Evidenced-Based Guidelines for Diabetes
AOA Health Promotions Committee

- Decision-making using the best clinical research evidence available, in conjunction with individual clinical experience and patient preferences
- Takes into account risk and benefits of clinical decisions

Disclaimer
Recommendations made in this guideline do not represent a standard of care. Instead, the recommendations are intended to assist the clinician in the decision-making process. Patient care and treatment should always be based on a clinician’s independent professional judgment, given the individual’s circumstances, state laws and regulations.

Evidence-Based Clinical Practice Guidelines
- Provides practitioners a clear explanation of the logical relationship between alternative care options and health outcomes.
- Based on a systemic review of existing evidence.
- Developed by a knowledgeable, multidisciplinary panel of experts and key stakeholders.

Key Features in the Guideline
- Strength of Evidence and Clinical recommendations are graded with ‘Strength of Evidence’ listed first/ followed by ‘Clinical Recommendation’
- Clinical Action Items highlighted in ‘Action’ boxes

Historical Perspective
- Caring for the Patient with Diabetes Mellitus
  1. 1993 – 1st Clinical Practice Guideline to be produced
  2. Clinical Care Center of AOA → 20 CPG’s
  3. An Investment in Optometry’s future
Clinical Practice Guidelines Are:

- Public Documents
- Covering Billable Procedures and Examinations
- Professional Liaison Documents
- Part of the OD Curriculum
- Supporting Documents ➔ Scope and Expansion
- Supporting optometrists on the front lines

Insulin–Dependent Diabetes Mellitus (IDDM)

- Results from destruction of islet cells in the pancreas.
- More common in persons under 20 years of age.
- Etiology both genetic and environmental.
- Patients acutely symptomatic at the time of onset. ("the polys")

For more information or to see the Guidelines, please visit: www.aoa.org/evidence

Non–Insulin Dependent Diabetes Mellitus (NIDDM)

- Resistance of body tissues to the action of insulin:
  - Insulin resistance
  - Beta-cell failure
- Usually occurs after age 40
- Gradual onset of symptoms (half are unaware)

Diabetes: A Definition

- Group of metabolic diseases
- Failure of the pancreas to produce sufficient amounts of the hormone insulin
  - or -
- Resistance of the body's cells to the action of insulin

Pre–Diabetes

- Comes before type 2 diabetes
- Blood glucose are higher than normal, but not yet diabetes
- Most people with prediabetes don't know they have it

<table>
<thead>
<tr>
<th>Prediabetes Ranges</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Plasma Glucose Test</td>
<td>100-125 mg/dl</td>
</tr>
<tr>
<td>Oral Glucose Tolerance Test</td>
<td>140-199 mg/dl</td>
</tr>
</tbody>
</table>

(Change graphic-modified)
Gestational Diabetes

- Onset or first recognition during pregnancy
- Limited to the term of the pregnancy
- 35–60% chance of developing type 2 in subsequent 10–20 yrs

Risk Factor

Type 1
- Family History
- Viral Exposure
- Autoimmune conditions

Type 2
- Family History
- Overweight
- Age
- Ethnicity

Other Forms

- May develop from:
  - genetic defects
  - pancreatic diseases or endocrinopathies
  - medications
  - toxic chemicals
  - infections
  - uncommon immune-mediated diabetes (e.g., “stiff man syndrome”)

Diabetic Retinal Disease

Nonproliferative Diabetic Retinopathy (NPDR)
- Hemorrhages and/or Microaneurysms
- Hard exudates
- Soft exudates (cotton wool spots)
- Intraretinal microvascular abnormalities (IRMA)
- Venous looping
- Venous beading

Epidemiology

- 26 million Americans have diabetes
  - 90% have type 2 diabetes
- 79 million more Americans are at high risk for developing diabetes within 10 years
- 1.8 million new cases diagnosed each year

Mild NPDR

- At least one retinal microaneurysm
  - the severity is less than that depicted in ETDRS standard photograph 2A
  - No other diabetic retinal lesion or abnormality associated with diabetes is present

(Standard photo 2A)
Moderate NPDR

- Hemorrhages and/or microaneurysms greater than ETDRS standard photograph 2A in one to three retinal quadrants and soft exudates, venous beading, and IRMAs may be present to a mild degree.

Severe NPDR

- Characterized by any one of the following:
  - Hemorrhages/Microaneurysms greater than ETDRS standard photograph 2A in four retinal quadrants.
  - Venous Beading (exemplified by that in standard photograph 6B) in two or more retinal quadrants.

Very Severe NPDR

- Two or more criteria for severe NPDR are met, in the absence of frank neovascularization.

Proliferative Diabetic Retinopathy (PDR)

- Severe sight-threatening form of diabetic retinopathy.
- 50% of eyes with PDR are blind within 5 years, as reported by ETDRS.

Prominent IRMA (greater than ETDRS standard photograph 8A) in at least one retinal quadrant.

