Diabetes Care for Older Adults: 2012 ADA Consensus Conference Recommendations
Disclosures

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Research support from Sanofi Aventis
Diabetes in Older Adults: A Consensus Report

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PharmD, CDE, Richard E. Pratley, MD, and Carrie S. Swift, MS, RD, BC-ADM, CDE
Lecture Outline

1. What is the epidemiology and pathogenesis of diabetes in older adults?
2. What is the evidence for preventing and treating diabetes and its common comorbidities in older adults?
3. What current guidelines exist for treating diabetes in older adults?
4. What issues need to be considered in individualizing treatment recommendations for older adults?
5. What are consensus recommendations for treating older adults with or at risk for diabetes?
6. How can gaps in the evidence best be filled?
Epidemiology of DM in Older Adults
Distribution of Age at Diagnosis of Diabetes Among Adults Incident (18–79 years) US

Adults ≥ 60 years accounted for 35.1% of all new cases of DM in 2011

http://www.cdc.gov/diabetes/statistics/age/fig1.htm
Incidence of Diagnosed DM/1,000 Population 18–79 Years by Age

http://www.cdc.gov/diabetes/statistics/age/fig1.htm
Prevalence of Type 2 Diabetes Among Elderly People (NHANES III)

Pathogenesis of DM in Older Adults
Model for Age-Related Hyperglycemia

Diabetes Risk Factors in Aging

- Decreased physical activity
- Increased adiposity
- Age effects on insulin action
  - Medications
  - Genetics
  - Coexisting illness
  - Inflammation
  - Age effects on β cells

INSULIN RESISTANCE

DECREASED INSULIN SECRETION

Impaired adaptation:
No ↑ insulin

IGT / IFGT / Type 2 diabetes

Chang & Halter. AJP 284:E7-E12, 2003
Pathophysiology of DM in older adults

Insulin resistance increases with aging due to:

- Weight gain
- Inactivity
- Decrease in muscle mass and quality
- Medications: e.g. steroids, high dose diuretics, beta blockers etc.
- Changes in physiology (+/- increase in hepatic glucose production; decrease insulin-mediated glucose disposal)
Pathophysiology of DM in older adults

Progressive decrease in β cell function due to:

- Increased intracellular lipid
- Decreased number of GLUT-2 transporters
- Decreased responsiveness to endogenous incretins
- Decreased conversion of pro-insulin to insulin
Glucose and Insulin Responses during OGTT in young and middle-aged subjects

MEN

WOMEN

Insulin Resistance and Aging

Young and elderly subjects matched for lean body and fat mass. No medications

<table>
<thead>
<tr>
<th></th>
<th>Young (13)</th>
<th>Elderly (15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>27 ± 2</td>
<td>70 ± 2*</td>
</tr>
<tr>
<td>Weight</td>
<td>71 ± 4</td>
<td>70 ± 3</td>
</tr>
<tr>
<td>Fat mass</td>
<td>20 ± 2</td>
<td>20 ± 2</td>
</tr>
<tr>
<td>% fat mass</td>
<td>28 ± 3</td>
<td>29 ± 2</td>
</tr>
<tr>
<td>Lean body mass</td>
<td>54 ± 5</td>
<td>49 ± 3</td>
</tr>
<tr>
<td>BMI</td>
<td>23 ± 8</td>
<td>25 ± 0.5</td>
</tr>
</tbody>
</table>
Elderly subjects have higher basal FFA with normal suppression during an OGTT

Petersen KF et al  Science  300:1140  2003
Metabolic parameters in young and elderly subjects

- EGP
- Rd Glu
- Muscle lipid
- Hepatic lipid
- Mit TCA flux
- ATP

Young vs. Elderly

* indicates significant difference

Petersen KF et al. Science 300:1140 2003
Mitochondria

- The “power plants” of a cell – i.e. the major source of energy
- Responsible for the breakdown of fatty acids
- Impairment of mitochondrial function causes buildup of fats and fatty acids inside muscle that can produce insulin resistance
- Accumulation of intracellular lipid contributes to the development of diabetes later in life.
- Impairment of mitochondrial generation of ATP within the beta cell may also play a role in age-associated reductions in insulin secretion

Petersen KF et al Science 300:1140 2003
Diabetes, inflammation, and functional decline in older adults

The Health, Aging and Body Composition (ABC) study

2895 healthy adults aged 70–79 years grouped according to CRP or IL-6 levels

Functional limitation defined as difficulty climbing 10 steps or walking one-quarter mile on two consecutive semiannual assessments.

