

# Gender Disparities in Cardiovascular Complications of Type 2 Diabetes: Are Females More Frequently in Risk ?

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## ABSTRACT

Cardiovascular Disease (CVD) continues to be a major cause of death and dejection for people with Type 2 Diabetes Mellitus (T2DM). However, an increasing amount of evidence suggests that there is a gender difference in the risk and rate of cardiovascular problem development among T2DM patients. Due to disparities in hormone levels, metabolic regulation, and the impact of traditional cardiovascular risk factors, women, especially postmenopausal women, may be more vulnerable to heart attack or stroke than men. Gazing into the clinical, behavioral, and biological factors that influence this variation, the present investigation investigates the relationship between gender and cardiovascular problems in type 2 diabetes. Understanding these gender-based differences is essential to improving treatment outcomes, preventative strategies, and clinical care of women with type 2 diabetes.

**Keywords:** Cardiovascular Disease (CVD), Evaluation of Cardiovascular Outcome Results, GLP-1, Sodium Glucose Co-Transporter-2 (SGLT2), LEADER (Liraglutide Effect and Action in Diabetes).

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## INTRODUCTION

Numerous individuals worldwide suffer from Type 2 Diabetes Mellitus (T2DM), a progressive metabolic condition which is strongly linked with Cardiovascular Disease (CVD). The high frequency of illness and death associated with T2DM and cardiovascular problems has made the junction between these illnesses a critical topic of investigation.<sup>[5,6]</sup> A growing database of research indicates that whereas cardiovascular events are at an increased risk and is gender independent with type 2 diabetes, women may bear a proportionally higher risk than males.<sup>[1-7]</sup>

Major issues concerning the underlying reasons and therapeutic implications are brought up by the gender difference in cardiovascular outcomes among T2DM patients. Factors such as hormonal fluctuations in women, especially during menopause, could potentially contribute to the elevated risk of cardiovascular disease.<sup>[8,9]</sup> Furthermore, by the time of diagnosis, women frequently have worse glycemic control and come with more advanced stages of CVD. The reported gaps are also influenced by social and behavioral factors, such as access to medical care and therapy commitment (Figures 1 and 2).<sup>[10]</sup>

This research looks into the clinical, behavioral, and biological factors that increase a woman's risk of cardiovascular disease in order to determine the gender differences in cardiovascular risks among type 2 diabetic patients. Understanding these variations can help direct afterwards research, improve clinical supervision, and promote individualized care for females with type 2 diabetes (Figure 3).<sup>[11,12]</sup>

## Inflammation

TNF- $\alpha$ , IL-6, IL-1, and INF- $\gamma$  are cytokines and macrophages that cause oxidative stress and epigenetic changes. Insulin resistance and the generation of glucose in the liver: Hyperglycemia is made worse by increased glucose production in the liver brought on by insulin resistance.

## Adipose tissue contribution

Adipokines (leptin, resistin, and adiponectin) and other factors (free fatty acid, IL-1, and TNF- $\alpha$ ) exacerbate inflammation, glucose intolerance, and cardiovascular risk. Endothelial dysfunction: A number of variables, including MCP-1, VEGF, and MMP, promote endothelial damage, atheromatous plaque formation, and reduced vasodilation.

The impact of hormones, chemical messengers secreted by bodily glands, on physiological functions is referred to as a hormonal factor. Hormonal variables significantly influence how men and



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women experience the course and considering the chance of cardiovascular issues linked to Type 2 Diabetes Mellitus (T2DM), especially about variations in these consequences between genders.<sup>[13,14]</sup>

### Gender-Specific Impacts of Hormones on Cardiovascular Risk Factors

Those who have been diagnosed with Type 2 Diabetes (T2D) have a fourfold greater chance of Heart Failure (HF) than individuals without T2D; women are affected more frequently than males. Men and women have different pathophysiologies, however as of right now, the diagnostic algorithm for heart failure in diabetic patients does not include suggestions based on a patient's gender.<sup>[15]</sup>

