

# SGLT2-Inhibitoren aus Sicht der Nephrologie

Alexander Kirsch

Grazer Fortbildungstage

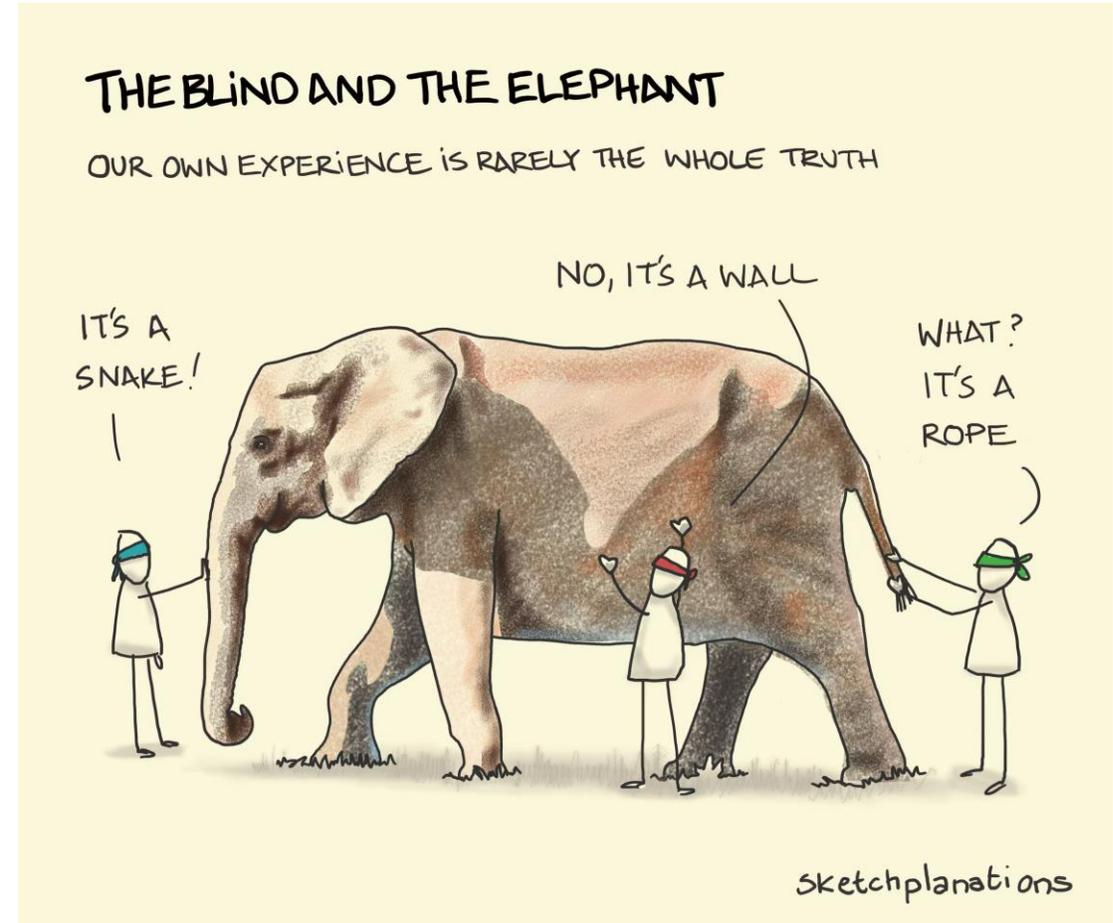
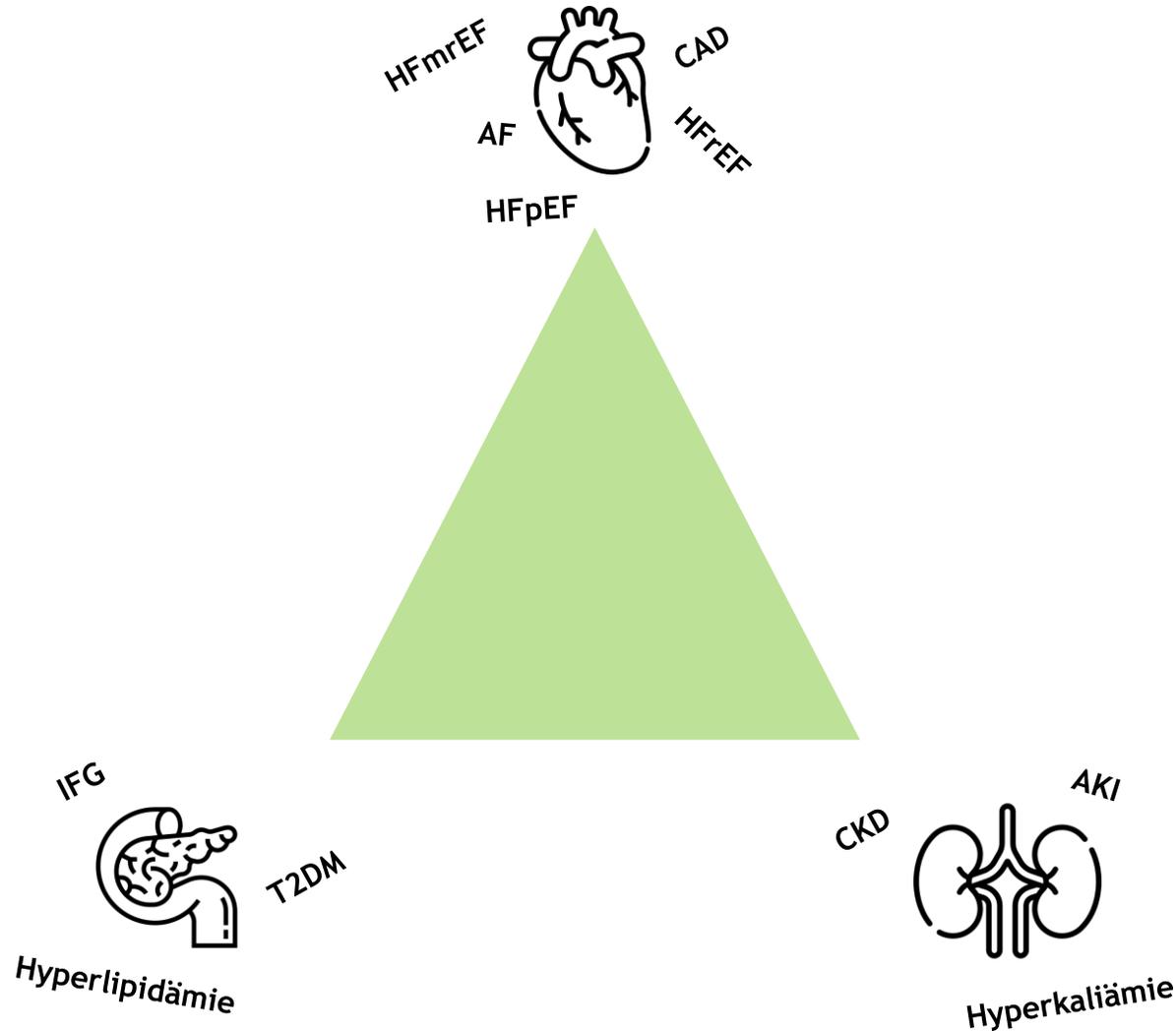
*11.10.2024*

# Disclosures

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- ▶ Astra Zeneca
- ▶ Vifor
- ▶ Bayer
- ▶ Boehringer Ingelheim
- ▶ Otsuka
- ▶ Baxter
- ▶ Astellas
- ▶ MSD

