# Hypertension and Kidney Disease: a Nephrologist's Perspective

## Alan Jardine

## University of Glasgow

University of Glasgow

Kidney Research UK
Funding research to save lives

British Heart Foundation

# Natural history of PRD

CV Risk

x 3-5

x 10-20

x 3-5

```
┌─────────────┐
│     CKD     │
└─────────────┘
       ↓
┌─────────────┐
│   Dialysis  │
└─────────────┘
       ↓
┌─────────────┐
│     Tx      │
└─────────────┘
```

Graft Failure
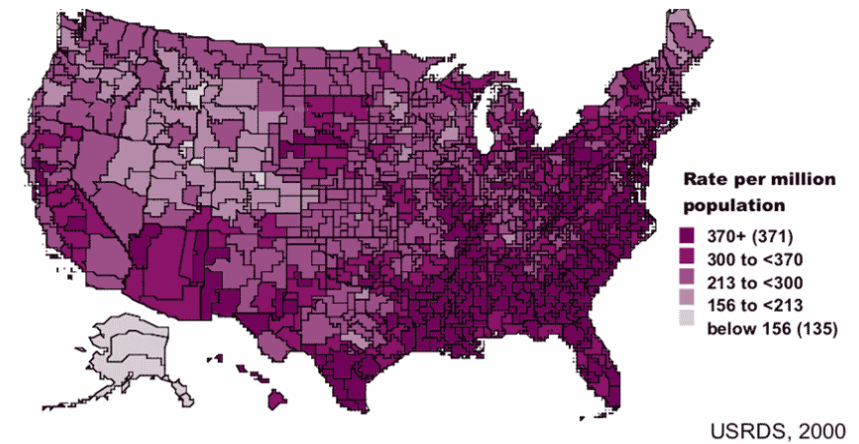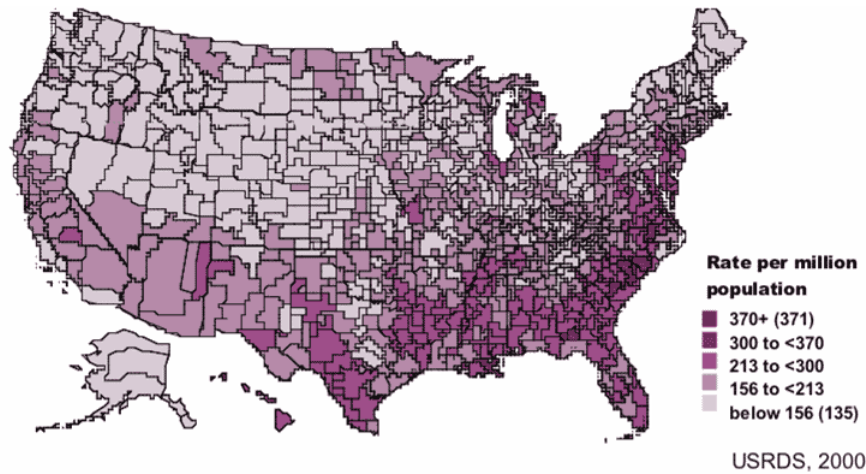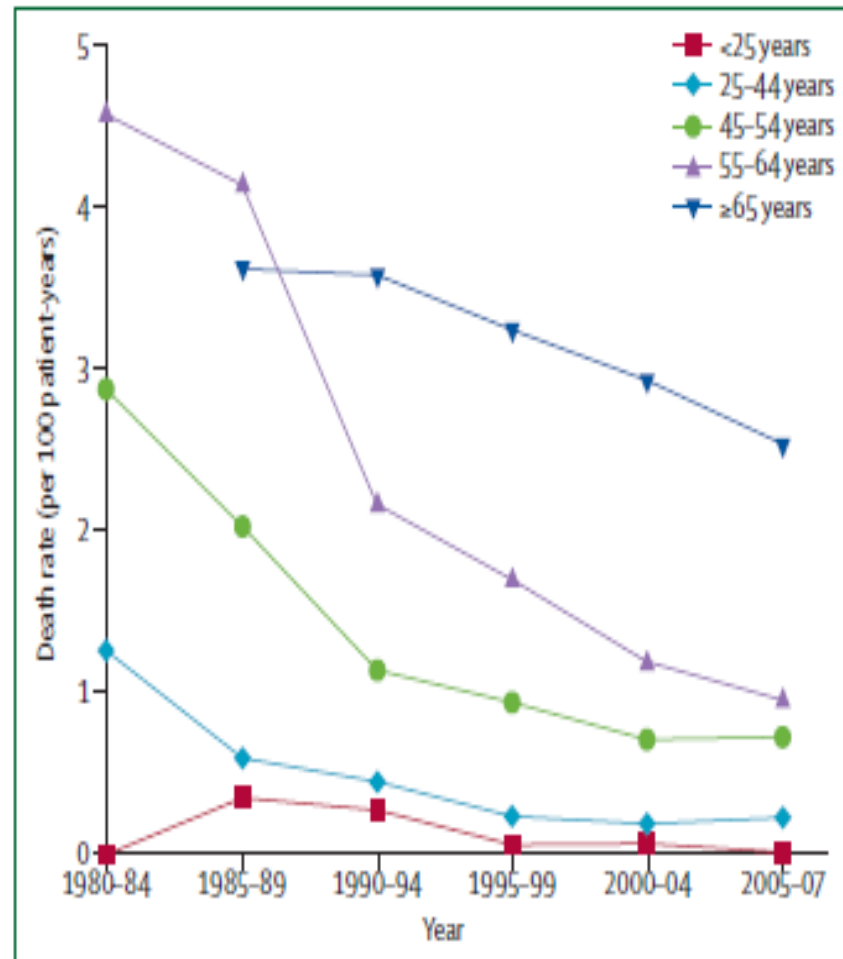
# Incidence of Kidney Failure