#### Estrogen

##### *In women*

The main sex hormone of women, estrogen, protects the cardiovascular system by encouraging normal cholesterol levels and preserving blood vessel elasticity. After menopause, when estrogen levels decline, this protection wanes and postmenopausal women are more prone to encounter cardiovascular illnesses.<sup>[16]</sup>

##### *In Men*

Compared to women, men have lower amounts of estrogen and do not undergo the dramatic hormonal decrease that occurs in women after menopause. They so have a lifelong cardiovascular risk profile that is more constant.<sup>[17,18]</sup>

#### Testosterone

##### *In Men*

The main sex hormone in men, testosterone, affects muscle mass, insulin sensitivity, and fat distribution, all of which have an impact on cardiovascular health. Reduced testosterone levels in men enhance the possibility of cardiovascular disease, including greater rates of dietary syndrome and type 2 diabetes.<sup>[19,20]</sup>

##### *In Women*

Small amounts of testosterone are also produced by women, and variations in testosterone levels, especially in PCOS, might affect insulin resistance and cardiovascular risk.<sup>[21-23]</sup>

#### Insulin

A key hormone in the metabolism of glucose is insulin. Elevated blood glucose levels result from insulin resistance which results in type 2 diabetes, where the body fails to use insulin properly. Type 2 diabetic women have dominant levels of insulin resistance than men do, a condition that is mostly attributed to hormonal fluctuations, especially after menopause.<sup>[24,25]</sup>

#### Progesterone

Progesterone, a different female sex hormone, functions in tandem with estrogen. It can affect blood pressure and vascular function, but its direct impact on cardiovascular health is not as strong as that of estrogen. Increased cardiovascular stress during pregnancy due to higher progesterone levels which may have long-term consequences on the cardiovascular health of women.<sup>[26-30]</sup>

#### Leptin

The hormone leptin affects men and women differently which controls metabolism and appetite. Women often have higher leptin levels than males do, and leptin resistance in T2DM patients can lead to obesity, which is a significantly linked with cardiovascular problems. Additionally, leptin and estrogen interact, potentially having distinct effects on cardiovascular outcomes for different women.<sup>[31]</sup>

#### Cortisol

Cortisol, sometimes referred to as the "stress hormone," affects blood pressure, inflammation, and glucose metabolism. Heart risks can be made worse by persistently high cortisol levels, which are frequently brought on by stress or inadequate glycemic management. Hormonal cycles may cause women to respond to cortisol differently, which may alter their risk profile.<sup>[32,33]</sup>

### Sex-Specific Treatments in Cardiovascular Complications of T2DM

#### *Hormone Replacement Therapy (HRT) for Postmenopausal Women*

##### *Reason*

Although it has a preventive effect on cardiovascular health, estrogen levels sharply decline after menopause. This hormonal change is associated with a greater chance of heart attack or stroke in women with type 2 diabetes.<sup>[34]</sup>

##### *Treatment*

Hormone Replacement Therapy (HRT) has the probability of lowering the danger of heart failure by restoring estrogen levels. Research suggests that beginning Hormone Replacement Therapy (HRT) early in menopause could reduce the risk of cardiac events. However, before using it, one must carefully assess the risks of thrombosis, ischemic stroke, and malignancy.<sup>[35]</sup>

##### *Challenges*

Not all women should use HRT, and rigorous risk assessment is necessary based on individual health profiles.<sup>[36]</sup>

## Antihypertensive Therapy Adjustments

### Reason

Type 2 Diabetes commonly causes hypertension in both men and women but women typically experience a greater increase in blood pressure during menopause because of estrogen loss.<sup>[37-39]</sup>

### Treatment

Antihypertensive medication adjustments may be required in response to sex-specific reactions. Men may respond more favourably to ACE inhibitors or ARBs, whereas women may respond better to specific blood pressure drugs like diuretics and calcium channel blockers. Angiotensin-Converting Enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARBs) are two oral medications that can lower blood pressure and protect the kidneys and heart.<sup>[40-42]</sup>

## Lipid-Lowering Therapy

### Reason

Primarily post-menopause, women with type 2 diabetes had poorer lipid assessments than men, with higher LDL and lower HDL cholesterol. They are more likely to develop cardiovascular disease as a result.<sup>[43,44]</sup>

