

# Diabetes – en hjärtkärlsjukdom

## Risker, komplikationer och prevention

Preventiv kardiologi 2024-11-05, Sigtuna

*Anna Norhammar,*

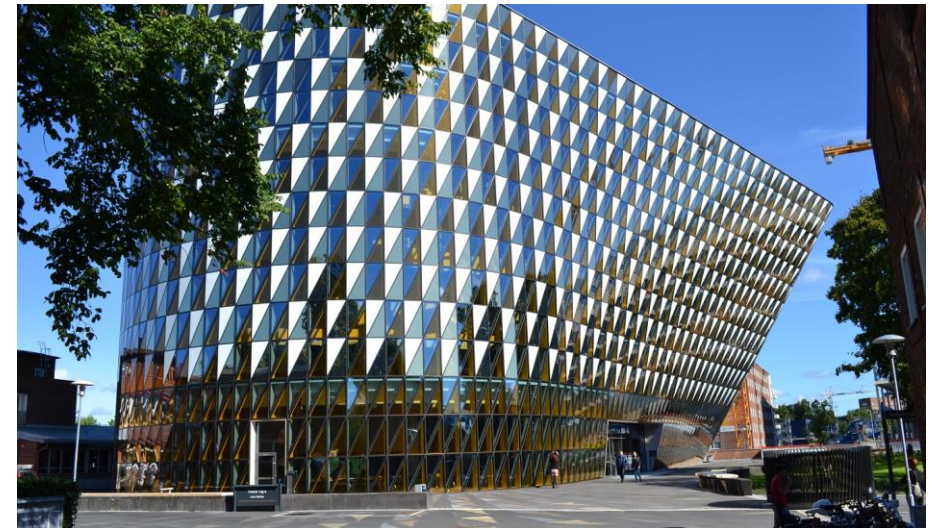
*Professor cardiology*

*Cardiology Unit, Department of Medicine*

*Karolinska Institutet, Stockholm*

*Senior consultant Capio S:t Görans hospital*

*Sweden*



# Diabetes och hjärtkärlsjukdom

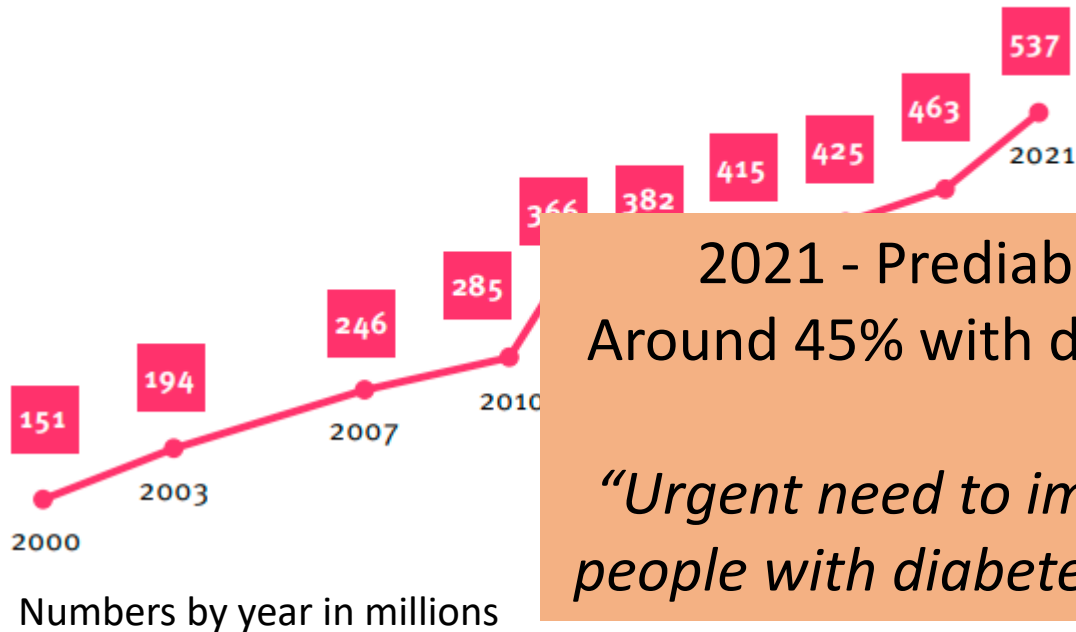
1. Epidemiologi, prevalens och incidens
2. Kardiovaskulär risk – trender och dagsläget
3. Betydelsen av riskfaktorkontroll
4. Kvarstående kardiovaskulära problem
5. Nya möjligheter – kardiovaskulära utfallsstudier

SGLT-2i

GLP-1 RA

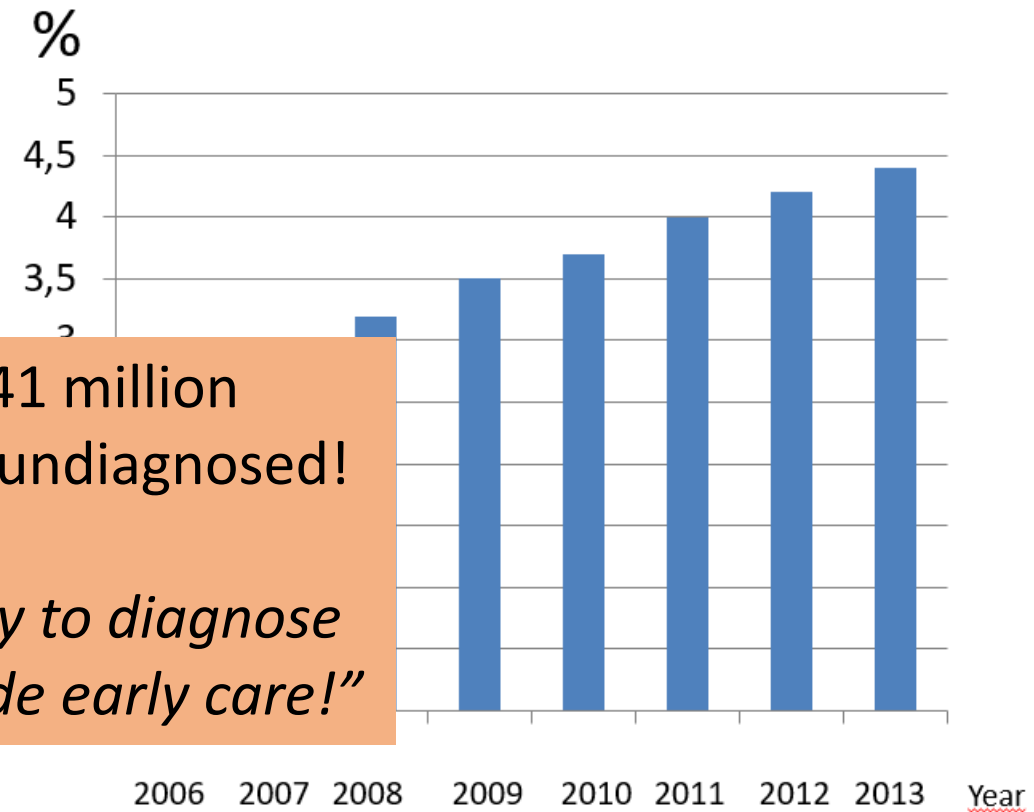
# Global diabetes prevalence

Yr 2001 151 million - 4.6%  
 Yr 2021 537 million - 10.5%  
 Yr 2030 643 million - 11.3% ???  
 Yr 2045 783 million - 12.2% ??



# Prevalence increases in Sweden

60% increase T2DM yr; 2006-2013



# Hyperglycaemia in pregnancy

This IDF Diabetes Atlas 10th edition

One of new highlights in IDF 10<sup>th</sup> Atlas

*“This IDF Diabetes Atlas 10th edition also shows that hyperglycaemia in pregnancy affects approximately one in six pregnancies”*

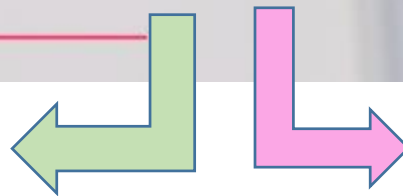


## HYPERGLYCAEMIA

■ Pregnant women with gestational diabetes can have babies that are large for gestational age, increasing the risk of pregnancy and birth complications for the mother and baby

### Child

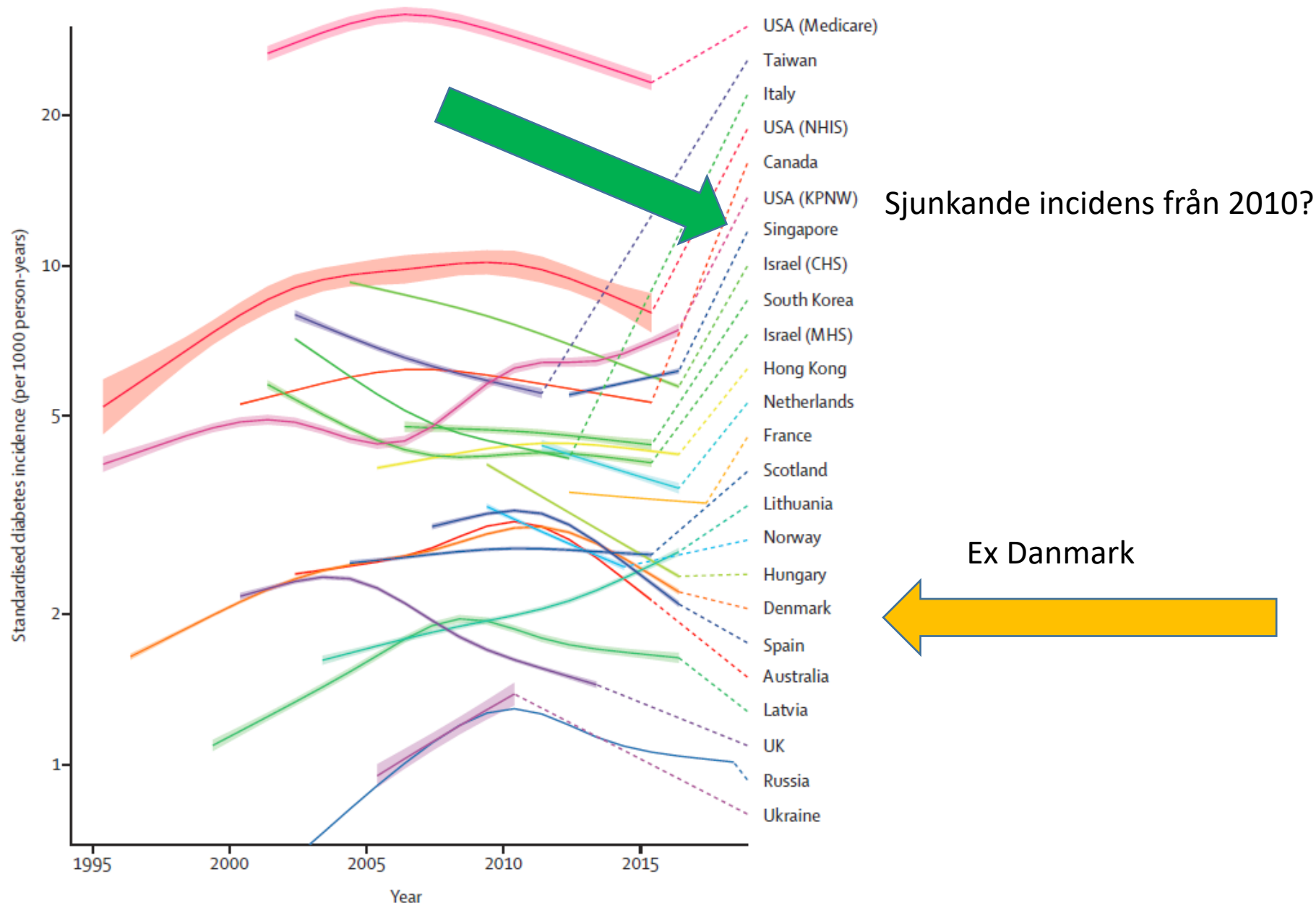
1. Large babies, birth defects
2. Birth complications
3. First days hypoglycaemia risk
4. Future diabetes risk



### Mother

1. Birth complications
2. Increased preeclampsia
3. **Future risk for mother at risk for diabetes and CVD**

# Incidens av diabetes - globala trender är stabila eller sjunkande



# Diabetes och hjärtkärlsjukdom

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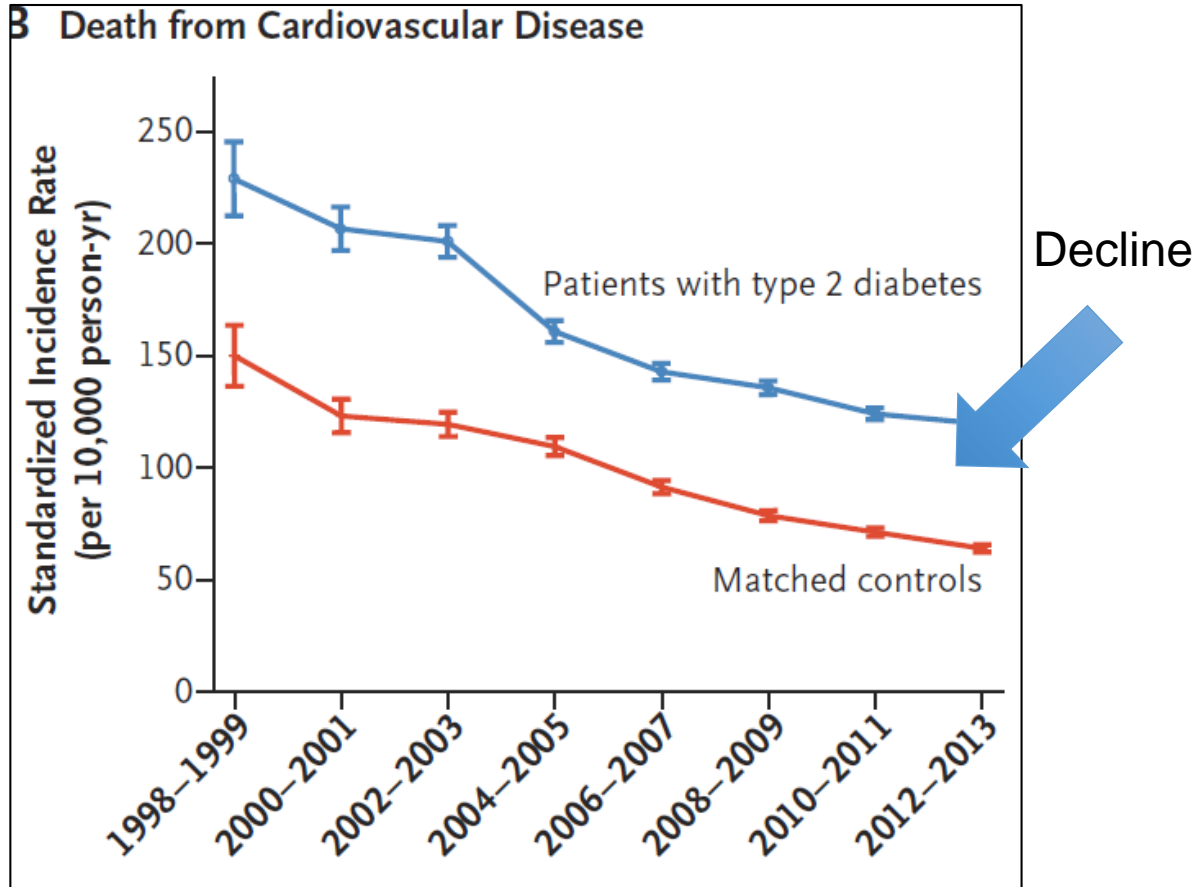
SGLT-2i

GLP-1 RA

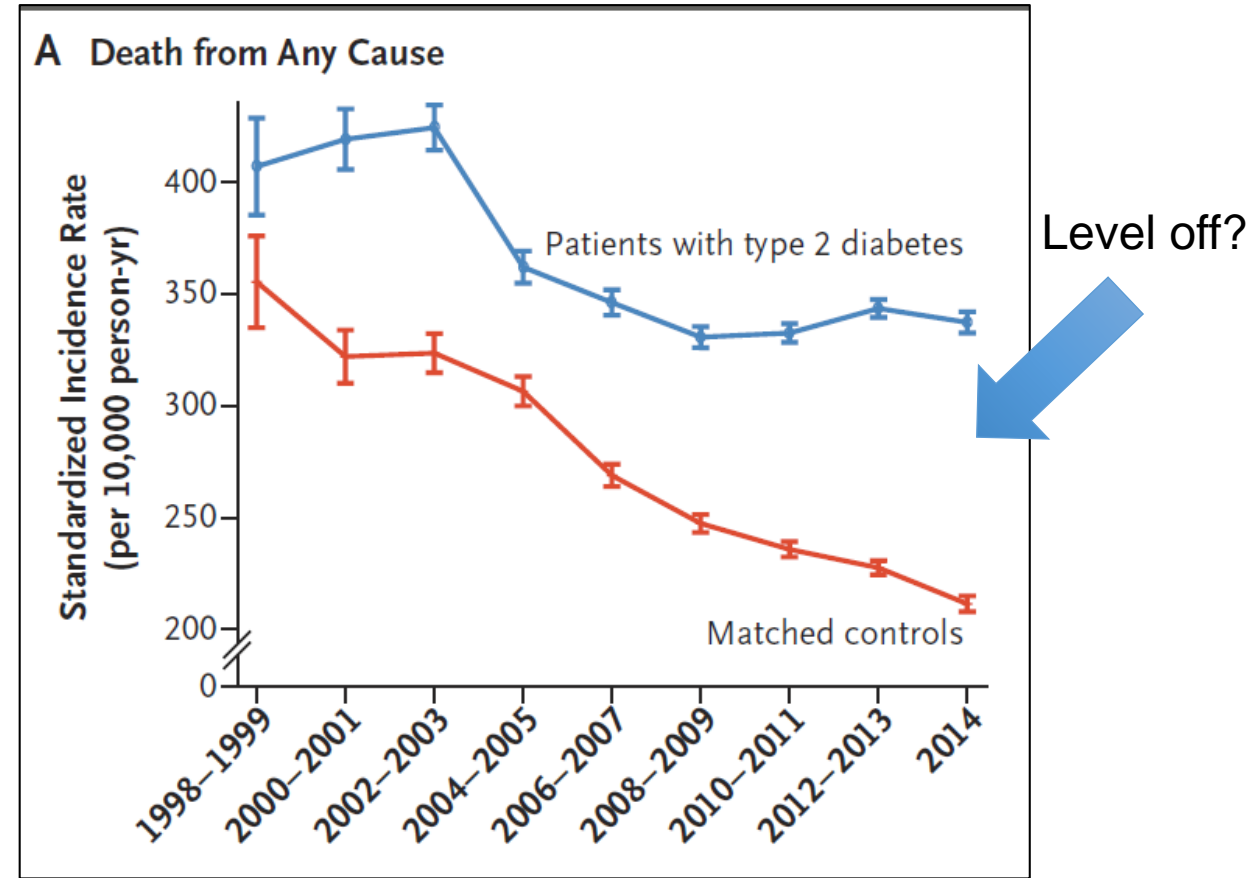
# Favorable all-cause mortality trends globally latter decades

Sweden 1998-2013, CV-mortality decreases, all-cause level off?

