

Metabolic Disease

New Twists on an Old Problem

Optometric Education Consultants

Twin Cities Power Hours

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September 12, 20/20

Disclosure Statement
(next slide)



Disclosures- Greg Caldwell, OD, FAAO

- ☞ Will mention many products, instruments and companies during our discussion
 - ★ I don't have any financial interest in any of these products, instruments or companies
- ☞ Pennsylvania Optometric Association –President 2010
 - 📅 POA Board of Directors 2006-2011
- ☞ American Optometric Association, Trustee 2013-2016
- ☞ I never used or will use my volunteer positions to further my lecturing career
- ☞ Lectured for: Aerie, Alcon, Allergan, BioTissue, Maculogix, OptoVue
- ☞ Advisory Board: Allergan, Maculogix, Sight Sciences, Sun, Takeda
- ☞ Envolve: PA Medical Director, Credential Committee
- ☞ Optometric Education Consultants- Scottsdale, St. Paul, Quebec City, Nashville, and Orlando/Disney OCT Users meeting; Owner



Disclosures: Tracy Offerdahl, PharmD

👁️ Dr. Offerdahl has the following financial disclosure:

★ Boiron: honorarium, webinar/speaker

👁️ Has not received any assistance from any commercial interest in the development of this course

Financial Obligations



Financial Obligations



Learning Objectives

- Review the prevalence and pathophysiology associated with diabetes mellitus (Type 2 DM) and hyperlipidemia
- Describe updates and changes to guidelines used in the management of diabetes mellitus, and hyperlipidemia
- List and describe medications used in the treatment of diabetes mellitus and hyperlipidemia, including systemic and ocular adverse effects, precautions, and any potential drug interactions

Metabolic Diseases

Pre-Diabetes

★ R73.03

Metabolic Syndrome

★ E88.81

Diabetes

★ E10

★ E11

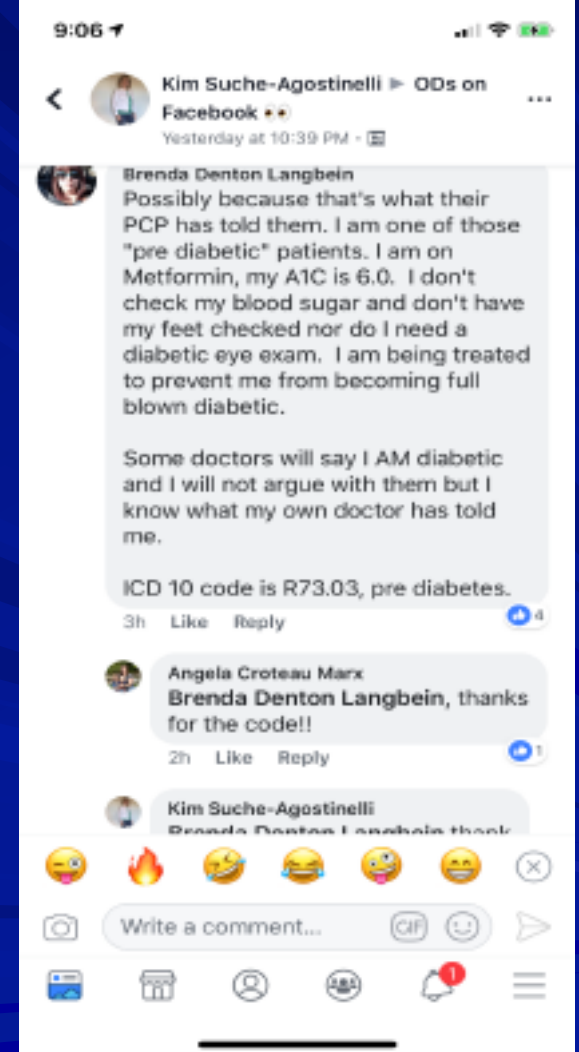
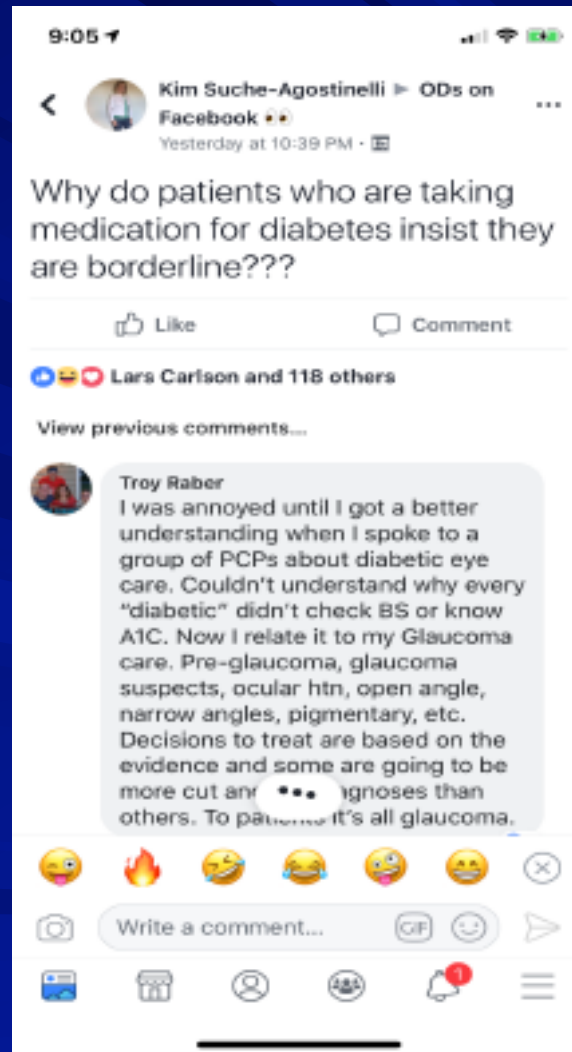
Dyslipidemia

Hypertension

How Many Times Have You Seen and Heard

- ⌘ A patient on metformin and lisinopril
- ⌘ Patient claims he/she is not diabetic
- ⌘ Patient claims he/she does not have hypertension

ODs on Facebook



ODs on Facebook

So I hate the dx of pre-diabetes because patients get really confused....but besides that....do we still provide same care as far as diabetic exams go with letters to pcp etc. It's such a grey area and I have been treating them the same as diabetic patients but wondering what the standard is. Because the patient is often confused it's hard to explain to them why it's a medical visit and possibly hits deductible etc when they are in complete denial they have a problem even though they are on metformin etc.

 7

41 Comments

 Like

 Comment

If a patient is on Metformin or another dm drug they are diabetic! If they are not on any medication then they are not. Very simple

Like · Reply · 4y

They still could be diabetic, absent treatment.

Like · Reply · 4y

 2

True, but if they are under care, their md needs to make the call unless you are going to do the workup and prescribe

Like · Reply · 4y

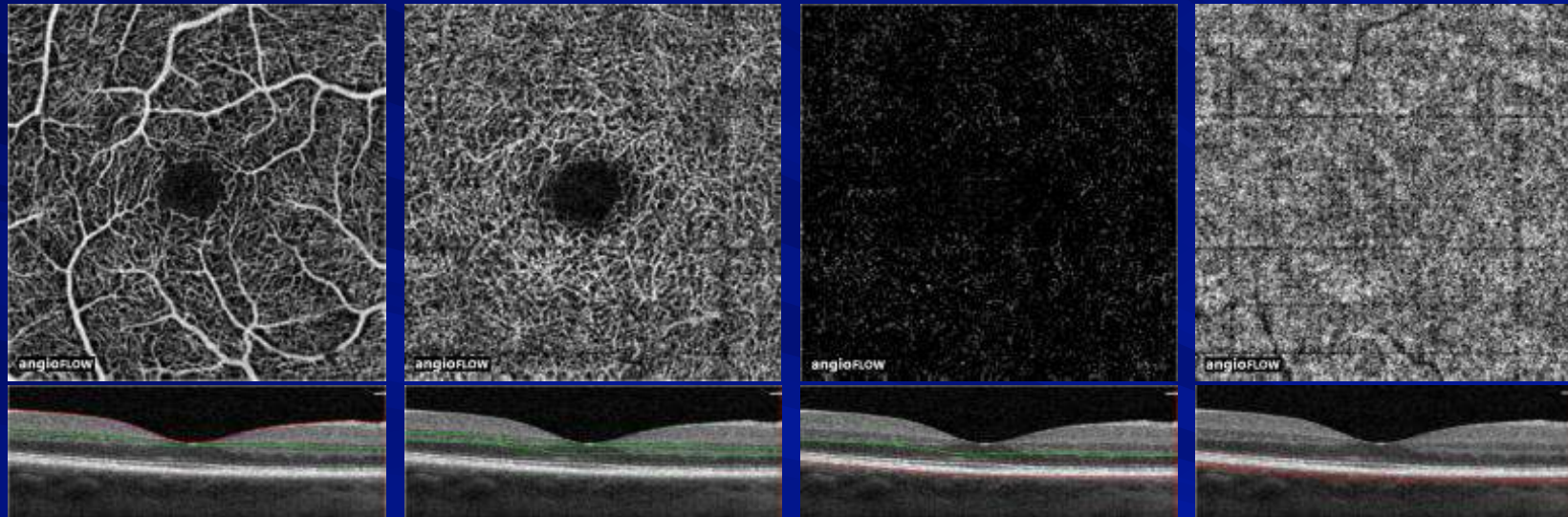


Rick Hawley About 7-8% of "pre-diabetics" have retinopathy. I treat them the same as far as letters, medical billing, etc.

