Screening for Diabetes 2012

- BMI ≥25 plus other risk factors
  - Inactivity
  - Low HDL or high TG
  - First degree relative
  - PCOS
  - High-risk ethnicity
  - Acanthosis nigricans
  - Gestational DM
  - Hx CVD
  - HTN
- Age 45

ADA Diabetes Care, 2012
**Diagnosis of Diabetes 2012**

- A1C $\geq 6.5\%$ *(New, 2010)*
- FPG $\geq 126 \text{ mg/dl} (7.0 \text{ mmol/L})$
- 2-h plasma glucose $\geq 200$ during OGTT
- Symptoms and random plasma glucose $\geq 200 \text{ mg/dl} (11.1 \text{ mmol/L})$
- Need two separate measurements

**Advantages of HbA1c as a Diagnostic Test**

- Non fasting
- Lower intra-individual variation
  - HbA1c: 2%
  - FPG: 6.5%
  - 2 hour plasma glucose: 16-17%
Diagnosis of Pre-Diabetes 2012

- A1C 5.7 – 6.4% \textbf{(New, 2010)}
- FPG 100 - 125 mg/dl  (5.6mmol/L - 6.9 mmol/L)
- 2-h plasma glucose 140 mg/dl – 199 mg/dl during OGTT (7.8mmol/L – 11.0 mmol/L)

ADA Diabetes Care, 2012

Risk of Pre-Diabetes 2012

- Increased risk of progression to diabetes
- 44,203 individuals; 16 studies, 5.6 years

- A1C 5.5 – 6.0: risk of DM 9 - 25%
- A1C 6.0 – 6.5: risk of DM 25 – 50%

ADA Diabetes Care, 2012
Treatment of Pre-Diabetes 2012

- Weight loss 7%; physical activity 150 min/week

- Metformin (but only metformin) may be considered, especially for those with BMI >35, age <60, and women with history of gestational DM

ADA Diabetes Care, 2012

Treatment of Pre-Diabetes 2012: DPP Outcomes Study

- Observational study of those randomized in DPP; 1990 participants

- Results: return to normal glucose during DPP associated with 56% reduction in diabetes risk

- Results unaffected by group assignment

Perreault et al, Lancet 2012
2012 Practice Guidelines: ASA

- ASA: only in those at increased CV risk (10 year risk >10%. Typically men over 50, women over 60 with other risk factors)

2009:
- ASA: over age 40 and for those with other CHD risk factors

2012 Practice Guidelines: HTN and Lipids and Tobacco

- BP: Goal less than 130 and less than 80

- LDL: Goal less than 70 (with CVD); less than 100 (without CVD)

- Don’t forget tobacco
CURRENT ISSUES IN DIABETES MANAGEMENT

Intensive BP Control in Type 2 DM: ACCORD

- RCT of 4733 patients with type 2 DM
- Compare BP less than 120 mm Hg vs 140

<table>
<thead>
<tr>
<th>BP</th>
<th>120</th>
<th>140</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>119</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>CV events plus death</td>
<td>1.87%</td>
<td>2.09%</td>
<td>.20</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.28%</td>
<td>1.19%</td>
<td>.55</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.32%</td>
<td>0.53%</td>
<td>.01</td>
</tr>
<tr>
<td>Adverse events</td>
<td>3.3%</td>
<td>1.3%</td>
<td>.001</td>
</tr>
</tbody>
</table>

In type 2 DM: treating to 120 mm Hg did not reduce the rate of composite fatal and non-fatal CV events

Case 1

70 yo woman with type 2 diabetes, hypertension, and coronary heart disease (s/p MI in 2003).

