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Combined physical exercise and mindfulness therapy for psychophysiological and glycemic regulation in type 2 diabetes mellitus: A systematic review

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder with substantial psychophysiological components. Integrated therapeutic approaches combining physical exercise and mindfulness practices may address both glycemic and psychological aspects, yet comprehensive evidence remains limited. This systematic review evaluated the effectiveness of combined physical exercise and mindfulness interventions on glycemic regulation and psychophysiological outcomes in patients with T2DM. A systematic search of PubMed, ScienceDirect, and Google Scholar identified experimental and quasi-experimental studies published between 2021 and 2025. Eligible studies included adult patients with T2DM who received combined physical exercise and mindfulness interventions. Outcomes assessed included glycemic control (HbA1c, fasting blood glucose) and psychophysiological parameters (stress, depression, quality of life). Narrative synthesis and comparison tables were used for qualitative analysis, and risk of bias was evaluated using the Cochrane RoB 2 tool and the Newcastle–Ottawa Scale. Five studies met the inclusion criteria (n = 386 participants). Combined interventions produced greater improvements than single-component or control conditions. Mean HbA1c reduction ranged from 0.7% to 1.1%, fasting blood glucose decreased by 12.5 to 23.07 mg/dL, and depression or stress scores declined by 20% to 45%. Additional benefits included better nerve conduction velocity, self-efficacy, medication adherence, and quality of life. Proposed mechanisms involved modulation of the hypothalamic-pituitary-adrenal axis, enhanced insulin sensitivity, and increased neuroplasticity. In conclusion, combined physical exercise and mindfulness interventions demonstrate superior effectiveness over single-modality or standard care approaches in improving glycemic control and psychophysiological well-being in T2DM. This integrated strategy represents a promising adjunct for T2DM management. Further randomized controlled trials with larger cohorts and extended follow-up are needed to substantiate clinical recommendations.

Keywords: type 2 diabetes mellitus, exercise therapy, mindfulness, glycemic control, psychological stress

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder characterized by pancreatic beta-cell dysfunction and insulin resistance in peripheral tissues, including skeletal muscle, liver, and adipose tissue (Galicia-Garcia et al., 2020; Silva Rosa et al., 2020). At the molecular

level, insulin resistance involves impaired post-receptor insulin signaling. Insulin binding to its receptor (IR) on the cell membrane induces tyrosine autophosphorylation of the receptor's β-subunit, which activates downstream signaling cascades, primarily the PI3K/Akt pathway (Saini, 2010). This pathway regulates the translocation of GLUT4 to the cell membrane, facilitating cellular glucose uptake. In insulin-resistant states, decreased tyrosine phosphorylation of the insulin receptor and increased serine/threonine phosphorylation of insulin receptor substrate-1 (IRS-1) occur through the activation of kinases such as JNK and IKKβ. These alterations disrupt PI3K interaction and inhibit GLUT4 translocation (Boura-Halfon and Zick, 2009; El-Ashmawy et al., 2022; van Gerwen et al., 2023).

Chronic psychological stress significantly contributes to worsening insulin resistance through activation of the hypothalamic-pituitary-adrenal (HPA) axis (Yaribeygi et al., 2022). Activation of the HPA axis triggers the release of corticotropin-releasing hormone (CRH) from the hypothalamus, which stimulates the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH). ACTH then stimulates the adrenal cortex to produce cortisol (Janssen, 2022). As the primary glucocorticoid, cortisol promotes insulin resistance through several long-term mechanisms (Joseph and Golden, 2017). First, cortisol increases hepatic gluconeogenesis by inducing the expression of key enzymes such as phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase. Second, cortisol decreases peripheral glucose utilization by inhibiting GLUT4 translocation, partly through elevated expression of inhibitory proteins such as PCK1 and reduced PI3K activity. Third, cortisol enhances serine phosphorylation of IRS-1 via activation of kinases such as JNK and IKK, impairing the tyrosine phosphorylation necessary for normal insulin signaling (Beaupere et al., 2021; Torres-Torres et al., 2024). In addition, cortisol can downregulate insulin receptor expression and increase lipolysis, resulting in elevated free fatty acids that further exacerbate insulin resistance through lipotoxic mechanisms (Sears and Perry, 2015).

