The 22nd Budapest Nephrology School

Nephrology, Hypertension, Dialysis, Transplantation, Nephropathology

Under the Auspices of

ISN, ERA-EDTA, RPS, IFKF and ISP

26–31 August, 2015

Nephroprotection: Where are we in 2015?

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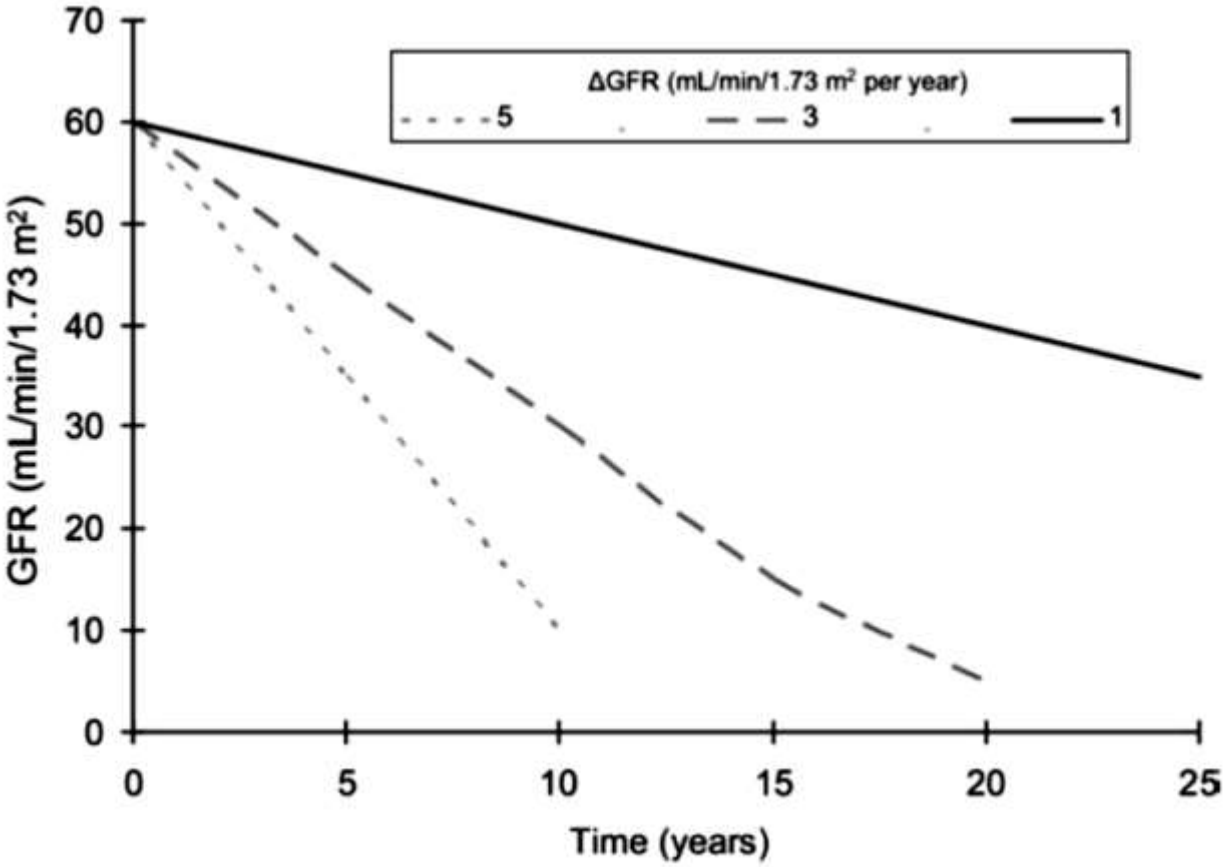
Decline of GFR in patients with diabetic nephropathy

Rate of annual kidney function decrease has an important role on time to reach end-stage renal disease



Turgut F. et al.: Am. J. Kidney Dis., 2010; 55: 928-940

Stages of Chronic Kidney Disease

GFR categories in CKD

GFR category	GFR (ml/min per 1.73 m^2)	Terms
G1	⩾90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level.
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Levin A., Stevens P.E., Kidney Int., 2014, 85, 49-61

Categories of Albuminuria

Albuminuria categories in CKD

Category	AER (mg/24 h)	ACR (approximate equivalent) (mg/mmol)	ACR (approximate equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30–300	3–30	30–300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: ACR, albumin-to-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease.

*Relative to young adult level.

**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 h (ACR >2220 mg/g; >220 mg/mmol)).

Levin A., Stevens P.E., Kidney Int., 2014, 85, 49-61

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min per 1.73 m²) 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 >30 mg/mmol
	G1	Normal or high	⩾90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red, very high risk.

Levin A., Stevens P.E., Kidney Int., 2014, 85, 49-61

Referral decison making by GFR and albuminuria)

GFR categories (ml/min per 1.73 m²) 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 >30 mg/mmol
	G1	Normal or high	⩾90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor	Monitor	Refer
	G4	Severely decreased	15–29	Refer*	Refer*	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

Referral decision making by GFR and albuminuria. *Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring.

Levin A., Stevens P.E., Kidney Int., 2014, 85, 49-61

Guide to frequency of monitoring (number of times per year) by GFR and albuminuria category

GFR categories (ml/min per 1.73 m^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 >30 mg/mmol
	G1	Normal or high	⩾90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year).

Levin A., Stevens P.E., Kidney Int., 2014, 85, 49-61

Nephrol Dial Transplant (2014) 29: 1073–1082
doi: 10.1093/ndt/gft351
Advance Access publication 3 October 2013

The prevalence of chronic kidney disease and its relation to socioeconomic conditions in an elderly Polish population: results from the national population-based study PolSenior

Jerzy Chudek[1,2], Katarzyna Wieczorowska-Tobis[3], Jan Zejda[4], Katarzyna Broczek[5], Anna Skalska[6], Tomasz Zdrojewski[7] and Andrzej Wiecek[1]

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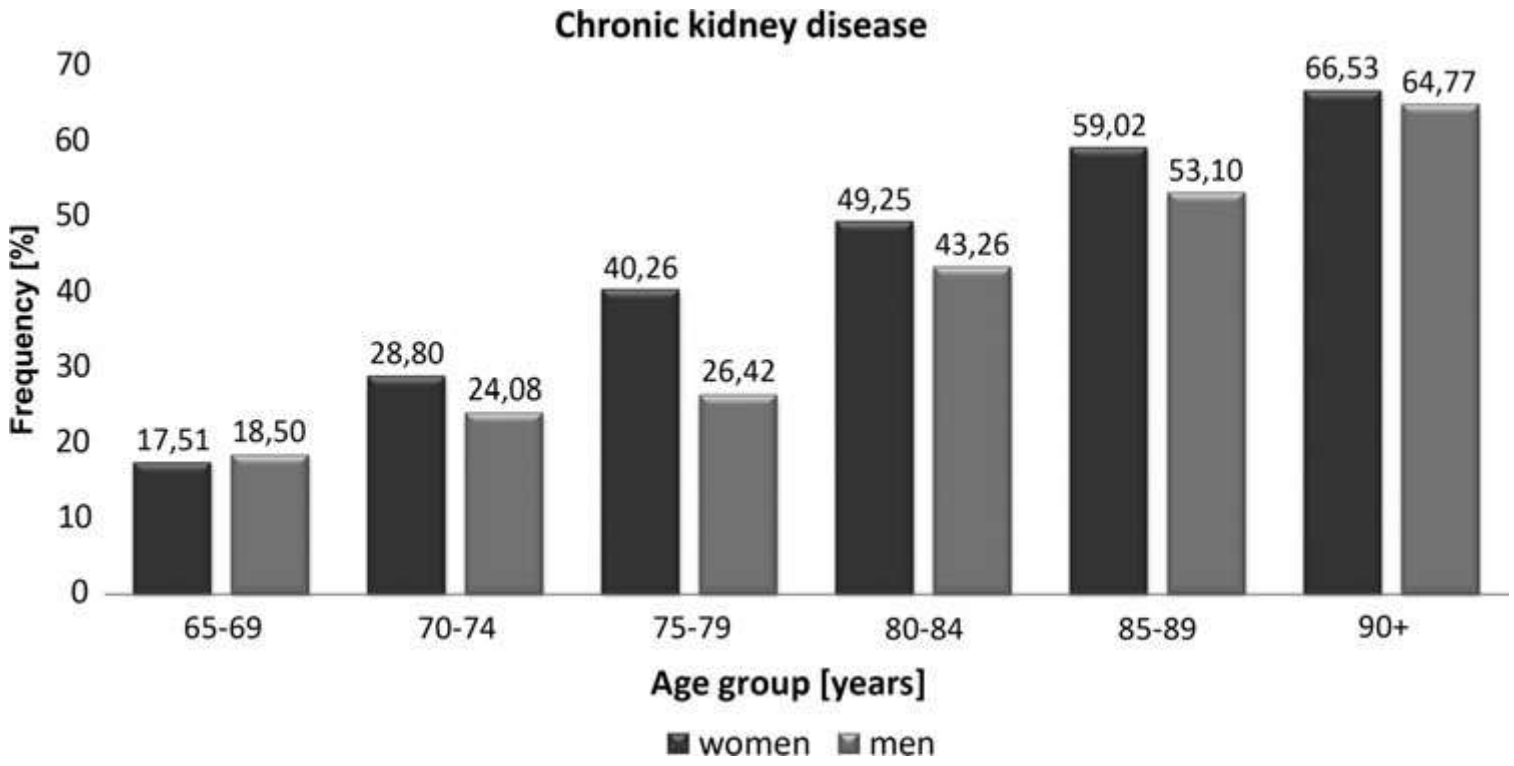
Frequency of CKD (eGFR <60 mL/min/1.73 m2 or ACR ≥30 mg/g) according to age and gender in the PolSenior study

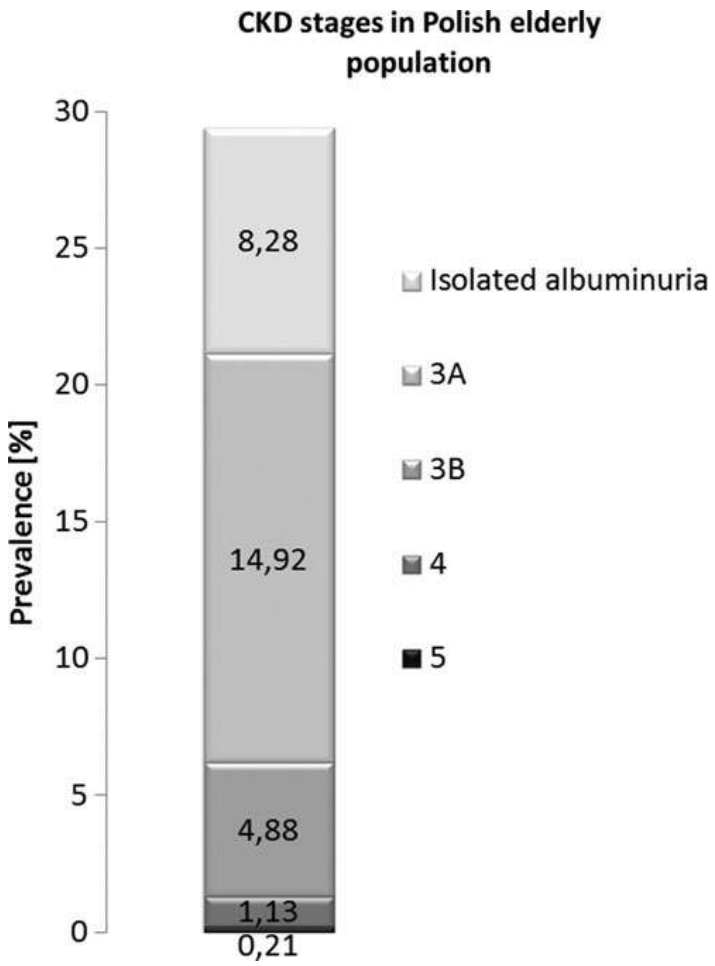
3793 subjects



Chudek J. et al. Nephrol, Dial. Transplant., 2014, 29: 1073–1082

Prevalence of CKD stages in Polish elderly population
(isolated albuminuria was defined when eGFR ≥60 mL/min/1.73 m2

3793 subjects



Chudek J. et al. Nephrol, Dial. Transplant., 2014, 29: 1073–1082

Nephroprotection: Where are we in 2015?

With confirmed benficial effect:

- Reduction of blood pressure
- Blockade of the RAAS (beyond BP reduction)
- Reduction of BMI
- Reduction of protein intake
- Correction of phosphatemia
- Correction of metabolic acidosis
- Correction of glucose (HBA1C) in DM patients
- Supplementation of Vitamin D
- Renal denervation

Nephroprotection: Where are we in 2015?

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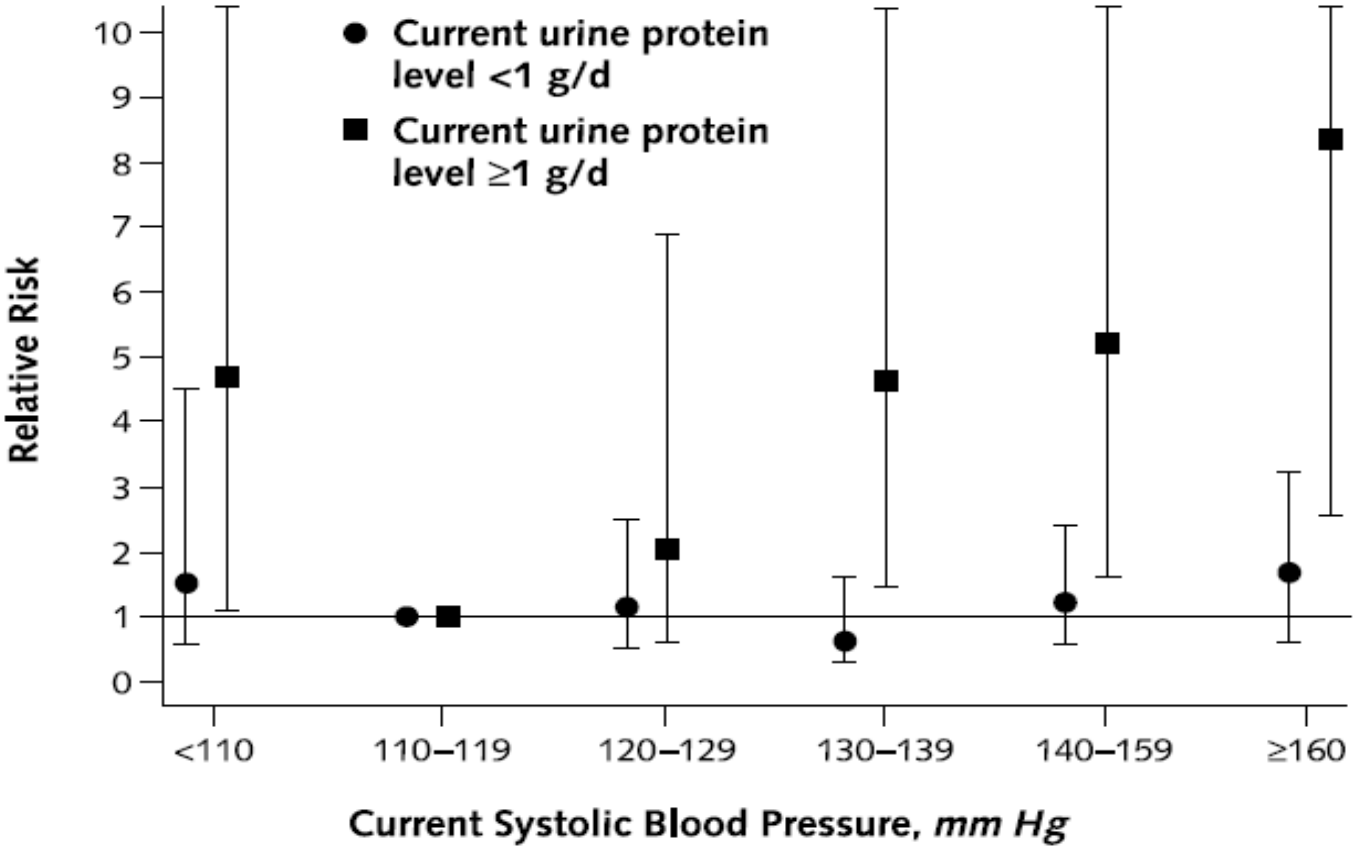
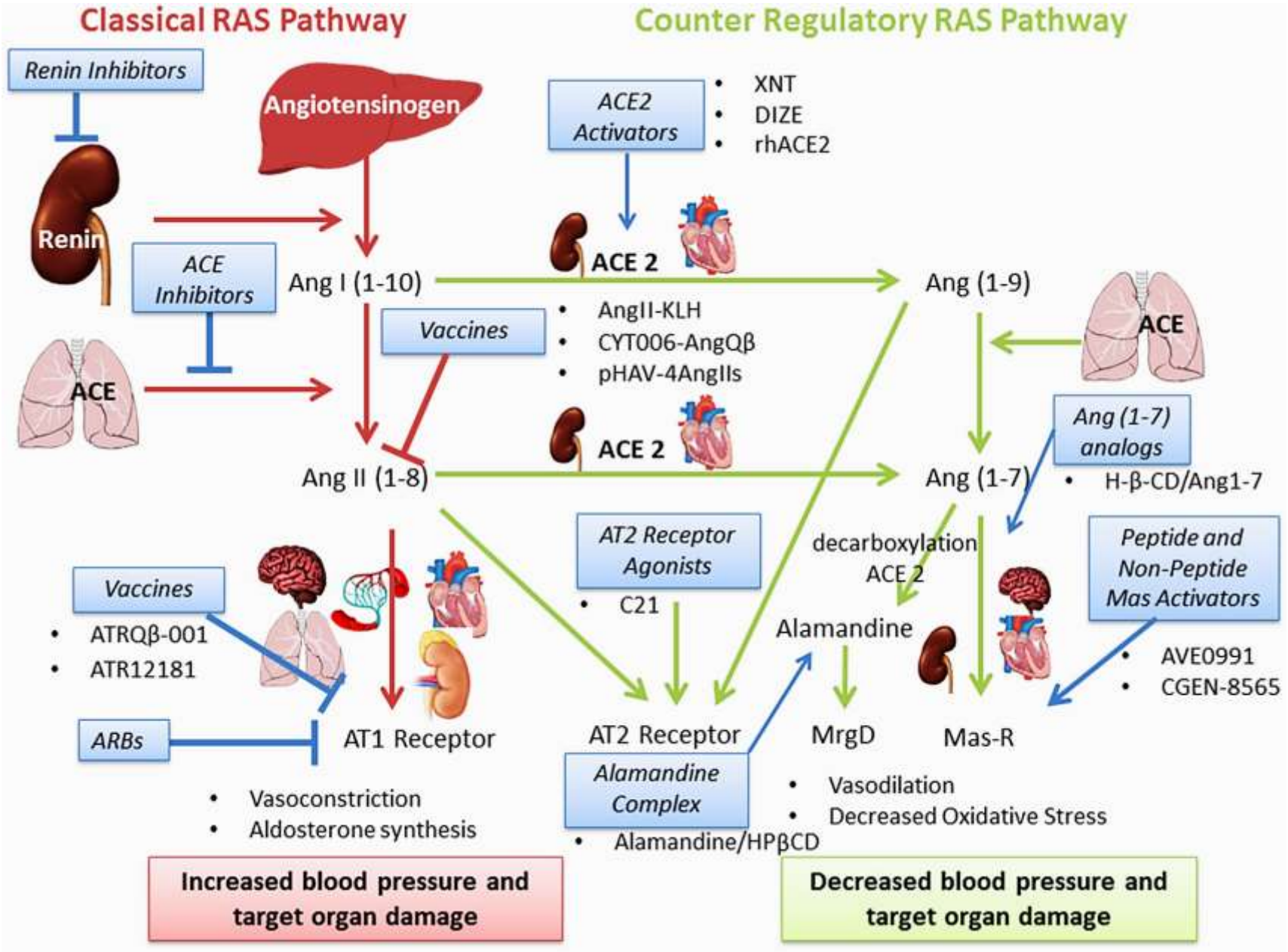
Relative risk for kidney disease progression based on current level of systolic blood pressure and current urine protein excretion



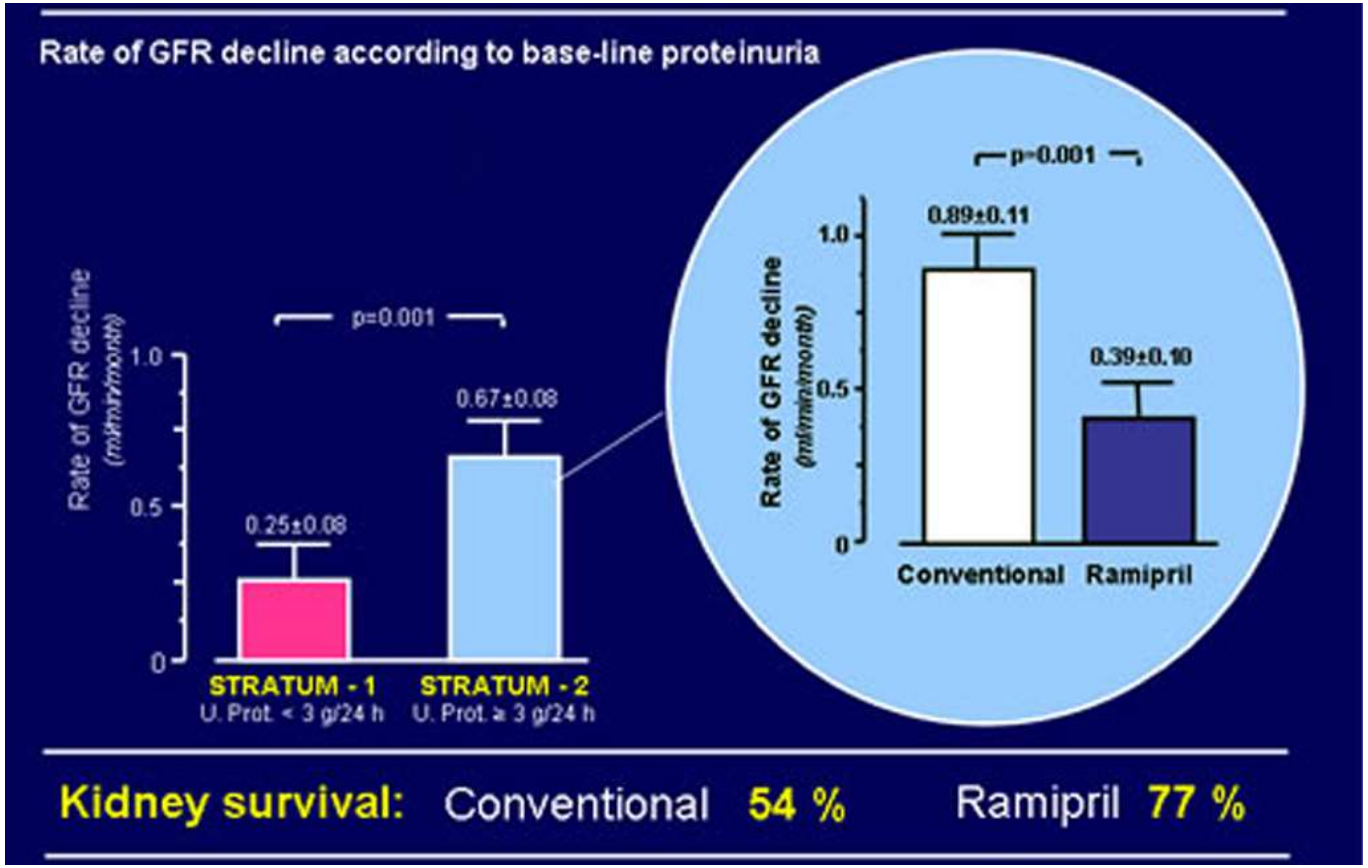
Progression of Chronic Kidney Disease: The Role of Blood Pressure Control, Proteinuria, and Angiotensin-Converting Enzyme Inhibition A Patient-Level Meta-Analysis

Jafar T.H. Ann Intern Med 2003, 193, 244-252



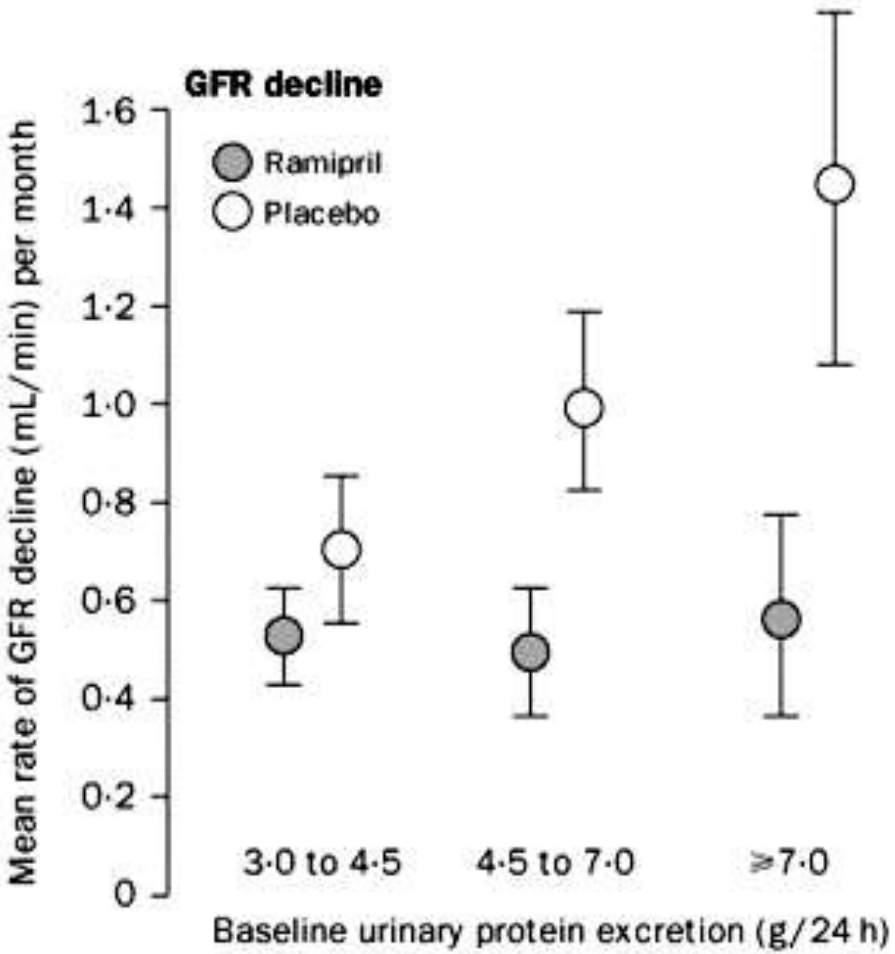
Oparil S., Schmiered R., Circ Res. 2015;116:1074-1095

