

Diabetes Microvascular Complications

Screening, Management, and Referral

Eric L. Johnson, M.D.

Associate Professor

Department of Family and Community Medicine

Assistant Medical Director

Altru Diabetes Center



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Diabetes Complications

Macrovascular Complications

- Cardiovascular disease
 - Coronary Heart disease (CHD)
 - Stroke
 - Peripheral arterial disease (PAD)/amputation



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Diabetes Complications

Microvascular Complications

- Eye disease (retinopathy)
- Kidney disease (nephropathy)
- Nerve disease (neuropathy)



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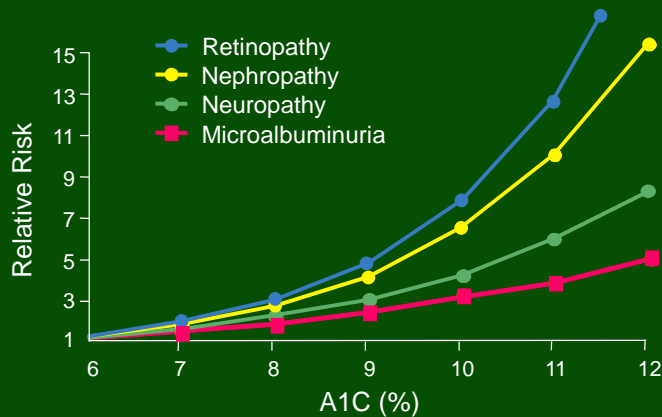
Microvascular Complications



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Type 1 Diabetes: DCCT

Microvascular Complications



Adapted with permission from Skyler J. *Endocrinol Metab Clin North Am.* 1996;25:243
DCCT Research Group. *N Engl J Med.* 1993;329:977



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DCCT/EDIC (type 1)

- Diabetic eye disease by 76 percent
- Advancement of eye disease by about half (54 percent), in people with some eye disease at the beginning of the study.
- Diabetic kidney disease by 50 percent.
- Diabetic nerve disease by 60 percent

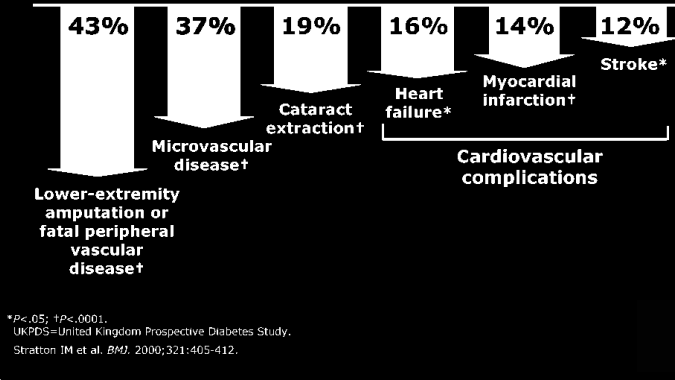
NIDDK
N Engl J Med 1993; 329:977-986
N Engl J Med. 2005;353(25):2643-53.



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Type 2 Diabetes: UKPDS

UKPDS: 1% A1C Decrease and Reduced Risk of Complications



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Goals of Glucose Management

Targets for glycemic control for many patients:

A1c (%)	<7
Fasting (preprandial) plasma glucose	80-130 mg/dL
Postprandial (after meal) plasma glucose	<180 mg/dL



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Kidney Disease



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Diabetic Kidney Disease

- Characterized by proteinuria and declining eGFR
- Occurs in 30% of type 1
- Occurs in 40% of type 2
- More common in African Americans, Asians, and Native Americans
- Associated with risk of CVD
- Diabetes is leading cause of ESRD

NKF
NIDDK
Med Clin North Am 97: 1-18, 2013
Am J Kid Dis June 2018



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Chronic Kidney Disease—Screening New for 2020

- At least once a year, assess urinary albumin (e.g., spot urinary albumin-to-creatinine ratio) and estimated glomerular filtration rate (eGFR) in patients with type 1 diabetes with duration of ≥ 5 years and in all patients with type 2 diabetes regardless of treatment.
- Patients with urinary albumin >30 mg/g creatinine and/or an eGFR <60 mL/min/1.73m² should be monitored twice annually to guide therapy
- Start at 5 years in type 1, at or near diagnosis in type 2



