SID
Società Italiana di Diabetologia

Lo scompenso cardiaco nel diabete tipo 1, una realtà sottovalutata?

Sandro Inchiostro

Direzione Percorso Aziendale
di Cura del Diabete
APSS – Trento

14 GIUGNO 2024 | ROZZANO (MI) | Centro Congressi Humanitas

DICHIARAZIONE CONFLITTO DI INTERESSI

Il sottoscritto_____Inchiostro Sandro_____

In ottemperanza alla normativa ECM ed al principio trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario, il ***docente deve "rilasciare al provider o all'organizzatore la dichiarazione di conflitto d'interessi (ultimi 2 anni rapporti diretti con aziende) e che successivamente debba informare l'aula all'atto della sua presentazione o comunque prima della lezione/relazione dichiarandolo ai discenti".***

Dichiara che negli ultimi due anni sono stato relatore o membro di board scientifico per eventi scientifici ECM, aventi il supporto incondizionato delle seguenti aziende:

Astra Zeneca

Bayer

Boehringer Ingelheim

Eli Lilly

Novo Nordisk

Sanofi Aventis

Glycaemic control and incidence of heart failure in 20 985 patients with type 1 diabetes: an observational study

Marcus Lind, Ioannis Bounias, Marita Olsson, Soffia Gudbjörnsdottir, Ann-Marie Svensson, Annika Rosengren

Lancet 2011; 378: 140–46

All patients (aged ≥18 years) with type 1 diabetes and no known heart failure who were registered in the national diabetes registry between January, 1998, and December, 2003.

These patients were followed up until hospital admission for heart failure, death, or end of follow-up on Dec 31, 2009.

20 985 patients with mean age of 38·6 years (SD 13·3) at baseline.

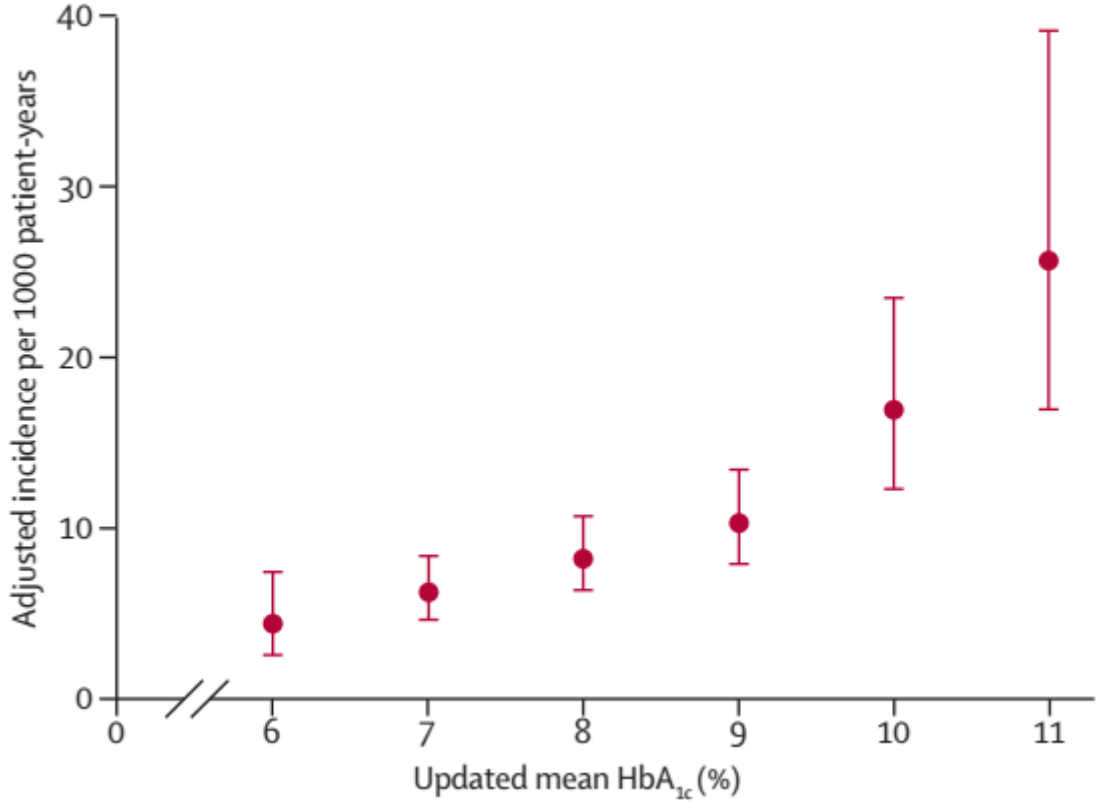
Glycaemic control and incidence of heart failure in 20 985 patients with type 1 diabetes: an observational study

Marcus Lind, Ioannis Bounias, Marita Olsson, Soffia Gudbjörnsdottir, Ann-Marie Svensson, Annika Rosengren

Lancet 2011; 378: 140–46

Incidence of heart failure in patients aged 56–60 years with T1D diagnosed at 11–20 years of age T1D without no known HF. Swedish National Diabetes Registry January, 1998 - December, 2003

Incidence of 3·38 events per 1000 patient-years (95% CI 3·12–3·65)



25% increase for 1% increment of updated mean HbA1c (fully adjusted analysis)

Long-term excess risk of heart failure in people with type 1 diabetes: a prospective case-control study

Lancet Diabetes Endocrinol
2015; 3: 876–85

Annika Rosengren, Daniel Vestberg, Ann-Marie Svensson, Mikhail Kosiborod, Mark Clements, Araz Rawshani, Aldina Pivodic, Soffia Gudbjörnsdottir, Marcus Lind

In this prospective case-control study, we identified all individuals with type 1 diabetes registered in the Swedish National Diabetes Registry between Jan 1, 1998, and Dec 31, 2011 and five controls randomly selected from the general population for each patient.

33 402 patients (mean age at baseline 35 years [SD 14]), 45% women.

Mean duration of diabetes 20·1 years (SD 14·5).

Mean follow-up of 7·9 years.

Long-term excess risk of heart failure in people with type 1 diabetes: a prospective case-control study

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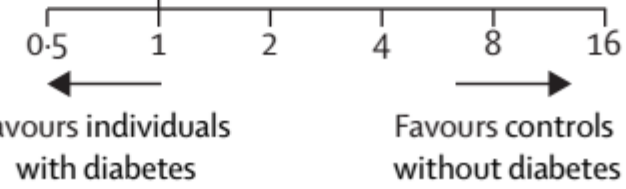
Unadjusted hazard ratios for admission to hospital for heart failure

The HR for all individuals with T1D versus controls was 4·69 (95% CI 3·64–6·04)

Age (years)	Type 1 diabetes	Reference (%)	HR (95% CI)	p value
Men				
<55	37 (0·4%)	43 (0·1)	4·36 (2·81–6·76)	<0·0001
55–64	149 (3·1%)	148 (0·6)	5·32 (4·24–6·68)	<0·0001
65–74	255 (9·2%)	372 (2·7)	3·90 (3·33–4·58)	<0·0001
≥75	148 (22·8%)	301 (9·9)	3·23 (2·65–3·94)	<0·0001
Women				
<55	19 (0·2%)	15 (0·0)	6·43 (3·27–12·66)	<0·0001
55–64	101 (2·6%)	60 (0·3)	8·77 (6·37–12·08)	<0·0001
65–74	219 (9·3%)	158 (1·4)	7·94 (6·47–9·75)	<0·0001
≥75	134 (21·5%)	228 (7·6)	4·04 (3·26–5·01)	<0·0001



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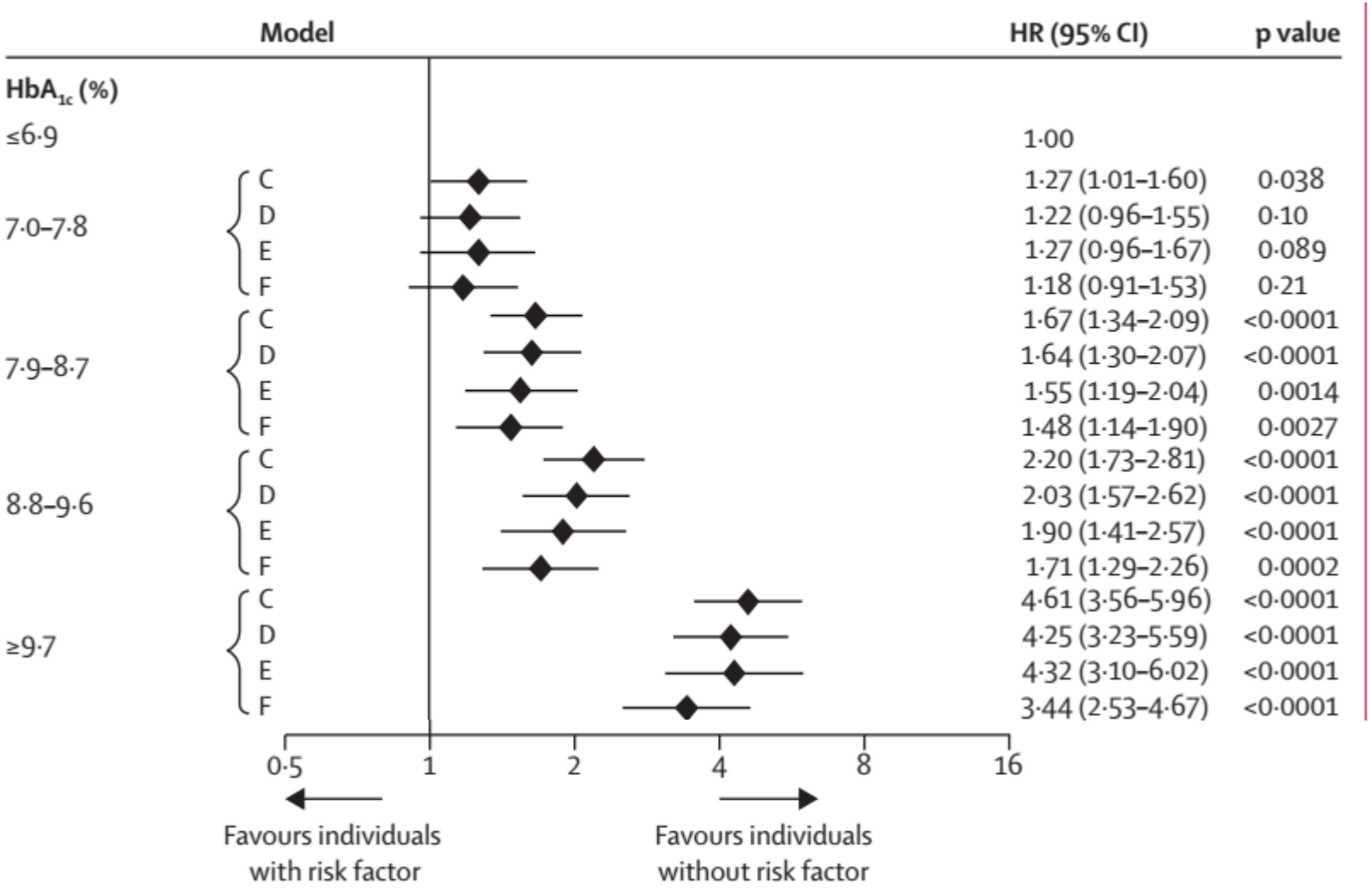
Adjusted hazard ratios for admission to hospital for heart failure

