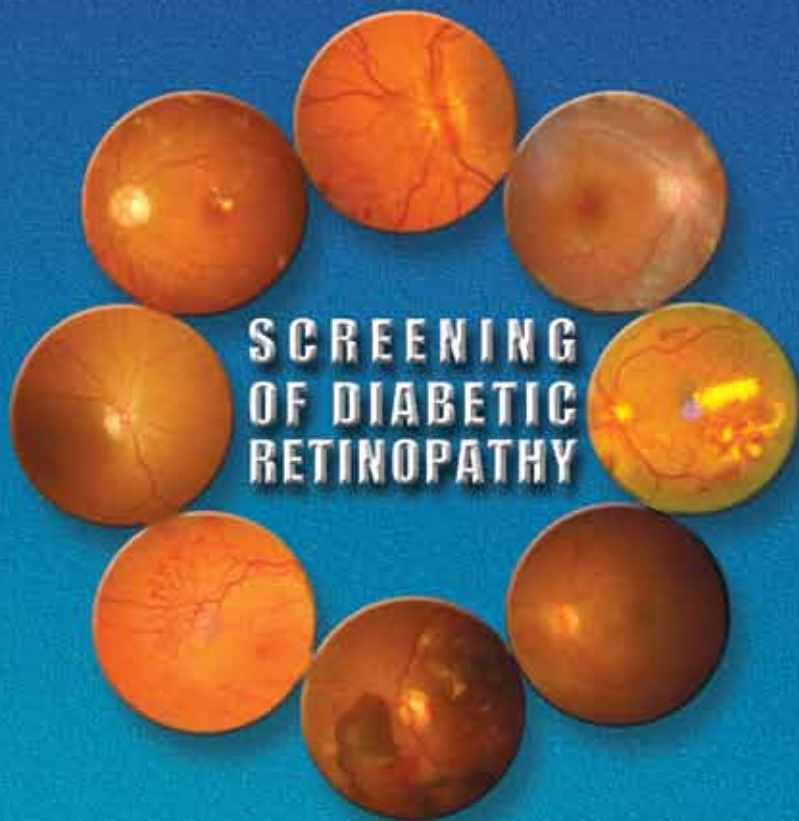


# CLINICAL PRACTICE GUIDELINES

JUNE 2011

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MINISTRY OF HEALTH  
MALAYSIA



MALAYSIAN SOCIETY OF  
OPHTHALMOLOGY



ACADEMY OF MEDICINE  
MALAYSIA

## STATEMENT OF INTENT

These clinical practice guidelines (CPG) are meant to be guides for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

These guidelines were issued in 2011 and will be reviewed in 2015 or sooner if new evidence becomes available.

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<http://www.moh.gov.my>

<http://www.acadmed.org.my>

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## LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II -1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

SOURCE: US / CANADIAN PREVENTIVE SERVICES TASK FORCE

## GRADES OF RECOMMENDATION

<b>A</b>	At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population
<b>B</b>	Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT
<b>C</b>	Evidence from expert committee reports, or opinions and / or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality

SOURCE: MODIFIED FROM THE SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK (SIGN)

Note: The grades of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

# GUIDELINES DEVELOPMENT AND OBJECTIVES

## GUIDELINES DEVELOPMENT

The Development Group for these Clinical Practice Guidelines (CPG) was from the Ministry of Health (MOH) and Ministry of Higher Education. They consisted of ophthalmologists, a paediatrician, an obstetrician & gynaecologist, a public health physician, a family medicine specialist, an optometrist, an assistant medical officer and a nursing sister. There was active involvement of the Review Committee during the process of development of these guidelines.

Literature search was carried out at the following electronic databases: Guidelines International Network (G-I-N); Centre for Reviews and Dissemination (CRD); PubMed; Ovid Medline, EBM Reviews - Cochrane Database of Systemic Reviews, EBM Reviews - Health Technology Assessment, Journals full text via OVID search engine (refer to **Appendix 1** for Search Terms). In addition, the reference lists of all retrieved articles were searched to identify relevant studies. Experts in the field were also contacted to identify further studies. All searches were conducted between September 2009 and January 2011. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Seretariat.

Reference was also made to other guidelines on Diabetic Retinopathy such as The American Academy of Ophthalmology Preferred Practice Pattern Diabetic Retinopathy (2008) and National Health and Medical Research Council (NHMRC) Australia Guidelines for the Management of Diabetic Retinopathy (2008). These CPGs were evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) prior to them being used as references.

The clinical questions were developed under three major subtopics and members of the Development Group were assigned individual questions within these subtopics (refer to **Appendix 2** for Clinical Questions). The group members met a total of 16 times throughout the development of these guidelines. All literature retrieved was appraised by at least two members and presented in the form of evidence tables and discussed during Development Group meetings. All statements and recommendations formulated were agreed upon by both the Development Group and Review Committee. Where evidence was insufficient, the recommendations were made by consensus of both groups. These CPG are based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.

The articles were graded using the US/Canadian Preventive Services Task Force Level of Evidence (2001), while the grading of recommendation in these guidelines was modified from grades of recommendation of the Scottish Intercollegiate Guidelines Network (SIGN).

The draft guidelines were posted on the MOH Malaysia official website for comment and feedback. It had also been presented to the Technical Advisory Committee for CPG and the HTA-CPG Council, MOH Malaysia for review and approval.

## OBJECTIVE

The objective of these CPG is to provide evidence-based recommendations in the screening of Diabetic Retinopathy. This would prevent or reduce the risk of visual loss, thereby maintaining or improving vision-related quality of life.

## CLINICAL QUESTIONS

Refer to **Appendix 2**

## TARGET POPULATION

All patients with Diabetes Mellitus including children and pregnant women

## TARGET GROUP/USER

These guidelines are applicable to all healthcare professionals who are involved in the screening of Diabetic Retinopathy:-

- Nurses/Assistant Medical Officers
- Family Medicine Specialists
- Optometrists
- General Practitioners/Medical Officers
- Physicians/ Paediatricians/ Obstetricians & Gynaecologists/ Endocrinologists
- Diabetic Support Groups
- Ophthalmologists

## HEALTHCARE SETTING

Outpatient, inpatient and community settings



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The draft guidelines were reviewed by a panel of independent expert referees from both public and private sectors including non-governmental organisation and patient advocate, who were asked to comment primarily on the comprehensiveness and accuracy in the interpretation of evidence supporting the recommendations in the guidelines.

