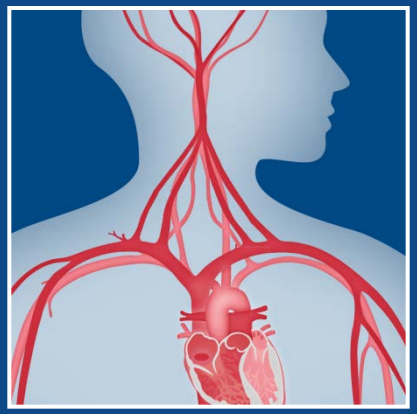
Nephro Update Europe 2018

5-6 October, Budapest

Cardiovascular Disease



Danilo Fliser, Germany

Conflicts of Interest

Lecturing: Amgen, Bayer, Boehringer Ingelheim, FMC, Vifor, Roche

Consulting activities: Amgen, Boehringer Ingelheim, FMC, Vifor

CV mortality, risk factors & biomarkers in CKD

State of the art

- CKD patients are characterized by high CV mortality, traditional and **non-traditiona**l (CKD-related) CV risk factors play a role

- Causes of CV death may differ from those in the general population. The utility of measures to reduce CV morbidity and mortality, and of CV risk biomarkers may differ as well

CV mortality in CKD

Study design and patients

- Prospective observational multicenter Coronary Artery Disease and REnal Failure **(CAD-REF)** Registry
- 3,352 patients with angiographically documented CAD, and baseline eGFR measurement
- Follow-up 2 years

Engelbertz C et al. ***Int J Cardiol*** 2017; 243: 65

CV mortality in CKD

Results and interpretation

- CAD worsened with decreasing kidney function
- Overall 2 year mortality was **6.5%**, with highest mortality in patients with CKD stages 4 and 5 (**22.4%**). Significant risk factors were higher age, lower eGFR, smoking, reduced LVEF and diabetes mellitus
- An eGFR reduction of **10 ml/min/1.73m^2** increased the risk of mortality by **19%** regardless of other risk factors

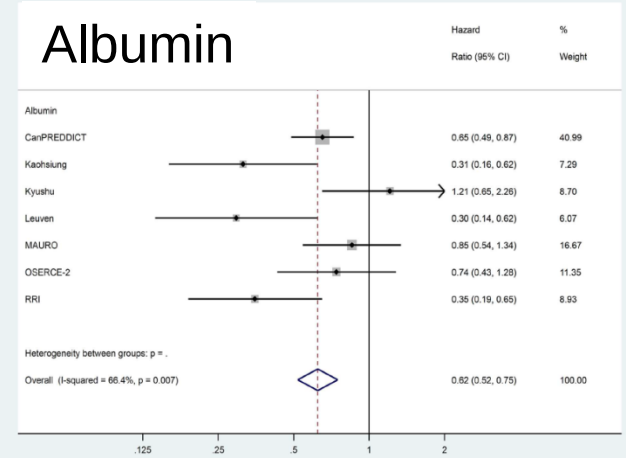
Engelbertz C et al. ***Int J Cardiol*** 2017; 243: 65

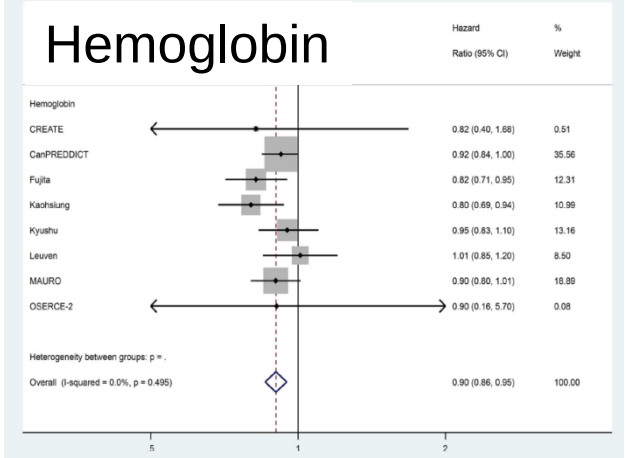
CV risk factors in CKD

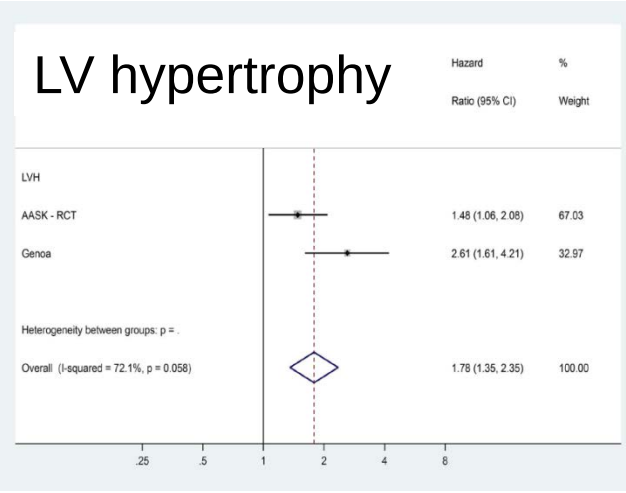
Study Name	Age	Gender	Ethnicity	DM	HTN	CVD	Lipids	BMI	Smoking	eGFR	Proteinuria	Total
AASK[25]	●	●	N/A	N/A	N/A		●			●	●	5
Ankara[26]	●	●		●	●				●	●		6
CARE FOR HOMe[19]	●	●	N/A	●		●				●	●	6
CanPREDDICT[27]	●			●	●	●				●		5
CREATE[39]	●	●		●	●	●						5
CRIC[29]	●	●	●	●	●	●^	●	●	●	●	●	11
CRISIS[30]	●	●	N/A	●	●	●			●	●*		6
Digitalis[31]	●	●	●	●	●	N/A		●				6
Fujita[32]	●	●		●		●				●	●	6
Genoa[33]	●	●	N/A	●	●	●	●			●	●	8
ICKD[20]	●	●		●	●	●	●	●	●	●	●	10
Kaohsiung[34]				●	●	●				●		4
Kyushu[21]	●		N/A		●	●		●		●		5
Leuven[22]	●	●	N/A		●	●				●	●	6
Madrid[23]	●		N/A	●		●				●		4
MAURO[24]	●	●	N/A	●	●		●	●	●	●	●	9
Naples[35]	●	●	N/A	●	●	●		●		●	●	8
OSERCE-2[36]	●		N/A	●	●	●	●		●	●		7
Pravastatin[37]	●		N/A	●	●	●	●		●			6
RRI[38]	●	●	●	●	●	●	●	●	●	●	●	11
TREAT[39]	●	●	●	N/A		●					●	5
Total	**95.2%**	**71.4%**	**40.0%**	**89.5%**	**80.0%**	**85.0%**	**38.1%**	**33.3%**	**38.1%**	**81.0%**	**52.4%**	

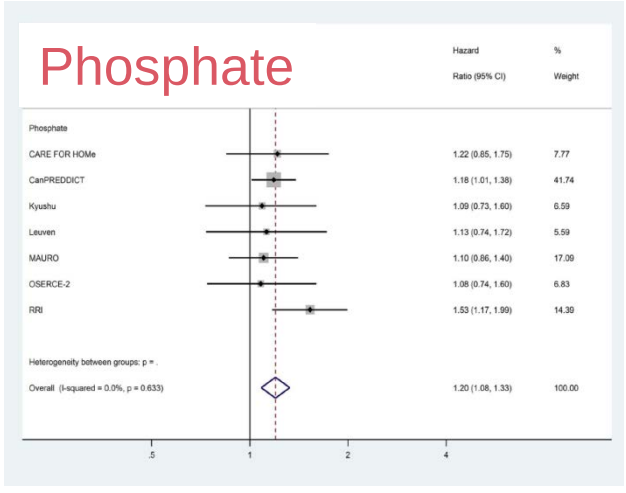
Major RW et al. ***PLoS ONE*** 2018; 13: e0192895

CV risk factors in CKD









Major RW et al. ***PLoS ONE*** 2018; 13: e0192895

Coronary artery calcification in CKD

Study design and patients

- Chronic Renal Insufficiency Cohort (**CRIC**) including 1,541 adults with an eGFR of 20–70 ml/min/1.73 m^2
- Coronary artery calcification was assessed with computer tomography
- **Incidence of CVD** (myocardial infarction, heart failure, stroke) and all-cause mortality were assessed during a follow-up of 5,9 years

Chen J et al. ***JAMA Cardiol*** 2017; 2: 635

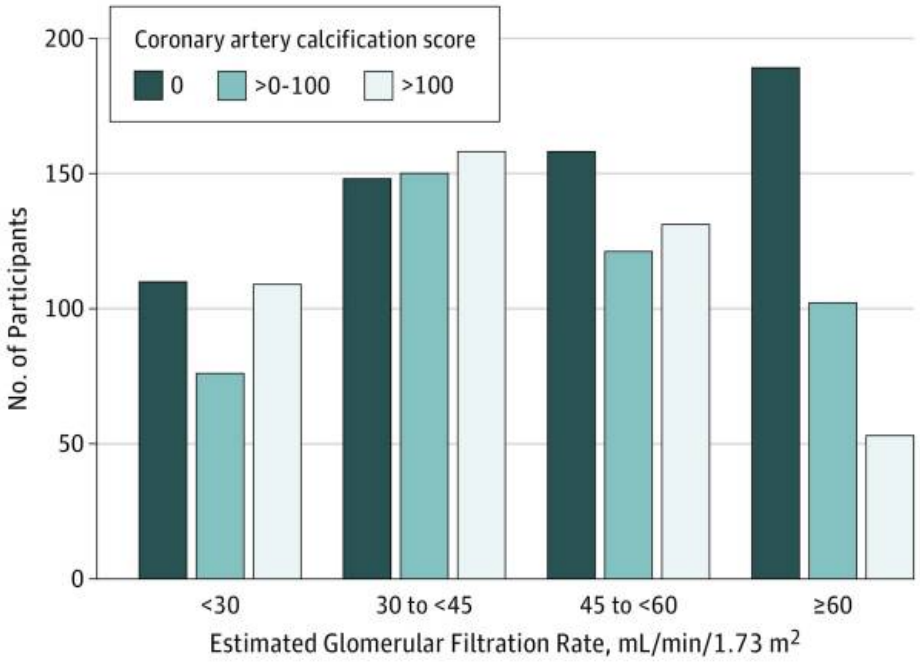
Coronary artery calcification in CKD

Study design and patients

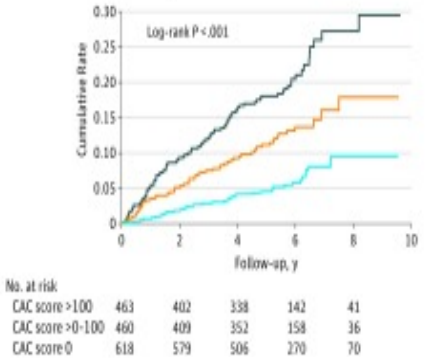
- The event rate was adjusted for
  - age, sex, race, site, education level, physical activity, total cholesterol, high-density lipoprotein cholesterol, systolic BP, antihypertensive treatment, smoking, diabetes, HbA_1c, body mass index
  - hs-CRP, phosphate, troponin T, NT pro-BNP, fibroblast growth factor 23, eGFR, proteinuria

Chen J et al. ***JAMA Cardiol*** 2017; 2: 635

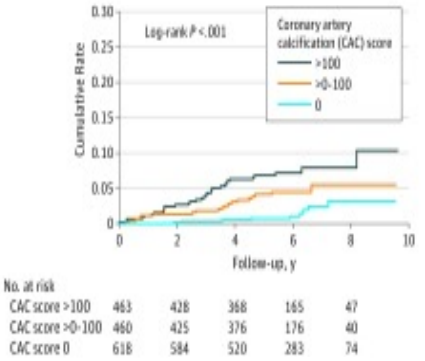
Coronary artery calcification in CKD



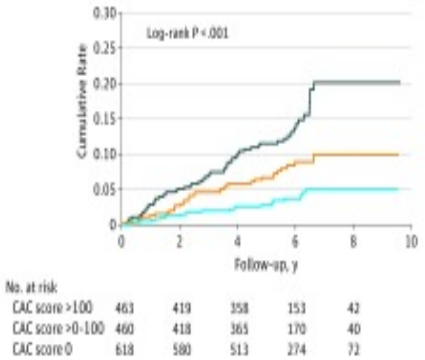
CVD



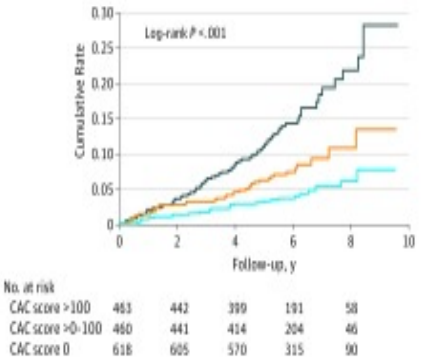
myocardial infarction



heart failure



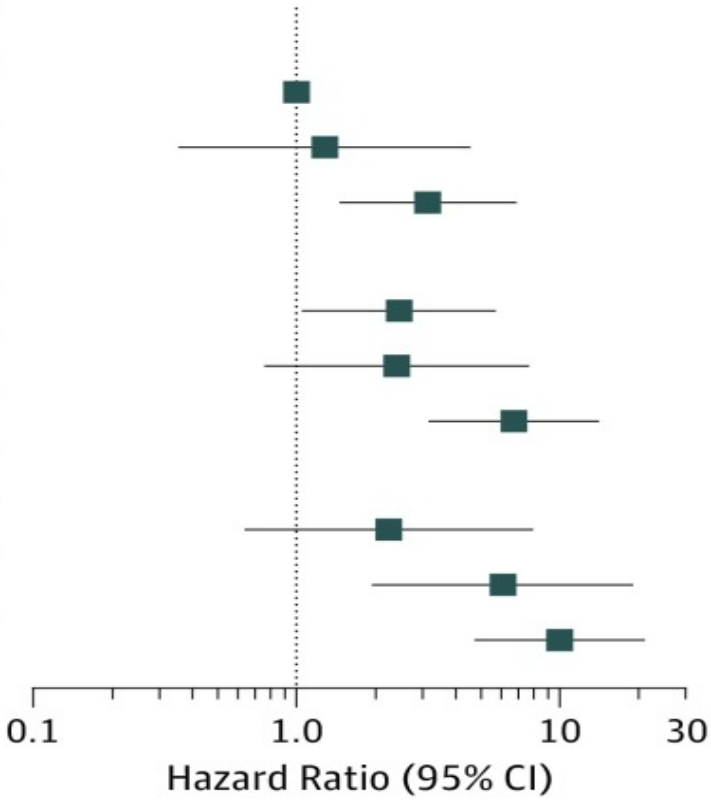
mortality



Chen J et al. ***JAMA Cardiol*** 2017; 2: 635

Coronary artery calcification in CKD

ACC/AHA Atherosclerotic Cardiovascular Disease Risk Score Category	Hazard Ratio (95% CI)
<5.0%	
CAC score 0	1 [Reference]
CAC score >0-100	1.28 (0.36-4.60)
CAC score >100	3.16 (1.46-6.84)
5.0%-7.5%	
CAC score 0	2.45 (1.05-5.71)
CAC score >0-100	2.41 (0.76-7.64)
CAC score >100	6.70 (3.18-14.10)
>7.5%	
CAC score 0	2.25 (0.64-7.93)
CAC score >0-100	6.09 (1.94-19.10)
CAC score >100	10.00 (4.76-21.00)