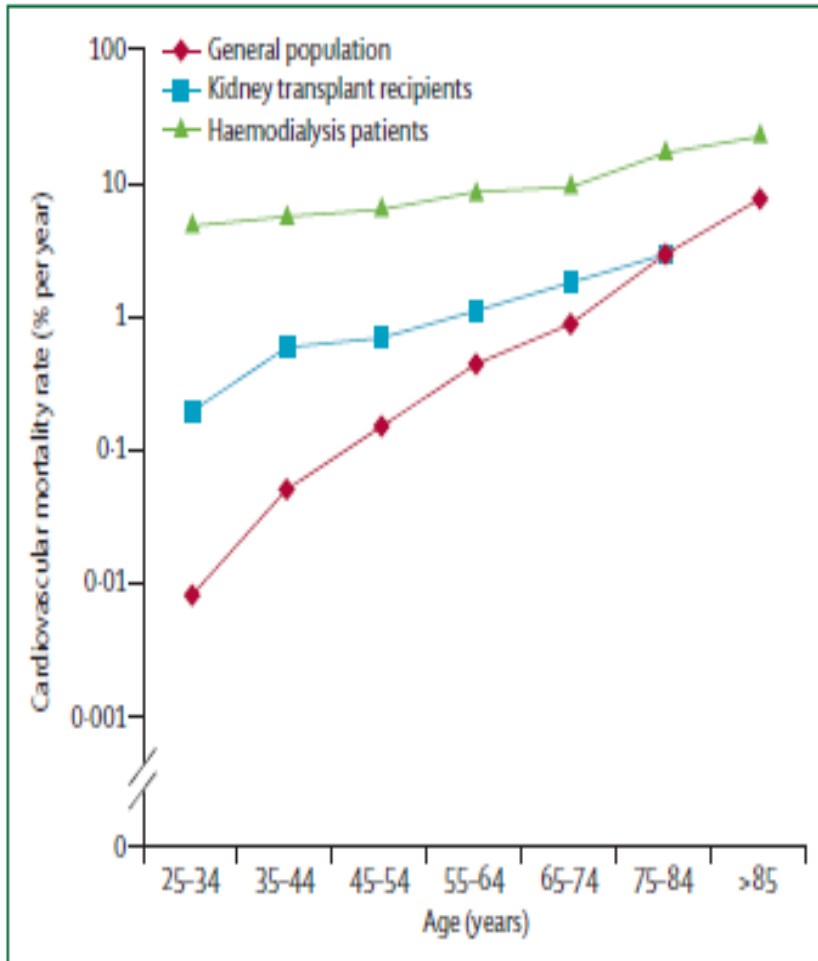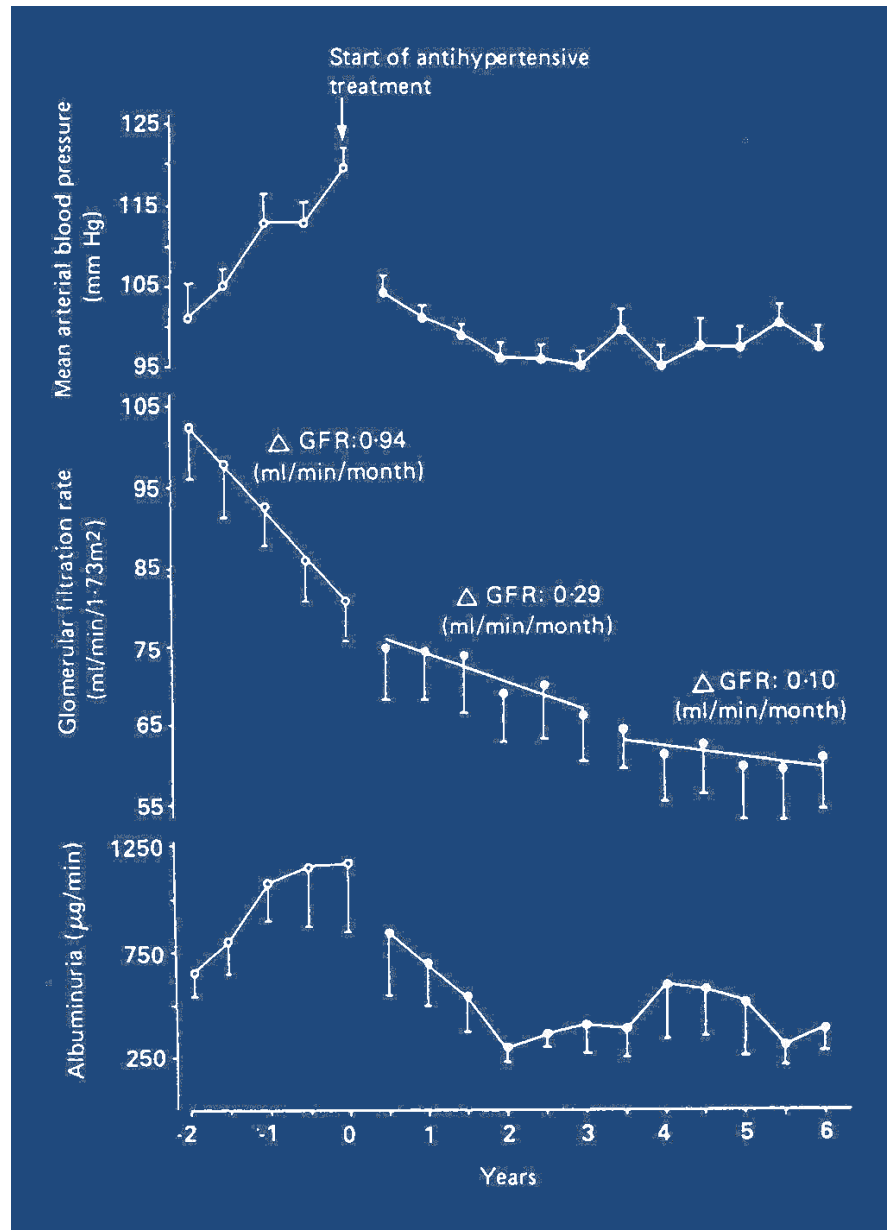per million population, 1990-2000, by HSA, unadjusted



USRDS, 2000

# Prevention of cardiovascular disease in adult recipients of kidney transplants

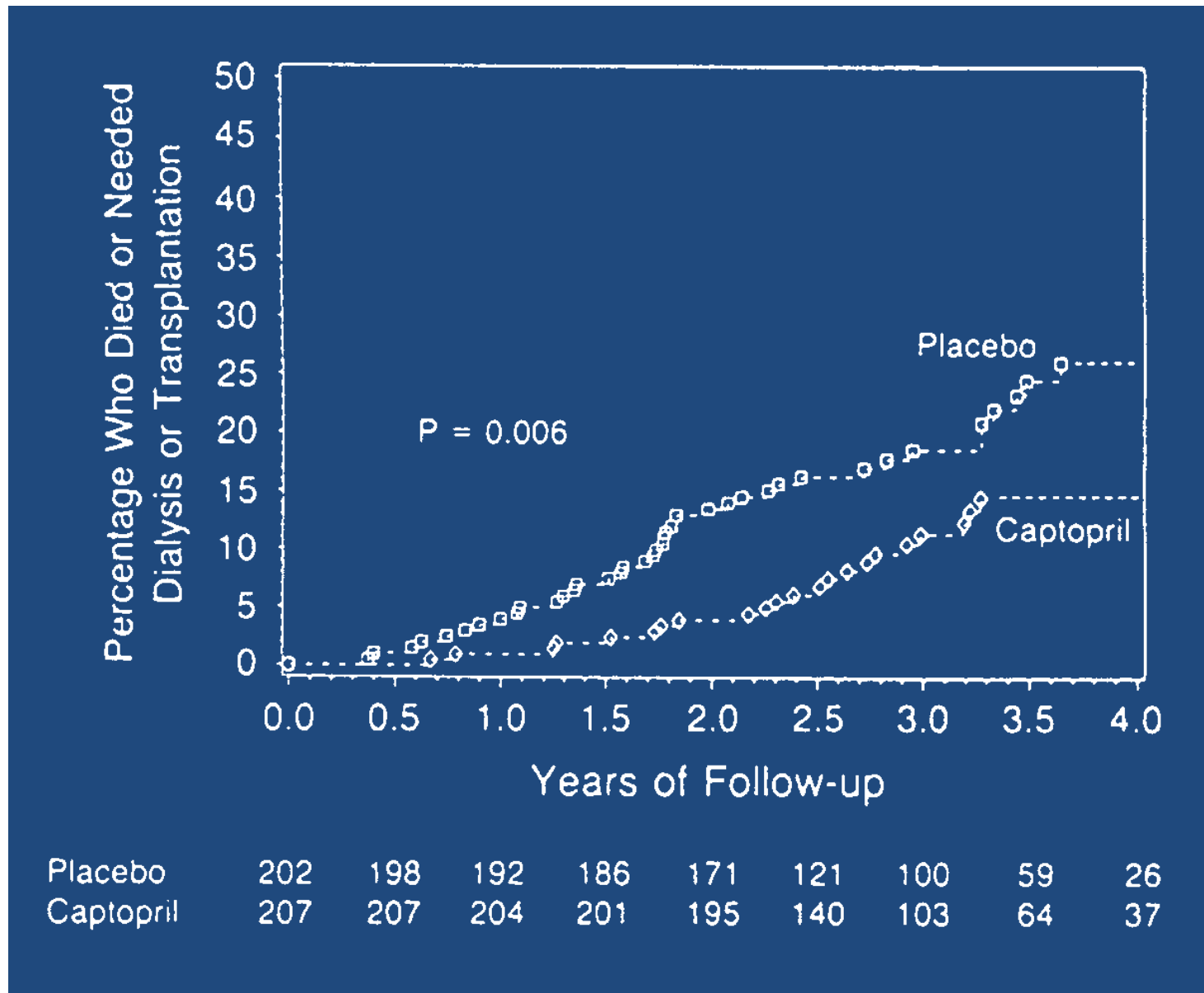Alan G Jardine, Robert S Gaston, Bengt C Fellstrom, Hallvard Holdaas