Recent studies indicate that HPA axis dysregulation in T2DM is frequently associated with systemic inflammation and oxidative stress (Mosili et al., 2024). Chronic hyperglycemia and elevated free fatty acids can activate inflammatory pathways such as NF-κB, increasing the production of proinflammatory cytokines including TNF-α and IL-6 (Caturano et al., 2025; Hoca, 2023). These cytokines can further activate JNK and IKKβ, amplifying serine phosphorylation of IRS-1 and impairing insulin signaling (Woo et al., 2024). This process establishes a vicious cycle linking inflammation, oxidative stress, and insulin resistance (Keane et al., 2015). Consequently, interventions that modulate HPA axis activity and reduce

inflammation, such as regular physical exercise and mindfulness-based practices, may improve insulin resistance both by enhancing insulin sensitivity and by lowering cortisol and inflammatory marker levels (Li et al., 2025).

Over the past decade, research has increasingly supported a bidirectional relationship between mental and metabolic health in T2DM. Patients with depression have approximately a 60 percent higher risk of developing T2DM, while individuals with T2DM have twice the risk of experiencing depression. This relationship is mediated not only by behavioral factors but also by biological mechanisms involving HPA axis hyperactivity, systemic inflammation, and autonomic dysfunction (Chae et al., 2024; Liu et al., 2024; Mezuk et al., 2008). Therefore, therapeutic approaches that integrate interventions targeting both psychological and metabolic domains are becoming increasingly important in clinical practice (Zhu et al., 2022). This systematic review evaluated the effectiveness of combined physical exercise and mindfulness interventions on glycemic regulation and psychophysiological outcomes in patients with T2DM.

METHOD

A systematic literature search was conducted using PubMed, ScienceDirect, Google Scholar, the Cochrane Library, and Scopus. The search strategy included combinations of the following keywords: “type 2 diabetes mellitus” or “T2DM,” “exercise” or “physical activity” or “aerobic training” or “resistance training,” “mindfulness” or “meditation” or “stress reduction” or “mind-body therapy,” “glycemic control” or “HbA1c” or “fasting blood glucose,” and “stress” or “depression” or “quality of life” or “cortisol.” The search was restricted to articles published between 2021 and 2025. In addition, a manual review of the reference lists of relevant studies was conducted to identify any additional eligible publications.

The population of interest consisted of adults aged 18 years and older diagnosed with type 2 diabetes mellitus, with or without complications. The interventions included combined approaches that integrated a structured physical exercise component, such as aerobic, resistance, or circuit training, together with a mindfulness, meditation, or stress management component, including meditation, breathing exercises, mindful eating, or acceptance therapy. The comparison groups consisted of single-component interventions, such as exercise only or mindfulness only, as well as usual care or other active control conditions. The primary outcomes were glycemic parameters, specifically HbA1c and fasting blood glucose levels.

Secondary outcomes included psychological parameters, such as depression and stress scores, biomarkers of stress such as cortisol, as well as quality of life, adherence, and physical or neurological function. Eligible study designs included randomized controlled trials, quasi-experimental studies, and pre-post studies with control groups, published in either English or Indonesian.

Two independent researchers screened the titles and abstracts of identified articles, assessed the eligibility of full-text studies, and extracted relevant data using a standardized form. Extracted information included study characteristics such as author, year of publication, and study design; participant characteristics; detailed descriptions of the interventions, including type, duration, and frequency; outcome measures and corresponding assessment tools; primary findings; and reported limitations.

The risk of bias for randomized controlled trials was assessed using the Cochrane Risk of Bias Tool version 2.0. For non-randomized studies, the Newcastle-Ottawa Scale was employed. All assessments were independently performed by two researchers, and any discrepancies were resolved through consensus. Due to the heterogeneity of interventions and outcome measures across studies, a narrative synthesis supported by comparison tables was undertaken. The effects of interventions were described in terms of mean differences, along with corresponding p-values and effect sizes when available.