*This “4-2-1” rule is an important clinical tool for determining the risk of progressing to proliferative diabetic retinopathy.*
New vessels on or within one disc diameter of the disc (NVD), new vessels elsewhere on the retina (i.e., not on or within one disc diameter of the optic disc) (NVE)

Fibrous proliferation on or within one disc diameter of the optic disc (FPD) or elsewhere on the retina (FPE)

High-Risk PDR

- NVD > one-fourth to one-third DA in size (ETDRS standard photograph 10A)
- NVD < one-fourth DA in size with fresh VH or PRH present
- NVE > one-half DA in size with VH or PRH present

(Add photo 10A)

Diabetic Macular Edema

- Intraretinal fluid in the macular with or without lipid exudates or cystoid changes
- Visual acuity is generally compromised when DME affects the fovea

Early Proliferative Diabetic Retinopathy

- NVE or NVD < ETDRS standard photograph 10A.
- PRH and NVE < one-half disk area (DA), without NVD.
- (Add photo 10A)

Clinically Significant Macular Edema (CSME)

- Thickening of the retina ≤ 500 microns (1/3 DD) from the center of the macula.
- Hard exudates ≤ 500 microns (1/3 DD) from the center of the macula with thickening of the adjacent retina.
- A zone or zones of retinal thickening ≥ 1 DA in size, any portion of which is ≤ 1 DD from the center of the macula.
Loss of visual acuity
Refractive error changes
Changes in color vision
Accommodative dysfunction
Visual Field Changes
Eye Movement Anomalies
Pupillary Reflexes

Conjunctiva changes
Tear film abnormalities
Corneal changes (Decreased sensitivity, slower healing, difficulty with abrasions)
Depigmentation of the iris with subsequent pigment deposition on the corneal endothelium

Neovascularization of the iris
Neovascular glaucoma
Cataracts
Vitreous degeneration and posterior vitreous detachment
Papillopathy
Ischemic optic neuropathy
Open angle glaucoma

Optic Nerve Damage

Eye Muscle Problems
Cataract

**CPG Relevant Action:**
Patients should be questioned about the awareness of their personal diabetes ABCs (A1C, blood pressure, cholesterol levels, and their history of smoking).

**Individuals with Undiagnosed Diabetes Mellitus**
- Patient History
  - Common ocular symptoms
  - Systemic symptoms
- Diabetes Risk Assessment
  - Diabetes Risk Calculator
  - Weill-Cornell Medical College Patient Self-Assessment Score for Diabetes

**Individuals with Diagnosed Diabetes Mellitus**
- Patient History
  - Quality of vision
  - Ocular history
  - Medical history
  - Duration of diabetes
  - Recent values for the ABCs of diabetes (A1c, Blood Pressure, Cholesterol, Smoking)
  - Prescribed management

**CPG Relevant Action Item:**
The individual’s primary care physician should be informed of eye examination results following each examination, even when retinopathy is minimal or not present.

**Ocular Examination**
- Best corrected visual acuity
- Pupillary reflexes
- Ocular motility
- Refractive status
- Confrontation visual field testing or visual field evaluation
- Slit lamp biomicroscopy
- Tonometry
- Dilated retinal examination
Ocular Examination Schedule
Determined on the basis of:
◦ Type of diabetes
◦ Duration
◦ Age
◦ Level of adherence and understanding of their treatment plan
◦ Concurrent medical status
◦ Ocular findings and symptoms
◦ Subjective changes in vision

Patient Education
◦ Disease process
◦ Complications and risks
◦ Patients to report all ocular symptoms
◦ Follow-up examinations and management
◦ Diabetes education programs
◦ Smoking cessation programs

CPG Relevant Action Item:
◦ As diabetes may go undiagnosed for many years, any individual with type 2 diabetes should have a comprehensive dilated eye examination soon after the diagnosis of diabetes

CPG Relevant Action Item:
◦ Individuals should be advised of the risks of smoking related to diabetes and encouraged to quit smoking and/or seek smoking cessation assistance

CPG Relevant Action Item:
◦ The individual’s primary care physician should be informed of eye examination results following each examination, even when retinopathy is minimal or not present.

Glycemic Control
◦ According to the American Diabetes Association, reducing A1C levels to less than 7 percent has been shown to reduce microvascular complications
◦ However, standards emphasize individualization
◦ Intensive glycemic therapy also increases the relative risk of severe hypoglycemia by 30 percent
Optometrists should have a rapid-acting carbohydrate (glucose gel or tablets, sugar-sweetened beverage or fruit juice) in their offices for use with diabetes patients who experience acute hypoglycemia during an eye examination.

Patients with diabetes are at increased risk of chronic vision loss, subsequent functional impairment, and resultant disability.

Patients with diabetes-related vision loss should be evaluated to determine their potential to benefit from comprehensive low vision rehabilitation.

Patients who experience vision loss from diabetes should be provided, or referred for, a comprehensive examination of the visual impairment by a practitioner who is trained or experienced in vision rehabilitation.

Case 1 – Patient JTM

- 54 y/o male diagnosed x 1 month with T2DM
- Case History
  - Q 1 - Do you know what your latest A1c test result is? That’s the test that measures your average blood sugar levels over the last 3 months and predicts your likelihood of developing diabetes complications, especially those affecting your eye health (Action Item)

Sidebar – Important Note About A1c

- Action ITEM: The glycemic goal for persons with diabetes should be individualized, taking into consideration the risk of hypoglycemia, anticipated life expectancy, duration of disease and comorbid conditions
  - Low A1c increases risk of death in some older pts with CVD, and children
  - An 85 y/o with no DR does not need an A1c < 6.5%
  - COMMUNICATE with the PCP/Endo about glycemic targets

Patient JTM (Cont.)

