Course 3: Our Obesogenic Culture: A Continuum of Obesity, Prediabetes, and Diabetes

Session 8: Diabetes Control: Barriers and Solutions

Learning Objectives

- Describe at least 3 obstacles to effective diabetes control in medical practice and at least one clinical mechanism to address each obstacle.
- Identify 3 clinical solutions to overcoming barriers to diabetes control that will result in more effective diabetes management.

Faculty
Leonard Fromer, MD, FAAFP, ABFM
Assistant Clinical Professor
David Geffen School of Medicine at the University of California at Los Angeles

Dr Fromer received his medical degree magna cum laude from the State University of New York Downstate Medical Center in Brooklyn. He completed his residency in family medicine at the University of California, Irvine, Long Beach Memorial Medical Center. He is a fellow of the American Academy of Family Physicians and a diplomate of both the American Board of Family Practice and the National Board of Medical Examiners. He has been in private practice in Santa Monica, California, with Prairie Medical Group for 28 years. Dr Fromer has served on the group’s board of directors and has been its managing director as well as its chief financial officer.

Dr Fromer’s practice includes a second field of concentration in allergy and asthma. He sits on the California Department of Health Services IMAP Advisory Panel for Allergy and Asthma, and he is on the faculty of the Department of Family Medicine at the University of California, Los Angeles.

Dr Fromer currently serves on the international editorial board of the International Primary Care Respiratory Journal. He is a past president of the California Academy of Family Physicians and has served more than 10 years as a member and chairman of the American Academy of Family Physicians Commission on Health Care Services. He has also served on the Physicians Capital Source Project Steering Committee for the American Medical Association, the advisory board for the American Medical Informatics Association, and the advisory board for the World Foundation for Studies of Female Health. Dr Fromer has lectured extensively on the topics of allergy, asthma, and health system reform and has been featured on CBS News and ABC News and in the Wall Street Journal.

Dr Fromer is a member of the board of TransforMED, LLC, and acts as a consultant to TransforMED in the area of clinical integration center of excellence quality improvement in the chronic diseases, coupled with successful practice transformation to the patient-centered personal medical home model of care. He is also executive medical director of the Group Practice Forum, where he leads a team engaged in national projects with group practices that deliver education, tools, and services to achieve success in their clinical integration efforts.

Faculty Financial Disclosure Statement
The presenting faculty reports the following:
Dr Fromer has no relationships to disclose.
### AAFP Evidence-Based Recommendations

<table>
<thead>
<tr>
<th>Practice Recommendation</th>
<th>As first-line therapy, encourage weight loss of 5%-7% in patients with impaired glucose tolerance or impaired fasting glucose to delay the onset of diabetes. If therapy goals are not achieved in a reasonable time frame through lifestyle interventions alone, add drug therapy with metformin.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Kaiser Permanente Care Management Institute; National Guideline Clearinghouse</td>
</tr>
<tr>
<td>Strength of Evidence</td>
<td>“A” (strong): The intervention is strongly recommended for eligible patients.</td>
</tr>
<tr>
<td>Date</td>
<td>December 2005</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Practice Recommendation</th>
<th>Individualize A1c target goal for each patient; aiming to achieve the lowest possible level may be modified based upon presence or absence of microvascular and/or macrovascular complications and life expectancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Joslin Diabetes Center; National Guideline Clearinghouse</td>
</tr>
<tr>
<td>Strength of Evidence</td>
<td>“1A” (strong recommendation with high quality of evidence)</td>
</tr>
<tr>
<td>Date</td>
<td>October 2006</td>
</tr>
</tbody>
</table>
## Diagnostic Criteria: Prediabetes and Diabetes

### Prediabetes
- Impaired fasting glucose 100-125 mg/dl
- (IFG) (Fasting plasma glucose) and/or
- Impaired glucose tolerance 140-199 mg/dl
- (IGT) (2-hr post 75g glucose challenge)

### Diabetes
- Random plasma glucose > 200 mg/dl with symptoms (polyuria, polydipsia, and unexplained weight loss) and/or
- Fasting plasma glucose > 126 mg/dl* and/or
- 2-hr plasma glucose > 200 mg/dl* post 75g glucose challenge

*Repeat to confirm on subsequent day unless symptoms are present

## Treatment Goals for the ABCs of Diabetes

<table>
<thead>
<tr>
<th>A1C</th>
<th>Blood pressure (mmHg)</th>
<th>Cholesterol Profile (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 7% for patients in general**</td>
<td>&lt; 130 / &lt; 80</td>
<td>LDL-C &lt; 100</td>
</tr>
<tr>
<td>Preprandial plasma glucose 70-130 mg/dl</td>
<td></td>
<td>HDL-C</td>
</tr>
<tr>
<td>Peak postprandial plasma glucose &lt; 180 mg/dl</td>
<td></td>
<td>Men &gt; 40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Women &gt; 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Triglycerides &lt; 150</td>
</tr>
</tbody>
</table>

**Individualize target levels:**
- A1C target as close to normal (< 6%) as possible without significant hypoglycemia in selected individuals, especially those with little comorbidity and long life expectancy.
- Less stringent A1C target for children and for people with severe or frequent hypoglycemia, limited life expectancy, comorbid conditions such as cardiovascular disease, or those with longstanding diabetes and minimal or stable microvascular disease.

