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Kardiologische Probleme beim Diabetiker

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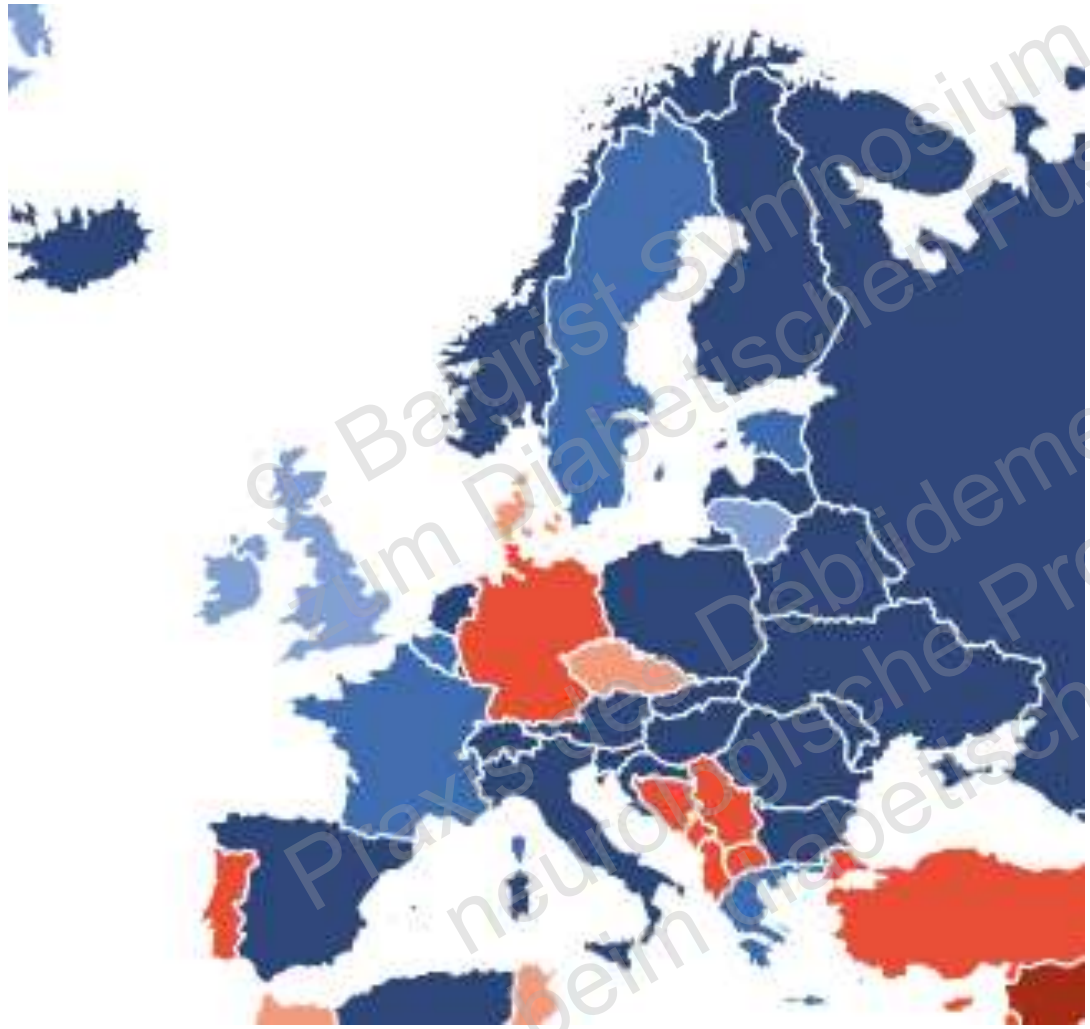
Hintergrund: Diabetes-Prävalenz bei 20-79jährigen in 2019



- <4%
- 4–<5%
- 5–<7%
- 7–<9%
- 9–<12%
- ≥12%
- No estimates made

Table 3.24 **Top 10 countries or territories for mean health expenditure (USD) per person with diabetes (20–79 years) in 2019**

Rank	Country or territory	Mean health expenditure per person with diabetes (USD)
1	Switzerland	11,916
2	United States of America	9,506
3	Norway	9,061
4	Luxembourg	7,978
5	Sweden	6,643
6	Ireland	6,598
7	Iceland	6,403
8	Denmark	5,521
9	Netherlands	5,380
10	Austria	5,259

Diabetes mellitus ist (auch) eine kardiovaskuläre Erkrankung

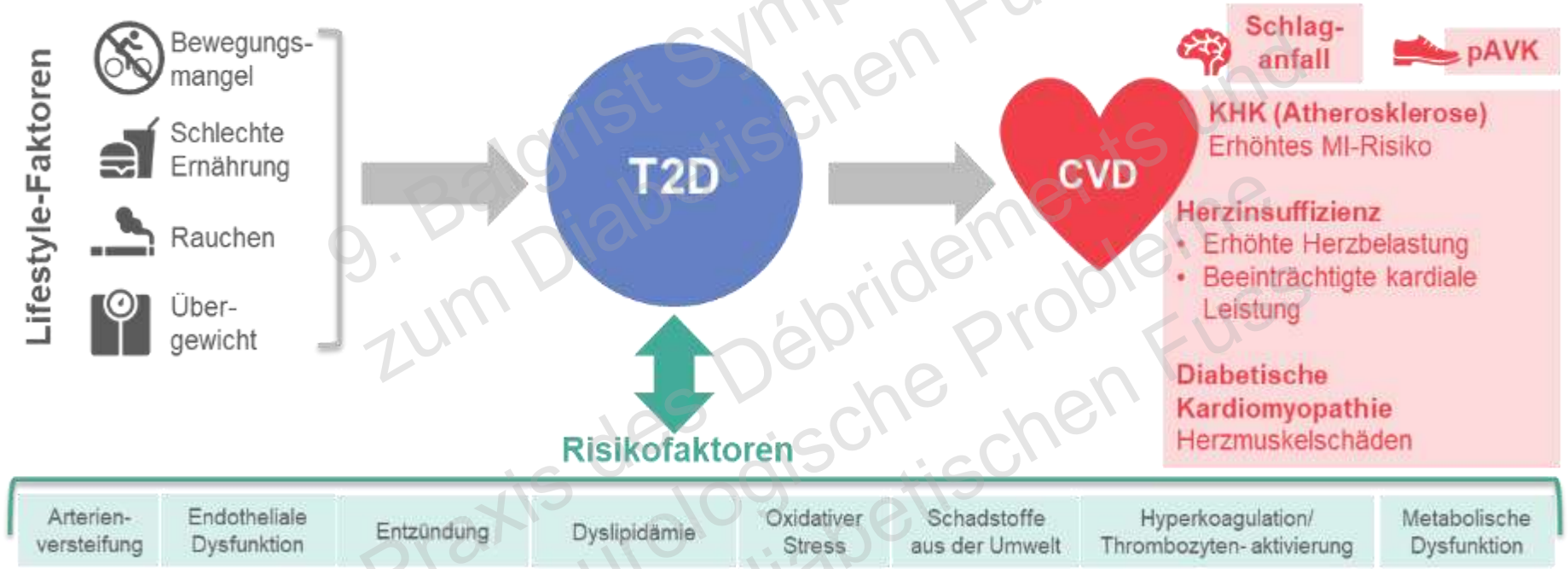
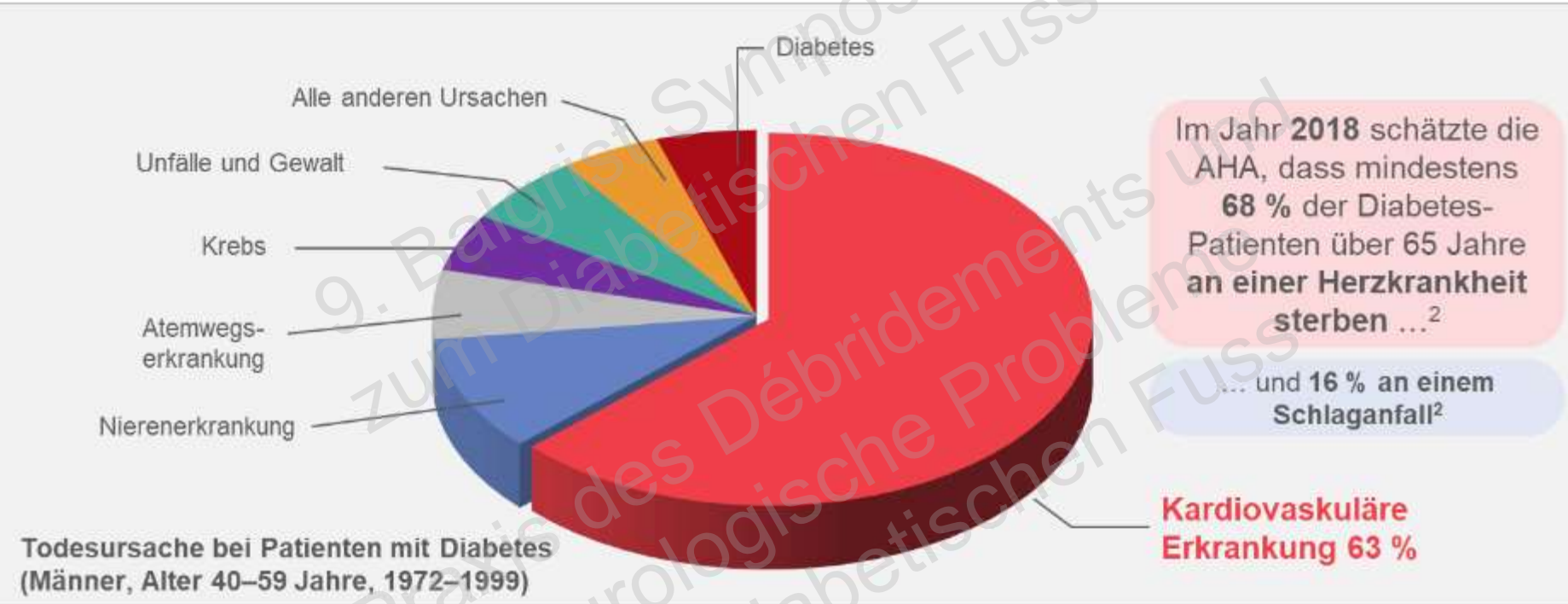