# Cardio-renal-metabolisches Syndrom



# CKD Guidelines - 2024

## KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease



**Nur 6 Empfehlungen unverändert beibehalten**



## KDIGO 2024 CLINICAL PRACTICE GUIDELINE FOR THE EVALUATION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE

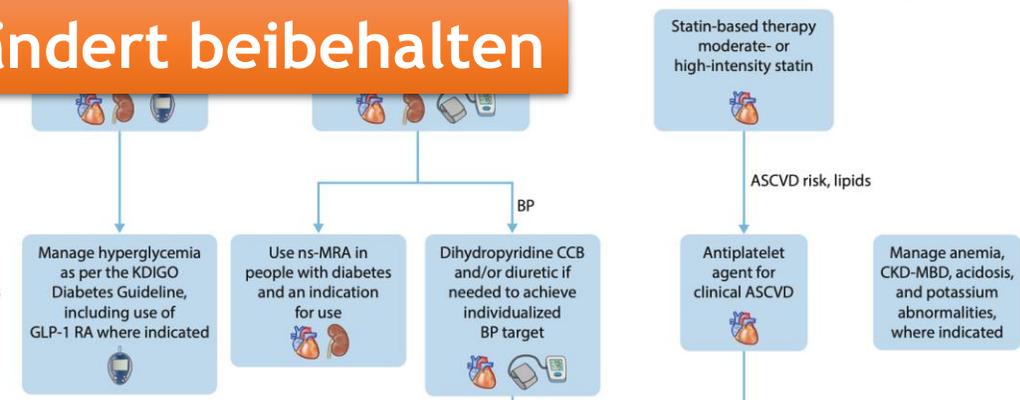
Lifestyle



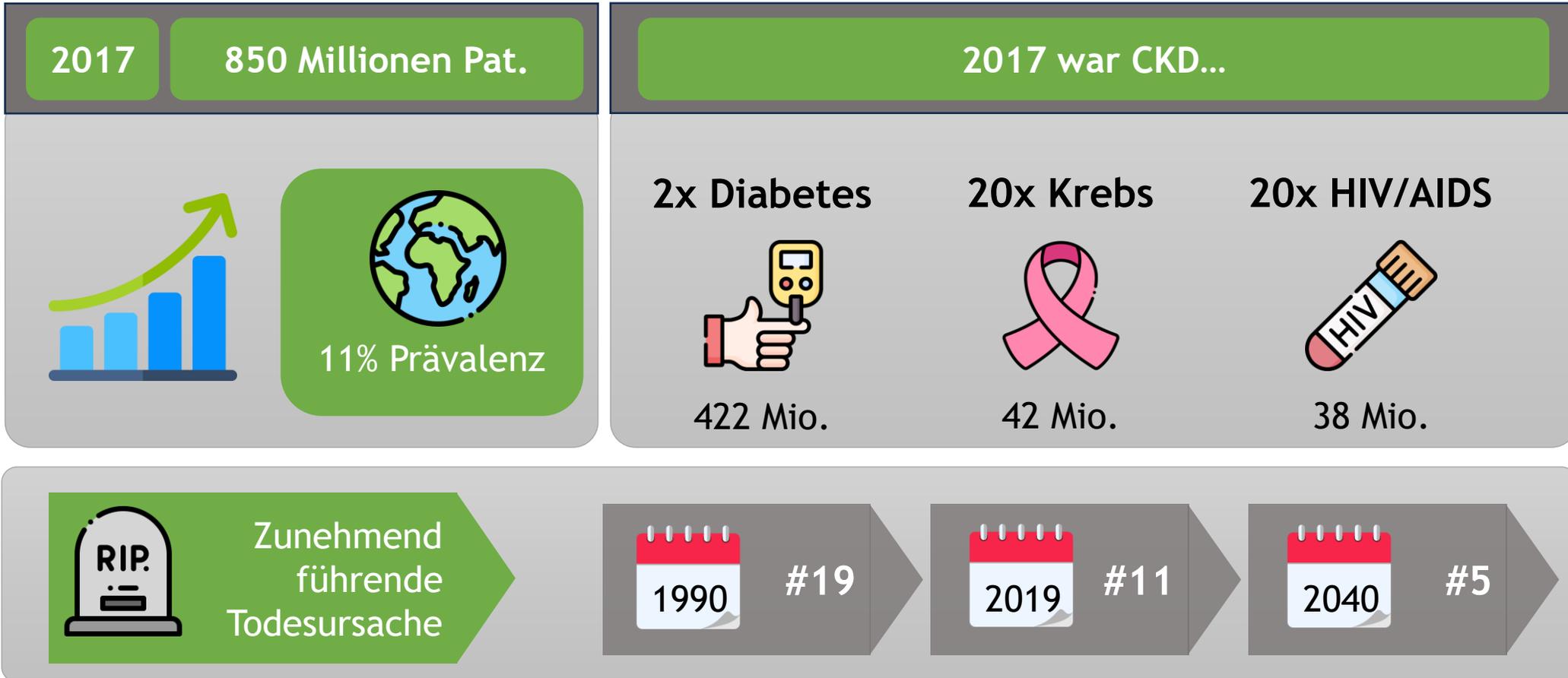
Regular risk factor reassessment (every 3–6 months)

most patients

Targeted therapies for complications



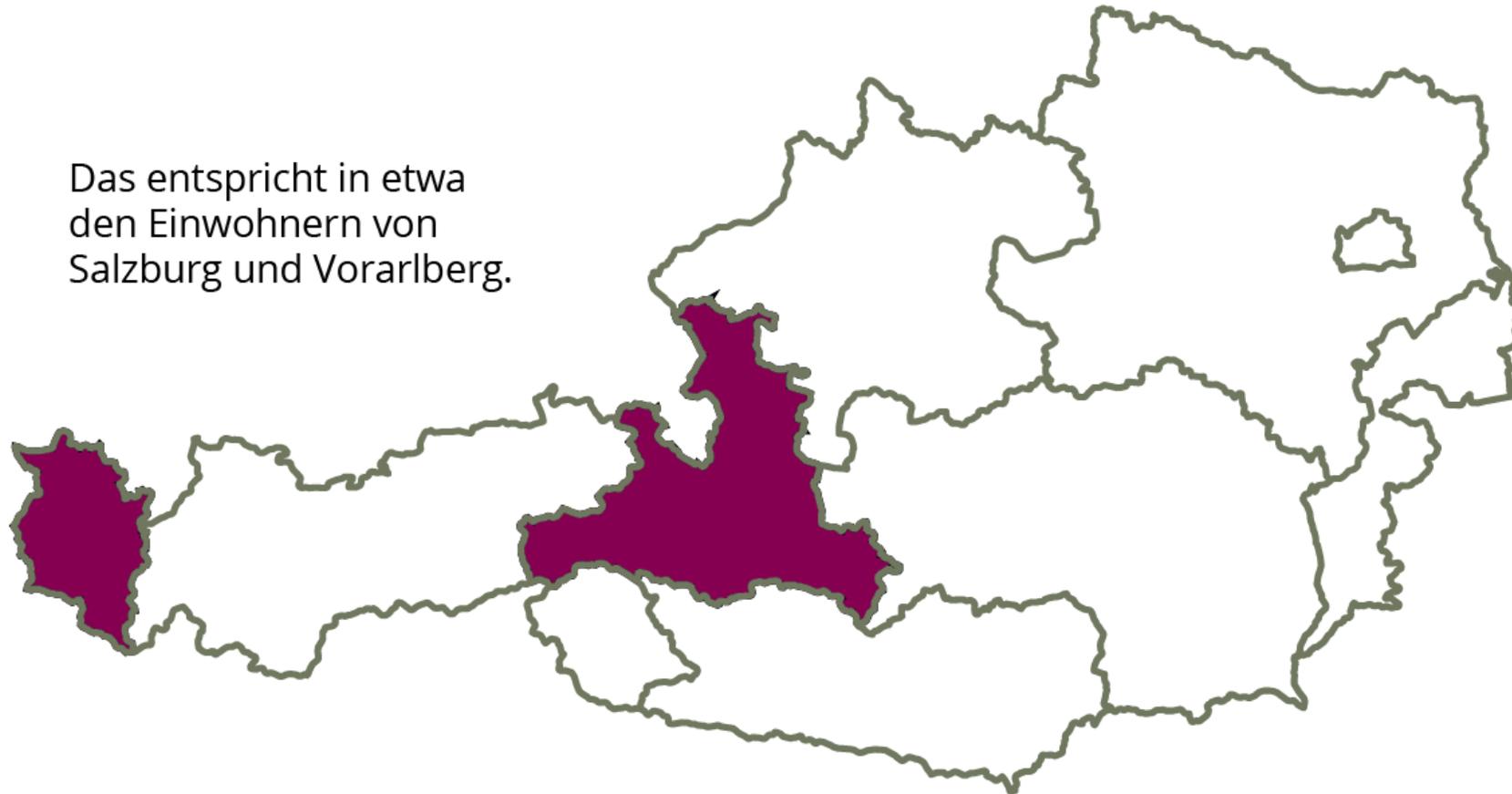
# CKD Epidemiologie



# CKD Prävalenz in Österreich

Ca. 10% der Bevölkerung haben eine chronisch eingeschränkte Nierenfunktion

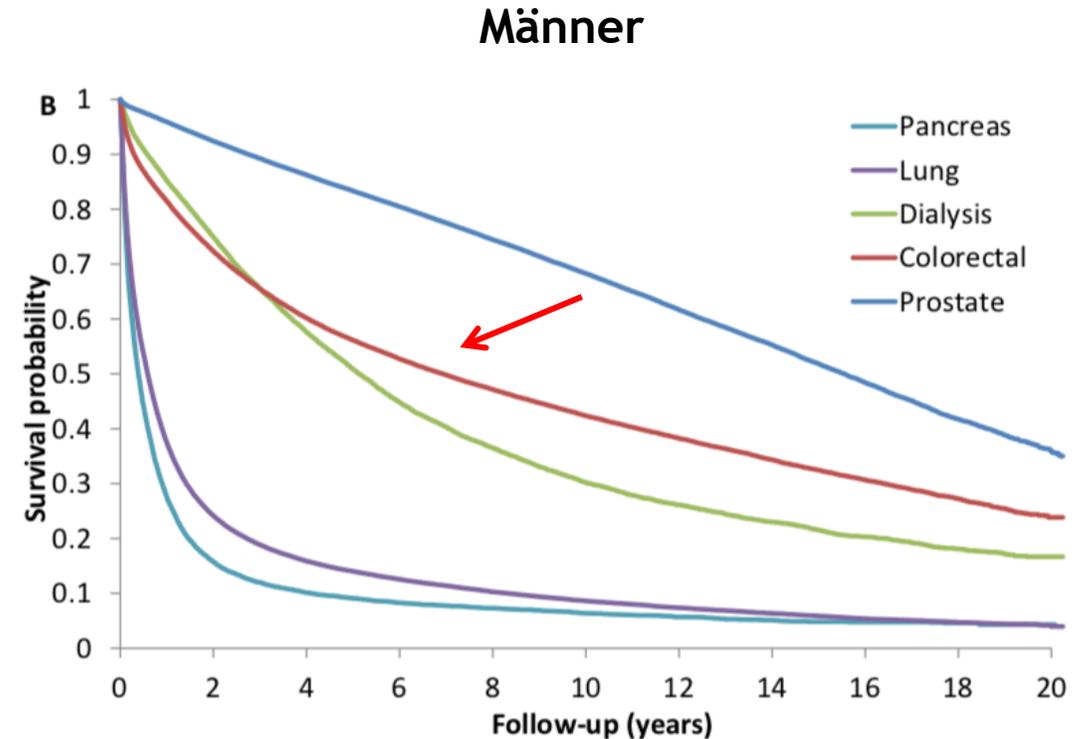
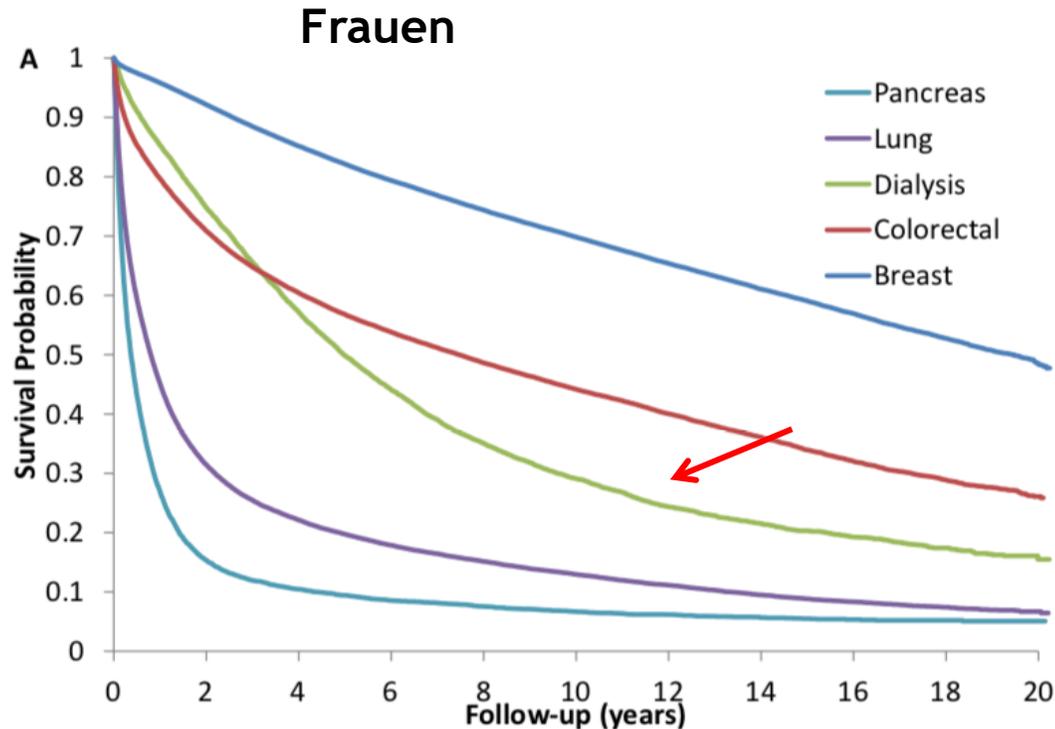
Das entspricht in etwa  
den Einwohnern von  
Salzburg und Vorarlberg.



