

# Diabetic Retinopathy: Current Treatment and Thailand Perspective

Sukhum Silpa-archa MD\*,  
Paisan Ruamviboonsuk MD\*

\* Department of Ophthalmology, Faculty of Medicine, Rajavithi Hospital, College of Medicine, Rangsit University,  
Bangkok, Thailand

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*Diabetes mellitus is a common and chronic metabolic disorder involving multiple organ systems. Major eye involvements include diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR). With a significantly increasing global number of cases of diabetes and the tendency towards an aging population, sight-threatening diabetic retinopathies are expected to increase from 37.3 million in 2011 to 56.3 million worldwide by 2030. Besides good glycemic and metabolic disease control, appropriate diabetic retinopathy (DR) screening and prompt treatments are crucial in order to minimize visual impairment from DR. The first-line therapy of DME is anti-vascular endothelial growth factor while panretinal photocoagulation laser remains the main treatment for PDR. Fortunately, in Thailand, these conditions have been included in the fundamental rights to eye care treatment, though an extension of geographic coverage and equal accessibility to care is needed. The Ministry of Public Health of Thailand has recently launched an area health initiative named the Service Plan, integrating 13 centers of excellence for certain specialties. As one of the 13 specialties, ophthalmic care includes centers of excellence in retina diseases. The policy implementation is aimed at drastically reducing preventable visual impairment resulting from various retinal diseases.*

**Keywords:** Diabetes, Diabetic retinopathy, Diabetic macular edema, Anti-vascular endothelial growth factor, Laser, Service plan, Screening

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Diabetes mellitus is a chronic illness with complex pathophysiology leading to multiple macrovascular and microvascular complications. Owing to people's longer life expectancy and increasingly unhealthy lifestyles, the prevalence of diabetes has been soaring, rising from 108 million adults (4.7%) in 1980 to 422 million (or 8.5% of the population) in 2014, with most of these living in developing countries<sup>(1)</sup>. As such, the complications commonly following diabetes are increasing in number. Diabetic retinopathy (DR), the second most common microvascular complication of diabetes<sup>(2)</sup>, can seriously threaten quality of life because for human beings, up to 80% of all information received from the outside world is processed through the visual pathway<sup>(3)</sup>. Together with uncorrected refractive error and cataract, which are modifiable

causes, DR has been ranked as a major cause of global blindness<sup>(4)</sup>. The reported global prevalence of DR has varied due to the different setting and designs of the studies which have been performed. Yau et al recently conducted a systematic review of 35 population-based studies revealing that the prevalence rates of DR, proliferative diabetic retinopathy (PDR), diabetic macular edema (DME), and vision-threatening diabetic retinopathy (VTDR) among individuals with diabetes were 34.6%, 7.0%, 6.8% and 10.2% respectively<sup>(5)</sup>. It is feared that the global number of patients with DR could possibly grow from 126.6 million in 2011 to 191.0 million by 2030 while the number of cases of VTDR may increase from 37.3 million to 56.3 million if no urgent action is taken<sup>(6)</sup>. In Thailand, the prevalence of DR is 24-31% in type 2 diabetes, comprising 21-23% non-proliferative diabetic retinopathy (NPDR) and 2.3-9.4% PDR<sup>(7-10)</sup>.

Though diabetic treatment is continuously evolving, the treatment outcomes regarding blood sugar control and complications prevention in Thailand have been suboptimal<sup>(11)</sup>. The proportion of patients following hemoglobin A1c (HbA1c) testing annually

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**Correspondence to:**

Silpa-archa S, Department of Ophthalmology, Faculty of Medicine, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok 10400, Thailand.

