Medical Overview of Diabetes in Older Adults

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Case Studies of Diabetes Mellitus in Older Adults

- Describe a broad spectrum of diabetes in older adults
- Illustrate specific points about the approach and management of diabetes in older adults in 3 cases
Natural History - Type 2 Diabetes

Genetics
Environment
- aging
- obesity
- sedentary lifestyle

Onset

Complications

Disability

Prediabetes: IGT, IFG

Insulin resistance
Atherosclerosis
Hyperinsulinemia
Hypertension
Dyslipidemia

Hyperglycemia

Retinopathy
Nephropathy
Neuropathy
Depression

Blindness
Renal failure
Amputation
CVD

Death
New ADA Recommendations for Diagnosing Diabetes

Table 3—Criteria for the diagnosis of diabetes

1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
   OR
2. FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.*
   OR
3. 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGGT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
   OR
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l).

*In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.
Prevalence of Diabetes in USA

CDC Diabetes Data and trends,
www.cdc.gov/diabetes/statistics/prev/national/figbyage.htm
Preventing Diabetes in Older Adults

Cumulative Incidence of Diabetes According to Study Group

All Subjects

<table>
<thead>
<tr>
<th></th>
<th>Old Subjects (Cases/100 person-yrs)</th>
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<tbody>
<tr>
<td>Placebo</td>
<td>10.8</td>
</tr>
<tr>
<td>Metformin</td>
<td>9.6</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Adapted from Diabetes Prevention Program Research Group, NEJM 2002;346:393-403
ADA Guidelines for Adults with Diabetes

• Hemoglobin $A_{1c} < 7$
  - Fasting BG 80-120 mg/dL
  - Post-prandial BG 100-150 mg/dL
• Nutrition Therapy
• Exercise
• Anti-platelet agents
• Blood Pressure Control
• Lipids
• Safe use of combination therapy

• Screen for complications
  - Renal
  - Neural
  - Retinal
  - Cardiovascular
• Foot Care
• Education

• Specifics for older adults addressed 1$^{st}$ time in 2005
A1C and Relative Risk of Microvascular Complications: DCCT

Adapted from Skyler J. Endocrinol Metab Clin North Am. 1996;25:243
Control of Type 2 Diabetes Predicts Cardiovascular Disease in Older Patients

BUT, does epidemiology predict trial results?

Multifactorial Intervention Helps
STENO-2

Reduced Microvascular Complications:

<table>
<thead>
<tr>
<th></th>
<th>RR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephropathy</td>
<td>0.4</td>
<td>.003</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>0.3</td>
<td>.02</td>
</tr>
<tr>
<td>Autonomic Neuropathy</td>
<td>0.4</td>
<td>.002</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>1.1</td>
<td>.66</td>
</tr>
</tbody>
</table>

STENO-2 Trial. NEJM 348:393, 2003
Summary of Revisions for the 2006 Clinical Practice Recommendations

Beginning with the 2005 supplement, the Clinical Practice Recommendations contained only the “Standards of Medical Care in Diabetes” and selected other position statements. This change was made to emphasize the importance of the “Standards” as the best source to determine ADA recommendations. The position statements in the supplement are updated yearly. Position statements not included in the supplement will be updated as necessary and republished when completed. A list of the position statements not included in this supplement appears on p. 575.

Format changes
• Page numbers now appear in the “Contents” for ease in locating particular sections
• Recommendations are now listed at the beginning of each section

Additions to the Standards of Medical Care in Diabetes
• Medical nutrition therapy (MNT)—extensively enhanced

- Diabetes self-management education (DSME)
- Physical activity
- Neuropathy

Summary of Revisions to Standards of Medical Care for Diabetes
• Assessment of glycemic control
  • Use of point-of-care testing for HbA1c (A1C) allows for timely decisions on therapy changes, when needed (E)
• Glycemic goals
  • The A1C goal for patients in general is <7% (B)
  • The A1C goal for the individual patient is an A1C as close to normal (<6%) as possible without significant hypoglycemia (E)
• Nephropathy
  • To reduce the risk of nephropathy, protein intake should be limited to the Recommended Dietary Allowance (RDA) (0.8 g/kg) in those with any degree of chronic kidney disease (CKD) (B)
  • Serum creatinine should be measured at least annually for the estimation of glomerular filtration rate (GFR) in all adults with diabetes regardless of the degree of urine albumin excretion. The serum creatinine alone should not be used as a measure of kidney function but rather used to estimate GFR and stage the level of CKD (E)