Figaro MK et al Diabetes Care. 29(9):2039-45 2006
What is the evidence for preventing diabetes in older adults?
## Categories of Glucose Tolerance

<table>
<thead>
<tr>
<th>Category</th>
<th>Fasting Glucose mg/dl</th>
<th>OGTT or 2 hour pp BG mg/dl</th>
<th>HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;100</td>
<td>&lt;140</td>
<td>&lt;5.7</td>
</tr>
<tr>
<td>Impaired (Pre-diabetes)</td>
<td>100-125</td>
<td>&lt;200</td>
<td>5.7-&lt;6.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>≥ 126</td>
<td>&gt;200</td>
<td>≥ 6.5</td>
</tr>
</tbody>
</table>

Screening for Diabetes

- Annual fasting glucose for all adults > age 45
- More frequent screening for obese adults with other risk factors

- Symptoms of hyperglycemia may be masked in older adults by:
  - Diuretic use
  - BPH in men
  - Other conditions associated with incontinence and/or polyuria
  - Age-related decrease in thirst which blunts polydipsia

Diabetes Prevention Program

Diet and exercise in prevention of type 2 diabetes in elderly individuals

Is diabetes preventable in older adults?

Number needed to treat for 3 yrs:

6.9 (CI 5.4-9.5) in lifestyle intervention

13.9 (CI 8.7-33.9) in metformin group

What is the evidence for treating diabetes and associated comorbidities in older adults?
### Summary of Major Clinical T2D Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean Age</th>
<th>Microvascular</th>
<th>CVD</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UKPDS</strong></td>
<td>63</td>
<td>↓</td>
<td>⇨</td>
<td>↓</td>
</tr>
<tr>
<td><strong>ACCORD</strong></td>
<td>62</td>
<td>↓</td>
<td>⇨</td>
<td>↑</td>
</tr>
<tr>
<td><strong>ADVANCE</strong></td>
<td>66</td>
<td>↓</td>
<td>⇨</td>
<td>⇨</td>
</tr>
<tr>
<td><strong>VADT</strong></td>
<td>60</td>
<td>↓</td>
<td>⇨</td>
<td>⇨</td>
</tr>
</tbody>
</table>

**UKPDS Group. Holman RR et al. NEJM 2008;359:1577.**  
Nathan DM et al. NEJM 2005;353:2643  
Gerstein HC et al. NEJM. 2008;358:2545.  
Patel A et al. NEJM 2008;358:2560  
Glycemic Control, Co-morbidity and CVD Outcomes in Diabetes

N = 2613 Subjects

Those with higher co-morbidity derived less benefit from intensive glucose control

Mean age: 62 ± 10 64 ± 10

All Cause Mortality and A1C

27,965 ≥ age 50 with type 2 diabetes from UK GP Research Database (1986-2008)
# Lipid Lowering Trials in T2D

<table>
<thead>
<tr>
<th>Statin Trials</th>
<th>Age Group</th>
<th>Outcomes</th>
<th>Elderly Subanalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CARDS</td>
<td>40-75</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ASCOT-ALL</td>
<td>40-79</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HPS</td>
<td>40-80</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>9 others</td>
<td>Up to age 80</td>
<td>All +</td>
<td>Not done</td>
</tr>
<tr>
<td><strong>Elderly</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSPER</td>
<td>70-82</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Diabetes + Elderly</td>
<td></td>
<td>??</td>
<td></td>
</tr>
<tr>
<td><strong>Fibrates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIELD</td>
<td>50-75</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>DAIS</td>
<td>50-65</td>
<td>+</td>
<td>NA</td>
</tr>
</tbody>
</table>

*From Cigolle et al. Clinics in Geriatric Medicine, November 2009*
# BP Lowering Trials in T2D

