Diabetes Complications: Screening, Avoidance and Management

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Objectives

• Identify potential diabetes complications
• Screen for diabetes complications
• Implement guideline based management of diabetes complications
Diabetes Guideline Management

- **AACE**: Endocrine Practice 2011;17 (suppl2)
- **ADA**: Diabetes Care January 2012; 35 (Supplement 1)
- Both Guideline sets recommend comprehensive approach for risk factors
Diabetes Complications

Macrovascular Complications

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

Microvascular Complications

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

Other complications

• Liver disease (NAFLD, NASH)
• All cause mortality risk
Diabetes and All-Cause Mortality

• Diabetes deaths annually in the U.S. ~233,000

• Meta-analysis 97 studies 820,900 people

• HR 1.8 death from any cause

• HR 1.25 death from cancer

• HR 2.32 death from vascular disease

• HR 1.73 death from any other cause

Diabetes and All-Cause Mortality

Diabetes also associated with death from:

- Pneumonia and other infectious diseases
- Mental disorders
- Nonhepatic digestive diseases
- External causes and intentional self-harm
- Nervous-system disorders
- COPD

Risks for Complications in Diabetes

- Abnormal blood sugar
- Abnormal cholesterol
- Abnormal blood pressure
- Sedentary lifestyle
- Smoking
Avoiding Diabetes Complications

• Blood glucose control A1C <7%

• Treat cholesterol profiles to targets
  – Total cholesterol <200
  – Triglycerides <150
  – HDL (“good”) >40 men, >50 women
  – LDL (“bad”) <100, <70 high risk

• Treat blood pressure to target <130/<80

For most non-pregnant adults
Avoiding Diabetes Complications

• Lifestyle
  - smoking cessation
  - exercise/activity
  - meal planning
Diabetes Complications

• First, we’ll discuss A1C and it’s relationship to complications
• Then, we’ll discuss systems and other risk factors
Blood Glucose/A1C and Relationship to Complications
Many questions about A1C in recent years with relationship to complications

Let's try to sort it out.....
A1C ~ “Average Glucose”

<table>
<thead>
<tr>
<th>A1C</th>
<th>eAG</th>
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<tr>
<td>%</td>
<td>mg/dL</td>
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<tr>
<td>6</td>
<td>126</td>
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<tr>
<td>6.5</td>
<td>140</td>
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<tr>
<td>7</td>
<td>154</td>
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<td>169</td>
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<td>197</td>
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<tr>
<td>9</td>
<td>212</td>
</tr>
<tr>
<td>9.5</td>
<td>226</td>
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</table>

Formula: \(28.7 \times A1C - 46.7 - eAG\)
Targets for Glycemic (blood sugar) Control In Most Non-Pregnant Adults

<table>
<thead>
<tr>
<th></th>
<th>ADA</th>
<th>AACE</th>
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</thead>
<tbody>
<tr>
<td>A1c (%)</td>
<td>&lt;7*</td>
<td>≤6.5</td>
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<tr>
<td>Fasting (preprandial) plasma glucose</td>
<td>70-130 mg/dL</td>
<td>&lt;110 mg/dL</td>
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<tr>
<td>Postprandial (after meal) plasma glucose</td>
<td>&lt;180 mg/dL</td>
<td>&lt;140 mg/dL</td>
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</table>

*<6 for certain individuals

Type 1 Diabetes: DCCT

Microvascular Complications

Relative Risk

- Retinopathy
- Nephropathy
- Neuropathy
- Microalbuminurinuria

A1C (%)
Type 2 Diabetes: UKPDS

UKPDS: 1% A1C Decrease and Reduced Risk of Complications

- 43% Lower-extremity amputation or fatal peripheral vascular disease†
- 37% Microvascular disease†
- 19% Cataract extraction†
- 16% Heart failure*†
- 14% Myocardial infarction†
- 12% Stroke*

Cardiovascular complications

*P<.05; †P<.0001.