# ESRD vs. Cancer Outcome



## Mortality in Incident Maintenance Dialysis Patients Versus Incident Solid Organ Cancer Patients:



# Definition der CKD

## KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of CKD

CKD ist definiert als Abnormalitäten der Nierenstruktur oder -funktion, die länger als 3 Monate andauern und Auswirkungen auf die Gesundheit hat

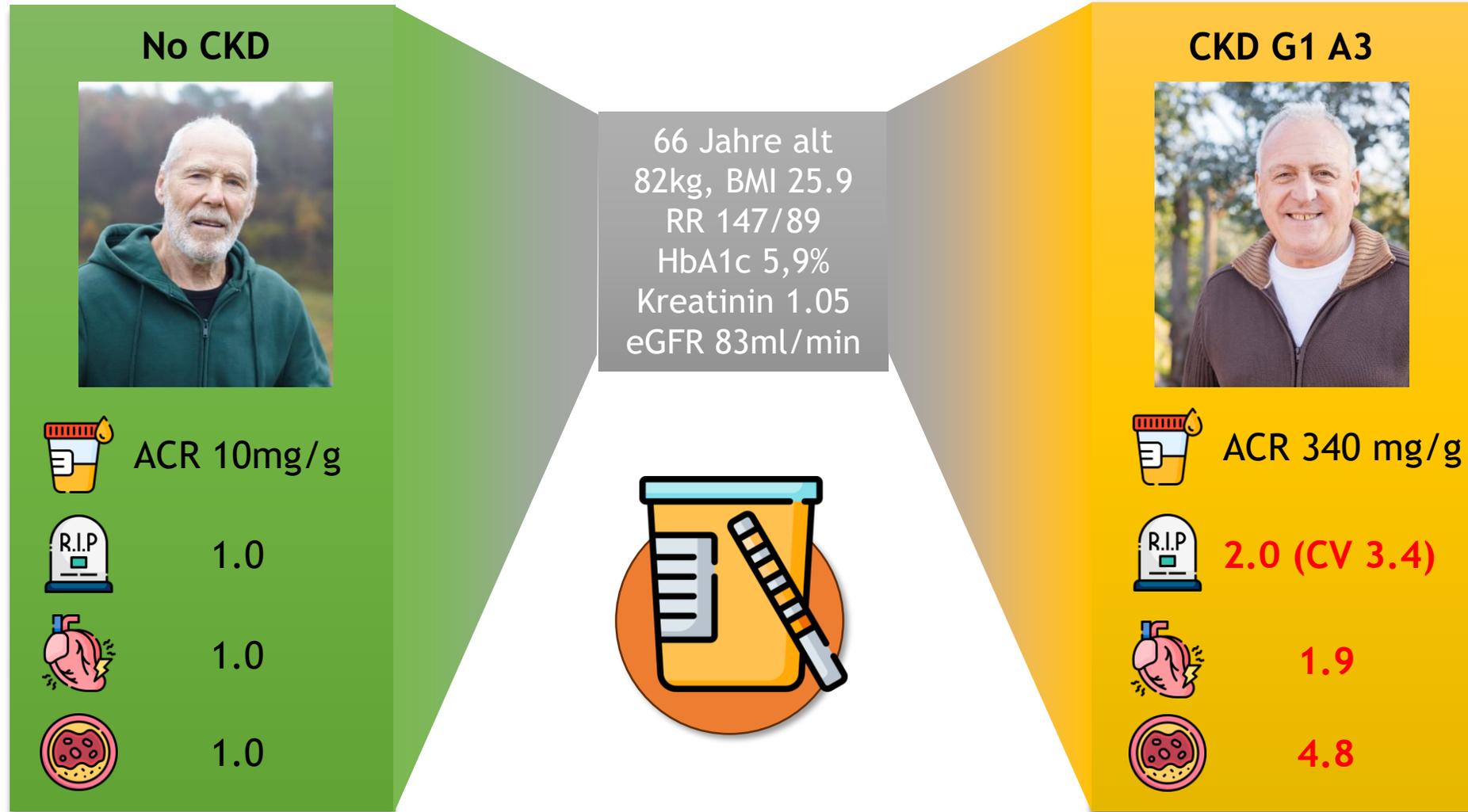
eGFR  $<60$  mL/min/1,73 m<sup>2</sup>

ODER

Anzeichen für eine Nierenschädigung, einschließlich persistierender Albuminurie (UACR  $\geq 30$  mg/g)

Für  $>3$  Monate

# Albuminurie als CV-Risikomarker



Grams ME, JAMA 2023; KDIGO Guidelines 2024

# Risikofaktoren für CKD

## Mehr als die „Klassiker“



# CKD Management (KDIGO 2024)

Lebensstil

Ernährung



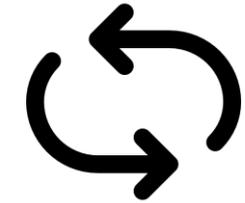
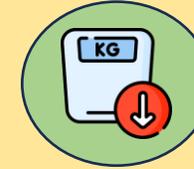
Bewegung



Rauchstop



Gewicht



Alle 3-6  
Monate

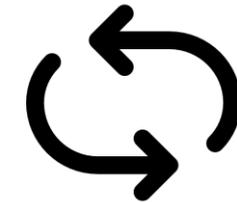
\*\*Standardized office BP

# CKD Management (KDIGO 2024)

Lebensstil

Ernährung Bewegung Rauchstop Gewicht



 Alle 3-6 Monate

Erstlinie

SGLT2i  
 Bis zur Dialyse



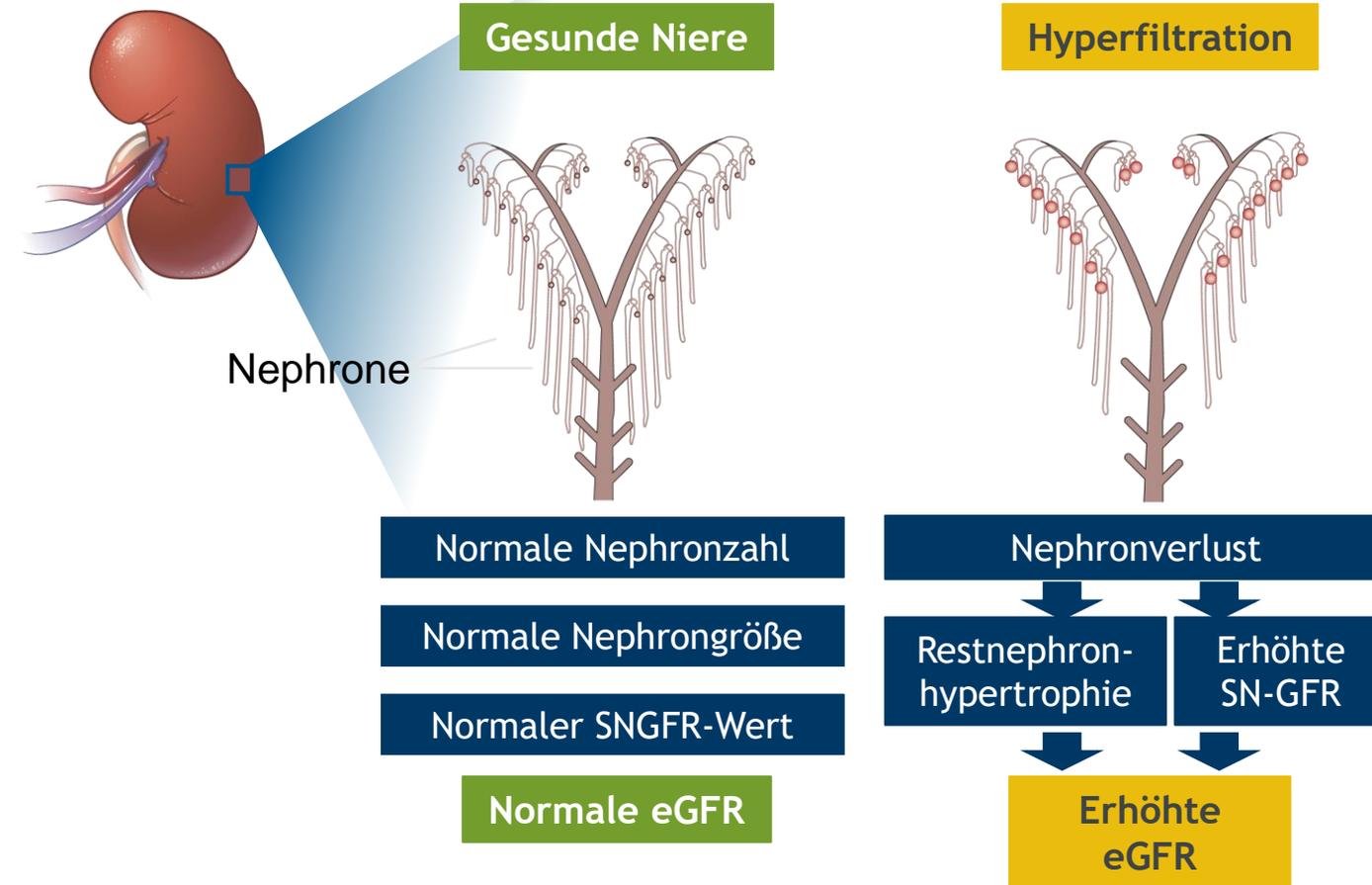

We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR  $\geq 20$  ml/min per 1.73 m<sup>2</sup> with an SGLT2i.