Like · Reply · 4y



1



Superficial Capillary Plexus

3 μ m Below ILM \rightarrow 15 μ m
Below IPL

Deep Capillary Plexus

15 μ m Below ILM \rightarrow 70 μ m
Below IPL

Outer Retina

70 μ m Below IPL \rightarrow 30 μ m
Below RPE Reference

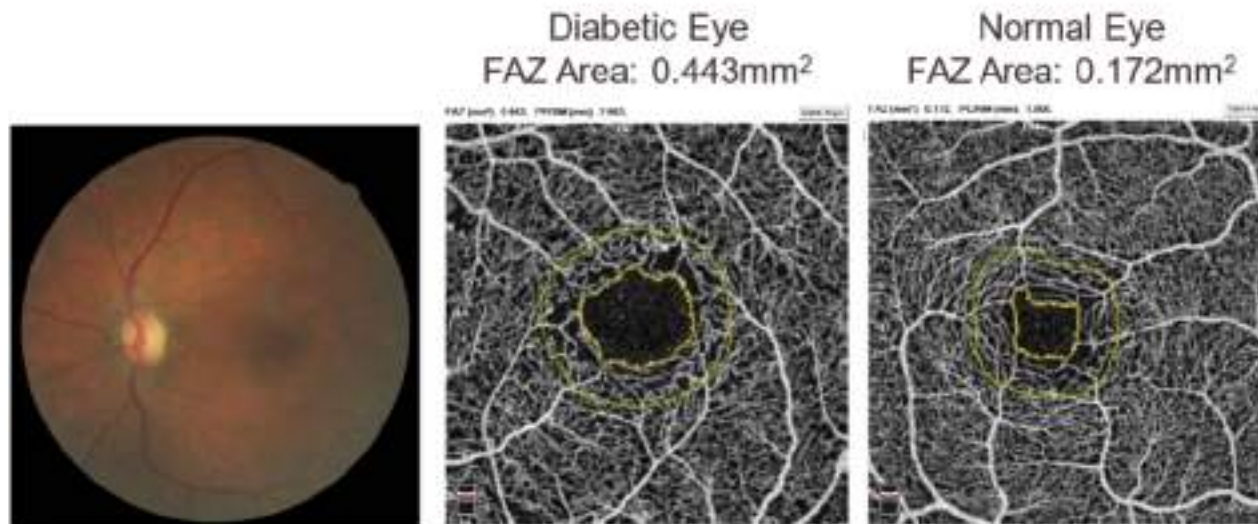
Choriocapillaris

30 μ m Below RPE Reference \rightarrow 60 μ m
Below RPE Reference

Normal Retinal Vasculature

Identify Early Vascular Changes in Diabetic Eyes

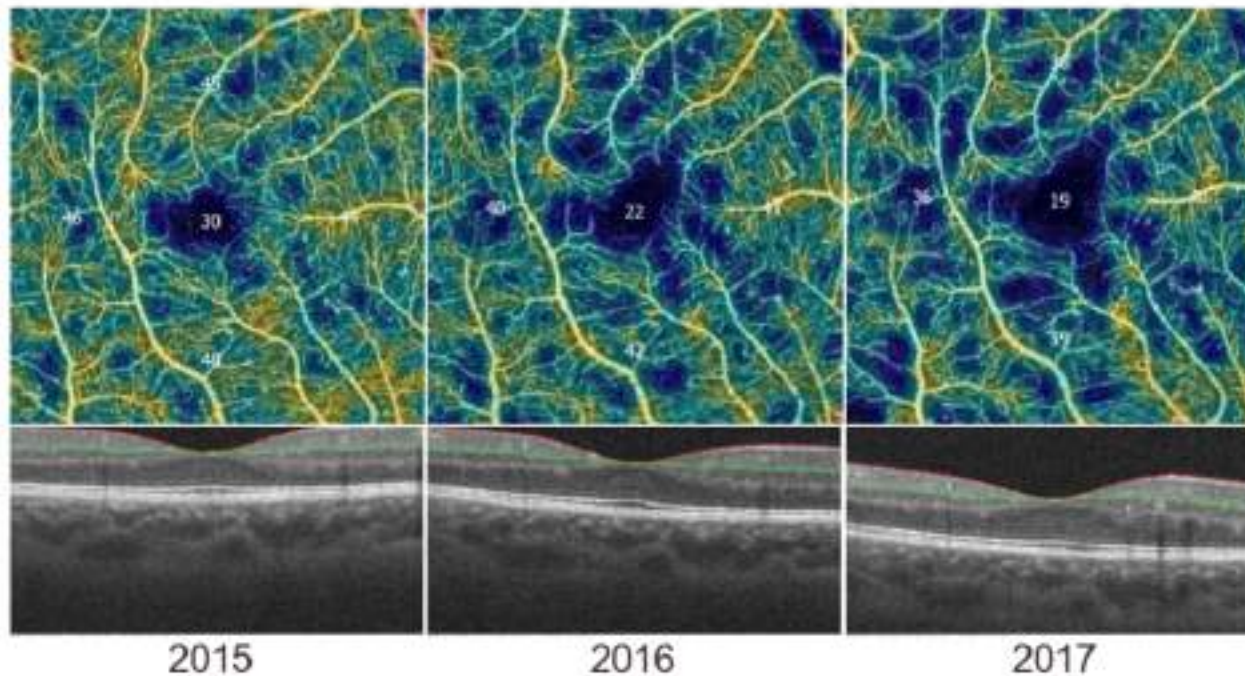
Patients with DM have a larger FAZ than healthy eyes.³



3. Di, G., Weihong, Y., Xiao, Z., et al. Graefes Arch Clin Exp Ophthalmology (2016) 254: 873. <https://doi.org/10.1007/s00147-015-3143-7>
Images courtesy of Julie Rodman, OD, FAAO

Assess Disease Progression with Multiscan View

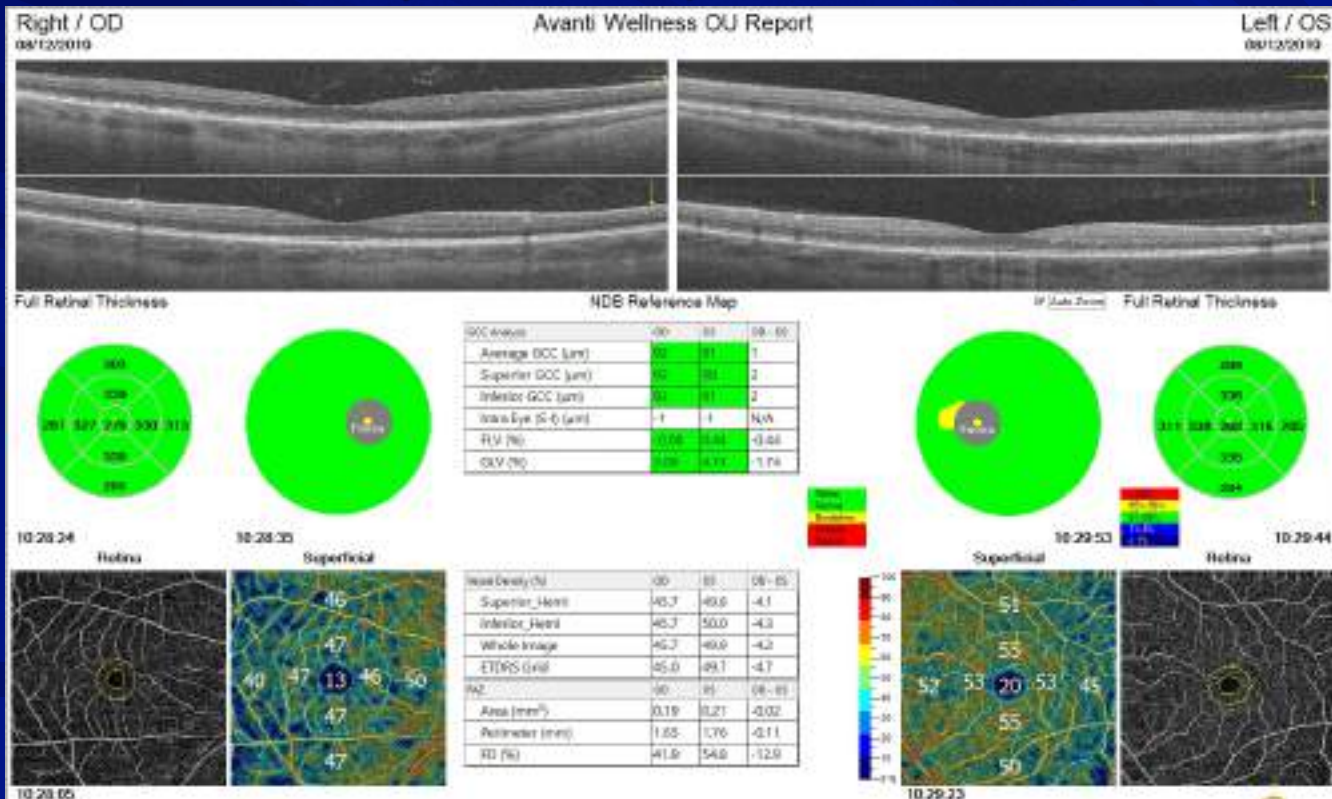
Vessel Density Decreases Significantly with Disease Severity⁴



4. Nesper FL, Roberts PK, Onishi AC, et al. Quantifying Microvascular Abnormalities With Increasing Severity of Diabetic Retinopathy Using Optical Coherence Tomography Angiography. *Investigative Ophthalmology & Visual Science*. 2017;58(6):BIO307-BIO315. doi:10.1167/iov.17-21787

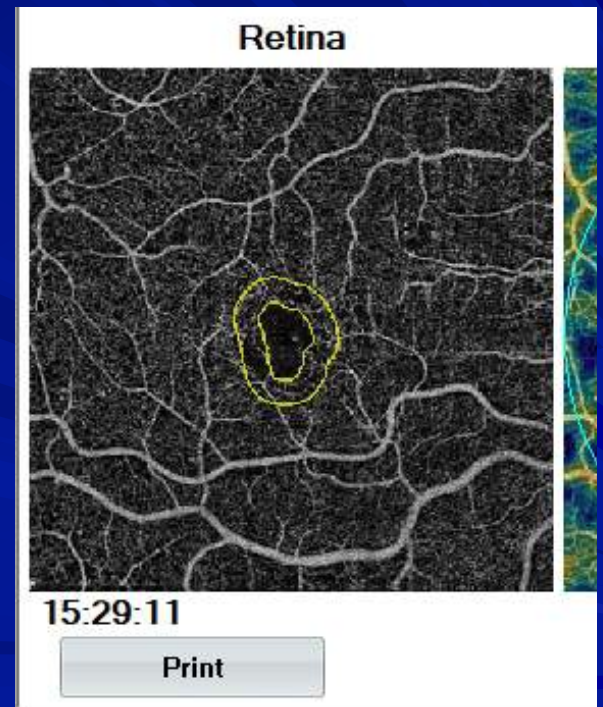
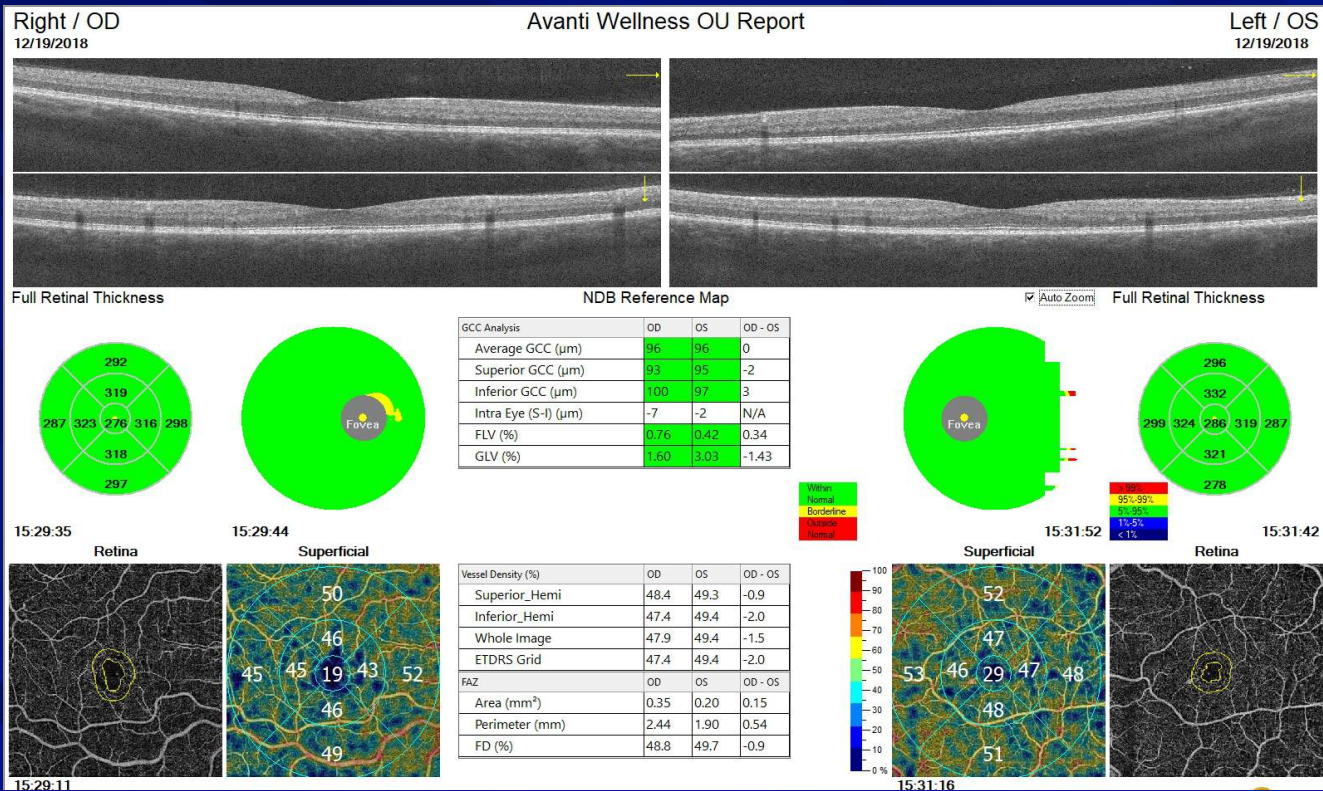
AngioWellness Report

