8th Annual Emirates Cardiac Society Conference

ACC Middle East Conference 2017

DUBAI

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UNIQUE EDUCATIONAL EXPERIENCE IN YOUR REGION

Diabetes and the Heart

By

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ACC Middle East Conference 2017

Disclosure

- None, related to this presentation

DIABETES

WITHOUT

COMPLICATIONS™

Road Map

- Is cardiac affection different in Diabetes?
- Is dysglycemia the only factor to be blamed?
- Diabetic cardiomyopathy!!!
- Hypoglycemia and heart
- Should ALL diabetes subjects be tested for heart disease?
- Glucose correction and heart disease !!!

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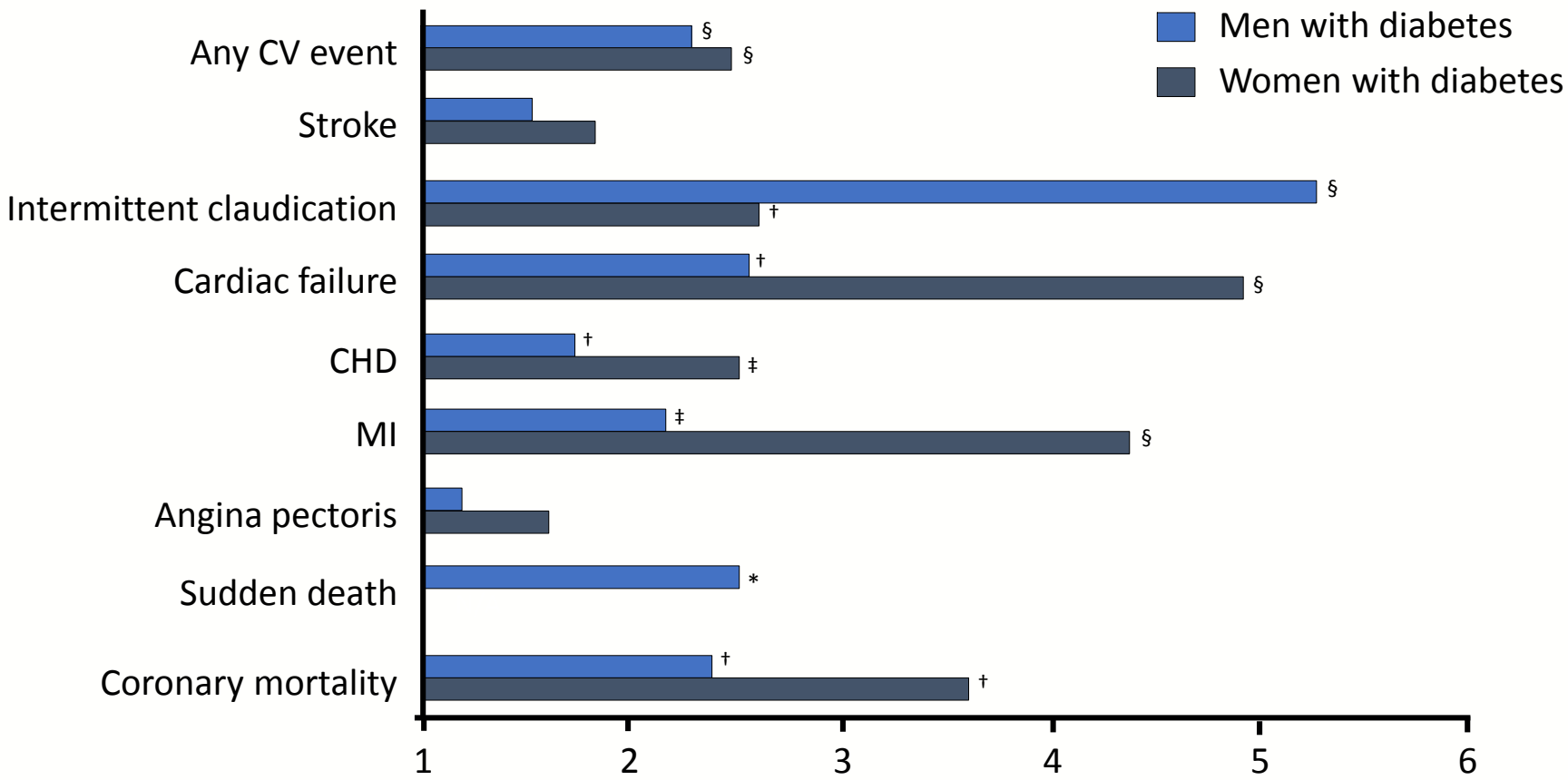
Type 2 diabetes increases the risk of CVD