Members of the Professional Practice Committee
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Kenneth Copeland, MD
Marjorie L. Cypress, MS, RN, CDE
Hertzl C. Gerstein, MD, Msc, FRCPC
Irl Hirsch, MD
Steven Kahn, MB, ChB
Elizabeth Mayer-Davis, MS, PhD, RD
James Meigs, MD, MPH
Michael P. Pignone, MD, MPH
Janet H. Silverstein, MD
Geralyn R. Spollett, MSN, C-ANP, CDE
Judith Wylie-Rosett, RD, EdD
Nathaniel G. Clark, MD, MS, RD (Staff)
Individualizing Treatment Goals

Approach to management of hyperglycemia:

- Patient attitude and expected treatment efforts
  - More stringent: Highly motivated, adherent, excellent self-care capacities
  - Less stringent: Less motivated, non-adherent, poor self-care capacities

- Risks potentially associated with hypoglycemia, other adverse events
  - More stringent: Low
  - Less stringent: High

- Disease duration
  - More stringent: Newly diagnosed
  - Less stringent: Long-standing

- Life expectancy
  - More stringent: Long
  - Less stringent: Short

- Important comorbidities
  - More stringent: Absent
  - Less stringent: Few/mild

- Established vascular complications
  - More stringent: Absent
  - Less stringent: Few/mild

- Resources, support system
  - More stringent: Readily available
  - Less stringent: Limited

Position Statement of the ADA & EASD. DIABETES CARE. 2012
Antidiabetic Agents: Major Sites of Action

- Sulfonylureas
- Meglitinides
- GLP-1 agonists
- Incretins
- Gli tract
- $\alpha$-Glucosidase Inhibitors
- GLP-1 agonists
- Metformin
- Incretins
- DPP IV
- Pancreas
- Liver
- Plasma glucose
- Glucose Uptake
- Glucose Production
- Carbohydrate Absorption
- Injected Insulin
- Muscle/Fat
- Amylin or analog
- TZD’s
- Insulin Secretion
- Carbohydrate Absorption
- Glucose Production
- Insulin Secretion
# Antidiabetic Agents for Type 2 DM

<table>
<thead>
<tr>
<th>Class</th>
<th>Oral Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>biguanide</td>
<td>metformin</td>
</tr>
<tr>
<td>sulfonylurea</td>
<td>glimepiride, glipizide, glyburide, 1st-gen. SU’s</td>
</tr>
<tr>
<td>thiazolidinedione</td>
<td>pioglitazone, rosiglitazone</td>
</tr>
<tr>
<td>non-SU secretagogue</td>
<td>repaglinide, nateglinide</td>
</tr>
<tr>
<td>α-Glucosidase inhibitor</td>
<td>acarbose, miglitol</td>
</tr>
<tr>
<td>DPPIV inhibitor</td>
<td>Sitagliptin, saxagliptin</td>
</tr>
<tr>
<td>Others</td>
<td>Bromocriptine, colesevelam</td>
</tr>
<tr>
<td>combinations</td>
<td>metformin/glyburide, glipizide/metformin, pioglitazone/glimeperide, sitagliptin/metformin</td>
</tr>
<tr>
<td>Injection</td>
<td></td>
</tr>
<tr>
<td>incretin mimetic</td>
<td>Exenatide, liraglutide</td>
</tr>
<tr>
<td>Insulin</td>
<td>NPH, Reg, 70/30, aspart, lispro, glulisine, glargine, detemir, pens, pumps</td>
</tr>
<tr>
<td>Amylin analog</td>
<td>pramlintide</td>
</tr>
</tbody>
</table>
What would you choose?
Healthy eating, weight control, increased physical activity