## CV-mortality



## All-cause mortality



# Hjärtkärlkomplikationer vid typ 2 diabetes -2-faldigt ökad risk för hjärtsvikt och hjärtinfarkt

Risk jämfört med populationen i Sverige 2006-2013

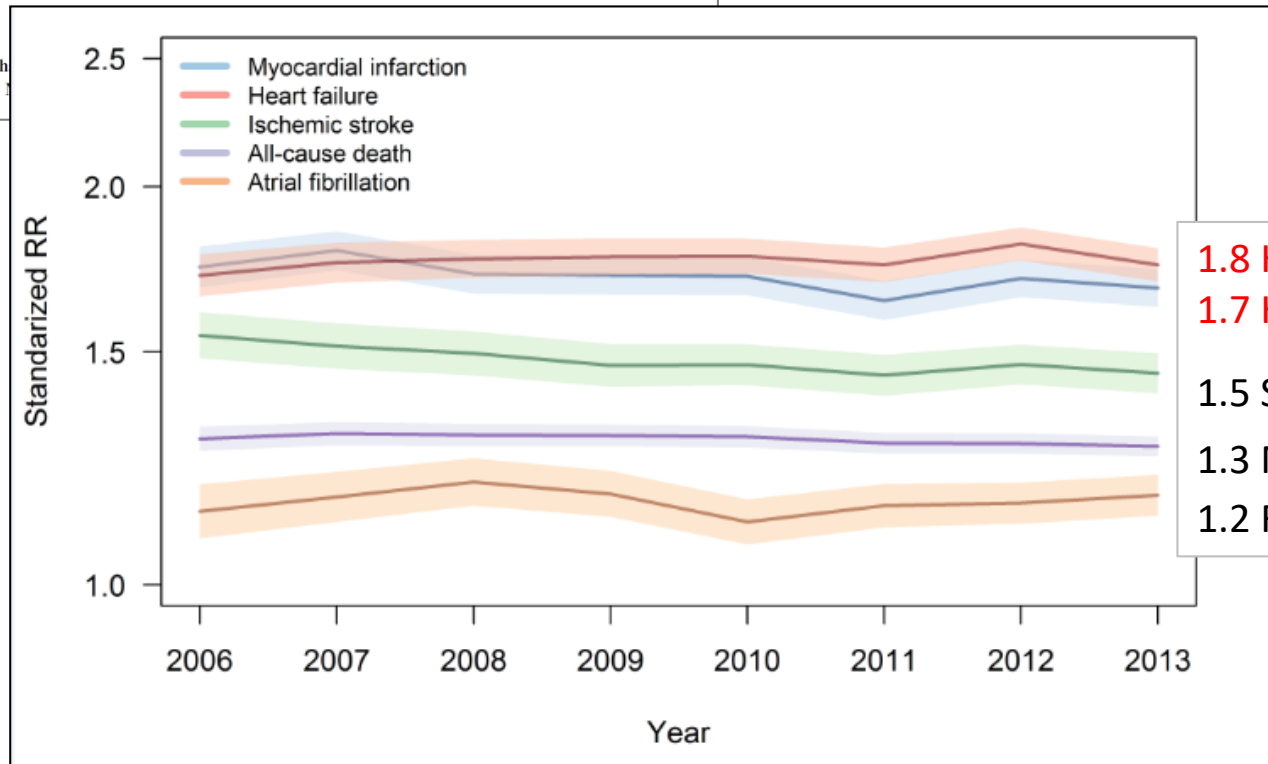
Läkemedelsbehandlad typ 2 diabetes år 2013, n=352,436

Diabetologia  
DOI 10.1007/s00125-016-3971-y

ARTICLE

**Incidence, prevalence and mortality of type 2 diabetes requiring glucose-lowering treatment, and associated risks of cardiovascular complications: a nationwide study in Sweden, 2006–2013**

Anna Norhammar<sup>1,2</sup> · Johanna Carlsson<sup>1,2</sup> · Jan W. Eriksson<sup>6</sup> · David ...

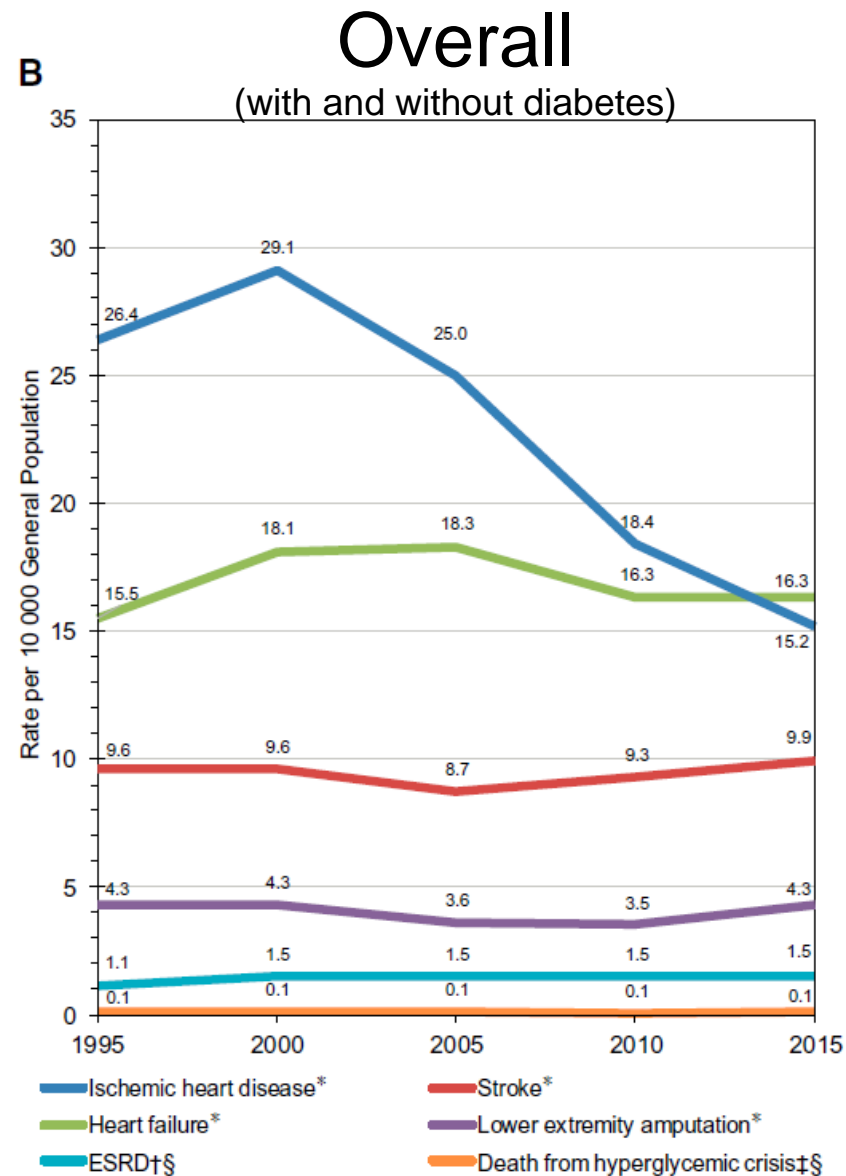
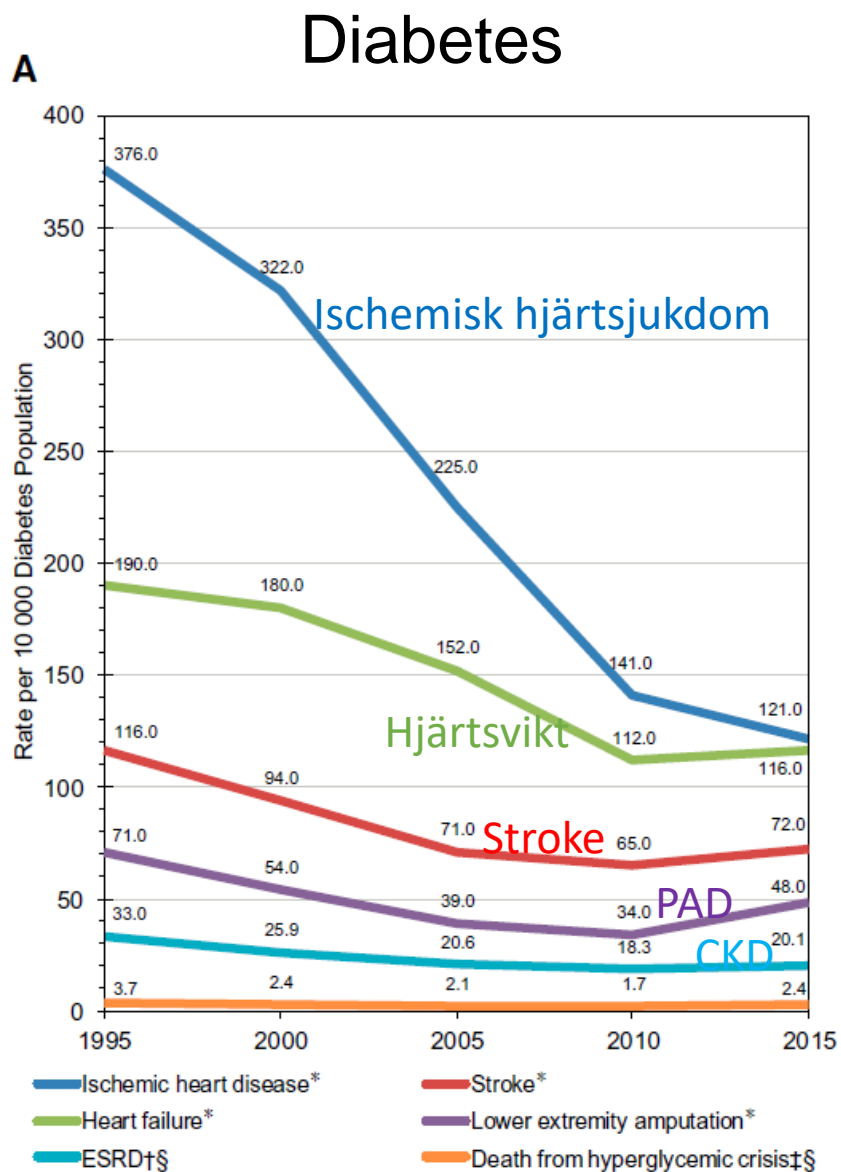


- 1.8 Hjärtsvikt
- 1.7 Hjärtinfarkt
- 1.5 Stroke
- 1.3 Mortalitet
- 1.2 Förmaksflimmer

Risken varierar med ålder och riskfaktorer



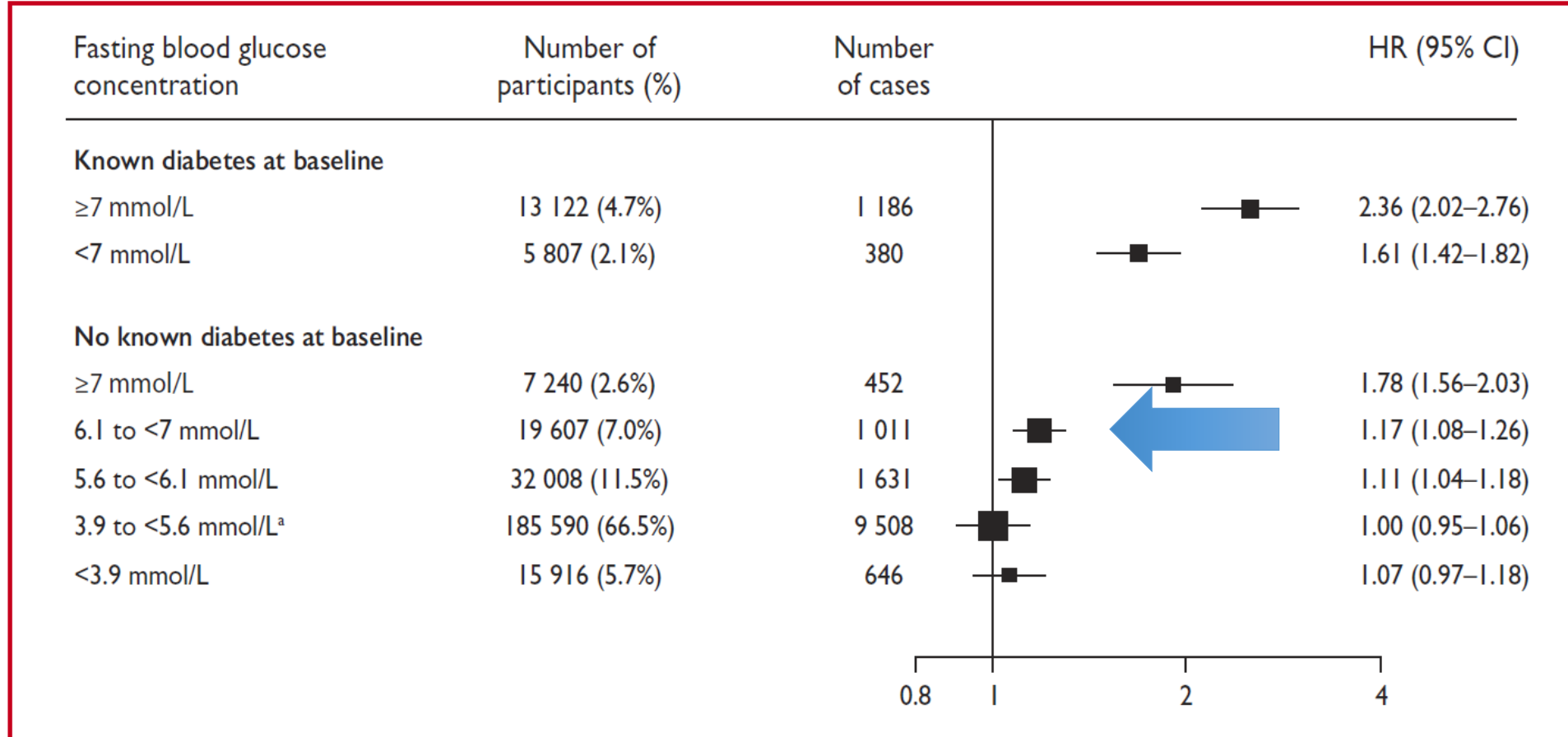
# Trender i hjärtskärlkomplikationer i USA 1995 till 2015



# Risk för hjärtsjukdom även nedom diabetesgräns

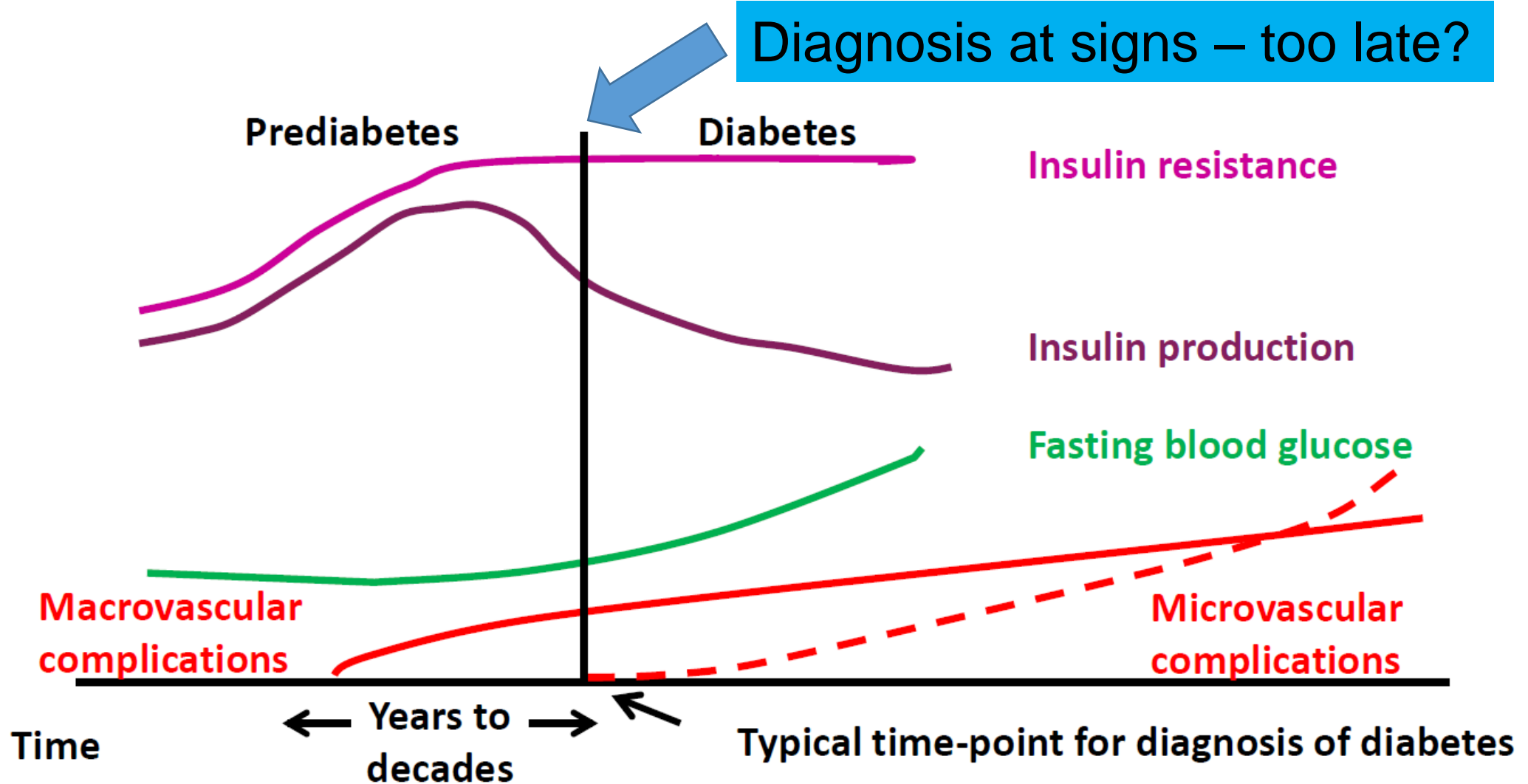
N=279 290, (14 814 fall).