Meds: Metformin, glipizide, aspirin, lisinopril, metoprolol, and simvastatin

Exam: BP 130/80, BMI 29 kg/m²
Normal exam
CURRENT ISSUES IN DIABETES MANAGEMENT

Case 1

Her glycemic goal should be:

1. HbA1c <6.0%
2. HbA1c <6.5%
3. HbA1c <7.0%
4. HbA1c <7.5%
5. HbA1c <8.0%

Glycemic Control Update

- 3 newer trials
  - ADVANCE
  - ACCORD
  - VA Diabetes Trial
ACCORD Trial

- NIH RCT in DM 2, 10,251 patients, known CVD or risk factors, mean A1c 8.1%
- Intensive vs. standard BP (120 v. 140)
- Lipid control (statins v. statins + fibrates)
- Normalization v. standard BS control (A1c 6 v. 7-7.9)
- Outcomes: CV events. Also microvascular events, quality of life, others

ACCORD trial

<table>
<thead>
<tr>
<th></th>
<th>Intensive</th>
<th>Standard</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c achieved:</td>
<td>6.5%</td>
<td>7.5%</td>
<td>-</td>
</tr>
<tr>
<td>1° outcome:</td>
<td>352</td>
<td>371</td>
<td>0.90 (0.78-1.04)</td>
</tr>
<tr>
<td>Total mortality</td>
<td>5.0%</td>
<td>3.1%</td>
<td>1.22 (1.01-1.46)</td>
</tr>
<tr>
<td>CVD mortality</td>
<td>2.6%</td>
<td>1.8%</td>
<td>1.35 (1.04-1.76)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>10.5%</td>
<td>3.5%</td>
<td>-</td>
</tr>
<tr>
<td>Wt. gain&gt;10 kg</td>
<td>27.8%</td>
<td>14.1%</td>
<td>-</td>
</tr>
</tbody>
</table>
current issues in diabetes management

ACCORD Trial

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>Intensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>203</td>
<td>257</td>
</tr>
<tr>
<td>11/1000/y</td>
<td>14/1000/y</td>
<td></td>
</tr>
</tbody>
</table>

Number Needed to Harm: 333

February 2008 (after 3.5 years): NIH stops this arm of study

ACCORD Trial

5-Year Outcomes

- Additional follow-up of 1.5 years
- All subjects treated to HbA1c of 7-7.9% during this period
- Results:
  - Mortality still higher in intensive group (7.6% vs 6.4%; HR 1.19)

ACCORD. NEJM. 2011
**Outcome of Intensive Glucose Lowering in Type 2 DM**

Meta-analysis of 13 RCTs in DM 2; 34,533 pts

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>1.04 (0.91 – 1.19)</td>
<td></td>
</tr>
<tr>
<td>CV death</td>
<td>1.11 (0.86 – 1.43)</td>
<td></td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>0.85 (0.74 – 0.96)*</td>
<td></td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>0.90 (0.85 – 0.96)*</td>
<td></td>
</tr>
<tr>
<td>Severe hypoglycemia</td>
<td>2.33 (21.62 -3.36)*</td>
<td></td>
</tr>
</tbody>
</table>

* P <0.001

*Boussageon, BMJ 2011*

---

**Outcome of Intensive Glucose Lowering in Type 2 DM**

Over five year period:

<table>
<thead>
<tr>
<th>Prevention</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNT to prevent one MI</td>
<td>117-150</td>
</tr>
<tr>
<td>NNT to prevent one microalbuminuria</td>
<td>32- 142</td>
</tr>
<tr>
<td>NNT to cause one episode of severe hypoglycemia</td>
<td>15-52</td>
</tr>
</tbody>
</table>

*Boussageon, BMJ 2011*
CURRENT ISSUES IN DIABETES MANAGEMENT

ORIGEN Trial

- RCT, 12,537 subjects; impaired FBS, IGT, or new diabetes, and high CV risk
- Mean FBS 131 mg/dl
- Glargine to FBS <95 mg/dl; 6.2 years
- Results: No difference in CV outcomes

ORIGEN, NEJM, 2012

Glucose Control and Renal End Points

- Meta-analysis of 7 RCTs; 28,065 adults; 2-15 years
- Intensive vs. conventional BS control
- Results:
  - Reduced micro (-14%) and macro albuminuria (-26%)
  - No significant difference in doubling of creatinine, ESRD, or death from renal disease