We recommend treating adults with CKD with an SGLT2i for the following (1A):

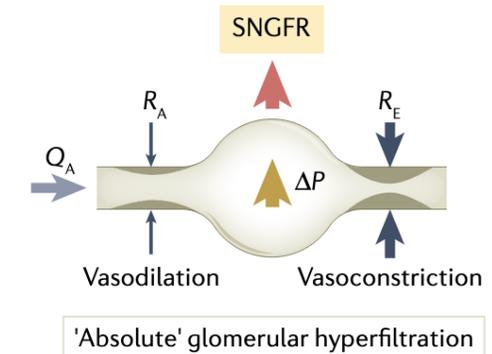
- eGFR >20 ml/min per 1.73 m<sup>2</sup> with urine ACR >200 mg/g (>20 mg/mmol), or
- heart failure, irrespective of level of albuminuria.

# Der Kompensationsmechanismus - Was passiert vor dem eGFR Abfall?

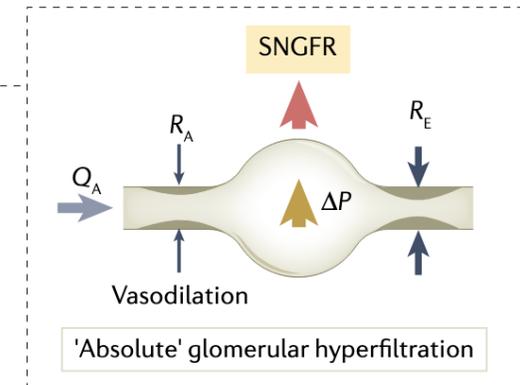
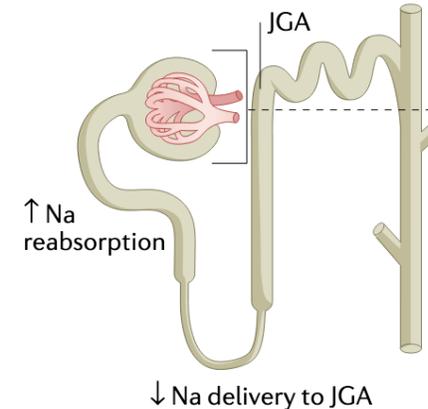


## a Haemodynamic hypothesis

- Imbalance of vasoactive mediators
- RAAS activation
  - Activation of the endothelin-1 pathway
  - COX2-derived prostanoids
  - Nitric oxide



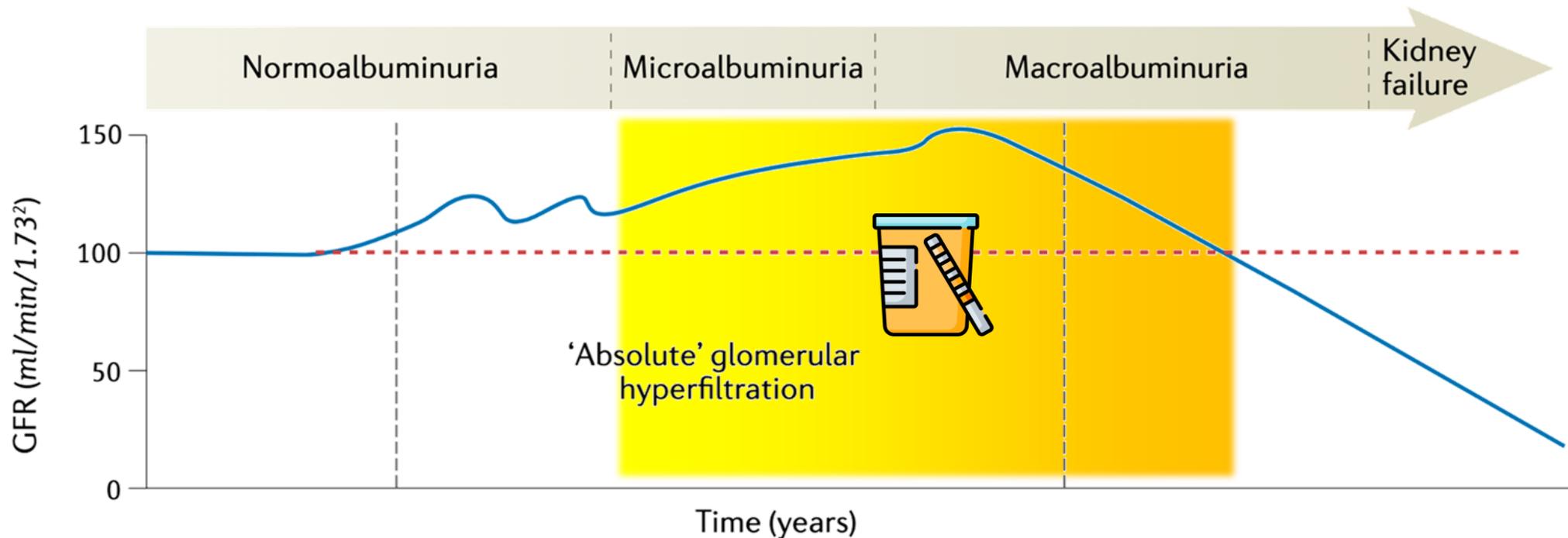
## b Tubular hypothesis



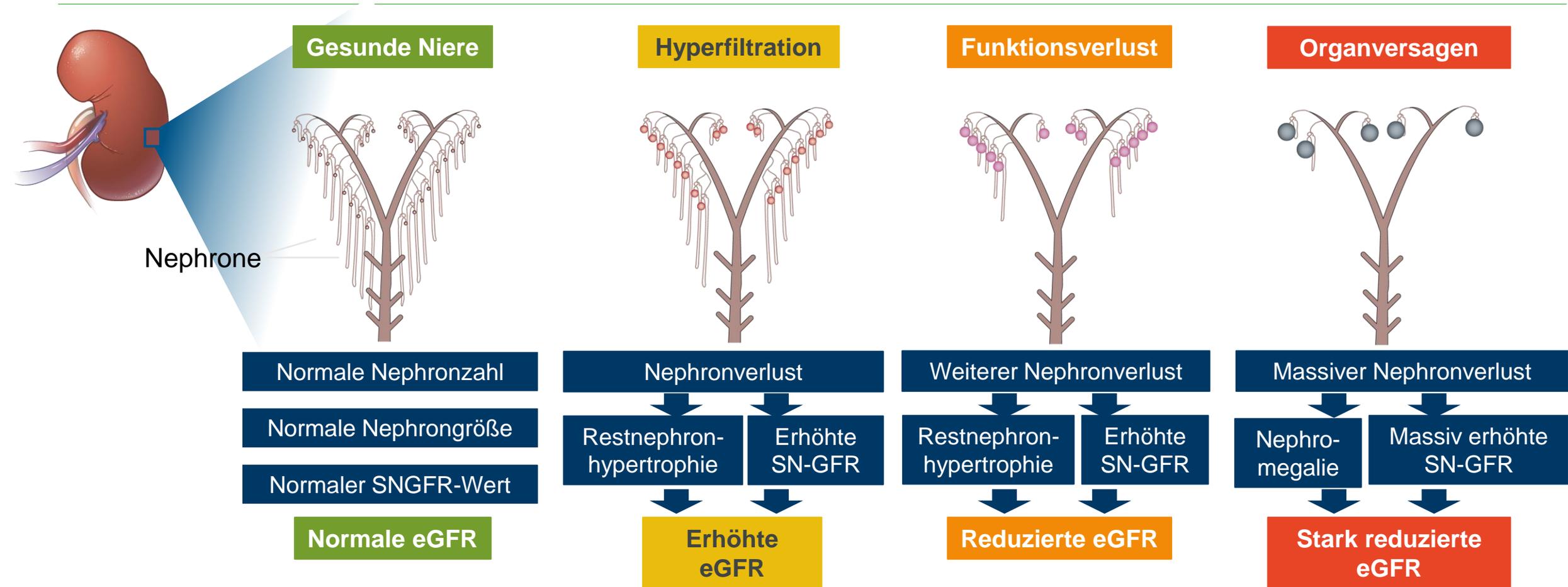
SN-GFR = glomeruläre Filtrationsrate eines einzelnen Nephrons  
CKD = chronische Nierenerkrankung; eGFR = geschätzte glomeruläre Filtrationsrate;

Anders HJ et al. Nat Rev Nephrol 2018; Szczech LA et al. PLoS One. 2014; Cortinovis M, Nature Rev Nephrol 2022

