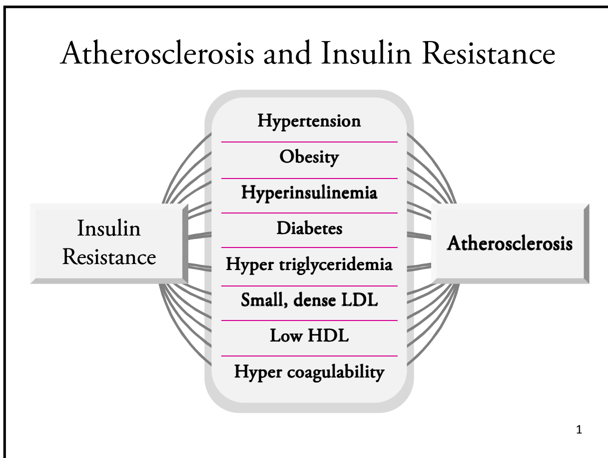
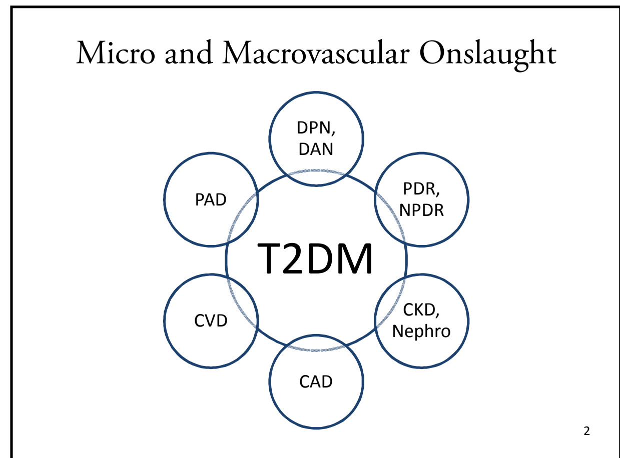
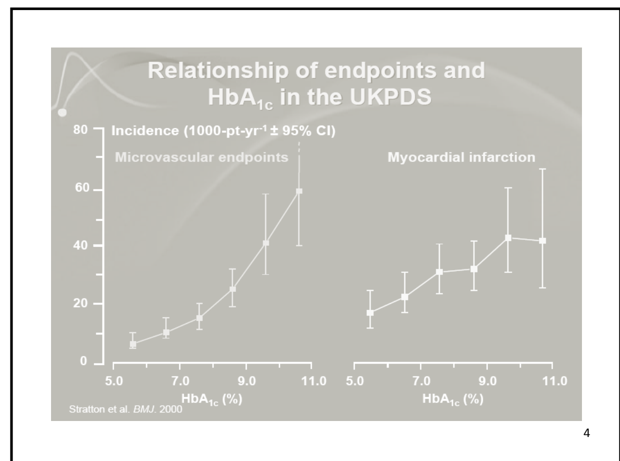