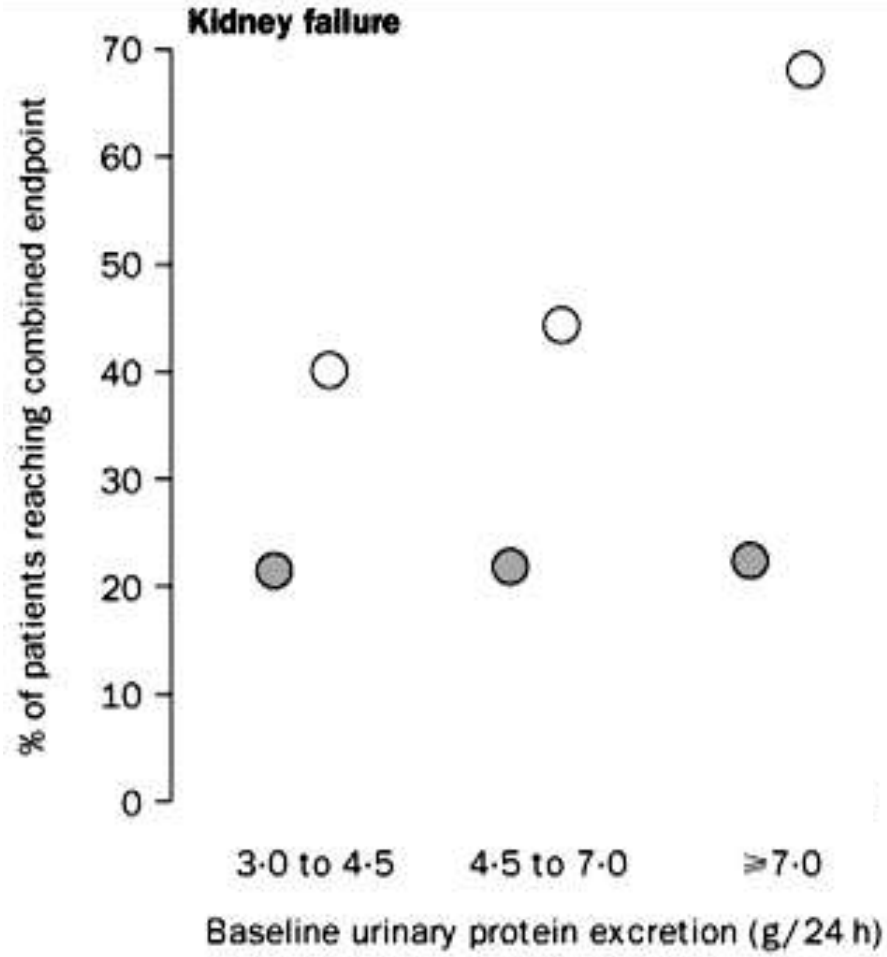
REIN Study



GISEN Group, Lancet 1997; 349: 1857-1863

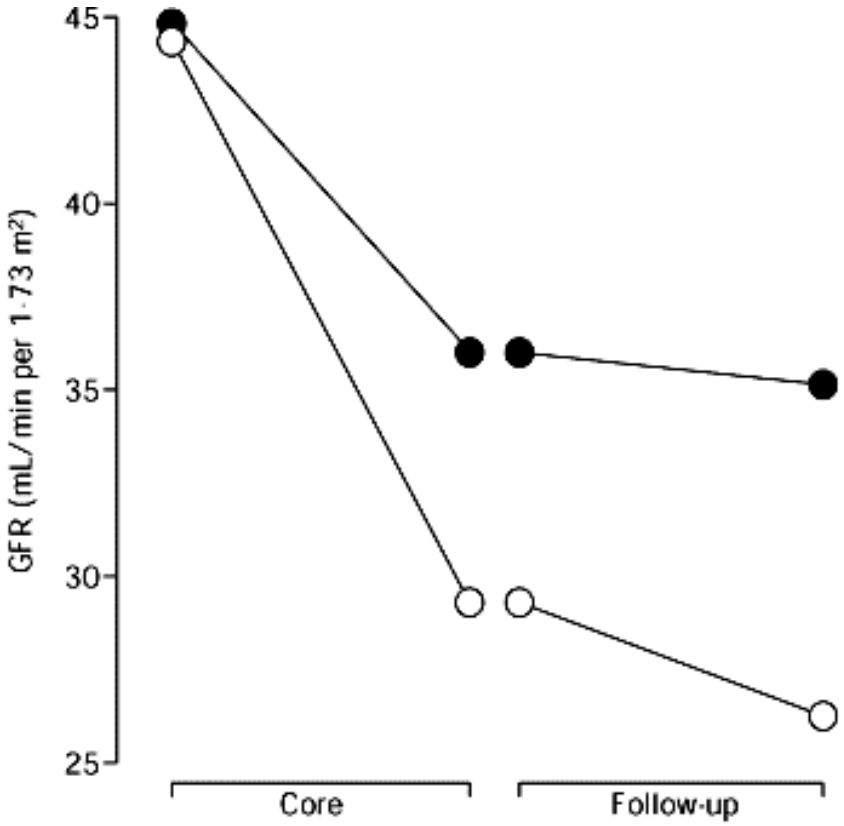
REIN Study





GISEN Group, Lancet 1997; 349: 1857-1863

REIN: Core and Follow-up Study

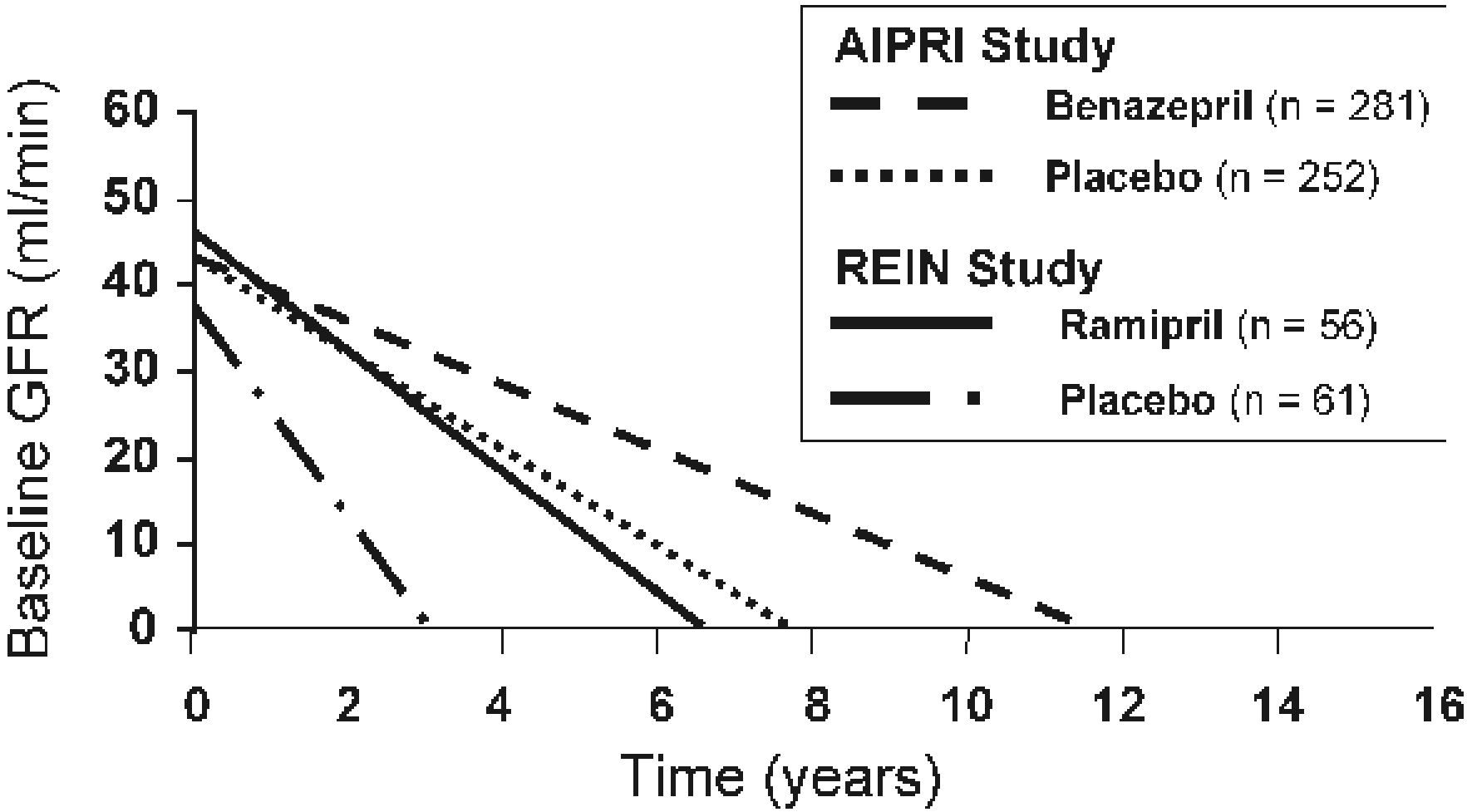


GFR decline (mL/min per 1·73 m² per month)

Group			p
● Continued ramipril	−0·44 (0·54)	−0·10 (0·50)	0·017
○ Switched to ramipril	−0·81 (1·12)	−0·14 (0·87)	0·017

GISEN Group, Lancet 1997; 349: 1857-1863

Treatment with ACEi and time to ESRD in patients with non-diabetic CKD

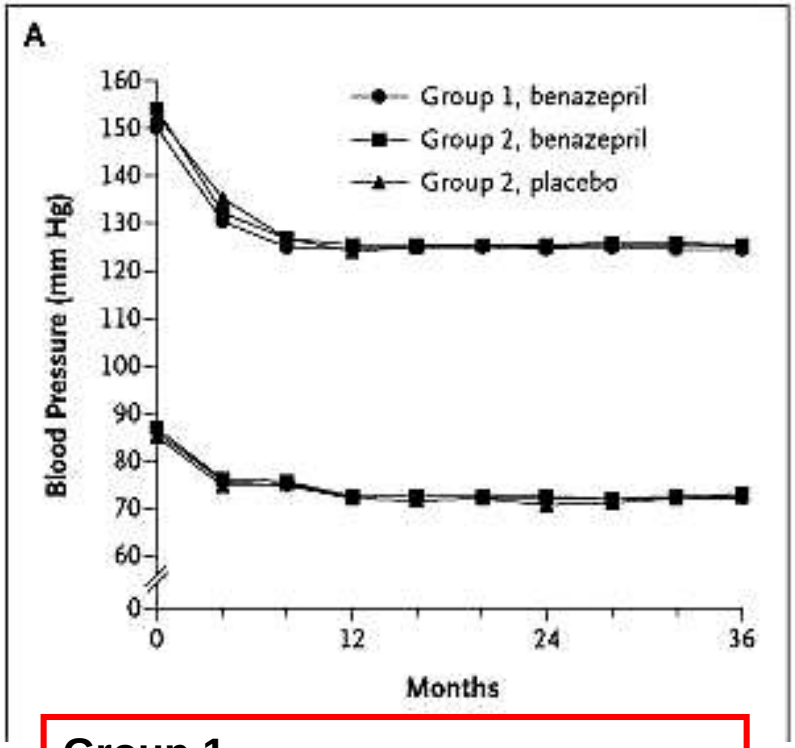


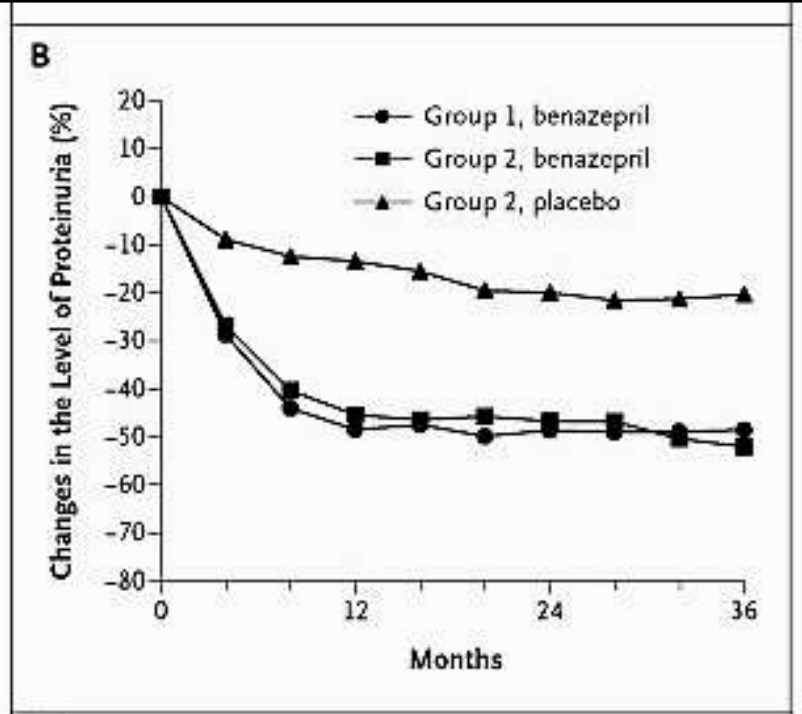
Maschio G. et al.: N Engl J Med 1996; 334: 939-45
The GISEN Group: Lancet 1997; 349: 1857-63

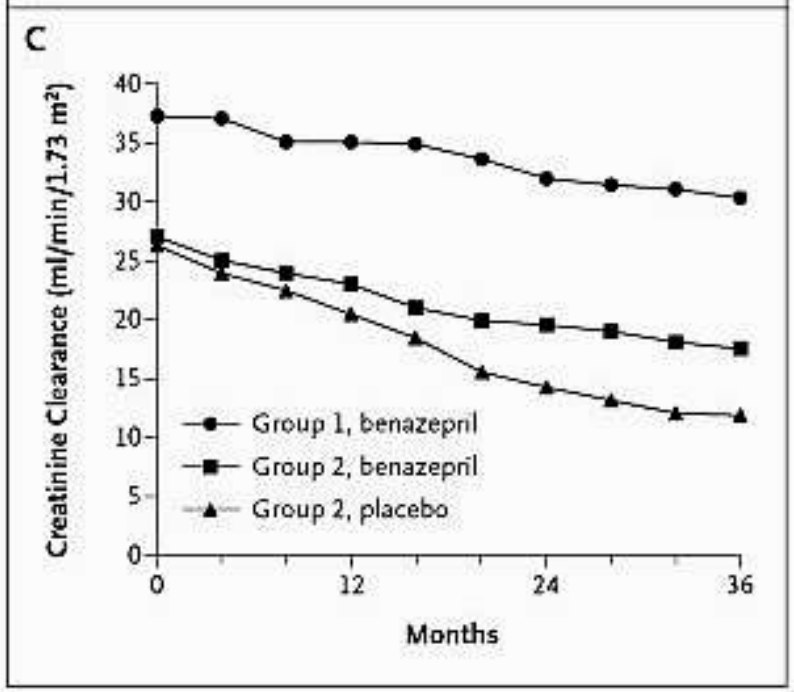
Large, RCTs with ACEi or ARB and RR of ESRD in patients with non - diabetic or diabetic CKD

Study	Year	Patients	Comparison	RR
Captopril study	1993	N 409; type 1 diabetes and proteinuria	Captopril versus placebo	45%
AIPRI	1996	N 583; various nephropathies	Benazapril versus placebo	56%
REIN	1997	N 323; non-diabetic nephropathies	Ramipril versus placebo	52%
UKPDS	1998	N 758; type 2 diabetes and hypertension	Captopril versus atenolol	NS
IDNT	2001	N 1715; type 2 diabetes and hypertension	Irbesartan versus placebo Irbesartan versus amlodipine	20% 23%
RENAAL	2001	N 1513; type 2 diabetes and nephropathy	Losartan versus placebo	16%
IRMA	2001	N 590; type 2 diabetes and microalbuminuria	Irbesartan 150mg versus placebo irbesartan 300mg versus placebo	39% 70%

Changes in Blood Pressure (Panel A), the Level of Proteinuria (Panel B), and Creatinine Clearance (Panel C) during Follow-up



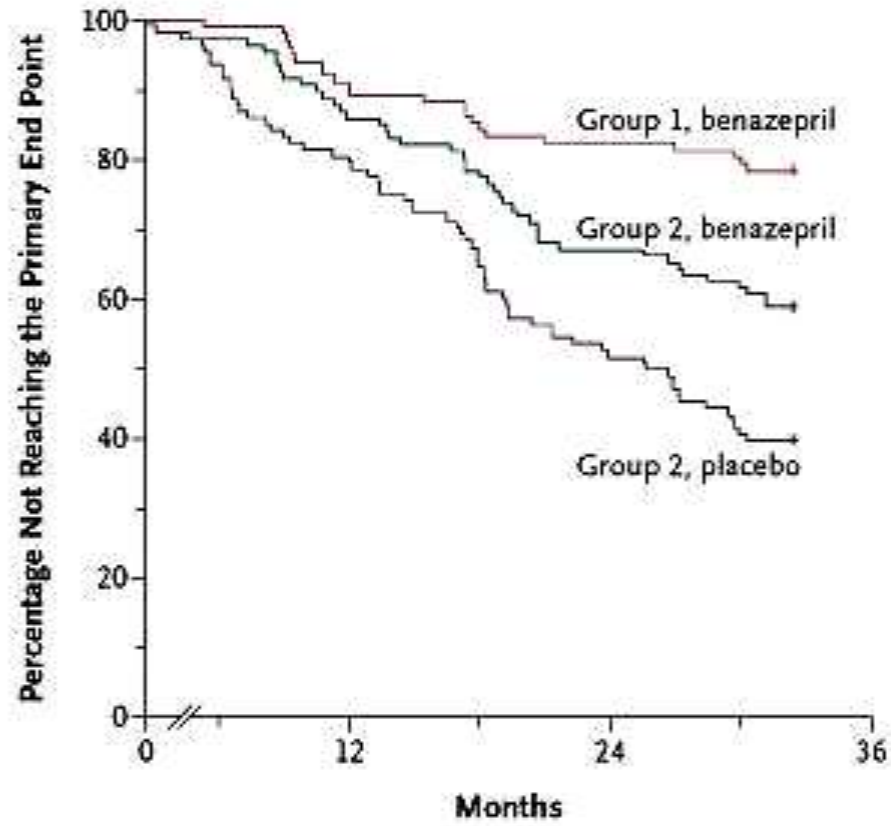




Group 1
Creatinine 1,5-3,0 mg%
(133-265 μmol/
Group 2
Creatinine 3,1-5,0 mg%
(274-442 μmol/l)

Hou, F. F. et al.,N Engl J Med 2006; 354: 131-140

Kaplan-Meier Estimates of the Percentage of Patients Not Reaching the Primary Composite End Point of a Doubling of the Serum Creatinine Level, End-Stage Renal Disease, or Death



No. at Risk				
Group 1, benazepril	102	96	84	40
Group 2, benazepril	107	96	73	32
Group 2, placebo	108	88	59	22

Group 1
Creatinine 1,5-3,0 mg%
(133-265 μmol/
Group 2
Creatinine 3,1-5,0 mg%
(274-442 μmol/l)

Hou, F. F. et al.,N Engl J Med 2006; 354: 131-140

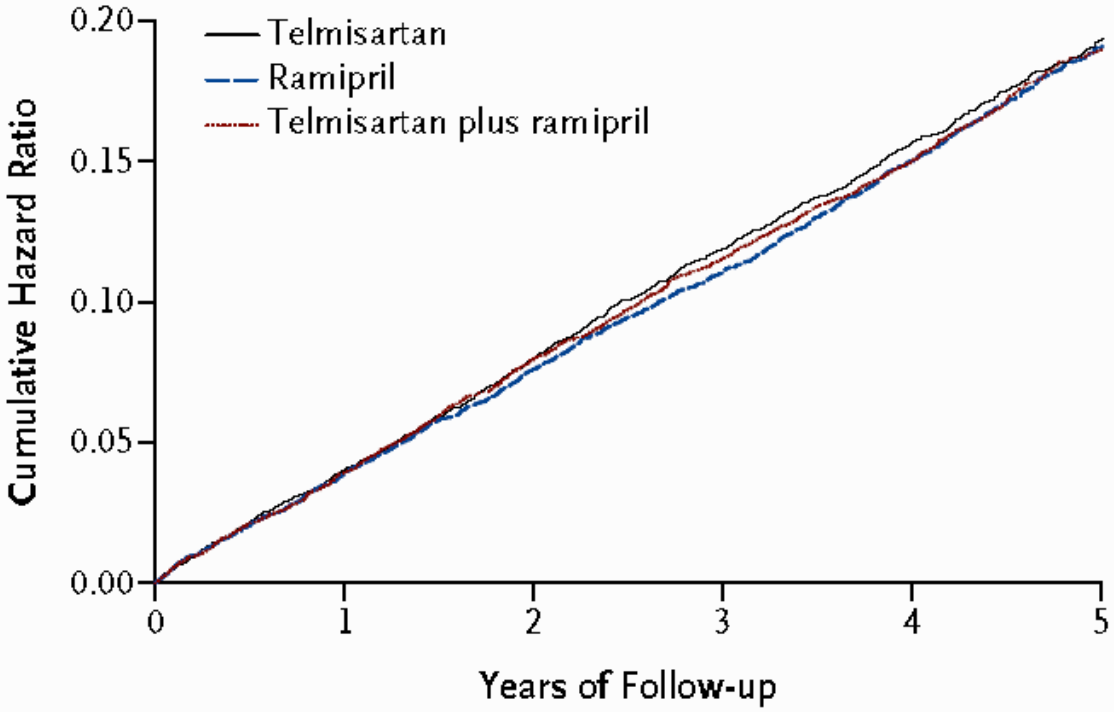
ONTARGET Study

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Ramipril (N=8576)	Telmisartan (N=8542)	Combination Therapy (N=8502)
Age — yr	66.4±7.2	66.4±7.1	66.5±7.3
Blood pressure — mm Hg†	141.8±17.4/82.1±10.4	141.7±17.2/82.1±10.4	141.9±17.6/82.1±10.4
Heart rate — beats/min	67.9±12.2	68.0±12.3	67.7±12.2
Body-mass index‡	28.1±4.5	28.1±4.6	28.0±4.5

N.Engl.J.Med. 2008; 358; 10:1547-1559

ONTARGET Study

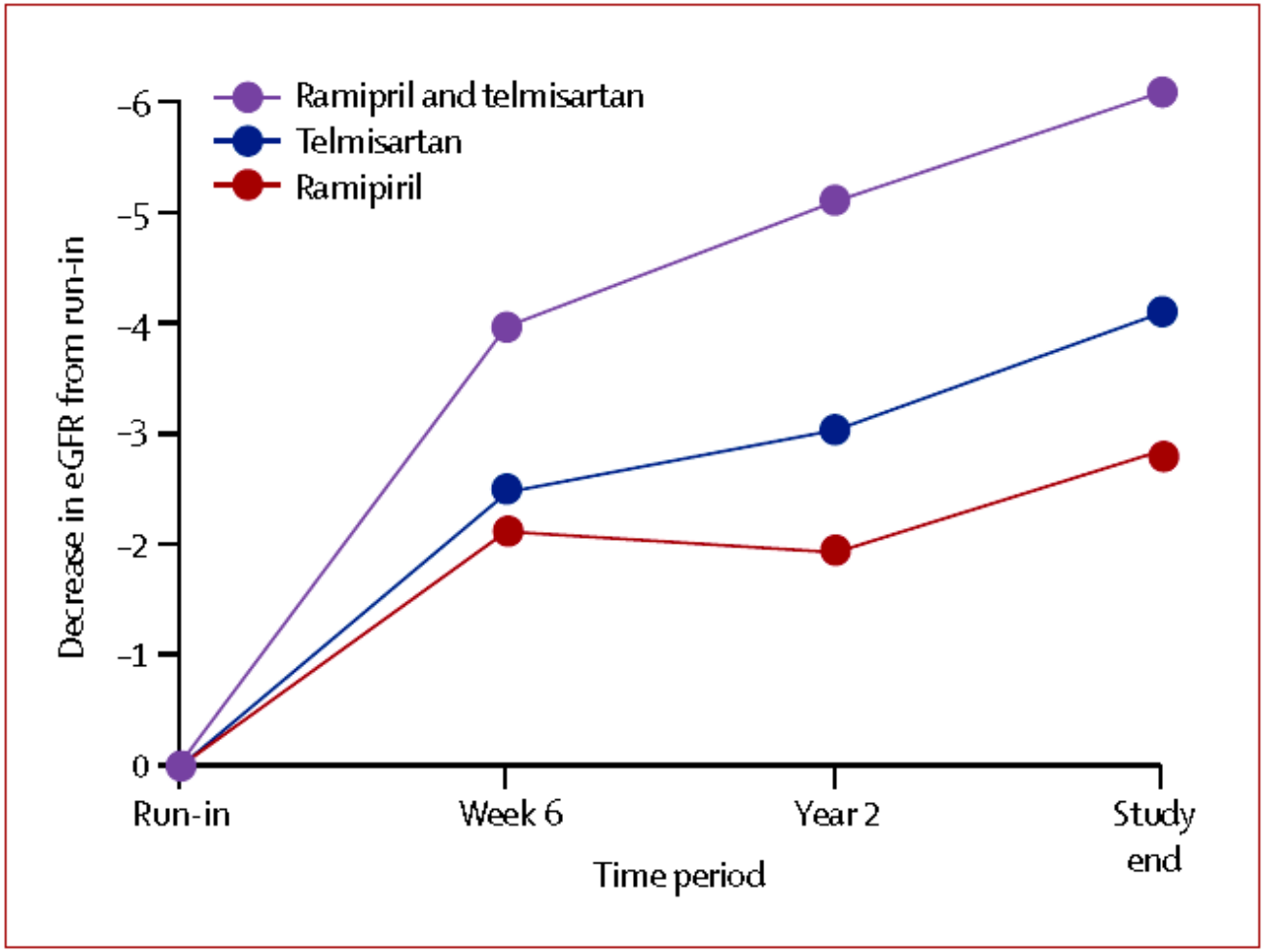


No. at Risk						
Telmisartan	8542	8177	7778	7420	7051	1687
Ramipril	8576	8214	7832	7472	7093	1703
Telmisartan plus ramipril	8502	8133	7738	7375	7022	1718

N.Engl.J.Med. 2008; 358; 10:1547-1559

ONTARGET Study

Changes of GFR in patients treated with ramipryl and/or telmisartan



JF Mann et al. Lancet 2008; 372: 547–53

ONTARGET Study

Table 2. Discontinuation of Study Medications and Selected Reasons for Permanent Discontinuation.*

Variable	Ramipril (N=8576)	Telmisartan (N=8542)	Combination Therapy (N=8502)	Telmisartan vs. Ramipril		Combination Therapy vs. Ramipril	
				Relative Risk	P Value	Relative Risk	P Value
		number (percent)					
Total no. of discontinuations†	2099 (24.5)	1962 (23.0)	2495 (29.3)	0.94	0.02	1.20	<0.001
Reason for permanent discontinuation							
Hypotensive symptoms	149 (1.7)	229 (2.7)	406 (4.8)	1.54	<0.001	2.75	<0.001
Syncope	15 (0.2)	19 (0.2)	29 (0.3)	1.27	0.49	1.95	0.03
Cough	360 (4.2)	93 (1.1)	392 (4.6)	0.26	<0.001	1.10	0.19
Diarrhea	12 (0.1)	19 (0.2)	39 (0.5)	1.59	0.20	3.28	<0.001
Angioedema	25 (0.3)	10 (0.1)	18 (0.2)	0.4	0.01	0.73	0.30
Renal impairment	60 (0.7)	68 (0.8)	94 (1.1)	1.14	0.46	1.58	<0.001

* There were no predefined criteria for each of the adverse events listed. Reasons listed are those provided by the investigator for the discontinuation of study drug.

† A patient could have multiple discontinuations, since patients were encouraged to restart study medications whenever possible after discontinuation.

N.Engl.J.Med. 2008; 358; 10:1547-1559

The NEW ENGLAND JOURNAL of MEDICINE

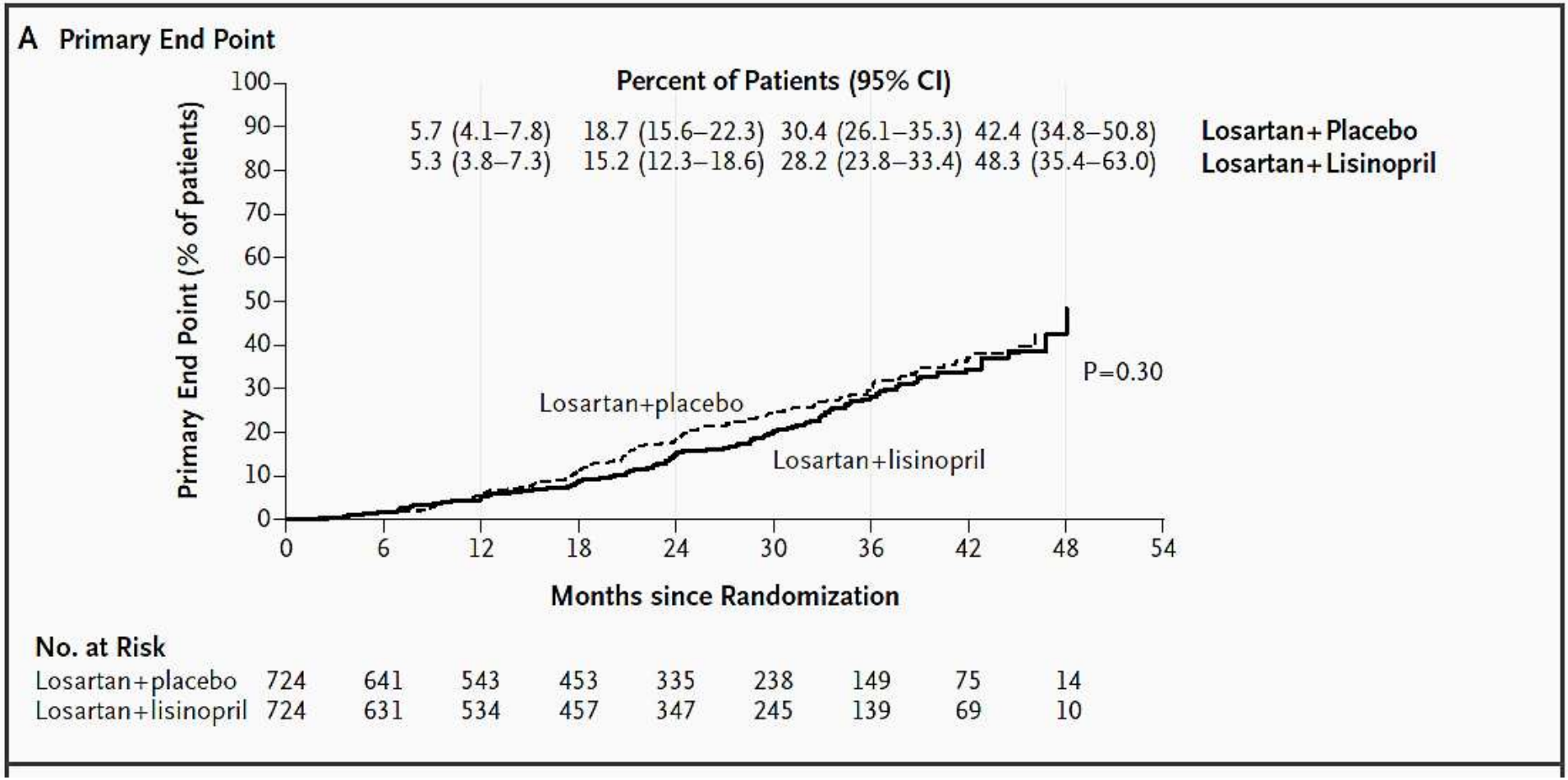
ORIGINAL ARTICLE

Combined Angiotensin Inhibition for the Treatment of Diabetic Nephropathy

Linda F. Fried, M.D., M.P.H., Nicholas Emanuele, M.D., Jane H. Zhang, Ph.D., Mary Brophy, M.D., Todd A. Conner, Pharm.D., William Duckworth, M.D., David J. Leehey, M.D., Peter A. McCullough, M.D., M.P.H., Theresa O'Connor, Ph.D., Paul M. Palevsky, M.D., Robert F. Reilly, M.D., Stephen L. Seliger, M.D., Stuart R. Warren, J.D., Pharm.D., Suzanne Watnick, M.D., Peter Peduzzi, Ph.D., and Peter Guarino, M.P.H., Ph.D., for the VA NEPHRON-D Investigators*