# Klassischer Verlauf der DN



# Der Kompensationsmechanismus - Was passiert vor dem eGFR Abfall?



SN-GFR = glomeruläre Filtrationsrate eines einzelnen Nephrons

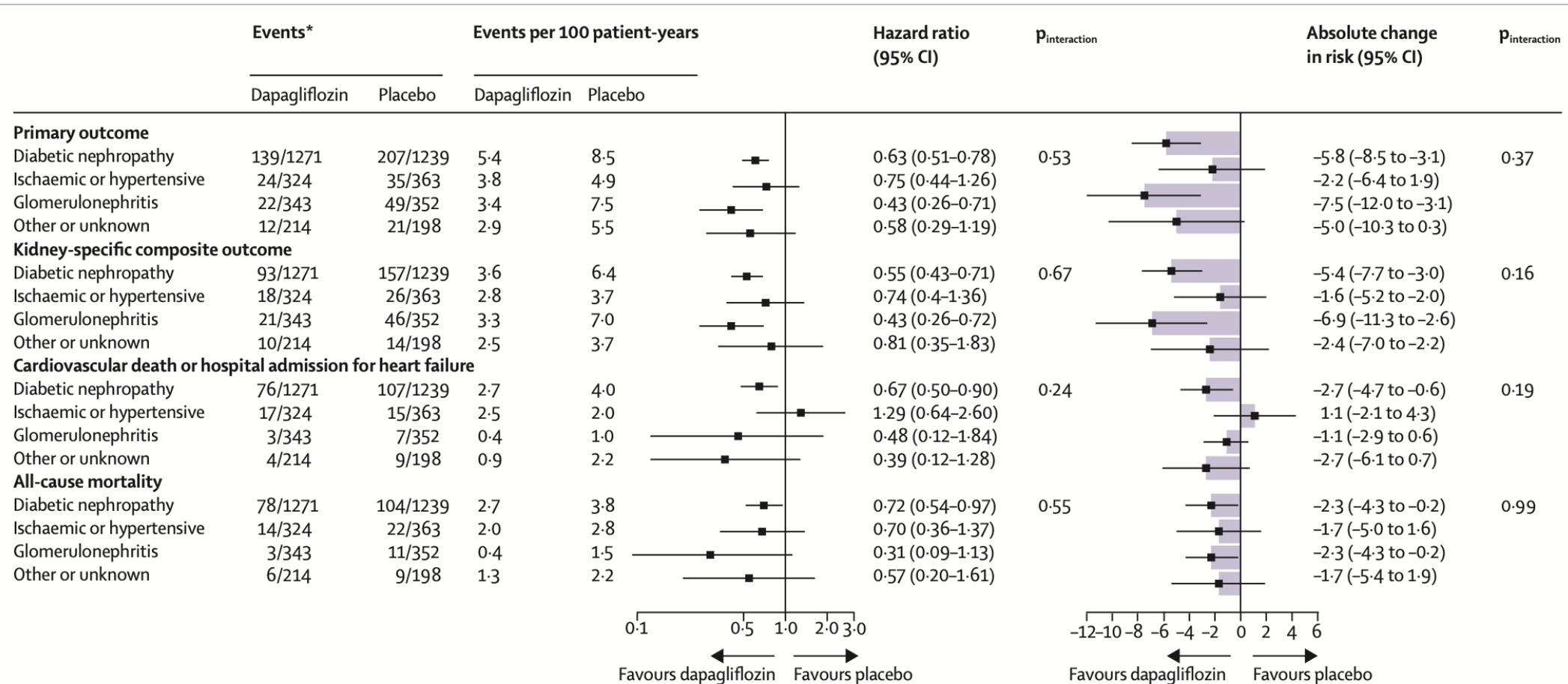
CKD = chronische Nierenerkrankung; eGFR = geschätzte glomeruläre Filtrationsrate;

Anders HJ et al. Nat Rev Nephrol 2018;14:361-377; Szczech LA et al. PLoS One. 2014;9:e110535

# Empa-Kidney: Effekt unabhängig von Grunderkrankung

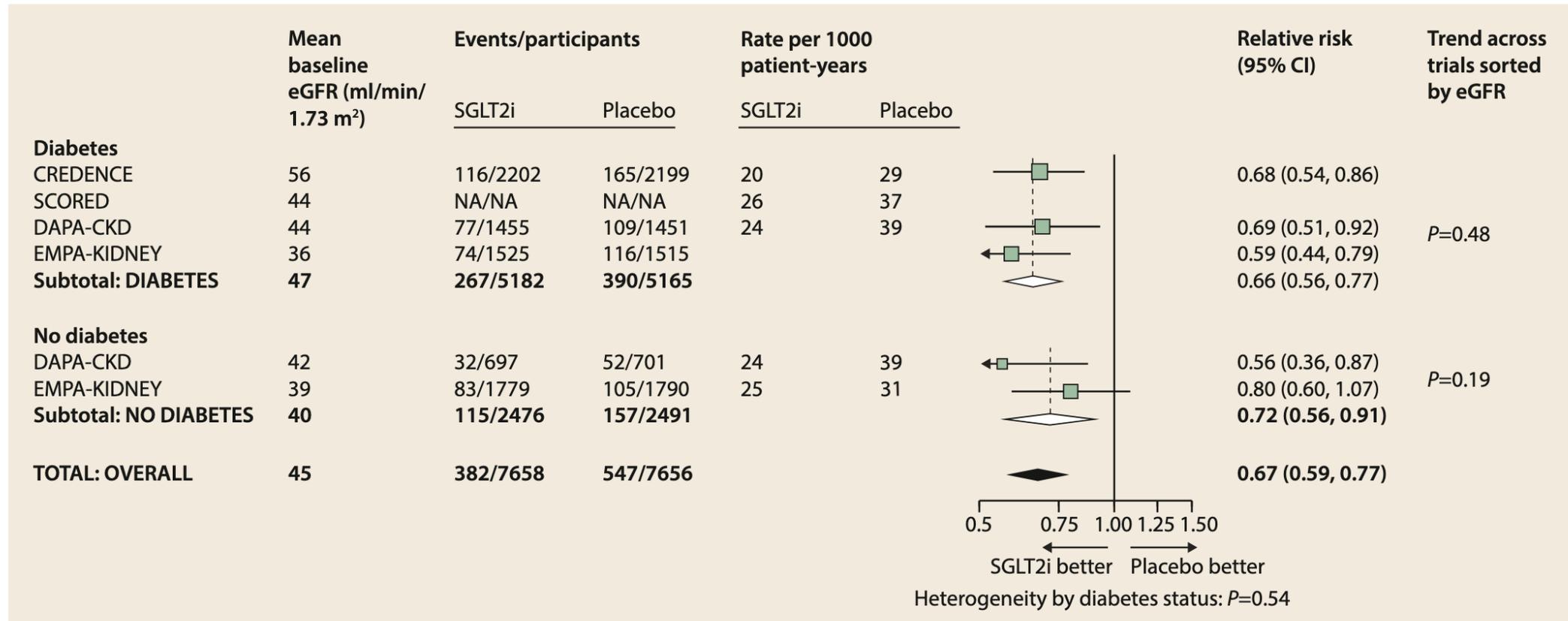
	Empagliflozin group (n=3304)		Placebo group (n=3305)		Hazard ratio (95% CI)	p <sub>heterogeneity</sub> *
	n (%)	Events per 100 person-years	n (%)	Events per 100 person-years		
<b>Primary outcome and its components</b>						
Primary outcome: progression of kidney disease or death from cardiovascular causes	..	..	..	..	..	0.56
Diabetic kidney disease	161 (15.6%)	8.10	223 (21.8%)	11.41	0.65 (0.53–0.80)	..
Hypertensive or renovascular disease	82 (11.6%)	5.95	96 (13.0%)	6.92	0.82 (0.61–1.11)	..
Glomerular disease	117 (13.7%)	7.48	142 (17.4%)	9.66	0.77 (0.60–0.98)	..
Other or unknown	72 (10.1%)	5.24	97 (13.4%)	6.84	0.73 (0.54–1.00)	..
Overall	432 (13.1%)	6.85	558 (16.9%)	8.96	0.72 (0.64–0.82)	..