**At each regular diabetes visit:**
- Measure weight and blood pressure.
- Inspect feet if 1 or more high-risk foot conditions are present.
- Review self-monitoring glucose record.
- Review/adjust medications to control glucose, lipids, and blood pressure. Include regular use of low-dose aspirin for CVD prevention as appropriate.
- Review self-management skills, dietary needs, and physical activity.
- Assess for depression or other mood disorder.
- Counsel on smoking cessation and alcohol use.

**Quarterly:**
- Obtain A1C in patients whose therapy has changed or who are not meeting glycemic goals (twice a year if at goal with stable glyceremia).

**Annually:**
- Obtain fasting lipid profile (every 2 years if patient has low-risk lipid values).
- Obtain serum creatinine to estimate glomerular filtration rate and stage the level of CKD.
- Perform urine test for albumin-to-creatinine ratio in patients with type 1 diabetes > 5 years and in all patients with type 2 diabetes.
- Refer for dilated eye exam (if normal, an eye care specialist may advise an exam every 2–3 yrs).
- Perform comprehensive foot exam.
- Refer for dental/oral exam at least once a year.
- Administer influenza vaccination.
- Review need for other preventive care or treatment.

**Lifetime:**
- Administer pneumococcal vaccination (repeat if < 64 yo or immunocompromised and last vaccination was < 5 yrs ago).

American Diabetes Association Standards of Medical Care. *Diabetes Care.* 2008;31(suppl 1):S12-S54. See source materials for treatment recommendations. The US Department of Health and Human Services’ National Diabetes Education Program (NDEP) is jointly sponsored by the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) with the support of more than 200 partner organizations. Updated March 2008 NDEP-12.
ADA T2DM Algorithm: 2009

Tier 1: Well-validated core therapies

**At diagnosis:**
- Lifestyle + Metformin

**Step 1**
- Lifestyle + Metformin + Basal insulin

**Step 2**
- Lifestyle + Metformin + Sulfonylurea
- Lifestyle + Metformin + Pioglitazone + GLP-1 agonist

**Step 3**
- Lifestyle + Metformin + Intensive insulin
- Lifestyle + Metformin + Pioglitazone + Sulfonylurea
- Lifestyle + Metformin + Basal insulin

Tier 2: Less well validated therapies

Algorithm for the metabolic management of type 2 diabetes. Reinforce lifestyle interventions at every visit and check A1C every 3 months until A1C is <7% and then at least every 6 months. The interventions should be changed if A1C is \( \geq 7\% \). * Sulfonylureas other than glybenclamide (glyburide) or chlorpropamide. ** Insufficient clinical use to be confident regarding safety.


A1C and Estimated Average Glucose (eAG)*

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>eAG (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>126</td>
</tr>
<tr>
<td>6.5</td>
<td>140</td>
</tr>
<tr>
<td>7</td>
<td>154</td>
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<tr>
<td>7.5</td>
<td>169</td>
</tr>
<tr>
<td>8</td>
<td>183</td>
</tr>
<tr>
<td>8.5</td>
<td>197</td>
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<tr>
<td>9</td>
<td>212</td>
</tr>
<tr>
<td>9.5</td>
<td>226</td>
</tr>
<tr>
<td>10</td>
<td>240</td>
</tr>
</tbody>
</table>

*David Nathan et al found that there is a linear relationship between A1C and average blood glucose levels. ADA now recommends using eAG in practice. A calculator is available at:

http://professional.diabetes.org/GlucoseCalculator.aspx

For Better Practice: Diabetes Care Flow Sheet

Patient name: __________________________
ID/Insurance #: __________________________

1. Record today’s date in the “Dates of Service,” “Dates of Results;” etc., row.
2. Note compliance or record values in appropriate boxes.

### History

<table>
<thead>
<tr>
<th>Dates of Service</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes history and self-management history taken or updated</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(See Diabetes History and Self-Management Checklist in this chapter of the toolkit)

### Physical Examination

<table>
<thead>
<tr>
<th>Dates of Service</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure—every visit</td>
<td></td>
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<tr>
<td>Weight—every visit</td>
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<tr>
<td>Body mass index—every visit</td>
<td></td>
<td></td>
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<tr>
<td>Foot examination Inspect every visit; full exam annually</td>
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<tr>
<td></td>
<td>Sensory (monofilament)</td>
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<tr>
<td></td>
<td>Pulses</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vibratory sensation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dilated eye exam—annually</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(See Standing Orders in this chapter of the toolkit)

### Laboratory Values

<table>
<thead>
<tr>
<th>Dates of Results</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin A1C—3 times/year</td>
<td></td>
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</tr>
<tr>
<td>Urine microalbumin—annually</td>
<td></td>
<td></td>
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<tr>
<td>Cholesterol—annually</td>
<td></td>
<td></td>
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<tr>
<td>Triglycerides—annually</td>
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<td></td>
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<tr>
<td>HDL cholesterol—annually</td>
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</tr>
<tr>
<td>LDL cholesterol—annually</td>
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</tr>
</tbody>
</table>

(See Standing Orders in this chapter of the toolkit)

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For Better Health: Your Diabetes Test Record

Name: __________________

Use this form to record your test results at each diabetes visit so you can keep track of how you are doing. The doctor, nurse, or diabetes educator will help you get started. Your doctor may add other tests to this list, such as creatinine or microalbuminuria (measures of kidney function). When you see that a test is due, mention it to the doctor or nurse to make sure that it is scheduled.

