Case 1: Type 2 Diabetes

59 year old male, diagnosed with T2DM six months ago

- Nonsmoker
- Father died myocardial infarction age 45
- Has hypertension, 144/89, on a Calcium Channel blocker
- Height, weight WNL (BMI 19)
- Total cholesterol 243 mg/dL or 6.28 mmol/L
- LDL-C 172 mg/dL or 4.45 mmol/L
- HDL-C 36 mg/dL or 0.94 mmol/L
- Triglycerides 168 mg/dL or 1.89 mmol/L
- Fasting glucose 129 mg/dL or 7.1 mmol/L
- HgA1C of 6.9%
**Case 1 questions**

- What features are of concern?
- What impact of hypertension?
- What impact of lipid profile? What are goals?
- How does this gentleman risk compare to the myocardial infarction risk that his father had: higher, lower, same?
- What if this gentleman was 79 years old?
- What if female instead male?

---

**ADVANCE: Combined Glycaemia and BP Effects on Death**

![Graph showing the impact of glucose arm and blood pressure arm on annual event rate (%)]

Effect of early intensive multifactorial therapy on 5 year outcomes in individuals with type 2 Diabetes

- N = 3055 persons, men, mostly Caucasian
- Mean age 60
- Many with history of MI or CVA
- Mean duration follow-up 5.3 years
- Goals: B/P < 135/85
  - Cholesterol < 5mmol (194 mg/dL) primary prevention, <4.5mmol (174 mg/dL) secondary prevention
  - HgA1c < 7 %


CV events and mortality in the two treatment groups

<table>
<thead>
<tr>
<th>Event</th>
<th>Routine care N = 1377</th>
<th>Intensive care N = 1678</th>
<th>Hazard Ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite CV events</td>
<td>117 (8.5%)</td>
<td>121 (7.2%)</td>
<td>0.83 (.65 - 1.05)</td>
</tr>
<tr>
<td>CV Death</td>
<td>22 (1.6%)</td>
<td>26 (1.5%)</td>
<td>0.88 (.51 – 1.51)</td>
</tr>
<tr>
<td>Total mortality</td>
<td>92 (6.7%)</td>
<td>104 (6.2%)</td>
<td>0.91 (.69 – 1.21)</td>
</tr>
</tbody>
</table>

All cause mortality 1997-2002 in Danish population study: Comparing non-diabetics with no MI with, prior MI patients, diabetes alone patients with those with both

<table>
<thead>
<tr>
<th></th>
<th>No diabetes</th>
<th>No diabetes</th>
<th>Diabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No MI</td>
<td>Prior MI</td>
<td>No prior MI</td>
<td>Prior MI</td>
</tr>
<tr>
<td>Men</td>
<td>114,931</td>
<td>14,375</td>
<td>1,851</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(7.7%)</td>
<td>(29.1%)</td>
<td>(44.6%)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>129,844</td>
<td>8,393</td>
<td>1,146</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(7.9%)</td>
<td>(35.3%)</td>
<td>(50.5%)</td>
<td></td>
</tr>
</tbody>
</table>

Case 1: Type 2 Diabetes
What if: Add Albuminuria?

- Last two clinic visits:
  - 57 mg/g alb/creat
    - (6.4 mg/mmol)
  - 77 mg/g alb/creat
    - (8.7 mg/mmol)

  Applicant FAXs new UA from his doctor:
  - 585 mg/g alb/creat
    - (66 mg/mmol)

- Definitions:
  - Normal
    - ≤ 30 mg/g creat
    - (3.4 mg/mmol creat)

  - Microalbuminuria
    - 30-300 mg/g creat
    - (3.4-34 mg/mmol)

  - Macroalbuminuria
    - >300 mg/g creat
    - (34 mg/mmol creat)
Myocardial Infarction and Microvascular Disease

Updated mean HbA1c (%)