# Dapagliflozin: Effekt unabhängig von Grunderkrankung



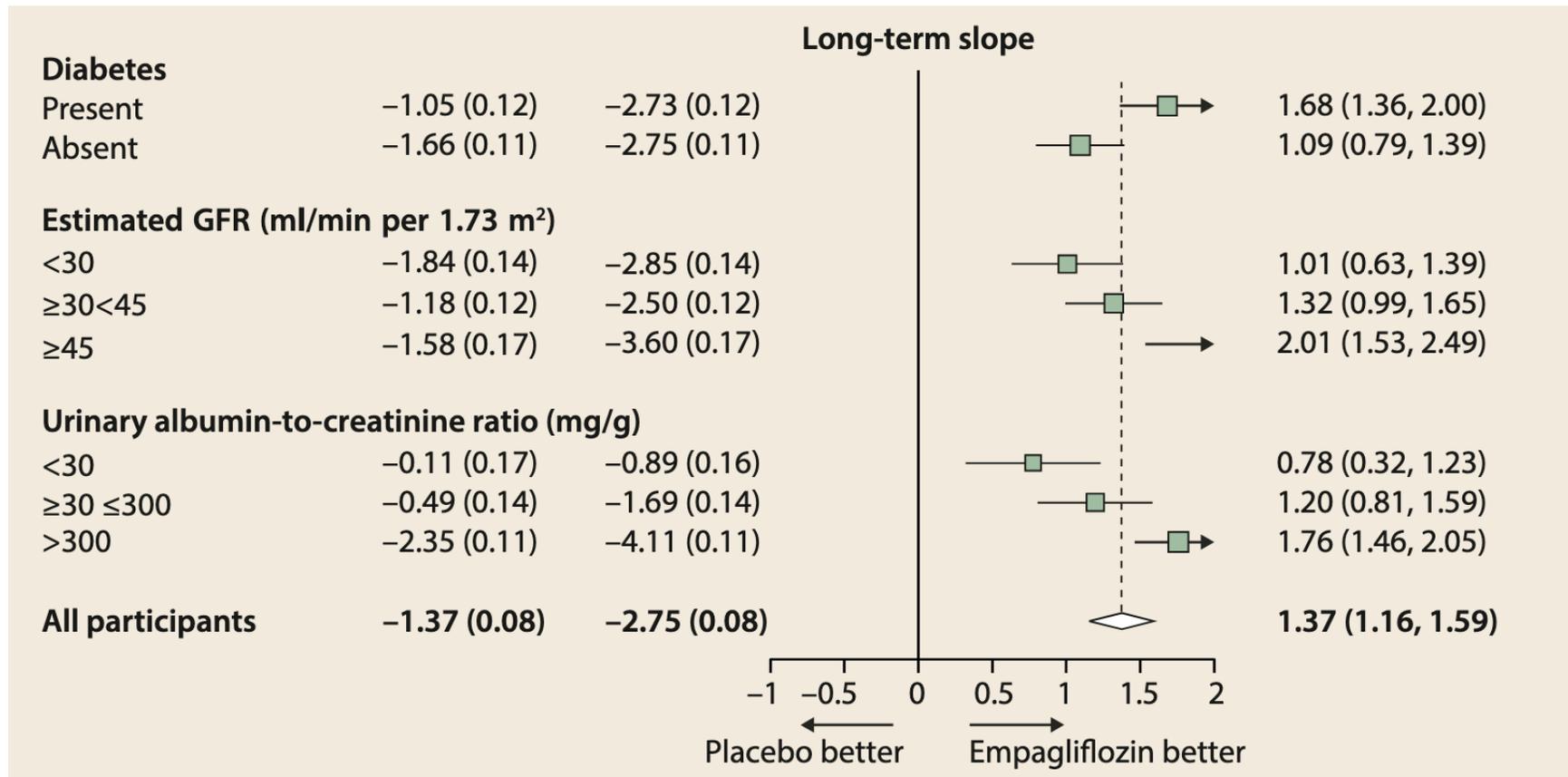
# SGLT2-Inhibitoren bei CKD

## Endpunkt: Nierenversagen



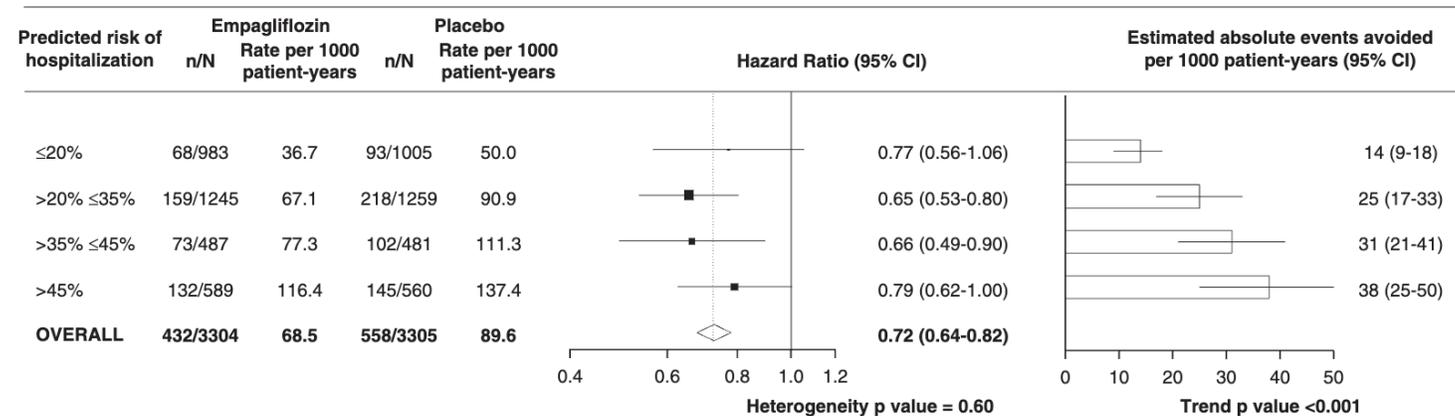
# SGLT2-Inhibitoren bei CKD

## Empa: Endpunkt Long Term Slope

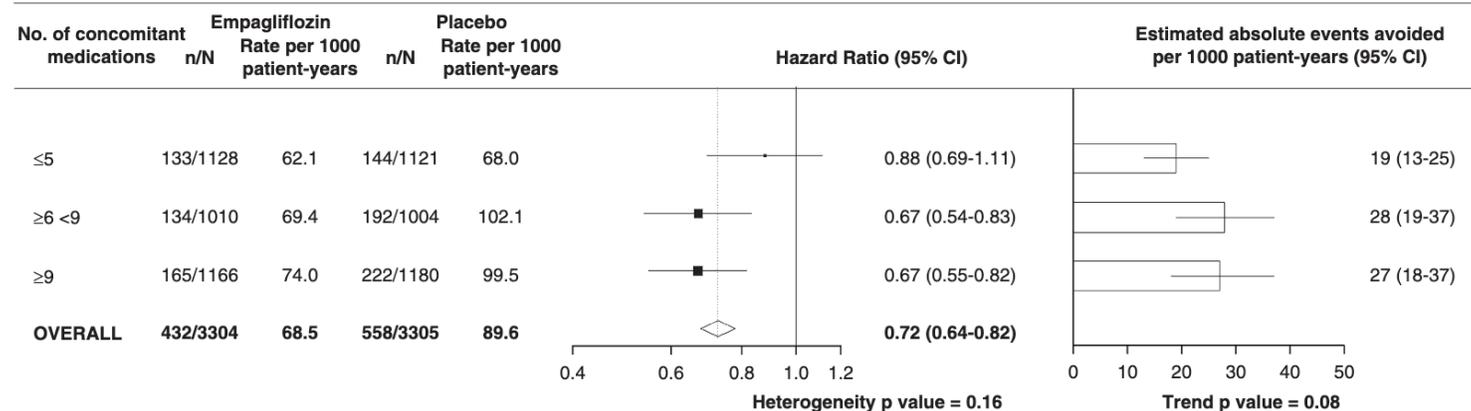


# SGLT2-Inhibitoren bei Frailty

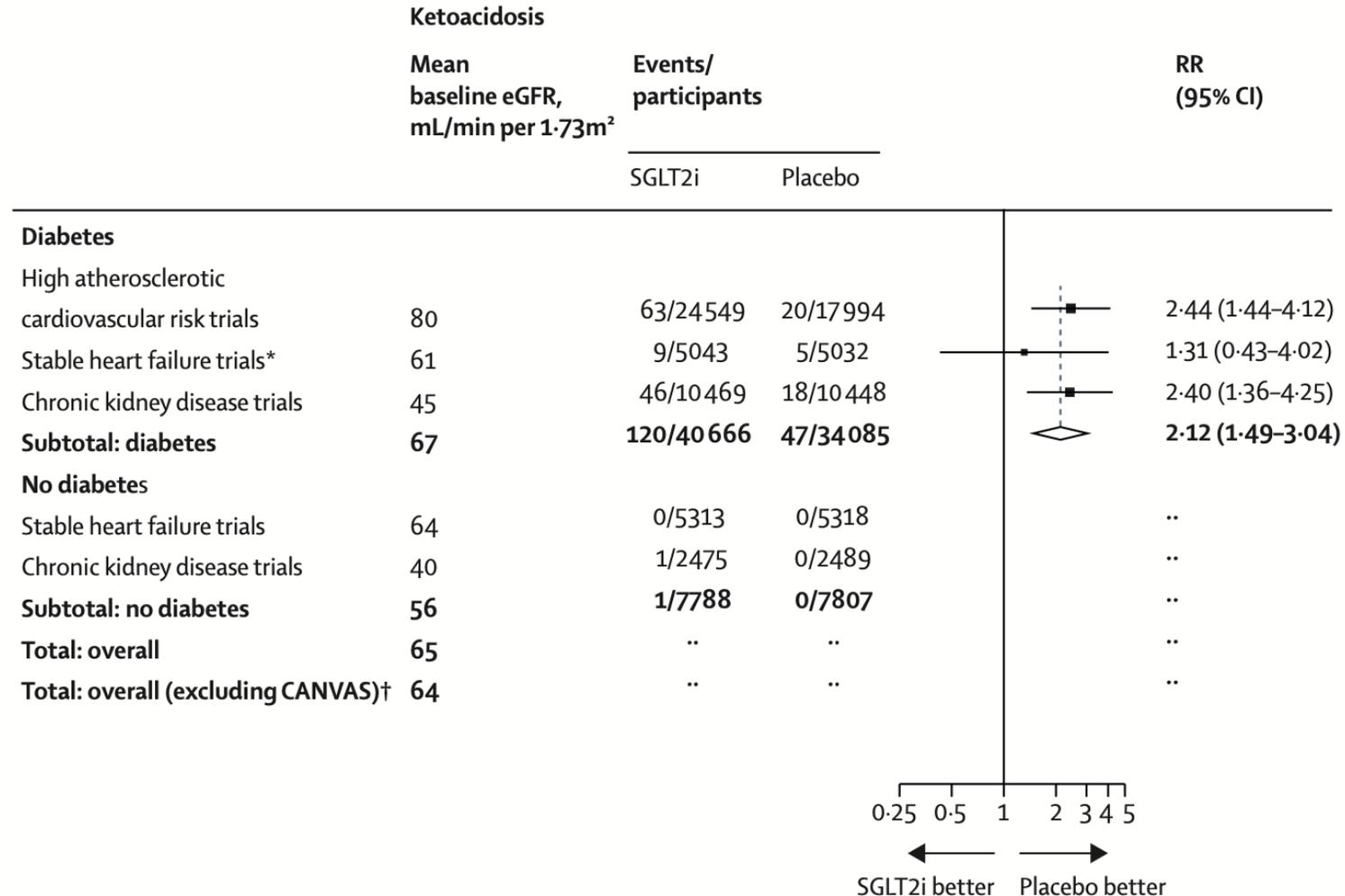
## Hospitalisierungsrisiko (2 Jahre)