Abbildung modifiziert nach Ref. 3 und 4

1. Grundy et al. Circulation 1999;100:1134–46. 2. Davies et al. Diabetologia 2018;61:2461–98. 3. Newman et al. J Am Coll Cardiol 2017;70:883–93. 4. Vulesevic et al Biochem Soc Trans 2014;42:523–7.

Schätzungsweise 2/3 der T2D-Patienten sterben an einer kardiovaskulären Erkrankung[1]

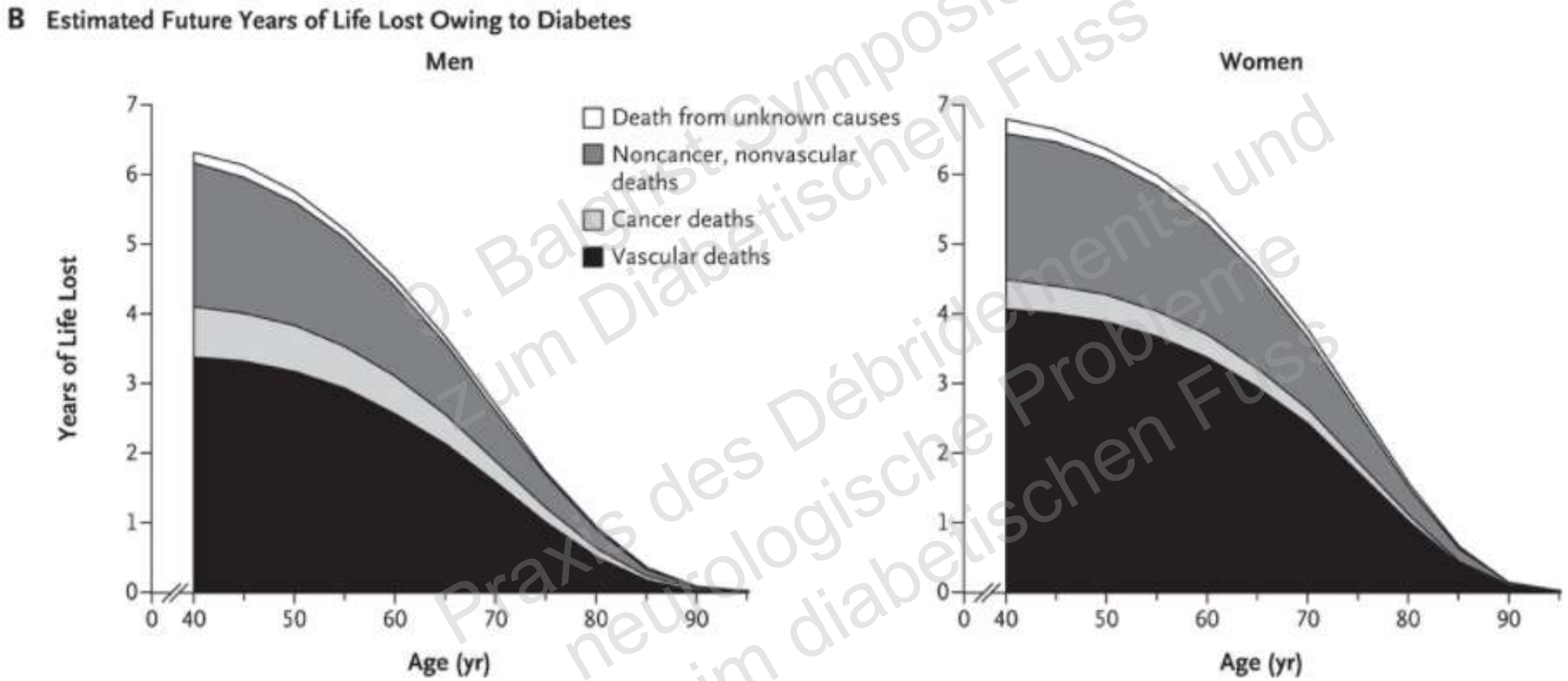


AHA, American Heart Association.

1. Laing, 1999. BSC TCT Symposium. 2. Heart.org. [https://www.heart.org/en/health-topics/diabetes/why-diabetes-matters/cardiovascular-disease--diabetes]. Zugriff im Okt. 2018.

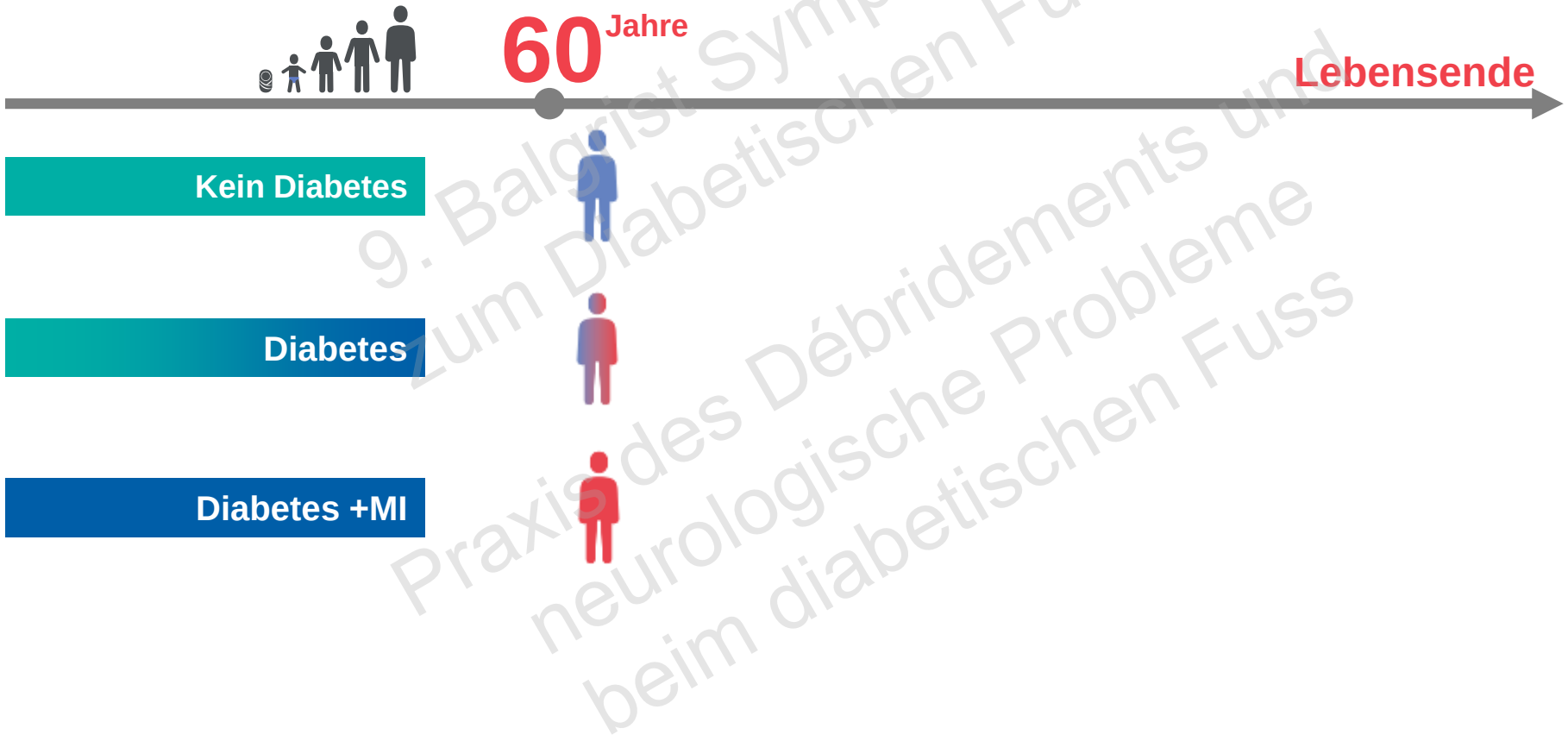
Diabetes mellitus führt zu einer früheren Sterblichkeit