Incidence per 1000 patient-years

- Microvascular disease (retinopathy/nephropathy)
- Myocardial infarction

UKPDS 35. BMJ 2000; 321: 405-12

Renal Outcomes in T2DM

Table 3. Cumulative Incidence of Renal Outcomes in the Trials*  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Kumaresan²</th>
<th>UKPDS 32⁷</th>
<th>UKPDS 34⁷</th>
<th>UKPDS Feasibility trial²</th>
<th>ACCORD²</th>
<th>ADVANCE³</th>
<th>VAQI⁴¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of follow up, median, y</td>
<td>6</td>
<td>10</td>
<td>10.7</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>11.6</td>
<td>23.8</td>
<td>23</td>
<td>44</td>
<td>23.5</td>
<td>24.7</td>
<td>11.5</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>5.7 ⁸</td>
<td>NA</td>
<td>10.5</td>
<td>4.6</td>
<td>3.5</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>Declining of creatinine level</td>
<td>NR</td>
<td>2.1 ⁹</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>eGFR</td>
<td>NR</td>
<td>0.9¹⁰</td>
<td>0.8</td>
<td>NR</td>
<td>0.0</td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Death from renal failure</td>
<td>NR</td>
<td>0.8¹¹</td>
<td>0.4</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Abbreviations: eGFR, estimated glomerular filtration rate. For other abbreviations, see Table 1.
*Combined incidence in treated and control arms.
²At 6 year follow-up.
³At 9 year follow-up.
⁴At study's end (median follow up: 11.1 years).

Role of Intensive Glucose Control in Development of Renal End Points in Type 2 Diabetes Mellitus: Systematic Review and Meta-analysis

Arch Intern Med. 2012 May 28;172(10):761-9
### A. Microalbuminuria

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Weight %</th>
<th>Risk Ratio M-H Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALADDIN-14</td>
<td>170</td>
<td>3290</td>
<td>17.3</td>
<td>0.88 (0.80-0.96)</td>
</tr>
<tr>
<td>ADHERE62</td>
<td>1318</td>
<td>3936</td>
<td>79.3</td>
<td>0.95 (0.86-1.05)</td>
</tr>
<tr>
<td>K heatmap21</td>
<td>9</td>
<td>52</td>
<td>9.7</td>
<td>0.97 (0.89-1.06)</td>
</tr>
<tr>
<td>UKPDS-37</td>
<td>368</td>
<td>377</td>
<td>10.2</td>
<td>0.86 (0.78-0.96)</td>
</tr>
<tr>
<td>UKPDS-347</td>
<td>19</td>
<td>347</td>
<td>0.75</td>
<td>1.03 (0.77-1.38)</td>
</tr>
<tr>
<td>VA Diabetes Trial2</td>
<td>60</td>
<td>460</td>
<td>0.6</td>
<td>1.19 (0.81-1.73)</td>
</tr>
<tr>
<td>VA Possible Trial2</td>
<td>7</td>
<td>42</td>
<td>0.56</td>
<td>0.35 (0.13-0.92)</td>
</tr>
<tr>
<td>Meta (95% CI)</td>
<td>11575</td>
<td>10750</td>
<td>100.0</td>
<td>0.86 (0.76-0.96)</td>
</tr>
</tbody>
</table>

Total events: 2540

Heterogeneity: I² = 79%, P = 0.01, 100%

### B. Microalbuminuria

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Weight %</th>
<th>Risk Ratio M-H Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALADDIN-14</td>
<td>105</td>
<td>4301</td>
<td>39.3</td>
<td>0.27 (0.06-0.98)</td>
</tr>
<tr>
<td>ADHERE62</td>
<td>758</td>
<td>5011</td>
<td>47.5</td>
<td>0.67 (0.42-1.08)</td>
</tr>
<tr>
<td>K heatmap21</td>
<td>9</td>
<td>56</td>
<td>0.7</td>
<td>0.97 (0.89-1.06)</td>
</tr>
<tr>
<td>UKPDS-37</td>
<td>7</td>
<td>307</td>
<td>10.4</td>
<td>0.24 (0.04-1.50)</td>
</tr>
<tr>
<td>UKPDS-347</td>
<td>12</td>
<td>373</td>
<td>4.2</td>
<td>0.46 (0.26-0.81)</td>
</tr>
<tr>
<td>VA Diabetes Trial2</td>
<td>3</td>
<td>74</td>
<td>1.4</td>
<td>0.38 (0.11-1.26)</td>
</tr>
<tr>
<td>VA Possible Trial2</td>
<td>3</td>
<td>23</td>
<td>0.6</td>
<td>0.35 (0.11-1.25)</td>
</tr>
<tr>
<td>Meta (95% CI)</td>
<td>133/4</td>
<td>117/3</td>
<td>100.0</td>
<td>0.74 (0.65-0.85)</td>
</tr>
</tbody>
</table>