Phone: +66-2-3548108 ext. 2221, Fax: +66-2-2062946

E-mail: [sisukhum@gmail.com](mailto:sisukhum@gmail.com)

has reached only 77.6%<sup>(2)</sup>. Though the American Diabetes Association encourages individuals with diabetes to keep their HbA1C at 7.0% or less, only one third of diabetic patients achieve those levels<sup>(12)</sup>. Lowering HbA1c levels in people with type 1 and type 2 diabetes results in lower incidence and reduced severity of DR<sup>(13-17)</sup>. DR can cause deterioration of visibility in three ways: DME; retinal neovascularization (NV) and sequel; and macular ischemia. Macular laser photocoagulation, a classic treatment modality of DME which provides only visual stabilization, has been superseded by anti-vascular endothelial growth factor (anti-VEGF), a new drug which provides visual improvement with reliable outcomes<sup>(18)</sup>. At certain degrees of NV in PDR, patients have been treated with full panretinal photocoagulation as the standard regimen to prevent severe visual loss<sup>(19)</sup>. Alternative treatments for DME include local corticosteroid injections and novel implantable devices. This review has two aims: (1) to summarize the current regimen of DR treatment according to global trends; and (2) to identify the current status and treatment policy of DR, including an economic perspective in Thailand.

## Material and Method

A literature search was performed on the PubMed database from 1979 to April 2016. Search terms included “diabetic retinopathy”, “diabetic macular edema”, “proliferative diabetic retinopathy”, “diabetic retinopathy in Thailand”, “diabetes”, “diabetes in Thailand”, “anti-VEGF”, “bevacizumab for diabetic macular edema”, “ranibizumab for diabetic macular edema”, “triamcinolone for diabetic macular edema”, “dexamethasone Intravitreal Implant for diabetic macular edema”, “panretinal laser photocoagulation”, “age-related macular degeneration”, “cost analysis of diabetic macular edema”, “visual impairment”, “visual impairment in Thailand”, “economic burden of blindness”, “cost of blindness”, “cost of diabetes”, and “cost of diabetic retinopathy”. In addition, policy and global report data were obtained from the official websites of the World Health Organization, the National Health Security Office, The World Bank, the International Diabetes Federation, and the World Diabetes Foundation through Google’s search engine. Inclusion criteria were any relevant articles in English or Thai published up to April 2016, with preference given to articles published in the last 10 years.

## Current treatment of diabetic retinopathy

Diabetic retinopathy can be categorized into

nonproliferative (NPDR) and proliferative diabetic retinopathy, and both patterns can be seen with DME. Patients with NPDR without center-involved DME (CDME) are generally asymptomatic and need only regular follow-up while those who have the proliferative level and/or CDME should receive appropriate interventions. Examination of the fundus with slit-lamp biomicroscopy or indirect ophthalmoscopy for DME has been a standard procedure in grading edematous levels<sup>(20)</sup>. The evolution of optical coherent tomography (OCT) over the past decade from time-domain to spectral-domain integrating with confocal scanning laser ophthalmoscopy fundus imaging has rendered OCT reliable and resulted in its becoming the standard modality of choice in evaluation of DME with quantifiable outcomes<sup>(21-24)</sup>. This part of the review focuses on updates to the current therapeutic options for DR-related visual impairment conditions: DME and PDR, including medical and surgical intervention.

## Diabetic macular edema

### First-line therapy:

After the establishment of the Early Treatment in Diabetic Retinopathy Study (ETDRS), a classic and landmark study of DR treatment, laser photocoagulation became a mainstay treatment for DME before the modality of laser treatment was modified to minimize laser-related complications<sup>(25)</sup>. However, the outcome of such therapy ensured only maintenance of visual acuity without significant improvement of vision<sup>(26-28)</sup> until the dawn of a new treatment by antiangiogenic drugs, which yielded a greater benefit than grid laser photocoagulation. The efficacy of anti-VEGF in restoring vision in CDME has been proven<sup>(18)</sup>. Ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA), a humanized recombinant monoclonal antibody fragment, was the first anti-VEGF officially approved by the US FDA for DME in 2012. Numerous major randomized control trials have certified the usefulness and safety of ranibizumab in DME patients<sup>(29-33)</sup>. However, the cost of ranibizumab is beyond the reach of the resources available in real-world healthcare scenarios. Bevacizumab (Avastin, Genentech Inc., San Francisco, CA) is a full-length humanized monoclonal antibody which has similar mechanisms of actions to those of ranibizumab. Despite its off-label status, it has become the most popular anti-VEGF for CDME around the world because of its cheaper price, parallel efficacy and safety compared to ranibizumab<sup>(34-36)</sup>. Aflibercept (Eylea, Regeneron-Bayer HealthCare), a fully human soluble recombinant decoy