Year ________

<table>
<thead>
<tr>
<th>Tests</th>
<th>My Goal</th>
<th>Date of Tests</th>
<th>My Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td></td>
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<td></td>
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<tr>
<td>Blood pressure</td>
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<tr>
<td>A1C</td>
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<td>LDL</td>
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<td>HDL</td>
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<td>Triglycerides</td>
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<tr>
<td>Eye exam</td>
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<tr>
<td>Foot exam</td>
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</tbody>
</table>

Year ________

<table>
<thead>
<tr>
<th>Tests</th>
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<th>My Notes</th>
</tr>
</thead>
<tbody>
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<td>Weight</td>
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<td>Eye exam</td>
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<tr>
<td>Foot exam</td>
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</tbody>
</table>

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ACP Diabetes Care Guide • http://diabetes.acponline.org
For Better Practice: Sensory Foot Exam Findings

Put a plus sign where your patient can feel the 10-g nylon filament and a min where your patient cannot feel the filament.

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

Date ________
Bottom of right foot  Bottom of left foot

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# Sample Blood Sugar Log

<table>
<thead>
<tr>
<th>Date</th>
<th>Day</th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Dinner</th>
<th>Bedtime</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
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</tbody>
</table>

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## Resources

**Patient Education**
- [WWW.MEDLINEPLUS.GOV](http://WWW.MEDLINEPLUS.GOV)
- [WWW.MYPYRAMIDTRACKER.GOV](http://WWW.MYPYRAMIDTRACKER.GOV)

**Diabetes Education**
- [WWW.NDEP.NIH.GOV](http://WWW.NDEP.NIH.GOV)
- [WWW.CDC.GOV](http://WWW.CDC.GOV)

**Practice Improvement Resources**
- [WWW.ACPQUEST.ORG](http://WWW.ACPQUEST.ORG)
  - Diabetes Initiative – American College of Physicians
- [WWW.NCQA.ORG](http://WWW.NCQA.ORG)
  - Diabetes Physicians Recognition Program
  - Sponsored by ADA and NCQA meets certain ABIM and ABFM requirements
- [www.ama-assn.org](http://www.ama-assn.org)
  - Physician consortium for performance improvement
- [WWW.AAFP.ORG](http://WWW.AAFP.ORG)
Diabetes Control: Barriers and Solutions
Leonard Fromer, MD, FAAFP, ABFM

Part 2: Diabetes—Agenda
- The Importance of Glycemic Control
- Challenges to Achieving Glycemic Control
- Implementing Antihyperglycemic Therapy in T2DM

Learning Objectives
At the conclusion of this session, learners should be better able to:
1) Describe at least 3 obstacles to effective diabetes control in medical practice and at least 1 clinical mechanism to address each obstacle
2) Identify 3 clinical solutions to overcoming barriers to diabetes control that will result in more effective diabetes management

Diabetes Statistics
- 10.7% of Americans aged 20 and older (23.5 million people)¹
- 90%-95% have T2DM¹
- The average patient has T2DM for 9 to 12 years before diagnosis²
- ~1/4 of all T2DM patients are undiagnosed¹
- Patients with diabetes lose approximately 4 to 19 years of life, not to mention lost quality of life (QOL)³


Diabetes Prevalence by Race/Ethnicity (age-adjusted)

The Mounting Toll of Diabetes in the United States

*Every 24 Hours . . .
- New Cases: 4384
- Deaths¹: 640
- Amputations: 194
- Kidney Failure¹: 128
- Blindness: 33-66

¹ Figures are averages based on yearly incidence data.
² Deaths in which diabetes was a contributing factor.
³ People with diabetes who began treatment for end-stage kidney disease in the United States and Puerto Rico.
ACE/AACE Outpatient Diabetes Mellitus Consensus Position Statement

- The longer people live with uncontrolled diabetes, the greater their risk for developing vascular complications, including:
  - Retinopathy
  - End-stage renal disease
  - Neuropathy
  - Coronary heart disease
- In 2007, diabetes cost the United States an estimated $174 billion.
- Majority of costs are related to treatment and consequences of diabetic complications.


The Importance of Glycemic Control

Blood Glucose Levels

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>FPG (mg/dL)</th>
<th>OGTT (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Diabetes</td>
<td>&lt;100</td>
<td>&lt;140</td>
</tr>
<tr>
<td>Pre-diabetes</td>
<td>100-125</td>
<td>140-199</td>
</tr>
<tr>
<td>Diabetes</td>
<td>≥126</td>
<td>≥200</td>
</tr>
</tbody>
</table>


ARS Question

Which of the following is the most important measure of glycemic control?

