Bluthochdruck, Diabetes und Nierenerkrankung

Aktuelle Therapieziele für das nächste Jahrzehnt

MEDIZIN IM DIALOG

mit Prof. Dr. Gunnar Heine

Dienstag
25.02.2020
18.00 Uhr

© AGAPLESION FRANKFURTER DIAKONIE KLINIKEN | Prof. Dr. med. Gunnar Heine, Chefarzt der Medizinischen Klinik II am AGAPLESION MARKUS KRANKENHAUS

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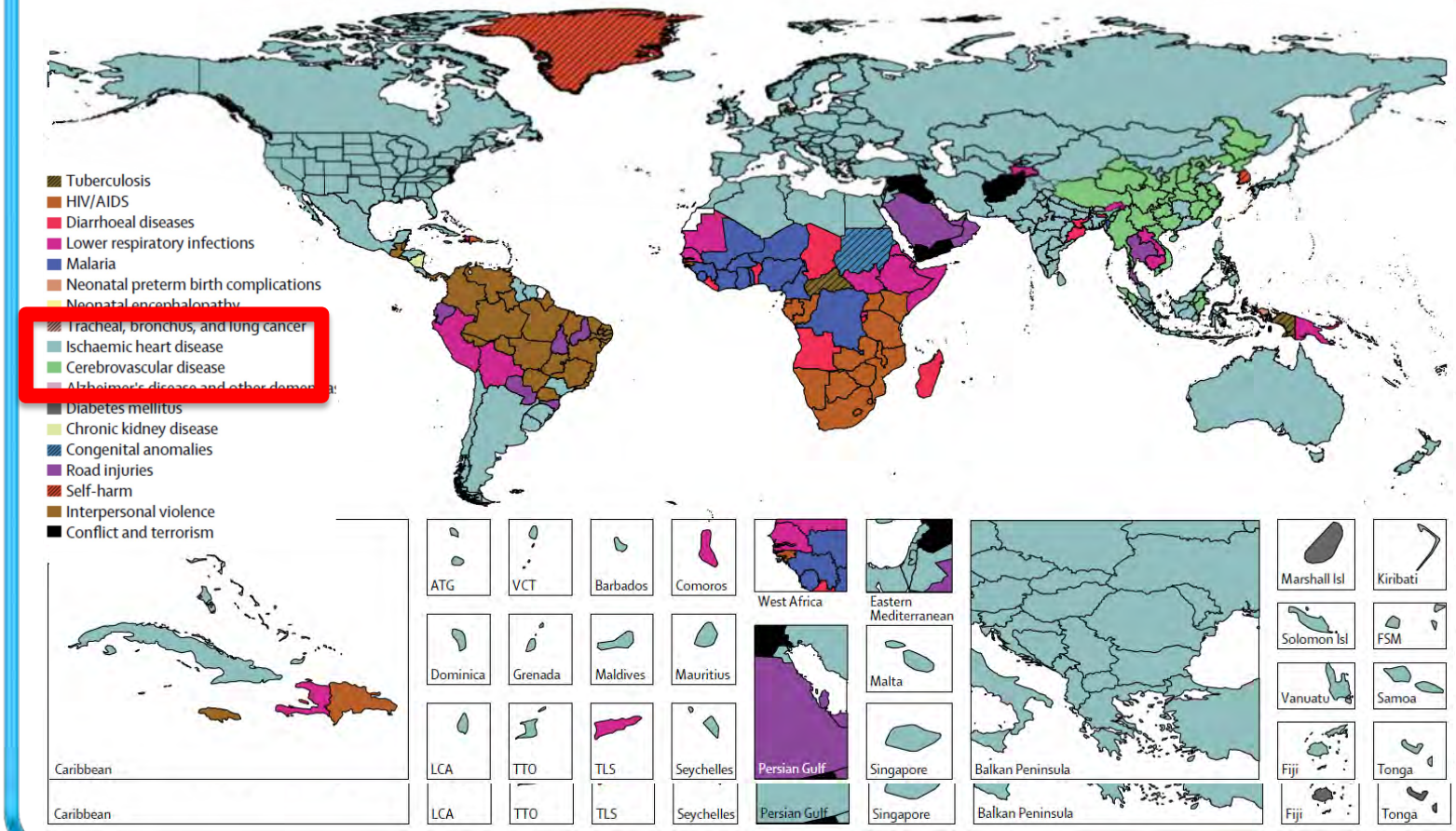
GBD 2016 Causes of Death Collaborators Lancet 2017

Führende Gründe für „verlorene Lebensjahre“

(Pläänuesr)



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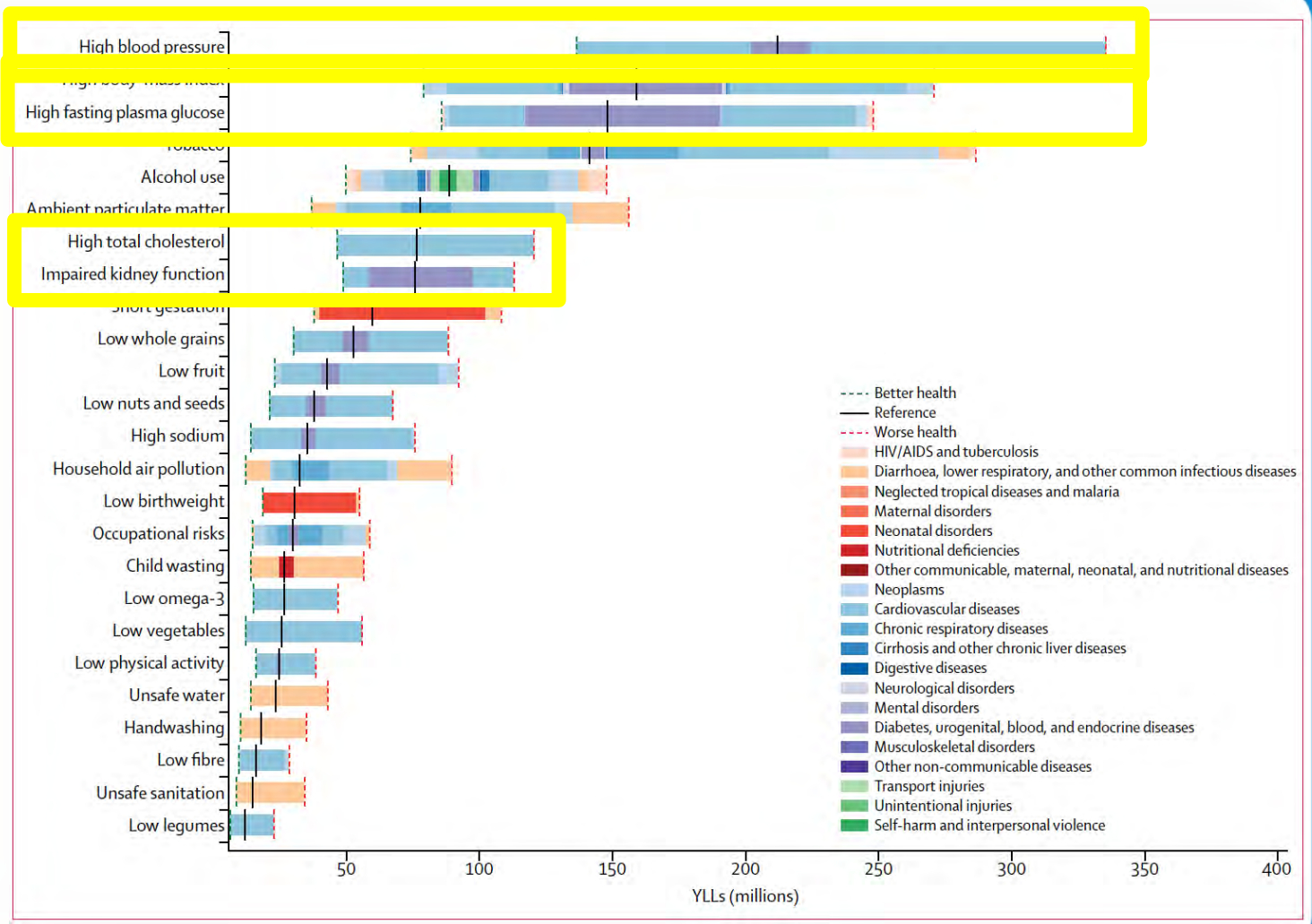
Foreman KJ *et al* Lancet 10th November 2018

Leading RF: all-cause attributable YLLs



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Definition arterielle Hypertonie ESH / ESC 2018

Praxisblutdruck

Kategorie[a]	Systolisch (mmHg)		Diastolisch (mmHg)
Optimal	< 120	und	< 80
Normal	120–129	und/oder	80–84
Hochnormal	130–139	und/oder	85–89
Hypertonie Grad 1	140–159	und/oder	90–99
Hypertonie Grad 2	160–179	und/oder	100–109
Hypertonie Grad 3	≥ 180	und/oder	≥ 110
Isolierte systolische Hypertonie[b]	≥ 140	und	< 90

Definition Bluthochdruck

Kategorie	SBP (mmHg)		DBP (mmHg)
Praxisblutdruck[a]	≥ 140	und/oder	≥ 90

Konferenz von Jalta, 4. – 11.02.1945

„The greatest danger to a man with high blood pressure lies in its discovery, because then some fool is certain to try and reduce it.“

J.H. Hay, 1931

„Hypertension may be an important compensatory mechanism which should not be tampered with, even were it certain that we could control it.“

Paul Dudley White, 1937

Kannel WB *et al.* Am J Public Health Nations Health 1965

National Health Act

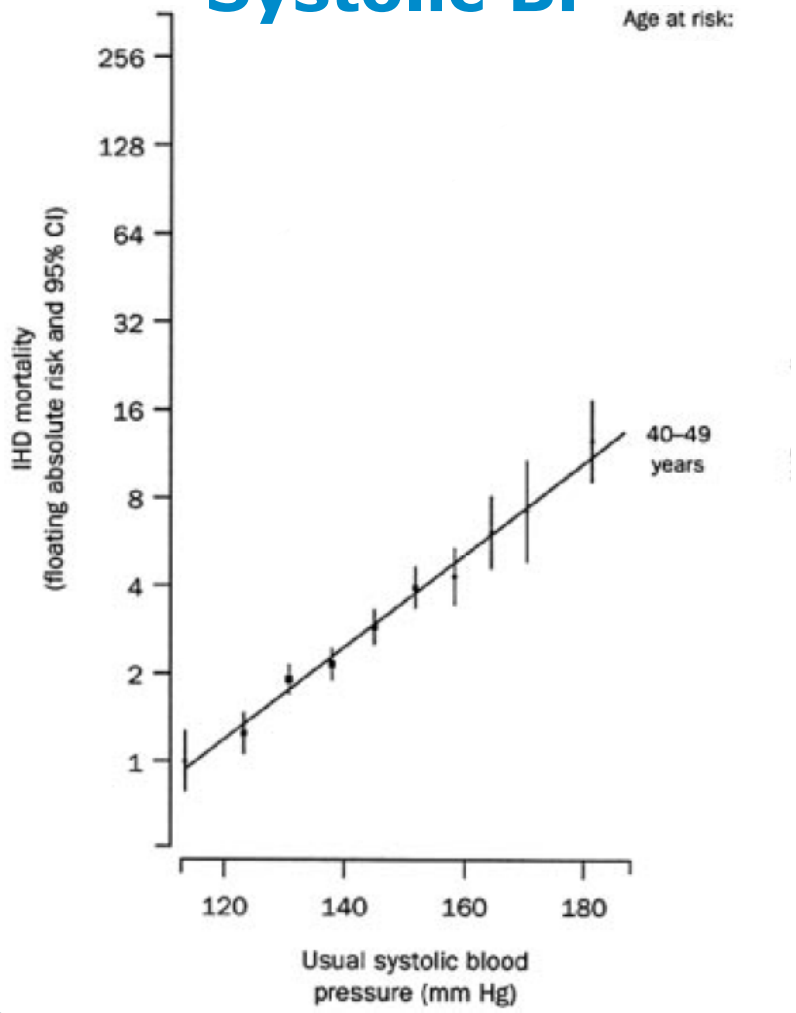
"The Nation's health is seriously threatened by diseases of the heart and circulation, including high blood pressure...

More than one in every three of our people die from them."

Initial Hypertensive Status†	mmHg	New Cases Developing in 12 Years: Brain Infarction Obs.	Brain Infarction Exp.	Brain Infarction M. R.*	Myocardial Infarction Obs.	Myocardial Infarction Exp.	Myocardial Infarction M. R.*
Normotensive	< 140 / 90	9	20.6	44	37	63.5	58
Borderline	others	15	21.0	71	72	59.1	122
Hypertensive	> 160 / 95	31	13.4	232	48	34.4	140

Lewington S *et al.* Lancet 2002

Systolic BP



Diastolic BP

VA Cooperate Study Group JAMA 1967

142

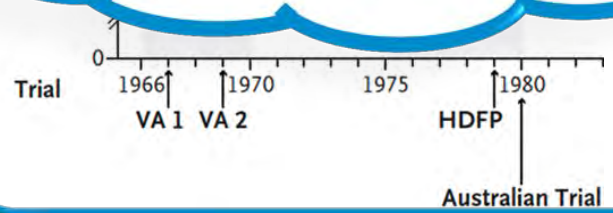
Diastolischer BD

115 – 129 mmHg

Therapie vs Placebo

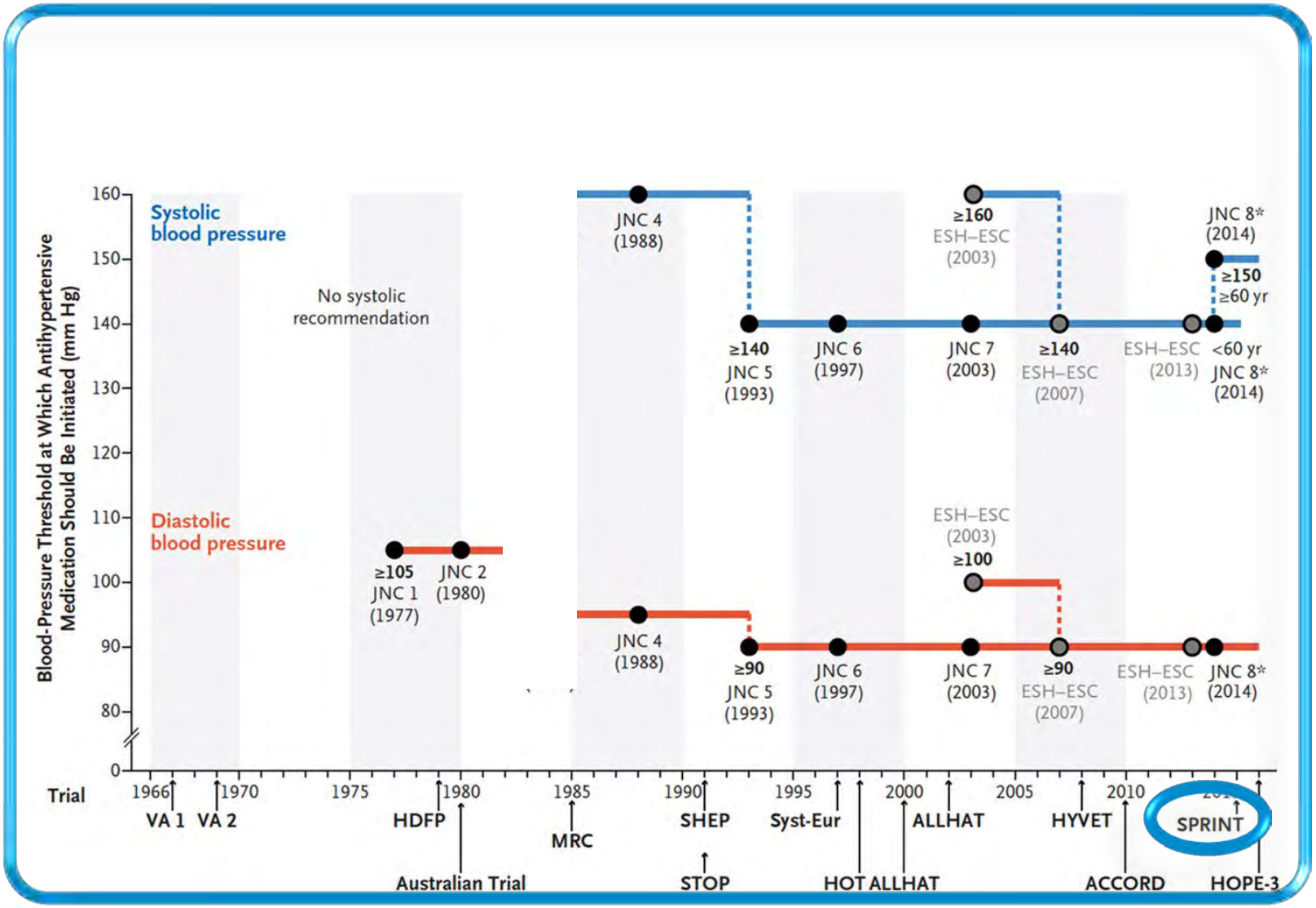
	Therapie	Placebo
BD dia (mmHg)	91.6	119.7
Komplikationen	2	27
Todesfälle	0	4

