

***‘New Clinical Solutions  
in Diabetes Care’  
‘Triumphing Against  
Adversity’***

# **UKPDS AND CVD RISK ASSESSMENT ARE RISK ASSESSMENT TOOLS USEFUL?**

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# Why do we treat Diabetes?

Symptoms

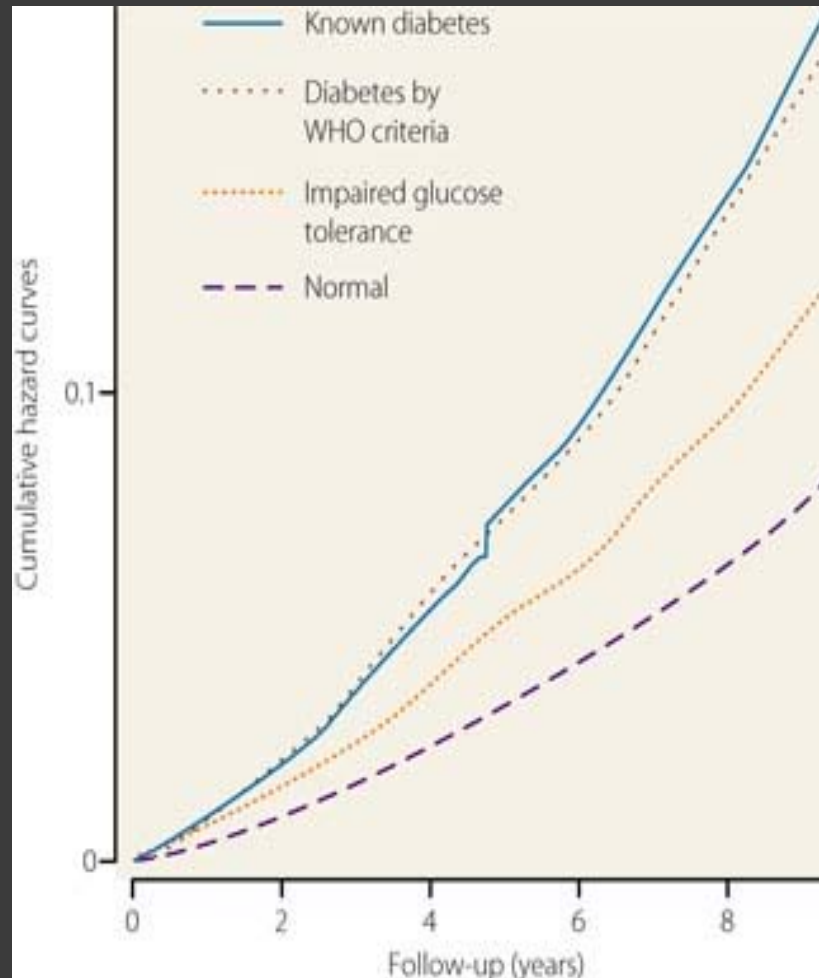
Acute Complications (DKA, HHS)