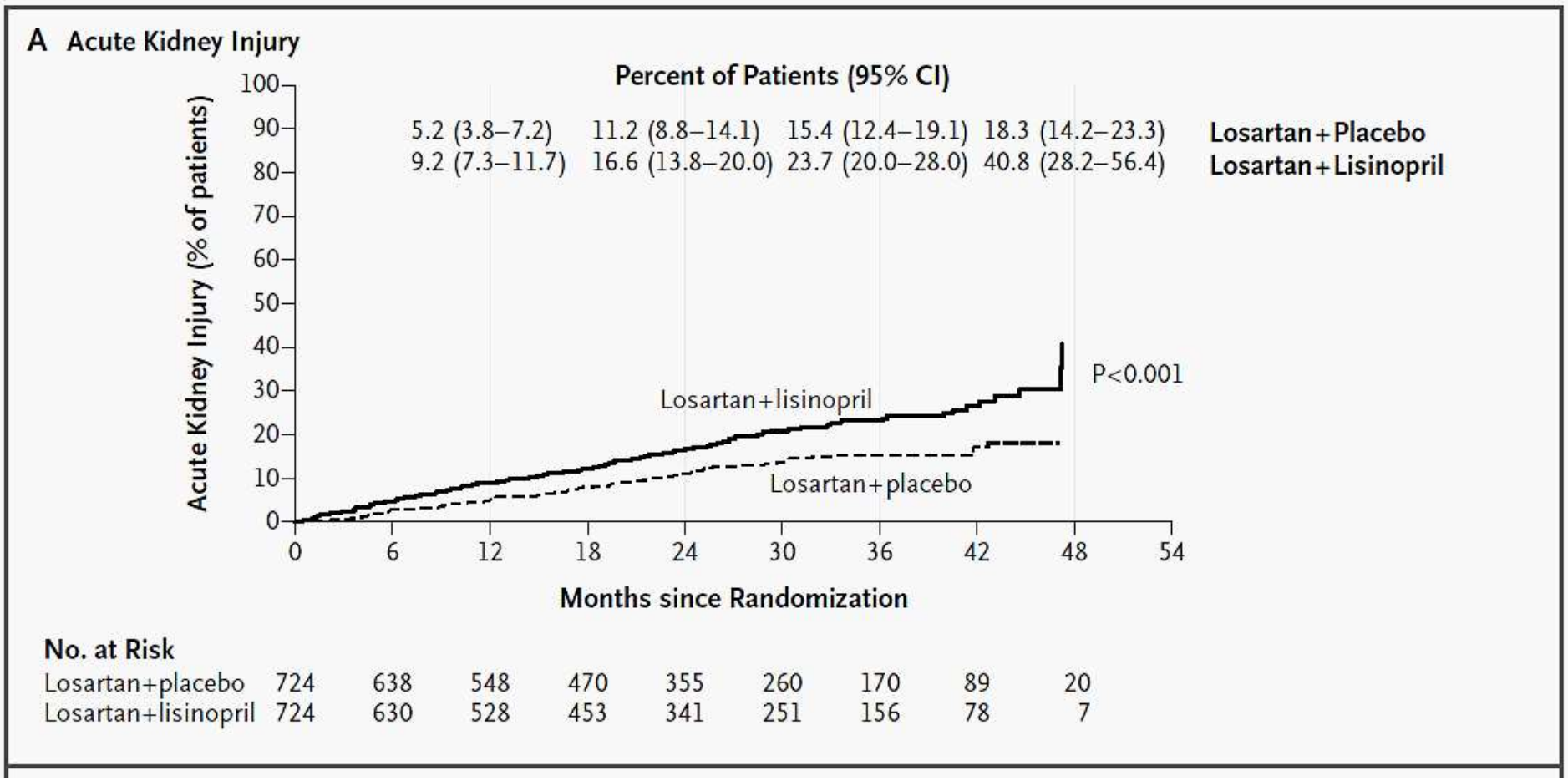
N. Engl. J. Med.,2013;369:1892-903

Kaplan–Meier Plot of Cumulative Probabilities of the Primary End Points



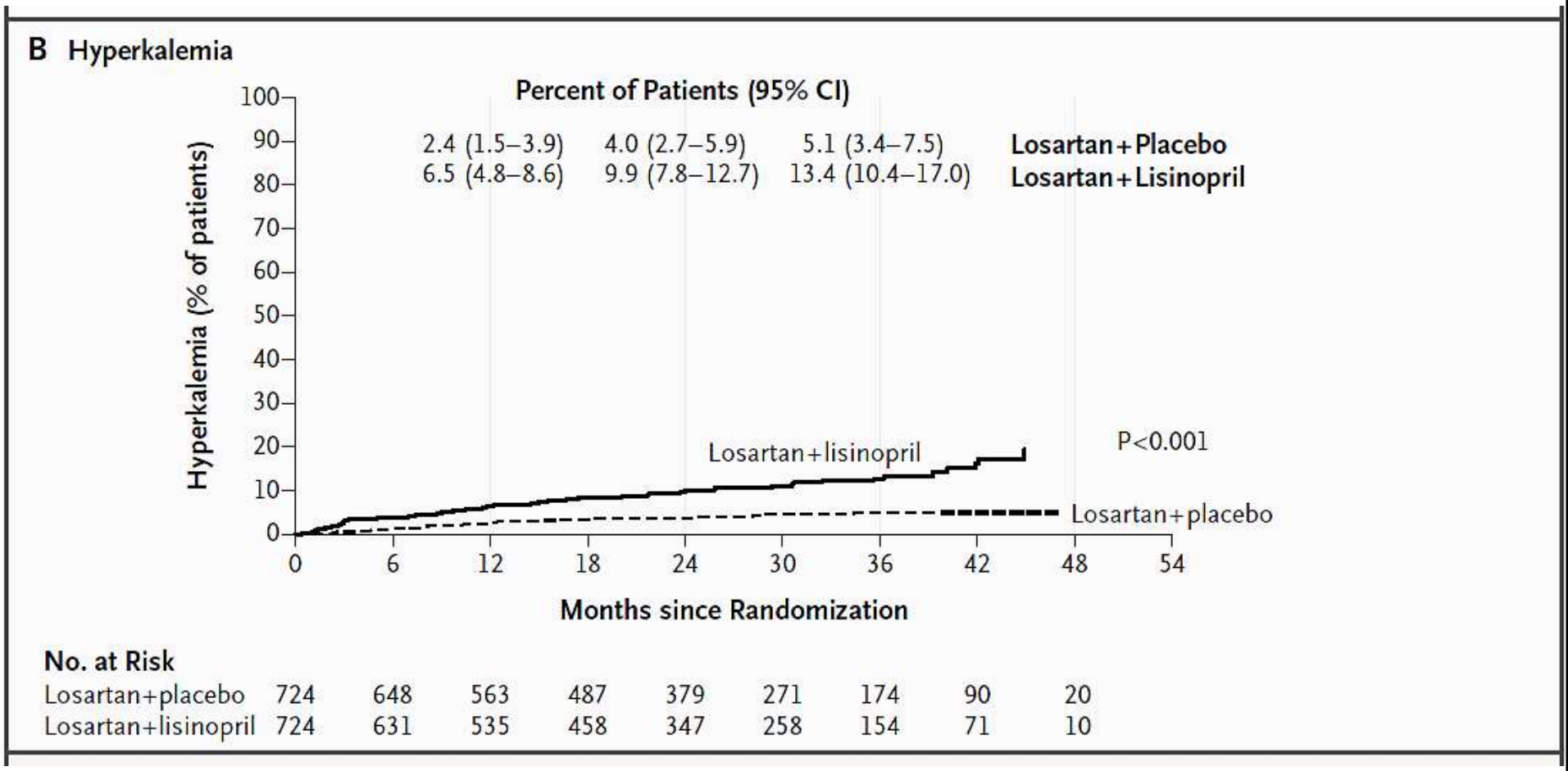
Fried L.F et al.,N. Engl. J. Med.,2013;369:1892-903

Kaplan–Meier Plot of Cumulative Probabilities of Acute Kidney Injury in Patients with ADPKD



Fried L.F et al.,N. Engl. J. Med.,2013;369:1892-903

Kaplan–Meier Plot of Cumulative Probabilities of Hyperkalemia in Patients with ADPKD



Fried L.F et al.,N. Engl. J. Med.,2013;369:1892-903

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Blood Pressure in Early Autosomal Dominant Polycystic Kidney Disease

Robert W. Schrier, M.D., Kaleab Z. Abebe, Ph.D., Ronald D. Perrone, M.D., Vicente E. Torres, M.D., Ph.D., William E. Braun, M.D., Theodore I. Steinman, M.D., Franz T. Winklhofer, M.D., Godela Brosnahan, M.D., Peter G. Czarnecki, M.D., Marie C. Hogan, M.D., Ph.D., Dana C. Miskulin, M.D., Frederic F. Rahbari-Oskoui, M.D., Jared J. Grantham, M.D., Peter C. Harris, Ph.D., Michael F. Flessner, M.D., Ph.D., Kyongtae T. Bae, M.D., Charity G. Moore, Ph.D., M.S.P.H., and Arlene B. Chapman, M.D., for the HALT-PKD Trial Investigators*

N. Engl. J. Med., 2014 Dec 11;371(24

The NEW ENGLAND JOURNAL of MEDICINE

Angiotensin Blockade in Late Autosomal Dominant Polycystic Kidney Disease

Vicente E. Torres, M.D., Ph.D., Kaleab Z. Abebe, Ph.D., Arlene B. Chapman, M.D., Robert W. Schrier, M.D., William E. Braun, M.D., Theodore I. Steinman, M.D., Franz T. Winklhofer, M.D., Godela Brosnahan, M.D., Peter G. Czarnecki, M.D., Marie C. Hogan, M.D., Ph.D., Dana C. Miskulin, M.D., Frederic F. Rahbari-Oskoui, M.D., Jared J. Grantham, M.D., Peter C. Harris, Ph.D., Michael F. Flessner, M.D., Ph.D., Charity G. Moore, Ph.D., M.S.P.H., and Ronald D. Perrone, M.D., for the HALT-PKD Trial Investigators*

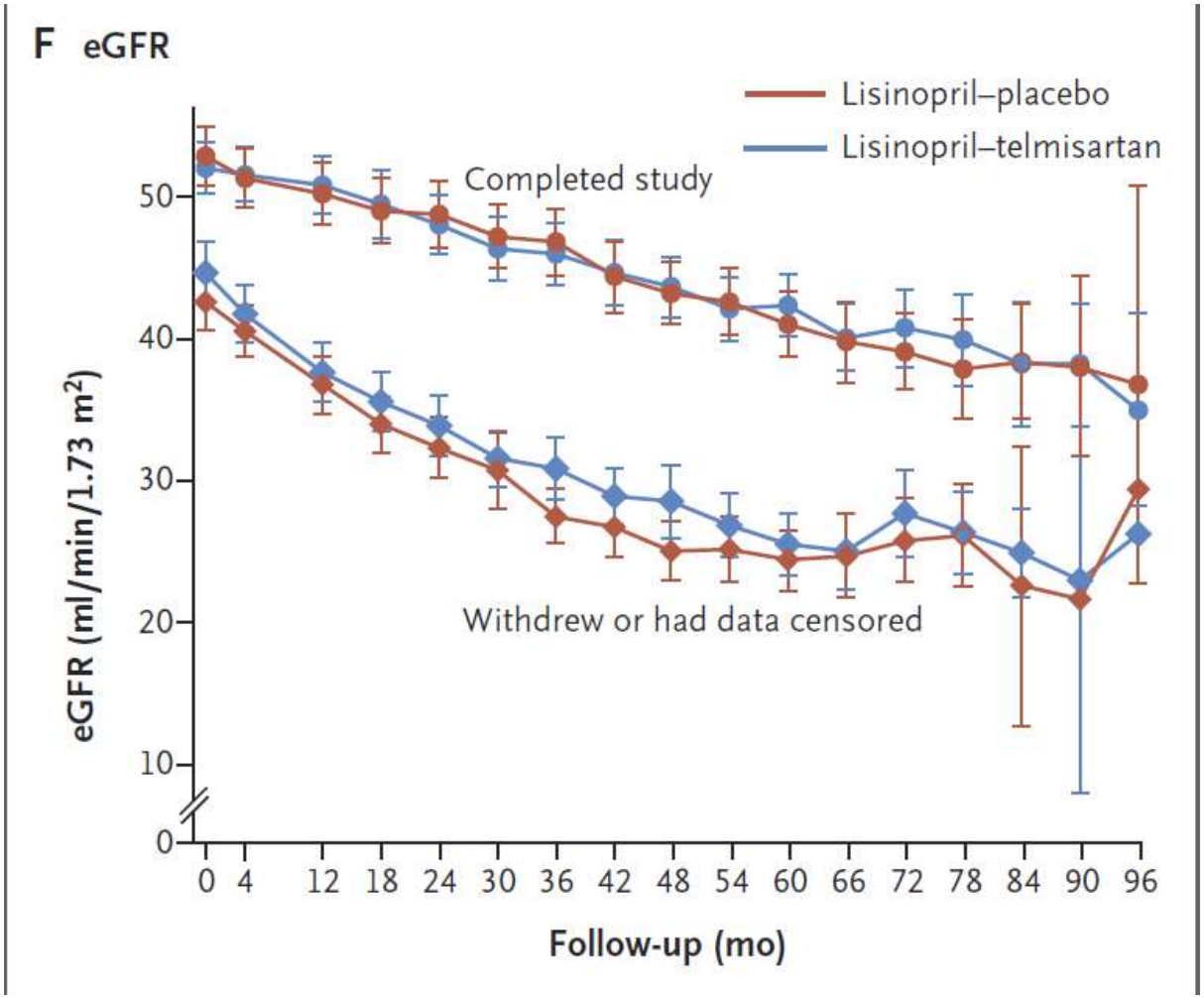
N. Engl. J. Med., 2014 Dec 11;371(24):2267-2276

Baseline characteristic of patients with ADPKD

Characteristic	Lisinopril–Telmisartan (N=244)	Lisinopril–Placebo (N=242)
Age — yr	48.6±8.5	48.9±8.1
Male sex — no. (%)	115 (47.1)	120 (49.6)
Body-mass index§	28.0±4.9	28.0±5.5
Serum creatinine — mg/dl¶	1.5±0.4	1.6±0.4
Estimated GFR — ml/min/1.73 m^2‖	48.5±11.5	47.9±12.2
Urinary sodium — mmol/24 hr	177.4±78.2	178.2±84.0
Urinary aldosterone — μg/24 hr	10.2±8.4	9.1±5.8
Urinary albumin — mg/24 hr		
Median	29.7	28.1
Interquartile range	16.6–71.8	17.3–78.0

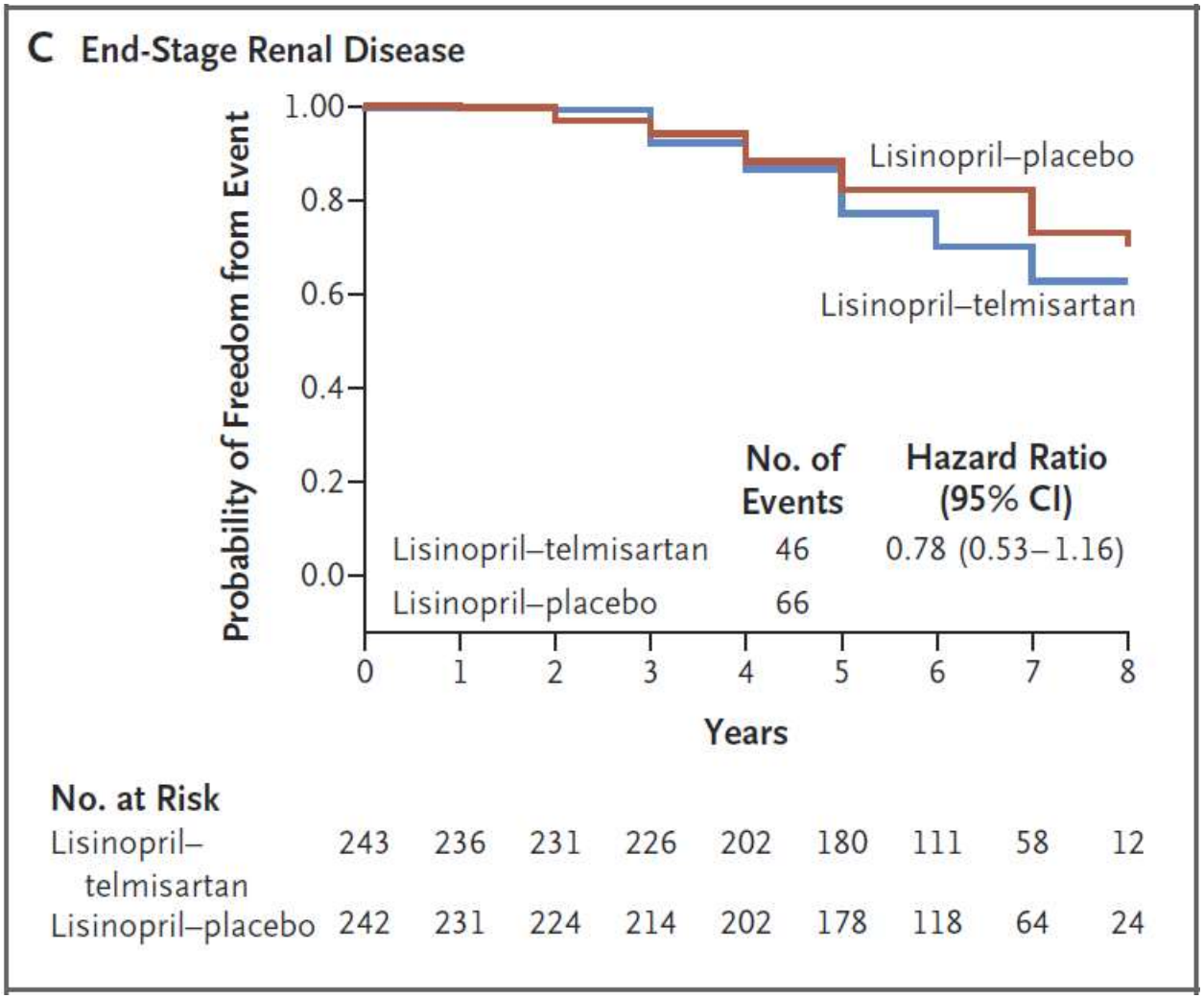
Torres V.E. i ws. , N. Engl. J. Med., 2014 Dec 11;371(24):2267-2276

Changes of eGFR



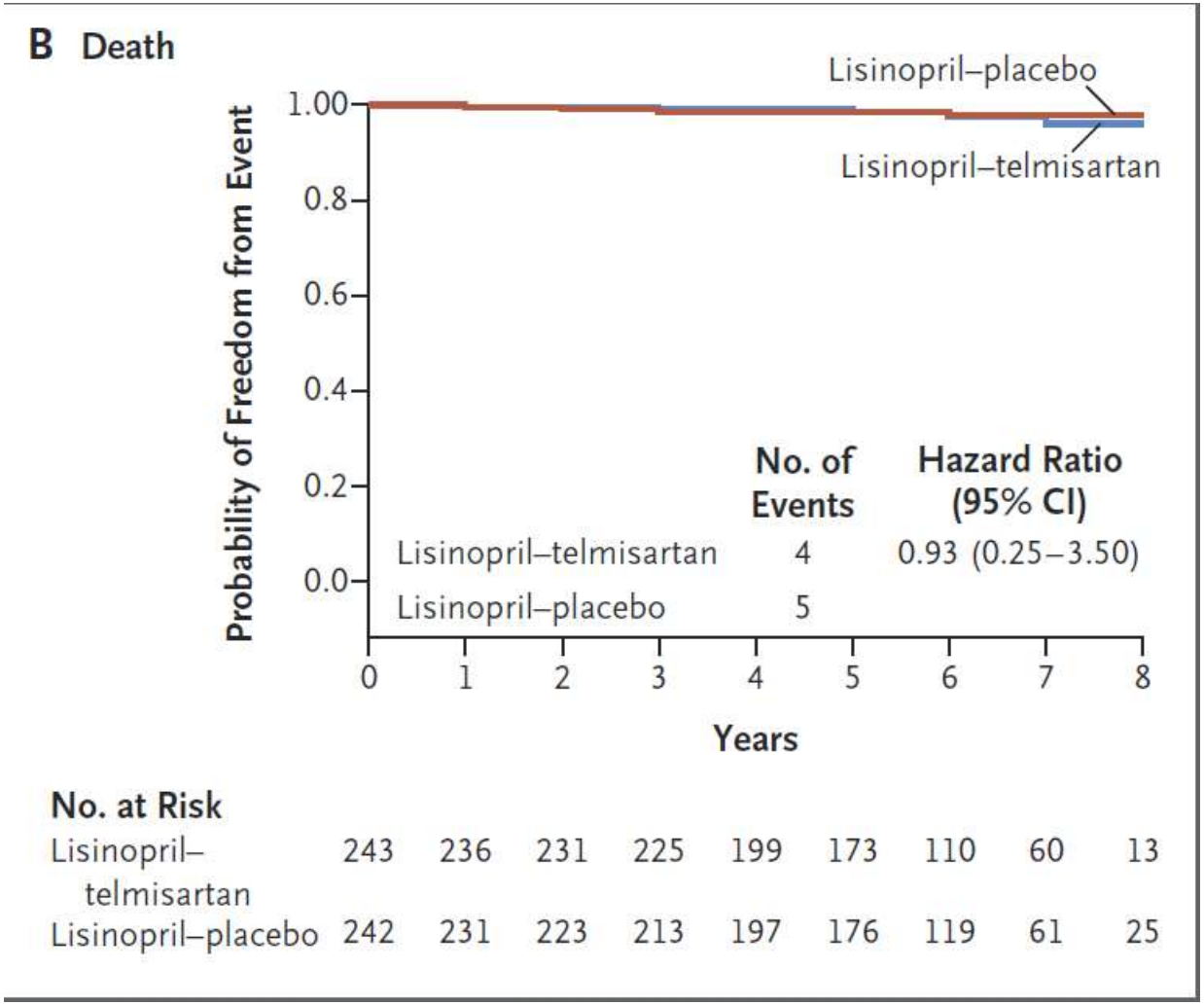
Torres V.E. i ws. , N. Engl. J. Med., 2014 Dec 11;371(24):2267-2276

Risk of ESRD in patients with ADPKD



Torres V.E. i ws. , N. Engl. J. Med., 2014 Dec 11;371(24):2267-2276

Death in patients with ADPKD



Torres V.E. i ws. , N. Engl. J. Med., 2014 Dec 11;371(24):2267-2276

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Future Perspectives

Am J Nephrol 2014;39:46–49
DOI: 10.1159/000357593

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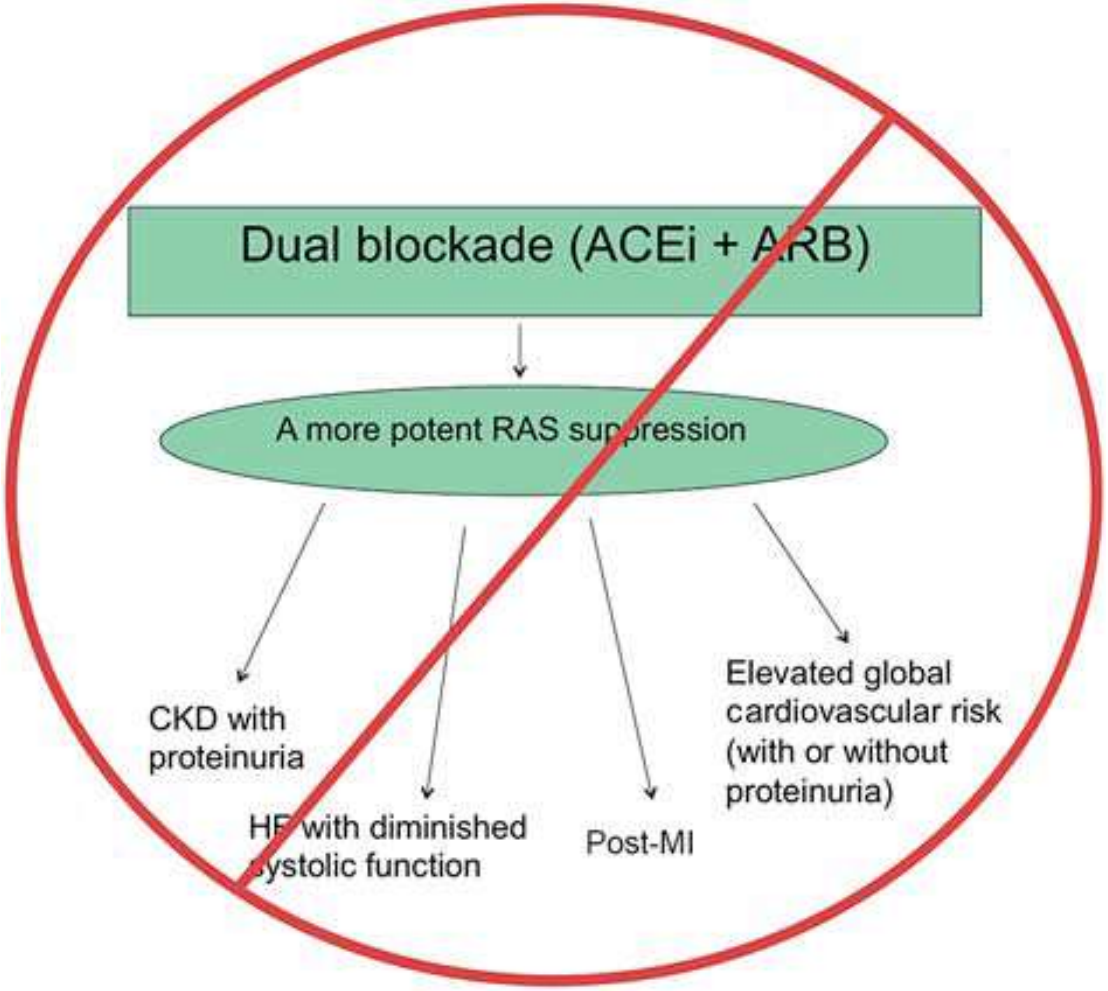
Perspective on Combination RAS Blocking Therapy: Off-TARGET, Dis-CORD, MAP-to-Nowhere, Low ALTITUDE, and NEPHRON-D

Friedrich C. Luft

Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Medical Faculty of the Charité, Berlin, Germany; Department of Clinical Pharmacology, Vanderbilt University School of Medicine, Nashville, Tenn., USA

A common schema of the putative advantages afforded by 'double blockade' of the RAAS.
Recent trails suggest that this view should be revised



????

Luft. F.C. Am J Nephrol 2014;39:46–49

RAS BLOCKADE

Nephroprotection by dual RAS blockade—a welcome back

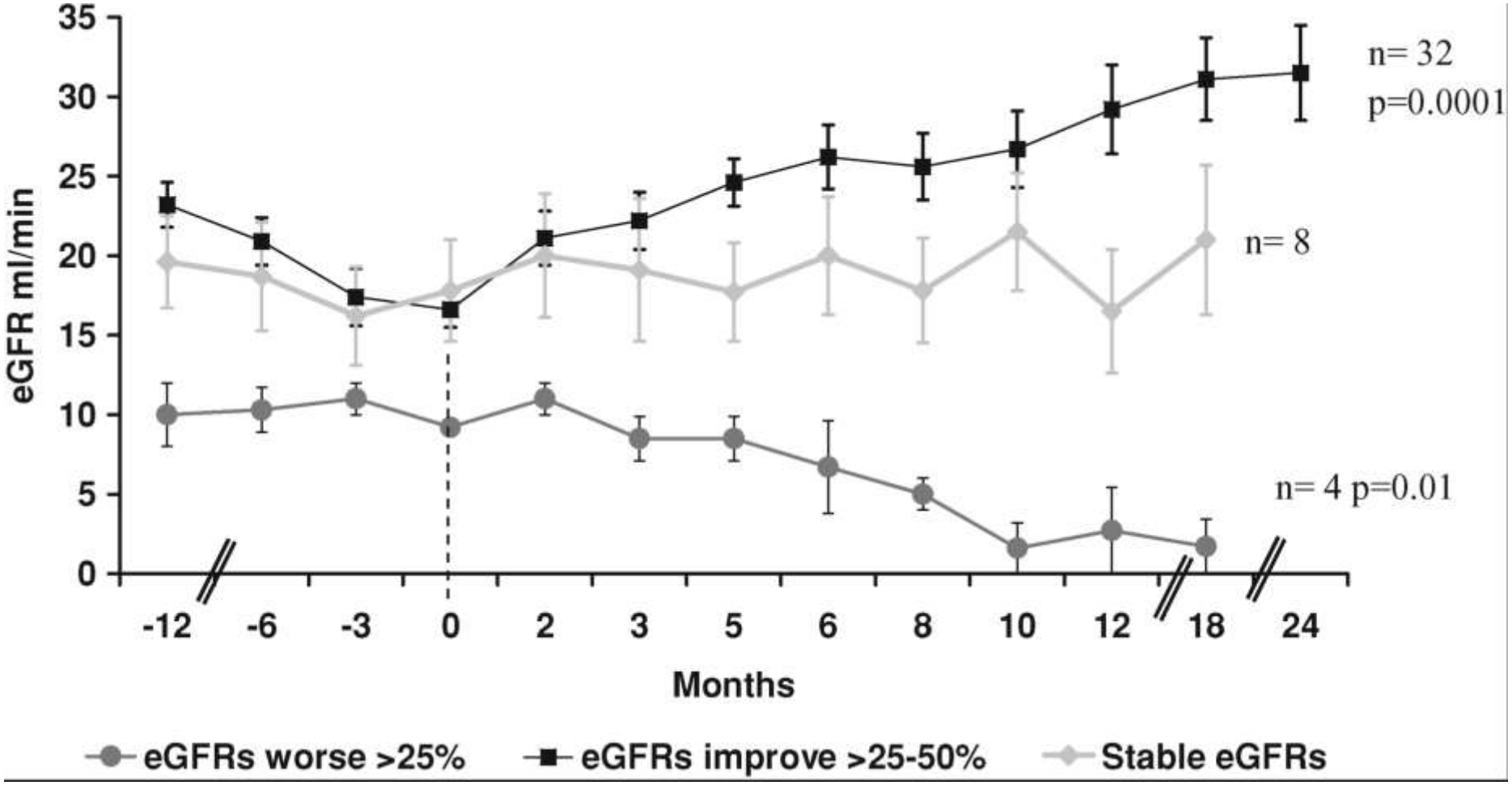
Piero Ruggenenti and Giuseppe Remuzzi

Refers to Palmer, S. C. *et al.* Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease: a network meta-analysis. *Lancet* **385**, 2047–2056 (2015)

A new meta-analysis shows that dual blockade of the renin–angiotensin system is the most effective approach to prevent end-stage renal disease in patients with diabetes and kidney disease. Combination therapy should therefore be reconsidered as the most powerful tool for nephroprotection, provided that treatment is individually tailored by careful dose-titration.