<table>
<thead>
<tr>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sulfonylureab</strong></td>
<td><strong>Thiazolidinedione</strong></td>
<td><strong>DPP-4 Inhibitor</strong></td>
<td><strong>GLP-1 receptor agonist</strong></td>
<td><strong>Insulin (usually basal)</strong></td>
</tr>
<tr>
<td>high</td>
<td>high</td>
<td>intermediate</td>
<td>high</td>
<td>highest</td>
</tr>
<tr>
<td>moderate risk</td>
<td>low risk</td>
<td>low risk</td>
<td>high</td>
<td>low risk</td>
</tr>
<tr>
<td>gain</td>
<td>neutral</td>
<td>loss</td>
<td>gain</td>
<td>variable</td>
</tr>
<tr>
<td>hypoglycemia</td>
<td>edema, HF, Fx's</td>
<td>GLi</td>
<td>hypoglycemia</td>
<td>variable</td>
</tr>
<tr>
<td>low</td>
<td>high</td>
<td>rare</td>
<td>high</td>
<td>variable</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

If needed to reach individualized HbA1c target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference).

<table>
<thead>
<tr>
<th>Metformin +</th>
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<th>Metformin +</th>
<th>Metformin +</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sulfonylureab</strong> +</td>
<td><strong>DPP-4-i</strong></td>
<td><strong>GLP-1-RA</strong></td>
<td><strong>Insulin</strong></td>
</tr>
<tr>
<td>or DPP-4-i or GLP-1-RA or Insulin</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>or TZD or</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>or SU or</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td>or GLP-1-RA or insulin</td>
<td>or</td>
<td>or</td>
<td>or</td>
</tr>
</tbody>
</table>

If combination therapy that includes basal insulin has failed to achieve HbA1c target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with one or two non-insulin agents:

**Insulin** (multiple daily doses)
Themes From AGS Guidelines for Older Adults

1. Individualize care and education
2. Provide aggressive treatment to prevent and manage cardiovascular risk factors
3. Help prevent and manage microvascular complications through glycemic control
4. Screen for and treat geriatric syndromes that are more common in older adults with diabetes

Conditions Associated with DM in Older Adults

Associated Conditions:
- Premature death
- Functional disability
- Hypertension
- CAD
- CVA
- Depression
- Cognitive impairment
- Urinary incontinence
- Injurious falls
- Pain
- Polypharmacy

Other Adverse Outcomes:
- Blindness
- Renal failure
- Amputations
- Infections
- CHF
- GERD
- Hospitalization
- In-hospital complications
- Disability

Accessible at: www.americangeriatricsociety.com
Figure. Overview of the Chronic Care Model

Community
- Resources and policies
  - Self-management support

Health system
- Organization of health care
  - Delivery system design
  - Decision support
  - Clinical information systems

Informed, activated patient

Prepared, proactive practice team

Productive interactions

Functional and clinical outcomes

adapted from Norris and Olson. Geriatrics, 2004
Update on Cardio-Vascular Disease in T2DM, 2008

- ACCORD
- VADT
- ADVANCE
- STENO-2

- Nephropathy prevented
- Control Risk Factors
- Blood Pressure
- Lipids

- Limited benefit, possibly harm from strict glycemic control
- Reasons for lack of benefit unclear
Diabetes in Older Adults: Case 1

Active 68 year old man with cardiovascular risk
• Complained of exertional chest pain at work, referred by colleague to seek medical attention
• Lifelong overweight, gained 30 lbs. in past 3 years
• Remote cigarettes, light alcohol intake
• Hypertension controlled with thiazide
• Elevated cholesterol (not treated with medications)

Contributory Family and Social History
• Family history significant for mother with DM d. 85yo from MI, father d. 88yo with dementia, brother with DM and obesity
Diabetes in Older Adults: Case 1

Contributory Medications and Comorbidities
• No major comorbid illness

Targeted elements of physical exam
• MMSE 30/30
• BP 135/90, HR 70, weight 245 lbs., height 5’10”, waist 44”
• ECG = NSR, leftward axis