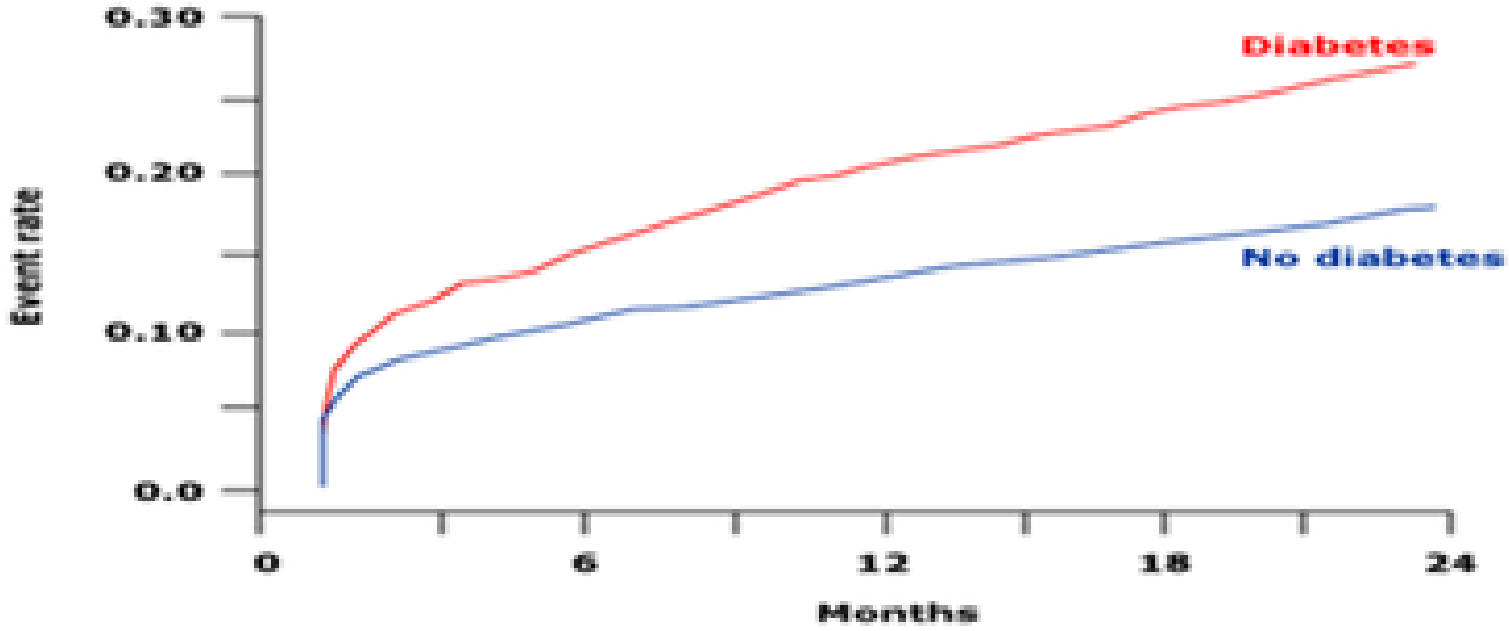


$P < 0.1$ †$P < 0.05$; ‡$P < 0.01$; §

Adapted from Kannel WB, et al. Am Heart J 1990; 120:672–6

Diabetes and ACS

Diabetics with a non-ST elevation ACS have a worse outcome than nondiabetics



In the OASIS registry of 8013 patients with a non-ST elevation acute coronary syndrome (unstable angina or non Q-wave myocardial infarction), 21 percent had diabetes. After a two-year follow-up, diabetic patients had a significantly higher combined event rate (cardiovascular death, new myocardial infarction, stroke, new heart failure) than nondiabetics (relative risk 1.56).

Data from Malmberg K, Yusuf S, Gerstein HC, et al. Circulation 2000; 102:1014.

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What are the priorities in diabetes management + CAD?

?

?

?

?

Cholesterol?

