulation, are neither uniform nor fully resolved at the molecular level. The conflicting findings on receptor desensitization, together with the possibility that rs1042714 reflects linkage with another functional variant, suggest that the path from genotype to phenotype is not direct. This mechanistic ambiguity foreshadows the inconsistent obesity associations reported in the epidemiological literature, reinforcing that Gln27Glu's relevance to obesity cannot be assumed from receptor biology alone and must be evaluated empirically across populations and environments.

The Association of *ADRB2* rs1042714 with Obesity and Body Composition

A significant body of research links the G allele (Glu27) of the *ADRB2* polymorphism to an increased risk of obesity, though these findings are often specific to certain populations or sexes. A study by Moore et al.[10] demonstrated a strong association in individuals with the GG genotype; specifically, women with this genotype had a 10-fold higher risk of obesity, corresponding to an increase in fat mass of approximately 20 kg. Women with the GG genotype also tended to have higher body weight and BMI, which was attributed to a significantly greater body fat percentage and total fat mass.[11] This positive association with increased adiposity has been echoed in other ethnicities. Research by Lange et al.[33] and Large et al.[34] in Hispanic populations also found a positive relationship between the G allele and both BMI and visceral adipose tissue, noting that subjects with the GG genotype had an average excess fat mass of 20 kg.

More recent studies have reinforced this link. A 2023 study by Kachkovska[32] involving 648 subjects demonstrated a statistically significant relative risk for obesity in both dominant (RR 1.95; p=0.03) and additive (RR 1.65; p=0.04) inheritance models. The results indicated that individuals carrying the G allele (genotypes CG and GG) had a 1.75-fold higher risk of obesity compared to individuals with the CC genotype (p=0.03). This is consistent with a meta-analysis by Zhang et al.[35], which concluded that this variant is significantly associated with obesity in both heterozygous (CG vs CC; p=0.009) and dominant (CC vs CG+GG; p=0.004) models. Furthermore, a study on a Japanese population by Mori et al.[36] found that the G allele frequency was significantly higher in subjects with obesity compared to non-obese or intermediate groups. Interestingly, the phenotypic effect of this polymorphism appears to be context-dependent and may be modulated by the subject's nutritional status.[37] In non-obese subjects, for example, individuals with the G allele have been observed to have lower body fat mass and higher levels of free fatty acids compared to non-carriers. This suggests that the variant may influence fat storage and mobilization differently, particularly in individuals who are not obese.[38]

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

Further complicating the narrative, some studies report an inverse association, suggesting the G allele (Glu27) may be protective against obesity. A study by Meirhaeghe et al.[38] in a French population found that the CC (Gln27Gln) genotype was associated with an *increased* risk of obesity. Men with the CC genotype exhibited higher body weight, BMI, waist and hip circumference, and waist-to-hip ratio compared to those with other genotypes. This effect was reportedly exacerbated in individuals who also carried the Arg16 allele, another variant of the *ADRB2* gene. Supporting this line of evidence, Saliba et al.[15] in Brazil also found that G allele carriers had a statistically significant lower mean BMI ($p = 0.006$), indicating a protective effect. This effect may be highly specific and context-dependent; another study linked the CG genotype to lower BMI values, particularly in women aged 30–39 with a low socioeconomic status.[39] While a study in an Oceanian population[40] initially found a significant association between the G allele and obesity ($p = 0.013$), the relationship did not remain significant after adjusting for other variants, as the two SNPs were in linkage disequilibrium. According to one mechanistic model, the Gln27Gln (CC) genotype itself functions as a risk factor for adiposity. This hypothesis posits that the CC genotype leads to a greater degree of β2-AR downregulation on the surface of adipocytes. This increased downregulation effectively blunts the catecholamine signal required for lipolysis. This signaling failure to efficiently catabolize fat subsequently manifests clinically as an accumulation of fat mass and an increase in BMI, as was observed in the subjects within the CC group.[20,41]

The variant's influence is often sex-dependent. Research by Sánchez et al.[42], for instance, reported that the allele could be a risk factor for visceral fat accumulation in men, but not in women. The same study found that obese men with the GG genotype had a significantly higher mean BMI ($p = 0.013$) compared to men with the CC or CG genotypes. However, no such difference was found in the female subjects.[42] The variant's effect also appears to be masked or rendered insignificant in populations with an extremely high baseline prevalence of obesity. A study involving 1,022 subjects from a Tongan population (where obesity prevalence was 84% in men and 93% in women) found no significant association between the G allele and BMI, body composition, or glucose metabolism parameters. This aligns with the hypothesis that in a population already experiencing overwhelming obesity, this specific variant may not play a significant or detectable role.[43]

The Gln27Glu polymorphism (rs1042714) represents the substitution of glutamine (Gln) with glutamic acid (Glu) at the 27th position of the β2-AR. This alteration has been directly linked to modifications in receptor downregulation, the mechanism that reduces receptor density on the cell surface after prolonged activation. According to this hypothesis, individuals with the Glu27 variant (G allele) reportedly demonstrate resistance to receptor downregulation. This resistance is thought to facilitate the β2-AR signaling pathway, thereby increasing the receptor's capacity to induce lipolysis in response to catecholamines. Consequently, lipolysis efficiency is improved, which may provide a metabolic advantage in energy balance and lower the risk of excess fat accumulation.[31] Conversely, individuals with the Gln27 (C allele) variant would exhibit higher rates of receptor downregulation. This functional impairment would reduce the receptor's ability to facilitate lipolysis, potentially inhibiting triglyceride breakdown and leading to reduced energy availability during periods of increased metabolic demand.[31]

This profound inconsistency in the literature strongly suggests that the variant's role is not deterministic but is instead critically modulated by environmental factors, particularly diet. This gene-environment interaction was precisely the focus of a study by Martí et al.[44] in a Spanish population. Their research demonstrated that the risk of obesity associated with the Gln27Glu polymorphism was dependent on nutritional context. They found that in women, carrying the Glu27 (G) allele was associated with a significantly higher risk of obesity only when combined with a high carbohydrate intake (defined as >49% of total energy). In contrast, the genotype had no significant effect on obesity risk among women with lower carbohydrate consumption. This finding was pivotal, providing a strong explanation for previous contradictory results: the genetic susceptibility conferred by the *ADRB2* variant may only be unmasked or expressed under specific dietary conditions.[37]

The Critical Role of Ethnicity

One critical factor that may explain the widespread heterogeneity in the literature is the statistically significant difference in the G allele (Glu27) frequency distribution across global ethnic populations. This variation is well-documented in numerous population genetics studies and genomic databases. Caucasian (European) populations, for instance, exhibit a relatively high G allele frequency, often reported to be between 25% and 40%. In contrast, populations of African-American descent show a frequency of approximately 19%, while East

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

Asian populations (e.g., Japanese, Korean, and Chinese) consistently demonstrate a markedly low G allele frequency, generally ranging from 5% to 9%.[45–49] This low frequency has a direct methodological consequence: studies in Asian populations possess significantly lower statistical power to detect any association with the G allele. The absolute rarity of the homozygous GG genotype in Asian populations (1.1% reported by Kim et al.[50]) renders statistical comparisons difficult, making the analysis susceptible to false-negative results or unstable effect estimates. Beyond statistical power, this divergence in allele frequency likely reflects distinct genetic backgrounds and different selective evolutionary pressures between continents. This raises the hypothesis that the same allele may confer a different phenotypic impact depending on the population-specific genetic. This hypothesis is strongly supported by a meta-analysis from Jalba et al.[51] which specifically concluded that the C allele (Gln27) acts as a significant risk factor for obesity in Asian populations. Therefore, the apparent contradiction between studies is likely not an error, but rather a reflection of a genuine, population-specific genetic effect.