Total events: 520

Heterogeneity: I² = 73%, P = 0.05, 100%

### C. Outcomes of Other Conditions

#### C.1. Diabetic Retinopathy

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Weight %</th>
<th>Risk Ratio M-H Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALADDIN-14</td>
<td>138</td>
<td>572</td>
<td>40.0</td>
<td>1.00 (0.73-1.35)</td>
</tr>
<tr>
<td>ADHERE62</td>
<td>12</td>
<td>373</td>
<td>7.5</td>
<td>1.00 (0.99-1.01)</td>
</tr>
<tr>
<td>K heatmap21</td>
<td>2</td>
<td>432</td>
<td>0.4</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>UKPDS-37</td>
<td>2</td>
<td>139</td>
<td>1.5</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>UKPDS-347</td>
<td>7</td>
<td>343</td>
<td>4.2</td>
<td>1.00 (0.71-1.39)</td>
</tr>
<tr>
<td>VA Diabetes Trial2</td>
<td>17</td>
<td>133/4</td>
<td>100.0</td>
<td>0.99 (0.90-1.09)</td>
</tr>
</tbody>
</table>

Total events: 174

Heterogeneity: I² = 0.00, P = 0.12, 100%

#### C.2. Cardiovascular Disease

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Weight %</th>
<th>Risk Ratio M-H Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALADDIN-14</td>
<td>15</td>
<td>257</td>
<td>73.5</td>
<td>0.24 (0.13-0.44)</td>
</tr>
<tr>
<td>ADHERE62</td>
<td>8</td>
<td>377</td>
<td>4.6</td>
<td>1.07 (0.57-2.05)</td>
</tr>
<tr>
<td>K heatmap21</td>
<td>2</td>
<td>54</td>
<td>0.5</td>
<td>0.40 (0.33-0.48)</td>
</tr>
<tr>
<td>UKPDS-37</td>
<td>2</td>
<td>71/11</td>
<td>100.0</td>
<td>0.98 (0.55-1.78)</td>
</tr>
</tbody>
</table>

Total events: 29

Heterogeneity: I² = 0.00, P = 0.15, 100%

#### C.3. Kidney Disease

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>Weight %</th>
<th>Risk Ratio M-H Random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALADDIN-14</td>
<td>15</td>
<td>257</td>
<td>73.5</td>
<td>0.24 (0.13-0.44)</td>
</tr>
<tr>
<td>ADHERE62</td>
<td>8</td>
<td>377</td>
<td>4.6</td>
<td>1.07 (0.57-2.05)</td>
</tr>
<tr>
<td>K heatmap21</td>
<td>2</td>
<td>54</td>
<td>0.5</td>
<td>0.40 (0.33-0.48)</td>
</tr>
<tr>
<td>UKPDS-37</td>
<td>2</td>
<td>71/11</td>
<td>100.0</td>
<td>0.98 (0.55-1.78)</td>
</tr>
</tbody>
</table>

Total events: 29

Heterogeneity: I² = 0.00, P = 0.15, 100%
Kaplan-Meier plots of proportion of patients with microalbuminuria, macroalbuminuria, reduced creatinine clearance (CrCl), doubling of plasma creatinine, or any one of these, after diagnosis of diabetes.

UKPDS
Retnakaran R et al. Diabetes 2006;55:1832-1839

Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64)

From Proportion of patients alive (95% CI) ten years later
No nephropathy 87.1% (86.8–87.3)
Microalbuminuria 70.8% (67.4–74.2)
Macroalbuminuria 65.1% (57.5–72.6)
Elevated plasma creatinine or renal replacement therapy 8.5% (0–100)

Impact of Nephropathy on Risk of Death

- No nephropathy: Annual Risk 1%
- Microalbuminuria: Annual Risk 3%
- Macroalbuminuria: Annual Risk 5%
- ESRD: Annual Risk 19%

DEATH

Case 1: Type 2 Diabetes
What if: add Diabetic Retinopathy?
Onset of retinopathy precedes diagnosis of type 2 diabetes

Prevalence of retinopathy in relation to years after onset of diabetes among patients in southern Wisconsin (blue circles) and rural western Australia (red squares). At diagnosis (year zero), retinopathy was already present in 10 to 20% of patients. The lines extrapolate back to an estimated onset of retinopathy four to seven years before the clinical diagnosis was made.

