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REVIEW

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The silent toll: understanding the complications of type 2 diabetes mellitus in the male body: a narrative review article

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Abstract

Diabetes mellitus (DM) is a significant global health concern, with a higher prevalence in males compared to females. This narrative review explores the biological, hormonal, and psychosocial factors contributing to sex-specific differences in the development, progression, and complications of type 2 diabetes (T2D) in men. A comprehensive literature search was conducted using PubMed, Scopus, Web of Science, and Google Scholar. The study focused on male-specific complications of diabetes, including cardiovascular disease, sexual dysfunction, neuropathy, renal and ocular complications, mental health, and behavioural influences. Inclusion criteria encompassed peer-reviewed articles focusing on adult males with DM and studies reporting sex-disaggregated data. Men with T2D exhibit distinct clinical features, such as hepatic insulin resistance, testosterone deficiency, and increased susceptibility to erectile dysfunction, cardiovascular complications, and foot ulcers. Testosterone plays a crucial role in glucose metabolism and vascular health, with low levels linked to worsened glycemic control and increased cardiovascular risk. Gender disparities exist in diagnosis and treatment responses, with men often showing lower adherence to screening programs and delayed healthcare-seeking behaviors. Additionally, psychosocial factors such as stigma, masculinity norms, and health literacy significantly influence diabetes management outcomes in men. This review highlights the need for a male-focused approach in diabetes care to improve early detection, personalized therapy, and complication prevention. Tailored interventions addressing hormonal imbalances, cardiovascular risks, sexual health, and psychosocial barriers are essential for optimizing health outcomes in men with diabetes.

Keywords

Type 2 diabetes; Male-specific complications; Testosterone deficiency; Erectile dysfunction; Cardiovascular disease; Insulin resistance; Sexual health

1. Introduction

1.1 Global and regional burden of Type 2 diabetes in men

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose levels due to impaired insulin secretion, action, or both—often resulting from abnormal β-cell function [1]. In 2021, an estimated 529 million (500–564 million) people of all ages worldwide were living with DM, corresponding to a global age-standardized prevalence of 6.1%. Type 2 diabetes (T2D) accounted for 96.0% of all diabetes cases. The prevalence was higher among males (6.5%) compared to females (5.8%), resulting in a male-to-female ratio of 1.14 [2]. Between 1990 and 2022, the age-standardized prevalence of diabetes went up in 131 countries for women and in 155 countries for men [3]. In terms of disease burden, diabetes contributed to 79.2 million disability-adjusted life years (DALYs), including 37.8 million years of life lost (YLLs) and 41.4 million years lived with disability (YLDs) [2].

1.2 Biological sex differences in T2D

1.2.1 Pathophysiology

Emerging evidence highlights important sex-specific differences in T2D pathophysiology, particularly in insulin resistance, fat distribution, and androgen levels. Women generally exhibit greater insulin sensitivity than men, partly due to the protective effects of oestrogen and differences in fat distribution—women typically have more subcutaneous fat and less visceral fat. However, this advantage may diminish with age, especially post-menopause, or as insulin resistance and T2D progress [4, 5]. Over the past two decades, research has shown that regional fat distribution—especially visceral adipose tissue (VAT)—is a stronger predictor of T2D than total body fat [6–8]. This association is stronger in females, particularly White and Hispanic women, than in males [9].

Additionally, lower testosterone levels are commonly observed in men with T2D and are linked to increased insulin resistance. The complex interplay between testosterone and glucose metabolism is discussed in detail in the following section.

1.2.2 Diagnosis

Although sex-based differences in diagnostic test performance exist, no single test has proven superior for men or women. For example, some biomarkers better predict T2D in women, while glycated hemoglobin (HbA1c) alone tends to underdiagnose T2D in men by underestimating fasting plasma glucose (FPG) levels [10]. Some researchers suggest that the oral glucose tolerance test (OGTT) may detect T2D more effectively in women, whereas FPG may be more suitable for men [11]. This variability in diagnostic accuracy underscores the need for sex-specific diagnostic thresholds or composite strategies.

1.2.3 Treatment outcomes

Biological sex differences influence T2D clinical outcomes through genetic and hormonal effects on disease mechanisms, symptoms, diagnosis, and treatment response [12, 13]. Hormonal fluctuations across the female lifespan contribute to greater variability in cardiometabolic risk, including T2D [4]. Additionally, gender-related psychosocial and cultural determinants, including health behaviors, lifestyle, and attitudes toward prevention and treatment, also affect T2D risk and progression [13]. Sex differences also influence treatment responses, yet sex-specific pharmacological guidelines for T2D remain underdeveloped. Women generally respond better to thiazolidinediones (TZDs), which enhance insulin sensitivity, while men benefit more from sulfonylureas, which stimulate insulin secretion. For instance, sulfonylureas reduce HbA1c more in obese men, whereas TZDs are more effective in obese women [14]. Furthermore, newer anti-diabetic drugs, such as glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT-2is), exhibit sex-related differences in efficacy and side effects. Reviews and cohort studies indicate that GLP-1RAs promote greater weight loss in women but are also associated with higher rates of gastrointestinal side effects such as nausea and vomiting, possibly due to sex-specific receptor expression and hormonal influences [15, 16]. A population-based analysis found that both GLP-1RAs and SGLT-2is, when combined with metformin, reduced major adverse cardiovascular events compared to sulfonylureas, with cardiovascular benefits more pronounced in women, especially for GLP-1RAs [17]. These findings emphasize the importance of tailoring pharmacologic treatment to sex-specific responses and tolerability.