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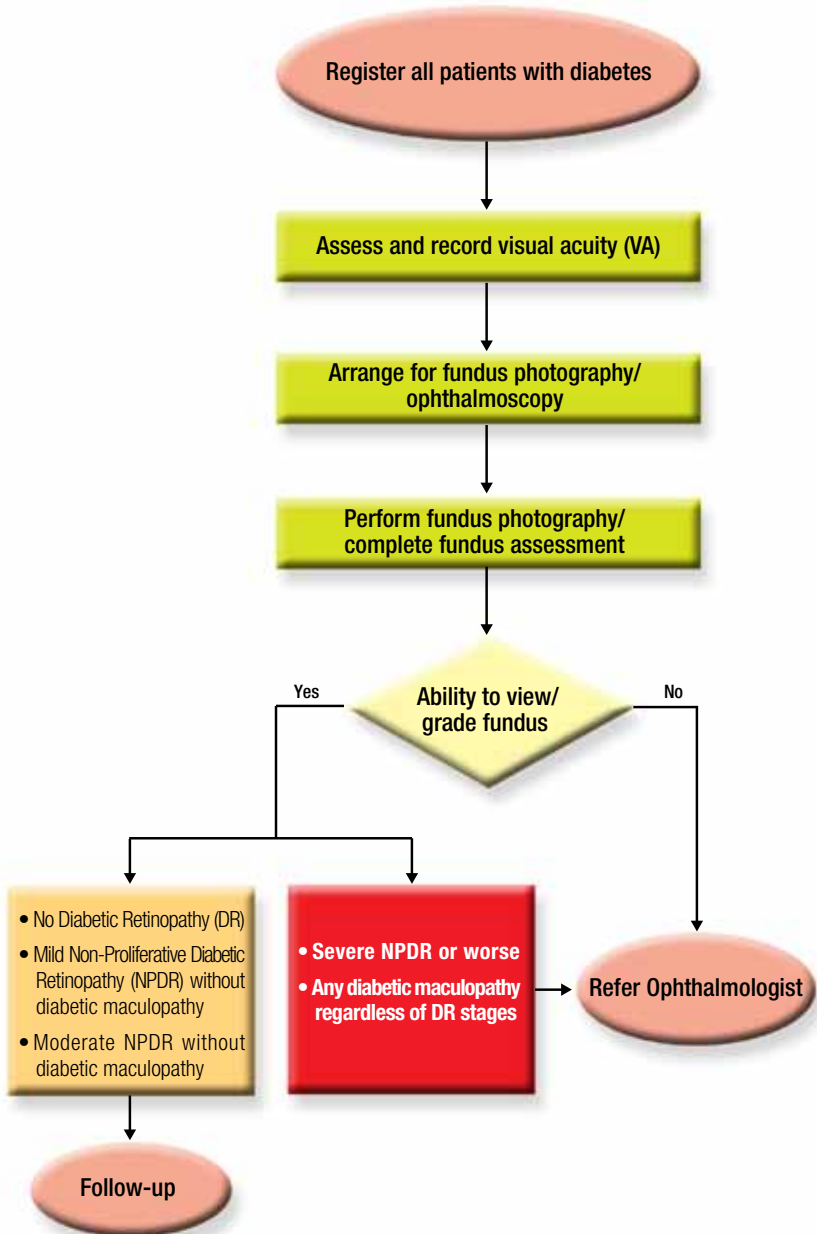
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## ALGORITHM FOR SCREENING OF DIABETIC RETINOPATHY TO PREVENT BLINDNESS



## 1.0 INTRODUCTION

Diabetes Mellitus (DM) is an important public health concern. Globally there is a rising trend in the prevalence of DM due to many factors such as aging, urbanisation and increasing prevalence of obesity and physical inactivity. The International Diabetes Federation (IDF) predicts that the prevalence of DM in South East Asia will increase by two folds by the year 2025.<sup>1, level III</sup> The World Health Organization (WHO) has estimated that in the year 2030, Malaysia would have a total of 2.48 million people with DM.<sup>2, level III</sup> In Malaysia, the first National Health and Morbidity Survey I (NHMS I) conducted in 1986 reported a DM prevalence of 6.3%. This had risen to 8.3% in the NHMS II 1996 report. In the latest NHMS III 2006 report, the overall prevalence of DM was 11.6% and 14.9% in those aged above 18 and 30 years respectively. NHMS I and II involved subjects aged above 30 years while NHMS III was conducted among subjects above 18 years of age.<sup>3, level III</sup>

DM is a complex disease with end organ complications. However, good control of DM will prevent the onset or retard progression of the various complications including diabetic retinopathy (DR). In Malaysia, diabetic eye disease is the commonest cause of visual loss among adults of working age. Prevalence of DR is closely linked to the duration of DM. At diagnosis, less than 5% will have retinopathy while the prevalence rises to 40 - 50% after 10 years. Almost all patients with type 1 diabetes mellitus (T1DM) and more than 60% patients with type 2 diabetes mellitus (T2DM) have some degree of retinopathy after 20 years of the disease.<sup>2, level III</sup> Screening and early treatment can prevent substantial visual loss in many cases. Late presentation continues to be a major challenge of prevention and alleviation of blindness.

DM prevalence in Malaysia has dramatically risen to almost twice in the magnitude over the last decade. In view of this, efforts to control this chronic disease and early detection of complications such as DR should be intensified. This is important as DR is asymptomatic in its early stage when it is most easily amenable to treatment.

Therefore, a DR screening programme must be comprehensive, covering all individuals with DM in Malaysia.

## 2. EPIDEMIOLOGY OF DIABETES MELLITUS AND DIABETIC RETINOPATHY

WHO estimates that the global prevalence of DM will increase from 2.8% to 4.4% from the year 2000 to 2030.<sup>4, level III</sup> Due to its chronicity, severity of complication and complexity of management, DM is a costly disease both for the affected individuals and the health sector as a whole.

DR is the leading cause of blindness and visual disability in adults of economically developed societies in the Western Pacific Region.<sup>1, level III</sup> Its prevalence is closely linked to the duration of DM and varies among nations and ethnicity.<sup>5, level III</sup>

### 2.1 Prevalence and Incidence of Diabetes Mellitus

#### 2.1.1 Adults

The prevalence of DM among those aged more than 30 years in Malaysia has increased alarmingly from 6.3% (1986) to 8.3% (1996) and 14.9% in 2006. There was also an increasing trend in the prevalence with age (2.0% among those aged 18 - 19 years to 20.8 - 26.2% among aged 50 - 64 years). Based on ethnicity, Indians have the highest prevalence followed by Malays and Chinese.<sup>3, level III</sup> Among those with DM for more than 15 years, approximately 2% became blind and 10% developed severe visual handicap.<sup>1, level III</sup>

It has been recommended that all DM patients should have at least a yearly eye examination.<sup>6, level III</sup> However, the NHMS III 2006 reported that only 45% of patients with known DM ever had an eye examination.<sup>3, level III</sup>

#### 2.1.2 Children and Adolescents

T1DM accounts for over 90% of childhood and adolescent diabetes in most western countries.<sup>7, level III</sup> The incidence of T1DM is on the increasing trend worldwide. The average annual increase is 4% in Asia, 3.2% in Europe and 5.3 % in North America.<sup>8, level III</sup> In the Asian population, T2DM occurs at a much greater prevalence ranging between 50% and 90%.<sup>9, level III</sup>

According to the Diabetes in Children and Adolescents Registry from April 2006 to June 2007, T1DM (69.2%) was more common than T2DM (17.5%).<sup>10, level III</sup> However there is no available data on the prevalence of DM in children and adolescents in Malaysia.