<table>
<thead>
<tr>
<th>Study</th>
<th>Age Group</th>
<th>Outcomes</th>
<th>Elderly Subanalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASCOT-BPLA</td>
<td>40-79</td>
<td>Comp. effectiveness</td>
<td>+</td>
</tr>
<tr>
<td>ALLHAT</td>
<td>&gt; 55</td>
<td>Comp. effectiveness</td>
<td>Not done</td>
</tr>
<tr>
<td>HOT</td>
<td>50-80</td>
<td>+ (BP target)</td>
<td>Not done</td>
</tr>
<tr>
<td>ABCD</td>
<td>40-74</td>
<td>+ (BP target)</td>
<td>Not done</td>
</tr>
<tr>
<td>UKPDS/HDS</td>
<td>25-65</td>
<td>- (10 yr f/u)</td>
<td>Not done</td>
</tr>
<tr>
<td>ADVANCE</td>
<td>&gt; 55</td>
<td>+ (ACE)</td>
<td>+</td>
</tr>
<tr>
<td>RENAAL</td>
<td>31-70</td>
<td>+ (ARB)</td>
<td>+</td>
</tr>
<tr>
<td>HOPE</td>
<td>&gt; 55</td>
<td>+ (ACE)</td>
<td>Not done</td>
</tr>
<tr>
<td>DM + Elderly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syst-Eur</td>
<td>&gt; 60</td>
<td>+ (BP target)</td>
<td>NA</td>
</tr>
<tr>
<td>SHEP</td>
<td>&gt; 60</td>
<td>+</td>
<td>NA</td>
</tr>
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</table>

From Cigolle et al. Clinics in Geriatric Medicine, November 2009
What current guidelines exist for treating diabetes in older adults?
### ADA Recommendations for adults with T2D

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Goal</th>
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<tbody>
<tr>
<td>Preprandial BG (mg/dl)</td>
<td>70-130</td>
</tr>
<tr>
<td>Peak postprandial BG (mg/dl)</td>
<td>&lt;180</td>
</tr>
<tr>
<td>A1c (%)</td>
<td>&lt;7.0%</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>&lt;140/80</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>&lt;100</td>
</tr>
</tbody>
</table>

*More or less stringent goals may be appropriate for individual patients*

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Screening for DM Related Complications

- Yearly retinal exam
  - Include screen for glaucoma, macular degeneration, and cataracts

- Annual creatinine and urine microalbumin

- Annual fasting lipid profile

- Regular BP checks

- Yearly foot exam
  - Instructing patients to examine their own feet
  - Medicare covers special footwear

Components of Diabetic Shoewear

Extra Depth: allows room for orthotics
Ventilation
Seamless/lightweight construction
Arch support
Room for toes
Good fitting heel
Thick soles
What issues need to be considered in individualizing treatment recommendations for older adults?
Qualifications of Glycemic Goals

Goals should be individualized based on:

- Duration of diabetes
- Age/life expectancy
- Comorbid conditions
- Presence of CVD or advanced microvascular complications
- Hypoglycemia unawareness (more common in elderly)
- Individual patient considerations

Consideration for treating diabetes in older adult population

- Complications such as neuropathy and retinopathy can impair independence
- Diabetes can lead to or worsen changes in cognitive function
- Diabetes increases risk for depression in men and women
- Geriatric syndrome (polypharmacy, depression, impaired vision, cognitive decline/dementia, fall risk, urinary incontinence, chronic pain, and various physiological changes) can make diabetes in the elderly more complicated to manage than in the non-elderly

Preventing Chronic Complications

Elderly patients with diabetes may have:

• Longstanding diabetes with associated microvascular and macrovascular complications

• Newly diagnosed diabetes with evidence of end organ complications at the time of presentation

• Newly diagnosed diabetes without evidence of complications
Health Status of Older Adults with Diabetes by Age
Health and Retirement Study