Long Term Complications

    Macrovascular

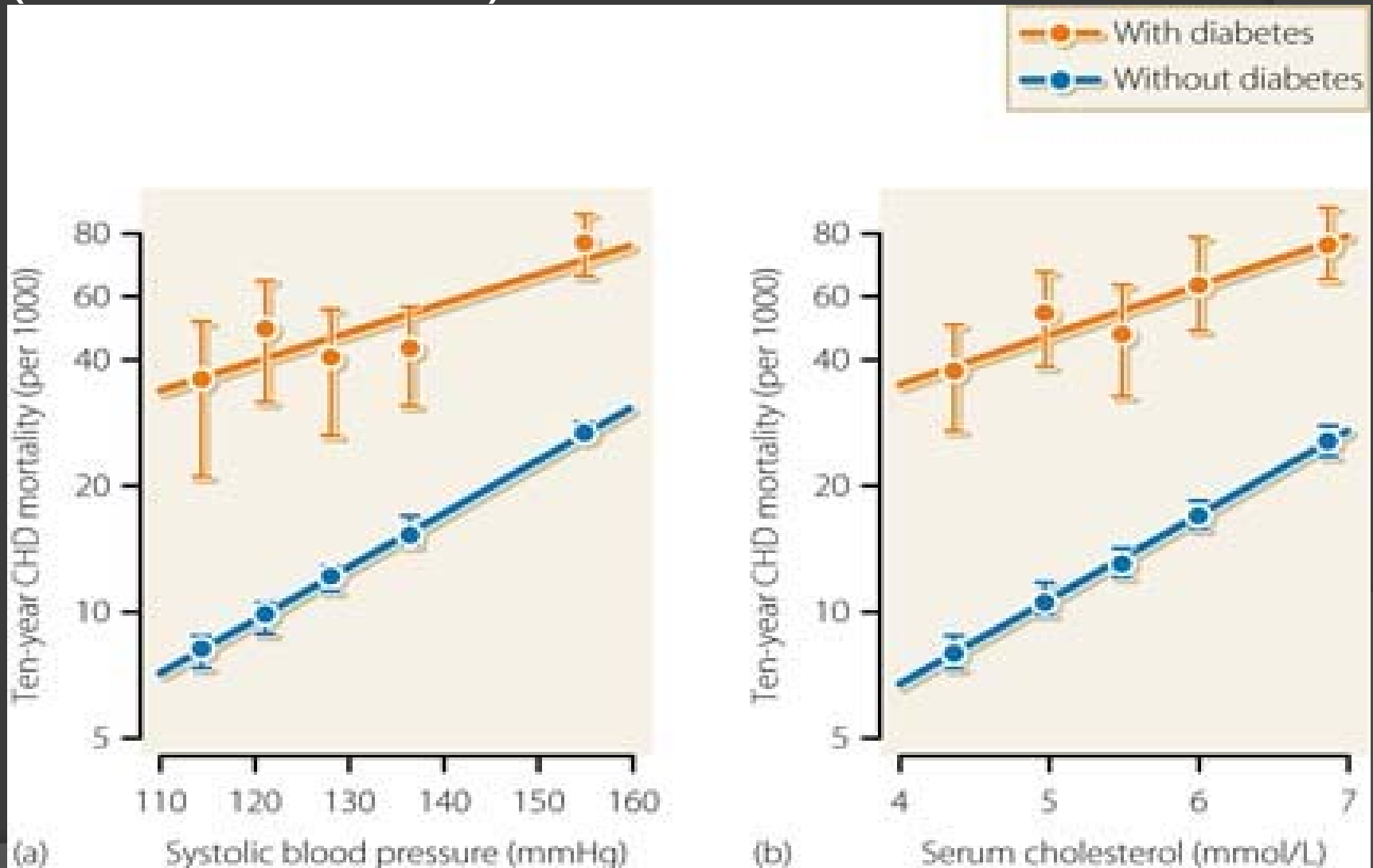
    Microvascular

# Diabetes is bad for you



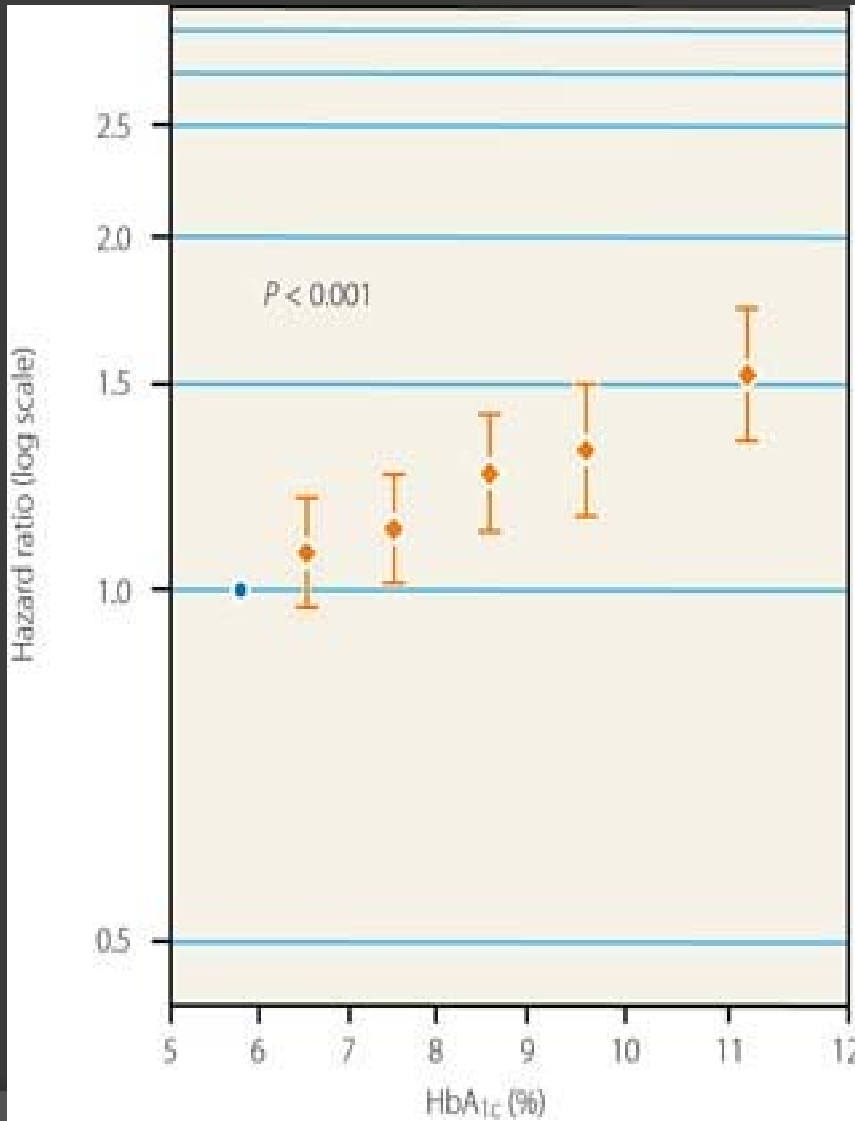
- DECODE STUDY
- Lancet 1999