vascular endothelial growth factor (VEGF) receptor or VEGF-trap, is a novel compound which blocks VEGF with an affinity stronger than that of ranibizumab and bevacizumab. The US FDA recently officially approved intravitreal aflibercept injection for DME treatment. Table 1 demonstrates the therapeutic options of DR in Thailand, including details of US FDA approval, coverage of health care system, cost per treatment and indicative role. Diabetic Retinopathy Clinical Research (DRCR) funded by the United States government's National Eye Institute was established in 2002 to implement multicenter clinical research initiatives focused on diabetes-induced retinal disorders. Recent data from DRCR did not show any clinically significant differences between bevacizumab, ranibizumab and aflibercept in treatment of CDME<sup>(34)</sup>. Moreover, laser photocoagulation has been outshone by ranibizumab injections in the latest report which found no difference between ranibizumab with early and deferred (>6 months) laser treatment groups<sup>(32)</sup>.

#### ***Second-line therapy:***

Corticosteroids are considered to be a reliable therapy for DME. Two routes of corticosteroids are useful in DME treatment: intravitreal triamcinolone injection (IVTA) and implantable corticosteroid devices<sup>(37-41)</sup>. They have proven to be useful in certain cases of DME: refractory/chronic DME, contraindication for anti-VEGF or VEGF-trap such as a recent arterial thromboembolic event<sup>(37,38,42-44)</sup>. IVTA has limited use in pseudophakic patients with common complications such as cataract and glaucoma<sup>(45)</sup>. The novel intravitreal sustained-release corticosteroids implant has proved to be a promising strategy for DME in providing substantial visual benefit for up to 3 years<sup>(39-41)</sup>. There are two options for sustained-release corticosteroid implants approved by the US FDA for DME treatment: Ozurdex (Allergan Inc., Irvine, CA), a biodegradable implant, which releases dexamethasone to the vitreous cavity over a six-month period; and a non-biodegradable cylindrical tube that releases fluocinolone acetonide for up to 3 years (Iluvien, Alimera Science, Alpharetta, GA). Though Ozurdex has a shorter duration of treatment than Iluvien, it has shown reliable efficacy with an acceptable rate of complications and is the only sustained-release implant available in Thailand<sup>(46,47)</sup>. However, given the risk of visual impairment from cataracts, glaucoma and intraocular infection with the use of intravitreal steroids, Ozurdex tends to be backlogged for use in patients poorly responsive to anti-VEGF therapy for CDME.

#### ***Proliferative diabetic retinopathy***

Since first reporting in 1978, the diabetic retinopathy Study (DRS) has highlighted the significant role of laser photocoagulation in the substantial reduction of severe visual loss for high-risk PDR cases. Later, in 1991, the Early Treatment in Diabetic Retinopathy Study (ETDRS) emphasized the effectiveness of laser treatment and retreatment protocols in PDR<sup>(48-50)</sup>. Since then, panretinal laser photocoagulation (PRP) has become the standard treatment for high-risk PDR or conditions approaching high risk, and it is also recommended by the American Academy of Ophthalmology's Preferred Practice Pattern for Diabetic Retinopathy<sup>(20)</sup>. As a result, retinal photocoagulation lasers have been made available in eye care services around the world. However, some limitations of laser treatment persist, for example, in dense, nonclearing vitreous hemorrhage, traction retinal detachment involving macula, combined tractional and rhegmatogenous retinal detachment, etc<sup>(51,52)</sup>. These conditions need vitrectomy interventions which help to clear up hazy vitreous hemorrhage and release vitreoretinal tractions to reattach retina. Interestingly, recent studies have revealed that patients with DME treated with ranibizumab were found to have reduced risk of DR progression and regression<sup>(27)</sup>. A recent report performed by DRCR showed the non-inferiority of ranibizumab to PRP for PDR therapy in terms of mean visual acuity letter improvement while, compared to the ranibizumab group, the PRP group had significantly higher rates of peripheral visual field sensitivity loss, vitrectomy and DME development<sup>(53)</sup>. Another advantage of anti-VEGF injection is that it is time-saving which may make it helpful and feasible for treating PDR patients needing anti-VEGF injection in settings with long waiting lists for laser treatment.

