

# Impact of Biologic Therapies and Multidisciplinary Care in Managing Diabetic Eye Disease

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## Abstract

**Objective:** To evaluate the impact of current and emerging biologic therapies on the treatment of diabetic eye diseases, specifically diabetic retinopathy and diabetic macular edema, and to examine how integrating these therapies with early detection, multidisciplinary collaboration, and patient-centered care improves long-term visual outcomes in patients with diabetes. **Background:** Diabetic retinopathy (DR) and diabetic macular edema (DME) are among the most common and vision-threatening complications of diabetes mellitus. As global diabetes prevalence continues to rise, so does the burden of diabetic eye disease. Many patients face barriers to care, and substantial gaps remain in treatment accessibility and long-term adherence. Although treatments such as anti-vascular endothelial growth factor (anti-VEGF) agents and corticosteroids have transformed the management of DR and DME, novel therapies may pose challenges, including increased costs or complexity associated with injection administration. A comprehensive, multidisciplinary strategy that integrates biologic therapies with early screening and coordinated care may further improve clinical outcomes and reduce the risk of vision loss in this high-risk population. **Methods:** This review synthesizes evidence from controlled trials, observational studies, and treatment guidelines published between 2010 and 2025. It evaluates pharmacologic interventions, including anti-VEGF agents and corticosteroids, analyzing their efficacy, dosing strategies, and adverse effects. Various interdisciplinary care models and public health factors, such as screening adherence and access disparities, were examined and summarized. **Results:** Biologic agents targeting VEGF and inflammatory pathways demonstrate strong efficacy in preserving or improving visual acuity in patients with DME and DR, particularly when administered at individualized intervals. However, high treatment burden, limited adherence, and disparities

in access present ongoing challenges. Studies show that early ophthalmologic screening, routine HbA1c monitoring, and collaborative care among healthcare professionals lead to significantly better disease management and reduced progression to vision-threatening stages. **Conclusions:** The management of diabetic eye disease is undergoing a paradigm shift with the advent of biologic therapies. When coupled with routine screening, patient education, and a multidisciplinary care model, these interventions can substantially improve visual and systemic outcomes in diabetic patients. Ongoing innovations in drug delivery, gene therapy, and integrin-targeting biologics hold additional promise, although increased accessibility and personalized treatment strategies are crucial to ensuring equitable care across diverse populations.

## Keywords

Pharmacist Intervention, Ophthalmology Disorders, Medication Management, Ophthalmology Treatment

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## 1. Introduction/Background

Diabetes impacts over 422 million individuals, and nearly 1.6 million die annually across the world [1]. It is projected to rise to 700 million individuals by 2045 [1], leading to numerous ophthalmic complications. Broadly known as diabetic eye diseases, these include diabetic retinopathy (DR), which is often complicated by diabetic macular edema (DME), and can progress to vision impairments [2]. Roughly one-third of diabetic patients over 40 years old present with some signs of DR, and these risks increase when diabetes is left untreated [2]. DME frequently co-occurs in patients with DR, which is a leading cause of blindness in American adults [3]. Fortunately, tools exist for early detection and treatment that can significantly reduce the risk of blindness [2]. Therefore, understanding the foundation of how DR and DME affect the vision and quality of life of patients is an essential process to understanding these conditions.

## 2. Pathophysiology of DR and DME

DR is a significant complication of diabetes and can cause severe visual impairment. It is the direct result of prolonged hyperglycemia, defined as blood glucose levels exceeding 125 mg/dL during fasting or above 180 mg/dL two hours post-prandial [4]. Long-term glycemic control is evaluated using glycated hemoglobin (HbA1C), with values  $\geq 6.5\%$  indicating diabetes and values between 5.7% and 6.4% suggesting prediabetes [5] [6]. Chronic hyperglycemia triggers a cascade of structural changes within the retinal microvasculature, initiating the first stage of DR: non-proliferative diabetic retinopathy (NPDR) [7]. In NPDR, elevated blood glucose levels lead to the formation of harmful molecules known as advanced glycation end-products (AGEs), which increase oxidative stress, promote vascular permeability, and activate inflammatory pathways within the retina [7] [8]. These