1.2.4 Complications

Moreover, the incidence of diabetes-related complications shows inconsistency across studies. Studies in Canada and Ethiopia reported that females were more susceptible to complications [18, 19], while others found males to be at higher risk [20]. Additionally, several studies indicated that specific complications were more prevalent in men, whereas others were more common in women [21].

1.3 Role of testosterone in male T2D outcomes

Testosterone plays a critical role in the development and progression of T2D in men. Men with T2D commonly exhibit lower total serum testosterone levels—by approximately 2.66 nmol/L compared to non-diabetic men—which contributes to increased insulin resistance and poorer glycemic control [22]. The relationship between testosterone and glucose metabolism appears bidirectional: diabetes can reduce testosterone production, while low testosterone increases the risk of developing T2D [23, 24]. Testosterone enhances insulin sensitivity in muscle and adipose tissue. Therefore, androgen deficiency may exacerbate insulin resistance and worsen metabolic control. Clinical studies have shown that testosterone replacement therapy can improve glycemic outcomes in hypogonadal men with T2D, although this intervention remains controversial due to the uncertainty about long-term safety, cost-effectiveness, and the risk of adverse effects [25, 26]. Beyond glycemic regulation, testosterone also impacts cardiovascular health, a major concern for men with T2D. Low testosterone levels are associated with unfavorable lipid profiles, endothelial dysfunction, and increased risk of atherosclerosis and cardiovascular diseases (CVDs) [27, 28]. Despite these findings, diagnosing androgen deficiency remains complex. Many symptoms overlap with other chronic conditions, and while some men exhibit classical hypogonadism, most do not. Therefore, testosterone deficiency may be more of a biomarker of poor overall health than a direct cause of metabolic dysfunction [29]. These findings highlight the importance of assessing testosterone levels in men with T2D—not only for diagnostic purposes but also as part of a broader, individualized treatment strategy aimed at improving metabolic and cardiovascular outcomes.

1.4 Rationale for a male-focused perspective

Men with T2D often exhibit distinct clinical features, including pronounced hepatic insulin resistance and differential responses to medication. Despite these differences, current diagnostic and treatment approaches rarely account for sex-specific variations. Adopting a male-focused perspective is critical to enhancing early detection, personalizing therapy, and improving health outcomes in men. This narrative review explores the biological and gender-related factors influencing

the development, progression, and complications of T2D in males. It examines how genetic, hormonal, and psychosocial factors shape diabetes risk and clinical outcomes, particularly in men. A male-centric approach is essential due to the unique physiological and hormonal influences on disease progression. For instance, men with diabetes are at heightened risk for complications such as hypogonadism and male-specific complications (*i.e.*, erectile dysfunction (ED)). Moreover, CVDs—often emerging earlier—are also a major concern among T2D male patients due to the synergistic impact of diabetes and testosterone deficiency. Recognizing these differences enables more targeted research, tailored interventions, and better health outcomes for men with diabetes [30–32].

2. Methodology

2.1 Literature search strategy

A comprehensive literature search was conducted using the databases PubMed, Scopus, Web of Science, and Google Scholar. The search targeted English-language articles from inception till 10 May 2025. Search terms included combinations of "diabetes complications", "men's health", "male diabetes", "gender differences in diabetes", "testosterone and diabetes", "diabetic cardiovascular risk in males", "diabetic erectile dysfunction", "diabetic neuropathy in men", "male diabetic nephropathy", "mental health in diabetic men", and "masculinity and diabetes care". The search focused on literature related to sex-specific manifestations and complications of diabetes in males, with the main thematic categories including:

- Biological and hormonal aspects.
- Cardiovascular disease.
- Sexual and reproductive health.
- Neuropathy and foot complications.
- Renal and ocular complications.
- Mental health and psychosocial factors.
- Behavioural and lifestyle influences.

Peer-reviewed original research articles, clinical guidelines, meta-analyses, and systematic reviews were included to ensure depth and quality of evidence.

2.2 Inclusion and exclusion criteria

Inclusion criteria:

- Studies focusing specifically on adult males (aged $\geq$18 years) with T2D.
- Articles reporting sex-disaggregated data on any of the above complication themes.
- Studies examining the biological, clinical, psychological, or behavioural dimensions of male diabetes.

Exclusion criteria:

- Studies that did not distinguish data by gender.
- Paediatric populations or studies focused on individuals under 18.
- Animal studies or preclinical investigations.
- Non-peer-reviewed articles, letters, or editorials.

3. Results

3.1 Diabetes related complications

Fig. 1 shows complications of DM in different men's body systems.