## 2.2 Prevalence and Incidence of Diabetic Retinopathy

DR is a leading complication of DM. The prevalence of DR worldwide ranges from 6.8 to 44.4% in patients with diabetes mellitus.<sup>11 - 15, level III</sup>

In Malaysia, the prevalence of DR from the 2007 Diabetic Eye Registry was 36.8%<sup>16, level III</sup> which was comparable to the prevalence of 35% found in the Singapore Malay Eye Study 2006.<sup>5, level III</sup> Other unpublished local data obtained from primary care screening centres showed a prevalence ranging between 12.3% and 16.9%.<sup>17 - 18, level III</sup>

In a study conducted in New South Wales, Australia, the prevalence of early DR in children less than 11 years was 8% as compared to 25% of adolescents older than 11 years.<sup>19, level II-2</sup> However, there is no retrievable data on the prevalence of DR in children and adolescents in Malaysia.

## 2.3 Prevalence of Blindness and Sight Threatening Diabetic Retinopathy

The prevalence of sight threatening DR ranges from 4.0 to 22.2%.<sup>5, level III; 20 - 21, level III; 22, level II-2; 23 - 24, level III</sup> In Malaysia, the National Eye Database (NED) 2007 and 2008 reported that the proportion of patients with sight threatening DR was 15.6% and 11.5% respectively. The proportion of patients with blindness was 9.0%.<sup>16, level III</sup>



### 3. RISK FACTORS

There are many risk factors for DR. The duration of DM is significantly associated with the development and severity of DR with odds ratio (OR) ranging from 1.07 to 8.62.<sup>5, level III; 20 - 21, level III; 23, level III, 25</sup>

Significant systemic risk factors include hypertension and high HbA<sub>1c</sub>, systolic blood pressure (SBP), pulse pressure, serum lipoprotein level and body mass index (BMI).<sup>5, level III; 20 - 21, level III; 22, level II-2; 23 - 24, level III; 25; 26, level III</sup> Other documented risk factors include renal disease/nephropathy, genetic factors, high waist-hip-ratio (abdominal obesity), upper socioeconomic status, urban residence, higher plasma total homocysteine level, male gender, insulin treatment and pregnancy.<sup>20, level III; 23 - 24, level III ; 25; 27, level III</sup>

The risk factors for sight threatening DR are chronic kidney disease (OR=4.45, 95% CI 2.18 to 9.07), previous stroke (OR=3.74, 95% CI 1.24 to 11.26), cardiovascular disease (OR=2.23, 95% CI 1.08 to 4.62),<sup>5, level III</sup> duration of DM (OR=1.38, 95% CI 1.02 to 1.87)<sup>21, level III</sup> and hypercholesterolemia.<sup>25</sup>

#### Recommendation

- Screening for diabetic retinopathy should be done in all patients with diabetes mellitus. **(Grade C)**

## 4. DIABETIC RETINOPATHY GRADING

To improve communication worldwide between ophthalmologists and primary healthcare providers in managing patients with DM, an international clinical disease severity scale was developed for DR and Diabetic Macula Oedema (DME) (refer to **Table 1**). This scale is based on the Early Treatment for Diabetic Retinopathy Study (ETDRS) Classification of DR and on the data collected in clinical trials and epidemiologic studies of DR.

**Table 1: International Clinical Diabetic Retinopathy and Diabetic Macula Oedema Disease Severity Scale**

RETINOPATHY STAGE	FINDINGS ON OPHTHALMOSCOPY
No apparent retinopathy	No abnormalities
Mild non-proliferative DR (NPDR)	Microaneurysms only
Moderate NPDR	More than just microaneurysms but less than severe NPDR
Severe NPDR	Any of the following: <ol style="list-style-type: none"> <li>1. More than 20 intraretinal haemorrhages in each of 4 quadrants</li> <li>2. Definite venous beading in 2 or more quadrants</li> <li>3. Prominent intraretinal microvascular abnormalities in 1 or more quadrants AND no signs of proliferative retinopathy</li> </ol>
Proliferative DR (PDR)	One of the following: <ol style="list-style-type: none"> <li>1. Neovascularisation</li> <li>2. Vitreous/preretinal haemorrhage</li> </ol>
Advanced Diabetic Eye Disease (ADED)	One of the following: <ol style="list-style-type: none"> <li>1. Formation of fibrovascular tissue proliferation</li> <li>2. Traction retinal detachment due to formation of posterior vitreous detachment</li> <li>3. Dragging of retinal/distortion</li> <li>4. Rhegmatogenous retinal detachment</li> </ol>

MACULA OEDEMA	FINDINGS ON OPHTHALMOSCOPY
Absent	No retinal thickening or hard exudates in posterior pole
Present	<ul style="list-style-type: none"> <li>• Mild – some retinal thickening or hard exudates in posterior pole but distant from the macula</li> <li>• Moderate – retinal thickening or hard exudates approaching the centre of the macula but not involving the centre</li> <li>• Severe – retinal thickening or hard exudates involving the centre of the macula</li> </ul>

**Source:** Wilkinson CP, Ferris FL III, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology* 2003; 110:1679-80

Examples of fundus appearance according to DR Stages are shown in **Appendix 3**.

## 5. ASSESSMENT OF DIABETIC RETINOPATHY

A variety of screening modalities are available in detecting and classifying DR. Ophthalmoscopy is the most commonly used technique to screen for DR. However, non-mydratic digital fundus photography is now being widely used. There is a wide variation in the sensitivities and specificities of different screening modalities performed by different screeners.