changes directly impair the endothelial cells that line the retinal capillaries, causing early microvascular dysfunction [7] [8]. One of the earliest signs of NPDR is the loss of pericytes, which help stabilize the capillary walls [9]. Damage to these cells causes the capillaries to become fragile and prone to leakage, which leads to microaneurysm formation [10]. Simultaneously, thickening of the basement membrane and disassembly of tight junctions contribute to the breakdown of the blood-retinal barrier (BRB) [11]. The BRB regulates the selective movement of molecules between the retinal tissue and the bloodstream [12]. As endothelial cells are damaged, the tight junctions that maintain this barrier are disrupted [9]. As a result, fluid, plasma proteins, and lipids leak into the retinal tissue [9] [13]. These changes cause microaneurysms, intraretinal hemorrhages, hard exudates, and cotton wool spots, which are distinctive features of NPDR [11] [14]. However, patients may be asymptomatic in this stage, which further exacerbates the challenge in diagnosing and treating DR before it progresses [11]. As capillary occlusion in the retina continues, the retina begins to produce elevated levels of VEGF, which is a standard characteristic of proliferative diabetic retinopathy (PDR), a more advanced stage of DR [15]. In PDR, increased VEGF promotes the growth of abnormal blood vessels at the retina and optic disc, a process referred to as neovascularization [14]. These new vessels are highly susceptible to rupture and can cause vitreous hemorrhage [14]. Furthermore, as fibrous tissue begins to develop with neovascularization, it can contract and pull on the retina. This excessive force increases the risk of tractional retinal detachment and can cause irreversible vision loss in diabetic patients [9] [14]. DME is another complication of diabetes and can develop at any stage of DR. As the blood retinal barrier is damaged, fluid leaks into the macula, the center region of the retina [15]. The macula is responsible for high acuity vision. This buildup of fluid in the macula leads to macular thickening, the formation of cysts, and a loss of central visual acuity [12]. As DME worsens, extracellular fluid accumulation disrupts the retina's overall structure, further exacerbating vision impairment.

### 3. Current Pharmaceutical Treatments

Ophthalmologic disease states are the leading complications for diabetic patients [9]. DR is known as one of the most common complications of diabetes, and can be complicated by DME at any point throughout the disease progression, contributing to vision loss [9]. The goals of treatment in DR and DME are to preserve vision by reducing disease progression.

Treatment options may include laser therapy, eye drops, or surgical intervention in advanced cases [16]. Previously, laser photocoagulation treatments have traditionally been the gold standard for treating DR and DME [9]. The destructive nature of laser therapy, however, risks permanent damage to retinal cells and reduced vision, and has rendered its current role a rescue therapy adjuvant to anti-VEGF therapy [9].

Current pharmacological treatment options include corticosteroids, anti-VEGF

therapy, and biologics, all of which are used in combination with glycemic management. Anti-VEGF agent is the first-line therapy for DR and DME in patients due to its high efficacy and safety profile [17]. Although anti-VEGF therapies seem promising, their short half-life poses limitations with frequent injections, as well as adverse effects and financial burdens [9]. Thus, the treatment for diabetic eye disease remains challenging, emphasizing the urgency for understanding and developing newer treatments [9].

### 3.1. Anti-VEGF Agents

VEGF increases vascular permeability and is closely linked to blood vessel leakage [16]. Inhibiting VEGF, utilizing anti-VEGF therapy, has shown its potency against neovascular age-related macular degeneration and complications of DR [18]. A network meta-analysis of nearly 20 trials found high-quality evidence that anti-VEGF therapies, such as aflibercept, bevacizumab, and ranibizumab, offer greater vision benefits than traditional laser photocoagulation treatments [19]. As shown in **Table 1**, which outlines available corticosteroids, their injection frequency, and clinical pearls based on approvals, off-label use, discontinuation and effectiveness. Two phase 3 clinical trials (YOSEMITE and RHINE) have further explored the safety and efficacy of faricimab in the application of DME [20]. Overall, most anti-VEGF agents are similarly efficacious, and selection of therapy is typically made based on patient factors such as the presence of other concurrent conditions or financial barriers.

While most anti-VEGF agents are administered by intravitreal injection, intravitreal implants are also available as an option for patients. Ranibizumab, for example, is available as both an injection and a 6-month implant to treat DME, but there is a black boxed warning for significantly increased risks of endophthalmitis [21].

**Table 1.** Summary of intravitreal anti-VEGF agents for DR/DME [22].

Anti-VEGF	Injection Frequency	Pearls
aflibercept	every 4 weeks (monthly) for the first 5 injections, followed by every 8 weeks (every 2 months)	Approved for DME 2014
bevacizumab	every 4 weeks (monthly) based on visual assessment	Approved 2004, off-label (must be repackaged)
faricimab	every 4 weeks (monthly) for 4 - 6 doses, followed by every 4 - 16 weeks based on visual assessment	Approved for DME 2022
pegaptanib	n/a	Discontinued 2018
ranibizumab	every 4 weeks (monthly) for 3 doses, may be followed by every 2 - 4 weeks based on visual assessment	Implant lasting 6 months; available for DME. Approved for DME in 2012.