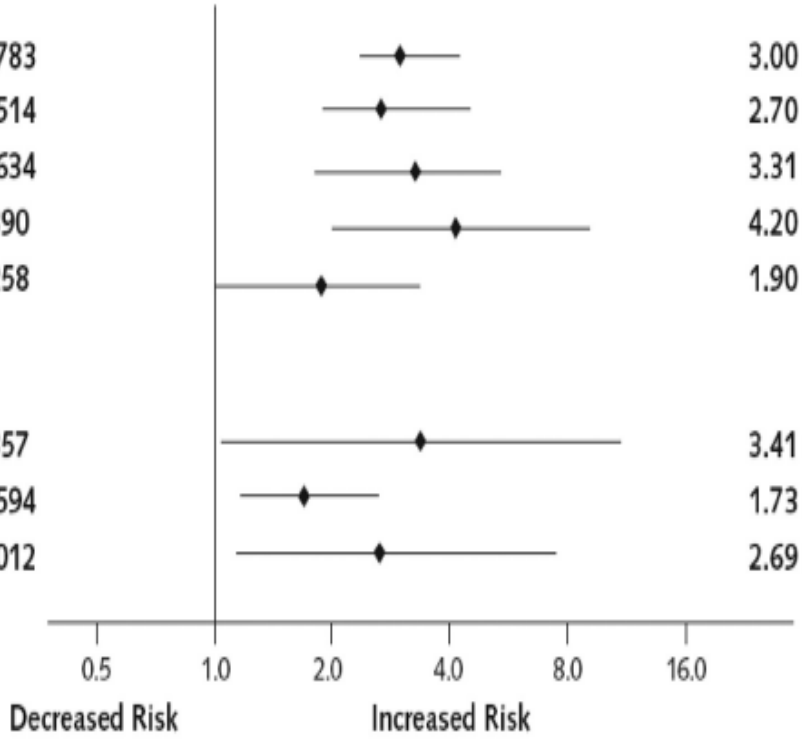


Chen J et al. ***JAMA Cardiol*** 2017; 2: 635

CV biomarkers in CKD

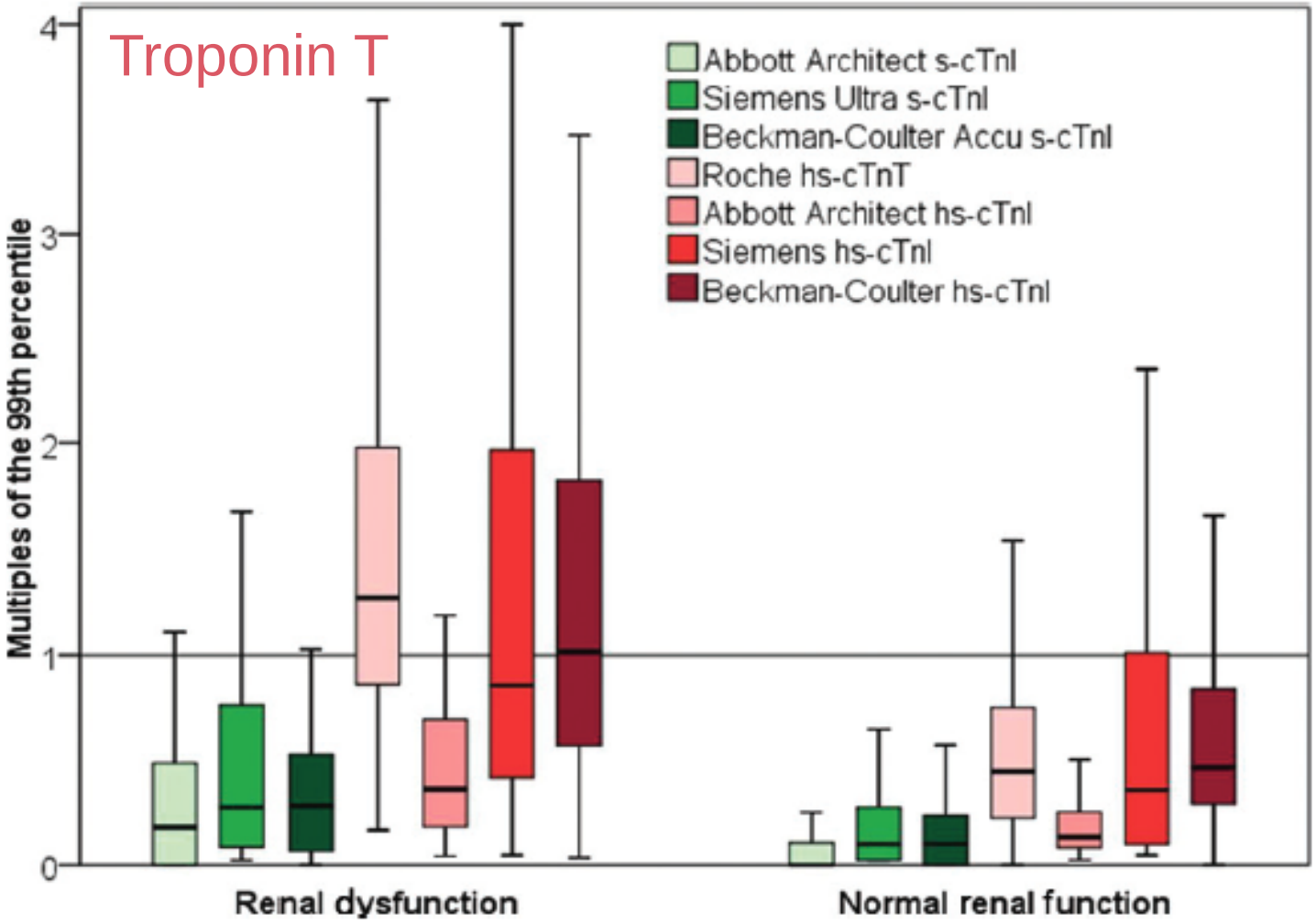
Troponin T

Outcome	Troponin assay	Studies, n	Patients, n	HR (95% CI)	SOE
Patients receiving dialysis					
All-cause mortality	cTnT	11	2783	3.00 (2.36–4.26)	Moderate
All-cause mortality	cTnI	7	1514	2.70 (1.90–4.57)	Moderate
CVD mortality	cTnT	5	1634	3.31 (1.81–5.43)	Moderate
CVD mortality	cTnI	3	390	4.20 (2.01–9.20)	Moderate
MACE	cTnT	1	258	1.90 (1.02–3.40)	Moderate
Patients not receiving dialysis					
All-cause mortality	cTnT	2	357	3.41 (1.06–10.99)	Moderate
All-cause mortality	cTnI	2	2594	1.73 (1.17–2.65)	Moderate
MACE	cTnT	4	2012	2.69 (1.14–7.60)	Moderate



DeFilippi CR & Herzog CA. ***Clin Chem*** 2017; 63: 59

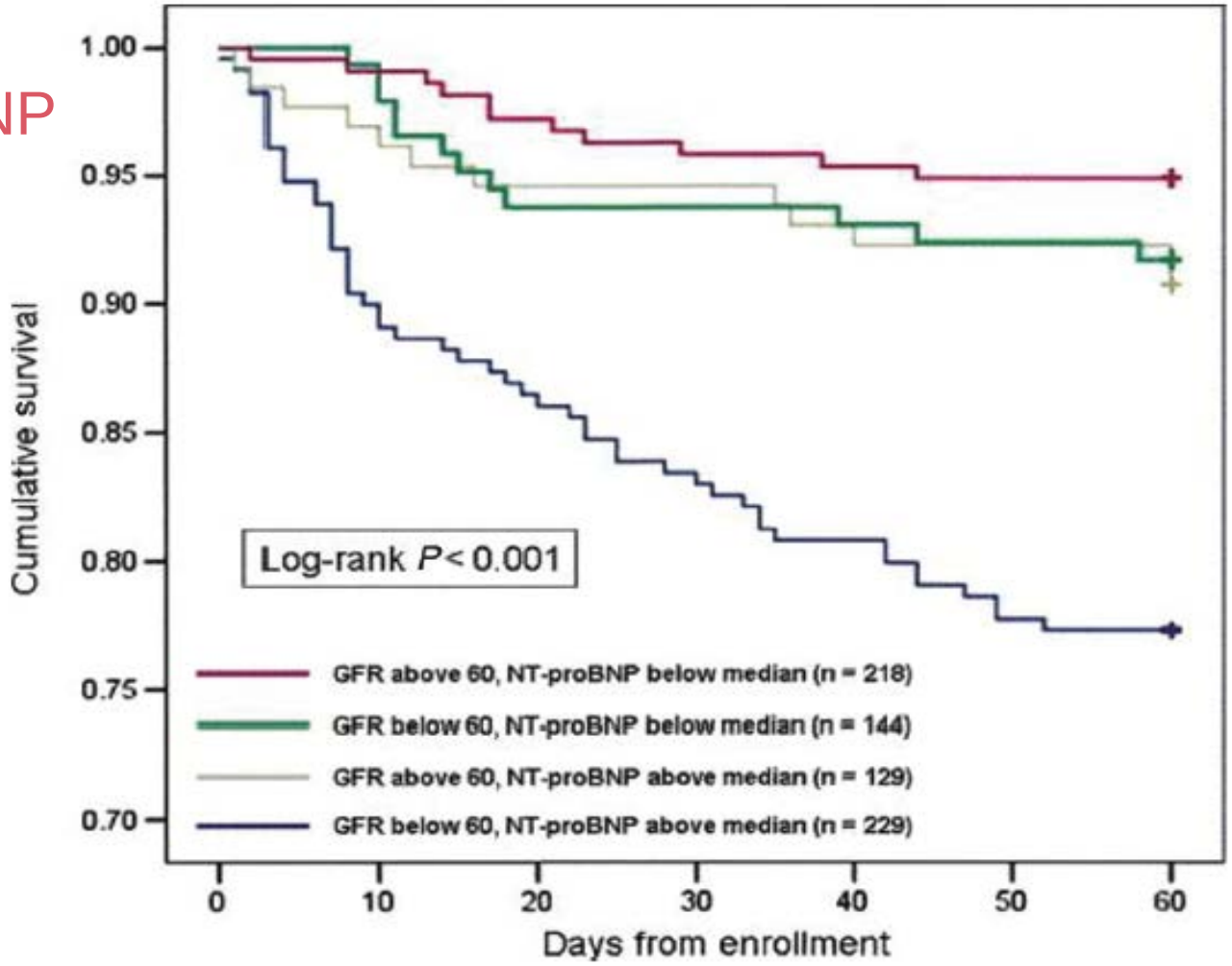
CV biomarkers in CKD



DeFilippi CR & Herzog CA. ***Clin Chem*** 2017; 63: 59

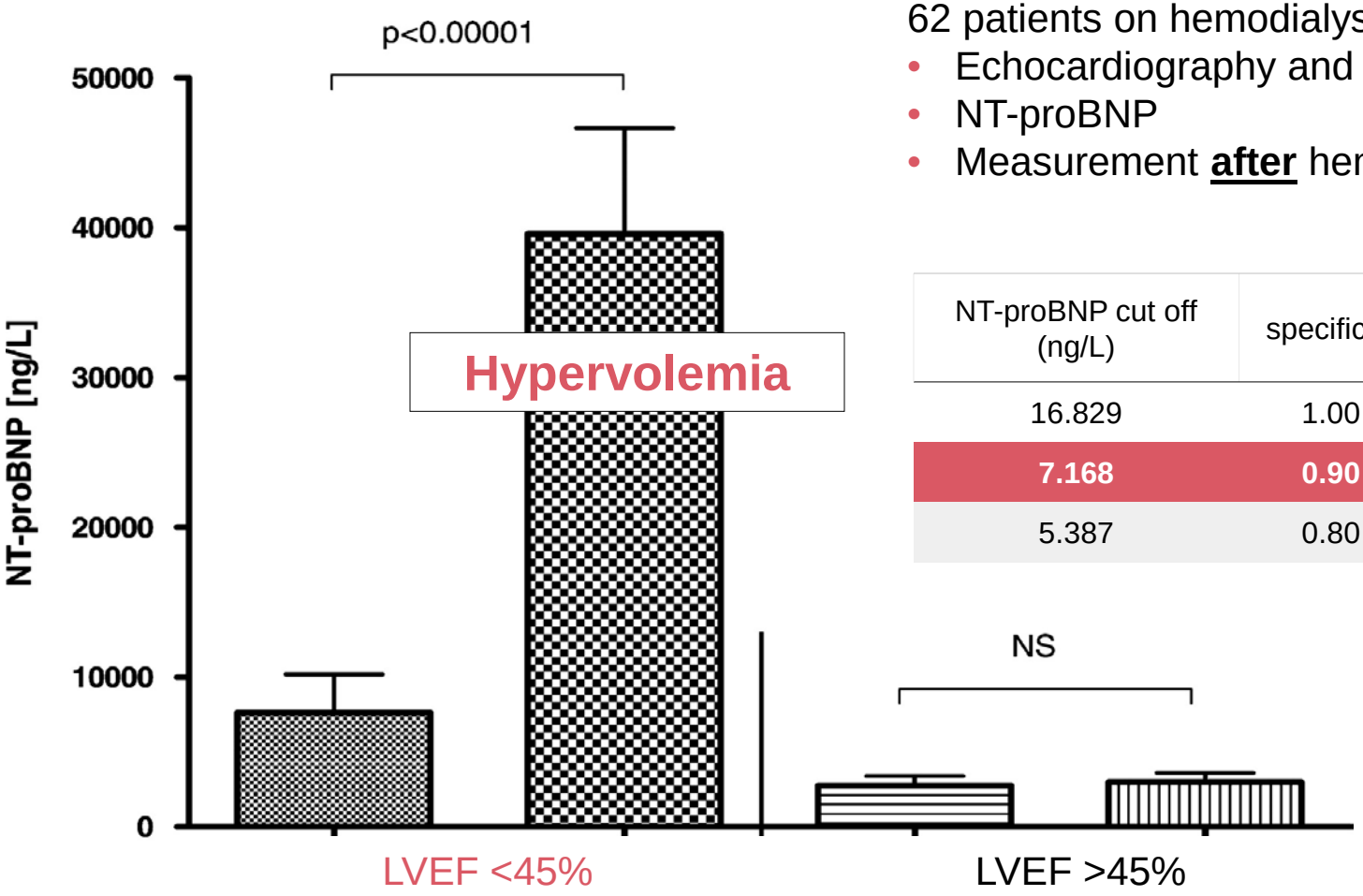
CV biomarkers in CKD

NT-proBNP



DeFilippi CR & Herzog CA. ***Clin Chem*** 2017; 63: 59

CV biomarkers in CKD



62 patients on hemodialysis

- Echocardiography and BIS
- NT-proBNP
- Measurement **after** hemodialysis

NT-proBNP cut off (ng/L)	specificity	sensitivity
16.829	1.00	0.65
7.168	**0.90**	**0.79**
5.387	0.80	0.93

David S et al. ***Nephrol Dial Transplant*** 2008; 23: 1370

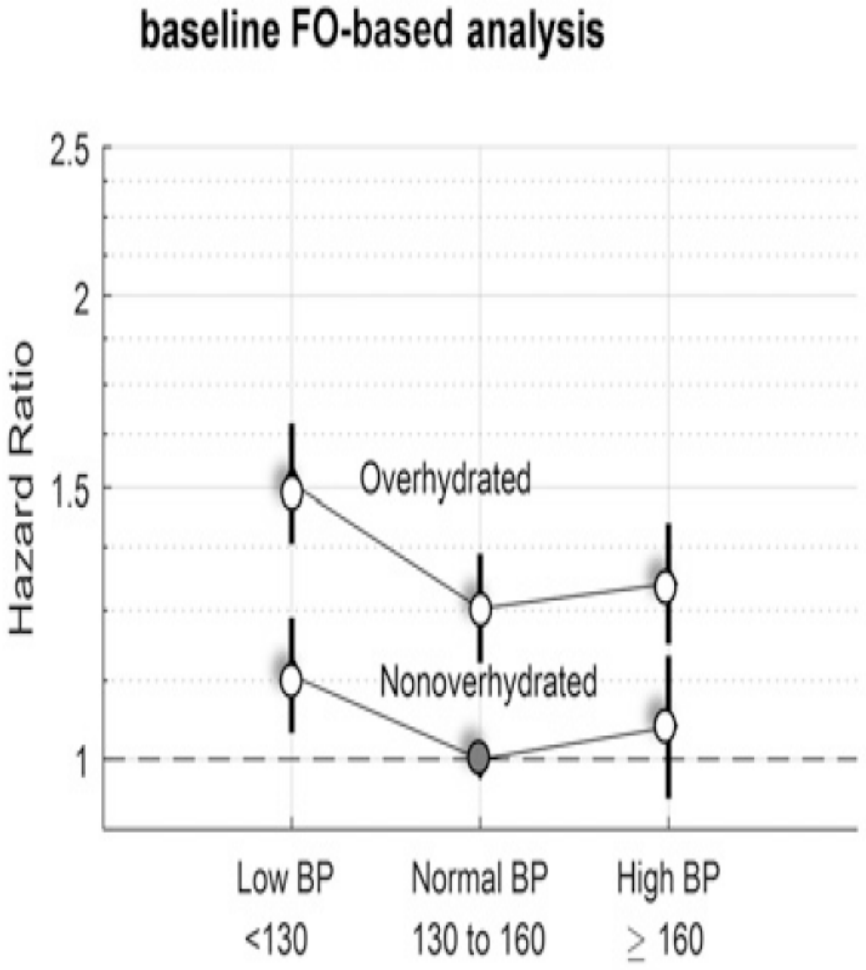
Volume and mortality in CKD

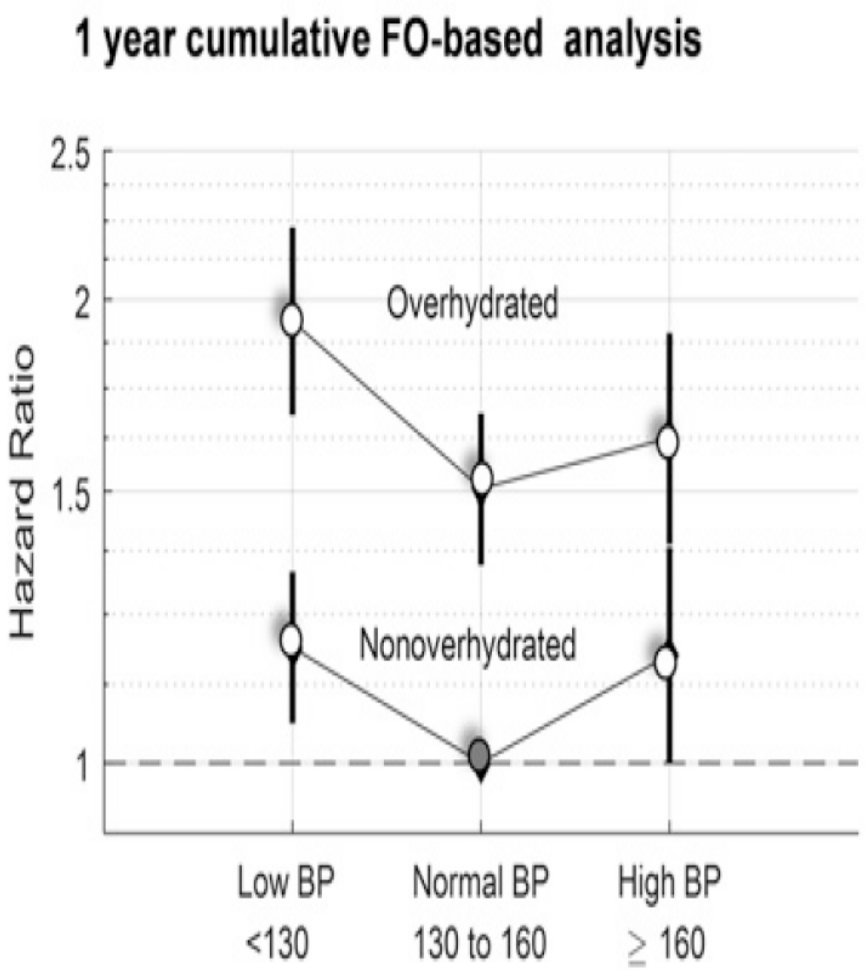
Study design and patients

- 39,566 hemodialysis patients from a large dialysis network (26 countries)
- Assessment of volume status at baseline and during follow-up using bioelectrical impedance spectroscopy (>200,000 measurements!)
- All-cause mortality was assessed during 12 months of follow-up