Hydrochlorothiazide + Reserpin + Hydralazinhydrochlorid

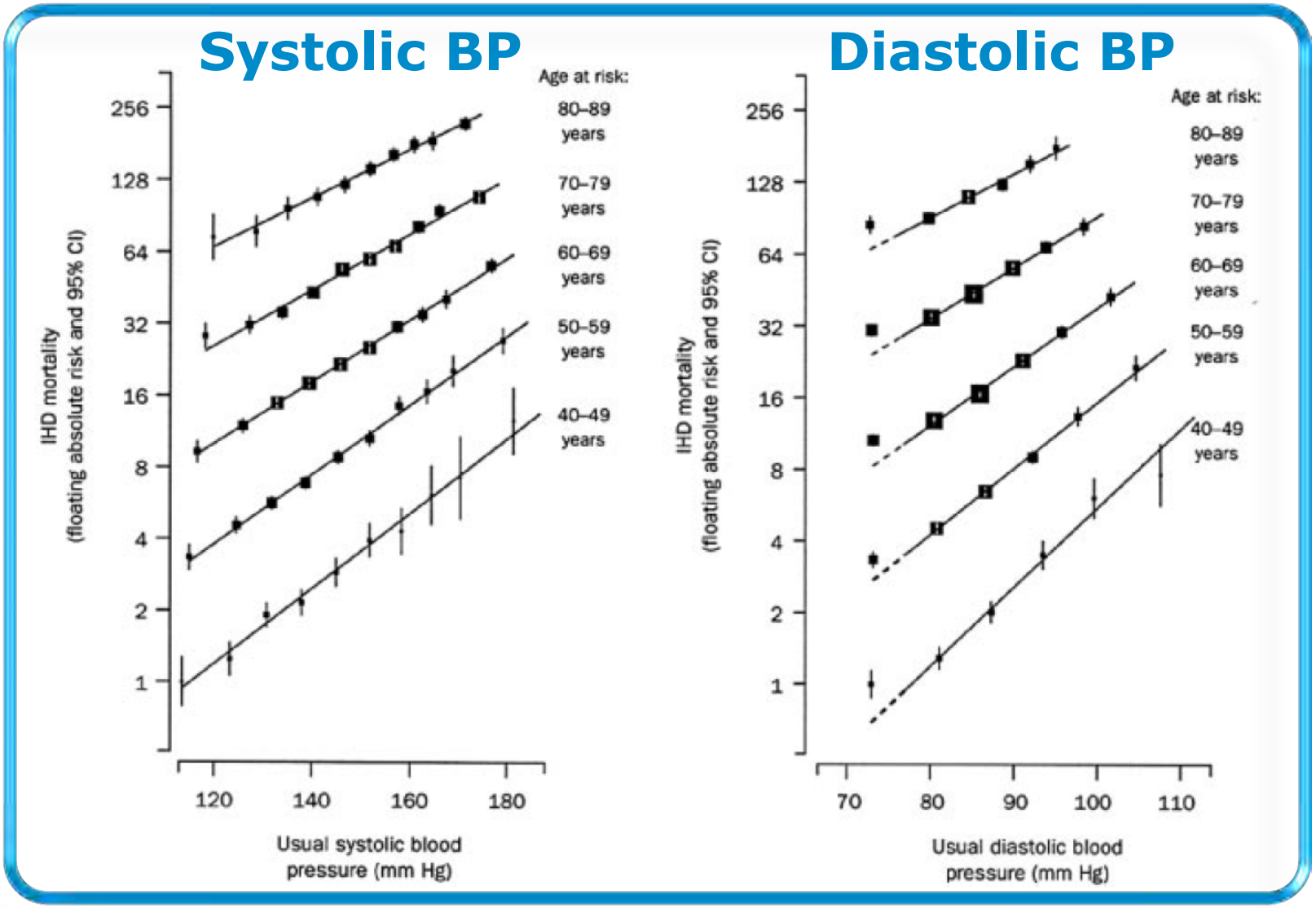


Herzinfarkte, Schlaganfälle, …

Lüscher TF Eur Heart J 2018



Lewington S *et al.* Lancet 2002



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Preprint New Engl J Med 2015

Ausschluss:
DM
Proteinurie > 1 g /d
Z. n. Schlaganfall

Alter ≥ 50 Jahre +
SBP 130 mmHg +
Erhö siko

20th Aug 2015

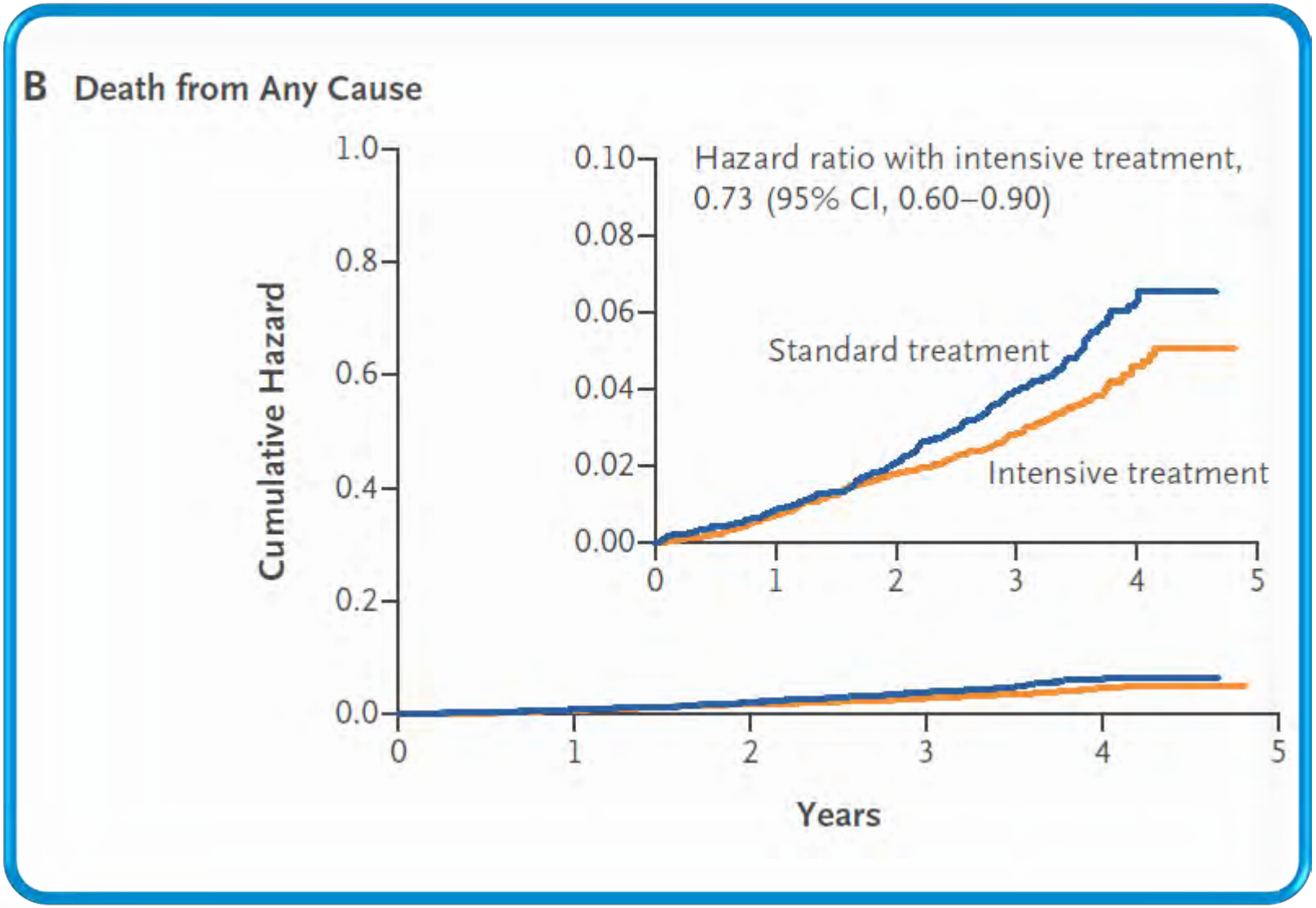
Ziel Office BP
135 – 140 mmHg
(n = 4683)

4 – 6 Jahre
geplantes FU
(bis Nov 2016)

Ziel Office BP
< 120 mmHg
(n=4678)

Primärer Endpunkt:
Myokardinfarkt / akutes Koronarsyndrom / Schlaganfall / akute kardiale Dekompensation / CV Tod

The SPRINT Research Group New Engl J Med 2015

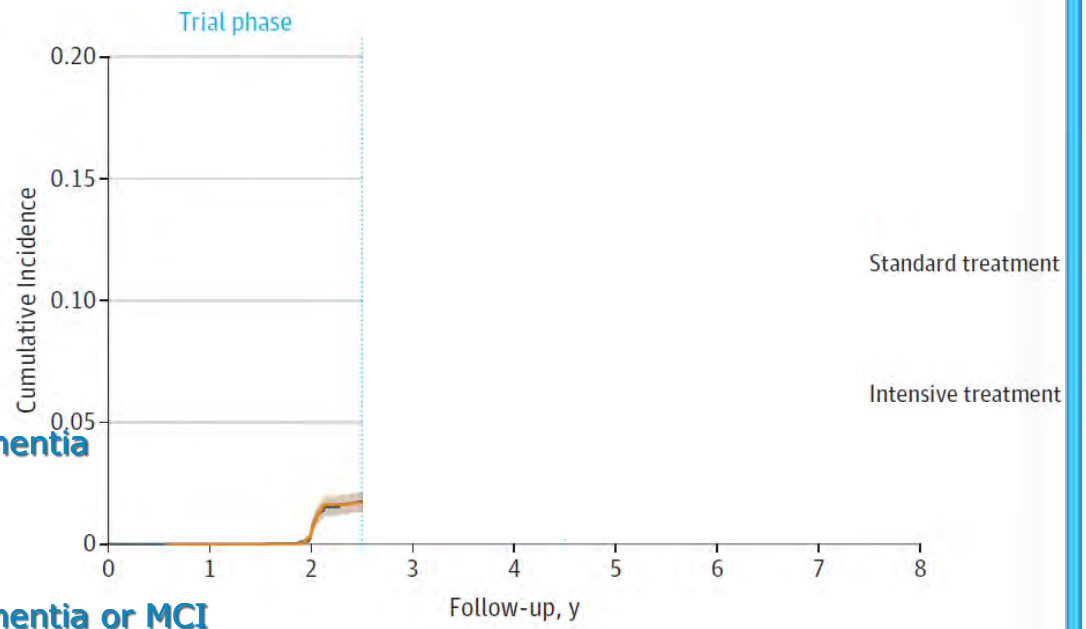


SPRINT MIND Investigators JAMA 2019

Probable dementia: **HR 0.83 (95 % CI 0.67 – 1.04; p = 0.10)**

MCI: **HR 0.81 (95 % CI 0.69 – 0.95)**

Probable dementia or MCI: **HR 0.85 (95 % CI 0.74 – 0.97)**



1st cognitive outcome:

Occurrence of probable dementia

2nd cognitive outcomes:

Occurrence of MCI

Occurrence of probable dementia or MCI

No. at risk

Standard treatment	4285	4282	4168	3886	2829	2107	989	87	0
Intensive treatment	4278	4277	4171	3917	2893	2189	1027	93	0

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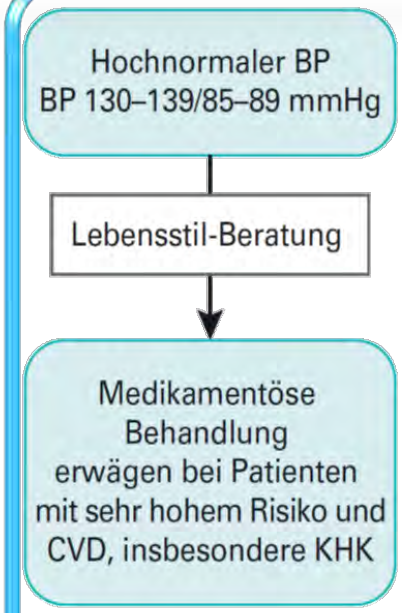
Definition arterielle Hypertonie ESH / ESC 2018



Definition arterielle Hypertonie ESH / ESC 2018

Tabelle 18: Praxisblutdruck-Zielbereiche für die Behandlung

Altersgruppe	Praxis-SBP-Behandlungszielbereiche (mmHg)			
	Hypertonie	+ Diabetes	+ KHK	+ Schlaganfall[a]/ TIA
18–65 Jahre	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120

JD Williamson *et al* JAMA 2016

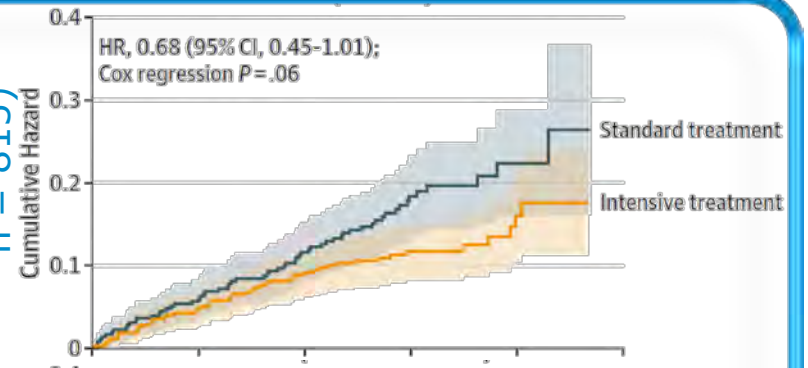
≥ 75 J (n = 2636)