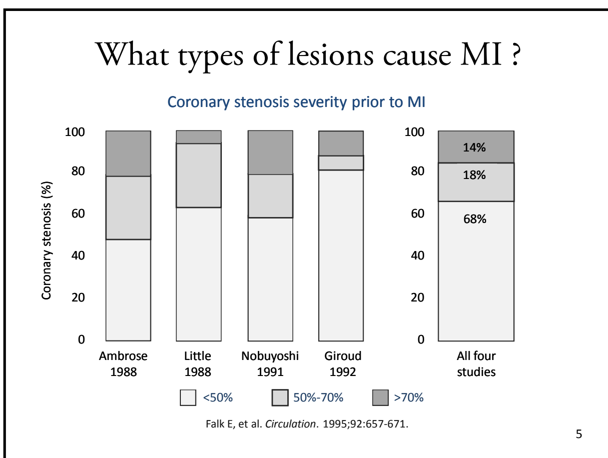



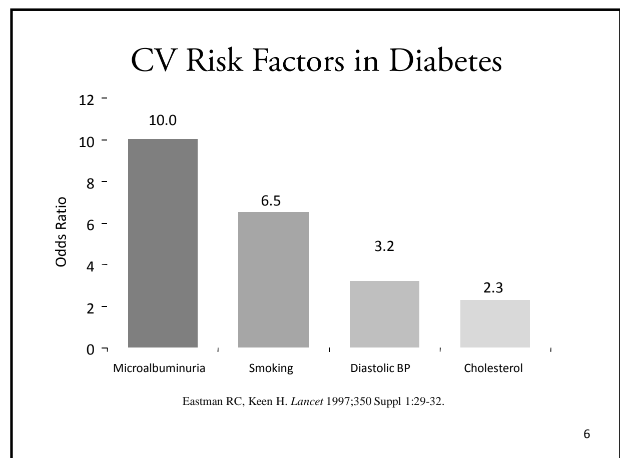

# Ticking Clock of T2DM

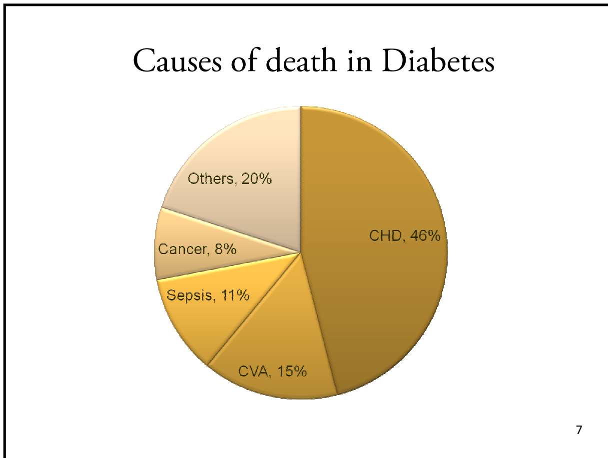
1. Micro-vascular (DR, CKD, DPN, DAN)
   - At the onset of hyperglycemia
   - Control of hyperglycemia essential
   - The A1c target of less than 7 must (A)
2. Macro-vascular (CAD, CVD, PVD)
   - At the onset of insulin resistance
   - Blood pressure goal of 130/80 (B)
   - Control of lipid abnormalities (C)

