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Apple Cider Vinegar in the Combat Against Type 2 Diabetes and Obesity – An Overview of Recent Research

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ABSTRACT

Introduction

Apple Cider Vinegar, primarily composed of acetic acid, is gaining more recognition for its possible health advantages, especially its anti-diabetic effects and its beneficial impact on weight loss.

Aim of this study

The aim of this review is to discuss the current state of knowledge regarding the influence of ACV on glycemic indices and weight management in diabetic and obese patients, explore the possibilities of preventing comorbidities, and assess the safety of ACV consumption.

Materials and Methods

Research was performed based on Pubmed and Google Scholar databases. The literature was reviewed using the keywords : Apple Cider Vinegar, Diabetes, Glucose, Obesity.

Results

Studies have confirmed that apple cider vinegar exhibits significant anti-obesity and anti-diabetic properties. It demonstrates dose- and time-dependent effects on reducing fasting glucose, postprandial glucose, glycated hemoglobin, and lipid parameters. It positively impacts weight loss, reducing waist and hip circumference, and enhances tissue sensitivity to insulin. Additionally, apple cider vinegar has been shown to potentiate the effects of metformin, with liquid consumption yielding better results than pill form.

Conclusions

Although initial findings are encouraging, additional research with a larger participant pool and an extended duration of vinegar consumption is necessary. The brevity of the study period restricts the observation of long-term effects, and a larger sample size would improve the applicability of the findings.

Keywords: apple cider vinegar; diabetes; glucose; obesity

INTRODUCTION

Diabetes mellitus is considered a major cause of mortality and reduced life expectancy. The global burden of diabetes had increased significantly since 1990 and became one of the biggest global public health concerns. [1] The World Health Organization (WHO) has predicted that DM will become the 7th leading cause of mortality by the year 2030. [2] As susceptibility to diabetes can be attributed to modifiable risk factors, it is a duty of the utmost importance to explore the possibilities of treatment and prevention.

Modern therapies have achieved significant progress in controlling type 2 diabetes (T2D). Nevertheless, due to the substantial social and financial implications of diabetes and its burden on the healthcare system, there is growing interest in complementary and alternative therapies for managing and controlling diabetes and its complications. The use of natural supplements or foods has seen a notable increase in recent years, reflecting a broader trend towards integrating natural and holistic approaches in chronic disease management. [3] Natural food products are associated with fewer side effects compared to medical therapies. In addition, obese individuals, typically reluctant to reduce their daily caloric intake, tend to use dietary supplements or alternative products for weight reduction and other metabolic benefits. [4] In recent years, interest in examining the antidiabetic and antiobesity effects of apple cider vinegar has been growing. Therefore, in this work we will address its impact on the treatment of diabetes and obesity.

ACV in history

The historical use of vinegar dates back over 10,000 years, with flavored varieties appearing around 5,000 years ago. Ancient civilizations like the Babylonians flavored vinegars with fruit, honey, and malt. Historical references, including those from the Old Testament, indicate the medicinal use of vinegar for wound management. [10] Since the era of Hippocrates vinegar has been used as an antifungal and antibacterial agent for the treatment of numerous infections and ailments, including persistent coughs, head lice, insect bites, warts, ear infections, and wounds. In recent decades, however, there has been increasing interest in the metabolic effects of vinegar. [9] Research on ACV indicates promising and expanding prospects. [11]

Apple Cider Vinegar – composition and mechanisms of action

ACV is a plant-derived food product typically produced from apples through either home or industrial processes. [3] The quality of vinegar is influenced by production techniques, impacting its composition. Traditional methods, characterized by slower production, are known to enhance aroma and flavor development. [12] The formation of vinegar, known as acetic acid, occurs through two biochemical processes: alcoholic fermentation and acid fermentation. [4]

The main active constituent of ACV is acetic acid, to which it owes its characteristic sour taste and distinctive smell. The other ingredients are other organic acids (formic, lactic, malic, citric, succinic, tartaric), amino acids, peptides, vitamins, mineral salts, and polyphenolic compounds such as catechin, caffeic, ferulic acid. [9]