# What kills people with diabetes? (MRFIT 1993)



# Poor Control is worse for CVD

- New Zealand Diabetic Med 2008





# What works?

1/ Blood pressure control

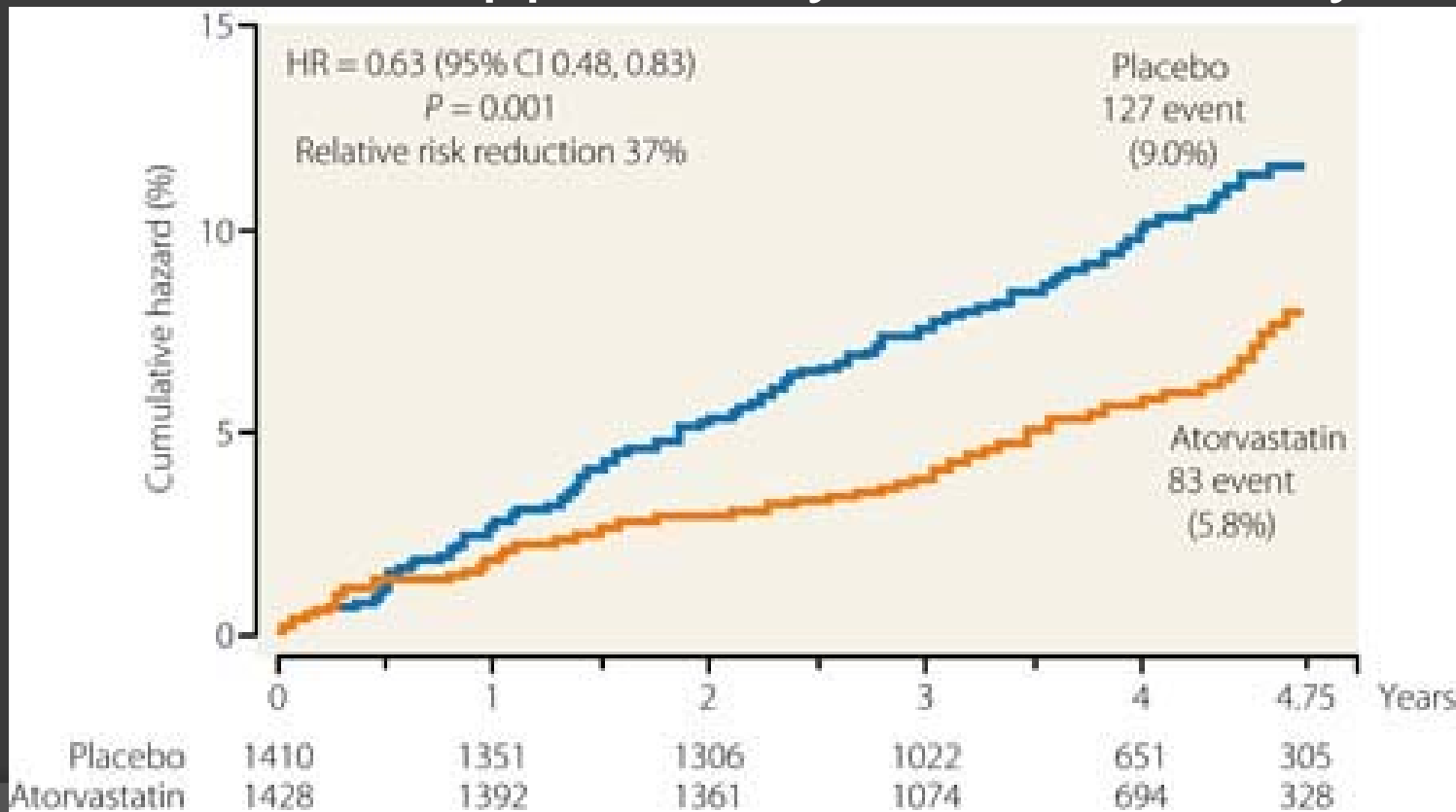
UKPDS BMJ 1998

44% RRR for CVA (21% NS for MI)