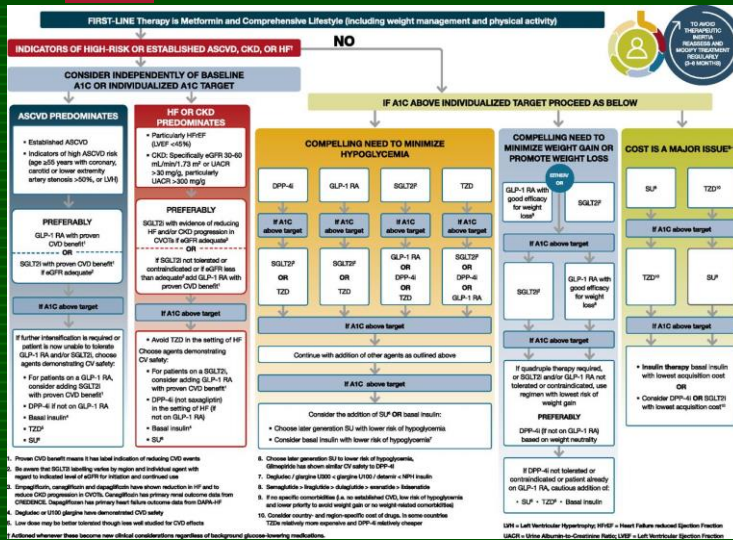
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Kidney Disease Management

- ACEI or ARB for albuminuria or proteinuria
- Serum creatinine and GFR monitoring
- Optimize blood pressure to target $<140/<90$ ($<130/<80$ without undue burden)
- Optimize blood glucose control (i.e., A1C <7) for appropriate patients
- Nephrology referral if eGFR <30 , uncertain diagnosis, difficult to manage or rapid progression, albuminuria/proteinuria
- SGLT-2 for appropriate patients

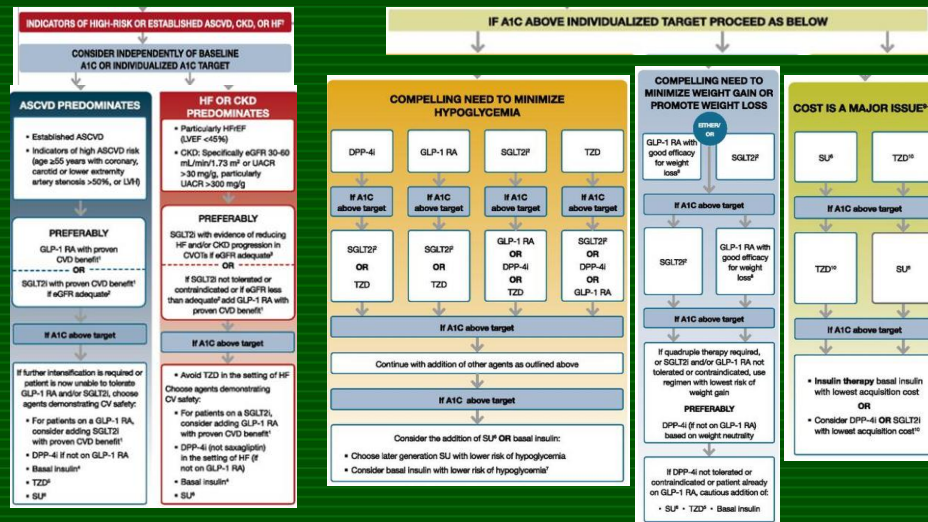


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Glucose-lowering Medication in Type 2 Diabetes: Overall Approach

Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2020, Diabetes Care 2020;43(Suppl. 1):S98-S110*



Choosing Medications in DKD

Medication	Renal effect-progression of DKD	Renal effect-dosing
Metformin	neutral	Contraindicated GFR<30
SGLT-2 inhibitors	benefit	Renal dosing, generally not used GFR<45-60
GLP-1 RA	Benefit-liraglutide	Renal dosing for exenatide, lixisenatide Watch for dehydration, kidney injury
DPP-IV inhibitors	neutral	Renal dosing
TZD's	neutral	FDA Black box warning-HF, fluid retention
Sulfonylureas	neutral	Glyburide-not recommended, watch for hypoglycemia (often not used)
insulin	neutral	Lower doses with lower GFR

Adapted from American Diabetes Association
Diabetes Care 2019 Jan; 42(Supplement 1): S90-S102



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Very Advanced Kidney Disease Diabetes Medications

- Insulin
- Maybe GLP-1
- Be sure to refer to nephrology



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ACEI/ARB in Diabetes

- Not prescribed only for the diagnosis of diabetes
- Used for hypertension or albuminuria/proteinuria in the absence of hypertension



Retinopathy



Retinopathy Screening

- Type 1 annual starting after age 10 or after 5 years post diagnosis
- Type 2 annual starting shortly after diagnosis
- Consider less frequent if one or more normal exams (not usually done)



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Retinopathy Screening New for 2020

Screening for diabetic retinopathy recommendations were revised to include consideration of retinal photograph with remote reading or use of a validated assessment tool as a way to improve screening access



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Retinopathy Management

- A1C < 7 for appropriate patients
- Laser photocoagulation by ophthalmologist or retinologist



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Diabetic Neuropathy



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Diabetic Distal Symmetric Polyneuropathy

- DSPN
 - At least 20% of type 1 diabetes after 20 years
 - 10-15% of new type 2 diabetes
 - 50% after 10 years of type 2 diabetes
- Feet typical initial presentation, burning, tingling, numbness
- Neuropathy contributes to amputations
- Up to 50% of DSPN may be asymptomatic