Data from Harris, M, Klein, R, Welborn, TA, Knudman, MW, Diabetes Care 1997; 15:815

UKPDS Glucose Study Results

A monotherapy approach, which achieved a median HbA1c difference of 0.9% (7.0% vs. 7.9%) over 10 years, reduced risk by:

- 12% any diabetes related endpoint, \( p = 0.029 \)
- 16% myocardial infarction, \( p = 0.052 \)
- 25% microvascular disease, \( p = 0.0099 \)
- 21% retinopathy at twelve years, \( p = 0.015 \)
- 33% albuminuria at twelve years, \( p = 0.000054 \)

A step-wise, treat-to-target approach, which achieved a mean blood pressure difference of 10/5 mmHg over 8 years (144/82 vs. 154/87), reduced risk by:

<table>
<thead>
<tr>
<th>Event</th>
<th>Relative Risk Reduction</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes-related endpoint</td>
<td>24%</td>
<td>0.0046</td>
</tr>
<tr>
<td>Fatal and non-fatal stroke</td>
<td>44%</td>
<td>0.013</td>
</tr>
<tr>
<td>Microvascular disease</td>
<td>37%</td>
<td>0.0092</td>
</tr>
<tr>
<td>Retinopathy progression</td>
<td>34%</td>
<td>0.0038</td>
</tr>
<tr>
<td>Deterioration of vision</td>
<td>47%</td>
<td>0.0036</td>
</tr>
</tbody>
</table>

**UKPDS Blood Pressure Study Results**

**Myocardial Infarction and Microvascular Disease**

Incidence per 1000 patient-years

- Microvascular disease
- Retinopathy/nephropathy
- Myocardial infarction

**UKPDS 35. BMJ 2000; 321: 405-12**
Case 1: Type 2 Diabetes
What if: add Peripheral Neuropathy?

UKPDS

- At T2DM diagnosis
  - 36% men
  - 21% women
  Had evidence of neuropathy

- At 12 years
  - Of those free of any neuropathic abnormality
    - 64% men
    - 44% women
  Developed at least one neuropathy endpoint
  (vibratory sensory threshold, ankle jerk reflex, ED in males)
Multifactorial intervention and CVD in patients with type 2 DM

Peripheral Neuropathy
Vibratory sensory threshold
Ankle jerk reflex
ED in males

Case 2: Type 1 Diabetes

24 year old female diagnosed with Type 1 DM since age 12

- On insulin pump with sensor last 3 years
- No major hypoglycemic events
- Had healthy baby last year
- Background retinopathy
- No renal disease
- Recent evaluation for lightheadedness
Case 2: Type 1 Diabetes

24 year old female diagnosed with Type 1 DM since age 12

- 5 ft 5 inches 177 lbs (165cm 80.5 kg)
- B/P 90/68, 94/64, 100/70
- Glucose 61 mg/dL (3.36mmol/L)
- HgA1C 7.3%
- Normal urinalysis
- Total cholesterol 119 mg/dL (3.08 mmol/L)
- LDL-C 67 mg/dL (1.73 mmol/L)
- HDL-C 42 mg/dL (1.09 mmol/L)
- Triglycerides 50 mg/dL (0.56 mmol/L)

Case 2: Type 1 Diabetes

24 year old female diagnosed with Type 1 DM since age 12

- Any impact of insulin pump therapy?
- What about recent pregnancy?
- What about the background retinopathy?
- What about the lightheadedness?
- What other evaluations would you like to see?
Autonomic Neuropathy Testing
ANSAR ANX 3.0

DATE: 

PATIENT NAME: 

REFERRING PROVIDER: 

HEART RATE VARIABILITY

- BASELINE: Normal/Abnormal
- DEEP BREATHING (Primarily parasympathetic): Normal/Abnormal
- Valsalva (Primarily sympathetic): Normal/Abnormal
- STANDING: 30-15, Combined autonomic tone, primarily sympathetic:
  Heart Rate response: Normal/Abnormal
  Blood Pressure response: Normal/Abnormal

RHYTHM STRIP INTERPRETATION: NSR

CONCLUSION: Normal/Early/Intermediate/Advanced

RECOMMENDATIONS: 
- Alpha Lipoic Acid 400mg bid
  - Repeat 6/17/21
  - ETT: To be arranged/Question discuss with PCP
Time trends in mortality in patients with type 1 diabetes: nationwide population based cohort study

Table 1: All cause standardised mortality ratios (SMRs) at 20 years duration of diabetes in early onset type 1 diabetes cohort (0-14 years) and late onset type 1 diabetes cohort (15-29 years) diagnosed between 1970 and 1980.