Justerade hazard ratios

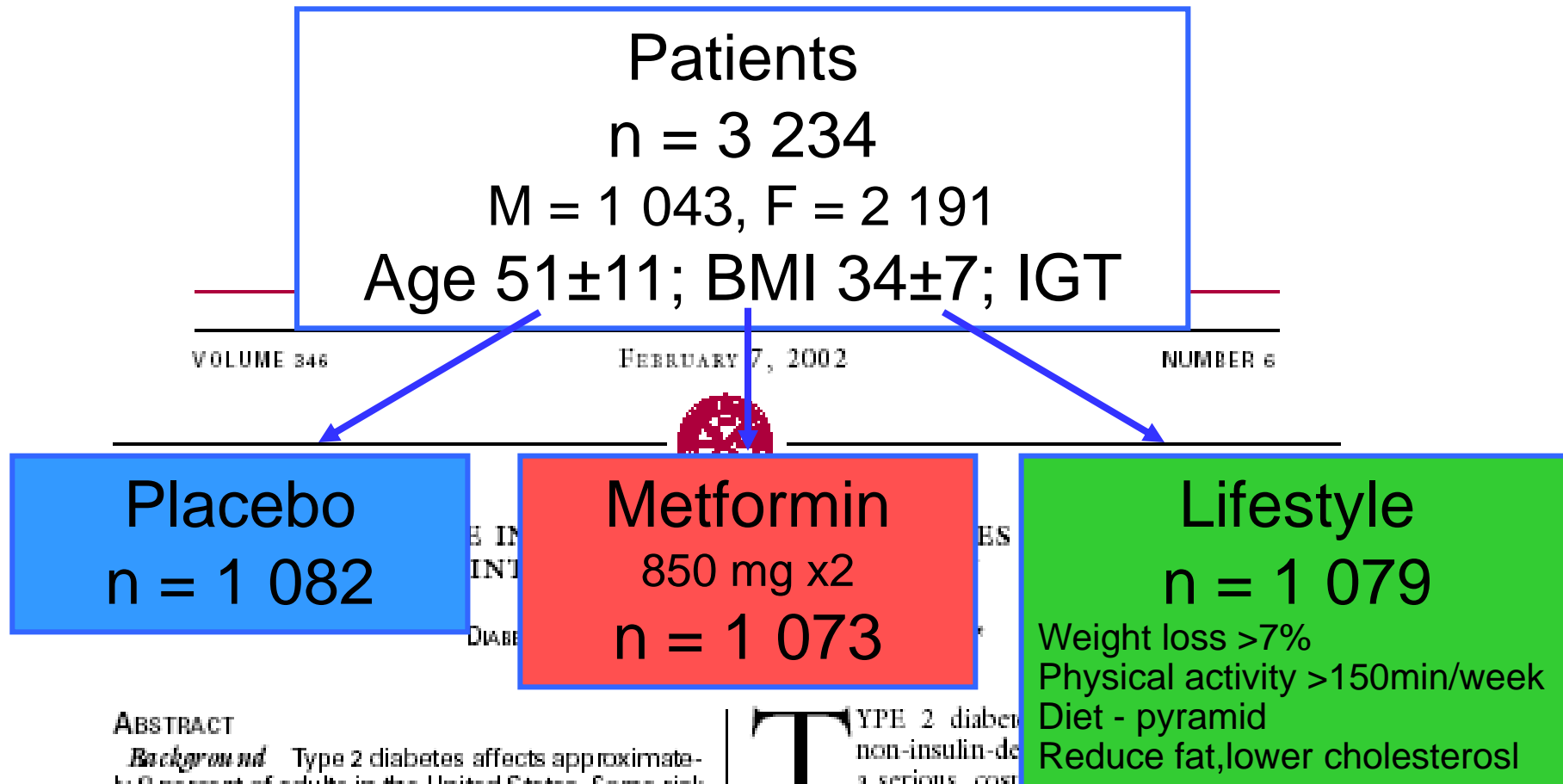


Risken för hjärtsjukdom startar under diabetesgränsen

# Development of type 2 diabetes



# Lifestyle and metformin prevents diabetes



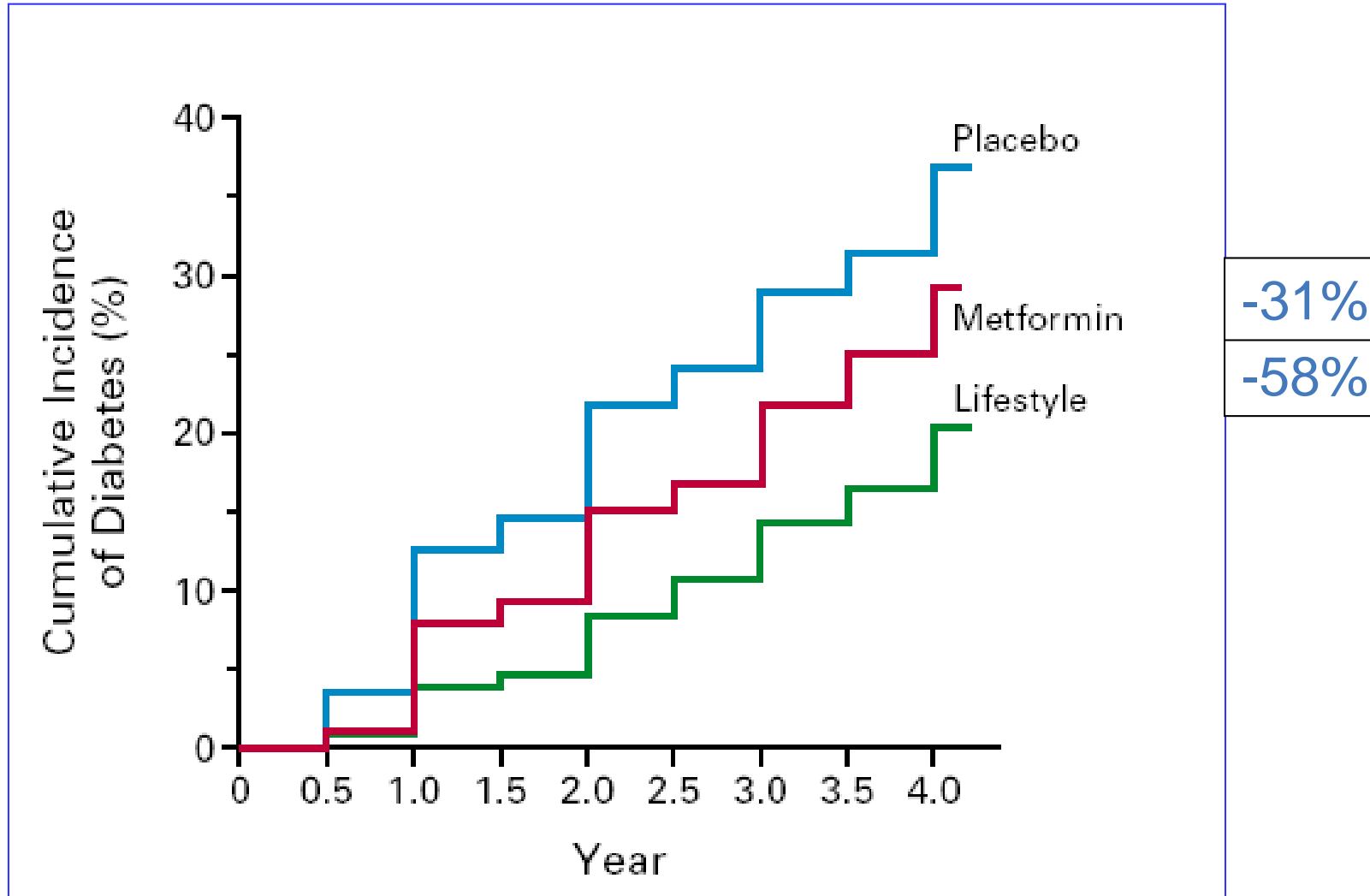
## ABSTRACT

**Background** Type 2 diabetes affects approximately 8 percent of adults in the United States. Some risk factors — elevated plasma glucose concentrations in the fasting state and after an oral glucose load, overweight, and a sedentary lifestyle — are potentially reversible. We hypothesized that modifying these factors with a lifestyle-intervention program or the administration of metformin would prevent or delay

**T**YPE 2 diabetes, a non-insulin-dependent form of diabetes, is a serious, costly disease that affects approximately 8 percent of adults in the United States.<sup>1</sup> Treatment prevents some of its devastating complications<sup>2,3</sup> but does not usually restore normoglycemia or eliminate all the adverse consequences. The diagnosis is often delayed until complications are

# Lifestyle and metformin prevents diabetes

Incidence of diabetes by OGTT



# Diabetes och hjärtkärlsjukdom

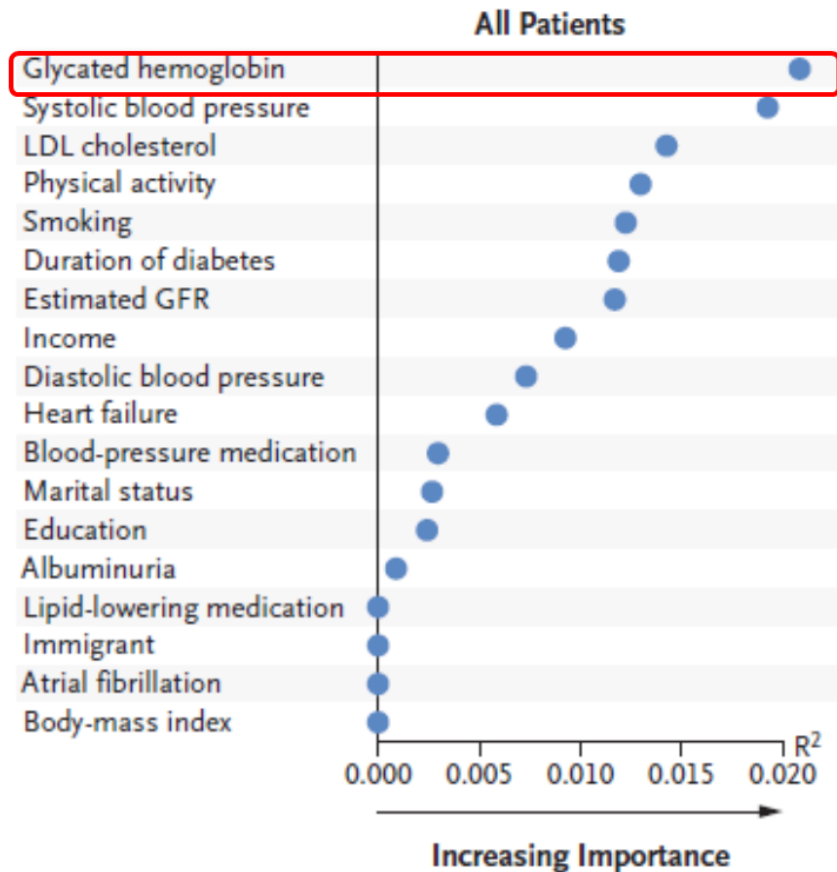
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SGLT-2i

GLP-1 RA

# NDR – riskfaktorer för hjärtinfarkt

## B Acute Myocardial Infarction



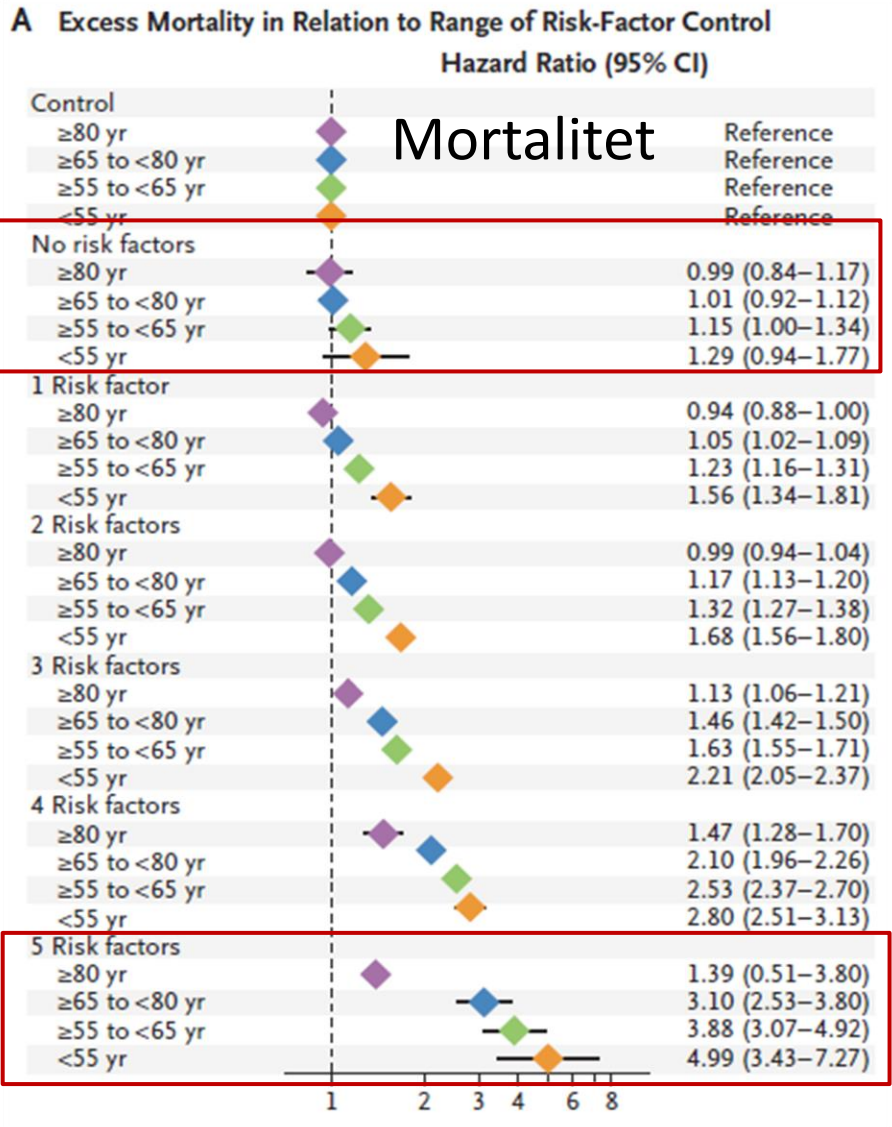
*Glukoskontroll viktig  
men ej tillräckligt att kontrollera<sup>1-8</sup>*

Rawshani A et al. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 2018;379:633-44. DOI: 10.1056/NEJMoa1800256

1. UKPDS Group. Lancet. 1998;352(9131):854-65. 2. Holman RR et al. N Engl J Med. 2008;359(15):1577-89. 3. DCCT. N Engl J Med 1993;329(14):977-86. 4. Nathan DM, et al. N Engl J Med. 2005;353(25):2643-53. 5. ACCORD Study Group. N Engl J Med. 2008;358(24):2545-59. 6. ACCORD Study Group. N Engl J Med. 2010;363(3):233-44. 7. ADVANCE Collaborative Group. N Engl J Med. 2008;358(24):2560-72. 8. Duckworth W et al. N Engl J Med. 2009;360(2):129-39

# Prevention lönar sig - betydelse av god riskfaktorkontroll

T2DM Swedish diabetes registry 1998-2012, uppföljning 5,7 år, risk för död  
 n=271,174, Kontroller n=1,355,870



Fem riskfaktorer  
 HbA1c, LDL, albuminuria, rökning, BP



Om alla fem välkontrollerade - låg risk!

*Preventiv behandling viktigt !!!  
 Tidigt!*



# Diabetes och hjärtkärlsjukdom

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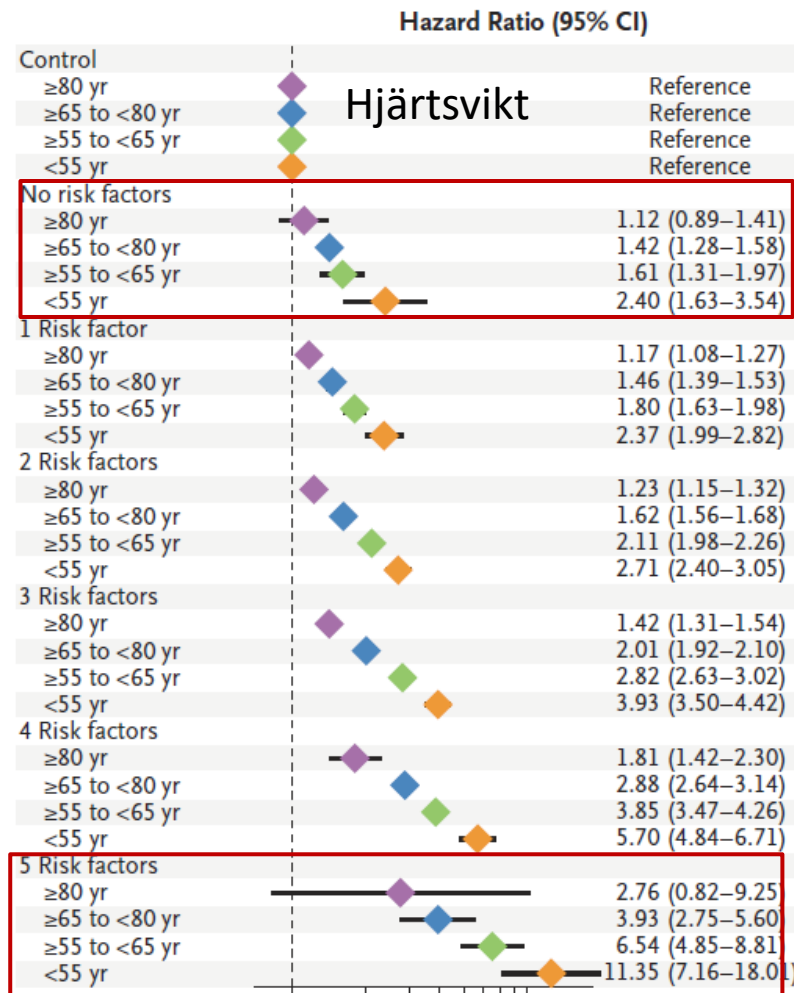
GLP-1 RA