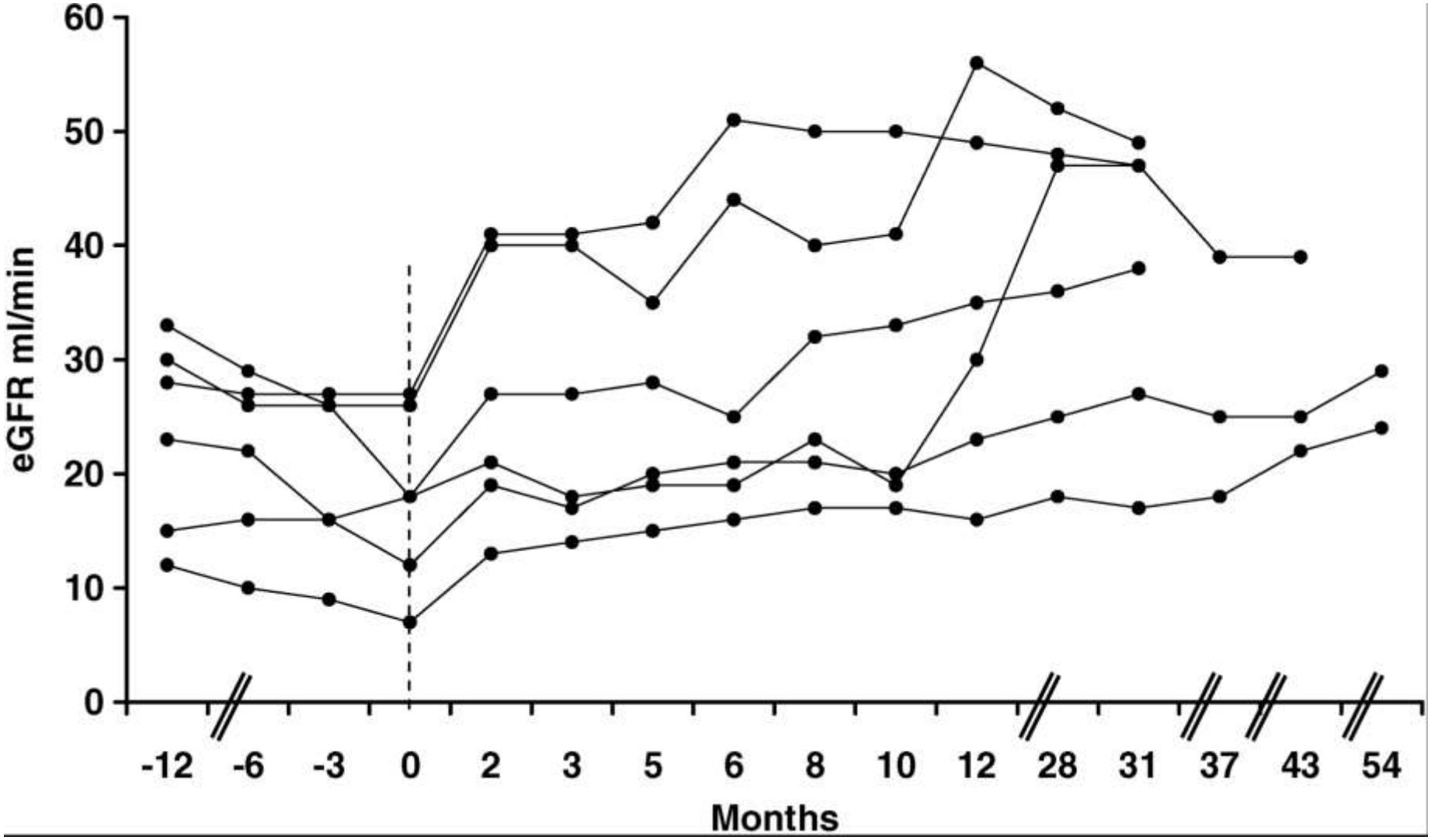
NATURE REVIEWS | NEPHROLOGY ,Published online 4 August 2015

Changes in eGFR after stopping ACEi/ARB in patients with advanced CKD



Aimun K. et al., Nephrol. Dial. Transplant., 2010, 25: 3977–3982

Example of the course of selected patients with sustained improvement in eGFR (>25%) up to 54 months after stopping ACEi/ARB



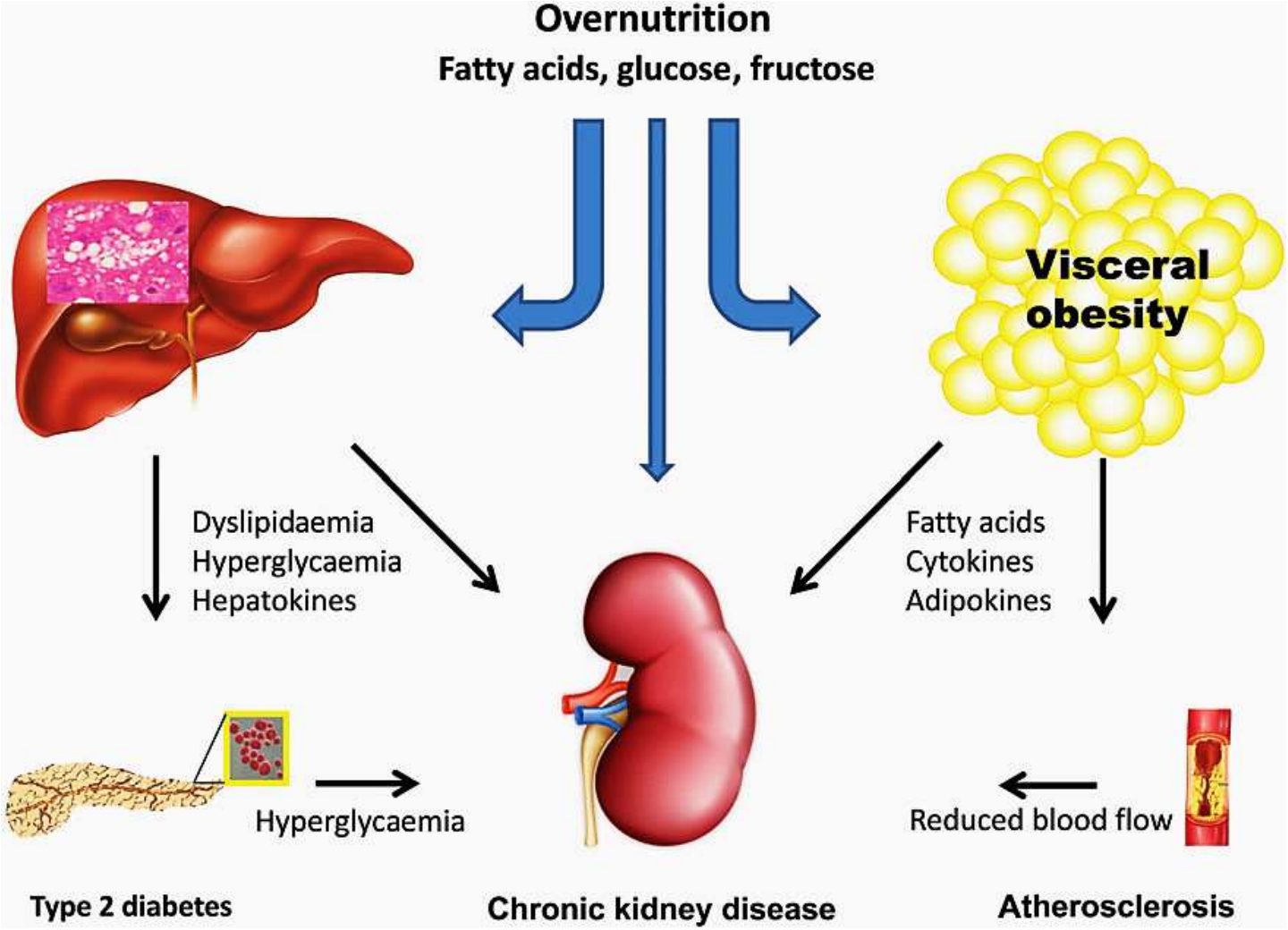
Aimun K. et al., Nephrol. Dial. Transplant., 2010, 25: 3977–3982

Nephroprotection: Where are we in 2015?

With confirmed benficial effect:

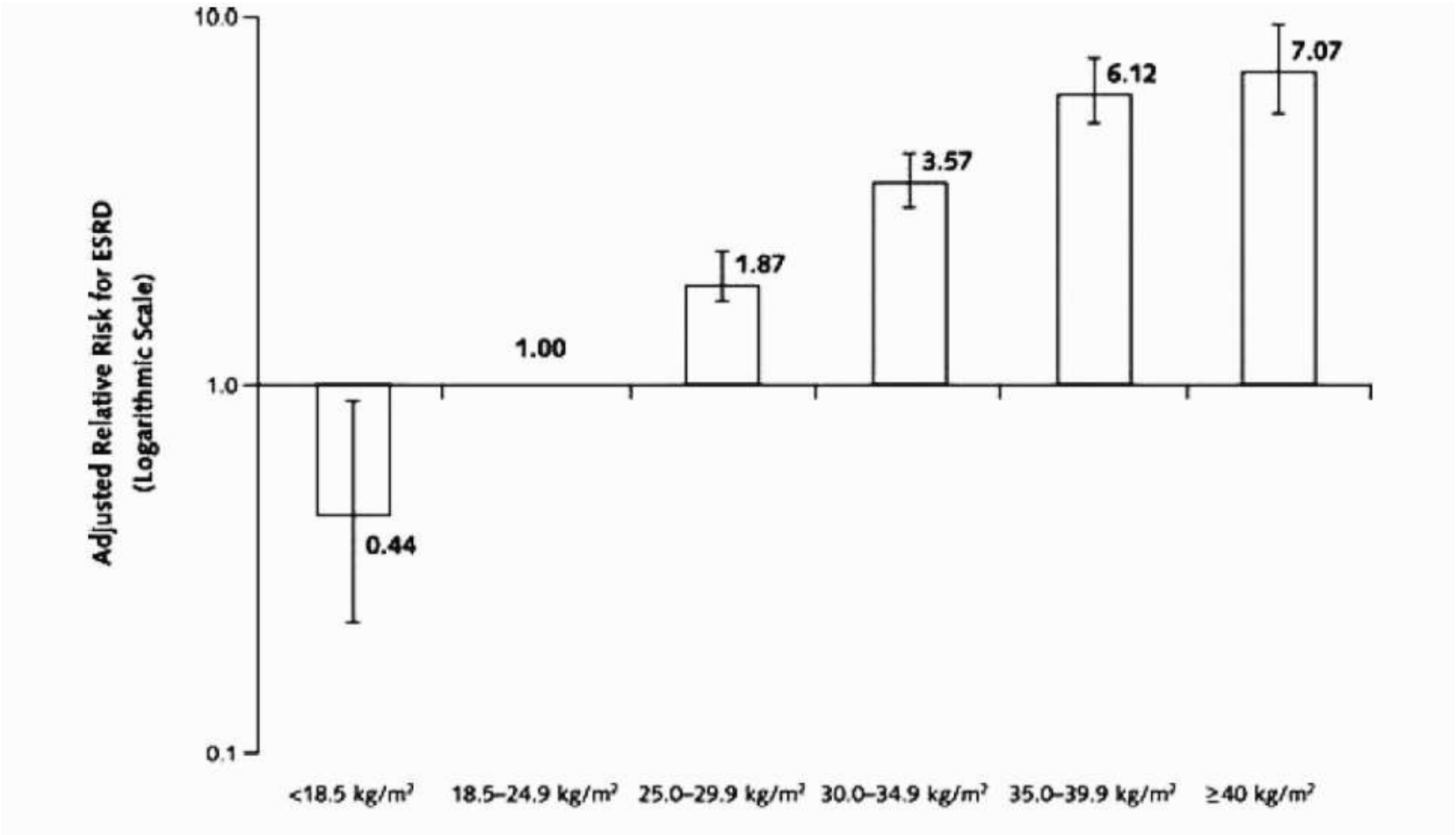
- Reduction of blood pressure
- Blockade of the RAAS (beyond BP reduction)
- Reduction of BMI
- Reduction of protein intake
- Correction of phosphatemia
- Correction of metabolic acidosis
- Correction of glucose (HBA1C) in DM patients
- Supplementation of Vitamin D
- Renal denervation

Obesity-associated pathways in the development of CKD



Stefan N. et al. Nephrol. Dial. Transplant., 2014, advanced publication

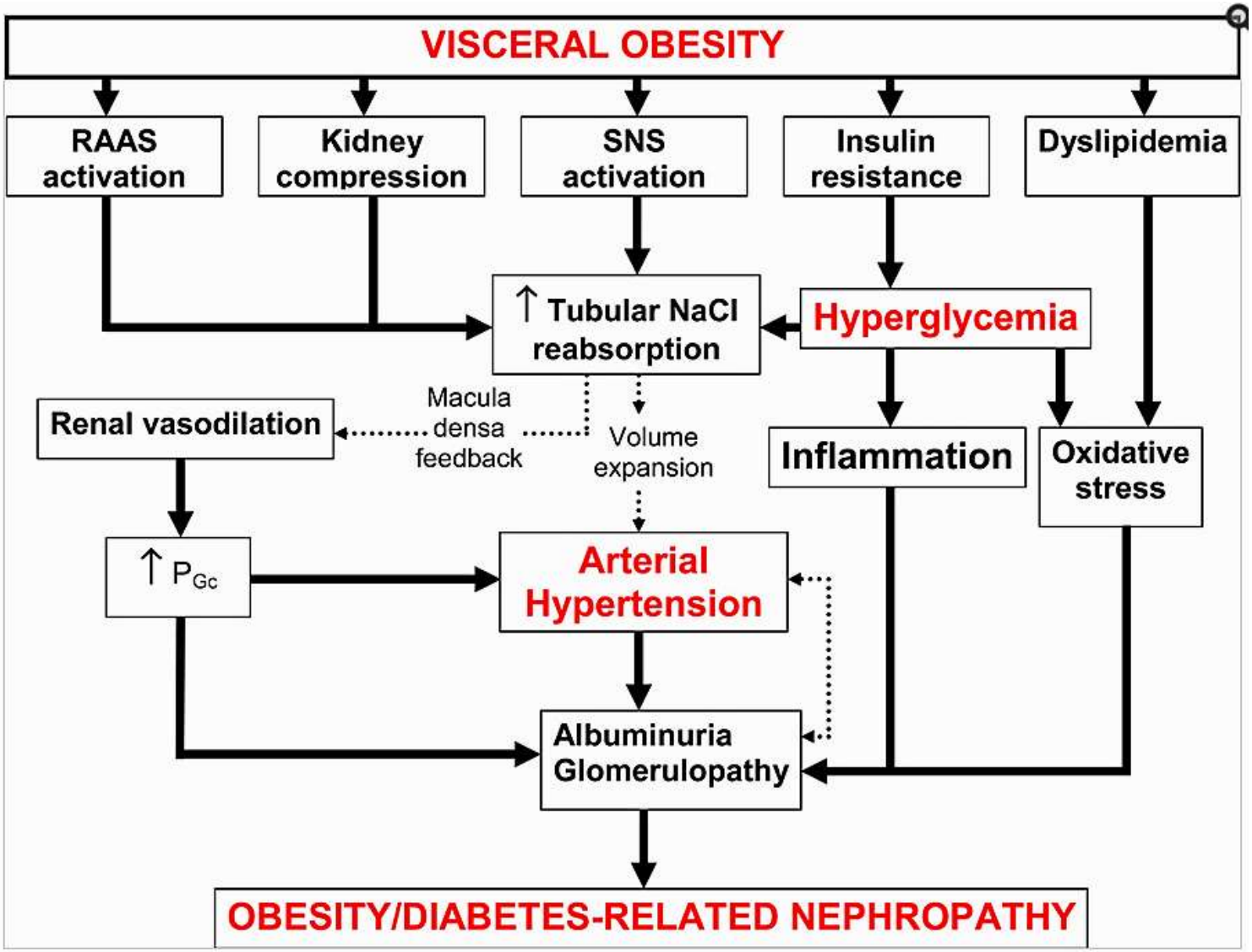
Adjusted relative risk for end-stage renal disease (ESRD) by body mass index (BMI)



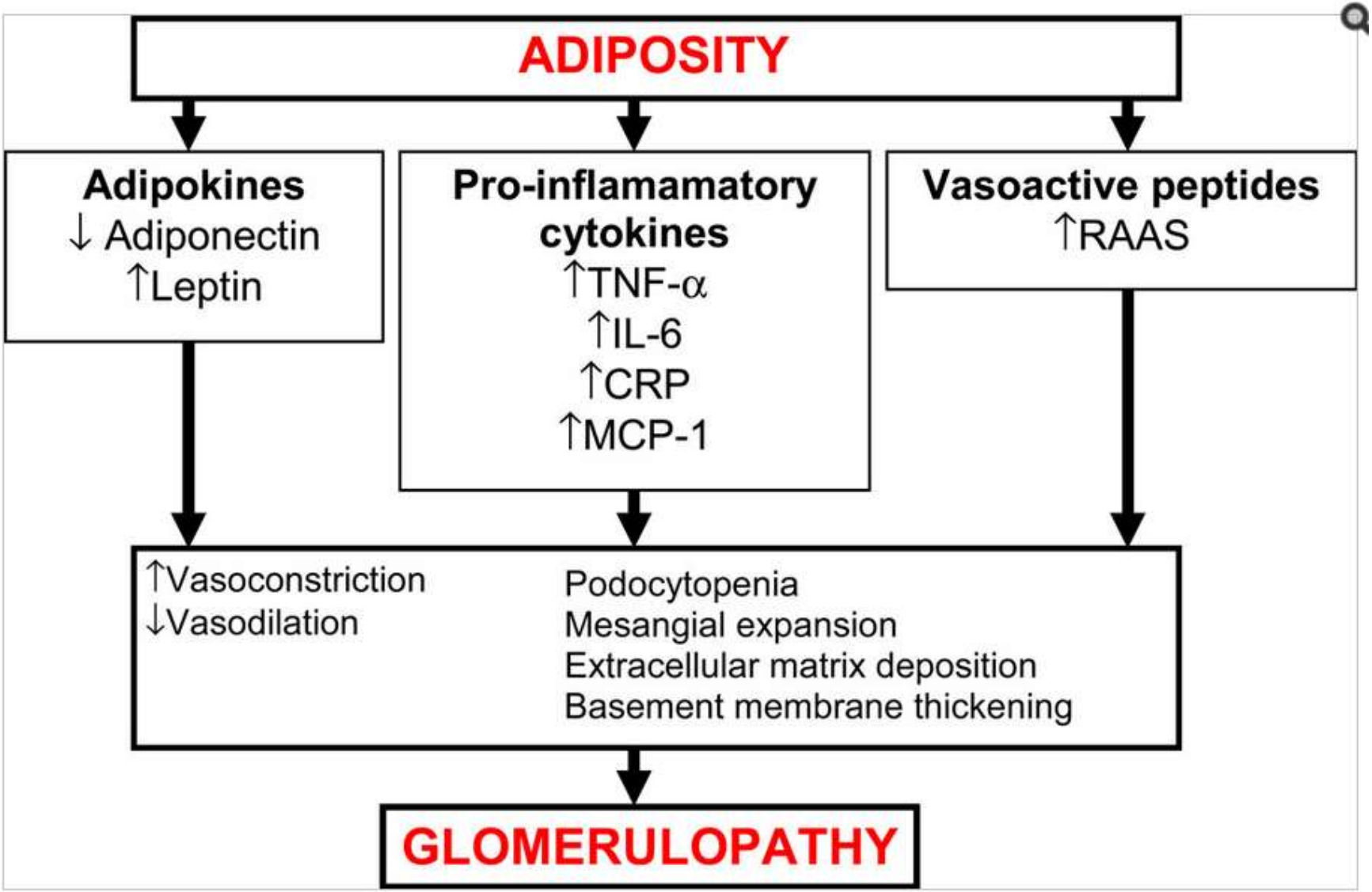
Model adjusted for multiphasic health checkup period, age, sex, race, education level, smoking status, history of myocardial infarction, serum cholesterol level, proteinuria, haematuria and serum creatinine level

Hsu et al. Ann. Intern. Med. 2006; 144: 21–28

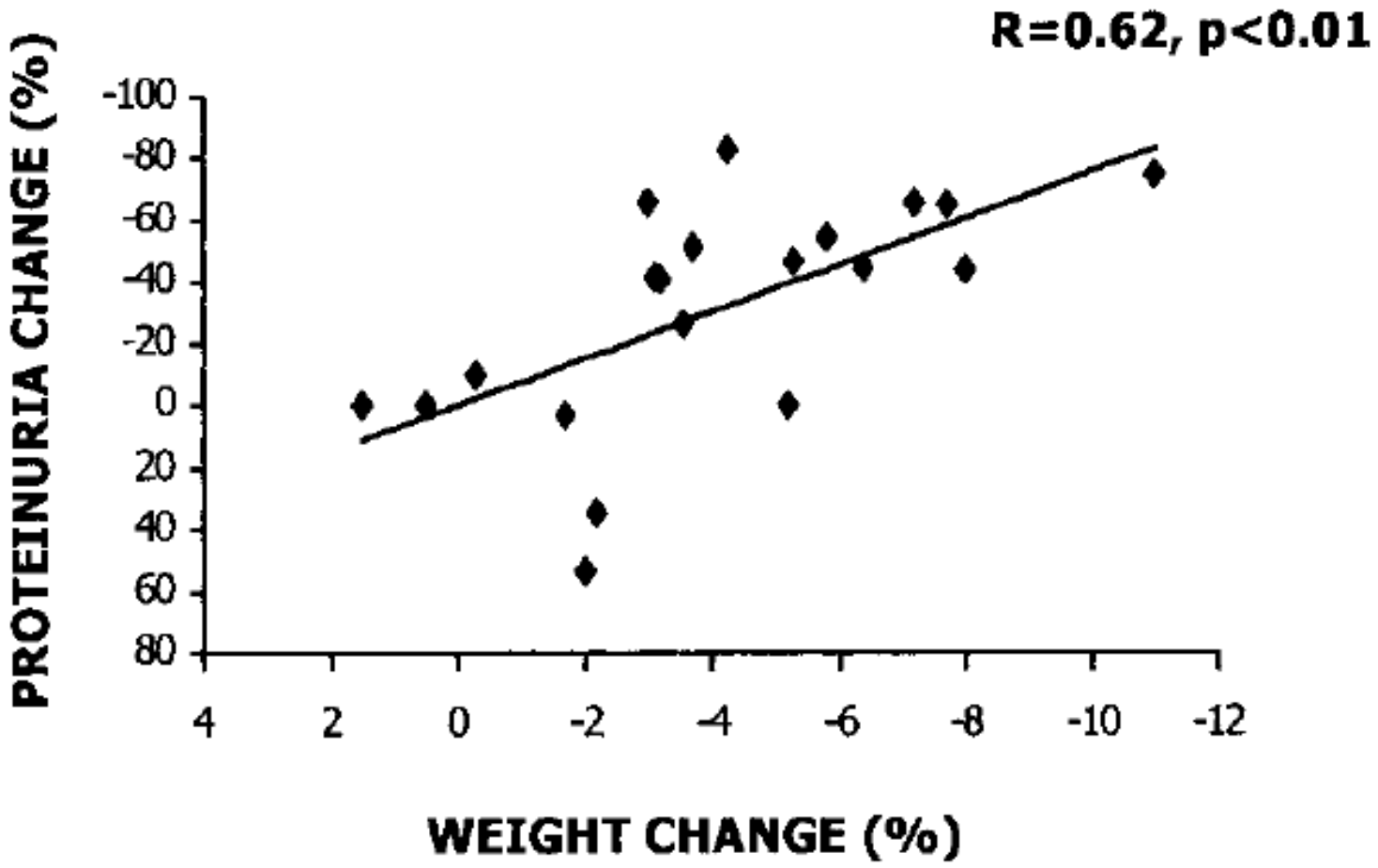
Interaction between metabolic and hemodynamic pathways in the pathophysiology of obesity related hypertension and renal disease



Mechanisms of obesity-related CKD



Relationship of proteinuria and weight changes in diet-group patients



Morales E. et al., Am. J. Kidney Dis., 2003, 41: 319-327

Exercise augments weight loss induced improvement in renal function in obese metabolic syndrome individuals

Nora E. Straznicky[a], Mariee T. Grima[a], Elisabeth A. Lambert[a], Nina Eikelis[b], Tye Dawood[a], Gavin W. Lambert[a], Paul J. Nestel[c], Kazuko Masuo[a], Carolina I. Sari[a], Reena Chopra[a], Justin A. Mariani[d] and Markus P. Schlaich[b]

Objective Metabolic syndrome (MetS) obesity is an independent risk factor for chronic kidney disease. This study was conducted to examine the effects of lifestyle interventions on renal parameters and putative metabolic, neuroadrenergic and hemodynamic mediators of renal injury.

Methods Untreated men and women (mean age 55 ± 1 years; BMI $32.7 \pm 0.6\,kg/m^2$) without pre-existing renal dysfunction, who fulfilled MetS criteria were randomized to dietary weight loss (WL, $n = 13$), weight loss combined with aerobic exercise (WL + EX, $n = 13$), or no treatment (control, $n = 12$). Estimated glomerular filtration rate (eGFR), 24 h urinary albumin excretion, plasma renin activity (PRA), muscle sympathetic nerve activity (MSNA), baroreflex sensitivity (BRS), anthropometric, metabolic and fitness variables were measured at baseline and week 12.

Conclusion Moderate weight loss in obese MetS patients is associated with a reduction in albuminuria and an improvement in eGFR which is augmented by exercise co-intervention. *J Hypertens* 29:553–564 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.

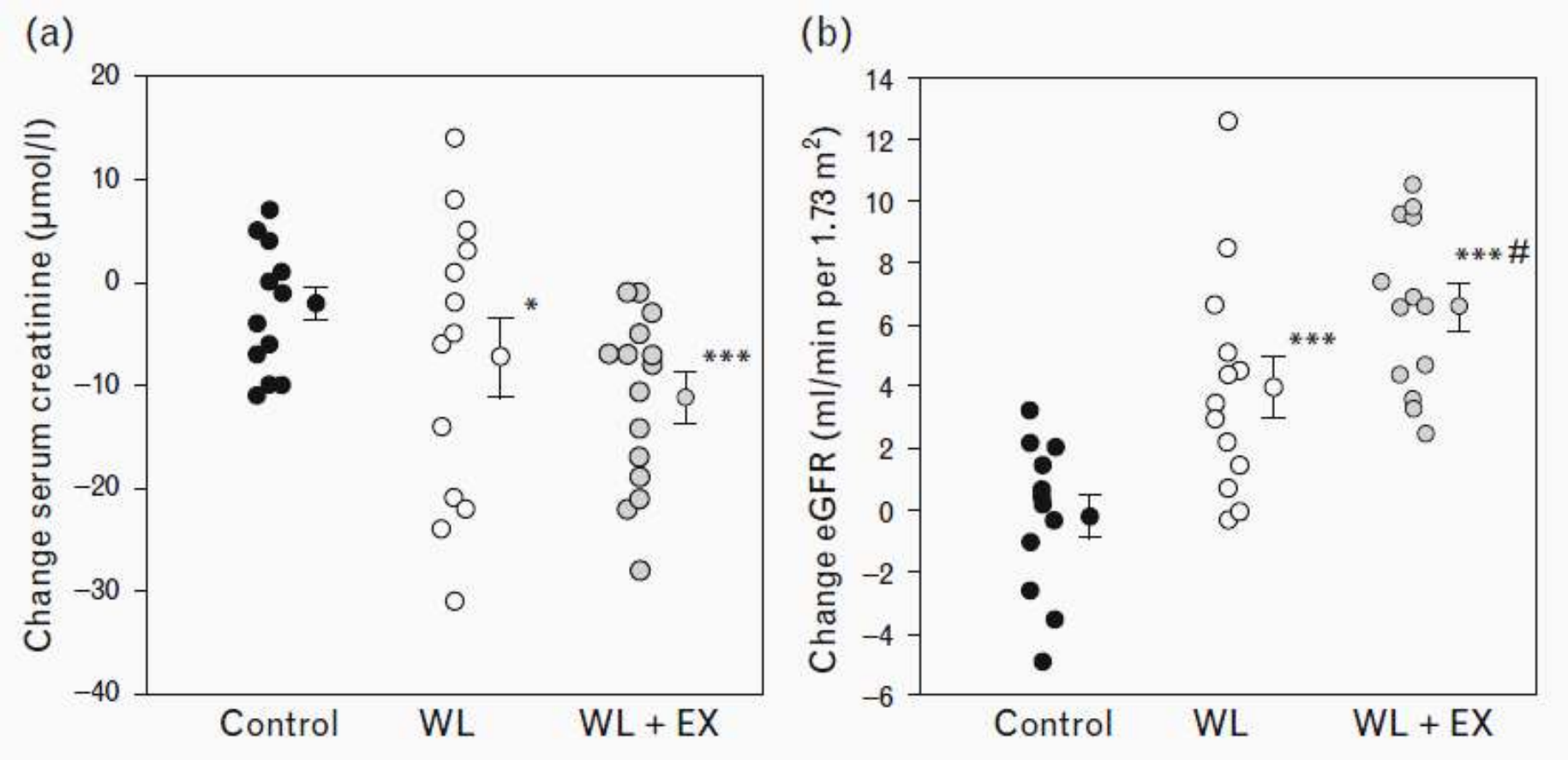
Journal of Hypertension 2011, 29:553–564

Keywords: aerobic exercise, albuminuria, metabolic syndrome, obesity, renal function, sympathetic nervous system, weight loss

Abbreviations: BRS, baroreflex sensitivity; CKD, chronic kidney disease; DASH, Dietary Approaches to Stop Hypertension; DEXA, dual-energy X-ray absorptiometry; eGFR, estimated glomerular filtration rate; hs-CRP, high sensitivity C-reactive protein; MDRD, Modification of Diet in Renal Disease; MetS, metabolic syndrome; MSNA, muscle sympathetic nervous activity; NEFA, non-esterified fatty acids; OGTT, oral glucose tolerance test; PRA, plasma renin activity; RAAS, renin–angiotensin–aldosterone system; SNS, sympathetic nervous system; $\dot{V}O_{2max}$, maximal oxygen consumption during incremental cycle ergometry protocol; WL, weight loss by hypocaloric diet; WL + EX, weight loss by hypocaloric diet and aerobic exercise

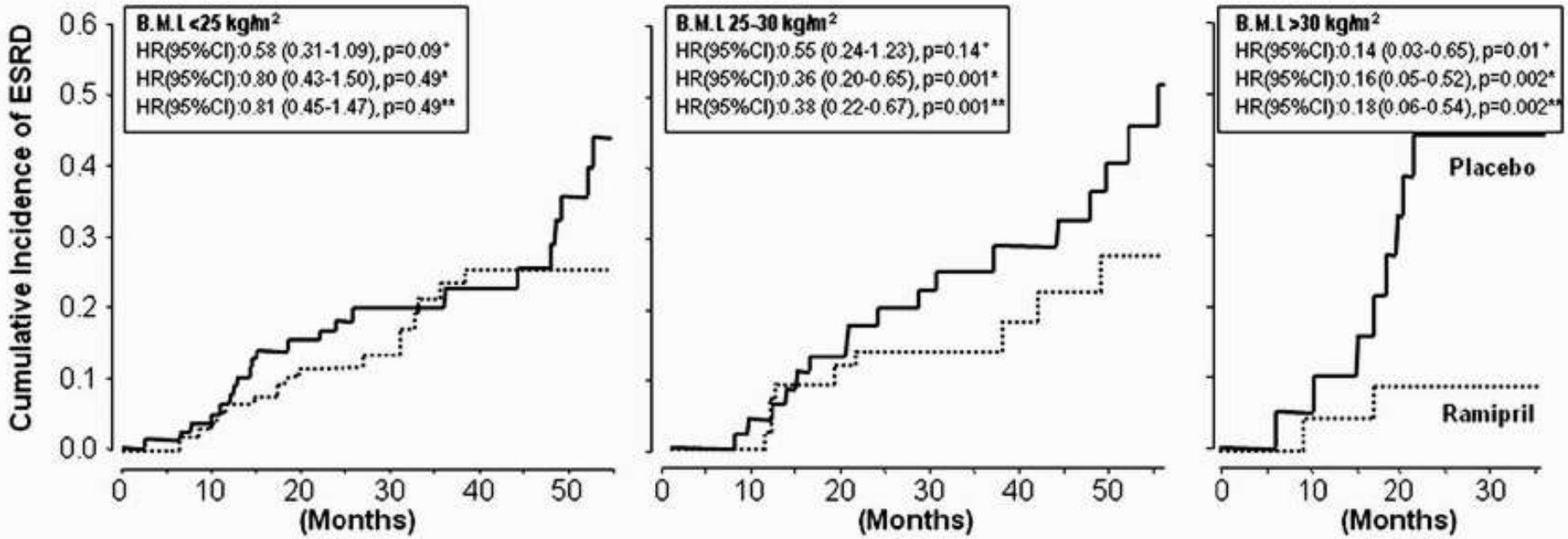
Straznicky N.E. et al., J. Hypertens., 2011, 29, 553-564

Individual and average changes in serum creatinine (a) and eGFR (b) after 12 weeks lifestyle intervention with weight loss by caloric restriction (WL)weight loss by caloric restriction and aerobic exercise (WL+EX) or no treatment (Control)