3.1.1 Cardiovascular complications

Sex differences in T2D are often overlooked, especially regarding CVDs risk and outcomes. Research shows that women with T2D face a higher CVD risk compared to men, despite generally having a lower risk than men in the general population due to oestrogen protective effects before menopause. This advantage disappears for women with T2D, as they experience a heightened CVD risk at a younger age, indicating that diabetes undermines oestrogen's cardioprotective benefits [33–35]. While women with diabetes are significantly affected by cardiovascular complications, men also warrant considerable attention, as numerous factors can elevate their risk. These include the presence of other comorbidities and lifestyle risk factors such as smoking, alcohol consumption, unhealthy diets, and lack of exercise. These combined factors, when superadded to chronic hyperglycemia, insulin resistance, and dyslipidemia, collectively promote the development and progression of atherosclerotic plaques. These plaques can obstruct blood flow to the heart, leading to acute coronary syndrome, myocardial infarction, and even death [36, 37]. Furthermore, the interconnection between diabetes and hormonal imbalances, such as low testosterone levels, can exacerbate the risk of atherosclerosis and coronary artery disease in men. Testosterone deficiency, often observed in men with diabetes, is associated with increased visceral adiposity, inflammation, and endothelial dysfunction, all of which contribute to the pathogenesis of atherosclerosis and increase the likelihood of adverse cardiac outcomes [38, 39].

3.1.2 Cerebrovascular complications

Globally, stroke ranks as the second leading cause of death [40]. From 1990 to 2021, the global burden of stroke increased significantly, with a 70.0% rise in stroke incidence, a 44.0% increase in deaths from stroke, and a 86.0% increase in stroke prevalence [40]. Diabetic men face a significantly increased risk of stroke compared to their non-diabetic counterparts [41, 42]. Evidence indicates notable sex differences in diabetes-related stroke risk. Among men, the crude incidence of stroke was 1000 per 100,000 in those with diabetes compared to 247 per 100,000 in non-diabetic men, corresponding to a relative risk (RR) of 4.1 (95% Confidence Interval (CI): 3.2–5.2). In women, although the absolute incidence was lower (757 *vs.* 152 per 100,000), the relative risk was higher at 5.8 (95% CI: 3.7–6.9). These findings suggest that while diabetic men bear a higher absolute burden of stroke, diabetic women experience a greater proportional increase in risk, underscoring the sex-specific vulnerability and the need for tailored preventive strategies [43, 44]. Ischemic stroke, the most common type, is particularly prevalent, and the presence of diabetes exacerbates underlying vascular damage, increasing the likelihood of thrombotic events. Approximately one-third of all stroke patients have diabetes [45]. Several mechanisms contribute to the increased risk of stroke in men with diabetes. Chronic hyperglycemia and insulin resistance promote atherosclerosis,

leading to the formation of plaques that can occlude cerebral blood vessels, causing ischemic stroke. Diabetes also increases the risk of small vessel disease (lacunar stroke) and predisposes individuals to cardioembolism due to associated cardiac abnormalities like atrial fibrillation. Furthermore, diabetes-related damage to blood vessels can impair cerebral blood flow autoregulation, making the brain more vulnerable to ischemia [42, 46]. Insulin resistance, a key feature of T2D, is a major contributor to the development of hypertension in men. This condition increases blood vessel stiffness and sodium retention by the kidneys, both of which elevate blood pressure. Several factors contribute to this process: inappropriate activation of the renin-angiotensin-aldosterone system (RAAS) and the autonomic nervous system, inappropriate mitochondrial function, elevated oxidative stress, inflammatory markers, gut microbiota imbalance, and disturbances in glucagon-like peptide-1 (GLP-1) and sodium-glucose cotransporter 2 (SGLT2) [47, 48]. Hypertension trends in diabetic men are concerning, with a significantly higher prevalence compared to their non-diabetic peers [48]. Studies have reported hypertension in 30% to 80% of diabetic patients [47, 49, 50]. Specifically, the prevalence of hypertension in males with T2D was found to be 34.1% by Taheri *et al*. [51] and 32.5% by Wang *et al*. [52]. The coexistence of hypertension and diabetes creates a synergistic effect, markedly increasing the risk of cardiovascular events, including stroke, myocardial infarction, and kidney disease [53, 54]. Moreover, the risk of cardiovascular events is significantly amplified in diabetic men who smoke. Smoking promotes endothelial dysfunction, increases oxidative stress, and impairs vascular repair mechanisms, thereby exacerbating the harmful effects of diabetes on the cardiovascular system [55, 56]. Obesity is another major factor that significantly increases the risk of CVDs in men with diabetes. Obesity, particularly abdominal or visceral obesity, is associated with increased insulin resistance, dyslipidemia, and inflammation, all of which contribute to the development of atherosclerosis