Glycemic Control Summary

- No consistent evidence that tight glycemic control reduces risk of CVD in DM 2
- Possible subgroups with benefit:
  - shorter diabetes duration, no CVD
- Strong evidence to support decrease in microvascular disease outcomes with more intensive glucose control
- More hypoglycemia and weight gain with more intensive regimens

2012 Practice Guidelines: Glucose Control

- Goal A1C ≤7 for most
- Goal A1C <6.5 for some: short duration, long life expectancy, and no CVD
- Goal less stringent (≤8) for history of hypoglycemia, limited life expectancy, micro or macrovascular complications, comorbid conditions, and those in whom the goal is difficult to attain

ADA Diabetes Care, 2012
**Critically Ill patients?**
Meta-analysis of 29 RCTs (n=8,432 patients)

<table>
<thead>
<tr>
<th></th>
<th>Mortality Rates</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tight</td>
<td>Usual</td>
</tr>
<tr>
<td>Overall</td>
<td>21.6%</td>
<td>23.3%</td>
</tr>
<tr>
<td>Very tight, ≤110 mg/dl</td>
<td>23.0%</td>
<td>25.2%</td>
</tr>
<tr>
<td>Moderate, &lt;150 mg/dl</td>
<td>17.3%</td>
<td>18.0%</td>
</tr>
<tr>
<td>Medical ICU</td>
<td>26.9%</td>
<td>29.7%</td>
</tr>
<tr>
<td>Surgical ICU</td>
<td>8.8%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Med-Surg ICU</td>
<td>26.1%</td>
<td>27.0%</td>
</tr>
</tbody>
</table>

**Glycemic Control Summary**

- No consistent evidence that tight glucose control improves mortality in hospitalized patients.
2012 Practice Guidelines: Glucose Control in Hospital

- Critically ill: Goal 140 - 180.
  - IV protocol

- Non-critically ill: premeal <140 if can be done safely; random < 180. Less stringent if severe comorbidities
  - Scheduled subcu insulin with basal, nutritional, and correction components

Case 1

Her glycemic goal should be:

1. HbA1c <6.0%
2. HbA1c <6.5%
3. HbA1c <7.0%
4. HbA1c <7.5%
5. HbA1c <8.0%
In my practice, I have initiated:

1. Exenatide (Byetta™) or Liraglutide (Victoza™)

2. Sitagliptin (Januvia™) or Saxagliptin (Onglyza™)

3. Both exenatide and sitagliptin

4. Pramlintide (Symlin™)

5. All three of the above

6. None of the above
Case 2: 48 yo woman with DM, BMI 33, on diet and exercise and max dose metformin. HbA1C is now 8.5. Your next best step is:

1. Continue current therapy
2. Begin a sulfonylurea
3. Begin pioglitizone
4. Begin NPH insulin or long-acting insulin analogue
5. Begin exenatide (Byetta™), liraglutide (Victoza™), sitagliptin (Januvia™) or saxagliptin (Onglyza™)

<table>
<thead>
<tr>
<th>HgA1c</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from Drug A to B, C, or D</td>
<td>Add Drug A to B, or B to A</td>
</tr>
<tr>
<td>Add Drug C</td>
<td>Add Drug D</td>
</tr>
</tbody>
</table>

**Generic Oral Hypoglycemic Slide**
Metformin: The Safest Hypoglycaemic Agent in Chronic Kidney Disease?

“There is no evidence from prospective comparative trials or from observational cohort studies that metformin is associated with an increased risk of lactic acidosis, or with increased levels of lactate, compared with other oral hypoglycaemic treatments.”


WHAT ABOUT THIAZOLIDINEDIONES?