UKPDS=United Kingdom Prospective Diabetes Study.
Blood Glucose, A1C, and CVD

- ACCORD, ADVANCE, VADT did not show improved CVD outcomes with A1C less than ~6.0%-6.5%
- ADVANCE confirmed less microvascular disease (nephropathy) in tightly controlled
- Other data suggest post-prandial, variable glucose, difficult to target may contribute to CVD
- Lower A1C associated with less microvascular disease (nephropathy, neuropathy, retinopathy) (UKPDS, DCCT)

Diabetes Care October 2011 34 (10) 2237-2243
Blood Glucose, A1C, and CVD

• Recent study showed A1C=6 or >8, higher CVD risk

• Meta-analysis of Five Trials
  UKPDS2, PROactive3, ADVANCE4, ACCORD5, VADT6

Intensive therapy reduced cardiovascular death, but not all cause mortality

Colayco DC et al *Diabetes Care*. 2011;34(1):77-83
Ray K et al *The Lancet*. 2009; 373:1765 - 1772
A1C and Complications

• So?

• What Now?........
Intensive Glycemic Control and the Prevention of Cardiovascular Events: Implications of the ACCORD, ADVANCE, and VA Diabetes Trials

A position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association.
A1C and Complications

• Data suggests lower A1C’s earlier in course of diabetes beneficial
• Long term poor control may not benefit from more stringent control now, particularly with reference to CVD

Diabetes Care January 2009;32 (1) 187-192
Summarizing Blood Glucose, A1C, and Diabetes Complications

• A1C
  Probably more associated with microvascular complications

• Glucose variability, post-prandial glucose
  Probably more associated with macrovascular complications

• Optimal A1C may be unclear for all patients with CVD risk
Optimal A1C

- Age
- Co-Morbid Conditions/Complications
- Length of Diabetes
- Resources
- Ability to manage complex regimens
- Hypoglycemia
Rethinking Glycemic “Control”

Importantly, utilizing the percentage of diabetic patients who are achieving an HbA1c of <7.0% as a quality indicator, as promulgated by various health care organizations, is inconsistent with the emphasis on individualization of treatment goals.

Diabetes Care 2012 Diabetologia 2012
Cardiovascular Disease
Cardiovascular Disease

• Risk:
  – Stroke 2 to 4 times higher
  – Heart Disease 2 to 4 times higher

• ~75% of diabetes patients have high blood pressure (hypertension)

• ~75% of people with diabetes have a dyslipidemia (cholesterol disease)
Cardiovascular Disease

• Heart disease and stroke ~65% of diabetes deaths

• Routine screening of asymptomatic not recommended

• Treat risk factors (lipids, BP, smoking, etc)

Diabetes Care January 2012; 35 (Supplement 1)
Lipid Targets

- Treat cholesterol profiles to targets
- Total cholesterol <200
- Triglycerides <150
- HDL ("good") >40 men, >50 women
- LDL ("bad") <100, <70 high risk
Commonly Used Anti-Lipid Medications

- **Statins**
  - Potent
  - Lower total cholesterol, LDL most effectively
  - Cut CVD risk by ~30%

- **Fibrates**
  - Target triglycerides
  - Often used in combo with Statins
  - Benefit uncertain in TG’s <400?

- **Niacin**

- **Omega-3 fish oils**

- **Colestevelam (Welchol)**
Blood Pressure Goals

- <130/<80 for most adults with diabetes
- Individual targets may vary (elderly, etc)
Common Anti-Hypertensives

• ACEI: Lisinopril (Prinivil), Ramipril (Altace), others
• ARB: Valsartan (Diovan), Losartan (Cozaar), others
• Beta-Blockers: atenolol, metoprolol (Toprol), carvedilol (Coreg-mixed function), others
Common Anti-Hypertensives

• Calcium Channel Blockers- Amlodipine (Norvasc), Verapamil (Covera, Verelan), Diltiazem (Cardizem), others
• Diuretics- Hydrochlorothiazide, others
Hypertension Medications

- ACEI and ARB medications are initial drugs of choice for HTN in DM
- Benefit of lowering blood pressure, reducing heart attack, stroke, and kidney disease
Diabetes and Cardiovascular Disease

- Aspirin Therapy is indicated in DM Men >50 y/o, Women >60 y/o or 10 year CVD risk >10% (consider risk of GI bleed, etc.)
- 81-325mg daily depending on risk factors and co-morbidities
- CV risk reduction 15-50%
- Smoking cessation
- Lifestyle
Diabetes and Cardiovascular Disease

• Death rates for cardiovascular disease in diabetes are declining in North Dakota
  – Men: CHD 8.7/1000 >> 6.5/1000
    Stroke 1.2/1000 >> 0.75/1000
  – Women: CHD 6.1/1000 >> 4.4/1000
    Stroke 1.4/1000 >> 0.5/1000

• Better recognition and treatment?