Comprehensive Eye Exam - Healthy



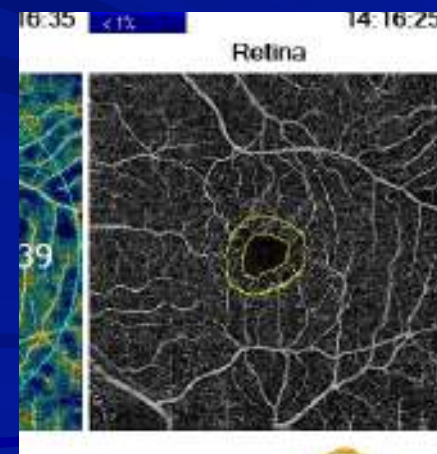
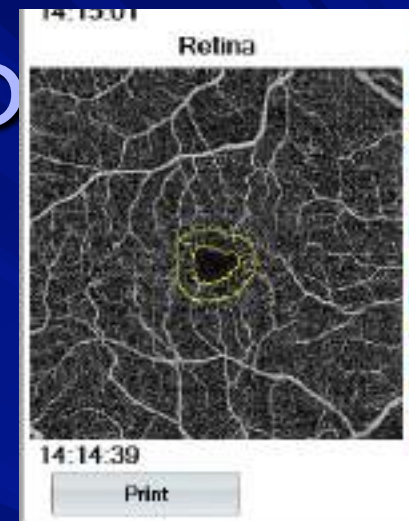
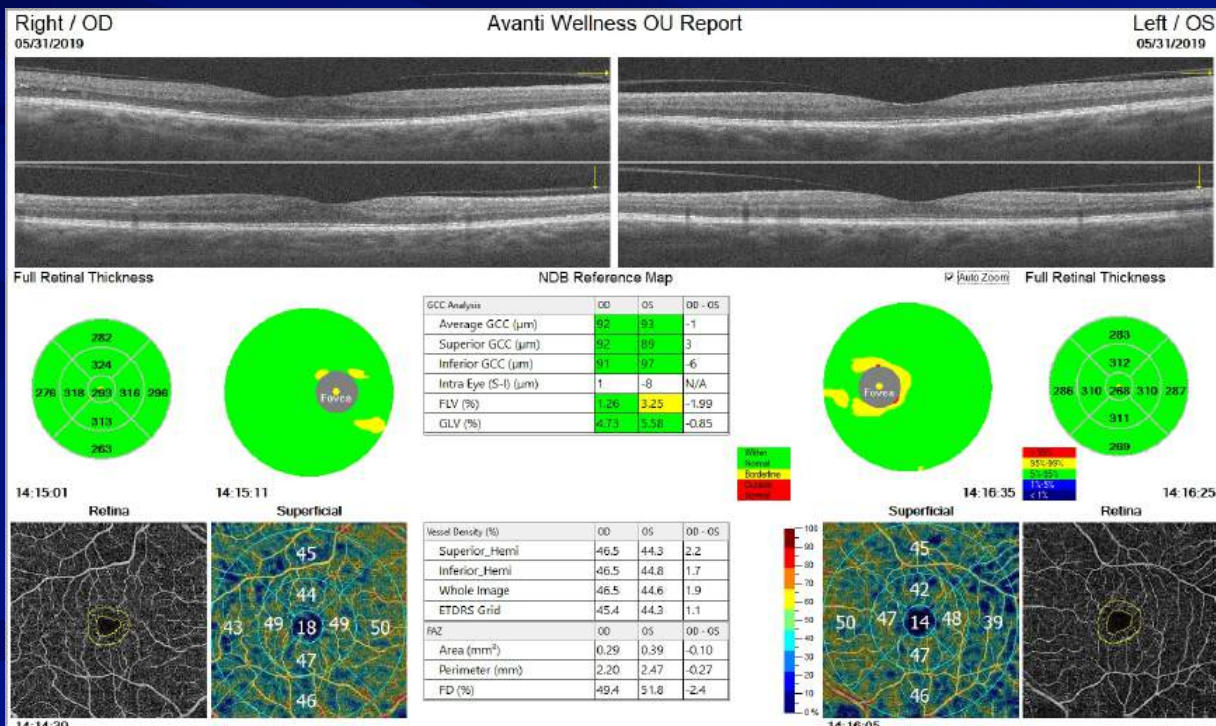
AngioWellness Report

Patient 1 with Diabetes



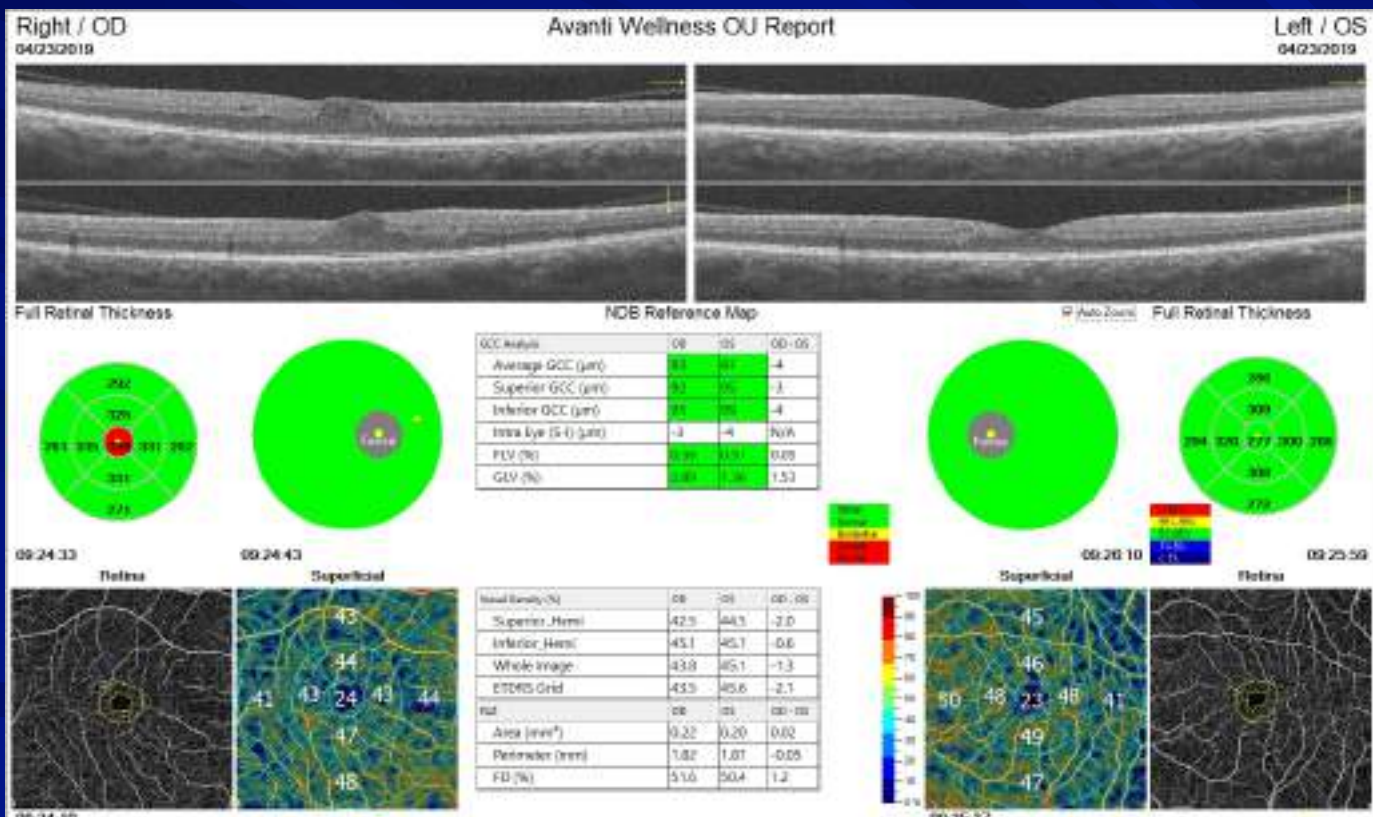
AngioWellness Report

Patient 2 with Diabetes



AngioWellness Report

Patient 3 with Diabetes



58-year-old man with diabetes

- 👓 New patient to the practice
- 👓 BS: unsure, last HbA1c unsure
- 👓 DM meds: metformin, glyburide, Invokana
- 👓 Vision 20/20
- 👓 Anterior segment: normal

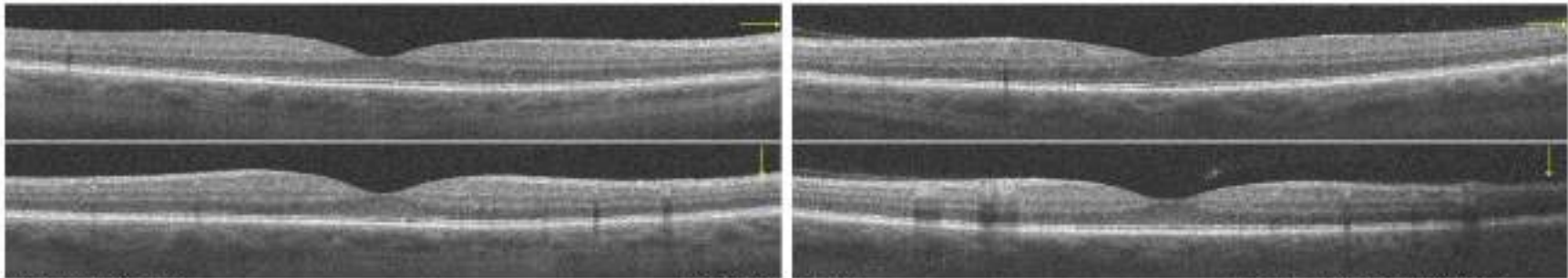
Widefield Imaging



Right / OD
08/18/2020

Avanti Wellness OU Report

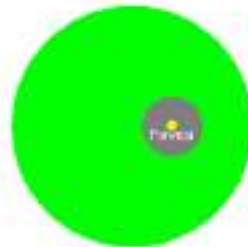
Left / OS
08/18/2020



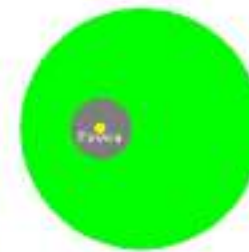
Full Retinal Thickness

NDB Reference Map

Full Retinal Thickness

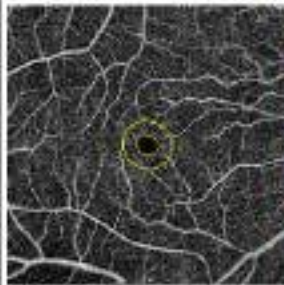


SCC Analysis	OD	OS	OD - OS
Average GCC (µm)	107	110	-3
Superior GCC (µm)	105	107	-2
Inferior GCC (µm)	110	113	-3
Intra Eye (S-I) (µm)	-5	-6	N/A
FLV (%)	0.02	0.00	0.02
GLV (%)	0.02	0.00	0.02