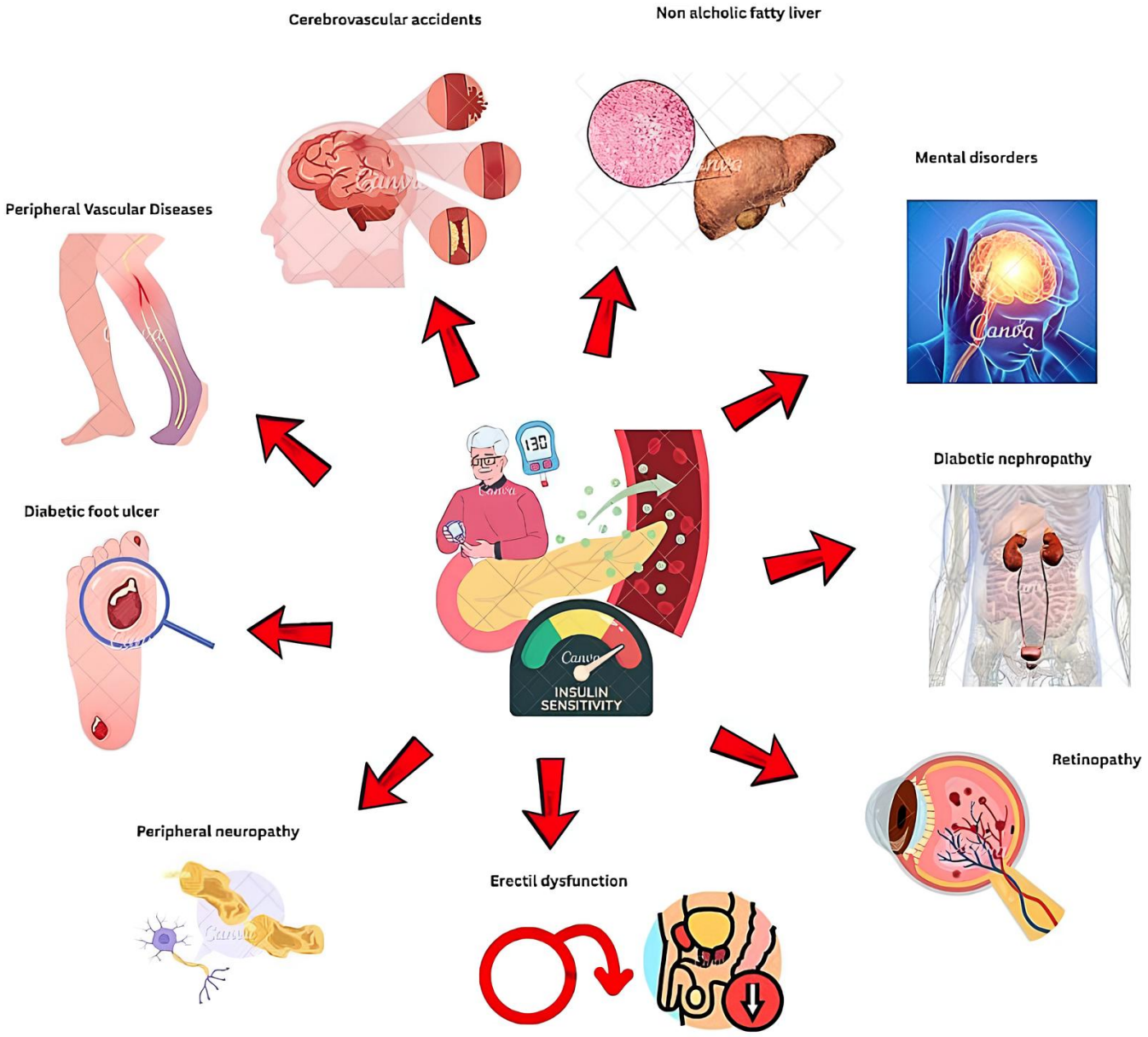

FIGURE 1. Diabetes related complications among men.

and increase the risk of coronary artery disease, heart failure, and stroke [57, 58].