# Renal Protection

## The effect of antihypertensive treatment



Parving et al; BMJ 1987

# ACE INHIBITORS AND RENAL FUNCTION



Lewis et al: NEJM 1993

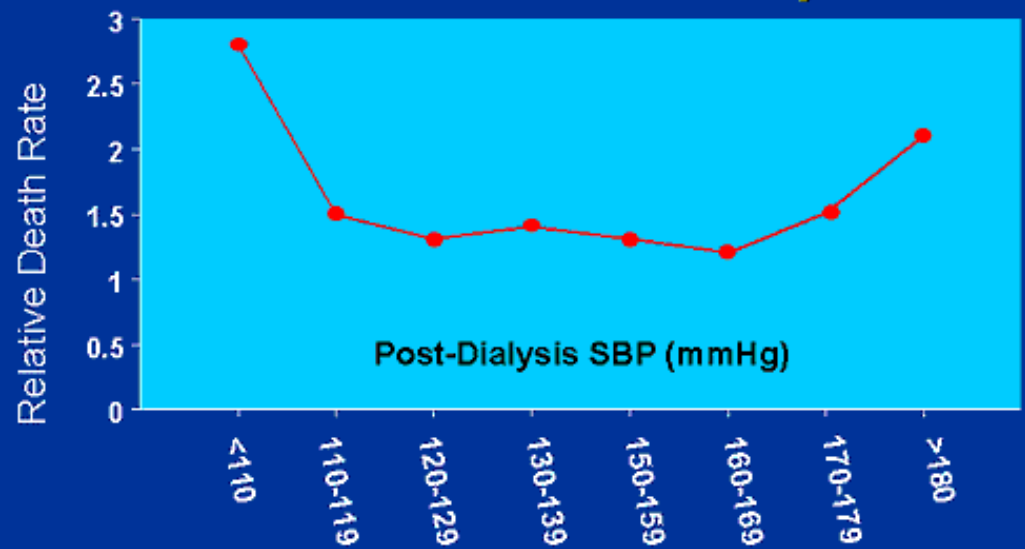| | Losartan vs placebo | Irbesartan vs placebo | Irbesartan vs amlodipine | amlodipine vs placebo |
|---|---|---|---|---|
| X2 creat, ESRD, death | 16 $p=0.024$ | 20 $p=0.024$ | 23 $p=0.006$ | -4 NS |
| x2 creat | 25 $p=0.006$ | 33 $p=0.003$ | 37 $p=0.001$ | -6 NS |
| ESRD | 28 $p=0.002$ | 23 $p=0.07$ | 23 $p=0.007$ | 0 NS |
| Death | -2 | "NS" | "NS" | "NS" |
| ESRD or death | 20 | N/A | N/A | N/A |
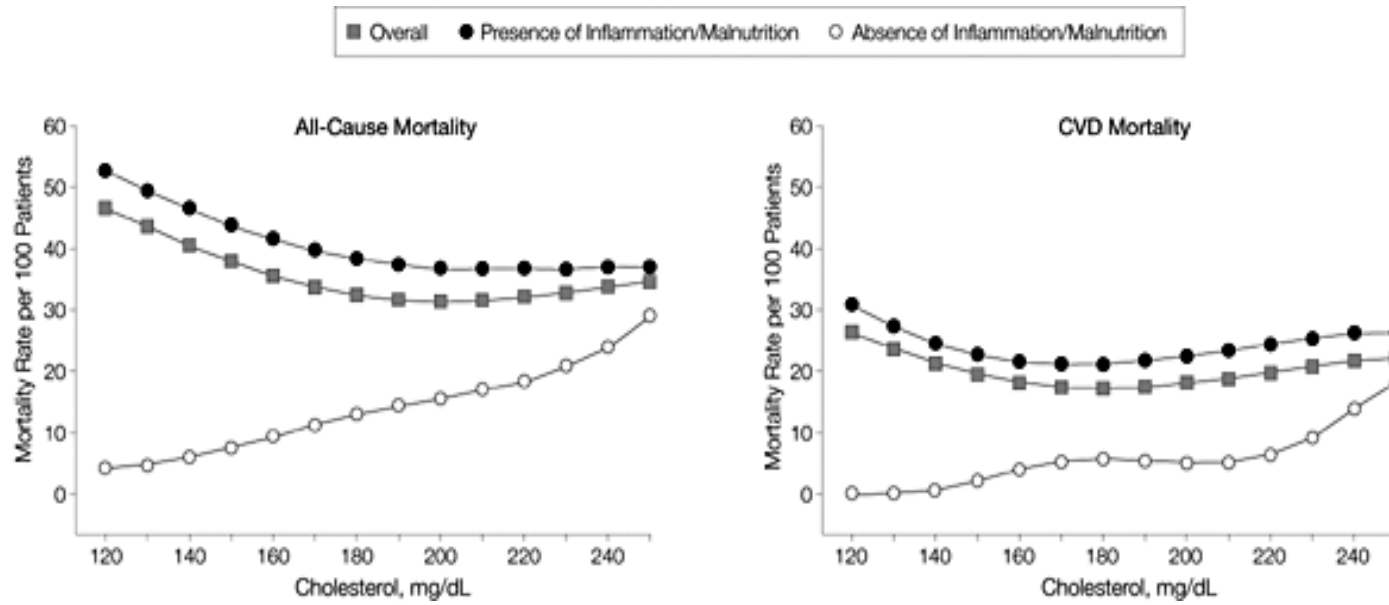
Liu Y, et al., *JAMA* 291: 451-459, 2004

**Hypertension is Not a Risk for Mortality – Low Predialysis BP Increases Mortality Risk**
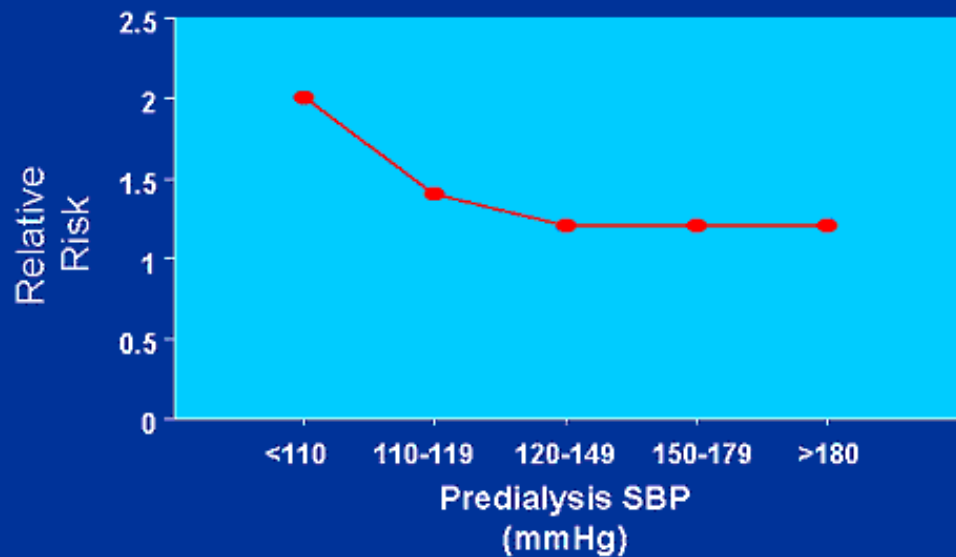
Port FK et al, AJKD 33:507, 1999

**"U" Curve Association Between BP and Mortality**

Zager PG et al, KI 54:561, 1998

Rate reduction 17% (95% CI 6–26%)
Log-rank p=0·0021

Placebo
Simvastatin plus ezetimibe
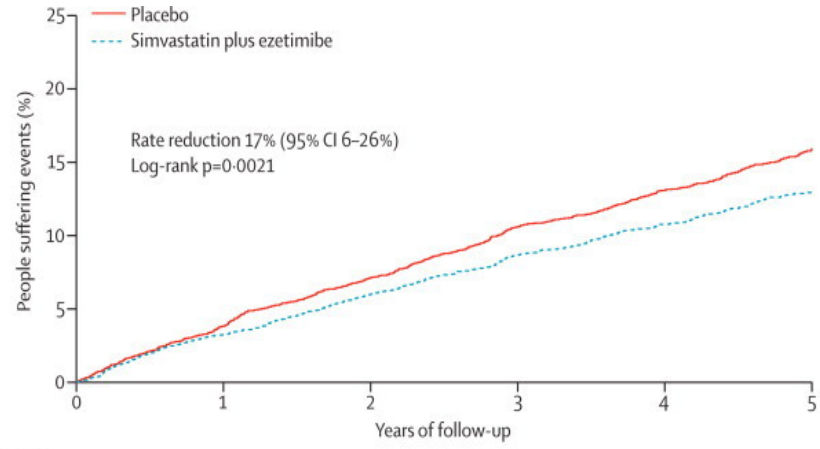
**Number at risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 4620 | 4204 | 3849 | 3469 | 2566 | 1269 |
| Simvastatin plus ezetimibe | 4650 | 4271 | 3939 | 3546 | 2655 | 1265 |