# Prevention lönar sig – men finns kvarstående ökad risk för hjärtsvikt

T2DM Swedish diabetes registry, 1998-2012, follow-up 5.7 years

n=271,174 controls 1,355,870

D Excess Heart Failure in Relation to Range of Risk-Factor Control



## Fem riskfaktorer

HbA1c, LDL, albuminuria, rökning, BP

## Risk för hjärtsvikt

Ingen riskfaktor

HR 1.12 up to 2.40

5 riskfaktorer

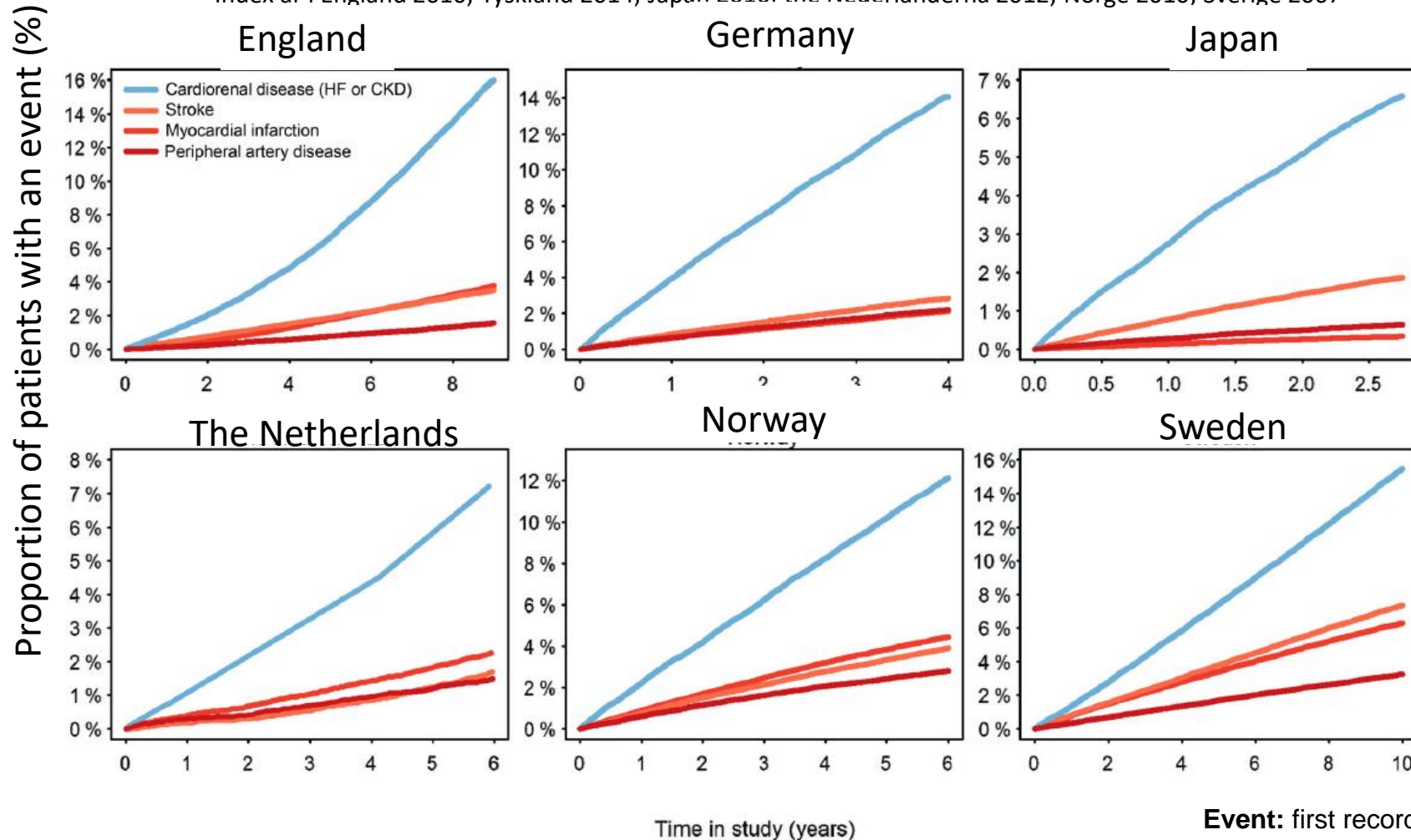
HR 2.76 up to 11.35

*Prevention viktigt!  
Men ännu ej tillräckligt för att  
hindra hjärtsvikt!*

# Hjärtsvikt och njursvikt är idag första kardiiovaskulära presentationen vid typ 2 diabetes

N=705 000 Hjärtkärifriska med typ 2 diabetes

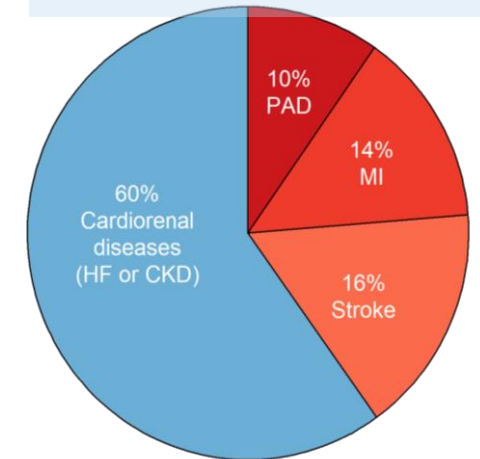
Index år i England 2010; Tyskland 2014; Japan 2016; the Nederländerna 2012; Norge 2010; Sverige 2007



Event 18% (n=137 081)

CKD	36%	} 60%
HF	24%	
Stroke	16%	
MI	14%	
PAD	10%	

Most frequent CKD+HF  
Across all countries



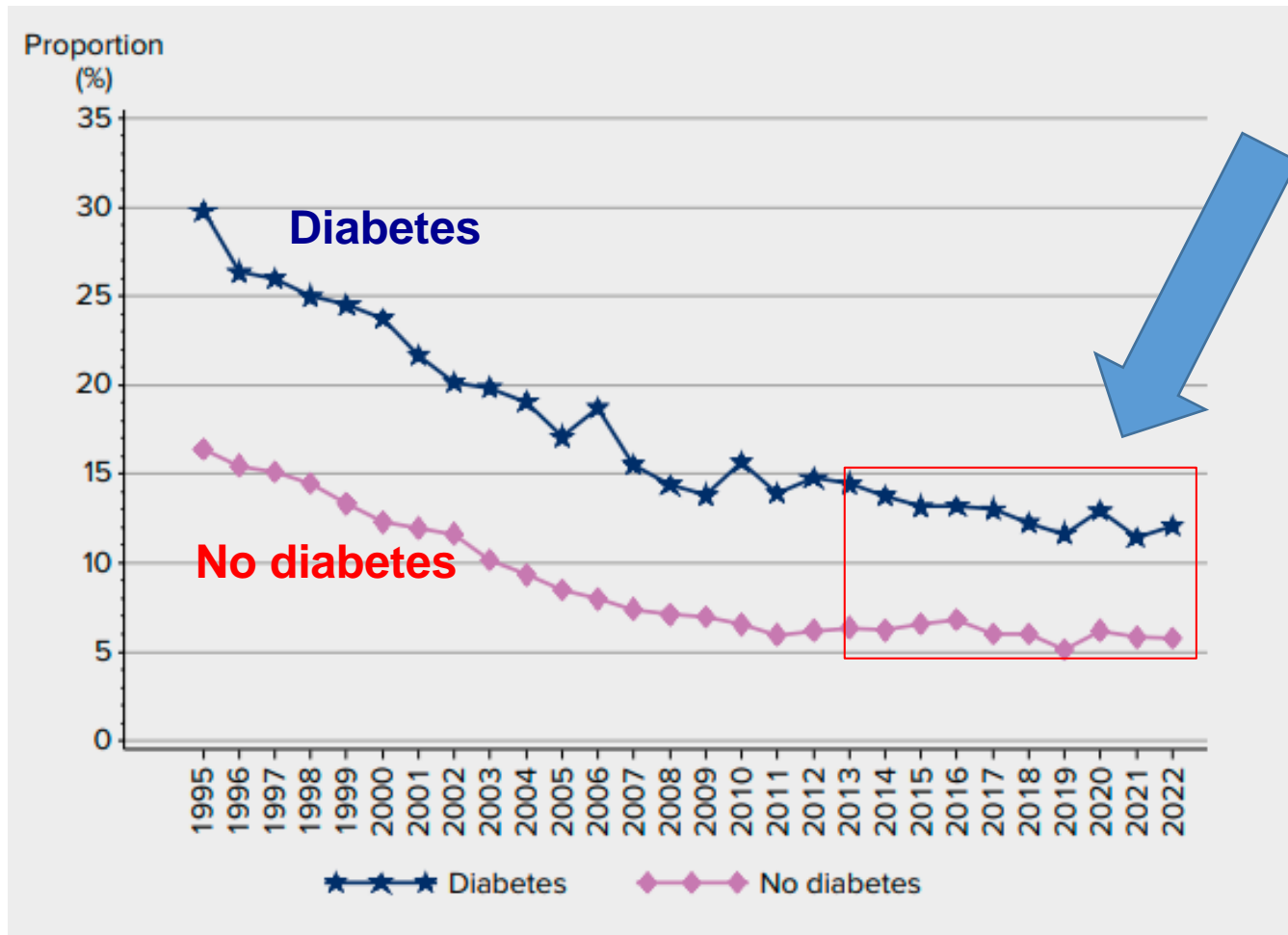
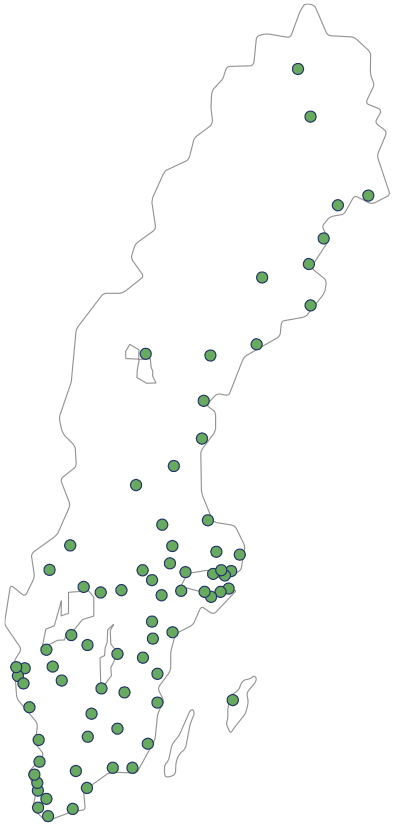
**Event:** first recorded hospitalised (in or out visit)

**CKD defined as;** diabetic nephropathy, acute kidney failure, CKD, unspecified kidney disease, hypertensive kidney failure and dialysis

# Prognos

## 1-årsdödlighet efter hjärtinfarkt

The SWEDEHEART registret, 1-årsdödlighet efter AMI 1995-2022



Mer än 50% minskad dödlighet efter hjärtinfarkt, efter justering

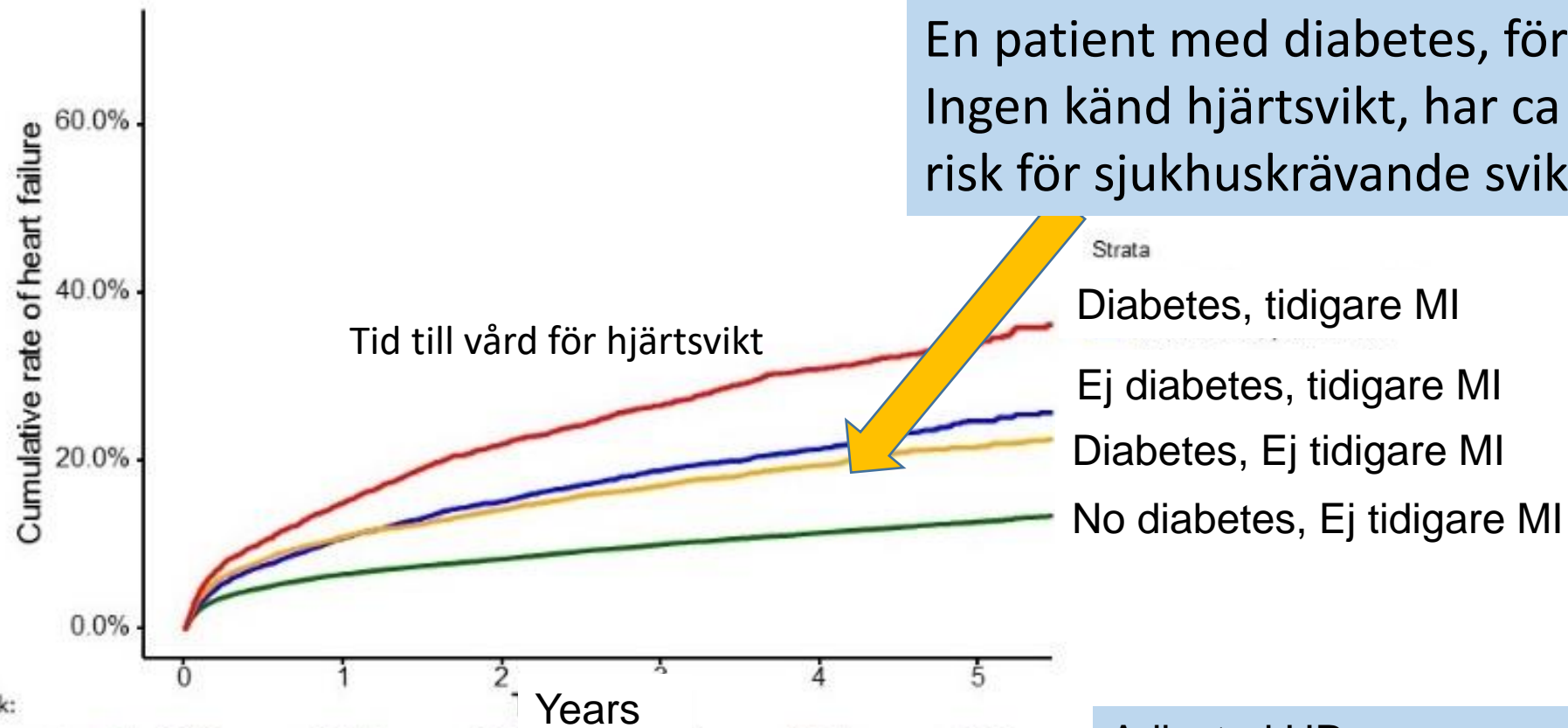
Finns en kvarstående överrisk vid diabetes!



# Hur är långtidsrisken efter hjärtinfarkt?

## Hög risk för hjärtsvikt efter AMI om diabetes

73 959 patienter med och utan diabetes åren 2012-2017 med AMI i SWEDEHEART-registret



En patient med diabetes, första hjärtinfarkt  
Ingen känd hjärtsvikt, har ca 50% ökad risk för sjukhuskrävande svikt

Numbers at risk:

	0	1	2	3	4	5
No diabetes, no previous MI	46059	33726	25992	18592	11646	5250
No diabetes, previous MI	7797	5500	4173	2933	1891	833
Diabetes, no previous MI	10992	7364	5491	3793	2261	1004
Diabetes, previous MI	4368	2869	2046	1427	854	373

Adjusted HR

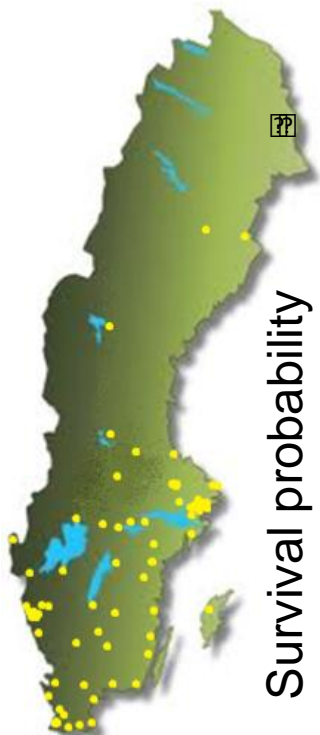
First MI, no previous HF 1.48 [1.40-1.57]

First MI, LVEF  $\geq$  50% 1.56 [1.39-1.76]

# Still dismal survival after HHF in Sweden 2003-2011

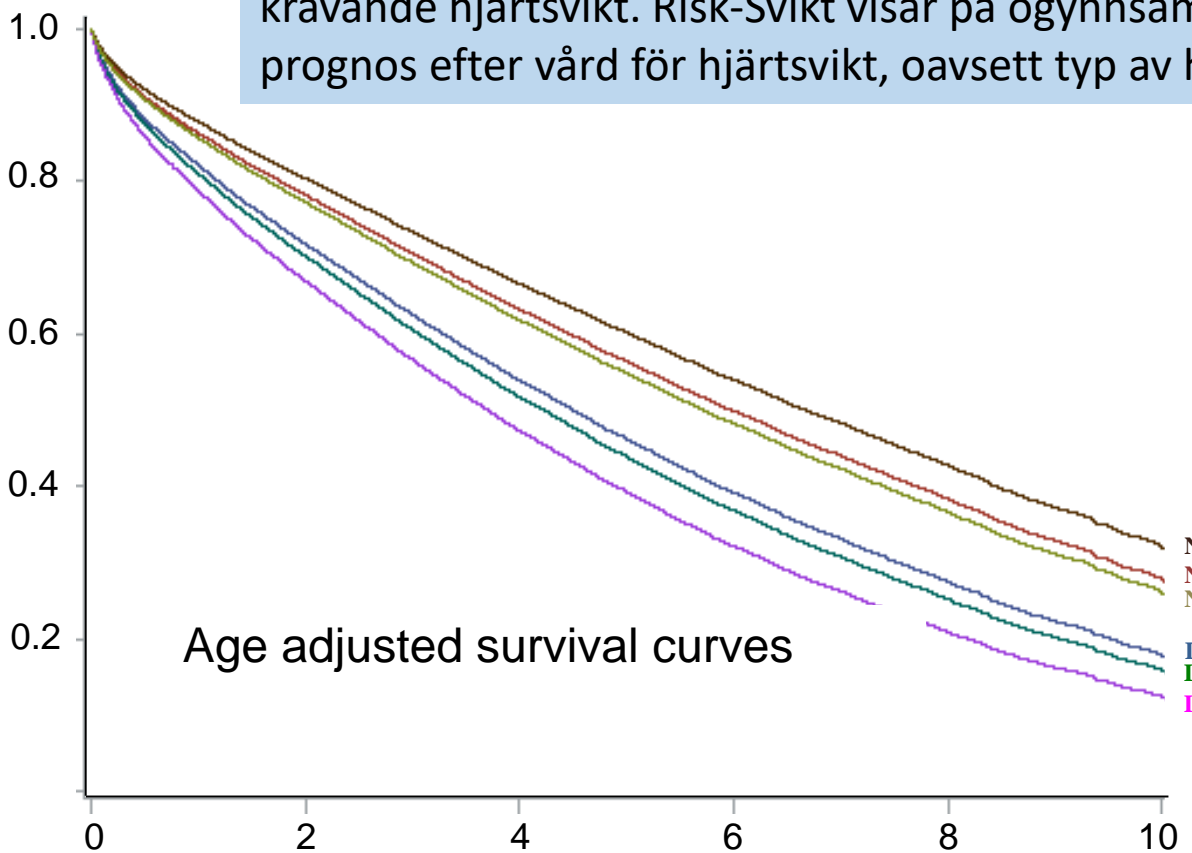
N=30 606, Diabetes in 25% (n=7487), Swedish Heart Failure registry