AMI, ACS,

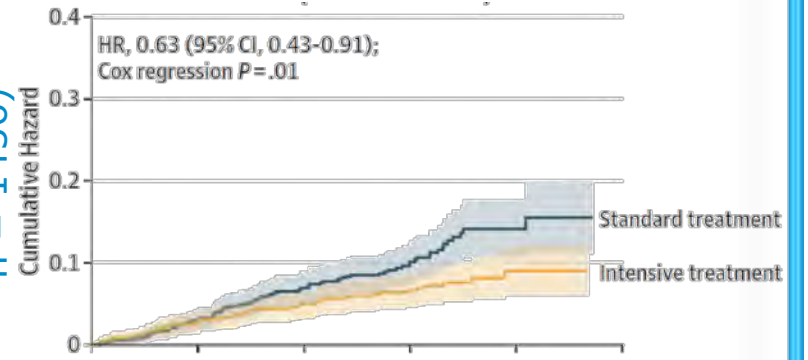
Stroke, HF, CV Tod

ø GFR 63 $\frac{ml}{\min * 1{,}73 m^2}$

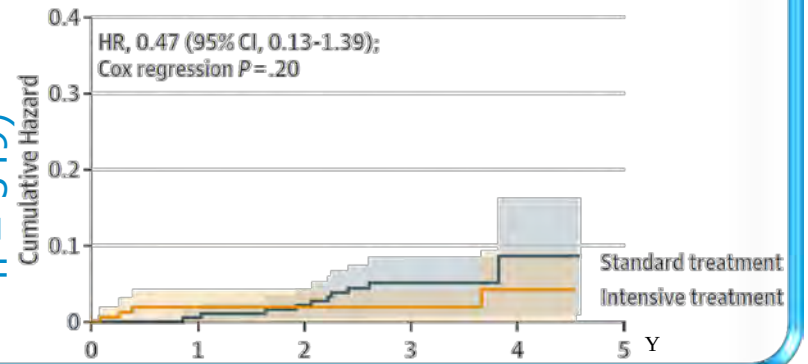
Frail (FI > 0.21; n = 815)



Less Fit (FI 0.11 – 0.21; n = 1456)



Fit (FI ≤ 0.10; n = 349)



Definition arterielle Hypertonie ESH / ESC 2018

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18–65 Jahre	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	70–79
65–79 Jahre[b]	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *Wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	70–79
≥ 80 Jahre[b]	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	70–79

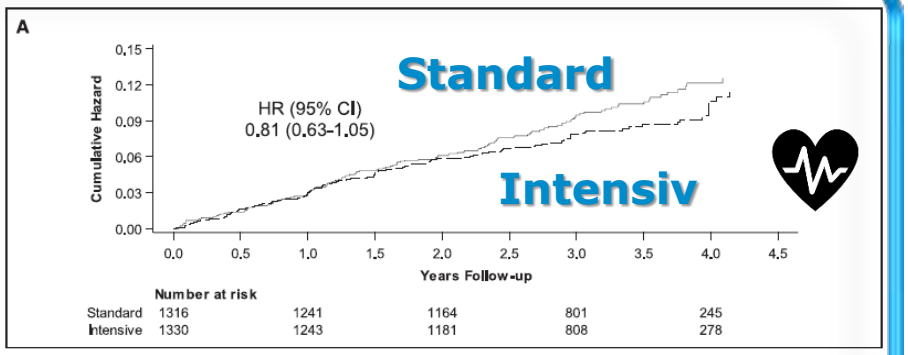
AK Cheung *et al* J Am Soc Nephrol 2017

CKD: 2464 (28 %)

AMI, ACS,

Stroke, HF, CV Tod

ESRD, GFR ↓ 50 %



Definition arterielle Hypertonie ESH / ESC 2018

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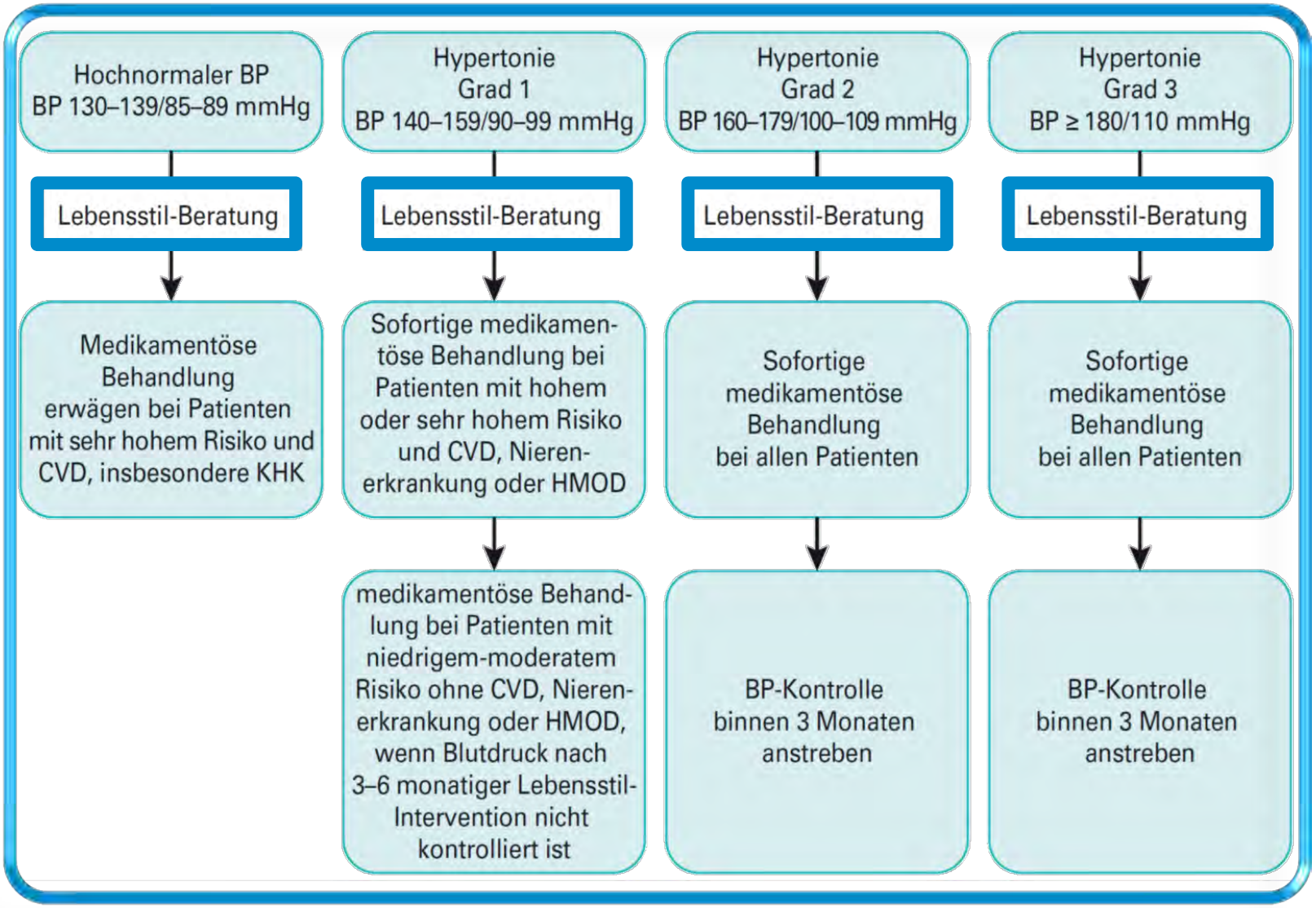
	Hypertonie	+ Diabetes	+ CKD	+ KHK	+ Schlaganfall[a]/ TIA	
18–65 Jahre	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf** [illegible] bis [illegible]enn vertrag[illegible]	**zielen auf ≤ 130** wenn vertragen Nicht < 120	**zielen auf ≤ 130** wenn vertragen Nicht < 120	70–79
65–79 Jahre[b]	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	**zielen auf 13**[illegible] *wenn* [illegible]*tragen*	**zielen auf 130–139** *Wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	70–79
≥ 80 Jahre[b]	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	**zielen auf 1**[illegible]**9** *wenn* [illegible]*tragen*	**zielen auf 130–139** *wenn vertragen*	**zielen auf 130–139** *wenn vertragen*	70–79

2020 Guidelines BD in CKD:

Ziel-BD (AOBP) < 120 mmHg!

Definition arterielle Hypertonie ESH / ESC 2018



ESC / ESH Blood Pressure Guidelines 2018

Moderate dynamische
Belastung ≥ 30 min
5 – 7 Tage / Woche

Kein Nikotin
ggf supportive care /
Entwöhnungsprogramm

BMI 20 – 25 kg/m²
M: Taillenumfang < 94 cm
F: Taillenumfang < 80 cm

M < 14 Gläser / Woche
F < 8 Gläser / Woche

Gemüse, frisches Obst,
Fisch, Nüsse, fettarme
Milchprodukte, ~~rotes~~
~~Fleisch~~, ungesättigte FS

< 5 g Kochsalz

Voskoboinik A *et al.* New Engl J Med 2020

140

≥ 10 Getränke

SR + AF

(paroxysmal / persistent)

Recurrent AF / AF Burden

Alkoholkonsum (Gläser / Wo)

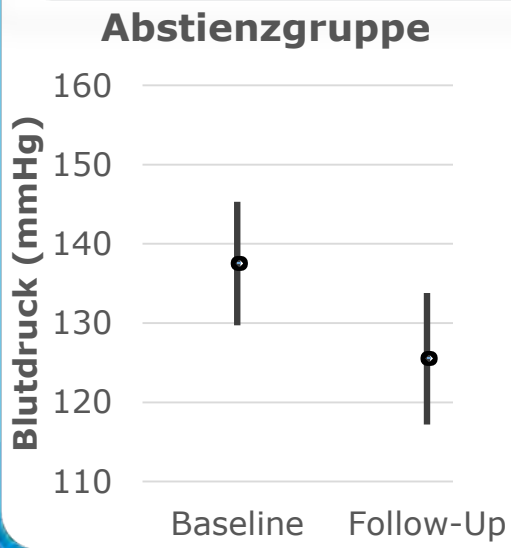
Abstinenzgruppe

prä: 16,8 ± 7,7 post: 2,1 ± 3,7

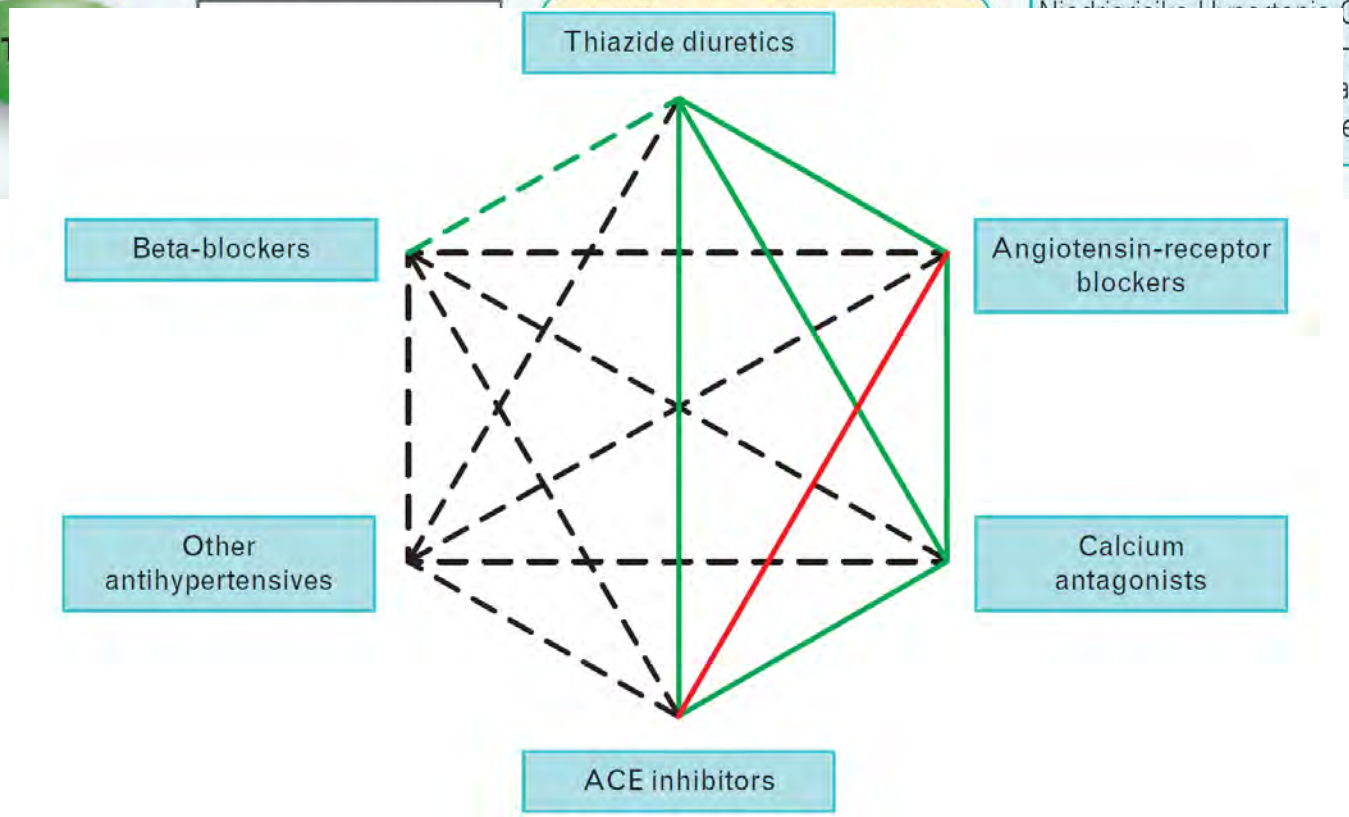
Komplette Abstinenz: 61 %

Kontrollgruppe

prä: 16,4 ± 6,9 post: 13,2 ± 6,5



ESC / ESH Blood Pressure Guidelines 2018



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ACCORD New Engl J Med 2008

Plasma Glukose (nüchtern)	**≥ 126 mg/dL** (7.0 mmol/L)	Keine Kalorienzufuhr für 8 Std