### Treatment

Men and women with T2DM are frequently administered statins, which reduce cholesterol levels. To obtain the best cholesterol control, women might need to use various dosages or other lipid-lowering medications like PCSK9 inhibitors or ezetimibe.<sup>[45]</sup>

## Sex-Specific Considerations

Women are more susceptible than men to suffer from the adverse effects of statins like muscle soreness, thus careful observation is necessary.<sup>[46]</sup>

## Antiplatelet Therapy

### Reason

Compared to men, women with T2DM have an increased risk of thrombotic events (such as heart attacks or strokes), particularly in the postmenopausal stage.<sup>[47,48]</sup>

### Treatment

For high-risk patients, aspirin at small doses or other antiplatelet medications are frequently administered to prevent clot formation. Early antiplatelet medication initiation may be more beneficial for women, particularly if they have additional risk factors (such as obesity or hypertension).<sup>[49]</sup>

## Sex-Specific Considerations

The likelihood between women and men may vary to experience bleeding, therefore monitoring and dosage adjustments are necessary.<sup>[50,51]</sup>

## Diabetes Management and Glycemic Control

### Reason

Diabetes medicines may react differently in women with Type 2 Diabetes (T2D) and they frequently exhibit elevated ranges of insulin resistance than in males, which can have an impact on cardiovascular outcomes.<sup>[3,52-54]</sup>

### Treatment

Strategies for individualized glucose management ought to take these gender variations into account.<sup>[55]</sup> For example:

#### Metformin

Good for both sexes, however, because to possible gastrointestinal side effects in women, dose adjustments may be necessary.

#### GLP-1 receptor agonists (e.g., liraglutide)

Considering that type 2 diabetic women often have higher rates of obesity, these may be more advantageous for women, especially in terms of weight loss and cardiovascular protection.

#### SGLT-2 inhibitors

Although sex-specific data on side effects is still developing, these drugs may lower CVD, particularly in women with ischemic stroke or renal illness.<sup>[12,56,57]</sup>

## Obesity Management

### Reason

Type 2 diabetic women are more likely to be obese, which raises their risk of cardiovascular disease. A major risk indicator for both type 2 diabetes and cardiovascular disease is adiposity.<sup>[52,58,59]</sup>

### Treatment

Women's distinct metabolic and hormonal demands can be catered for in sex-specific weight loss strategies, such as lifestyle modifications, medication (e.g., GLP-1 receptor agonists), and even bariatric surgery.<sup>[60]</sup>

## Exercise and Lifestyle Interventions

### Reason

The impact of sedentary lifestyles on cardiovascular health may be particularly dominant in type 2 diabetic women because of hormonal changes and postmenopausal weight gain.<sup>[61]</sup>

### Treatment

Exercise regimens and physical activity levels should be customized for each sex, accounting for variations in muscle mass, fat distribution, and the cardiovascular system's general response to exercise. Programs aimed at enhancing bone density, which is essential after menopause, and cardiovascular health may be beneficial to women.<sup>[62]</sup>

## Psychosocial Interventions

### Reason

Women with type 2 diabetes are more likely to experience depression, stress, and anxiety, which can have a detrimental effect on glucose management and cardiovascular health.<sup>[63,64]</sup>

### Treatment

Stress management courses and cognitive behavioral therapy are two examples of psychological and social support interventions that can be extremely important for increasing treatment compliance and lowering women's cardiovascular risk.<sup>[2,65]</sup>

## Gender-Specific Cardiovascular Risks in Type 2 Diabetes: A Closer Look at Women's Increased Vulnerability

Even after adjusting for well-known risk variables like blood pressure and cholesterol, recent research has revealed that women with Type 2 Diabetes (T2D) are more likely than males to experience cardiovascular problems. In addition to biological variations, diabetes exacerbates cardiovascular risk factors in women, which accounts for these discrepancies.<sup>[2,52,65,66]</sup>