HbA1c %



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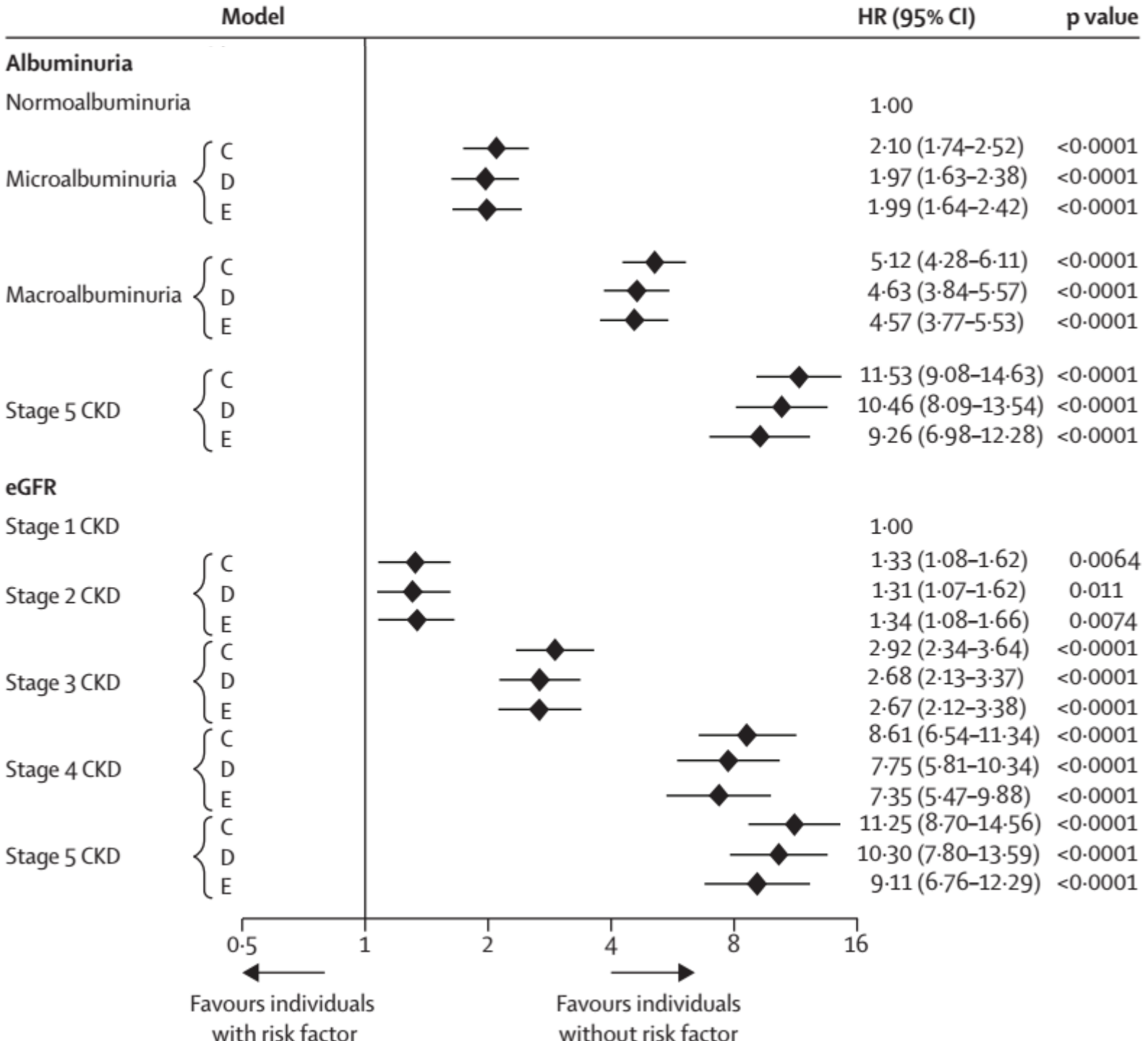
Albuminuria

CKD



Lancet 2018; 392: 477–86

Excess mortality and cardiovascular disease in young adults with type 1 diabetes in relation to age at onset: a nationwide, register-based cohort study

Araz Rawshani, Naveed Sattar*, Stefan Franzén, Aidin Rawshani, Andrew T Hattersley, Ann-Marie Svensson, Björn Eliasson, Soffia Gudbjörnsdottir*

Individuals with type 1 diabetes in the Swedish National Diabetes Register and matched controls from the general population.
We included patients with at least one registration between Jan 1, 1998, and Dec 31, 2012,
mean age 29 years

Using Cox regression, and with adjustment for diabetes duration, we estimated the excess risk of …….. heart failure …..

Individuals with type 1 diabetes were categorised into five groups, according to age at diagnosis:
0–10 years, 11–15 years, 16–20 years, 21–25 years, and 26–30 years

27195 individuals with type 1 diabetes and 135178 matched controls were selected for this study.
Median follow-up ~ 10 years

Lancet 2018; 392: 477–86

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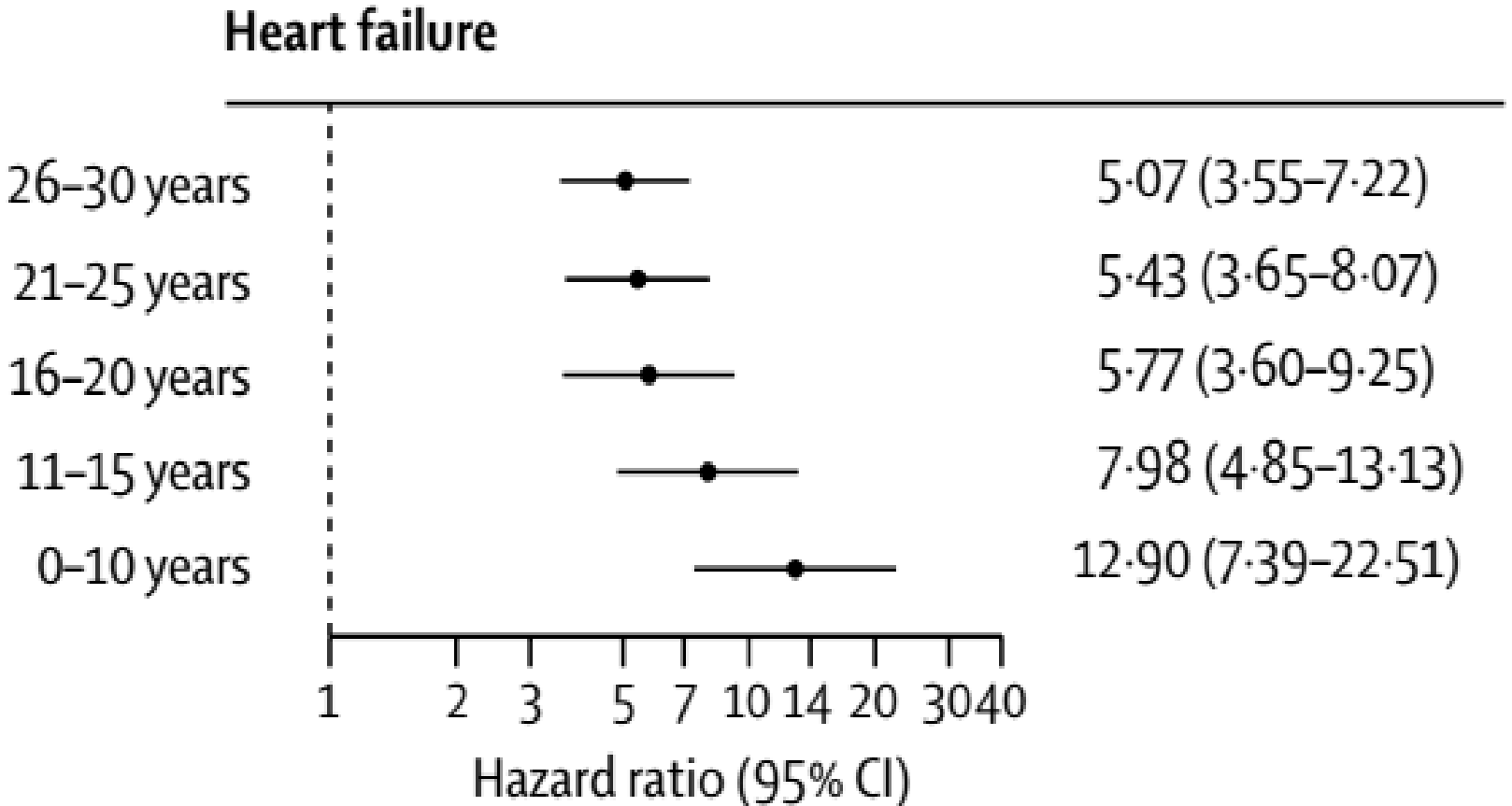
Adjusted hazard ratios for Heart Failure, according to age at type 1 diabetes diagnosis



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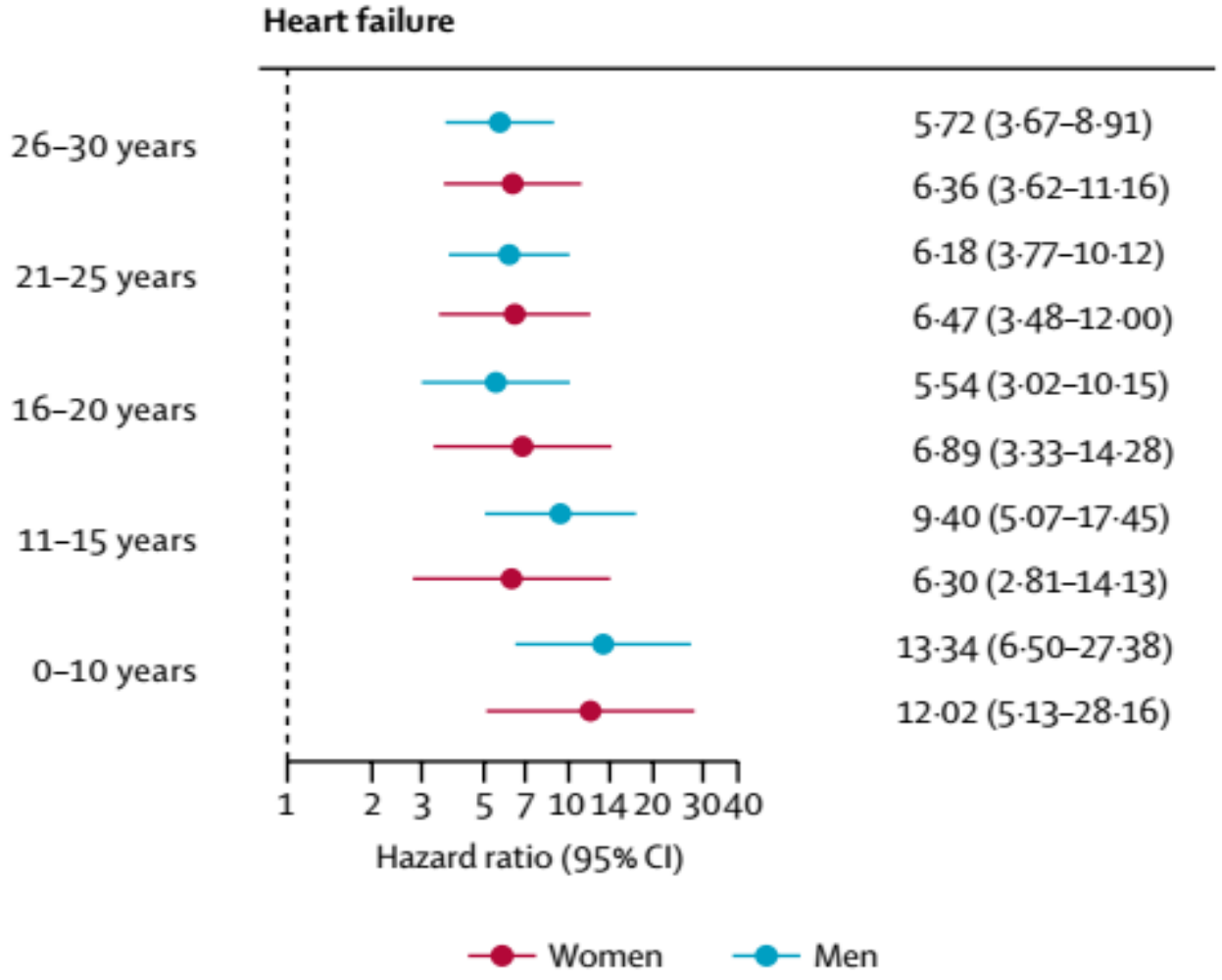
Adjusted hazard ratios for Heart Failure, according to age at type 1 diabetes diagnosis and sex