The use of pre-or intraoperative bevacizumab is also indicated to reduce early postoperative vitreous hemorrhage. Moreover, patients treated with a combination of bevacizumab and vitrectomy are more likely to gain 3 or more lines of visual acuity<sup>(54,55)</sup>. Nevertheless, laser photocoagulation remains the mainstay PDR treatment if there are no indications for surgery, while the role of anti-VEGF for PDR still needs to be evaluated in long-term follow-up and to undergo risk-cost-benefit analysis.

#### ***DR status and policy in Thailand***

Thailand is a developing Southeast Asian country with an upper middle income level, and it has a population of 67 million people with gross domestic

**Table 1.** Therapeutic options of diabetic retinopathy in Thailand: coverage of health care system, Cost per treatment and indicative role

Diseases	Treatments available in Thailand	US FDA approval for DME/PDR	National drug lists	Thai health scheme coverage <sup>a</sup>	Cost per treatment <sup>b</sup> in US\$ <sup>c</sup>	Indicative role
DME	IVT Bevacizumab	N	ED	UC (6 injections per year) SS, CS (unlimited)	23 <sup>d</sup>	First line
	IVT Ranibizumab	Y	NED	CS	1,518 <sup>d</sup>	First line
	IVT Aflibercept	Y	NED	CS	1,503 <sup>d</sup>	First line
	IVT Triamcinolone	N	ED	UC, SS, CS	2 <sup>d</sup>	Second line
	Dexamethasone implant	Y <sup>e</sup>	NED	CS	1,355 <sup>d</sup>	Second line
	Laser photocoagulation	Y	-	UC, SS, CS	106 (any types)	Second line for CDME
PDR	Laser photocoagulation	Y	-	UC, SS, CS	106 (any types)	First line for NCDME
	Vitrectomy	Y	-	UC, SS, CS	639-927 <sup>f</sup>	First line (if indicated)
	IVT Bevacizumab	N	ED	SS, CS	23 <sup>d</sup>	Second line/adjunct for vitrectomy
	IVT Ranibizumab/ Aflibercept	N	NED	CS	As above	Second line/adjunct for vitrectomy

<sup>a</sup> Coverage of UC and CS are universal among government hospitals while SS coverage depends on local hospital committees

<sup>b</sup> Price list of department of pharmacy and operating room department, Rajavithi Hospital on April, 2016

<sup>c</sup> Exchange rate 1 US\$ = 33 THB

<sup>d</sup> Does not include procedure fee

<sup>e</sup> For use in adult patients with diabetic macular edema who have had an artificial lens implant or are scheduled for cataract surgery

<sup>f</sup> Average rate of vitrectomy package including tamponade agents and 3-day hospitalization

DME = diabetic macular edema; PDR = proliferative diabetic retinopathy; IVT = intravitreal injection; ED = essential drugs; NED = non-essential drugs; UC = universal healthcare coverage; SS = social security scheme for employees; CS = civil servant medical benefit scheme; CDME = center involved diabetic macular edema; NCDME = non-center involved diabetic macular edema