Standards of Diabetes Care 2020

Typ 1 Diabetes Mellitus

Absoluter Insulinmangel

Therapie: Insulin

Typ 2 Diabetes Mellitus

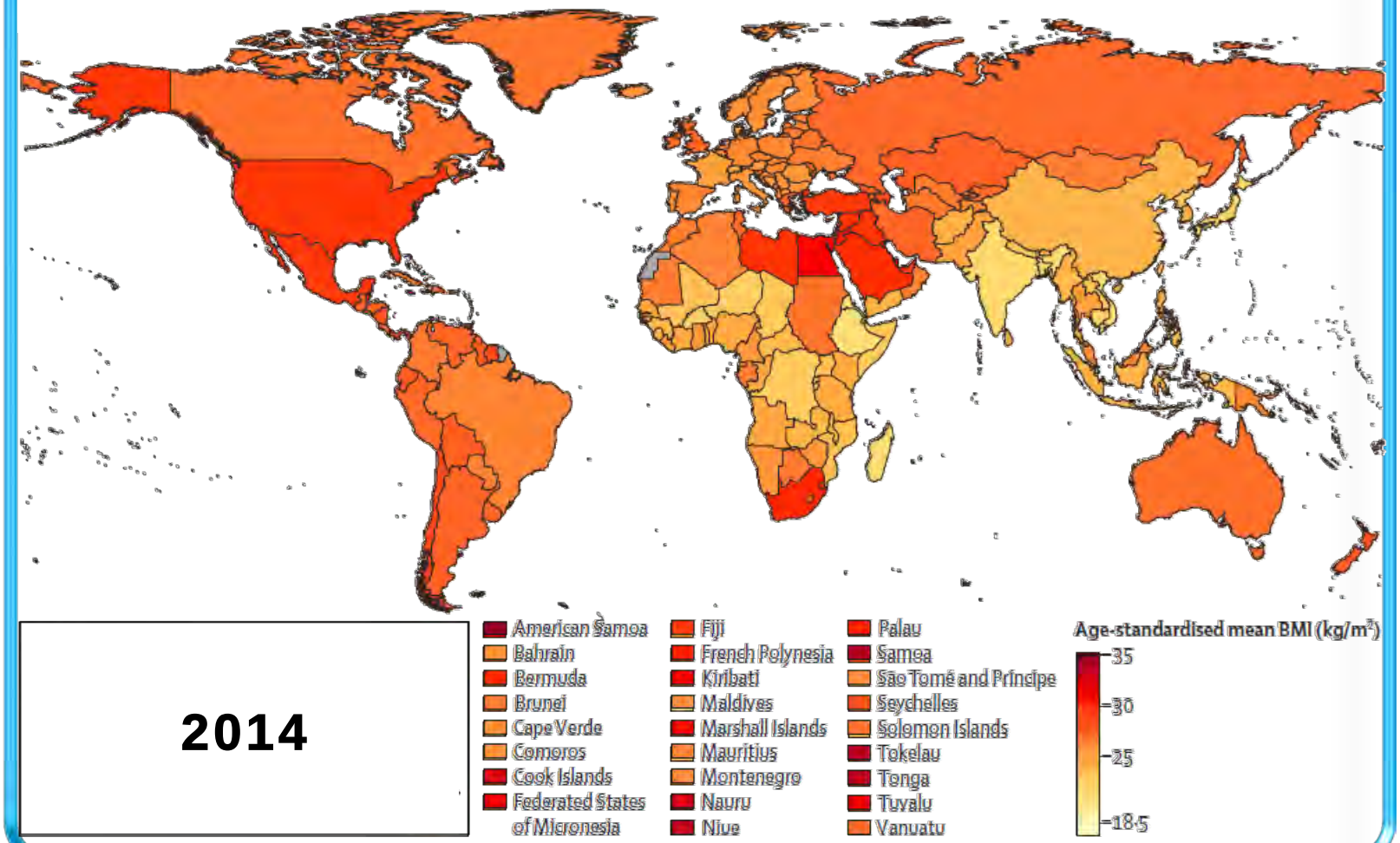
Insulinresistenz, relativer Insulinmangel

Risikofaktoren

https://www.diabetes.org/risk-test

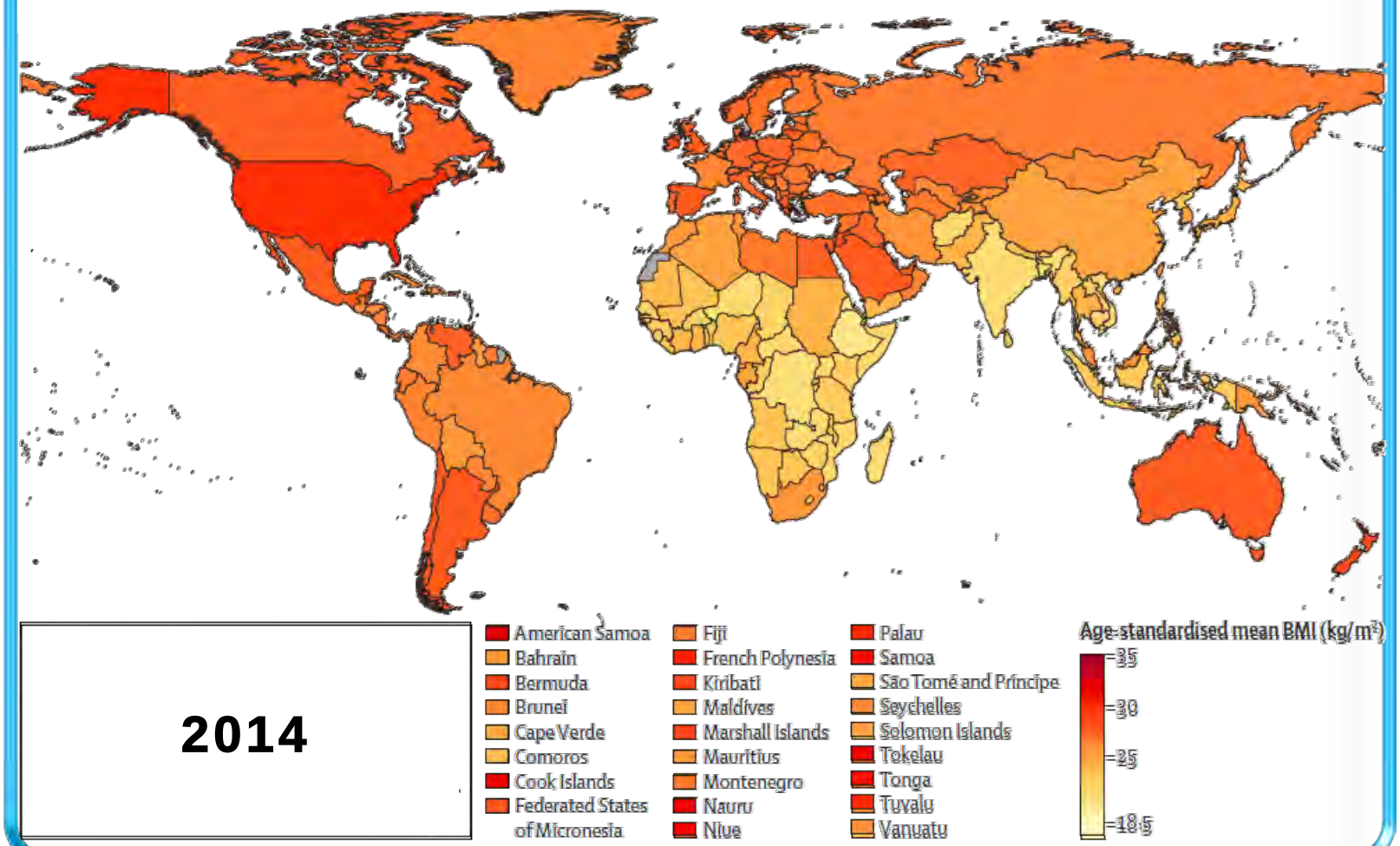
NCD Risk Factor Collaboration Lancet 2016