Zoccali C et al. ***J Am Soc Nephrol*** 2017; 28: 2491

Volume and mortality CKD





Zoccali C et al. ***J Am Soc Nephrol*** 2017; 28: 2491

Volume and mortality in CKD

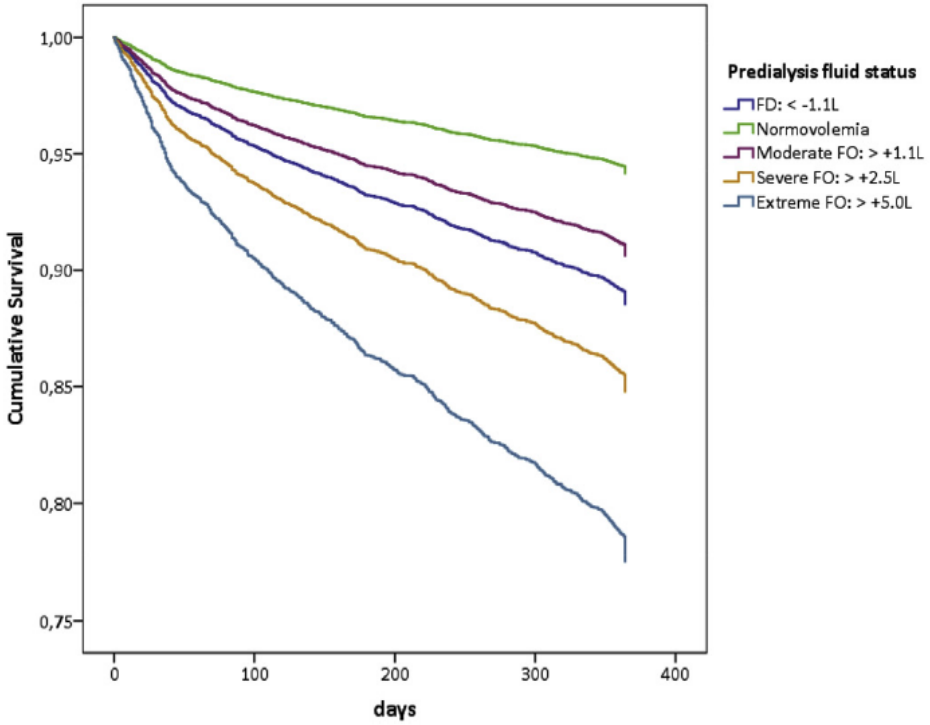
Study design and patients

- 8,883 hemodialysis patients from the MONDO database
- Assessment of baseline serum hs-CRP and volume status using bioelectrical impedance spectroscopy
- All-cause mortality was assessed during 12 months of follow-up

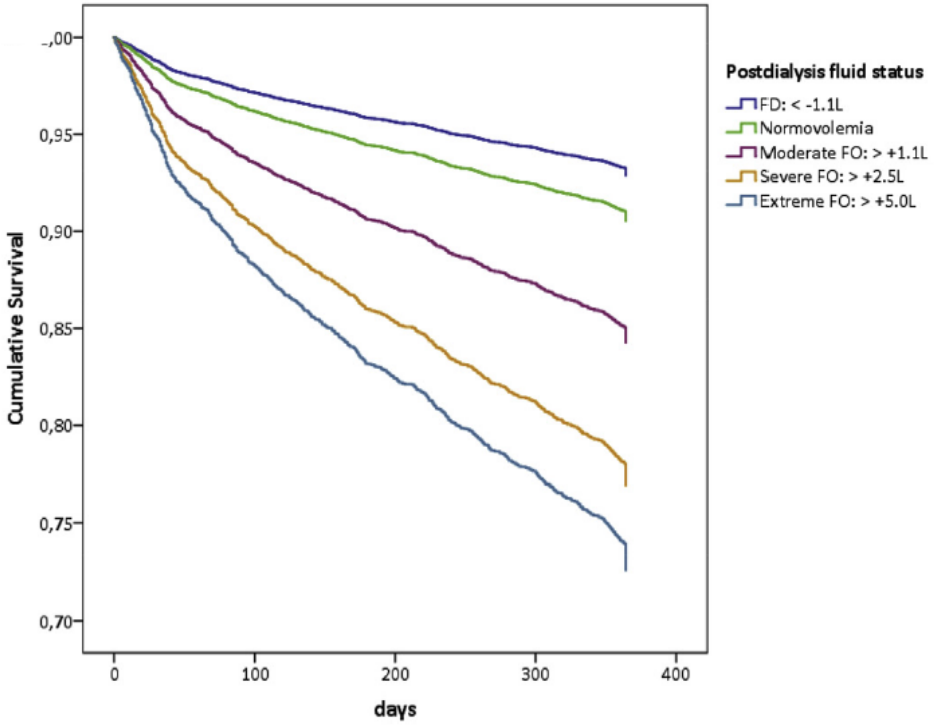
Dekker MJE et al. ***Kidney Int*** 2017; 91: 1214

Volume and mortality CKD

Pre-dialysis BIS

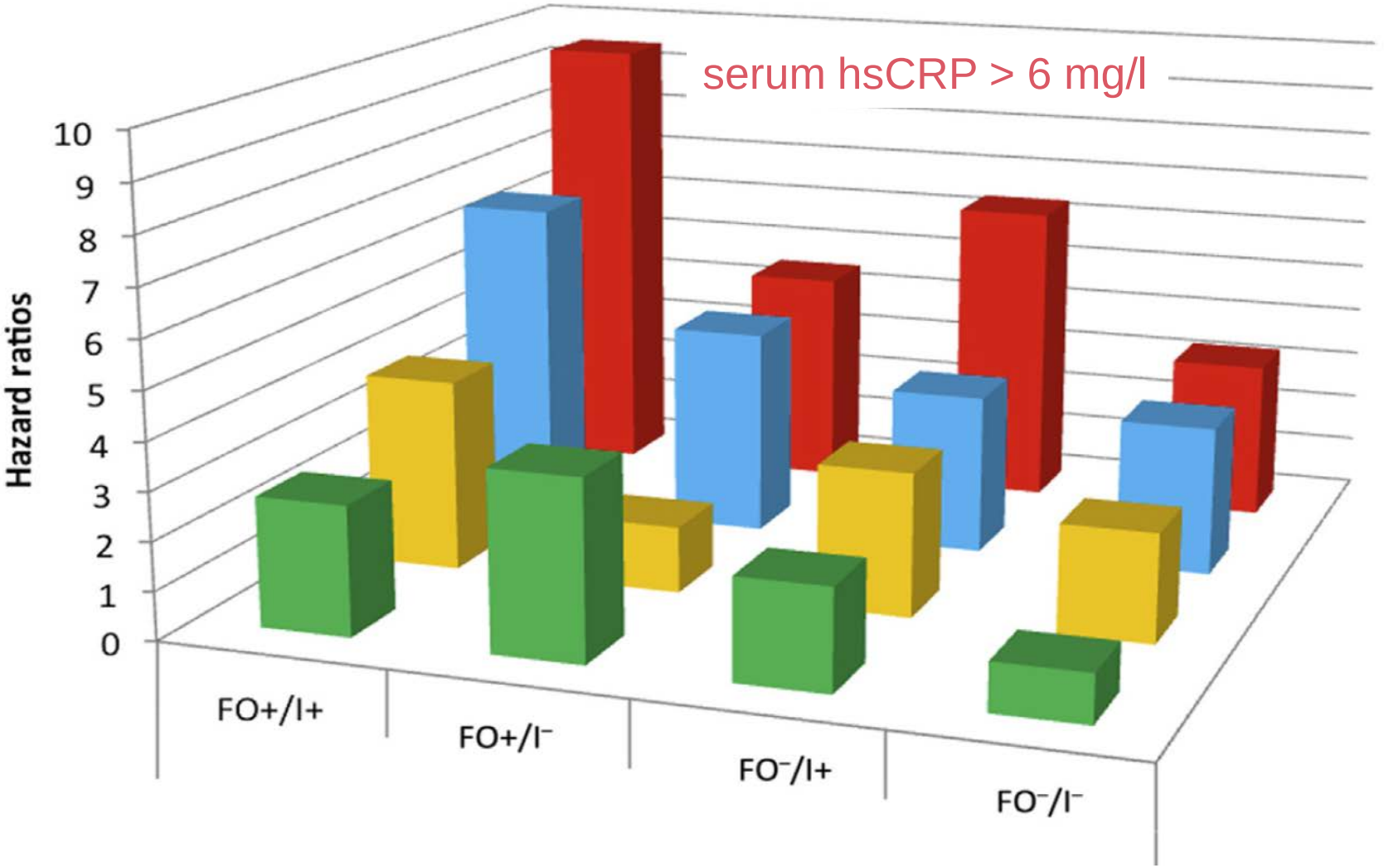


Post-dialysis BIS



Dekker MJE et al. ***Kidney Int*** 2017; 91: 1214

Volume and mortality CKD



Dekker MJE et al. ***Kidney Int*** 2017; 91: 1214

ICD and CV mortality in CKD

Study design and patients

- Kaiser Permanente health care beneficiaries with heart failure **(LVEF <40%)** and CKD (eGFR <60 ml/min/1.73 m^2)
- Patients who received and did not receive an **ICD** were matched (1:3) on CKD status
- All-cause death, hospitalizations due to heart failure, and any-cause hospitalizations were assessed

Bansal N et al. ***JAMA Int Med*** 2018; 178: 390

ICD and CV mortality in CKD

Results and interpretation

- 5,877 matched adults with CKD (1,556 with and 4,321 without an ICD) were identified
- **No difference in all-cause mortality** (HR 0.96; 95% CI 0.87–1.06), but ICD placement was associated with **increased risk** of subsequent hospitalization due to heart failure and any-cause hospitalization among CKD patients

Bansal N et al. ***JAMA Int Med*** 2018; 178: 390

Take-Home Message

- CV morbidity and mortality increase with progressive CKD
- CV risk biomarkers such as NT-proBNP can be used in CKD patients with appropriate interpretation
- Coronary artery calcification may be assessed in CKD patients for risk stratification

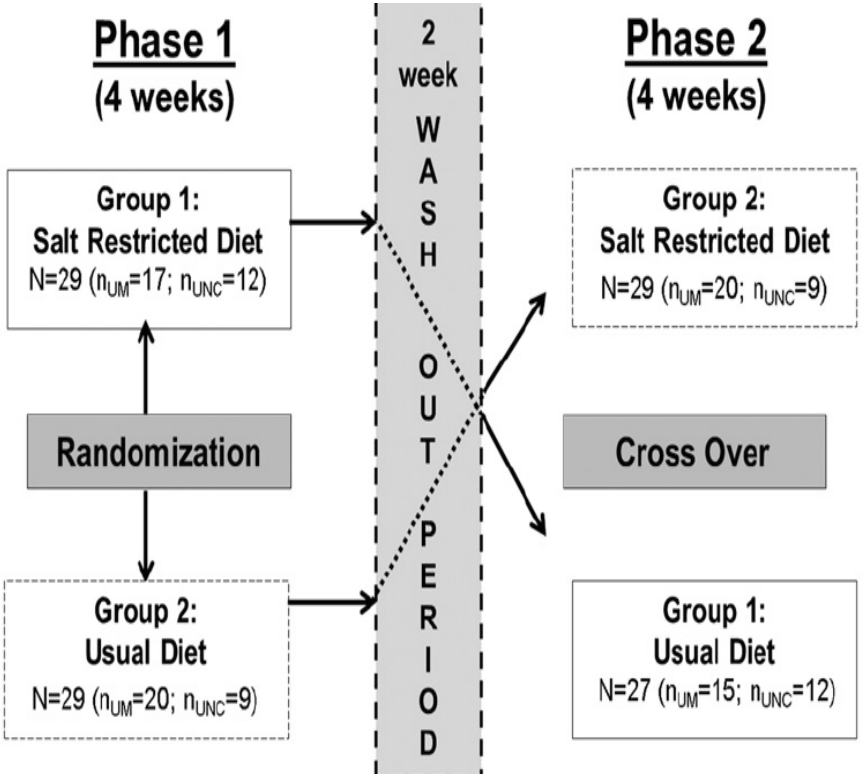
Volume & blood pressure control in CKD

State of the art

- CKD patients are characterized by volume expansion due to NaCl retention
- CKD patients may benefit from BP reduction, but the target level is a matter of debate
- It is unclear if intensive BP reduction in CKD patients has adverse effects

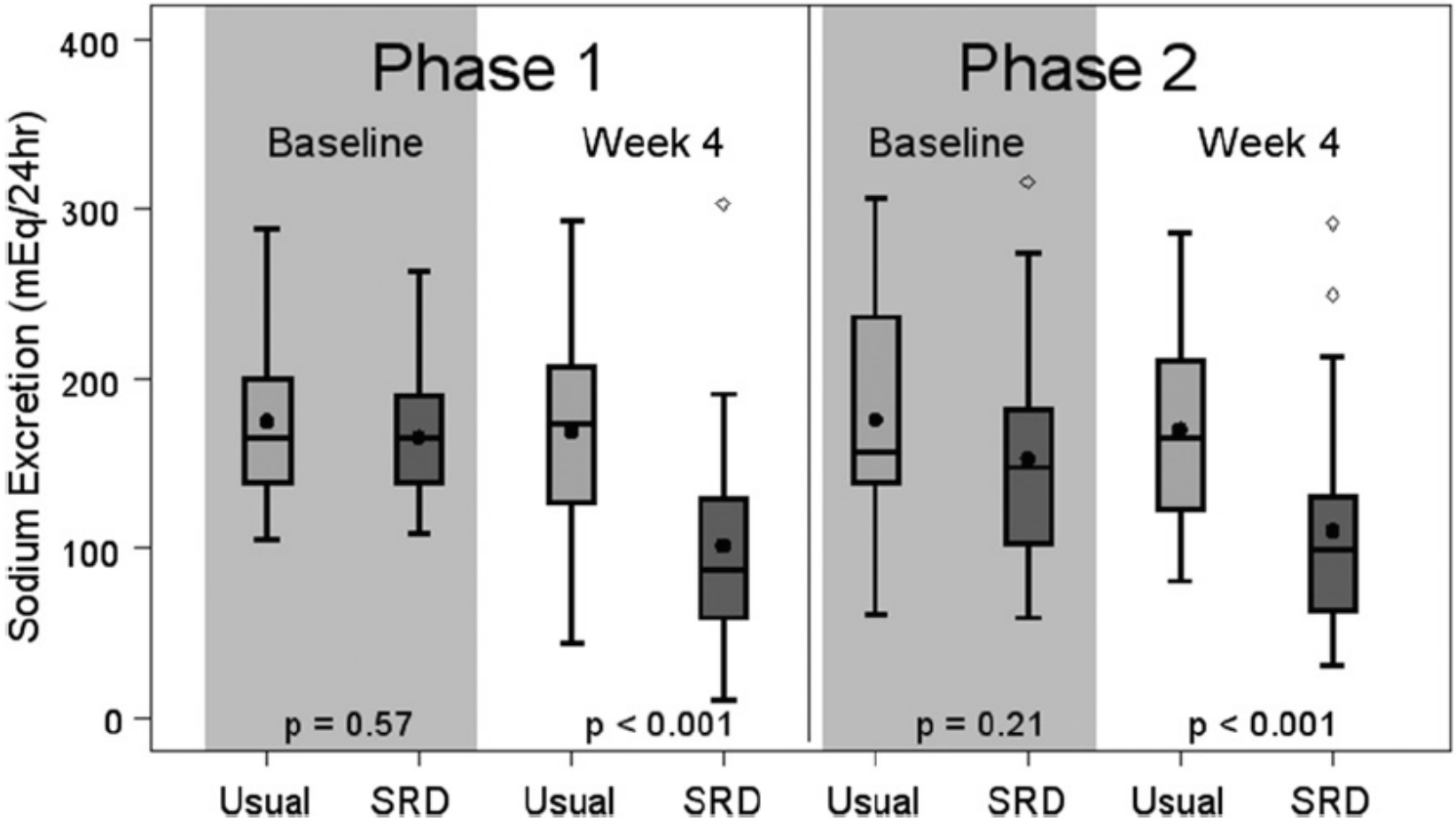
NaCl restriction in CKD

- 58 CKD stage 3–4 patients
- 2 x 4 week treatments
- Usual vs. restricted (<100 mmol/day) salt intake
- Hydration status assessed by bioelectrical impedance spectroscopy