product of US\$ 404 billion. Health expenditure per capita has been soaring, increasing from US\$ 124 in 2005 to US\$ 360 in 2014<sup>(56)</sup>. After the 4<sup>th</sup> national eye survey in 2006, the 5<sup>th</sup> Thailand national program for prevention of blindness was conducted in a Thai population aged 50 years or older and reported by Isipradit et al in 2014. The current burden of blindness is estimated at 100,532 people (0.6%), while low vision is estimated at 2.2 million (13.9%). DR is the third most common cause of blindness (5.1%) behind untreated cataract (69.7%) and non-specific posterior segment disorders (6.1%), and ahead of glaucoma and corneal opacity. Furthermore, among the leading causes of blindness, DR is the only cause related to a systemic and chronic disease i.e. diabetes mellitus<sup>(57)</sup>. The National Health Security Office annual report of 2014 revealed that the eye screening rate of type 2 DM patients was 75.5% in the fiscal year 2010-2014<sup>(2)</sup>. As mentioned above, the increasing number of cases of VTDR raises a major concern amidst rising numbers of DM patients with suboptimal glycemic control, longer life span and increasingly unhealthy diet.

#### ***Screening policy and service plan for DR Screening program:***

The screening program for DR in Thailand has been introduced because of the fact that there are not enough ophthalmologists to perform eye examinations to detect DR in patients with diabetes. There are approximately 1,300 ophthalmologists in Thailand compared with approximately 4,000,000 patients with diabetes. In addition, the majority of patients live in areas where their community hospitals have no ophthalmologists, and they have to travel 100 kilometers on average to be examined for DR checkup. Before the establishment of national DR screening programs, the average level of DR screening was just 30.0% for the whole country.

The program focuses on forming DR screening units in communities. The unit includes a retinal camera and a team of community non-physician health care personnel with different tasks: a retinal image capturer and reader, vision screener, data manager and general manager. For non-physician personnel, a comprehensive instruction course with specific continuing education is essential to achieve reliability in grading and to maintain their expertise<sup>(58)</sup>. The Excellence Center for Retinal Diseases at Rajavithi Hospital has played an important role in training personnel in the unit. Two-day training courses for DR Management are conducted to train personnel from all

parts of Thailand in vision screening, retinal image capture and interpretation as well as data management to detect DR for referral to ophthalmologists.

A web-based application has also been created to provide additional self-learning and consultation. The web-based application is also used for quality control of screeners who are required to log in to read 50 retinal images and interpret each of them as “Referral” or “Non-referral”. After that, trainers are able to log in to assess the sensitivity of the trainees. The required level of sensitivity and specificity of the trainees is 80%.

For treatment of the referrals, the National Health Security Office of Thailand has provided a budget for laser treatment on indicated patients. In addition, bevacizumab is also approved in the Thai National List of Essential Medicine (NLEM). This policy has successfully assisted in driving the DR screening program.

The Ministry of Public Health of Thailand (MoPH) has also included DR management in their Service Plan policy (see below). The DR screening rate among patients with diabetes is currently one of the Key Performance Indicators (KPI) of success in national ophthalmic care. The KPI for DR screening for the whole country is currently set at 60% and is expected to increase by 5% each year. The KPI for DR treatment is also expected to rise in the future.

#### ***Service plan:***

In the past, failures in the health care system in Thailand brought about major problems regarding inequality of efficacy and quality of service, with an disorganized inter-area referral system causing overcrowding in tertiary care hospitals. To alleviate these concerns, the MoPH has been implementing a health initiative, the Service Plan, by geographically dividing service areas into 12 regional MoPH areas (service plan) with a seamless health service network. Each zone is designated to be fully organized at primary, secondary and tertiary care levels, integrating with centers of excellence for certain specialties. The eye service has been included as one of the 13 specialties.

The ultimate goal of this policy for ophthalmic care is to have at least one well-established retinal center in each region. The center should have at least 2 retinal specialists with full equipment for performing most kinds of retinal diagnosis and treatment including retinal surgery. Apart from DR management, the center will also focus on prevention of childhood blindness due to retinopathy of prematurity, another leading cause of



blindness of Thailand.

The recent strategy of the service plan in Thailand is a collaborative effort between the MoPH and Ministry of Education which has led to a memorandum of understanding (MOU) being signed between the 2 ministries to establish national centers of medical excellence in different regions of the country. Medical schools all over Thailand have collaborated with regional hospitals in different areas to set up the centers. Centers of excellence in retina diseases are expected to be established and management of DR as well as other essential retina diseases will be increasingly focused on in the future.