Frauen

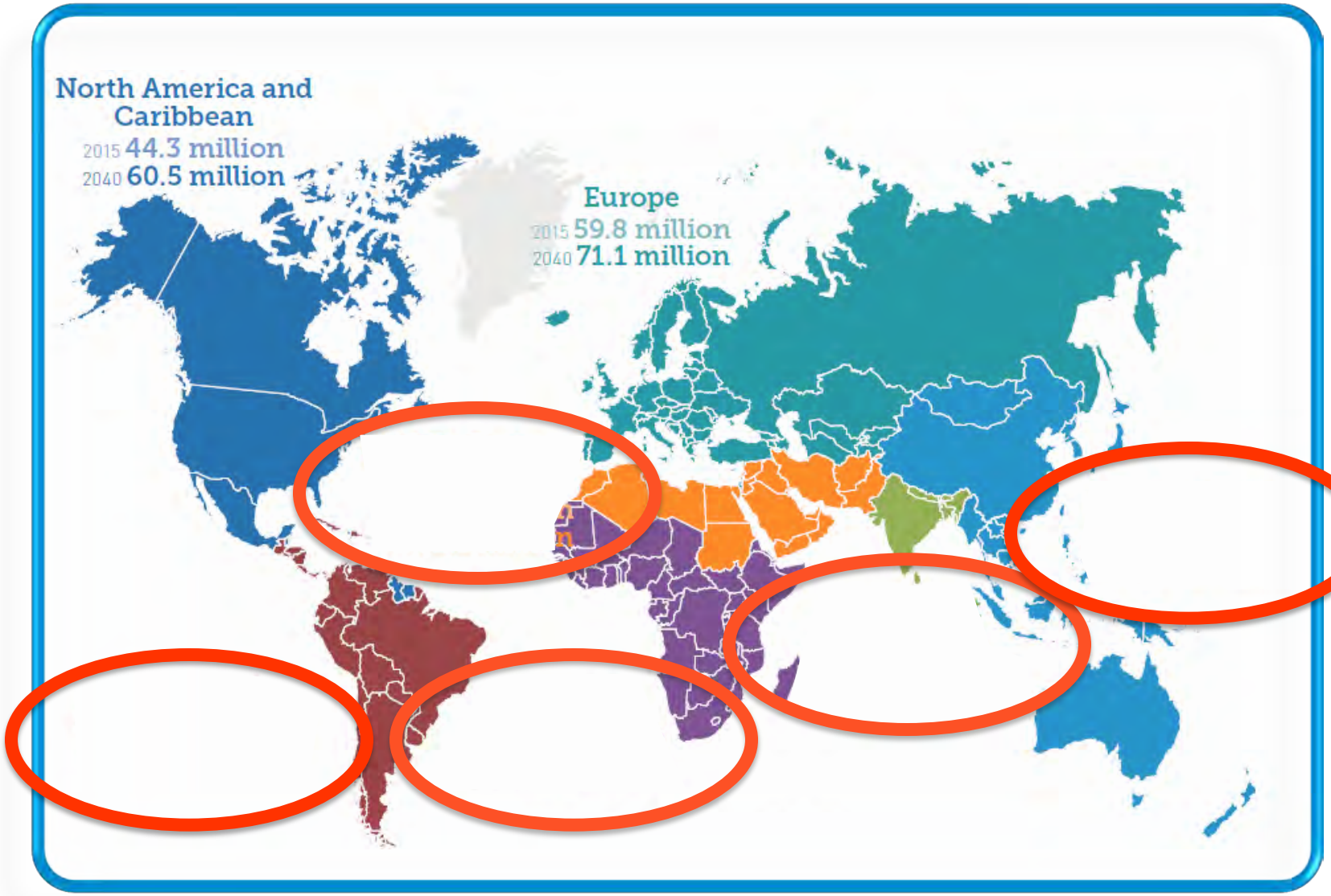


NCD Risk Factor Collaboration Lancet 2016

Männer



Prevalence of DM (20 – 79 y) IDF Diabetes Atlas 2015



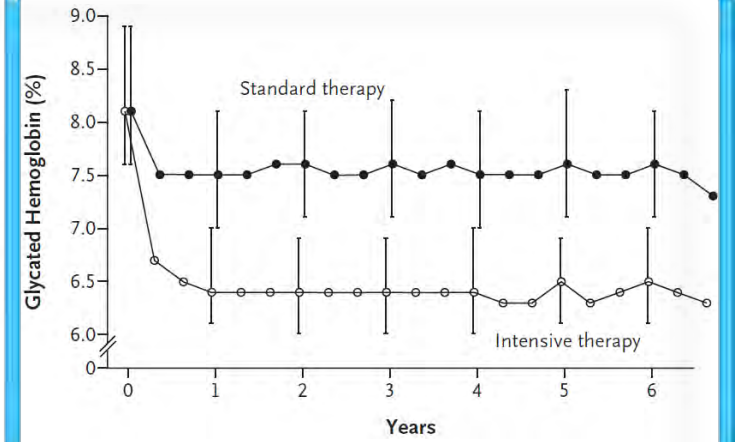
ACCORD New Engl J Med 2008

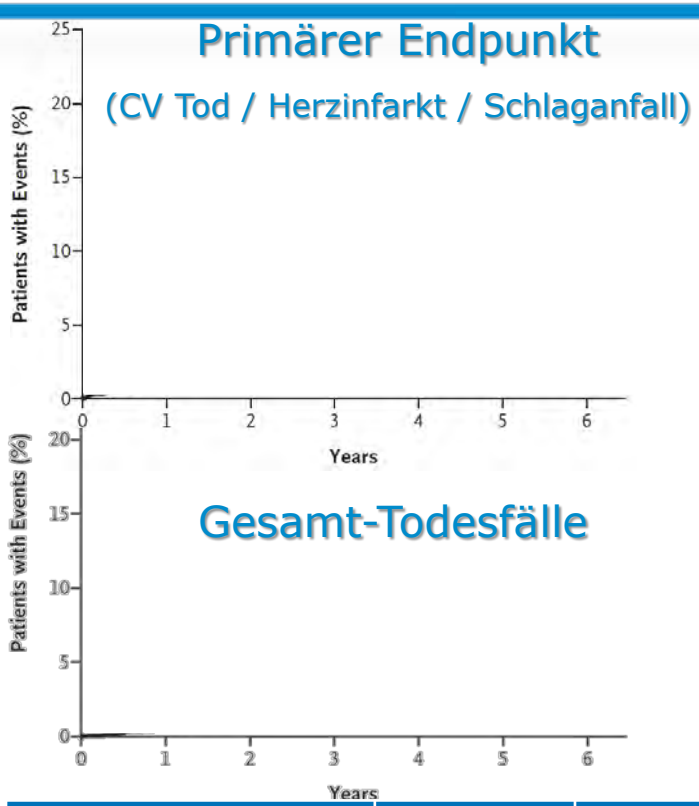
10251 Typ 2 DM

ø 3,5 Jahre

Kreatinin ≤ 1,5 mg/dl

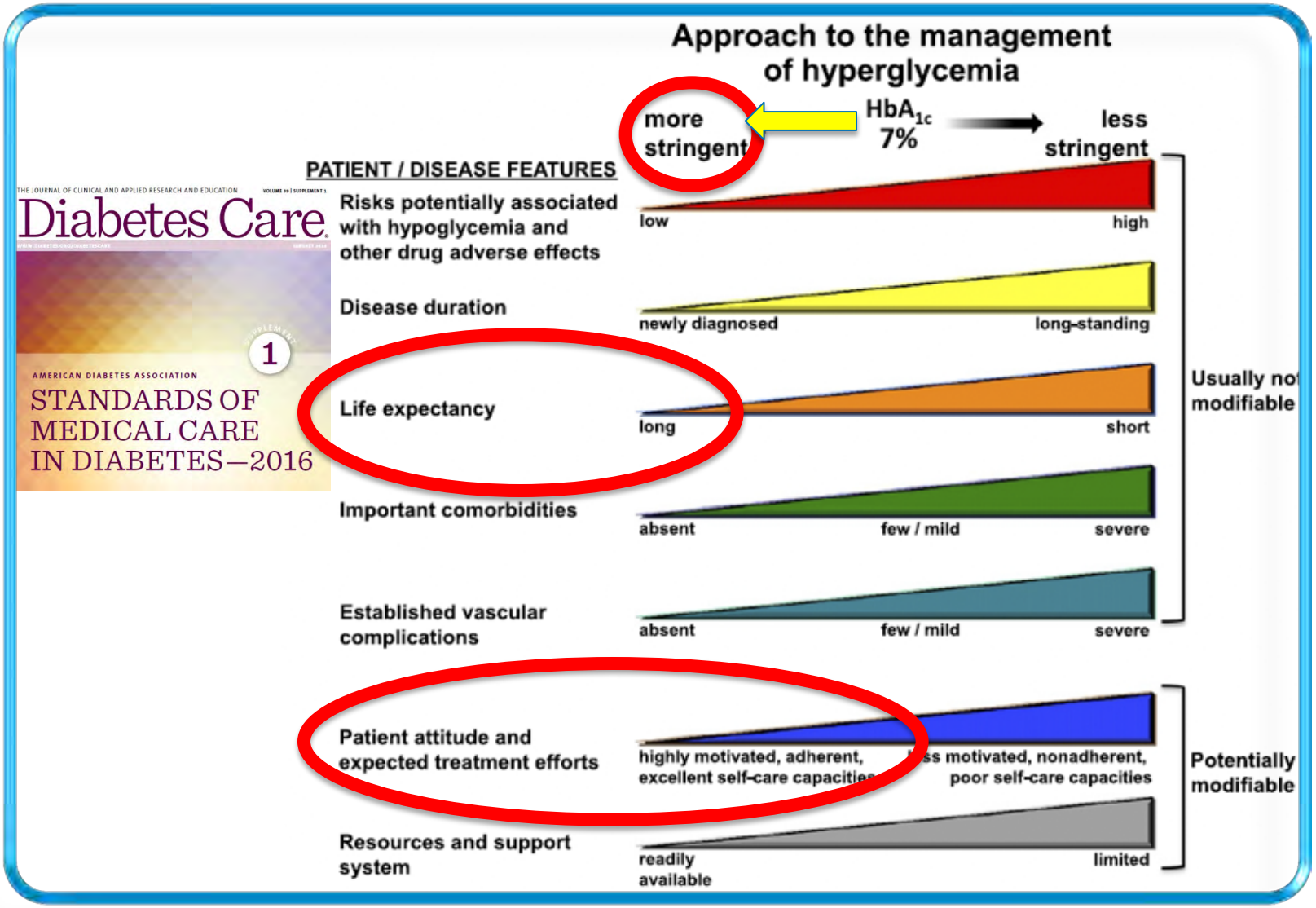
Hba1c < 6.0 % vs 7,0 – 7,9 %



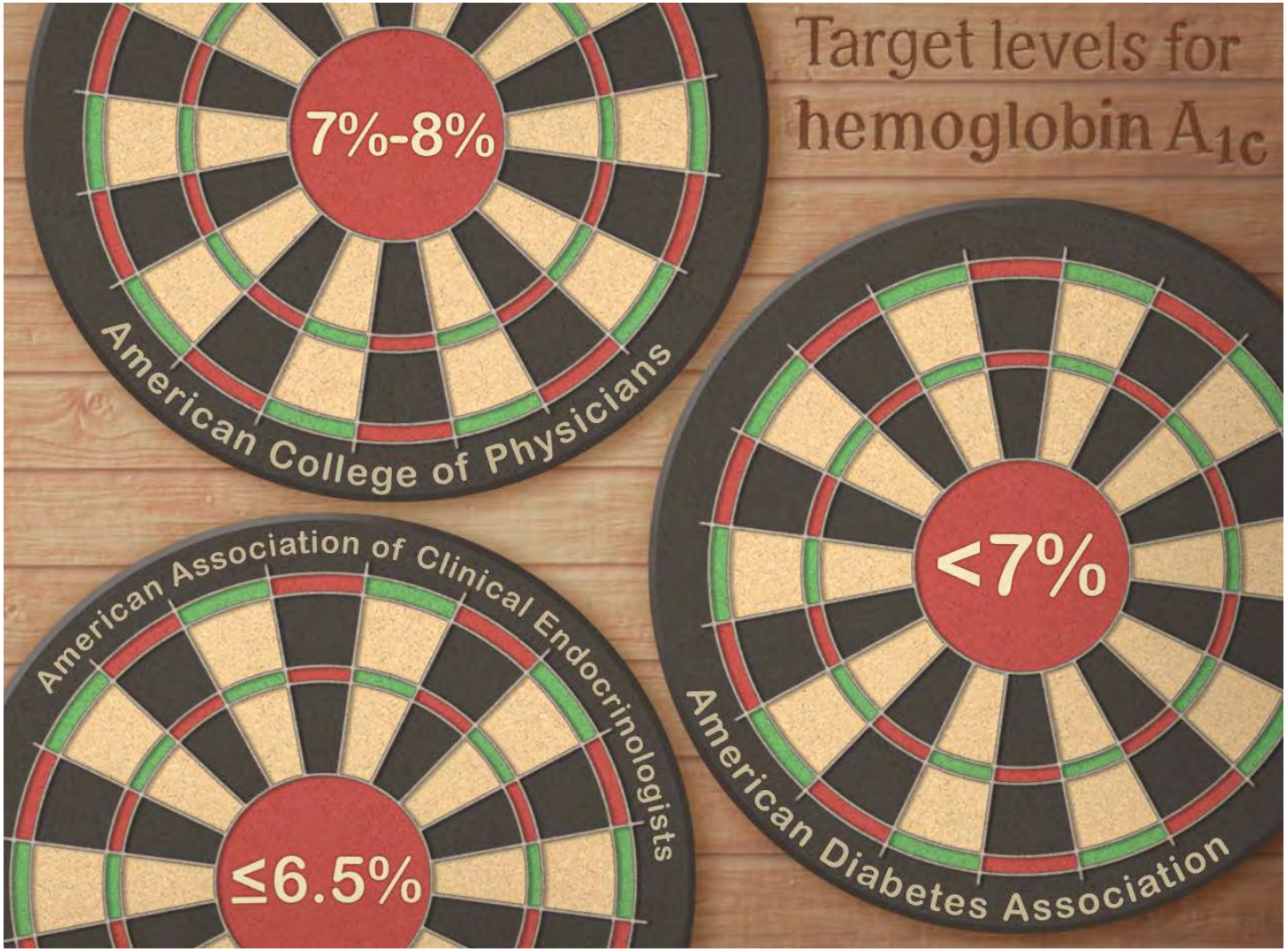


	Intensiv	Standard
Blutzucker ↓ + Med. Hilfe	10,5 %	3,5 %
Blutzucker ↓ + Hilfe	16,2 %	5,1 %
Herzversagen	3,0 %	2,4 %
KG Anstieg > 10 kg	27,6 %	14,1 %

Diabetes Mellitus – Hba1c targets Diabetes Care 2016



Diabetes Mellitus – Hba1c targets J Abbasi JAMA 2018



Standards of Diabetes Care 2020

	Potenz	BZ -	KG
Metformin	++	Nein	0 / -
SGLT-2 I (-gliflozin)	+	Nein	-
GLP-1 GA (-glutid)	++	Nein	-
DPP-4 I (-gliptin)	+	Nein	0
Sulfanyl-Hst	++	Ja	+
Insulin	+++	Ja	+

Phase 3 Studien SGLT-2 Inhibitoren

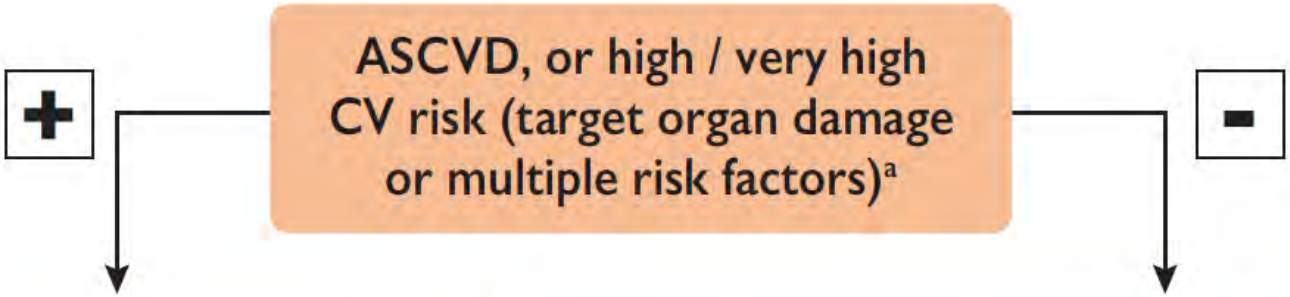
EMPA	EMPA-REG OUTCOME
DAPA	DECLARE-TIMI 58
CANA	CANVAS / CANVAS-R

Standards of Diabetes Care 2020

	Potenz	BZ -	KG
Metformin	++	Nein	0 / -
SGLT-2 I (-gliflozin)	+	Nein	-
GLP-1 GA (-glutid)	++	Nein	-
DPP-4 I (-gliptin)	+	Nein	0
Sulfanyl-Hst	++	Ja	+
Insulin	+++	Ja	+

ESC Guidelines 2019

A Type 2 DM - Drug naïve patients



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Prävalenz CKD KDIGO 2012 / NHANES 1999 - 2006

Percentage of US Population by eGFR and Albuminuria Category: KDIGO 2012 and NHANES 1999-2006

GFR categories (ml/min/ 1.73m^2) Description and range			Persistent albuminuria categories Description and range		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30mg/mmol
G1	Normal or high	≥90	NKD		
G2	Mildly decreased	60-89			
G3a	Mildly to moderately decreased	45-59	CKD		
G3b	Moderately to severely decreased	30-44			
G4	Severely decreased	15-29			
G5	Kidney failure	<15			

Prävalenz CKD KDIGO 2012 / NHANES 1999 - 2006

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nhanes

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			<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30mg/mmol
G1	Normal or high	≥90	NKD 88.5 %		
G2	Mildly decreased	60-89			
G3a	Mildly to moderately decreased	45-59	CKD 10.5 %		
G3b	Moderately to severely decreased	30-44			
G4	Severely decreased	15-29			
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nhanes

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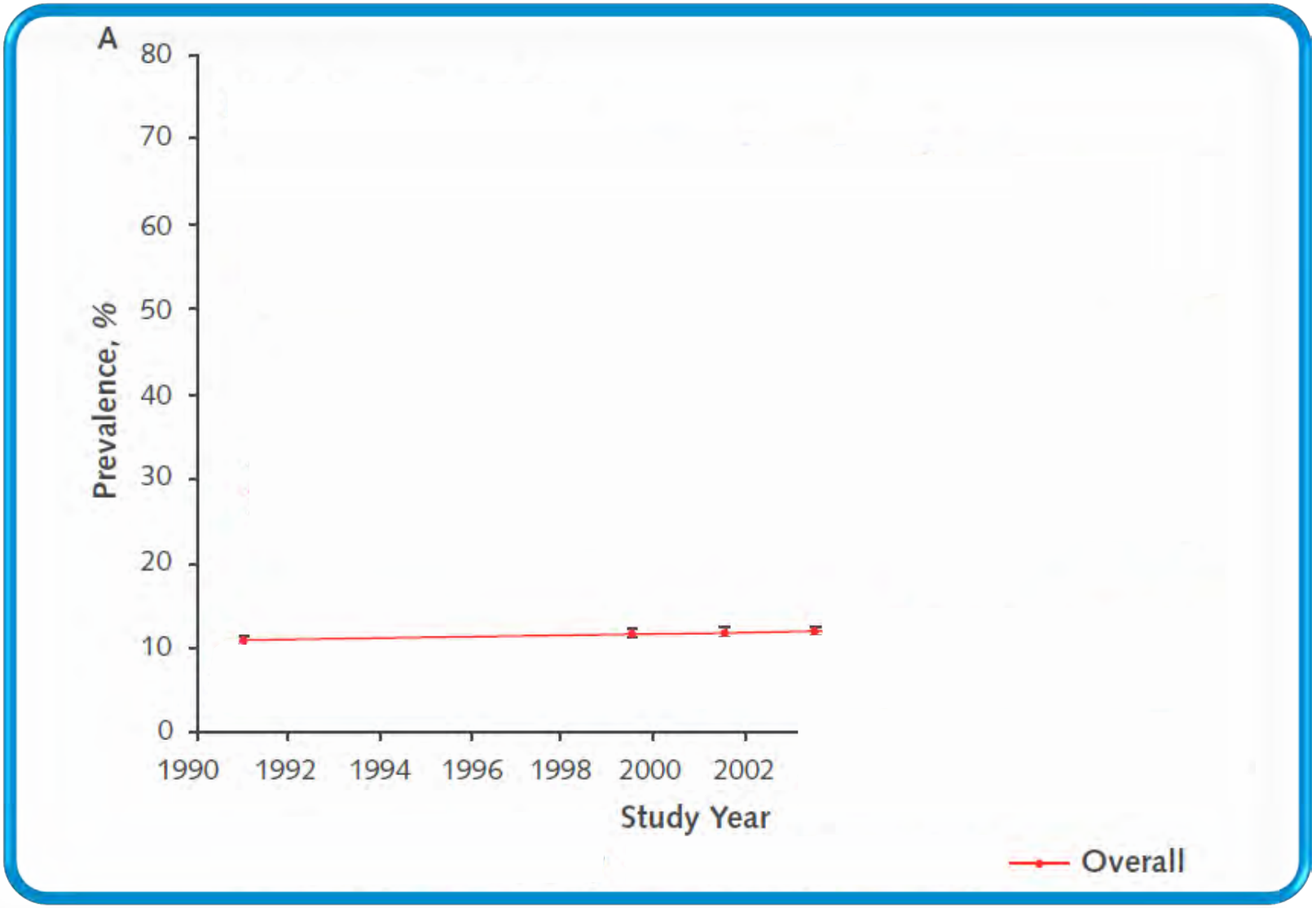
CKD NHANES 1988 – 2012 D Murphy Ann Intern Med 2016

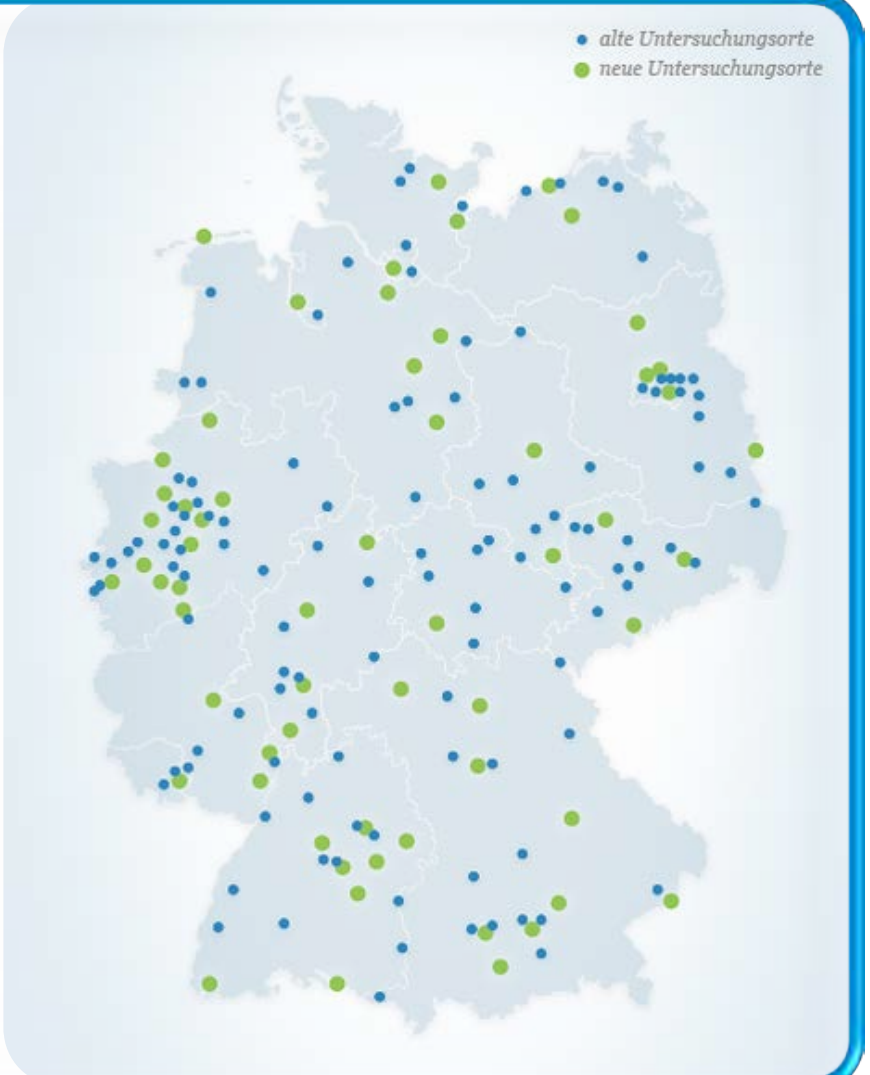


THIS IS NOT AMERICA!

