Diabetes Is Primary 2020
Case Studies
Outline

• Glycemic control and medications in clinical trials
• Data from real-world practice
• Comparison of geriatric diabetes care guidelines
• Case study
Trends in the prevalence of diagnosed diabetes* among older adults with diabetes, U.S., 1997-2010

*Self-reported
Source: National Health Interview Survey

Diabetes in America, 3rd Edition
Projected Direct Medicare Spending on Diabetes and Its Complications for Different Cohorts, 2009-2034

# High Prevalence of Co-Occurring Chronic Diseases

<table>
<thead>
<tr>
<th>Index Condition (%)</th>
<th>Weighted Prevalence (%) of Other Conditions Among Respondents Having Index Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAD</td>
</tr>
<tr>
<td>CAD (8.7)</td>
<td>17%</td>
</tr>
<tr>
<td>CHF (4.8)</td>
<td>58%</td>
</tr>
<tr>
<td>T2DM (19.4)</td>
<td>24%</td>
</tr>
<tr>
<td>UI (25.0)</td>
<td>19%</td>
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<tr>
<td>Falls (23.2)</td>
<td>23%</td>
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</table>

Questions Driving Research

• How do we best treat the individual older patient with diabetes?
• How intensively should we control glucose?
• What medications should we use?
Glycemic Control and Medications in Trials
United Kingdom Prospective Diabetes Study

**Intervention Trial**
Median follow-up 10.0 years

- RR = 0.88 (0.79-0.99)
- P = 0.029

**Intervention Trial + Post-trial monitoring**
Median follow-up 16.8 years

- RR = 0.91 (0.83-0.99)
- P = 0.040

*Conventional Sulfonylurea/Insulin*

**References**
- NEJM 2008; 359:1577-1589
# Late 2000s Glycemic Control Trials

<table>
<thead>
<tr>
<th></th>
<th>ACCORD</th>
<th>ADVANCE</th>
<th>VADT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean</strong></td>
<td>62.2</td>
<td>66</td>
<td>60.4</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>10 yrs (median)</td>
<td>8 yrs (mean)</td>
<td>11.5 yrs (mean)</td>
</tr>
<tr>
<td><strong>A1C Achieved</strong></td>
<td>7.5% vs. 6.4%</td>
<td>7.3% vs. 6.5%</td>
<td>8.4% vs. 6.9%</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>1.22, CI (1.01-1.46)</td>
<td>0.93, CI (0.83-1.06)</td>
<td>1.07, CI (0.81, 1.42)</td>
</tr>
<tr>
<td><strong>Cardio-vascular</strong></td>
<td>Non-fatal and fatal cardiovascular disease 0.90 (0.78-1.04)</td>
<td>Macrovascular 0.94 (0.84-1.06)</td>
<td>Cardiovascular events 0.88 (0.74-1.05)</td>
</tr>
<tr>
<td></td>
<td>Non-fatal myocardial infarction 0.76 (0.62-0.92)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Micro-vascular</strong></td>
<td>0.86 (0.77-0.97)</td>
<td></td>
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</table>

Glycemic Control Trials and Patients over 80

• ACCORD
  – Initially enrolled patients over 80 but stopped after observing high rates of hypoglycemia

• Japan Elderly Diabetes Intervention Trial
  – Attempted to evaluate a multiple risk factor intervention in patients 65-85 (N=1173)
  – Unable to achieve separation in A1C
  – Attributed to fear of inducing hypoglycemia
Gaps in glucose control trial literature

- Trials not designed to compare multiple glucose targets (target 1 vs. target 2)
- Trials do not include full span of age, >75 years of age
- Trials do not include older patients with varying levels of comorbidity, functional status, frailty
- As a result, we do not have a stratified analysis by comorbidity, functional status, frailty
EMPA-REG OUTCOME (SGLT-2 Inhibitor)

**A** Primary Outcome
- Hazard ratio, 0.86 (95.02% CI, 0.74–0.99)
- P=0.04 for superiority

**B** Death from Cardiovascular Causes
- Hazard ratio, 0.62 (95% CI, 0.49–0.77)
- P<0.001

**C** Death from Any Cause
- Hazard ratio, 0.68 (95% CI, 0.57–0.82)
- P<0.001

**D** Hospitalization for Heart Failure
- Hazard ratio, 0.65 (95% CI, 0.50–0.85)
- P=0.002

*NEJM 2015; 373: 2117*
Figure 2: Pooled Kaplan-Meier curves and hazard ratios comparing new users of SGLT2 inhibitors and new users of other glucose-lowering drugs for cardiovascular mortality and major adverse cardiovascular events. Groups were matched 1:3 by propensity score. SGLT2=sodium-glucose co-transporter-2. HR=hazard ratio.
Gaps in CVOT Trial Literature

• Many older people with CVD will benefit from GLP-1 agonists and SLGT-2 inhibitors

• However:

• Mean ages 62-66… trials do not include full span of age, >75 years of age

• Trials do not include older patients with varying levels of comorbidity, functional status, frailty