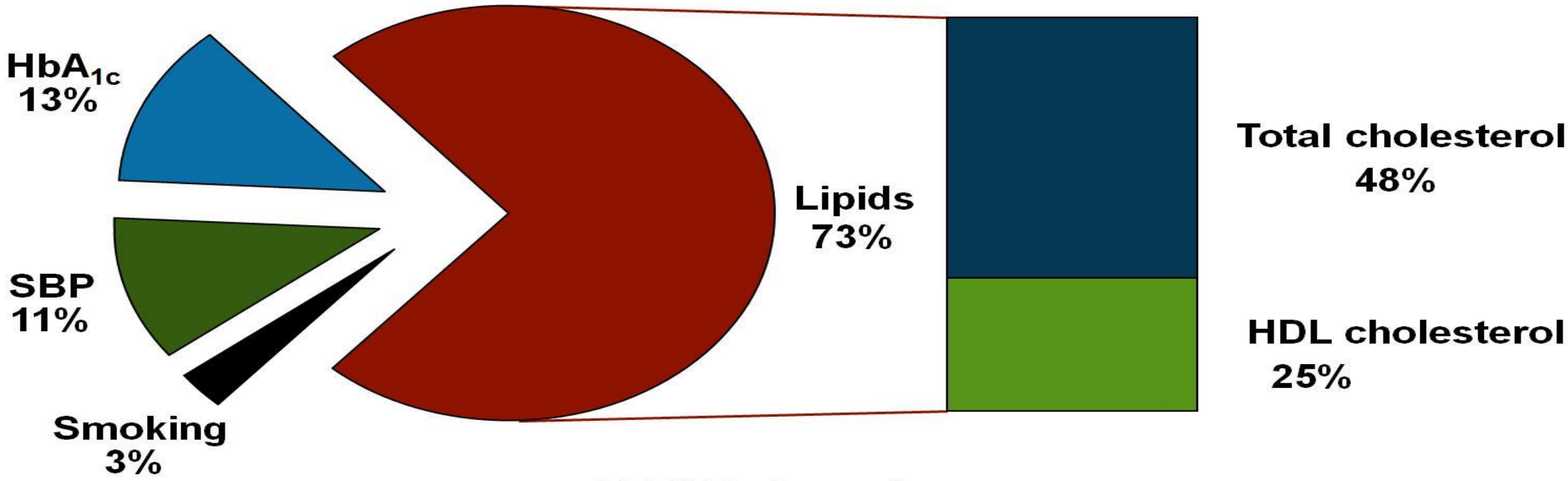
Glucose?

- ❑ Endothelial Dysfunction
- ❑ AGEs

Blood pressure?

Principles for Multifactorial Management in Individuals With T2D

Actual contribution of each risk factor in improving the UKPDS coronary heart disease risk score in the STENO-2 intensive arm



STENO-2 study

Gaede P, et al. *Diabetes*. 2004;53(suppl 3):S39-S47.

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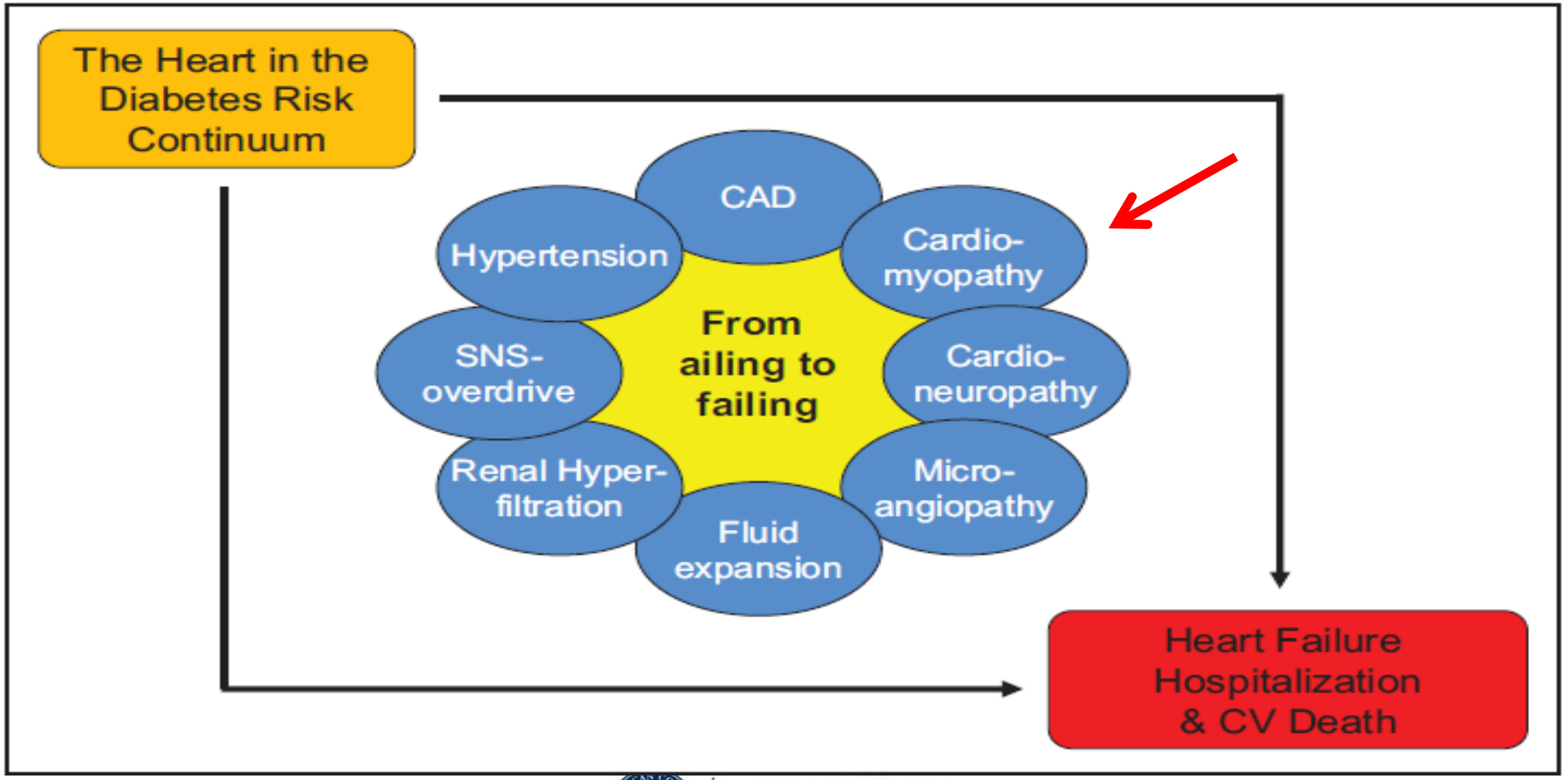
Heart Failure & DM