Neuropathy Position Statement
Diabetes Care 2017;40:136-154



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Neuropathy Screening

- Screen at diagnosis for type 2, 5 years after diagnosis for type 1, and annual thereafter
- Foot inspection every visit plus annual/prn:
 - 10g monofilament testing
 - Vibratory testing (128 HZ)
 - Temperature and pinprick
 - Reflexes
- Assess for autonomic neuropathy in those with DSPN



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Neuropathy: Treatment

- Optimize blood glucose control (i.e., A1C <7) for appropriate individuals for reducing incidence of DPN and CV autonomic neuropathy in those with type 1 diabetes (better evidence in type 1 diabetes)
- Optimize blood glucose control to prevent progression of DSPN in persons with type 2 diabetes
- Pregabalin or duloxetine recommended first line
- Gabapentin may also be considered first line
- Opioids not recommended
- Tricyclic antidepressants use with caution



Other neuropathies

- Autonomic
 - Cardiovascular
 - Gastrointestinal
 - Urogenital
 - Sudomotor
- Mononeuropathy
 - Cranial or peripheral nerve
- Radiculopathy
- Pressure palsies
- B12 deficiency from long term metformin use
- Related hypothyroidism



Case 1: MT

- MT is a 58-year-old Hispanic female
- T2DM x 11 years with dyslipidemia, HTN, albuminuria, non-painful peripheral neuropathy, obesity, non-alcoholic fatty liver disease (NAFLD), history of myocardial infarction (MI) 3 years ago
- Current medications:
 - Metformin 1000 mg orally twice a day
 - Glipizide 10 mg orally once daily
 - Pioglitazone 30 mg orally once daily
 - Lisinopril 20 mg orally once daily
 - Metoprolol XL 25 mg orally once daily
 - Atorvastatin 80 mg orally once daily
 - Aspirin 81 mg orally once daily



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Case 1: MT

- **Physical exam**
 - Nonproliferative retinopathy, normal heart and lung sounds, obese, decreased vibratory and filament sensation in otherwise healthy appearing feet
- **Concerns**
 - Many blood sugars in 200-300s mg/dL , but occasionally less than 70 mg/dL
 - Fatigue
 - Difficulty losing weight
 - Urinary frequency
- **Labs**
 - A1C 10.2%
 - Lipids in target range (on high intensity statin), serum creatinine 0.9 mg/dL, GFR 54 mL/minute/1.73 m², hepatic function revealing minor transaminase elevation, urine albumin 110 mg/24 hr (normal <30 mg/24 hr)

What next?



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Case 1:MT

- This patient has **macrovascular** disease
 - ASCVD
- This patient has **microvascular** disease
 - Early CKD, neuropathy, early retinopathy



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Case 1: MT

- Recall current standards of care recommend an **SGLT-2 inhibitor** or a **GLP-1 agonist** in the patient with established cardiovascular disease
- Recall current standards of care recommend an **SGLT-2 inhibitor** in the patient with chronic kidney disease with appropriate GFR
- One of patient's main complaints is difficulty losing weight, both of these drug classes are weight-neutral or may promote weight loss
- Basal insulin could also be considered here- A1C greater than 10% with symptoms



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Case 1: MT

- **Could do any of the following in the patient with established CVD**
 - Add drug class: GLP-1 agonist
 - Add drug class: SGLT-2 inhibitor
 - Using both GLP-1 agonist or SGLT-2 inhibitor for maximal weight loss
- **Could do any of the following in the patient with established CKD**
 - Preferentially add drug class SGLT-2 inhibitor if eGFR is satisfactory
- **Would definitely**
 - Continue metformin (renal function is OK for this)
 - Refer to diabetes educator and dietician for interprofessional team care
 - Assess well-being/lifestyle factors
- **Would consider**
 - Stop glipizide
 - Stop pioglitazone
 - As we have onboarded more appropriate medications for this patients individual needs



Case 1: MT Summary

- What if A1C was not at target in 3 months?
 - if not on insulin yet, would definitely consider
- **Advance therapy, avoid clinical inertia**
- Remember appropriate interprofessional team-based diabetes self-management education and support



Case 2: CG

- 60 year old Hispanic male
- Metformin, DPP-IV inhibitor
- Started on ACEI for HTN
- Serum creatinine at start 1.1
- 4 weeks later 2.9
- Now what?



Case 2: CG

- Renal ultrasound shows bilateral renal artery stenosis





Standards of Care Resources

- Full version available
- Abridged version for PCPs
- Free app, with interactive tools
- Pocket cards with key figures
- Free webcast for continuing education credit

[Professional.Diabetes.org/
SOC](https://Professional.Diabetes.org/SOC)

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Summary

- Diabetes complications can be avoided or minimized with good glucose control
- Appropriate, guideline based screening is important for early detection
- Know when to make appropriate referrals



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