According to a 2021 study, compared to men, those with diabetes and coronary artery disease had a greater risk of cardiac failure in part because they have worse glycemic control and more cases of hypertension. In addition, women typically experience worse outcomes from diabetes-related cardiac problems and are less likely to receive adequate cardiovascular risk management. Additionally, women are also more inclined than men to have

vascular diseases, such as coronary artery disease, probably because their metabolic degradation is more severe. The increased risk may additionally be clarified by the fact that women may already have worse cardiovascular health than males when they are diagnosed with diabetes.<sup>[66]</sup>

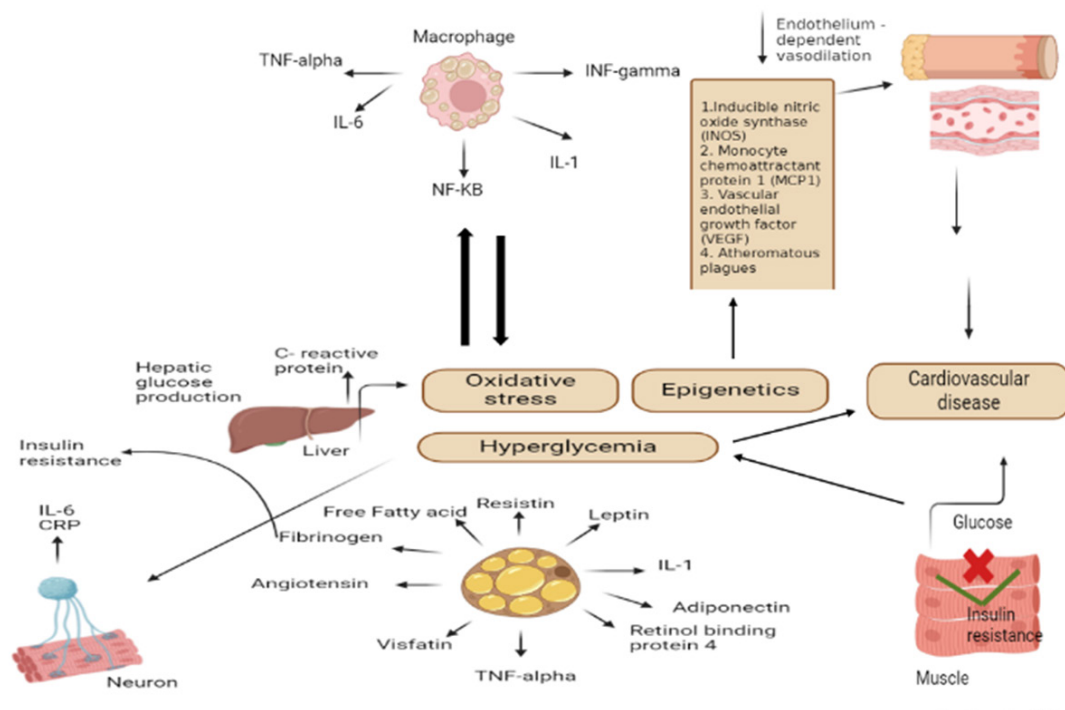
These findings highlight the need for more focused diabetes management strategies for women because, compared to males, their cardiovascular risk factors tend to deteriorate more quickly.<sup>[67]</sup>

## Recent Drugs Trials

Current clinical trials have examined a range of drugs targeted at lowering cardiovascular problems in individuals with Type 2 Diabetes (T2DM), with particular attention to variations in gender. Semaglutide and SGLT2 inhibitors, such as empagliflozin, are two potential medications that have been demonstrated to improve cardiovascular health in both men and women, while some research suggests that their effectiveness varies depending on the sex.<sup>[68-70]</sup>