- Case History
  - Q 2 – Do you know what blood pressure your primary care doctor/endocrinologist has recommended for you? It’s important because high blood pressure damages the eyes in people with diabetes more than people without diabetes
Patient JTM (Cont.)

- Case History
  - Q3: Do you know what your blood cholesterol levels are, especially your levels of good and bad cholesterol? It’s important because these levels affect your risk of eye and heart disease.

Retinal Imaging is…

- Wonderful and extremely useful

  BUT

- Does not substitute for clinical examination, especially in a court of law...

Patient JTM (Cont.)

- Case History
  - Q4: Do you smoke cigarettes or use tobacco? It’s important because tobacco use increases the risk of eye complications from diabetes.

Send a Diabetes Eye Examination Report

Available at www.aoa.org/diabetes

Patient JTM – Ocular examination

- Perform a dilated retinal examination with stereoscopic assessment of the disk and macula.

- OD: Many people have diabetes for several years before they are diagnosed, so we are going to dilate, or enlarge your pupils to thoroughly check for changes to the tiny blood vessels inside your eyes and I will send a report of my findings to your PCP and endocrinologist.

Patient JTM –

- You notice your patient seems to be ‘spacing out’ during your examination or consult.

- You check the chart to determine if he is taking any diabetes medications that can cause hypoglycemia, especially insulin or a sulfonylurea drug like Glyburide, Amaryl® or Micronase®.
JTM has started insulin therapy – rapid-acting Novolog® and the basal insulin, Levemir®

You ask JTM if he feels weak or shaky, and if he has his blood glucose meter

- JTM self tests and his spot glucose is 54 mg/dl or
- JTM has no meter, so you test with the office meter you wisely purchased for such a common event and find his spot glucose is 54 mg/dl or
- You assume JTM is hypoglycemic based on his Sx and then you…..

Hypoglycemia
Always have a rapid-acting carbohydrate in the office (juice, sugared soda, glucose gel) for pts on meds that can cause low blood glucose....

15gm CHO will ↑ BG ~ 30-40 mg/dl (1.7-2.2 mmol/L)

Patient JTM
You ask JTM if he feels weak or shaky, and if he has his blood glucose meter with him

- JTM self tests and his spot glucose is 54 mg/dl or
- JTM has no meter, so you test with the office meter you wisely purchased for such a common event and find his spot glucose is 54 mg/dl or
- You assume JTM is hypoglycemic based on his Sx and then you…..

Symptoms of Hypoglycemia
- Shaking
- Sweating
- Fast heart beat
- Dizziness
- Anxious
- Hunger
- Impaired vision

Action Item
- Optometrists should have a rapid-acting carbohydrate (glucose gel or tablets, sugar-sweetened beverage or fruit juice) in their offices for use with diabetic patients who experience acute hypoglycemia during an eye examination

Symptoms of severe low blood sugar
- Seizure
- Loss of consciousness (coma)
- Stroke
- Death
Treatment of Hypoglycemia

15 to 20 grams of carbohydrate (that puts glucose into bloodstream in about 5 minutes. Any quick-sugar food will raise your blood sugar about 30 milligrams per deciliter (mg/dL) in about 15 to 20 minutes.

Check blood sugar level again 15 minutes. Have person drink ½ glass of juice or regular soft drink, or 1 glass of milk.

If symptoms persist, call internist.

Follow up with a light snack (½ peanut butter or meat sandwich and ½ glass of milk)

Patient KG
- 44 y/o male with T1DM x 22 years
- Last HbA1c = 11.6%
- In–office BP = 126/78
- Meds: Lantus®, Novolog®
- BCVA is 20/30 OD and 20/100 OS
- 1+ PSC OD/OS No NVI seen
- IOP = 17/18
- “I am seeing lines in my vision for the last week”
- “I got a shot in my right eye last year and had to pay $900 (high-deductible insurance), so never went back”

What’s The Diagnosis
- May be more than one answer
  - Mild NPDR
  - Moderate NPDR
  - Severe NPDR
  - PDR
  - High-Risk PDR
  - Traction Retinal Detachment
  - DME
  - CSME  Not enough information to be sure
Proper Management?

- Take photos and monitor x 1 month
- Referral to ophthalmology
- Prompt referral to a vitreo-retinal surgeon
- Stat referral to an ophthalmologist experienced in the management of diabetic retinal disease
- Stat referral to the endocrinologist or PCP for better glucose control

Outcome for KG

- PRP performed OU by retinal specialist
- A1c improved to 8% under endocrinologists’ care (target = 7.5 - 8%)
- Vitrectomy performed for vitreo-macular traction (VMT) OD and traction retinal detachment (TRD) OS
- Cataract surgery performed OU
  - BCVA 20/80 and 20/1000
  - KG referred to vision low vision specialist
- Diagnosed with autonomic cardiomyopathy

Relevant CPG Action Items

- Patients with high-risk proliferative diabetic retinopathy (PDR) should receive referral to an ophthalmologist experienced in the management of diabetic retinal disease for prompt pan-retinal photocoagulation
- Prompt referral to a vitreo-retinal surgeon is indicated when a vitreous hemorrhage, a retinal detachment or other evidence of PDR is present