These patterns, taken as a whole, indicate that allele frequency differences across ethnic groups are not simply a technical issue of statistical power, but may reflect genuinely distinct selective and genetic backgrounds that shape how the Glu27 allele behaves phenotypically. This reinforces a central aim of the present review: that any interpretation of this variant clinical relevance must account for population-specific genetic context rather than assuming a universal effect.

Gene-Diet Interactions: Nutritional Modulation of rs1042714's Effect

A clinically relevant aspect of the rs1042714 polymorphism is its function as a modulator of an individual's response to dietary interventions. Evidence suggests that the variant's influence on body composition is not static but is dynamically altered by nutritional context, particularly caloric intake and macronutrient composition. This has given rise to a central paradox in the literature: the allele (Glu27) associated with a higher risk of obesity at baseline appears, in some contexts, to confer a distinct advantage during weight-loss efforts. However, the investigation into this interaction is characterized by conflicting findings. Several studies have reported a null association. Saliba et al.[15] analyzed 139 overweight and obese Brazilian women during a 16-week weight-loss intervention and concluded that the *ADRB2* Gln27Glu polymorphism did not significantly influence the changes in weight, BMI, or body composition among the different genotype groups. This finding is supported by preliminary research from Ruiz et al.[52] Their 8-week study of 45 obese Spanish women on an energy-restricted diet also found no significant differences in body weight or composition changes between genotypes, leading them to conclude the variant was not a significant predictor of weight-loss success in that cohort.

In direct contrast to these findings, recent research by de Luis et al.[26] provides strong evidence that the rs1042714 variant can, in fact, predict dietary response. This study focused on 95 premenopausal women with severe obesity (BMI > 35) undergoing a 12-week meal-replacement hypocaloric diet. Their results showed a significant gene-diet interaction: carriers of the G allele (Glu27) exhibited a better response to the diet. This group experienced a significantly greater reduction in body weight, BMI, fat mass, and waist circumference. Furthermore, this cohort showed superior improvements in glucose metabolism, including greater decreases in fasting insulin and HOMA-IR. This finding is particularly notable as it suggests that, in this specific intervention, the G allele was associated with a more favorable metabolic outcome.

The discrepancy in the literature ranging from the significant, positive response for G-allele carriers can likely be attributed to key differences in study design, intervention specificity, and participant characteristics. One of the most critical differences is the specificity of the dietary intervention. De Luis et al. study[26], which found a significant effect, utilized a highly specific meal-replacement hypocaloric diet. This type of intervention is highly controlled with a fixed macronutrient composition. In contrast, the studies by Saliba et al.[15] and Ruiz et al.[52] used more general weight-loss or energy-restricted diets. It is plausible that the specific macronutrient profile of the meal-replacement diet is the key factor that interacts with the *ADRB2* variant, an effect that would be obscured in less-controlled, general energy restriction. Participant characteristics also differ significantly. De Luis et al. study[26] focused on women with severe obesity (BMI > 35), who may have more pronounced metabolic dysregulation. The genetic effect might only become detectable in this specific, more severe phenotype. The other studies included broader ranges of overweight and obese individuals. Furthermore, the ethnic differences (Brazilian vs. Spanish) are a known confounder for this specific gene, complicating direct comparisons. Finally, statistical power is a concern. Ruiz et al. study[52] was explicitly preliminary with a very small sample (N=45) and was likely underpowered to detect a subtle gene-diet

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

interaction. While the other studies had larger cohorts, the true effect may still be small and require even larger samples to detect reliably. Therefore, the positive finding in the de Luis study[26] does not necessarily conflict with the others, it may instead highlight a highly specific interaction, suggesting the G allele's favorable response is uniquely triggered by a specific nutritional environment and is most detectable in individuals with severe obesity.

These findings support the argument that the metabolic consequences of the Glu27 allele are not fixed, but conditional on dietary context, with the type, intensity, and specificity of the nutritional intervention shaping whether the variant confers metabolic risk or benefit. This gene-diet interaction stands as one of the clearest demonstrations that this variant relevance to obesity cannot be evaluated independently of nutritional intake, directly addressing this review's objective of clarifying how diet modulates the gene-phenotype relationship.

Macronutrient-Specific Effects: The Influence of Carbohydrate Intake

The effect of the Gln27Glu polymorphism on obesity risk may not be direct, but rather dependent on the specific macronutrient composition of the diet. A pivotal study by Martí et al. [44] in a population of Spanish women provides direct evidence for this gene-diet interaction. The researchers investigated whether the association between the *ADRB2* variant and obesity was modulated by dietary intake. Their findings demonstrated that the genetic risk was entirely dependent on carbohydrate consumption. The Glu27 (G) allele was associated with a significantly higher risk of obesity (Odds Ratio = 2.56) only among women with a high carbohydrate intake (defined as >49% of total energy). In stark contrast, for women who consumed a lower-carbohydrate diet, the Gln27Glu polymorphism had no significant effect on their obesity risk. This study was one of the first to strongly suggest that the metabolic risk conferred by the Glu27 allele is not deterministic and may be unmasked or expressed only within the specific nutritional environment of a high-carbohydrate diet.

A large cross-sectional study in a Japanese population by Nanri et al.[53] investigated the associations between dietary patterns and serum triglyceride levels, as modulated by the Gln27Glu polymorphism. The study identified a significant gene-diet interaction, specifically with the Western dietary pattern (characterized by high intakes of fat, oils, meat, and processed foods). The results showed that the Glu27 (G allele) was significantly associated with higher serum triglyceride levels, but only among individuals in the highest tertile for adherence to the Western diet. For subjects on a Prudent or Traditional Japanese diet, the Gln27Glu variant had no significant effect on triglycerides. This reinforces the concept that the metabolic consequences of the Glu27 allele are strongly dependent on macronutrient context, becoming detrimental when combined with a diet high in fats and processed foods.

These two lines of evidence, together, point to macronutrient composition, rather than overall caloric intake, as the feature of diet most relevant to the Glu27 allele's metabolic impact, with risk concentrated among individuals consuming high-carbohydrate or Western-pattern diets. These findings reinforce that dietary composition, not merely caloric intake, is a critical determinant of whether rs1042714 translates into adverse metabolic outcomes, lending further support to the review's emphasis on nutrition as a key modulator of this variant's clinical relevance.