#### ***DR and the health economic burden in Thailand***

From a health economics perspective, total health expenditure includes direct medical costs, direct non-medical costs and indirect costs. Interestingly, direct medical costs, including all costs from resources attributable to the use of a health care intervention or illness, are outweighed by direct non-medical costs (transportation and additional paid caregiver time), and indirect costs (caused by morbidity and productivity losses)<sup>(59)</sup>. Thus the social and financial costs of visual impairment and blindness are significant not only to those directly affected and their families, but also to communities and entire countries<sup>(60)</sup>. Direct medical costs are generally estimated more precisely than indirect ones. Chatterjee et al conducted a diabetes care cost analysis in Thailand and demonstrated that diabetic patients with complications cost three times as much (USD 480, 1 USD = 32 Thai Baht) as diabetic patients without complications (USD 115). The expenditure on DM with microvascular complications per capita, including DR, diabetic nephropathy and diabetic neuropathy, (USD 641) was almost twice as much as that of DM with macrovascular complications (USD 366)<sup>(59)</sup>.

Regarding eye perspective, AMD has been the only retinal diseases with cost analysis data. The study, aimed at determining healthcare resource utilization and the economic burden of patients with AMD in Thailand, revealed that the average direct and non-direct medical costs were US\$ 3,604±4,530 and US\$ 2,920±6,560 per year respectively<sup>(61)</sup>. However, although AMD treatment options are primarily anti-VEGF like DME, patients' characteristics in the study did not reflect the real situation of AMD treatments in public health facilities in Thailand given that the research was carried out in a university-affiliated hospital and the ratio of ranibizumab-treated

patients to bevacizumab-treated patients was 1.77. As a result, direct medical costs reported in the study seemed higher than direct non-medical costs. Although many researchers have revealed results of epidemiologic studies of visual impairment/blindness including the prevalence of DR in Thailand, information about the economic costs of DR has been lacking. While it may be difficult to discriminate the eye cost from total diabetes health-care cost, given that diabetes is a metabolic problem that affects multiple systems in people with diabetes<sup>(62,63)</sup>, the study of the economic impact of visual impairment and cost-benefit analysis of the interventions seems more feasible and appears necessary.

#### ***Accessibility to standard treatments of DR and inequalities***

The Thailand government health insurance system includes three major schemes: universal healthcare coverage (UC), the social security scheme (SS), and the civil servant medical benefits scheme (CS). Table 2 demonstrates the characteristics of government health insurance schemes as updated in 2014<sup>(2,64)</sup>.

As the most comprehensive coverage, UC for all Thai citizens has increased from 71% in the fiscal year 2001 to 99.8%, covering 48 million people, in the fiscal year 2014. However, UC has not eliminated problems with quality of care and access to specific services, particularly with regard to preventive and self-management services. Rajavithi Hospital is a major referral center for ophthalmology in the central region of the Thai public health system, catering mostly for patients in the UC government health insurance scheme. Regarding the proportion of access to eye care services in this setting, the author recently reported the epidemiology of uveitis patients visiting outpatient service at 60% for UC<sup>(65)</sup>. As for disabled people registered to the UC scheme, 11.3% of 1,127,097 cases had blindness or low vision<sup>(2)</sup>.

Regarding the right to access standard DR treatment, people under all schemes have been allowed unlimited access to laser retinal photocoagulation treatments for DR, and the procedure has been generally available countrywide<sup>(66)</sup>. Luckily, the standard treatment of anti-VEGF injections has also been permitted and included in the NLEM, which is available to all three government health insurance schemes. For people under UC, there are some limitations: (1) this includes only DME, not PDR or surgical interventions of DR; (2) the sole anti-VEGF covered is bevacizumab; and (3) a limited number of injections per year is allowed,