## Polypharmazie

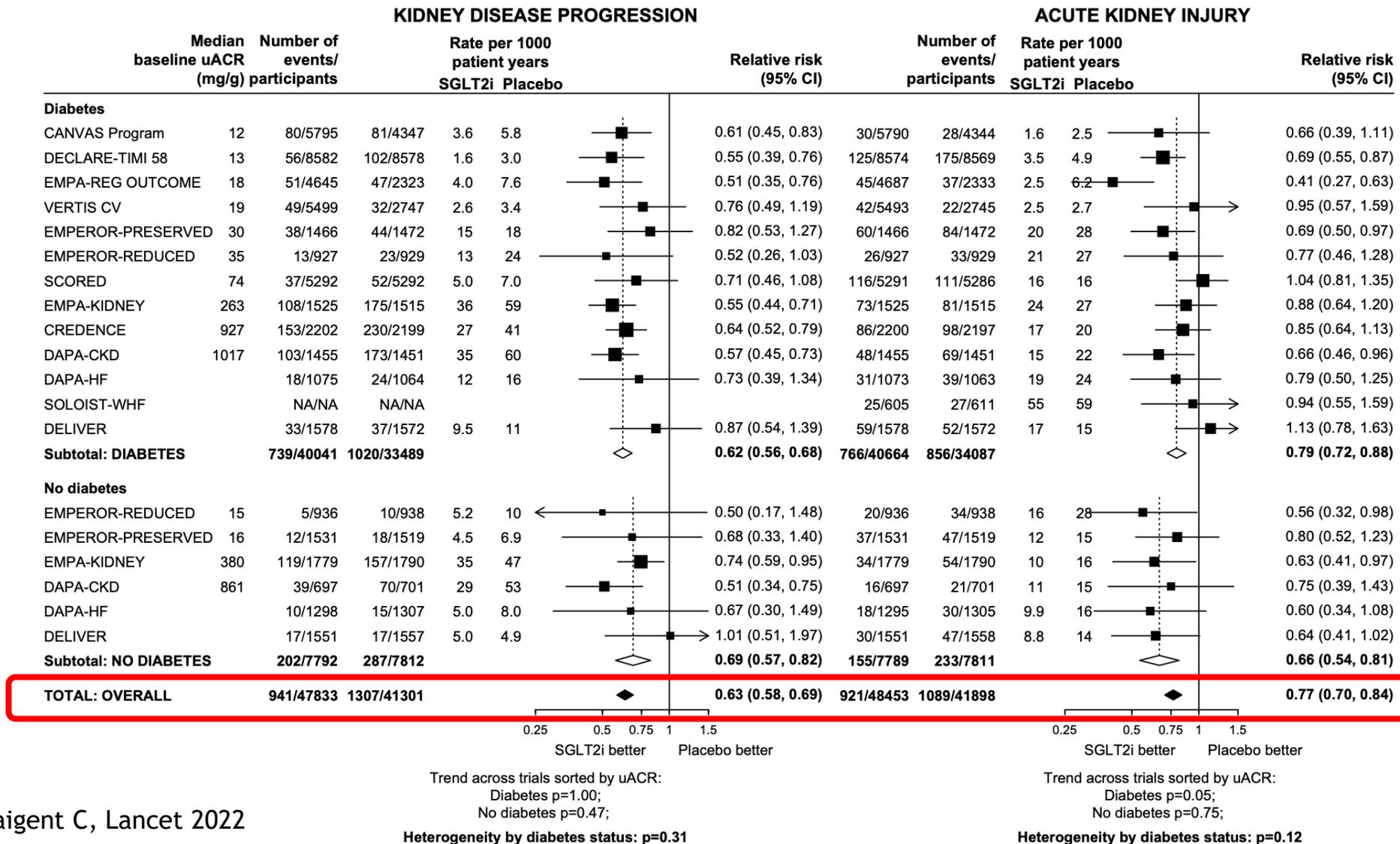


# Euglykämie Ketoazidose kommt bei Nicht-Diabetikern nicht vor



Baigent C, Lancet 2022

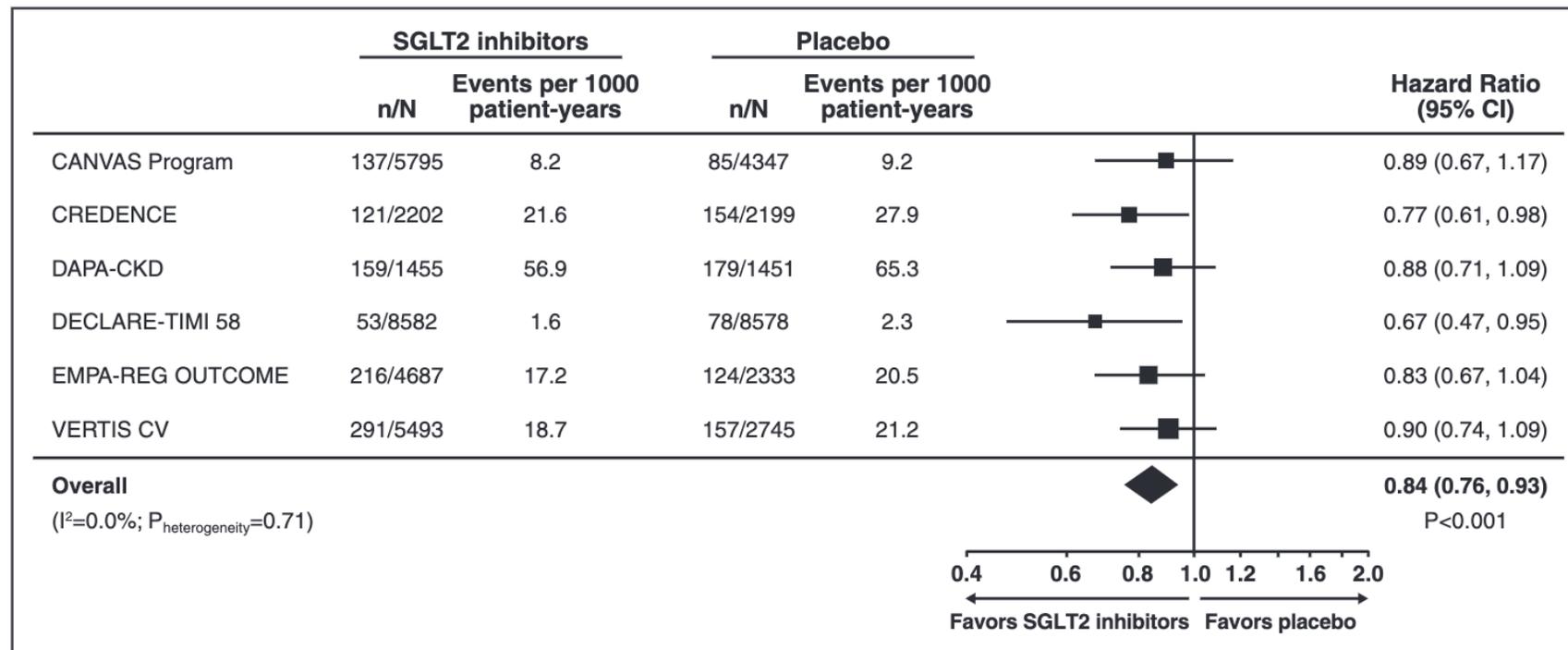
# Akutes Nierenversagen & SGLT-2i



Baigent C, Lancet 2022

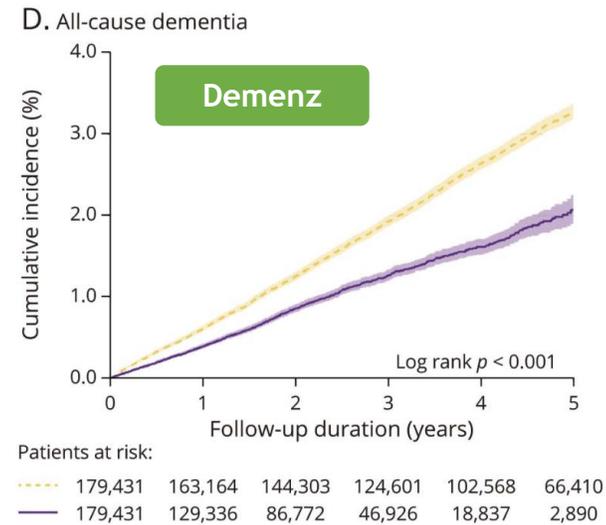
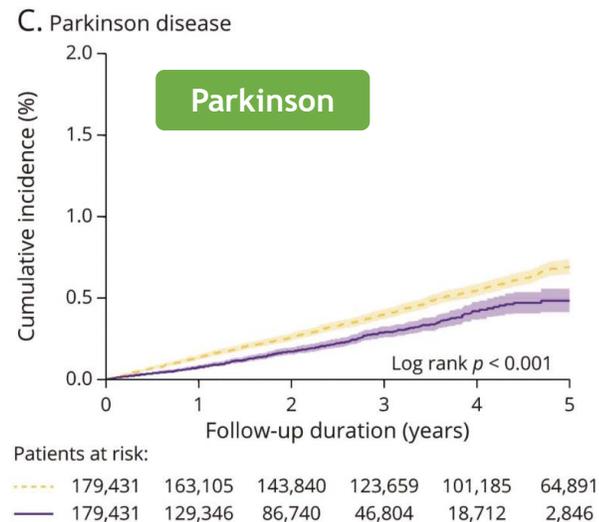
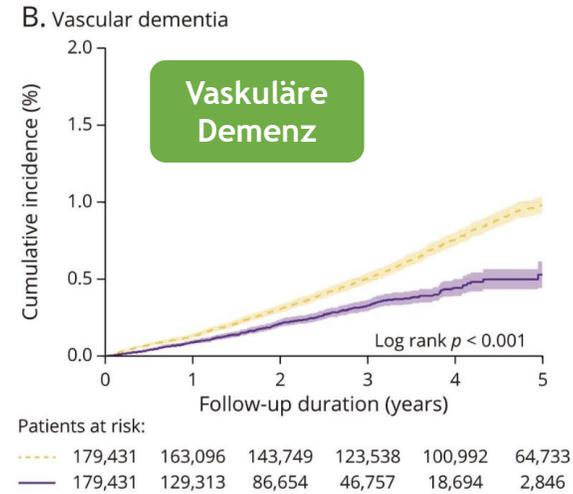
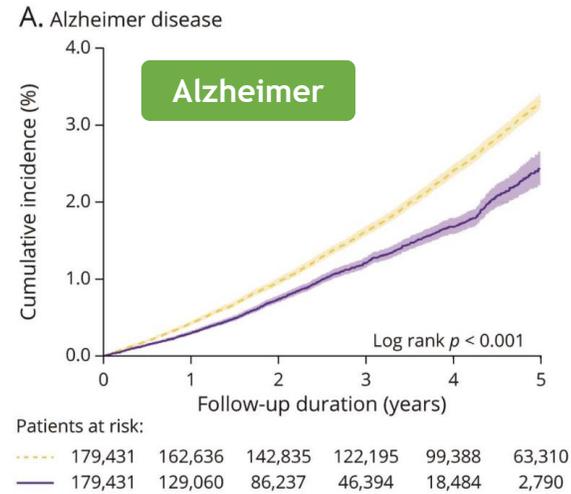
# SGLT2-Inhibitoren und HyperK

- ▶ N=50.000 Typ 2 Diabetiker aus CREDENCE, CANVAS, EMPA-REG, DECLARE-TIMI, DAPA-CKD, VERTIS-CV)