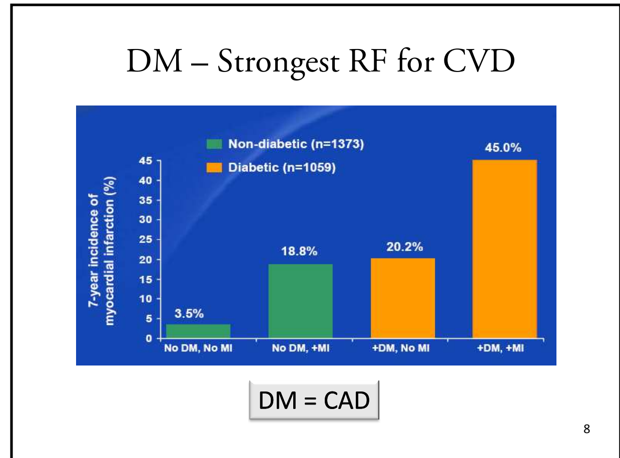
3

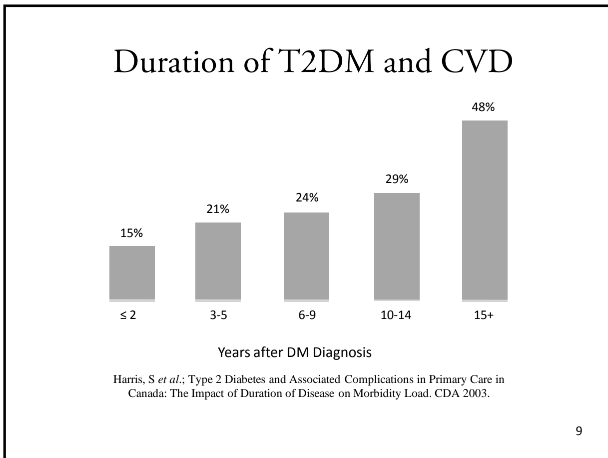


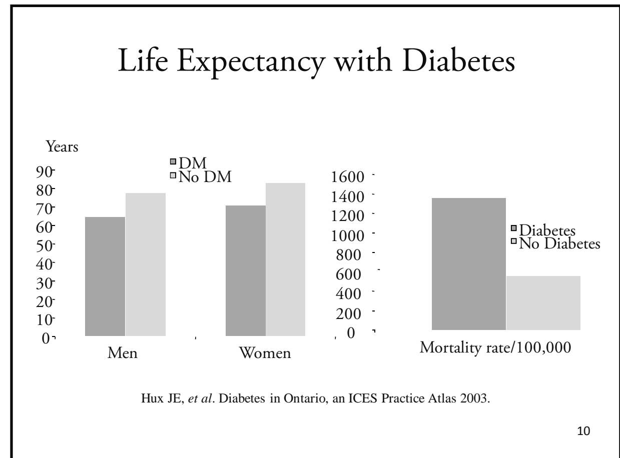



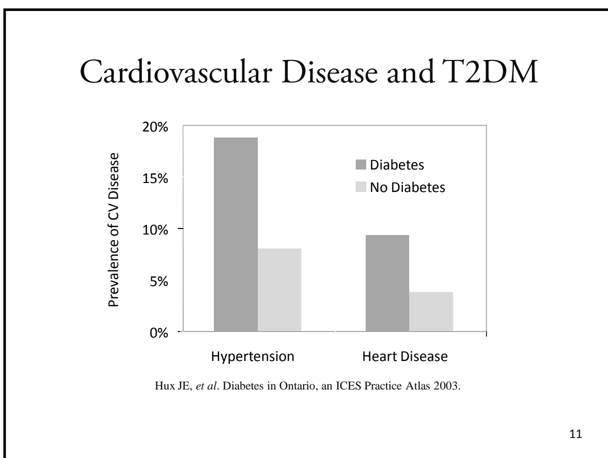



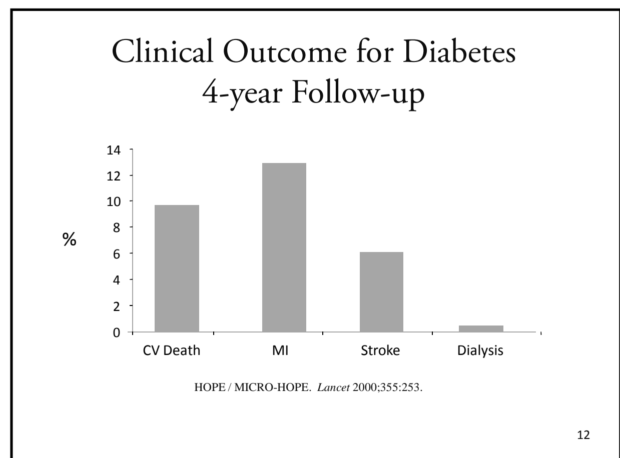

Causes of death in Diabetes
Others, 20%
CHD, 46%
Cancer, 8%
Sepsis, 11%
CVA, 15%
7


DM – Strongest RF for CVD
Non-diabetic (n=1373)
Diabetic (n=1059)
7-year incidence of myocardial infarction (%)
3.5%
18.8%
20.2%
45.0%
No DM, No MI
No DM, +MI
+DM, No MI
+DM, +MI
DM = CAD
8