Circulation

ORIGINAL RESEARCH ARTICLE

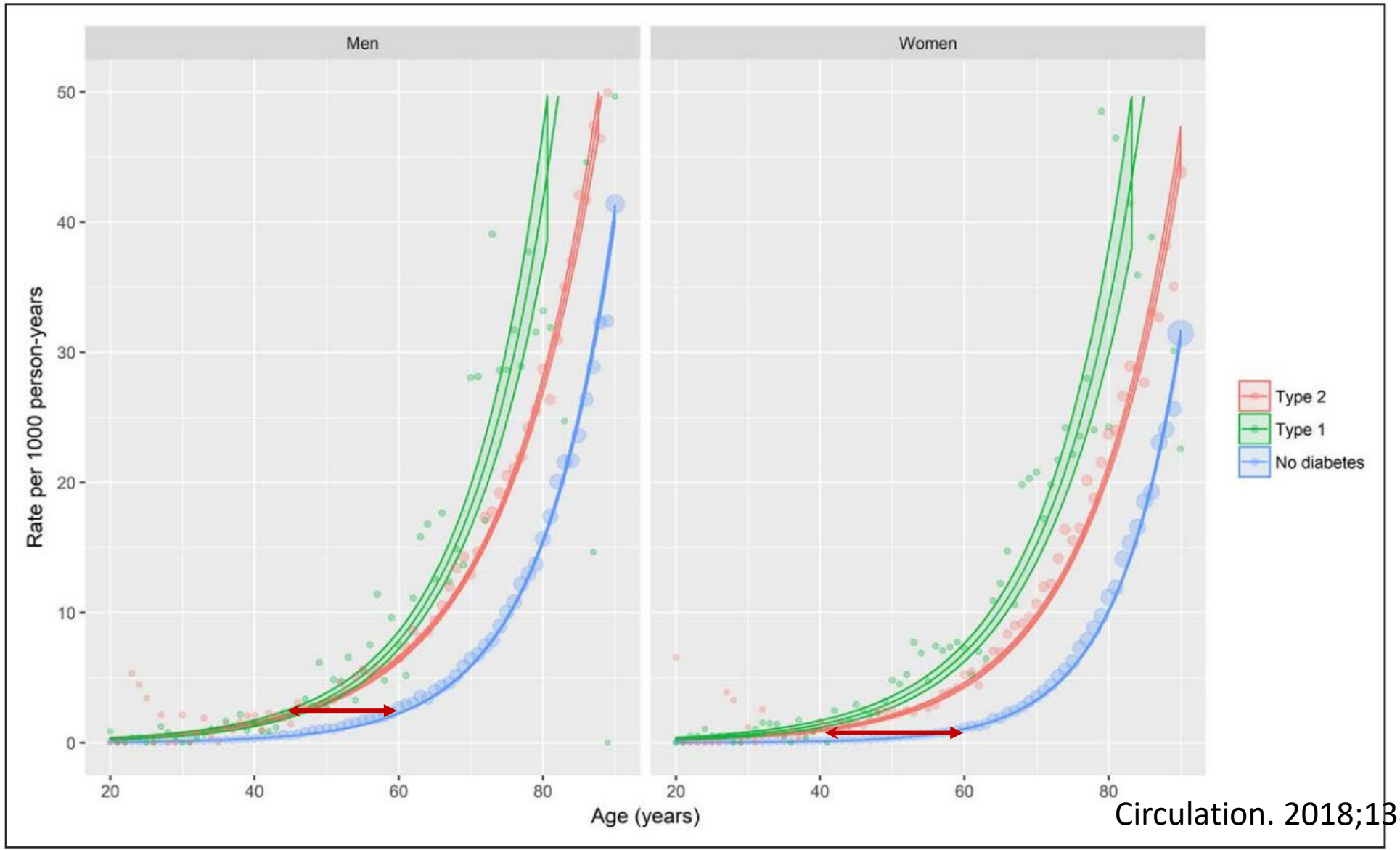
Incidence of Hospitalization for Heart Failure and Case-Fatality Among 3.25 Million People With and Without Diabetes Mellitus

We examined the incidence and case-fatality of heart failure hospitalizations in the entire population aged ≥30 years resident in Scotland during 2004 to 2013.

10-year period of follow-up

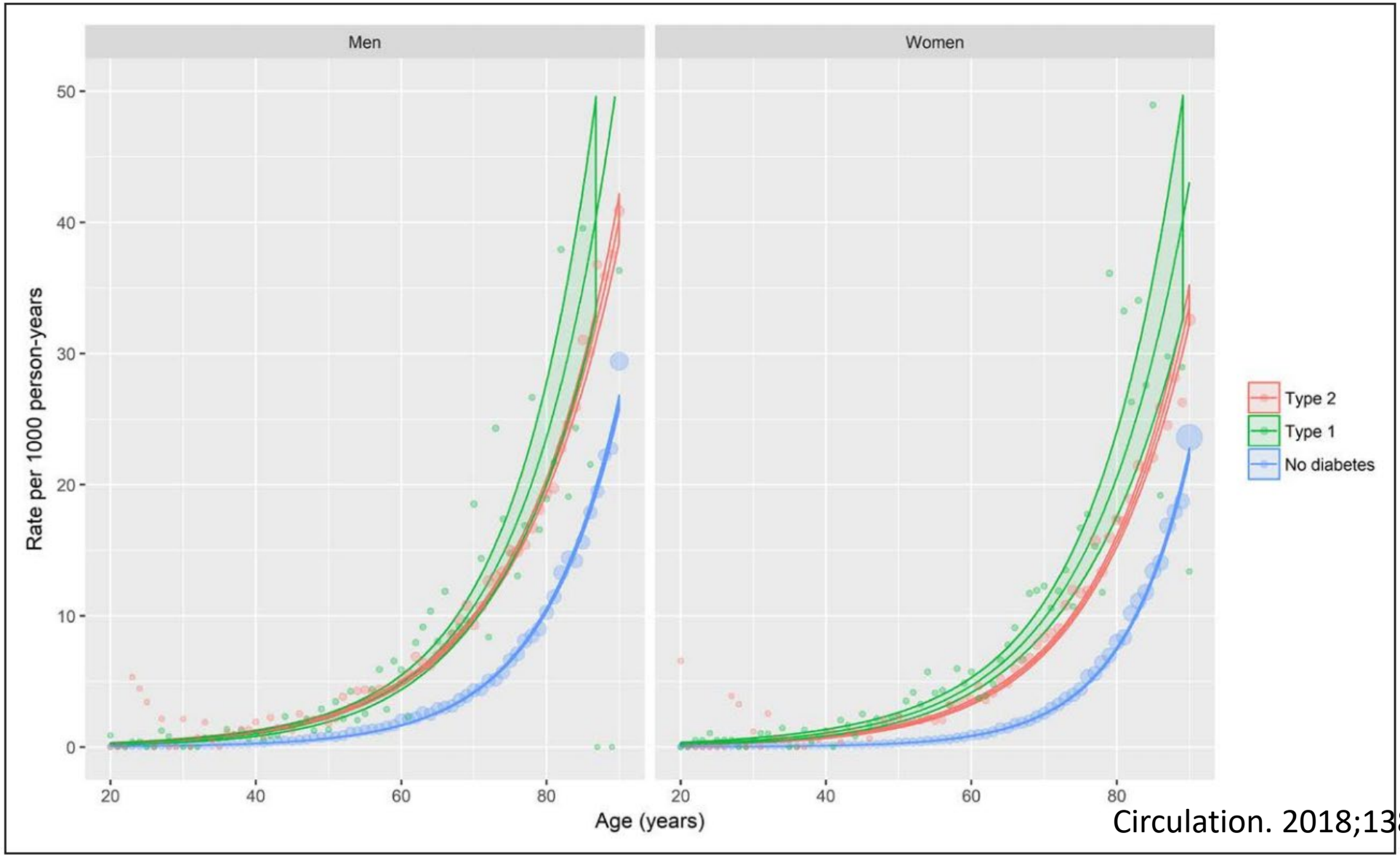
Circulation. 2018;138:2774–2786

Incidence of heart failure hospitalization



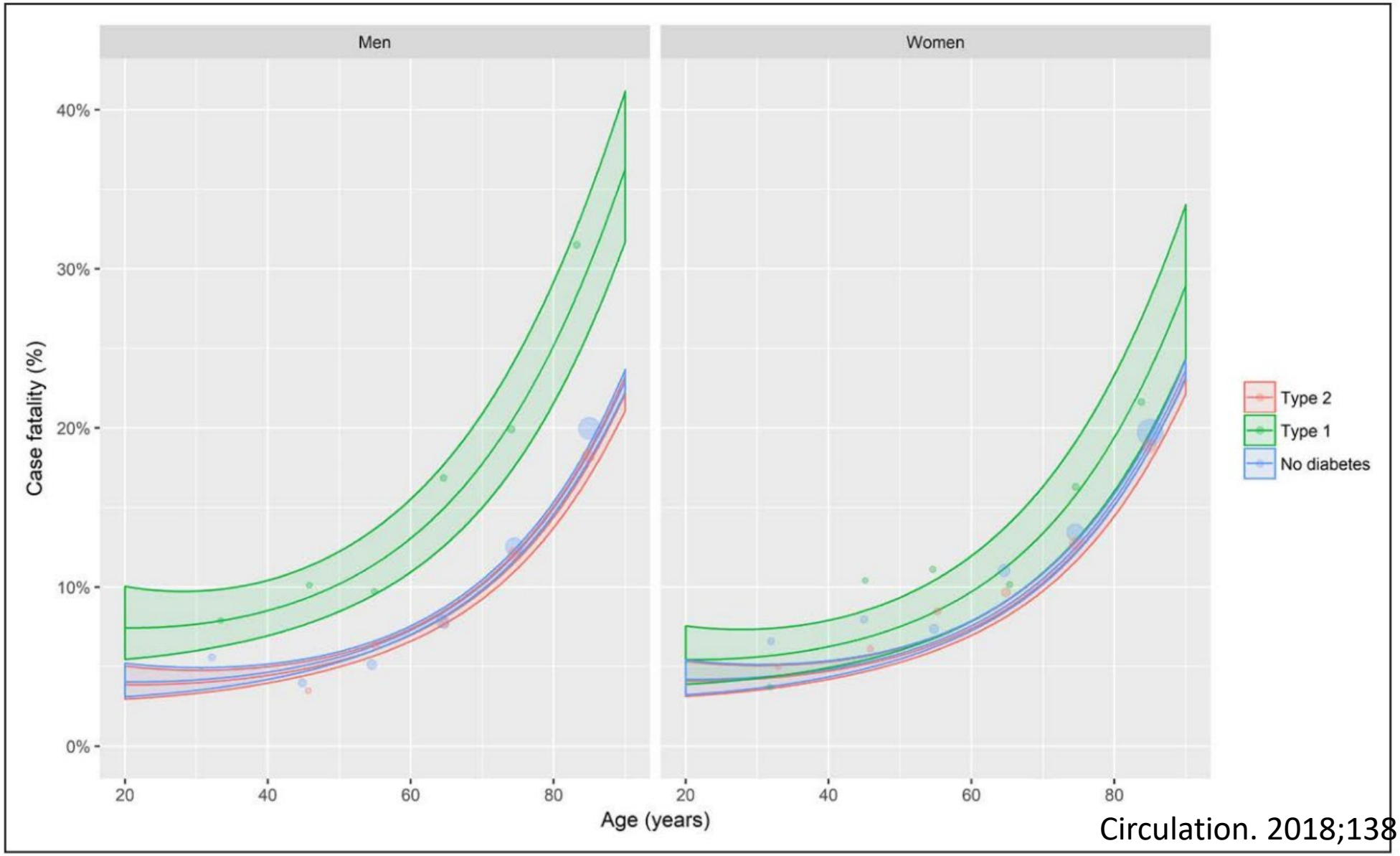
Circulation. 2018;138:2774–2786

Incidence of heart failure hospitalization in people without previous ischemic heart disease.



Circulation. 2018;138:2774–2786

30-day case-fatality of incident heart failure hospitalization



Circulation. 2018;138:2774–2786

Cardiovascular and Renal Disease Burden in Type 1 Compared With Type 2 Diabetes: A Two-Country Nationwide Observational Study

Robin Kristófi,[1] Johan Bodegard,[2] Anna Norhammar,[3,4] Marcus Thuresson,[5] David Nathanson,[6] Thomas Nyström,[7] Kåre I. Birkeland,[8] Jan W. Eriksson[1]

Diabetes Care 2021;44:1211–1218 | https://doi.org/10.2337/dc20-2839

Type 1 diabetes (T1D) and type 2 diabetes (T2D) increase risks of cardiovascular and renal disease (CVRD). Direct comparisons between T1D and T2D are scarce. We examined this by pooling full-population cohorts in Sweden and Norway.

RESEARCH DESIGN AND METHODS

A total of 59,331 patients with T1D and 484,241 patients with T2D, aged 18–84

Mean follow-up 2.6 years from 31 December 2013.