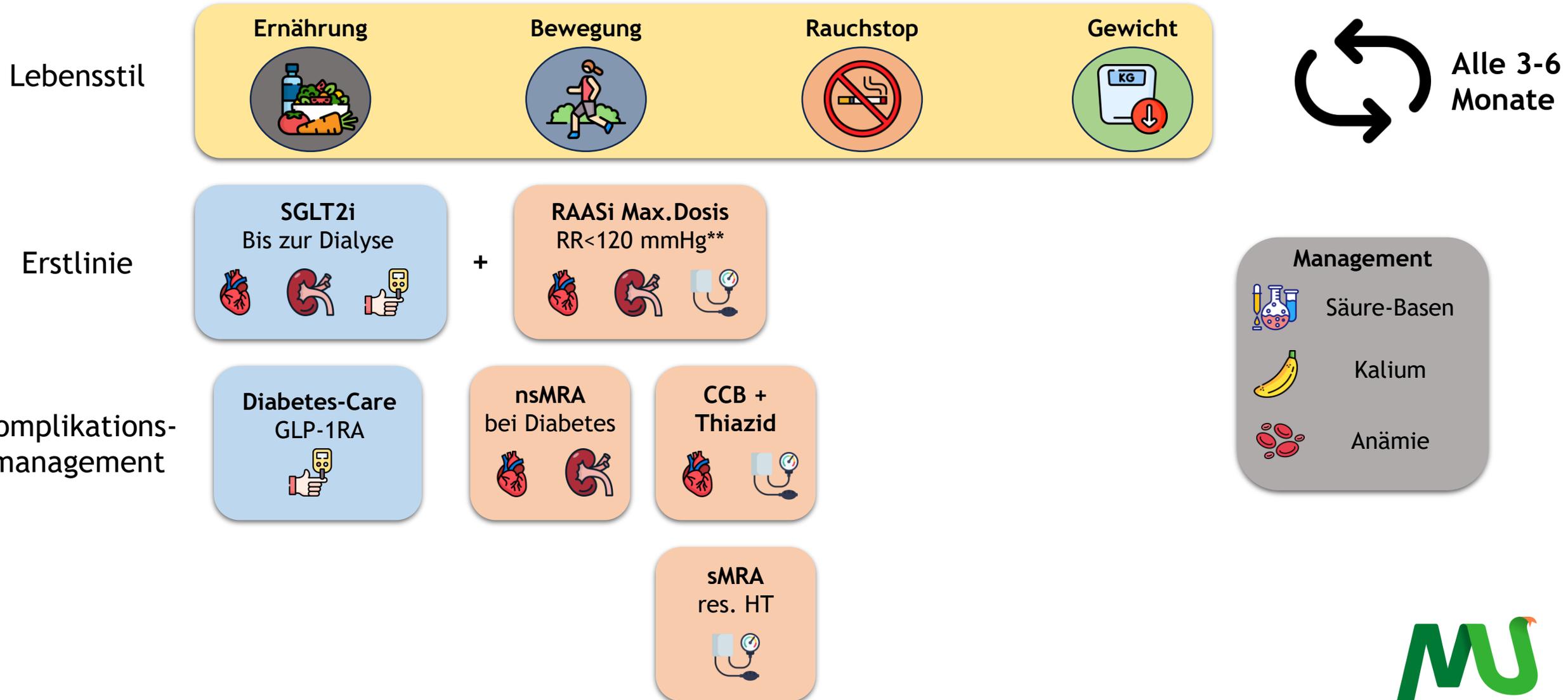


**Figure 1.** Effects of SGLT2 inhibitors on serious hyperkalemia (central laboratory-determined serum potassium  $\geq 6.0$  mmol/L).

# SGLT2-Inhibitoren und neurodegenerative Erkrankungen

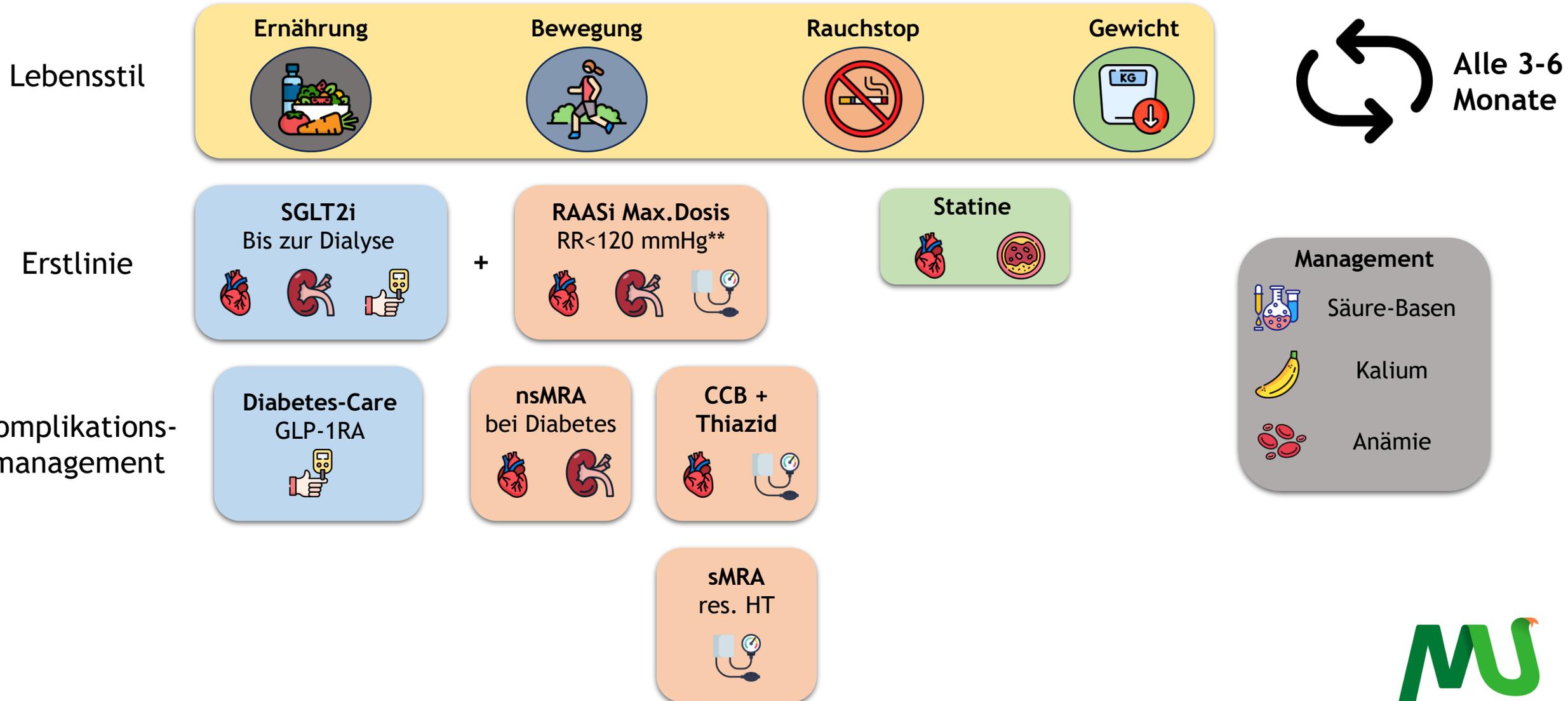


# CKD Management (KDIGO 2024)



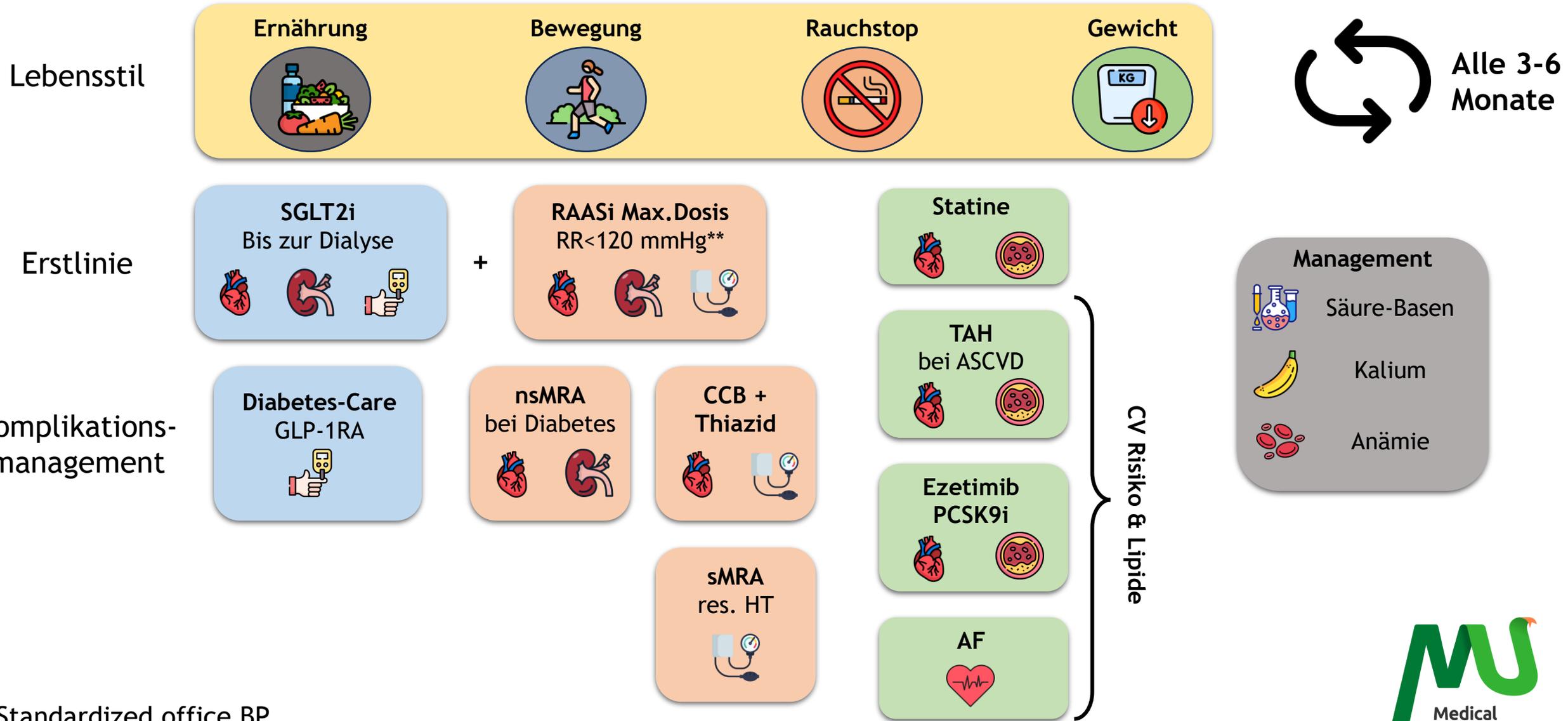
\*\*Standardized office BP

# CKD Management (KDIGO 2024)



\*\*Standardized office BP

# CKD Management (KDIGO 2024)



# SGLT2i nephrologisch

- ▶ Fokus auf frühe Erkennung: Albuminurie
  - CKD: GFR  $<60$  oder GFR  $> 60$  und pathologische Albuminurie
  - Albuminurie: Albumin-Kreatinin Ratio im Spontanharn
- ▶ SGLT2-Hemmer: Grundpfeiler der modernen CKD Therapie
  - CKD mit GFR 90-20/75-25 zusätzlich zu ACEi/ARB
  - Bei abnehmender GFR bis zur Dialyse
  - **bei wem nicht (routinemäßig)? ADPKD, Typ 1 DM (NTx Patient, Immunsuppression)**
- ▶ Frühe Erkennung → Frühe Therapie → mehr Benefit

My understanding  
of the kidney

stuff happens in there...  
something about Potassium  
and maybe sodium & calcium, too.  
urea? filtration n' junk.