More Relevant Action Items

- The glycemic goal for persons with diabetes should be individualized, taking into consideration their risk of hypoglycemia, anticipated life expectancy, duration of disease and co-morbid conditions
- Individuals who experience vision loss from diabetes should be provided or referred for a comprehensive examination by a practitioner trained/experienced in vision rehabilitation

Relevant CPG Action Items

- The individual’s primary care physician should be informed of eye examination results following each examination, even when retinopathy is minimal or not present
- As part of the proper management of diabetes, the optometrist should make referrals for concurrent care when indicated
### TABLE 1
Prevalence of Diagnosed and Undiagnosed Diabetes: Americans Aged 20 Years or Older (2010)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number or percentage who have diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged 20 years or older</td>
<td>25.6 million, or 11.3% of all people in this age group</td>
</tr>
<tr>
<td>Aged 65 years or older</td>
<td>10.9 million, or 26.9% of all people in this age group</td>
</tr>
<tr>
<td>Men</td>
<td>13.0 million, or 11.8% of all men ages 20 years or older</td>
</tr>
<tr>
<td>Women</td>
<td>12.6 million, or 10.8% of all women ages 20 years or older</td>
</tr>
<tr>
<td>Non-Hispanic Whites</td>
<td>15.7 million, or 10.2% of all non-Hispanic whites ages 20 years or older</td>
</tr>
<tr>
<td>Non-Hispanic Blacks</td>
<td>4.9 million, or 19.7% of all non-Hispanic blacks ages 20 years or older</td>
</tr>
</tbody>
</table>


### TABLE 2
Duration of Diabetes Mellitus and Presence of Diabetic Retinopathy and Diabetic Macular Edema

<table>
<thead>
<tr>
<th>Diabetes</th>
<th>Duration of Disease</th>
<th>Ocular Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>&gt; 5 years</td>
<td>17 to 29% have some retinopathy</td>
</tr>
<tr>
<td></td>
<td>&gt; 10 years</td>
<td>60% have some retinopathy</td>
</tr>
<tr>
<td></td>
<td>&gt; 15 years</td>
<td>78 to 97% have some degree of retinopathy; 25% progress to proliferative diabetic retinopathy</td>
</tr>
<tr>
<td></td>
<td>&gt; 20 years</td>
<td>60 to 60% progress to proliferative retinopathy</td>
</tr>
<tr>
<td></td>
<td>&gt; 25 years</td>
<td>29% have diabetic macular edema; 17% have clinically significant macular edema</td>
</tr>
<tr>
<td>Type 2</td>
<td>At diagnosis</td>
<td>20 to 39% have some retinopathy</td>
</tr>
<tr>
<td></td>
<td>&gt; 4 years</td>
<td>4% progress to proliferative retinopathy</td>
</tr>
<tr>
<td></td>
<td>&gt; 10 years</td>
<td>25% of individuals on insulin have diabetic macular edema; 14% on oral medications have diabetic macular edema</td>
</tr>
<tr>
<td></td>
<td>&gt; 15 years</td>
<td>60 to 80% have some retinopathy; up to 20% progress to proliferative retinopathy</td>
</tr>
</tbody>
</table>
### TABLE 3

<table>
<thead>
<tr>
<th>Severity of Condition</th>
<th>Natural Course Rate of Progression to PDR (1 year)</th>
<th>HR PDR (5 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild NPDR</td>
<td>5%</td>
<td>15%</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>12 to 27%</td>
<td>33%</td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>52%</td>
<td>60 to 75%</td>
</tr>
<tr>
<td>Non-high-risk PDR</td>
<td></td>
<td>75%</td>
</tr>
</tbody>
</table>

Twenty-five to forty percent of individuals with high-risk proliferative diabetic retinopathy (HR PDR) develop severe vision loss within 2 years.

### TABLE 4:

**Frequency and Composition of Evaluation and Management Visits for Retinal Complications of Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Severity of Condition</th>
<th>Natural Course Rate of Progression to</th>
<th>Frequency of Follow-up</th>
<th>Components of Follow-up Evaluations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PDR (1 year)</td>
<td>HR (5 years)</td>
<td>Fundus Photography</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>5%</td>
<td>15%</td>
<td>No</td>
</tr>
<tr>
<td>No macular edema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macular edema</td>
<td></td>
<td>4 to 6 months</td>
<td>Yes</td>
</tr>
<tr>
<td>CSME</td>
<td></td>
<td>2 to 4 months**</td>
<td>Yes</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>12-27%</td>
<td>33%</td>
<td>No</td>
</tr>
<tr>
<td>No macular edema</td>
<td></td>
<td>6 to 8 months</td>
<td>Yes</td>
</tr>
<tr>
<td>Macular edema (not CSME)</td>
<td></td>
<td>4 to 6 months</td>
<td>Yes</td>
</tr>
<tr>
<td>CSME</td>
<td></td>
<td>2 to 4 months**</td>
<td>Yes</td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>52%</td>
<td>60-75%</td>
<td>No</td>
</tr>
<tr>
<td>No macular edema</td>
<td></td>
<td>3 to 4 months</td>
<td>Yes</td>
</tr>
<tr>
<td>Macular edema (not CSME)</td>
<td></td>
<td>2 to 3 months</td>
<td>Yes</td>
</tr>
<tr>
<td>CSME</td>
<td></td>
<td>2 to 3 months**</td>
<td>Yes</td>
</tr>
<tr>
<td>Very Severe NPDR</td>
<td>75%</td>
<td>75%</td>
<td>No</td>
</tr>
<tr>
<td>No macular edema</td>
<td></td>
<td>2 to 3 months</td>
<td>Yes</td>
</tr>
<tr>
<td>Macular edema (not CSME)</td>
<td></td>
<td>2 to 3 months</td>
<td>Yes</td>
</tr>
<tr>
<td>CSME</td>
<td></td>
<td>2 to 3 months**</td>
<td>Yes</td>
</tr>
<tr>
<td>Non-high-risk PDR</td>
<td>75%</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>No macular edema</td>
<td></td>
<td>2 to 3 months</td>
<td>Yes</td>
</tr>
<tr>
<td>Macular edema</td>
<td></td>
<td>2 to 3 months</td>
<td>Yes</td>
</tr>
</tbody>
</table>
### TABLE 4 (continued)