Cardiovascular and Renal Disease Burden in Type 1 Compared With Type 2 Diabetes: A Two-Country Nationwide Observational Study

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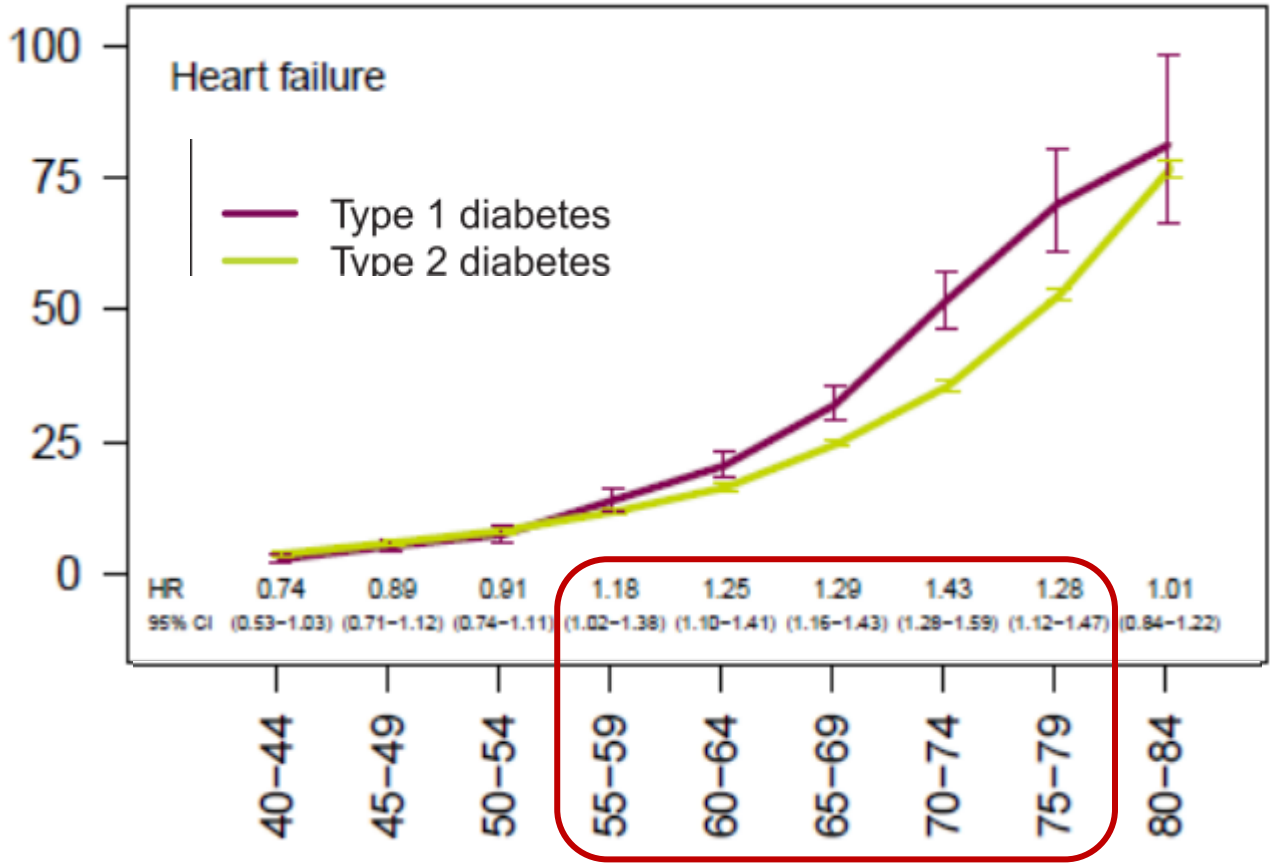
Diabetes Care 2021;44:1211–1218 | https://doi.org/10.2337/dc20-2839

Incidence of Heart Failure



Check for updates

Cardiovascular and Renal Disease Burden in Type 1 Compared With Type 2 Diabetes: A Two-Country Nationwide Observational Study

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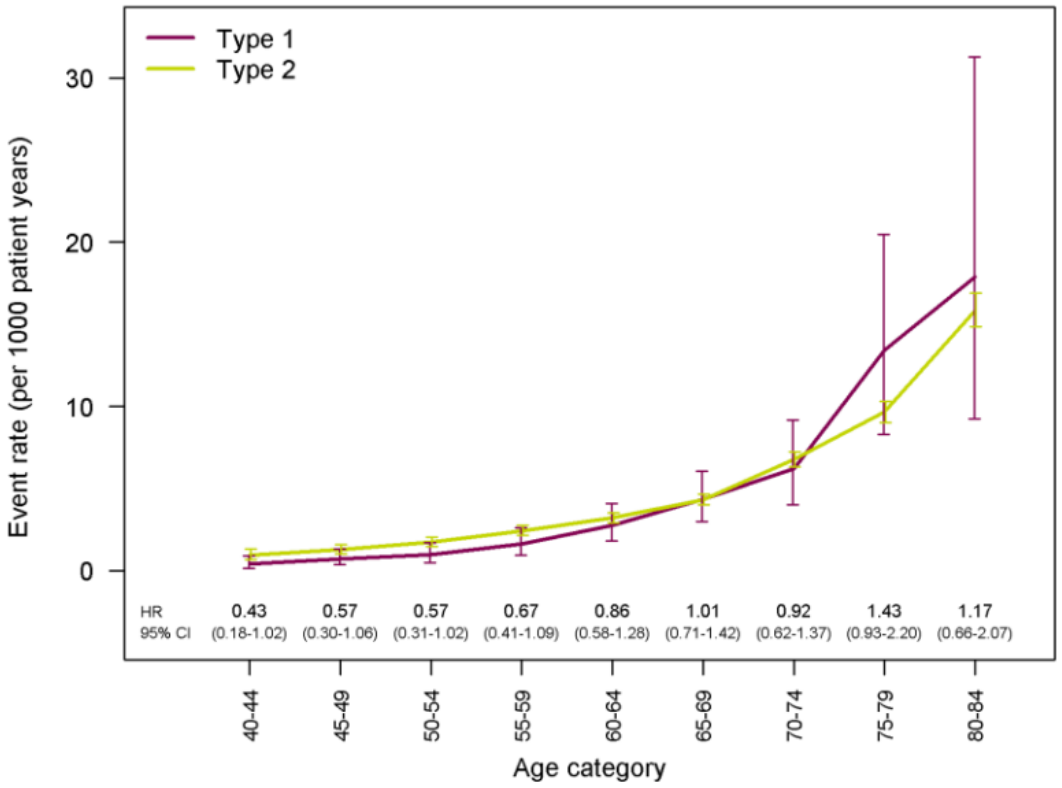
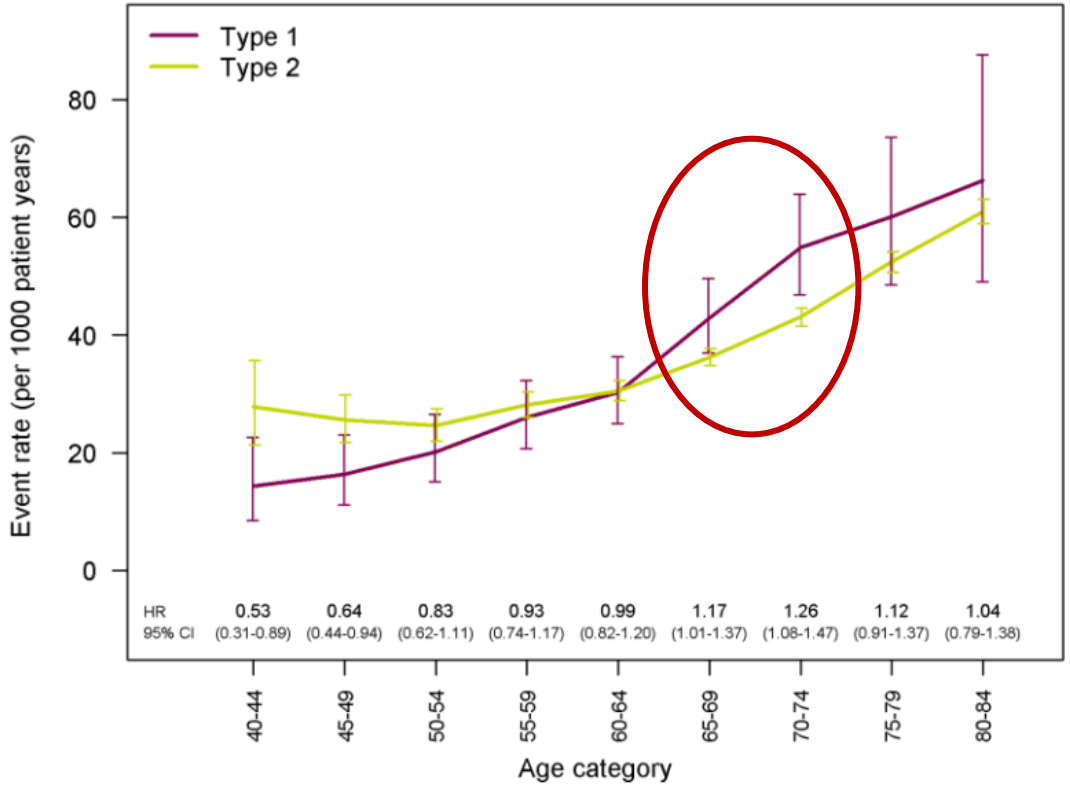
Figures S5. Event rates in subjects without CVRD at baseline

Figures S6. Event rates in subjects with previous CVRD at baseline

Incidence of Heart Failure





Circulation

Circulation. 2019;139:1900–1912

ORIGINAL RESEARCH ARTICLE

Relative Prognostic Importance and Optimal Levels of Risk Factors for Mortality and Cardiovascular Outcomes in Type 1 Diabetes Mellitus

Swedish National Diabetes Register from 1998 to 2014

Relative prognostic importance of 17 risk factors for death and cardiovascular outcomes

Analysis: Cox regression and machine learning analyses.

32611 patients with type 1 diabetes mellitus
Follow-up of 10.4 years.

Circulation. 2019;139:1900–1912

Risk Factors for First and Subsequent CVD Events in Type 1 Diabetes: The DCCT/EDIC Study

Diabetes Care 2020;43:867–874 | https://doi.org/10.2337/dc19-2292

*Ionut Bebu,[1] David Schade,[2] Barbara Braffett,[1] Mikhail Kosiborod,[3,4] Maria Lopes-Virella,[5] Elsayed Z. Soliman,[6] William H. Herman,[7] David A. Bluemke,[8] Amisha Wallia,[9] Trevor Orchard,[10] and John M. Lachin,[1] on behalf of the DCCT/EDIC Research Group**

1,441 DCCT/EDIC participants, mean age at baseline 27 years

Median follow-up of 29 years

17 partecipants had 22 episodes of CHF

Risk Factors for First and Subsequent CVD Events in Type 1 Diabetes: The DCCT/EDIC Study

*Ionut Bebu,[1] David Schade,[2] Barbara Braffett,[1] Mikhail Kosiborod,[3,4] Maria Lopes-Virella,[5] Elsayed Z. Soliman,[6] William H. Herman,[7] David A. Bluemke,[8] Amisha Wallia,[9] Trevor Orchard,[10] and John M. Lachin,[1] on behalf of the DCCT/EDIC Research Group**

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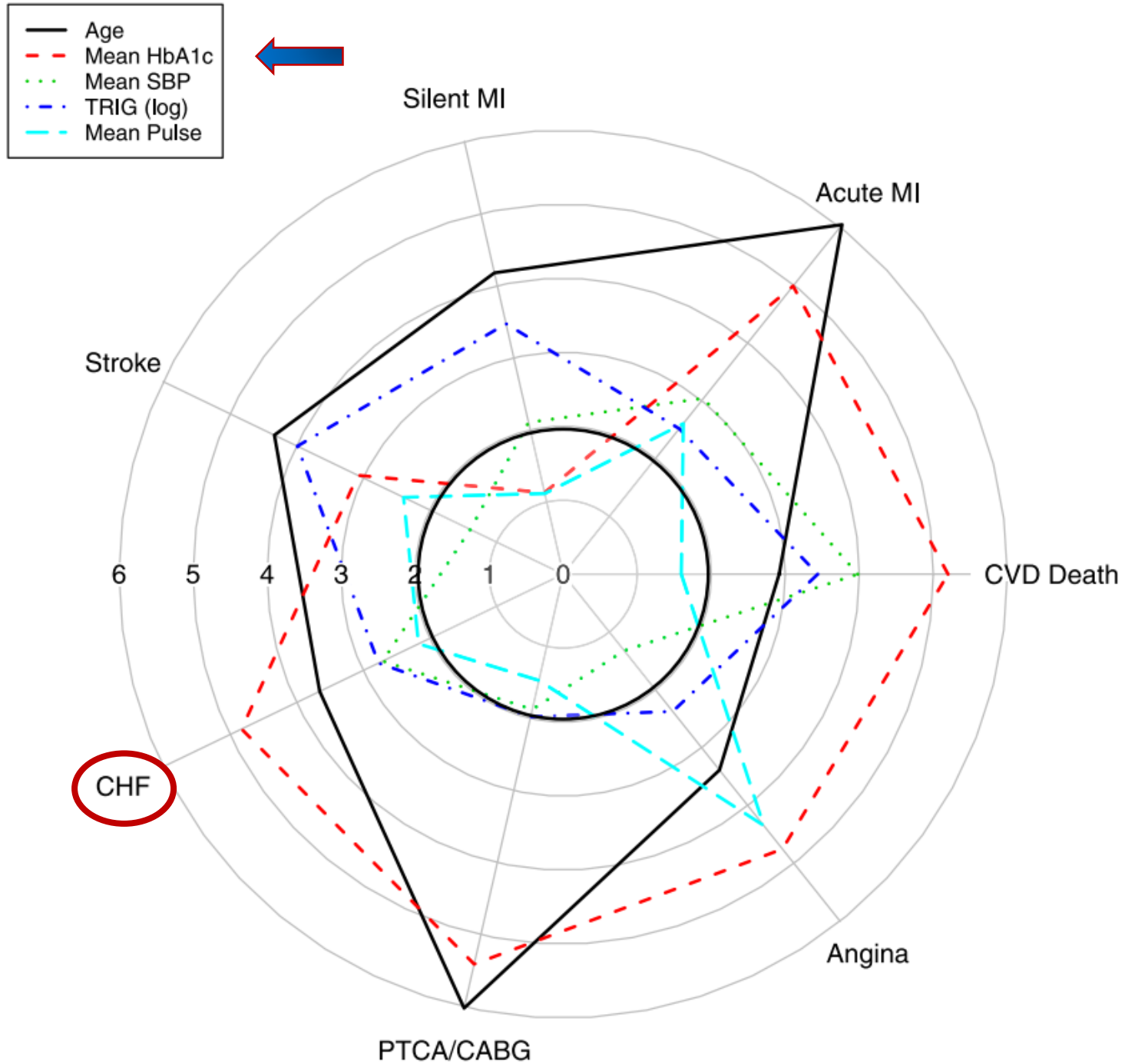


