Type 1 Diabetic

- 53 year old man diagnosed with T1DM age 15. Family Hx significant for father who as ASCVD with CABG age 65 and Paternal GF who died of MI age 65
  - A1c since 2003 A1c 5.6-6.1%
- In 2003 at age 42
  - weighed 170 lbs, BMI 23.5
  - BP 100/60
  - A1c 5.6%
  - TC 196 LDL 132, HDL 44, TG 101
  - Urine microalbumin/creat + 69 (<30)
  - No retinopathy
  - Training for a triathlon
### Type 1 Diabetic Risk Assessment

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Your Answer</th>
<th>Points</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: Male, Female</td>
<td>Male</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Age: 42 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker: Yes, No</td>
<td>Yes</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>Diabetes: Yes, No</td>
<td>Yes</td>
<td>2</td>
<td>High</td>
</tr>
<tr>
<td>Blood Pressure: 100/60 mm Hg</td>
<td></td>
<td>0</td>
<td>Very Low</td>
</tr>
<tr>
<td>LDL Cholesterol:</td>
<td>132 mg/dl</td>
<td>0</td>
<td>Moderate</td>
</tr>
<tr>
<td>HDL Cholesterol:</td>
<td>44 mg/dl</td>
<td>1</td>
<td>High</td>
</tr>
</tbody>
</table>

**Total Points:** 4  
**7% risk of heart disease in 10 years**

Average 10-year risk = 7% (for others in your age group)

Low 10-year risk = 4% (for others in your age group)

---

### Type 1 Diabetic Risk Assessment

#### Framingham Risk Score

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Your Answer</th>
<th>Points</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: Male, Female</td>
<td>Male</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Age: 53 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker: Yes, No</td>
<td>Yes</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>Diabetes: Yes, No</td>
<td>Yes</td>
<td>2</td>
<td>High</td>
</tr>
<tr>
<td>Blood Pressure: 132/84 mm Hg</td>
<td></td>
<td>1</td>
<td>Moderate</td>
</tr>
<tr>
<td>LDL Cholesterol:</td>
<td>121 mg/dl</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>HDL Cholesterol:</td>
<td>40 mg/dl</td>
<td>1</td>
<td>High</td>
</tr>
</tbody>
</table>

**Total Points:** 7  
**14% risk of heart disease in 10 years**

Average 10-year risk = 14% (for others in your age group)

Low 10-year risk = 6% (for others in your age group)
Type 1 Diabetic

- 53 year old diagnosed with T1DM age 15. Family Hx significant for father who as ASCVD with CABG age 65 and Paternal GF who died of MI age 65
  - A1c since 2003 A1c 5.6-6.1%

- In 2013 at age 53
  - weighed 181 lbs, BMI 26.2
  - BP 132/84
  - A1c 6.7%
  - TC 182 LDL 121, HDL 40, TG 120
  - Urine microalbumin/creat + 69 (<30)
  - No retinopathy

- Reports left arm numbness and dyspnea walking up 4-5 flights of stairs
Type 1 Diabetic UKPDS 10 & 20 yr Risk Assessment

- **UKPDS Risk Score**

<table>
<thead>
<tr>
<th>Information</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53 years</td>
</tr>
<tr>
<td>Weight</td>
<td>82 kg</td>
</tr>
<tr>
<td>Height</td>
<td>178 cm</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.1 mmol/L</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>5.068 mmol/L</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>132 mmHg</td>
</tr>
<tr>
<td>Smoker</td>
<td>No</td>
</tr>
<tr>
<td>Afro-Caribbean ethnicity?</td>
<td>No</td>
</tr>
<tr>
<td>HbA1c</td>
<td>6.7 %</td>
</tr>
<tr>
<td>Time Period</td>
<td>10 years</td>
</tr>
<tr>
<td>Regular Exercise per week</td>
<td>2 Times</td>
</tr>
</tbody>
</table>

10 yr risk 11.95%, 32.76% if Caucasian

---

Type 1 Diabetic

- EKG unremarkable
- Referred to cardiologist that afternoon
- Given his story and risk factors, coronary catheterization was recommended.
- What did the cath show?
Type 2 Diabetic