Placebo
Rosuvastatin

Hazard ratio, 0.96
P=0.59
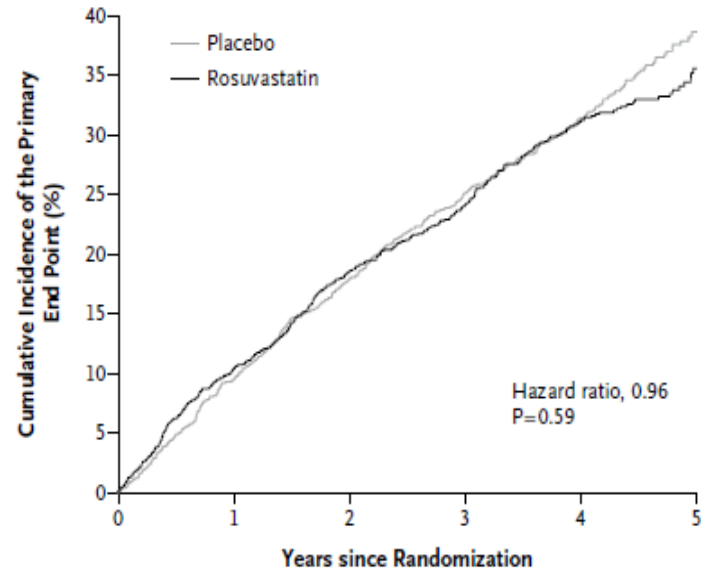
**No. at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 1384 | 1163 | 952 | 809 | 534 | 153 |
| Rosuvastatin | 1390 | 1152 | 962 | 826 | 551 | 148 |

# Is CVD the same in CKD?

| | 4D | ALERT | 4S | AURORA |
|---|---|---|---|---|
| EP | Placebo | Placebo | Placebo | Placebo |
| CD | 23% | 5.1% | 8.5% | 23.4% |
| AMI (NF) | 12% | 6.3% | 22.6% | 7.7% |
| Non-CVD | 25% | 6.2% | 2.2% | 19.4% |

# Is CVD the same in CKD?

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Baseline variable

| Importance |

# Risk Factors – MI
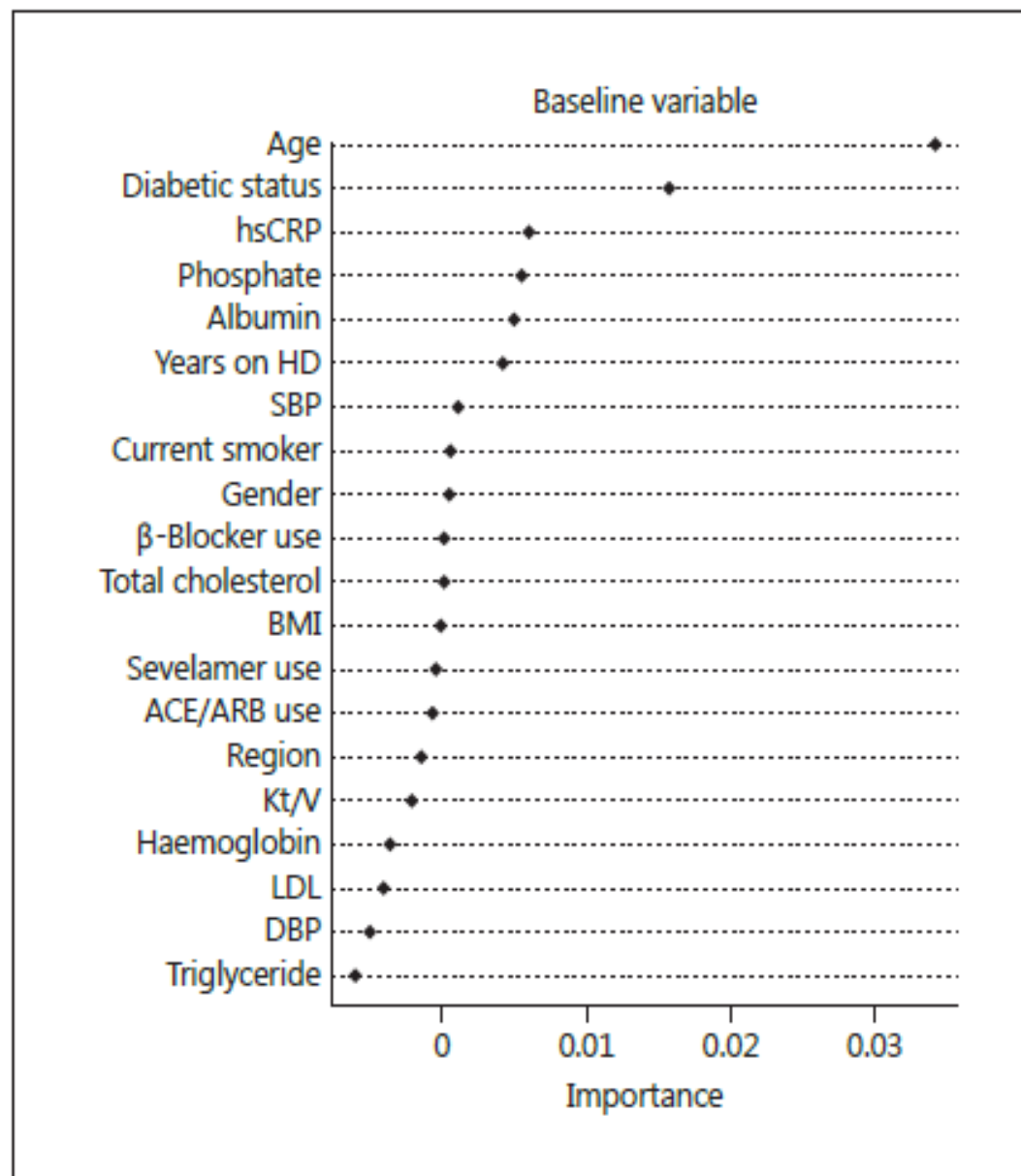
|  | RR | CI | P |
|---|---|---|---|
| Age | 1.03 | (1.00,1.05) | 0.0211 |
| Diabetes | 2.36 | (1.42,3.04) | 0.0010 |
| Smoking | 2.31 | (1.78,5.63) | 0.0017 |
| CHD | 3.17 | (2.08,5.18) | 0.0001 |
| LDL | 1.41 | (1.12,1.77) | 0.0038 |

# Risk Factors – Cardiac death

|        | RR   | CI            | P       |
|--------|------|---------------|---------|
| Age    | 1.05 | (1.02,1.08)   | 0.0001  |
| Diabetes | 2.82 | (1.62,4.91) | 0.0002  |
| Smoking | 1.55 | (0.86,2.80)  | 0.1490  |
| CHD    | 3.60 | (1.96,6.63)   | <0.0001 |
| LDL    | 1.28 | (0.99, 1.65)  | 0.0607  |
| SBP    | 1.01 | (1.00,1.03)   | 0.0506  |
| PP     | 1.01 | (1.00,1.03)   | 0.0034  |
| LVH    | 2.08 | (1.11, 3.89)  | <0.0001 |
| ST-T   | 3.59 | (2.07, 6.21)  | <0.0001 |