# What works?

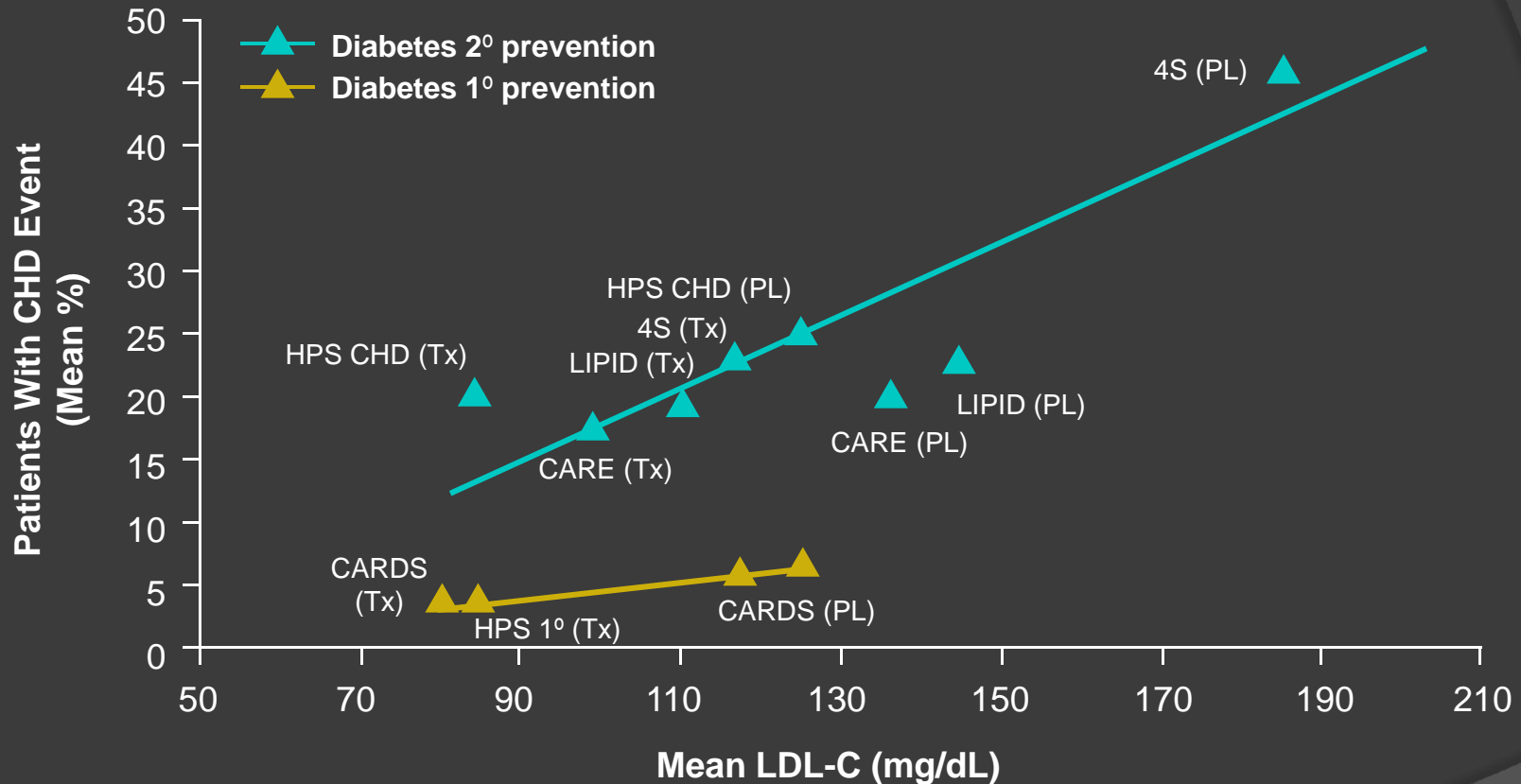
## 2/ Cholesterol Control

### CARDS – stopped early due to efficacy



# Results From Statin Trials

Reducing LDL reduces the risk of CHD events



Colhoun HM and the CARDS Investigators. Lancet. 2004;364:685-696.

Collins R and the Heart Protection Study Collaborative Group. Lancet. 2003;361:2005-2016.

Keech A et al. Diabetes Care. 2003;26:2713-2721.

Goldberg RB and the CARE Investigators. Circulation. 1998;98:2513-2519.

Pyörälä K et al. Diabetes Care. 1997;20:614-620.

# Calculations

- Framingham / CardioRisk
- UKPDS/ UKPDS (stroke)
- PROCAM
- SCORE
- DECODE
- Archimedes

<400 diabetics

poor discrimination

self reported diabetes

?CVD at start

theoretical physiology

# UKPDS vs Framingham

- ◉ Framingham underestimates
- ◉ UKPDS overestimates in males
- ◉ Both good at identifying high risk
- ◉ Both poor validity below 40yo
- ◉ UKPDS more recent and includes glycaemia as continuous variable (and ethnicity)
- ◉ No allowance for
  - ◉ Microalbuminuria
  - ◉ Strong Family History
  - ◉ Secondary prevention

# NICE / RCP Advisory Group

- “.... Manage nearly all people with Type 2 diabetes as having risk >20%/10-years particularly as outcome from MI is known to be worse for those with diabetes”
- Unless
  - Not overweight and
  - Normotensive and
  - Does not have microalb and
  - Does not smoke and
  - Does not have a high risk lipid profile
  - Has no family history of CVD

# JBS 2 2005

- ⦿ HPS; reduction in CHD and CVA similar to non diabetic
- ⦿ ASCOT; non significant as stopped early
- ⦿ CARDS primary prevention in diabetes. 2800 pts with dm and one other risk factor. 36% reduction in cardiac and 48% reduction in CVA
- ⦿ Recommend for all over 40 or for under 40 if microvasc or poor dm control or on antihypertensives or total chol >6 or fh
- ⦿ Uses Framingham- only 337 diabetics

# Treatment Goals in Type-2 Diabetes ESC/EASD

- ⦿ Glycaemic control
  - Maintain glycaemic targets for HbA1c (<7.0%)
- ⦿ Blood lipids
  - Reduce cholesterol to <4.5mmol/L (176mg/dL) and LDL to <2.5mmol/L (98mg/dL)
- ⦿ Blood pressure
  - Maintain at <130/80 mm Hg
- ⦿ Lifestyle
  - Maintain BMI at <25 kg/m<sup>2</sup>
  - Physical activity <30-45 min/day
  - Smoking cessation
  - Reduce intake of salt and dietary fat