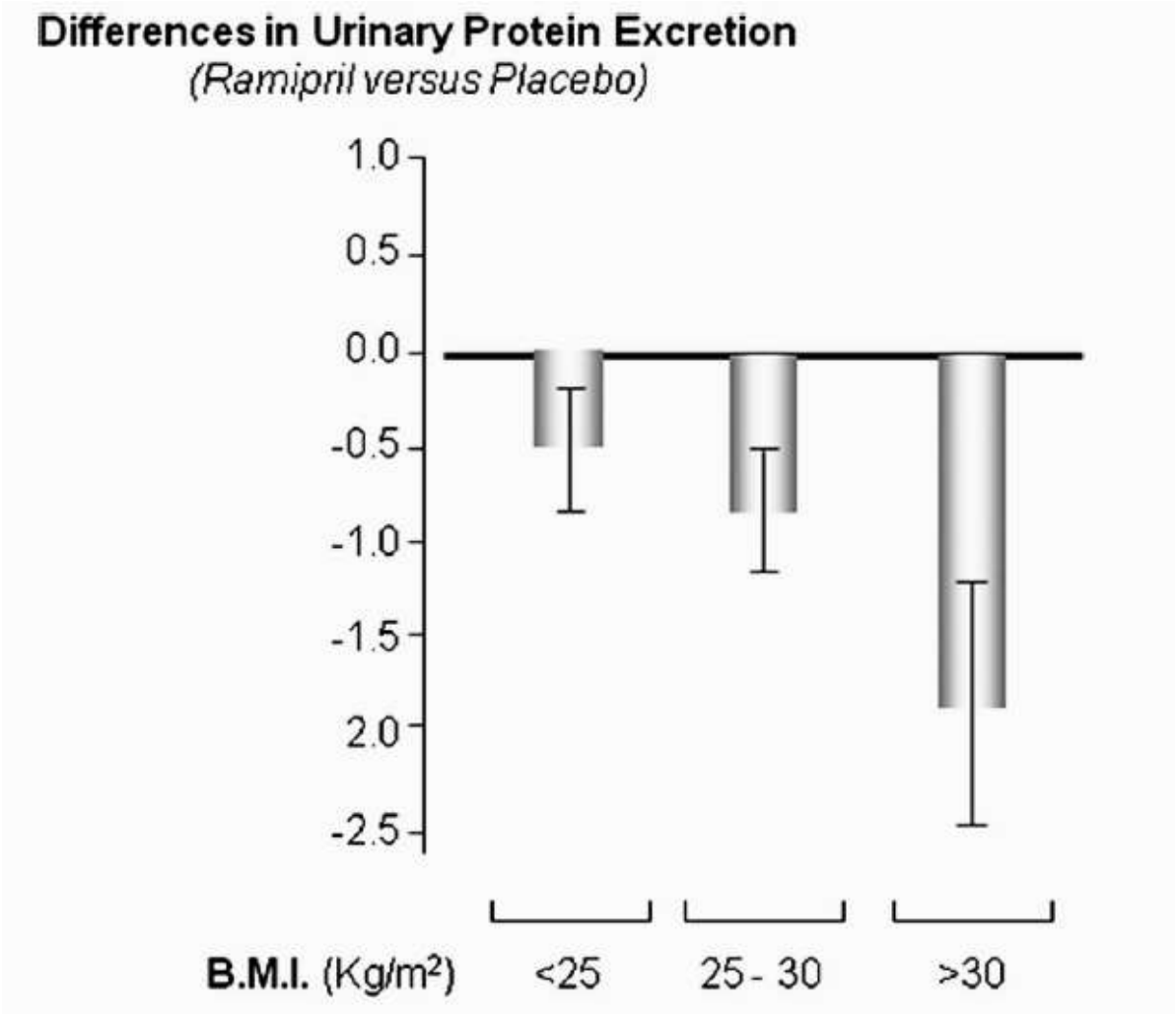
Straznicky N. E. et al., J. Hypertens., 2011, 29, 553-564

Ramipril markedly attenuates the risk of ESDR in overweight and obese patients



Mallamaci F. et al. J. Am. Soc.Nephrol., 2011, 22, 1122-1128

Anti-proteinuric effect of ramipril



Mallamaci F. et al. J. Am.Soc.Nephrol., 2011; 22: 1122-1128

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- Reduction of protein intake
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- Correction of metabolic acidosis
- Correction of glucose (HBA1C) in DM patients
- Supplementation of Vitamin D
- Renal denervation

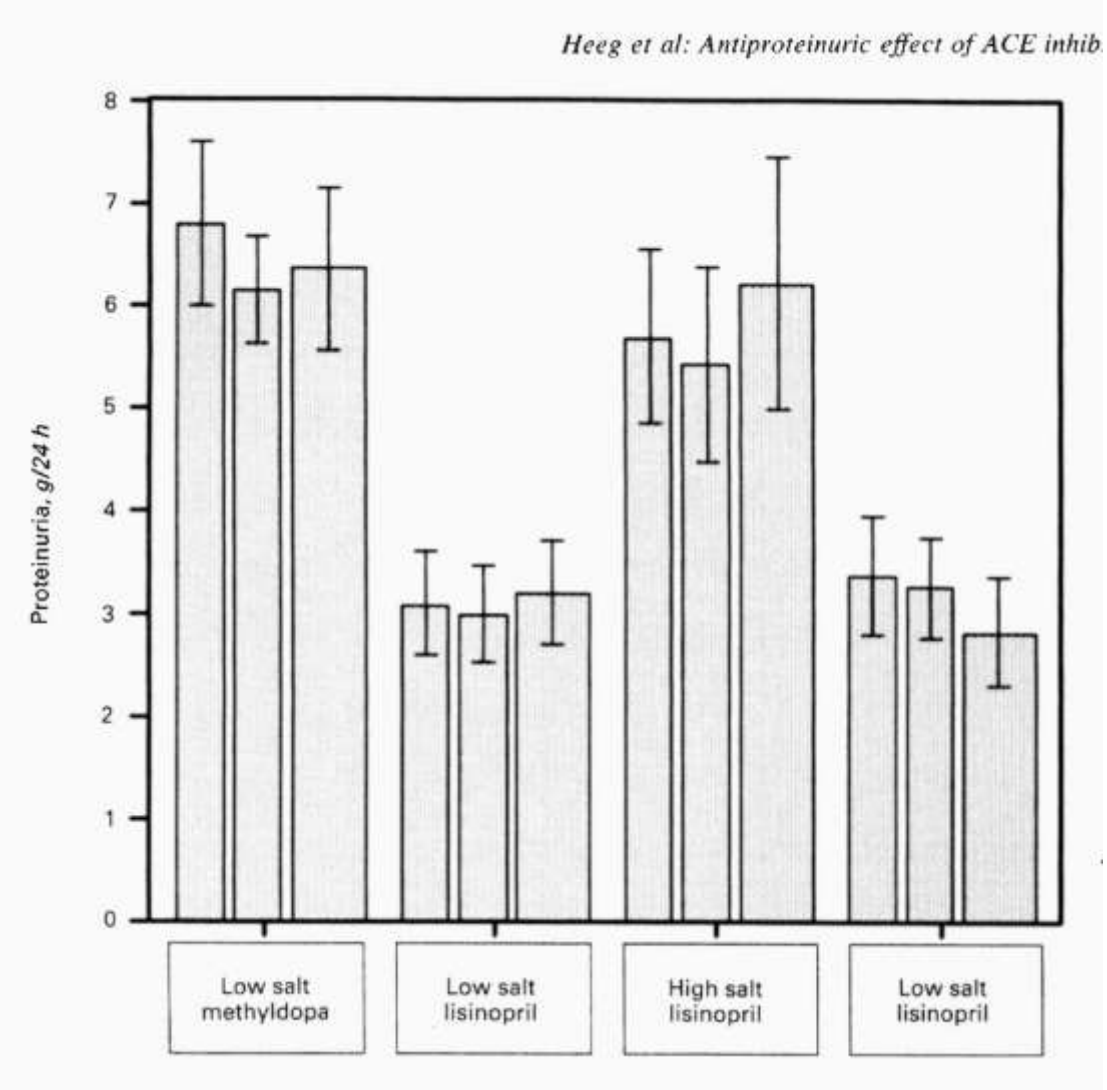
Diet and progression of CKD

Table 1 The influence of diet on the progression of renal insufficiency

1. Changes in the measurement of the rate of loss of kidney function [20]
   (a) An acute change in dietary protein causes a parallel change in measured glomerular filtration rate (GFR)
2. Creatinine production changes with dietary protein [20]
   (a) An increase or decrease in protein intake reciprocally change serum creatinine or eGFR
   (b) The new steady state after changing the diet occurs in ~4 months
3. Protein-associated dietary factors affecting progression of CKD
   (a) Salt and hypertension [4–6, 41]
   (b) Uric acid and hypertension/inflammation [7–9]
   (c) Phosphates and kidney injury [10–12, 28, 29]
4. Direct effects of protein intake and progression of CKD
   (a) Net acid load and aldosterone/hypertrophy [18–21, 24, 25]
   (b) Albuminuria/proteinuria via hyperfiltration [13, 17–23]
   (c) Protein-derived nephrotoxins (e.g., indoxyl sulfate) [26, 27]

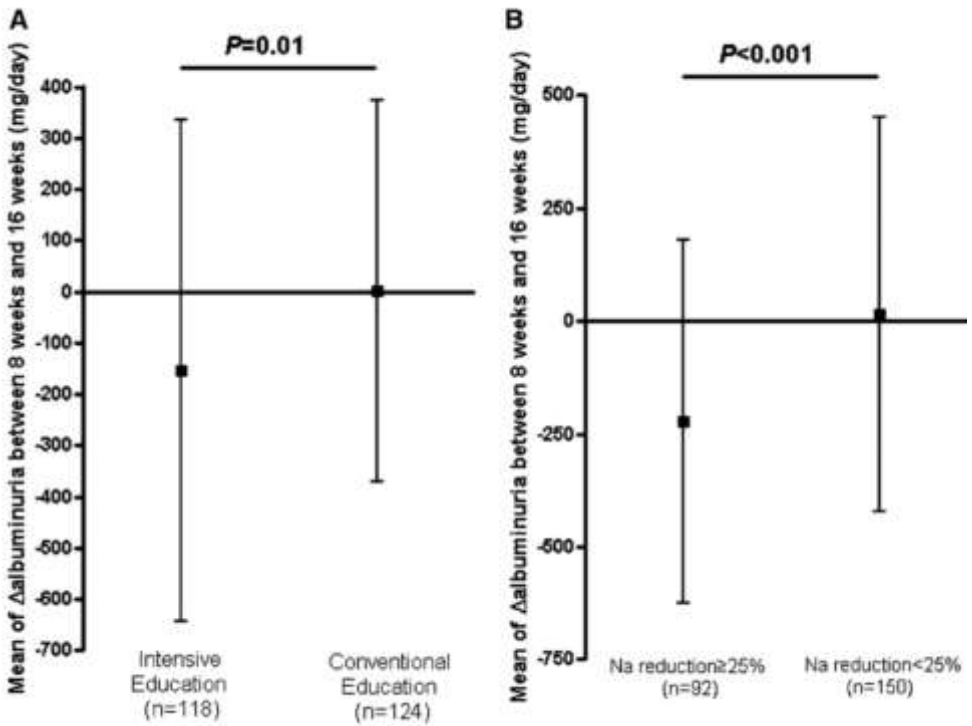
Riccio E. et al., Clin. Exp. Nephrol., 2015, 19:161–167

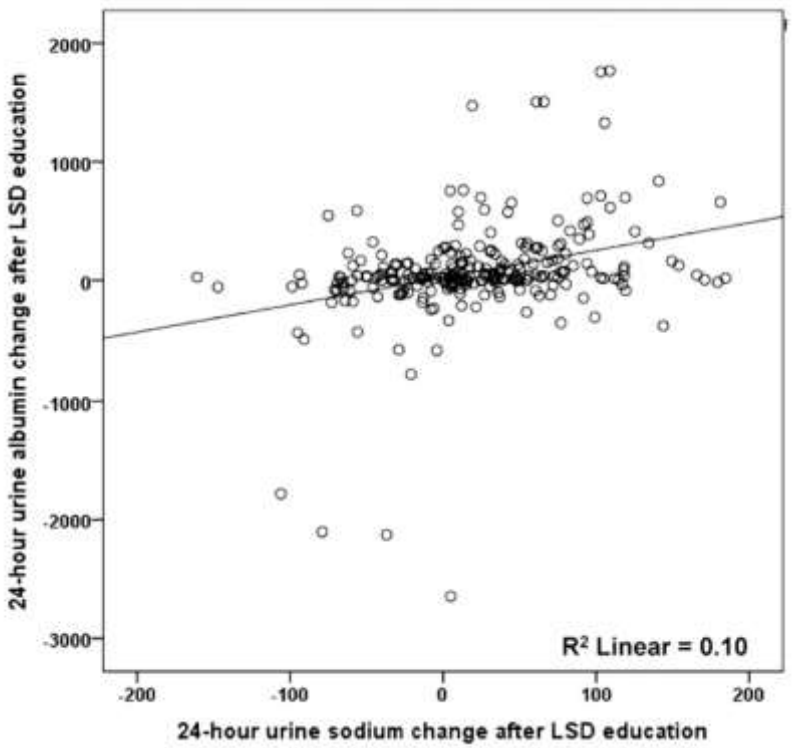
Salt, ACEi and proteinuria



Heeg J.E. et al., Kidney Int., 1987, 32, 78-83

Salt, education and proteinuria





Hwang J.H. et al, CJASN 2014;9:2059-2069

Randomized Placebo-Controlled EPPIC Trials of AST-120 in CKD

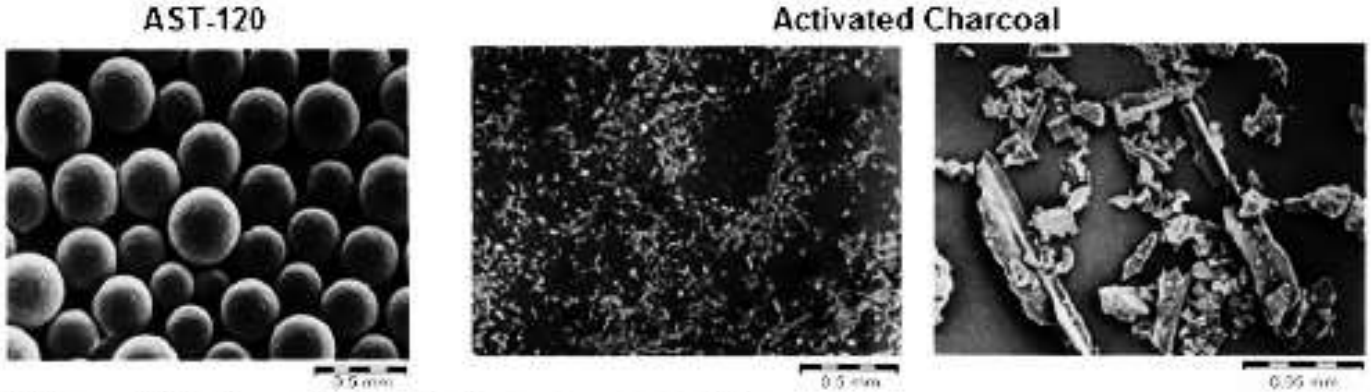
Gerald Schulman,* Tomas Berl,† Gerald J. Beck,‡ Giuseppe Remuzzi,§ Eberhard Ritz,‖ Kiyoshi Arita,¶ Akira Kato,** and Miho Shimizu¶

*Vanderbilt University School of Medicine, Nashville, Tennessee; †University of Colorado Health Sciences Center, Denver, Colorado; ‡Cleveland Clinic Foundation, Cleveland, Ohio; §Mario Negri Institute for Pharmacological Research, Bergamo, Italy; ‖University of Heidelberg, Heidelberg, Germany; ¶Mitsubishi Tanabe Pharma Corporation, Tokyo, Japan; and **Kureha Corporation, Tokyo, Japan

ABSTRACT

Reduced GFR in patients with CKD causes systemic accumulation of uremic toxins, which has been correlated with disease progression and increased morbidity. The orally administered spherical carbon adsorbent AST-120 reduces systemic toxin absorption through gastrointestinal sequestration, which may slow disease progression in these patients. The multinational, randomized, double-blind, placebo-controlled Evaluating Prevention of Progression in CKD (EPPIC)-1 and EPPIC-2 trials evaluated the effects of AST-120 on the progression of CKD when added to standard therapy. We randomly assigned 2035 adults with moderate to severe disease (serum creatinine at screening, 2.0–5.0 mg/dl for men and 1.5–5.0 mg/dl for women) to receive either placebo or AST-120 (9 g/d). The primary end point was a composite of dialysis initiation, kidney transplantation, and serum creatinine doubling. Each trial continued until accrual of 291 primary end points. The time to primary end point was similar between the AST-120 and the placebo groups in both trials (EPPIC-1: hazard ratio, 1.03; 95% confidence interval, 0.84 to 1.27; P=0.78) (EPPIC-2: hazard ratio, 0.91; 95% confidence interval, 0.74 to 1.12; P=0.37); a pooled analysis of both trials showed similar results. The estimated median time to primary end points for the placebo groups was 124 weeks for power calculations, but actual times were 189.0 and 170.3 weeks for EPPIC-1 and EPPIC-2, respectively. Thus, disease progression was more gradual than expected in the trial populations. In conclusion, the benefit of adding AST-120 to standard therapy in patients with moderate to severe CKD is not supported by these data.

J Am Soc Nephrol 26: 1732–1746, 2015. doi: 10.1681/ASN.2014010042

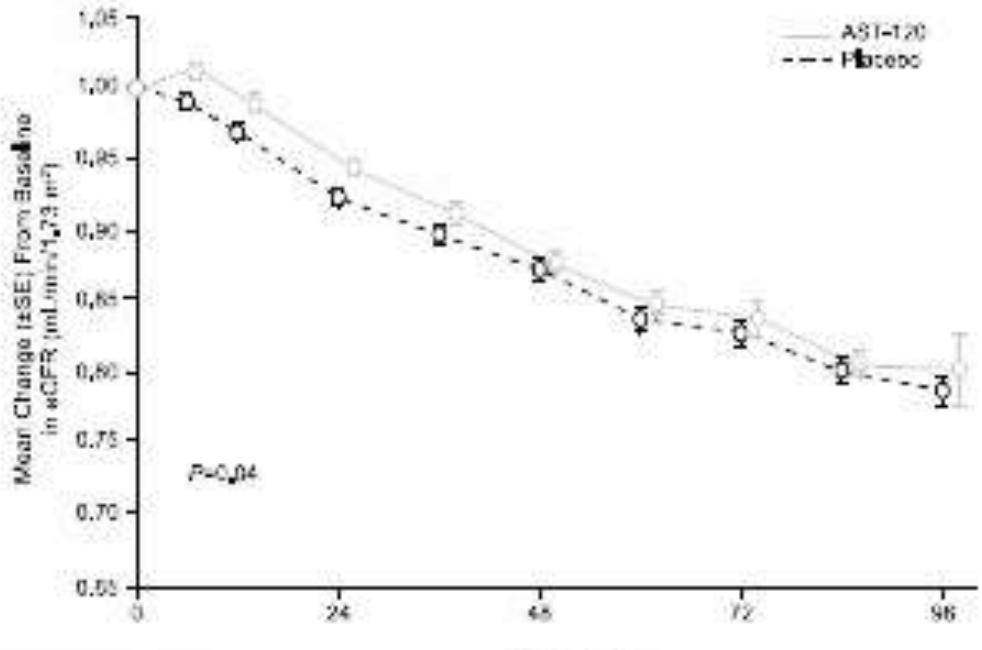


High-resolution transmission electron microscopic picture

Figure 1. Structural features of AST-120 and activated charcoal (United States Pharmacopeia). High-resolution transmission electron microscopy studies demonstrate that AST-120 differs structurally from activated charcoal (United States Pharmacopeia). AST-120, spherical carbon adsorbent, presents as black, odorless, spherical particles approximately 0.2–0.4 mm in diameter. Composed mainly of carbon (approximately 96%), AST-120 exhibits adsorption ability similar or superior to that of activated charcoal for certain acidic and basic organic compounds known to be increased in renal failure; however, AST-120 has lower adsorption ability than activated charcoal for digestive enzymes.

Schulman G. et al., J. Am. Soc. Nephrol.,2015, 26: 1732–1746

Mean change of GFR from baseline



Patients with eGFR data, n

AST-120	1000	885	765	656	499
Placebo	999	860	733	623	479

Schulman G. et al., J. Am. Soc. Nephrol.,2015, 26: 1732–1746

Nephrol Dial Transplant (2013) 28: 632–640
doi: 10.1093/ndt/gfs477
Advance Access publication 19 November 2012

ndt
Nephrology Dialysis Transplantation

Original Articles

Phosphate attenuates the anti-proteinuric effect of very low-protein diet in CKD patients

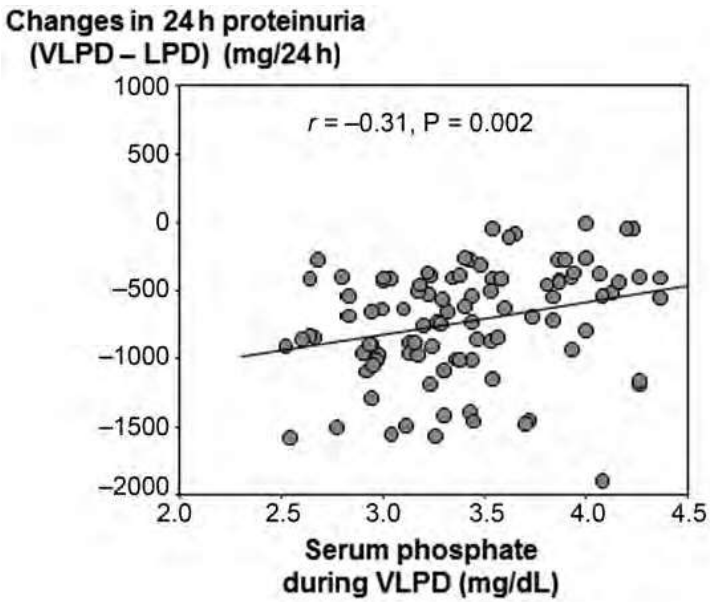
Biagio R. Di Iorio[1], Vincenzo Bellizzi[2], Antonio Bellasi[3], Serena Torraca[1], Graziella D'Arrigo[4], Giovanni Tripepi[4] and Carmine Zoccali[4]

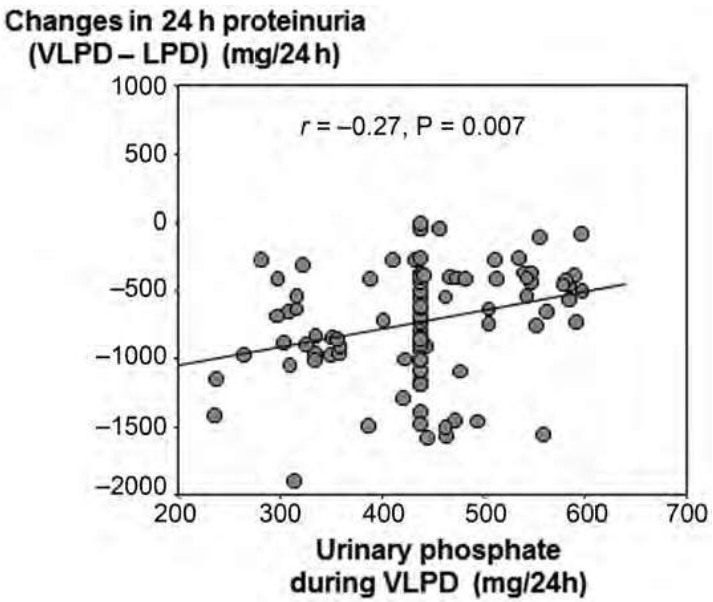
[1]Division of Nephrology, 'A. Landolfi' Hospital, Solofra, Avellino, Italy,
[2]Division of Nephrology, Dialysis and Renal Transplantation, University Hospital 'San Giovanni di Dio e Ruggi d'Aragona', Salerno, Italy,
[3]Division of Nephrology, 'Sant'Anna' Hospital, Como, Italy and
[4]Renal and Transplantation Unit and CNR-IBIM, Ospedali Riuniti, Reggio Cal, Italy

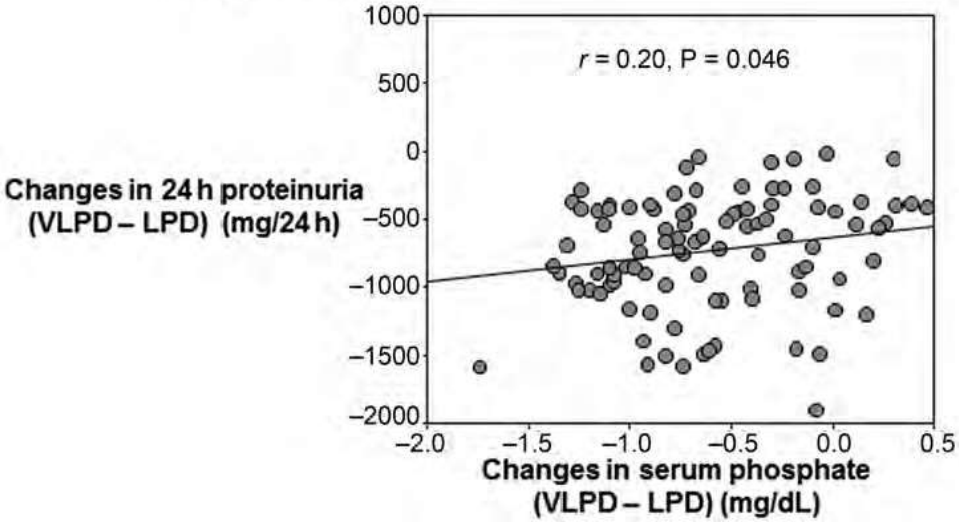
Correspondence and offprint requests to: Biagio R. Di Iorio; E-mail br.diiorio@gmail.com

Keywords: chronic kidney disease, phosphate intake, proteinuria

Relationships of changes in 24-h urinary protein between VLPD and LPD with serum and urinary phosphate

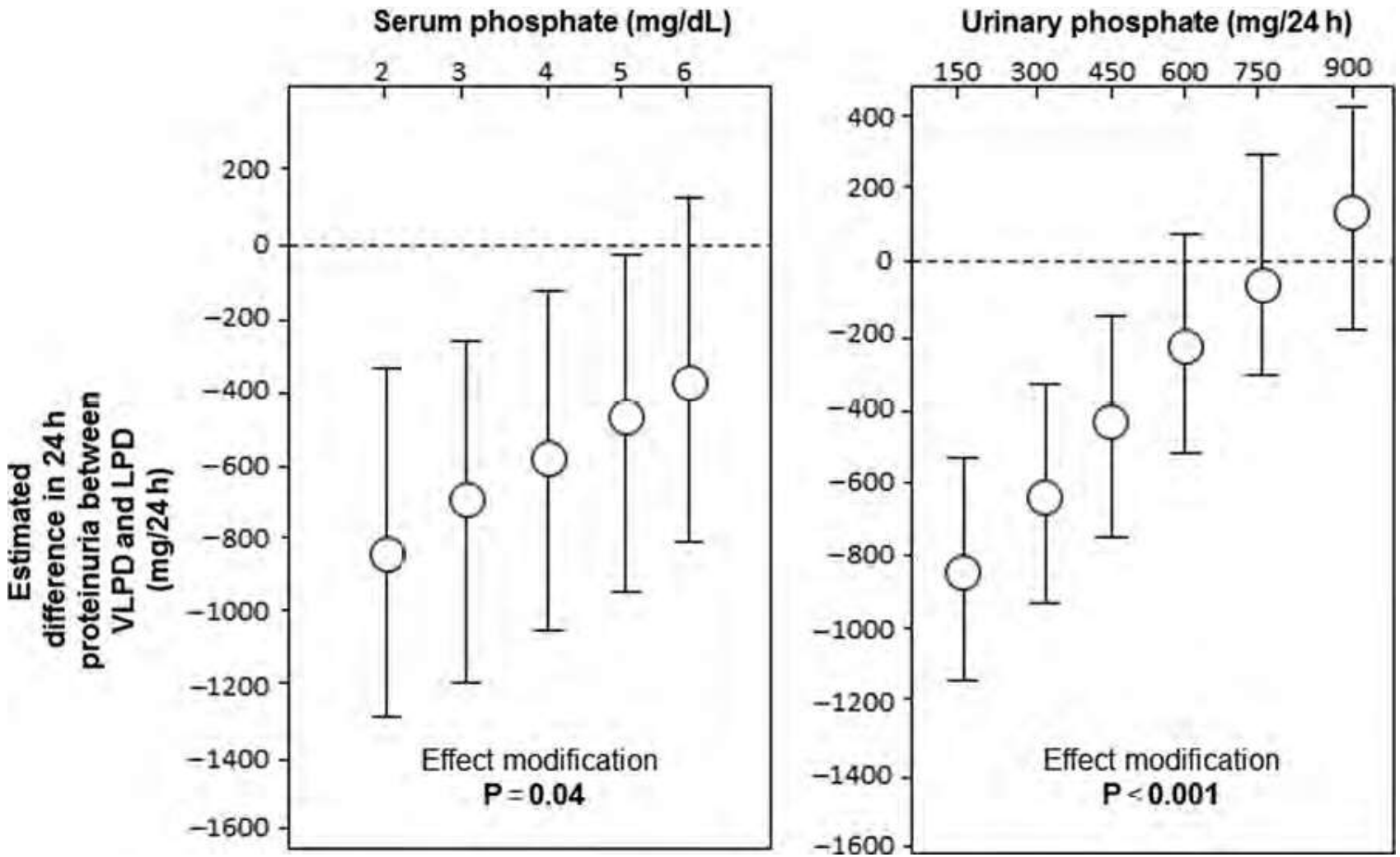






Iorio B.R.D. et al., Nephrol. Dial. Transplant., 2013, 28: 632–640

Effect modification analyses of serum and urinary phosphate of the efficacy of VLPD when compared with LPD for reducing 24-h proteinuria



Iorio B.R.D. et al., Nephrol. Dial. Transplant., 2013, 28: 632–640

- Phosphate appears to be an important modifier of the anti-proteinuric response to VLPD supplemented with keto-analogues in patients with proteinuric CKD

- Interventions aimed at reducing phosphate burden may reduce proteinuria and slow the progression of renal insufficiency in CKD patients, an issue that remains to be tested in specific clinical trials

Iorio B.R.D. et al., Nephrol. Dial. Transplant., 2013, 28: 632–640

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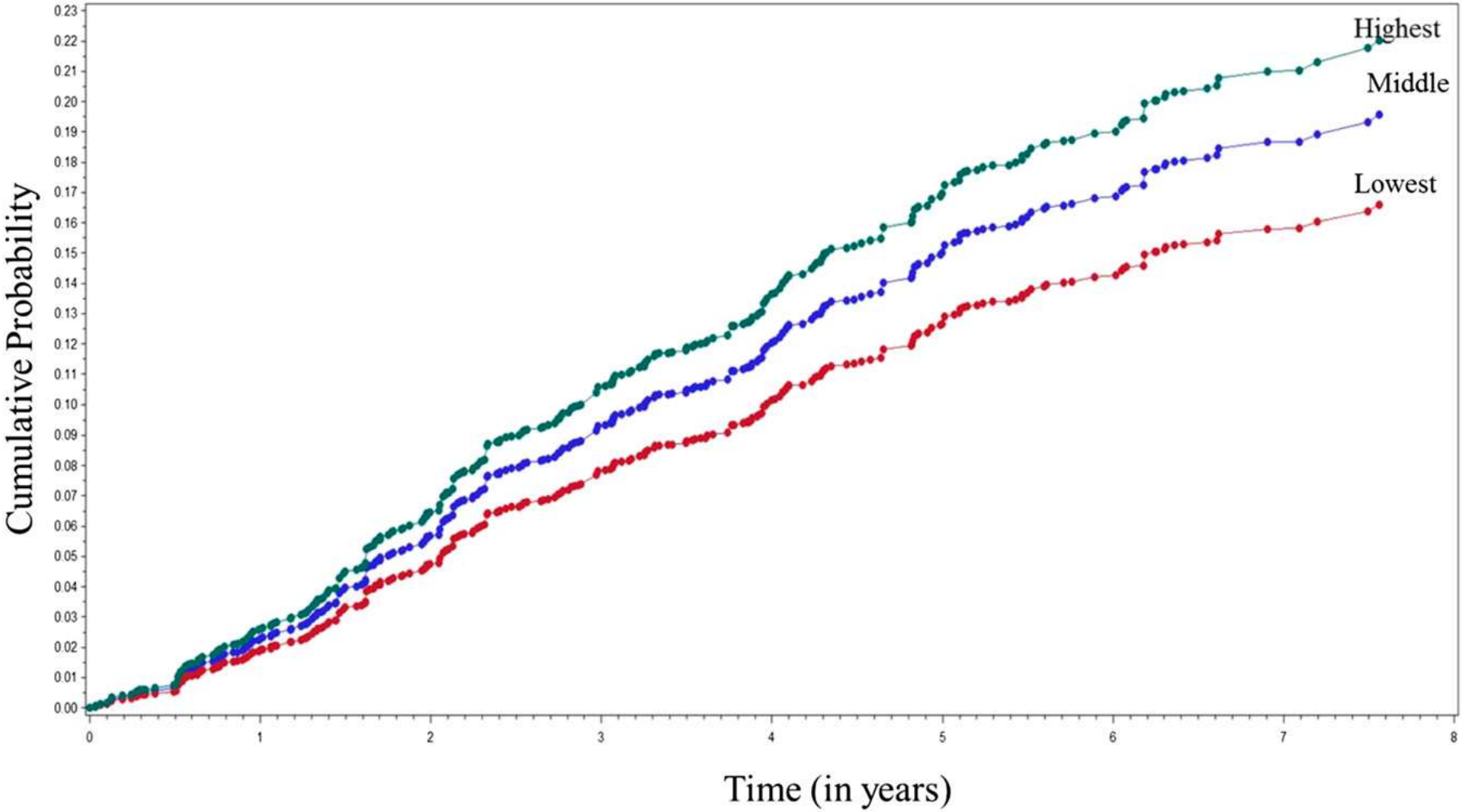
- Correction of metabolic acidosis
- Correction of glucose (HBA1C) in DM patients
- Supplementation of Vitamin D
- Renal denervation