University of Glasgow

# The Uraemic Heart

VASCULAR BIOLOGY – HEMODYNAMICS – HYPERTENSION

# Electrocardiographic abnormalities and uremic cardiomyopathy

GRAHAM A. STEWART, RON T. GANSEVOORT, PATRICK B. MARK, ESTHER ROONEY,
THERESA A. MCDONAGH, HENRY J. DARGIE, R. STUART, C. RODGER, and ALAN G. JARDINE
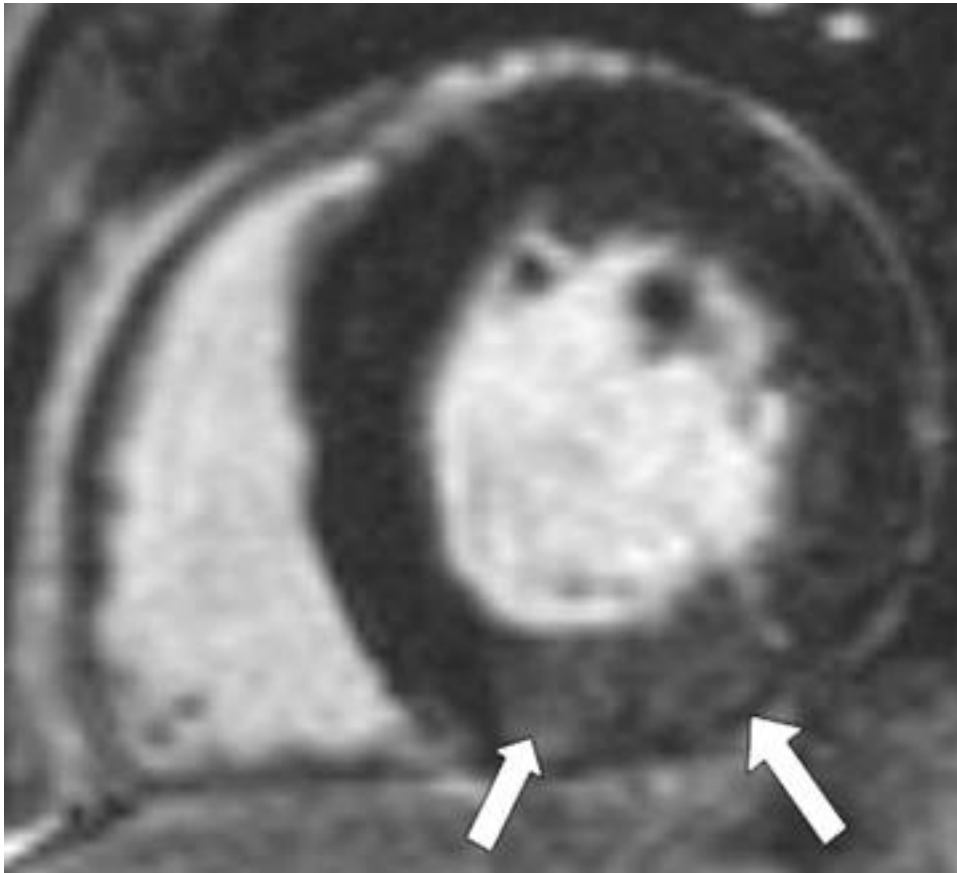


Stewart GA et al., KI 2006;67:217-26
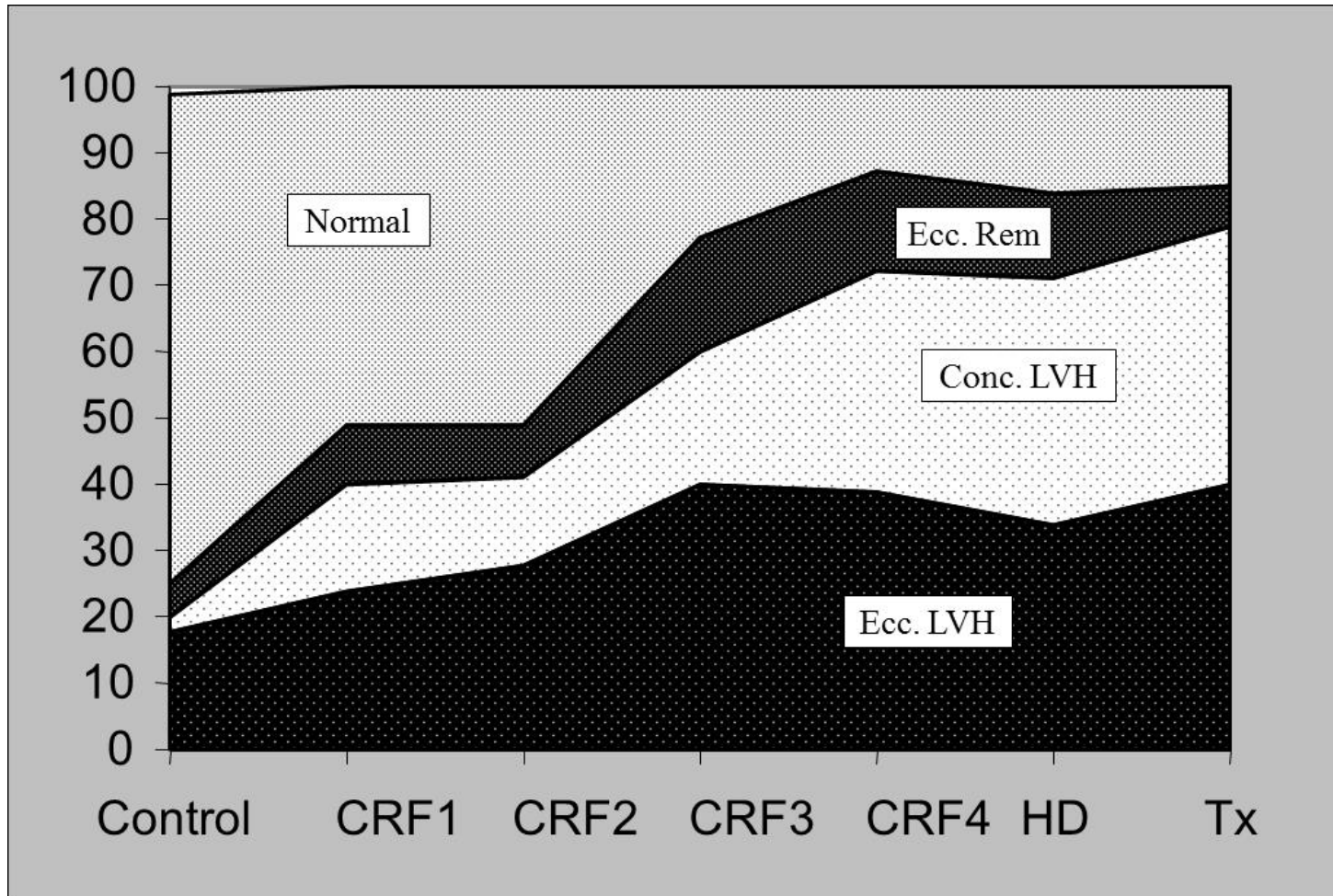
# Redefinition of uremic cardiomyopathy by contrast-enhanced cardiac magnetic resonance imaging

PB Mark[1,2], N Johnston[3], BA Groenning[3], JE Foster[3], KG Blyth[3], TN Martin[3], T Steedman[3], HJ Dargie[3] and AG Jardine[1,2]



Mark PB et al., Kid. Int. 2006;69:1839-45
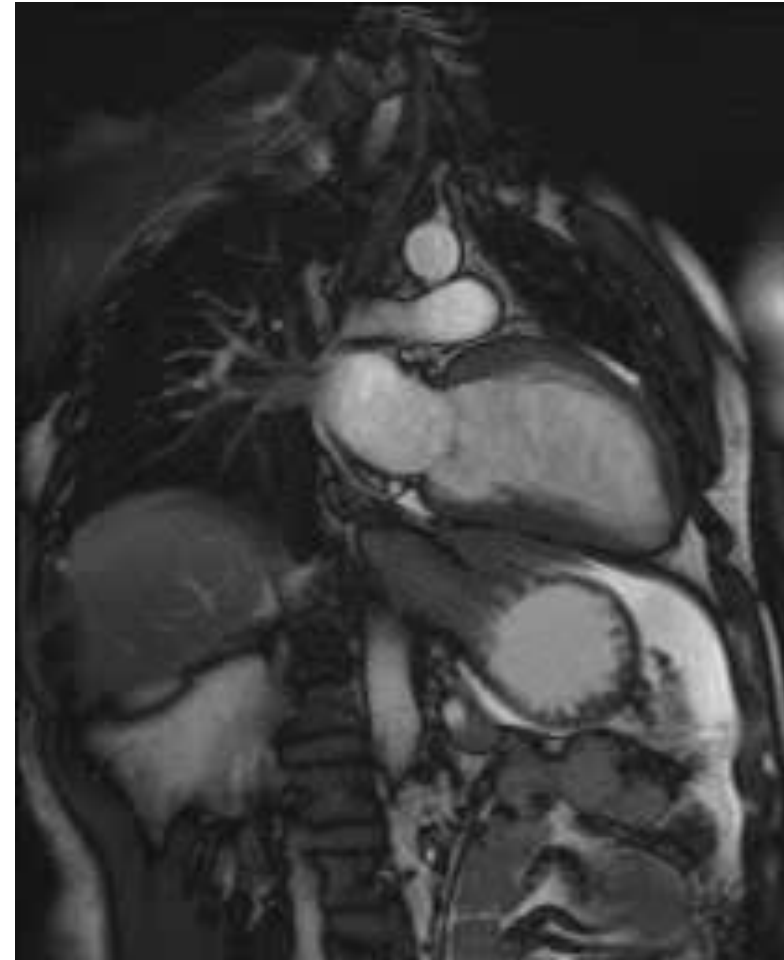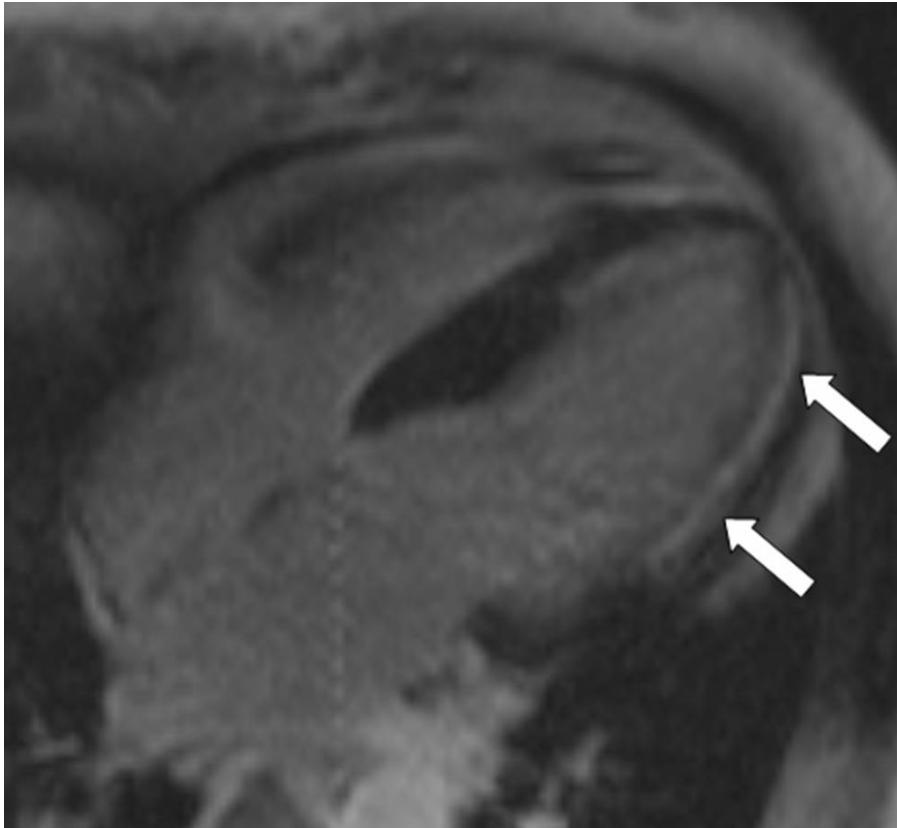
Mark PB et al., Kid. Int. 2006;69:1839-45