# ADA 2008

- ⊙ >40 and
  - Smoker
  - Systolic >140 or on treatment
  - HDL <1.04 female, <1.3 male
  - Family history
- ⊙ <40 with “multiple risk factors
- ⊙ LDL >2.6mmol/l
- ⊙ Audit at EASD showed only 65% compliance in Cleveland Ohio (not the real Cleveland)

# SIGN

- “Lipid Lowering therapy with Simvastatin 40mg or Atorvastatin 10mg is recommended for primary prevention in all over 40yo regardless of baseline cholesterol”



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- > Conferences
- > Publications
- > Slides
- > Webcasts

#### Software

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- > EXSCEL
- > TECOS
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DIABETES TRIALS UNIT  
The Oxford Centre for Diabetes  
Endocrinology and Metabolism

# UKPDS Risk Engine

## Download

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The UKPDS Risk Engine is intended primarily for use by health care professionals to assist in the management of people with type 2 diabetes. The UKPDS Risk Engine is not a replacement for formal medical assessment and should only be used by patients in consultation with their trained medical adviser.

### Download the UKPDS Risk Engine

The Risk Engine software calculates coronary heart disease and stroke risk estimates for a single individual with Type 2 diabetes.

- [Windows](#)
- [Mac Classic and MacOS X](#)
- [Palm](#)
- [PocketPC](#)



## Input

Age now:  years

HbA1c:  %

Diabetes duration:  years

Systolic BP:  mm Hg

Sex:  Male  Female

Total cholesterol:  mmol/l

Atrial fibrillation:  No  Yes

HDL cholesterol:  mmol/l

Ethnicity:  ▼

Smoking:  ▼

Options <

## Number of values\*

HbA1c:

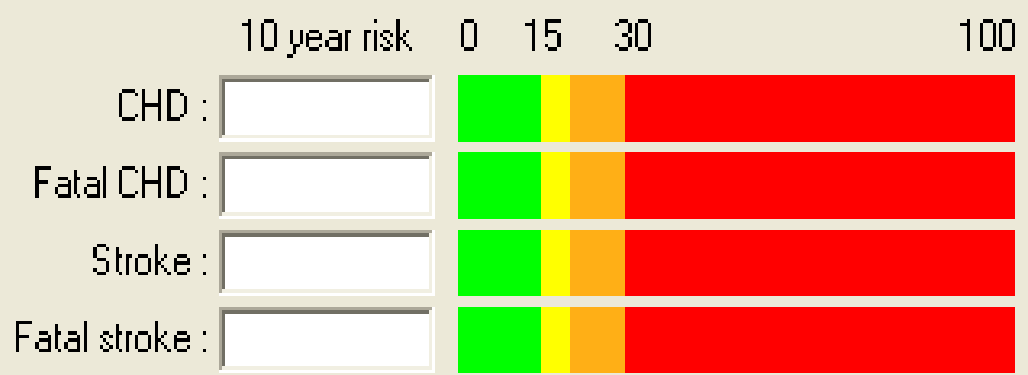
Systolic BP:

Total cholesterol:

*\* used to adjust for regression dilution*

Units:  mmol/l  
 mg/dl

## Output



## Risk interval

Risk over next  years

Calculate

Copy

Print

Defaults

Help

Exit

# Individualisation

- ⦿ Attitude to risk
- ⦿ Explanation of risk
- ⦿ Perception of side effects (muscle ache in upto 25% statin and placebo)
- ⦿ Deprivation / educational attainment- as risk factor (ACCORD) but also as challenge to compliance and negotiated management plan

# My patient

- Roper's paper
  - Beer- triglycerides
  - Sugar in tomato sauce
  - "can't afford fruit"
  - "all my family are this size"
  - ?Mental Health Problems / Learning Disabilities
  - Lack of supportive wife
  - Lack of exercise
- Communicating in terms of *a 10 year relative or absolute risk ratio for cardiovascular disease* is of limited value





Input

Age now :  years

HbA1c :  %

Diabetes duration :  years

Systolic BP :  mm Hg

Sex :  Male  Female

Total cholesterol :  mmol/l

Atrial fibrillation :  No  Yes

HDL cholesterol :  mmol/l

Ethnicity :

Smoking :

Options <

Number of values\*

HbA1c :

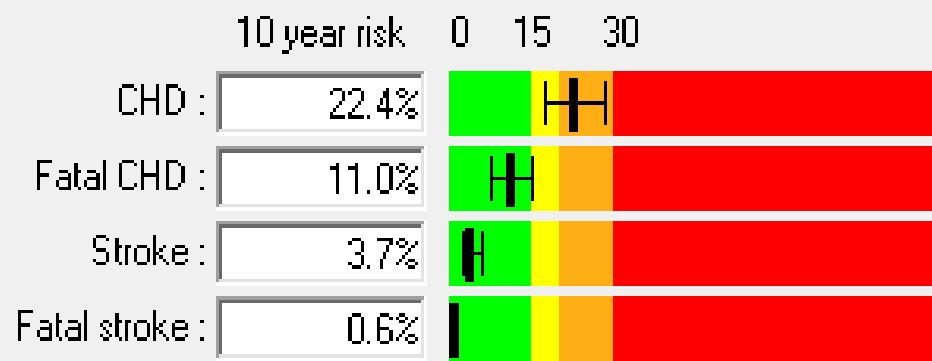
Systolic BP :

Total cholesterol :

\* used to adjust for regression dilution

Units :  mmol/l  
 mg/dl

Output



Risk interval

**Underestimates**

- Pack years
- Microalb
- Family history
- Lack of exercise
- ?late presentation
- ?20 year risk
- Etc.....