>500‘000 Patienten ohne kardiovaskuläre Erkrankung



Emerging Risk Factors Collaboration, NEJM 2011

Die Lebenserwartung wird bei Diabetes-Patienten* mit Myokardinfarkt um 12 Jahre reduziert

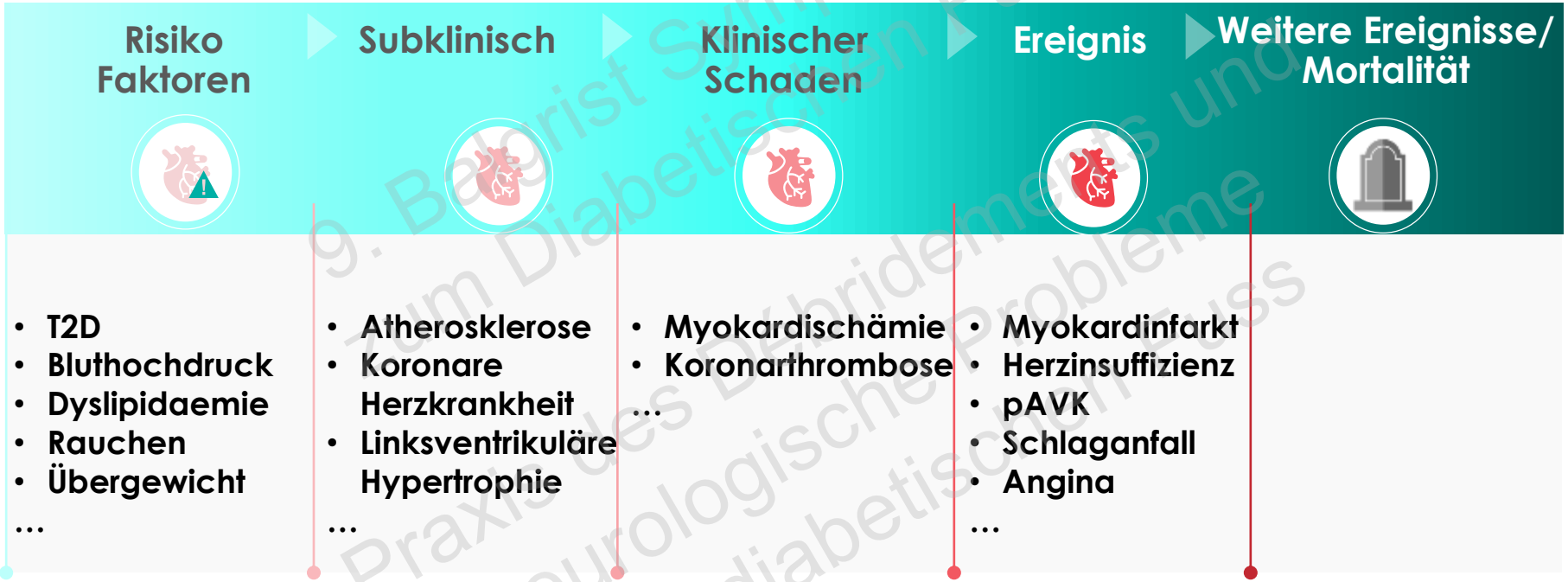


Kardiovaskulärer Tod bedeutet in diesem Fall Tod durch Myokardinfarkt oder Schlaganfall.
MI: Myokardinfarkt
*60 Jahre alt.

Di Angelantonio E. et al., Association of Cardiometabolic Multimorbidity With Mortality. JAMA 2015;314(1):52-60

Kontinuum Kardiovaskulärer Erkrankungen bei T2D Patienten

Patienten sind im Krankheitsverlauf einem kv Risiko ausgesetzt, auch schon vor Diagnosestellung

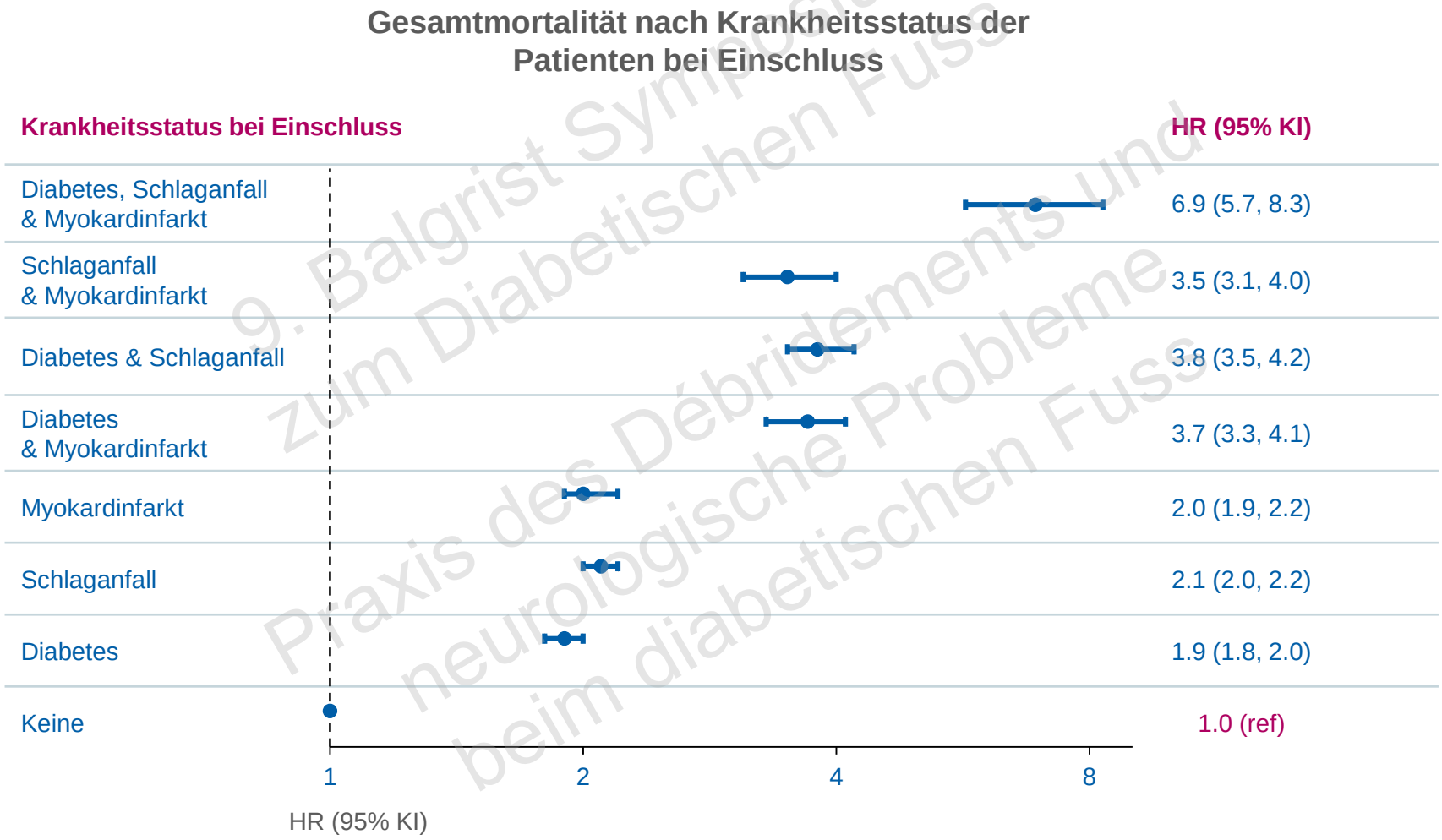


KV, kardiovaskular; pAVK, peripheren arteriellen Verschlusskrankheit; T2D, Typ-2-Diabetes