RESULTS

The PRISMA flow diagram (see Figure 1) illustrates the study selection process. Initially, 352 records were retrieved from Google Scholar (n=280), Pubmed (n=58), and ScienceDirect (n=14). After removing 125 duplicates, 227 records remained for screening. Of these, 212 were excluded after title and abstract review. Fifteen full-text articles were assessed for eligibility, and ten were excluded due to non-combined interventions, irrelevant populations, or being non-primary research. Five studies met all inclusion criteria and were included in the synthesis.

Table 1 summarizes the characteristics of the included studies. The five studies, published between 2022 and 2025, involved a total of 386 participants. Study designs comprised two randomized controlled trials (RCTs), two quasi-experimental studies, and one experimental study. Participants were from Iran, India, Egypt, Thailand, and China. The interventions combined aerobic exercise, circuit training, or Tai Chi with mindfulness meditation, stress-

reduction techniques, or mindful eating programs. The intervention duration ranged from 5 to 16 weeks.

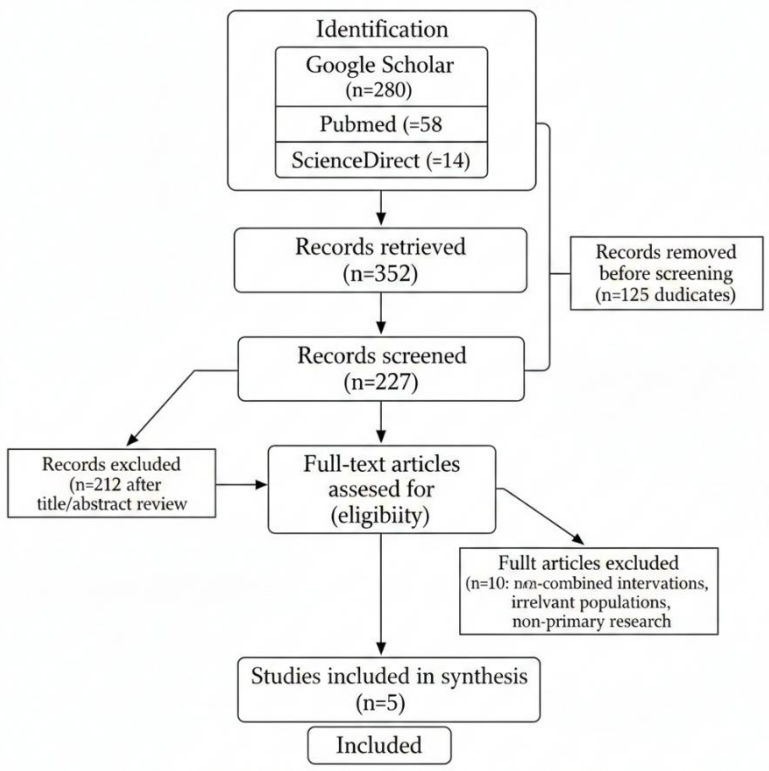

Figure 1. PRISMA flow diagram

Consistent with prior evidence, combined interventions demonstrated additive benefits for glycemic regulation. In a study involving 60 Iranian women, Aslani et al. (2025) reported that a 12-week regimen combining aerobic treadmill exercise with Mindfulness-Based Stress Reduction (MBSR) significantly lowered fasting blood glucose (FBG) levels to 117.13 mg/dL, outperforming both the aerobic-only group (133.07 mg/dL) and the mindfulness-only group (130.40 mg/dL). Similarly, HbA1c levels in the combined-intervention group declined to 5.39%, compared with values exceeding 6.20% in single-intervention groups.

This finding was corroborated by Juby & Jagtap (2025) in an Indian cohort, where a five-week circuit training program integrated with breathing exercises reduced FBG from approximately 156 mg/dL to 114.94 mg/dL ($p < 0.0001$). Furthermore, Sukchaisong et al. (2022) demonstrated that incorporating family support into mindfulness practice prevented the deterioration of glycemic control observed in control groups, resulting in a decrease in HbA1c from 8.4% to 7.8% over 16 weeks.

Mindfulness interventions specifically address the psychological burden of diabetes, which in turn influences physiological stress markers. Obaya et al. (2023) reported that adding deep breathing and mindfulness to aerobic training in Egyptian women led to a 30.29% reduction in serum cortisol levels, a significantly greater improvement than the 20.16% reduction achieved through aerobic exercise alone.