1. FPG
2. OGTT
3. Glycosylated hemoglobin (A1c) or estimated average glucose (eAG)
4. Absence of end-organ damage

A1c: Gold Standard for Assessing Glycemic Control

- A1c represents the sum of both fasting and PPG excursions (normal < 6.1%)

Interpretation:
- The lower the A1c, the greater the contribution of the FPG.
- The higher the A1c, the greater the contribution of the PPG.

A1c and eAG

- There is a linear relationship between A1c and average blood glucose levels.
- ADA now recommends using “eAG” in practice.
- A1c can now be shown using the same units (mg/dL or mmol/L) as blood glucose measurements.

A1c Predicts Complications of Diabetes

Lowering A1c Reduces Complications

<table>
<thead>
<tr>
<th></th>
<th>DCCT1</th>
<th>Kumamoto2</th>
<th>UKPDS3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c (%)</td>
<td>9.1 → 7.3</td>
<td>9.4 → 7.1</td>
<td>7.9 → 7.3</td>
</tr>
<tr>
<td>(eAG, mg/dL)</td>
<td>(214 →163)</td>
<td>(221 →159)</td>
<td>(180 →154)</td>
</tr>
</tbody>
</table>

Rhabdopathy ↓ 63% to 65% ↓ 21%
Nephropathy ↓ 54% ↓ 57% ↓ 24%
Neuropathy ↓ 90% Sig improved ↓ 16%
Macrovascular disease ↓ 41% ↓ – ↓ 16%

* Not statistically significant.


The Evidence FAVORING Intensive Glycemic Control

Reemphasized importance of comprehensive treatment of glycemia, BP, and dyslipidemia in T2DM

DCCT, Kumamoto, and ADVANCE, and STENO-2, and UKPDS

Studies Raising Concerns About Intensive Glycemic Control

ACCORD, ADVANCE, and VADT

<table>
<thead>
<tr>
<th>CVD Events</th>
<th>Hypoglycemia</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attempts to achieve near-normal A1c did not decrease CV risk versus usual care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower rates of primary CVD outcomes with intensive therapy not statistically significant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased risk of severe hypoglycemia with intensive glucose control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predictor of CVD events in VADT but not in ACCORD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


The Case for Intensive Treatment

• Intensive treatment of diabetes can decrease chronic complications
• There appears to be no glycemic threshold for reduction of complications1,2

The lower the A1c, the lower the rate of complications3

Recent contrasting evidence suggests that this may not be true for ALL patients.3


The A1c Connection to Risk

1% absolute increase1 in A1c above homeostatic level predicts → 20% relative increase in incidence of CVD events1

1% A1c reduction results in → 30% reduction in microvascular complications2

Therefore:
- The higher the A1c (eAG), the greater the benefit of lowering A1c (eAG)
- Decreasing A1c from 10 to 9 (eAG from 240 to 212) results in greater decrease in complications than does reducing A1c from 7 to 6 (eAG from 154 to 126)


The Evidence Favoring Intensive Glycemic Control

Reemphasized importance of comprehensive treatment of glycemia, BP, and dyslipidemia in T2DM

DCCT, Kumamoto, and ADVANCE, and STENO-2, and UKPDS

The Case for Intensive Treatment

• Reaching the ADA clinical guideline target of A1c <7% (eAG <154) with goal of normalization (A1c 4%-6%; eAG 68 to 126) will improve quality and quantity of life for the vast majority of patients1
• Though life is finite, the goal to compress illness into the last few years of life should be discussed to avoid nihilism as an excuse for not embracing these goals

1. According to the February 2005 “Implementation Conference for ACE Outpatient Diabetes Mellitus Consensus Conference Recommendations: Position Statement,” the current target for glycemic control is A1c <6.5%.2
Interpreting ACCORD,1,2 ADVANCE,1,3 and VADT4

Glycemic Targets

- Absence of CVD RFs

<table>
<thead>
<tr>
<th>Target A1c</th>
<th>Absence of CVD RFs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target A1c level of ~7% may be appropriate in high-risk patients with multiple RFs and/or CVD</td>
<td></td>
</tr>
<tr>
<td>Did not address strategies for treating A1c in low-risk patients with CVD or additional CVD RFs</td>
<td></td>
</tr>
<tr>
<td>In ACCORD, intensive-treated patients who did not have a CVD event history or whose baseline A1c was &lt;8% had significantly fewer fatal and nonfatal CVD events than those patients at higher risk</td>
<td></td>
</tr>
</tbody>
</table>

Recent ADA, ACC Foundation, and AHA Consensus Statement

"The evidence obtained from ACCORD, ADVANCE, and VADT does not suggest the need for major changes in glycemic control targets but, rather, additional clarification of the language that has consistently stressed individualization... Therefore, the A1c goal for nonpregnant adults in general is 7%."5

Recent ADA, ACC Foundation, and AHA Consensus Statement

Who Is Treating Diabetes Patients?