<table>
<thead>
<tr>
<th>Category</th>
<th>CSME</th>
<th>2 to 3 months**</th>
<th>Yes</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk PDR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No macular edema</td>
<td></td>
<td>2 to 3 months</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Macular edema</td>
<td></td>
<td>1 to 2 months</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CSME</td>
<td></td>
<td>1 to 2 months**</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*HPC = High-risk category
**Follow-up is typically monthly for the first year of treatment if intravitreal anti-VEGF injections are given.

### TABLE 5

**Management of Non-retinal Ocular Complications of Diabetes**

<table>
<thead>
<tr>
<th>Category</th>
<th>Ocular /Visual Complications</th>
<th>Management*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional</td>
<td>Loss of visual acuity</td>
<td>Assess visual acuity as recommended in the Optometric Clinical Practice Guideline on Adult Eye and Vision Examination, Pediatric Eye and Vision Examination, or Care of the Patient with Visual Impairment.</td>
</tr>
<tr>
<td></td>
<td>Refractive error changes</td>
<td>Assess refractive error, distance and near and pinhole acuity as recommended in the Optometric Clinical Practice Guidelines on Care of the Patient with Myopia and Care of the Patient with Hyperopia. Change in spectacle or contact lenses prescription, as indicated by the patient’s visual requirements, with special attention to the person’s level of glycemic control. Counsel patients about variable refractive status due to fluctuations in blood glucose.</td>
</tr>
<tr>
<td></td>
<td>Changes in color vision</td>
<td>Perform color vision assessment that is sensitive to acquired (i.e., generally blue/yellow) color vision loss.</td>
</tr>
<tr>
<td></td>
<td>Changes in visual fields</td>
<td>Assess visual field changes and manage as recommended in the Optometric Clinical Practice Guideline on Care of the Patient with Visual Impairment. Rule out other causes of visual field changes.</td>
</tr>
<tr>
<td>Eye movement anomalies</td>
<td>Cranial nerve palsy</td>
<td>Assess multiple diagnostic positions of gaze; tests of smooth pursuits (versions and ductions), and saccades. Rule out other cranial nerve palsy or other etiologies.</td>
</tr>
<tr>
<td>Pupils</td>
<td>Sluggish pupillary reflexes</td>
<td>Rule out optic neuropathy and other neurological etiologies.</td>
</tr>
<tr>
<td></td>
<td>Afferent pupillary defects</td>
<td></td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>Bilbar microaneurysms</td>
<td>Monitor</td>
</tr>
<tr>
<td>Category</td>
<td>Ocular /Visual Complications</td>
<td>Management*</td>
</tr>
<tr>
<td>------------</td>
<td>-----------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Tear film</td>
<td>Dry eye syndrome</td>
<td>Recommend use of artificial tears, ocular lubricants, and other dry eye</td>
</tr>
<tr>
<td></td>
<td></td>
<td>management techniques as recommended in the **Optometric Clinical Practice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Guideline** on Care of the Patient with Ocular Surface Disease.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor for corneal complications.</td>
</tr>
<tr>
<td>Cornea</td>
<td>Reduced corneal sensitivity</td>
<td>Monitor for abrasions, keratitis, or ulcerations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor contact lens wear as recommended in the **Optometric Clinical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Practice Guideline** on Care of the Patient with Contact Lenses.</td>
</tr>
<tr>
<td></td>
<td>Basement membrane anomalies</td>
<td>Recommend lubricating drops/artificial tears.</td>
</tr>
<tr>
<td></td>
<td>Recurrent corneal erosions</td>
<td>Prescribe sodium chloride solution/ointment or ocular surface lubricant.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bandage contact lenses or patching, as necessary.</td>
</tr>
<tr>
<td>Iris</td>
<td>Rubecosis Iridis</td>
<td>Gonioscopy to rule out anterior chamber angle involvement and neovascular</td>
</tr>
<tr>
<td></td>
<td>(neovascularization on the</td>
<td>glaucoma.</td>
</tr>
<tr>
<td></td>
<td>Iris)</td>
<td>Dilated retinal examination to evaluate proliferative diabetic retinopathy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Refer to an ophthalmologist experienced in the management of diabetic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>retinal disease for possible panretinal photocoagulation and/or anti-VEGF</td>
</tr>
<tr>
<td>Eyelids</td>
<td>Ptosis</td>
<td>Determine etiology (neurologic, mechanical, immunological).</td>
</tr>
<tr>
<td>Category</td>
<td>Ocular /Visual Complications</td>
<td>Management*</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Lens</td>
<td>Cataracts</td>
<td>Assess and monitor degree of lens opacification. Refraction to obtain best visual acuity. If functional deficits remain, manage as recommended in the <em>Optometric Clinical Practice Guideline</em> on Care of the Patient with Visual Impairment. Surgery may be indicated, if adequate visualization of the retina is no longer possible or if visual acuity is decreased secondary to the cataract. Refer to <em>Optometric Clinical Practice Guideline</em> on Care of the Adult Patient with Cataract for more information.</td>
</tr>
<tr>
<td>Vitreous</td>
<td>Premature syneresis/degeneration</td>
<td>Dilated retinal examination. Ultrasound, if retinal view is obscured. Consultation with an ophthalmologist experienced in the management of diabetic retinal disease.</td>
</tr>
<tr>
<td></td>
<td>Hemorrhage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Detachment</td>
<td></td>
</tr>
<tr>
<td>Optic Disc</td>
<td>Papillopathy</td>
<td>Management of diabetic papillopathy or ischemic optic neuropathy may require consultation with a neuro-ophthalmologist or neurologist to rule out all other potential etiologies.</td>
</tr>
<tr>
<td></td>
<td>Ischemic optic neuropathy</td>
<td></td>
</tr>
</tbody>
</table>