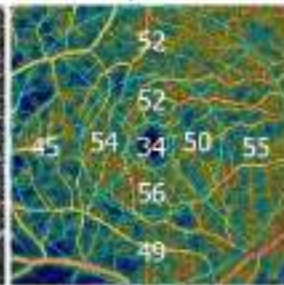
10:06:26

Retina



10:06:35

Superficial

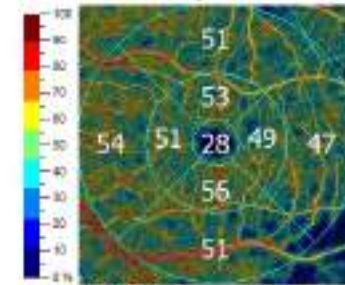


Hard Density (%)	OD	OS	OD - OS
Superior_Hemi	50.7	50.0	0.7
Inferior_Hemi	49.5	49.1	0.4
Whole Image	50.1	49.5	0.6
ETDRS Grid	50.3	50.4	-0.1
NAZ	OD	OS	OD - OS
Area (mm ²)	0.15	0.24	-0.09
Perimeter (mm)	1.49	1.52	-0.43
FD (%)	55.5	55.8	0.5



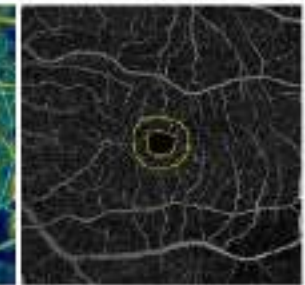
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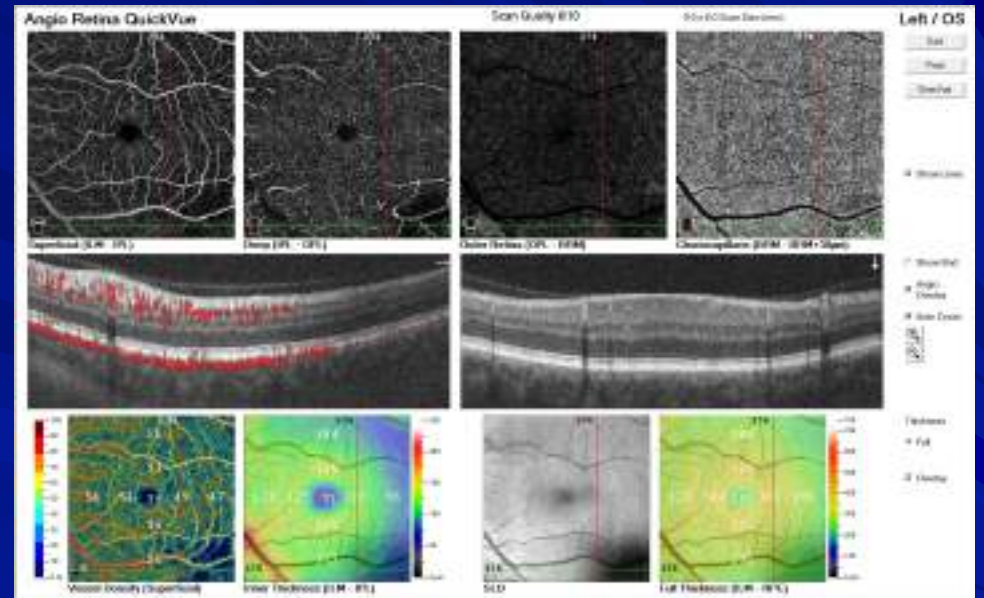
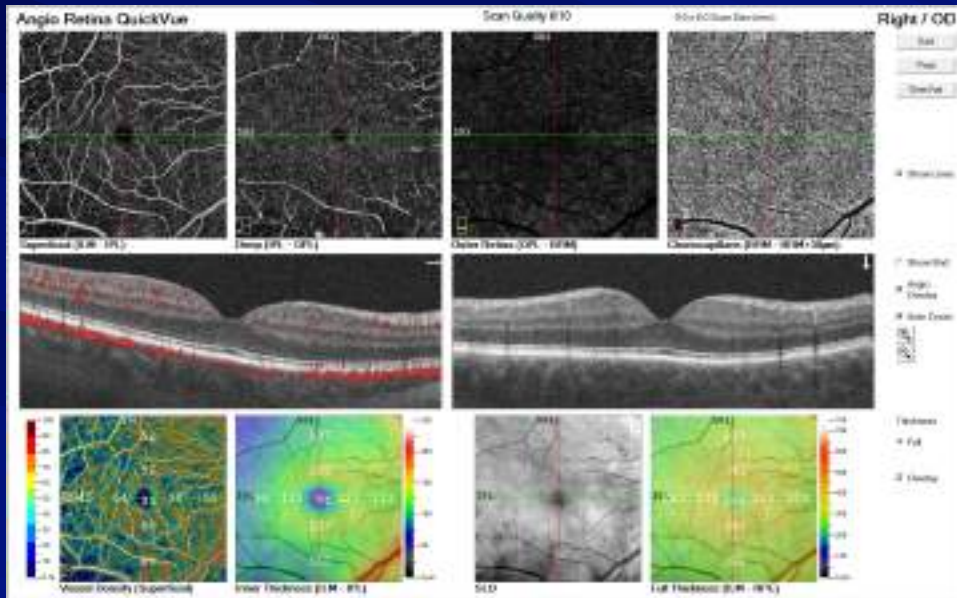
Superficial