Labs
• Fasting blood glucose = 164 & 138 mg/dL
• HbA$_{1c}$ = 8.0%
• Cholesterol 210, LDL 140, HDL 39, TG 160 (mg/dL)
• BUN/Cr = 18/1.2, Urine Albumin = 8 mg/day
Diabetes in Older Adults: Case 1

Treatment Goals

Standard Type 2 DM and major AGS themes guidelines apply for this patient

- Aggressively Prevent and Manage Cardiovascular Risk Factors through lifestyle management and medication adherence
  - Smoking
  - Lipids
  - Blood Pressure
  - Exercise and Diet
  - Glycemic control:
    - Nutrition therapy
    - Lifestyle
    - Monitoring
    - HbA\textsubscript{1c}, fasting and post-prandial goals
    - Oral or injectable agents all have potential roles
Diabetes in Older Adults: Case 1
Therapeutic Approach

Pharmacological goals related to CV risk:

• Glycemic Control
• Blood Pressure
• Lipids
• Anti-platelet agents
Diabetes in Older Adults: Case 1 Summary

• Provide aggressive treatment to prevent and manage cardiovascular risk factors
• Help prevent and manage microvascular complications through glycemic control
• Follow same DM guidelines as younger adults (unless specific factors need consideration)
• Pursue additional conditions associated with DM in older adults
• Use multifactorial approach in majority of patients
• Individualize approach for every patient…
Healthy eating, weight control, increased physical activity

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Efficacy</th>
<th>Hypoglycemia</th>
<th>Weight</th>
<th>Side effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>high</td>
<td>low risk</td>
<td>neutral/loss</td>
<td>GI/lactic acidosis</td>
<td>low.</td>
</tr>
</tbody>
</table>

If needed to reach individualized HbA1c target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):

- **Metformin + Sulfonylurea**
  - high
  - moderate risk
  - gain
  - hypoglycemia
  - low

- **Metformin + Thiazolidinedione**
  - high
  - low risk
  - gain
  - edema, HF, Fx's
  - high

- **Metformin + DPP-4 Inhibitor**
  - intermediate
  - low risk
  - neutral
  - GI
  - rare

- **Metformin + GLP-1 receptor agonist**
  - high
  - low risk
  - loss
  - gain
  - hypoglycemia
  - variable

If needed to reach individualized HbA1c target after ~3 months, proceed to three-drug combination (order not meant to denote any specific preference):

- **Metformin + Sulfonylurea + TZD**
  - high
  - moderate risk
  - gain
  - hypoglycemia
  - low

- **Metformin + Thiazolidinedione + SU**
  - high
  - low risk
  - gain
  - edema, HF, Fx's
  - high

- **Metformin + DPP-4 Inhibitor + TZD**
  - intermediate
  - low risk
  - neutral
  - GI
  - rare

- **Metformin + GLP-1 receptor agonist + Insulin**
  - high
  - low risk
  - loss
  - gain
  - hypoglycemia
  - variable

If combination therapy that includes basal insulin has failed to achieve HbA1c target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with one or two non-insulin agents:

- **Insulin (multiple daily doses)**
Metformin

- Generally first choice medication
- Reduces hepatic glucose output
- Effective in many studies
- Mild weight loss
- Reduce GI ADE’s by starting low dose
- Low risk of hypoglycemia as monotherapy
- Prevents DM in younger patients in DPP
Effect of metformin as monotherapy or in combination with glyburide

Change in fasting plasma glucose (mg/dL)

Diet + placebo

Diet + metformin

Week

Glyburide

Metformin

Metformin + glyburide

Week

* $P < 0.001$
† $P < 0.001$ glyburide-metformin vs glyburide
‡ $P < 0.001$ metformin vs glyburide
§ $P < 0.01$ metformin vs glyburide

Metformin

• High rate of GI adverse effects
• Mild weight loss
• Lactic acidosis
  – Rare (1/40,000) and usually associated with another risk factor
• Contraindications:
  – Renal disease
  – Hepatic disease
  – Hypoxic or acidotic conditions
Metformin: Use in the elderly?