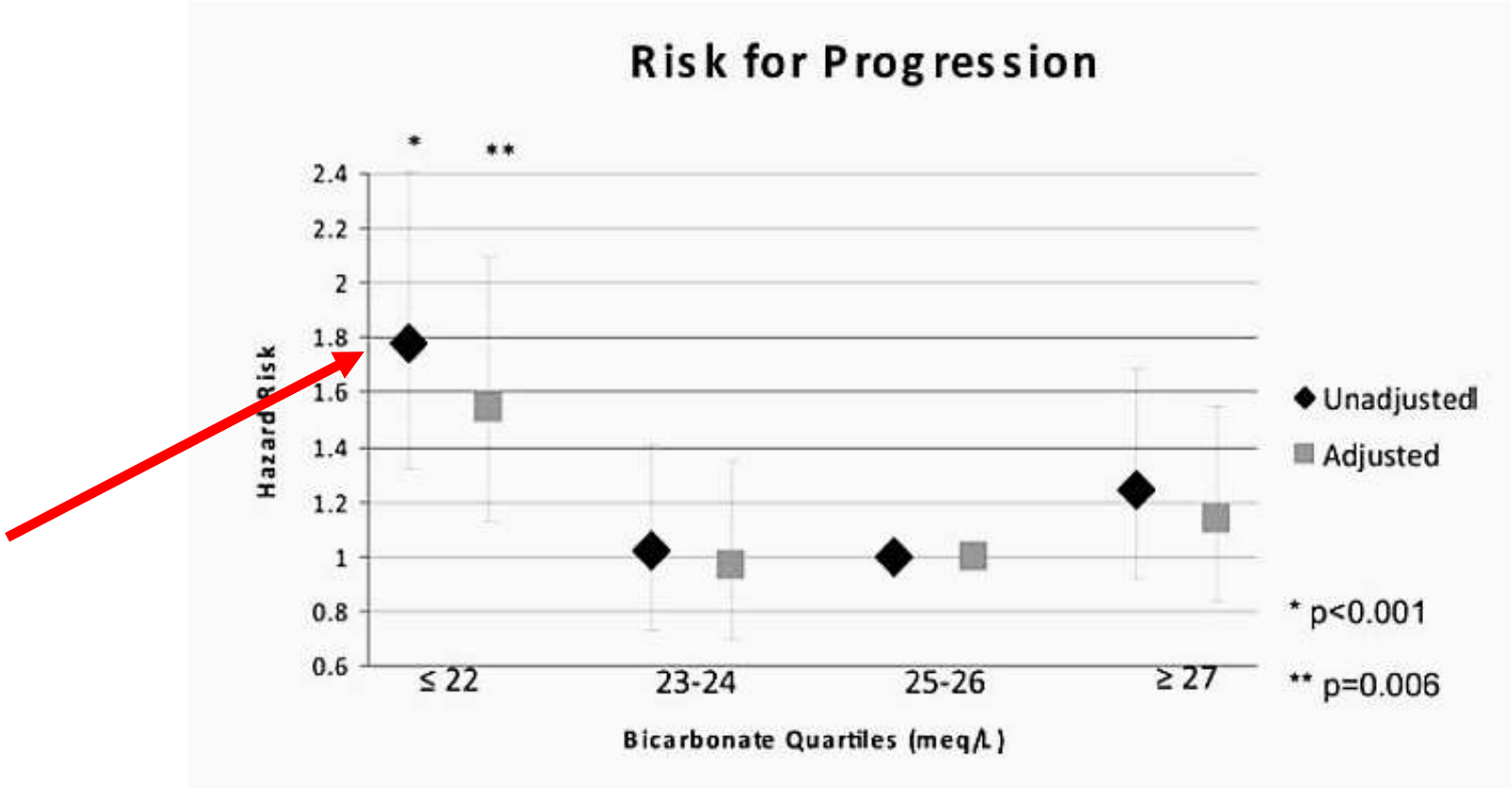
A greater risk of ESRD is associated with a higher dietary acid load



Banerjee T. et al.,J. Am. Soc. Nephrol., 2,015 26: 1693–1700

Metabolic acidosis and prognosis in CKD

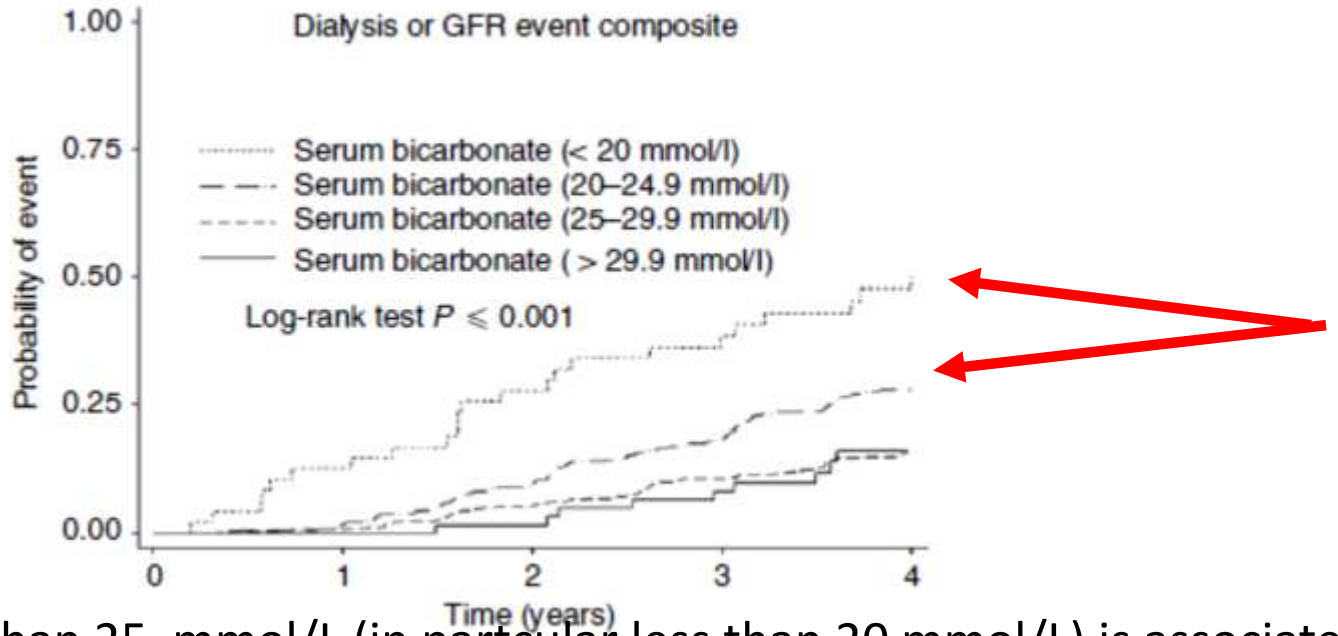
- Observational, retrospective study
- 5422 patients (9% with eGFR < 60 ml/min)
- Endpoints: decline of eGFR > 50% or eGFR < 15 ml/min.



Shah S.N. et al. Am J Kidney Dis 2009; 54: 270-277

Metabolic acidosis and prognosis in CKD

- Prospective, observational study; 4 years observation period
- 1094 adult African-American patients with hypertensive nephropathy (AASK study) ; mean age 68 years
- Endpoints: decline of eGFR > 50% or eGFR <25ml/min. or starting renal replacement therapy

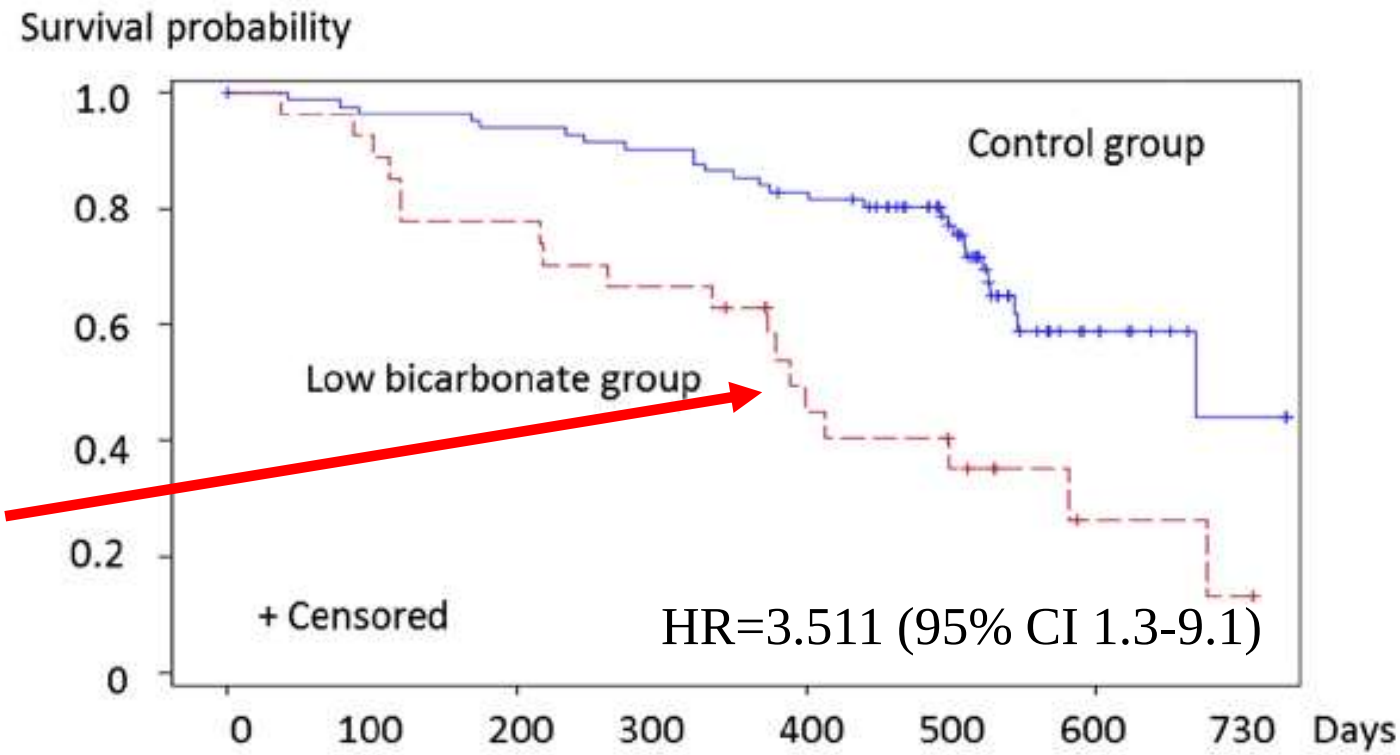


- $[HCO_3^-]$ less than 25 mmol/L (in partcular less than 20 mmol/L) is associated with acceleration of CKD progression
- Higher by 1mmol/L $[HCO_3^-]$ is associated with 6% reduction in the risk of achieving the endpoint

Raphael K.L. et al. Kidney Int 2011; 79: 356-362

Metabolic acidosis and prognosis in CKD

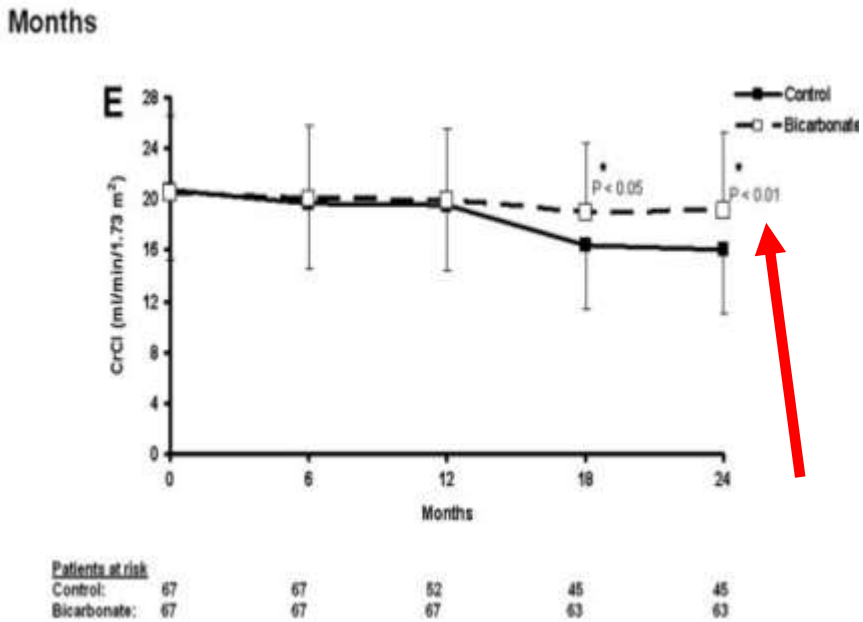
- Retrospective study
- 113 CKD erderly patients without metabolic acidosis
- Patients with $[HCO_3^-]$ < 25,5 mmol/L *vs* patients with $[HCO_3^-]$ > 25,5mmol/L
- Endpoints: reduction in eGFR > 25% or starting dialysis

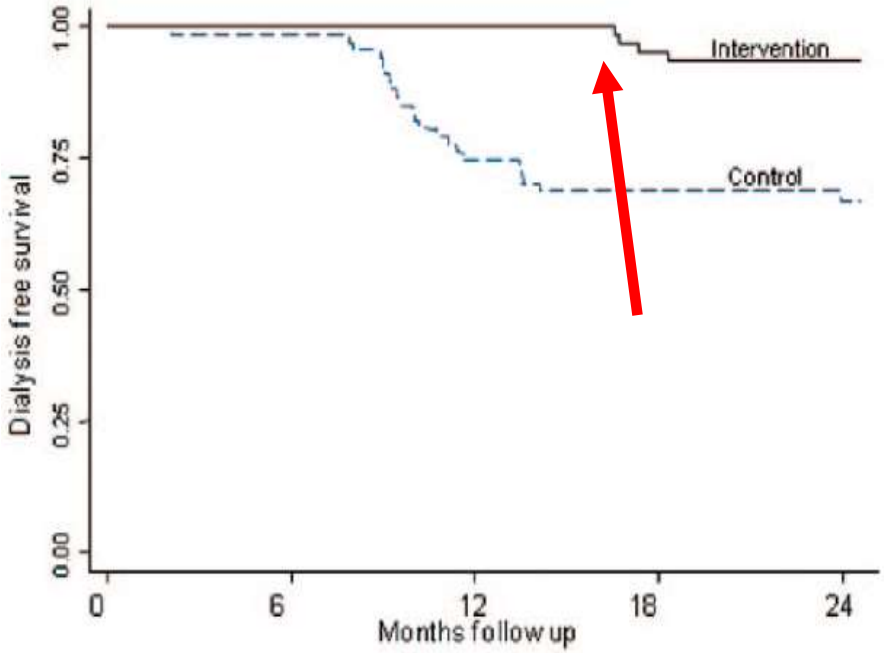


Higher by 1mmol/L $[HCO_3^-]$ is associated with 21% reduction of the risk of achieving the endpoint

Kanda E. et al. BMC Nephrology 2013; 14: 4

Treatment of metabolic acidosis inhibits the progression of CKD



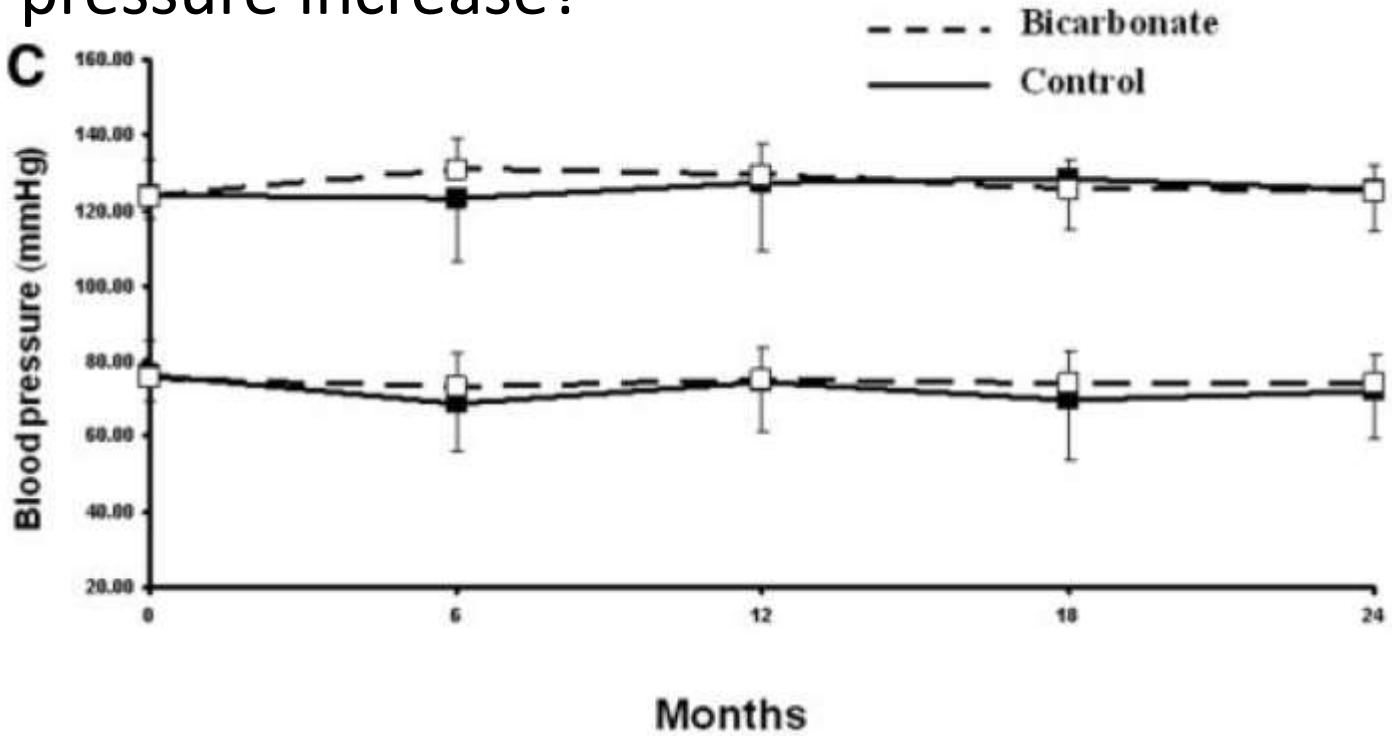


- In the group treated with sodium bicarbonate the rate of decline in eGFR (1.88 vs 5.93 ml/min/1.73 m^2/year) was reduced
- In the group treated with sodium bicarbonate significantly lower number of patients requiring dialysis (4 *vs* 22)

De Bristo-Ashurst I. et al. J Am Soc Nephrol 2009; 20: 2075-2084

The safety of alkalizing drugs

Does use of sodium bicarbonate or sodium citrate lead to blood pressure increase?



Adverse Events	Control (% of Patients)	Bicarbonate (% of Patients)	*P*
Hospitalization for CHF	0	0	N/A
Worsening hypertension requiring increase in therapy	48	61	0.17

De Bristo-Ashurst I. et al. J Am Soc Nephrol 2009; 20: 2075-2084

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- Renal denervation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes

S. Zoungas, J. Chalmers, B. Neal, L. Billot, Q. Li, Y. Hirakawa, H. Arima, H. Monaghan, R. Joshi, S. Colagiuri, M.E. Cooper, P. Glasziou, D. Grobbee, P. Hamet, S. Harrap, S. Heller, L. Lisheng, G. Mancia, M. Marre, D.R. Matthews, C.E. Mogensen, V. Perkovic, N. Poulter, A. Rodgers, B. Williams, S. MacMahon, A. Patel, and M. Woodward, for the ADVANCE-ON Collaborative Group*

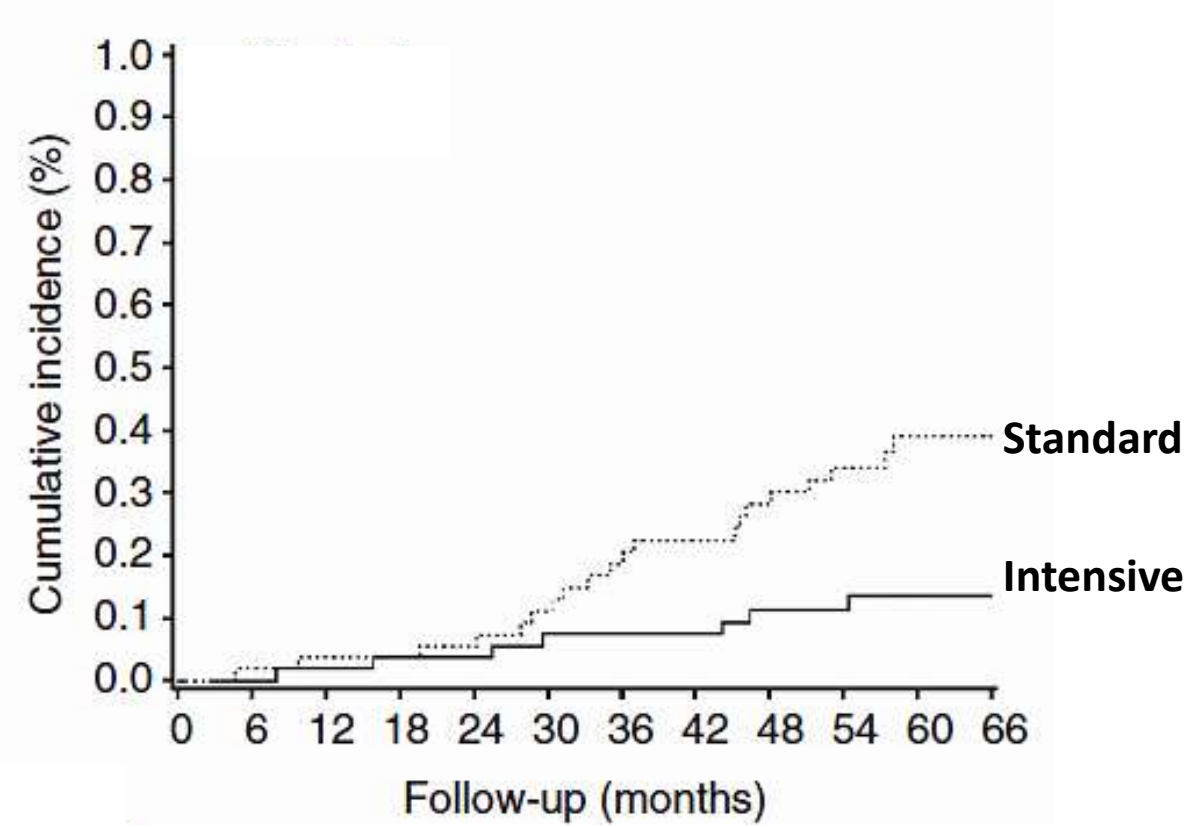
ABSTRACT

BACKGROUND

In the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) factorial trial, the combination of perindopril and indapamide reduced mortality among patients with type 2 diabetes, but intensive glucose control, targeting a glycated hemoglobin level of less than 6.5%, did not. We now report results of the 6-year post-trial follow-up.

Zoungas Z. i wsp. N Engl J Med 2014;371:1392-406

End-stage kidney disease (dialysis or renal transplantation)



Relative risk reduction 65%
95% CI: 15 to 83%, p=0.02
20 vs 7 events

ADVANCE

Kidney Int 2013;83:517-523

HbA1c levels

Glucose arm	HbA1c level (%) Mean±SD	
	Standard	Intensive
Pre-randomisation	**7.5±1.5**	**7.5±1.6**
Last randomised visit	**7.2±1.1**	**6.5±0.8**

ADVANCE-ON

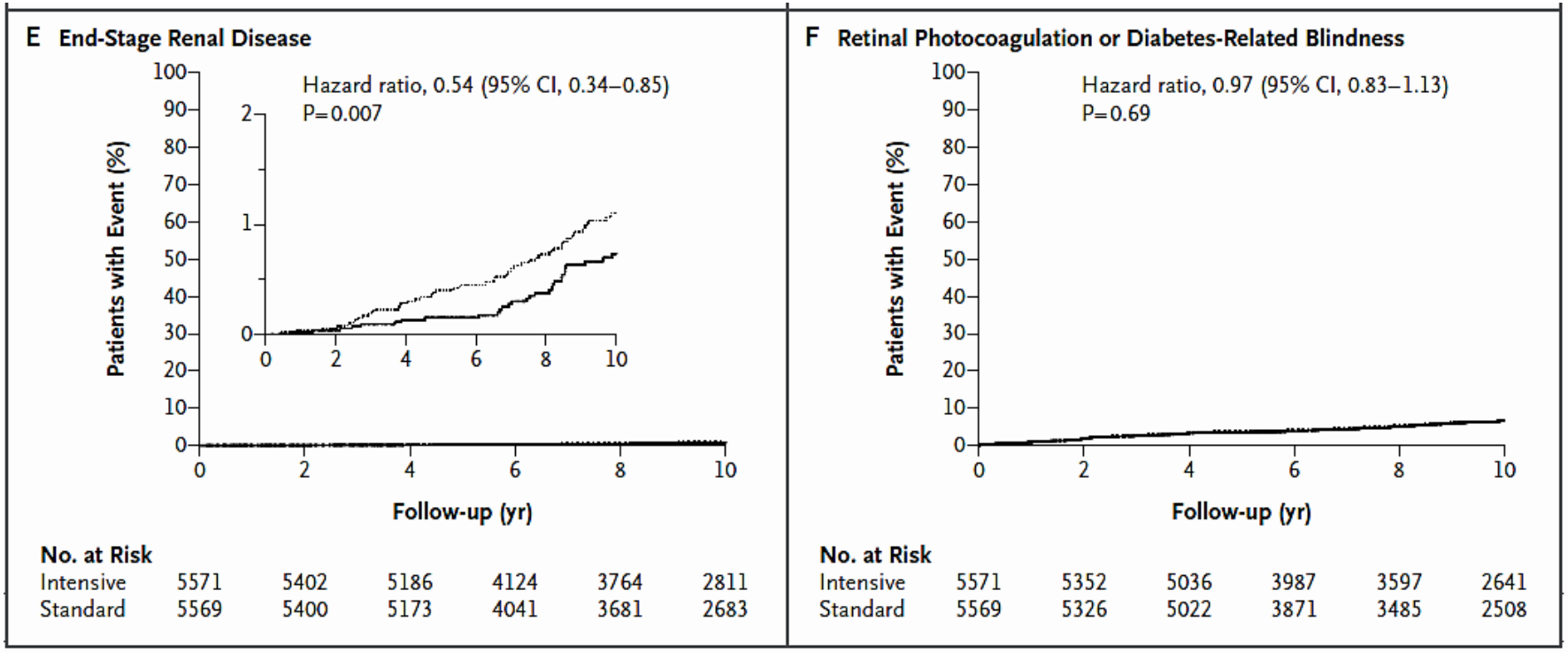
HbA1c levels

Glucose arm	HbA1c level (%) Mean±SD	
	Standard	Intensive
Pre-randomisation	**7.5±1.5**	**7.5±1.6**
Last randomised visit	**7.2±1.1**	**6.5±0.8**
First ADVANCE-ON visit	**7.3±1.3**	**7.3±1.4**
Final ADVANCE-ON visit	**7.4±1.3**	**7.2±1.2**

ADVANCE-ON

N Engl J Med 2014;371:1392-1406

Standard vs intensive treatment in patients with t.2 DM



Cumulative Incidence of Events,According to Glucose-Control Study Group

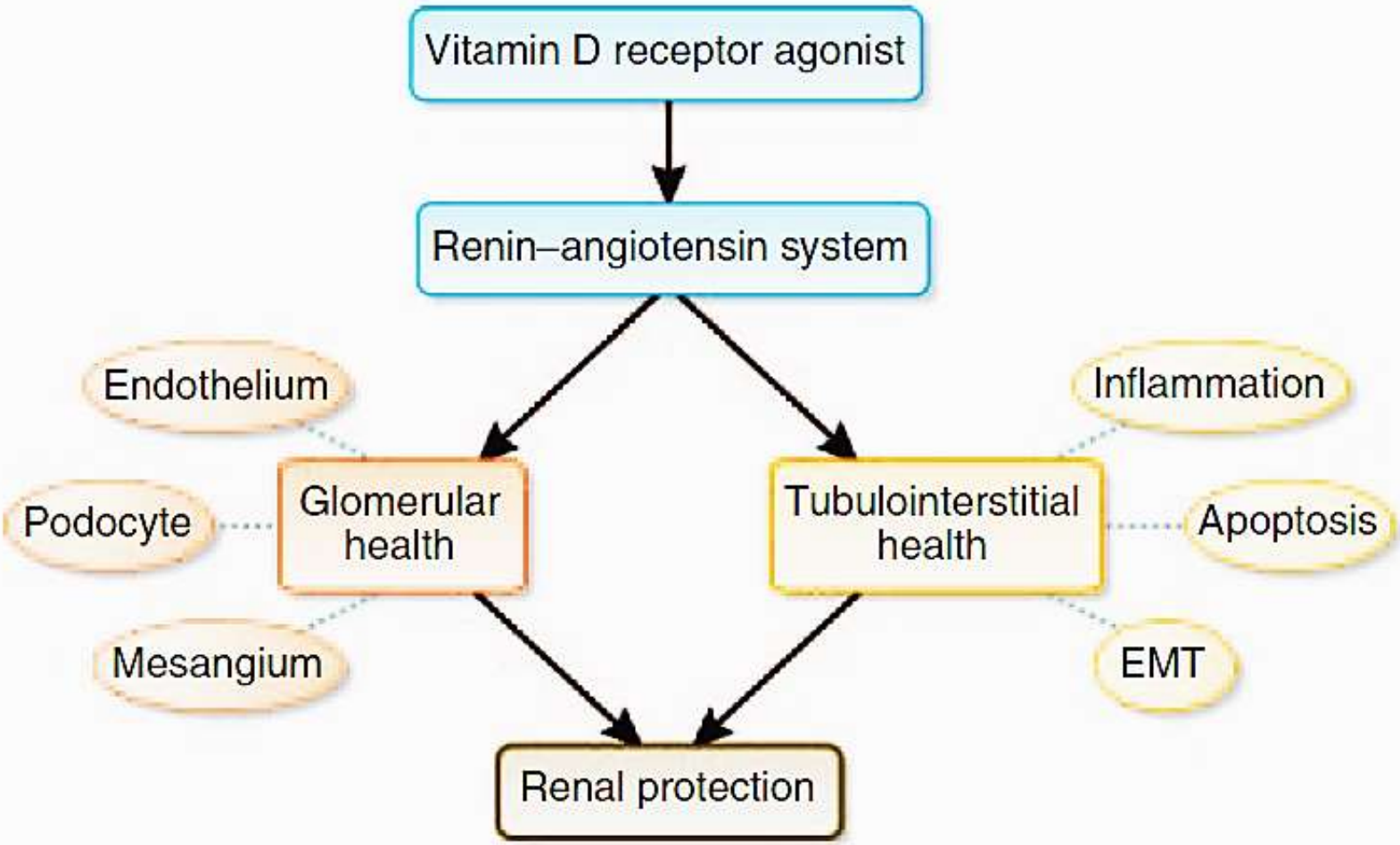
Zoungas Z. i wsp. N. Engl. J. Med., 2014;371:1392-406

Nephroprotection: Where are we in 2015?