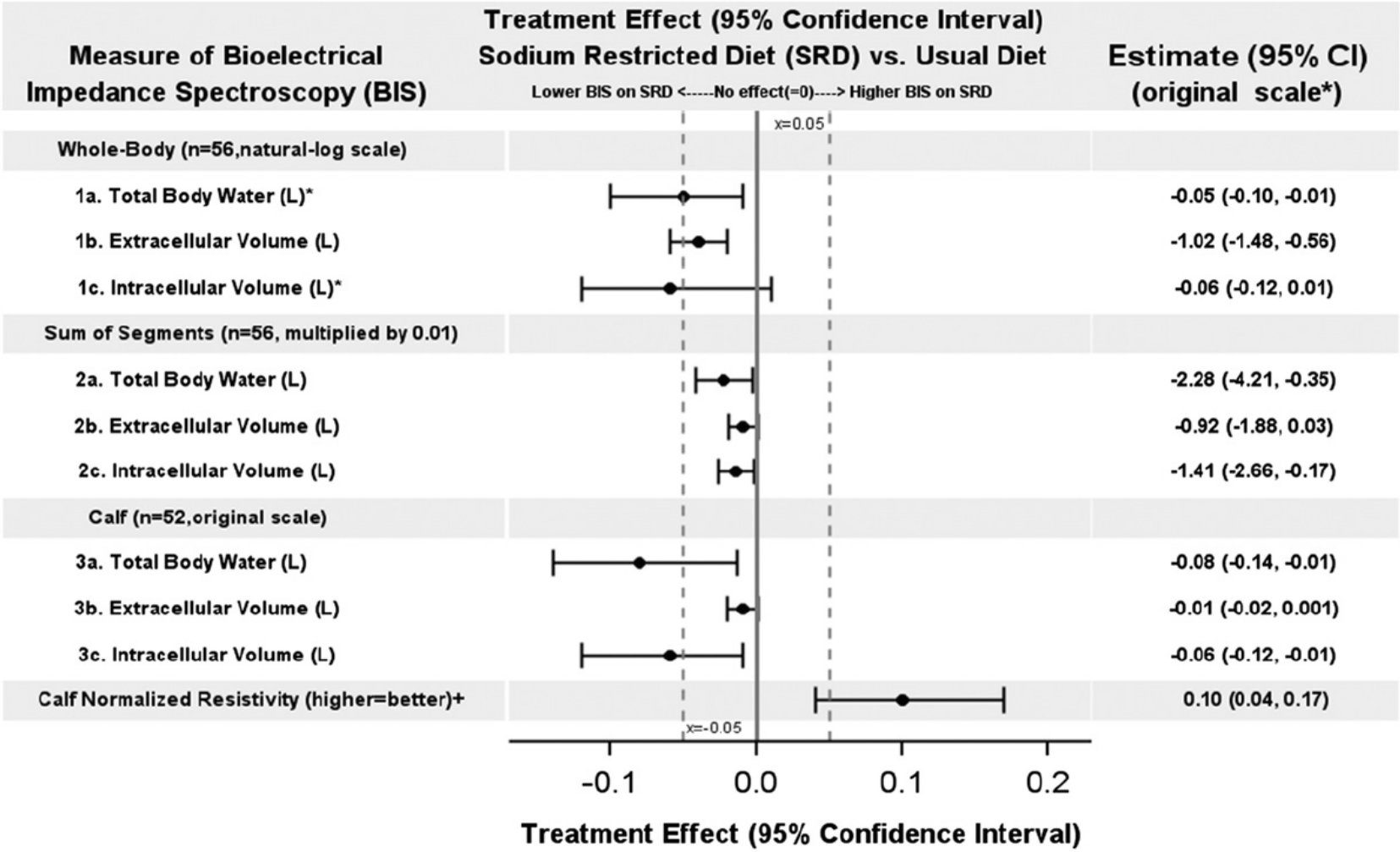
Saran R et al. ***Clin J Am Soc Nephrol*** 2017; 12: 399

NaCl restriction in CKD



Saran R et al. ***Clin J Am Soc Nephrol*** 2017; 12: 399

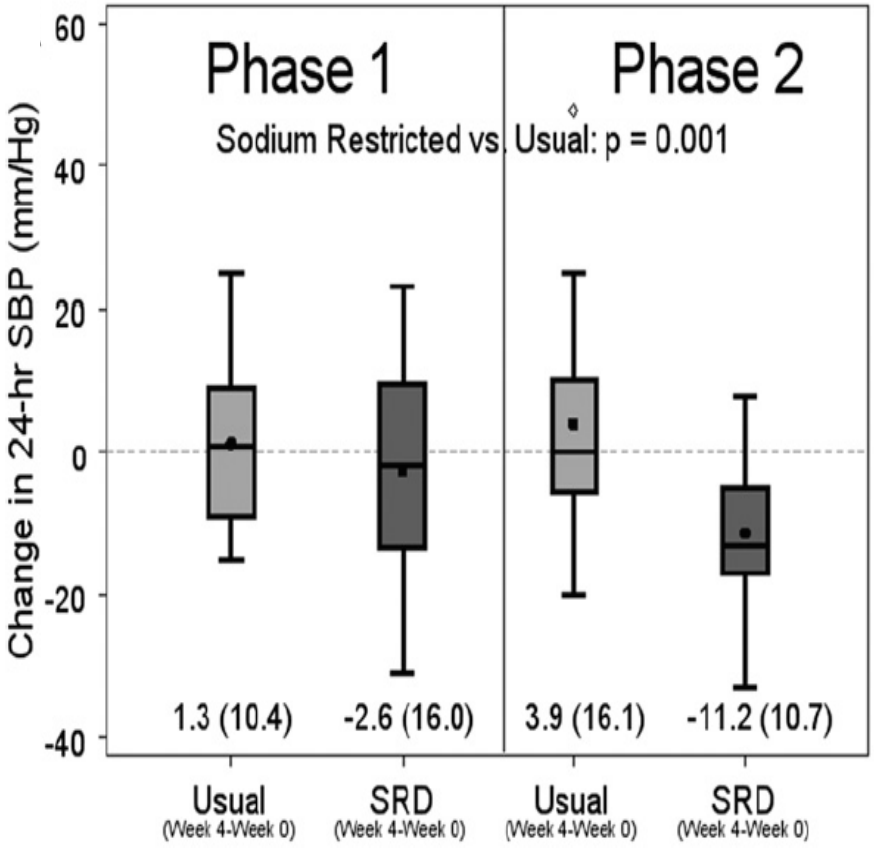
NaCl restriction and volume in CKD



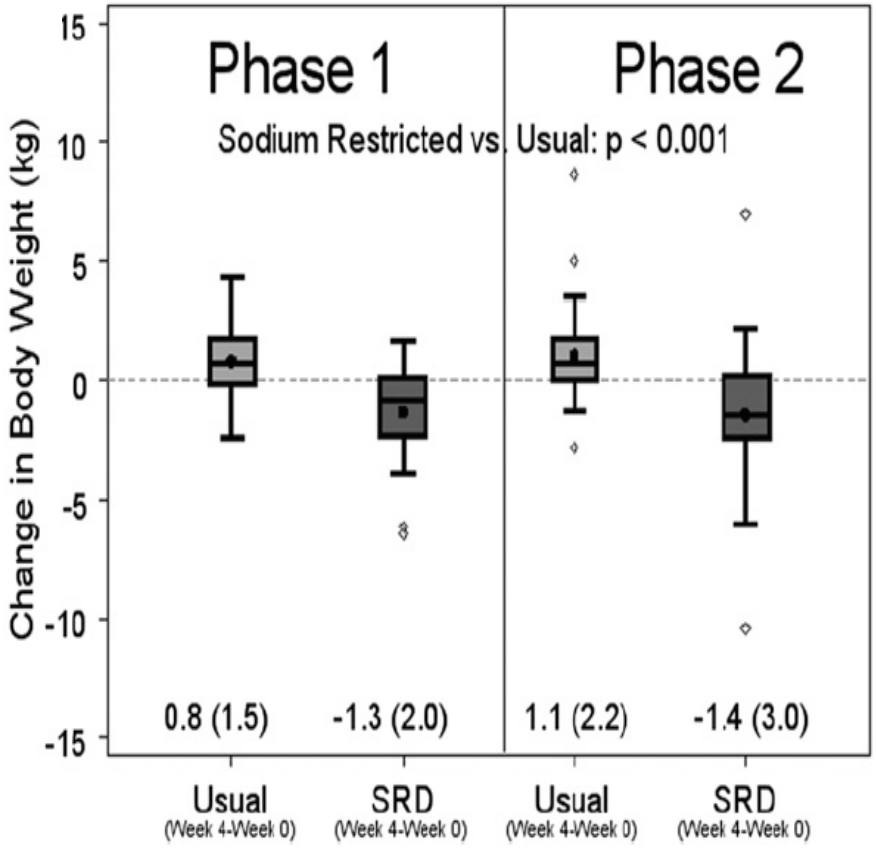
Saran R et al. ***Clin J Am Soc Nephrol*** 2017; 12: 399

NaCl restriction and BP in CKD

Blood pressure



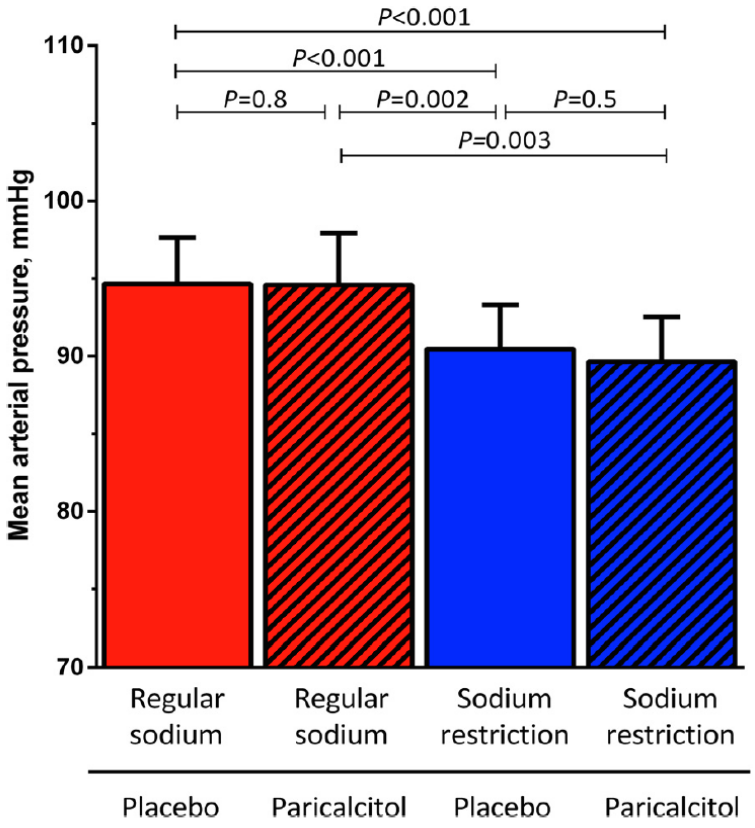
Body weight



Saran R et al. ***Clin J Am Soc Nephrol*** 2017; 12: 399

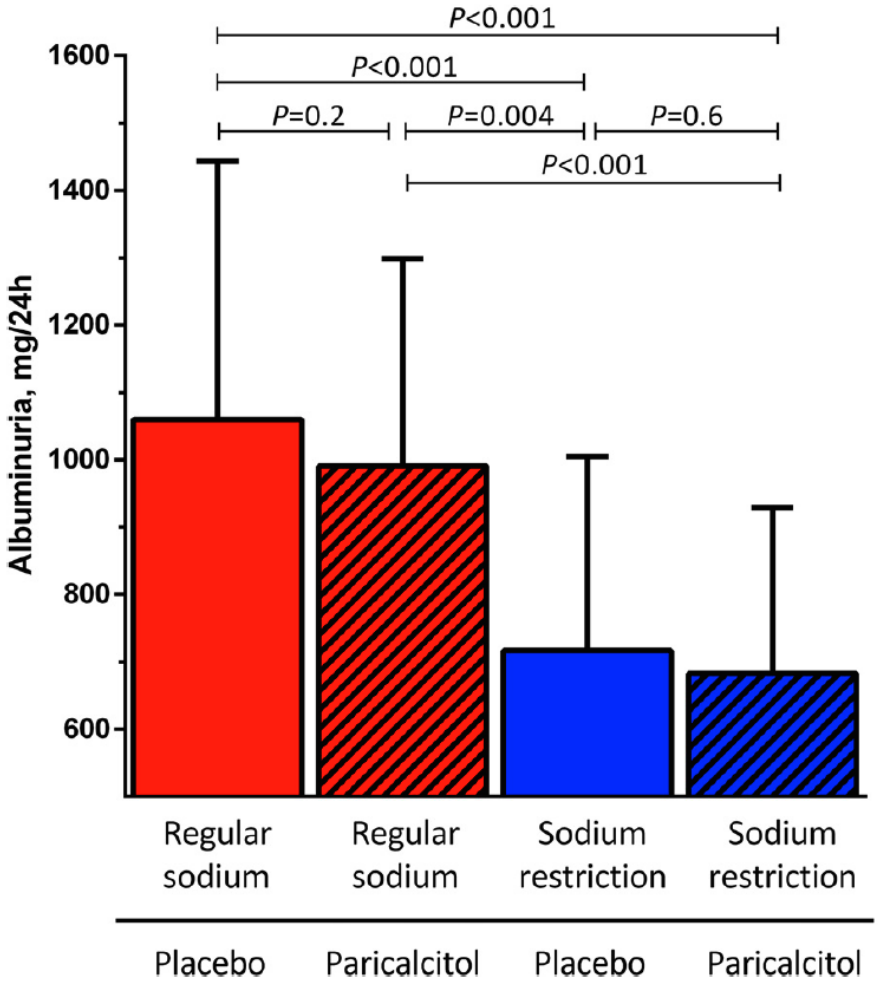
NaCl restriction + Vitamin D in CKD

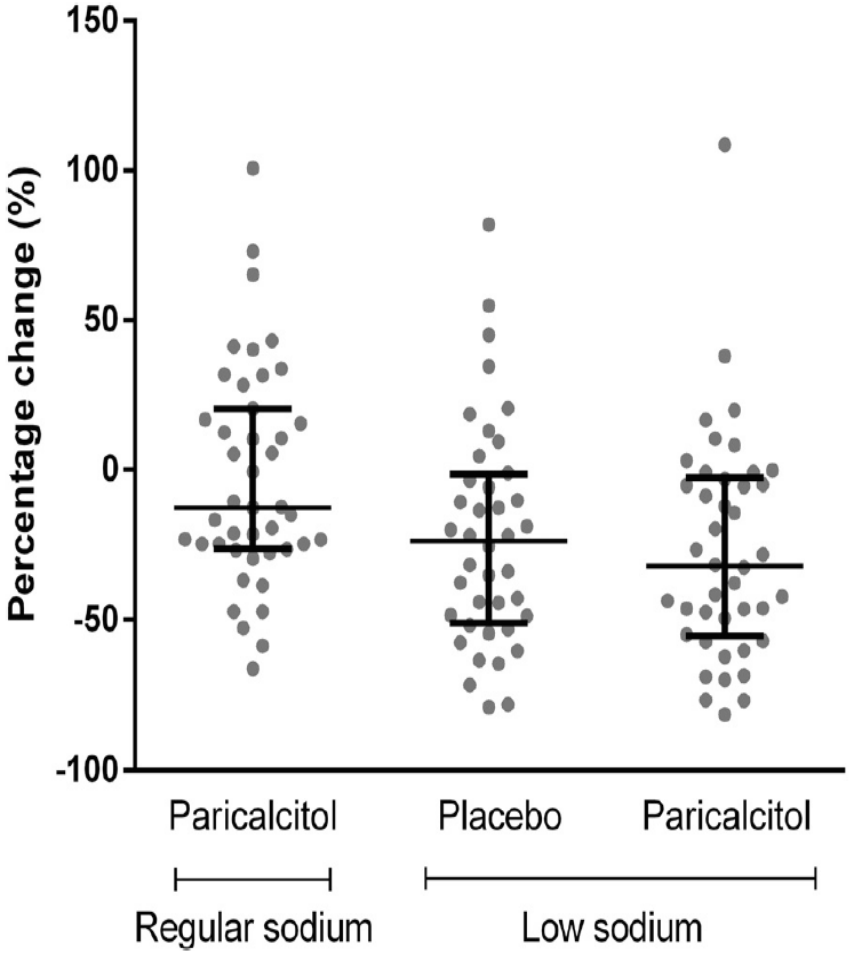
- 45 CKD stage 1–3 patients and albuminuria > 300 mg/day
- Fix dose ACEI (10 mg ramipril)
- 4 x 8 week treatments
- Normal (200 mmol/day) vs. low (50 mmol/day) salt intake
- Paracalcitol (2 µg/day) vs. placebo