Mechanisms of action of ACV include delayed gastric emptying and intestinal absorption, inhibition of endogenous production of glucose by the liver, enhanced glucose metabolism in skeletal muscle, and increased flow-mediated vasodilation. Vinegar ingestion improves insulin secretion and reduces lipogenesis through the inhibition of the metabolic pathways of cholesterogenesis (by activation of AMPK - an inhibitor of fatty acid and sterol synthesis) and reduction in the transcripts of several lipogenic genes in the liver. It also increases transcripts of several lipolytic genes, stimulates fecal bile acid excretion, increases satiety and enhances energy expenditure. ACV is also believed to inhibit the hunger center in the central nervous system. [9,13]

Definition of diabetes mellitus

Diabetes mellitus (DM) is a chronic metabolic disorder with multiple etiologies, characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) involves insulin resistance and an inadequate compensatory insulin secretion. The majority of individuals with T2DM are obese, exhibiting a higher percentage of body fat or abnormal fat distribution, which contributes to the pathophysiology of the disease. Adipose tissue exacerbates insulin resistance by releasing elevated levels of free fatty acids. Additional contributing factors are dysregulation of hepatic glucose production, and both decreased beta-cell function and beta-cell failure. [5] In this

paper, we will focus on type 2 diabetes, the most common form of diabetes, marked by reduction in insulin action with progressive loss of beta cell function, resulting in insufficient insulin production by the pancreas. [6]

Treatment of type 2 diabetes

The primary goals of diabetes management are to prevent or delay the onset of complications, reduce mortality, and maintain a high quality of life. The best indicator of diabetes management is HbA1c, which reflects blood glucose control over the previous two to three months. [7] In addition, reducing complications and comorbidities of T2DM is effectively achieved through weight loss. A moderate weight loss of 5-10% can normalize blood pressure, improve glycemic control, and increase HDL cholesterol levels. [5] Pharmacotherapy should be initiated when adequate metabolic control is not achieved, either due to the patient's inability to maintain lifestyle modifications or despite consistent adherence to diet and exercise regimens, therapeutic targets are not met. [7] Healthcare providers should prioritize the use of glucose-lowering medications that also facilitate weight management to effectively address both glycemic control and weight-related goals in diabetes treatment. [8] However, managing obesity and T2DM primarily involves dietary modifications and lifestyle interventions, which can be difficult to maintain. [5] For this reason, the use of natural food supplements for addressing health issues has notably risen in recent times. [9]

CURRENT STATE OF KNOWLEDGE

Effects of Apple Cider Vinegar (ACV) consumption on glycemic indices in diabetic patients

Jafarirad et al., conducted a study proving the positive impact of prolonged consumption of ACV on blood glucose indices, lipids and anthropometric indices in type 2 diabetic patients. A randomized clinical trial was carried out and participants were divided into two groups: ACV (30 ml daily), and control. Before and after eight weeks, measurements were taken for fasting blood glucose, HbA1c, insulin, insulin resistance, total cholesterol (Chol), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. The initial positive impact of ACV was observed in the improvement of anthropometric indices:

reduced weight, BMI, waist and hip circumstance. Individuals who consumed ACV exhibited positive effects on postprandial hyperglycemia and fasting blood glucose, which was only significant in the ACV group. There was a significant difference in hemoglobin A1C levels between the two groups. In addition, LDL, Total Chol, LDL/HDL and Chol/HDL ratio decreased after the intervention period in the ACV group compared to the control group. [3]

Kausar, et al. carried out a study that showed the effect of oral apple cider vinegar consumption on blood biochemical factors in type 2 diabetic and hyperlipidemic patients. Blood glucose and insulin levels were measured after two hours after eating. It was found that vinegar can lower postprandial glucose levels but this effect is more noticeable in high glycemic index meals compared to meals with low glycemic index, even when the meals have similar calories content. [4]

A quasi experimental study was conducted by Padmapriya, et al., involving 50 diabetic patients. Experimental group was receiving oral supplementation of apple cider vinegar (15 ml once a day) for one month, and a control group continued their regular medications. The results showed a significant decrease in both fasting and postprandial blood sugar levels after one month of apple cider vinegar supplementation compared to baseline levels. [4]