- 56 year old African American man presents with new onset diabetes in 1996
- Family hx: + T2DM in sister, brother. Father died at age 85 of CHF
- BMI 29.2
- A1c is 7.8%
- Urine micro/creatinine 47 (<30)
- BP 142/90
- LDL 139, HDL 89
- Started on
  - ecASA
  - Metformin 1000 mg bid
  - Ramipril 5 mg daily
  - Lipitor 10 mg daily

UKPDS Risk Assessment

10 yr Risk 2.35, 20 yr risk 7.14
If HDL 30: 9.37, 26.43
UKPDS Risk Assessment 10 yrs. Later

<table>
<thead>
<tr>
<th>Information</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66</td>
</tr>
<tr>
<td>Weight</td>
<td>87.09</td>
</tr>
<tr>
<td>Height</td>
<td>172</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>0.801</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>4.42</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>102</td>
</tr>
<tr>
<td>Smoker</td>
<td>No</td>
</tr>
<tr>
<td>Afro-Caribbean ethnicity?</td>
<td>No</td>
</tr>
<tr>
<td>HbA1c</td>
<td>9</td>
</tr>
<tr>
<td>Time Period</td>
<td>20</td>
</tr>
<tr>
<td>Regular Exercise per week</td>
<td>More than 5 times</td>
</tr>
</tbody>
</table>

10 yr Risk: 3.61%, 20 yr Risk: 10.85%
IF HDL was 30: 14.14, 36.4

Type 2 diabetes
Evidence for interventions
Blood glucose or blood pressure?
UKPDS 38. BMJ 1998;317:703–713

- UKPDS provides the most important evidence
- Recruited 5,102 newly diagnosed diabetics, aged 25 to 65 (Fasting blood glucose > 6mmol/l)
- Initially treated for 3 months with diet and advice
- Three main components:
  - Blood glucose: intensive BG vs. conventional BG (+ insulin and sulphonylurea comparisons)
  - Metformin: intensive BG control with metformin vs. SU/insulin in overweight patients
  - Blood pressure: tight BP vs. less tight control (+ ACE Inhibitor and ß-blocker comparisons)

What did UKPDS show us?
UKPDS 38. BMJ 1998;317:703–713

Take 100 people such as those in UKPDS

If you control blood sugar intensively with insulin or sulphonylurea:
- Over 10 years, you stop about 3 people developing microvascular complications (mainly because about 3 people don’t need retinal photocoagulation)
- You don’t stop anyone going blind, or prevent any deaths, strokes or (probably) any heart attacks

If you use metformin to control blood glucose (overweight & obese people):
- Over 10 years, you stop about 7 people having a heart attack and about 5 from dying from diabetes complications and about 8 from dying from any cause
- You don’t stop anyone developing microvascular complications

If you control their BP:
- Over 8 years, you stop about 4 people from having a stroke, about 5 from dying from diabetes complications and about 5 from having microvascular problems
Type 2 Diabetic 10 years later, age 66

- BMI 29.29
- A1c has ranged from 7.3 to 9.0%
- Urine micro/creatine 5 (<30)
- BP 102/66
- LDL 85, HDL 77
- Urine microalbumin/creatinine: normal
- Now on
  - ecASA
  - Metformin 1000 mg bid
  - Ramipril 5 mg daily
  - Cardura 4 mg daily
  - Lipitor 10 mg daily
  - Repaglinide 2 mg with meals
  - Lantus 25 units qhs

Type 2 Diabetic 18 years later, age 74

- BMI 29.07
- A1c has ranged from 7.6 to 9.0%
- Urine micro/creatine 15 (<30)
- BP 141/86
- LDL 75, HDL 69
- Now on
  - ecASA 81 mg daily
  - Metformin 1000 mg bid
  - Ramipril 5 mg daily
  - Cardura 4 mg daily
  - Lipitor 20 mg daily
  - Januvia 100 mg daily- often forgets
  - Lantus 25 units qhs
  - Novolog 6 units with meals- often forgets
10-year follow-up of UKPDS

...still no convincing evidence that tight control of blood glucose in type 2 diabetes reduces CV risk

- **Observational** follow-up of the blood glucose part of the study
- Baseline differences in mean HbA$_1c$ levels lost by 1 year, but despite this...
- ...**Continued reduction in microvascular risk and emergent reduction in macrovascular risk seen with intensive vs. conventional therapy**
- Significant risk reductions also persisted with metformin, in the sub-study of overweight patients