Calculate

Copy

Print

Help

Exit

# Your patients?

- Regular exercise
- Good compliance
  - Diet
  - Medications
  - Consultations
- Early Presentation
  - Diabetes
  - Complications
- Probably developed diabetes later in life
- Probably stopped smoking
- Motivated to address diet
- Wife motivated to read the packets





Input

Age now:  years

HbA1c:  %

Diabetes duration:  years

Systolic BP:  mm Hg

Sex:  Male  Female

Total cholesterol:  mmol/l

Atrial fibrillation:  No  Yes

HDL cholesterol:  mmol/l

Ethnicity:  ▼

Smoking:  ▼

Options <

Number of values\*

HbA1c:

Systolic BP:

Total cholesterol:

\* used to adjust for regression dilution

Units:  mmol/l

mg/dl

Output

10 year risk 0 15 30

CHD:

Fatal CHD:

Stroke:

Fatal stroke:

*Adjusted for regression dilution*

Calculate

Copy

Print

Help

Exit

•With the same risk markers



Input

Age now:  years

HbA1c:  %

Diabetes duration:  years

Systolic BP:  mm Hg

Sex:  Male  Female

Total cholesterol:  mmol/l

Atrial fibrillation:  No  Yes

HDL cholesterol:  mmol/l

Ethnicity:

Smoking:

Options <

Number of values\*

HbA1c:

Systolic BP:

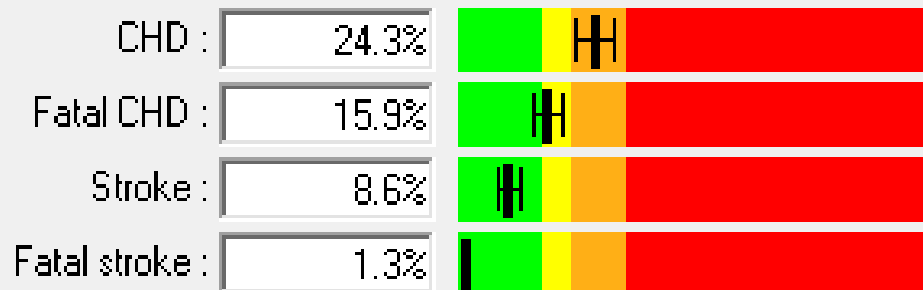
Total cholesterol:

\* used to adjust for regression dilution

Units:  mmol/l  
 mg/dl

Output

10 year risk 0 15 30



*Adjusted for regression dilution*

Risk interval

•And with better controlled risk factors.....