3.1.3 Sexual and reproductive health

Sexual dysfunction (SD) is a multifactorial and heterogeneous condition characterized by clinically significant impairments in the ability to engage in or enjoy sexual activity [59, 60]. SD is particularly prevalent among individuals with diabetes; the global pooled prevalence of SD among individuals with diabetes is estimated at 61.4% (95% CI: 51.80–70.99) [61]. Female sexual dysfunction (FSD) remains a frequently overlooked complication of diabetes, despite its high prevalence (20–80%) and doubled risk among affected patients [62]. FSD comprises three primary diagnostic categories: female sexual interest/arousal disorder (FSIAD), female orgasmic disorder, and genito-pelvic pain/penetration disorder. FSD in diabetes has a multifactorial etiology, encompassing not only metabolic disturbances but also psychological, social, and cultural determinants [63]. While FSD is often shaped by a complex interplay of hormonal, psychological, and sociocultural factors, ED represents the most common and well-studied manifestation of sexual dysfunction in diabetic men. Diabetic men experience SD more frequently and at an earlier age compared to non-diabetic men [61, 64]. Common manifestations include arousal disorders like ED and orgasmic issues such as premature ejaculation, retrograde ejaculation, and anorgasmia [65]. ED, formerly termed impotence, refers to the persistent or recurrent inability to achieve or maintain an erection sufficient for satisfactory sexual activity. Key risk factors associated with ED in diabetic patients include age over 40 years, diabetes duration exceeding 10 years, presence of peripheral vascular disease, and body mass index (BMI) greater than 30 kg/m^2 [66]. ED in diabetes arises from several interrelated mechanisms. Chronic hyperglycemia leads to endothelial dysfunction, accumulation of advanced glycation end products, oxidative stress, and neuropathy, all of which impair normal erectile function [67, 68]. Diabetic peripheral and autonomic neuropathy interfere with nerve signaling and weaken the penile blood flow regulation, further contributing to ED [69, 70]. Additionally, CVDs, common in diabetic patients, limits penile blood vessel dilation, compounding erectile difficulties [66]. ED in diabetic men can significantly impact relationships, reducing marital satisfaction, causing emotional stress and communication breakdowns, and potentially leading to divorce [67]. It also carries profound psychological consequences, including diminished self-esteem and worsened physical and mental health [71]. This creates a vicious cycle where diabetes, ED, and psychological distress reinforce each other, substantially affecting overall well-being [72, 73]. Phosphodiesterase type 5 (PDE5) inhibitors are the first-line treatment for ED; however, diabetic men often show reduced responsiveness compared to non-diabetic men. For those with treatment-resistant ED, alternative options such as intracavernosal injections, intraurethral prostaglandin, vacuum erection devices, or penile prostheses should be explored. Combination therapies—like PDE5 inhibitors with oral agents such as arginine or L-carnitine—may enhance treatment outcomes. Emerging approaches, including low-intensity shockwave therapy and stem cell therapy, also hold promise as targeted interventions for diabetic-related ED [74].

3.1.4 Diabetic peripheral neuropathy

The mechanisms underlying diabetic peripheral neuropathy (DPN) are complex and multifactorial. Chronic hyperglycemia is believed to be a primary contributor, leading to the accumulation of advanced glycation end products (AGEs), which can damage nerve fibres and impair their function. Increased oxidative stress, inflammation, and microvascular damage within the nerves also play significant roles in the development and progression of this condition [75, 76].

The prevalence of DPN in men with diabetes is substantial, with studies indicating that approximately 46.6% (95% CI: 40.3–52.9%) of men with T2D will develop DPN during their lifetime [77]. Hicks *et al*. [78] reported that the prevalence of DPN was 51.2% in diabetic men and 22.5% in non-diabetic men. Men tend to experience more frequent and severe structural nerve damage, referred to as polyneuropathy. In contrast, women report significantly higher levels of pain intensity and greater prevalence of pain, even though their objective neuropathy is milder. This difference in pain perception may be influenced by biological factors related to sex, such as hormonal variations or differences in central nervous system pain processing, as well as psychosocial factors associated with gender [79]. Early detection of DPN is paramount. Detection involves regular clinical assessments, including neurological examinations focused on sensory and motor functions, and quantitative sensory testing to evaluate nerve function. Electrophysiological studies, such as nerve conduction studies, are also crucial for confirming the diagnosis and determining the extent of nerve damage [80]. DPN typically progresses gradually. Symptoms often begin in the distal extremities—such as the feet and hands—and may spread proximally over time. Factors such as poor glycemic control, prolonged duration of diabetes, and the presence of other comorbidities, including hypertension and hyperlipidemia, can accelerate the progression of nerve damage. Regular monitoring and proactive management of risk factors are essential for slowing the progression and reducing the risk of complications associated with DPN [81, 82].

3.1.5 Diabetic foot ulcers and amputation risk

Diabetic foot ulcers (DFUs) are a major complication of diabetes and a significant precursor to lower-extremity amputations (LEAs), particularly among men. Globally, an estimated 131 million people, or 1.77% of the global population, suffer from lower-extremity complications related to diabetes. This includes 105.6 million individuals with neuropathy alone, 18.6 million with foot ulcers, and 6.8 million who have undergone amputations (4.3 million without prostheses and 2.5 million with prostheses). In 2016, these conditions collectively accounted for 16.8 million YLDs, representing 2.07% of the global YLDs. Neuropathic pain was the leading contributor, responsible for 12.9 million YLDs, followed by foot ulcers with 2.5 million YLDs and amputations, which accounted for a combined total of 1.5 million YLDs [83]. The development of DFUs is often multifactorial, with DPN, vascular insufficiency, and impaired wound healing playing key roles [84]. Neuropathy can result in a loss of protective sensation,

increasing the risk of undetected foot injuries, while peripheral vascular disease impairs blood flow, delaying healing and increasing the risk of infection and tissue necrosis [85]. The consequences of LEAs are profound, leading to significant disability, reduced quality of life, increased mortality, and substantial healthcare costs [86–88]. Although these mechanisms are shared by all individuals with diabetes, growing evidence highlights important sex-based differences in both the incidence and outcomes of diabetic foot complications. Men with diabetes have a higher risk of developing DFUs and undergoing LEAs compared to women. This disparity may be attributed to a combination of factors, including a higher prevalence of DPN and peripheral artery disease (PAD) in men, as well as differences in health-seeking behaviour and adherence to preventive foot care. Additionally, gender-related differences in pain perception and care-seeking behavior may influence outcomes. Studies suggest that men and women may experience and report pain differently, with men more likely to underreport symptoms or delay medical consultation until complications become severe. These tendencies, influenced by biological factors (*e.g.*, cerebral cortex processing) and sociocultural norms that discourage expressions of vulnerability, may contribute to delayed diagnoses and increased risk of foot ulcers, infections, and amputations in men with diabetes [86–88].