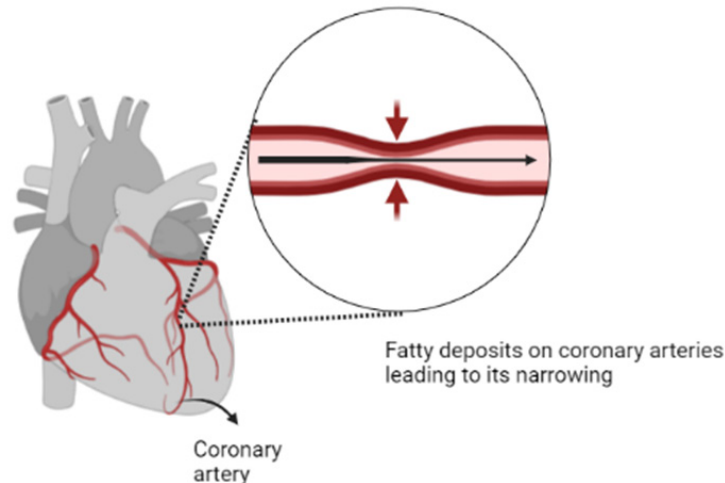
### Semaglutide

This drug is often used for weight loss and glycemic control and was discovered to reduce myocardial events in individuals at high risk, such as patients with type 2 diabetes was reduces by 20%, according to a recent study published in 2023. Benefits from this experiment included a decrease in heart attacks and strokes, and both men and women appeared to benefit equally from its cardiovascular effects.<sup>[71]</sup>



**Figure 1:** Type 2 Diabetes Mellitus (T2DM) is characterized by a complicated interplay between inflammatory processes, poor metabolism, and cardiovascular diseases within the framework of insulin resistance and high blood sugar levels.





**Figure 2:** Illustration of the impact of Atherosclerosis on coronary artery system.

### **SGLT2 inhibitors and GLP-1 receptor agonists**

Medication like empagliflozin and antagonists of GLP-1 receptors has been recommended to reduce cardiovascular risk, especially for those with existing Atherosclerotic Cardiovascular Disease (ASCVD) or Diabetic Kidney Disease (DKD). Recent guidelines indicate that these drugs have the potential to lower serious cardiovascular events and heart failure.<sup>[72]</sup>

Trials currently underway are investigating the response of different genders to these treatments, indicating that individualized treatment is becoming increasingly critical in preventing cardiovascular events in individuals with Type 2 diabetes mellitus.

### **An outline of the gender gap in association with Men, Women, and cardiovascular results in patients with type 2 diabetes**

It is well known that people with Type 2 Diabetes Mellitus (T2DM) have different cardiovascular outcomes depending on their gender. In broad terms, Cardiovascular Disease (CVD) is more likely to cause issues for women than for men. The differences between the sexes in the onset and consequences of cardiovascular events are highlighted by several recent studies.<sup>[73]</sup>

The coronary arteries supplying the heart muscle with oxygenated blood are depicted along the surface of the heart. The inset shows a close-up of a narrowed artery, where fatty deposits (atherosclerotic plaque) have accumulated, and reducing blood flow. This build up can result in Coronary Artery Disease (CAD). Trials currently underway are investigating the response of different genders to these treatments, indicating that individualized treatment is becoming increasingly critical in preventing cardiovascular events in individuals with Type 2 diabetes mellitus.

### **Higher Cardiovascular Risk in Women with T2DM**

#### **Negative Results for Women**

Studies show that estragon's ability to protect the cardiovascular system diminishes after menopause, increasing the risk of heart disease in women. Even after controlling for conventional risk variables like hypertension and cholesterol, women with type 2 diabetes still had a higher relative risk of coronary heart disease and stroke than males.<sup>[1,52,74]</sup>

#### **Delayed Diagnosis**

By the time of diagnosis, women frequently have more advanced stages of cardiovascular disease. This could be because of unusual symptoms like nausea or exhaustion, which can cause delays in the need for prompt cardiovascular measures.<sup>[75]</sup>

### **Differences in Treatment Response**

#### **Pharmacological Response**

Patients' reactions to drugs used to control cardiovascular risk varied depending on their sex. For example, women may be more sensitive to statin side effects than men, which may result in less aggressive lipid-lowering medication. The way that these medications are managed can have an impact on long-term results.<sup>[76]</sup>

#### **Under-Treatment of Women**

Compared to males, women with T2DM and CVD are frequently undertreated, especially when it comes to statins, antiplatelet treatment, and antihypertensive medications. Women who receive less therapy tend to have lower outcomes.<sup>[77]</sup>

### **Heart Failure and Mortality Rates**

#### **Higher Heart Failure Risk in Women**

Compared to males, women with type 2 diabetes have a higher risk of developing heart failure, especially Heart Failure with

preserved Ejection Fraction (HFpEF). This type of heart failure is linked to a higher death rate and offers fewer alternatives for therapy.<sup>[78]</sup>

### Increased Death Rates in Women

Women with type 2 diabetes had a significantly higher risk of dying from CVD than did men. Furthermore, the relative risk of dying from coronary heart disease is 50% higher in women with type 2 diabetes than in men with the same condition.