Calculate

Copy

Print

Help

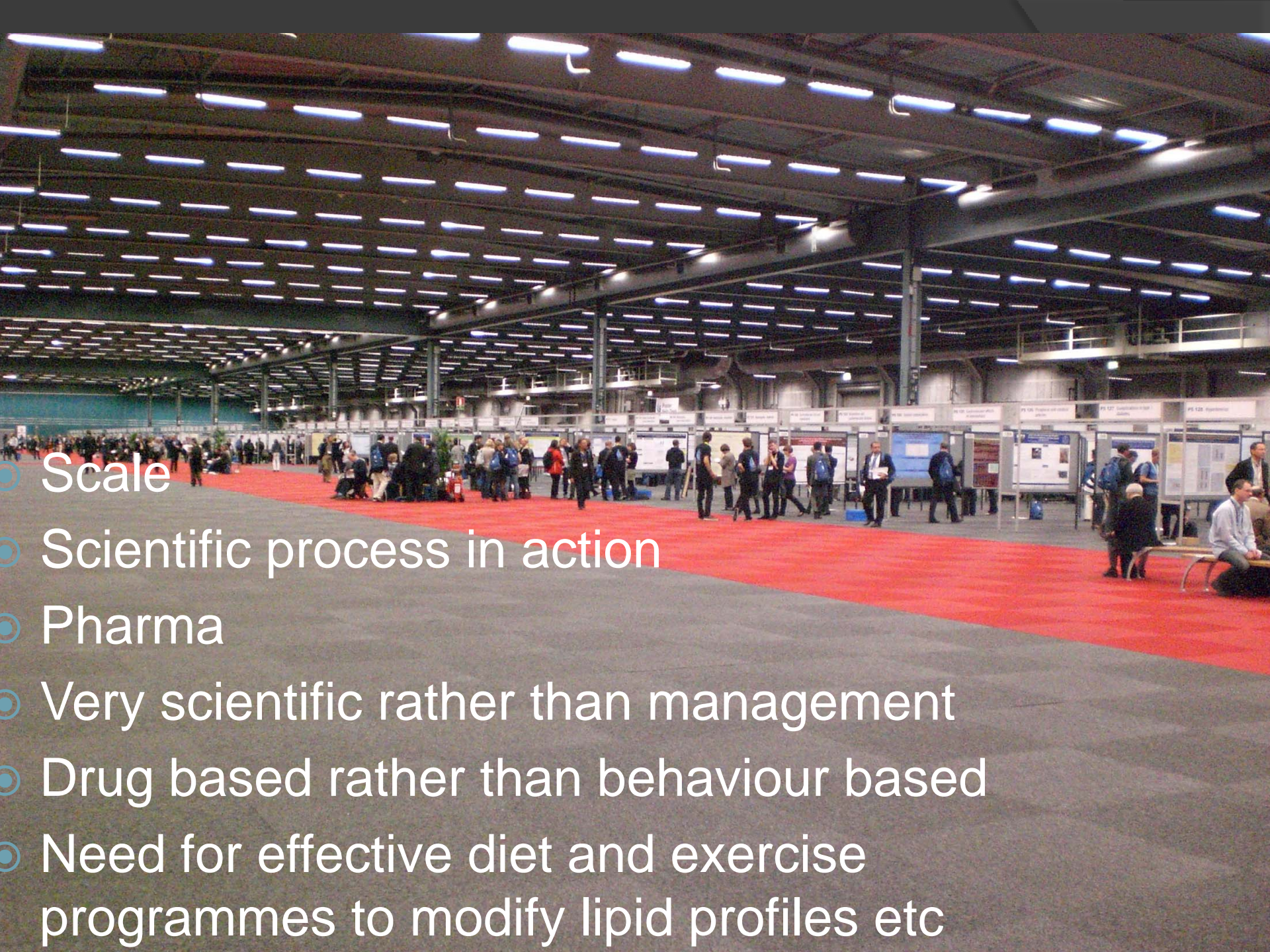
Exit



46th Annual Meeting

**EASD**

46th Annual Meeting of the European  
Association for the Study of Diabetes  
20 – 24 September 2010  
STOCKHOLM · SWEDEN



- Scale
- Scientific process in action
- Pharma
- Very scientific rather than management
- Drug based rather than behaviour based
- Need for effective diet and exercise programmes to modify lipid profiles etc

# ADDITION 2010

- UK Denmark Norway
- Screening followed by intensive/  
conventional
- Targeted screening viable
- No difference between groups
- Partly because conventional so good
- No comparison to non screened  
population

**UKPDS Risk Engine v2.0**

**Input**

Age now:  years      HbA1c:  %


Diabetes duration:  years      Systolic BP:  mm Hg


Sex:  Male  Female      Total cholesterol:  mmol/l


Atrial fibrillation:  No  Yes      HDL cholesterol:  mmol/l


**UKPDS Risk Engine**

The Risk Engine is not recommended for individuals who were under 20 when diabetes was first diagnosed.

CHD:  

Fatal CHD:  

Stroke:  

Fatal stroke:  