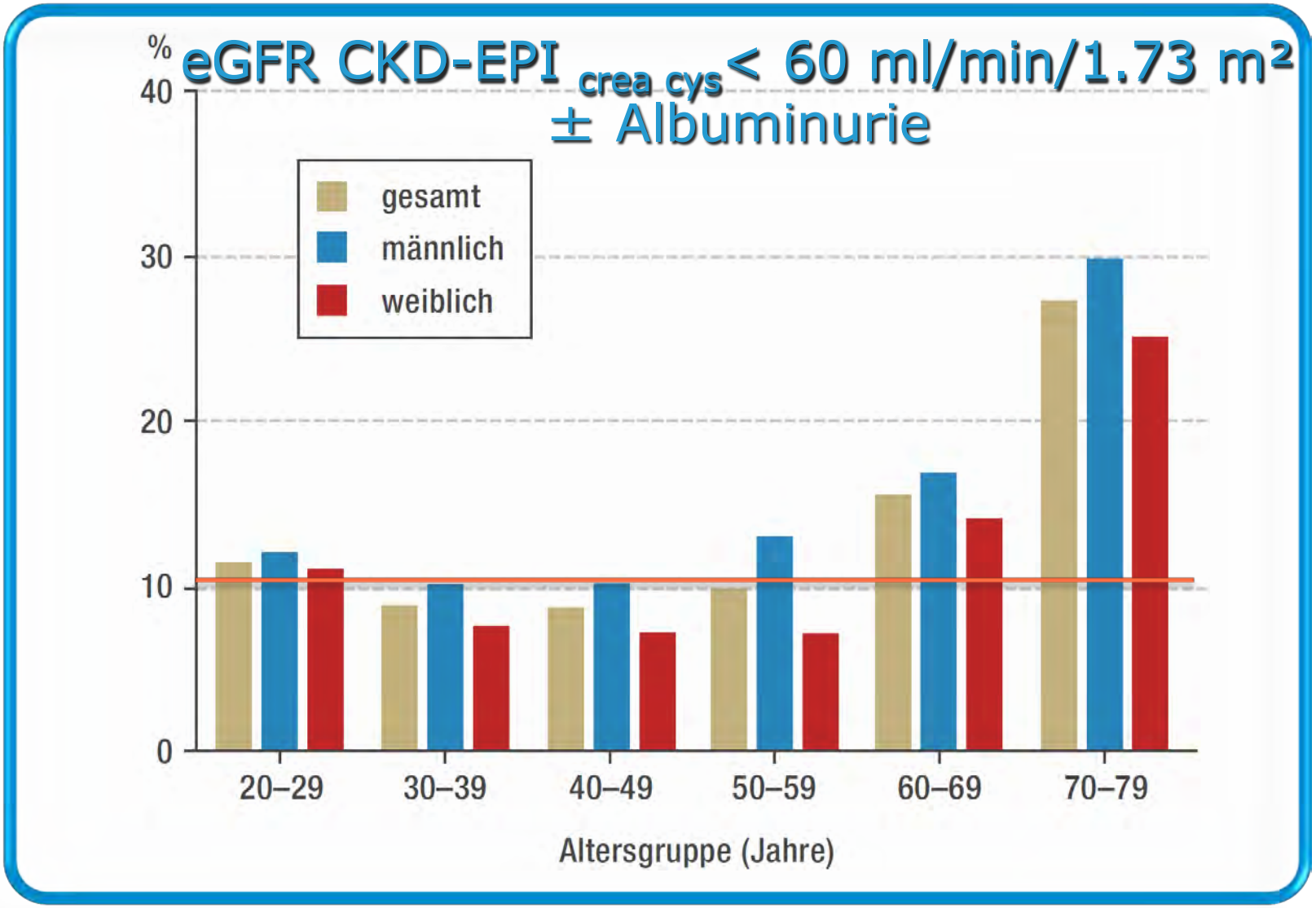
M Girndt *et al.* Dtsch Arztebl Int 2016

DEGS
Studie zur Gesundheit Erwachsener in Deutschland

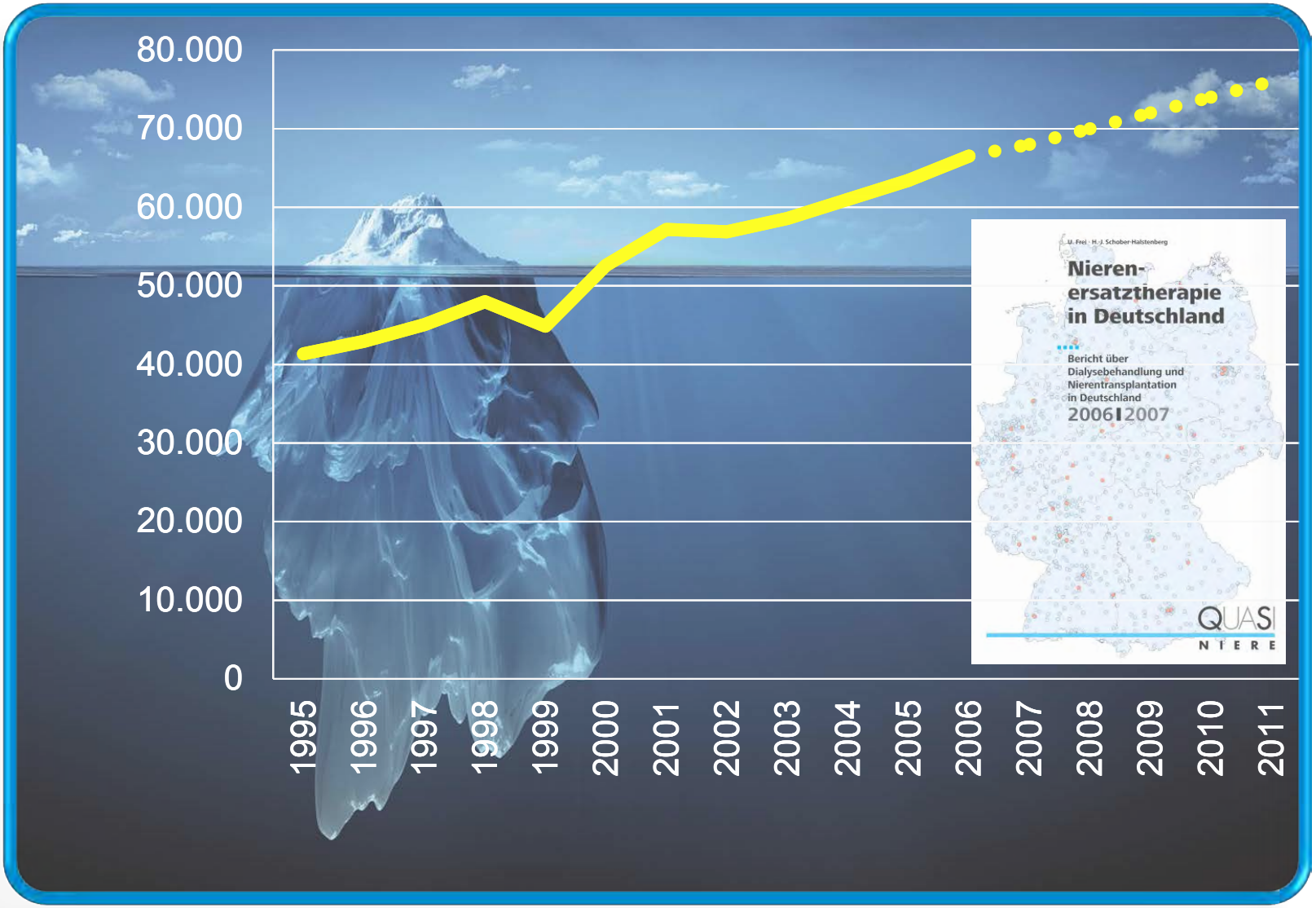
- 7 115 Probanden
- 180 Rekrutierungszentren
- eGFR: CKD-EPI$_{\text{crea cys}}$
- Micral-Stix



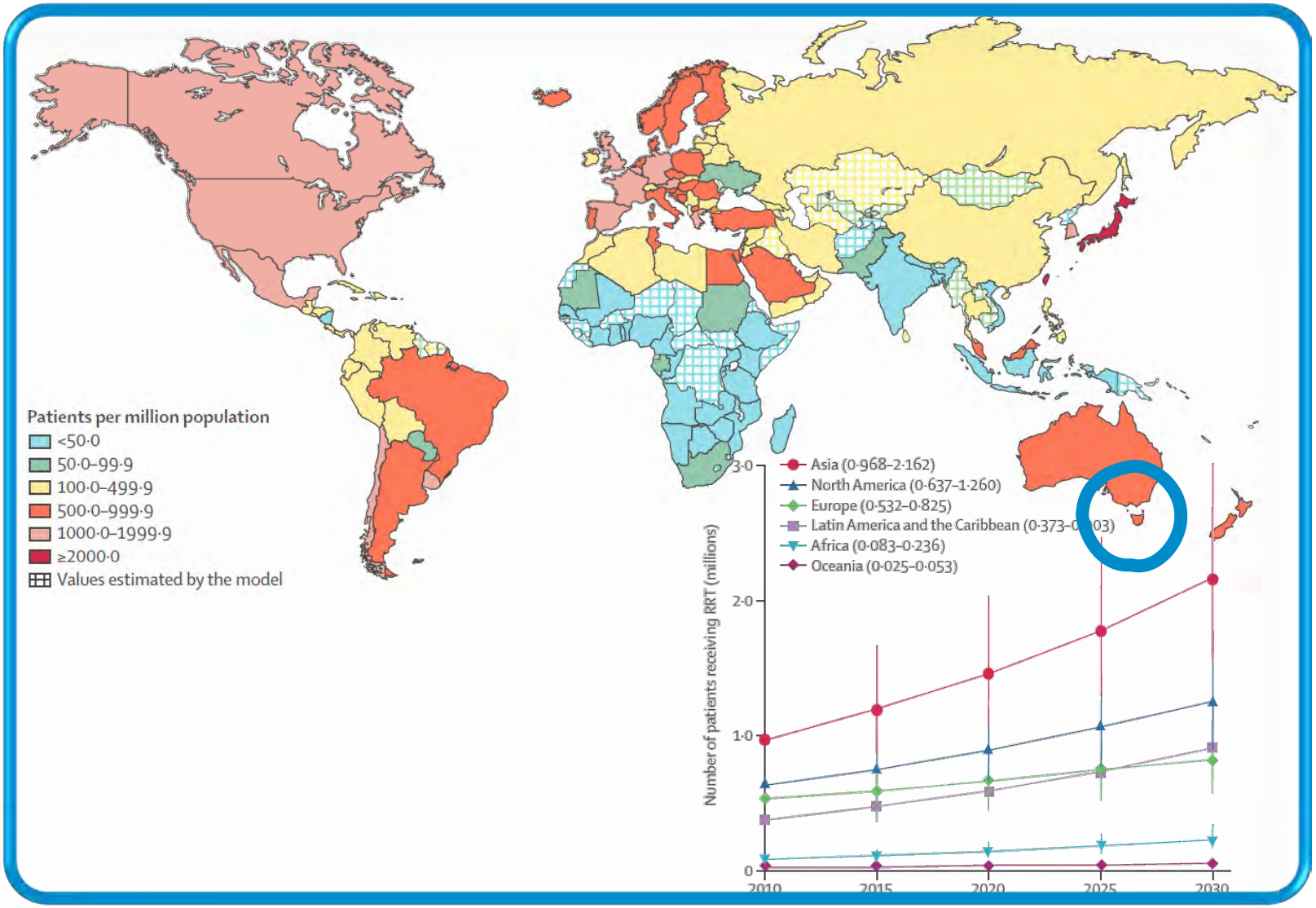
M Girndt *et al.* Dtsch Arztebl Int 2016