HFmrEF; EF=40-50%, HFrEF; EF<40%, HFpEF; EF≥50%



Viktigt att skydda vår patient från sjukhuskrävande hjärtsvikt. Risk-Svikt visar på ogynnsam prognos efter vård för hjärtsvikt, oavsett typ av hjärtsvikt

Survival probability



Age adjusted survival curves

No DM, HFpEF  
No DM, HFmrEF  
No DM, HFrEF  
DM, HFpEF  
DM, HFmrEF  
DM, HFrEF

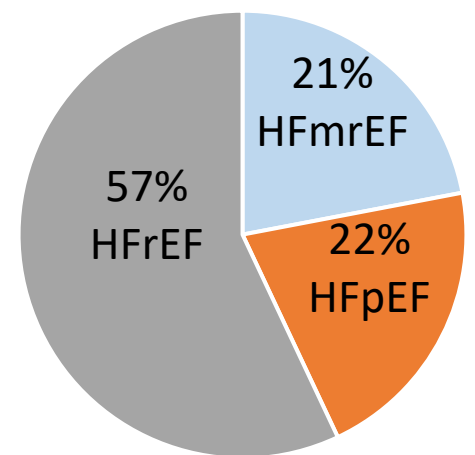
Diabetes

**HFpEF**  
DM vs. No DM  
Adj HR 1.32 ( 1.22-1.43)

**HFmrEF**  
DM vs. No DM  
Adj HR 1.51 (1.39-1.65)

**HFrEF**  
DM vs. No DM  
Adj HR 1.46 (1.39-1.54)

Proportion HF type in DM



RESEARCH

Open Access

Trends in prognosis and use of SGLT2i and GLP-1 RA in patients with diabetes and coronary artery disease



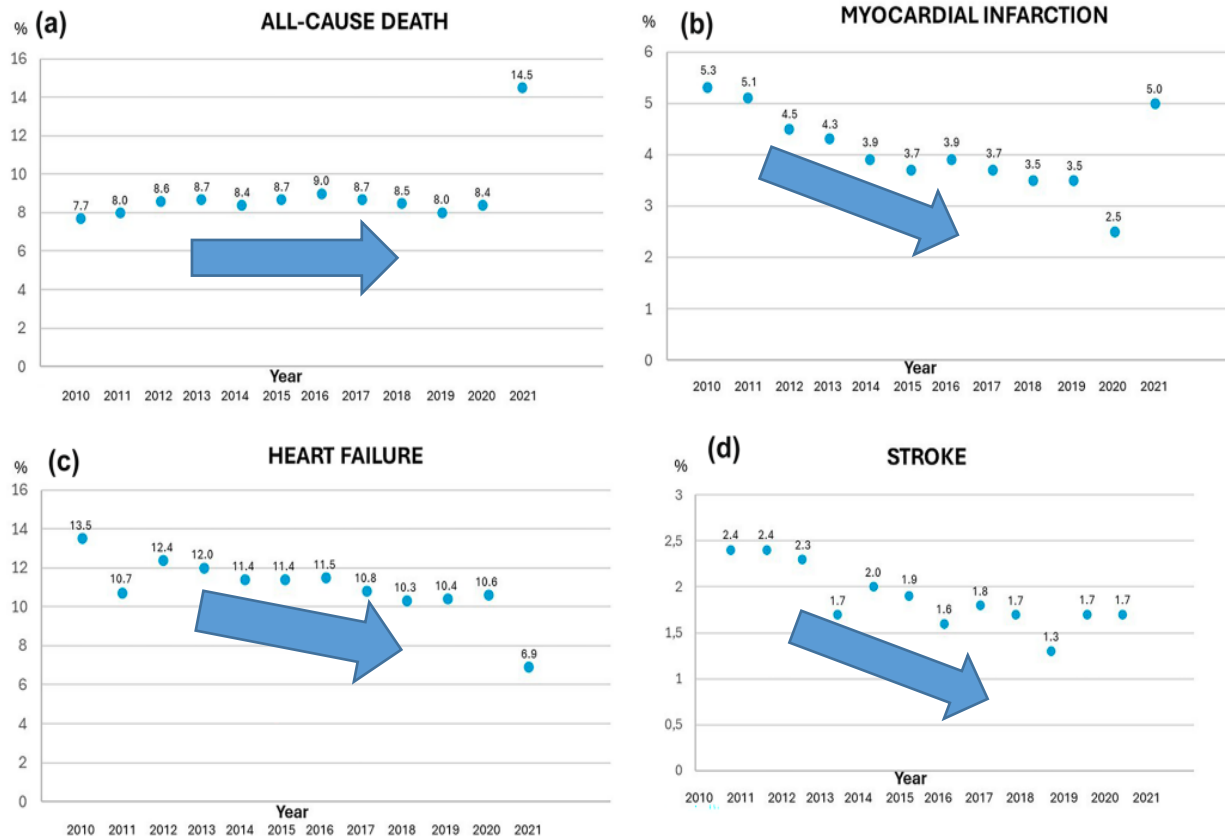
Viveca Ritsinger<sup>1,2\*</sup>, Kamila Avander<sup>3</sup>, Bo Lagerqvist<sup>4</sup>, Pia Lundman<sup>3</sup> and Anna Norhammar<sup>1,5</sup>

# Yearly event rate after CVD –improves

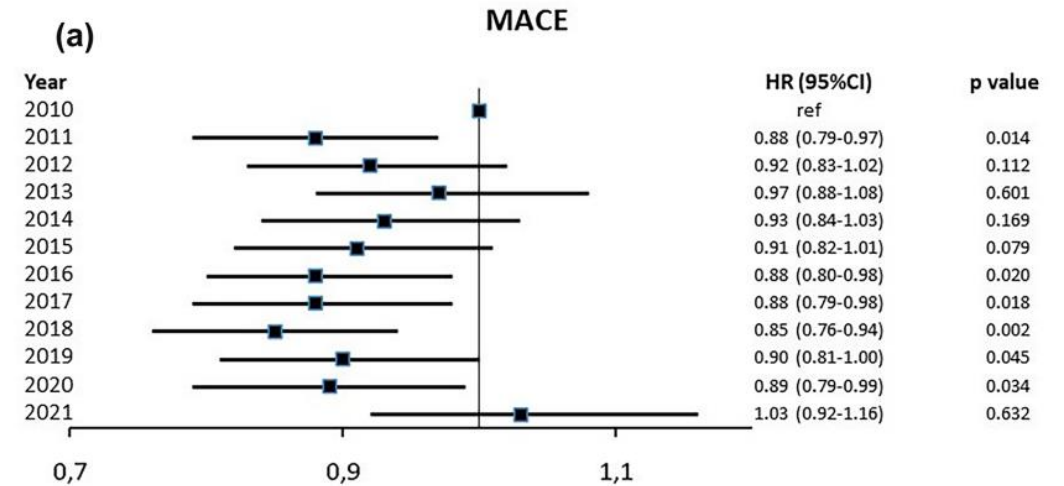
## SWEDHEART , 2010 to 2021, n=38,671 with DM

### 31% stable CAD, 69% STEMI/nonSTEMI infarction

Reduction in MI, Stroke, somewhat in HF, death stable



Yearly MACE reduced vs. yr 2010



RESEARCH

Open Access

Trends in prognosis and use of SGLT2i and GLP-1 RA in patients with diabetes and coronary artery disease

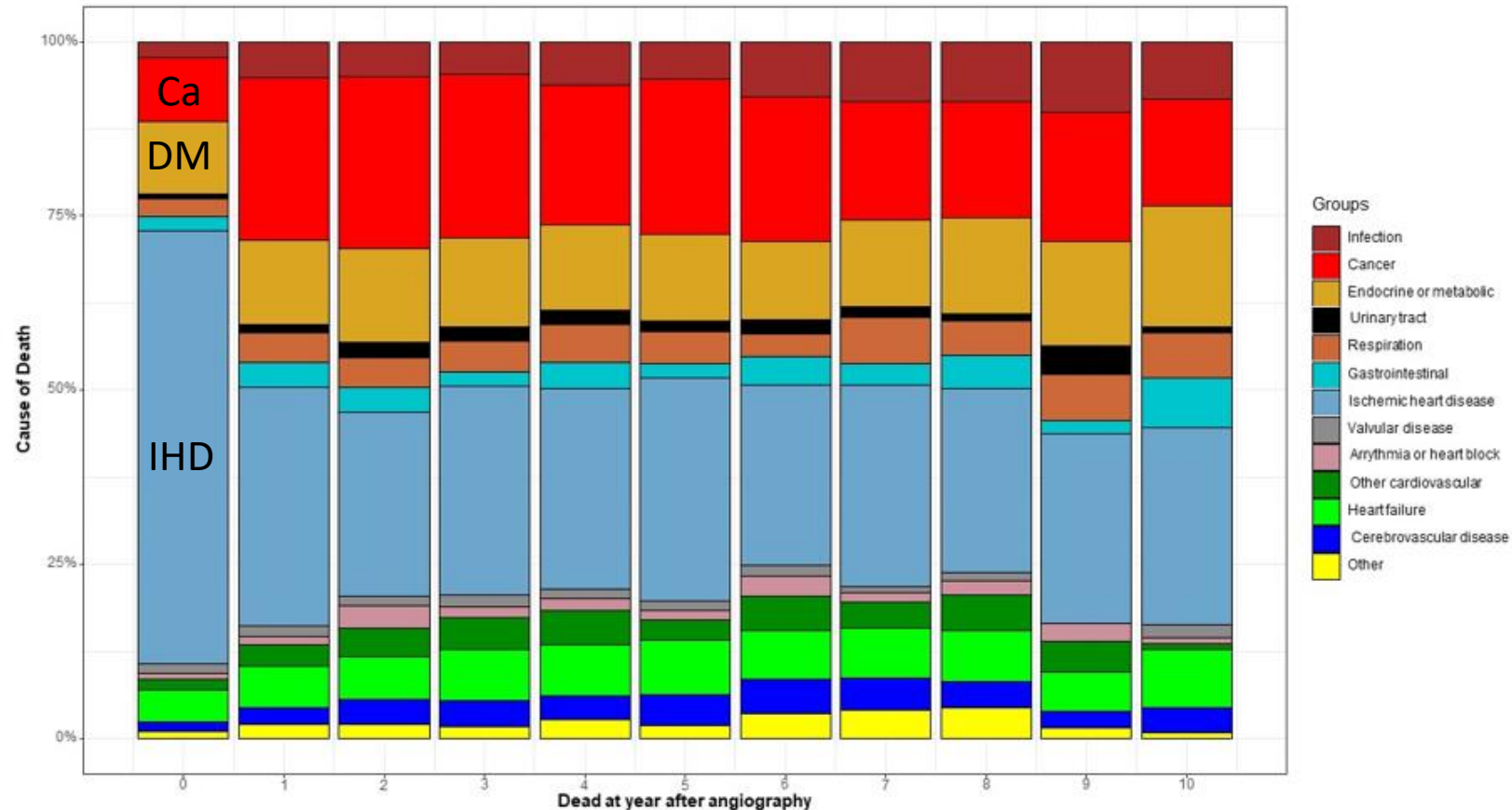


Viveca Ritsinger<sup>1,2\*</sup>, Kamila Avander<sup>3</sup>, Bo Lagerqvist<sup>4</sup>, Pia Lundman<sup>3</sup> and Anna Norhammar<sup>1,5</sup>

# Mortality cause after CVD in diabetes

SWEDHEART, 2010 to 2021, n=38,671 with DM  
31% stable CAD, 69% STEMI/nonSTEMI infarction

Mortality cause first year 60% IHD, second year cancer+ endocrine catches up





# Glukosstörningar vanligt ≈ 60% av patienter med hjärtinfarkt om OGTT

OGTT 4-5 dagar efter infarkt

**THE LANCET**

ARTICLES

**Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study**

*Anna Norhammar, Åke Tenerz, Göran Nilsson, Anders Hamsten, Suad Efendic, Lars Rydén, Klas Malmberg*

**Summary**

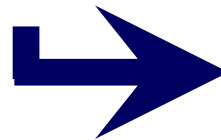
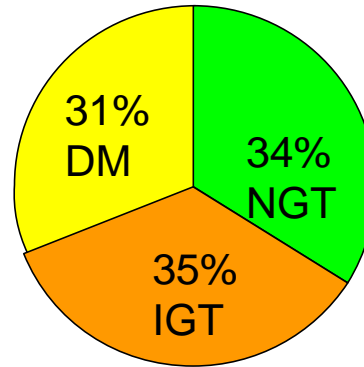
**Background** Glycometabolic state at hospital admission is an important risk marker for long-term mortality in patients with acute myocardial infarction, whether or not they have

**Introduction** Individuals with diabetes who have myocardial infarction are more likely to die than those without diabetes.<sup>1-3</sup> Furthermore, results of several large cohort studies<sup>4,5</sup> indicate that people with prediabetic

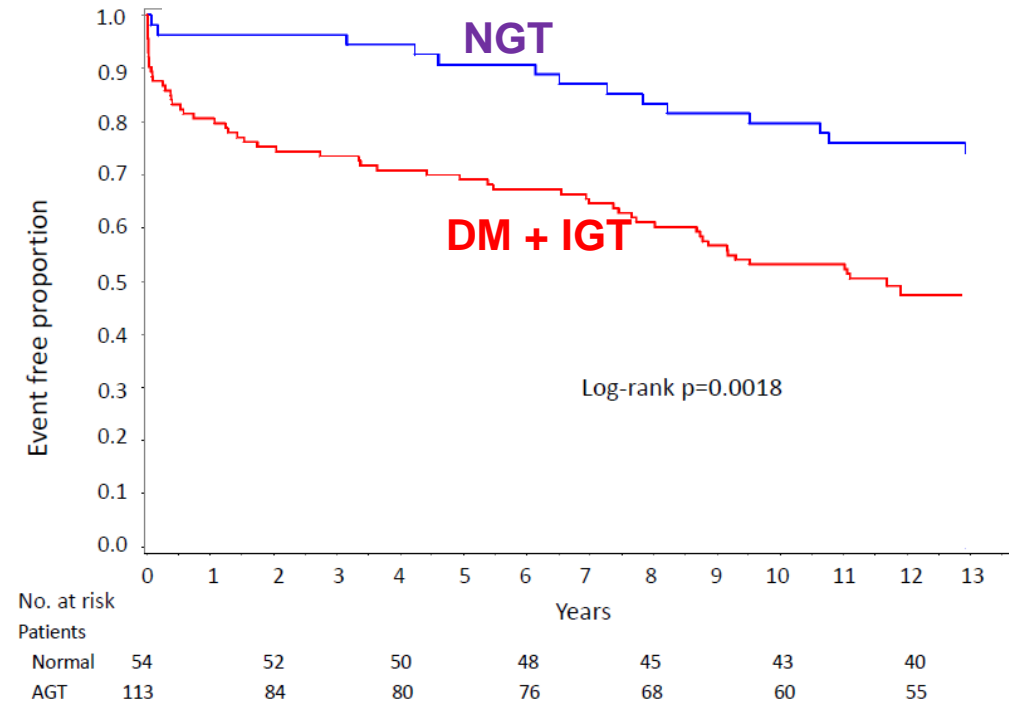


Norhammar et al Lancet 2002; 359: 2140

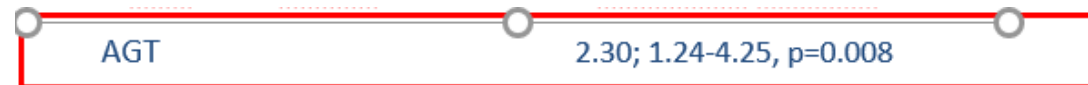
60%



10 års uppföljning  
CV event; CV death, MI, stroke, heart failure

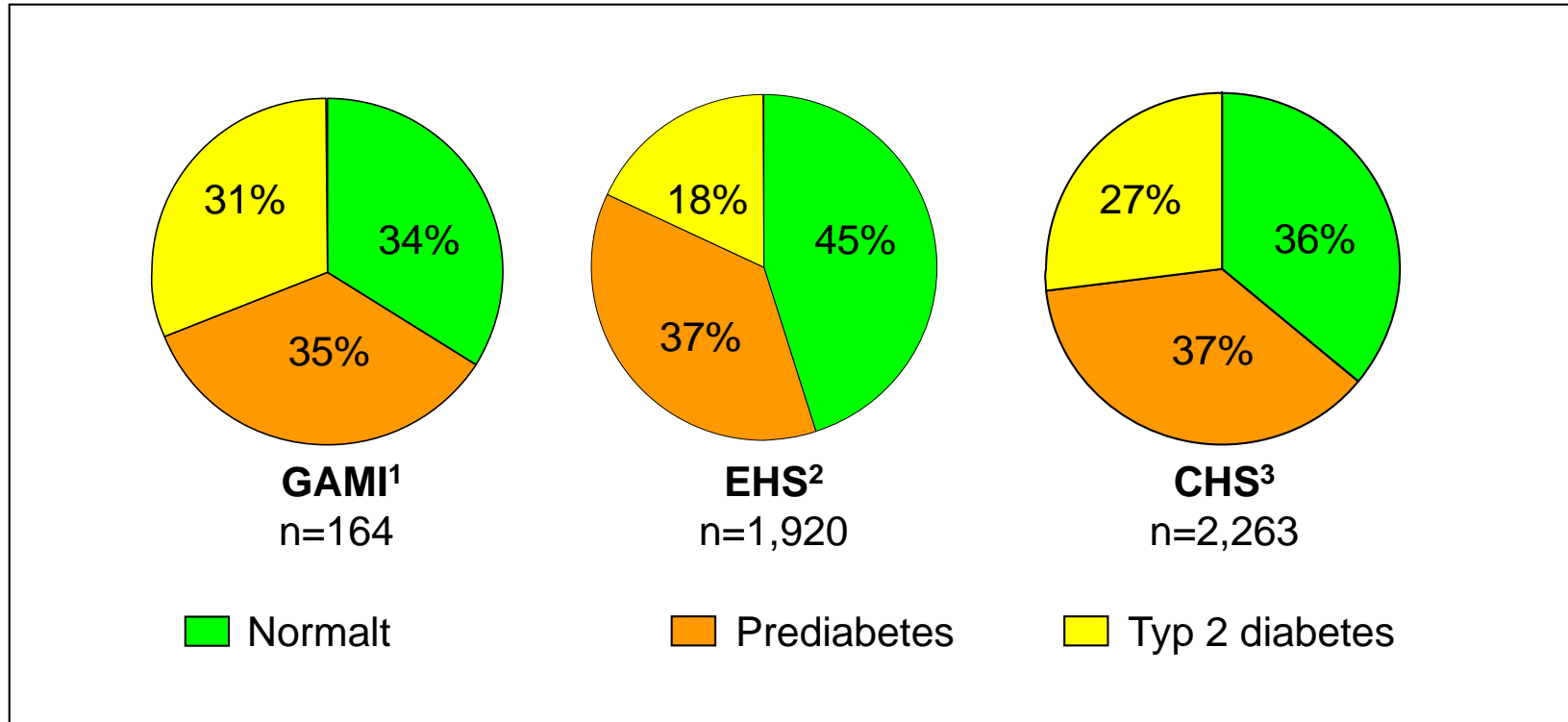


Ritsinger et al Diab Vas Dis Res 2014



# Glucose disturbances are common (60-65%) in AMI

Repeated results in Sweden, Europe, China.....