- Rate of Heart failure in DM is 2 to 5 times greater than those in the general population.
- About 30% of type 2 diabetes will develop heart failure
- Almost 40% of patients hospitalized for acute decompensated heart failure have diabetes

Ekeruo LA et al. Curr Cardiovasc Risk Rep 2013; 7: 417–22
Cowie CC, et al. Diabetes Care 2010; 33: 562-8
Nichols GA, et al. Diabetes Care. 2004;27:1879–84.
Joffe SW, et al. J Am Heart Assoc 2013, 2:e000053

Heart Failure and DM
(ominous Octet)



Standl E et al. Circ Res 2016

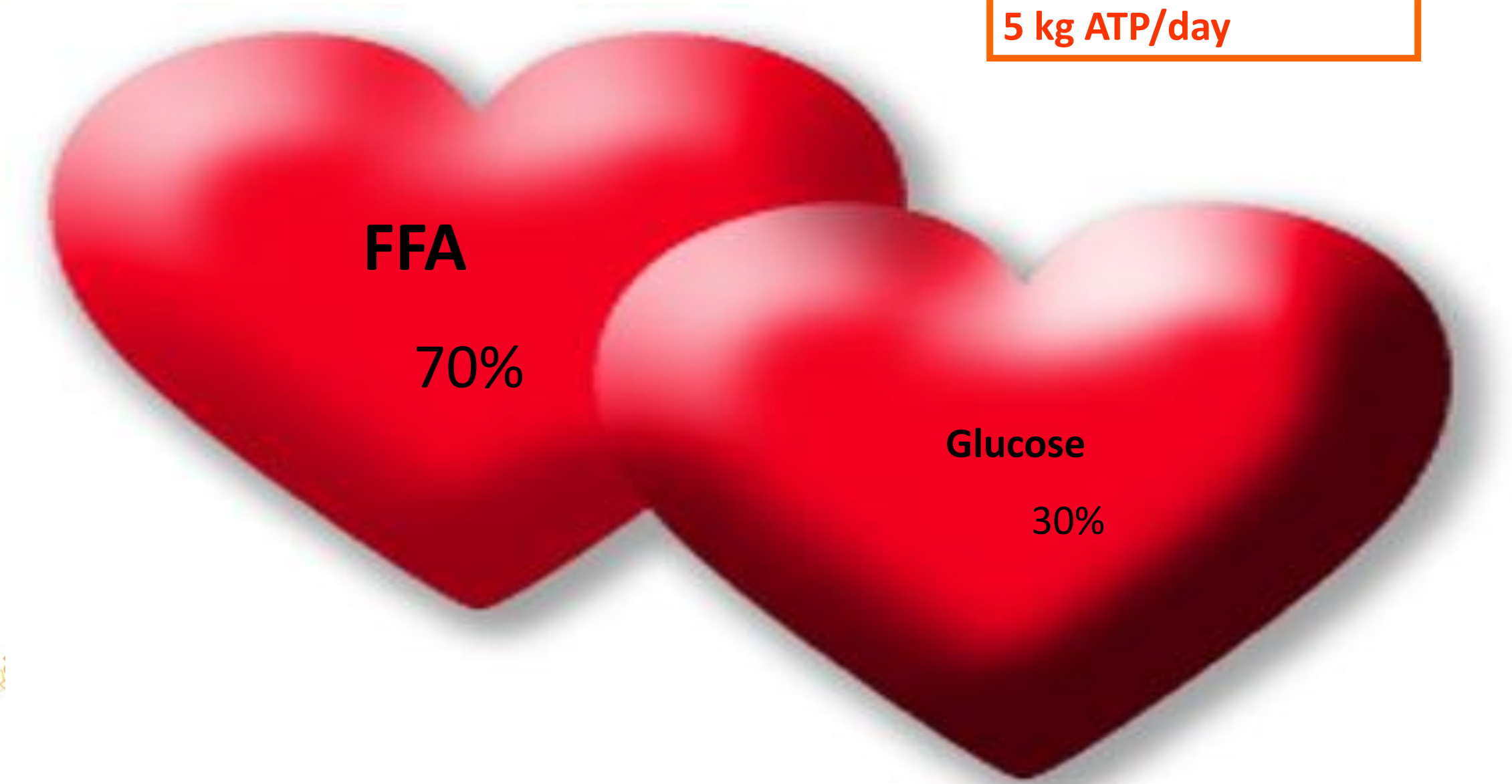
In the early 19th century, Laennec described Fatty Degeneration of the Heart