### 5.1 Screening Tools

The instruments that can be used for screening are:

- Direct ophthalmoscope
- PAN-ophthalmoscope
- Binocular indirect ophthalmoscope (BIO)
- Slit lamp biomicroscope
- Mydratic fundus camera
- Non-mydratic fundus camera

#### 5.1.1 Sensitivity and Specificity of Diabetic Retinopathy Screening Tools

The UK National Institute for Clinical Excellence (NICE) recommends that DR screening modalities should have a sensitivity of at least 80%, a specificity of at least 95% and a technical failure rate of no greater than 5%.<sup>28</sup>

**Table 2** describes the diagnostic accuracy of different screening tools. Non-mydratic fundus camera has high sensitivity and specificity. It eliminates the need for pupillary dilatation, promoting compliance, efficiency and safety. The findings by Aptel F et al showed that at least one field photo assessment was sufficient to detect DR. However, the Training Module for DR Screening in Malaysia recommends two fields photo assessment.<sup>29, level III</sup>

**Table 2: Sensitivity and Specificity of DR Screening Tools**

SCREENING TOOL	SENSITIVITY	SPECIFICITY
Direct ophthalmoscope <sup>25</sup>	45.0 - 98.0%	62.0 - 100%
Slit lamp biomicroscope <sup>30, level II-2</sup>	87.4%	94.9%
Mydriatic fundus camera <sup>25</sup>	73.0 - 96.0%	68.0 - 99.0%
Non-mydriatic fundus camera <sup>31, level II-2</sup>	92.0%	97.0%

### 5.1.2 Agreement between Non-mydriatic Fundus Camera versus Ophthalmoscope and Mydriatic Fundus Camera

As a screening tool, non-mydriatic fundus camera has good inter-rater reliability with ophthalmoscope ( $\kappa=0.90$ )<sup>31, level II-2</sup> and mydriatic fundus camera ( $\kappa=0.80$ ).<sup>32, level I</sup>

#### Recommendation

- Non-mydriatic fundus camera should be used as a screening tool for diabetic retinopathy (DR) when possible. **(Grade A)**
  - Two fields fundus photo assessment should be done. **(Grade C)**
- When there is no access to fundus camera, ophthalmoscope should be used for screening of DR. **(Grade C)**

### 5.2 Automated Diabetic Retinopathy Grading

Automated grading of DR is a growing research field aimed at decreasing the burden of grading. Various individual softwares have been developed.<sup>33 - 34, level II-2; 35 - 36, level III</sup> However, further evaluation and validation is required for local use.

### 5.3 Pupillary Dilatation

Non-mydriatic fundus photography generally does not require pupil dilatation if performed in an adequately darkened room. However, in cases of small pupil and ungradable photos, pupillary dilatation can increase the sensitivity of screening by over 50%. Those performing DR screening should be aware of the possibility of inducing acute angle closure glaucoma in high risk individuals (history of glaucoma and shallow anterior chamber). The use of tropicamide 1% alone has not been reported to cause this complication.<sup>37, level III</sup>

Those intending to use tropicamide 1% should be aware of the possible side effects.

#### Recommendation

- Tropicamide 1% should be used for pupillary dilatation in selected cases by trained personnel. **(Grade C)**

### 5.4. Examination and Grading of Diabetic Retinopathy by Healthcare Professionals

The screening and grading of DR can be performed with high accuracy by:<sup>38 - 42, level III</sup>

- Doctors (family medicine specialists, general practitioners and medical officers)
- Optometrists
- Assistant medical officers and nurses

All healthcare personnel need proper training before they can be privileged for DR screening so as to increase the interpretation and grading accuracy. Studies have shown that the sensitivity and specificity of interpretation increased after training.<sup>38 - 39, level III; 41, level III</sup> Jackson CL et al reported that brief training intervention had increased the accuracy of interpretation from 24% to 94%.<sup>41, level III</sup> In another study, trained primary care clinicians showed appropriate referral to the ophthalmologist with a sensitivity of 89.8% and a specificity of 93%.<sup>38, level III</sup>

Retinal screeners and graders require specific training, accreditation and regular performance assessment. Training module should include:

- Clinical knowledge and skills
- Imaging and computer skills
- Operational issues
- Fundus grading

A Training Steering Group has been established by the Ministry of Health (MOH) Malaysia. This group has produced a training manual and developed a training curriculum.<sup>29</sup> The MOH has accredited the training curriculum and training materials. Training should be adapted to the local setting to enable the trainees to handle available and relevant equipments.

### **Recommendation**

- All diabetic retinopathy (DR) screeners must undergo appropriate and standardised training as per DR screening training module. **(Grade C)**

## 6. EXAMINATION SCHEDULE

Early detection of sight threatening retinopathy by regular examination is the key to reduce visual loss and blindness from DR. Due to the sight threatening potential of DR and the availability of methods to slow down the rate of disease progression, a proper screening at an appropriate time is recommended.<sup>25</sup>

### 6.1 Timing of First Screening

The initial fundus examination for DR varies according to the types of DM:

- **Adults T1DM**

Adults with T1DM should have their first screening within three to five years after the initial diagnosis.<sup>43; 44, level III</sup>

- **Adults T2DM**

The time of onset of T2DM is often difficult to determine and may precede the diagnosis by a number of years. Therefore, patients should have their first fundus examination at the time of diagnosis.<sup>43; 44, level III</sup>

- **Pregnant Women with Pre-existing DM**

DR can worsen during pregnancy because of changes in metabolic status. Individuals with DM planning for pregnancy should have their eyes examined prior to conception and counselled on the risk of development and progression of DR.<sup>25; 43</sup>

- **Gestational DM (GDM)**

GDM is an abnormal glucose intolerance first detected during pregnancy. In general, DR screening is not required for GDM.<sup>25; 43</sup> However, if GDM is diagnosed in the first trimester of pregnancy, screening should be as per pre-existing DM.



- **Children and Adolescents**

Incidence of DR in young children is negligibly small and therefore children younger than 9 years old do not require screening for DR.<sup>45, level III</sup> International Society for Paediatric & Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines 2009 recommends timing of first screening as follows:<sup>46, level III</sup>

**a) T1DM:**

- At age 9 years with 5 years of diabetes duration
- At age 11 years with 2 years of diabetes duration

**b) T2DM:**

- At the time of diagnosis

### Recommendation

- First screening for diabetic retinopathy (DR) should be done at:
  - Adults type 1 diabetes mellitus (T1DM) - up to 3 years after diagnosis
  - Adults type 2 diabetes mellitus (T2DM) - at time of diagnosis
  - Pregnant women with
    - i. Pre-existing diabetes mellitus (DM) - prior to planned pregnancy
    - ii. Gestational DM (GDM) diagnosed in the first trimester - at the time of diagnosis. Otherwise not required.
  - Children T1DM
    - i. At age 9 years with 5 years of DM duration
    - ii. At age 11 years with 2 years of DM duration
  - Children T2DM - at time of diagnosis **(Grade C)**

## 6.2 Follow-up Examination Schedule

Individuals with DM should be screened at least every two years. High risk individuals (longer duration of diabetes or poor control of blood sugar, blood pressure or serum lipid) should be examined at least annually.<sup>25</sup>

The examination should include:

- Visual acuity assessment (Snellen chart and equivalent)
- Fundus photography or dilated fundus examination

Individuals with any signs of NPDR should be examined at 6 - 12 monthly intervals. Earlier follow-up may be required in:<sup>43; 44, level III</sup>

- High risk groups
- Presence of renal complications
- Progression of DR

The recommended intervals for eye examination for patients with DM are provided in **Table 3**.