• As a result, we do not have a stratified analysis by comorbidity, functional status, frailty
Older Adults with Diabetes in Real-World Clinical Practice
Classifying Older Adults with Diabetes by Comorbid Conditions (NSHAP)


Class 1: 9%  Class 2: 17%  Class 3: 33%
### Table 3. Sex- and Race-Adjusted Incidence of Diabetes Complications in Older Adults With Longer Duration\(^a\) of Type 2 Diabetes\(^b\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Age 60-69 y (95% CI)</th>
<th>Age 70-79 y (95% CI)</th>
<th>Age ≥80 y (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hyperglycemic event</td>
<td>1.85 (1.44-2.37)</td>
<td>1.76 (1.36-2.27)</td>
<td>2.35 (1.68-3.27)</td>
<td>.21</td>
</tr>
<tr>
<td>Acute hypoglycemic event</td>
<td>9.62 (8.70-10.64)</td>
<td>15.88 (14.56-17.32)</td>
<td>19.60 (17.48-21.98)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>7.92 (7.08-8.84)</td>
<td>7.64 (6.83-8.54)</td>
<td>5.75 (4.80-6.88)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Eye disease</td>
<td>20.26 (18.41-22.30)</td>
<td>14.97 (13.45-16.66)</td>
<td>14.89 (12.69-17.47)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>4.02 (3.47-4.67)</td>
<td>4.90 (4.25-5.64)</td>
<td>5.67 (4.67-6.88)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Lower limb amputation</td>
<td>3.94 (3.38-4.60)</td>
<td>4.26 (3.66-4.95)</td>
<td>3.92 (3.16-4.88)</td>
<td>.97</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>15.15 (13.89-16.51)</td>
<td>18.98 (17.50-20.59)</td>
<td>24.09 (21.55-26.92)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>13.83 (12.62-15.15)</td>
<td>23.86 (22.10-25.76)</td>
<td>33.10 (29.88-36.66)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Mortality</td>
<td>33.21 (31.55-34.95)</td>
<td>65.87 (63.28-68.56)</td>
<td>132.90 (127.09-138.98)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

\(^a\) Duration of diabetes was 10 years or more.

\(^b\) Information was obtained from Kaiser Permanente Northern California database, 2004-2010.
Figure Legend:
Rates of Estimated Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries With Diabetes Mellitus, 1999 to 2010. The circles and diamonds indicate observed values; the lines represent the smoothed trend over time.
A1C-Mortality Relationship in UK Diabetes Registry

Results of Simulated Trials (UKPDS) in Older, Sicker Patients

Diabetes Care Guidelines for Older Patients
### ADA Consensus Panel Framework

<table>
<thead>
<tr>
<th>HEALTH STATUS</th>
<th>RATIONALE</th>
<th>REASONABLE A1C GOAL</th>
<th>FASTING OR PREPRANDIAL GLUCOSE (mg/dl)</th>
<th>BEDTIME GLUCOSE (mg/dl)</th>
<th>BLOOD PRESSURE (mmhg)</th>
<th>LIPIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>Longer life expectancy</td>
<td>&lt;7.5%</td>
<td>90 – 130</td>
<td>90 – 150</td>
<td>&lt;140/80</td>
<td>Statin (unless contraindicated or not tolerated)</td>
</tr>
<tr>
<td>Complex/Intermediate Health</td>
<td>Intermediate life expectancy; high treatment burden; hypoglycemia vulnerability; fall risk</td>
<td>&lt;8.0%</td>
<td>90 – 150</td>
<td>100 – 180</td>
<td>&lt;140/80</td>
<td>Statin (unless contraindicated or not tolerated)</td>
</tr>
<tr>
<td>Very Complex Poor Health</td>
<td>Limited life expectancy; treatment benefit uncertain</td>
<td>&lt;8.5%</td>
<td>100 – 180</td>
<td>110 – 200</td>
<td>&lt;150/90</td>
<td>Consider benefit with statin; (secondary prevention &gt; primary)</td>
</tr>
</tbody>
</table>

**Healthy** - Few coexisting chronic illnesses, intact cognitive & functional status

**Complex/Intermediate Health** - Multiple coexisting chronic illnesses, or 2+ instrumental ADL impairments, or mild to moderate cognitive impairment

**Very Complex/Poor Health** - Long-term care or end-stage chronic illnesses or moderate to severe cognitive impairment or 2+ ADL dependencies

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### Comparison of Geriatric Guidelines