Kausar et al. measured the effect of apple cider vinegar on patients with type 2 diabetes mellitus (DM) who had poor glycemic control. The participants included adult patients with T2D who were already receiving standard medical therapy for diabetes, specifically metformin + sitagliptin. A single-blind, randomized, placebo-controlled trial was conducted on 110 eligible patients. The interventional group received 15 ml of ACV during dinner for 3 months, while the other group received a placebo. Significant mean changes were observed in the interventional group in HbA1c, fasting blood sugar, total cholesterol, triglyceride, and hip-waist ratio. No significant changes were noted in the mean values of these parameters in the placebo group. In addition, no significant shifts were observed in levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) in both groups. [2]

Another study conducted by Ghefleti et al. aimed to evaluate 70 participants diagnosed with type 2 diabetes and hyperlipidemia. Intervention group received 20 ml of apple vinegar per day for 8 weeks. Various parameters including fasting blood sugar (FBS), insulin resistance (HOMA-IR), beta-cell function (HOMA-B), insulin sensitivity (QUICKI), insulin

levels, oxidative stress markers (malondialdehyde and DPPH), homocysteine levels, and blood pressure were assessed. The results showed that apple vinegar led to significant improvements in FBS and antioxidant capacity (DPPH) within the intervention group. Additionally, there was a significant increase in malondialdehyde levels in the control group. Glycemic indices including insulin levels, HOMA-IR, HOMA-B, and QUICKI decreased significantly in both groups. [14]

Kumar et al. presented systematic review and network meta-analysis aiming to compare and assess the effects of various herbal formulations in the treatment of type 2 diabetes. 44 trials involving 3130 participants in the final analysis were included. Results indicated that ACV, cinnamon, curcumin, and fenugreek markedly decreased fasting blood glucose in comparison to placebo (all $p < 0.05$). Additionally, only ACV and fenugreek seeds were found to be significantly effective in reducing HbA1C levels. Among the herbs studied, ACV was identified as the most effective in reducing FBG compared to others. [15]

Halima et al. developed a double-blind trial study that investigated the effects of ACV on various blood biochemical parameters in individuals with type 2 diabetes. 46 patients were examined; 26 of them received 15ml of ACV with their midday meal for one month, while the rest were given placebo. Results revealed significant reductions in FBG, BMI, weight, triglycerides, very-low density lipoproteins (VLDL), and the total cholesterol to high-density lipoprotein-cholesterol ratio (TC/HDL-C) in the ACV group. However, total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), and the LDL-C to HDL-C ratio did not show significant changes. No substantial differences appeared in the placebo group. [31]

Synergistic activity of metformin and ACV

The objective of the next study was to evaluate the impact of Apple Cider Vinegar (ACV) in conjunction with metformin on the Body Mass Index and glycemic control of patients recently diagnosed with type 2 diabetes mellitus. Abid, et al. conducted a single-arm, pre-post quasi-experimental clinical trial. A total of 30 newly diagnosed type 2 diabetic patients were recruited for the study. After 12 weeks of treatment, which consisted of Metformin (750 mg) combined with 2 tablespoons of ACV daily, results indicated significant reduction in body weight and BMI. Furthermore, glycemic control showed major

improvements, with FBS and HbA1c levels decreasing significantly ($p<0.01$ for all comparisons). [16]

Another study findings indicate that the addition of Apple Cider Vinegar to conventional therapy, such as metformin, enhances glycemic control to a greater extent than treatment with metformin alone, as evidenced by improvements in Fasting Blood Sugar and Hemoglobin A1c levels in newly diagnosed diabetic patients. In this open-label, randomized controlled trial, 126 patients were enrolled and split into two groups: the first received metformin 750 mg daily, and the second received metformin 750 mg plus 2 tablespoons of apple cider vinegar per day. Participants were evaluated for weight, BMI, Fasting Blood Sugar, and HbA1c. After 12 weeks all parameters showed a significant reduction. However, a significant difference was observed in the post-treatment comparisons of FBS and HbA1c. In contrast, no substantial difference was noted in the post-treatment comparisons of weight and BMI between the groups. [17]