**Table 3: Recommended Follow-up Schedule**

STAGE OF RETINOPATHY	FOLLOW-UP
No DR	12 - 24 months
Mild NPDR without maculopathy	9 - 12 months
Moderate NPDR without maculopathy	6 months
Mild/Moderate NPDR with maculopathy	Refer to Ophthalmologist
Severe NPDR without maculopathy	
Any maculopathy	
Proliferative DR	Refer urgently to Ophthalmologist
Advanced Diabetic Eye Disease (ADED)	
No DR to Mild NPDR In Pregnant Women	Every 3 months
Moderate NPDR or Worse In Pregnant Women	Refer to Ophthalmologist

**Sources:**

1. American Academy of Ophthalmology Retina Panel. Preferred Practice Pattern Guidelines. Diabetic Retinopathy, San Francisco, CA: American Academy of Ophthalmology; 2008
2. Ministry of Health Malaysia. Diabetic Retinopathy. Kuala Lumpur: MOH; 1997

### 6.3 Referral Criteria to Ophthalmologist

The ultimate aim for screening of DR is to detect sight threatening DR and to ensure timely treatment in order to prevent vision loss. Appropriate referral to the ophthalmologist should be done.

Criteria for referral are:<sup>28</sup>

- Any level of Diabetic Maculopathy
- Severe NPDR
- Any PDR
- Unexplained visual loss
- If screening examination cannot be performed including ungradable fundus photo

The urgency of referral is as shown in **Table 4**.

**Table 4: Criteria for Urgent Referral**

URGENCY OF REFERRAL	OCULAR FEATURES
<b>Emergency (same day referral)</b>	<ul style="list-style-type: none"> <li>• Sudden severe visual loss</li> <li>• Symptoms or signs of acute retinal detachment</li> </ul>
<b>Within 1 week</b>	<ul style="list-style-type: none"> <li>• Presence of retinal new vessels</li> <li>• Preretinal haemorrhage</li> <li>• Vitreous haemorrhage</li> <li>• Rubeosis iridis</li> </ul>
<b>Within 4 weeks</b>	<ul style="list-style-type: none"> <li>• Unexplained drop in visual acuity</li> <li>• Any form of maculopathy</li> <li>• Severe NPDR</li> <li>• Worsening retinopathy</li> </ul>

**Source:** National Institute for Clinical Excellence. Management of Type 2 diabetes. Retinopathy screening and early management London: NICE; 2002

#### Recommendation

- Examination schedule and urgency of referral to an ophthalmologist should be based on the grade and severity of diabetic retinopathy as well as the presence of risk factors. **(Grade C)**

## 7.0 TREATMENT FOR DIABETIC RETINOPATHY

### 7.1 Current Treatment Modalities

Early detection of DR is important as it is reversible. There are many treatment modalities available (refer to **Table 5**). Laser photocoagulation remains the standard practice for treating DR. Stages of DR which require treatment includes severe NPDR, PDR, ADED and DME.

**Table 5: Summary of Treatment for Diabetic Retinopathy**

STAGE OF DR	MODE OF TREATMENT
<b>DME</b>	<ul style="list-style-type: none"> <li>• Laser - focal/ grid</li> <li>• Intraocular steroids*</li> <li>• Intraocular anti-vascular endothelial growth factor (anti-VEGF)*</li> </ul>
<b>Severe NPDR</b>	<ul style="list-style-type: none"> <li>• Laser - scattered pan-retinal photocoagulation (PRP)</li> </ul>
<b>PDR</b>	<ul style="list-style-type: none"> <li>• Laser - PRP</li> </ul>
<b>ADED</b>	<ul style="list-style-type: none"> <li>• Intraocular steroids</li> <li>• Intraocular anti-vascular endothelial growth factor (anti-VEGF)</li> <li>• Vitrectomy</li> </ul>

\*For refractory DME

## 7.2 Modifiable Risk Factors in Reducing Progression of Diabetic Retinopathy

The mainstay of current treatment involves risk factor modification by controlling blood glucose, blood pressure and serum lipids as shown in **Table 6**. Potential alternative therapeutic approaches that directly target diabetic microvascular complications include:<sup>25; 47</sup>

- Antiplatelet agents
- Advanced glycation end (AGE) product inhibitors
- Aldose reductase inhibitors (ARIs)
- Protein kinase C (PKC) inhibitors
- Angiotensin converting enzyme (ACE) inhibitors
- Fenofibrate

**Table 6: Target Level of Modifiable Risk Factors in Adults**

RISK FACTOR	TARGET LEVEL
<b>Glycaemic Control</b> <ul style="list-style-type: none"> <li>• Fasting</li> <li>• Non-fasting</li> <li>• HbA<sub>1c</sub></li> </ul>	4.4 - 6.1 mmol/L 4.4 - 8.0 mmol/L <6.5%
<b>Blood Pressure</b> <ul style="list-style-type: none"> <li>• Normal Renal Function</li> <li>• Renal Impairment/ micro- or macroalbuminuria</li> </ul>	≤130/80 mmHg ≤120/75 mmHg
<b>Lipids</b> <ul style="list-style-type: none"> <li>• Triglycerides</li> <li>• HDL cholesterol</li> <li>• LDL cholesterol</li> </ul>	≤1.7 mmol/L ≥1.1 mmol/L ≤2.6 mmol/L

**Source:** Ministry of Health Malaysia. Management of Type 2 Diabetes Mellitus (Fourth Edition). Putrajaya: MOH; 2009

Other modalities of risk factor modification include diet, exercise and stop smoking.<sup>48</sup>

## 8.0 IMPLEMENTING THE GUIDELINES

This chapter provides advice on the resource implications associated with implementing the key recommendations and advice on proposed clinical audit indicators for quality management to aid implementation.

Implementation of these CPG is an essential part of clinical governance. It should cater to the local individual hospitals, health clinics and community based on both economic and non-economic considerations. Mechanisms should be in place to review the existing healthcare system as compared to the CPG recommendations. Any differences should be assessed and addressed appropriately.

Important issues that should be considered when implementing these CPG in Malaysia are:-

- Establishment of a screening programme
- Proper DR database
- Adequate training and privileging of screeners and graders
- Availability of screening tools
- Co-ordinated referral system & availability of resources for necessary treatment

### 8.1 Existing Facilitators and Barriers in Applying Recommendations

The implementation of the CPG will be facilitated by the existing DR Screening Training Module of the MOH Malaysia. The module has been established since 2008 and involves the training of family medicine specialists, medical officers, optometrists, assistant medical officers and nurses. However, the Development Group will ensure that the contents of this training module will be in tandem with the recommendations in the CPG.