• Age is frequently listed as contraindication

• Really Shouldn’t be
  – Contraindications may be more common in older adults,
  – remain vigilant
Sulfonyl-Ureas

• Previous first choice medication
• Increase insulin secretion from beta-cells
glyburide, glipizide, glimeperide
• Long history
• Efficacy in multiple studies
Sulfonylureas and Hypoglycemia in Older Adults

Age was most common associated factor
- 80% over 60 yo
- Peak age 71-80

Other major factors:
- Renal function
- Energy intake
- Infection

Ben-Ami et al, Arch Int Med 1999
Sulfonyl-Ureas

- 2nd generation safer than 1st generation
- Highest risk of hypoglycemia
- Weight gain
- High risk of treatment “failure”
- Renal metabolism and excretion
- Glyburide may be more associated with cardiac arrhythmia risk
- Glipizide has shorter half-life
- Sulfa allergies
# Time Course of Action of Basal Insulin Preparations

<table>
<thead>
<tr>
<th>Insulin Preparation</th>
<th>Onset of Action (h)</th>
<th>Peak Action (h)</th>
<th>Effective Duration of Action (h)</th>
<th>Maximum Duration of Action (h)</th>
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</thead>
<tbody>
<tr>
<td>Long acting</td>
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<td></td>
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</tr>
<tr>
<td>Glargine (basal analog)</td>
<td>5</td>
<td>None</td>
<td>&gt;24</td>
<td>Unknown</td>
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<tr>
<td>Detemir (analog)</td>
<td>1</td>
<td>8-10</td>
<td>12-24</td>
<td>18-24</td>
</tr>
<tr>
<td>Intermediate acting</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>NPH (isophane)</td>
<td>2-4</td>
<td>6-10</td>
<td>10-16</td>
<td>14-18</td>
</tr>
</tbody>
</table>

Start with a daily dose
Advance dose until reaching safe fasting BG goal
Incretin Effect
Diminished in Type 2 Diabetes

Control Subjects (n=8)

Normal Incretin Effect

IR Insulin, mU/L

Time, min

Subjects With Type 2 Diabetes (n=14)

Diminished Incretin Effect

IR Insulin, mU/L

Time, min

ORAL glucose load

Intravenous (IV) glucose infusion

IR=immunoreactive.

GLP-1 Modulates Numerous Functions in Humans

GLP-1: Secreted upon the ingestion of food

Promotes satiety and reduces appetite

Alpha cells: ↓ Postprandial glucagon secretion

Liver: ↓ Glucagon reduces hepatic glucose output

Stomach: Helps regulate gastric emptying

Beta cells: Enhances glucose-dependent insulin secretion

Incretins broken down by DPP-IV

DPPIV Inhibitors

Sitagliptin, saxaglipitin (others in pipeline)

• Newest class on the market
• DPPIV normally proteolyzes GLP-1, GIP, glucagon to inactivate them
• Weight neutral
• Enhance insulin secretion
• No long-term safety or outcome data
• Probably safer in renal disease
• Probable additive effect with metformin
GLP-1 Analogs (exenatide, liraglutide)

- Incretin mimetic
- GLP-1 analog, not recognized by DPPIV
  - Increases duration and levels
- Multiple beneficial effects:
  - Weight loss
  - Decreased GI motility
  - Increased insulin secretion
  - Suppress glucagon
  - beta-cell preservation and growth
  - Suppress appetite
Exenatide, Liraglutide

- Modest improvement in glycemia
- Weight Loss
- Currently expensive
- Frequent GI ADE’s
- Injected
  - Exenatide (Byetta™) twice a day before meals
  - Liraglutide (Victoza™) daily
  - Exenatide weekly preparation (Bydureon™) just released
  - Others nearly available or in pipeline
- Benefits don’t correlate with physiological effects
- Case reports of pancreatitis
- No long term or outcome trials
Thiazolidinediones