Keyzer CA et al. ***J Am Soc Nephrol*** 2017; 28: 1296

NaCl restriction + Vitamin D in CKD





Keyzer CA et al. ***J Am Soc Nephrol*** 2017; 28: 1296

SPRINT Trial

Intensive vs. standard BP

Study design and patients

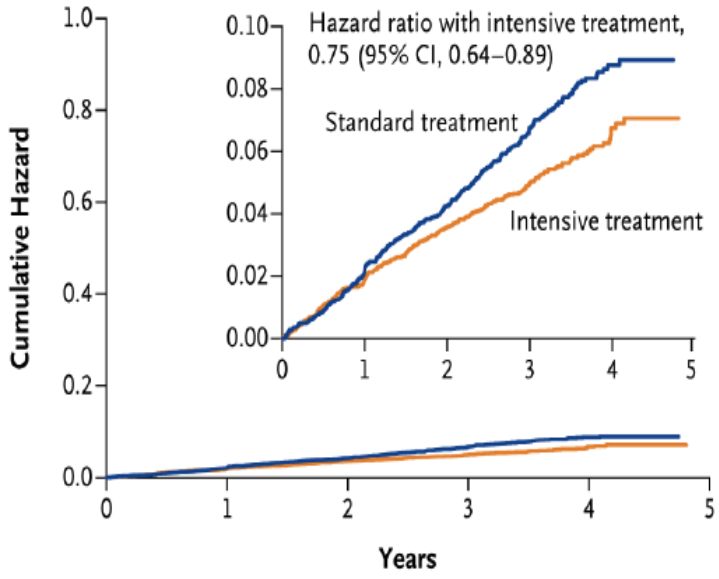
- 9,361 persons with a systolic BP of >130 mm Hg and an increased CV risk, but **without diabetes**
- Randomized comparison of 2 systolic BP targets:
  - **<120 mmHg** (intensive treatment)
  - **<140 mmHg** (standard treatment)
- Primary composite outcome: myocardial infarction, stroke, heart failure, or death from CV causes

SPRINT Research Group. ***N Engl J Med*** 2015; 373: 2103

SPRINT Trial

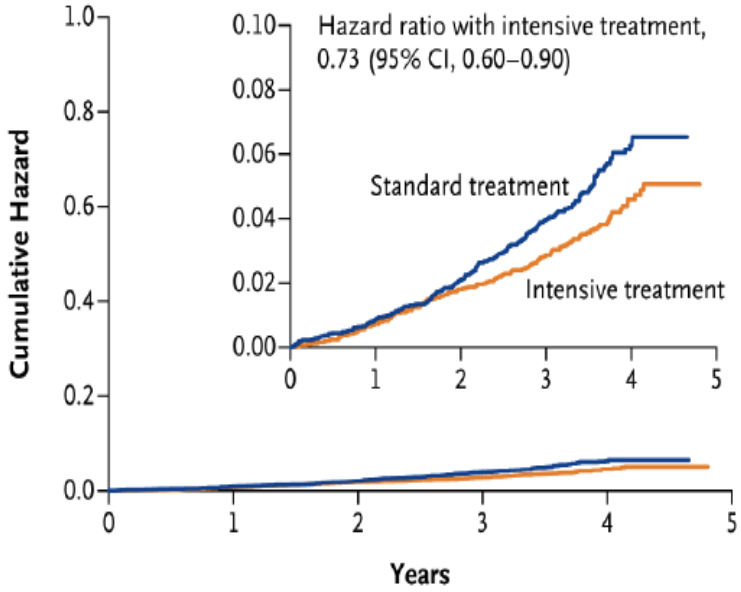
Intensive vs. standard BP

Primary outcome



No. at Risk					
Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

Death from any cause



No. at Risk					
Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

SPRINT Research Group. ***N Engl J Med*** 2015; 373: 2103

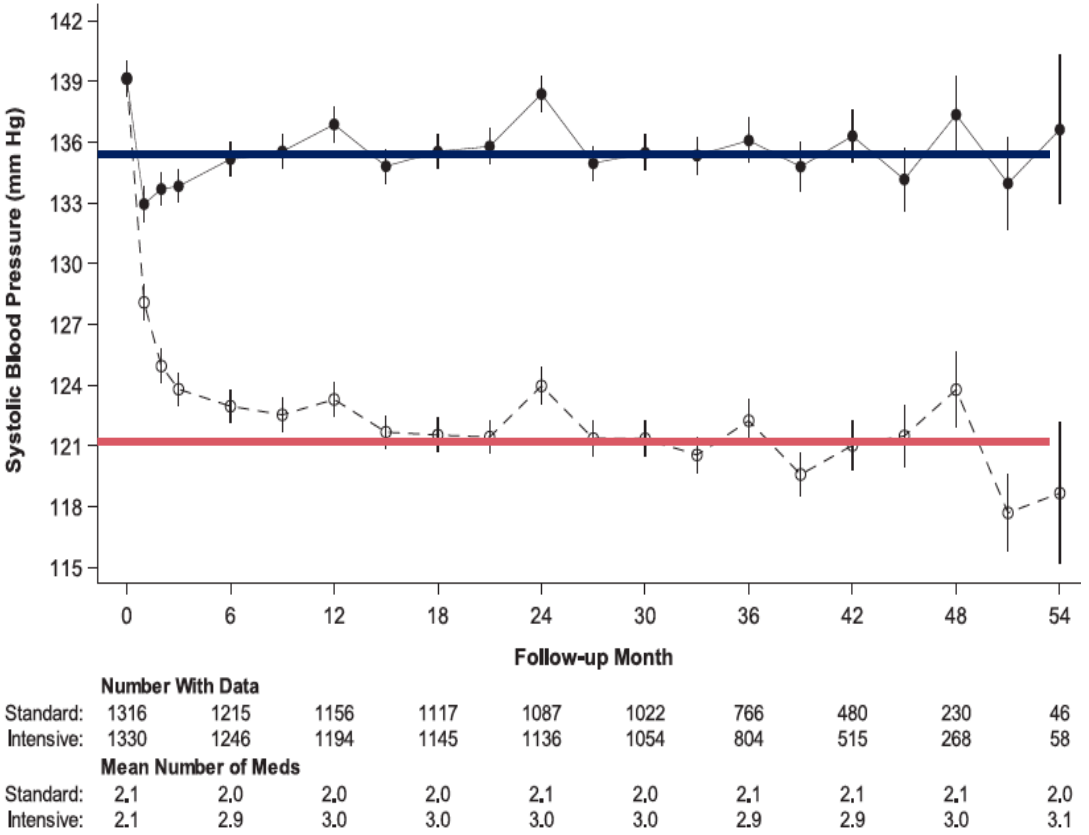
SPRINT Trial

Intensive BP treatment in CKD

Inclusion criteria:

- Hypertension
- High CV risk
- CKD stage 3-5
- Proteinuria <1g/day
- No diabetes

Total of 2,646 patients



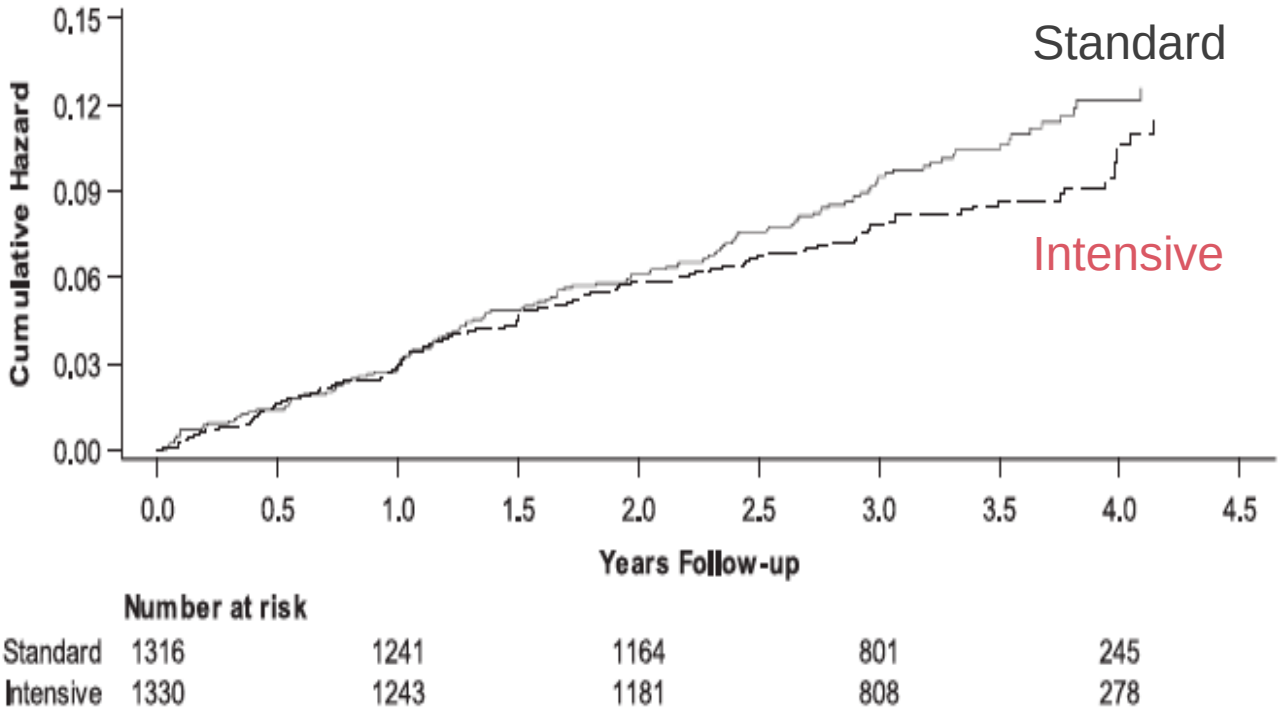
Cheung AK et al. ***J Am Soc Nephrol*** 2017; 28: 2812

SPRINT Trial

Intensive BP treatment in CKD

Primary CV outcome

HR 0.81 (95% CI 0.63-1.05)



2,646 patients

Cheung AK et al. ***J Am Soc Nephrol*** 2017; 28: 2812

Standard vs. lower BP in CKD

Study design and patients

- Meta-analysis of 18 randomized controlled trials (until June 2016) with **15,924 CKD patients stage 3–5**, but not on renal replacement therapy

- Comparison of two defined BP targets:
  - active BP treatment vs. placebo or no treatment
  - intensive vs. less intensive BP control

- **Primary outcome mortality** (total of 1,293 deaths)

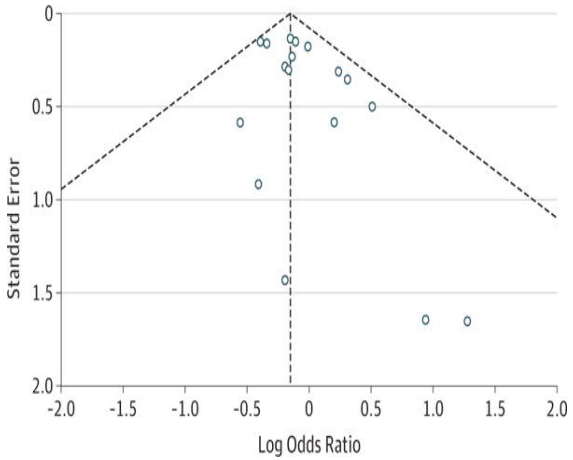
Malhotra R et al. ***JAMA Int Med*** 2017; 177: 1498

Standard vs. lower BP in CKD

Results

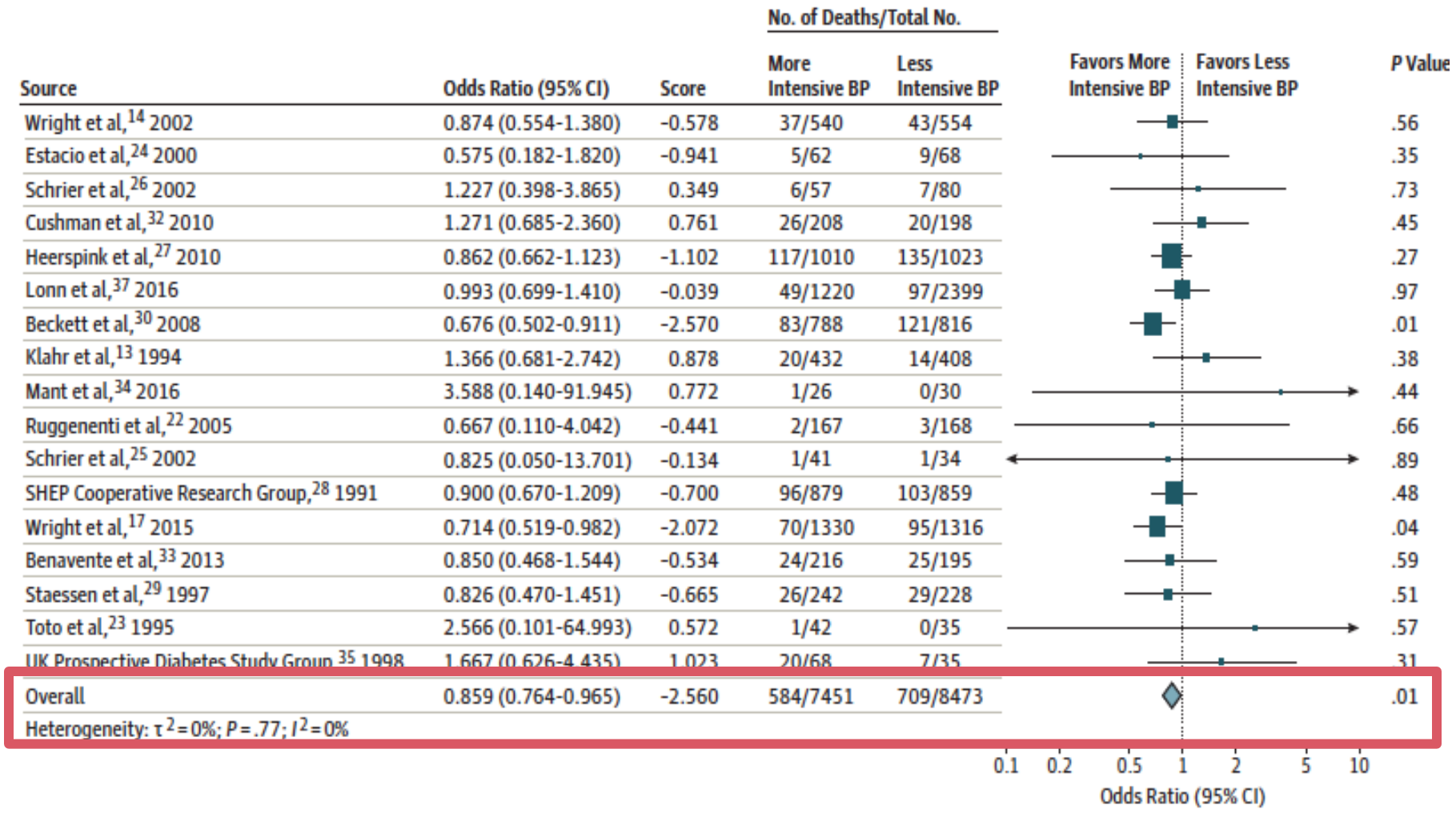
- Systolic BP was initially 148 mmHg, systolic BP reduction was **–8 mmHg** (standard) vs. **–16 mmHg** (lower)

- **Mortality** in the “intensively” treated group was **14% lower**, without significant heterogeneity across studies



Malhotra R et al. ***JAMA Int Med*** 2017; 177: 1498

Standard vs. lower BP in CKD



Source	Odds Ratio (95% CI)	Score	No. of Deaths/Total No. More Intensive BP	No. of Deaths/Total No. Less Intensive BP	P Value
Wright et al,[14] 2002	0.874 (0.554-1.380)	-0.578	37/540	43/554	.56
Estacio et al,[24] 2000	0.575 (0.182-1.820)	-0.941	5/62	9/68	.35
Schrier et al,[26] 2002	1.227 (0.398-3.865)	0.349	6/57	7/80	.73
Cushman et al,[32] 2010	1.271 (0.685-2.360)	0.761	26/208	20/198	.45
Heerspink et al,[27] 2010	0.862 (0.662-1.123)	-1.102	117/1010	135/1023	.27
Lonn et al,[37] 2016	0.993 (0.699-1.410)	-0.039	49/1220	97/2399	.97
Beckett et al,[30] 2008	0.676 (0.502-0.911)	-2.570	83/788	121/816	.01
Klahr et al,[13] 1994	1.366 (0.681-2.742)	0.878	20/432	14/408	.38
Mant et al,[34] 2016	3.588 (0.140-91.945)	0.772	1/26	0/30	.44
Ruggenenti et al,[22] 2005	0.667 (0.110-4.042)	-0.441	2/167	3/168	.66
Schrier et al,[25] 2002	0.825 (0.050-13.701)	-0.134	1/41	1/34	.89
SHEP Cooperative Research Group,[28] 1991	0.900 (0.670-1.209)	-0.700	96/879	103/859	.48
Wright et al,[17] 2015	0.714 (0.519-0.982)	-2.072	70/1330	95/1316	.04
Benavente et al,[33] 2013	0.850 (0.468-1.544)	-0.534	24/216	25/195	.59
Staessen et al,[29] 1997	0.826 (0.470-1.451)	-0.665	26/242	29/228	.51
Toto et al,[23] 1995	2.566 (0.101-64.993)	0.572	1/42	0/35	.57
UK Prospective Diabetes Study Group [35] 1998	1.667 (0.626-4.435)	1.023	20/68	7/35	.31
Overall	0.859 (0.764-0.965)	-2.560	584/7451	709/8473	.01
Heterogeneity: $\tau^2 = 0\%$; $P = .77$; $I^2 = 0\%$					