Association between excessive weight and diabetes

Obesity and excessive weight stands out as a paramount and crucial risk factor in the onset and progression of type 2 diabetes mellitus (DM) across all age brackets. The imbalance between surplus energy stored and energy expended by the body disrupts nutrient signaling and leads to inadequate energy utilization, which is the primary contributor to obesity. Numerous clinical studies have illustrated that moderate and sustained weight reduction can enhance blood glucose levels, insulin sensitivity, and diminish the necessity for diabetic medications. [5] Strong and consistent evidence indicates that interventions aimed at managing obesity can effectively postpone the progression from prediabetes to type 2 diabetes and offer significant therapeutic advantages in the treatment of type 2 diabetes. [8] Treatment objectives for individuals with diabetes should encompass both glycemic control and weight management to address hyperglycemia and its root pathophysiological cause (obesity), thereby promoting comprehensive well-being. [8] The complex interplay of pathophysiological mechanisms between obesity and type 2 DM exacerbates the occurrence of insulin resistance, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), and various metabolic disorders in obese patients. Elevated body mass index and abdominal fat deposition heighten the risk of type 2 DM through alterations in adipose tissue biology, leading to insulin

resistance and beta cell dysfunction. Abdominal obesity, assessed by waist-to-hip ratio, independently contributes to the development of hypertension and elevated fasting glucose levels, even in individuals with excess abdominal fat who may not meet the BMI criteria for obesity. While type 2 DM susceptibility is influenced by non-modifiable factors such as genetic predisposition and ethnicity, interventions targeting modifiable risk factors like obesity can aid in its prevention and management. [5] Therefore, we will take a look at the effects of apple cider vinegar on weight, which is an important factor in the prevention of diabetes.

Effects of apple cider vinegar on obesity

Khezri et al. conducted a randomized clinical trial and assessed the impact of ACV incorporated into a restricted calorie diet and its beneficial effects on body weight and serum metabolic profiles among overweight or obese individuals. The study included a total of 39 participants who were randomly assigned to either the ACV group, where individuals followed a restricted calorie diet (RCD) with a 250 kcal/day energy deficit and consumed 30 ml/day of ACV, or the control group, which followed the RCD alone, for a duration of 12 weeks. The findings revealed significant improvements among participants in the ACV group, including reductions in body weight, BMI, hip circumference, visceral adiposity index, and appetite score. Moreover, individuals in the ACV group exhibited notable decreases in plasma triglyceride and total cholesterol levels, along with a significant increase in HDL-C concentration compared to the control group. [18]

Another double-blind, randomized clinical trial was conducted by Abou-Khalil, et al. over a 12-week period. A total of 120 patients with Body Mass Index (BMI) values between 27 and 34 kg/m^2 were enrolled in this study. Participants received either a daily dose of ACV at 5, 10, or 15 ml (on an empty stomach) or a placebo, composed of water containing lactic acid to simulate the taste of vinegar. The diet diary and physical activity levels did not differ significantly among the groups throughout the study. ACV consumption resulted in significant, time- and dose-dependent decreases in serum glucose, triglycerides, and total cholesterol levels at weeks 4, 8, and 12, with the most significant reductions seen with 15 ml of ACV over 12 weeks. No significant changes were observed in the placebo group. [19]

Khalid et al. did a study, demonstrating that apple cider vinegar has more effective results in obese/overweight people compared to healthy ones. This randomized controlled trial, aimed to evaluate the effects of ACV on weight management, blood glucose levels, HbA1c, and lipid profile. The intervention group included 30 obese or overweight patients who received ACV before lunch and dinner (total dose of 30 ml). The control group consisted of 30 healthy individuals, receiving ACV at the same time and dosage as the intervention group. Results showed a significant reduction in body weight and BMI among obese/overweight patients. Additionally, significant improvements in HbA1c, cholesterol, and triglyceride levels were observed in the intervention group. Measurements in the control group did not yield significant results. [20]

Pusparatha et al. aimed to evaluate the effects of apple cider vinegar (ACV) on individuals with diabetes and obesity. A total of 10 diabetic and 10 obese patients were enrolled into the study. They were administered 20 ml of ACV diluted in 200 ml of water daily before bedtime for a duration of 30 days. For diabetic patients, fasting blood glucose levels were measured, while body mass index (BMI) were recorded in obese individuals. The findings revealed a significant reduction in BMI, with values decreasing from 27.4 ± 0.33 to 26.9 ± 0.32. Moreover, diabetic patients exhibited a decrease in fasting blood glucose levels from 140.6 ± 2.13 to 121.9 ± 2.28. However, the short duration of the study and the small number of participants should be considered while drawing conclusions from the above study. [21]