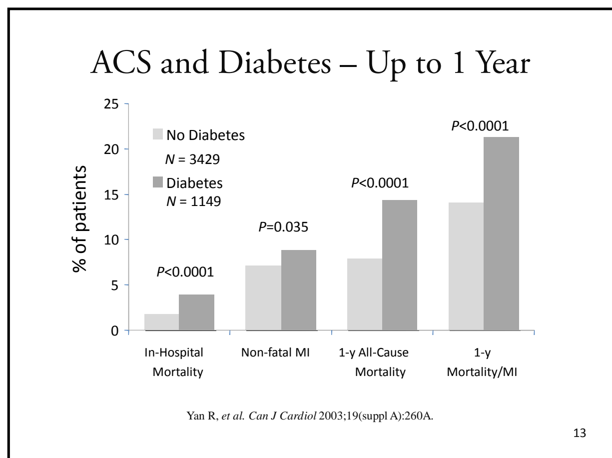

Duration of T2DM and CVD
15%
21%
24%
29%
48%
≤ 2
3-5
6-9
10-14
15+
Years after DM Diagnosis
Harris, S et al.; Type 2 Diabetes and Associated Complications in Primary Care in Canada: The Impact of Duration of Disease on Morbidity Load. CDA 2003.
9


Life Expectancy with Diabetes
Years
DM
No DM
Men
Women
Diabetes
No Diabetes
Mortality rate/100,000
Hux JE, et al. Diabetes in Ontario, an ICES Practice Atlas 2003.
10


Cardiovascular Disease and T2DM
Prevalence of CV Disease
Diabetes
No Diabetes
Hypertension
Heart Disease
Hux JE, et al. Diabetes in Ontario, an ICES Practice Atlas 2003.
11


Clinical Outcome for Diabetes
4-year Follow-up
%
CV Death
MI
Stroke
Dialysis
HOPE / MICRO-HOPE. Lancet 2000;355:253.
12

## ACS and Diabetes – Up to 1 Year




Yan R, *et al. Can J Cardiol* 2003;19(suppl A):260A.

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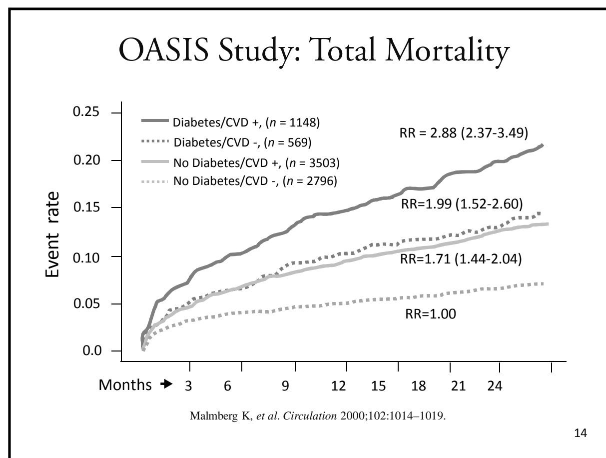
## OASIS Study: Total Mortality




Malmberg K, *et al. Circulation* 2000;102:1014–1019.

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## Predictors of CV Risk in DM

- **Age; But Gender looses its power**
- **MAU (Microalbuminuria)**
- **W/Ht Ratio (Abdominal Obesity)**
- **LP(a) (Lipoprotein small 'a')**
- **LDL Cholesterol**
- **Not the Glycemic levels !!**

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## DM = CAD - Because

- CVD is responsible for 60 - 75% of mortality in T2DM
- CVD is 4 times more prevalent in diabetes; CADI is more
- CVD prevalence increases with age, so is T2DM
- CVD in DM is often severe, silent, poor prognosis and fatal
- Diabetes ↑ mortality, 50% pre adm / recurrent MI and ACS
- Diabetes erases the protection conferred to women
- At diagnosis of T2DM, most patients have evidence of CVD
- Abnormal Glucose tolerance is a strong CV Risk factor