With confirmed benficial effect:

- Reduction of blood pressure
- Blockade of the RAAS (beyond BP reduction)
- Reduction of BMI
- Reduction of protein intake
- Correction of phosphatemia
- Correction of metabolic acidosis
- Correction of glucose (HBA1C) in DM patients
- Supplementation of Vitamin D
- Renal denervation

Renoprotective mechanisms of Vitamin D receptor agonists



Agarwal R.: Kidney Int. 2010; 77: 943-945

Comparison of reduction of proteinuria after treatment with Paricalcitol – results from different clinical trials

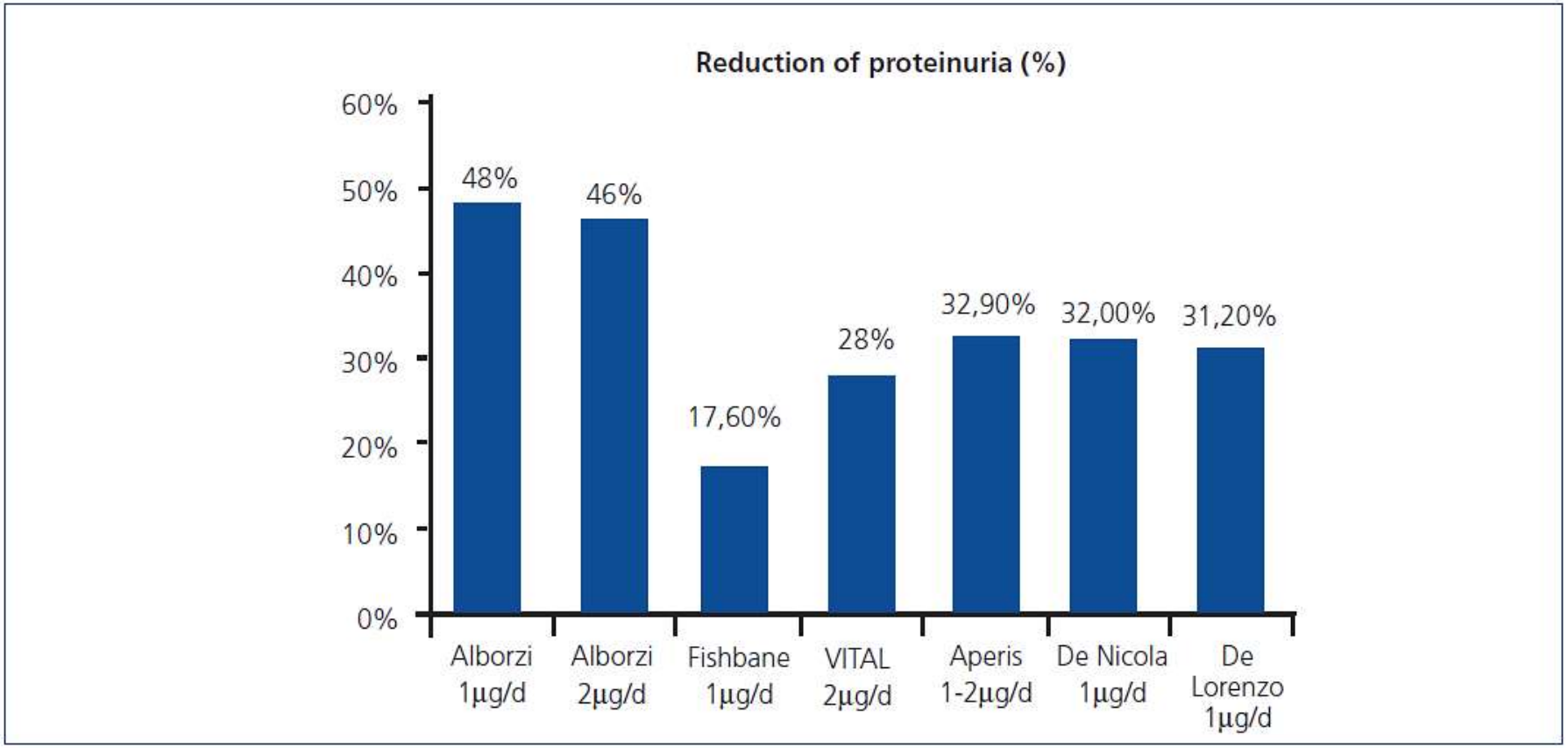
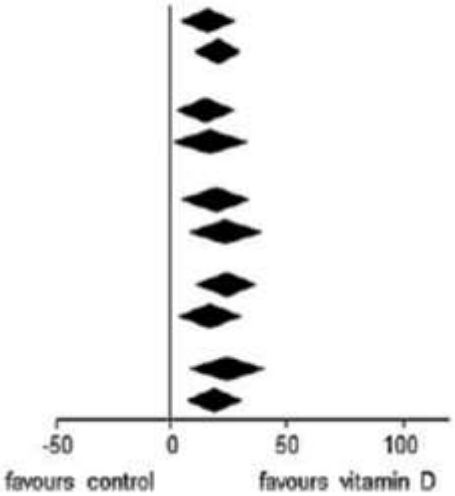


Figure 2. Comparision of proteinuria reduction.
The results of this study are compared alongside those of previous studies of paricalcitol on proteinuria reduction. Percent of reduction in the study performed by Agarwal et al. not published (proteinuria determined by means of a dipstick test). Proteinuria reduction with 1µg/d in VITAL study resulted no significant.

De Lorenzo et al., Nefrologia, 2013, 33, 709-715

Vitamin D effect on proteinuria in CKD 2

		Number of studies	Number of patients (vitamin D/control)	Mean difference (95% CI)	p for subgroup differences
Study drug	paricalcitol	3	264 / 171	16% (5 to 28%)	0.16
	calcitriol	2	72 / 69	31% (14 to 48%)	
Paricalcitol dose	1 ug/day	2	123 / 118	16% (3 to 28%)	0.86
	2 ug/day	2	141 / 141	17% (1 to 34%)	
Patient population	diabetic nephropathy only	2	230 / 133	20% (4 to 35%)	0.69
	not (only) diabetic nephropathy	3	106 / 107	24% (8 to 40%)	
Duration of follow-up	<24 weeks	2	77 / 75	24% (11 to 38%)	0.46
	≥ 24 weeks	3	259 / 165	17% (3 to 31%)	
Study size	number of participants <80	3	57 / 54	24% (8 to 41%)	0.61
	number of participants ≥80	3	279 / 186	19% (7 to 31%)	



Active Vitamin D Treatment for Reduction of Residual Proteinuria: A Systematic Review

Martin H. de Borst,* Reza Hajhosseiny,†‡ Hector Tamez,† Julia Wenger,† Ravi Thadhani,† and David J.A. Goldsmith‡

J. Am.Soc. Nephrol., 2013, 24, 1863-1871

Nephrol Dial Transplant (2014) 29: 1012–1019
doi: 10.1093/ndt/gft434
Advance Access publication 5 November 2013

Antifibrotic, nephroprotective effects of paricalcitol versus calcitriol on top of ACE-inhibitor therapy in the COL4A3 knockout mouse model for progressive renal fibrosis

Diana Rubel†, Johanna Stock†, Ayse Ciner, Henrik Hiller, Rainer Girgert, Gerhard-Anton Müller and Oliver Gross

Department of Nephrology and Rheumatology, University Medicine Goettingen, Goettingen, Germany

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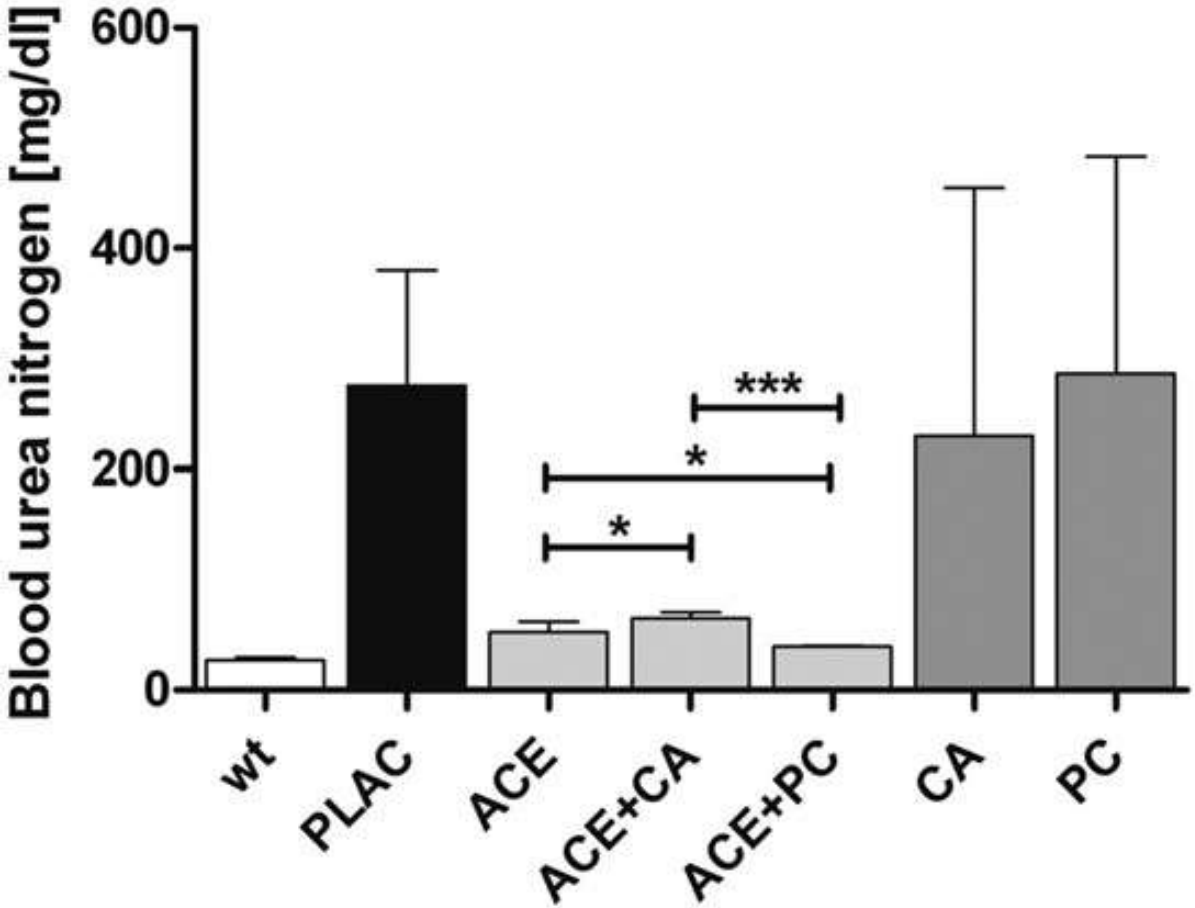
†Both authors contributed equally to this work.

Renal function.
Blood urea nitrogen in untreated miceversus different treatment modalities. wt, wild type



Rubel D. et al., Nephrol. Dial. Transplant., 2014, 29: 1012–1019

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- Correction of glucose (HBA1C) in DM patients
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- Renal denervation

Renal denervation preserves renal function in patients with chronic kidney disease and resistant hypertension

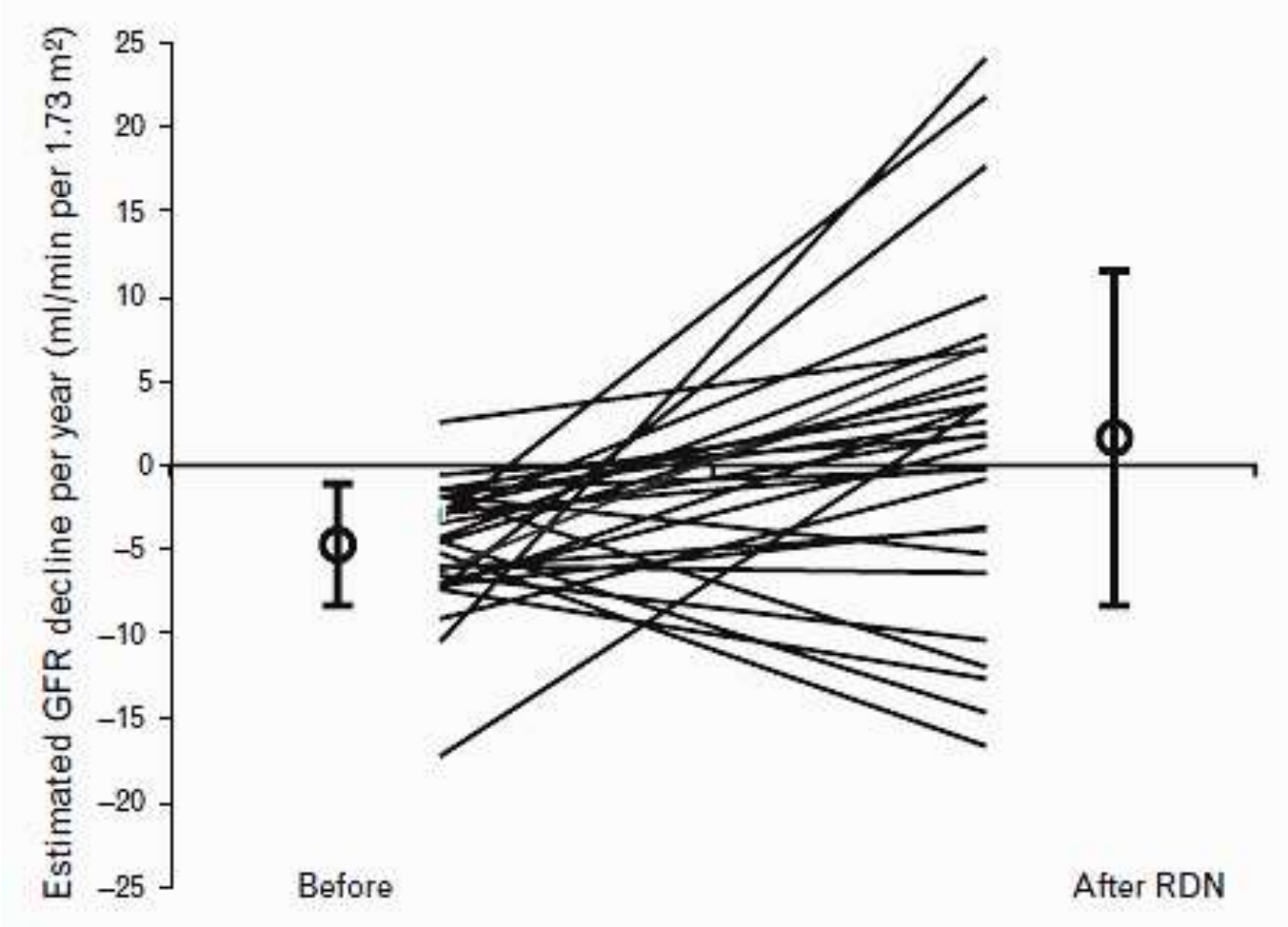
Christian Ott[a], Felix Mahfoud[b], Axel Schmid[c], Stefan W. Toennes[d], Sebastian Ewen[b]
Tilmann Ditting[a], Roland Veelken[a], Christian Ukena[b], Michael Uder[c], Michael Böhm[b]
Roland E. Schmieder[a]

TABLE 1. Clinical characteristics

Parameter	
Age (years)	63.4 ± 9.4
Gender (m/w)	22/5
BMI (kg/m^2)	31.2 ± 4.8
Number of antihypertensives (*n*)	6.2 ± 1.1
RAS-modulating agents (at least one)	26 (96)
Calcium-channel blockers	19 (70)
β-blockers	23 (85)
Diuretics	23 (85)
Central sympatholytics	20 (74)
Aldosterone antagonists	3 (11)
Vasodilators	14 (52)
CHD	10 (37)
Diabetes mellitus type 2	15 (56)
eGFR (ml/min per 1.73 m^2)[a]	48.5 ± 12

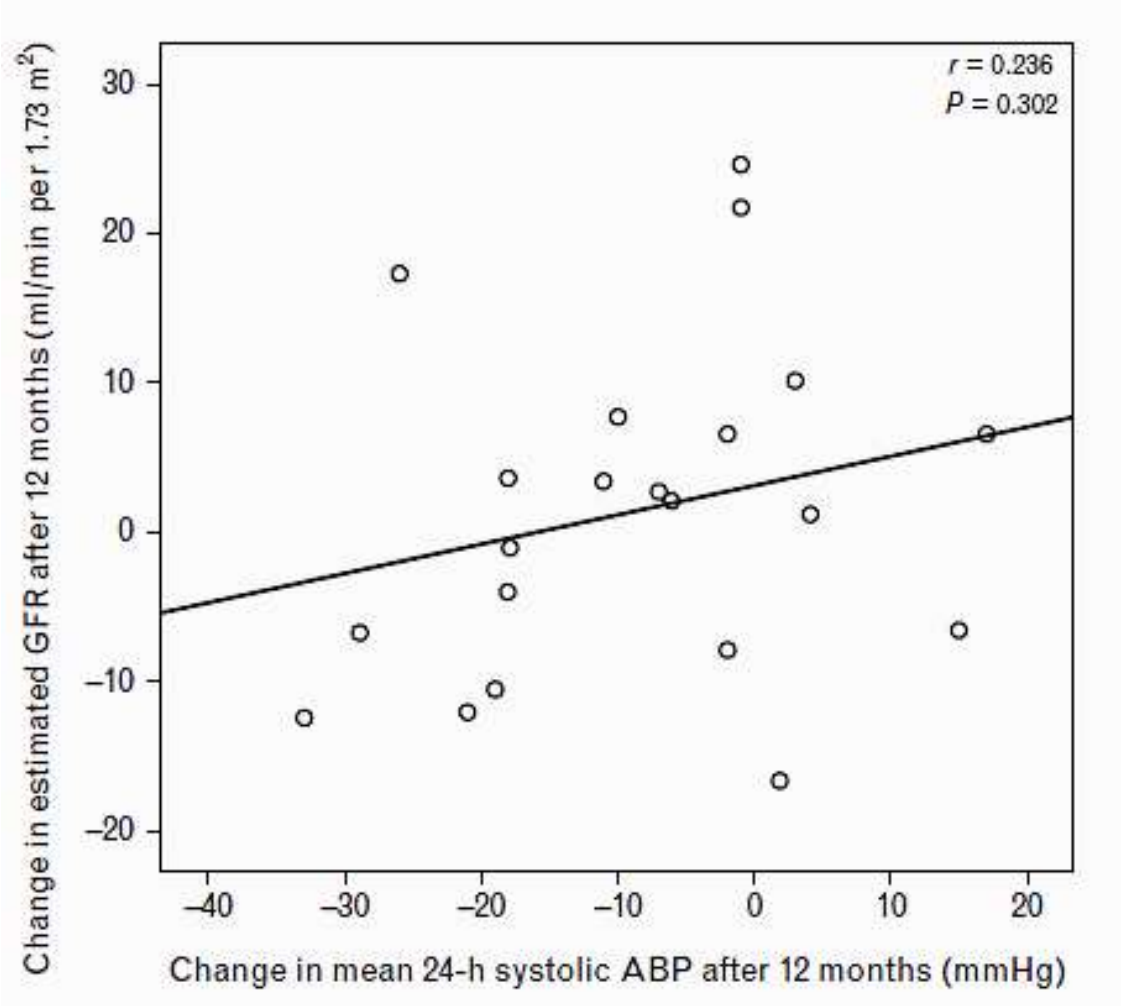
Ott Ch. et al. J. Hypertens., 2015 Jun;33(6):1261-1266

Decline of estimated glomerular filtration rate (GFR) per year before and after renal denervation (RDN) given in absolute number of each individual patient as well as median and standard deviation for whole study cohort



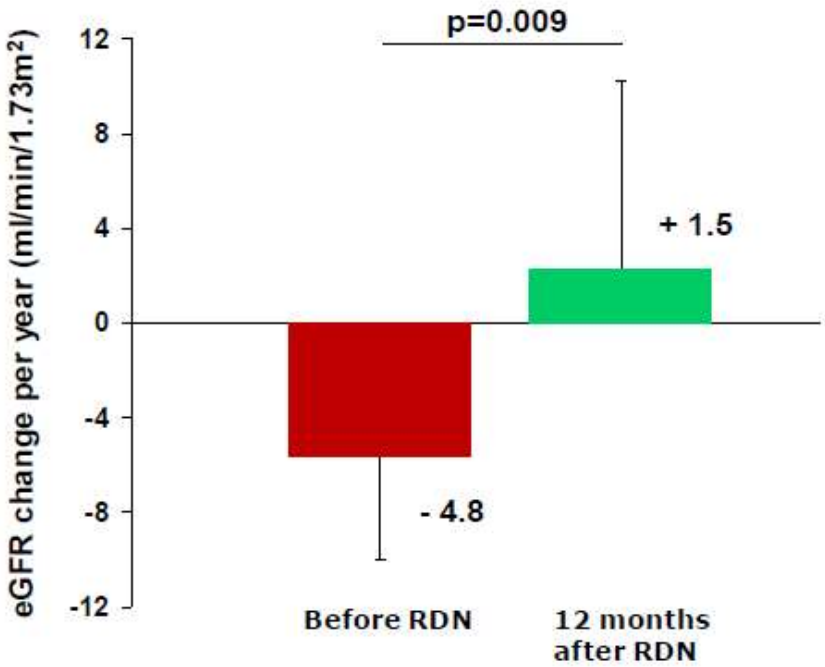
Ott Ch. et al. J. Hypertens., 2015 Jun;33(6):1261-1266

Correlation between the change of estimated glomerular filtration rate (GFR) and the change of mean 24-h systolic ambulatory blood pressure (ABP) 12 months after renal denervation



Ott Ch. et al. J. Hypertens., 2015 Jun;33(6):1261-1266

Renal Denervation: Response as judged by eGFR change per year



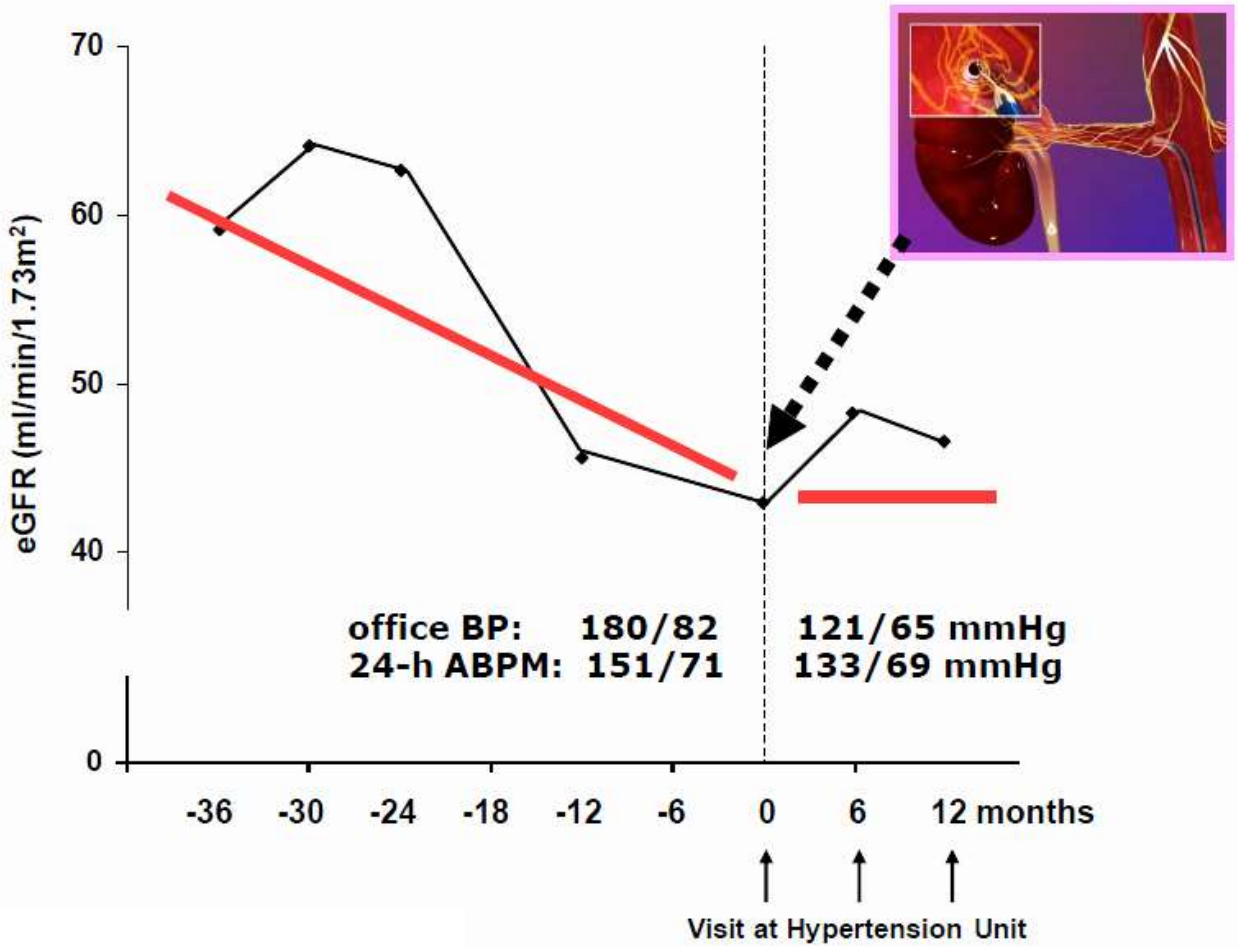
- On average mean eGFR decline before RDN was −4.8 ml/min/1.73 m^2 per year, which fits with the postulated decline of renal function (about −5 ml/min per year at MAP of 105 mmHg) based on a metaanalysis of long-term clinical trials (Bakris et al, Am J Kidney Dis 2000; 36:646-61).
- In contrast, eGFR remained stable (baseline: 48.5 12 vs. 1 year: 49.6 15 ml/min/1.73m^2), with a significance between eGFR change per year before vs. after RDN.
- **None of the patients developed a doubling of serum creatinine or required dialysis after RDN at any point of time.**

Schmieder RE, Ott C., EDA 2014

Ott Ch. et al. J. Hypertens., 2015 Jun;33(6):1261-1266

Case Study: Hypertensive patient CKD stage 3b

56 yr male patient (6 antihypert. drugs):



Schmieder R.E, Ott C. ERA-EDTA, Amsterdam, 2014

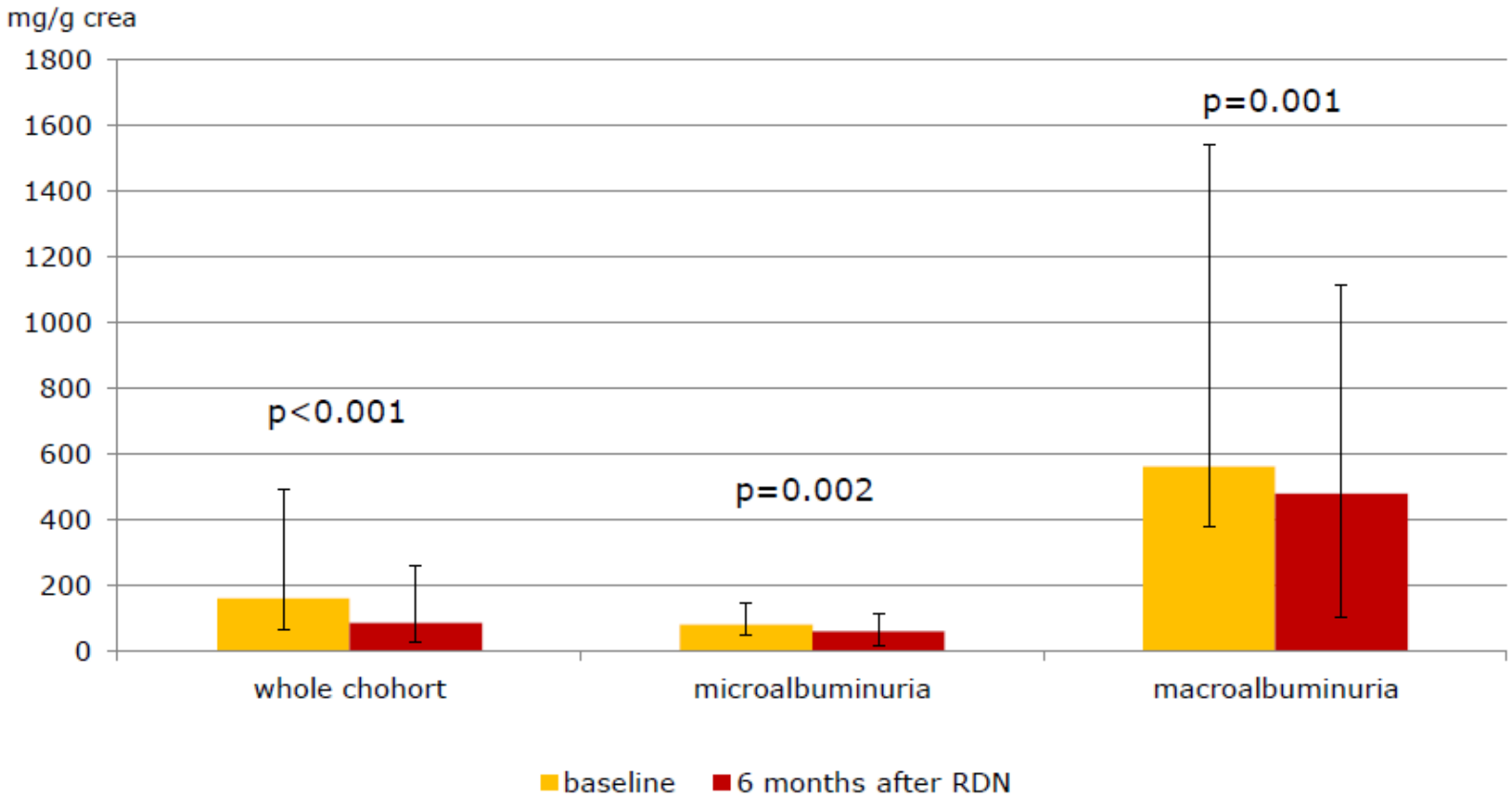
Renal denervation preserves renal function in patients with chronic kidney disease and resistant hypertension

Christian Ott[a], Felix Mahfoud[b], Axel Schmid[c], Stefan W. Toennes[d], Sebastian Ewen[b]
Tilmann Ditting[a], Roland Veelken[a], Christian Ukena[b], Michael Uder[c], Michael Böhm[b]
Roland E. Schmieder[a]

In conclusion, our observational pilot study suggests that RDN not only decreases office and ABP but, most importantly, also slows or even halts the decline of renal function in treatment-resistant hypertensive patients with CKD stages 3 and 4.