Modizifiert nach : Dzau VJ et al., The cardiovascular disease continuum validated: clinical evidence of improved patient outcomes: part I: Pathophysiology and clinical trial evidence (risk factors through stable coronary artery disease). Circulation 2006; 114:2850. Franklin BA et al., Recent advances in preventive cardiology and lifestyle medicine: a themed series. Circulation 2011; 123:2274

DIA_D_012020_Empagliflozin(Jardiance, Jardiance MET)/EM-CH-100065

Trotz Fortschritte in der kardiovaskulären Therapie, ist die Mortalität bei T2D Patienten hoch



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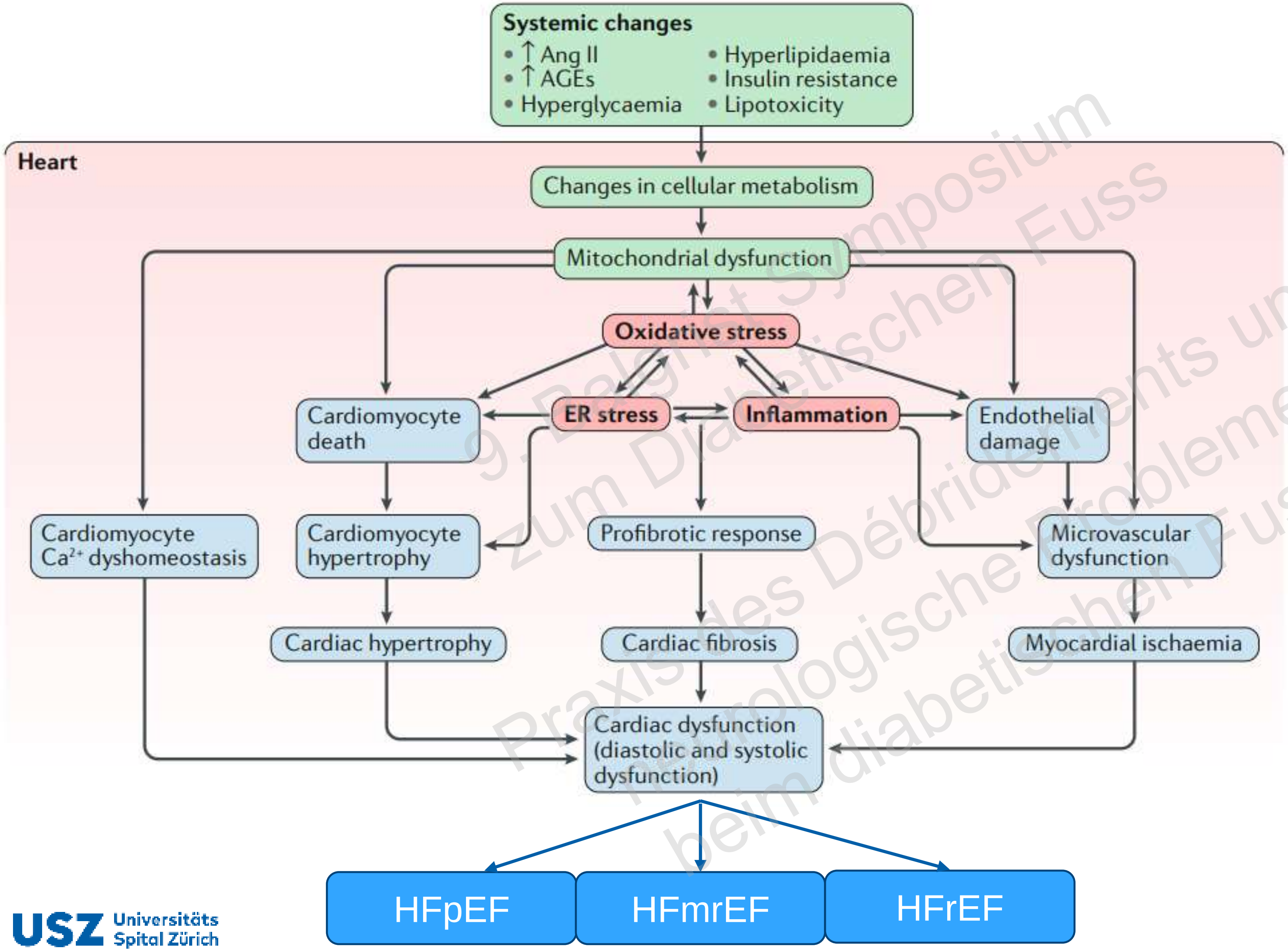
Di Angelantonio E. et al., Association of Cardiometabolic Multimorbidity With Mortality. JAMA 2015;314(1):52-60

Diabetes und Herzinsuffizienz



Potential Pathways that Could be Targeted to Modulate Specific Pathophysiologic Mechanisms that Contribute to Diabetes-Associated Heart Failure

- Altered Myocardial Substrate Metabolism
- Mitochondrial Bioenergetics
- Oxidative Stress
- Lipotoxicity
- Inflammation
- ER Stress
- Insulin Signaling
- β_2Adrenergic Receptor Signaling
- GRK2 Signaling
- Renin Angiotensin Aldosterone Signaling
- Autophagy
- AGEs

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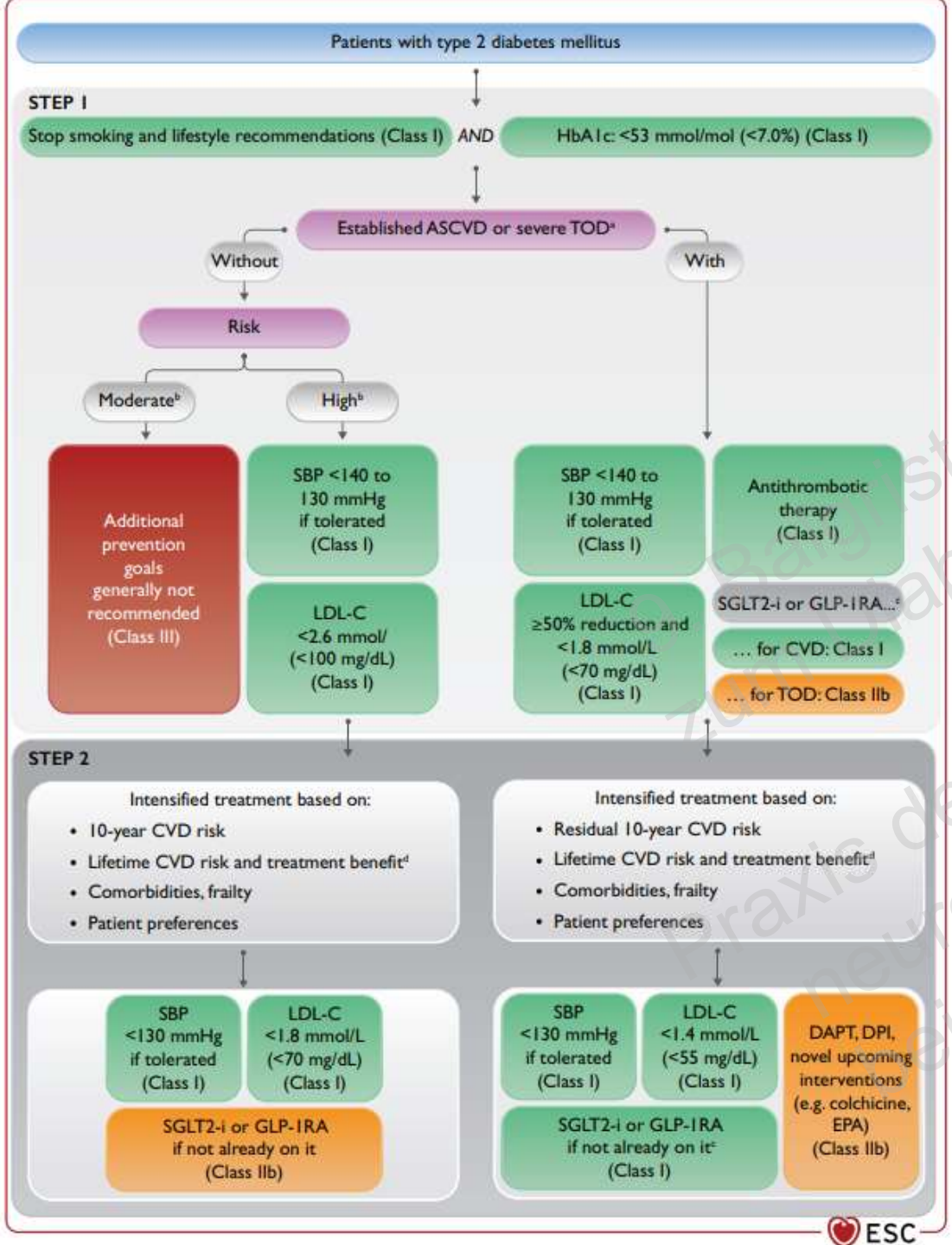
Tan et al; Nature Reviews Cardiology 2020