Table 1. Characteristics of Included Studies

Author (Year), Country	Design	Sample (n)	Combined Intervention	Comparison Group(s)	Duration	Key Outcomes Measured
Aslani et al. (2025), Iran	Quasi-experimental (4 groups)	60 (women)	Aerobic exercise + Mindfulness	Aerobic only, Mindfulness only, Usual care	12 weeks + 3-month FU	HbA1c, FBG, BDI-II
Juby & Jagtap (2025), India	Experimental (2 groups)	68 (M/F)	Circuit training + Stress-relieving techniques	Usual care	5 weeks	FBG, PPG, 6MWT, PSS
Obaya et al. (2023), Egypt	RCT (2 groups)	58 (women)	Aerobic + Deep breathing + Mindfulness	Aerobic only	6 weeks	FBG, Serum cortisol
Sukchaisong et al. (2022), Thailand	RCT (2 groups)	80 (M/F)	Mindfulness (eating, education) + Family support	Usual care	12 weeks + 16-week FU	HbA1c, FBG, Mindful eating, Self-efficacy
Weng et al. (2022), China	Experimental (3 groups)	120 (M/F)	Mindfulness + Aerobic exercise	Mindfulness only, Aerobic only	12 weeks	NCV, MAAS, TCSS, QoL

Abbreviations: FU: Follow-up; BDI-II: Beck Depression Inventory-II; PPG: Postprandial Glucose; 6MWT: 6-Minute Walk Test; PSS: Perceived Stress Scale; NCV: Nerve Conduction Velocity; MAAS: Mindful Attention Awareness Scale; TCSS: Toronto Clinical Scoring System; QoL: Quality of Life.

Subjective indicators of mental health showed parallel improvements. Aslani et al. (2025) found that combined interventions produced significantly lower Beck Depression Inventory-II (BDI-II) scores (13.00) compared with exercise-only or mindfulness-only approaches. Similarly, Juby and Jagtap observed a marked decline in Perceived Stress Scale scores, falling from 33.22 to 20.05.

Beyond metabolic regulation, combined interventions appear to alleviate diabetes-related complications such as peripheral neuropathy. Weng et al. (2022) found that integrating mindfulness with aerobic exercise improved sensory nerve conduction velocity in the median

nerve, increasing from 34.68 to 43.51 m/s. This combined approach also resulted in a greater reduction in Toronto Clinical Scoring System (TCSS) neuropathy severity scores compared with single-modality treatments. Additionally, functional capacity improved substantially, as Juby and Jagtap reported an increase of 116 meters in the 6-Minute Walk Distance among participants in the intervention group, whereas the control group demonstrated only minimal gains.

DISCUSSION

This systematic review synthesizes evidence from five recent studies examining the effects of combined physical exercise and mindfulness interventions in patients with type 2 diabetes mellitus (T2DM). The primary finding indicates that a dual-modality approach integrating aerobic or resistance training with psychological stress-reduction techniques yields superior outcomes compared to single-modality interventions or usual care. Specifically, the combined approach demonstrated additive benefits in improving glycemic parameters (HbA1c and FBG), lowering physiological stress markers (cortisol), and alleviating diabetes-related complications such as peripheral neuropathy.

The superior glycemic control observed in the combined intervention groups supports the hypothesis of a synergistic mechanism. Physical exercise is well-established to increase insulin sensitivity and enhance glucose uptake through muscle contraction. The addition of mindfulness appears to modulate the neuroendocrine components of diabetes management. As reported by Aslani et al. (2025) and Juby and Jagtap (2025), participants receiving the combined intervention achieved significantly lower FBG and HbA1c levels than those in exercise-only groups. These findings suggest that reducing psychological stress may amplify the physiological benefits of exercise. Chronic stress elevates counter-regulatory hormones such as catecholamines, which impair insulin action (Sharma et al., 2022). By attenuating this stress response, mindfulness practices likely create a more favorable hormonal environment for exercise-induced glucose metabolism.

This review underscores the critical role of the mind–body connection in T2DM management. The marked reduction in serum cortisol levels reported by Obaya et al. (2023) provides biological support for the observed improvements in psychological well-being, including lower depression scores (BDI-II) and reduced perceived stress. Unlike standard exercise protocols that primarily focus on metabolic expenditure, mindfulness practices, deep breathing, and family support address the psychological burden of chronic disease. This is particularly

relevant given the bidirectional relationship between diabetes distress and poor glycemic control. The combined approach appears effective in breaking this cycle by simultaneously targeting both physiological and psychological pathways.