There are three barriers in applying recommendations of the CPG in the local context:

#### i. Patient factors

- Lack of awareness of the possible complications of DM to the eye as DR may remain asymptomatic
- Poor access to eye care services
- Different cultural beliefs

#### ii. Healthcare professional factors

- Limited knowledge and/or poor attitude
- Limited resources
- High turnover of trained screeners and graders
- Lack of utilisation of screening tools

## iii. Health services factors

- Lack of linkages between services and providers
- Lack of recalls or reminders for defaulters
- Long waiting list for first screening and referral to see ophthalmologist
- Lack of optimisation of fundus cameras

With the availability of these national evidence-based CPG, the current nation-wide screening programme will be strengthened to prevent blindness among those with DM.

## 8.2 Potential Resource Implications in Applying Recommendations

In implementing the CPG, the Development Group recommends strengthening of the existing training module on DR screening. Financial allocation is proposed to individual hospitals, health clinics and communities to achieve adequate access to eye screening.

In view of the low percentage of DM patients screened for DR annually,<sup>3, level III</sup> the development group proposes the following **clinical audit indicators for quality management** as part of ensuring the implementation of recommendations in the CPG:-

<ul style="list-style-type: none"> <li>• Percentage of T2DM patients screened for DR for the first time</li> </ul>	=	$\frac{\text{Number of T2DM patients screened for DR for the first time within a year}}{\text{Total number of newly registered T2DM patients within the same year}}$	x 100%
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<ul style="list-style-type: none"> <li>• Percentage of ungradable fundus photo</li> </ul>	=	$\frac{\text{Number of patients with ungradable fundus photo within a year}}{\text{Total number of patients' fundus photos taken within the same year}}$	x 100%
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<ul style="list-style-type: none"> <li>• Percentage of diabetics screened with sight threatening DR</li> </ul>	=	$\frac{\text{Number of diabetics screened with sight threatening DR within a year}}{\text{Total number of diabetics screened for DR within the same year}}$	x 100%
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# APPENDICES



## Appendix 1

### SEARCH TERMS

The following MeSH terms or free text terms were used either singly or in combination:

“diabetes mellitus”[MeSH Terms], “diabetes mellitus, type 2”[MeSH Terms], “diabetes mellitus, type 1”[MeSH Terms], diabetes, “diabetic retinopathy”[MeSH Terms], “prevalence”[MeSH Terms], “epidemiology”[MeSH Terms], “worldwide prevalence”, “incidence”[MeSH Terms], “worldwide incidence”, “diabetes mellitus prevalence”, Malaysia, “prevalence diabetic retinopathy”, “risk factors”[MeSH Terms], HbA1c, “pregnancy”[MeSH Terms], duration, “hyperglycemia”[MeSH Terms], “hypertension”[MeSH Terms], “tobacco”[MeSH Terms], “Hyperlipidemia”[MeSH Terms], “dyslipidemias”[MeSH Terms], Nephropathy, “creatinine”[MeSH Terms], “serum creatinine”, age, gender, gestation, “classification”[MeSH Terms], grading, “grading system”, “fundus camera”, “retinal photography”, “retinal imaging”, “direct ophthalmoscope”, “ophthalmoscopes”[MeSH Terms], funduscope, “pan funduscope”, “binocular indirect ophthalmoscope”, BIO, “slitlamp biomicroscopy”, slitlamp, “Diabetic retinopathy screening”, guidelines, , “automated grading”, “software grading”, “automated grading”, automated, “dilated pupil”, “pupil dilation”, “mydriasis”[MeSH Terms], “pupillary dilatation”, “side effect”, “adverse effect”, “adverse drug reaction”, “glaucoma”[MeSH Terms], “tropicamide”[MeSH Terms], phenylephrine, screening, “non-ophthalmologist”, “accuracy of grading”, “optometrist”, “general practitioner”, “primary care physician”, accuracy, timing, “referral criteria”, criteria, referral, “diabetic retinopathy guideline”, “diabetes mellitus guideline”, “classification”[Mesh], “diagnosis”[Mesh], diabetic, “eye examination”, “eye assessment”, “eye screening”, “follow up”, schedule, detection, protocol, therapeutics”[MeSH Terms], “laser treatment”, “intravitreal triamcinolone”, “laser photocoagulation”, “vitrectomy”, blindness, “sight threatening”

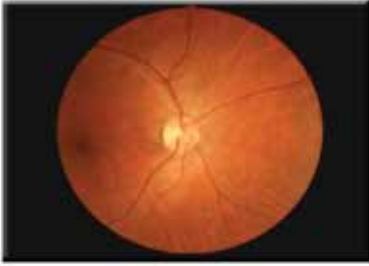
## Appendix 2

### CLINICAL QUESTIONS

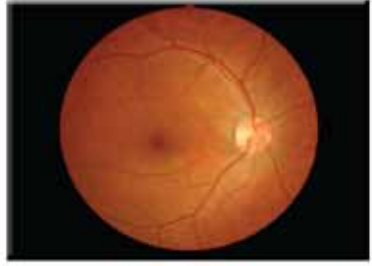
1. What is the prevalence of Type 1 DM and Type 2 DM in Malaysia and worldwide?
2. What is the prevalence of diabetic retinopathy in Type 1 and Type 2 DM in Malaysia and worldwide?
3. What is the prevalence of sight threatening DR or blindness due to diabetic retinopathy in Malaysia and worldwide?
4. Is there any difference in the risk of diabetic retinopathy for the different types of diabetes?
5. What are the current grading systems for diabetic retinopathy?
6. What are the sensitivity and specificity of screening tools to detect diabetic retinopathy?
  - i. Direct ophthalmoscope
  - ii. PAN-ophthalmoscope
  - iii. BIO
  - iv. Slit lamp
  - v. Fundus camera - mydriatic versus nonmydriatic
7. Is automated grading of diabetic retinopathy as efficient as manual grading?
8. When should the pupil be dilated and what are the potential side effects of pupillary dilation?
9. Who can perform examination and grade the status of diabetic retinopathy?
10. What are the criteria for referral of DR to the ophthalmologist?
11. What are the most appropriate timing and frequency of eye examinations in people with DM?
  - i. Established diabetics who are planning to get pregnant or who are already pregnant
  - ii. Children and adolescents
  - iii. Adults
12. What are the treatments for diabetic retinopathy?
13. Are there new modalities in treating diabetic retinopathy?