Circ Res 2019; Kenny and Abel

Behandlungsziele



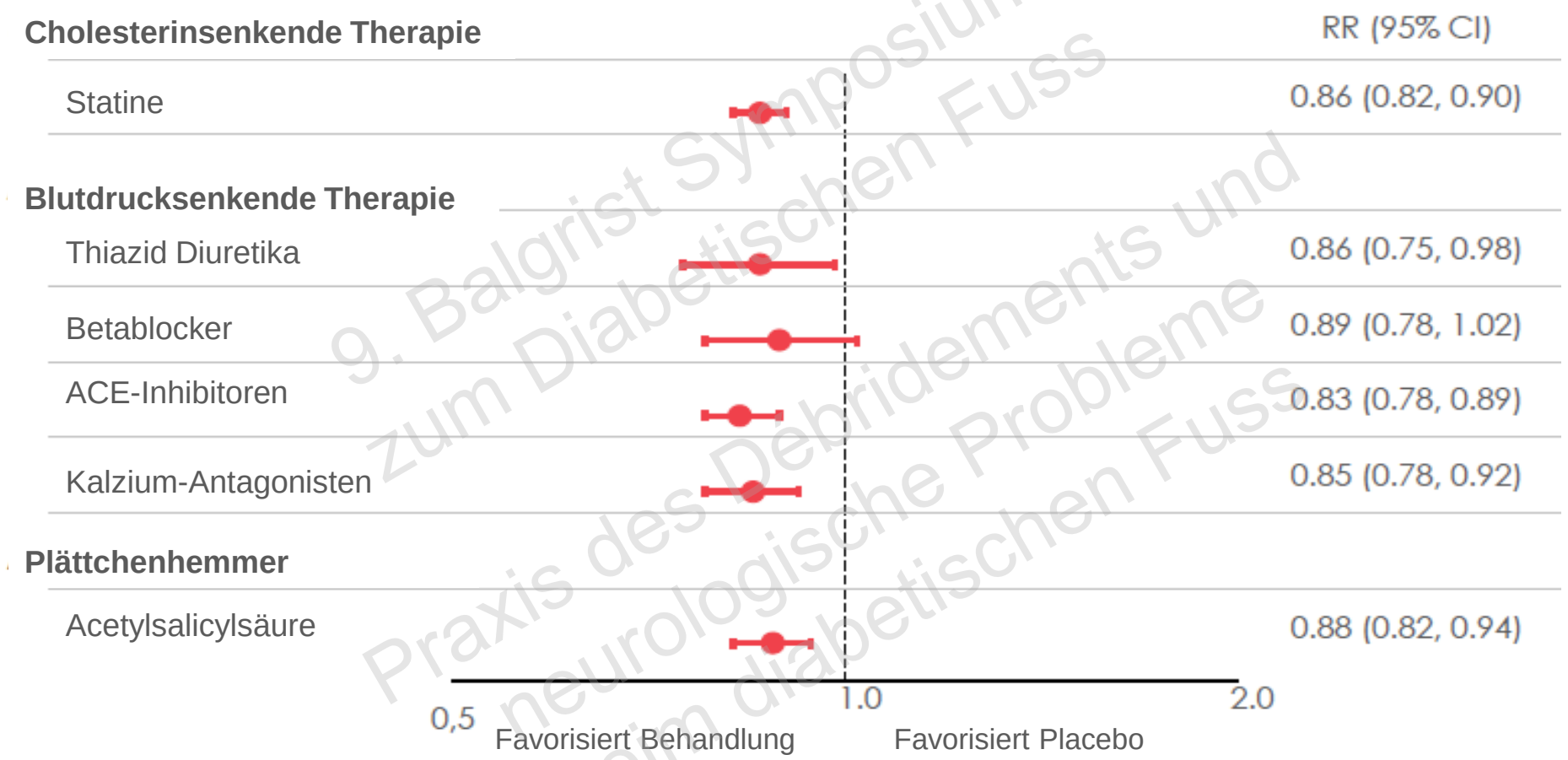
Lifetime CVD risk and treatment benefit estimation

Prevention of CVD by treating risk factors is usually done with a lifetime perspective. Lifetime CVD risk can be approximated by clinical experience with clinical criteria such as age, (change in) risk factor levels, risk modifiers, etc. or estimated in apparently healthy people, patients with established ASCVD, and persons with type 2 DM with specific lifetime CVD risk scores.

BD	**130-140 mmHg**
LDL-C	**<2.6 mmol/l (<1.8 mmol/l)**
Nikotin	**Stop**
HbA1c	**<7%**

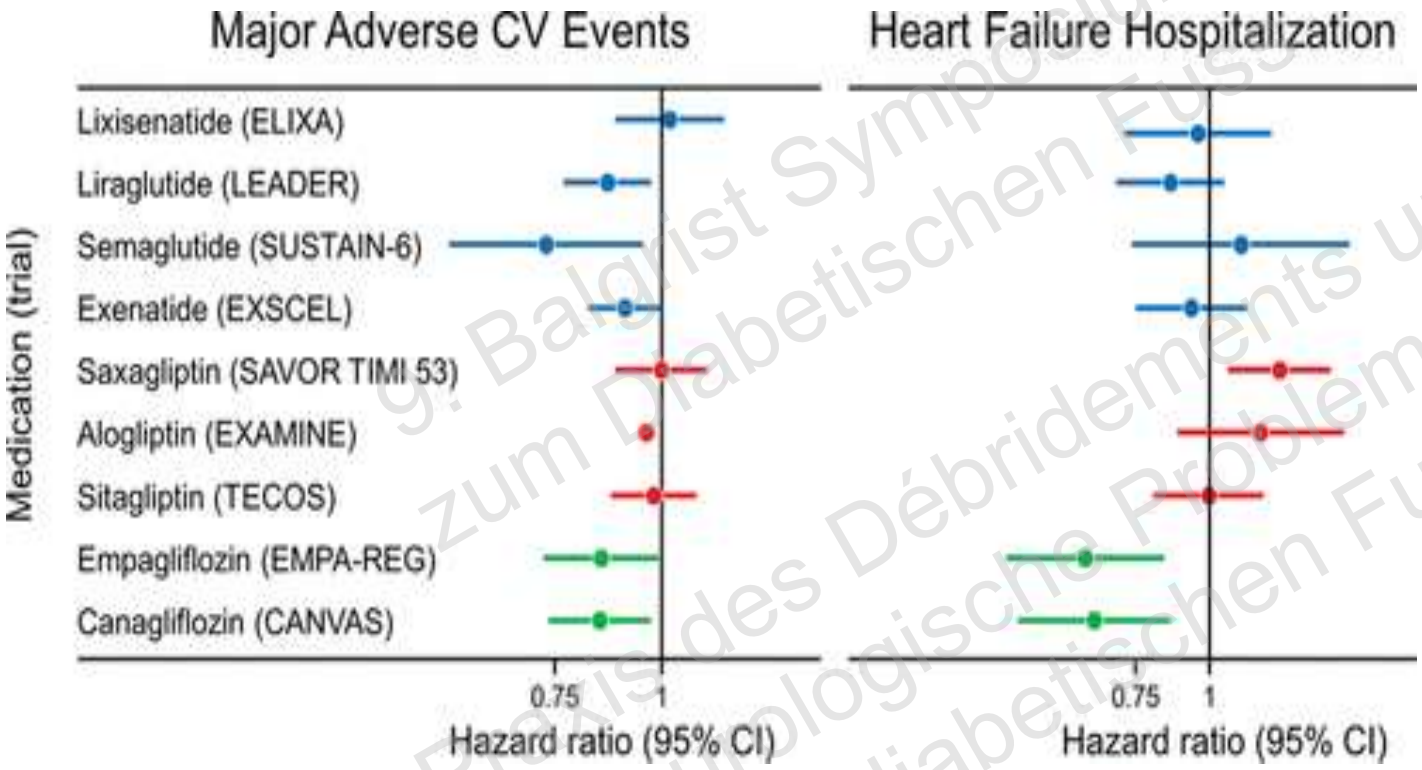
ESC Guidelines on cv disease prevention 2021