A noteworthy and clinically significant finding of this review is the potential impact on diabetes complications. Weng et al. (2022) demonstrated that mindfulness combined with aerobic exercise improved nerve conduction velocity and reduced neuropathy severity, as measured by TCSS scores. These results suggest that the benefits of combined interventions extend beyond glycemic regulation to include neuroprotective effects, possibly mediated through enhanced microvascular circulation and reduced oxidative stress. Moreover, the significant improvement in functional capacity (6MWT) reported by Juby and Jagtap indicates that these interventions enhance daily physical functioning, which is essential for long-term adherence to lifestyle modifications.

This review offers several strengths, including the synthesis of recent clinical trials (published through 2025) and the inclusion of diverse mindfulness modalities such as MBSR, mindful eating, and general stress-reduction programs. Nonetheless, several limitations warrant consideration. The total sample size (n=386) across five studies remains modest, which limits the generalizability of these findings. In addition, all studies were conducted in Asian or Middle Eastern countries (Iran, India, Egypt, Thailand, and China), which may reflect cultural influences on the acceptability and effectiveness of mindfulness-based practices compared to Western populations. The heterogeneity of intervention protocols, varying from 5 to 16 weeks and employing different exercise modalities, also prevents a definitive conclusion regarding the optimal duration, frequency, or type of combined intervention.

CONCLUSION

In conclusion, integrating physical exercise with mindfulness-based interventions represents a more effective approach for managing T2DM than exercise alone, offering comprehensive benefits for glycemic control, psychological health, and complication management. Clinicians are encouraged to adopt holistic treatment plans that combine stress-reduction strategies with evidence-based physical activity guidelines. Future research should focus on large-scale, multicenter randomized controlled trials with extended follow-up periods to determine the sustainability of these effects and to develop standardized intervention protocols for clinical application.

REFERENCES

Aslani F, Ranjbaripour T, Meschi F, et al. (2025) The Effectiveness of Aerobic Exercise With or Without Mindfulness on Fasting Blood Sugar, Hemoglobin A1C, and Depression Levels in Women With Type 2 Diabetes. *Physical Treatments - Specific Physical Therapy* 15(4): 333–344.

Beaupere C, Liboz A, Fève B, et al. (2021) Molecular Mechanisms of Glucocorticoid-Induced Insulin Resistance. *International Journal of Molecular Sciences* 22(2): 623.

Boura-Halfon S and Zick Y (2009) Phosphorylation of IRS proteins, insulin action, and insulin resistance. *American Journal of Physiology-Endocrinology and Metabolism* 296(4): E581–E591.

Caturano A, Rocco M, Tagliaferri G, et al. (2025) Oxidative Stress and Cardiovascular Complications in Type 2 Diabetes: From Pathophysiology to Lifestyle Modifications. *Antioxidants* 14(1): 72.

Chae WR, Kohring C, Rohde C, et al. (2024) Eight-year nationwide study of the bidirectional association between type 2 diabetes and depression in nearly 8 million German outpatients. *BMJ Open Diabetes Research & Care* 12(3): e003903.

El-Ashmawy N, Khedr E, Alfeky N, et al. (2022) Upregulation of GLUT4 and PI3K, and downregulation of GSK3 mediate the anti-hyperglycemic effects of proanthocyanidins. *Medicine International* 2(3): 14.

Galicia-Garcia U, Benito-Vicente A, Jebari S, et al. (2020) Pathophysiology of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences* 21(17): 6275.

Hoca M (2023) The Reciprocal Relationship between Inflammation and Diabetes: Importance of Medical Nutrition Therapy. *Cyprus Journal of Medical Sciences* 8(3): 166–172.

Janssen JAMJL (2022) New Insights into the Role of Insulin and Hypothalamic-Pituitary-Adrenal (HPA) Axis in the Metabolic Syndrome. *International Journal of Molecular Sciences* 23(15): 8178.