Risk factors, mortality trends, and cardiovascular diseases in people with Type 1 diabetes and controls in Sweden: An observational cohort study

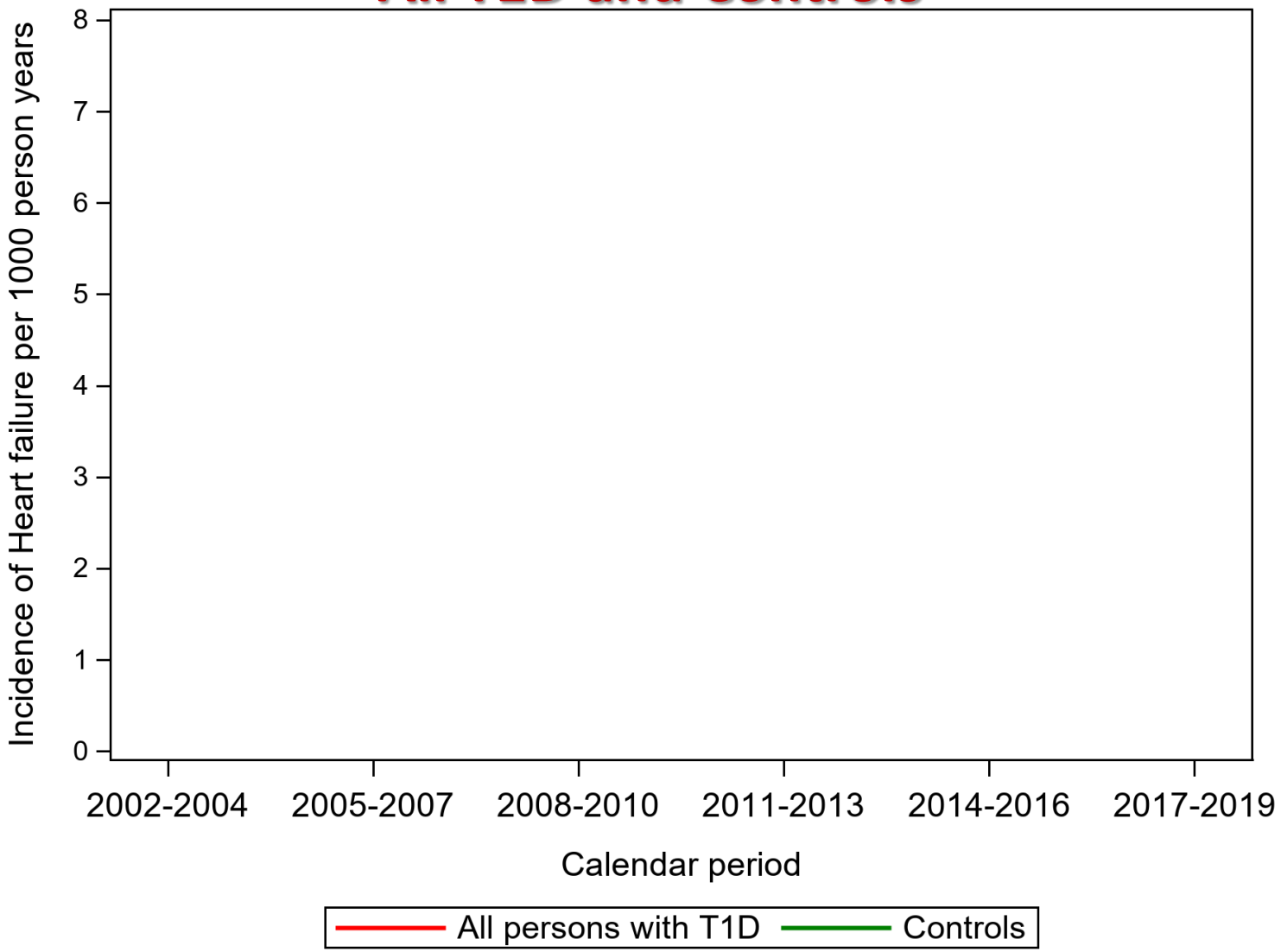
Sara Hallström,[a,b] Magnus Olof Wijkman,[c] Johnny Ludvigsson,[d] Per Ekman,[e] Marc Alan Pfeffer,[f] Hans Wedel,[g] Annika Rosengren,[b] and Marcus Lind[a,b,h]*

The Lancet Regional Health – Europe 2022;21: 100469

Risk factors, mortality trends, and cardiovascular diseases in people with Type 1 diabetes and controls in Sweden: An observational cohort study

Sara Hallström,[a,b,*] Magnus Olof Wijkman,[c] Johnny Ludvigsson,[d] Per Ekman,[e] Marc Alan Pfeffer,[f] Hans Wedel,[g] Annika Rosengren,[b] and Marcus Lind[a,b,h]

Standardized incidence rates per 1000 person years of heart failure. All T1D and Controls



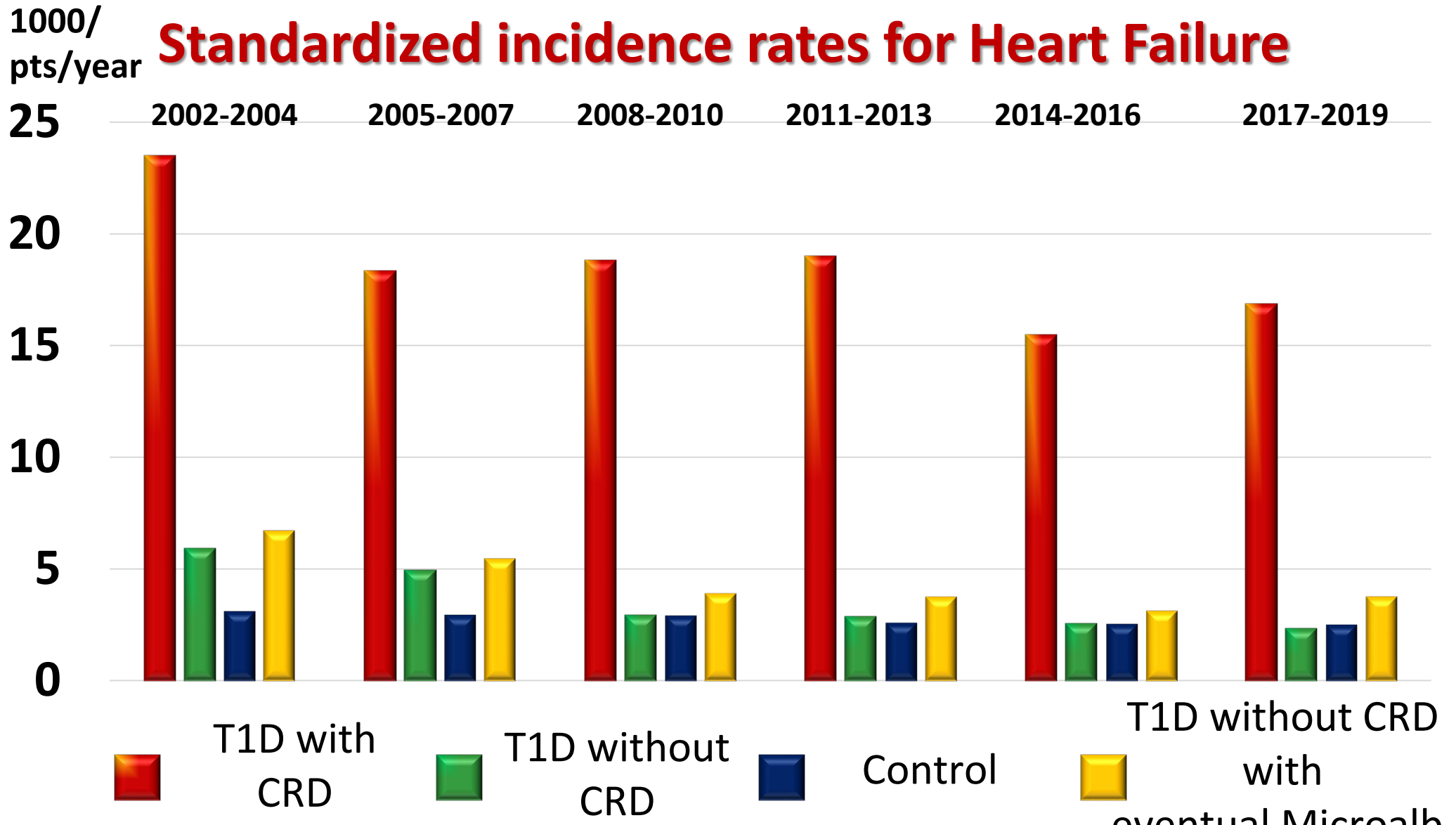
The Lancet Regional Health – Europe 2022;21: 100469

Standardized incidence rates

AGE (yrs)

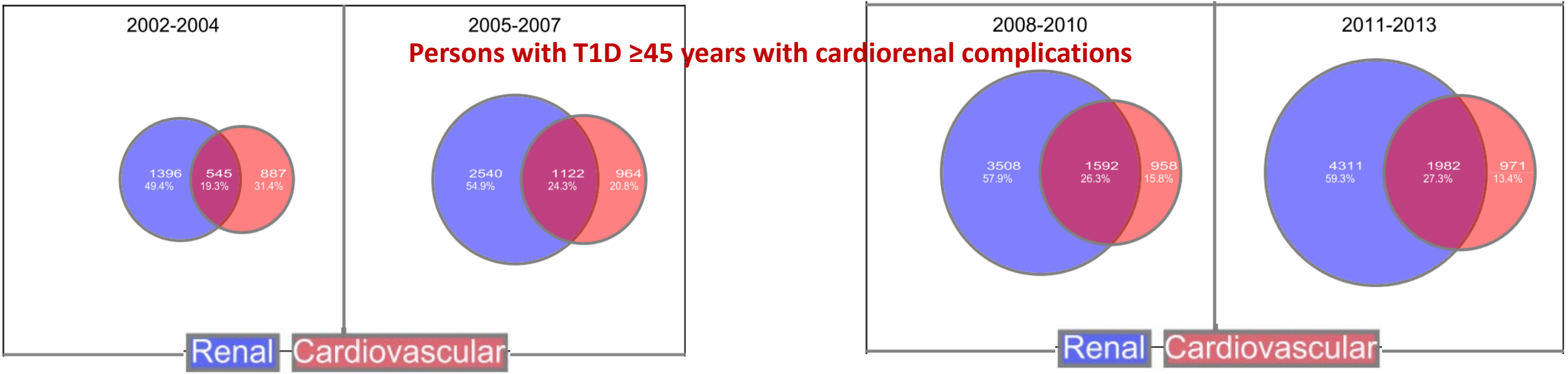
The Lancet Regional Health – Europe 2022;21: 100469