10:07:54

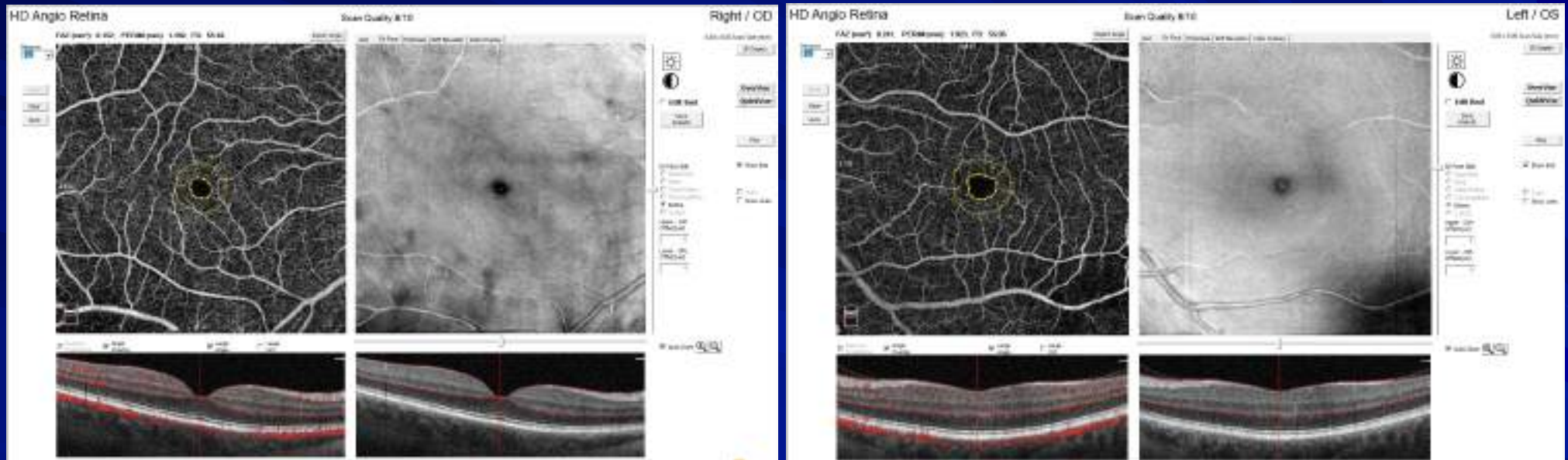
Retina





FAZ Damage – This is DR

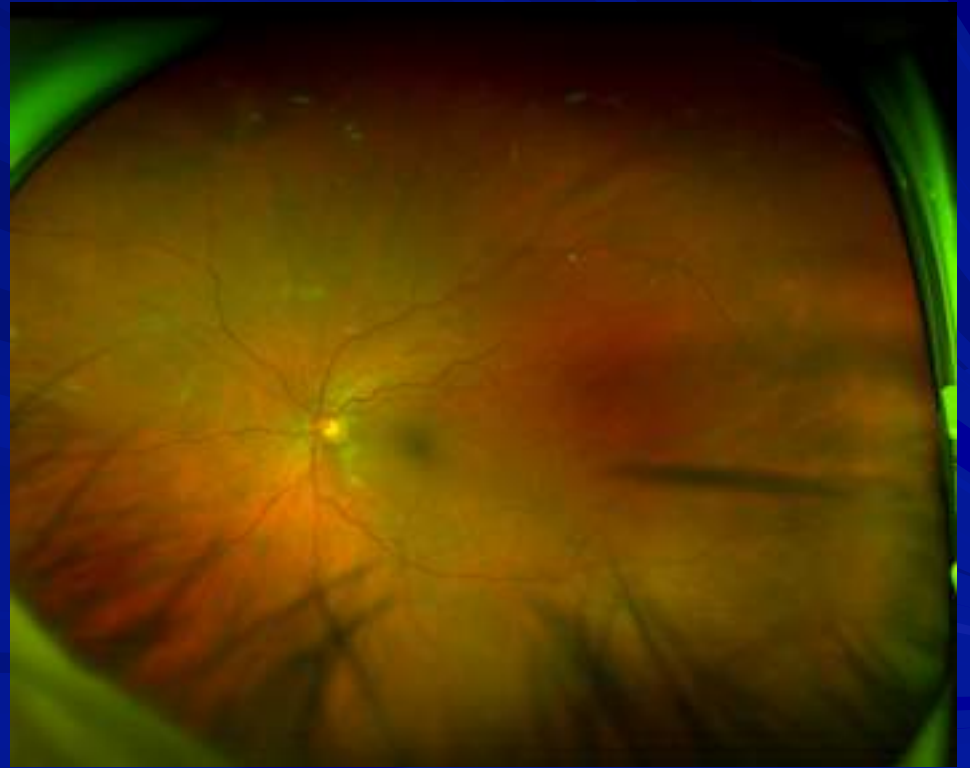
Time to get to know your BS and HBA1c



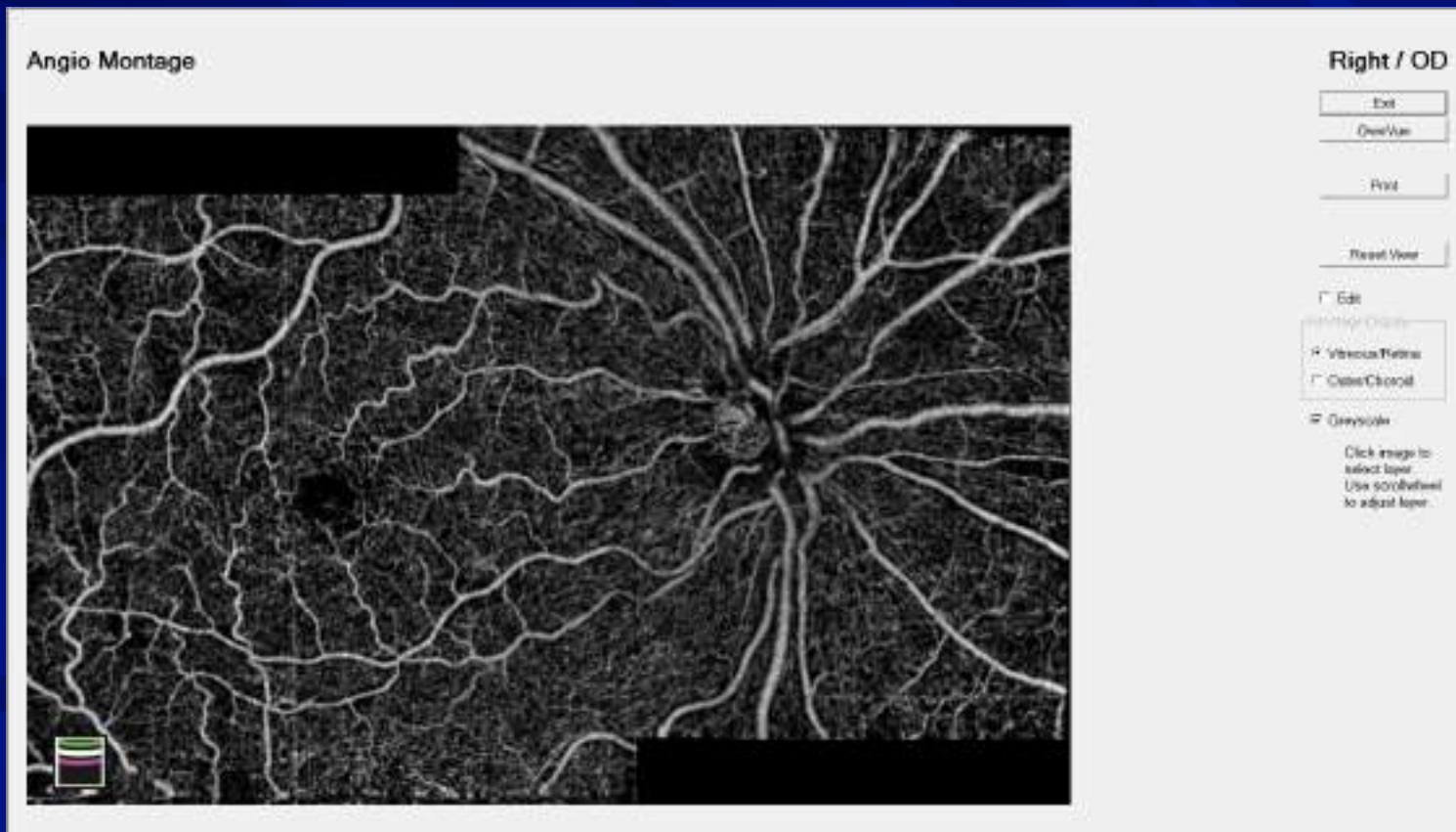
64-year-old man with diabetes

- BS: 134 this AM, last HbA1c 8.0
- DM meds: Novolog and Amaryl
- Vision 20/20
- Anterior segment: normal