### Biological and Hormonal Factors

#### Impact of Hormones

Estrogen offers a protective effect against cardiovascular events in premenopausal women, but this advantage declines sharply after menopause. The loss of Estrogen has been linked to the worsening of cardiovascular profiles, including higher cholesterol levels and increased insulin resistance.<sup>[34,36]</sup>

### Novel Therapies

New treatments for Type 2 Diabetes (T2DM) are coming on the scene, with an emphasis on immediate cardiovascular benefits as well as glycemic control.<sup>[81]</sup> The following are a few recent advancements in therapy:

Glucagon Like Peptidase-1 Receptor (GLP-1) Agonists (e.g., Semaglutide, Liraglutide).

#### Mechanism

By lowering oxidative stress and inflammation in blood vessels, these medications protect the cardiovascular system while also improving insulin production and glucose regulation.

### Evidence

GLP-1 receptor agonists prevent adverse cardiovascular events, especially in high-risk populations, such as men and women with existing cardiovascular disease, according to the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results i.e. (LEADER) trial and subsequent research.<sup>[79]</sup>

### Gender-Specific Outcomes

GLP-1 receptor antagonist may help women with Type 2 Diabetes (T2DM) lose weight more effectively, which is important for lowering cardiovascular risk. Additionally, it has been noted that these drugs reduce the risk of heart failure in both sexes; however, the benefits may differ greatly according on hormonal components.<sup>[55,80]</sup>

### SGLT2 Inhibitors (e.g., Empagliflozin, Dapagliflozin)

#### Mechanism

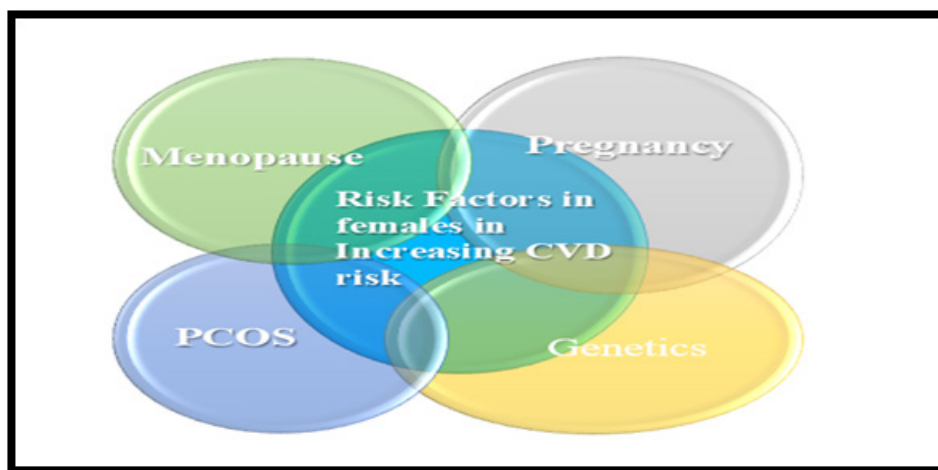
By encouraging the kidneys to eliminate more glucose through urine, SGLT2 inhibitors reduce blood sugar. Additionally, they have been demonstrated to enhance renal and cardiac health and reduce blood pressure.

### Evidence

SGLT2 inhibitors have been shown in recent large-scale trials to lower cardiovascular mortality and the danger of heart failure in diabetic patients. These trials were noteworthy for demonstrating advantages to both sexes, while men often have marginally superior results in measures related to heart failure.<sup>[58,81]</sup>

### Gender-Specific Considerations

Since women are more likely to develop Diabetic Kidney Disease (DKD), which is a major cause of cardiovascular problems, they may benefit from the renal protective effects of SGLT2 inhibitors, especially if they are postmenopausal.<sup>[82]</sup>



**Figure 3:** The risk Factors in Females Increasing Cardiovascular Disease (CVD) Risk: Menopause, Pregnancy, PCOS, and Genetics. All the above mentioned characteristics plays an interconnected role in gradual progression CVD risks closely associated with females.