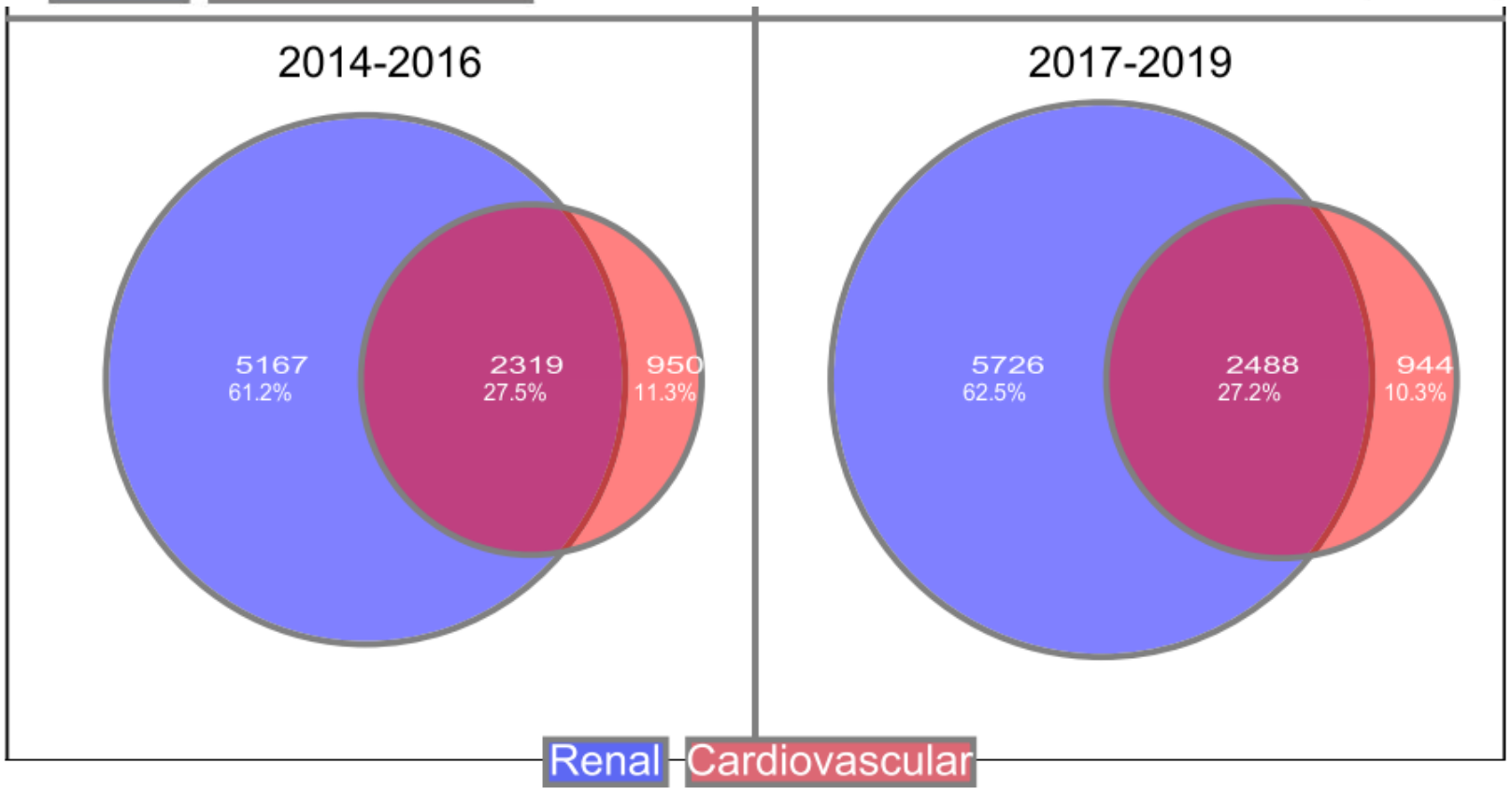
IMPACT OF CARDIORENAL DISEASE ON INCIDENCE OF HEART FAILURE



The Lancet Regional Health – Europe 2022;21: 100469

Persons with T1D ≥45 years with cardiorenal complications





72,5% of T1D with CVD have Renal Disease

30% of T1D with Renal Disease have CVD

Microvascular Burden and Incident Heart Failure Among Middle-Aged and Older Adults With Type 1 or Type 2 Diabetes

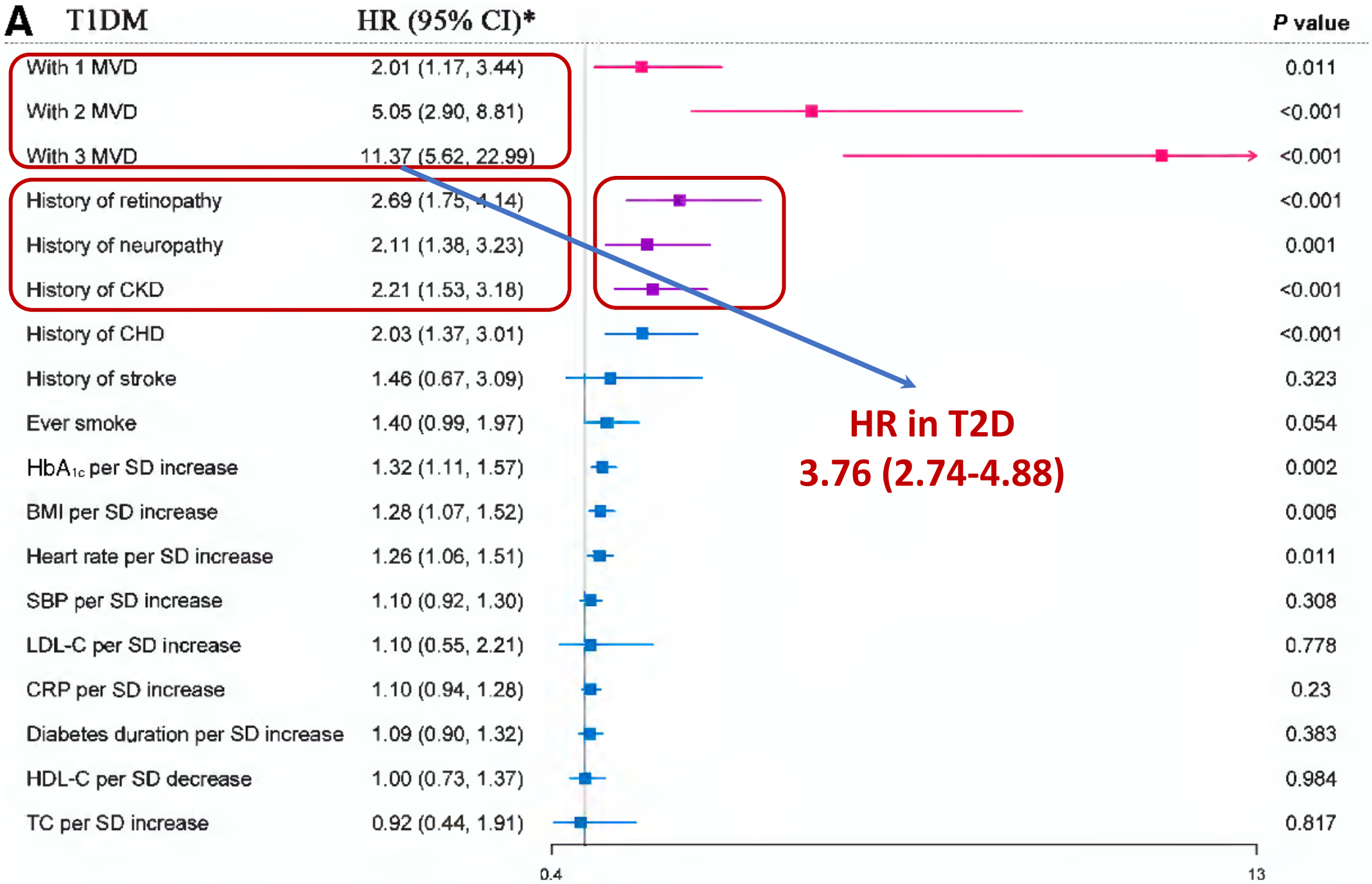
Fu-Rong Li,[1,2,3] Daniel Nyarko Hukportie,[2] Jing Yang,[4,5] Huan-Huan Yang,[6] Guo-Chong Chen,[4,7] and Xian-Bo Wu[2]

Diabetes Care 2022;45:2999–3006 | https://doi.org/10.2337/dc22-0177

We included 1,713 and 28,624 participants with T1DM and T2DM, respectively, from the UK Biobank who were free of HF during enrollment.

There were 145 and 2,515 incident cases of HF recorded among participants with T1DM and T2DM, respectively

Median follow-up of 11.5 years


A
T1DM
HR (95% CI)*
P value
With 1 MVD
2.01 (1.17, 3.44)
0.011
With 2 MVD
5.05 (2.90, 8.81)
<0.001
With 3 MVD
11.37 (5.62, 22.99)
<0.001
History of retinopathy
2.69 (1.75, 4.14)
<0.001
History of neuropathy
2.11 (1.38, 3.23)
0.001
History of CKD
2.21 (1.53, 3.18)
<0.001
History of CHD
2.03 (1.37, 3.01)
<0.001
History of stroke
1.46 (0.67, 3.09)
0.323
Ever smoke
1.40 (0.99, 1.97)
0.054
HbA1c per SD increase
1.32 (1.11, 1.57)
0.002
BMI per SD increase
1.28 (1.07, 1.52)
0.006
Heart rate per SD increase
1.26 (1.06, 1.51)
0.011
SBP per SD increase
1.10 (0.92, 1.30)
0.308
LDL-C per SD increase
1.10 (0.55, 2.21)
0.778
CRP per SD increase
1.10 (0.94, 1.28)
0.23
Diabetes duration per SD increase
1.09 (0.90, 1.32)
0.383
HDL-C per SD decrease
1.00 (0.73, 1.37)
0.984
TC per SD increase
0.92 (0.44, 1.91)
0.817
HR in T2D
3.76 (2.74-4.88)
0.4
13

Circulation

Circulation. 2020;141:1107–1109

RESEARCH LETTER

Cardiac Autoimmunity Is Associated With Subclinical Myocardial Dysfunction in Patients With Type 1 Diabetes Mellitus

DCCT/EDIC study

Poor glycemic control in patients with T1DM followed in the DCCT (Diabetes Control and Complications Trial), but not in patients with type 2 diabetes mellitus, is associated with positivity for multiple (≥2) **cardiac autoantibodies**, similar to a HF cohort with Chagas cardiomyopathy, raising the possibility of autoimmune-associated myocardial dysfunction in T1DM

Circulation. 2020;141:1107–1109

Table. **Association Between Cardiac Autoantibodies, Clinical Characteristics, and CMR Indices of Left Ventricular Structure and Function**

	Cardiac Autoantibody Status			
	No Autoantibodies (n=746)	1 Autoantibody (n=102)	≥2 Autoantibodies (n=44)	*P* for Trend*
CMR indices of left ventricular structure and function				
Minimally adjusted#				
End-diastolic volume, mL	136±1	133±2	151±3	<0.001§
End-systolic volume, mL	52±0	50±1	69±2	<0.001§
Stroke volume, mL	84±1	83±1	82±2	0.59
Ejection fraction, %	62±0	62±1	56±1	<0.001§
Cardiac output, L/min	5.9±0.0	6.0±0.1	5.8±0.2	0.52
Left ventricular mass, g	137±1	137±2	151±3	<0.001§
Fully adjusted**				
End-diastolic volume, mL	136±1	133±2	151±3	<0.001§
End-systolic volume, mL	52±1	50±1	69±2	<0.001§
Stroke volume, mL	84±1	83±1	82±2	0.65
Ejection fraction, %	62±0	62±1	55±1	<0.001§
Cardiac output, L/min	5.9±0.0	6.0±0.1	5.8±0.2	0.63
Left ventricular mass, g	137±1	135±2	149±3	<0.001§

Kerola et al. Cardiovascular Diabetology (2022) 21:177
https://doi.org/10.1186/s12933-022-01608-3

Cardiovascular Diabetology

RESEARCH Open Access

Long-term cardiovascular prognosis of patients with type 1 diabetes after myocardial infarction

Anne M. Kerola[1,2*], Anne Grete Semb[3], Markus Juonala[4], Antti Palomäki[4,5], Päivi Rautava[6,7] and Ville Kytö[8,9,10]

Patients with type 1 diabetes surviving 90 days after MI (n=1508; 60% male, mean age=62.1 years) or without any type of diabetes (n=62,785) in Finland during 2005–2018 were retrospectively studied using multiple national registries.

Median follow-up was 3.9 years (maximum 12 years).

Differences between groups were balanced by multivariable adjustments and propensity score matching (n=1401 patient pairs).