3.1.6 Renal complication

Persistent high blood glucose levels in patients with diabetes lead to disruption and damage of the kidneys' microvascular architecture. Research indicates that 20–40% of individuals with diabetes develop diabetic nephropathy (DN), characterized by reduced glomerular filtration rate and persistent albuminuria, which can progress to end-stage renal disease. DN is now a major cause of chronic kidney disease (CKD), renal failure, and end-stage renal disease (ESRD) [89, 90]. Between 1990 and 2021, the global burden of DN rose substantially. The number of deaths increased from 197.27 thousand to 571.29 thousand, and DALYs rose from 635.044 million to 151.5 million, reflecting 1.89-fold and 1.38-fold increases, respectively. The global mortality rate rose from 5.233 to 6.807 per 100,000, and the DALY rate increased from 152.759 to 176.286 per 100,000. While the overall DALY rate for DN increased, particularly for T2D, a slight decrease was noted among women with type 1 DM (T1D). Specifically, DALY rates for T1D in men rose from 51.439 to 53.209 per 100,000, but declined in women from 42.693 to 27.273 per 100,000. For T2D, DALY rates surged dramatically, from 121.653 to 1518.130 per 100,000 in men and from 93.543 to 1136.710 per 100,000 in women. Overall, the burden of DN was markedly higher in 2021 compared to 1990 [90]. Men with T2D have a higher risk of nephropathy compared to normoglycemic men, but this risk is not consistently observed in women [91]. However, women with T2D are more likely to experience kidney failure and renal insufficiency [92]. Additionally, studies suggest that women have a higher risk of developing diabetic end-stage renal disease, while men with newly diagnosed diabetes or pre-diabetes are at an increased risk of developing CKD. Testosterone is believed to play a significant role in the development of DN in males. Reduction of testosterone levels might help decrease kidney injury in males [93–95]. Moreover, a clear association has been observed between higher testosterone levels in younger men and the development of microalbuminuria [96].

3.1.7 Ocular complications

A meta-analysis conducted by Teo *et al.* [97] estimated the global and regional burden of diabetic retinopathy (DR) through 2045. Among people with diabetes, the global prevalence was 22.27% for DR, 6.17% for vision-threatening DR (VTDR), and 4.07% for clinically significant macular edema (CSME). In 2020, an estimated 103 million people had DR, projected to rise to 161 million by 2045. Ocular complications, particularly DR, appear to be more prevalent in men. For example, a multicenter cross-sectional study by Cherchi *et al.* [98] found a significantly higher DR prevalence in men (22.0%) compared to women (19.3%, $p < 0.0001$), even though women often exhibit fewer risk factors. This suggests that male sex may be an independent risk factor for DR. Supporting this, data from the Swedish National Diabetes Registry showed that men with T2D had a higher likelihood of developing DR than women, with an odds ratio of 1.10 [99]. The increased burden among men may also be linked to their higher rates of associated risk factors such as smoking, lower adherence to lifestyle modifications, and less frequent health monitoring. Moreover, hormonal differences may contribute by affecting retinal microvasculature and inflammatory pathways involved in DR [100, 101].

3.1.8 Non-alcoholic fatty liver disease (NAFLD)

NAFLD is the most prevalent chronic liver disorder globally. Approximately 32% of adults are affected—40% of men versus 26% of women—and the incidence is 47 cases per 1000 population, again higher in males [102]. The disease spectrum ranges from simple steatosis to non-alcoholic steatohepatitis (NASH; inflammation and hepatocyte injury). In diabetic patients, NASH more frequently progresses to cirrhosis and hepatocellular carcinoma [103]. Given these hepatologic features, several large-scale studies have quantified NAFLD's impact on diabetes risk and increased prevalence [104, 105]. A comprehensive meta-analysis of 33 longitudinal studies involving 501,022 adults—30.8% of whom had NAFLD—identified 27,953 new cases of diabetes over a median follow-up period of five years. The analysis found that NAFLD independently doubles the risk of developing T2D, with a hazard ratio of 2.19 (95% CI: 1.93–2.48). Individuals with more severe NAFLD had an even greater risk of developing diabetes, with a hazard ratio of 2.69 (95% CI: 2.08–3.49). Additionally, the risk increased significantly with advancing liver fibrosis, reaching a hazard ratio of 3.42 (95% CI: 2.29–5.11) [104]. Furthermore, NAFLD impairs glycemic control and actively contributes to the pathogenesis of chronic diabetic complications, particularly CVDs and CKD [106]. A separate meta-analysis of sex-stratified cohorts found that women had a 19% lower relative risk of NAFLD compared to men (pooled relative risk 0.81; 95% CI: 0.74–0.88), but a similar risk of NASH; paradoxically, women's risk of advanced fibrosis was 37% higher (especially post-menopause). These sex disparities may be attributed to differences in body fat distribution, estrogen levels, and

adipokine profiles between men and women [107].