Genotype-Dependent Changes in Metabolic Health Markers

The Gln27Glu (rs1042714) polymorphism's influence extends beyond simple obesity risk to a range of more specific metabolic and cardiovascular health markers. Research has progressively shifted from BMI to more precise phenotypes, revealing a complex, context-dependent role for the variant. The variant has been directly implicated in regional fat distribution, a critical determinant of metabolic health. A study by Kunnas et al.[54] in Finnish women reported that carriers of the Glu27 (G allele) were associated with a male-type (central) fat accumulation pattern, exhibiting a higher abdominal-to-gluteal fat ratio compared to Gln27Gln (CC homozygotes). This suggests the G allele may predispose individuals to store fat viscerally, a key marker of metabolic risk. This link to metabolic dysregulation is often stronger when analyzed by haplotype. Prior et al.[55] studying obese postmenopausal women, demonstrated that *ADRB2* haplotypes (which include the Gln27Glu locus) were significantly associated with glucose tolerance and insulin sensitivity.

The metabolic consequences of *ADRB2* variation may ultimately translate to hard cardiovascular endpoints. A large-scale prospective study by Schürks et al.[56] which followed 25,224 women, identified a haplotype (Gly16-Gln27-Thr164) that was associated with a significantly reduced risk of incident myocardial infarction (HR 0.75). Furthermore, the gene's influence is detectable at a fundamental physiological level. Atala et al.[57] found that *ADRB2* polymorphisms in

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

healthy young Brazilians significantly influence cardiac autonomic modulation and baroreflex sensitivity, key markers of nervous system control over cardiovascular function. The variant's association with metabolic markers is not universal and appears to be heavily modulated by genetic and environmental context. This is evident in population-specific studies, such as the one by Shakhanova et al.[58] in a Kazakh population, which found no association between the *ADRB2* polymorphism and the risk of hyperinsulinism or insulin resistance.

The metabolic impact is also complicated by epistasis (gene-gene interactions). Ukkola et al.[59] in the Quebec Family Study, demonstrated that interactions *among* the alpha2-, beta2-, and beta3-adrenergic receptor genes were significantly associated with obesity-related phenotypes, indicating the Gln27Glu variant does not act in isolation. Furthermore, the variant's effect can be modulated by pharmacological interventions. A study by Vardeny et al.[60] in heart failure patients found that the Glu27 (G allele) had opposing effects on insulin resistance depending on the specific beta-blocker prescribed: it was associated with lower insulin resistance (a favorable outcome) in patients on carvedilol, but higher insulin resistance (a detrimental outcome) in patients on metoprolol succinate. Finally, the gene's influence appears to be context-dependent even during dietary interventions. A 2023 study by de Luis et al.[26] on women with severe obesity found that G allele carriers had a paradoxically better metabolic response to a meal-replacement diet. This group showed significantly greater reductions in fasting glucose, cholesterol, triglycerides, and HOMA-IR scores, with an odds ratio of 0.26 for resolving impaired glucose metabolism. This suggests the G allele's metabolic impact may be unfavorable at baseline as seen in Kunnas et al.[54] but beneficial under specific conditions of caloric restriction.

Considered jointly, these studies show that rs1042714's influence reaches well beyond obesity risk alone, extending into fat distribution patterns, glucose-insulin dynamics, and cardiovascular endpoints, with additional layers of complexity introduced by epistatic gene-gene interactions and even by the specific pharmacological agents a patient receives. This breadth of context-dependency is consistent with the review's central thesis: that rs1042714 operates as a conditional modulator of metabolic health rather than a fixed, deterministic risk variant.

Gene-Exercise Interactions: The Complex Role of Physical Activity

The Gln27Glu polymorphism's influence on metabolism appears to be significantly modulated by physical activity. The variant's effect is not static but interacts dynamically with an individual's activity level, influencing baseline energy expenditure, metabolic response to exercise, and cardiovascular regulation. The interaction between rs1042714 and a sedentary lifestyle has been clearly demonstrated. A study by Rosado et al.[61] in 135 obese Brazilian women found a significant gene-environment interaction: carriers of the Glu27 (G) allele who were classified as sedentary had a significantly lower resting metabolic rate (RMR) compared to sedentary women with the Gln27Gln (CC genotype). The G allele was also associated with a higher body fat percentage in these sedentary individuals, suggesting it may contribute to a thrifty phenotype (lower energy expenditure) primarily in the absence of physical activity. G allele was shown to increase obesity risk even with moderate sedentary behavior.

Beyond baseline expenditure, the polymorphism appears to dictate the efficiency of the metabolic response to exercise, particularly regarding fat mobilization. A study by Macho-Azcarate et al.[62] in 52 obese Spanish women found that carriers of the Glu27 (G allele) exhibited a blunted lipolytic response during a standardized exercise test. They showed significantly lower plasma glycerol and free fatty acid (FFA) concentrations compared to CC homozygotes, indicating a reduced capacity to mobilize fat from adipose tissue during physical exertion. This finding of a less favorable metabolic response in G-allele carriers is further supported by other research. One study examining obese women during a maximum oxygen consumption test (VO2 max) noted that the GG genotype group had a worse metabolic profile during the recovery phase. Compared to the CC group, they demonstrated lower plasma glycerol, higher triglyceride and insulin:glucose ratios, and significantly lower fat oxidation. This suggests that for individuals with the GG genotype, physical activity may be less effective at stimulating lipolysis and fat oxidation.[63]

While the G allele is linked to blunted metabolic efficiency, the Gln27Gln (CC genotype) has been associated with adverse cardiovascular responses to exercise in high-risk patients. A study by Ferreira-Santos et al.[64] investigated neurovascular control in patients who had experienced an acute coronary syndrome (ACS). During a handgrip exercise test, patients with the CC genotype exhibited an exaggerated Muscle Sympathetic Nerve Activity (MSNA) and blood pressure response compared to G allele carriers. This finding is clinically relevant, as it links the CC genotype to a

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

higher-risk cardiovascular profile during exertion. Notably, the study also found that a 2 month exercise training program successfully normalized this exaggerated response, demonstrating a complex interplay between genotype and exercise adaptation.

Collectively, the studies summarized here confirm a profound lack of consensus regarding the direction of the Gln27Glu-obesity association, with the G allele variously reported as a risk factor, a protective factor, or unrelated to obesity depending on the population studied. Rather than reflecting inconsistent methodology alone, this divergence is consistent with the review's central premise that rs1042714 is not a deterministic obesity variant, but one whose phenotypic expression depends heavily on genetic background and environmental context, factors examined in detail in the sections that follow.