Joseph JJ and Golden SH (2017) Cortisol dysregulation: the bidirectional link between stress, depression, and type 2 diabetes mellitus. *Annals of the New York Academy of Sciences* 1391(1): 20–34.

Juby N and Jagtap V (2025) Impact of Combined Stress Relieving Technique and Circuit Training on Glycemic Control, Physical and Psychological Well-Being in Diabetic Patients. *Journal of Neonatal Surgery* 14(5S): 361–368.

Keane KN, Cruzat VF, Carlessi R, et al. (2015) Molecular Events Linking Oxidative Stress and Inflammation to Insulin Resistance and β -Cell Dysfunction. *Oxidative Medicine and Cellular Longevity* 2015: 1–15.

Li X, Huang J and Zhu F (2025) The Optimal Exercise Modality and Dose for Cortisol Reduction in Psychological Distress: A Systematic Review and Network Meta-Analysis. *Sports* 13(12): 415.

Liu Y, Huang S-Y, Liu D-L, et al. (2024) Bidirectional relationship between diabetes mellitus and depression: Mechanisms and epidemiology. *World Journal of Psychiatry* 14(10): 1429–1436.

Mezuk B, Eaton WW, Albrecht S, et al. (2008) Depression and Type 2 Diabetes Over the Lifespan. *Diabetes Care* 31(12): 2383–2390.

Mosili P, Mkhize BC, Sibiya NH, et al. (2024) Review of the direct and indirect effects of hyperglycemia on the HPA axis in T2DM and the co-occurrence of depression. *BMJ Open Diabetes Research & Care* 12(1): e003218.

Obaya HE, Abdeen HA, Salem AA, et al. (2023) Effect of aerobic exercise, slow deep breathing and mindfulness meditation on cortisol and glucose levels in women with type 2 diabetes mellitus: a randomized controlled trial. *Frontiers in Physiology* 14.

Saini V (2010) Molecular mechanisms of insulin resistance in type 2 diabetes mellitus. *World Journal of Diabetes* 1(3): 68.

Sears B and Perry M (2015) The role of fatty acids in insulin resistance. *Lipids in Health and Disease* 14(1): 121.

Sharma K, Akre S, Chakole S, et al. (2022) Stress-Induced Diabetes: A Review. *Cureus* 14(9).

Silva Rosa SC, Nayak N, Caymo AM, et al. (2020) Mechanisms of muscle insulin resistance and the cross-talk with liver and adipose tissue. *Physiological Reports* 8(19).

Sukchaisong N, Pichayapinyo P, Lagampan S, et al. (2022) Effectiveness of the Mindfulness-Based Diabetes Self- and Family Management Support Program among Adults with Uncontrolled Diabetes: A Randomized Controlled Trial. *Pacific Rim International Journal of Nursing Research* 26(3): 517–532.

Torres-Torres J, Monroy-Muñoz IE, Perez-Duran J, et al. (2024) Cellular and Molecular Pathophysiology of Gestational Diabetes. *International Journal of Molecular Sciences* 25(21): 11641.

van Gerwen J, Shun-Shion AS and Fazakerley DJ (2023) Insulin signalling and GLUT4 trafficking in insulin resistance. *Biochemical Society Transactions* 51(3): 1057–1069.

Weng X, Liao S, Wang F, et al. (2022) Evaluation of Mindfulness Training Combined with Aerobic Exercise on Neurological Function and Quality of Life in Patients with Peripheral Neuropathy Type 2 Diabetes Mellitus. *Contrast Media & Molecular Imaging* Hashmi MF (ed.) 2022(1).

Woo JR, Bae S-H, Wales TE, et al. (2024) The serine phosphorylations in the IRS-1 PIR domain abrogate IRS-1 and IR interaction. *Proceedings of the National Academy of Sciences* 121(17).

Yaribeygi H, Maleki M, Butler AE, et al. (2022) Molecular mechanisms linking stress and insulin resistance. *EXCLI Journal* 21(SE-Review articles): 317–334.

Zhu M, Li Y, Luo B, et al. (2022) Comorbidity of Type 2 Diabetes Mellitus and Depression: Clinical Evidence and Rationale for the Exacerbation of Cardiovascular Disease. *Frontiers in Cardiovascular Medicine* 9.