Ott Ch. et al. J. Hypertens., 2015 Jun;33(6):1261-1266

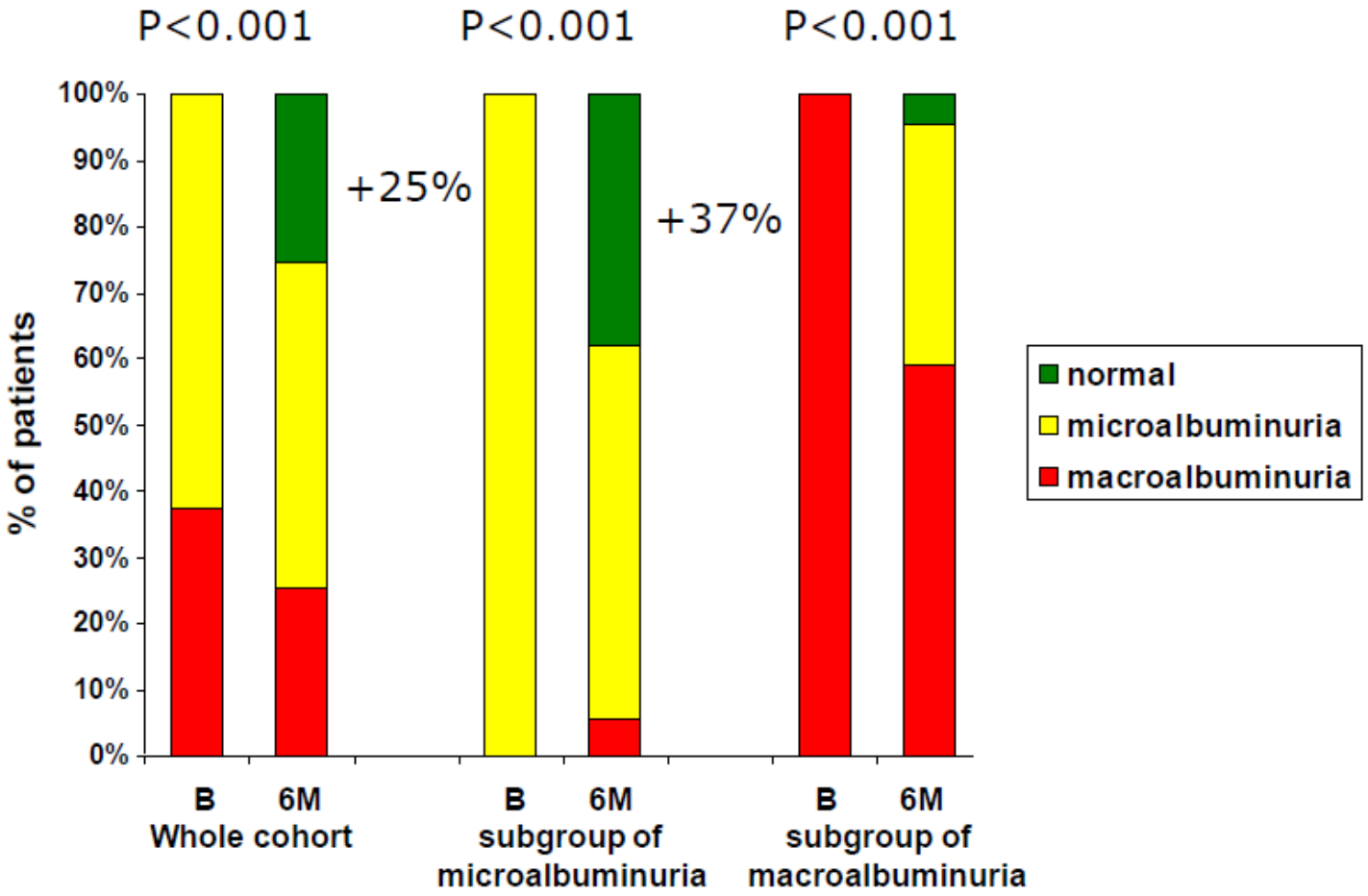
Albuminuria (UACR) between baseline and 6 months after RDN



Schmieder RE ACC 2014

Ott Ch. et al.,Int. J. Cardiol., 2014;173(2):311-315

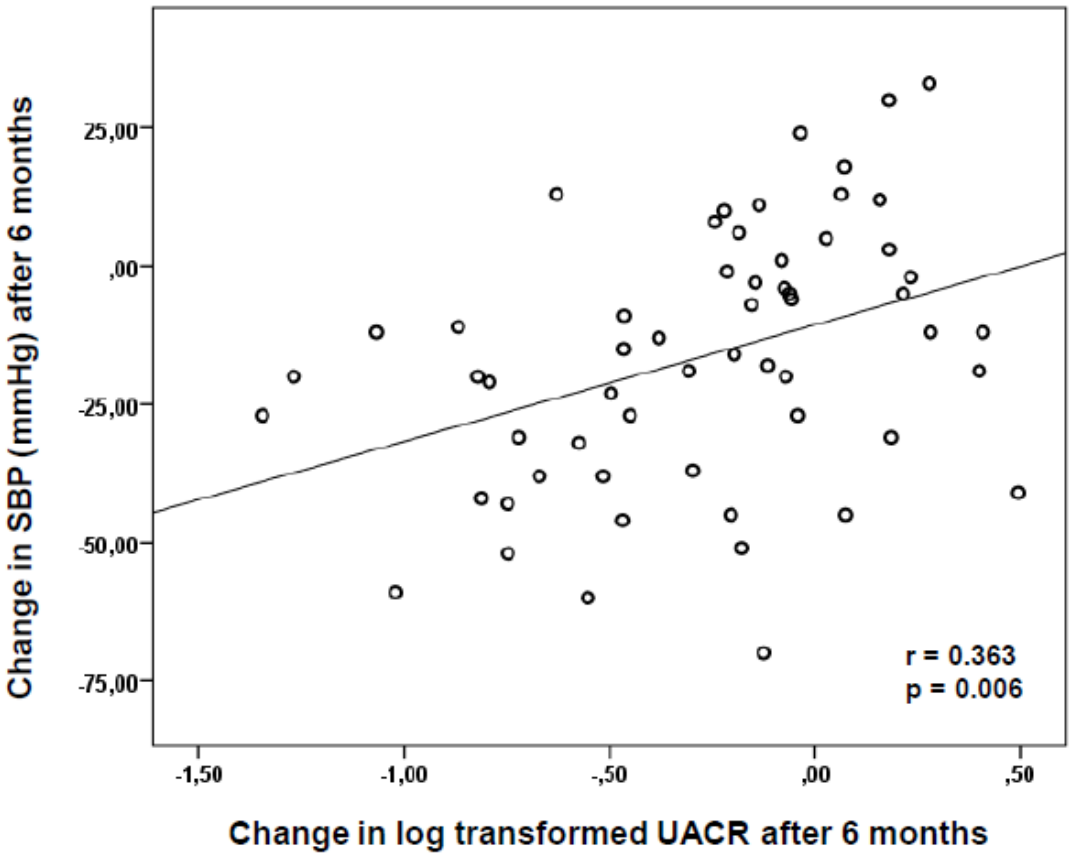
Change in categories of albuminuria



Schmieder RE ACC 2014

Ott Ch. et al.,Int. J. Cardiol., 2014;173(2):311-315

Correlation between decrease in systolic BP and decrease in albuminuria



Schmieder RE ACC 2014

Ott Ch. et al.,Int. J. Cardiol., 2014;173(2):311-315

Conclusion

1) Renal denervation reduced elevated albuminuria in treatment-resistant hypertensive patients:

   in mico- and macroalbuminuric patients

   in diabetic and non diabetic patients

2) The antiproteinuric effect appeared to be in part related to the decrease in blood pressure, and

3) decreased sympathetic activity to the kidneys may have played a role as well,
   but this cannot delineated from our trial

Nephroprotection: Where are we in 2015?

Without confirmed beneficial effect:

- Increased fluid intake
- Correction of anaemia
- Statins
- Sulodexide (it is a GAG that consists of heparin and dermatan sulfate, and is available for oral administration)
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Nephrol Dial Transplant (2014) 29: 1377–1384
doi: 10.1093/ndt/gft507
Advance Access publication 6 January 2014

ndt
Nephrology Dialysis Transplantation

Original Article

Fluid intake and all-cause mortality, cardiovascular mortality and kidney function: a population-based longitudinal cohort study

Suetonia C. Palmer[1], Germaine Wong[2], Samuel Iff[3], Jean Yang[4], Vivek Jayaswal[4], Jonathan C. Craig[2,3], Elena Rochtchina[5], Paul Mitchell[5], Jie Jin Wang[5] and Giovanni F.M. Strippoli[2,6,7,8]

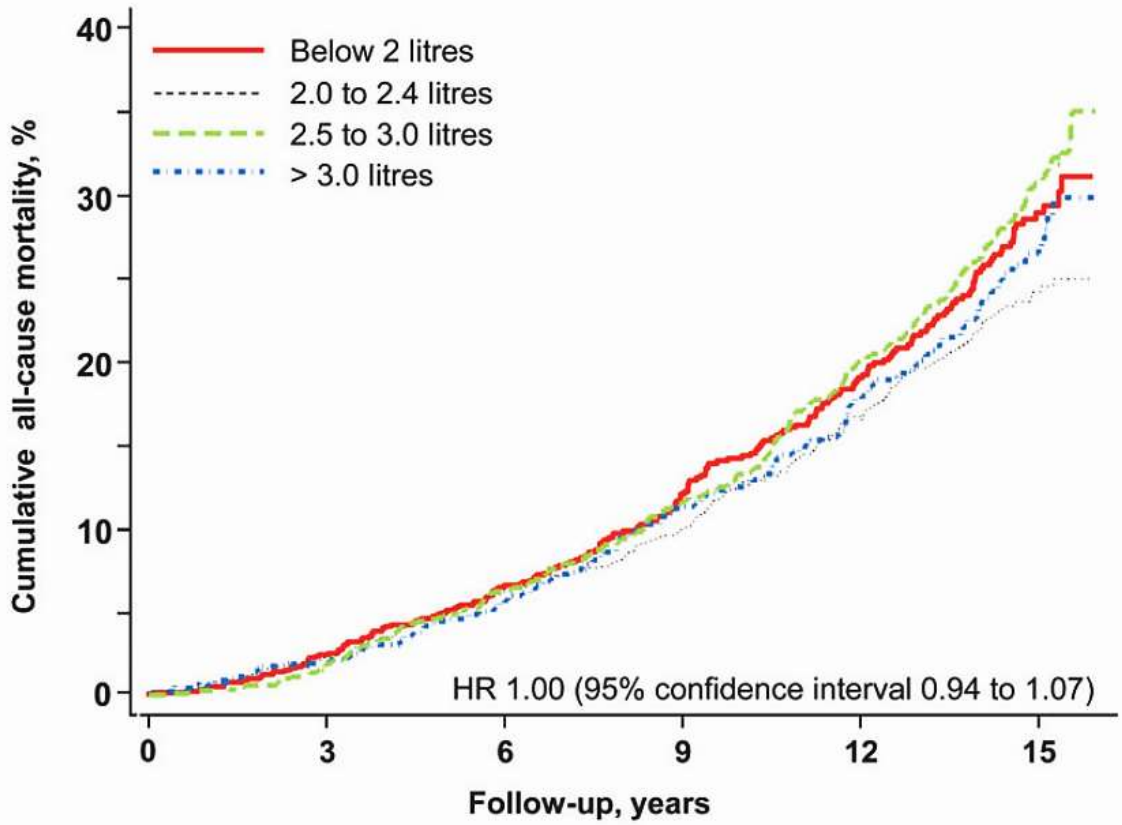
[1]Department of Medicine, University of Otago, Christchurch, New Zealand, [2]School of Public Health, Sydney Medical School, The University of Sydney, Sydney, NSW, Australia, [3]Centre for Kidney Research, Children's Hospital at Westmead, Westmead, NSW, Australia, [4]School of Mathematics and Statistics, The University of Sydney, Sydney, NSW, Australia, [5]Centre for Vision Research, Westmead Millennium Institute and Clinical Ophthalmology and Eye Health, Westmead Clinical School, The University of Sydney, C24 – Westmead Hospital, Sydney, NSW, Australia, [6]Department of Clinical Pharmacology and Epidemiology, Consorzio Mario Negri Sud, S. Maria Imbaro 66030, Italy, [7]Diaverum Scientific Office, Lund, Sweden and [8]Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy

Changes of eGFR in relation to the daily fluid intake

Characteristics	All n = 1207	Daily fluid intake (L) Quartile 1 (< 2 liters) n = 261	Quartile 2 (2-2.4 liters) n = 368	Quartile 3 (2.5-2.9 liters) n = 304	Quartile 4 (≥ 3.0 liters) n = 274	P value*
Demographics						
Age, mean (SD), years	73.6 (7.7)	73.5 (7.3)	74.2 (7.8)	73.3 (7.8)	73.3 (7.5)	0.3
Male, No. (%)	486 (40.2)	90 (34.4)	138 (37.5)	118 (38.8)	140 (51.1)	<0.001
White race, No. (%)	1200 (99.3)	257 (98.4)	365 (99.1)	304 (100)	273 (99.6)	0.5
Currently employed, No. (%)	359 (29.7)	75 (28.5)	100 (27.3)	101 (33.2)	83 (30.5)	0.2
Ever smoked, No. (%)	550 (45.5)	104 (39.8)	165 (44.8)	135 (44.4)	146 (53.3)	0.07
Estimated glomerular filtration rate (SD), ml/min/1.73m²) using the CKDEPI formula at baseline	76.2 (12.7)	76.1 (12.9)	74.3 (12.8)	76.9 (13.2)	78.2 (11.4)	0.009
Estimated glomerular filtration rate (SD), ml/min/1.73m² using the CKDEPI formula at 10 years	74.0 (16.1)	73.7 (17.6)	72.0 (15.6)	74.3 (16.9)	76.7 (13.7)	0.003
Percentage change in eGFR between baseline and follow-up (SD)	-3.3 (19.1)	-3.2 (20.0)	-3.5 (18.5)	-4.0 (19.1)	-2.3 (18.9)	0.8
Absolute change in eGFR between baseline and follow-up (SD), ml/min/1.73m²	-2.2 (10.9)	-2.4 (11.7)	-2.3 (9.7)	-2.6 (12.0)	-1.5 (10.5)	0.7

Palmer S.C., et al. Nephrol. Dial. Transplant., 2014, 29, 1377-1384

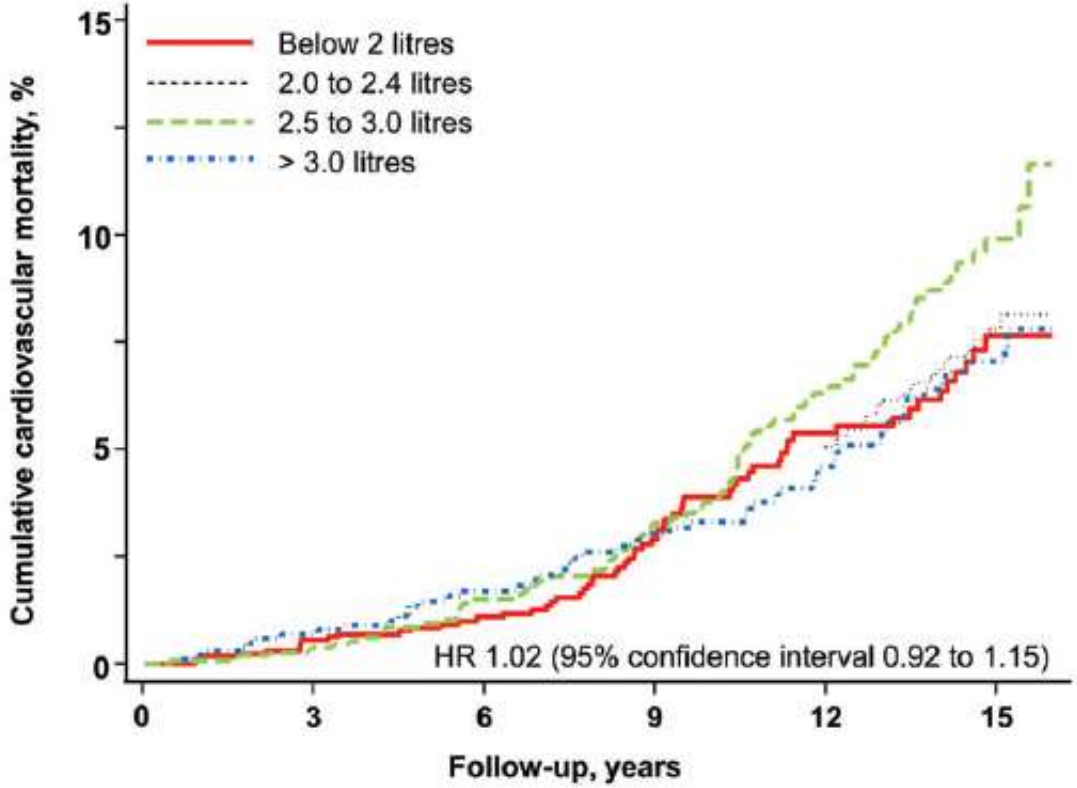
All-cause mortality, stratified by self-reported daily fluid consumption (n = 3858)



Number at risk						
Less than 2.0 litres	578	549	507	463	416	210
2.0 to 2.4 litres	665	635	587	550	497	232
2.5 to 3.0 litres	584	563	517	477	425	211
>3.0 litres	520	504	475	440	402	206

Palmer S.C., et al. Nephrol. Dial. Transplant., 2014, 29, 1377-1384

Cardiovascular mortality, stratified by self-reported daily fluid consumption (n = 3858)



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Palmer S.C., et al. Nephrol. Dial. Transplant., 2014, 29, 1377-1384

Risk factors for change in kidney function (n = 1207)

Table 3. Risk factors for change in kidney function (n = 1207)

Variable	Adjusted regression coefficient [change in eGFR (mL/min per 1.73 m^2) per 250 mL/day increase in fluid consumption]	P-value
Intercept	9.23	0.1
Age	−0.10	0.1
Systolic blood pressure	−0.086	0.004
Diastolic blood pressure	0.09	0.1
Fibrinogen	−0.63	0.06
History of angina	−3.62	0.02
Diabetes mellitus	−6.91	0.003
Fluid intake	0.06	0.6

Palmer S.C., at al. Nephrol. Dial. Transplant., 2014, 29, 1377-1384

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Palmer S.C., at al. Nephrol. Dial. Transplant., 2014, 29, 1377-1384

8 glasses a day ….

Conclusions. Fluid intake from food and beverages excluding water is not associated with improved kidney function or reduced mortality.

Palmer S.C., et al. Nephrol. Dial. Transplant., 2014, 29, 1377-1384

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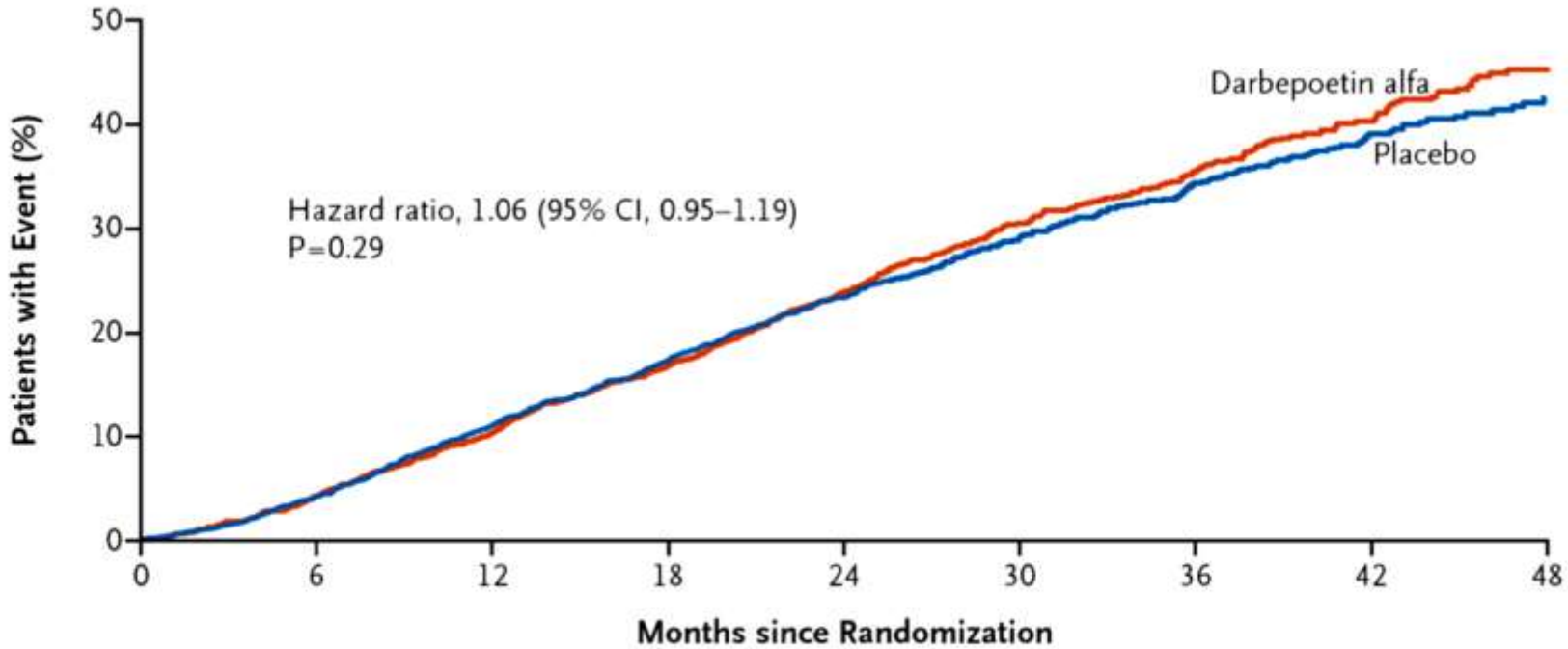
Effect of treatment with darpepoetin on CKD progression in the TREAT study (ESRD or death)



No. at Risk									
Darbepoetin alfa	2012	1910	1762	1544	1207	820	552	309	134
Placebo	2026	1915	1748	1519	1193	842	540	312	123

Pfeffer MA, et al. N Engl Med. 2009;361:2019-2032

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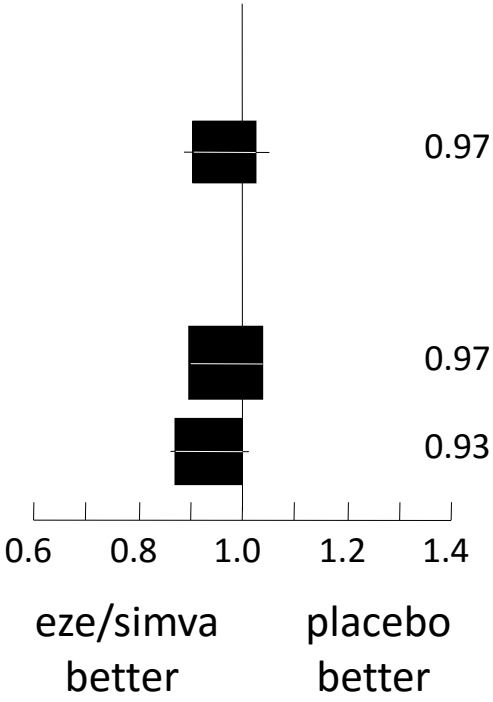
SHARP: No beneficial (or adverse) effect on pre-specified renal outcomes

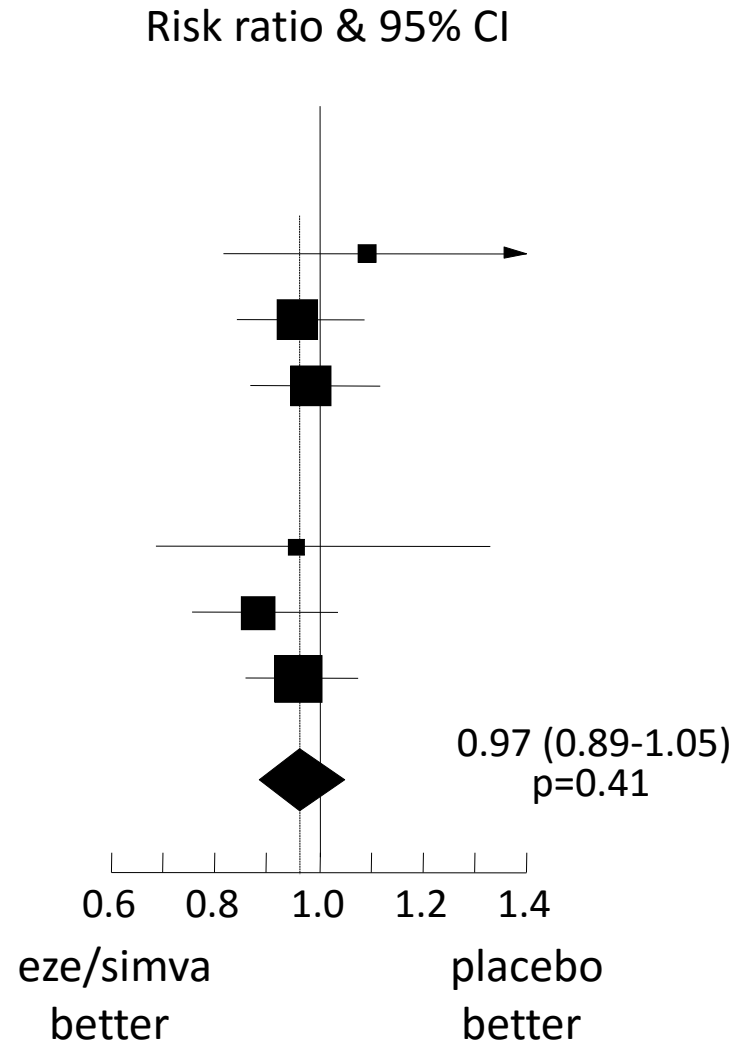
Event	eze/simva (n=3117)	placebo (n=3130)	Risk ratio & 95% CI
Main renal outcome			
End-stage renal disease	1057 (33.9%)	1084 (34.6%)	0.97 (0.89-1.05)
Tertiary renal outcomes			
ESRD or death	1477 (47.4%)	1513 (48.3%)	0.97 (0.90-1.04)
ESRD or 2 x creatinine	1190 (38.2%)	1257 (40.2%)	0.93 (0.86-1.01)



Baigent C. et al., Lancet, 2011, 377, 2181-2192

SHARP: Lack of effect on progression to end-stage renal disease subdivided by disease stage at start

Event	eze/simva (n=3117)	placebo (n=3130)
MDRD estimated GFR (mL/min/1.73m²)		
≥30 (stage 2-3)	96 (8.4%)	83 (7.6%)
≥15 and <30 (stage 4)	454 (36.4%)	489 (37.1%)
<15 (stage 5)	471 (76.7%)	473 (77.9%)
Urinary ACR (mg/g)		
<30 (normo)	68 (12.5%)	73 (13.0%)
≥30 and <300 (micro)	281 (27.2%)	323 (30.0%)
≥300 (macro)	621 (51.6%)	602 (52.1%)
All patients	1057 (33.9%)	1084 (34.6%)



Baigent C. et al., Lancet, 2011, 377, 2181-2192

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bardoxolone Methyl in Type 2 Diabetes and Stage 4 Chronic Kidney Disease

Dick de Zeeuw, M.D., Ph.D., Tadao Akizawa, M.D., Ph.D.,
Paul Audhya, M.D., M.B.A., George L. Bakris, M.D., Melanie Chin, Ph.D.,
Heidi Christ-Schmidt, M.S.E., Angie Goldsberry, M.S., Mark Houser, M.D.,
Melissa Krauth, M.B.A., Hiddo J. Lambers Heerspink, Pharm.D., Ph.D.,
John J. McMurray, M.D., Colin J. Meyer, M.D., Hans-Henrik Parving, M.D., D.M.Sc.,
Giuseppe Remuzzi, M.D., Robert D. Toto, M.D., Nosratola D. Vaziri, M.D.,
Christoph Wanner, M.D., Janet Wittes, Ph.D., Danielle Wrolstad, M.S.,
and Glenn M. Chertow, M.D., M.P.H., for the BEACON Trial Investigators*

CONCLUSIONS

Among patients with type 2 diabetes mellitus and stage 4 chronic kidney disease, bardoxolone methyl did not reduce the risk of ESRD or death from cardiovascular causes. A higher rate of cardiovascular events with bardoxolone methyl than with placebo prompted termination of the trial. (Funded by Reata Pharmaceuticals; BEACON ClinicalTrials.gov number, NCT01351675.)

N. Engl. J. Med. 2103, 369, 2492-2403

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Alcohol and kidney damage: a Janus-faced relationship

Elke Schaeffner[1] and Eberhard Ritz[2]

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It has been known for a long time that excessive consumption of alcohol has adverse effects, including adverse impact on kidneys and kidney disease. Recently, observational evidence has been provided that moderate alcohol consumption is associated with less cardiovascular and renal risk. These issues had been summarized and discussed at the recent congress of the European Society for Biomedical Research and Alcoholism in Vienna.

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KEYWORDS: acute renal failure; chronic kidney disease; diabetes; end-stage kidney disease; proteinuria

On occasion of the recent congress of the European Society for Biomedical Research on Alcoholism (ESBRA) in Vienna, 4–7 September 2011, one entire session had been devoted to the relationship between alcohol and the kidney. It was the goal of this session to provide an evenhanded analysis of the impact of alcohol consumption on the evolution of chronic kidney function and disease. The interest in the issue of alcohol and its effect on the kidney was aroused by the fact that—after several preceding negative analyses[1,2]—a number of stringent prospective observational studies had recently documented that moderate alcohol consumption has a beneficial effect both on the decline in renal function with age and the evolution of primary kidney disease.[3–6] The fact that one major session of the congress was devoted to the kidney indicates that these novel findings had a resonance even outside of nephrology. This was also reflected by an animated and constructive discussion.

Kidney International, 2012, 81: 816

Nephroprotection: Where are we in 2015?

How to improve the effectiveness of nephroprotection?

- To educate patients
- To educate doctors
- Educational materials
- Web programmes (e-learning) - UK
- Improve the health system (incentives for doctors in UK)

Thank you very much for your attention !

Andrzej Wiecek

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