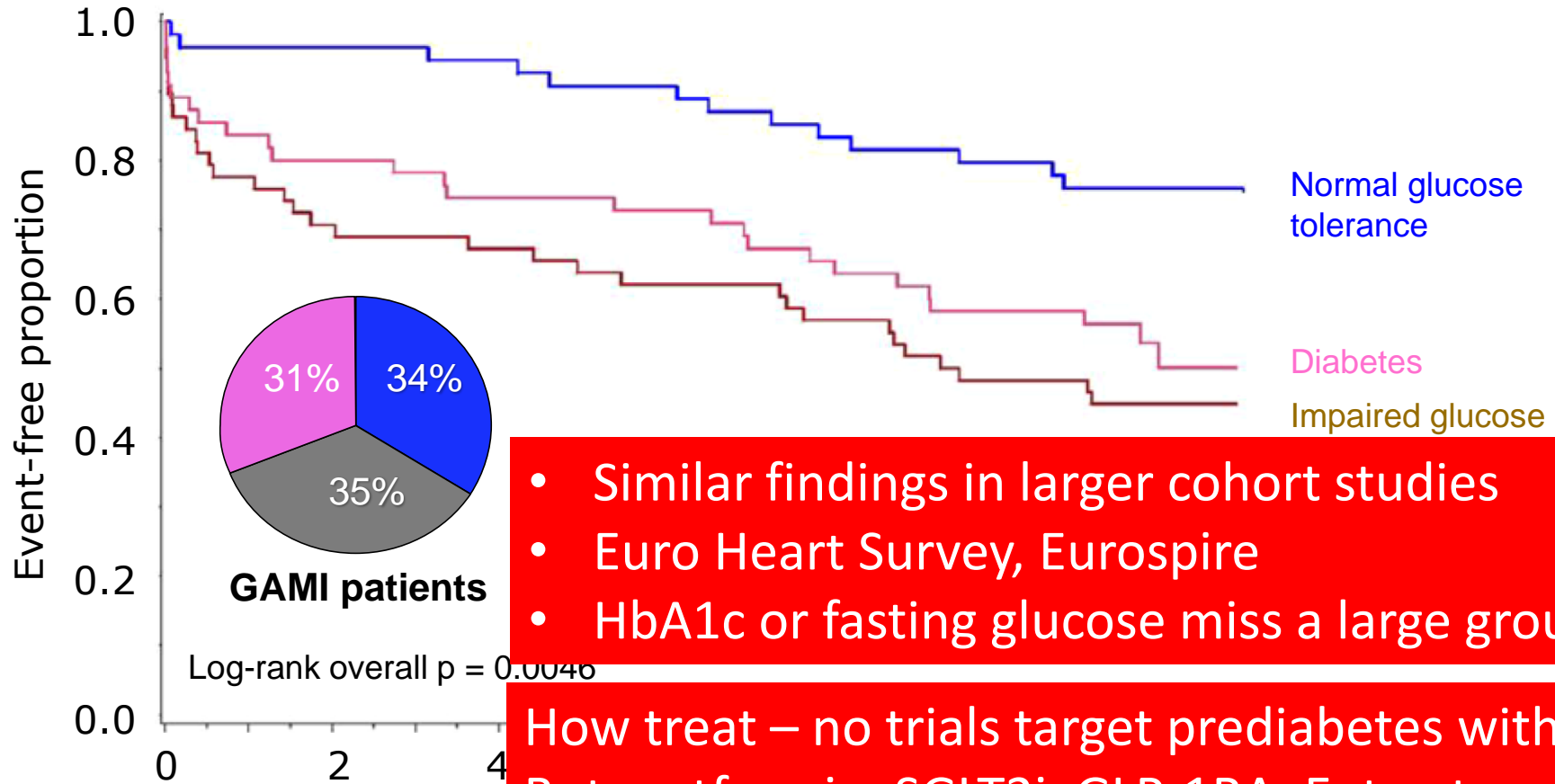
(1. Norhammar et al. Lancet. 2002;359:2140–4)

(2. Bartnik et al. Eur Heart J. 2004;25:1880–90)

(3. Hu et al. Eur Heart J. 2006;27:2573–9)

# Newly detected glucose abnormalities – at CV risk

OGTT 4-5 days after AMI; GAMI – long-term follow up  
First major event (death, MI, stroke or severe heart failure)



- Similar findings in larger cohort studies
- Euro Heart Survey, Eurospire
- HbA1c or fasting glucose miss a large group

How treat – no trials target prediabetes with CAD  
But metformin, SGLT2i, GLP-1RA, Entresto reduces glucose levels after AMI or HF with prediabetes

# Screening for diabetes – ESC 2023 diabetes guidelines

## Recommendation Table 1 — Recommendations for diagnosing diabetes

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Screening for diabetes is recommended in all individuals with CVD, <sup>c</sup> using fasting glucose and/or HbA1c. <sup>5–7,36,37,39</sup>	<b>I</b>	<b>A</b>
It is recommended that the diagnosis of diabetes is based on HbA1c and/or fasting plasma glucose, or on an OGTT if still in doubt. <sup>d,5–8,10,11</sup>	<b>I</b>	<b>B</b>

1. HbA1c/faste-glukos
2. OGTT om tveksamt resultat

**Table 5 Revised concepts 2023 Guidelines**

Focus of the Guidelines is prevention and management of cardiovascular disease in diabetes

The aspect of pre-diabetes is no longer covered in the current Guidelines.

# 2023 ESC guidelines on diabetes

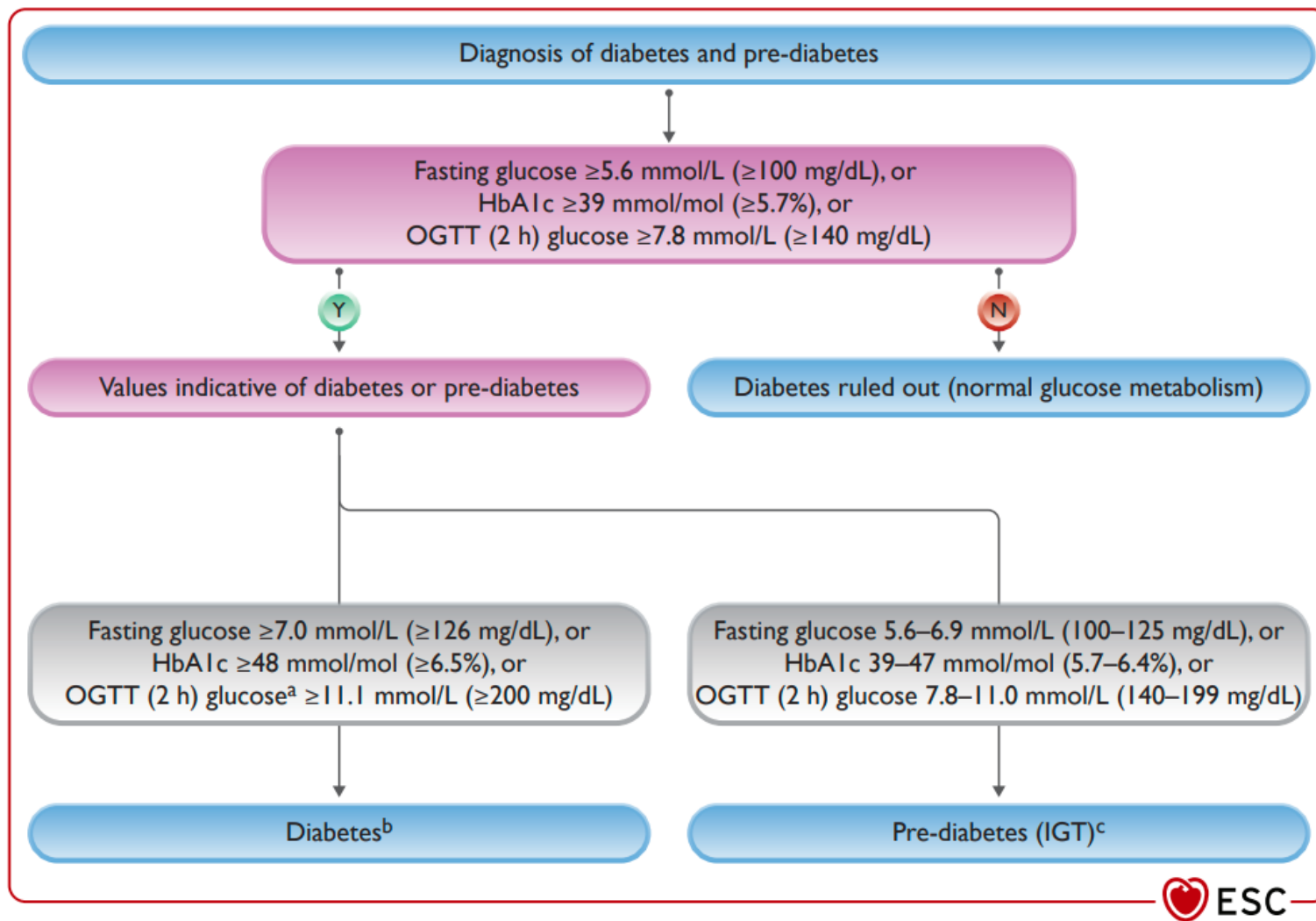
## Diagnostic criteria by WHO and ADA

**Table 6 Biochemical diagnostic criteria for diabetes and pre-diabetes according to the World Health Organization and the American Diabetes Association**

Glycaemic marker	WHO criteria (2011, 2019) <sup>5,6</sup>	ADA criteria (2021) <sup>7</sup>
	<b>Diabetes</b>	
FPG	≥7.0 mmol/L (≥126 mg/dL)	
2hPG (OGTT)	≥11.1 mmol/L (≥200 mg/dL)	
HbA1c	≥6.5% (≥48 mmol/mol)	
RPG	≥11.1 mmol/L (≥200 mg/dL)	
<b>Pre-diabetes</b>		
FPG	6.1–6.9 mmol/L (110–125 mg/dL)	5.6–6.9 mmol/L (100–125 mg/dL)
2hPG (OGTT)	7.8–11.0 mmol/L (140–199 mg/dL)	
HbA1c	6.0–6.4% (42–47 mmol/mol)	5.7–6.4% (39–47 mmol/mol)

ADA, American Diabetes Association; 2hPG, 2 h plasma glucose; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; RPG, random plasma glucose; OGTT, oral glucose tolerance test; WHO, World Health Organization.

# 2023 -ESC guidelines algorithm diagnosis diabetes and prediabetes



ADA criteria – very low fasting and HbA1c cutoffs!

**Figure 2** Diagnosis of diabetes and pre-diabetes. HbA1c, glycated haemoglobin; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test. <sup>a</sup>Rule out stress hyperglycaemia (often manifests as elevated glucose and normal HbA1c). <sup>b</sup>In the presence of symptoms, a single test is enough; in the absence of symptoms, two abnormal tests are required to make the diagnosis. <sup>c</sup>American Diabetes Association criteria are used in this scheme for the diagnosis of pre-diabetes.

# ESC guidelines on prediabetes screening 2023

## **Table 5** Revised concepts 2023 Guidelines

### **Focus of the Guidelines is prevention and management of cardiovascular disease in diabetes**

The aspect of pre-diabetes is no longer covered in the current Guidelines.

### **Cardiovascular risk assessment in diabetes**

For patients without ASCVD or severe target-organ damage, a novel T2DM-specific risk score (SCORE2-Diabetes) is introduced.

CV risk categories in T2DM are now defined based on the presence of ASCVD or severe target-organ damage or the 10-year CVD risk using SCORE2-Diabetes.

# Diabetes och hjärtkärlsjukdom

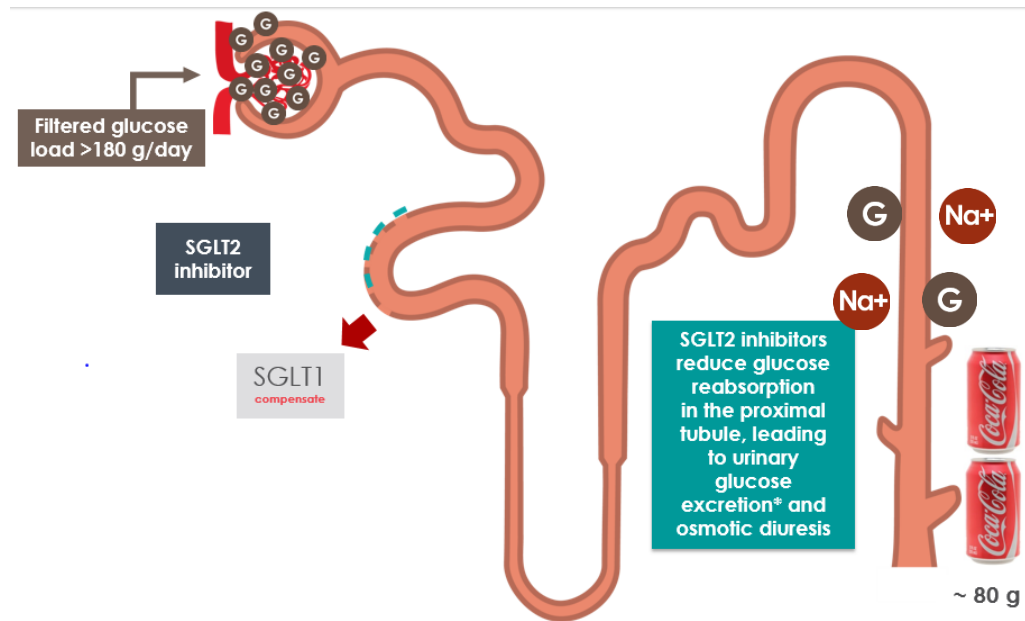
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**SGLT-2i**

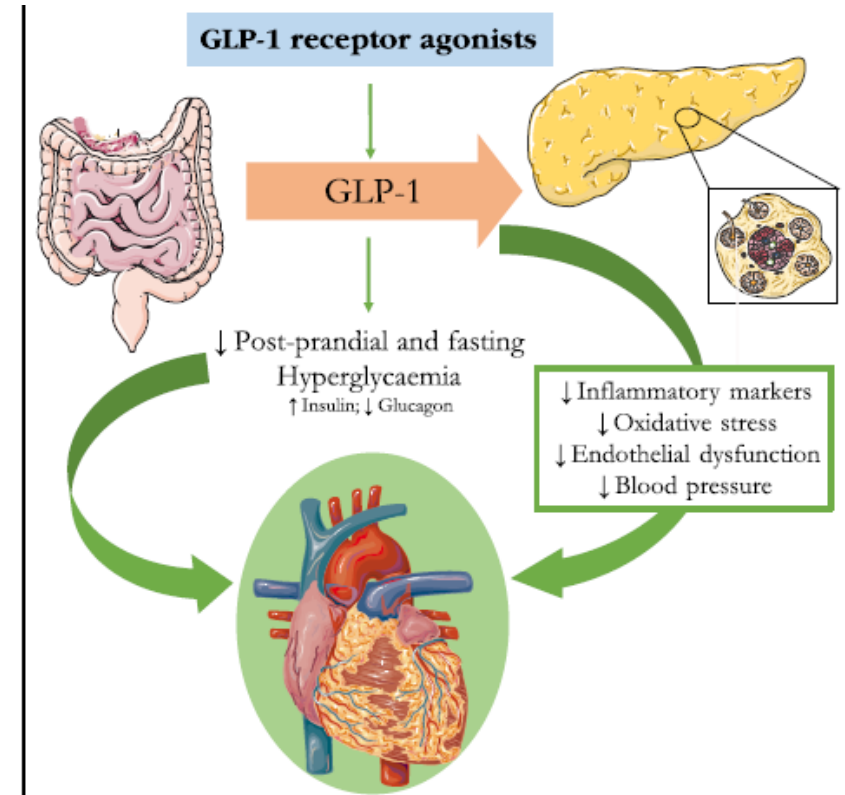


# SGLT-2i and GLP1 RA – have different mechanism

SGLT-2i increases glucose and sodium excretion to urine



GLP1 RA stimulates insulin and inhibits glucagon secretion



Adopted and By courtesy from BI

Bakris GL, et al. *Kidney Int.* 2009;75;1272–1277.

