

UNIVERSITI TEKNOLOGI MARA (UiTM)

**GENETIC VARIABILITY IN LIPID METABOLISM AND
ITS INFLUENCE ON WEIGHT LOSS: A SYSTEMATIC
REVIEW AND META-ANALYSIS**

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ABSTRACT

Genome-wide association studies have provided valuable information about the potential link between certain genetic polymorphisms related to lipid metabolism and obesity. These findings have led to the assessment of lipid metabolism genes in relation to weight loss outcomes after participation in a weight management program. A literature search was conducted using various databases, such as Pubmed, Google Scholar, Scopus, Web of Sciences and Cochrane Library, to identify studies investigating the influence of genetic variants in lipid metabolism genes on weight loss during a weight management program. Twelve studies focusing on single nucleotide polymorphisms (SNPs) in the ADRB3, FABP2 and PPARG genes were included. The SNP IDs rs4994, rs1799883, and rs1801282 were the subjects of these investigations. The analysis revealed that individuals with the TT genotype for rs4994 (MD = -0.44, 95% CI = -0.99 to 0.10) tended to lose weight more effectively. For rs1799883, those with the GA+AA genotypes (MD = 0.91, 95% CI = -1.50 to 3.32) also showed a tendency towards weight loss, although results varied. Individuals with the CG + GG genotypes for rs1801282 (MD = 1.18, 95% CI = 0.32 to 2.04) experienced significantly more weight loss compared to the CC genotype. This systematic review and meta-analysis suggest that specific genetic variants in ADRB3, FABP2 and PPARG genes may influence weight loss outcomes in weight management programs. However, the overall results are not statistically significant, indicating the need for further research with larger sample sizes to validate these findings.

The review is registered in PROSPERO's International Prospective Register of Systematic Reviews with the identification number CRD42024542178.

Keywords: “genetic variability”, “lipid metabolism genes”, “obesity”, “weight management program”, “weight loss”, “ADRB3”, “FABP2”, “PPARG”

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CHAPTER 1: INTRODUCTION

1.1 Research Background

Obesity has become a global epidemic over the past five decades, posing significant health risks (Blucher, 2019). There is also a global gender disparity in obesity, with a higher prevalence in women than men in all world regions (Ahmad et al., 2016). Obesity can dramatically elevate the chances of developing various diseases, including type 2 diabetes, fatty liver disease, hypertension, heart attack, stroke, dementia, osteoarthritis, obstructive sleep apnea and certain cancers (Sidik et al., 2021). Consequently, it leads to a decrease in both life expectancy and quality of life. World Obesity Atlas 2022 revealed that it is projected that by 2030, approximately one billion people worldwide will be affected by obesity. According to the World Health Organization (WHO), overweight and obesity are characterised by the abnormal or excessive accumulation of fat, which poses a health risk. Obesity results from an imbalance between the energy consumed and the amount expended (Chooi et al., 2019).

It is widely believed that genetic factors contribute to approximately 40-60% of the variation in obesity (Wardle et al., 2008). Genetic variants can influence metabolic processes, impacting how the body utilises and stores energy obtained from food. Body weight homeostasis is governed by a complex interplay of metabolic factors that are influenced by genetics and linked to body composition, physical activity, appetite regulation, insulin signalling, mitochondrial function, fat cell differentiation, lipid metabolism, energy balance, thermogenesis and energy efficiency (Abete et al., 2012).