<table>
<thead>
<tr>
<th>Diagnosis subgroup</th>
<th>Follow-up range (years)</th>
<th>Age range (years)</th>
<th>Mortality/100,000</th>
<th>Observed No. of deaths</th>
<th>Person years</th>
<th>Expected No. of deaths</th>
<th>SMR (95% CI)</th>
<th>P value for risk ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early onset†</td>
<td>1970-4</td>
<td>0-20</td>
<td>0-34</td>
<td>240</td>
<td>68</td>
<td>28,345</td>
<td>19.6</td>
<td>3.5 (2.7 to 4.4)</td>
</tr>
<tr>
<td></td>
<td>1970-0</td>
<td>0-20</td>
<td>0-34</td>
<td>218</td>
<td>64</td>
<td>20,865</td>
<td>13.9</td>
<td>2.4 (2.0 to 2.8)</td>
</tr>
<tr>
<td></td>
<td>1980-4</td>
<td>0-20</td>
<td>0-34</td>
<td>176</td>
<td>57</td>
<td>20,373</td>
<td>11.7</td>
<td>3.0 (2.3 to 3.8)</td>
</tr>
<tr>
<td></td>
<td>1980-0</td>
<td>0-20</td>
<td>0-34</td>
<td>99</td>
<td>19</td>
<td>19,219</td>
<td>10.1</td>
<td>1.9 (1.2 to 2.9)</td>
</tr>
<tr>
<td>Late onset†</td>
<td>1970-4</td>
<td>0-20</td>
<td>15-49</td>
<td>225</td>
<td>49</td>
<td>21,924</td>
<td>35.1</td>
<td>1.4 (1.0 to 1.8)</td>
</tr>
<tr>
<td></td>
<td>1970-0</td>
<td>0-20</td>
<td>15-49</td>
<td>236</td>
<td>68</td>
<td>22,951</td>
<td>37.4</td>
<td>1.8 (1.4 to 2.2)</td>
</tr>
<tr>
<td></td>
<td>1980-4</td>
<td>0-20</td>
<td>15-49</td>
<td>320</td>
<td>71</td>
<td>21,545</td>
<td>31.8</td>
<td>2.2 (1.8 to 2.6)</td>
</tr>
<tr>
<td></td>
<td>1980-0</td>
<td>0-20</td>
<td>15-49</td>
<td>406</td>
<td>57</td>
<td>12,995</td>
<td>19.0</td>
<td>2.0 (2.2 to 2.7)</td>
</tr>
</tbody>
</table>

NS: not significant
*Adjusted for age at diagnosis and duration of diabetes.
† value for trend < 0.05.
Glycemic control and incidence of heart failure in patients with type 1 diabetes—observational study

- N = 20,985 with mean age 38.6 years old
- Median follow-up 9 years
- N = 635 admitted for Congestive Heart Failure
- Incidence increased in relationship to HgA1C
  - 1.42/1000 patient years in those HgA1C < 6.5
  - 5.2/1000 patient years in those HgA1C > 10.5
  - Age and duration of DM increased risk
  - Hazard Ratio overall, 3.98 (CI 2.23-7.14)

Lind M et al. Lancet July 2011;vol 378:140-146

Rate of new cases of type 1 and type 2 diabetes among youth ages younger than 20 years, by race/ethnicity, 2002–2005

Source: SEARCH for Diabetes in Youth Study
NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics; API=Asians/Pacific Islanders; AI=American Indians

National Diabetes Statistics 2011 cdc.gov
Case 3: T2DM in Youth

14 Y/O MALE

- Height: 5’8”
  - (172.7 cm)
- Weight: 275#
  - (124.7 kg)
- BMI: 41.9 (95%)
- BP: 140/88 (>95%)

- Phone Call History:
  - T2DM X 4 years
  - Recently added pill for ‘kidneys’
  - Also ‘watching’ liver

- Medications:
  - “one for DM, one for kidneys, one for cholesterol…just like mom”
- Mom + Dad BMI = 91
Weight categories for adults and youth

<table>
<thead>
<tr>
<th>Category</th>
<th>Adults (≥18 yrs)</th>
<th>Youth (2-20 yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>BMI &lt;18.5</td>
<td>BMI &lt;5th percentile for age</td>
</tr>
<tr>
<td>Normal weight</td>
<td>BMI 18.5-24.9</td>
<td>BMI 5th to 85th percentile</td>
</tr>
<tr>
<td>Overweight</td>
<td>BMI 25-29.9</td>
<td>BMI 85th to 95th percentile</td>
</tr>
<tr>
<td>Obesity</td>
<td>BMI &gt;30</td>
<td>BMI &gt;95th percentile</td>
</tr>
<tr>
<td>Class III obesity</td>
<td>BMI &gt;40</td>
<td>Not used*</td>
</tr>
</tbody>
</table>

* In children, proposed definitions of severe obesity are BMI >120 percent of the 95th percentile, or BMI >99th percentile.