Pioglitazone now 1st (only?) choice

- Activates PPARγ nuclear receptor
- Mostly acts directly on fat and liver cells
- Enhances insulin action everywhere
- 3-6 weeks for glycemic effects
- Best results in preventive trials
- Longest duration of oral monotherapy in early diabetes
- Purported "pleiotrophic" benefits
- Low risk of hypoglycemia as monotherapy
Thiazolidinediones

ADE’s:
- Edema
- Macular edema
- CHF
- Weight Gain
- Hepatotoxicity
- Decreased bone density
- Variable lipid effects
  - Mild ↑LDL, Idiosyncratic ↑TG

New concerns:
- Increased CAD risk with rosiglitazone
- Increased Bladder Cancer risk with pioglitazone
SU-Receptor Binding Agents

Repaglinide and Nateglinide
• Rapid acting, bind to alternate sites of SU receptor
• Taken before meals
• Somewhat glucose dependent
  – Decreases hypoglycemia
• Less renal clearance than SU
• Still some hypoglycemia
SU-like agents and Hypoglycemia in Older Adults

Patients over 64 yo in clinical trials for nateglinide

Del Prato, Diabetes Care, 2003
Glucosidase Inhibitors

Acarbose and miglitol
- Blocks breakdown of carbohydrates to prevent absorption at gut
- GI ADE’s
- Modest glycemic benefit
- Take before CHO-rich meals
- No risk of hypoglycemia as monotherapy
- Benefit in preventive trial
Diabetes in Older Adults: Case 2

Frail woman with microvascular complications
- 65 yo woman with type 2 DM for 12 years
- Routine follow up
- Obesity, family history of DM, signs of gestational diabetes
- Home BG measurements:
  - AM (ave. = 165 mg/dL), rare PM values (all>180)
- Multiple complaints
- Sedentary lifestyle, limited by complaints

Diabetic Complications
- Nephropathy, Neuropathy, Retinopathy, Hypertension, Hyperlipidemia

Contributory Family and Social History
- Remote cigarettes
- No EtOH
- Daughter shops and cleans. Prepares some meals on her own.
- Recently stopped driving
Diabetes in Older Adults: Case 2

Contributing Medications and Comorbidities

- Multiple medicines prescribed, not all up-to-date
- Inconsistent emptying of bottles (23 bottles of 16 medications)
  Aspirin, ACE-I, beta-blocker, diuretic, “statin”, SU, metformin, NSAID, opiate, OTC analgesic, OTC sleep aid, PPI, OTC antacid, 2 antidepressants

Targeted elements of physical exam

- MMSE 26/30
- BP 140/90, HR 80, Weight 180 lbs, height 5’4”, waist 40”
- Unsteady gait
- BDR without bleeding
- Enlarged liver span
- Trace edema, preserved pulses, osteoarthritic changes, fails monofilament, impaired distal vibratory sensation

Labs

- HbA$_1^c$ = 8.5%
- Cr = 1.3
- LDL = 100, HDL = 38
Diabetes in Older Adults: Case 2

Follow a Multidisciplinary Approach

• The group of providers*
  – Self-management
  – Caregivers
  – Geriatric primary care
  – Diabetes education
  – Certified Diabetes Educators
  – Physician Assistants and Nurse Practitioners
  – Nurses, Directors of Nursing
  – Pharm.D. and Pharmacists
  – Nutritionist
  – Podiatrist
  – Subspecialty consultants

*an example similar to our model at the VA, (Neither all-inclusive nor exclusive)
Diabetes in Older Adults: Case 2

Treatment Goals

CV risk and Glycemic control

• Who benefits according to AGS guidelines
  – CV risk reduction for all
  – Glycemic control for:
    • Symptoms
    • Avoid progression of established microvascular complications
    • Greater than 8 years of projected mortality
Diabetes in Older Adults: Case 2
Therapeutic Approach

• Choose safest set of medications
  – Combination Therapy frequently necessary
    “polypharmacy” vs. Combination therapy:
      • Hypertension
      • Glycemic control
      • Pain control
      • Psychoactive medications
  – Avoid contraindicated medications
    • Metformin
    • Sulfonylurea
    • Thiazolidinediones
    • NSAID’s
  – Reduce un-necessary medications
    • Evaluate symptomatic needs judiciously
    • Reduce psychoactive medications appropriately
Polypharmacy

• Definition:
  “Whenever a drug is not indicated”
  • R. David Lee, MD

• The Triangle (work as a team)
  – Prescriber
  – Patient
  – Others: Nurse, Physician Assistant, Pharmacist, Social workers, Caregiver….