**Table 2.** Characteristics of government health insurance schemes

Insurance scheme	Population coverage	Coverage percentage (number)	Financing source	Access to service
Civil servant medical benefit scheme	Government employees plus dependents (parents, spouse and up to two children age <20)	7.4% (4.83 million)	General tax, non-contributory scheme	Free choice of public providers, no registration required
Social security scheme	Private sector employees, excluding dependents	16.9% (11.07 million)	Tripartite contribution, equally shared by employer, employee and the government	Registered public and private competing contractors
Universal healthcare coverage	The rest of the population not covered by CS and SS	73.8% (48.31 million)	General tax	Registered contractor provider, notably district health system

whereas people under SS and CS can obtain unrestricted indications of bevacizumab (Table 1). Accepted worldwide for preparation with off-label usage for DME and age-related macular degeneration (AMD), bevacizumab, primarily licensed for metastatic colorectal cancer, has been repackaged in small single-use syringes for intravitreal use by compounding pharmacies. In sterile conditions, it has been found to be stable for 3-6 months at 4°C, and for 7 days at room temperature in terms of activity, microbial contamination and physico-chemical stability. However a significant decrease in anti-VEGF activity was detected when syringes were exposed to UV light at a temperature of 37°C<sup>(67-69)</sup>. Though improving visual acuity, the drawback of the new injection therapy is its unequal accessibility and the necessity for the injected patient to follow up monthly after injection for at least the first three months, whereas laser treatment would require just a single 3-4 months' follow-up visit after treatment. The frequent visits are also major concerns for needy people, most of whom are in the UC scheme, as they involve repeat transportation and caregiver fees.

People suffering from AMD, another valid indication for bevacizumab, are eligible for 12 injections over one year in the UC scheme. Although both the percentage of all degrees of visual loss (blindness, severe visual loss, moderate visual loss) in DME patients<sup>(57)</sup> and the number of DME patients in need of bevacizumab administration were reportedly higher

than those of AMD sufferers<sup>(70)</sup>, patients with DME are allowed to receive bevacizumab administration only 6 times per year while AMD patients are eligible for 12 injections of bevacizumab per year if the stipulated indications are fulfilled. In addition, recent data from Maguire et al showed that anti-vascular endothelial growth factor treatment in AMD patients for 5 years failed to maintain vision gains during the first 2 years or even vision at baseline, while patients with CDME maintained vision gains obtained by the first year for 5 years with little additional treatment after the first 3 years<sup>(32,65)</sup>. As a result, UC diabetic patients whose vision is threatened by DME or non-approved conditions (vitreous hemorrhage and tractional retinal detachment), have to face out-of-pocket expenses after they have received 6 bevacizumab injections. Another DME therapeutic option included in NLEM is unlimited access to IVTA injection which is approved for treatment of refractory DME. However, because of the potential for cataracts and glaucoma, the use of IVTA should be limited and patients who receive such treatment should be closely monitored on a regular basis.

The other available DME treatments not included in NLEM encompass first-line DME treatments (ranibizumab and aflibercept) and second-line treatments (surgically implantable corticosteroids devices (Ozurdex)). These are considered non-essential treatments given that they are much more expensive

licensed drugs, approximately 50 times more costly per treatment than bevacizumab (Table 1). Thus, patients with diabetes under the UC and SS schemes are not eligible for these options. Nevertheless, these regimens are allowable for patients under the CS scheme who meet the specified indications. Furthermore, decisions regarding medicine registration into hospital drug lists are individual since local authorities play a role in selection decisions. Drug items such as bevacizumab are not included in some major state-owned hospitals' drug lists regardless of the availability of retinal specialists. As a result, some users divide the original volume of ranibizumab into smaller aliquots to be used for several patients, with satisfactory safety records. Hopefully, a UC expansion of bevacizumab indications will be considered, and all diabetic patients that need to be treated but are unable to afford the costly alternative drugs will be able to receive these effective treatments in order to prevent blindness.