Meta-analysis of 42 trials of rosiglitazone:

<table>
<thead>
<tr>
<th>Event</th>
<th>Odds</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>1.43</td>
<td>(1.03-1.98)</td>
</tr>
<tr>
<td>Death</td>
<td>1.64</td>
<td>(0.98-2.74)</td>
</tr>
</tbody>
</table>

Nissen, NEJM 2007
**RECORD TRIAL: Rosiglitazone**

RCT, 4447 patients, type 2 DM, A1C 7.9%, rosiglitazone plus metformin or sulfonylurea vs. the two together. Funded by GSK.

<table>
<thead>
<tr>
<th>Event</th>
<th>HR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac hosp or death*</td>
<td>0.99</td>
<td>NS</td>
</tr>
<tr>
<td>All death</td>
<td>0.86</td>
<td>NS</td>
</tr>
<tr>
<td>CV death</td>
<td>0.84</td>
<td>NS</td>
</tr>
<tr>
<td>MI</td>
<td>1.14</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.72</td>
<td>NS</td>
</tr>
<tr>
<td>CHF</td>
<td>2.10</td>
<td>0.0010</td>
</tr>
<tr>
<td>Fractures</td>
<td>1.36</td>
<td>NS</td>
</tr>
</tbody>
</table>

From: Lancet 2009

**PROactive Primary Endpoint: No Statistically Significant Difference vs Placebo in CV outcome**


Composite primary endpoint: all cause mortality, non-fatal MI (including silent MI), stroke, leg amputation, ACS, cardiac intervention, leg revascularization.
Rosiglitazone vs Pioglitazone

Observational study, FDA, 227,571 Medicare patients, over 3 years.

<table>
<thead>
<tr>
<th>Event</th>
<th>Rosi/Pio HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>1.06</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.27</td>
</tr>
<tr>
<td>CHF</td>
<td>1.25</td>
</tr>
<tr>
<td>Death</td>
<td>1.14</td>
</tr>
<tr>
<td>Composite</td>
<td>1.18</td>
</tr>
</tbody>
</table>

Number Needed to Harm with Rosiglitazone = 60 per year

Graham et al, JAMA 2010

Rosiglitzone (Avandia) to Be Pulled From Retail Pharmacy Shelves

Rosiglizone (Avandia) will be pulled from retail pharmacy shelves November 18, 2011.

Only certified MDs will be allowed to prescribe the drug. Prescriptions filled by mail order only through specific pharmacies.

May 2011
Oral Agent “Failure”
Why does this occur?

- Changing HbA1c goals
- Compliance, side effects
- Wrong diagnosis (LADA—latent autoimmune diabetes in adults 10%)
- Stress, diabetogenic medications
- Postprandial hyperglycemia
- Natural progression of the disease

Relative Contributions of Fasting and Postprandial Plasma Glucose to Total Glycemic Excursions as a Function of A1C

CURRENT ISSUES IN DIABETES MANAGEMENT

Natural History of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Months</th>
<th>Years of Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Glucose (mg/dL)

- Post-meal Glucose
- Fasting Glucose

Relative Function (%)

- Insulin Resistance
- Beta-cell failure
- Insulin Level

Obesity | IFG* | Diabetes | Uncontrolled hyperglycemia

*IFG = impaired fasting glucose

Natural History of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Lifestyle</th>
<th>SU</th>
<th>Biguanide</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-meal Glucose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin Resistance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-cell failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin Level</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Years of Diabetes

- Years of Diabetes
- Glucose (mg/dL)
- Relative Function (%)

Lifestyle

SU

Biguanide

Insulin
Insulin Plus Oral Agents

Introduction of insulin
  – Bedtime
  – Intermediate/Long-acting insulins
    • NPH, glargine, leemir
    • 10 units
  – Self-monitoring of blood glucose (hypoglycemia education)

Insulin plus other oral agent combinations (maintain effect on insulin sensitivity)

When to go to > 1 shot per day

✧ HgA1c >7
✧ Glucose in AM at goal but glucose before dinner >140

Options
✧ Add premeal lispro/aspart
✧ Add bid premixed insulin – 70/30, 75/25

Questions
✧ Continue metformin
✧ ? Sulfanylurea, ? Thiazolidinedione (mostly not)
CURRENT ISSUES IN DIABETES MANAGEMENT