- **BUT these are observational data**
  - Need to compare with original UKPDS RCT data
  - Should not be used to promote early, very intensive glucose-lowering treatment for all patients with type 2 diabetes

- **And we now have ACCORD, ADVANCE and VADT**
  - Large RCTs set up to assess whether intensive glucose control strategies offered any advantage over standard therapies with regard to major CV events
  - Found no significant improvements in macrovascular events with intensive glucose control
  - In ACCORD, intensive therapy was associated with an **increased** risk of death
What did the ACCORD study show?


- RCT of 10,251 patients (mean age 62 years) with type 2 diabetes and elevated CV risk
- Randomized to intensive glucose-lowering (target HbA1c <6.0%) or standard therapy (target HbA1c 7.0–7.9%)
- Intensive treatment stopped early, after 3.5 years, because of higher all-cause mortality
- Primary endpoint (MI, stroke or CV death) did not differ between groups

<table>
<thead>
<tr>
<th></th>
<th>Intensive therapy</th>
<th>Standard therapy</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable median HbA1c at 1 year</td>
<td>6.4%</td>
<td>7.5%</td>
<td>-</td>
</tr>
<tr>
<td>Primary endpoint (MI, stroke or CV death)</td>
<td>6.9%</td>
<td>7.2%</td>
<td>0.90 (0.78–1.04); P=0.16 Not significant</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>5.0%</td>
<td>4.0%</td>
<td>1.22 (1.01–1.46); P=0.04; NNH=95</td>
</tr>
</tbody>
</table>

What about ADVANCE?


- RCT of 11,140 patients (mean age 66 years) with type 2 diabetes and elevated CV risk
- Randomized to intensive gliclazide-based glucose-lowering (target HbA1c <6.5%) or standard therapy (target based on local guidelines)
- Median follow-up 5 years
- Intensive therapy showed no significant effect on macrovascular events or all-cause mortality, but it did reduce nephropathy

<table>
<thead>
<tr>
<th></th>
<th>Intensive therapy</th>
<th>Standard therapy</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HbA1c</td>
<td>6.5%</td>
<td>7.3%</td>
<td>-</td>
</tr>
<tr>
<td>Macrovascular primary endpoint (MI, stroke or CV death)</td>
<td>10.0%</td>
<td>10.6%</td>
<td>0.94 (0.84–1.06); P=0.32 Not significant</td>
</tr>
<tr>
<td>Microvascular primary endpoint (new or worsening nephropathy or retinopathy)</td>
<td>9.4%</td>
<td>10.9%</td>
<td>0.86 (0.77–0.97); P=0.01; NNT=67</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>8.9%</td>
<td>9.6%</td>
<td>0.93 (0.83–1.06); P=0.28 Not significant</td>
</tr>
</tbody>
</table>
And now the Veterans Affairs Diabetes Trial (VADT)

- Open-label RCT of 1,791 people (mean age 60 years) with type 2 diabetes
  - Most did not smoke, had well-controlled BP and were taking a statin
- Randomized to intensive or standard glucose control with oral hypoglycemic drugs (including rosiglitazone) plus insulin if necessary. Other CV risk factors were treated uniformly
- Over a median follow-up of 5.6 years, intensive treatment to achieve a median HbA\(_1c\) of 6.9% compared with standard control to a median of 8.4% did not statistically significantly reduce the risk of:
  - Major CV events (MI, stroke, death from CV causes, CHF, surgery for vascular disease, inoperable coronary disease, amputation for ischemic gangrene), HR 0.88; 95% CI 0.74 to 1.05, P=0.14 or any of these component endpoints
  - All-cause mortality, HR 1.07; 95% CI 0.81 – 1.42; P=0.62
  - Any microvascular outcomes (ophthalmic, nephropathic or neuropathic)
- Patients in the intensive treatment arm were more likely to experience hypoglycaemic episodes

HbA\(_1c\) will rise over time — no matter how hard we try to control blood glucose?