Diabetic Cardiomyopathy
1970s

Smith HL, Willius FA. Adiposiy of the Heart. Arch Int Med, 1933; 52: 811-931

Baseline

5 kg ATP/day



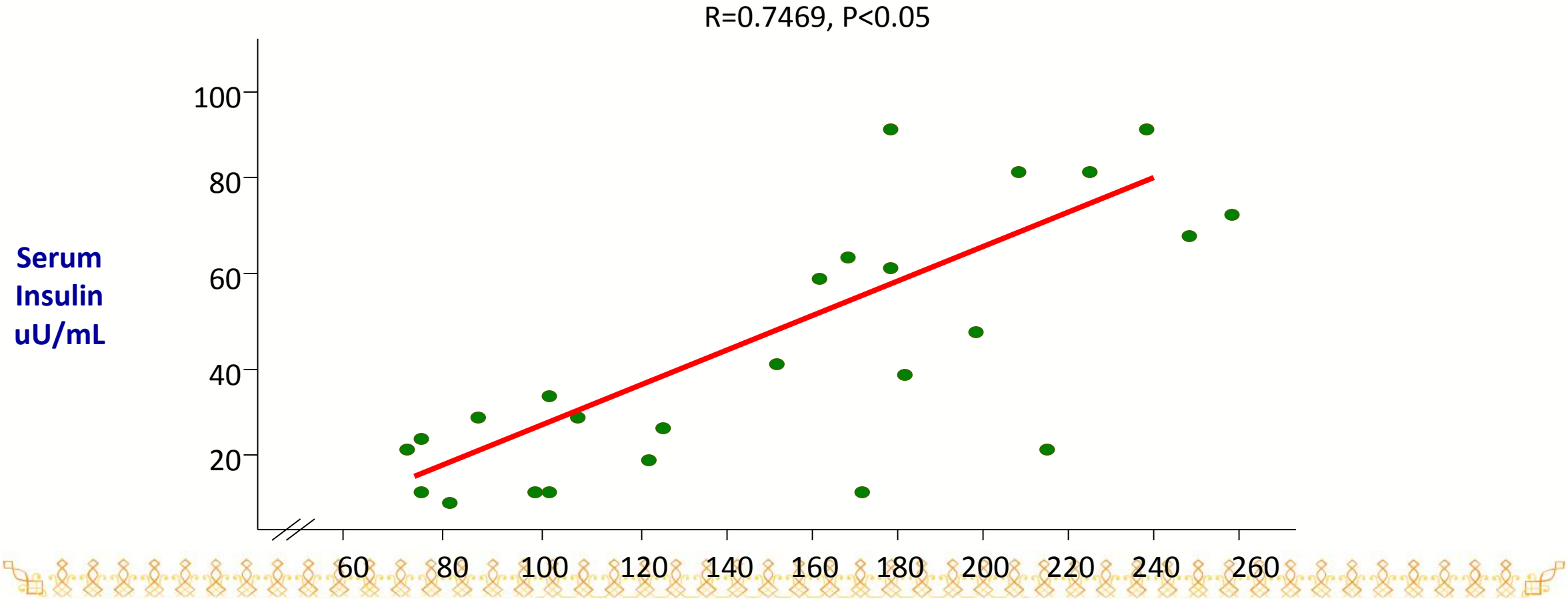
Injury

↑ **Energy Efficiency**

Insulin Resistance

↓Energy Efficiency

Relation of Insulin to Left Ventricular Mass



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Ayad W, Assaad SN et al, Bull Alex Fac Med 1997; 33: 327-30.