* Communication with the patient’s health care provider regarding ocular and visual findings, and patient education are an integral part of management for all conditions.
<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Hypoglycemic potential (Used alone)</th>
<th>Injectable</th>
<th>A1C reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>Metformin</td>
<td>Minimal</td>
<td>No</td>
<td>1.5-2%</td>
</tr>
<tr>
<td>Sulfonylurea &amp; glinides</td>
<td>Glyburide, Glipizide, Glimepiride, Nateglinide, Repaglinide</td>
<td>Yes</td>
<td>No</td>
<td>1-2%</td>
</tr>
<tr>
<td>Alpha-glucosidase Inhibitor</td>
<td>Acarbose, Miglitol</td>
<td>Minimal</td>
<td>No</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Thiazolidinedione</td>
<td>Rosiglitazone, Pioglitazone</td>
<td>Minimal</td>
<td>No</td>
<td>0.6-1.9%</td>
</tr>
<tr>
<td>DPP-IV inhibitor</td>
<td>Sitagliptin, Linagliptin, Saxagliptin</td>
<td>Minimal</td>
<td>No</td>
<td>0.6-0.8%</td>
</tr>
<tr>
<td>Bile acid sequestrant</td>
<td>Colesevelam</td>
<td>Minimal</td>
<td>No</td>
<td>0.5-0.6%</td>
</tr>
<tr>
<td>Dopamine agonist</td>
<td>Bromocriptine</td>
<td>Minimal</td>
<td>No</td>
<td>0.6-1.0%</td>
</tr>
<tr>
<td>SGLT2-Inhibitor</td>
<td>Canagliflozin</td>
<td>Minimal</td>
<td>No</td>
<td>0.9-1.1%</td>
</tr>
<tr>
<td>GLP-1 agonist/analog</td>
<td>Exenatide, Exenatide LAR, Liraglutide</td>
<td>Minimal</td>
<td>Yes</td>
<td>0.8-1.2%</td>
</tr>
<tr>
<td>Amylin analog</td>
<td>Pramlintide</td>
<td>Yes (when used with insulin)</td>
<td>Yes</td>
<td>0.6%</td>
</tr>
</tbody>
</table>
APPENDIX FIGURE 1
Optometric Management of the Patient With Undiagnosed Diabetes Mellitus: A Flowchart

Patient assessment

Suspect undiagnosed diabetes

No ocular manifestations

Request A1C or fasting blood glucose or refer for testing

A1C < 5.7% or fasting blood glucose < 110 mg/dL
- Schedule follow-up eye examination

A1C 5.7 to 6.4% or fasting blood glucose 110 - 125 mg/dL
- Re-test A1C or fasting blood glucose

A1C ≥ 6.5% or fasting blood glucose ≥ 126 mg/dL
- Refer for evaluation

Schedule follow-up eye examination

Ocular manifestations

Non-retinal abnormality
- Manage or refer per Guideline

Non-proliferative retinopathy
- Refer for treatment of diabetes

Proliferative retinopathy

Diabetic macular edema
APPENDIX FIGURE 2

Optometric Management of the Patient With Diagnosed Diabetes Mellitus: A Flowchart

Patient assessment

Individual known to have:

- No retinal manifestations
- Non-proliferative retinopathy
- Proliferative retinopathy
- Diabetic macular edema

No ocular manifestations

- Schedule follow-up eye examination
- Counsel patient regarding risk for ocular manifestations
- Communicate with physician treating patient’s diabetes

Manage or refer per Guideline

Communicate with physician treating person’s diabetes
## APPENDIX TABLE 1
Comparison of ETDRS and International Clinical Diabetic Retinopathy and Macular Edema Severity Scale