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## Dyslipidemia in DM and IRS

- Elevated total TG
- Reduced HDL
- Small, dense LDL

} LDL Level of 180 to 220 mg

- ↑ $HDL_3$ and ↓ $HDL_1$ and $HDL_2$
- LDL is not usually high
- Postprandial Hyper lipemia
- Lipemia Retinalis

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## Small Dense LDL and CHD
### Potential Atherogenic Mechanisms

- Increased susceptibility to oxidation
- Increased vascular permeability
- Increased binding to arterial wall proteoglycons
- Conformational change in Apo B
- ↓ Affinity for LDL receptor (↓ clearance)
- Association with insulin resistance syndrome
- Association with high TG and low HDL

Austin MA et al. *Curr Opin Lipidol* 1996;7:167-171.

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## Glycemic control alone is hopelessly inadequate !!

The A B C of Diabetes Management

A A1c (Hb A1c)
B Blood pressure (goal)
C Cholesterol (all lipids)

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## How to offer Vascular Protection ?

1. ACE inhibitors or ARBs
2. ASA (Acetyl Salicylic Acid)
3. Atorvastatin (Lipid management)
4. A1c control (Glycemic control)
5. Blood pressure goal (<130/80)
6. Control of Nephropathy, Proteinuria (MAU)
7. Cigarette smoking cessation
8. Weight and waist management
9. Physical Activity – at least 2 km/d x 5 d

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## Goals in T2DM for VP

| Risk Factor | Goal or Target |
|---|---|
| Glycemia | Hb A1c < 6.5% |
| Blood Pressure | < 130/80 mm Hg |
| LDL target | < 100 mg%; better < 70 |
| HDL target | > 40 men, > 50 women |
| TG target | < 150 mg% |
| BMI | < 25 kg/m² |
| Physical activity | At least 5 days - 2 km/day |

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## From Blood Sugar to Blood Vessel

| ACEi (Ramipril) | Vasoprotective, anti HT, ↓ ED |
|---|---|
| ASA (75 to 150 mg%) | Anti inflamm., Anti Platelet |
| Statin (Powerful, full) | ↓ LDL, TG, Corrects ED, Inflam |
| BP Goal | Vascular damage, LVH, CVA |
| Glycemic control | ↓ Micro vascular ? Macrovascular |
| Physical activity | ED, ↓ Inflammation, ↑ HDL |
| Diet and TLC | ↓ TG, LDL, Glycemia, Weight |
| Smoking cessation | ↓ ED and Inflammation |

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## ACEi in T2DM - VP

- Antihypertensive, vasoprotective, anti-thrombotic, and anti-inflammatory properties –Must for all DM
- Reduce CV events, Reduce atherosclerosis
- Reduce renal disease which is a strong CV risk factor
- Metabolically 'friendly' drugs that prevent rises in glucose & prevent diabetes
- Well-tolerated with few side effects

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## Paradigm Shift in T2DM

| About 10 to 15 years ago | Diabetes as of now |
|---|---|
| 1. Only Dysglycemia | 1. Cardiometabolic disease |
| 2. Urine, RBG, GTT | 2. Hb $A_1c$, FBG, PPBG |
| 3. Insulin deficiency | 3. Insulin Resistance, ID |
| 4. Secretagogues – SU | 4. Metformin, Glitazones |
| 5. β cell stimulation | 5. Beta cell preservation |
| 6. Insulin as a last resort | 6. Early Insulin use |
| 7. Treatment of DM only | 7. Prevention; Intense Rx. |
| 8. BG > 180, No IFG, IGT | 8. Pre DM (IFG, IGT), DM |
| 9. Blood Sugar Disease | 9. Blood vessel; guardian Rx. |
| 10. DM is a mild disease | 10. DM = CAD; Prevention |
| 11. Emphasis on complic. less | 11. MAU, Micro, Macro com. |

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