# Defining myocardial tissue abnormalities in end-stage renal failure with cardiac magnetic resonance imaging using native T1 mapping

CrossMark

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see commentary on page 729

Elaine Rutherford[1,2], Mohammed A. Talle[1], Kenneth Mangion[1], Elizabeth Bell[1], Samuli M. Rauhalammi[1], Giles Roditi[1], Christie McComb[1], Aleksandra Radjenovic[1], Paul Welsh[1], Rosemary Woodward[1], Allan D. Struthers[2], Alan G. Jardine[1], Rajan K. Patel[1], Colin Berry[1] and Patrick B. Mark[1]

[1]Institute of Cardiovascular and Medical Sciences, BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Scotland, UK; and
[2]University of Dundee, Division of Cardiovascular & Diabetes Medicine, Dundee, Scotland, UK
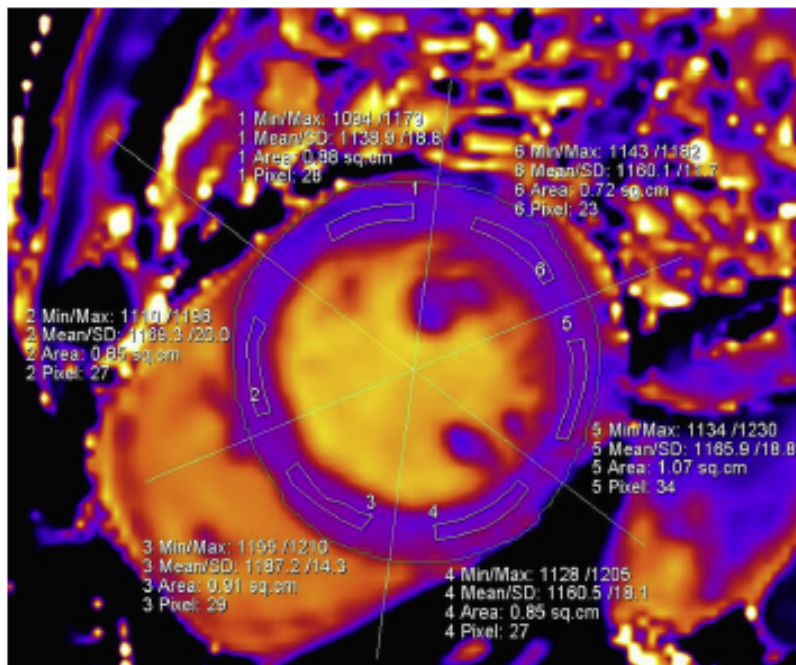
Figure 3 | A typically segmented T1 map of a basal myocardial slice in a hemodialysis patient. Min/Max, minimum/maximum.
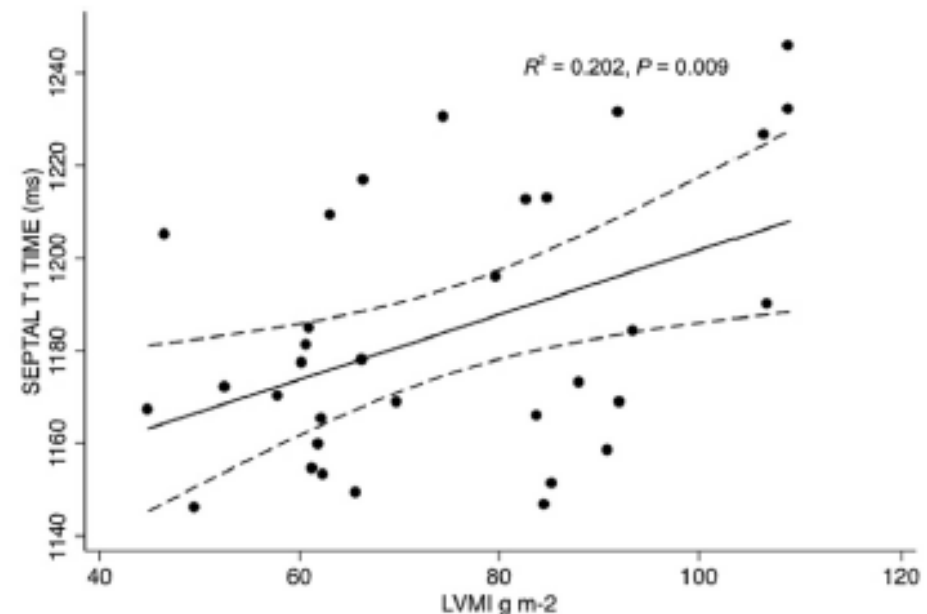


Figure 2 | Scatterplot of septal T1 times against left ventricular mass indexed to body surface area (LVMI) in hemodialysis patients. g m-2, grams per meter squared.

$R^2 = 0.202$, $P = 0.009$

Rutherford E et al., KI 2016; 90:845-52

# Novel cardiac nuclear magnetic resonance method for noninvasive assessment of myocardial fibrosis in hemodialysis patients

Matthew P.M. Graham-Brown[1,2,3], Daniel S. March[1,2], Darren R. Churchward[1,2], David J. Stensel[3], Anvesha Singh[4], Ranjit Arnold[4], James O. Burton[1,2,4] and Gerry P. McCann[4]

[1]John Walls Renal Unit, University Hospitals Leicester NHS Trust, Leicester, United Kingdom; [2]Department of Infection Immunity and Inflammation, School of Medicine and Biological Sciences, University of Leicester, Leicester, United Kingdom; [3]National Centre for Sport and Exercise Medicine, School of Sport, Exercise, and Health Sciences, Loughborough University, Loughborough, United Kingdom; and [4]Department of Cardiovascular Sciences, University of Leicester and NIHR Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital Leicester, Leicester, United Kingdom