Einfluss von pharmakologischen Interventionen auf das KV Risiko



1. Baigent C., et al., Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2010, 376: 1670-81.
2. 2. Law M. R., et al., Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009; 338 :b1665
3. 3. Baigent C., et al., Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009, 373: 1849-60.

Risiko für kardiovaskuläre Ereignisse und Herzinsuffizienz-Hospitalisationen



GLP1-RA

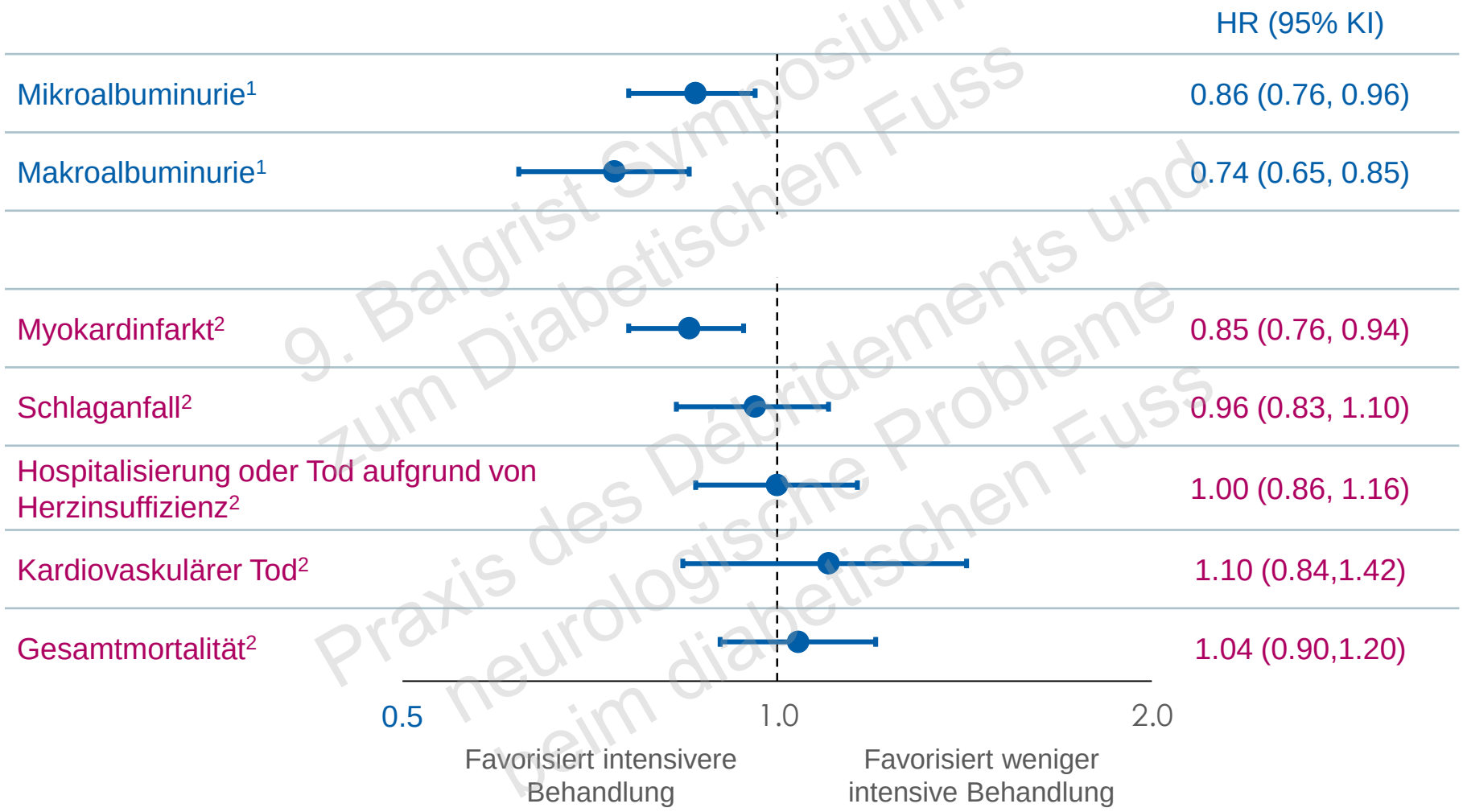
DPP4-I

SGLT2-I

Dunlay et al. Circulation 2019; 140 (7), Pages: e294-e324

Intensive glukosesenkende Therapien haben begrenzte Auswirkung auf makrovaskuläre Endpunkte und Mortalität

Sulfonylharnstoff, Metformin, Glitazone, Glinide, Insulin



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1.Coca SG et al., Arch Intern Med. 2012;172(10):761–769 . 2. Turnbull, F.M. et al., Intensive glucose control and macrovascular outcomes in type 2 diabetes. Diabetologia (2009) 52: 2288

New recommendations (8)

Recommendations	Class
Risk factors and interventions at the individual level (continued)	
In persons with type 2 DM and ASCVD, the use of a GLP-1RA or SGLT2 inhibitor with proven outcome benefits is recommended to reduce CV and/or cardiorenal outcomes.	I
In patients with type 2 DM and CKD, the use of an SGLT2 inhibitor is recommended to improve ASCVD and/or cardiorenal outcomes.	I
In patients with type 2 DM and HFrEF, use of an SGLT2 inhibitor with proven outcome benefits is recommended to lessen HF hospitalizations and CV death.	I
Participation in a medically supervised, structured, comprehensive, multidisciplinary EBCR and prevention programme for patients after ASCVD events and/or revascularization, and for patients with HF (mainly HFrEF), is recommended to improve patient outcomes.	I