<table>
<thead>
<tr>
<th>European Diabetes Working Party for Older People</th>
<th>American Geriatrics Society</th>
<th>Department of Veterans Affairs</th>
<th>American Diabetes Association</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description of patient stratum</strong></td>
<td><strong>A1C goal</strong></td>
<td><strong>A1C goal</strong></td>
<td><strong>A1C goal</strong></td>
</tr>
<tr>
<td>Without major comorbidities</td>
<td>Healthy 7.0-7.5%</td>
<td>None or very mild microvascular complications; life expectancy of 10-15 years</td>
<td>&lt;7.0% Healthy (few co-existing chronic illnesses; intact cognitive and functional status)</td>
</tr>
<tr>
<td>Frail patients (dependent; multi-system disease; care home residency, including those with dementia)</td>
<td>Moderate comorbidities 7.6-8.5%</td>
<td>Long duration of diabetes (&gt;10 years); requires combination drug regimen including insulin</td>
<td>&lt;8.0% Complex/intermediate (examples: multiple co-existing chronic illnesses*, ≥2 instrumental ADL impairments, or mild-moderate cognitive impairment)</td>
</tr>
<tr>
<td>Multiple comorbidities</td>
<td>Advanced microvascular complications and/or major comorbid illness; life expectancy &lt;5 years</td>
<td>8.0-9.0% Very complex/poor health (examples: long term care, end stage chronic illnesses†, moderate-severe cognitive impairment, or ≥2 ADL dependencies)</td>
<td>&lt;8.5%‡</td>
</tr>
</tbody>
</table>
Concepts Behind Stratified Approach

• Life expectancy of patient versus. Lag time to benefit
  – Competing mortality risk
• Relative benefit vs. Risk of therapy
• Comorbidity-therapy interaction
• Ability to adhere to therapy (function)
Clinical Pearls from Standards of Care

• Individualized approach requires regular assessment of medical, psychological, functional, and social domains

• Screen for geriatric syndromes (polypharmacy, cognitive impairment, depression, incontinence, falls, persistent pain)
  – Cognition: Mini-Cog, MOCA

• Screen for hypoglycemia and hypoglycemia awareness

• Drug selection in older adults is all about avoiding risk of adverse effects

• Deintensification of complex regimens is recommended to reduce hypoglycemia and polypharmacy if can be achieved with glycemic goal
Case Study
History

- 77 year old Caucasian male here for initial diabetes education
- Diabetes Hx: Diagnosed 4 years ago
- Complications and Comorbidities:
  - Hypertension (1988)
  - Dyslipidemia (2001)
  - Diabetes Type 2 (2005)
  - Dementia (2008)
  - Hx of TIA (March 2009)
  - Osteoarthritis (1999)
- Allergies: NKDA
- Social History:
  - Mr. Gates lives with his wife of 50 years in an independent apartment in Seattle. He has two adult children who do not live in this area. His wife is the primary care provider. Retired mechanical engineer.
- Non-smoker; drinks ETOH 2 drinks daily (Whiskey).
Current medications:

- Clopidogrel 75mg daily
- Ramipril 5mg daily
- Losartan 100mg daily
- Chlorthalidone 12.5mg daily
- Metoprolol 50mg BID
- Donepazil 10mg daily
- Memantine 10mg BID
- Fluoxetine 20mg daily
- Rosuvastatin 20mg daily
- Ezetimibe 10mg daily
- Pioglitazone 45 mg daily
- Insulin glargine 54 units SC QPM
- Insulin aspart 14 units SC QAM and 26 units QPM (AC)
- Exenatide 10 mcg sub-Q BID
- Acetaminophen 1,000 mg QID prn arthritis pain
Physical Exam

- BP = 109/56 mm/Hg  Pulse = 52 bpm, regular;
- Weight = 171 lbs (77 kg); Height = 5’ 9”; BMI = 25.2;
- MMSE 24/30

Laboratory Values

- Na = 139, K = 5.1, Cl = 100, CO3 = 22, BUN = 13, SCr = 1.1, eGFR 61 ml/min; AST = 22, ALT = 44,
- Gluc = 62, A1C = 6.3
- TChol = 144, LDL = 88, HDL = 44, TG = 82

- Blood glucose logbook (past 30 days):
  - Mean plasma glucose (N=30 in 30 days) 154 mg/dL
  - Fasting mean (N=20): 109 mg/dL
  - Pre-dinner mean (N=7): 201 mg/dL
  - Bedtime mean (N=3): 127 mg/dL
Functional Assessment

• Mr. Gates has difficulty drawing up his own insulin due to osteoarthritis in his hands and fingers.
• He occasionally is confused about his insulin dose.
• His wife is currently preparing and administering his doses.
• Occasionally, he will give his own insulin if she is not home, only if she has prepared the dose.
• With greater progression of his dementia, his wife has taken on the responsibility of organizing his medications, preparing meals, household chores, and finance management.
• He and his wife started walking 0.25 miles M-F at the mall about 2 months ago. He has noticed significant improvement in his energy since initiating exercise.
Functional Assessment Continued

- His meals are very consistent:
  - Breakfast: 2 eggs, toast, and bacon;
  - Lunch: Sandwich, fruit, and milk;
  - Dinner: Meat, potatoes/rice, and salad;
  - Does not snack but does like dessert – Vanilla ice cream with molasses each evening.

- He experiences hypoglycemia 1-2 times weekly requiring rescue with snacks – his wife usually notices a shift in his focus and mood but no other symptoms
Concerns

• Accompanied by his wife who manages the patient’s medications;
• No new symptoms or behavioral problems reported;
• His wife feels that managing his DM is difficult and is concerned that his blood glucoses often seem too low when she tests him, often below 90 mg/dL.
For more information visit:

Professional.Diabetes.Org