3.1.9 Mental health and psychosocial problems

Anxiety disorders (*e.g.*, generalized anxiety disorder, panic disorder, post-traumatic stress disorder (PTSD)) frequently co-occur with both T1D and T2D—often worsening around diagnosis or when complications arise [108, 109]. Anxiety symptoms can mimic hypoglycemia, leading to confusion and mismanagement, while needle fear can deter self-injection or blood testing. Fear of hypoglycemia may also prompt some patients to intentionally maintain hyperglycemia, increasing complication risk [110]. A substantial proportion of patients report diabetes-related stigma (76% of T1D, 52% of T2D) [111]. Men are consistently less likely than women to experience anxiety, depression, and stigma, with one study showing 30% lower odds of depression screening-positive in men versus women [112]. Biological factors (*e.g.*, hormonal fluctuations) and gender roles (*e.g.*, caregiving responsibilities) may increase women's vulnerability to psychological distress [113, 114].

3.2 Public health and clinical strategies

Because T2D often remains undiagnosed for 9–12 years, complications are frequently present at diagnosis. Patients are classified as having an "early" diagnosis if no diabetes-related complications (*e.g.*, neuropathy, retinopathy) documented at initial presentation; those with any existing complication are considered "late" diagnoses. Late-diagnosed patients exhibit a significantly higher prevalence of microvascular and macrovascular complications at the time of diagnosis [115]. Male patients demonstrate consistently lower adherence to diabetes screening programs than females—most notably among those aged 40–44, where men's adherence is approximately 15% lower. Although adherence among men improves with age—surpassing 80% in those ≥65 years—it remains lower than that of women across rural, urban, and socioeconomically deprived settings [116]. Additionally, men participate less in preventive measures—such as lifestyle modification, medication adherence, and routine health screenings—than women [117, 118]. These gender-based disparities in screening and prevention likely contribute to later diagnoses and more advanced complications in men. Tailored, gender-sensitive interventions—addressing barriers to awareness, accessibility, and healthcare engagement—are crucial, especially for younger men in early adulthood and those in underserved regions.

Artificial intelligence (AI) is a broad term encompassing a range of techniques that enable computers to simulate human intelligence. It includes various subfields such as machine learning, deep learning, and other computational approaches designed to perform tasks typically requiring human cognition. AI is hoped to offer numerous opportunities to enhance diabetes care across the entire healthcare continuum—from prevention and early diagnosis to personalized treatment and long-term management [119]. It would enable the analysis of large-scale clinical data, allowing systems to identify key predictive features and build models that support personalized treatment and enhance diagnostic accuracy [120]. Recently, AI has been increasingly utilized in the screening [121], treatment, and prediction of diabetes-related complications [122]. Looking ahead, AI-powered precision medicine is expected to play a pivotal role in forecasting and diagnosing these complications. Integrating AI into the healthcare system holds the potential to substantially reduce the burden of diabetes care by enabling a more proactive, efficient, and personalized approach to prevention, diagnosis, and management [119].

Community-based intervention for screening [123] and management of diabetes complications [124] involve self-care management support, a fundamental element of the Chronic Care Model, which focuses on empowering and equipping patients with the skills and knowledge needed to effectively manage their health [125]. This empowers patients to take an active role in managing their condition through health education and the development of essential skills, enabling them to achieve metabolic control targets, prevent or delay the onset of acute and chronic complications, and ultimately preserve their quality of life [123]. Community-based health interventions offer a promising solution for improving diabetes management, particularly in areas with limited healthcare access and resources. This intervention raises awareness of the disease and enhances self-care practices while addressing social and community-specific factors that are vital for the long-term treatment and prevention of diabetes and its complications. They help eliminate barriers to self-care and reduce stigma, leading to better patient-centered outcomes, increased acceptability, and ultimately, higher levels of patient engagement and satisfaction [126].

3.3 Research gaps and future directions

Despite the increasing awareness of sex-specific differences in diabetes, significant research gaps remain, particularly in understanding the unique pathophysiology, complications, and treatment responses in men. Many current diabetes studies do not separate data by sex, which results in a lack of insights focused on males. This is especially true regarding hormonal influences, such as testosterone deficiency, cardiovascular risks, and psychosocial barriers to care. Future research should prioritize longitudinal studies that disaggregate data by sex. This approach will help clarify how biological factors, like androgen levels and visceral adiposity, and gender-related factors, such as health-seeking behaviours and masculinity norms, affect diabetes progression in men. Clinical trials must actively recruit male participants to assess the effectiveness of sex-specific treatments, particularly therapies like testosterone replacement and SGLT2 inhibitors, which can help mitigate complications such as ED and CVDs. Moreover, public health programs should incorporate gender-sensitive strategies, including targeted screening for hypogonadism in diabetic men, community-based interventions to improve male health literacy, and AI-driven tools for early prediction of complications. Additionally, interdisciplinary collaboration is essential to explore the connections between metabolic health, mental well-being, and sexual function in men, ensuring a holistic approach to diabetes care. By addressing these gaps, future efforts can advance precision medicine approaches and

reduce the disproportionate burden of diabetes complications in male populations.