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Hemodynamic changes associated with hypoglycemia:

- Increase in **heart rate**
- **Increase** in peripheral **systolic blood pressure**
- **Reduced peripheral** arterial resistance (causing a widening of pulse pressure)
- **Increased myocardial** contractility, stroke volume, and cardiac output
- ECG changes: prolonged repolarization and a prominent U wave.

Diabetes Metab Res Rev 2008;24:353–363

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Who is at high risk of premature CV disease?

- Consider a person with T2DM to be at high risk of premature CV disease unless he or she:
  - Is not overweight, tailoring this with an assessment of body-weight associated risk according to ethnic group
  - Is normotensive (< 140/80 mmHg in the absence of antihypertensive therapy).
  - Does not have microalbuminuria
  - Does not smoke
  - Does not have a high-risk lipid profile
  - Has no history of CV disease
  - Has no family history of CV disease

NICE (2009) Type 2 Diabetes. The Management of Type 2 Diabetes. NICE Clinical Guideline 87. NICE, London. Available at: http://tiny.cc/CG87 (accessed at 9 August 2011).
CV, cardiovascular; T2DM, Type 2 diabetes mellitus

Canadian Diabetes Guidelines

A baseline resting ECG should be performed in individuals with any of the following [Grade D, Consensus]:

- Age >40 years
- Duration of diabetes >15 years and age >30 years
- End organ damage (microvascular, macrovascular)
- Cardiac risk factors

Canad J Diab 2013, 37 : suppl 1

Canadian Diabetes Guidelines

People with diabetes should undergo investigation for CAD by exercise ECG stress testing as the initial test [Grade D, Consensus] in the presence of the following:

- Typical or atypical cardiac symptoms (e.g. unexplained dyspnea, chest discomfort) [Grade C, Level 3]
- Signs or symptoms of associated diseases
  - Peripheral arterial disease (abnormal ankle-brachial index) [Grade D, Level]
  - Carotid bruits [Grade D, Consensus]
  - Transient ischemic attack [Grade D, Consensus]
  - Stroke [Grade D, Consensus]
- Resting abnormalities on ECG (e.g. Q waves) [Grade D, Consensus]

Canad J Diab 2013, 37 : suppl 1

ADA - Standards of Medical Care in Diabetes 2017

Screening

- In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as atherosclerotic cardiovascular disease risk factors are treated. A

Diabetes Care 2017;40(Suppl. 1):S75–S87

ADA - Standards of Medical Care in Diabetes 2017

- Consider investigations for coronary artery disease in the presence of any of the following: atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort); signs or symptoms of associated vascular disease including carotid bruits, transient ischemic attack, stroke, claudication, or peripheral arterial disease; or electrocardiogram abnormalities (e.g., Q waves). E