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

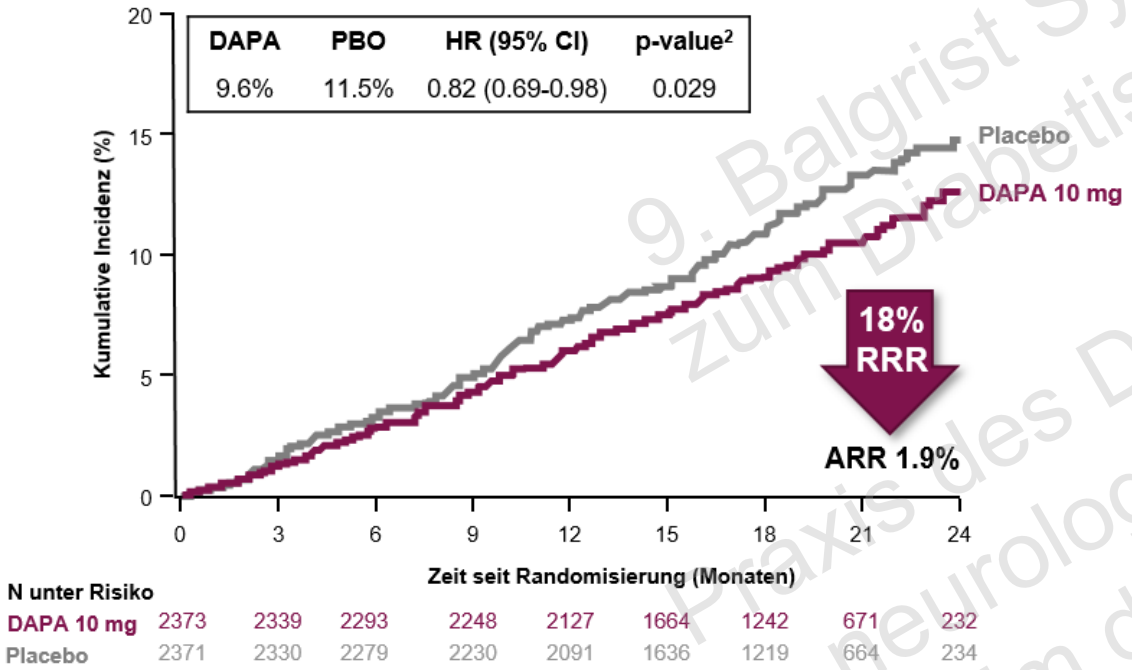
New recommendations (11)

Recommendations	Class
Risk factors and interventions at the individual level (continued)	
In patients with type 2 DM and TOD, the use of an SGLT2 inhibitor or GLP-1RA with proven outcome benefits may be considered to reduce future CVD and total mortality.	**IIb**
For primary prevention patients at very high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor may be considered.	**IIb**
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 X 2 g/day) may be considered in combination with a statin.	**IIb**
Initiation of statin treatment for primary prevention in older people aged ≥70 may be considered, if at high risk or above.	**IIb**

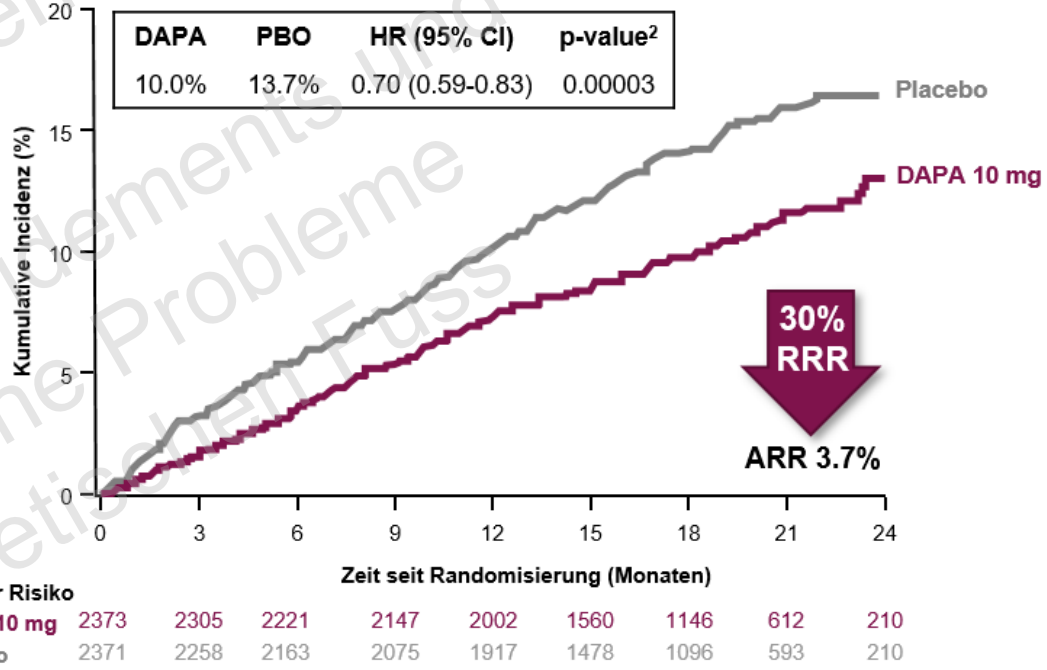
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

DAPA-HF:
signifikante Reduktion von Kardiovaskulärem Tod und Verschlechterung der Herzinsuffizienz

Kardiovaskuläre Tod



Verschlechterung der HI*



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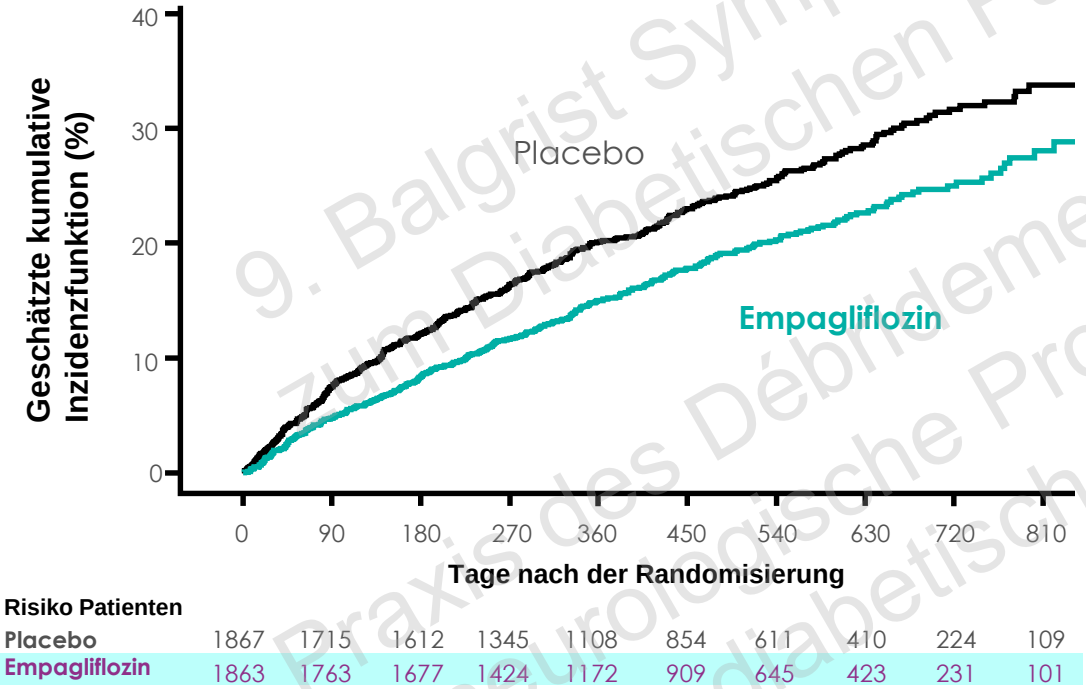
* Eine Verschlechterung der HI ist definiert als Hospitalisierung oder notfallmässiger Arztkontakt wegen HI.

ARR = absolute risk reduction; CI: confidence interval (Konfidenzintervall) DAPA = dapagliflozin; HI = Herzinsuffizienz; HR = hazard ratio; PBO = placebo; RRR = relative risk reduction

1. McMurray JJV et al. Dapagliflozin in Patients With Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019 Nov 21;381(21):1995–2008.