**Table 1: The effects of several hormones on cardiovascular health in men and women with type 2 diabetes mellitus.**

Hormone	Impact on Women	Impact on Men
Estrogen	Protects Cardiovascular systems; promotes normal cholesterol and vessel elasticity. Protection declines after menopause, increasing risk of cardiovascular disease (CVD).	Lower estrogen levels throughout life; no Lower estrogen levels throughout life; no dramatic post-menopausal hormonal drop, resulting in a more stable cardiovascular risk profile.
Testosterone	Low levels affect insulin resistance and cardiovascular risk, especially in PCOS.	It affects muscle mass, insulin sensitivity, and fat distribution; low testosterone increases the risk of CVD and metabolic syndrome.
Insulin	Higher levels of insulin resistance, particularly post-menopause, increasing risk of type 2 diabetes (T2D) and heart failure.	Lower insulin resistance than women, resulting in slightly lower cardiovascular risk related to T2D.
Progesterone	It affects blood pressure and vascular function; high levels during pregnancy can increase long-term cardiovascular stress.	Limited direct impact on cardiovascular health compared to women.
Leptin	Higher leptin levels; leptin resistance in T2DM linked to obesity and cardiovascular issues. Interaction with estrogen affects cardiovascular outcomes.	Lower leptin levels; less interaction with estrogen, resulting in different cardiovascular outcomes.
Cortisol	Hormonal cycles influence response to cortisol, potentially altering cardiovascular risk.	Higher persistent cortisol due to stress can worsen heart risks; generally, similar effects to women in cardiovascular terms.

## Dual GLP-1/GIP Receptor Agonists (Tirzepatide)

### Mechanism

By targeting both GLP-1 and GIP receptors, this unique class of medications improves glucose control and increases the body's sensitivity to insulin, all while encouraging weight loss.

### Evidence

In clinical trials, tirzepatide has demonstrated encouraging outcomes in lowering HbA1c levels and causing notable weight

loss. Although more extensive evidence is still needed, preliminary findings indicate that it might provide strong cardiovascular protection.<sup>[83]</sup>

## Potential Benefits for Women

Tirzepatide's ability to encourage weight loss and enhance glycemic control may be especially helpful for lowering the prevalence of obesity and severe insulin resistance in women with type 2 diabetes, which raises their risk of cardiovascular conditions.<sup>[84]</sup>

## Anti-inflammatory therapies (e.g., Canakinumab)

### Mechanism

Atherosclerosis is largely influenced by inflammation, especially in those with diabetes. Targeting interleukin-1 $\beta$ , Canakinumab is an anti-inflammatory monoclonal antibody that lowers vascular inflammation.

### Evidence

Regardless of the presence of diabetes, the CANTOS trial demonstrated that reducing inflammation could lower cardiovascular events in those who had previously experienced a myocardial infarction.

Anti-inflammatory strategies for cardiovascular protection in type 2 diabetes have gained attention as a result.

### Potential benefits for Women

Though further gender-specific research is required, medicines like Canakinumab may have a significant impact on improving outcomes for women with T2DM, as inflammation is a primary cause of CVD risk in postmenopausal women.<sup>[85]</sup>

## Non-Pharmacological Interventions

### Gender Considerations

Women with T2DM often experience more significant glycemic fluctuations, particularly during menopause. Artificial pancreas systems could help stabilize blood sugar levels and reduce long-term cardiovascular risks.<sup>[85]</sup>

## Artificial Pancreas Systems

Artificial pancreas devices, also referred to as closed-loop insulin administration systems, provide better glucose control at a lower cardiovascular risk. By maintaining stricter glucose control, these devices could have a major influence on the cardiovascular outcomes of patients with type 2 diabetes by adjusting the supply of insulin based on real-time glucose measurements.<sup>[86]</sup>