4. Conclusions

The burden of diabetes in men is compounded by unique physiological, hormonal, and psychosocial factors that contribute to distinct clinical presentations and complications. Biological differences, particularly testosterone deficiency, play a central role in promoting insulin resistance, metabolic dysregulation, and cardiovascular disease. Men also face specific challenges related to sexual dysfunction, neuropathy, and poor health-seeking behaviours, which can delay diagnosis and effective treatment. Current diagnostic and therapeutic strategies rarely account for these sex-specific differences, leading to suboptimal outcomes. A targeted, male-centered perspective in diabetes research and clinical practice is critical for improving early detection, personalizing interventions, and reducing the disproportionate burden of diabetes-related complications in men. Future efforts should focus on integrating gender-sensitive approaches into public health initiatives, leveraging AI for precision medicine, and promoting community-based interventions tailored to the needs of male populations.

4.1 Strengths of the study

A key strength of this narrative review is its thorough exploration of the biological, hormonal, and psychosocial factors contributing to sex-specific differences in T2D among men. We conducted an extensive literature search across reputable databases—PubMed, Scopus, Web of Science, and Google Scholar—ensuring access to a wide range of peer-reviewed studies up to 10 May 2025. This approach facilitated an in-depth look at male-specific complications such as CVDs, sexual dysfunction, and mental health issues. Additionally, the study goes beyond traditional clinical perspectives by integrating hormonal, genetic, and psychosocial dimensions, offering a multidisciplinary understanding of diabetes in men versus women. It also discusses public health strategies and emerging technologies like AI for early detection and personalized treatment.

4.2 Limitations of the study

The current study has several limitations that should be considered. As a narrative review, it lacks a structured methodology for synthesizing evidence, which may introduce selection bias. The absence of a formal quality assessment tool limits the ability to gauge the reliability of the findings. Moreover, excluding non-English language publications and grey literature may lead to publication bias. Additionally, the study does not include quantitative analysis. While it offers valuable qualitative insights into male-specific diabetes complications, it fails to quantify sex differences or statistically validate its findings. This reduces its relevance for evidence-based policy and clinical decision-making, where numerical data are crucial.

ABBREVIATIONS

AGEs, Advanced Glycation End Products; AI, Artificial Intelligence; BMI, Body Mass Index; CKD, Chronic Kidney Disease; CI, Confidence Interval; CVDs, Cardiovascular Disease; CSME, clinically significant macular edema; DALYs, disability-adjusted life years; DFUs, Diabetic Foot Ulcers; DR, Diabetic retinopathy; DM, Diabetes Mellitus; DN, Diabetic Nephropathy; DPN, Diabetic Peripheral Neuropathy; ED, Erectile Dysfunction; ESRD, End-Stage Renal Disease; FPG, Fasting Plasma Glucose; FSD, Female Sexual Dysfunction; FSIAD, Female Sexual Interest/Arousal Disorder; GLP-1RAs, Glucagon-Like Peptide-1 Receptor Agonists; HbA1c, Glycated hemoglobin; LEAs, Lower-Extremity Amputations; NAFLD, Non-Alcoholic Fatty Liver Disease; NASH, Non-Alcoholic Steatohepatitis; OGTT, Oral Glucose Tolerance Test; RR, relative risk; PAD, Peripheral Artery Disease; PDE5, Phosphodiesterase Type 5; PTSD, Post traumatic stress disorder; RAAS, Renin-Angiotensin-Aldosterone System; SD, Sexual Dysfunction; SGLT2, Sodium-Glucose Cotransporter 2; SGLT-2is, Sodium-Glucose Cotransporter-2 Inhibitors; T1D, Type 1 Diabetes mellitus; T2D, Type 2 Diabetes; TZDs, Thiazolidinediones; VAT, Visceral Adipose Tissue; YLDs, Years Lived with Disability; YLL: years of life lost; VTDR, vision-threatening DR.

AVAILABILITY OF DATA AND MATERIALS

All data supporting the findings of this review are derived from the existing literature and are available within the referenced articles and databases cited in the manuscript.

AUTHOR CONTRIBUTIONS

RMG—conceptualization, design, drafting and revising the manuscript, and final approval. MMA—literature search, data extraction, critical revision, and final approval. SAA—literature review, thematic analysis, and writing support. EE—methodology development, critical feedback, and editing. LMABO—data synthesis, writing, and formatting. SH—review of clinical aspects, editing, and quality assurance. HAHA—thematic input, interpretation of results, and review. HTE—critical evaluation of hormonal and metabolic components. FHA—contribution to cardiovascular and behavioral sections. AMFA—review of psychosocial and public health implications. AA—assistance with literature screening and organization. MFH—oversight of methodology, drafting the manuscript, final review, and validation. All authors read and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable. This study is a narrative review based on previously published literature and does not involve any primary data collection or human participants.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests. No financial or non-financial conflicts of interest exist regarding the content of this manuscript.

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