<table>
<thead>
<tr>
<th>Diabetic Retinopathy</th>
<th>ETDRS</th>
<th>International Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>No apparent DR</td>
<td></td>
<td>No abnormalities</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>At least one Ma</td>
<td>Ma only</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>H/Ma &gt; standard photo 2A or soft exudates, VB and IRMA present</td>
<td>More than just Ma, but less than severe NPDR</td>
</tr>
</tbody>
</table>
| Severe NPDR          | One of the following:  
  - H/Ma ≥ standard photo 2A in all 4 quadrants  
  - VB present in at least 2 quadrants  
  - IRMA ≥ standard photo 6A in at least 1 quadrant | No signs of PDR, with any of the following:  
  - >20 intraretinal hemorrhages in each of 4 quadrants  
  - Definite VB in ≥ 2 quadrants  
  - Prominent IRMA in ≥ 1 quadrant |
| PDR                  |       | One or both of the following:  
  - Neovascularization, Vitreous/ preretinal hemorrhage |
| Mild PDR             | One or more of the following:  
  - NVE, FPD or FPE present, NVD and NVE present |
| Moderate PDR         | One or more of the following:  
  - NVE elevated  
  - NVD < standard photo 10A  
  - VH/PRH and NVE < ½ DA  
  - NVD absent |
| High-risk PDR        | One or more of the following:  
  - NVD ≥ ½ to 1/3 DA (standard photo 10A)  
  - NVD and VH/PRH  
  - NVE ≥ ½ DA and VH/PRH |
### APPENDIX TABLE 1 (continued)

<table>
<thead>
<tr>
<th>Diabetic Macular Edema</th>
<th>ETDRS</th>
<th>International Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>DME apparently absent</td>
<td></td>
<td>No apparent retinal thickening or HE in posterior pole</td>
</tr>
<tr>
<td>DME apparently present</td>
<td></td>
<td>Some apparent retinal thickening or HE in posterior pole</td>
</tr>
<tr>
<td>Mild DME</td>
<td>Retinal thickening within 2 DD of center of the macula</td>
<td>Some retinal thickening or HE in posterior pole, but distant from center of the macula</td>
</tr>
<tr>
<td>Moderate DME</td>
<td></td>
<td>Retinal thickening or HE approaching, but not involving, the center of the macula</td>
</tr>
<tr>
<td>Severe DME</td>
<td></td>
<td>Retinal thickening or HE involving the center of the macula</td>
</tr>
<tr>
<td>CSME</td>
<td>• One or more of the following:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Thickening of the retina ≤ 500 microns from the center of the macula</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• HE ≤ 500 microns from the center of the macula with thickening of the adjacent retina</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• A zone or zones of retinal thickening ≥ 1 DA in size, any portion of which is ≤ 1 DD from the center of the macula</td>
<td></td>
</tr>
</tbody>
</table>

**Sources:**


DR – Diabetic retinopathy
NPDR – Non-proliferative diabetic retinopathy
PDR – Proliferative diabetic retinopathy
DME – Diabetic macular edema
CSME – Clinically significant macular edema
## APPENDIX TABLE 2

Effects of Systemic Medications on the Onset and Progression of Diabetic Retinopathy

<table>
<thead>
<tr>
<th>Agents for glycemic control</th>
<th>Actions</th>
<th>Systemic effects</th>
<th>Specific mechanism</th>
<th>References (Author or study)</th>
<th>Implications for diabetes eye care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Insulin, glucagon, somatostatin, somatostatin analogues, insulin</td>
<td>Regulates carbohydrate, lipid and protein metabolism</td>
<td>Increased VEGF gene expression**</td>
<td>LRP15**; DCCT**; DCM**</td>
<td>Glycemic control with HBA1c target of &lt;7% significantly reduces the risk of developing or worsening of DRS**; May reduce the need for laser treatment by 21%<strong>; Reduces the risk of developing or worsening of DRS</strong>; Reduces the risk of developing or worsening of DRS**.</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Rosiglitazone, Pioglitazone</td>
<td>Improves insulin sensitivity</td>
<td><strong>PPARγ agonist activity; Decreased VEGF production</strong></td>
<td>Shih et al.<strong>; Fong et al.</strong></td>
<td>Delays the onset of PDR**; May reduce the risk of DRS**.</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Metformin</td>
<td>Improves glycemic control, Cardioprotective effects</td>
<td>Decreased concentrations of TNF-α, IL-6 and CRP**</td>
<td>UKPDS**</td>
<td>First line oral hypoglycemic agent particularly beneficial in T2DM patients with overweight or obesity and cardiovascular risk factors**; Potential for preventing or delaying progression of DR**.</td>
</tr>
</tbody>
</table>

### Agents for lipid control

| Fibra | Fenofibrate, Clofibrate, Ezetimibe | Improves lipid parameters (increases HDL cholesterol levels, reduces levels of total and LDL cholesterol and triglycerides) | **PPARα agonist activity** | FIELD**; ACCORD Eye** | Reduces the need for laser treatment by 36%**; Reduces the risk of developing or worsening of DRS**; Reduces the risk of developing or worsening of DRS**. |

### Statins

| STAT | Atonozolast, Simvastatin | Improves lipid parameters (reduces total and LDL cholesterol levels) | **PPARα agonist activity** | STARK-2**; CAMEO** | Evidence insufficient to support primary use of statins to prevent DRS progression**; Reduces the risk of developing or worsening of DRS**; Reduces the risk of developing or worsening of DRS**. |