Table 1. Summary of Studies on ADRB2 rs1042714 and Obesity

Author (year)	Population	Sample size (N)	Variables	Key finding related to SNV rs1042714
Large et all. (1997)[34]	Swedish (Caucasian)	140 subjects	Age, BMI, waist-to-hip ratio (WHR), fat cell volume, and fasting plasma levels of glucose and insulin.	Significantly associated with obesity, (RR=7, OR=1). GG carrier had an average fat mass excess of 20 kg and approximately 50% larger fat cells than controls. G allele was more frequent in obese (41%) than in controls (31%).
Mori et al. (1999)[31]	Japanese	278 men (249 CC, 28 CG, 1 GG).	BMI and fat distribution (subcutaneous fat and visceral fat)	G allele was significantly higher in obese than in nonobese/intermediate subjects (0.11 vs 0.04, *P*= 0.004). The CG genotype had a significantly higher mean age-adjusted body-mass index (BMI) and mean age-adjusted subcutaneous fat area assessed by CT scan than the wild-type CC genotype, but not the mean age-adjusted visceral fat areas.
Meirhaeghe et al. (2000)[38]	French (Caucasian)	836 (419 men, 417 women)	Body weight, BMI, waist and hip circumferences and WHR.	CC genotype subjects had an increased risk of obesity (OR=1.77, *P*=0.005). This effect was mainly detected in men (OR=2.40, *P*=0.003). Men bearing the CC genotype had higher body weight, BMI, waist and hip circumferences and WHR.
Kim et al. (2002)[46]	Korean	195 subjects	BMI, % body fat, WHR, blood pressure, fasting plasma glucose, fasting serum insulin, LDL, HDL, TG, FFA	The frequency of the GG genotype was 1.1%. No significant differences in BMI, percentage body fat, waist–to-hip ratio (WHR), systolic blood pressure, diastolic blood pressure and concentrations of fasting plasma glucose, fasting serum insulin, serum low-density lipoprotein (LDL)-cholesterol, serum high-density lipoprotein (HDL)-cholesterol, serum triglyceride, and serum free fatty acids.
Azcarate et al. (2002)[65]	Spanish	15 obese women (7 CC, 8 GG)	Plasma triglycerides, glycerol, FFA, hydroxybutyrate, glucose and lactate were assayed by spectrophotometric methods. Insulin, leptin	A gene-exercise interaction was found. Carriers of the G allele showed a blunted lipolytic (fat breakdown) response during exercise. They had significantly lower concentrations of glycerol and FFAs compared to the CC homozygotes, indicating a reduced ability to mobilize fat for energy during physical activity.

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

Table 1. Summary of Studies on ADRB2 rs1042714 and Obesity(*Continue...)*

Author (year)	Population	Sample size (N)	Variables	Key finding related to SNV rs1042714
González et al. (2003)[42]	Spanish (Caucasian)	666 subjects (319 men, 347 women)	BMI, WHR, sagittal abdominal diameter (SAD), blood pressure, fasting glucose, total cholesterol, HDL, LDL, TG, insulin, proinsulin and leptin	GG genotype obese men had significantly higher BMI and SAD mean values than both CG and CC genotype obese men. Two-hour post-load plasma glucose concentration was higher in GG genotype than in CC genotype in the whole population and only in men when stratified by gender.
Duarte et al. (2003)[43]	Tongan	1022 subjects	BMI, fat-free mass, percentage fat and WHR	The frequency of the GG genotype was 0.1%. The mean BMI for men and women was not significantly different in groups.
Martínez et al. (2003)[44]	Spanish	313 subjects (159 obese, 154 non obese)	BMI, carbohydrate intake.	A gene-diet interaction was identified. G allele was associated with a significantly higher risk of obesity *only* in women with high carbohydrate intake (>49% of total energy). The genotype had no effect on obesity risk in women with low carbohydrate intake.
Lange et al. (2005)[33]	African-American and Hispanic-American	992 subjects (565 women, 427 men)	Adipose tissue deposition (measured by CT, including visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT)), BMI, and VAT-to-SAT ratio.	The G allele was positively associated with body mass index (p=0.025), visceral adipose tissue (p=<0.0001) and visceral-to-subcutaneous adipose ratio (p=0.009), but not with subcutaneous adipose tissue (p=0.952) in recessive model.
Jocken et al. (2007) [63]	Dutch	108 subjects (65 men, 43 women) overweight and obese	Energy expenditure (EE), respiratory quotient (RQ), circulating free fatty acid (FFA) and glycerol levels	The frequency of the GG genotype was 21,3%. Genetic variation in the ADRB2 gene is associated with disturbances in in vivo b-adrenoceptor-mediated lipolysis and fat oxidation during b-adrenergic stimulation in overweight and obese subjects; these effects are influenced by gene–gender interactions.
Jalba et al. (2008)[51]	Multiple populations	A meta-analysis including 38 studies for the Gln27Glu variant	BMI	The frequency of G allele carriers, ranged from 6.71% in Aymara American Indians to 78.29% in a Dutch population. The frequency of Arg16 allele carriers varied from 51.4 to 64.6% in Europeans and from 71.1 to 85.6% in East Asians. In race groups with low Glu27 allele frequency (Asians, Pacific Islanders, and American Indians), ORs revealed a significant obesity risk associated with rs1042714.
Rooyen et al. (2008)[37]	African.	102 women	Anthropometric variables, resting blood pressure, plasma glucose, insulin, free fatty acids (FFA), ghrelin, leptin and lipids, HOMA-IR.	The percentage body fat was significantly lower and the FFA significantly higher in lean subjects with the G allele compared to subjects with the C allele of the ADRB2 gene.

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

Table 1. Summary of Studies on ADRB2 rs1042714 and Obesity(*Continue...)*

Author (year)	Population	Sample size (N)	Variables	Key finding related to SNV rs1042714
Kunnas et al. (2009)[54]	Finnish	112 women	Fat distribution, WHR, BMI.	Visceral fat was significantly higher in women with the G allele compared to CC genotyoe. The waist-hip ratio also tended to be higher in women with the G allele compared to CC genotype.
Prior et al. (2011)[55]	Caucasian and African American	123 women	Glucose tolerance and insulin sensitivity (measured by OGTT)	The study focused on haplotypes (combinations of variants). The haplotype containing Gln27 (C allele) was associated with worse glucose tolerance and lower insulin sensitivity.
Pereira et al. (2011)[45]	Japanese	4,193 subjects (1,911 women and 2,282 men).	BMI	The Gln27Glu variant by itself was not associated with obesity. However, a significant gene-gene interaction (synergism) was found. Individuals who carried both the *ADRB2* Glu27 (G) allele and the *LEPR* 223Arg allele had a significantly increased risk of obesity.
Ruiz et al. (2011)[52]	Spanish (Caucasian)	78 obese women	Intervention: 8-week energy-restricted diet	Interaction effect between the Gln27Glu polymorphism and diet-induced changes on body weight, BMI, and LM observed. Women carrying the G allele had a greater reduction in body weight than noncarriers. Women with the G allele lost more LM than the CC genotype.
Beason et al. (2011)[25]	African	1,893 men	Body composition (measured by DEXA), BMI, waist circumference	The frequency of the GG genotype was 2.2%. The study focused on haplotypes (combinations of variants). The haplotype containing G alelle was equally frequent in low, medium, and high tertiles of percentage of body fat mass.
Naka et al. (2013)[40]	Oceanic	694 subjects	BMI	The 27Glu was also significantly associated with obesity in the single-point association. However, this association was no longer significant after adjustment for rs34623097 since these SNPs were in linkage disequilibrium with each other. .
Zhang et al. (2014)[1]	Multiple populations	A meta-analysis of 18 studies	Obesity	rs1042714 was associated with significantly increased obesity risk in the heterozygote model and the dominant model, whereas no significant association was found in the other models for rs1042714.
Saliba et al. (2014)[15]	Brazilian	109 women	Intervention: 7-week weight loss diet intervention	The intervention did not result in a statistically significant difference in weight loss between polymorphism carriers and non-carriers. Gln27Glu polymorphism carriers showed a lower BMI compared to non-carriers.
Rosado et al. (2015)[66]	Brazilian	60 obese women	Intervention: energy-restricted diet for 10 weeks	The GG genotype showed a positive relation with EE in physical activity and fat oxidation. The environmental factors and Gln27Glu variant did not influence the nutritional status and EE of obese women, but physical activity in obese women with the variant in the ADRβ_2 gene can promote fat oxidation.