## FUTURE PROSPECTS

With the development of precision medicine and novel therapies such as GLP-1 receptor agonists and SGLT2 inhibitors, it is now feasible to customize treatment regimens for the gender of each

patient and lessen the gaps associated with Type 2 Diabetes (T2DM). The number of women taking part in clinical trials should be increased, hormone therapy for postmenopausal women should be researched, and preventative care tailored to each woman's risk profile should be integrated. These tactics aim to reduce the increased cardiovascular risk in women with type 2 diabetes and ensure more equitable health outcomes.<sup>[87]</sup>

## CONCLUSION

Intending to treat cardiovascular problems in type 2 diabetes, these innovative treatments-which include anti-inflammatory drugs, SGLT2 inhibitors, dual agonists like tirzepatide, and more-offer fresh hope. More research is required to properly understand how these medicines operate in women vs. males, especially in light of the particular hormonal and metabolic aspects affecting women with type 2 diabetes, even though the majority of trials have shown broad efficacy across both genders. The review emphasizes how women are more likely than men to encounter cardiovascular problems from Type 2 Diabetes Mellitus (T2DM). These differences are substantial. In women, hormonal fluctuations, especially following menopause, increase the danger of coronary artery disease due to biological causes. Also, women experience worse outcomes like heart failure and greater death rates due to delayed diagnoses, less aggressive treatment, and underuse of preventative medicines. Though sex-specific research and tailored treatment plans are necessary to maximize outcomes for both men and women, recent therapeutic advances, such as GLP-1 receptor antagonists, SGLT2 blockers, and innovative medications like tirzepatide, show promise in resolving these inequalities. For women with type 2 diabetes, closing these gaps with customized strategies can enhance long-term cardiovascular health.<sup>[88]</sup>

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**T2DM:** Type 2 Diabetes Mellitus; **CVD:** Cardiovascular Disease; **HF:** Heart Failure; **GLP-1:** Glucagon Like Peptide-1; **SGLT2:** Sodium Glucose co-Transporter-2; **LEADER:** Liraglutide Effect and Action in Diabetes; **PCOS:** Polycystic Ovary Syndrome; **HRT:** Hormone Replacement Therapy; **ACE:** Angiotensin-Converting Enzyme; **ARBs:** Angiotensin Receptor Blockers; **LDL:** Low-Density Lipoproteins; **HDL:** High-Density Lipoproteins; **HFpEF:** Heart Failure with preserved Ejection Fraction;

**TNF- $\alpha$ :** Tumor Necrosis Factor-alpha; **IL-6:** Interleukin-6; **IL-1:** Interleukin-1; **INF- $\gamma$ :** Interferon-gamma; **MCP-1:** Monocyte Chemoattractant Protein-1; **VEGF:** Vascular Endothelial Growth Factor; **MMP:** Matrix Metalloproteinase; **DKD:** Diabetic Kidney Disease; **ASCVD:** Atherosclerotic Cardiovascular Disease; **CANTOS:** Canakinumab Anti-inflammatory Thrombosis Outcomes Study; **SPSS:** Statistical Package for the Social Sciences; **HCl:** Hydrochloric Acid; **H<sub>2</sub>SO<sub>4</sub>:** Sulfuric Acid; **KMnO<sub>4</sub>:** Potassium Permanganate; **NH<sub>4</sub>OH:** Ammonium Hydroxide; **USTP:** University of Science and Technology of Southern Philippines; **RBC:** Red Blood Cells; **IBM:** International Business Machines.

## SUMMARY

- Significant differences in T2DM patients' risk of cardiovascular problems related to the gender of the patient.
- Women with type 2 diabetes have a higher relative risk of heart disease, especially after menopause.<sup>1</sup>
- The likelihood of a female receiving a diagnosis of cardiovascular disease due to hormonal fluctuations, abnormalities in metabolism, and delayed diagnosis.<sup>2</sup>
- The negative effects of traditional cardiovascular risk factors, such as obesity and hypertension, can change based on the gender of an individual.<sup>3</sup>
- To tackle the specific cardiovascular risks that women with type 2 diabetes face, tailored treatment programs are required.<sup>4</sup>

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