Blaum C et al. Medical Care 2010: 48;327
## Characteristics of Middle-aged and Elderly Subjects with & without Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Age 40-64</th>
<th></th>
<th>Age ≥ 65</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No DM</td>
<td>DM</td>
<td>No DM</td>
<td>Diabetes Onset</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>3391</td>
<td>374</td>
<td>2344</td>
<td>272</td>
</tr>
<tr>
<td><strong>Age at Dx (y)</strong></td>
<td></td>
<td></td>
<td></td>
<td>46.7</td>
</tr>
<tr>
<td><strong>Yrs since dx(%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td>25.4</td>
<td></td>
<td>76.7</td>
<td>10.9</td>
</tr>
<tr>
<td>5-10</td>
<td>26.9</td>
<td></td>
<td>17.6</td>
<td>24.1</td>
</tr>
<tr>
<td>&lt;5</td>
<td>47.7</td>
<td></td>
<td>5.7</td>
<td>65.0</td>
</tr>
<tr>
<td><strong>Complications (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD</td>
<td>5.6</td>
<td>13.9</td>
<td>19.6</td>
<td>26.1</td>
</tr>
<tr>
<td>CVA</td>
<td>1.7</td>
<td>5.0</td>
<td>7.8</td>
<td>14.0</td>
</tr>
<tr>
<td>CHD</td>
<td>4.3</td>
<td>10.4</td>
<td>14.0</td>
<td>30.1</td>
</tr>
<tr>
<td>PAD</td>
<td>2.4</td>
<td>6.0</td>
<td>12.0</td>
<td>22.4</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>7.9</td>
<td>16.9</td>
<td>21.5</td>
<td>35.5</td>
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<tr>
<td>Retinopathy</td>
<td>--</td>
<td>24.8</td>
<td>--</td>
<td>39.4</td>
</tr>
</tbody>
</table>

*Selvin E et al. Diabetes Care. 29:2415 2006*
What are the consensus recommendations for treating older adults with or at risk for diabetes?
### Framework for glycemic and metabolic goals in older adults with Diabetes

<table>
<thead>
<tr>
<th>Patient Characteristics/Health Status</th>
<th>A1C Goal</th>
<th>FBG or Pre-Meal</th>
<th>HS BG</th>
<th>BP</th>
<th>Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>&lt;7.5%</td>
<td>90-130</td>
<td>90-150</td>
<td>&lt;140/80</td>
<td>Statin*</td>
</tr>
<tr>
<td>Longer remaining life expectancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex/Intermediate</td>
<td>&lt;8.0%</td>
<td>90-150</td>
<td>100-80</td>
<td>&lt;140/80</td>
<td>Statin*</td>
</tr>
<tr>
<td>Intermediate remaining life expectancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very Complex/Poor Health</td>
<td>&lt;8.5%†</td>
<td>100-180</td>
<td>110-200</td>
<td>&lt;150/90</td>
<td>**</td>
</tr>
<tr>
<td>Limited remaining life expectancy makes benefit uncertain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Unless contraindicated or not tolerated

**Consider likelihood of benefit with statin (secondary > primary prevention)

*Kirkman MS et al Diabetes Care and JAGS Dec 2012*
Definitions and contingencies of the published framework

Healthy: Few co-existing chronic illnesses, intact cognitive and functional status

Intermediate: Multiple co-existing chronic illnesses or 2+ instrumental ADL impairments or mild-moderate cognitive impairment. High treatment burden, hypoglycemia vulnerability, fall risk

Very complex/poor health: long-term care or end-stage chronic illnesses or moderate-severe cognitive impairment or 2+ ADL dependencies

Chronic illnesses defined as conditions serious enough to require medications or lifestyle management. Includes arthritis, CA, CHF, depression, COPD, falls, HTN, incontinence, ≥Stage 3 CKD, MI, stroke. Multiple defined as ≥ 3 chronic conditions

Kirkman MS et al Diabetes Care and JAGS Dec 2012
Hypoglycemia

Particularly dangerous in the elderly

• Especially when on insulin or secretagogues
• The ability to sense hypoglycemia declines with age
• Age-related impairment in counterregulatory response to hypoglycemia
• Elderly brain is more sensitive to the insult of hypoglycemia

Patient education regarding symptoms and treatment of hypoglycemia can help prevent severe episodes with associated sequellae.
Prevention of hypoglycemia