Prävalenz der dialysepflichtigen CKD in Deutschland

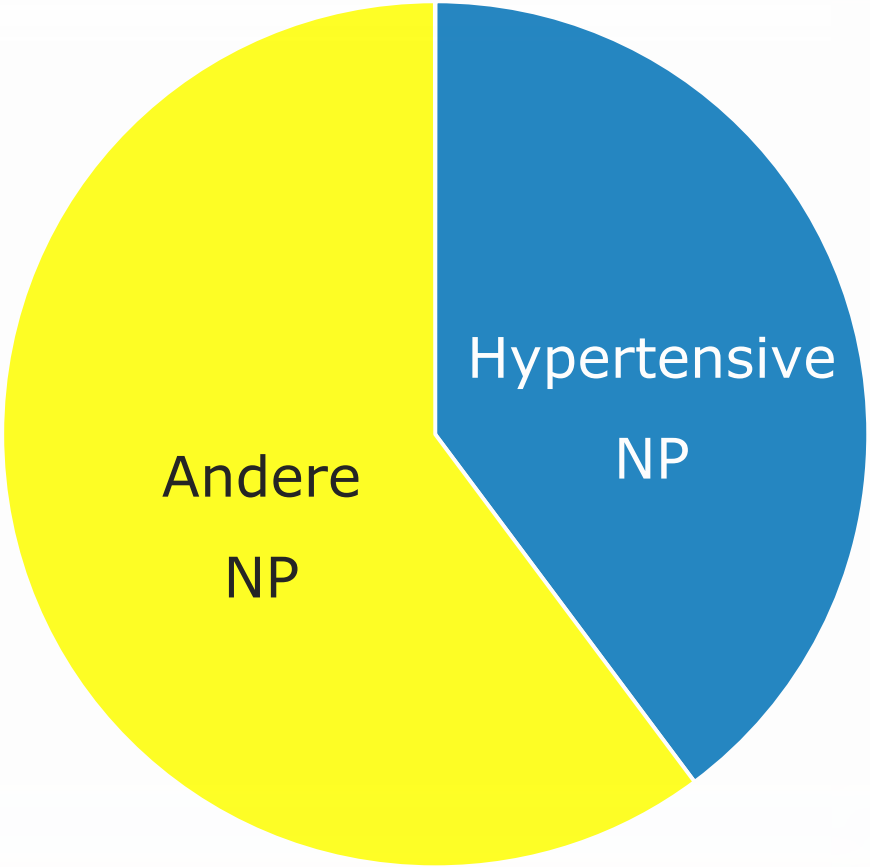


T Liyanage et al Lancet 2015

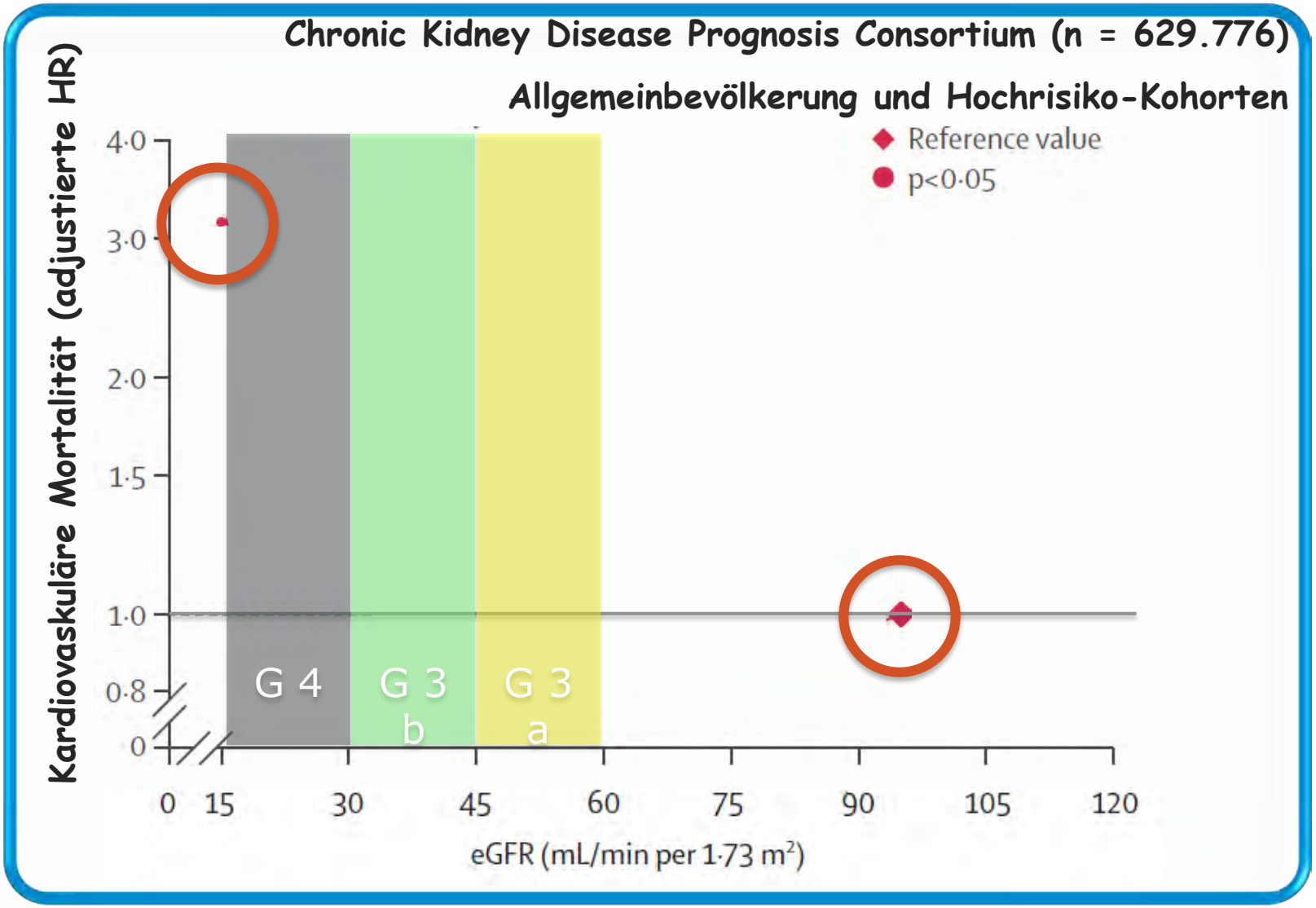


CARE FOR HOMe

CKD - Ursache



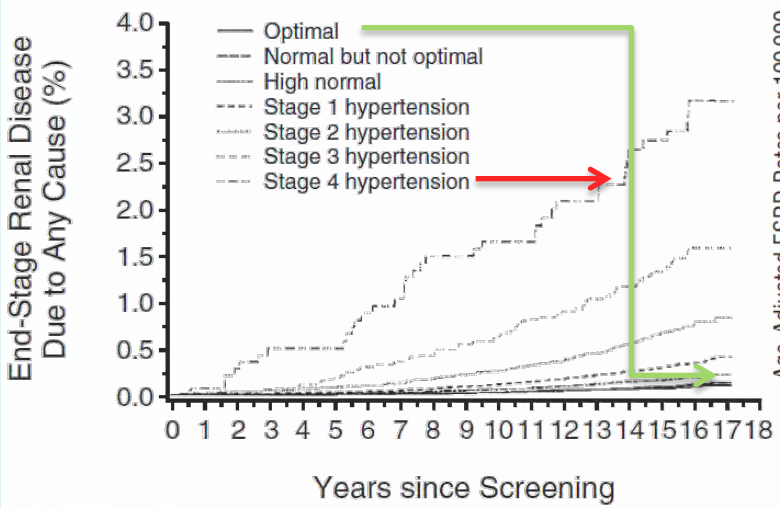
K Matsushita *et al.* Lancet Diabetes Endocrinol 2015



Klag *et al* N Engl J Med 1996 Hsu *et al* Arch Intern Med 2005

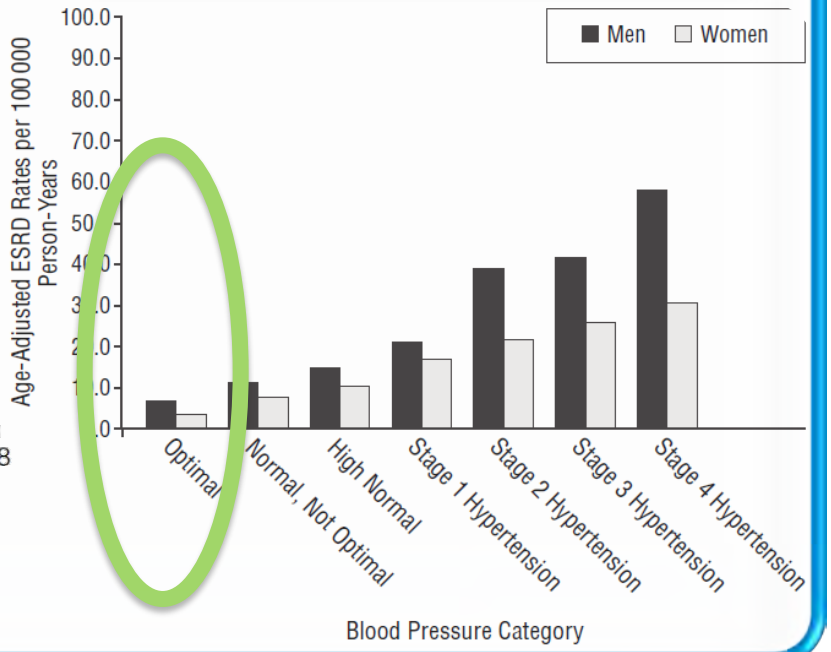
MrFIT

332,544 Männer
(35 - 57 Jahre)
Screening 1973 - 1975

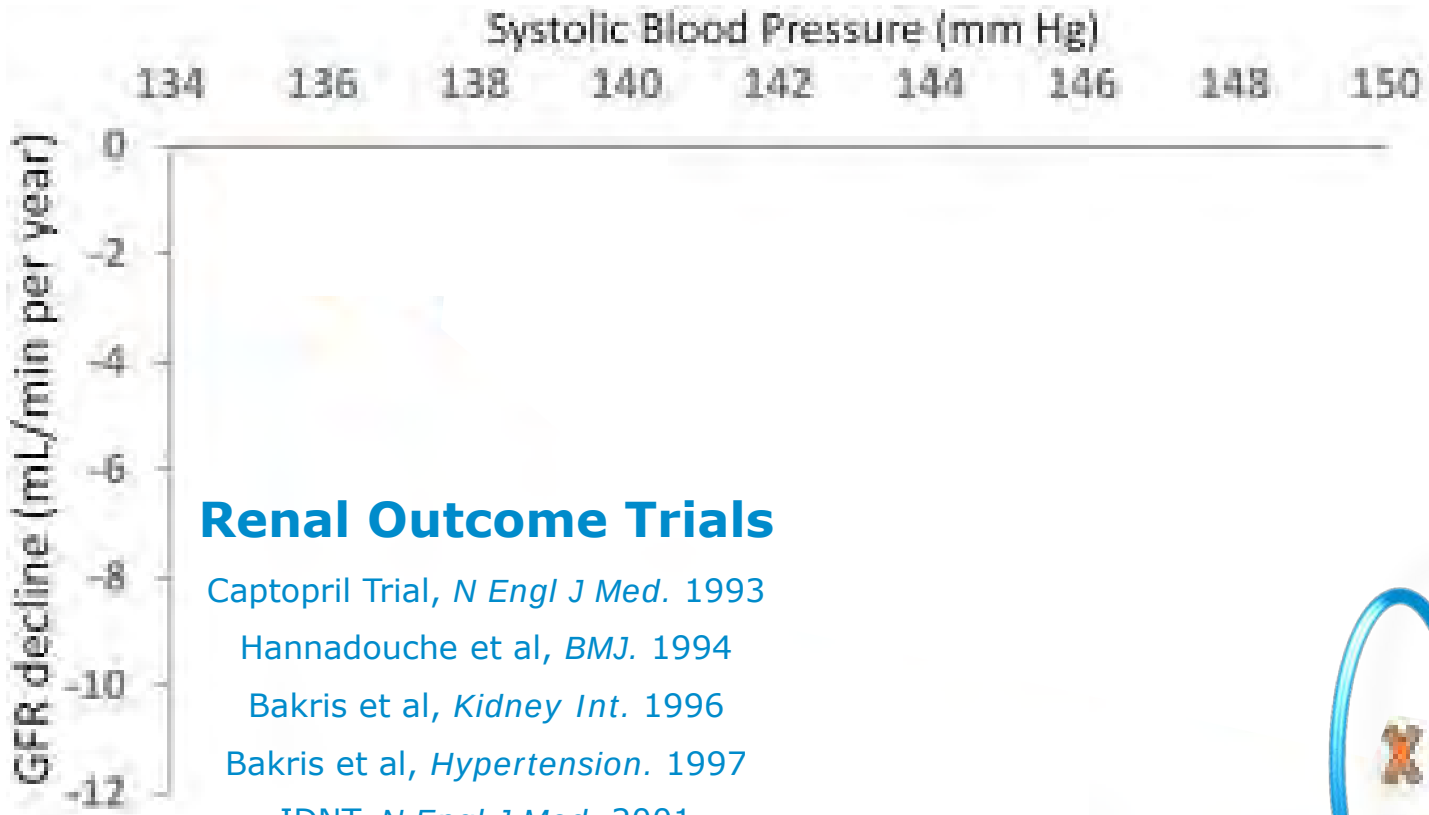


Kaiser Permanente of Northern California

316 675 Männer / Frauen
eGFR > 60 ml/min/1.73 m²
∅ Proteinurie / Hämaturie



G Bakris Am J Kidney Dis 2019



Renal Outcome Trials

Captopril Trial, *N Engl J Med.* 1993

Hannadouche et al, *BMJ.* 1994

Bakris et al, *Kidney Int.* 1996

Bakris et al, *Hypertension.* 1997

IDNT, *N Engl J Med.* 2001

RENAAL, *N Engl J Med.* 2001

Phase 3 Studien SGLT-2 Inhibitoren

EMPA	EMPA-REG OUTCOME	Nierenersatztherapie: 11 - 27 Pat
DAPA	DECLARE-TIMI 58	Nierenersatztherapie: ? Pat
CANA	CANVAS / CANVAS-R	Nierenersatztherapie: 18 Pat

AGAPLESION FRANKFURTER DIAKONIE KLINIKEN

Ausschluss:
Immunsuppression
MRA

...ovic V *et al.* CREDENCE New Engl J Med 2019

DM Typ 2 + CKD G 2 –3b A 3
(eGFR 30 – 89 ml/min/1,73 m² ACR 301 – 5000 mg/g)
unter RAS Inhibitoren

Canagliflozin 100 mg
(n =2202)

Geplant:
844 Ereignisse
Interim Analyse:
495 Ereignisse
Medianes FU
2,6 Jahre

Placebo
(n=2199)

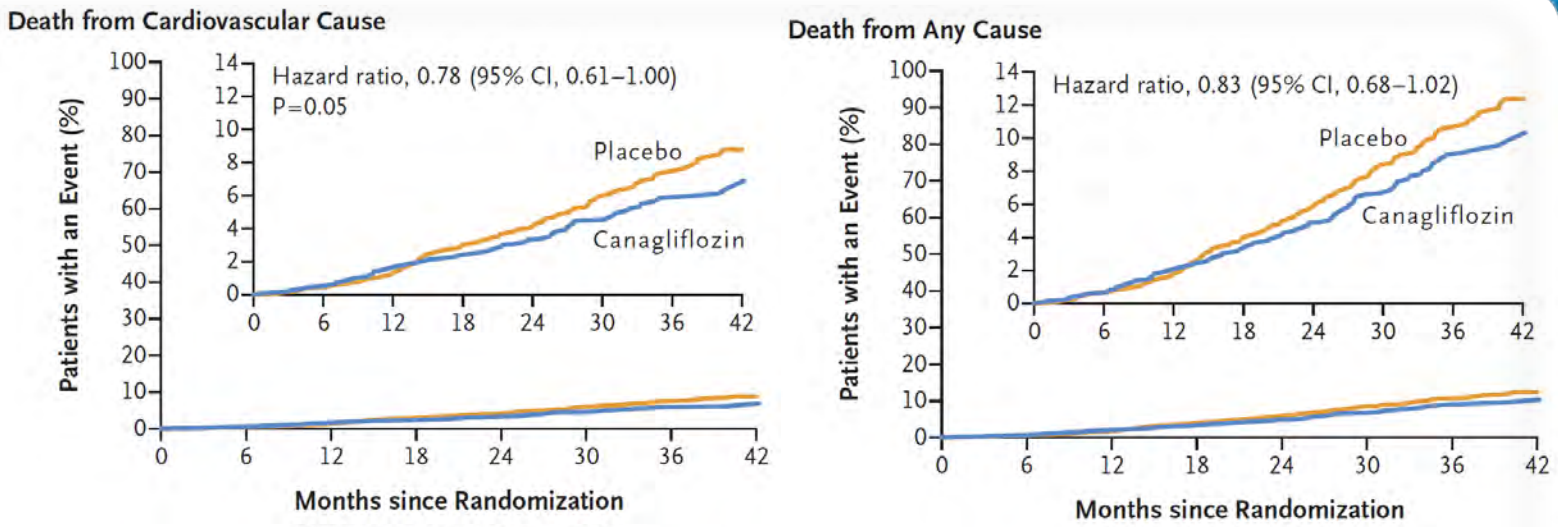
Primärer Endpunkt:

ESRD (Dialyse / Transplantation / pers. eGFR < 15 $\frac{ml}{min * 1{,}73\ m^2}$)