Lee, J Am Board Fam Prac, 1998
Diabetes in Older Adults: Case 2
Summary

Established microvascular complications and has already developed associated conditions

• Focus on CV risk
• Prevent progression of established DM microvascular disease with glycemic control
• Identify associated conditions that occur in older people with DM
• Avoid the “tyranny of complaints” – utilize Chronic Care Model
Position Statement of the ADA & EASD. DIABETES CARE. 2012

Healthy eating, weight control, increased physical activity

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Metformin</th>
<th>Sulfonylurea&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Thiazolidinedione</th>
<th>DPP-4 Inhibitor</th>
<th>GLP-1 receptor agonist</th>
<th>Insulin (usually basal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy (↓HbA&lt;sub&gt;1c&lt;/sub&gt;)</td>
<td>high</td>
<td>moderate risk</td>
<td>high</td>
<td>intermediate</td>
<td>high</td>
<td>highest</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td>high</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>high</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td>gain</td>
<td>gain</td>
<td>neutral</td>
<td>loss</td>
<td>gain</td>
</tr>
<tr>
<td>Side effects</td>
<td></td>
<td>hypoglycemia</td>
<td>edema, HF, Fx's&lt;sup&gt;c&lt;/sup&gt;</td>
<td>rare&lt;sup&gt;c&lt;/sup&gt;</td>
<td>GL&lt;sup&gt;e&lt;/sup&gt;</td>
<td>hypoglycemia&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Costs</td>
<td></td>
<td>low</td>
<td>high</td>
<td></td>
<td>high</td>
<td>variable</td>
</tr>
</tbody>
</table>

If needed to reach individualized HbA<sub>1c</sub> target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference).

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<tr>
<th>Drug Combination</th>
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<th>Sulfonylurea&lt;sup&gt;b&lt;/sup&gt; or DPP-4-i or GLP-1-RA or Insulin&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Thiazolidinedione or SU&lt;sup&gt;b&lt;/sup&gt; or DPP-4-i or GLP-1-RA or Insulin&lt;sup&gt;d&lt;/sup&gt;</th>
<th>DPP-4 Inhibitor or TZD or Insulin&lt;sup&gt;d&lt;/sup&gt;</th>
<th>GLP-1 receptor agonist or SU&lt;sup&gt;b&lt;/sup&gt; or TZD or Insulin&lt;sup&gt;d&lt;/sup&gt;</th>
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</table>

If combination therapy that includes basal insulin has failed to achieve HbA<sub>1c</sub> target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with one or two non-insulin agents:

- Insulin<sup>e</sup> (multiple daily doses)
Diabetes in Older Adults: Case 3

Frail man with microvascular complications & associated conditions
- 68 yo man with type 2 DM for 12 years
- Losing weight
- Falls in the home
- Highly variable home BG measurements, poor hypoglycemic awareness

Diabetic Complications
- All microvascular complications
- CAD – s/p CABG with CHF and LVEF 30%,
- Gastroparesis
- Hyperglycemic symptoms
- Weekly hypoglycemia
- COPD from cigarettes on oxygen at night and with exertion

Contributory Family and Social History
- Multiple dependencies
Diabetes in Older Adults: Case 3

Contributory Medications and Comorbidities
- Complicated by hypoglycemia
- Multiple medications
- Multiple co-morbidities reflect limited remaining life-span

Targeted Elements of Physical Exam
- MMSE 26/30
- BP 125/65, HR 56 (no variation), Weight 178 lbs., Height 5’6”
- Unsteady gait, new mild left sided weakness
- Carotid bruit on right, systolic murmur at Aortic area
- Truncal adiposity, induration at injection sites
- Failed monofilament, 1+ distal edema, 0-1+ DTR’s, interossial wasting