- Approximately 95% of patients with T2DM receive their care from PCPs1
- Only 8% of all office visits for diabetes were made to a diabetes/endocrinology specialist in 1990-1991

Challenges to Achieving Glycemic Control

Diabetes Control: Elusive for Decades

64.2% of patients with T2DM have A1c ≥7.0%
37.2% have A1c >8.0%
25.2% have A1c >9.0%
12.4% have A1c >10.0%
ADA recommended target (<7.0%)
AACE recommended target (≤6.5%)
Upper limit of normal range (<6.0%)

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ADA Treatment Recommendations for T2DM

- Monitor A1c/eAG every 3 months\(^1,2\)
- Intensify treatment until A1c < 7.0% (eAG < 154)\(^1,2\)
- Use multiple agents\(^2\)
- Although 3 oral agents can be used, insulin therapy is preferred\(^1,2\)


Why Aren’t Practitioners Intensifying Treatment?

- Disappointing levels not isolated to a specific region, socioeconomic group, or practice type
- Why does diabetic control remain so elusive when we have more tools than ever?
  - 19 classes of drugs and more than 30 choices of medicines

Factors Influencing Achievement of Glycemic Goals

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Physician Factors</th>
<th>Process Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence</td>
<td>Knowledge</td>
<td>17-minute visit</td>
</tr>
<tr>
<td>Access</td>
<td>Presumptuous behavior</td>
<td>Clinical demands</td>
</tr>
<tr>
<td>Socioeconomic issues</td>
<td>Clinical inertia</td>
<td>1600 guidelines</td>
</tr>
<tr>
<td>Health literacy</td>
<td></td>
<td>Clinical demands</td>
</tr>
<tr>
<td>Natural history of diabetes</td>
<td></td>
<td>Fragmented system</td>
</tr>
</tbody>
</table>

Patient Adherence

- 44% of clinicians surveyed cited medication adherence as one of their biggest barriers when managing diabetes.

ARS Question

Medication adherence __________.

1. is primarily a concern in the elderly
2. is related more directly to the number of medicines than to the doses
3. approaches 50% with 4-times-daily dosing
4. and medication reconciliation are closely associated
Medication Adherence: The Cost Factor

Percent of the Public Who Say They or a Family Member Have Done Each of the Following in the Past Year Because of the Cost
(poll conducted between October 8, 2008 and October 13, 2008)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Put off or postponed getting healthcare you needed</td>
<td>30%</td>
</tr>
<tr>
<td>Skipped a recommended medical test or treatment</td>
<td>31%</td>
</tr>
<tr>
<td>Didn’t fill a prescription</td>
<td>27%</td>
</tr>
<tr>
<td>Cut pills or skipped doses of medicine</td>
<td>22%</td>
</tr>
<tr>
<td>Had problems getting mental healthcare</td>
<td>12%</td>
</tr>
<tr>
<td>Did any of the above</td>
<td>47%</td>
</tr>
</tbody>
</table>

Dealing With Medication Adherence

An approach such as . . .

“I know it must be difficult to take all your medications regularly. How often do you miss taking them?”

. . . will help to more accurately assess adherence.

Also, provide a medication list for the patient.

Minimizing Dose Frequency Increases Adherence

Minimizing the total number of daily doses is more important in promoting adherence than minimizing the total number of medications.²

Health Literacy:

“The capacity of individuals to access, understand, and use health information to make informed and appropriate health-related decisions.”


Challenges in Diabetes Health Literacy:

<table>
<thead>
<tr>
<th>Functional</th>
<th>Communicative</th>
<th>Critical</th>
</tr>
</thead>
<tbody>
<tr>
<td>extent to which patients read instructions or leaflets from hospitals and pharmacies without experiencing difficulties</td>
<td>extent to which patients extract and communicate diabetes-related information</td>
<td>extent to which patients critically analyze information and use it to make decisions</td>
</tr>
</tbody>
</table>

Good complication awareness and high health literacy result in good diabetic control, BUT . . .

- Print DM education materials meet few criteria for usability by patients with low literacy, limited prior medical knowledge, and/or limited resource availability

Health Literacy Varies by Age:

Least Among Older Adults and Hispanic People

Health Literacy Varies by Ethnicity:

Least Among Older Adults and Hispanic People

Diabetes Self-Management Education (DSME):

- Recommended, according to national standards
- Should be provided by qualified, trained HCPs
- Should address psychosocial issues
- Is covered by Medicare and most other payors
- Focuses on a skill-based approach
- Associated with
  - Improved diabetes knowledge
  - Improved self-care behavior
  - Improved clinical outcomes
  - Lower self-reported weight
  - Improved quality of life

Clinical Inertia

A “wait-until-next-visit” approach
What Is Clinical Inertia?