Kerola et al. Cardiovascular Diabetology (2022) 21:177
https://doi.org/10.1186/s12933-022-01608-3

Cardiovascular Diabetology

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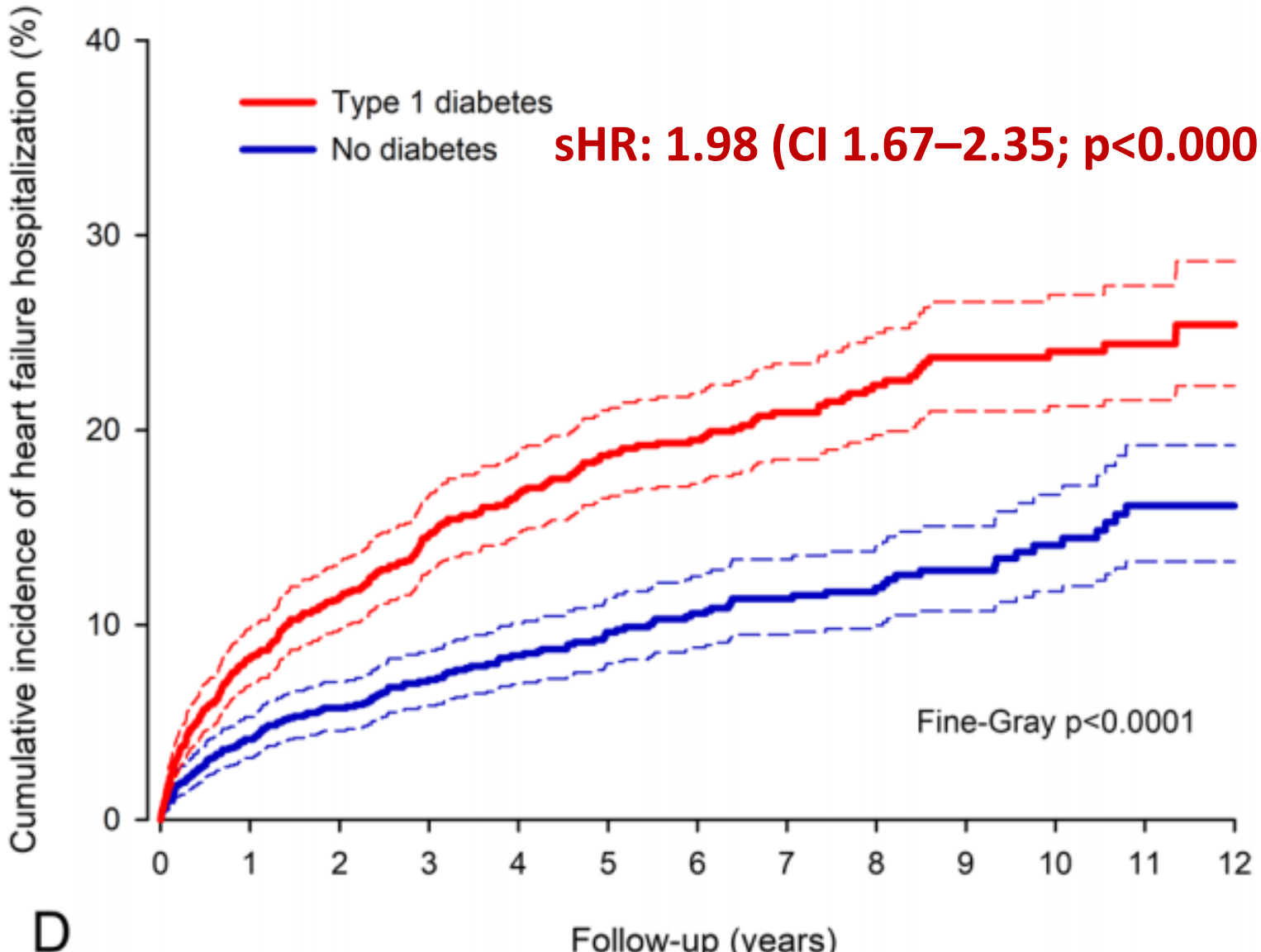
Heart Failure Hospitalization



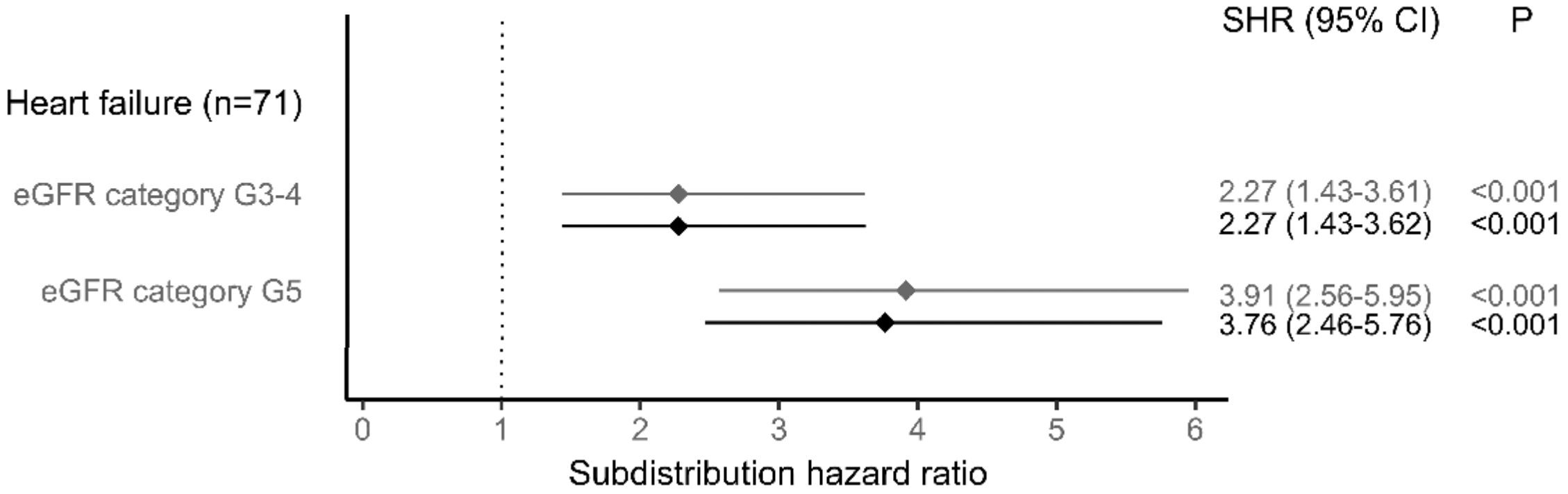
D

Prognosis After First-Ever Myocardial Infarction in Type 1 Diabetes Is Strongly Affected by Chronic Kidney Disease

*Patrik Smidtslund,[1–3] Fanny Jansson Sigfrids,[1–3] Anni Ylinen,[1–3,5] Nina Elonen,[1–3] Valma Harjutsalo,[1–3] Per-Henrik Groop,[1–4] and Lena M. Thorn,[1–3,5] on behalf of the FinnDiane Study Group**

Diabetes Care 2023;46:197–205 | https://doi.org/10.2337/dc22-1586

Observational follow-up study of 4,217 individuals from the Finnish Diabetic Nephropathy (FinnDiane)



RIASSUNTO 1

- ✓ **Nel T1D il rischio di andare incontro ad insufficienza cardiaca è:**
  - ✓ **quattro-sei volte superiore rispetto alla popolazione generale,**
  - ✓ **tanto più elevato quanto più precoce è l'insorgenza del diabete,**
  - ✓ **maggiore rispetto al T2D, soprattutto nell'età più avanzata.**

- ✓ **Il rischio relativo nelle donne con T1D rispetto alla popolazione generale è simile a quello del sesso maschile nell'età giovanile, mentre nell'età più avanzata diventa maggiore.**

RIASSUNTO 2

- ✓ **Il maggior fattore clinico associato all'insufficienza cardiaca nel T1D è la CKD e la complicanza microvascolare nel suo insieme con potente effetto additivo/moltiplicativo.**

- ✓ **Accanto all'età e alla durata del diabete il controllo glicemico si pone come un ulteriore importante fattore di rischio di insufficienza cardiaca.**

- ✓ **I fattori di rischio e le patologie concomitanti subcliniche o cliniche sono strettamente intercorrelati tra loro, come elementi reciprocamente causali e sinergici nel determinare il rischio di sviluppare insufficienza cardiaca.**

TAKE HOME MESSAGE

L’insufficienza cardiaca è sicuramente una realtà sottovalutata nel diabete tipo 1.

La prevenzione dell’insufficienza cardiaca deve essere estremamente precoce attraverso il controllo di tutti i fattori di rischio che possono portare al danno metabolico, micro e macroangiopatico e neurologico, che sono i presupposti fisiopatologici dell’insufficienza cardiaca nel diabete di tipo 1.

La ricerca dell’insufficienza cardiaca subclinica è indispensabile per attuare

Grazie per l’attenzione!

Prognosis After First-Ever Myocardial Infarction in Type 1 Diabetes Is Strongly Affected by Chronic Kidney Disease

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Diabetes Care 2023;46:197–205 | https://doi.org/10.2337/dc22-1586

In this observational follow-up study of 4,217 individuals from the Finnish Diabetic Nephropathy (FinnDiane) Study with no prior MI or coronary revascularization, we verified 253 (6.0%) MIs from medical records or death certificates

Median post-MI survival time of 3.07 years

↓

71 experienced HF

Legend:

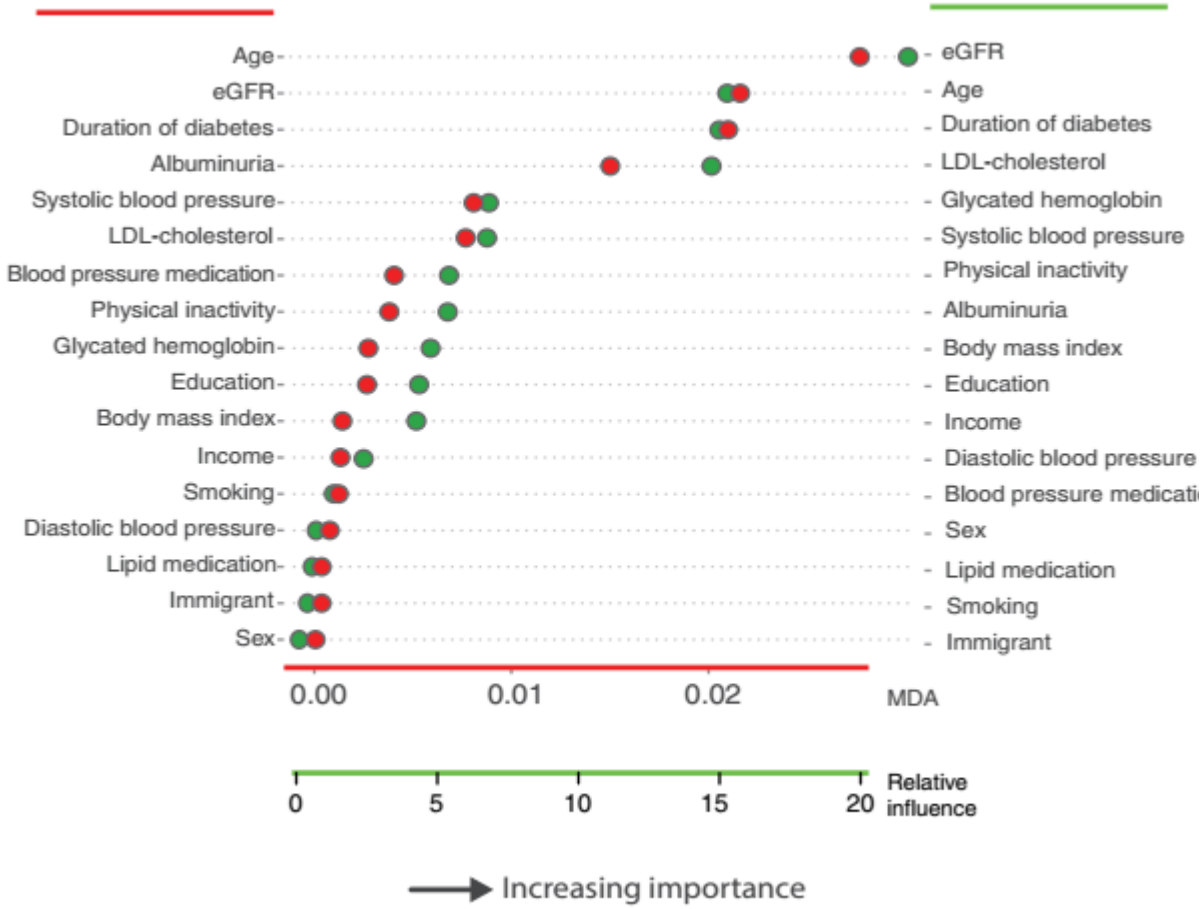
Random forest (mean-decrease accuracy)

Gradient boosting (relative influence)