Obesity among children

NOTE: Obesity is body mass index (BMI) for age and sex at or above the 95th percentile of the CDC growth charts.
SOURCE: CDC/NCHS, Health, United States, 2010, Figure 13. Data from the National Health and Nutrition Examination Survey.
Source: SEARCH for Diabetes in Youth Study
NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics; API=Asians/Pacific Islanders; AI=American Indians

National Diabetes Statistics 2011  cdc.gov

Criteria for the diagnosis of diabetes

1. A1C ≥6.5 percent. The test should be performed in a laboratory using a method that is NCEP-certified and standardized in the United States.

2. Fasting plasma glucose ≥126 mg/dL (7.0 mmol/L) fasting is defined as no carbohydrate intake for at least 8 h.

3. 2-h post-75-g oral glucose tolerance test (OGTT) plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. 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.

4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

A1C: glycated hemoglobin; NCEP: national cholesterol education program; T2DM: type 2 diabetes mellitus; OGTT: oral glucose tolerance test; *In the absence of unequivocal hyperglycemia, criterion 1 is not to be confirmed by repeat testing.
T2DM in Youth: Comorbidities

- **HTN**
  - 12-32% HTN at diagnosis of T2DM
  - >95% of BP 120-130 systolic
  - Treatment Goal: <90% 120/80
  - ACE/ARBs vs. ?

- **Dyslipidemia**
  - 30% at dx (<adults)

- **NAFLD**
  - 20% ALT> 2X

- **Retinopathy**
  - <4%

- **Nephropathy**
  - 14-22% at dx
  - 60% at 10 yrs.

- **Vascular?**

- **Depression/eating disorders**

TODAY Study
Treatment Options for T2DM in Adolescents and Youth Study

- **Approx. 700**
- **T2DM < 2 yrs.**
- **3.8 yr follow up**

- **Failure Rate:**
  - goal: HgA1c 8%
  - Metformin 51.7%
  - Metformin plus Avandia 38.6%
  - Metformin plus lifestyle 46.6%

Ped. Diabetes 2007 April;8(2):74-81
Case 4: Gestational Diabetes

- 30 year old female
  - Hx of gestational diabetes
  - NSVD 6 months ago.
  - Had been treated with insulin
  - GDM previous 3 pregnancies
  - Current BMI 37.5

- Application information: No Medications
- (No lab obtained due to low amount of coverage)

Gestational Diabetes: Definitions

**OVERT DIABETES**

- FPG ≥ 126 mg/dL (7.0 mmol/L)
- A1C ≥ 6.5%
- Random GLU ≥ 200

**GESTATIONAL DIABETES**

- FPG ≥ 92 (5.1 mmol/L)
- At 24-28 weeks
  - 75 gm 2 hour GTT
  - At least one of the following:
    - FPG: ≥ 92 mg/dL (5.1 mmol/L) but ≤ 126 mg/dL (7.0 mmol/L)
    - 1 HOUR: ≥ 180 mg/dL (10.0 mmol/L)
    - 2 HOUR: ≥ 153 mg/dL (8.5 mmol/L)

2010 International Association of Diabetes and Pregnancy Study Group
2011 American Diabetes Association
Gestational Diabetes

- 10% either T2DM or Latent Type 1
- 1/3-2/3 GDM in subsequent pregnancy
- 20% IGT post partum
- Risk of T2DM
  - 20-60% in next 10 years
  - 50-75% if BMI > 30
  - RR 4.69 at 5 yrs.
  - RR 9.34 > 5 yrs.