Animal studies

The main aim of the subsequent study was to evaluate the impact of apple vinegar on metabolic alterations caused by a high-calorie diet in Wistar rats. In this in vivo study conducted by Ousaaid et al. adult Wistar rats were divided into two groups: one group was given a 10% D-glucose solution and the other group received water for five weeks. During this period, the rats on the D-glucose diet were also administered apple vinegar daily. The treatment with D-glucose over five weeks led to increases in plasma glucose, lipid profile, hepatic enzyme levels, urea, and creatinine. However, the simultaneous administration of apple vinegar ameliorated these metabolic parameters. [22]

In the next study, Halima et al. investigated the noteworthy properties of ACV in preventing complications related to diabetes in the liver and kidneys in normal and diabetic rats. The animals were fasted overnight, and diabetes mellitus was induced by an injection of streptozotocin. Control rats received an injection of citrate buffer. ACV was given orally for four weeks. The results showed that ACV supplementation elevated the activity of antioxidant enzymes: superoxide dismutase, catalase, glutathione peroxidase, and thiol. It reduced lipid peroxidation levels and decreased indices of toxicity in the liver and kidneys by significantly lowering the activities of AST and ALT, as well as total and direct bilirubin levels. Additionally, ACV reduced urea and creatinine levels, increased the plasma concentrations of magnesium, calcium and copper, while decreasing iron levels. [23]

Next study conducted by Bukhari, et al. aimed to assess the effects of green tea and apple cider vinegar on obesity and liver function in comparison to pharmaceutical drugs. Thirty-six adult male albino rats were divided into control and experimental groups and high-calorie, hyperlipidemic diets were then administered. Treatment groups received either green tea, apple cider vinegar, orlistat, or chitocal. All treated groups showed a significant decrease in body weight compared to the control group. Additionally, all treatment groups improved liver function, with chitocal and apple cider vinegar showing the greatest effect on ALT levels. Apple cider vinegar emerged as the most effective natural weight control formula. [24]

Halima et al. investigated the impact of daily ACV intake on cardiovascular risk factors associated with obesity in high-fat diet (HFD)-induced hyperlipidemic Wistar rats. The obese rats exhibited elevated serum levels of total cholesterol, triglycerides, LDL-C, VLDL, and atherogenic index after 6 and 9 weeks of HFD consumption. Notably, ACV significantly mitigated these parameters. Oxidative stress, evident after 6 weeks of HFD, was significantly reduced. ACV administration normalized various biochemical and metabolic alterations, demonstrating a significant decrease in malondialdehyde levels and an increase in thiol group concentrations. These findings suggest that HFD disrupts the oxidant-antioxidant balance, leading to reduced antioxidant enzyme activities and vitamin E levels, and increased lipid peroxidation. [25]

Safety of ACV consumption

Apple Cider Vinegar seems to be a safe natural supplement that helps regulate blood sugar and lipid profiles. Only a handful of papers have touched on the side effects of using this specific drug. [26] Human studies on ACV are limited by small sample sizes and short durations, necessitating more extensive, high-quality, long-term clinical studies to validate health claims. [27] Individuals allergic to apples and pectin should avoid ACV. There is insufficient evidence on the safety of vinegar use in pregnancy , so it is not recommended to be consumed by pregnant and breastfeeding women. Caution should be exercised when using ACV alongside hypoglycemic agents and medications that reduce potassium, due to potential synergistic effects. Additionally, patients with diabetic gastroparesis should use ACV cautiously, as it may delay gastric emptying. [27] The chronic consumption of excessive amounts of vinegar can lead to severe health complications. For instance, a case study documented a 28-year-old patient who regularly consumed approximately 250 ml of vinegar per day over a period of 6 years. This excessive intake resulted in elevated urinary excretion of potassium, sodium, and bicarbonate, as well as increased plasma renin activity. The patient presented to the hospital with symptoms of muscle cramps and hypokalemia. Moreover, cute ingestion of vinegar was associated with ulcerative injury to the oropharynx and esophagus in a case involving a 39-year-old woman who consumed one tablespoon of white vinegar to alleviate a lodged crab shell in her throat. [28]

In conclusion, these cases underscore the importance of caution when using vinegar, particularly in excessive amounts or for unproven therapeutic purposes, as it can lead to serious adverse effects and complications. [28] Although data on the long-term side effects of apple cider vinegar supplementation are currently limited, individual case reports provide insights into potential adverse effects and highlight areas where caution is warranted.