Function of Insulin in Regimens

Meal coverage (carbohydrates)

Basal insulin

Correction of high blood sugar

More Options

Incretin mimetics

Exenatide (Byetta™) 4/05
Sitagliptin (Januvia™) 6/06
Saxagliptin (Onglyza™) 8/09
Liraglutide (Victoza™) 1/10
Exenatide LA (Bydureon™) 1/12

Amylinomimetics (amylin analog)

Pramlintide (Symlin™) 3/05
CURRENT ISSUES IN DIABETES MANAGEMENT

INCRETINS

Gut factors that promote insulin secretion in response to nutrients

Major incretins: GLP-1, CCK, GIP

Oral Glucose Promotes More Insulin Release than IV Glucose - Indicating a Role for Incretins
**Incretin Drugs**

<table>
<thead>
<tr>
<th>GLP Agonists</th>
<th>DPP IV Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide</td>
<td>Sitagliptin</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>Saxagliptin</td>
</tr>
<tr>
<td>Exenatide LA</td>
<td>Vildagliptin</td>
</tr>
<tr>
<td>Semaglutide</td>
<td>Alogliptin</td>
</tr>
<tr>
<td>Aliaglutide</td>
<td>Linagliptin</td>
</tr>
<tr>
<td>Taspoglutide</td>
<td>Dutogliptin</td>
</tr>
<tr>
<td>Exenatide Lar</td>
<td>Metogliptin</td>
</tr>
<tr>
<td>Lixsenatide</td>
<td></td>
</tr>
</tbody>
</table>

**Biological Diagram**

- Nutrients
- Food Intake
- Gastric Emptying
- Glucose Synthesis
- Insulin
- Glucagon
- GLP-1
- Islet mass
- Apoptosis
- L cells
**CURRENT ISSUES IN DIABETES MANAGEMENT**

### A1C (%) Effect (change from baseline)

<table>
<thead>
<tr>
<th></th>
<th>Placebo BID</th>
<th>5 mcg exenatide BID</th>
<th>10 mcg exenatide BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET</td>
<td>0.1</td>
<td>-0.4</td>
<td>-0.8</td>
</tr>
<tr>
<td>SFU</td>
<td>0.1</td>
<td>-0.5</td>
<td>-0.9</td>
</tr>
<tr>
<td>MET+SFU</td>
<td>0.2</td>
<td>-0.6</td>
<td>-0.8</td>
</tr>
</tbody>
</table>

Changes in A1C from baseline vs placebo statistically significant

### Weight (change from baseline) & Hypoglycemia

<table>
<thead>
<tr>
<th></th>
<th>Placebo BID</th>
<th>5 mcg exenatide BID</th>
<th>10 mcg exenatide BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-1.4</td>
<td>-3.1</td>
<td>-4.2</td>
</tr>
<tr>
<td>Hypoglycemia (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MET</td>
<td>5.3</td>
<td>4.5</td>
<td>5.3</td>
</tr>
<tr>
<td>SFU</td>
<td>3.3</td>
<td>14.4</td>
<td>35.7</td>
</tr>
<tr>
<td>MET + SFU</td>
<td>1.26</td>
<td>19.2</td>
<td>27.8</td>
</tr>
</tbody>
</table>

Open-label extension study to 90 weeks: persistence in weight loss and ↓A1C
CURRENT ISSUES IN DIABETES MANAGEMENT

Side Effects

GI
- Nausea (44% vs 18% with placebo); incidence lessens over time; 3% dropout rate due to nausea
- Vomiting (13% vs 4%)
- Diarrhea (13% vs 6%)

Headache (9% vs 6%)
Hypoglycemia (see previous slide)

Improvements in HbA1c With Initial Co-administration of Sitagliptin and Metformin