Practitioners recognize poor control . . .
AND
Agree medication should be intensified . . .
YET
TAKE NO ACTION

WHY?
• Overestimation of care provided
• Use of “soft” reasons to avoid intensification of therapy
• Lack of education, training, and practice organization


Recommendations for Avoiding Clinical Inertia

• Emphasize benefits of treating to therapeutic targets and dangers of clinical inertia
• Institute quality improvement efforts that focus on provider use of flow sheets and reminders
• Systematic self-measurement of practice performance (maintenance of certification/ACP initiatives)
• Regular interaction with peers or opinion leaders to obtain feedback on performance


Process Solutions

• DSME
  – Initial diagnosis (10 h) + annually 2 h/y
• Team-based approach
• Physician and patient reminders
• Practice redesign
• Web-based education
  – MedlinePlus
  – MyPyramid.gov
  – See list in handout

“A little knowledge that acts is worth infinitely more than much knowledge that is idle.”
Kahlil Gibran

Implementing Antihyperglycemic Therapy in T2DM

Case Study: Sharon

Medical History
55-year-old woman with HTN, menopausal symptoms, depression, and hypothyroidism presents c/o fatigue; 3 siblings with diabetes, 1 on dialysis

Physical Exam
Weight: 180 lb
BMI: 31 kg/m²
BP: 135/85 mm Hg
EKG: normal
Otherwise normal

Laboratory values
FPG: 140, PPG: 210 mg/dL
LDL-C: 120 mg/dL
HDL-C: 35 mg/dL
TC: 181 mg/dL
TGs: 130 mg/dL
Creatinine: 1.0 mg/dL
LFT: all normal
Urine: pos for protein

Medications
Ramipril 5 mg
Simvastatin 10 mg
Fluoxetine 10 mg
Levothyroxine 0.05 mg
Goals of Therapy

**ADA/EASD T2DM Algorithm: 2006**

<table>
<thead>
<tr>
<th>A1c (%)</th>
<th>FPG (mg/dL)</th>
<th>PPG (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7.0</td>
<td>&lt;=154</td>
<td>&lt;110</td>
</tr>
<tr>
<td>7.0-8.0</td>
<td>110-130</td>
<td>110-140</td>
</tr>
<tr>
<td>8.0-9.0</td>
<td>140-180</td>
<td>140-160</td>
</tr>
<tr>
<td>&gt;9.0</td>
<td>&gt;180</td>
<td>&gt;180</td>
</tr>
</tbody>
</table>

**ADA/EASD T2DM Algorithm: 2009**

**Tier 1: Well-validated core therapies**

- Lifestyle + MET + Basal insulin
- Lifestyle + MET + Intensive insulin
- Lifestyle + MET + Basal insulin + GLP-1 agonist
- Lifestyle + MET + Basal insulin + Pioglitazone
- Lifestyle + MET + Basal insulin + SGLT-2 inhibitor

**Tier 2: Less well-validated therapies**

- Lifestyle + MET + Basal insulin + GLP-1 agonist + Pioglitazone + SGLT-2 inhibitor

**Relative Contributions of FPG and PPG to Overall Hyperglycemia Depending on A1c Quintiles**

<table>
<thead>
<tr>
<th>A1c (%)</th>
<th>Contribution (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7.0</td>
<td>69.5</td>
</tr>
<tr>
<td>7.0-8.0</td>
<td>45.5</td>
</tr>
<tr>
<td>8.0-9.0</td>
<td>40.0</td>
</tr>
<tr>
<td>9.0-10.0</td>
<td>69.5</td>
</tr>
<tr>
<td>&gt;10.0</td>
<td>30.5</td>
</tr>
</tbody>
</table>

**Treatment Targets Based on A1c**

- At elevated A1c levels, initially target FPG
  - As A1c decreases toward goal and FPG approaches normal, target PPG
  - Recent changes in glycemic control are overrepresented in A1c
    - ~50% of A1c is determined in the month before measurement
    - ~25% of A1c is determined 30 to 60 days before measurement
    - ~25% of A1c is determined 60 to 120 days before measurement
  - A1c is inaccurate in presence of hemoglobin variants or shortened RBC survival

---

**Case Study: Sharon**

After diagnosing T2DM (A1c = 8.5; eAG = 197), in addition to referral to DSME and dietician or nutritionist, what is your next step?

1. Initiate sulfonylurea and reevaluate in 3 months
2. Initiate MET and reevaluate in 1 month
3. Increase levothyroxine and reevaluate in 4 to 6 months
4. Increase ramipril, fluoxetine, and simvastatin, start MET, and reevaluate in 3 to 6 months
5. As patient has microalbuminuria, refer to nephrologist and endocrinologist to consider insulin therapy

---

Conventional Antihyperglycemics and Incretins: Effect on FPG, PPG, and A1c

<table>
<thead>
<tr>
<th>Lowering Effect</th>
<th>FPG</th>
<th>PPG</th>
<th>A1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>✔️</td>
<td>✔️</td>
<td>1.5-3.5</td>
</tr>
<tr>
<td>MET</td>
<td>✔️</td>
<td>✔️</td>
<td>1-2</td>
</tr>
<tr>
<td>SUs</td>
<td>✔️</td>
<td>✔️</td>
<td>1-2</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>✔️</td>
<td>✔️</td>
<td>0.5-1.5</td>
</tr>
<tr>
<td>TZDs</td>
<td>✔️</td>
<td>✔️</td>
<td>0.5-1.4</td>
</tr>
<tr>
<td>Alpha-glucosidase Inhibitors</td>
<td>✔️</td>
<td>✔️</td>
<td>0.5-0.8</td>
</tr>
<tr>
<td>GLP-1 Agonists</td>
<td>✔️</td>
<td>✔️</td>
<td>0.6-0.8</td>
</tr>
<tr>
<td>DPP-4 Inhibitors</td>
<td>✔️</td>
<td>✔️</td>
<td>0.5-0.8</td>
</tr>
</tbody>
</table>