Malhotra R et al. ***JAMA Int Med*** 2017; 177: 1498

Standard vs. lower BP in CKD

Limitations

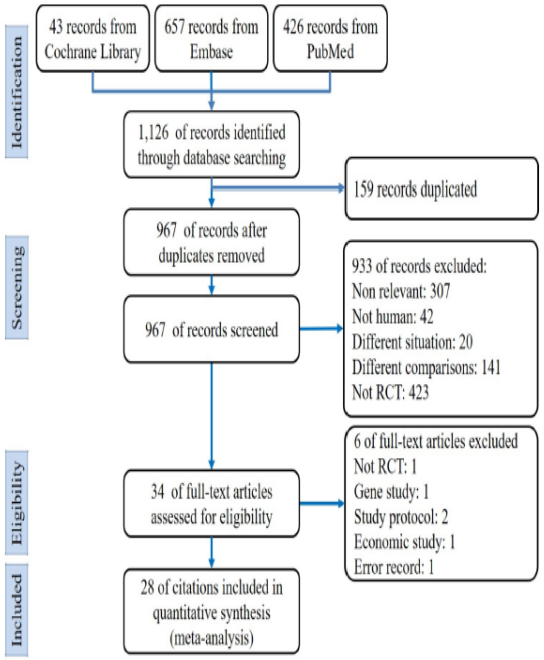
- Only mortality as an endpoint (not progression)
- No adverse effects assessed
- Different treatments (medication vs. placebo, lower vs. higher BP)
- Different levels of BP target

Malhotra R et al. ***JAMA Int Med*** 2017; 177: 1498

CCB vs. ACEI/ARB in CKD

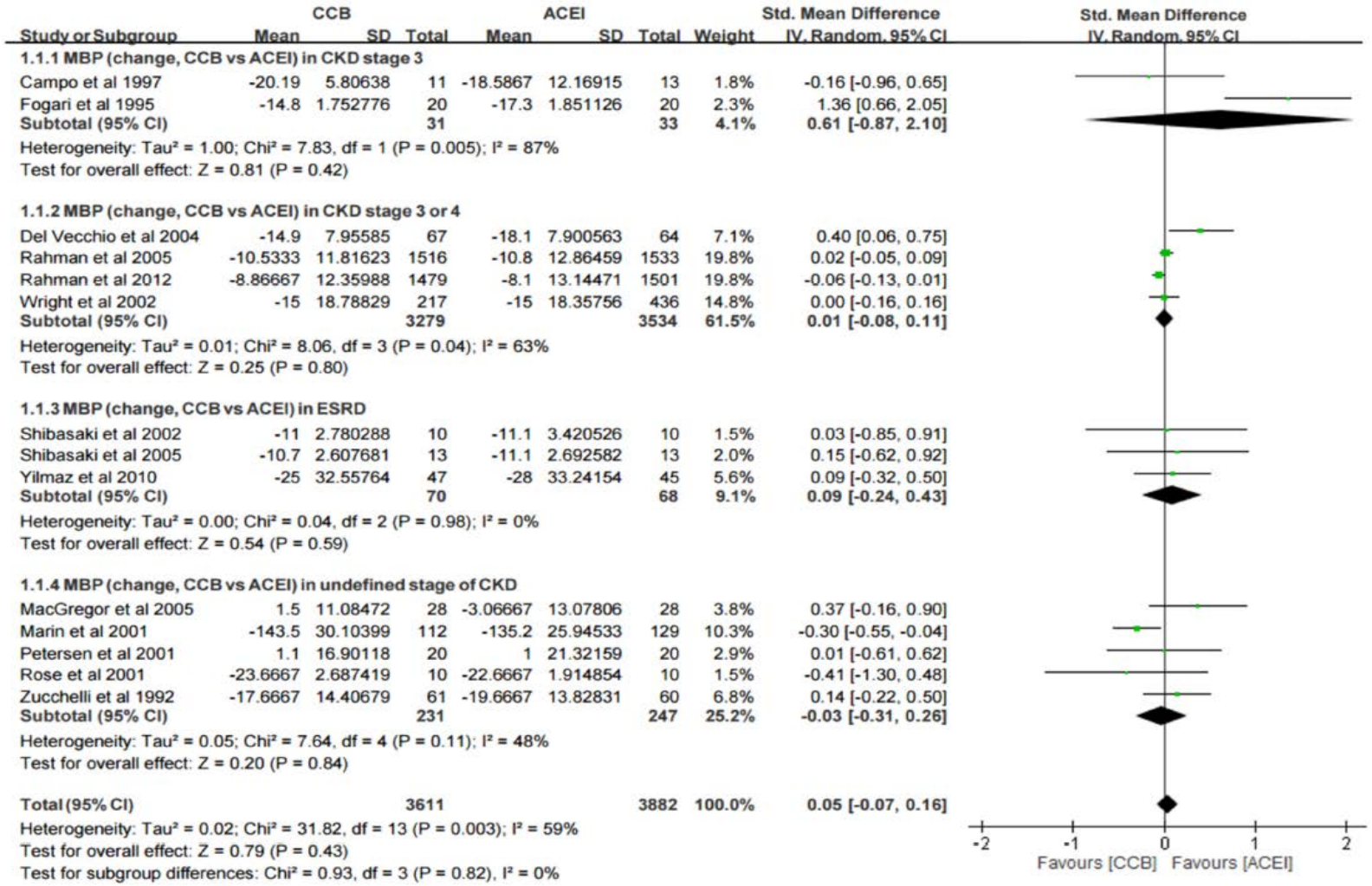
Study design and patients

- Meta-analysis of 28 randomized controlled trials with 9,492 patients **CKD stage 3–5D**
- Comparison of CCB vs. ACEI/ARB
- Outcome: BP change, mortality, heart failure, stroke or cerebrovascular and renal events



Lin YC et al. ***PLoS ONE*** 2017; 12: e0188975

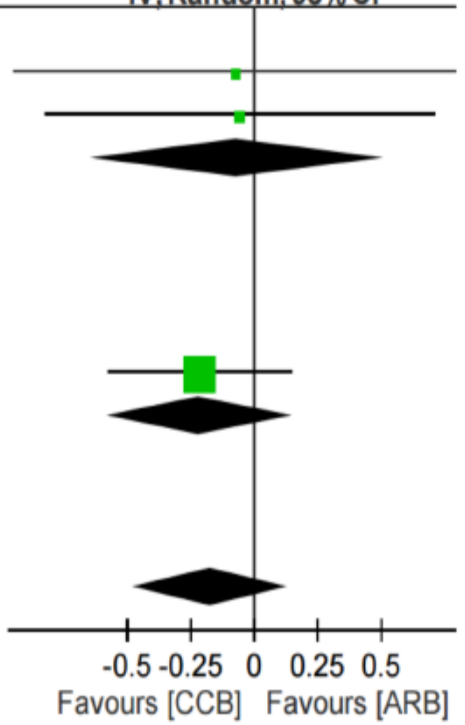
CCB vs. ACEI in CKD



Lin YC et al. ***PLoS ONE*** 2017; 12: e0188975

CCB vs. ARB in CKD

Study or Subgroup	CCB Mean	CCB SD	CCB Total	ARB Mean	ARB SD	ARB Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 MBP(change, CCB vs ARB) in ESRD								
Shibasaki et al 2002	-11	2.780288	10	-10.7	4.716991	10	12.3%	-0.07 [-0.95, 0.80]
Shibasaki et al 2005	-10.7	2.607681	13	-10.5	3.996248	13	16.0%	-0.06 [-0.83, 0.71]
Subtotal (95% CI)			**23**			**23**	**28.3%**	**-0.06 [-0.64, 0.51]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.98); I² = 0%								
Test for overall effect: Z = 0.22 (P = 0.83)								
1.2.2 MBP(change, CCB vs ARB) in undefined stage of CKD								
Iino et al 2004	-16.2333	10.84097	59	-13	18.28004	58	71.7%	-0.21 [-0.58, 0.15]
Subtotal (95% CI)			**59**			**58**	**71.7%**	**-0.21 [-0.58, 0.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.15 (P = 0.25)								
Total (95% CI)			**82**			**81**	**100.0%**	**-0.17 [-0.48, 0.14]**
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 2 (P = 0.91); I² = 0%								
Test for overall effect: Z = 1.09 (P = 0.27)								
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%								



Lin YC et al. ***PLoS ONE*** 2017; 12: e0188975

Take-Home Message

- Even modest dietary salt restriction enhances volume and BP control in CKD patients
- Intensive (systolic) BP control improves CV outcome in CKD patients, but CKD progression is not retarded, with more serious renal events, e.g. acute kidney injury
- CCB and ACEI/ARB are comparable with respect to CV protection in CKD patients

Lipids, inflammation and other CV risk factors

State of the art

- Reducing low-density cholesterol with statin-based therapy reduces CV risk in CKD patients

- CKD patients are characterized by a high level of microinflammation that is induced e.g. by uremic lipoprotein modifications

Statins in CKD

Study design and patients

- Post-hoc analysis of the **IMPROVE-IT** study
- Ezetimibe plus simvastatin versus simvastatin alone
- 18,015 patients with CVD and creatinine clearance > 30 ml/min stabilized within 10 days of acute coronary syndrome

Stanifer JW et al. ***J Am Soc Nephrol*** 2017; 28: 3034

Statins in CKD

Results and interpretation

- For the primary CV endpoint the relative risk reduction of combination therapy vs. monotherapy differed by eGFR (p=0.04)

- Combination therapy was associated with a 12% risk reduction (HR 0.88; 95% CI 0.82–0.95) in patients with a baseline eGFR of <60 ml/min/1.73 m^2 and with a 13% risk reduction (HR 0.87; 95% CI 0.78–0.98) in those with a baseline eGFR of <45 ml/min/1.73m^2

Stanifer JW et al. ***J Am Soc Nephrol*** 2017; 28: 3034

PCSK9 inhibition in CKD

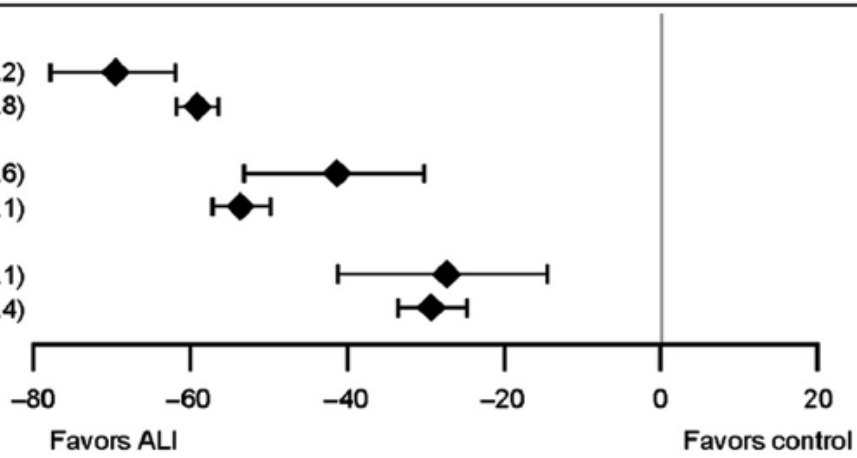
Study design and patients

- 4,629 patients from eight phase 3 ODYSSEY trials (double-blind treatments of 24–104 weeks)
- Alirocumab 150 mg or 75/150 mg every 2 weeks vs. placebo or ezetimibe
- **10%** of patients had **eGFR 30–59** ml/min/1.73 m^2 and over 99% were receiving statin treatment

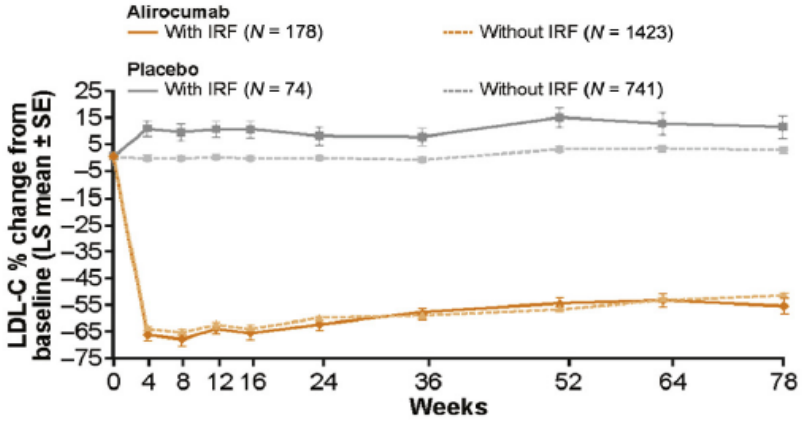
Toth PP et al. ***Kidney Int*** 2018; 93: 1397

PCSK9 inhibition in CKD

Study pool	Subgroup	N	% change from baseline LS mean (SE) Control	% change from baseline LS mean (SE) ALI	Difference in % change from baseline LS mean difference (95% CI) ALI - Control	Interaction *P* value
LDL-C						
ALI 150 mg vs. PBO	With IRF	252	7.9 (3.4)	–62.2 (2.2)		0.0158
	Without IRF	2164	–0.2 (1.1)	–60.1 (0.8)		
ALI 75/150 mg vs. PBO	With IRF	92	–4.3 (4.7)	–46.1 (3.6)		0.0507
	Without IRF	951	5.1 (1.5)	–48.8 (1.1)		
ALI 75/150 mg vs. EZE	With IRF	117	–25.6 (5.5)	–53.6 (4.1)		0.8489
	Without IRF	988	–18.7 (1.8)	–48.3 (1.4)		



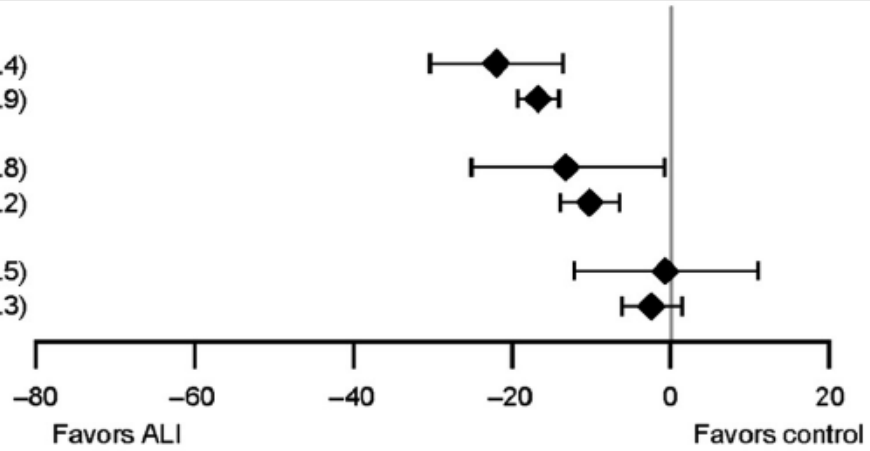
Low-density cholesterol



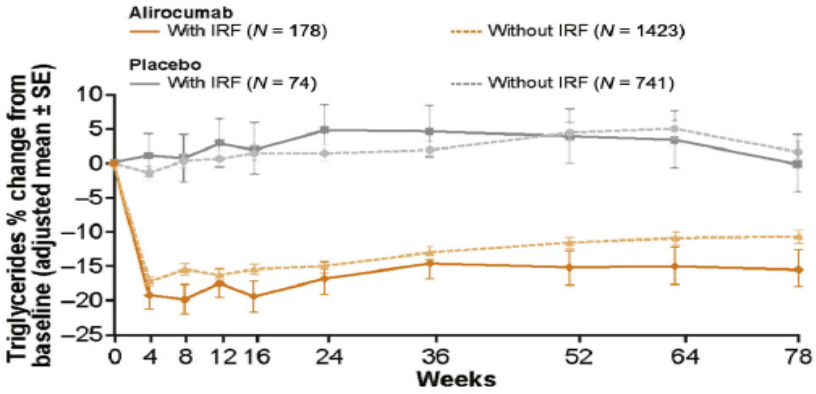
Toth PP et al. ***Kidney Int*** 2018; 93: 1397

PCSK9 inhibition in CKD

Study pool	Subgroup	N	% change from baseline Adjusted mean (SE) Control	ALI	Difference in % change from baseline Adjusted mean difference (95% CI) ALI - Control	Interaction *P* value
Triglycerides						
ALI 150 mg vs. PBO	IRF	252	4.9 (3.7)	−16.8 (2.4)		0.2598
	Without IRF	2164	1.4 (1.2)	−15.1 (0.9)		
ALI 75/150 mg vs. PBO	IRF	92	−0.1 (4.9)	−12.9 (3.8)		0.6691
	Without IRF	951	1.6 (1.6)	−8.5 (1.2)		
ALI 75/150 mg vs. EZE	IRF	117	−11.9 (4.8)	−12.1 (3.5)		0.7784
	Without IRF	988	−11.2 (1.5)	−13.1 (1.3)		