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

Table 1. Summary of Studies on ADRB2 rs1042714 and Obesity(*Continue...)*

Author (year)	Population	Sample size (N)	Variables	Key finding related to SNV rs1042714
Nanri et al. (2016)[53]	Japanese	1720 subjects	4 diatery patterns, serum TG	No interaction between *ADR*β*2* Gln27Glu and the seafood pattern (*p* for interaction = 0.52), this pattern was significantly positively associated with triglyceride levels among Gln/Gln homozygotoes after adjustment for all confounding factors (*p* for trend = 0.03).
Jesus et al. (2019)[7]	Brazilian	44 subjects	Body composition, insulin, lipid profile, abdominal subcutaneous and visceral adiposities	The frequency of the G allele was 29,5%. The group of adolescent carriers of the G presented higher mean adiposity indicators (abdominal circumference, trunk fat mass and visceral fat), as well as lower IL-10 concentrations when compared to non-carriers.
De luis et al. (2023)[26]	Spanish	95 women	Intervention: 12-week meal-replacement hypocaloric diet.	Significant interaction effects between *ADRB2* variant and pMR-induced changes in dominant model on body weight, BMI, fat mass, waist circumference, glucose, total cholesterol, LDL, TG, and fasting insulin levels.
Kachkovska et al. (2023)[32]	Ukrainian	648 subjects	BMI	Obesity relative risk estimation showed a statistically significant correlation related to the dominant (p=0.03) and additive (p=0.04) models of inheritance. The risk of obesity in minor allele carriers (Glu/Glu+Gln/Glu) was 1.75 times higher than that in the major allele homozygotes (p=0.03).
Da Fonseca et al. (2024)[67]	Brazilian	501 subjects (305 obese and 196 controls).	Body weight, waist, hip circumference, fasting plasma glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), and triglyceride (TG)	No significant association was found.

CONCLUSION

This narrative review set out to summarize and critically analyze the scientific literature regarding the ADRB2 rs1042714 variant, with particular attention to how its relationship with obesity is shaped by dietary intake and physical activity. Taken together, the evidence reviewed here indicates that the ADRB2 Gln27Glu (rs1042714) polymorphism functions not as a deterministic factor for obesity, but as a context-dependent modulator of human energy metabolism. Its association with baseline adiposity is markedly inconsistent across the literature, with the G allele reported as a risk factor, a protective factor, or non-significant depending on the study population. This variability is attributable, in large part, to population-specific differences in allele frequency and genetic background, which differ substantially between Caucasian, East Asian, African, and Hispanic populations and likely reflect distinct evolutionary and selective pressures.

Beyond ethnicity, this review demonstrates that the variant's most clinically meaningful role lies in modulating an individual's metabolic response to their environment rather than in exerting a fixed, independent effect on adiposity. The gene-diet interaction evidence indicates that the metabolic consequences of the Glu27 allele depend on both the

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

specificity of the dietary intervention and its macronutrient composition, with risk most consistently unmasked under high-carbohydrate or Western-pattern diets, while more controlled interventions such as meal-replacement regimens may reveal a paradoxically favorable response in G allele carriers. Similarly, the gene-exercise interaction evidence shows that the metabolic disadvantages associated with the Glu27 allele, including blunted lipolysis and reduced resting energy expenditure, are most pronounced under sedentary conditions and may be attenuated by regular physical activity. Together, these patterns support a gene-environment mismatch framework, in which a variant that may once have conferred a survival advantage under conditions of caloric scarcity becomes metabolically maladaptive in an obesogenic environment characterized by energy-dense diets and low physical activity.

Limitation

This review has several limitations that should be considered when interpreting its findings. First, because this was conducted as a narrative rather than a systematic review, a formal PRISMA-style screening process with a flow diagram was not implemented, and exact counts of articles identified, screened, and excluded at each stage were not formally tracked. As a result, the selection of articles, while guided by explicit inclusion and exclusion criteria, retains an inherent degree of subjectivity characteristic of narrative reviews, and the absence of a documented screening flow limits the reproducibility of the search process. In total, approximately 30 primary research articles and 2 meta-analyses meeting the inclusion criteria were retained and form the evidence base for this review, supplemented by additional mechanistic and background literature to contextualize the biological pathways discussed. Future systematic reviews or meta-analyses on this topic would benefit from a fully reproducible search protocol with pre-registered search strings and a complete PRISMA-style screening flow diagram to allow more rigorous quantification of study selection at each stage.