MET: First-Line Drug Therapy

- Most effective, least costly, and safest
- Universally agreed to be initiated upon diagnosis
- Achieves significant effect on A1c vs other agents
- Consistently leads to weight loss or is weight neutral
- Decreases LDL-C, TGs, and BP
- Increases or has neutral effect on HDL-C
- Not associated with hypoglycemia
- Decreased CV and total mortality rates
- Contraindicated with ↑ creatinine, IV contrast agents

Polybrominated Diphenyl Ethers (PBDEs) and Their Metabolites

- MET and Lactic Acidosis

**Cochrane Database of Systematic Reviews**

“Risk of fatal and nonfatal lactic acidosis with MET use in type 2 diabetes mellitus”

| 274 trials | 59,321 patient-years |

Conclusions:
No evidence from prospective comparative trials or from observational studies that MET is associated with increased risk of lactic acidosis or with increased levels of lactate, compared with other antihyperglycemic treatments

**Comparative Effectiveness and Safety of Oral Medications**

- Similar or superior effects on
  - Glycemic control
  - Lipids
  - Other intermediate endpoints compared with newer, more expensive agents

**Thiazolidinedione Update to ADA/EASD Algorithm**

The concerns
- Potential risk of MI with rosiglitazone
- Two-fold risk of fluid retention and resultant CHF
- Increased risk of fractures

Current position of ADA/EASD Writing Group
- Weight of the evidence warrants more careful consideration before using TZDs—rather than insulin or sulfonylureas—as second step


Titration of MET 2009

1. Begin with low-dose MET (500 mg) taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day.
2. After 5 to 7 days, if gastrointestinal side effects have not occurred, advance dose to 850 or two 500-mg tablets, twice per day (medication to be taken before breakfast and/or dinner).
3. If gastrointestinal side effects appear as dose is advanced, decrease to previous lower dose and try to advance the dose at a later time.
4. The maximum effective dose can be up to 1000 mg twice per day but is often 850 mg twice per day. Most likely greater effectiveness has been observed with doses up to about 2500 mg/day. Gastrointestinal side effects may limit the dose that can be used.
5. Given cost considerations, generic MET is the first choice of therapy. A longer-acting formulation is available in some countries and can be given once per day.


Are Discouraged

Regular Sliding-Scale Insulin Regimens Are Discouraged

- Ineffective as monotherapy in patients with established insulin requirements
- Unacceptably high rates of hyperglycemia and hypoglycemia
- Iatrogenic diabetic ketoacidosis
- Sliding scale insulin – time to stop sliding

Common Insulin Preparations

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset (h)</th>
<th>Peak (h)</th>
<th>Duration (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting (isophane, aspart)</td>
<td>0.5-1.5</td>
<td>0.5-1.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Short-acting (regular insulin)</td>
<td>0.5</td>
<td>0.5-2</td>
<td>3.4</td>
</tr>
<tr>
<td>Intermediate-acting (human NPH)</td>
<td>2-5</td>
<td>4-10</td>
<td>12-18</td>
</tr>
<tr>
<td>Long-acting (lente)</td>
<td>4-6</td>
<td>None</td>
<td>20-24</td>
</tr>
</tbody>
</table>

Biphasic insulin mixtures

- Biphasic human insulin mixtures
- Biphasic insulin lispro 50/50
- Biphasic insulin aspart 70/30
- Biphasic human insulin 70/30
- Biphasic insulin glargine
- NPH/Reg 70%/30%

Basal-Bolus Insulin Treatment

With Insulin Analogues

- Lispro, glulisine, or aspart

The Physiologic Insulin Profile

Meatime insulin excursions

- Rapid rise; short duration
- Smooth, steady basal insulin profile

Insulin Requirements in Health and Illness

Components of insulin requirement are divided into basal, prandial or nutritional, and correction insulin. When writing insulin orders, the basal and prandial/nutritional insulin doses are written as programmed (scheduled) insulin, and correction-dose insulin is written as an algorithm to supplement the scheduled insulin. Programmed and correction insulin are increased to meet the higher daily basal and prandial or nutritional requirements. Total insulin requirements may vary widely.

Regular Sliding-Scale Insulin Regimens Are Discouraged

- Ineffective as monotherapy in patients with established insulin requirements
- Unacceptably high rates of hyperglycemia and hypoglycemia
- Iatrogenic diabetic ketoacidosis
- Sliding scale insulin – time to stop sliding

Approximate Pharmacokinetic Profiles of Human Insulin and Analogues

- Rapid-acting (isophane, aspart)
- Regular
- NPH
- Detemir
- Extended zinc insulin
- Glargine

Relative Plasma Insulin Levels

- 0.00-2.00
- 2.00-4.00
- 4.00-6.00
- 6.00-8.00
- 8.00-10.00
- 10.00-12.00
- 12.00-14.00
- 14.00-16.00
- 16.00-18.00
- 18.00-20.00
- 20.00-22.00
- 22.00-24.00

General Principles of Insulin Use

1. Usually initiate basal insulin. Oral agents (sensitizers and/or secretagogues) are usually continued at same dose.
2. Fix the fasting first: control the prebreakfast glucose first to <120 mg/dL.
3. If PPG remains elevated despite normal FBS, add prandial insulin. At this point, secretagogues can be stopped, but insulin sensitizers should be continued in obese, insulin-resistant persons.