Triglycerides

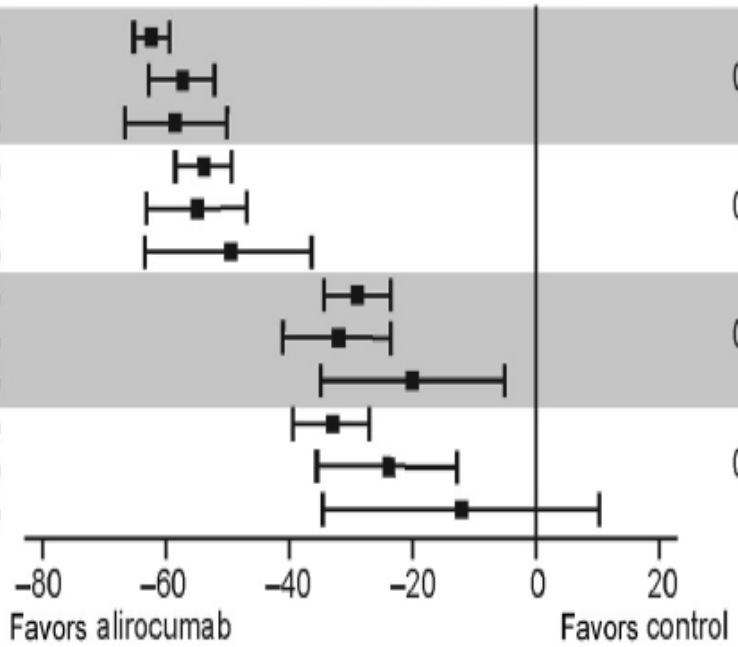


Toth PP et al. ***Kidney Int*** 2018; 93: 1397

PCSK9 inhibition in CKD

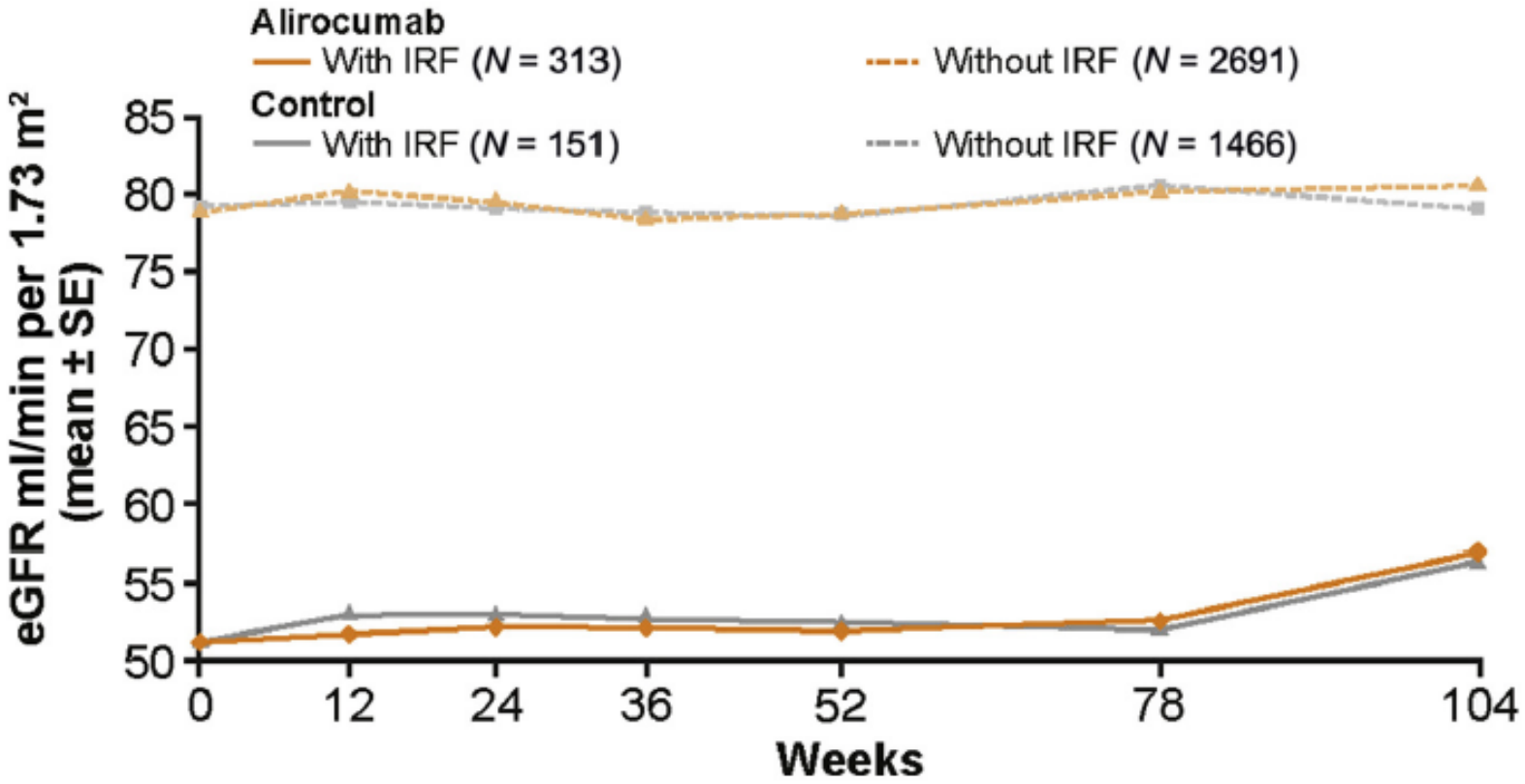
Low-density cholesterol

Study pool	Proteinuria subgroup	n	% change from baseline LS mean (SE) Control	% change from baseline LS mean (SE) Alirocumab	Interaction *P* value
Alirocumab 150 mg vs. placebo (with statins)	Negative	1564	2.2 (1.3)	−60.4 (0.9)	0.2290
	Trace	489	−3.3 (2.3)	−60.8 (1.6)	
	Positive	208	−1.0 (3.4)	−59.7 (2.6)	
Alirocumab 75/150 mg vs. placebo (with statins)	Negative	565	4.3 (2.0)	−50.0 (1.5)	0.7969
	Trace	203	7.4 (3.6)	−48.0 (2.4)	
	Positive	95	5.1 (6.1)	−44.9 (3.4)	
Alirocumab 75/150 mg vs. ezetimibe (with statins)	Negative	714	−20.4 (2.2)	−49.5 (1.7)	0.4050
	Trace	247	−15.0 (3.3)	−47.4 (3.1)	
	Positive	98	−23.2 (6.1)	−43.5 (4.6)	
Alirocumab 75/150 mg vs. ezetimibe (without statins)	Negative	229	−13.3 (2.3)	−46.8 (2.2)	0.1079
	Trace	71	−14.5 (4.0)	−38.8 (4.3)	
	Positive	19	−27.4 (8.7)	−39.9 (7.4)	



Toth PP et al. ***Kidney Int*** 2018; 93: 1397

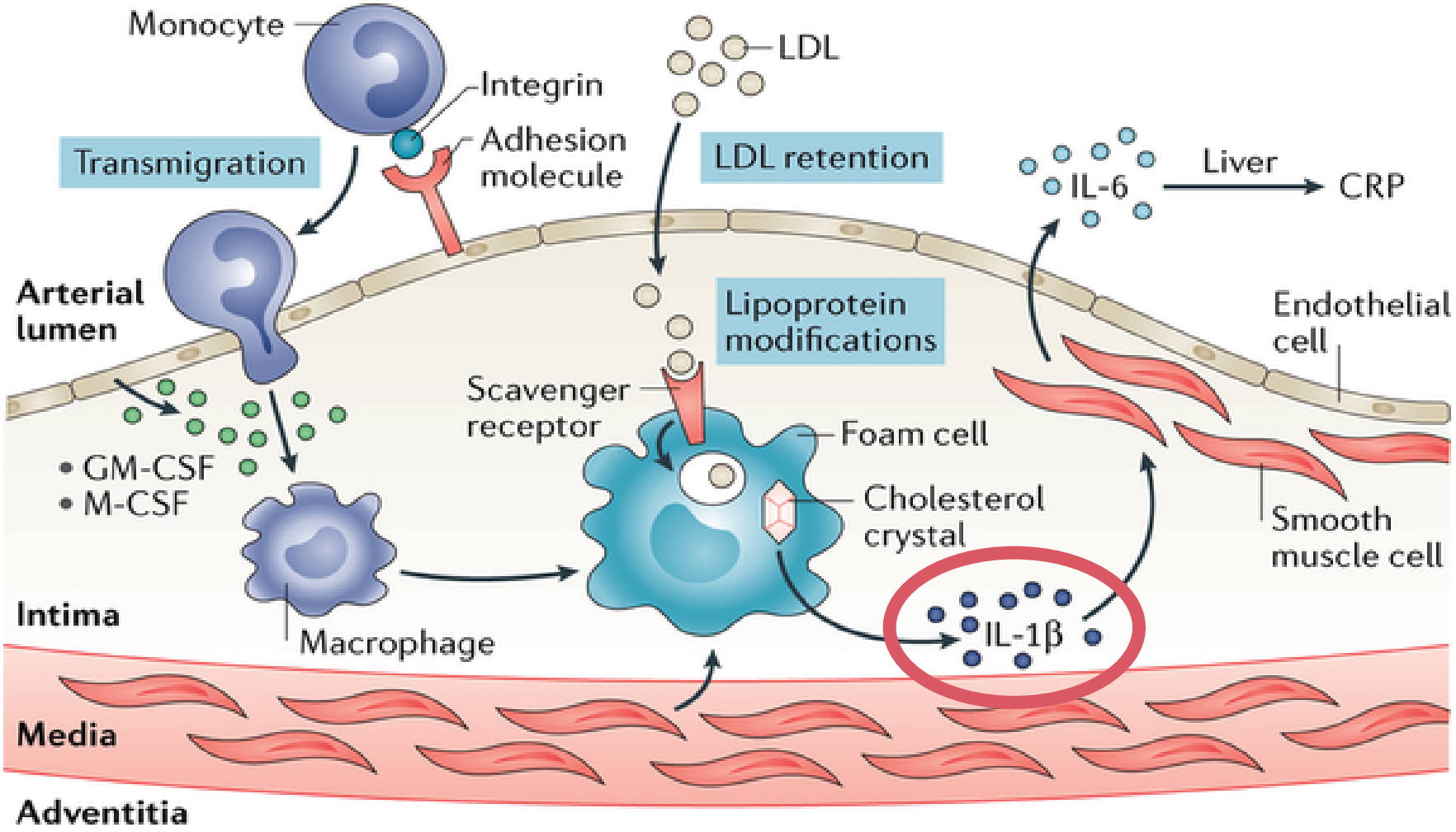
PCSK9 inhibition in CKD



Low-density cholesterol

Toth PP et al. ***Kidney Int*** 2018; 93: 1397

Inflammation and atherosclerosis

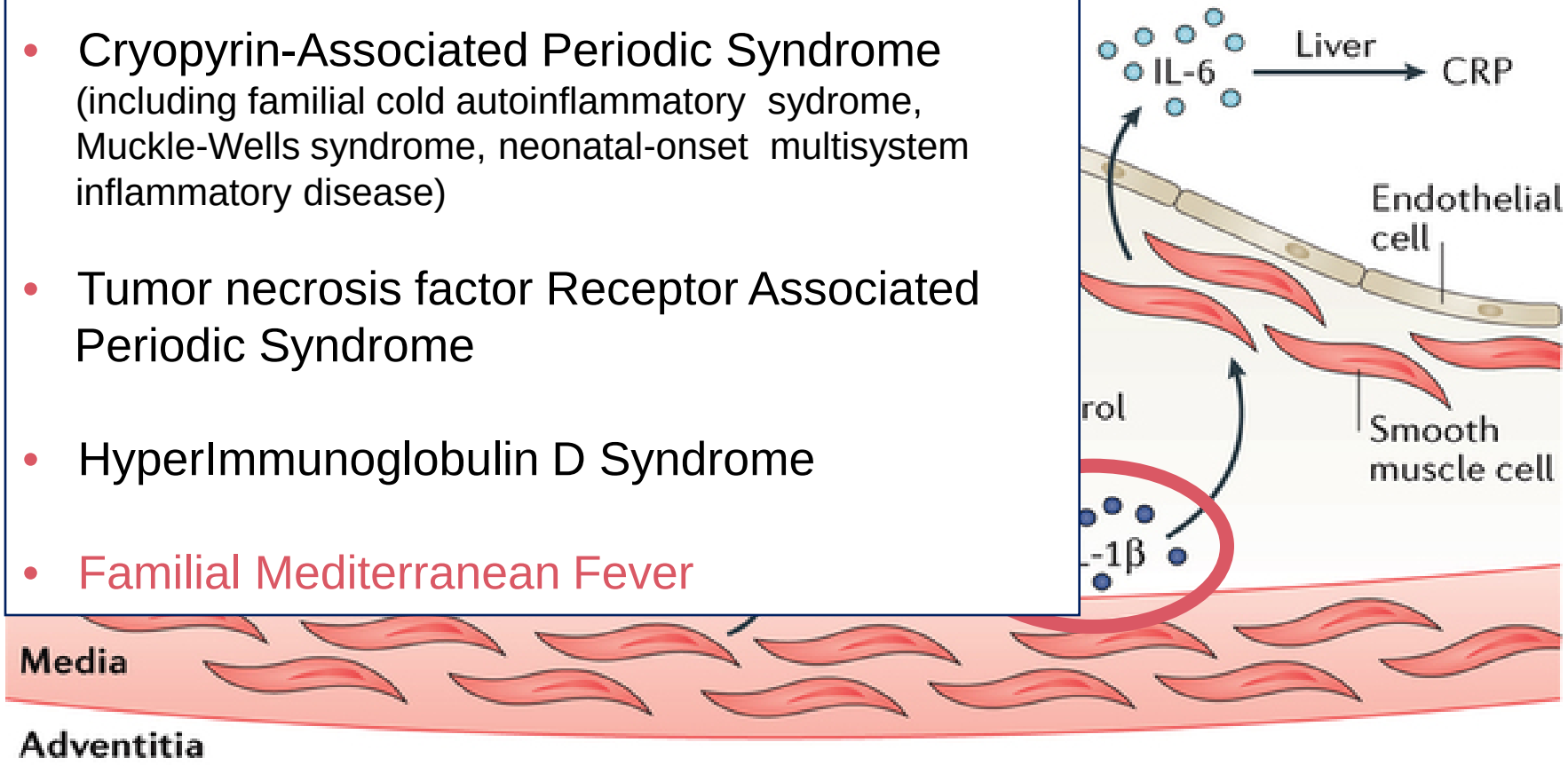


Gistera A & Hansson GK. ***Nat Rev Nephrol*** 2017; 13: 368

Inflammation and atherosclerosis

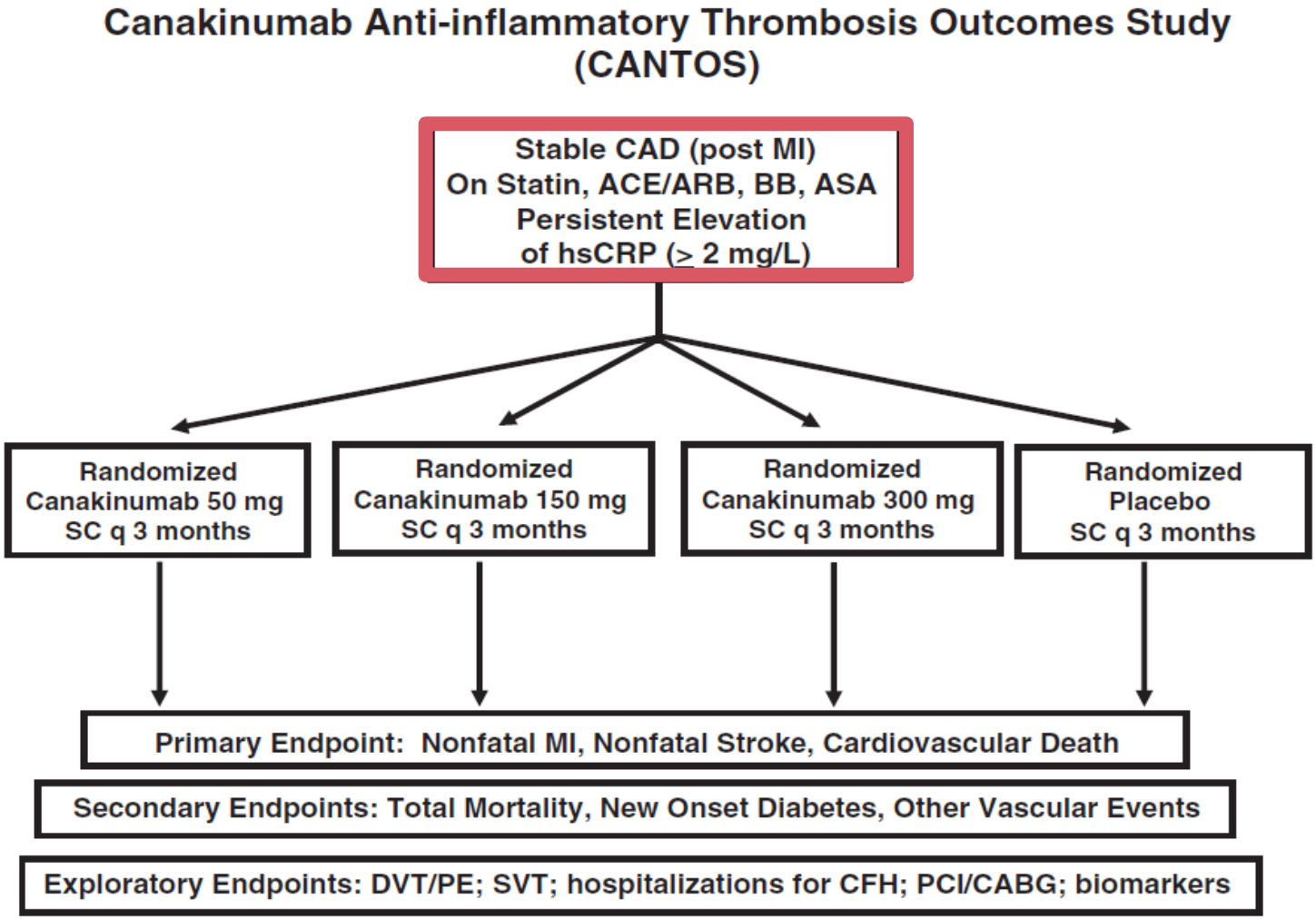
Canakinumab – antibody against IL-1ß in

- Cryopyrin-Associated Periodic Syndrome (including familial cold autoinflammatory sydrome, Muckle-Wells syndrome, neonatal-onset multisystem inflammatory disease)
- Tumor necrosis factor Receptor Associated Periodic Syndrome
- HyperImmunoglobulin D Syndrome
- Familial Mediterranean Fever