REFERENCES

1. Zhang H, Wu J, Yu L. Association of Gln27Glu and Arg16Gly polymorphisms in Beta2-adrenergic receptor gene with obesity susceptibility: a meta-analysis. PLoS One. 2014;9(6):e100489. doi:10.1371/journal.pone.0100489 PubMed PMID: 24960039.
2. Boutari C, Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. Metabolism. 2022 Aug;133:155217. doi:10.1016/j.metabol.2022.155217
3. McPherson R. Genetic contributors to obesity. Canadian Journal of Cardiology. 2007 Aug;23:23A-27A. doi:10.1016/S0828-282X(07)71002-4
4. Bouchard C. Genetics of Obesity: What We Have Learned Over Decades of Research. Obesity. 2021 May 26;29(5):802–20. doi:10.1002/oby.23116
5. Mahmoud R, Kimonis V, Butler MG. Genetics of Obesity in Humans: A Clinical Review. Int J Mol Sci. 2022 Sep 20;23(19). doi:10.3390/ijms231911005 PubMed PMID: 36232301.
6. da Fonseca ACP, Assis IS da S, Salum KCR, Palhinha L, Abreu G de M, Zembrzuski VM, et al. Genetic variants in DBC1, SIRT1, UCP2 and ADRB2 as potential biomarkers for severe obesity and metabolic complications. Front Genet. 2024 May 22;15. doi:10.3389/fgene.2024.1363417
7. Jesus ÍC de, Alle LF, Tureck LV, Silva LR da, Lopes WA, Moraes Junior FB de, et al. ADRB2 GLN27GLU POLYMORPHISM ASSOCIATED WITH ADIPOSITY INDICATORS AND IL-10 IN ADOLESCENTS. Revista Brasileira de Medicina do Esporte. 2019 Aug;25(4):322–7. doi:10.1590/1517-869220192504214836
8. Collins S. β-adrenoceptor signaling networks in adipocytes for recruiting stored fat and energy expenditure. Front Endocrinol (Lausanne). 2011;2. doi:10.3389/fendo.2011.00102
9. Ishida Y, Matsushita M, Yoneshiro T, Saito M, Fuse S, Hamaoka T, et al. Genetic evidence for involvement of β2-adrenergic receptor in brown adipose tissue thermogenesis in humans. Int J Obes. 2024 Aug 17;48(8):1110–7. doi:10.1038/s41366-024-01522-6
10. Arner P, Hoffstedt J. Adrenoceptor genes in human obesity. J Intern Med. 1999 Jun 25;245(6):667–72. doi:10.1046/j.1365-2796.1999.00495.x
11. Moore GE, Shuldiner AR, Zmuda JM, Ferrell RE, McCole SD, Hagberg JM. Obesity gene variant and elite endurance performance. Metabolism. 2001 Dec;50(12):1391–2. doi:10.1053/meta.2001.28140
12. Jocken JWE, Blaak EE, Schiffelers S, Arner P, van Baak MA, Saris WHM. Association of a beta-2 adrenoceptor (ADRB2) gene variant with a blunted in vivo lipolysis and fat oxidation. Int

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

J Obes. 2007 May 28;31(5):813–9. doi:10.1038/sj.ijo.0803499
13. Takenaka A, Nakamura S, Mitsunaga F, Inoue-Murayama M, Udono T, Suryobroto B. Human-Specific SNP in Obesity Genes, Adrenergic Receptor Beta2 (ADRB2), Beta3 (ADRB3), and PPAR γ2 (PPARG), during Primate Evolution. PLoS One. 2012 Aug 24;7(8):e43461. doi:10.1371/journal.pone.0043461
14. Salas-Martínez MG, Saldaña-Alvarez Y, Cordova EJ, Mendiola-Soto DK, Cid-Soto MA, Luckie-Duque A, et al. Genetic variability of five ADRB2 polymorphisms among Mexican Amerindian ethnicities and the Mestizo population. PLoS One. 2019 Dec 2;14(12):e0225030. doi:10.1371/journal.pone.0225030
15. Saliba LF, Reis RS, Brownson RC, Hino AA, Tureck L V., Valko C, et al. Obesity-related gene ADRB2, ADRB3 and GHRL polymorphisms and the response to a weight loss diet intervention in adult women. Genet Mol Biol. 2014;37(1):15–22. doi:10.1590/S1415-47572014000100005
16. Sarpeshkar V, Bentley DJ. Adrenergic-β2 receptor polymorphism and athletic performance. J Hum Genet. 2010 Aug 30;55(8):479–85. doi:10.1038/jhg.2010.42
17. Zechner R, Zimmermann R, Eichmann TO, Kohlwein SD, Haemmerle G, Lass A, et al. FAT SIGNALS--lipases and lipolysis in lipid metabolism and signaling. Cell Metab. 2012 Mar 7;15(3):279–91. doi:10.1016/j.cmet.2011.12.018 PubMed PMID: 22405066.
18. Mullins GR, Wang L, Raje V, Sherwood SG, Grande RC, Boroda S, et al. Catecholamine-induced lipolysis causes mTOR complex dissociation and inhibits glucose uptake in adipocytes. Proceedings of the National Academy of Sciences. 2014 Dec 9;111(49):17450–5. doi:10.1073/pnas.1410530111
19. Jönsson C, Castor Batista AP, Kjølhede P, Strålfors P. Insulin and β-adrenergic receptors mediate lipolytic and anti-lipolytic signalling that is not altered by type 2 diabetes in human adipocytes. Biochemical Journal. 2019 Oct 15;476(19):2883–908. doi:10.1042/BCJ20190594
20. Blondin DP, Nielsen S, Kuipers EN, Severinsen MC, Jensen VH, Miard S, et al. Human Brown Adipocyte Thermogenesis Is Driven by β2-AR Stimulation. Cell Metab. 2020 Aug;32(2):287-300.e7. doi:10.1016/j.cmet.2020.07.005
21. Arner P, Hoffstedt J. Adrenoceptor genes in human obesity. J Intern Med. 1999 Jun 25;245(6):667–72. doi:10.1046/j.1365-2796.1999.00495.x
22. Kunnas T, Lahtio R, Kortelainen ML, Kalela A, Nikkari ST. Gln27Glu variant of Beta2-adrenoceptor gene affects male type fat accumulation in women. Lipids Health Dis. 2009;8(1):43. doi:10.1186/1476-511X-8-43
23. Wu J, Boström P, Sparks LM, Ye L, Choi JH, Giang AH, et al. Beige Adipocytes Are a Distinct Type of Thermogenic Fat Cell in Mouse and Human. Cell. 2012 Jul;150(2):366–76. doi:10.1016/j.cell.2012.05.016
24. Salas-Martínez MG, Saldaña-Alvarez Y, Cordova EJ, Mendiola-Soto DK, Cid-Soto MA, Luckie-Duque A, et al. Genetic variability of five ADRB2 polymorphisms among Mexican Amerindian ethnicities and the Mestizo population. PLoS One. 2019;14(12):e0225030. doi:10.1371/journal.pone.0225030 PubMed PMID: 31790415.
25. Beason TS, Bunker CH, Zmuda JM, Wilson JW, Patrick AL, Wheeler VW, et al. ADRB2 gene variants, dual-energy x-ray absorptiometry body composition, and hypertension in Tobago men of African descent. Metabolism. 2011 May;60(5):698–705. doi:10.1016/j.metabol.2010.07.004
26. de Luis DA, Izaola O, Primo D, Gómez JJL. Role of beta-2 adrenergic receptor polymorphism (rs1042714) on body weight and glucose metabolism response to a meal-replacement hypocaloric diet. Nutrition. 2023 Dec;116:112170. doi:10.1016/j.nut.2023.112170
27. Takenaka A, Nakamura S, Mitsunaga F, Inoue-Murayama M, Udono T, Suryobroto B. Human-Specific SNP in Obesity Genes, Adrenergic Receptor Beta2 (ADRB2), Beta3 (ADRB3), and PPAR γ2 (PPARG), during Primate Evolution. PLoS One. 2012 Aug 24;7(8):e43461. doi:10.1371/journal.pone.0043461
28. Drolet R, Richard C, Sniderman AD, Mailloux J, Fortier M, Huot C, et al. Hypertrophy and hyperplasia of abdominal adipose tissues in women. Int J Obes. 2008 Feb 28;32(2):283–91. doi:10.1038/sj.ijo.0803708
29. Giralt M, Villarroya F. White, Brown, Beige/Brite: Different Adipose Cells for Different Functions? Endocrinology. 2013 Sep 1;154(9):2992–3000. doi:10.1210/en.2013-1403
30. Frühbeck G, Méndez-Giménez L, Fernández-Formoso JA, Fernández S, Rodríguez A. Regulation of adipocyte lipolysis. Nutr Res Rev.