Mean Baseline HbA1c = 8.8%
N=1091

* Placebo-subtracted LS mean change from baseline at Week 24.
Sita=sitagliptin. Met=metformin.
Aschner P, et al. Oral presentation at the EASD 42nd Annual Meeting; 14-17 September 2006; Copenhagen.
CURRENT ISSUES IN DIABETES MANAGEMENT

Sitagliptin – adverse reactions

<table>
<thead>
<tr>
<th></th>
<th>Sitagliptin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>n = 443</td>
<td>n = 363</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>23 (5.2)</td>
<td>12 (3.3)</td>
</tr>
<tr>
<td>+ pioglitazone</td>
<td>n = 175</td>
<td>n = 178</td>
</tr>
<tr>
<td>Upper resp. infection</td>
<td>11 (6.3)</td>
<td>6 (3.4)</td>
</tr>
</tbody>
</table>

Small increase in WBC – neutrophil count higher by 200 on Sitagliptin

No nausea or vomiting

No weight loss

Increased Incidence of Pancreatitis and Cancer Among Patients Given Glucagon Like Peptide-1 Based Therapy

- Sitagliptin or exenatide increased the odds ratio for pancreatitis 6-fold (P < 2 x 10^{-16}).

- Pancreatic cancer was more commonly reported among patients that took sitagliptin or exenatide, (P < 0.033, P < 2x10^{-4})

- All other cancers occurred more frequently among patients that took sitagliptin, (P < 1x10^{-4})

Gastroenterology (2011)
CURRENT ISSUES IN DIABETES MANAGEMENT

Natural History of Type 2 Diabetes

- Incretins/Others?
- Thiazolidinedione? - Biguanide
- Lifestyle
- SU
- Insulin

Glucose (mg/dL)

- Post-meal Glucose
- Fasting Glucose

Relative Function (%)

- Insulin Resistance
- Insulin Level

Beta-cell failure

Years of Diabetes

Drug Cost Comparison

<table>
<thead>
<tr>
<th>Drug and Dose</th>
<th>Cost/month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose strips (2 per day)</td>
<td>$66</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td></td>
</tr>
<tr>
<td>Generic</td>
<td>$4-14</td>
</tr>
<tr>
<td>Brand</td>
<td>$50</td>
</tr>
<tr>
<td>Rapaglinide 2 mg tid</td>
<td>$193</td>
</tr>
<tr>
<td>Acarbose 100 mg tid</td>
<td>$88</td>
</tr>
<tr>
<td>Metformin 1000 bid</td>
<td></td>
</tr>
<tr>
<td>Generic</td>
<td>$4-32</td>
</tr>
<tr>
<td>Brand</td>
<td>$161</td>
</tr>
<tr>
<td>Rosiglitazone 8 mg qd</td>
<td>$266</td>
</tr>
<tr>
<td>Pioglitazone 45 mg/d</td>
<td>$245</td>
</tr>
<tr>
<td>Sitagliptin/Saxagliptin</td>
<td>$207/190</td>
</tr>
<tr>
<td>Exenatide 10 mcg/Liraglutide 1.2mg</td>
<td>$271/280</td>
</tr>
<tr>
<td>Glargine, 45 U/d</td>
<td>$150</td>
</tr>
<tr>
<td>24 hour fitness Center</td>
<td>$35</td>
</tr>
<tr>
<td>YMCA</td>
<td>$65</td>
</tr>
</tbody>
</table>
Case 2: 48 yo woman with DM, BMI 33, on diet and exercise and max dose metformin. HbA1C is now 8.5. Your next best step is:

1. Continue current therapy
2. Begin a sulfonylurea
3. Begin pioglitizone
4. Begin NPH insulin or long-acting insulin analogue
5. Begin exenatide (Byetta™), liraglutide (Victoza™), sitagliptin (Januvia™) or saxagliptin (Onglyza™)
Conclusions

- Tight glycemic control not effective in lowering total mortality or CV mortality.
- Many newer diabetes agents available, all with some side effects and higher costs...few with hard outcome data.
- Glucose control may be more important early in diabetes.
- Good BP and lipid control is important throughout the diabetes life course.