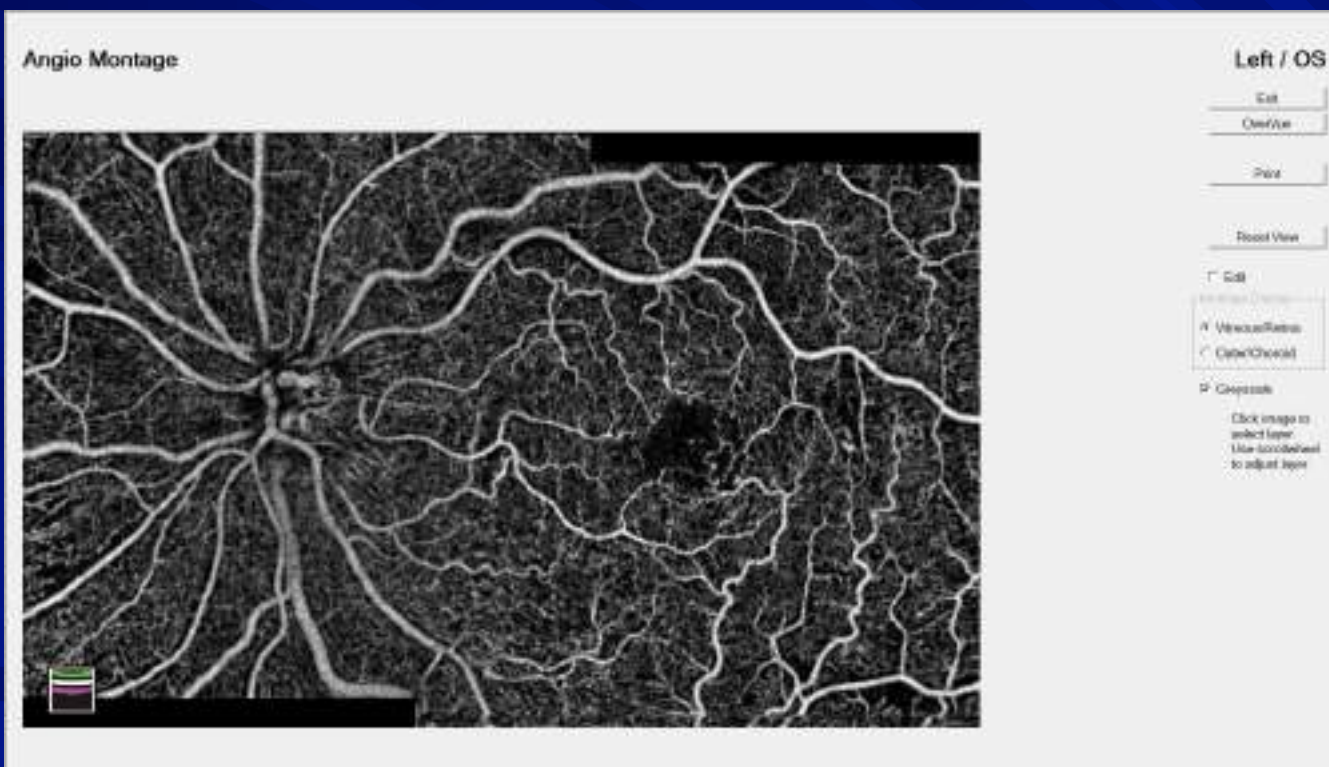
Widefield Imaging



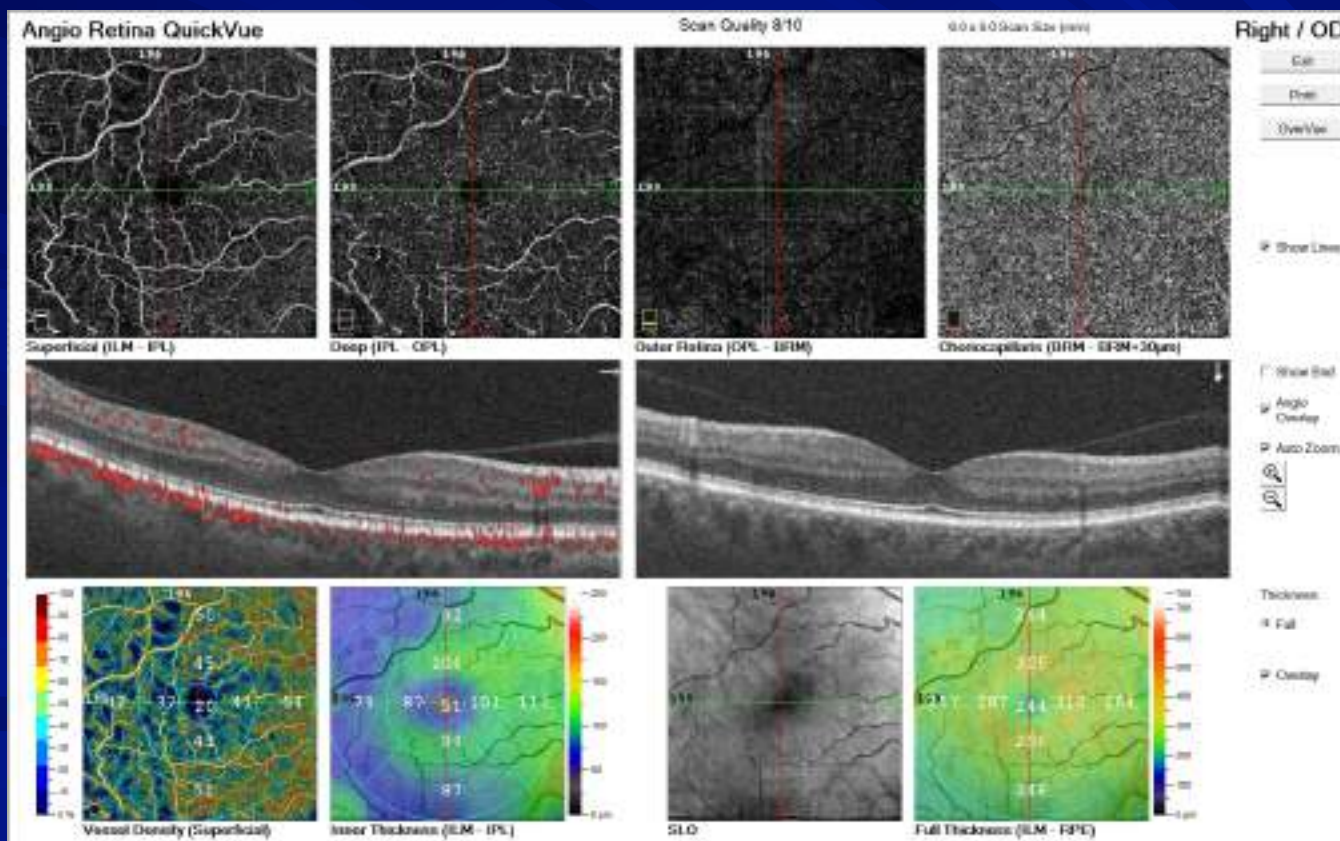
64-year-old man with diabetes



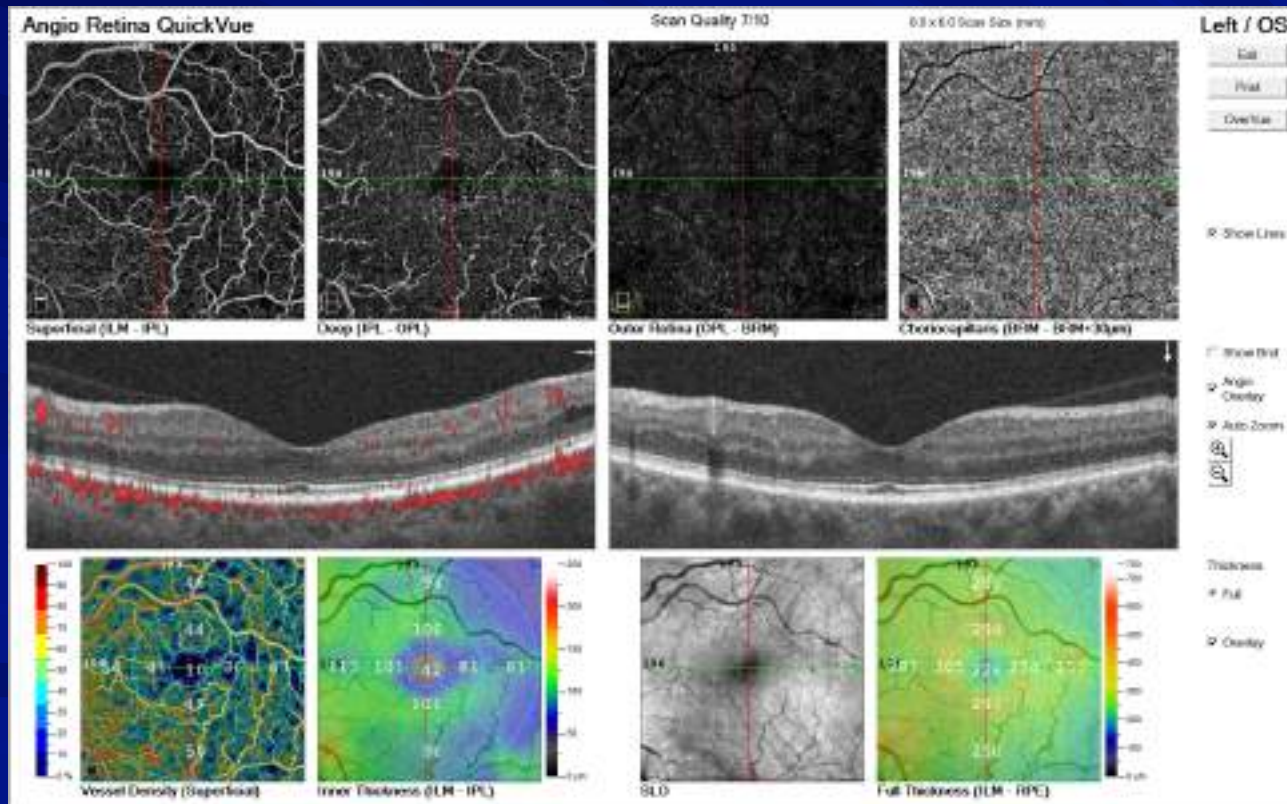
64-year-old man with diabetes



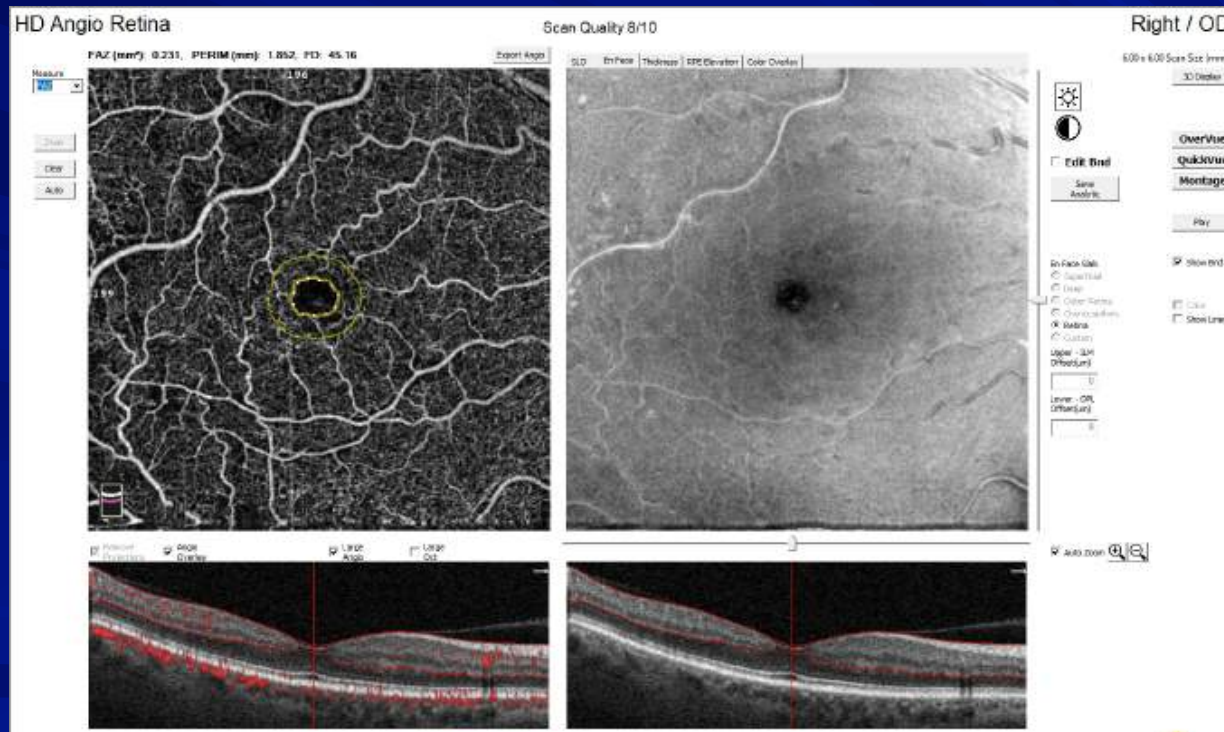
64-year-old man with diabetes



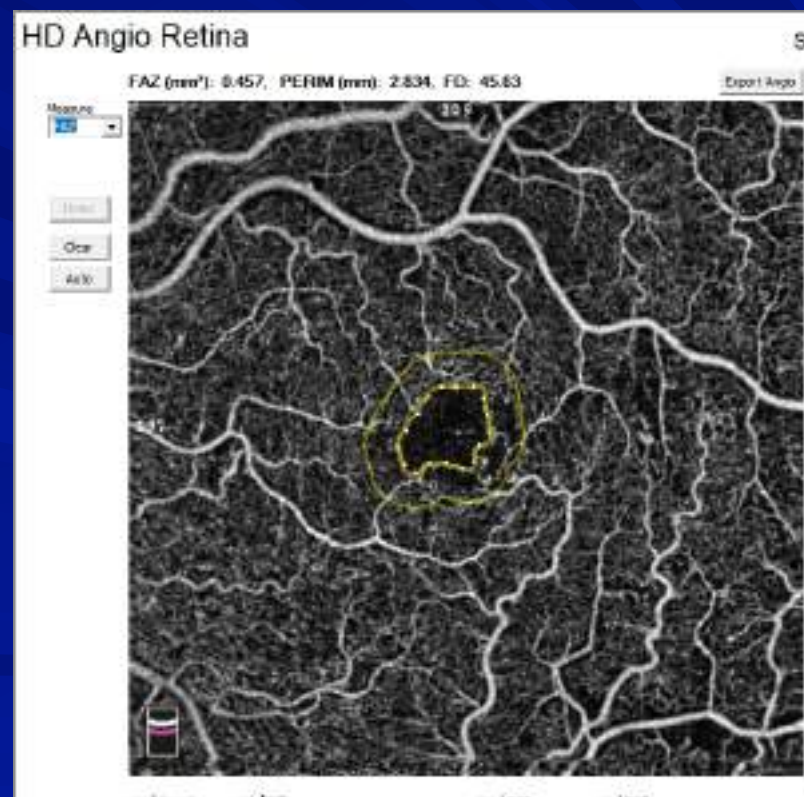
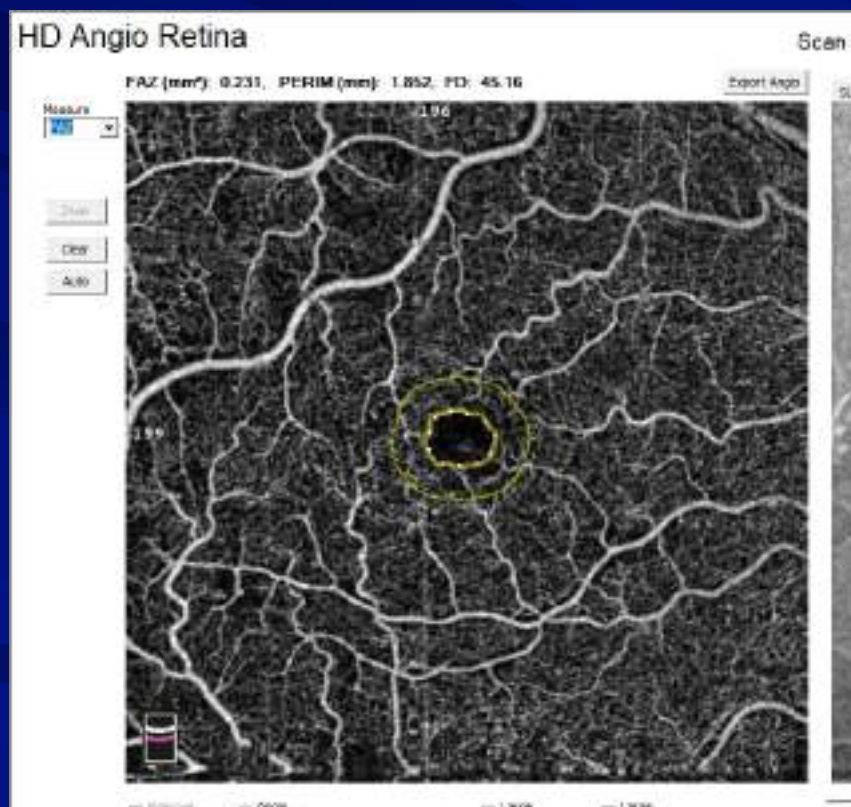
64-year-old man with diabetes



64-year-old man with diabetes



64-year-old man with diabetes



OCT and OCT-A

👓 Treatment?

👓 Certainly useful, beneficial, essential, and important in following the patient with diabetes

👓 Improved HbA1c

ODs on Facebook

What ICD code do you use for a patient who is "pre-diabetic" and on metformin. Patient insists you don't call it DM bc they are afraid it will be on their record forever.

38 Comments

Like Comment

The patient isn't "pre-diabetic" if he/she is on metformin. Call the managing doctor and ask what he/she codes. I guarantee it's a diabetic code.

Like Reply · 0y

I used to agree with you Jason, but many PCPs are treating pre-diabetes with metformin now. I guess it's been shown to be beneficial long term, especially in those high risk to develop full blown diabetes.

Like Reply · 0y

Where do these people come up with these terms? Its as ridiculous as saying a person is pre-dead if they are living.

Like Reply · 0y

True Susan, I think they consider 100-120 FBS to be pre-diabetic though. I could be off on that though. Kinda see how 2 weeks after conception a woman is 4 weeks pregnant. I never understood that one.

Like Reply · 0y

The pcps vs endocrine Dx of diabetes vs diabetic suspect? Same as glaucoma vs glaucoma suspect. In my mind if you're treating it, it's the Dx.

Like Reply · 0y

Like Reply · 0y

While "pre-diabetic" can be used in lay terms to describe a patient that is flirting with high enough blood sugars to warrant considering a diabetes diagnosis and thus treating the condition, I would say that if the patient is actually on metformin to treat their high blood sugar that they have crossed that line in the eyes of their physician and are diabetic. It's your record at the end of the day. Call it as you see it.

Like Reply · 0y

Diabetes

Table 2.2—Criteria for the diagnosis of diabetes

FPG \geq 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG \geq 200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C \geq 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose \geq 200 mg/dL (11.1 mmol/L).

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diabetes care. 2020;43(Supplement 1):S14-S31.

Pre-Diabetes Criteria for Testing

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥ 25 kg/m² or ≥ 23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
 - First-degree relative with diabetes
 - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
 - History of CVD
 - Hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
 - HDL cholesterol level < 35 mg/dL (0.90 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L)
 - Women with polycystic ovary syndrome
 - Physical inactivity
 - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C $\geq 5.7\%$ [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

CVD, cardiovascular disease; GDM, gestational diabetes mellitus.

American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diabetes care. 2020;43(Supplement 1):S14-S31.

Criteria Defining Pre-Diabetes- R73.03

Table 2.5—Criteria defining prediabetes*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)

OR

2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

OR

A1C 5.7–6.4% (39–47 mmol/mol)

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; 2-h PG, 2-h plasma glucose. *For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range.

Metabolic Syndrome

↳ A cluster of conditions that increase the risk of:

- ★ Heart disease
- ★ Stroke
- ★ Diabetes
- ★ Dementia
- ★ Cancer
 - ↳ Loves sugar
- ★ Polycystic ovarian syndrome
- ★ Non-alcoholic fatty liver disease

The Cluster of Conditions

↳ Elevated glucose

- ★ Insulin resistance
- ★ ie >100 fasting or HbA1c >6.5

↳ High blood pressure

- ★ ie >120 systolic

↳ Obese/overweight

- ★ ie BMI >25
- ★ Abdominal obesity

↳ Abnormal cholesterol/ratios, dyslipidemia

- ★ High triglycerides ie >150
- ★ Low HDL cholesterol ie <40

↳ Proinflammatory and prothrombotic states

3 of these 5 leads to:
Heart disease, stroke, DM,
dementia, cancer...