### Conclusion

Diabetic retinopathy remains a major concern as one of the leading causes of preventable blindness. To prevent vision-threatening sequelae, adequate control of glycemic levels in line with other metabolic problems, blood pressure control, appropriate DR screening and prompt DR treatment are necessary. Overall, the national ophthalmic care included in Thailand's health policy has covered comprehensive management of DR nationwide, although extension of geographic coverage and equal accessibility of the care need to be implemented. A well-established Service Plan integrated with centers of excellence in retina diseases equipped with retinal specialists will bring about a brighter future in the reduction of blindness caused by various retinal diseases nationwide.

### What is already known on this topic?

As the prevalence of diabetes has been soaring, the prevalence of sight-threatening diabetic retinopathies is expected to reach 56.3 million worldwide by 2030.

The first-line therapy of diabetic macular edema is anti-vascular endothelial growth factor while panretinal photocoagulation laser remains the main treatment for proliferative diabetic retinopathy.

### What this study adds?

In Thailand, anti-vascular endothelial growth factor therapy has been diversely covered by different government-sponsored health insurance schemes. The

conditions which need to be fulfilled in order to receive treatment are also different depending on patients' health scheme, treatment setting and clinical practice guidelines.

The Ministry of Public Health of Thailand has also included diabetic retinopathy management in their Service Plan policy, integrating with centers of excellence in retina diseases, and this will help to bring about a brighter future in reduction of blindness caused by various retinal diseases nationwide.

### Potential conflicts of interest

None.

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## ภาวะเบาหวานขึ้นจอตา: มาตรฐานการรักษาในปัจจุบัน และสถานการณ์ในประเทศไทย

สุขุม ศิลปอาชา, ไพศาล ร่มวิบูลย์สุข

เบาหวานเป็นโรคทางเมตาบอลิซึมที่พบบ่อยและเกี่ยวข้องกับอวัยวะสำคัญในร่างกายหลายระบบรวมถึงดวงตา โรคทางตาที่เกิดขึ้นจากเบาหวานที่สำคัญได้แก่ ภาวะจลรัศัภาพบวม และเบาหวานขึ้นจอตาชนิดมีเส้นเลือดงอกใหม่ ซึ่งทั้งสองภาวะทำให้สูญเสียการมองเห็น และมีแนวโน้มจะเพิ่มขึ้นตามความชุกของโรคเบาหวานที่เพิ่มขึ้น โดยอาจเพิ่มขึ้นถึง 56.3 ล้านคนทั่วโลกในปี พ.ศ. 2574 ทั้งนี้ นอกเหนือจากการคุมระดับน้ำตาลและโรคเมตาบอลิซึมอื่นให้ดีขึ้นแล้ว การตรวจคัดกรองภาวะเบาหวานขึ้นจอตา และการรักษาอย่างทันต่วงที่ก็มีความจำเป็นในการป้องกันภาวะสายตาสั้นเลือนรางที่จะเกิดขึ้น การรักษาภาวะจลรัศัภาพบวมจากเบาหวานในปัจจุบันใช้การฉีด Anti-vascular endothelial growth factor ส่วนการรักษาภาวะเบาหวานขึ้นจอตาชนิดมีเส้นเลือดงอกใหม่มักยังใช้การยิงเลเซอร์ Panretinal photocoagulation ในประเทศไทยสิทธิการรักษาของรัฐบาลครอบคลุมถึงการรักษาทั้ง 2 วิธีนี้ แม้จะยังไม่ทั่วถึงเท่าที่ควร ขณะนี้กระทรวงสาธารณสุขไทยได้ริเริ่มแผนการจัดระบบบริการสุขภาพ (Service Plan) โดยแบ่งเขตสาธารณสุขเป็น 13 เขตทั่วประเทศ มีการจัดตั้งศูนย์ความเป็นเลิศในหลากหลายสาขาการแพทย์ ซึ่งรวมถึงศูนย์ความเป็นเลิศทางจักษุและจอประสาทตา ที่มีนโยบายในการป้องกันภาวะสายตาสั้นเลือนรางและตาบอดอันมีสาเหตุหลักมาจากโรคทางจอตา

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