## Appendix 3

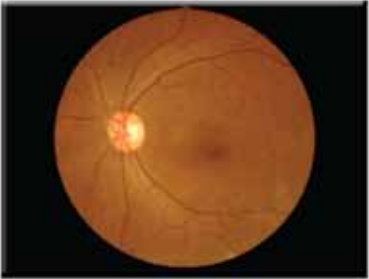
### FUNDUS APPEARANCE ACCORDING TO DR STAGES



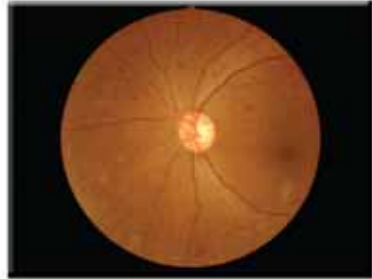
No DR



Mild NPDR



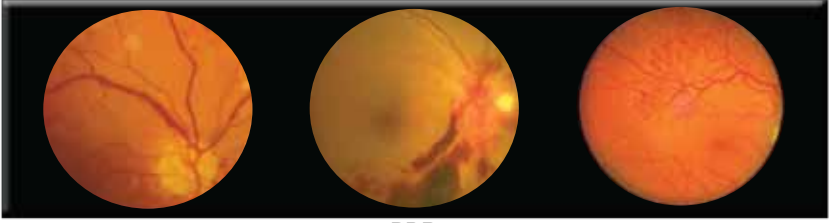
Moderate NPDR



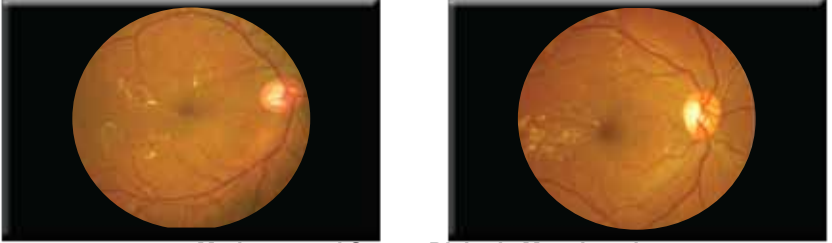
Severe NPDR



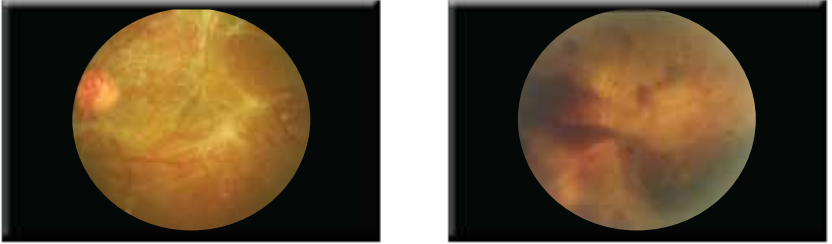




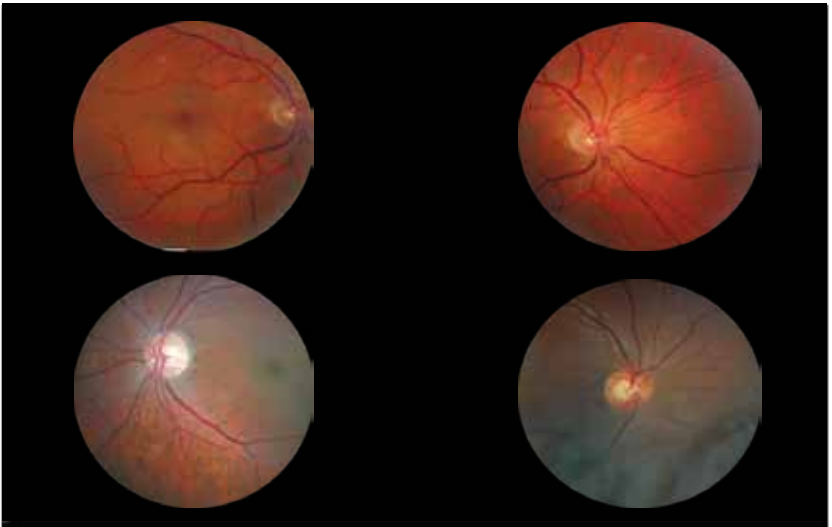
**PDR**



**Moderate and Severe Diabetic Maculopathy**



**ADED and Vitreous Haemorrhage**



**Ungradable Photos**

## Appendix 4

LIST OF HEALTH CLINICS WITH FUNDUS  
CAMERA IN MINISTRY OF HEALTH 2011

No.	State/District	Health Clinic	Total Fundus Camera	
1.	<b>Perlis</b>		2	
		Kangar		Klinik Kesihatan Kangar
				Klinik Kesihatan Arau
2.	<b>Kedah</b>		12	
		Kubang Pasu		Klinik Kesihatan Kepala Batas
		Padang Terap		Klinik Kesihatan Naka
		Kota Setar		Klinik Kesihatan Pokok Sena
				Klinik Kesihatan Simpang Kuala
		Pendang		Klinik Kesihatan Pendang
		Yan		Klinik Kesihatan Guar Chempedak
		Sik		Klinik Kesihatan Jeniang
		Kuala Muda		Klinik Kesihatan Bandar Sungai Petani
		Baling		Klinik Kesihatan Tawar
		Kulim		Klinik Kesihatan Kulim
Klinik Kesihatan Padang Serai				
Bandar Baharu	Klinik Kesihatan Serdang			
3.	<b>Pulau Pinang</b>		4	
		Seberang Perai Utara		Klinik Kesihatan Butterworth
		Seberang Perai Tengah		Klinik Kesihatan Seberang Jaya
		Seberang Perai Selatan		Klinik Kesihatan Nibong Tebal
		Timur Laut		Klinik Kesihatan Jalan Perak
4.	<b>Perak</b>		8	
		Kinta		Klinik Kesihatan Jelapang
				Klinik Kesihatan Greentown
		Larut Matang		Klinik Kesihatan Taiping
		Manjung		Klinik Kesihatan Sitiawan
		Hilir Perak		Klinik Kesihatan Hutan Melintang
		Batang Padang		Klinik Kesihatan Tanjung Malim
		Kuala Kangsar		Klinik Kesihatan Padang Rengas
Kerian	Klinik Kesihatan Bagan Serai			