**Input**

Age now :  years

HbA1c :  %

Diabetes duration :  years

Systolic BP :  mm Hg

Sex :  Male  Female

Total cholesterol :  mmol/l

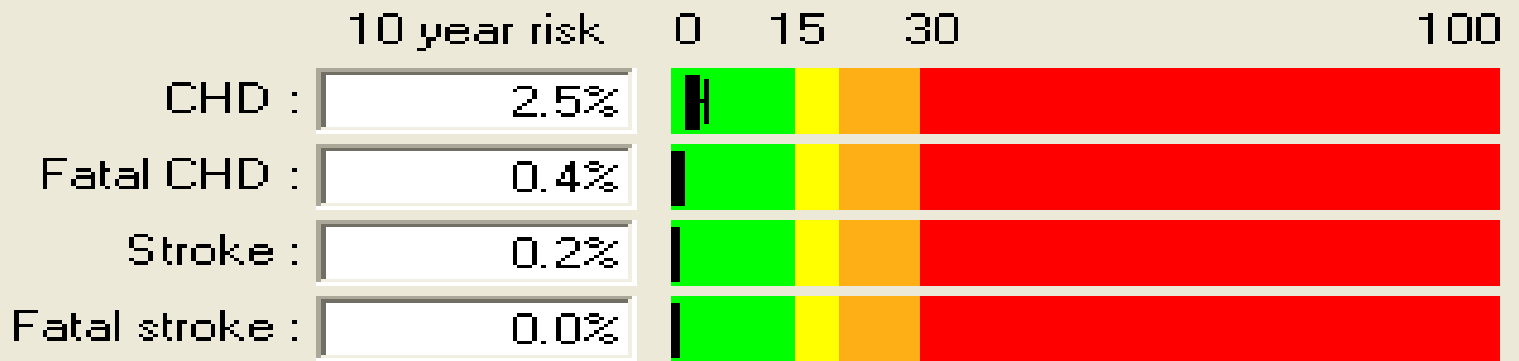
Atrial fibrillation :  No  Yes

HDL cholesterol :  mmol/l

Ethnicity :  ▼

Smoking :  ▼

**Output**

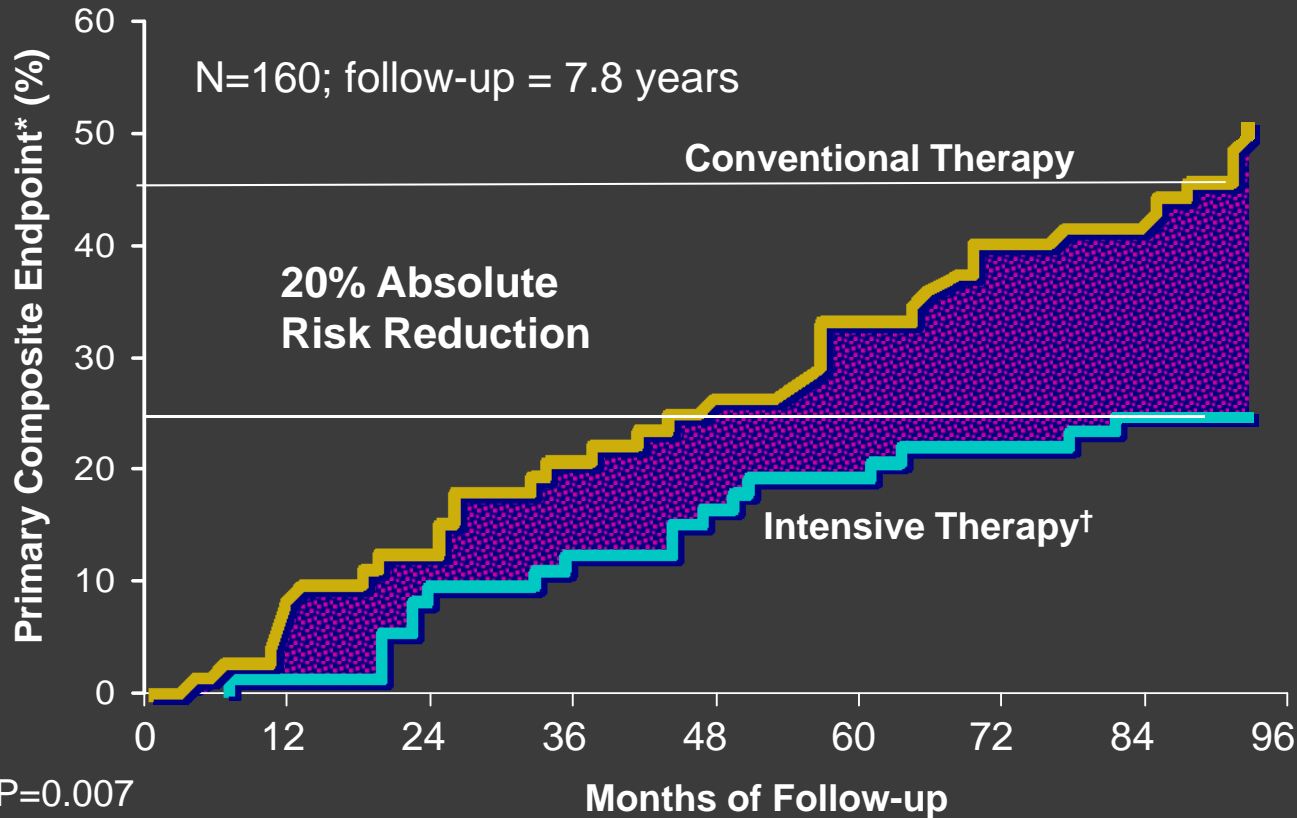


*Adjusted for regression dilution*

# STENO-2 Study

Intensive MRF management significantly reduces risk of CV events

Multiple risk-factor intervention study comparing conventional vs intensive treatment of risk factors in a high-risk population with type-2 diabetes



Intensive therapy<sup>†</sup>:

- Microalbuminuria with ACEIs, ARBs, or combination
- Hypertension
- Hyperglycaemia
- Dyslipidaemia
- Secondary prevention of CVD

Conventional treatment was in accordance with national guidelines

Primary composite endpoint: conventional therapy (44%) and intensive therapy (24%).

\*Death from CV causes, nonfatal MI, CABG, PCI, nonfatal stroke, amputation, or surgery for peripheral atherosclerotic artery disease; <sup>†</sup>Behavior modification and pharmacologic therapy

MRF: Multiple risk factor

# Recent Trials Providing Conflicting Evidence for Macrovascular Risk Reduction

## UKPDS

- Early intensive glucose control **reduces the risk** of MI and mortality over the long-term<sup>1,2</sup>

## ADVANCE

- Intensive glucose control has **no significant effect** on MaV events<sup>3</sup>

## ACCORD

- Non-significant increases in mortality were observed<sup>4</sup>
- After a mean follow-up of 3.5 years, ACCORD was stopped due to higher mortality in intensive Tx group

1. Holman R. Oral presentation at EASD 2008.  
2. Holman RR, et al. N Engl J Med. 2008;359:1577-89.  
3. ACCORD Group. N Engl J Med 2008;358:2545-59.  
4. ACCORD Group. N Engl J Med 2008;358:2545-59.

# Summary

- UKPDS calculator is useful in developing a balance between “individualisation” and early “multiple Risk Factor Intervention”
- UKPDS calculator is the best we have available but does not accommodate all known risk factors
- UKPDS calculator is effective at identifying high risk patients and less useful in younger and low risk patients