Labs
- HbA$_{1c}$ = 8.5%
- Cr = 2 mg/dL, Urine Albumin = 400 mg/day
- LDL = 125, HDL = 38
Functional Status and DM Predict CV Disease and Mortality

DM in Older Adults: Case 3

Treatment Goals

• Continued benefit from focus on CV risk
• Restate glycemic goals
• HbA$_{1c}$ of secondary importance
• Reduce medications
• Reduce fall risk
• Enhance support structure and re-direct education
• Observe for associated conditions: depression, dementing illness, progression of underlying diseases, pain, etc.
DM in Older Adults: Case 3

Treatment Goals

• HbA$_1$c

• Blood Glucose Testing
  “HbA$_1$c goal of 8%”
  (per AGS guidelines)

• Avoid hypoglycemia and symptomatic hyperglycemia

n.b. VA A1c Guidelines also tend to be higher
Diabetes in Older Adults: Case 3

Therapeutic Approach

• Glycemic control
  – Use appropriate insulin if necessary
  – State safe goals

• CV Risk Reduction
  – Safe anti-platelet, BP, and cholesterol lowering therapy

• Control of Associated Conditions
  – Pain, cognitive decline, depression, sensory impairment, falls, urinary dysfunction
  – Informed consent and end-of-life decisions
DM in Older Adults: Case 3

Summary

Individualize care
  – Use HbA$_{1c}$ as a guide if necessary
  – Avoid hypoglycemia and symptomatic hyperglycemia

Areas that need further research:
• What levels of care are helpful for each associated condition?
• What is the impact of glycemic control on associated conditions?
# Time Course of Action of Insulin Preparations

<table>
<thead>
<tr>
<th>Insulin Preparation</th>
<th>Onset of Action (h)</th>
<th>Peak Action (h)</th>
<th>Effective Duration of Action (h)</th>
<th>Maximum Duration of Action (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lispro (analog)</td>
<td>0.25-0.50</td>
<td>0.5-1.5</td>
<td>3-4</td>
<td>4-6</td>
</tr>
<tr>
<td>Aspart (analog)</td>
<td>0.25-0.50</td>
<td>0.5-1.5</td>
<td>3-4</td>
<td>4-6</td>
</tr>
<tr>
<td>Glulisine (analog)</td>
<td>0.25-0.50</td>
<td>0.5-1.5</td>
<td>3-4</td>
<td>4-6</td>
</tr>
<tr>
<td><strong>Short acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular (soluble)</td>
<td>0.5-1</td>
<td>2-3</td>
<td>3-6</td>
<td>6-8</td>
</tr>
<tr>
<td><strong>Intermediate acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH (isophane)</td>
<td>2-4</td>
<td>6-10</td>
<td>10-16</td>
<td>14-18</td>
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</thead>
<tbody>
<tr>
<td>Long acting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargine (basal analog)</td>
<td>5</td>
<td>None</td>
<td>&gt;24</td>
<td>Unknown</td>
</tr>
<tr>
<td>Detemir (analog)</td>
<td>1</td>
<td>8-10</td>
<td>12-24</td>
<td>18-24</td>
</tr>
<tr>
<td>Combinations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70/30 (70% NPH, 30% regular)</td>
<td>0.5-1</td>
<td>Dual</td>
<td>10-16</td>
<td>14-18</td>
</tr>
<tr>
<td>50/50 (50% NPH, 50% regular)</td>
<td>0.5-1</td>
<td>Dual</td>
<td>10-16</td>
<td>14-18</td>
</tr>
<tr>
<td>Lispro mix 75/25, (75% NPL+25%lispro)</td>
<td>0.25-0.5</td>
<td>Dual</td>
<td>10-16</td>
<td>14-18</td>
</tr>
<tr>
<td>or Novolog 70/30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Themes From AGS Guidelines

1. Individualize care and education
2. Provide aggressive treatment to prevent and manage cardiovascular risk factors
3. Help prevent and manage microvascular complications through glycemic control
4. Screen for and treat geriatric syndromes that are more common in older adults with diabetes