Journal Diab Compl March-April 2009
Children with DM
Hypertension and Lipids

• Lipids: start screening in childhood if strong FH, or at age 10
• Hypertension: BP >90th percentile for height and weight or >130/>80
• Consider medications (statins, ACE) if necessary

American Diabetes Association. *Diabetes Care.* 2012;35(suppl 1)
Peripheral Arterial Disease (PAD)
Peripheral Arterial Disease

• Blockage of arteries in legs
• Contributing factor to amputations in diabetes:
  – ~60% of lower limb amputations occur in people with diabetes
  – ~71,000 lower limb amputations annually in people with diabetes
  – Amputation rate is 10 times higher in diabetes
Peripheral Artery Disease: Avoidance

• A1C <7%

• Treat same risk factors as heart attack and stroke
  – Treat to target blood pressure
  – Treat to target cholesterol
  – Daily aspirin
Peripheral Arterial Disease: Treatment

- “Bypass” surgery (usually femoral artery to popliteal artery)
- Medications
  - Aspirin daily
  - Clopidogrel
- Amputation for severe disease
  - Tissue death
  - Severe infection (“gangrene”)
Nephropathy
Diabetic Nephropathy

- Characterized by proteinuria
- Prevalence 15-40% in type 1
- Prevalence 5-20% in type 2
- More common in African Americans, Asians, and Native Americans
- Associated with risk of CVD
## NKF-K/DOQI Stages of CKD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>2</td>
<td>Mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney Failure</td>
<td>&lt; 15 or dialysis</td>
</tr>
</tbody>
</table>
Nephropathy Avoidance

- Optimize blood glucose control
- Optimize blood pressure control
Nephropathy Screening/Avoidance/Treatment

• Annual microalbumin and serum creatinine screening
• A1C <7.0
• BP’s <130/<80, weight reduction, lipid control, avoidance of NSAIDS if possible, tobacco cessation
• Usually treated with ACEI or ARB, other BP meds if needed, dietary sodium and protein restriction
Retinopathy
Diabetic Retinopathy

- Non-proliferative diabetic retinopathy (NPDR), microaneurysms only
- Proliferative diabetic retinopathy, neovascularization or vitreous/preretinal hemorrhage
Retinopathy: Avoidance/Treatment

- A1C <7.0, less glucose variability?
- Annual dilated eye exams/fundal photography by eye care professional
- Screen more frequently in pregnancy or if disease present
- Laser photocoagulation, vitrectomy for overt retinopathy
- New medications on the horizon
Diabetic Eye Disease - Other Conditions

• Cataracts
• Macular edema
• Glaucoma
Neuropathy
Diabetic Neuropathy

• Diabetic Peripheral Neuropathy (DPN)
• Focal and Mononeuropathies
• Autonomic Neuropathy
• Radiculoplexic Neuropathy-more proximal
• Painful Diabetic Neuropathy
Diabetic Peripheral Neuropathy

- DPN affects ~60-70% of patients with diabetes
  - Feet typical initial presentation, burning, tingling, numbness

- Neuropathy contributes to amputations
Neuropathy: Avoidance

- Optimize glucose control
Neuropathy: Screening

- Foot inspection
- 10mg filament testing
- 128 hz vibratory testing
- Reflexes
- At least annual or prn
Neuropathy: Treatment

- Optimize blood glucose control
- Consider other differentials, i.e. B12 deficiency in metformin users, thyroid
- Anti-seizure meds (gapapentin, pregabalin)
- Tricyclic anti-depressants (amitriptyline)
- Duloxetine-antidepressant with neuropathy indication
- Capsazin creme
Liver Disease
Fatty Liver

• NAFLD (non-alcoholic fatty liver disease)
• NASH (non-alcoholic steatohepatitis)
• At least 30% of type 2 patients
• Underdiagnosed
• Current treatment is weight loss, possible future medication role
• Type 2 also higher risk of hepatitis C

Tolman KG et al Diabetes Care 2007;30: 734-743
Johnson EL Journal of Family Practice 2012
Fatty Liver