Graham Brown MPM et al., KI 2016; 90:835-44
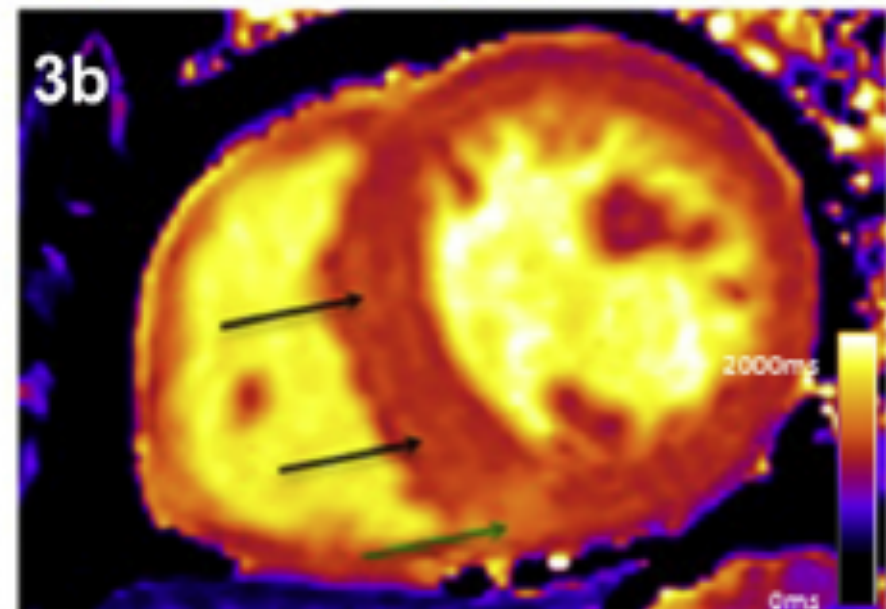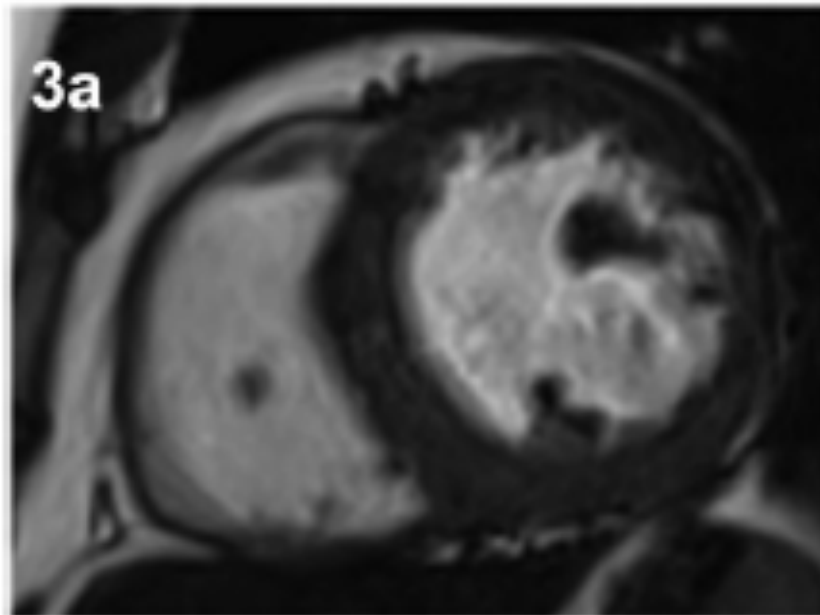
# Diffuse Interstitial Fibrosis and Myocardial Dysfunction in Early Chronic Kidney Disease

Nicola C. Edwards, PhD[a,b,*], William E. Moody, MBChB[a,b], Mengshi Yuan, MBChB[b], Manvir K. Hayer, MBChB[c], Charles J. Ferro, MD[a,c], Jonathan N. Townend, MD[a,b], and Richard P. Steeds, MD[a,b]
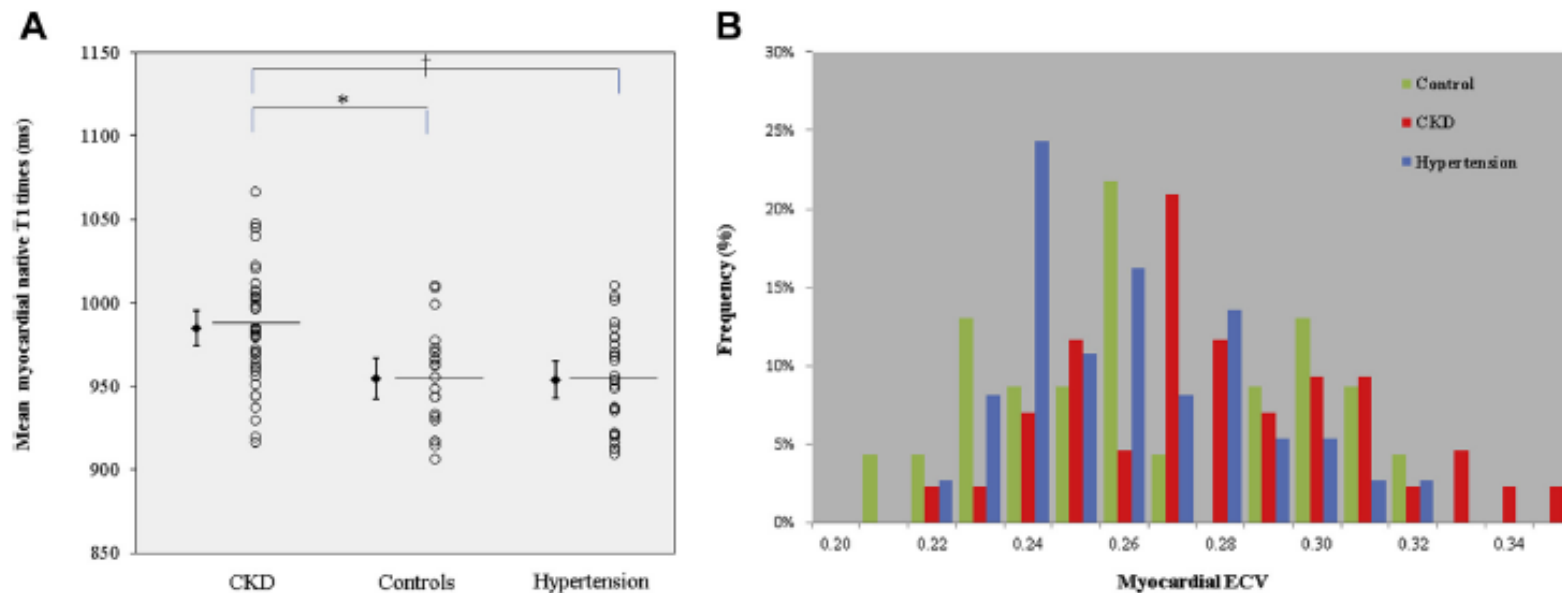
Figure 3. (A) Box scatter plot of native myocardial T1 times. Error bars are standard error of the mean x2. Myocardial T1 time were assessed in the LV septum from the basal and mid-ventricular levels and averaged to yield a "global T1 time." Measurements excluded RV insertion point late gadolinium enhancement. *p <0.05 CKD versus control, †CKD versus hypertension. (B) Frequency histogram of myocardial ECV. The histogram for CKD is shifted rightward with a higher mean septal ECV in the left ventricle but with greater scatter.
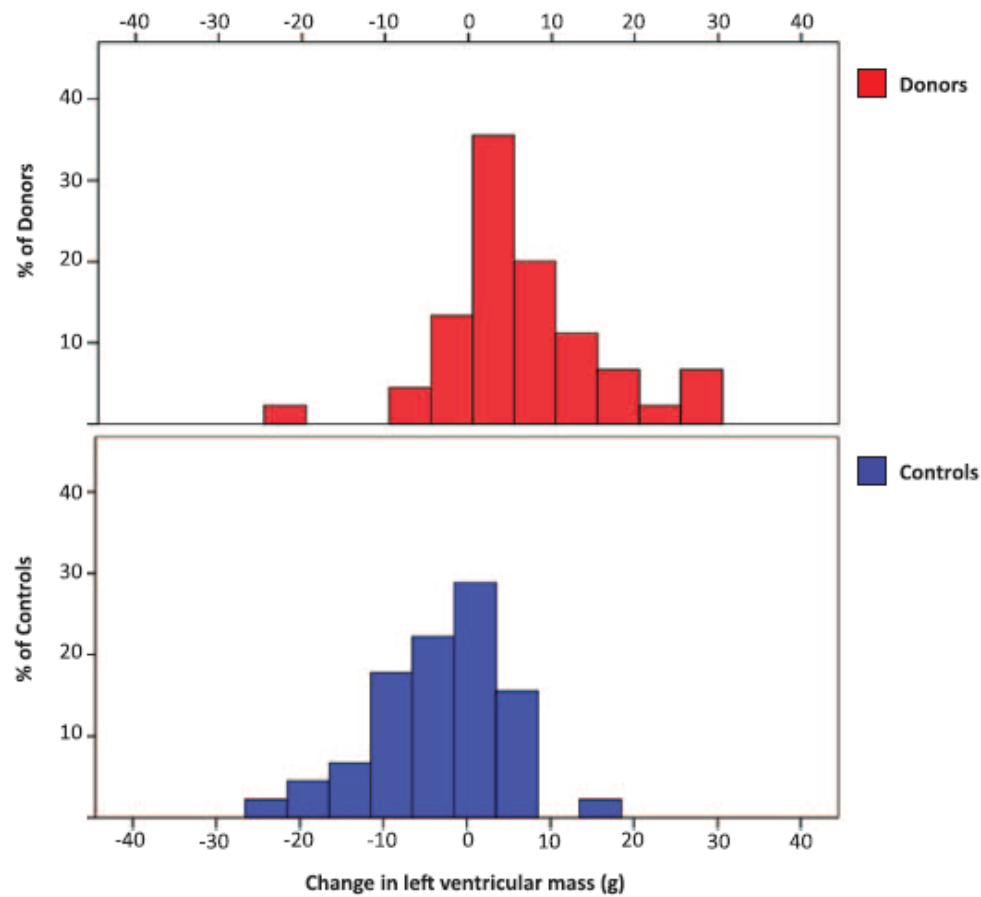
Edwards NC et al., Am J Cardiol 2015;115:1311-1317