Tablets do not provide the same effectiveness as the solution

Next study compared the effects of liquid vinegar and commercial vinegar pills on insulin resistance and postprandial glycemia in healthy adults. In an 8-week parallel-arm randomized controlled trial, conducted by Feise and Johnston, participants ingested either liquid vinegar (2 tablespoons twice a day with meals) or vinegar pills (2 tablets daily with meals). Eleven participants in the liquid vinegar group and twelve in the pill group completed

the trial. After 8 weeks, the first group experienced a 12% reduction in insulin resistance, while the pill group saw a 7% increase. [29]

Additionally, a crossover trial suggests that commercial vinegar pills, with acetic acid content ranging from 45–700 mg per serving, are ineffective in improving glycemic control in healthy adults. 12 participants were enrolled into the study, where the effects of liquid vinegar and vinegar pills on postprandial glycemia were compared. Blood glucose levels measured 30 minutes after consuming a meal were reduced by 12% in the liquid vinegar group compared to the pill group and a no-vinegar control. [29]

Moreover, the following crossover trial has shown that commercial vinegar tablets taken whole at mealtime are less effective than liquid vinegar in reducing postmeal glucose excursions in young, healthy adults. Twelve young individuals participated in this 4-arm Latin square crossover trial. Participants consumed a test meal (64 g carbohydrate) immediately following one of four oral treatments: control (60 g water), liquid vinegar (25 g vinegar with 5% acidity), whole vinegar tablets (four tablets containing 1.50 g acetic acid), and crushed vinegar tablets (four tablets dissolved in 60 g water). Blood glucose was measured while fasting and at 30 and 60 minutes post meal. The 60-minute glucose excursion differed significantly between treatments. Post hoc analysis showed a 31% reduction in postmeal glucose excursion for the liquid vinegar compared to the control and whole tablet groups. [30]

DISCUSSION

The analyzed papers varied in their findings on the effects of vinegar use on certain parameters, but all demonstrated a clear trend of lowering diabetic indices and, in most cases, showed a positive impact on weight. These differences could be due to various factors, including the vinegar dosage, timing of vinegar intake, study duration, physiological characteristics of humans and animals, vinegar acidity, pancreatic secretion levels, insulin secretion levels, and the glycemic index of the meal. [4] Positive effects have also been validated in animal studies. They have demonstrated promising effects in reversing organ damage caused by obesity and diabetes. It has also been shown that the best results come from using vinegar in liquid form, while tablets have proven ineffective, although they may seem more convenient to use. Despite the research on the side effects of vinegar use is limited, caution is advised, and excessive consumption of ACV should be avoided. In conclusion,

ACV could serve as an alternative for weight reduction medicines, potentially minimizing side effects associated with drug use. Natural products offer positive effects without associated risks. [24]

CONCLUSIONS

According to research on publishing trends, the field of ACV in human health holds unexplored potential. [11] The latest reports confirm the antidiabetic and antiobesity effects of Apple Cider Vinegar. However, it should be noted that despite promising results, further studies with a greater number of participants and a longer period of vinegar intake are warranted. The short study duration limits the ability to observe long-term effects, and a larger sample size would enhance the generalizability of the results. That suggests that additional research is essential to discover long-term effects of consuming vinegar, possible side effects and to optimize the use of vinegar potentially maximizing the benefits of ACV as a functional food in the therapy of diabetes and obesity. Moreover, further research is needed to explore the effect of vinegar on the timing of initiation of antidiabetic drugs or insulin, and the extent to which it prevents the development of diabetes and its complications. The potential synergistic effects of ACV with commonly used, besides metformin, first-line drugs such as GLP-1 agonists, should also be investigated. Studies covering diverse populations would be important.

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