- Education regarding peak times for insulin (or oral agent action)
- Home glucose monitoring
- Adjustments diabetes regimen for exercise or food intake
  - Insulin treated patients can be advised to decrease their prandial insulin by 1-2 units for the meals preceding and following exercise
  - Patients treated with an insulin secretogogue can be advised to reduce the dose, exercise before taking the medication, OR to have a snack prior to exercise
Treatment of hyperglycemia

Medical Nutrition Therapy

Exercise

Home blood glucose monitoring
  Glucose sensors

Pharmacologic therapy

  Oral agents
    Non-insulin injectable therapies
      Pramlintide
      Glucagon-like peptide analogs
  Insulin
Mediterranean vs Low Fat Diets in Overweight Subjects with Type 2 DM

Log-rank test, $P = 0.001$

Hazard ratio, $0.63$ (95% CI, 0.51–0.86)
Aerobic vs Resistance Exercise Training in Type 2 Diabetes

Mean age 55.8 ± 8.7 yrs
Range 30-75

Church, T. S. et al. JAMA 2010;304:2253-2262
Algorithm for Management of T2DM*

*Emphasis on Individualizing therapy

Inzucchi SE et al. Diabetes Care 35:1364 2012
<table>
<thead>
<tr>
<th>Class</th>
<th>Considerations for use in OA</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylureas/ Short acting Insulin Secretagogues</td>
<td>High risk for hypoglycemia (glyburide &gt; all other SU)</td>
<td>$</td>
</tr>
<tr>
<td>Biguanides (metformin)</td>
<td>GI side effects in 5% of patients</td>
<td>$</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Exacerbation of edema and CHF</td>
<td>$$</td>
</tr>
<tr>
<td>α-Glucosidase Inhibitors</td>
<td>Bloating, abdominal discomfort</td>
<td>SS</td>
</tr>
<tr>
<td>DPP IV Inhibitors</td>
<td>More URI/UTI in some studies</td>
<td>SSS</td>
</tr>
<tr>
<td>SGLT2 inhibitors</td>
<td>UTI, polyuria, Vulvovaginitis</td>
<td>UNK</td>
</tr>
</tbody>
</table>
## Proposed Update to Metformin Labeling
Submitted to FDA 2013

<table>
<thead>
<tr>
<th>eGFR ml/min/1.73m²</th>
<th>Action</th>
</tr>
</thead>
</table>
| ≥ 60               | No renal contraindication  
                        Monitor renal function annually |
| <60 and ≥ 45       | Continue use  
                        Monitor renal function every 3-6 months |
| <45 and ≥ 30       | Do not start metformin  
                        **For patients already on metformin:**  
                        Use metformin with caution at lower doses (max:1 G/day)  
                        Monitor renal function every 3 months |
| <30                | Stop metformin |


## Major Classes of Injectable Agents for DM

<table>
<thead>
<tr>
<th>Class</th>
<th>Considerations for use in OA</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1 receptor agonists</td>
<td>GI (nausea, diarrhea) ? Pancreatitis Medullary thyroid cancer</td>
<td>SSS</td>
</tr>
<tr>
<td><em>Exenatide, liraglutide</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amylin mimetic</td>
<td>GI (nausea) Hypoglycemia (when used with insulin) Dosing before each meal</td>
<td>$$$</td>
</tr>
<tr>
<td><em>Pramlintide</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>Hypoglycemia Weight gain Mitogenicity Training requirements Quality of life issues Potential need for multiple doses</td>
<td>Varies</td>
</tr>
</tbody>
</table>
Summary:

2012 ADA Recommendations for DM in Older Adults

• One out of every 3-4 individuals age >65 has diabetes

• Annual screening in older adults permits early identification of individuals at risk for diabetes

• Lifestyle intervention with diet and exercise is effective at reducing risk for progression to T2D in older adults

• Goal directed therapy of glucose, BP, and lipids modified according to life expectancy and or illness burden reduces risk for micro- and macrovascular complications

• There are no absolute contraindications to use of any diabetes medications in the elderly population, including insulin

Kirkman MS et al Diabetes Care and JAGS Dec 2012