Diabetes Care 2017;40(Suppl. 1):S75–S87

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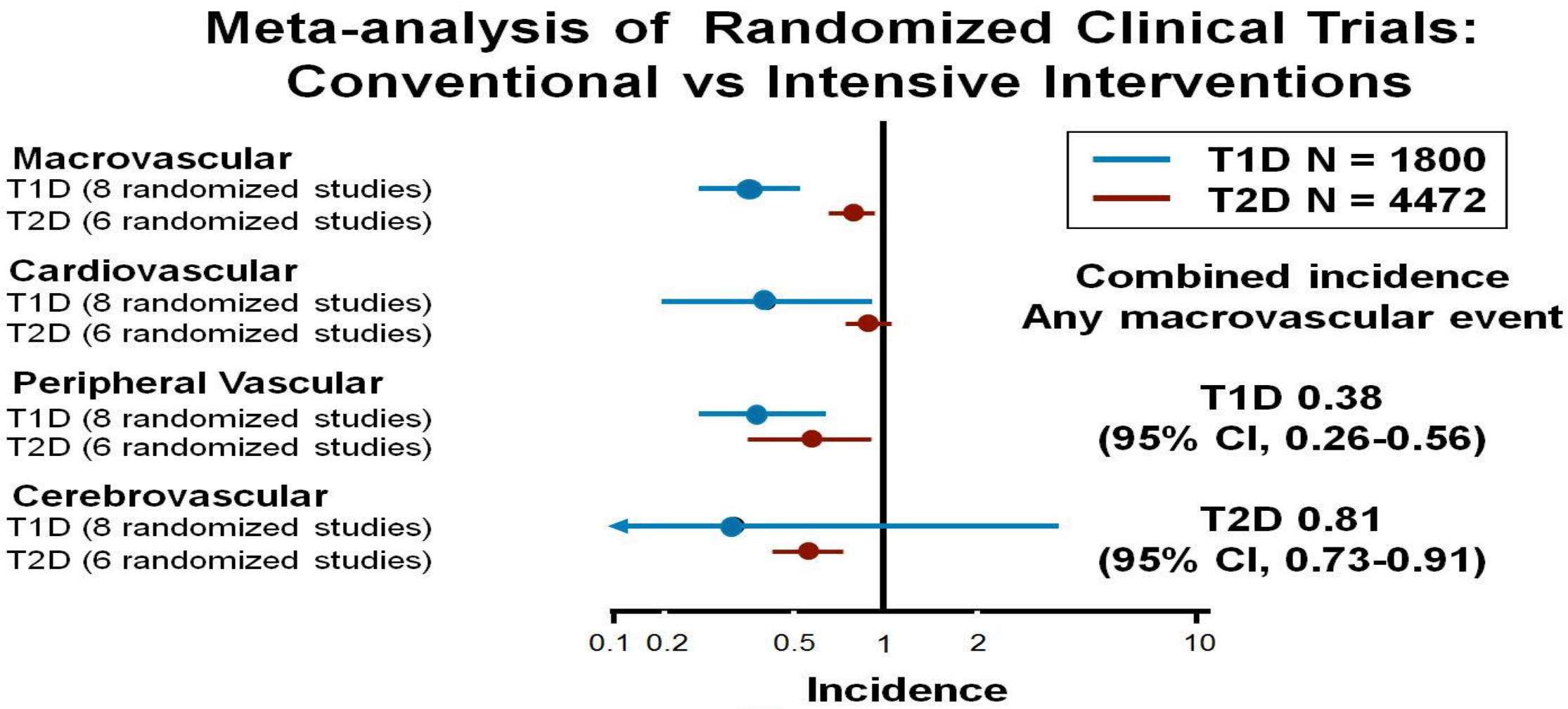
Meta-analysis: Improved Glucose Reduction in Macrovascular Events



Stettler C, et al, *Am Heart J.* 2006;152:27-38.[20]

Impacting Macrovascular Disease

- Treat patients as aggressively as possible without hypoglycemia
- Treat as early as possible