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

2014 Jun 28;27(1):63–93. doi:10.1017/S095442241400002X

31. Mori Y, Kim-Motoyama H, Ito Y, Katakura T, Yasuda K, Ishiyama-Shigemoto S, et al. The Gln27Glu β2-Adrenergic Receptor Variant Is Associated with Obesity Due to Subcutaneous Fat Accumulation in Japanese Men. Biochem Biophys Res Commun. 1999 Apr;258(1):138–40. doi:10.1006/bbrc.1999.0607
32. Kachkovska V. Association between Gln27Glu Polymorphism in the B2 Adrenergic Receptor Gene and Obesity Risk in Patients with Early-Onset and Late-Onset Bronchial Asthma. Georgian Med News. 2023;(340–341):254–8. PubMed PMID: 37805907.
33. Lange LA, Norris JM, Langefeld CD, Nicklas BJ, Wagenknecht LE, Saad MF, et al. Association of adipose tissue deposition and beta-2 adrenergic receptor variants: the IRAS family study. Int J Obes. 2005 May 18;29(5):449–57. doi:10.1038/sj.ijo.0802883
34. Large V, Hellström L, Reynisdottir S, Lönnqvist F, Eriksson P, Lannfelt L, et al. Human beta-2 adrenoceptor gene polymorphisms are highly frequent in obesity and associate with altered adipocyte beta-2 adrenoceptor function. Journal of Clinical Investigation. 1997 Dec 15;100(12):3005–13. doi:10.1172/JCI119854
35. Zhang H, Wu J, Yu L. Association of Gln27Glu and Arg16Gly Polymorphisms in Beta2-Adrenergic Receptor Gene with Obesity Susceptibility: A Meta-Analysis. PLoS One. 2014 Jun 24;9(6):e100489. doi:10.1371/journal.pone.0100489
36. Mori Y, Kim-Motoyama H, Ito Y, Katakura T, Yasuda K, Ishiyama-Shigemoto S, et al. The Gln27Glu β2-Adrenergic Receptor Variant Is Associated with Obesity Due to Subcutaneous Fat Accumulation in Japanese Men. Biochem Biophys Res Commun. 1999 Apr;258(1):138–40. doi:10.1006/bbrc.1999.0607
37. Rooyen J, Pretorius P, Britz M, Huisman H, Schutte A, Towers G, et al. Genetic Polymorphisms of β_2 - and β_3 -Adrenergic Receptor Genes Associated with Characteristics of the Metabolic Syndrome in Black South African Women. Experimental and Clinical Endocrinology & Diabetes. 2008 Apr 7;116(04):236–40. doi:10.1055/s-2007-992785
38. Meirhaeghe A, Helbecque N, Cottel D, Amouyel P. Impact of polymorphisms of the human β2-adrenoceptor gene on obesity in a French population. Int J Obes. 2000 Mar 13;24(3):382–7. doi:10.1038/sj.ijo.0801168
39. Saliba LF, Reis RS, Brownson RC, Hino AA, Tureck L V., Valko C, et al. Obesity-related gene ADRB2, ADRB3 and GHRL polymorphisms and the response to a weight loss diet intervention in adult women. Genet Mol Biol. 2014;37(1):15–22. doi:10.1590/S1415-47572014000100005
40. Naka I, Hikami K, Nakayama K, Koga M, Nishida N, Kimura R, et al. A functional SNP upstream of the beta-2 adrenergic receptor gene (ADRB2) is associated with obesity in Oceanic populations. Int J Obes. 2013 Sep 11;37(9):1204–10. doi:10.1038/ijo.2012.206
41. da Fonseca ACP, Assis IS da S, Salum KCR, Palhinha L, Abreu G de M, Zembrzuski VM, et al. Genetic variants in DBC1, SIRT1, UCP2 and ADRB2 as potential biomarkers for severe obesity and metabolic complications. Front Genet. 2024 May 22;15. doi:10.3389/fgene.2024.1363417
42. González Sánchez JL, Proenza AM, Martínez Larrad MT, Ramis JM, Fernández Pérez C, Palou A, et al. The glutamine 27 glutamic acid polymorphism of the β_2 -adrenoceptor gene is associated with abdominal obesity and greater risk of impaired glucose tolerance in men but not in women: a population-based study in Spain. Clin Endocrinol (Oxf). 2003 Oct 18;59(4):476–81. doi:10.1046/j.1365-2265.2003.01871.x
43. DUARTE NL, COLAGIURI S, PALU T, WANG XL, WILCKEN DEL. Obesity, Type II diabetes and the β2 adrenoceptor gene Gln27Glu polymorphism in the Tongan population. Clin Sci. 2003 Mar 1;104(3):211–5. doi:10.1042/cs1040211
44. Martínez JA, Corbalán MS, Forga L, Marti A, Sánchez-Villegas A, Martínez-González MA. Obesity Risk Is Associated with Carbohydrate Intake in Women Carrying the Gln27Glu β2-Adrenoceptor Polymorphism. J Nutr. 2003 Aug;133(8):2549–54. doi:10.1093/jn/133.8.2549
45. Pereira T V., Mingroni-Netto RC, Yamada Y. *ADRB2* and *LEPR* Gene Polymorphisms: Synergistic Effects on the Risk of Obesity in Japanese. Obesity. 2011 Jul 10;19(7):1523–7. doi:10.1038/oby.2010.322
46. Kim SH, Kim DJ, Seo IA, Min YK, Lee MS, Kim KW, et al. Significance of [beta]2-adrenergic receptor gene polymorphism in obesity and type 2 diabetes mellitus in Korean subjects. Metabolism. 2002 Jul;51(7):833–7. doi:10.1053/meta.2002.33347
47. Iwamoto N, Ogawa Y, Kajihara S, Hisatomi A, Yasutake T, Yoshimura T, et al. Gln27Glu β2-adrenergic receptor variant is associated with hypertriglyceridemia and the development of fatty liver. Clinica Chimica Acta. 2001