No.	State/District	Health Clinic	Total Fundus Camera
5.	<b>Selangor</b>		7
	Gombak	Klinik Kesihatan Taman Ehsan	
	Hulu Langat	Klinik Kesihatan Kajang	
	Klang	Klinik Kesihatan Pandamaran	
	Kuala Langat	Klinik Kesihatan Telok Datuk	
	Kuala Selangor	Klinik Kesihatan Kuala Selangor	
	Sabak Bernam	Klinik Kesihatan Sungai Besar	
Hulu Selangor	Klinik Kesihatan Serendah		
6.	<b>WP Kuala Lumpur &amp; Putrajaya</b>		4
	Putrajaya	Klinik Kesihatan Putrajaya	
	Kuala Lumpur	Klinik Kesihatan Jinjang	
		Klinik Kesihatan Cheras Baru	
Klinik Kesihatan Tanglin			
7.	<b>Negeri Sembilan</b>		11
	Seremban	Klinik Kesihatan Seremban	
		Klinik Kesihatan Ampangan	
		Klinik Kesihatan Rantau	
	Kuala Pilah	Klinik Kesihatan Kuala Pilah	
		Klinik Kesihatan Juasseh	
	Jelebu	Klinik Kesihatan Jelebu	
	Jempol	Klinik Kesihatan Bahau	
		Klinik Kesihatan Palong 4,5,6	
Rembau	Klinik Kesihatan Rembau		
Tampin	Klinik Kesihatan Tampin		
Port Dickson	Klinik Kesihatan Port Dickson		
8.	<b>Malacca</b>		5
	Malacca Tengah	Klinik Kesihatan Ayer Keroh	
	Alor Gajah	Klinik Kesihatan Masjid Tanah	
	Jasin	Klinik Kesihatan Selandar	
		Klinik Kesihatan Umbai	
Jabatan Pesakit Luar Jasin			

No.	State/District	Health Clinic	Total Fundus Camera
9.	<b>Johor</b>		12
	Johor Bahru	Klinik Kesihatan Pasir Gudang	
		Klinik Kesihatan Mahmodiah	
	Muar	Klinik Kesihatan Bandar Maharani	
		Klinik Kesihatan Parit Jawa, Muar	
		Klinik Kesihatan Paya Mas, Muar	
	Batu Pahat	Klinik Kesihatan Batu Pahat	
	Kluang	Klinik Kesihatan Mengkibol	
	Pontian	Klinik Kesihatan Pontian	
	Segamat	Klinik Kesihatan Segamat	
	Kota Tinggi	Jabatan Pesakit Luar Kota Tinggi	
	Mersing	Klinik Kesihatan Endau	
	Ledang	Klinik Kesihatan Paya Mas	
10.	<b>Pahang</b>		9
	Kuantan	Klinik Kesihatan Bandar Kuantan	
		Klinik Kesihatan Balok	
		Klinik Kesihatan Jaya Gading	
	Temerloh	Klinik Kesihatan Temerloh	
	Bera	Klinik Kesihatan Triang	
	Lipis	Klinik Kesihatan Benta	
	Maran	Klinik Kesihatan Maran (tidak berfungsi)	
		Klinik Kesihatan Bandar Jengka	
	Rompin	Klinik Kesihatan Kuala Rompin	

No.	State/District	Health Clinic	Total Fundus Camera
11.	<b>Terengganu</b>		12
	Kuala Terengganu	Jabatan Pesakit Luar Hospital Sultanah Nur Zahirah	
		Klinik Kesihatan Hciliran	
		Klinik Kesihatan Batu Rakit	
	Dungun	Klinik Kesihatan Ketengah Jaya	
	Marang	Klinik Kesihatan Marang	
		Klinik Kesihatan Bukit Payong	
	Besut	Klinik Kesihatan Kuala Besut	
	Setiu	Klinik Kesihatan Pemaisuri	
	Kemaman	Klinik Kesihatan Kerteh	
	Hulu Terengganu	Klinik Kesihatan Ajil	
		Klinik Kesihatan Kuala Berang	
		Klinik Kesihatan Tengkawang	
12.	<b>Kelantan</b>		14
	Gua Musang	Klinik Kesihatan Gua Musang	
	Kuala Krai	Klinik Kesihatan Kuala Krai	
	Pasir Puteh	Klinik Kesihatan Selising	
	Tumpat	Klinik Kesihatan Wakaf Baru	
	Jeli	Klinik Kesihatan Jeli	
		Klinik Kesihatan Ayer Lanas	
	Kota Bharu	Klinik Kesihatan Kota Bharu	
		Klinik Kesihatan Ketereh	
	Machang	Klinik Kesihatan Labok	
	Pasir Mas	Klinik Kesihatan Pasir Mas	
		Klinik Kesihatan Tendong	
	Tanah Merah	Klinik Kesihatan Batu Gajah	
	Bachok	Klinik Kesihatan Bachok	
		Klinik Kesihatan Gunong	

No.	State/District	Health Clinic	Total Fundus Camera
13.	<b>Sabah</b>		3
	Kota Kinabalu	Klinik Kesihatan Luyang	
	Sandakan	Klinik Kesihatan Sandakan	
	Penampang	Klinik Kesihatan Penampang	
14	<b>Sarawak</b>		4
	Miri	Klinik Kesihatan Miri	
	Sibu	Klinik Kesihatan Lanang	
	Kuching	Klinik Kesihatan Jalan Masjid	
Klinik Kesihatan Sentosa			
<b>Total</b>			<b>107</b>

## LIST OF ABBREVIATIONS

<b>ACE</b>	Angiotensin Converting Enzyme (ACE) Inhibitors
<b>ADED</b>	Advanced Diabetic Eye Disease
<b>AGE</b>	Advanced Glycation End (AGE) Product Inhibitors
<b>Anti-VEGF</b>	Anti-Vascular Endothelial Growth Factor
<b>ARIs</b>	Aldose Reductase Inhibitors (ARIs)
<b>BIO</b>	Binocular Indirect Ophthalmoscope
<b>BMI</b>	Body Mass Index
<b>CI</b>	Confidence Interval
<b>CPG</b>	Clinical Practice Guidelines
<b>DM</b>	Diabetes Mellitus
<b>DR</b>	Diabetic Retinopathy
<b>DRS</b>	Diabetic Retinopathy Screening
<b>ETDRS</b>	Early Treatment for Diabetic Retinopathy Study
<b>GDM</b>	Gestational Diabetes Mellitus
<b>IDF</b>	The International Diabetes Federation
<b>MOH</b>	Ministry of Health
<b>NED</b>	National Eye Database
<b>NPDR</b>	Non-Proliferative Diabetic Retinopathy
<b>OR</b>	Odds Ratio
<b>PDR</b>	Proliferative Diabetic Retinopathy
<b>PKC</b>	Protein Kinase C (PKC) Inhibitors
<b>PRP</b>	Pan-Retinal Photocoagulation
<b>RCT</b>	Randomised Controlled Trial
<b>SBP</b>	Systolic Blood Pressure
<b>T1DM</b>	Type 1 Diabetes Mellitus
<b>T2DM</b>	Type 2 Diabetes Mellitus
<b>VA</b>	Visual Acuity

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