Scirica BM, et al. N Engl J Med 2013
White WB, et al. N Engl J Med 2013

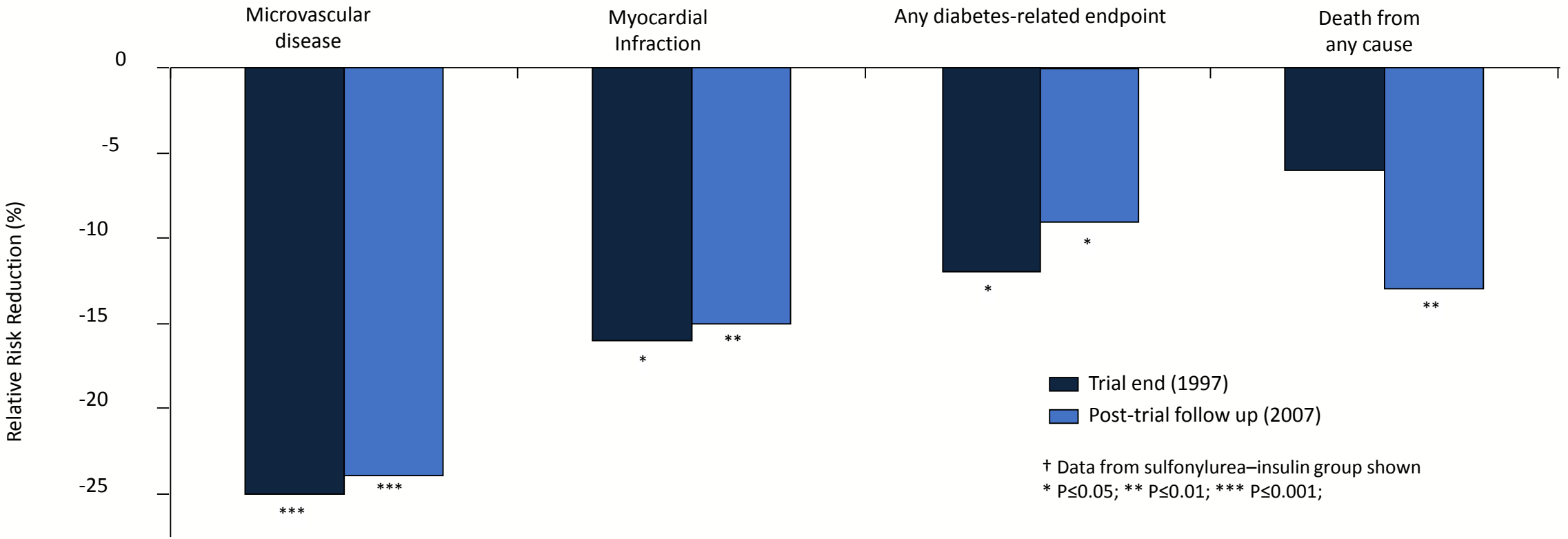
Metabolic Memory

Control As Early As Possible

T1DM → DCCT/EDIC
T2DM → UKPDS

Early glycemic control provides lasting protection: The legacy effect

10-year post-trial monitoring from 1997 to 2007 of UKPDS Study†



- Randomized intervention to achieve either intensive or conventional targets - stopped at the trial end (1997)
- Differences in mean HbA_{1c} between the two groups were lost by year 1 of post-trial follow-up.
- Relative reductions in risk in patients who had been treated to intensive goals, compared with conventional targets, persisted after 10 years

The legacy effect – a reduction in complications persists 10 years after intensive therapy

1. UKPDS 33 Study Group. *Lancet.* 1998;352:837-853;
2. 2. Holman RR, et al. *N Engl J Med.* 2008;359:1577-1589.
3. Chalmers J and Cooper ME. *N Engl J Med*. 2008; 359: 1618–1620.

Challenges in Initiating/Monitoring Glucose-lowering Therapy in Type 2 Diabetes and Coronary Artery Disease

- Choosing the most appropriate antidiabetic drug or drug combination
- Evaluating the cardiovascular impact of the drug or drug combination
- Deciding on the glycemic target

CV Outcomes Trials of Glucose-Lowering Drugs in T2DM

Trial	Tested Agents	Outcome	Status
Insulin			
ORIGIN	Insulin glargine vs SoC	CV death, MI, stroke	Reported
DEVOTE	Insulin degludec vs glargine	CV death, MI, stroke	Reported
DPP-4 inhibitors			
SAVOR-TIMI 53	Saxagliptin vs placebo	CV death, MI, stroke	Reported
EXAMINE	Alogliptin vs placebo	CV death, MI, stroke	Reported
TECOS	Sitagliptin vs placebo	CV death, MI, UA, stroke	Reported
CAROLINA	Linagliptin vs glimepiride	CV death, MI, UA, stroke	Ongoing
CARMELINA	Linagliptin vs placebo	CV death, MI, UA, stroke	Ongoing
OMNEON	Omarigliptin vs placebo	CV death, MI, UA, stroke	Ongoing
GLP-1 RAs			
ELIXA	Lixisenatide vs placebo	CV death, MI, UA, stroke	Reported
REWIND	Dulaglutide vs placebo	CV death, MI, stroke	Ongoing
LEADER	Liraglutide vs placebo	CV death, MI, stroke	Completed
EXSCEL	Exenatide weekly vs placebo	CV death, MI, stroke	Ongoing
SUSTAIN 6	Semaglutide vs placebo	CV death, MI, stroke	Reported
FREEDOM-CVO	Exenatide vs placebo	CV death, MI, UA, stroke	Ongoing
SGLT2 inhibitors			
EMPA-REG OUTCOME	Empagliflozin vs placebo	CV death, MI, UA, stroke	Reported
DECLARE-TIMI 58	Dapagliflozin vs placebo	CV death, MI, stroke	Ongoing
VERTIS-CVO	Ertugliflozin vs placebo	CV death, MI, stroke	Ongoing
CANVAS	Canagliflozin vs placebo	CV death, MI, UA, stroke	Reported
CREDENCE	Canagliflozin vs placebo	CV, renal death, ESRD, 2XCr	Ongoing

US National Institutes of Health: ClinicalTrials.gov

Summary

- Is cardiac affection different in Diabetes? **YES**
- Is dysglycemia the only factor to be blamed? **NO**
- Diabetic cardiomyopathy**!!!**
- Is Hypoglycemia bad for the heart ? **YES**
- Should ALL diabetes subjects be tested for heart disease? **NO**
- Glucose correction and heart disease **? ?**


Alexandria
OLD PORT

THANK YOU

References

- Kannel WB, et al. Diabetes, fibrinogen, and risk of cardiovascular disease: the Framingham experience. Am Heart J 1990; 120:672–676
- Gaede P, et al. Intensive integrated therapy of type 2 diabetes: implications for long-term prognosis. Diabetes 2004;53 Suppl 3: S39-4
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- Stettler C, et al. Glycemic control and macrovascular disease in types 1 and 2 diabetes mellitus: Meta-analysis of randomized trials. Am Heart J 2006 Jul;152(1):27-38.