How to Code - E88.81

← → ↻ <https://www.icd10data.com/ICD10CM/Codes/E00-E89/E70-E89/E88-E88.81> ☆ 📄 📄 📄 📄 📄 📄

ICD10Data.com Search All ICD-10 🔍

2019 Codes ▾ Indexes ▾ Conversion DRG Rules ▾ Analytics ▾ Changes ▾ HCPCS ▾ Disclaimer


ICD-10-CM Codes ▾ E00-E89 Endocrine, nutritional and metabolic diseases ▾ E70-E88 Metabolic disorders ▾ E88- Other and unspecified metabolic disorders ▾

▸ **2019 ICD-10-CM Diagnosis Code E88.81** 🇺🇸 🇬🇧

Metabolic syndrome

2019 2017 2018 2025 **Billable/Specific Code**

- E88.81 is a billable/specific ICD-10-CM code that can be used to indicate a diagnosis for reimbursement purposes.
- The 2019 edition of ICD-10-CM E88.81 became effective on October 1, 2018.
- This is the American ICD-10-CM version of E88.81 - other international versions of ICD-10 E88.81 may differ.



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Applicable To

- Dyametabolic syndrome x

Use Additional ⓘ

- codes for associated manifestations, such as:
- obesity (E66.- ⓘ)

The following code(s) above E88.81 contain annotation back-references ⓘ that may be applicable to E88.81:

- [E00-E89](#) ⓘ Endocrine, nutritional and metabolic diseases
- [E70-E88](#) ⓘ Metabolic disorders
- [E88](#) ⓘ Other and unspecified metabolic disorders

Approximate Synonyms


- Drug resistance to insulin
- Dyametabolic syndrome x
- Insulin resistance
- Metabolic syndrome x

Clinical Information

- A cluster of metabolic risk factors for cardiovascular diseases and type 2 diabetes mellitus. The major components of metabolic syndrome x include excess abdominal fat; atherogenic dyslipidemia; hypertension; hyperglycemia; insulin resistance; a proinflammatory state; and a prothrombotic (thrombosis) state.

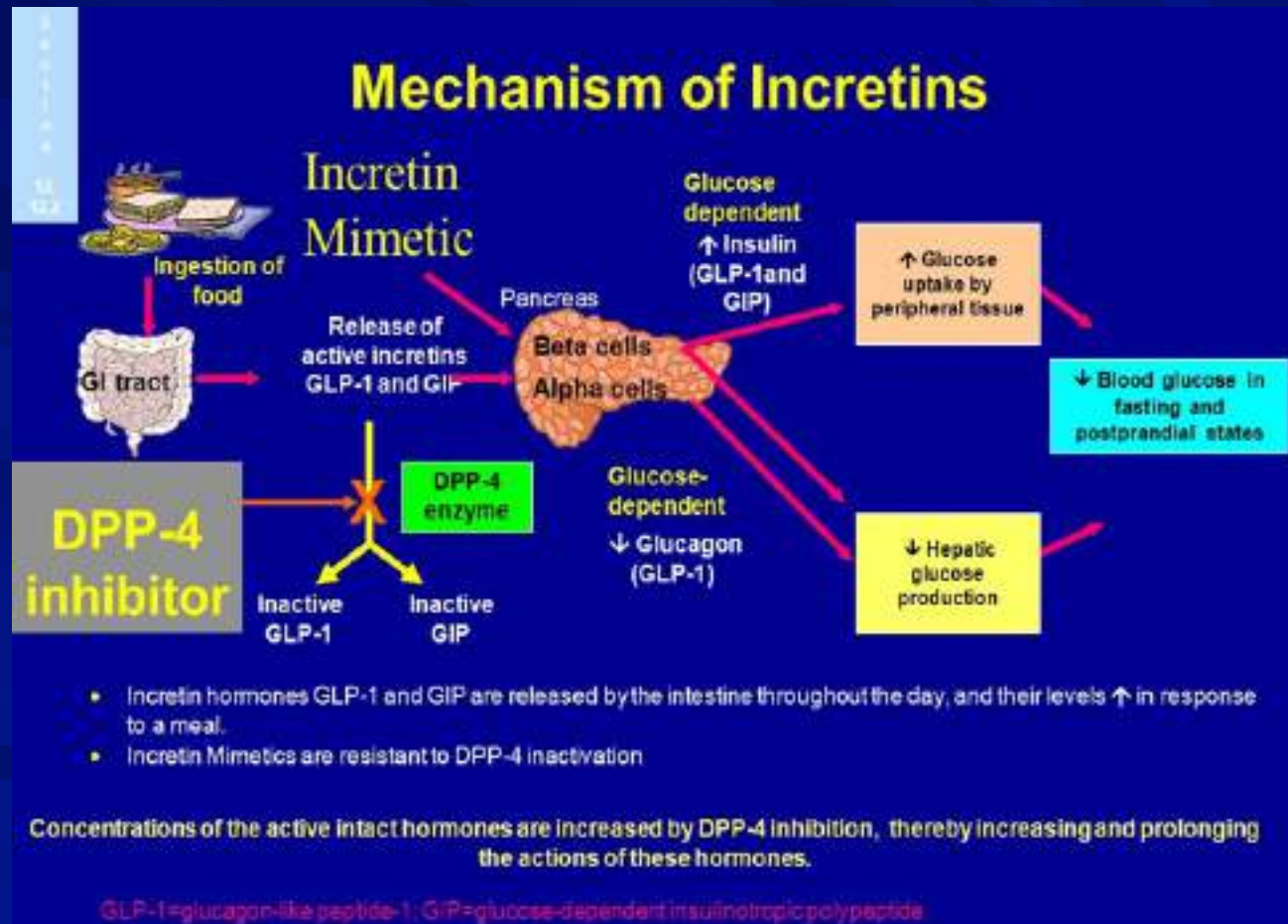
Metabolic Diseases and the “Syndrome”

What is Optometry’s Role Now and in the Future?

The background is a solid dark blue color with a pattern of lighter blue diagonal lines that create a sense of depth and movement, radiating from the top right towards the bottom left.

Let's Discuss the
Conditions and Agents
Used to Treat
Metabolic Diseases

Endocrinology-Incretin System



Diabetes Mellitus

Pathophysiology Reminder

👓 Type 1 DM

- ★ Pancreatic beta cells are destroyed = subsequent severe or absolute lack of insulin

👓 Type 2 DM

- ★ insulin resistance in tissue
- ★ AKA a decrease in insulin sensitivity

Hemoglobin A1c

☞ A1c \leq 6.5%

- ★ More “stable” patients
- ★ For patients without comorbidities
- ★ Low hypoglycemia risk

☞ A1c $>$ 6.5%

- ★ Less “stable” patients
- ★ For patients with comorbidities
- ★ High hypoglycemia risk

Updates on Treatment

☞ **Type 1 = exogenous insulin injections**

- ★ Newer insulin products = products that offer more flexibility
- ★ More closely resemble endogenous insulin secretion and “basal” insulin levels

Updates on Treatment

👁️ **Type 2 = Metformin as 1st line agent**

★ If HgA1c is >10% and/or blood glucose is > 300mg/dL, then patients may start with TWO agents

📄 Insulin

📄 GLP-1 Agonists

📄 DPP4 Inhibitor

Gestational Diabetes

☞ Standard has always been insulin injections

☞ Metformin is the newest choice and has become treatment of choice

Basic Mechanisms

☞ Type 2 Patients = primary dysfunction is hyperinsulinemia = insulin resistance

- ★ Insulin and insulin-secreting meds = hypoglycemia and weight gain
- ★ NEED MEDS that “re-teach” the body how to use the endogenous insulin that is already in the bloodstream!
- ★ All mechanism are NOT created equal!

Side-Effect Comparison

🕒 Drugs that cause hypoglycemia as MONOTHERAPY

★ Those drugs that cause the pancreas to RELEASE MORE INSULIN

- 📄 Insulin (ACTUAL insulin)
- 📄 Sulfonylureas
- 📄 Meglitinides

🕒 Drugs that cause weight loss or are weight neutral

★ All other agents cause weight gain over time

- 📄 Metformin
- 📄 GLP-1 Agonists
- 📄 DPP4 inhibitors
- 📄 SGLT2 Inhibitors

Precautions/Contraindications & Drug interactions

🕒 Patients on >1 anti-diabetic agent

★ MUCH higher likelihood of hypoglycemia

🕒 Renal impairment = contraindicated in patients on metformin

Biguanide

☞ Metformin (Glucophage)

- ★ Initial Drug of Choice / Cornerstone of Therapy

☞ Mechanism of Action (MOA)

- ★ Inhibits hepatic and renal gluconeogenesis
- ★ Stimulation of glucose uptake in peripheral tissues
 - ☐ Decreases insulin resistance = improves insulin sensitivity

Sulfonylureas

☞ **MOA:** Stimulate release of insulin from functioning pancreatic beta cells

☞ **2nd Generation Agents (preferred):**

- ★ glyburide (DiaBeta, Micronase, Glynase)
- ★ glipizide (Glucotrol, Glucotrol XL)
- ★ glimepiride (Amaryl)

Insulin Preparations

- ☞ Drug therapy of choice for all patients with type 1 DM and those with type 2 DM who cannot control their condition with diet, exercise, and 1st-line agents
 - ★ metformin
- ☞ **MOA:** Regulates glucose metabolism in the muscle and other tissues
- ☞ Semisynthetic “human” – identical amino acid composition to endogenous human insulin

Insulin Preparations

http://www.diabetesed.net/page/_files/Insulin-PC-3-2015.pdf

Insulin PocketCard™

Diabetes Education SERVICES

15 years

Action		Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Rapid Acting Analogs	Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs	Bolus insulin lowers after-meal glucose. Post meal BG reflects efficacy. Basal insulin controls BG between meals and nighttime. Fasting BG reflects efficacy. Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/kg body wt/day. Discard opened insulin vials after 28 days.
		Lispro (Humalog)				
		Glulisine (Apidra)				
	Short Acting	Regular	30 - 60 min	2 - 3 hrs	5 - 8 hrs	
Concentrated Regular Insulin 500 units/mL reg insulin "U-500"		30 - 60 min	2 - 3 hrs	Up to 24 hrs		
Basal	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	
	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
		Glargine (Lantus)	2 - 4 hrs	No peak	20 - 24 hrs	
		Concentrated Glargine (Toujeo) 300 units/mL in 1.5 mL Pen	6 hrs	No Peak	24 hrs	
Basal + Bolus	Intermediate + short	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	
	Intermediate + rapid	Novolog® Mix - 70/30 Humalog® Mix - 75/25 or 50/50	5 - 15 min			

Insulin action times can vary with each injection, time periods listed here are general guidelines only; please consult prescribing information for details.