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

Dec;314(1–2):85–91. doi:10.1016/S0009-8981(01)00633-7

48. Mori Y, Kim-Motoyama H, Ito Y, Katakura T, Yasuda K, Ishiyama-Shigemoto S, et al. The Gln27Glu β2-Adrenergic Receptor Variant Is Associated with Obesity Due to Subcutaneous Fat Accumulation in Japanese Men. Biochem Biophys Res Commun. 1999 Apr;258(1):138–40. doi:10.1006/bbrc.1999.0607
49. Ishiyama-Shigemoto S, Yamada K, Yuan X, Ichikawa F, Nonaka K. Association of polymorphisms in the ?2-adrenergic receptor gene with obesity, hypertriglyceridaemia, and diabetes mellitus (Short Communication). Diabetologia. 1999 Jan 11;42(1):98–101. doi:10.1007/s001250051120
50. Kim SH, Kim DJ, Seo IA, Min YK, Lee MS, Kim KW, et al. Significance of [beta]2-adrenergic receptor gene polymorphism in obesity and type 2 diabetes mellitus in Korean subjects. Metabolism. 2002 Jul;51(7):833–7. doi:10.1053/meta.2002.33347
51. Jalba MS, Rhoads GG, Demissie K. Association of Codon 16 and Codon 27 β2-Adrenergic Receptor Gene Polymorphisms with Obesity: A Meta-analysis. Obesity. 2008 Sep 6;16(9):2096–106. doi:10.1038/oby.2008.327
52. Ruiz JR, Larrarte E, Margareto J, Ares R, Labayen I. Role of β_2 -Adrenergic Receptor Polymorphisms on Body Weight and Body Composition Response to Energy Restriction in Obese Women: Preliminary Results. Obesity. 2011 Jan 6;19(1):212–5. doi:10.1038/oby.2010.130
53. Nanri H, Nishida Y, Nakamura K, Tanaka K, Naito M, Yin G, et al. Associations between Dietary Patterns, ADRβ2 Gln27Glu and ADRβ3 Trp64Arg with Regard to Serum Triglyceride Levels: J-MICC Study. Nutrients. 2016 Sep 6;8(9):545. doi:10.3390/nu8090545
54. Kunnas T, Lahtio R, Kortelainen ML, Kalela A, Nikkari ST. Gln27Glu variant of Beta2-adrenoceptor gene affects male type fat accumulation in women. Lipids Health Dis. 2009;8(1):43. doi:10.1186/1476-511X-8-43
55. Prior SJ, Goldberg AP, Ryan AS. *ADRB2* Haplotype Is Associated With Glucose Tolerance and Insulin Sensitivity in Obese Postmenopausal Women. Obesity. 2011 Feb 6;19(2):396–401. doi:10.1038/oby.2010.197
56. Schürks M, Kurth T, Ridker PM, Buring JE, Zee RYL. Association between polymorphisms in the beta2-adrenergic receptor gene with myocardial infarction and ischaemic stroke in women. Thromb Haemost. 2009 Feb;101(2):351–8. PubMed PMID: 19190821.
57. Atala MM, Goulart A, Guerra GM, Mostarda C, Rodrigues B, Mello PR, et al. Arg16Gly and Gln27Glu β2 adrenergic polymorphisms influence cardiac autonomic modulation and baroreflex sensitivity in healthy young Brazilians. Am J Transl Res. 2015;7(1):153–61. PubMed PMID: 25755837.
58. Shakhanova A, Aukenov N, Nurtazina A, Massabayeva M, Babenko D, Adiyeva M, et al. Association of polymorphism genes LPL , ADRB2 , AGT and AGTR1 with risk of hyperinsulinism and insulin resistance in the Kazakh population. Biomed Rep. 2020 Nov;13(5):35. doi:10.3892/br.2020.1342 PubMed PMID: 32843963.
59. Ukkola O, Rankinen T, Weisnagel SJ, Sun G, Pérusse L, Chagnon YC, et al. Interactions among the alpha2-, beta2-, and beta3-adrenergic receptor genes and obesity-related phenotypes in the Quebec Family Study. Metabolism. 2000 Aug;49(8):1063–70. doi:10.1053/meta.2000.7708 PubMed PMID: 10954027.
60. Vardeny O, Detry MA, Moran JJM, Johnson MR, Sweitzer NK. The beta2 adrenergic receptor Gln27Glu polymorphism affects insulin resistance in patients with heart failure: possible modulation by choice of beta blocker. J Cardiovasc Pharmacol. 2008 Dec;52(6):500–6. doi:10.1097/FJC.0b013e31818f5739 PubMed PMID: 19034036.
61. Rosado EL, Bressan J, Martínez JA. Environmental Factors and Beta2-Adrenergic Receptor Polymorphism: Influence on the Energy Expenditure and Nutritional Status of Obese Women. Lipids. 2015 May 18;50(5):459–67. doi:10.1007/s11745-015-4012-1
62. Macho-Azcarate T, Marti A, Calabuig J, Martinez J. Basal fat oxidation and after a peak oxygen consumption test in obese women with a β2 adrenoceptor gene polymorphism. J Nutr Biochem. 2003 May;14(5):275–9. doi:10.1016/S0955-2863(03)00035-4
63. Jocken JWE, Blaak EE, Schiffelers S, Arner P, van Baak MA, Saris WHM. Association of a beta-2 adrenoceptor (ADRB2) gene variant with a blunted in vivo lipolysis and fat oxidation. Int J Obes. 2007 May 28;31(5):813–9. doi:10.1038/sj.ijo.0803499
64. Ferreira-Santos L, Martinez DG, Nicolau JC, Moreira HG, Alves MJ, Pereira AC, et al. Neurovascular control during exercise in acute coronary syndrome patients with Gln27Glu polymorphism of β2-adrenergic receptor. PLoS One. 2017;12(2):e0173061.

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)

doi:10.1371/journal.pone.0173061 PubMed PMID: 28235084.

65. Macho-Azcarate T, Marti A, González A, Martinez J, Ibañez J. Gln27Glu polymorphism in the beta2 adrenergic receptor gene and lipid metabolism during exercise in obese women. Int J Obes. 2002 Nov 13;26(11):1434–41. doi:10.1038/sj.ijo.0802129
66. Rosado EL, Bressan J, Martínez JA. Environmental Factors and Beta2-Adrenergic Receptor Polymorphism: Influence on the Energy Expenditure and Nutritional Status of Obese Women. Lipids. 2015 May 18;50(5):459–67. doi:10.1007/s11745-015-4012-1
67. da Fonseca ACP, Assis IS da S, Salum KCR, Palhinha L, Abreu G de M, Zembrzuski VM, et al. Genetic variants in DBC1, SIRT1, UCP2 and ADRB2 as potential biomarkers for severe obesity and metabolic complications. Front Genet. 2024;15:1363417. doi:10.3389/fgene.2024.1363417 PubMed PMID: 38841722.

Copyright © 2026 by the Authors, Published by Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Journal of Nutrition College Volume 15 (4) Oktober 2026, P-ISSN: 2337-6236; E-ISSN: 2622-884X
This is an open access article under the CC BY-SA License(https://creativecommons.org/licenses/by-sa/4.0/)