From UKPDS 33
Type 1 DM with high CV risk

- 2003: 57 y/o woman with T2 DM, Dyslipidemia
- Presented with diabetes at age 50 after steroid treatment for a rash. Treated with pravachol 20 mg for hypercholesterolemia. Insulin added soon after diagnosis: 70/30 Regular bid then NPH and R.
- Weight 167 lbs. BMI 28.72
- BP 118/64
- A1C 11.2
- CHOL 192
- HDL 70
- TRI 73
- LDL 107
- No meter and states she usually does not check glucose
- Measured anti-bodies and stimulated C-Peptide
64 y/o Type 1 DM with high CV risk

- 2011: On Lantus and Humalog
- Has developed hypertension treated to 124/63 on Valsartan 40 mg daily
- A1C 10.7 7/25/2011
- CHOL 262 7/25/2011
- HDL 62 7/25/2011
- TRI 104 7/25/2011
- LDL 179 7/25/2011

- 2012 presents because she is “about to run out of meds.” Frequency of glucose monitoring: Few times per week. Has "given up"
10 year risk: 15.94%, 20 year risk: 41.83%

64 year old woman with Type 1 DM

- **2011**
  - A1C 10.7 7/25/2011
  - CHOL 262 7/25/2011
  - HDL 62 7/25/2011
  - TRI 104 7/25/2011
  - LDL 179 7/25/2011

- **2012** presents because she is “about to run out of meds.” Frequency of glucose monitoring: Few times per week. Has "given up"
Morbidly Obese Type 2 Diabetic

- 50 y/o with T2DM, HTN, Dyslipidemia
- Strong family hx of DM and ASCVD
- 331 lbs, BMI 50.3
- BP 160/86
- On: Glucophage, Glucotrol, Actos
- On: Lopressor 25 mg bid, Zestoretic 20/12.5 mg daily
- On: Lipitor 20 mg daily, ecASA 81 mg daily
- Labs
  - A1c 7.6%
  - LDL 94, HDL 41, TC 220
  - Urine microalbumin/cr 47

UKPDS Risk Assessment

10 year Risk: 13.22%, 20 yr Risk: 35.76%
Type 2 Diabetic, 1 yr. Post Gastric Bypass

- 50 y/o with T2DM, HTN, Dyslipidemia
- Strong family hx of DM and ASCVD
- 228 lbs, BMI 33.67
- BP 128/80
- On: Glucophage
- On: Lopressor 25 mg bid, Zestril 20 mg daily
- On: Lipitor 5 mg daily, ecASA 81 mg daily
- Labs
  - A1c 5.6%
  - LDL 57, HDL 43, TC 106
  - Urine microalbumin/cr 5-resolved

New UKPDS Risk Assessment?

10 yr Risk: 3.86%, 20 year Risk: 11.55%

vs.

10 year Risk: 13.22%, 20 yr Risk: 35.76%
# MESA-HNR diabetes CHD risk score

<table>
<thead>
<tr>
<th>Category</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Year risk: Add points from the 5 categories</td>
<td></td>
</tr>
<tr>
<td>Age:</td>
<td></td>
</tr>
<tr>
<td>&gt;65 years,</td>
<td>4</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Male,</td>
<td>4</td>
</tr>
<tr>
<td>Systolic bp:</td>
<td></td>
</tr>
<tr>
<td>&gt;135,</td>
<td>2</td>
</tr>
<tr>
<td>Duration of diabetes:</td>
<td></td>
</tr>
<tr>
<td>&gt;0 years,</td>
<td>3</td>
</tr>
<tr>
<td>Coronary Calc. Score</td>
<td></td>
</tr>
<tr>
<td>&lt;25,</td>
<td>-2</td>
</tr>
<tr>
<td>25 to &lt;125,</td>
<td>0</td>
</tr>
<tr>
<td>125 to &lt;400,</td>
<td>4</td>
</tr>
<tr>
<td>≥400,</td>
<td>16</td>
</tr>
</tbody>
</table>

Coronary Calc. Score

Less than 1 point indicates less than 1% risk, otherwise 1 point is ~1% risk of 8 year coronary heart disease event. He is 7%

## Failings of these Risk Calculators

- Doesn’t take into account the number of drugs needed to control diabetes, hypertension
- Doesn’t take into account previous control of these measures/metabolic memory
- UKPDS does not have a category for “no exercise”
Questions?