Insulin Therapy in T2DM: Current Strategies

- **Fix the Fasting First**: Basal Insulin Therapy
  - NPH at bedtime
  - Long-acting insulin once daily

- **Basal-Bolus Therapy**
  - Human or analogue premixed (biphasic) insulin
    - Once daily at dinner
    - Twice daily (breakfast and bedtime)
  - Full basal-bolus therapy
    - Basal + regular human insulin or rapid-acting analogue insulin
    - Once daily at largest meal
    - Twice daily (based on BG profile)
    - Three times daily
    - Insulin pump therapy

Additional Drugs for T2DM

<table>
<thead>
<tr>
<th>Drug</th>
<th>A1c Reduction (%)</th>
<th>Weight</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>0.5-1</td>
<td>Neutral</td>
<td>TID dosing; GI side effects</td>
</tr>
<tr>
<td>Glinides</td>
<td>1-1.5</td>
<td>Increase</td>
<td>Shorter onset of action and half-life, TID dosing</td>
</tr>
<tr>
<td>Pramlintide</td>
<td>0.5-1.0</td>
<td>Decrease</td>
<td>Injections, TID dosing, GI side effects, less experience</td>
</tr>
<tr>
<td>Obgetse/Incretins</td>
<td>0.6-0.8</td>
<td>Neutral+/+</td>
<td>Little experience, reduce dose with renal insufficiency</td>
</tr>
</tbody>
</table>

Synthetic Amylin

- **Action**: Works with insulin to reduce PPG levels, inhibits secretion of glucagon, slows gastric emptying, and enhances satiety
- **Injections**, given with meal
  - Dose 60 mg BID to TID before meals, titrate to 120 mg
- **Efficacy**
  - Reduces A1c levels 0.5% to 0.7%
- **Side effects**
  - Nausea
  - Modest weight loss
- **Medication in this class**: pramlintide

Incretin Mimetics

- **Action**: Augment insulin secretion, lower glucagon levels, slow gastric emptying, and increase satiety1-3
- **Adjust therapy to MET and/or sulfonylurea1-3**
- Can also be prescribed with TZD or without MET4
- Fixed-dose prefilled pens: 5 ug BID and 10 ug BID3
- **Efficacy**
  - Reduces A1c 0.5% to 1.0%5
- **Side effects**
  - Hypoglycemia, especially if given with (high-dose) SU1,2
  - Nausea1,3
  - Weight loss1,3
- **Medication in this class**: exenatide1,3

DPP-4 Inhibitors

- **Action**: Augment secretion of insulin from beta cells and inhibit glucagon release from alpha cells
- **Monotherapy or in combination with a TZD or MET
- **Dose**: 100 mg QD
  - Modify for CRI to CR CI <30-25 mg/daily, CR CL 30-50 mg/daily
- **Efficacy**
  - Lowers FPG and PPG levels
  - Reduces A1c 0.6% to 1.4%
- **Other side effects**
  - Nasopharyngitis
  - Headache
  - Diarrhea
  - Upper respiratory infection
  - Joint pain
  - Urinary tract infection
- **Medication in this class**: sitagliptin

References:

ADA/EASD T2DM Algorithm: 2009

**Tier 1: Well-validated core therapies**

At diagnosis:
- Lifestyle +MET
- Basal insulin
- Sulfonylurea*
- Intensive insulin
- Pioglitazone
- Basal insulin
- Pioglitazone
- GLP-1 agonist†

**Tier 2: Less well validated therapies**

Algorithm for the metabolic management of T2DM. Reinforce lifestyle interventions at every visit and check A1c every 3 months until A1c is <7% and then at least every 6 months. The interventions should be changed if A1c is >7%.

* Sulfonylureas other than glybenclamide (glyburide) or chlorpropamide.
† Insufficient clinical use to be confident regarding safety.


Summary

- Treat to target
  - It’s less important how you get there
- Assess adherence/literacy
- Fix the FPG first
- Escalate therapy THIS VISIT
  - Avoid clinical inertia
- Develop a team-based approach

The First Chinese Medical Text, 2600 BC

"inferior doctors treat full-blown disease,
mediocre doctors treat disease before it is evident,
superior doctors prevent disease”

Huang Dee, Nai-Chian

ARS Question

Which of the following is the most important measure of glycemic control?

1. FPG
2. OGTT
3. Glycosylated hemoglobin (A1c) or estimated average glucose (eAG)
4. Absence of end-organ damage

ARS Question

Medication adherence ________.

1. is primarily a concern in the elderly
2. is related more directly to the number of medicines than to the doses
3. approaches 50% with 4-times-daily dosing
4. and medication reconciliation are closely associated