CASE 5: Pre Diabetes

- 50 year old male
  - 5’10” (152 cm)
  - 220 # (99.7 kg)
  - BMI 31.6
  - BP 132/84
  - Screening Blood Chemistry Profile
    - HgA1C 6.1%
    - Repeated at his MD: HgA1C 5.8%
Pre-Diabetes Definition

A1C Level and Future Risk of Diabetes: A Systematic Review
Diabetes Care 33:1665-1673, 2010

Risk of Future T2DM

- HgA1C 6.0-6.5%
  - 5 yr risk 25-50%
  - Annualized risk 54% if ≥ 6.1%
- HgA1C 5.5-6.0%
  - 5 yr risk 9-25%
- HgA1C 5.0-5.5%
  - 5 yr risk <9%
  - Annualized risk 0.1% if ≤ 5.0%

“This systematic review of prospective studies confirms a strong, continuous association between A1C and subsequent diabetes risk.”

A1C Level and Future Risk of Diabetes: A Systematic Review
Diabetes Care 33:1665-1673, 2010
Haemoglobin A1c cut-off point to identify a high risk group of future diabetes: Omiya MA Cohort Study

Diabetic Medicine 2012 Jul;29(7):905-910
A1C linear with mortality

HbA1c concentration as a predictor of mortality

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>&lt;5.0 (n=1304)</th>
<th>5.0-5.4 (n=1608)</th>
<th>5.5-6.0 (n=1611)</th>
<th>&gt;7.0 (n=31)</th>
<th>Known DM (n=180)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause death</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>5.0</td>
<td>6.0</td>
</tr>
<tr>
<td>CVR death</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>5.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>

In a study of men ages 45 to 79, HbA1c, a marker of blood glucose concentration, was correlated with cardiovascular (red bars) and all cause (blue bars) mortality, even within the nondiabetic range.


Appendix
## Meta-analysis: All-cause Mortality

<table>
<thead>
<tr>
<th>Trials</th>
<th>Number of Events (Annual Event Rate, %)</th>
<th>Favor More Intensive</th>
<th>Favor Less Intensive</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCORD</td>
<td>More Intensive: 257 (1.41) Less Intensive: 203 (1.14)</td>
<td>1.01</td>
<td>1.22 (1.01 - 1.46)</td>
<td></td>
</tr>
<tr>
<td>ADVANCE</td>
<td>More Intensive: 498 (1.88) Less Intensive: 533 (1.99)</td>
<td>-0.72</td>
<td>0.93 (0.83 - 1.00)</td>
<td></td>
</tr>
<tr>
<td>UKPDS</td>
<td>More Intensive: 123 (0.13) Less Intensive: 53 (0.25)</td>
<td>-0.66</td>
<td>0.96 (0.70 - 1.33)</td>
<td></td>
</tr>
<tr>
<td>VADT</td>
<td>More Intensive: 102 (2.22) Less Intensive: 95 (2.06)</td>
<td>-1.16</td>
<td>1.07 (0.81 - 1.42)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>More Intensive: 980 Less Intensive: 884</td>
<td>-0.88</td>
<td>1.04 (0.89 - 1.20) (Q=5.71, p=0.13, I²=47.5%)</td>
<td></td>
</tr>
</tbody>
</table>


## Meta-Analysis: Probability of Death with intensive glucose-lowering versus standard treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKPDS</td>
<td>0.79 (0.53, 1.20)</td>
<td>10.05</td>
</tr>
<tr>
<td>PPROactive</td>
<td>0.96 (0.77, 1.19)</td>
<td>21.47</td>
</tr>
<tr>
<td>ADVANCE</td>
<td>0.93 (0.82, 1.05)</td>
<td>29.38</td>
</tr>
<tr>
<td>VADT</td>
<td>1.09 (0.81, 1.47)</td>
<td>15.46</td>
</tr>
<tr>
<td>ACCORD</td>
<td>1.28 (1.06, 1.54)</td>
<td>23.64</td>
</tr>
<tr>
<td>Overall</td>
<td>1.02 (0.87, 1.19)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

I-squared = 58% (95% CI 0% to 84%), p = 0.048

Intensive therapy better vs. standard therapy better
KYOTO HEART Study

- To examine whether valsartan added to conventional anti-hypertensive treatment influences CV events in high-risk Japanese patients w/ uncontrolled HTN

- Two groups (n = 3031)
  - Valsartan add-on
    - 80 mg Q AM initially then double after 4 weeks if target BP >140/90 mmHg (or >130/80 in pts with diabetes or renal disease)
  - Conventional therapy
    - All other anti hypertensives to target BP except ACEI and ARBs

Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Valsartan (n = 1517)</th>
<th>Non-ARB (n = 1514)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 (11)</td>
<td>66 (11)</td>
</tr>
<tr>
<td>Men/Women</td>
<td>861/656 (57/43%)</td>
<td>867/647 (57/43%)</td>
</tr>
<tr>
<td>HF</td>
<td>84 (6%)</td>
<td>109 (7%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>401 (26%)</td>
<td>406 (27%)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>63 (10)</td>
<td>63 (9)</td>
</tr>
<tr>
<td>SCR</td>
<td>0.87 (0.35)</td>
<td>0.84 (0.38)</td>
</tr>
<tr>
<td>Meds at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEIs</td>
<td>289 (19%)</td>
<td>305 (20%)</td>
</tr>
<tr>
<td>CCBs</td>
<td>825 (54%)</td>
<td>832 (55%)</td>
</tr>
<tr>
<td>BBs</td>
<td>264 (17%)</td>
<td>277 (18%)</td>
</tr>
<tr>
<td>Statin</td>
<td>491 (32%)</td>
<td>503 (33%)</td>
</tr>
<tr>
<td>Antiplatelet Agent</td>
<td>402 (26%)</td>
<td>427 (28%)</td>
</tr>
</tbody>
</table>
RESULTS

- In both groups, BP:
  - Baseline = 157/88 mmHg
  - End of Study = 133/76 mmHg

- Compared with non-ARB arm, valsartan add-on arm had fewer primary endpoints
  - 83 vs. 155; HR 0.55, 95% CI 0.42–0.72, P < 0.0001

### Top 10 Countries/territories of number of people with diabetes (20-79 years), 2011 and 2030

<table>
<thead>
<tr>
<th>COUNTRY / TERRITORY</th>
<th>2011 MILLIONS</th>
<th>COUNTRY / TERRITORY</th>
<th>2030 MILLIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. China</td>
<td>90.0</td>
<td>1. China</td>
<td>129.7</td>
</tr>
<tr>
<td>2. India</td>
<td>61.3</td>
<td>2. India</td>
<td>101.2</td>
</tr>
<tr>
<td>3. United States of America</td>
<td>23.7</td>
<td>3. United States of America</td>
<td>29.6</td>
</tr>
<tr>
<td>4. Russian Federation</td>
<td>12.6</td>
<td>4. Brazil</td>
<td>19.6</td>
</tr>
<tr>
<td>5. Brazil</td>
<td>12.4</td>
<td>5. Bangladesh</td>
<td>16.8</td>
</tr>
<tr>
<td>6. Japan</td>
<td>10.7</td>
<td>6. Mexico</td>
<td>16.4</td>
</tr>
<tr>
<td>7. Mexico</td>
<td>10.3</td>
<td>7. Russian Federation</td>
<td>14.1</td>
</tr>
<tr>
<td>8. Bangladesh</td>
<td>8.4</td>
<td>8. Egypt</td>
<td>12.4</td>
</tr>
<tr>
<td>9. Egypt</td>
<td>7.3</td>
<td>9. Indonesia</td>
<td>11.8</td>
</tr>
<tr>
<td>10. Indonesia</td>
<td>7.3</td>
<td>10. Pakistan</td>
<td>11.4</td>
</tr>
</tbody>
</table>

International Diabetes Federation, Diabetes Atlas, 5th Edition

### Table 2.1. Top 10 countries/territories for prevalence* (%) of diabetes (20-79 years), 2011 and 2030

<table>
<thead>
<tr>
<th>COUNTRY / TERRITORY</th>
<th>2011 PREVALENCE (%)</th>
<th>COUNTRY / TERRITORY</th>
<th>2030 PREVALENCE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Kiribati</td>
<td>65.7</td>
<td>1. Kiribati</td>
<td>26.3</td>
</tr>
<tr>
<td>4. Nauru</td>
<td>20.7</td>
<td>4. Tuvalu</td>
<td>20.8</td>
</tr>
<tr>
<td>5. Lebanon</td>
<td>20.2</td>
<td>5. Nauru</td>
<td>20.7</td>
</tr>
<tr>
<td>7. Saudi Arabia</td>
<td>20.0</td>
<td>7. Lebanon</td>
<td>20.4</td>
</tr>
<tr>
<td>8. Bahrain</td>
<td>19.9</td>
<td>8. Qatar</td>
<td>20.4</td>
</tr>
<tr>
<td>10. United Arab Emirates</td>
<td>19.2</td>
<td>10. United Arab Emirates</td>
<td>19.8</td>
</tr>
</tbody>
</table>

*comparative prevalence

International Diabetes Federation, Diabetes Atlas, 5th Edition