Ferranini E, *Cell* 2017 review

Hiddo J.L. Heerspink et al review; *Kidney International* (2018) 94, 26–39

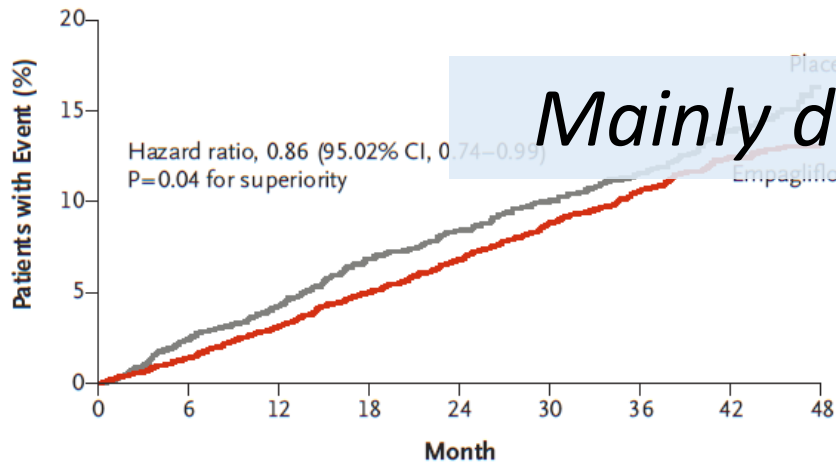
Lotte Bjerre Knudsen *Frontiers in Endocrinology* April 2019

Daniel Drucker *Diabetes* 2018;67:1710–1719

# MACE (primary endpoint- CV-death/MI/Stroke)

## EMPAREG OUTCOME

N= 7020, 100% CVD



**HR 0.86 (0.74-0.99)**

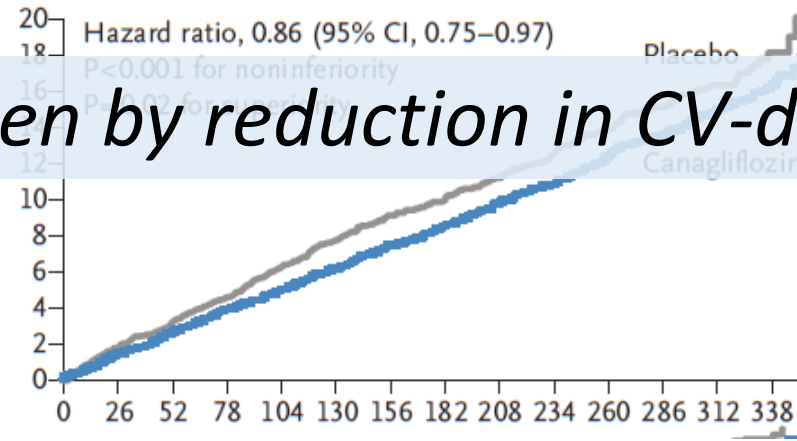
Superiority p=0.04

Zinman et al. N Engl J Med 2015; 373:2117

**Mortality HR 0.68 (0.57-0.82)**

## CANVAS Program

N= 10142, 66% CVD



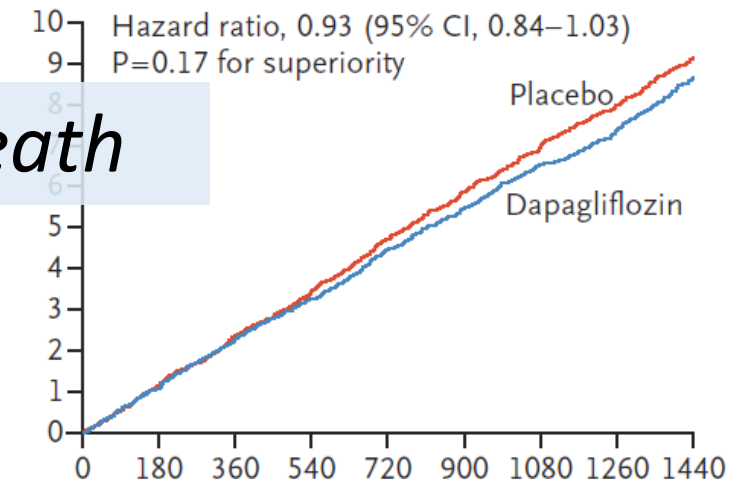
**HR 0.86 (0.75-0.97)**

Superiority p=0.02

Neal B et al. N Engl J Med. 2017

## DECLARE TIMI-58

N= 17160, 40% CVD



**HR 0.93 (0.84-1.03)**

Superiority p=0.17

Wiviott SD et al. N Engl J Med. 2018 Nov.10

*Mainly driven by reduction in CV-death*

# Hospitalisation for heart failure and renal events

(Renal events; renal function, renal transplantation, renal death)

	Heart failure	Renal events
<b>EMPAREG OUTCOME</b> N= 7020, 100% CVD	<b>HR 0.66</b> (0.50-0.85)	<b>HR 0.61</b> (0.53-0.70)
<b>CANVAS Program</b> N= 10142, 66% CVD	<b>HR 0.67</b> (0.52-0.87)	<b>HR 0.60</b> (0.47-0.77)
<b>DECLARE TIMI-58</b> N= 17160, 40% CVD	<b>HR 0.73</b> (0.61-0.88)	<b>HR 0.53</b> (0.43-0.66)

Consistent robust  
significant reductions  
in HF and renal events

Ftichett D European Heart Journal (2016) 37, 1526

Wanner N Engl J Med 2016;375:323-34.

Neal B et al. N Engl J Med. 2017

Wiviott SD et al. N Engl J Med. 2018 Nov.10

SGLT2-hämmare - ny hjärtsvikt medicin  
vid HFrEF och HFpEF, med eller utan  
diabetes

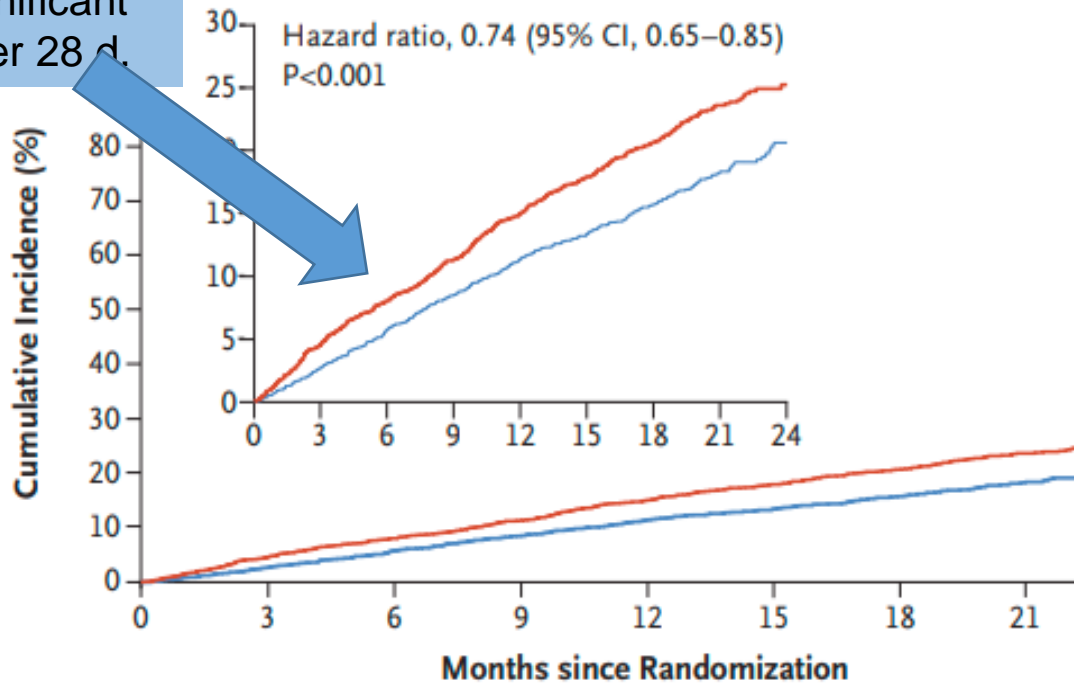
# Chronic HFrEF; primary outcome

## DAPA-HF 2019

N=4744, LVEF ≤40%, NYHA 2-4, EGFR > 30 ml/min  
Primary outcome; CV-death + worse HF/urgent HF  
SGLT-2i 10 mg dapagliflozin vs placebo  
Mean age 66, mean EF 31%

**HR 0.74 (0.65-0.85)**

Fast effect  
significant  
after 28 d.



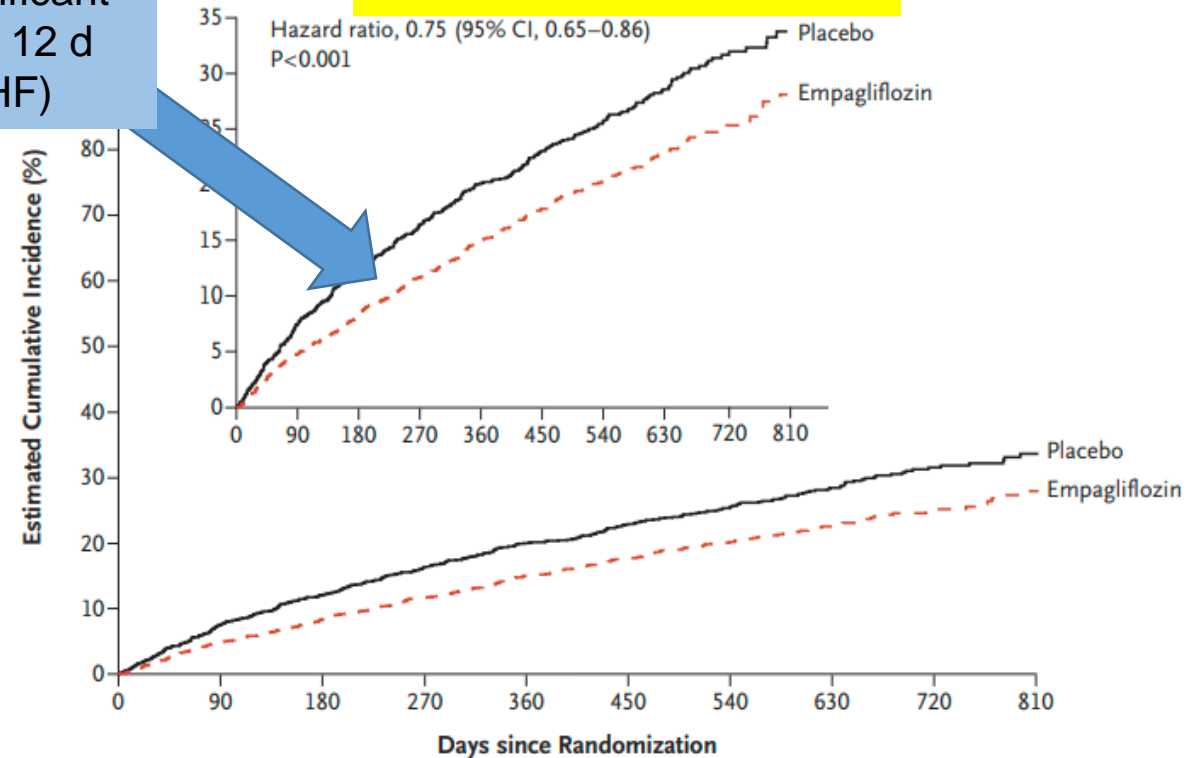
J.J.V. McMurray, NEJM 2019

## EMPEROR-Reduced 2020

N=3730, LVEF ≤40%, NYHA 2-4, eGFR > 20ml/min  
Primary outcome; CV-death + worse HF  
SGLT-2i 10 mg empagliflozin vs placebo  
Mean age 67, mean EF 27%

**HR 0.75 (0.65-0.86)**

Significant  
after 12 d  
(all HF)



M. Packer, NEJM 2020 & M Packer Circulation 2021

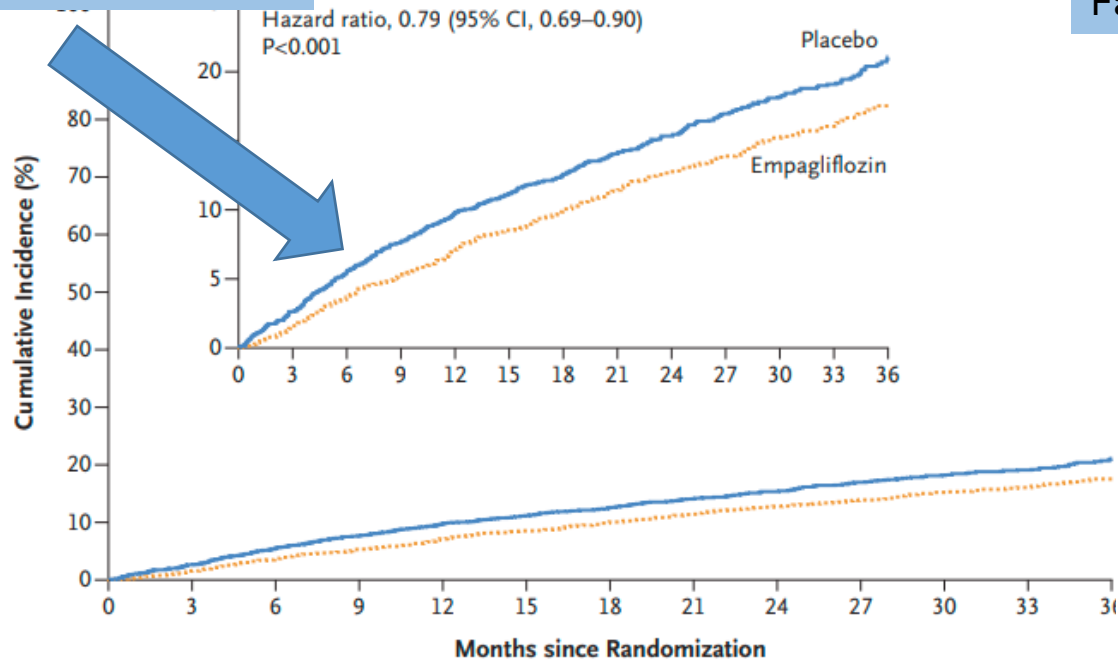
# HFpEF/HFmrEF; primary outcome

EMPEROR-preserved 2021

N=5998, LVEF >40%+ structural HF, NYHA 2-4, eGFR > 19 ml/min  
Primary outcome; CV-death + hosp HF  
SGLT-2i empagliflozin 10 mg vs placebo  
Mean age 72, mean EF 54.3%, mean follow-up 26.2 months

**HR 0.79 (0.69-0.90)**

Fast effect, mainly HHF



S.D. Anker et al, NEJM 2021

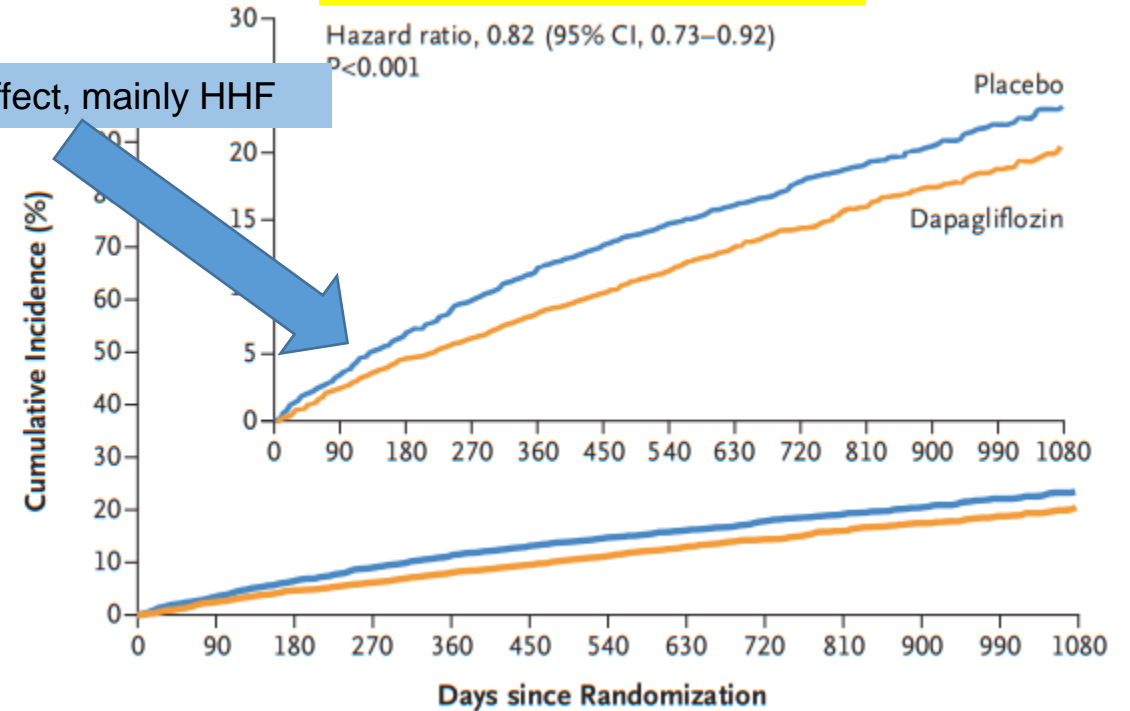
DELIVER 2022

N=6263, LVEF >40%+ structural HF, NYHA 2-4, eGFR > xx ml/min  
Primary outcome; CV-death + hosp HF+ urgent HF  
SGLT-2i dapagliflozin 10 mg vs placebo  
Mean age 72, mean EF 54%, mean follow-up 2.3 yr.

**HR 0.82 (0.73-0.92)**

A Primary Outcome

Fast effect, mainly HHF



S.D. Solomon et al, NEJM 2022

# Diabetes och hjärtkärlsjukdom

1. Kardiovaskulär risk – trender och dagsläget
2. Betydelsen av riskfaktor kontroll
3. Kvarstående kardiovaskulära problem
4. Nya möjligheter – kardiovaskulära utfallsstudier

SGLT-2i

**GLP-1 RA**

# GLP1-RA; 4 major CVOT trials CV-preventive effects

Different modified GLP-1 RA

**Leader  
2016  
liraglutide**  
THE NEW ENGLAND JOURNAL of MEDICINE

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**ORIGINAL ARTICLE**

**Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes**

Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Frandsen, Peter Kristensen, M.D., E.M.B.A., Johannes F.E. Mann, M.D., Michael A. Nauck, M.D., Steven E. Nissen, M.D., Stuart Pocock, Ph.D., Neil R. Poulter, F.Med.Sci., Lasse S. Ravn, M.D., Ph.D., William M. Steinberg, M.D., Mette Stockner, M.D., Bernard Zinman, Richard M. Bergenstal, M.D., and John B. Buse, M.D., Ph.D., for the LEADER Steering Committee on behalf of the LEADER Trial Investigators

**Daily injection  
81% CVD**

Marso et al. N Engl J Med 2016

**SUSTAIN-6  
2016  
semaglutide**  
THE NEW ENGLAND JOURNAL of MEDICINE

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**ORIGINAL ARTICLE**

**Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes**

Steven P. Marso, M.D., Stephen C. Bain, M.D., Agostino Consoli, Freddy G. Eliaschewitz, M.D., Esteban Jódar, M.D., Lawrence A. Leiter, Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Julio Rosenstock, M.D., Jochen Seufert, M.D., Ph.D., Mark L. Warren, M.D., Vincent Woo, Oluf Hansen, M.Sc., Anders G. Holst, M.D., Ph.D., Jonas Pettersson, and Tina Vilsboll, M.D., D.M.Sc., for the SUSTAIN-6 Investigators

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**ABSTRACT**

**Weekly injection  
83% CVD**

Marso SP et al. N Engl J Med 2016

**Harmony  
2018  
albiglutide**

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**Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial**

Adrian F Hernandez, Jennifer B Green, Salim Jammohamed, Ralph B D'Agostino Sr, Christopher B Granger, Nigel P Jones, Lawrence A Leiter, Anne E Rosenberg, Kristina N Sigmon, Matthew C Somerville, Karl M Thorpe, John J V McMurray, Stefano Del Prato, for the Harmony Outcomes committees and investigators

**Summary**  
Background Glucagon-like peptide 1 receptor agonists differ in chemical structure, duration of action, and in their effects on cardiovascular outcomes.