### 3.2. Corticosteroids

Corticosteroids have a significant role within the management of DME and DR,

especially when biologic therapies aren’t sufficient [23]. Restoring the blood-retinal barrier can reduce macular edema by regulating ion and water channels [24]. Intravitreal steroids are considered a second-line treatment [25]. As shown in **Table 2**, which outlines available corticosteroids, their injection frequency, and clinical pearls based on approvals, off-label use, and effectiveness. Monotherapy with an agent such as intravitreal triamcinolone injections or implants may be suggested in patients with DME unresponsive to first-line agents [26]. However, the benefits of steroids are often overshadowed by their increased risk of side effects such as glaucoma and cataracts [26]. The overall effects of corticosteroids are localized and may minimize systemic exposure, resulting in a temporary impact that requires repeated injections [24]. Sustained-release corticosteroid implants, such as dexamethasone and fluocinolone acetonide, have been approved for the treatment of DME [24]. Though its use is limited, glucocorticoids can activate the mineralocorticoid receptor (MR) pathway within the retinal tissue, contributing to retinal fluid accumulation and choroidal vasodilation [24]. Sometimes, side effects may lead to central serous chorioretinopathy (CSCR) [24]. As a result, mineralocorticoid receptor (MR) therapeutics may be safer and targeted for long-term management of DME and DR cases [24].

**Table 2.** Summary for Corticosteroid agents for DR/DME [27] [28].

Corticosteroid	Injection Frequency	Pearls
Triamcinolone acetonide	Every 3 months; injection	Used off-label; effective in anti-VEGF resistant DME
Dexamethasone	Every 3 - 6 months (Ozurdex implant)	Effective for chronic DME; FDA-approved
Fluocinolone acetonide	Once every 3 years (Iluvien implant)	Effective for chronic DME; FDA-approved

3.3. Clinical Trials in Progress

Future directions for treating diabetic eye diseases continue to focus on developing additional biologic drugs, particularly in increasingly complex disease settings. One ongoing Phase 1b clinical trial aims to assess the safety of escalating doses of a novel intravitreal drug in DME secondary to non-proliferative DR [29]. Additional recent studies, such as the HORNBILL trial, investigate the tolerability of intravitreal injections of a novel drug in patients with DR complicated with diabetic macular ischemia [30].

4. Disparities and Access to Treatments

While anti-VEGF therapies are safe and effective in preventing vision impairment in patients with DR and DME, intravitreal drugs such as these must be injected into the vitreous cavity of the eye by a professional [2]. Dosing regimens are typically more frequent in the first several doses, such as faricimab, which may be

administered once every 4 weeks for at least 4 doses, then every 4 to 8 weeks, or even every 16 weeks, based on visual assessment [31]. The invasive nature of the injectable drug may contribute to non-adherence or undertreatment. Some trials suggest that alternative dosing regimens with extended intervals of at least 12 weeks may alleviate this treatment burden [26].

With anti-VEGF therapy, the time and resources necessary to attend frequent in-office visits may pose further barriers to access for patients, especially in rural or underserved communities. Potential adverse effects of VEGF inhibitors include transient increases in intraocular pressure, mild injection-site discomfort despite local anesthesia, and rare but severe cases of infectious endophthalmitis have occurred as well [26].

The cost of anti-VEGF agents varies significantly between those approved by the FDA and those used off-label, so providers may also consider patient-specific factors and published efficacy data when selecting a treatment regimen.

Further limitations include the need for more efficacy data, especially in off-label uses or specific patient subgroups. Many clinical trials exclude enrolling patients who are pregnant or breastfeeding, as well as those who have received eye procedures such as cataract surgery within 3 months of the study [29].

Access to these biological therapies may be limited due to their high cost, frequent dosing requirements, and the need for regular clinic visits. However, early screening and detection of these conditions may help prevent these complications and serve to alleviate the overall burden.

## 5. Multidisciplinary Approach and Screenings

While therapeutic interventions, including anti-VEGF injections and biologic drugs, are essential in treating DR and DME, early detection screenings can directly prevent the onset of these diseases [32]. Early DR and DME are usually asymptomatic, often leading to delayed diagnosis in which retinal damage has already occurred. With routine eye exams, diabetic patients have higher rates of detecting DR and DME before these diseases progress [33]. The American Diabetes Association recommends that patients with type 1 diabetes receive an initial dilated eye examination within five years of diagnosis, while those with type 2 diabetes are encouraged to have proper screening when they are first diagnosed [13] [34]. Follow-up screenings are advised depending on the extent of the disease and risk of progression [32]. These screenings effectively allow early detection of microvascular abnormalities, such as microaneurysms, hemorrhages, or macular thickening, which are key indicators of early retinopathy and macular edema [10].