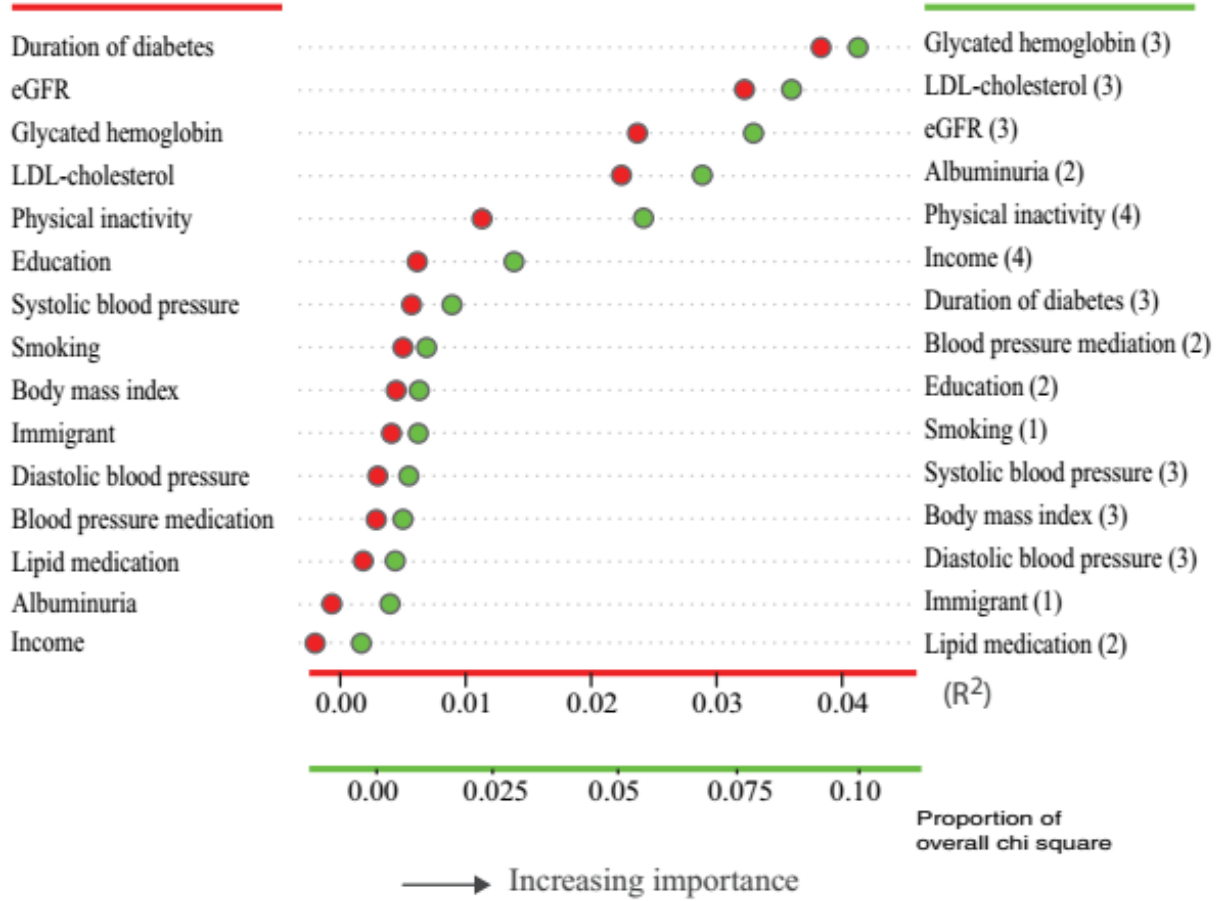
Cox hazards model (R^2 statistics)

Cox hazards model (explainable log-likelihood, Chi-square).

D HEART FAILURE



D HEART FAILURE



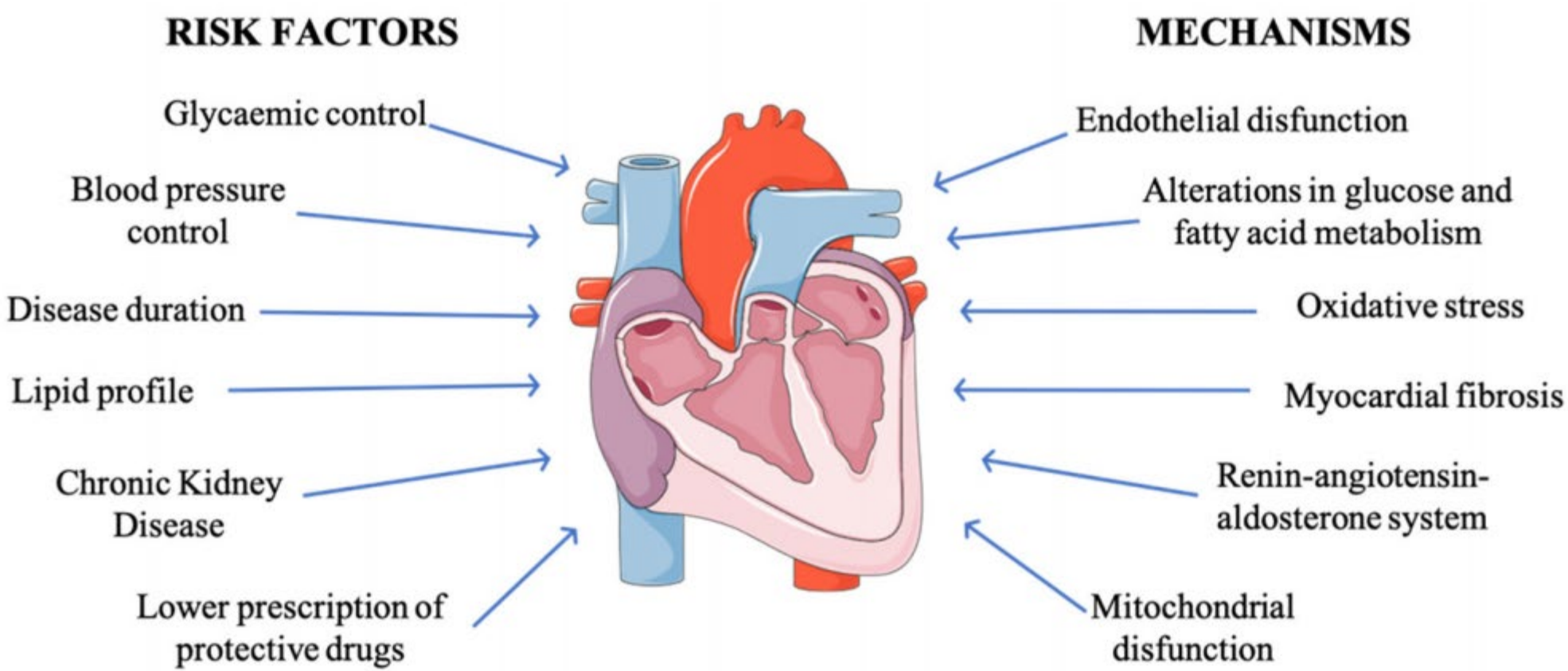

RISK FACTORS
Glycaemic control
Blood pressure control
Disease duration
Lipid profile
Chronic Kidney Disease
Lower prescription of protective drugs
MECHANISMS
Endothelial disfunction
Alterations in glucose and fatty acid metabolism
Oxidative stress
Myocardial fibrosis
Renin-angiotensin-aldosterone system
Mitochondrial disfunction

Table 1—Number and rate of CVD events separately by event type and the incidence ratios (IRs) for age- and mean HbA_{1c}–adjusted associations between risk factors and individual CVD outcomes in proportional rate models

	CVD death		Acute MI		Silent MI		Stroke		CHF		PTCA/CABG		Angina	
n (rate):*	35 (0.87)		86 (2.15)		73 (1.83)		28 (0.70)		22 (0.55)		181 (4.53)		56 (1.40)	
	IR (LL, UL)	*P* value	IR (LL, UL)	*P* value	IR (LL, UL)	*P* value	IR (LL, UL)	*P* value	IR (LL, UL)	*P* value	IR (LL, UL)	*P* value	IR (LL, UL)	*P* value
Group (INT vs. CON)	1.06 (0.53, 2.15)	0.86	0.87 (0.54, 1.42)	0.59	1.24 (0.78, 1.98)	0.37	1.06 (0.39, 2.88)	0.91	2.60 (0.84, 8.06)	0.10	0.69 (0.44, 1.1)	0.12	0.86 (0.46, 1.62)	0.64
Cohort (SCND vs. PRIM)	1.11 (0.58, 2.14)	0.75	1.86 (1.11, 3.1)	**0.02**	1.11 (0.68, 1.81)	0.68	1.12 (0.46, 2.73)	0.80	1.16 (0.44, 3.03)	0.77	1.38 (0.84, 2.27)	0.20	1.87 (0.97, 3.61)	0.06
Age (per 5 years)**	1.34 (1.1, 1.64)	**<0.01**	1.54 (1.34, 1.77)	**<0.01**	1.43 (1.21, 1.69)	**<0.01**	2.55 (1.67, 3.9)	**<0.01**	2.16 (1.43, 3.27)	**<0.01**	1.53 (1.33, 1.76)	**<0.01**	1.47 (1.18, 1.84)	**<0.01**
Sex (male vs. female)	2.28 (1.15, 4.5)	**0.02**	1.09 (0.68, 1.75)	0.71	0.97 (0.6, 1.57)	0.89	1.05 (0.46, 2.43)	0.91	1.75 (0.63, 4.83)	0.28	1.07 (0.66, 1.74)	0.78	0.64 (0.34, 1.22)	0.18
Mean HbA_{1c}** (per 1%)	2.54 (1.79, 3.61)	**<0.01**	1.79 (1.42, 2.25)	**<0.01**	1.14 (0.91, 1.44)	0.26	1.57 (1.18, 2.1)	**<0.01**	3.15 (1.98, 5.02)	**<0.01**	1.81 (1.46, 2.24)	**<0.01**	1.92 (1.47, 2.52)	**<0.01**
Mean SBP (per 10 mmHg)	2.00 (1.42, 2.82)	**<0.01**	1.46 (1.14, 1.87)	**<0.01**	1.35 (1.02, 1.79)	**0.04**	1.35 (0.89, 2.05)	0.16	2.21 (1.24, 3.92)	**0.01**	1.26 (0.99, 1.61)	0.06	1.26 (0.89, 1.78)	0.19
TRIG (log) (per 10 mg/dL)	2.68 (1.53, 4.70)	**<0.01**	1.84 (1.14, 2.97)	**0.01**	1.97 (1.34, 2.88)	**<0.01**	2.64 (1.64, 4.25)	**<0.01**	3.06 (1.39, 6.74)	**0.01**	1.43 (1, 2.03)	0.05	1.93 (1.12, 3.32)	**0.02**
Mean pulse (per 10 bpm)	1.58 (0.9, 2.79)	0.11	1.55 (1.11, 2.16)	**0.01**	1.30 (0.82, 2.04)	0.26	2.69 (1.2, 6.04)	**0.02**	1.94 (1.07, 3.52)	**0.03**	1.36 (0.9, 2.06)	0.14	2.38 (1.61, 3.52)	**<0.01**
Duration (per 5 years)	1.38 (0.93, 2.04)	0.11	1.53 (1.13, 2.08)	**0.01**	1.08 (0.82, 1.43)	0.59	0.94 (0.54, 1.61)	0.81	1.23 (0.66, 2.28)	0.52	1.40 (1.09, 1.79)	**0.01**	1.86 (1.27, 2.73)	**<0.01**
ACE inhibitor use (yes vs. no)	1.19 (0.57, 2.48)	0.64	0.60 (0.36, 0.99)	0.05	0.72 (0.43, 1.23)	0.23	0.29 (0.12, 0.7)	**0.01**	0.42 (0.16, 1.13)	0.09	1.02 (0.69, 1.49)	0.94	0.86 (0.45, 1.65)	0.65
FAM Hx MI (yes vs. no)	0.92 (0.47, 1.79)	0.80	1.68 (1.05, 2.69)	**0.03**	1.33 (0.82, 2.13)	0.24	1.05 (0.45, 2.46)	0.91	0.69 (0.25, 1.92)	0.48	2.17 (1.38, 3.4)	**<0.01**	2.87 (1.4, 5.89)	**<0.01**
Mean LDLc (per 10 mg/dL)	1.07 (0.91, 1.27)	0.39	1.17 (1.05, 1.3)	**<0.01**	1.06 (0.96, 1.19)	0.26	1.19 (1.01, 1.41)	**0.04**	0.93 (0.73, 1.19)	0.56	1.14 (1.03, 1.25)	**<0.01**	1.01 (0.91, 1.13)	0.85
Smoking (yes vs. no)	3.08 (1.53, 6.22)	**<0.01**	1.59 (0.92, 2.74)	0.09	1.49 (0.85, 2.61)	0.16	1.46 (0.61, 3.49)	0.39	1.75 (0.51, 5.97)	0.37	0.99 (0.62, 1.59)	0.97	1.10 (0.55, 2.19)	0.79

Covariates are listed in the descending order of importance in the multivariable risk factor model for the first of CVD events published previously (6). Treatment group, cohort, sex, and smoking were added to this list. *P* values <0.05 appear in boldface type. bpm, beats per minute; CON, conventional group; FAM Hx MI, family history of MI; INT, intensive group; LL, lower limit for 95% CI; PRIM, primary cohort; SCND, secondary cohort; TRIG, triglycerides; UL, upper limit for 95% CI. **n* is number of events (rate per 1,000 person-years). **Models for age were adjusted only for mean HbA_{1c}, and the models for mean HbA_{1c} were only adjusted for age. All of the other models were adjusted for both age and mean HbA_{1c}.

Diabetes Care Volume 42, July 2019

BMI, Mortality, and Cardiovascular Outcomes in Type 1 Diabetes: Findings Against an Obesity Paradox

Jon Edqvist,[1,2] Araz Rawshani,[1] Martin Adiels,[3] Lena Björck,[1,2] Marcus Lind,[1,4] Ann-Marie Svensson,[5] Sofia Gudbjörnsdottir,[5] Naveed Sattar,[6] and Annika Rosengren[1,2]

Diabetes Care 2019;42:1297–1304 | https://doi.org/10.2337/dc18-1446

Hazard ratios for hospitalization for HF