**Weekly injection  
100% CVD**

Hernandez Lancet 2018

**REWIND  
2019  
dulaglutide**

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**Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial**

Hertzel C Gerstein, Helen M Colhoun, Gilles R Dagenais, Rajat Das, Mark Lakhani, Prem Pais, Jeffrey Prins, Jeffrey S Rosenson, Matthew C Riddle, Lars Rydén, Dennis Xavier, Charles Messin Altman, Leanne Dyal, Staphanos Hall, Pavlana Rao-Melacini, Gladis Wong, Alvaro Avazum, Jan Basile, Namsik Chung, Ignacio Conget, William C Cushman, Edward Frank, Nicolae Hansa, Marko J Hladik, Shaun Holt, Petr Jansky, Matyas Kralivsky, Fernando Lanas, Lawrence A Leiter, Patricio Lopez-Jaramillo, Ernesto German Cardona Munoz, Valdis Pirags, Nana Pogossova, Peter J Raabheimer, Jonathan E Shaw, Wayne H-H Shea, Theodoros Terzoglou, Karim Tachibani, for the REWIND investigators

**Summary**  
Background Three different glucagon-like peptide-1 (GLP-1) receptor agonists reduce cardiovascular outcomes in people with type 2 diabetes at high cardiovascular risk with high glycaemic haemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) concentrations. We assessed the effect of the GLP-1 receptor agonist dulaglutide on major adverse cardiovascular events when added to the existing antihyperglycaemic regimens of individuals with type 2 diabetes with and without previous cardiovascular disease and a wide range of glycaemic control.

**Methods** This multicentre, randomised, double-blind, placebo-controlled trial was done at 371 sites in 24 countries. Men and women aged 18–85 years with type 2 diabetes and a wide range of glycaemic control were randomised to receive dulaglutide or placebo. Investigators listed in the appendix

**Weekly injection  
32% CVD**

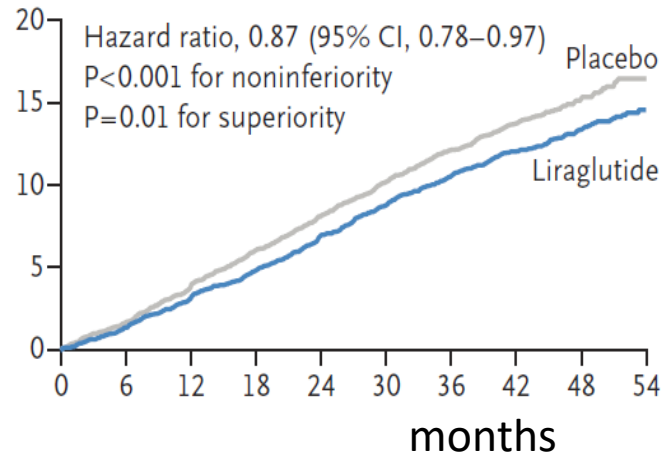
Gerstein H Lancet 2019;394: 121–30



# MACE (primary endpoint)

## LEADER

N= 9340, 81% CVD  
Once daily



**HR 0.87 (0.78-0.97)**  
Superiority p=0.01

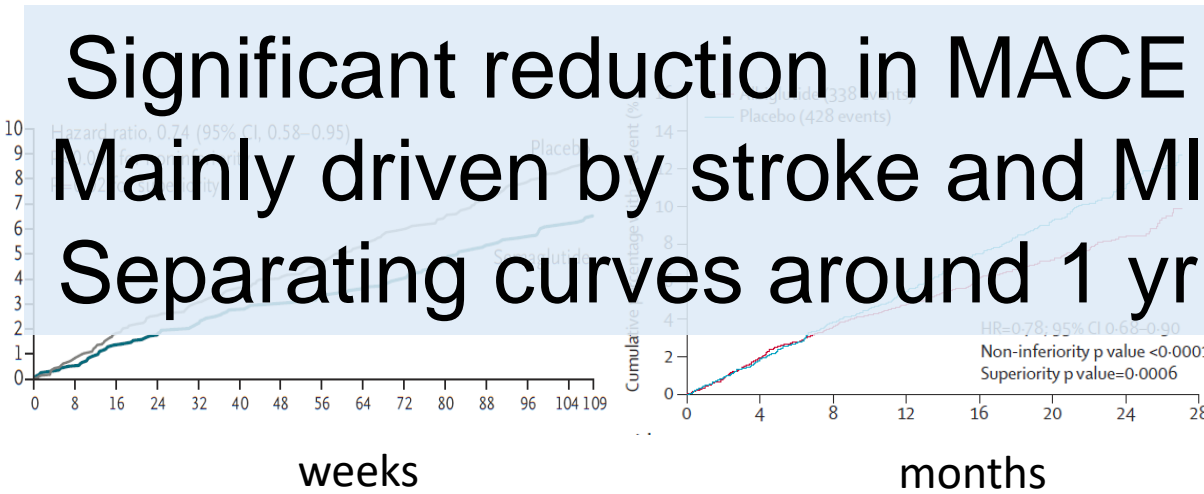
Mortality

**HR 0.85 (0.74-0.97)**

Marso et al. N Engl J Med 2016

## SUSTAIN-6

N= 3297, 83% CVD  
Weekly



**HR 0.74 (0.58-0.95)**  
Superiority p=0.02

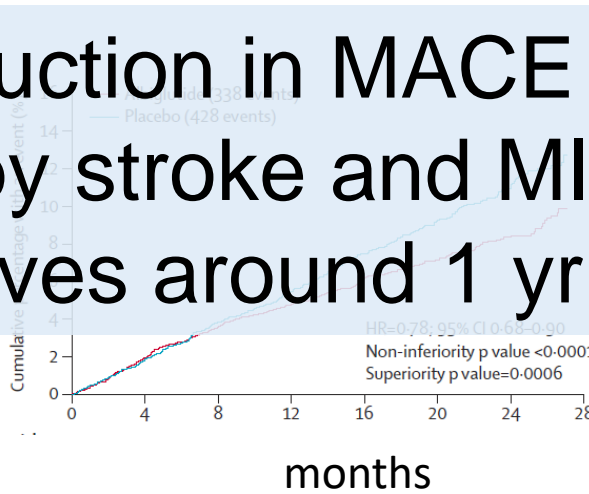
Mortality

**HR 1.05 (0.74-1.50)**

Marso SP et al. N Engl J Med 2016

## HARMONY

N= 17160, ~100% CVD  
Weekly



**HR 0.78 (0.68-0.90)**  
Superiority p=0.0006

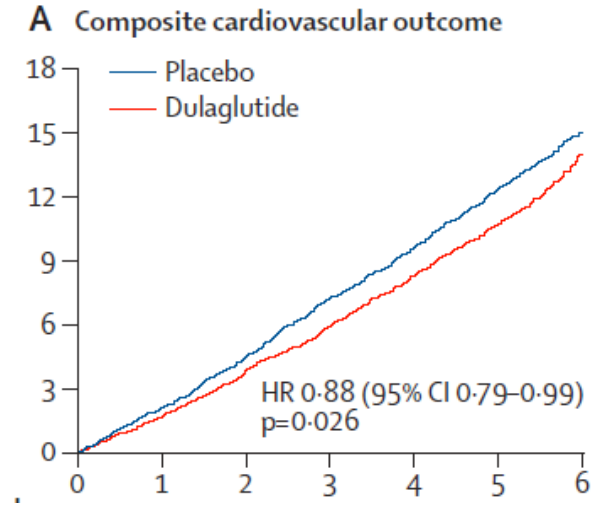
Mortality

**HR 0.95 (0.79-1.16)**

Hernandez Lancet 2018

## REWIND

N= 9901, 32% CVD  
Weekly



**HR 0.88 (0.79-0.99)**  
p=0.026

Mortality

**HR 0.90 (0.80-1.01)**

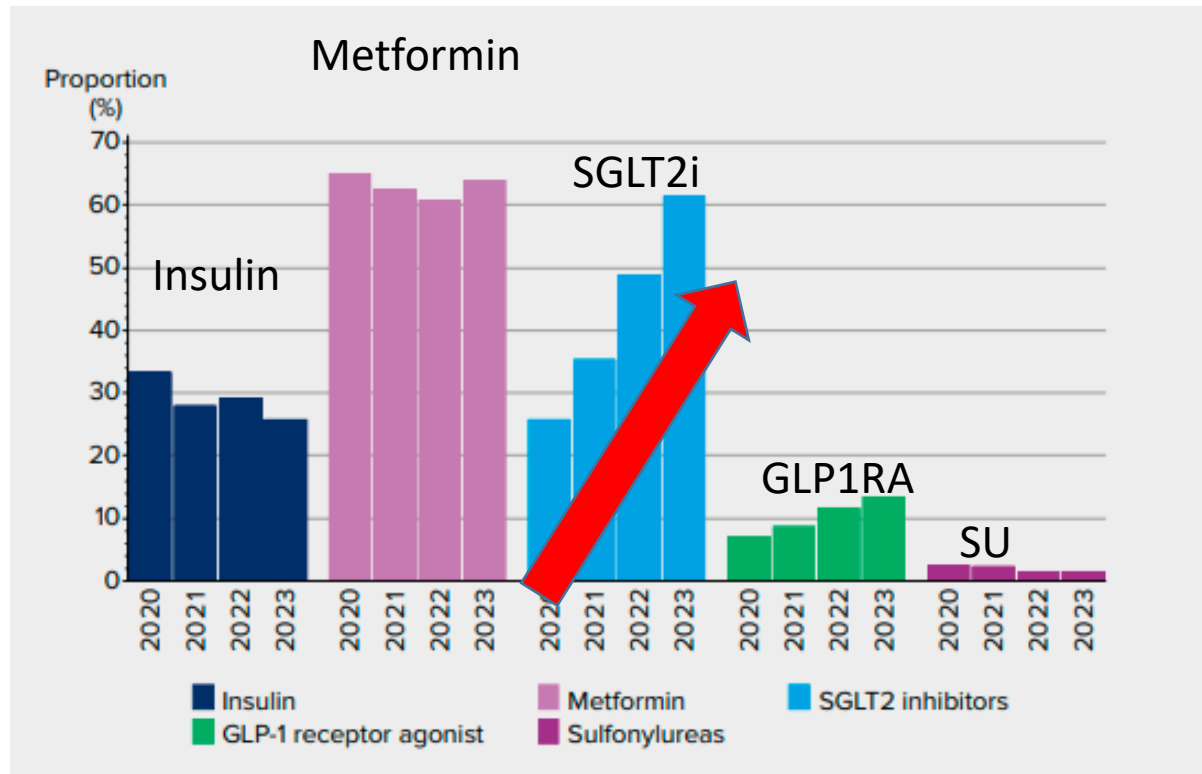
Gersein H Lancet 2019:394: 121–30

**Significant reduction in MACE  
Mainly driven by stroke and MI  
Separating curves around 1 yr**

# Implementation after myocardial infarction

## Use of glucose lowering agents in diabetes post-MI SWEDEHEART 2023

Year 2022



- ESC guidelines on diabetes 2019
- Consensus in Sweden 2020
- New diabetes variable pilot 2018
- Mandatory since 2020
- SGLT2 inhibitor and/ or a GLP-1 receptor agonist at the 1st follow-up was **65 %** in 2023
- A large increase in SGLT2i, **60 %** in 2023
- GLP1 RA around 15 % in 2023

RESEARCH

Open Access

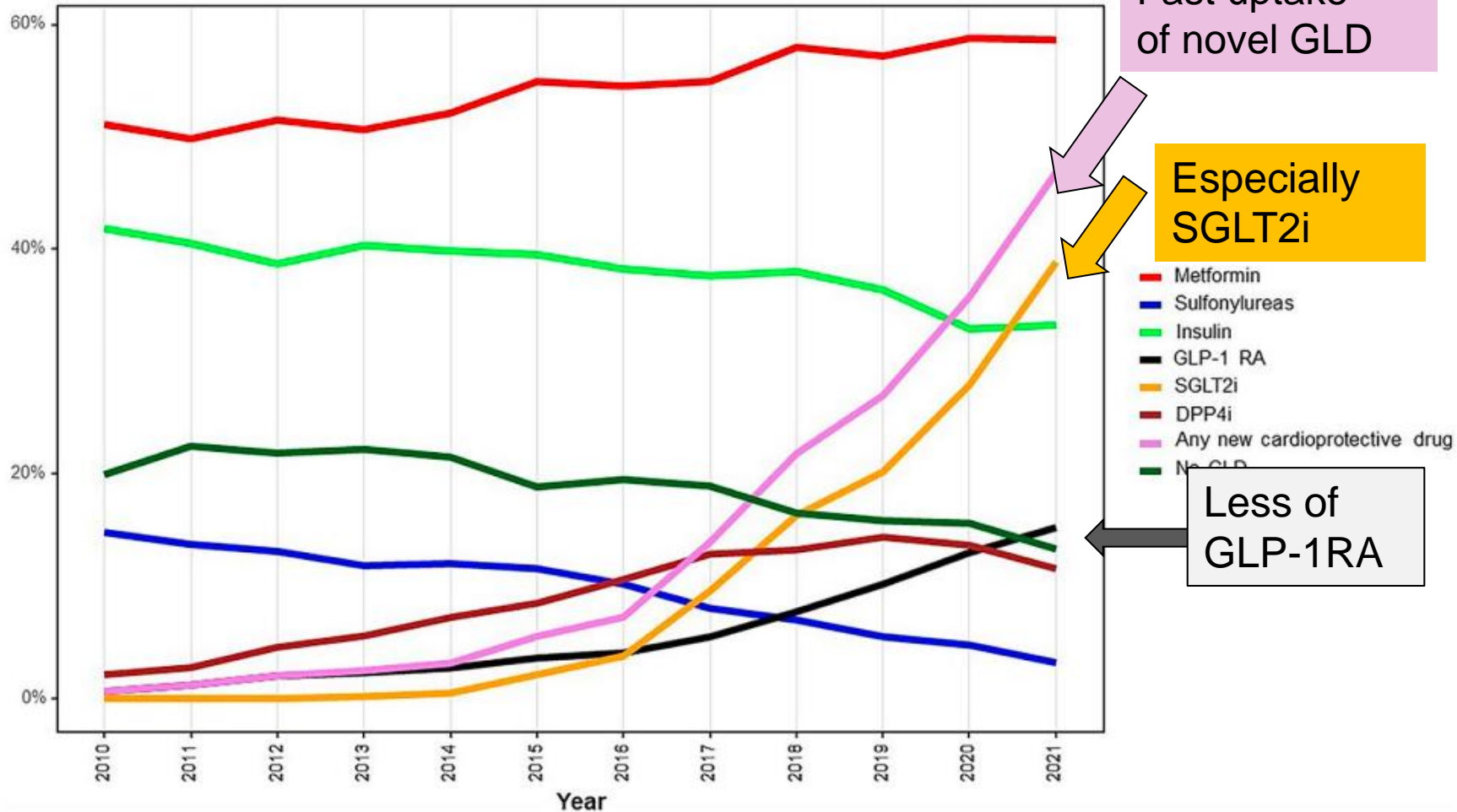
Trends in prognosis and use of SGLT2i and GLP-1 RA in patients with diabetes and coronary artery disease



Viveca Ritsinger<sup>1,2\*</sup>, Kamila Avander<sup>3</sup>, Bo Lagerqvist<sup>4</sup>, Pia Lundman<sup>3</sup> and Anna Norhammar<sup>1,5</sup>

# GLD after CVD in diabetes - underused

SWEDHEART, 2010 to 2021, n=38,671 with DM  
31% stable CAD, 69% STEMI/nonSTEMI infarction



Fast uptake of novel GLD

Especially SGLT2i

Less of GLP-1RA

- From 2016 to 2021 (7% till 47%),
- SGLT2i (4% to 38%)
- Less of GLP-1 RA (4% to 15%).
- Insulin reduced
- Metformin stable/increase
- No GLD reduced 20% to 13%
- **Less of novel GLD, vs elderly GLD**
  - Women
  - Elderly
  - Previous MI
  - Previous HF

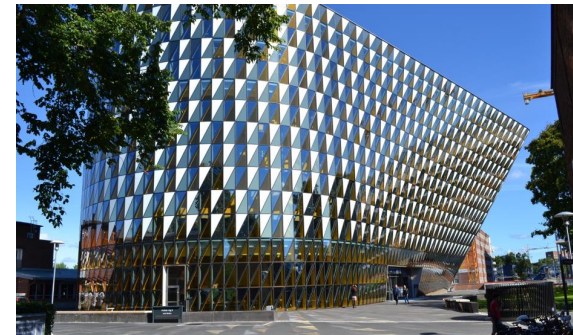
# Sammanfattning

- Diabetes typ 2 medför fortfarande ökad risk för hjärtkärlsjukdom och död
- Prediabetes och graviditetsdiabetes medför ökad hjärtkärlrisk
- Prevention är möjligt! Om god multifaktoriell riskfaktor kontroll, men räcker ej alltid
- Förändrat komplikationsmönster vid diabetes då fler överlever hjärtinfarkt, fler hinner få hjärtsvikt och njursvikt... (och cancer, demens, förmaksflimmer!), Dödsorsak efter hjärtinfarkt förändras
- SGLT2-hämmare förhindrar hjärtsvikt och skyddar mot försämrad njursjukdom samt förlänger liv och minskar hjärtkärlöd
- GLP-1 RA skyddar mot nya hjärtkärlhändelser hos de med etablerad hjärtkärlsjukdom/hög risk, ffa skyddas mot ateroskleroshändelser!
- Underutnyttjas – ges ej till de med hög CV-risk
- Obesitas även vanligt och farligt vid typ 2 diabetes!

# *Tack för att ni lyssnat!*

***Anna Norhammar, 2024-11-05***

*Professor cardiology  
Cardiology Unit, Department of Medicine  
Karolinska Institutet, Stockholm  
Senior consultant Capio S:t Görans hospital  
Sweden*



“Namaste”

anna@norhammar.se