Patient education is an effective tool that can prevent the onset and advancement of DR and DME. Many patients who are diagnosed with diabetes are unaware that chronically elevated blood glucose levels can impair their vision. They can mistake DR and DME for age-related vision deterioration rather than a direct result of their diabetes. Therefore, it is essential for healthcare providers to emphasize the connection between diabetes and ocular health consistently. In one

study, only 58% of individuals with diabetes indicated that their primary care providers had discussed the importance of regular eye checkups. A similar proportion recalled being informed about how diabetes could impact their vision, and just over half reported they were specifically advised to undergo ophthalmic screening [35]. This study effectively highlights the importance of patient education and awareness. Educational interventions, including community-based programs and pharmacist-led counseling, have been shown to improve screening rates and treatment compliance [36].

A multidisciplinary approach between primary care physicians (PCPs), endocrinologists, optometrists, ophthalmologists, and pharmacists are crucial for comprehensive diabetic control [33]. Primarily, PCPs and endocrinologists contribute by regularly monitoring patients' glucose levels, blood pressure, and cholesterol levels, which are key risk factors in the development of diabetes and diabetic eye diseases [15] [34]. Specifically, Hemoglobin A1c (HbA1c) is an effective marker for assessing a patient's long-term glycemic control, as it is strongly correlated with the onset and progression of DR [16]. Studies such as the Diabetes Control and Complications Trial (DCCT) demonstrate that maintaining HbA1c levels below 7% significantly reduces the risk of retinal complications [6]. With annual lab work, healthcare providers will be better informed of a patient's risk of diabetes and can effectively intervene.

Additionally, uncontrolled hypertension promotes capillary leakage and ischemia. Blood pressure control, particularly maintaining systolic blood pressure below 140 mmHg, has been shown to reduce the incidence and severity of DR [6]. Hyperlipidemia (HLD) may also play a role in the progression of diabetic eye diseases [15]. Although additional large-scale clinical trials are needed to investigate the direct relationship between lipids and diabetic eye diseases, several findings have shown that elevated serum lipids are associated with an increased risk of complex exudate formation and clinically significant macular edema [37]. By managing blood pressure and lipid levels, especially LDL cholesterol, providers can reduce the risk of retinal complications [38]. When patients are diagnosed with DR and DME, they are referred to optometrists who serve as the primary point of contact for advanced eye care. Through comprehensive dilated eye exams and advanced imaging techniques, including optical coherence tomography (OCT) and fundus photography, they assess the severity of the disease, the patient's current ocular health, and potential treatment plans [32]. Additionally, optometrists educate patients on the importance of glycemic control, blood pressure management, and lipid regulation to prevent disease progression [32]. They send referrals to ophthalmologists when vision-threatening pathology is present [13].

Ophthalmologists are specialists who use anti-VEGF injections and gene therapy to treat more advanced cases of DR and DME [39]. Pharmacists also play a crucial role in managing diabetes by reviewing medications, facilitating the interactions between different drugs, and providing patient education [40]. A clinical study investigating the role of pharmacists in managing patients' diabetes discov-



ered that pharmacist interventions helped reduce HbA1C levels by 0.76% across 2073 participants [41]. Additionally, a meta-analysis comprising 22 studies revealed a statistically significant decrease in HbA1c of 0.85%, suggesting that pharmacists can actively reduce the risk of diabetes and diabetic eye diseases [41]. Moreover, pharmacists play a key role in monitoring potential side effects of emerging therapies, including increased intraocular pressure and endophthalmitis [42]. As novel therapies continue to expand, pharmacists also help patients select the optimal treatments, considering efficacy, availability, and cost. A common misconception among patients is that community pharmacists are not certified to provide additional care related to their treatment. It is essential that this misunderstanding be addressed and corrected to improve patient outcomes.

## 6. Conclusion

Diabetes remains a significant factor in adult-onset blindness despite improvements in diabetes management [16]. Regular screening leads to early detection and preventions of DR and DME, allowing for timely treatment options [16]. Anti-VEGF therapy is a cornerstone in treating retinal disease and can significantly preserve or improve vision [43]. However, it carries potential ocular and systemic risks [43]. As a team, ophthalmologists, pharmacists, and healthcare providers should carefully weigh these benefits and risks and monitor the patient accordingly. Biologic therapies continue to play an essential role in this, as many manufacturers are working to develop therapies that benefit patients by minimizing the burden and restoring visual acuity [1]. Corticosteroids serve as a key therapeutic option due to their anti-inflammatory effects, which reduce the production of inflammatory mediators [25]. The combination of both anti-VEGF and corticosteroid therapy may lead to a new, broader approach to therapy [25], continuing to mark a transformative era in diabetic eye care, innovations and emerging therapies may offer hope for preserving vision and patient's quality of life. The combination of therapy management and a multidisciplinary approach to early screening may serve as a pivotal intervention in preventing irreversible damage and disease progression.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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