ODER Verdopplung S-Kreatinin

ODER renale / kardiovaskuläre Mortalität

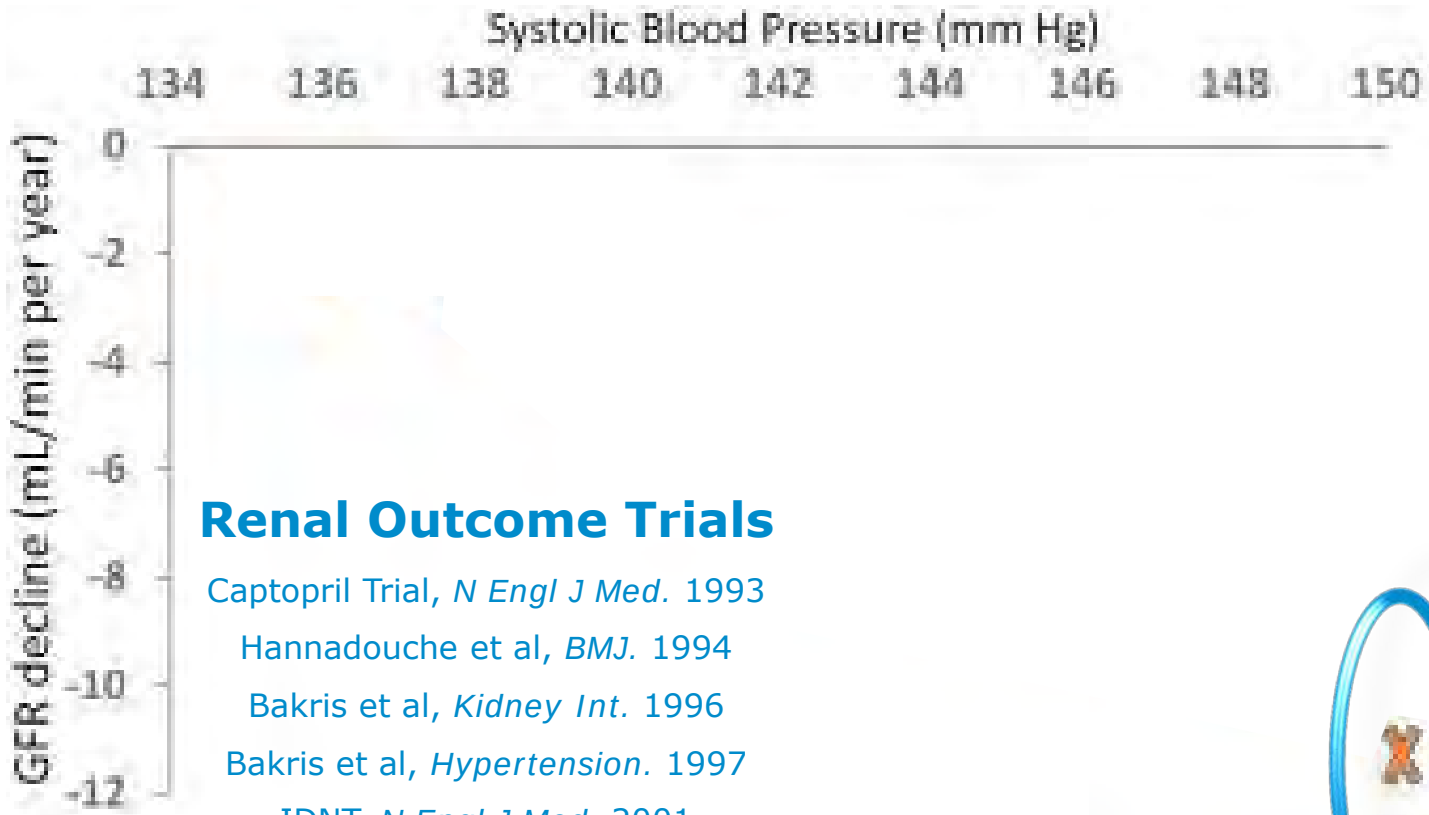
Perkovic V *et al.* CREDENCE New Engl J Med 2019



Sekundäre Endpunkte:

1: CV Tod oder HF (KH Aufnahme)	$p < 0.001$
2: CV Tod, MI oder Schlaganfall	$p = 0.01$
3. HF (KH Aufnahme)	$p < 0.001$
4. ESRD, Verdopplung S-Kreatinin oder renale Mortalität	$p < 0.001$
5. CV Mortalität	
6. Gesamtmortalität	
7. CV Mortalität, MI, Schlaganfall, oder HF / instablie Angina (KH Aufnahme)	

G Bakris Am J Kidney Dis 2019



Renal Outcome Trials

Captopril Trial, *N Engl J Med.* 1993

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Bakris et al, *Kidney Int.* 1996

Bakris et al, *Hypertension.* 1997

IDNT, *N Engl J Med.* 2001

RENAAL, *N Engl J Med.* 2001

Phase 3 Studien SGLT-2 Inhibitoren

EMPA	EMPA-REG OUTCOME	EMPEROR-Preserved EMPEROR-Reduced	EMPA-Kidney
DAPA	DECLARE-TIMI 58	DAPA-HF	DAPA-CKD
CANA	CANVAS / CANVAS-R		CREDENCE

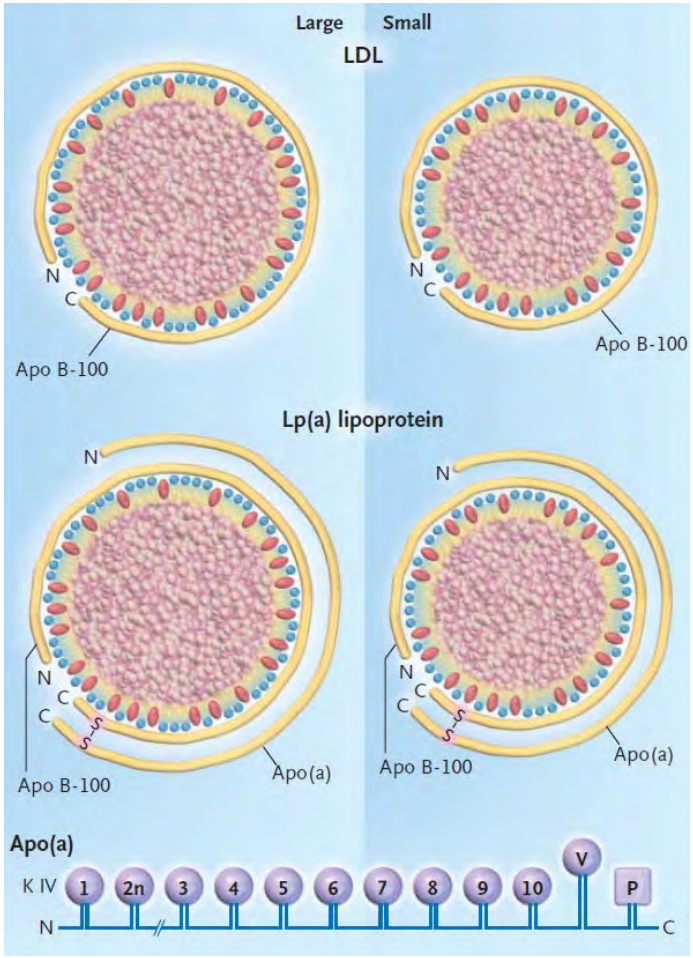
EMPA-KIDNEY

EMPA-KIDNEY

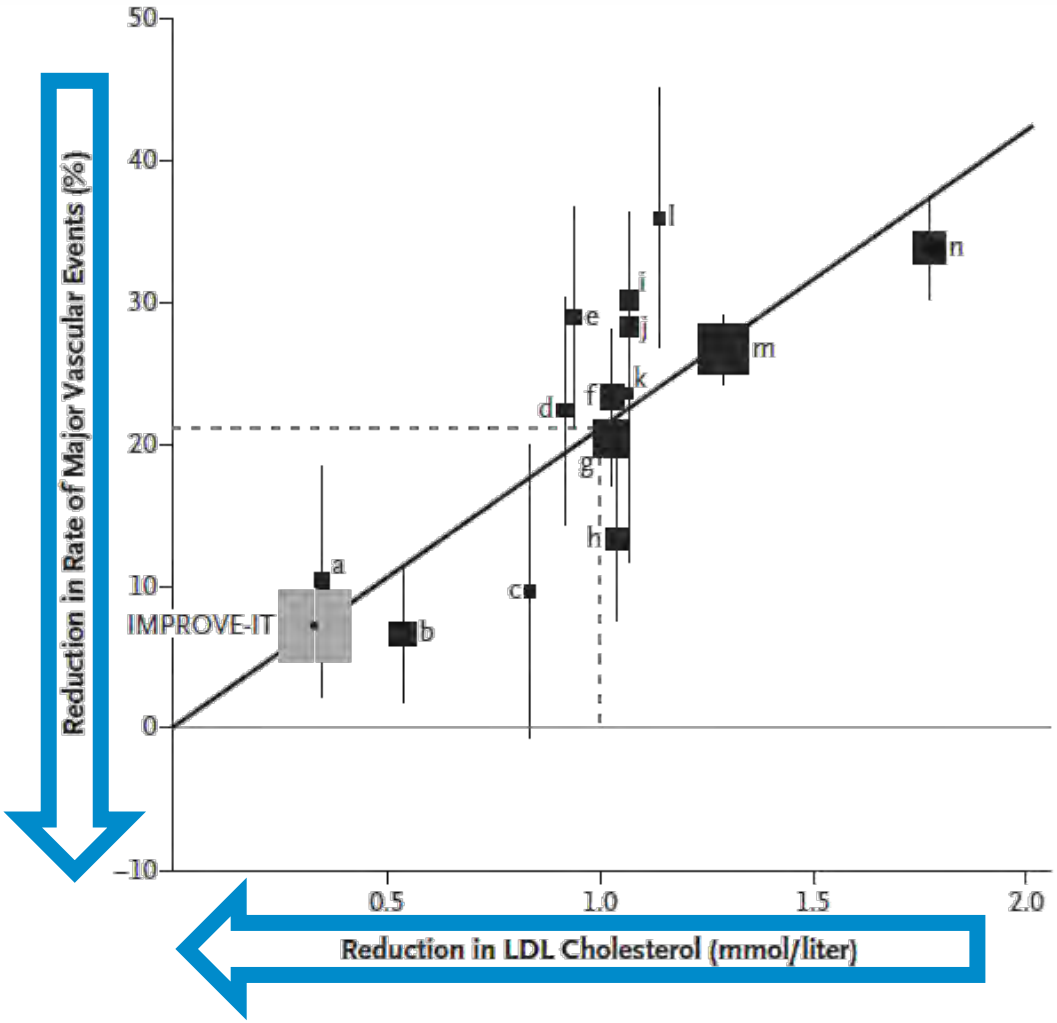
The study of heart and kidney protection with empagliflozin

NO
TIME
TO
DIE
007
NO
TIME
TO
DIE
007

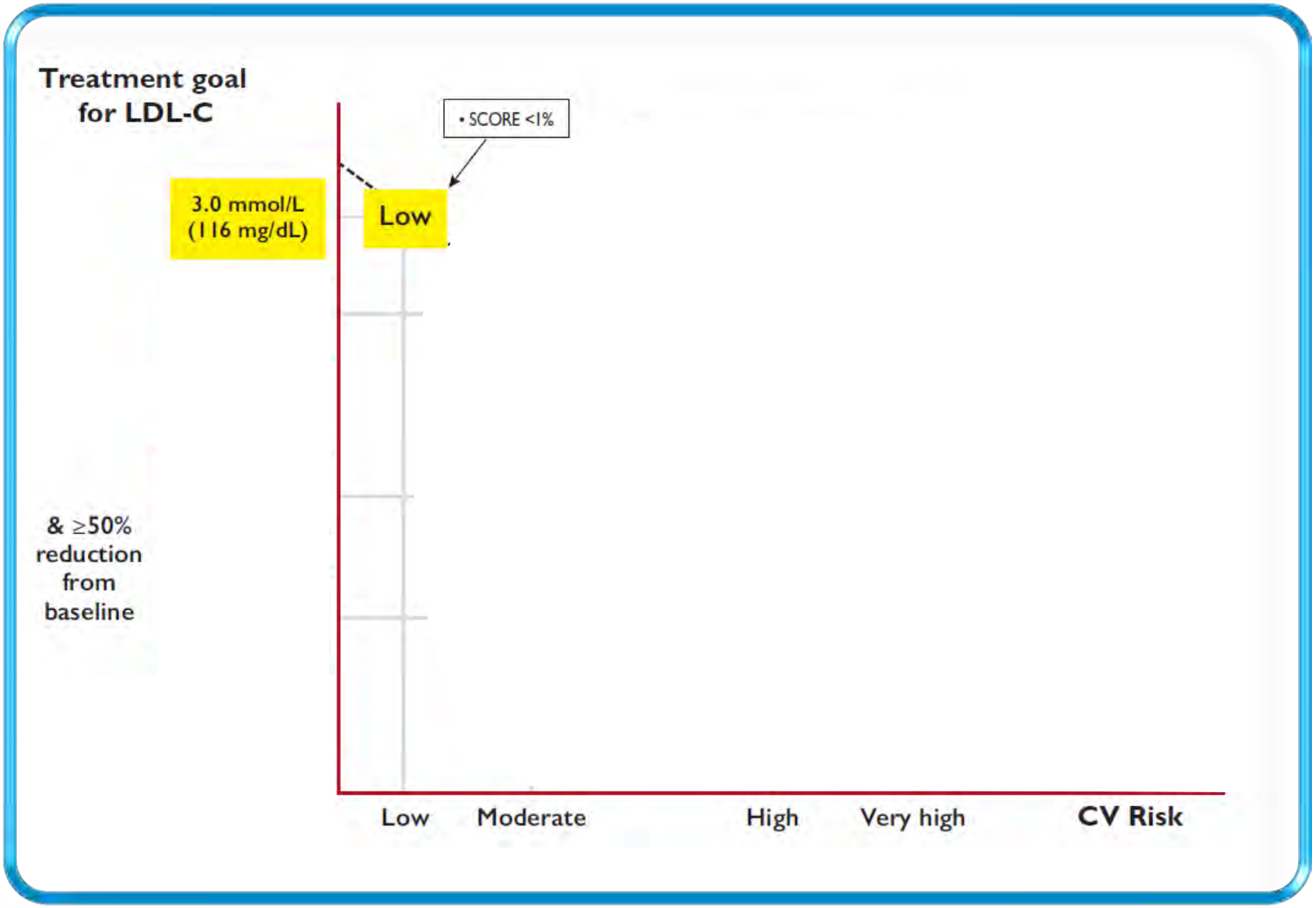
Scanu A N Engl J Med 2003



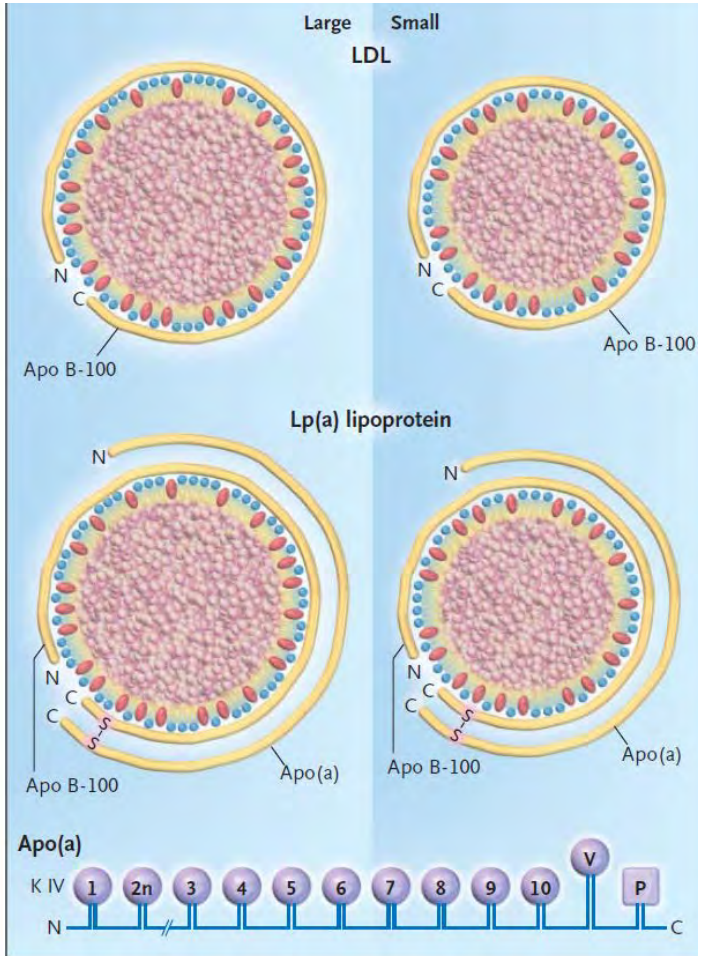
Cannon C *et al.* N Engl J Med 2015



ESC Guidelines 2019



Scanu A N Engl J Med 2003



2019	2020
Statine	Statine
Ezetimib	Ezetimib
Evolocumab	Evolocumab
	Inclisiran
	Bempedoic acid
(Evolocumab)	(Evolocumab)
	(Inclisiran)

01.09.2020 18 Uhr AGAPLESION MARKUS KRANKENHAUS