EMPEROR-Reduced:
Primärer Endpunkt: Zeit bis zur ersten Hospitalisierung durch Herzinsuffizienz oder CV-Tod



Risiko Patienten										
Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

RRR 25%

ARR 5.2%

NNT = 19

HR 0.75
(95% CI 0.65, 0.86)
p<0.001

Empagliflozin:
361 Patienten mit Ereignis
Bewerten: 15,8/100 Patientenjahre
Placebo:
462 Patienten mit Ereignis
Bewerten: 21,0/100 Patientenjahre

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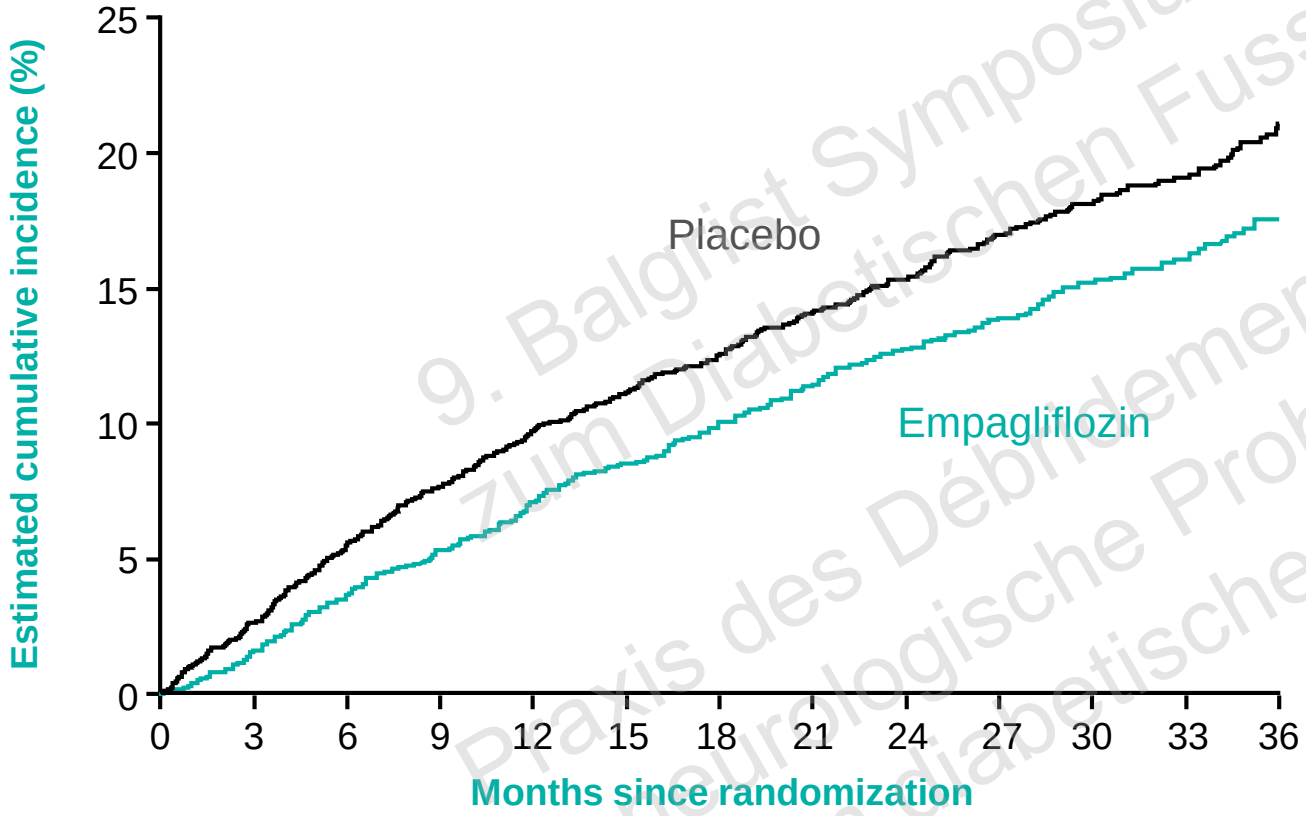
Packer M et al. NEJM 2020

EMPEROR-Preserved:
21% RRR in the composite primary endpoint of CV death or HHF



Patients at risk

Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

RRR 21%

ARR 3.3%

NNT*=31

HR: 0.79
(95% CI: 0.69, 0.90)
p<0.001

Empagliflozin:
415 (13.8%) patients with event
Rate: 6.9/100 patient-years
Placebo:
511 (17.1%) patients with event
Rate: 8.7/100 patient-years

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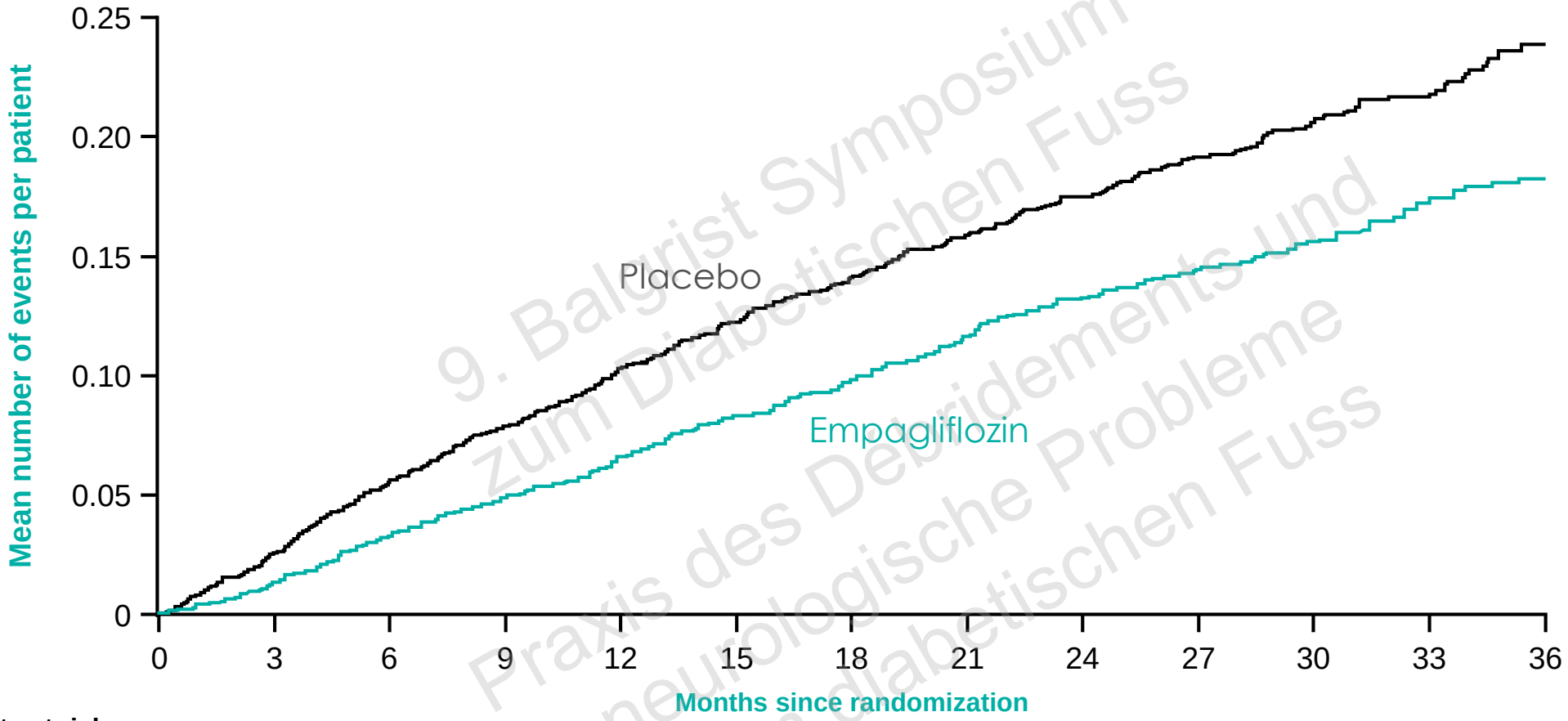
Anker S *et al. NEJM* 2021

EMPEROR-Preserved:
Empagliflozin reduced first and recurrent HHF by 27%



Patients at risk

Placebo	2991	2945	2901	2855	2816	2618	2258	1998	1695	1414	1061	747	448
Empagliflozin	2997	2962	2913	2869	2817	2604	2247	1977	1684	1429	1081	765	446

RRR 27%

HR: 0.73
(95% CI: 0.61, 0.88)
p<0.001

Empagliflozin: 407 patients with event
Placebo: 541 patients with event

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Anker S *et al. NEJM* 2021

Zusammenfassung

- Diabetes mellitus ist häufig und verkürzt die Lebenserwartung signifikant
- Risiken für Myokardinfarkt, Schlaganfälle und pAVK sind signifikant erhöht
- Diabetes mellitus ist ein wichtiger Risikofaktor für Herzinsuffizienz (HFrEF und HFpEF)
- Neuere Behandlungsmethoden mit SGLT2-I und GLP1-RA zeigen erstmals einen Nutzen bzgl. kardiovaskulärer Mortalität/Morbidität
- positive Effekte der SGLT2-I bei Herzinsuffizienzpatienten sind mit/ohne T2D vorhanden
- Begleitende Risikofaktoren (Dyslipidämie, Hypertonie, Nikotin, …) müssen frühzeitig erkannt und optimal behandelt werden

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Vielen Dank für Ihre Aufmerksamkeit

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