### Agents for blood pressure control

| ACE Inhibitors | Captopril, Enalapril, Lisinopril | Block the conversion of angiotensin-I to angiotensin-II | Renin-angiotensin system blockade** | UKPDS**; LUCID**; RASSO** | Reduces the risk of developing or worsening of DRS**; Reduces the risk of developing or worsening of DRS**; Reduces the risk of developing or worsening of DRS**. |

| ARB | Conivaptan, Losartan, Telmisartan, Losartan | Block the activation of angiotensin-II | Renin-angiotensin system blockade** | RASSO**; DIRECT**; PREVAIL 1; PROTECT 1 and 2** | Treatment with losartan in nondiabetic patients with T2DM reduces the risk for two-step or more progression by 65%**; Treatment with lisinopril in nondiabetic patients with T2DM reduces the risk for two-step or more progression by 65%**; Treatment with losartan in nondiabetic patients with T2DM reduces the risk for two-step or more progression by 65%**. |

**Indicates significant findings at the p<0.05 level.**
## APPENDIX TABLE 2 (continued)

### Effects of Systemic Medications on the Onset and Progression of Diabetic Retinopathy

**REVIEW**

<table>
<thead>
<tr>
<th>Systemic agents</th>
<th>Prototypical drug</th>
<th>Systemic effects</th>
<th>Specific ocular mechanism</th>
<th>Reference (Author or study)</th>
<th>Implications for diabetes eye-care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agents for cardiac complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplated agents</td>
<td>Aspirin</td>
<td>Decreased platelet adhesion and aggregation</td>
<td>Decreased prostaglandin production</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Low doses</strong>: Inhibition of COX-1 and TPA production</td>
<td></td>
<td><strong>ETDRS</strong>, <strong>DAMK</strong>, <strong>TIMP-1</strong></td>
<td>Does not worsen DR or predispose to vitreous hemorrhage; At intermediate to high doses may theoretically slow the progression of early DR</td>
</tr>
<tr>
<td></td>
<td>Warfarin</td>
<td>Inhibits synthesis of clotting factors</td>
<td>Inhibits synthesis of clotting factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Di Gasparo et al.,</strong> <strong>Schechter et al.</strong>, <strong>Sa et al.</strong></td>
<td>If maintained at therapeutic range, it is not a contraindication for ocular surgery; Does not increase the risk for intracocular hemorrhage</td>
</tr>
<tr>
<td><strong>Cardiac glycosides</strong></td>
<td>Digoxin</td>
<td>Anti-arrhythmic agent, Inhibits Na+K-ATPase</td>
<td>Inhibition of RAS expression and reduced RAS activity</td>
<td><strong>Prosser et al.,</strong> <strong>Philipp et al.</strong></td>
<td>Can potentially inhibit ocular neovascularization and retinal vascular leakage; Studies are presently being conducted to determine safety and efficacy</td>
</tr>
<tr>
<td><strong>Agents for the treatment of anemia</strong></td>
<td>Erythropoiesis</td>
<td>Stimulates increased red blood cell production</td>
<td>VEGF-independent angiogenic factor</td>
<td><strong>Matrakakis et al.,</strong> <strong>Tong et al.</strong></td>
<td>Patients requiring treatment with erythropoietin should be monitored closely for the development or worsening of DR particularly in the setting of chronic renal disease and anemia</td>
</tr>
<tr>
<td><strong>Anti-inflammatory agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salicylates and COX-2 inhibitors</td>
<td>Salicylate</td>
<td>Inhibits prostaglandin synthesis</td>
<td>Inhibition of COX and prostaglandin production</td>
<td><strong>Reichmann et al.,</strong> <strong>Chew et al.</strong></td>
<td>Concern on cardiovascular safety with long-term use and higher doses</td>
</tr>
<tr>
<td></td>
<td>Celecoxib</td>
<td></td>
<td>Suppression of NF-κB-mediated pathway</td>
<td></td>
<td>Theoretically may slow the progression of early DR</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisone</td>
<td></td>
<td>Mediation of inflammatory response</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inhibition of prostaglandin release</td>
<td><strong>DRS</strong></td>
<td>An independent beneficial effect of systemic corticosteroids on the development or progression of DR and/or DME has not been reported and is likely overshadowed by adverse effects</td>
</tr>
<tr>
<td><strong>Antiangiogenic agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEGF inhibitors</td>
<td>Bevacizumab</td>
<td>Inhibits tumor growth and angiogenesis</td>
<td>Inhibition of all VEGF isoforms</td>
<td><strong>Machida et al.,</strong> <strong>Avery et al.,</strong> <strong>Scott et al.</strong>, <strong>Chen et al.,</strong> <strong>Amsel et al.,</strong> <strong>ORCET</strong></td>
<td>Systemic delivery limited by adverse effects; Intravitreal administration has shown benefit in regression of PDR and neovascularization of PDR; Benefit of intravitreal ranibizumab over bevacizumab reported</td>
</tr>
</tbody>
</table>

*Abbreviations: COX, cyclooxygenase; plus known as prostaglandin G/H synthase; DR, diabetic retinopathy; DME, diabetic macular edema; D, diabetic retinopathy; ETDRS, Early Treatment Diabetic Retinopathy Study; TIMP-1, tissue inhibitor of metalloproteinase 1; VEGF, vascular endothelial growth factor.*