REV 03/2015 ©2015

GLP-1 Agonists

- ↳ Exenatide injection (Byetta)
- ↳ Liraglutide injection (Victoza)
 - ★ Saxenda brand name = weight loss only
- ↳ Abiglutide (Tanzeum)
- ↳ Dulaglutide (Trulicity)
- ↳ Semaglutide (Ozempic)
- ↳ Lixisenatide (Adlyxin)

GLP-1 Agonists

🔗 Mechanism of Action

- ★ Stimulate the GLP-1 (incretin) receptor
- ★ Incretin stimulates insulin release from the beta cells in the pancreas
 - In response to high blood glucose levels
 - Releases insulin IN RESPONSE TO FOOD!
- ★ Inhibits the liver's production of glucose
 - 📄 Promotes insulin activity
 - 📄 Inhibits gluconeogenesis by preventing incretin inactivation Weight loss

DPP4 Inhibitors (dipeptidyl-peptidase-4)

- ☞ Sitagliptin (Januvia) tablets
- ☞ Saxagliptin (Onglyza) tablets
- ☞ Linagliptin (Tradjenta) tablets

☞ Mechanism of Action

- ★ Inhibits the breakdown of glucagon-like peptide-1 (incretin)

Sodium-Glucose Co-Transporter 2 SGLT2 Inhibitor

👓 **Canagliflozin (Invokana)**

👓 **Dapagliflozin (Farxiga)**

👓 **Empagliflozin (Jardiance)**

👓 **MOA**

★ Inhibition of the SGLT2

- 📄 Reduced absorption of filtered glucose
- 📄 Lowering of renal threshold for glucose
- 📄 Increasing of urinary excretion of glucose

Hypertension

👁️ **Very common comorbid condition**

★ “compelling indication”

★ “JNC 8”

📄 8th Joint National Committee – prevention and treatment of hypertension

📄 2014

👁️ **Pretty big changes**

Basic Principles of Treatment From the JNC VIII

☞ In persons > 60 years of age

- ★ Systolic blood pressure (SBP) ≥ 150 mmHg or
- ★ Diastolic blood pressure (DBP) ≥ 90 mmHg should be treated with meds
- ★ Goal should be SBP <150 mmHg and DBP <90 mmHg

☞ In persons < 60 years of age

- ★ Systolic blood pressure (SBP) ≥ 140 mmHg or
- ★ Diastolic blood pressure (DBP) ≥ 90 mmHg should be treated with meds
- ★ Goal should be SBP <140 mmHg and DBP <90 mmHg

Hyperlipidemia

👓 Common comorbidity in patients with diabetes

★ The “American triumvirate”

📄 DM/metabolic syndrome, hypertension, hypercholesterolemia

👓 Statins are the only group of drugs that consistently decrease mortality in patients with high cholesterol!

Proteinuria

👁️ Protein in the urine is a harbinger of doom

- ★ Chronic renal failure/hemodialysis
- ★ Prevention is the key!
- ★ Maintain normal blood pressure and blood glucose levels
 - 📄 Use Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-2 receptor blockers (ARBs)

Inflammation as a risk factor...

↳ CRP C-reactive protein

- ★ Marker for inflammation
- ★ Inflammation = increase in plaque formation
- ★ GCA, RA, celiac disease, DM, heart dz, food intolerances, etc.

Vitamins...

🔗 Vitamin D

- ★ Sun may NOT be enough
- ★ Two vitamins better absorbed through supplementation rather than from dietary sources: Vitamin D and folic acid!
- ★ ACTIVE vitamin D is the best option (D3)

- ★ Get vitamin and vitamin B-12 levels checked!
 - 📄 Don't forget that B-12 will likely be low in patients on metformin
 - 📄 Also in those taking proton-pump inhibitor
 - Prilosec, Nexium, etc.

Diabetic Neuropathy

↳ Peripheral vessels are largely affected

- ★ Decrease in pain sensitivity in feet and lower legs
- ★ Pain and amputation

↳ What about the gut??

- ★ Decrease in food and drug absorption

Hyperlipidemia Basic Treatment

👁 LDL – “bad cholesterol”

- ★ Drugs are usually the best choice

👁 HDL – “good cholesterol”

- ★ Protective
- ★ Exercise is the best treatment

👁 Triglycerides

- ★ Dietary changes and fish oil

The new guidelines recommend a statin for

- ☞ Anyone who has cardiovascular disease, including angina (chest pain with exercise or stress)
 - ★ previous heart attack or stroke,
 - ★ Other related conditions; EVEN DM!
- ☞ Anyone with a very high level of harmful LDL cholesterol
 - ★ Generally an LDL above greater than 190 milligrams per deciliter of blood [mg/dL]
- ☞ Anyone with diabetes between the ages of 40 and 75 years
- ☞ Anyone with a greater than 7.5% chance of having a heart attack or stroke
 - ★ Or developing other form of cardiovascular disease in the next 10 years
 - ★ AKA “Framingham Index/Score”

Statins

☞ **MOA:** decrease LDL, decrease TGs, increase HDL

☞ ****ONLY AGENTS PROVEN TO LOWER THE RISK OF CV EVENTS
in patients with high cholesterol**

Statin Treatment Table

Age	No Risk Factors	ASCVD Risk Factors	ASCVD
< 40 years old	No treatment	Mod/High Intensity dose	High Intensity dose
40-75 years old	Mod/High Intensity dose	High Intensity dose	High Intensity dose
> 75 years old	Mod/High Intensity dose	Mod/High Intensity dose	High Intensity dose

ASCVD= Atherosclerotic Cardiovascular Disease

Risk Factors: LDL \geq 100mg/dL, hypertension, smoking, obesity, family hx of premature ASCVD

Moderate-Intensity Doses:

Rosuvastatin (Crestor) 5-10 mg
Atorvastatin (Lipitor) 10-20 mg
Simvastatin (Zocor) 20-40 mg
Pravastatin (Pravachol) 40-80 mg
Lovastatin (Mevacor) 40 mg
Fluvastatin (Lescol) 80 mg
Pitavastatin (Livalo) 2-4 mg

High-Intensity Doses:

Rosuvastatin (Crestor) 20-40 mg
Atorvastatin (Lipitor) 40-80 mg

Statins

Side effects:

- ★ < 0.1 % myopathy/myalgia/myositis/rhabdomyolysis
 - 📄 Including ocular muscles!!
- ★ DM (FDA added warning of increased blood sugar and HgA1C to statin labeling)?
- ★ Memory loss

Hmmm

The screenshot displays a medical software interface for editing a patient encounter. The window title is "MainEyes - Electronic Health Records". The patient information at the top includes: "Date: 01/01/2018 - 00:00/01/1948", "Age: 69", "Race: Gregory Caldwell", and "Established".

Chief Complaint: "Astigmatism/Hypometropic/Presbyopia". The "HPI Notes" field contains: "Pt. is taking a new medication for asthma - but cannot remember what it is called. pt states fall & broke glasses".

Medications: A table with columns: "Detailed HPI", "Location", "Usual Qty", "Severity", "Duration", "Timing", "Condit", "Med. Fact.", "Signs & Smp.", "Up", "Down", "Edit", "Delete".

Procedures: A table with columns: "Date", "Surgery", "Type", "Location", "Surgon", "Notes", "Edit", "Delete". The entry shows "No Surgeries" and "General".

Major Illnesses: A table with columns: "Major Illnesses", "Notes", "Edit", "Delete".

Mental and Functional States: "Mood or affect: Normal", "Orientation: Oriented to person, place and time", "Functional Status", "Other Disability".

Blood Sugar: "HbA1C: 10.0".

Allergy History: A table with columns: "Reaction Date", "Allergy", "Reaction", "Allergy Type", "Status", "Source", "Modified Date", "Edit", "Delete".

The interface includes a sidebar on the left with a navigation menu, a top toolbar with "Save", "Cancel", and "Print" buttons, and a Windows taskbar at the bottom showing the time as 2:05 PM on 01/14/2018.

Niacin

Niaspan

- ★ Only other agent that decreases LDL, TG, and increases HDL
- ★ Not proven to decrease death
- ★ SEs:
 - ☐ Cutaneous flushing
 - ☐ GI problems (avoid in GERD or PUD)
 - ☐ Hyperuricemia
 - ☐ Loss of glycemic control in DM

Fibric Acid Derivatives

- 👁 Gemfibrozil (Lopid)
- 👁 Fenofibrate (Tricor)
- 👁 Fenofibric acid (Trilipix)

- 👁 Used for high triglycerides only
- 👁 No decrease in mortality

Fish Oil

👁 Lovaza (DHA and EPA), Vascepa (EPA only)

- ★ Used to treat high triglycerides only

👁 Many other benefits!

- ★ Inflammatory diseases

👁 SEs:

- ★ Fishy taste
- ★ Increased bleeding time

Types of fish oil...

☞ Triglyceride form

- ★ More “natural” and better tolerated
- ★ Less likely to cause fishy aftertaste

☞ Ethyl ester form

- ★ Cheaper to make
- ★ More likely to cause burps and fishy aftertaste

Cholesterol Absorption Inhibitor

👁 Ezetimibe (Zetia)

- ★ Lowers LDL only
- ★ No mortality data
- ★ Added to statins

👁 Ezetimibe + Simvastatin (Vytorin)

New Medication

☞ Bempedoic acid (Nexletol) – PO agent

- ★ Indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who need additional decrease in LDL
- ★ Mechanism: adenosine triphosphate-citrate lyase (ACL) inhibitor
- ★ No data yet on CV morbidity and mortality lowering
- ★ Side effects: hyperuricemia, muscle spasms, pain in extremities, increase in liver enzymes

PCSK9 Inhibitors

👉 Agents: Alirocumab (Praluent) & Evolocumab (Repatha)

👉 **MOA:**

- ★ PCSK9 (proprotein convertase subtilisin kexin type 9) is an enzyme – binds to LDL cholesterol receptors
 - 📄 PCSK9 receptor inhibitors increase the number of receptors that are available to bind to and clear LDL cholesterol
 - Increased LDL cholesterol clearance and lower LDL plasma levels
 - consistent decrease in LDL cholesterol by 60%

PCSK9 Inhibitors

Dosing:

- ★ SC injection; once or twice per month
- ★ \$10,000 per year (average estimate)

Who might benefit:

- ★ Certain types of familial hyperlipidemia
- ★ Statin-intolerant patients
- ★ Poor response to statins
- ★ Contraindications to statins

PCSK9 Inhibitors – Side Effects

👁️ Arthralgias

👁️ Myalgia (with increase in CPK levels)

👁️ Neurocognitive impairment

★ Amnesia, cognitive impairment, confusion

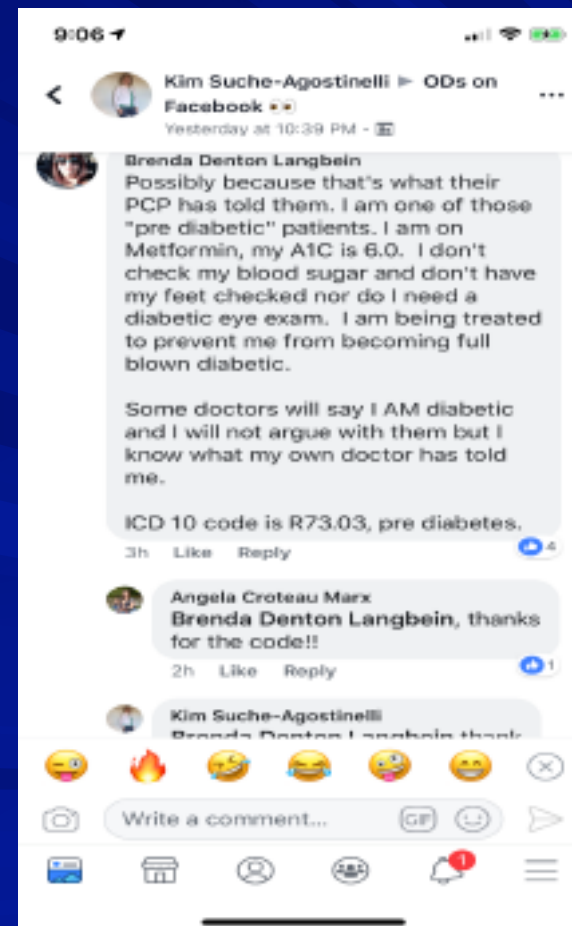
👁️ Ophthalmologic events

👁️ Impairment of glucose homeostasis

★ b/c PCSK9 enzyme is also found on pancreatic islet cells

★ Increased risk of developing DM

Hope this lecture helped with...



Thank You!

Questions