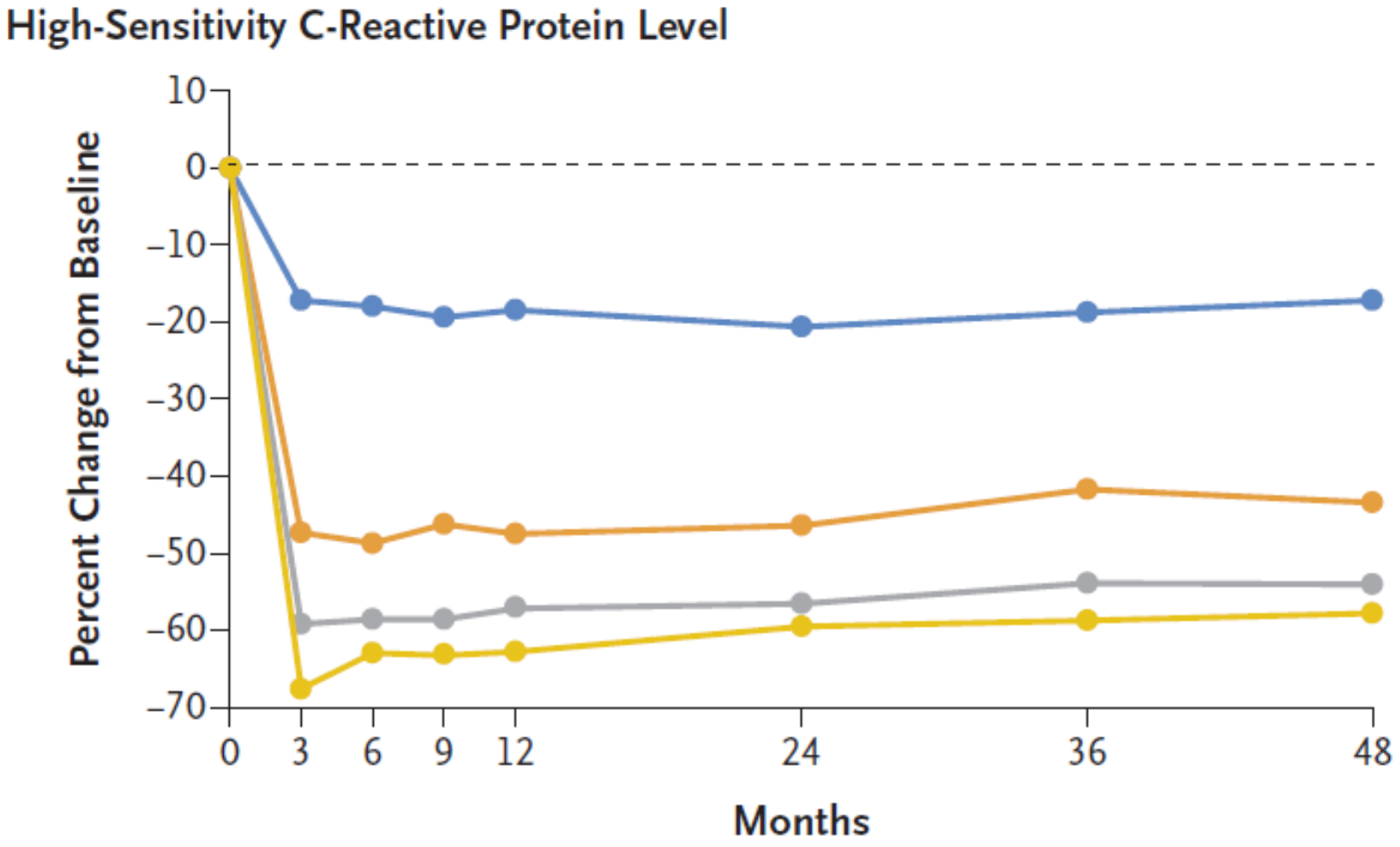
Gistera A & Hansson GK. ***Nat Rev Nephrol*** 2017; 13: 368

Antiinflamatory drugs in CAD



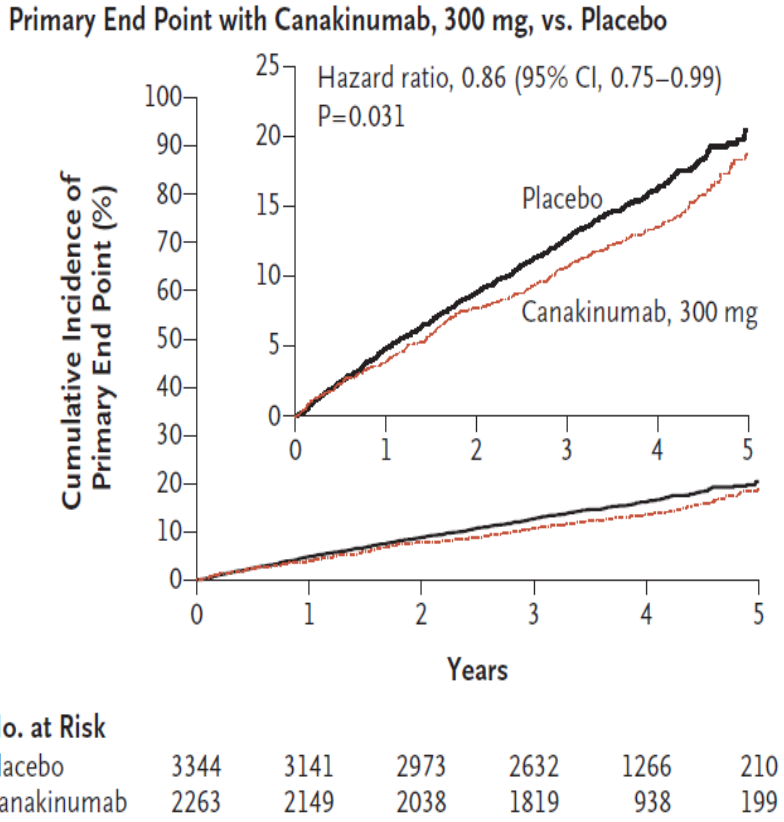
Ridker PM et al. ***Am Heart J*** 2011; 162: 597

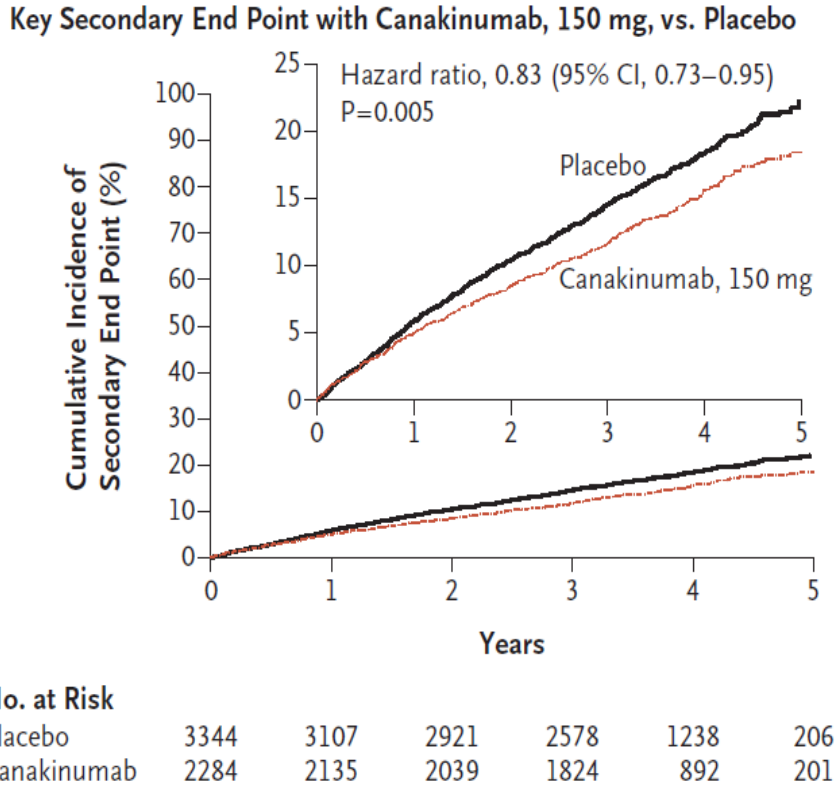
Antiinflamatory drugs in CAD



Ridker PM et al. ***New Engl J Med*** 2017; 377: 1119

Antiinflamatory drugs in CAD

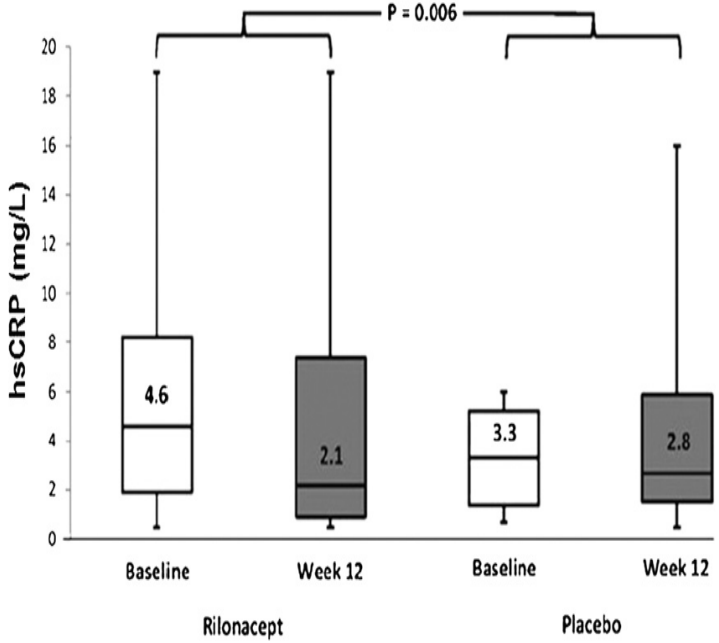




Ridker PM et al. ***New Engl J Med*** 2017; 377: 1119

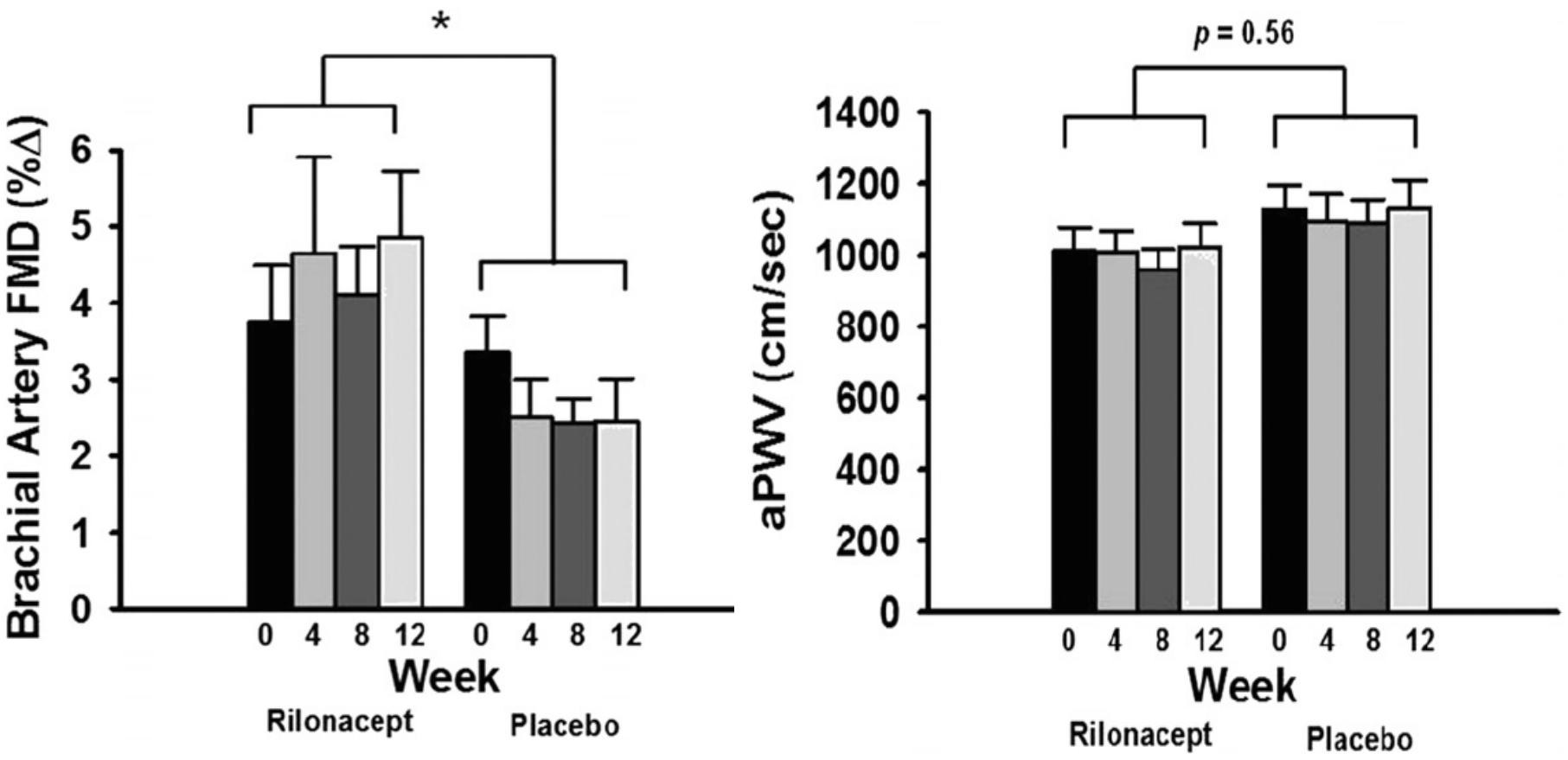
Antiinflamatory drugs in CKD

- 42 CKD stage 3–4 patients
- Treatment with IL-1ß trap rilonacept or placebo for 12 weeks
- Assessment of brachial artery flow-mediated dilation (FMD) and aortic pulse-wave velocity (aPWV)



Nowak KL et al. ***J Am Soc Nephrol*** 2017; 28: 971

Antiinflamatory drugs in CKD



Nowak KL et al. ***J Am Soc Nephrol*** 2017; 28: 971

Febuxostat vs. allopurinol

Study design and patients

- Multicenter, double-blind, **non-inferiority trial** in 6,190 patients with **gout** and CVD stratified according to kidney function and randomized to febuxostat or allopurinol
- Primary end point was composite of CV death, nonfatal myocardial infarction, nonfatal stroke, or unstable angina with urgent revascularization
- Median follow-up was 32 months

White WB et al. ***N Engl J Med*** 2018; 378: 1200

Febuxostat vs. allopurinol

Results and interpretation

- A primary end-point event occurred in 335 patients (10.8%) with febuxostat and in 321 patients (10.4%) with allopurinol (HR 1.03; 98.5% CI 1.23; P=0.002 for non-inferiority)

- All-cause (HR 1.22; 95% CI 1.01-1.47) and CV (HR 1.34; 95% CI 1.03-1.73) mortality were higher in the febuxostat group than in the allopurinol group

White WB et al. ***N Engl J Med*** 2018; 378: 1200

Take-Home Message

- Reducing low-density cholesterol with statin-based therapy reduces CV risk in CKD patients and has no significant long-term adverse effects

- Novel pharmacological treatment targets in CKD patients are PCSK9 inhibition, and reduction of microinflammation via inhibition of IL-1ß

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22. White WB et al. *N Engl J Med* 2018; 378: 1200

List of Abbreviations

- ACEI – angiotensin-converting enzyme inhibitors
- ARB – angiotensin receptor blocker
- BIS – bioelectrical impedance spectroscopy
- BP – blood pressure
- CAD – coronary artery disease
- CCB – calcium channel blocker
- CI – confidence interval
- CKD – chronic kidney disease
- CVD – cardiovascular disease
- eGFR – estimated glomerular filtration rate

List of Abbreviations

- ESKD – end-stage kidney disease
- hs-CRP – high-sensivity C-reactive protein
- HR – hazard ratio
- ICD – implantable cardioverter defibrillator
- IL-1ß – interleukin 1-beta
- LVEF – left ventricular ejection fraction
- NaCl – sodium chloride
- NT pro-BNP – N-terminal pro-B-type natriuretic peptide