- Usually marked by minor liver function test abnormalities (alkaline phosphatase, ALT, AST)
- No specific treatment, but metformin, TZD, glp-1, insulin may improve
- If persistent LFT abnormalities:
  - imaging (ultrasound, CT, MRI)
  - screen for hepatitis
  - consider gastroenterology referral
Dental
Dental Issues in Diabetes

- Tooth loss
- Peridontal disease
- Possible cause of diabetes/aggravator of diabetes/CVD
- Dentist every 6 months
Tobacco and Diabetes
The Deadly Intersection
Tobacco and Diabetes

- Smoking is a cause of type 2 diabetes
- Smoking worsens diabetes control
- Smoking increases risk of CVD and other complications
- Smoking cessation is critical in diabetes
- Refer to ND Quitline/Quitnet, MN Quitplan, other resources
Diabetes Clinical Encounters
Patient comes in today for follow up on type (1 or 2) diabetes

- (Other problem list)
- Home Blood glucose monitoring:
- Ambulatory/Home Blood Pressures:
- Current concerns:
- Last educator appointment:
- Last dietician appointment:
- Last eye appointment:
- Last dental:
- Flu vaccine (seasonal):
- Other recent appointments:
- Complete medication review
Diabetes Clinical Encounters
Review of Systems-My EHR Template

• General: Fatigue/Energy level, appetite, recent illnesses, polydipsia
• HEENT: Vision change, sore throat, neck pain/masses
• Cardiopulmonary: CP, dyspnea, palpitations
• Abdomen: Diarrhea, constipation, pain
Diabetes Clinical Encounters
Review of Systems (cont’d)

• Genitourinary: Polyuria, Dysuria, Urgency, Frequency, Nocturia
• Musculoskeletal: Muscle or Joint Pain, Foot or Leg Pain
• Neurologic: Dizzy, Lightheaded, Parasthesias, Weakness, Pain
• Skin: Rash or other
• Psych: Depression, Anxiety
Diabetes Clinical Encounters

Physical Exam

- VS: Height, Weight, BP (x2?), Pulse, Tobacco status
- Fundus exam
- Cardiopulmonary
- Carotids
- Thyroid
- Abdomen (enlarged liver-fatty liver)
Diabetes Clinical Encounters
Physical Exam (cont’d)

• Filament and vibratory testing (feet)
• General foot exam (skin, nails, lesions, color)
• General skin/injection sites
• Other complaint directed
• Growth parameters-children
Diabetes Clinical Encounters

- Other:
  Age appropriate recommendations
  (cancer screening, etc)

Vaccinations

See patients 2 to 4 times a year
Diabetes Labs

- A1C 2-4 times yearly
- Chemistry panel, to include renal and hepatic 1-2 times yearly, prn
- Urine for microalbumin annually
- CBC annually, particularly if on aspirin and/or renal disease
- Celiac screening in type 1 periodically (ever 3 years and prn)
- Thyroid screening usually annual in type 1

Diabetes Care 35: Supplement 1, 2012
The Diabetes Team

- **Physician**: Primary Care, Diabetologist, Endocrinologist
- **Mid-level provider**: Physician Assistant or Nurse Practitioner
- **Other appropriate specialists** (eye, kidney, heart, psychologist, foot, dentist)
The Diabetes Team

• Diabetes Nurse Educator or Certified Diabetes Educator (CDE)
• Registered Dietician
• The patient!
Team Approach

• Diabetes is a complex condition
• Different team members have different focus
• Integrate care to individualize care to the patient
Summary: Reducing Diabetes Complications

• A1C < 7% for most non-pregnant adults
• Treat blood pressure to target of <130/<80
• Treat cholesterol profiles to target
• Low dose aspirin for appropriate patients
• Lifestyle changes
  – Meal Plan
  – Appropriate exercise plan
  – Smoking Cessation
• Proper and timely follow-up with providers
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Slide Decks (Diabetes, Tobacco, other)
http://www.med.und.edu/familymedicine/slidedecks.html

iTunes Podcasts (Diabetes)
http://www.med.und.edu/podcasts/ or iTunes>>search UND Medcast (3/1/11 release)

WebMD Page:
http://www.webmd.com/eric-l-johnson

Diabetes e-columns (archived):
http://www.ndhealth.gov/diabetescoalition/DrJohnson/DrJohnson.htm