OPEN

# Cardiovascular Effects of Unilateral Nephrectomy in Living Kidney Donors

William E. Moody, Charles J. Ferro, Nicola C. Edwards, Colin D. Chue, Erica Lai Sze Lin,
Robin J. Taylor, Paul Cockwell, Richard P. Steeds, Jonathan N. Townend;
on behalf of the CRIB-Donor Study Investigators

# Microvolt T-Wave Alternans in End-Stage Renal Disease Patients—Associations with Uremic Cardiomyopathy

Rajan K. Patel,*[†] Patrick B. Mark,*[†] Crawford Halliday,[‡] Tracey Steedman,[‡] Henry J. Dargie,[‡] Stuart M. Cobbe,* and Alan G. Jardine*[†]
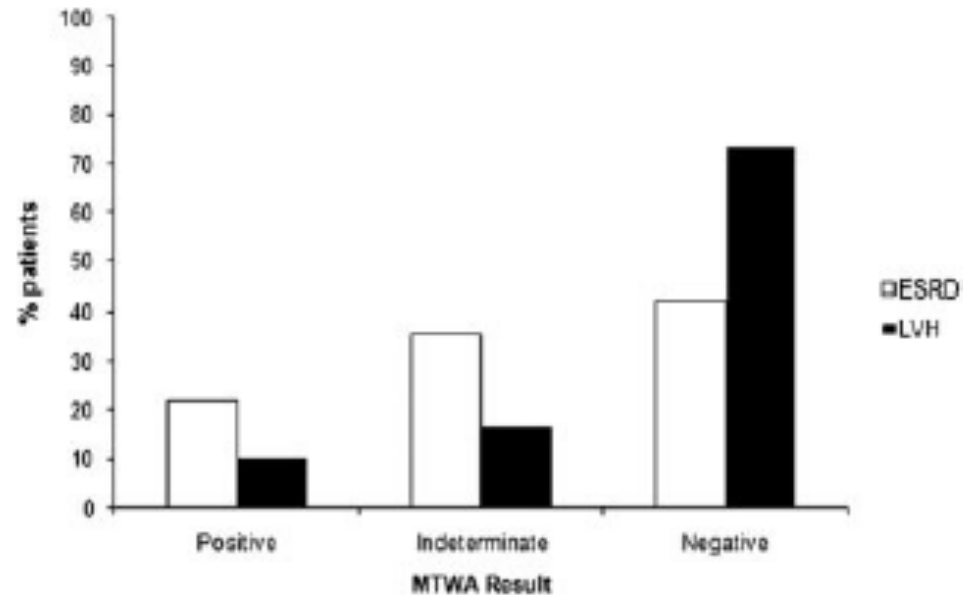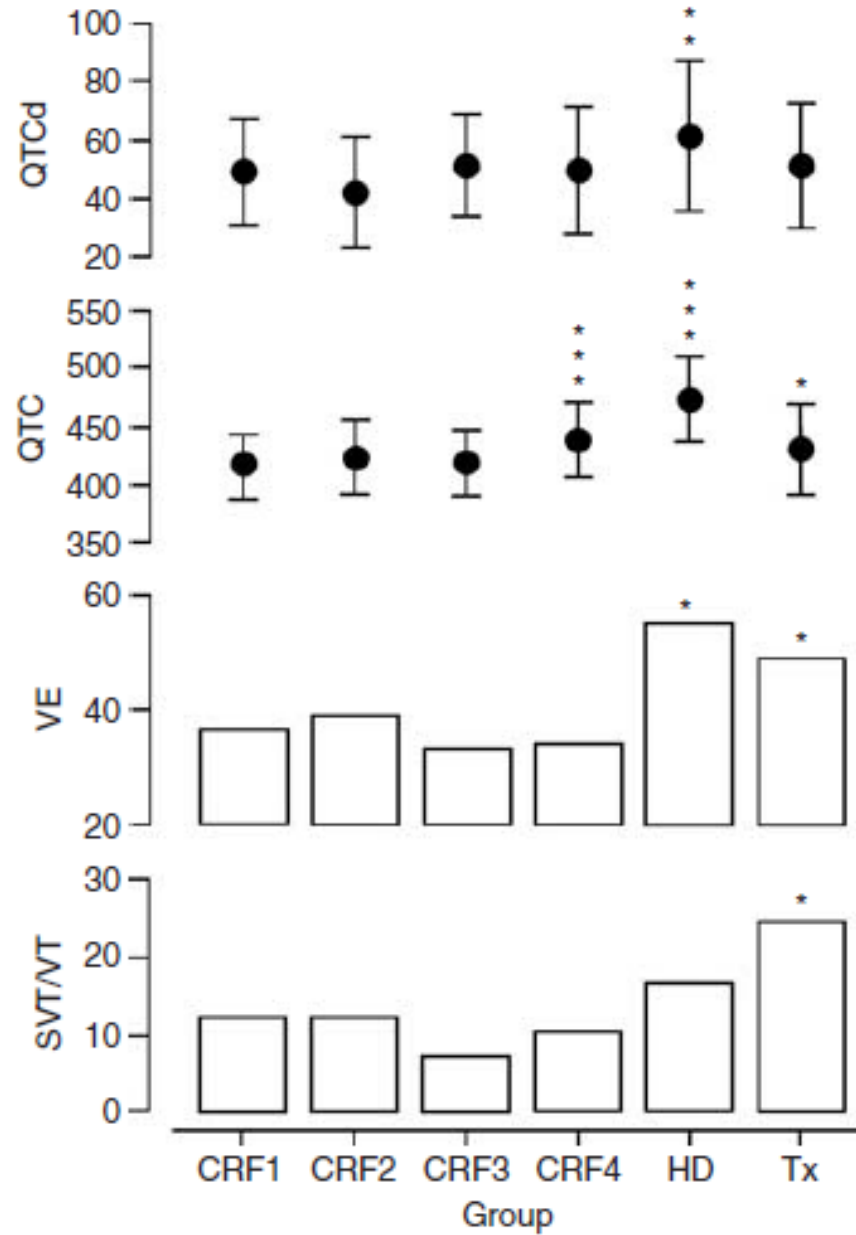
**Figure 1. | Bar chart showing MTWA result for ESRD and LVH patients.**

Patel RK et al., CJASN 2011;6:519-527

Stewart GA et al., KI 2006;67:217-26

# Determinants of Left Ventricular Mass and Hypertrophy in Hemodialysis Patients Assessed by Cardiac Magnetic Resonance Imaging

Rajan K. Patel,*[†] Scott Oliver,[†] Patrick B. Mark,*[†] Joanna R. Powell,*[†] Emily P. McQuarrie,*[†] James P. Traynor,[‡] Henry J. Dargie,[§] and Alan G. Jardine*[†]

Patel R et al. CJASN 2009;4:1477-83
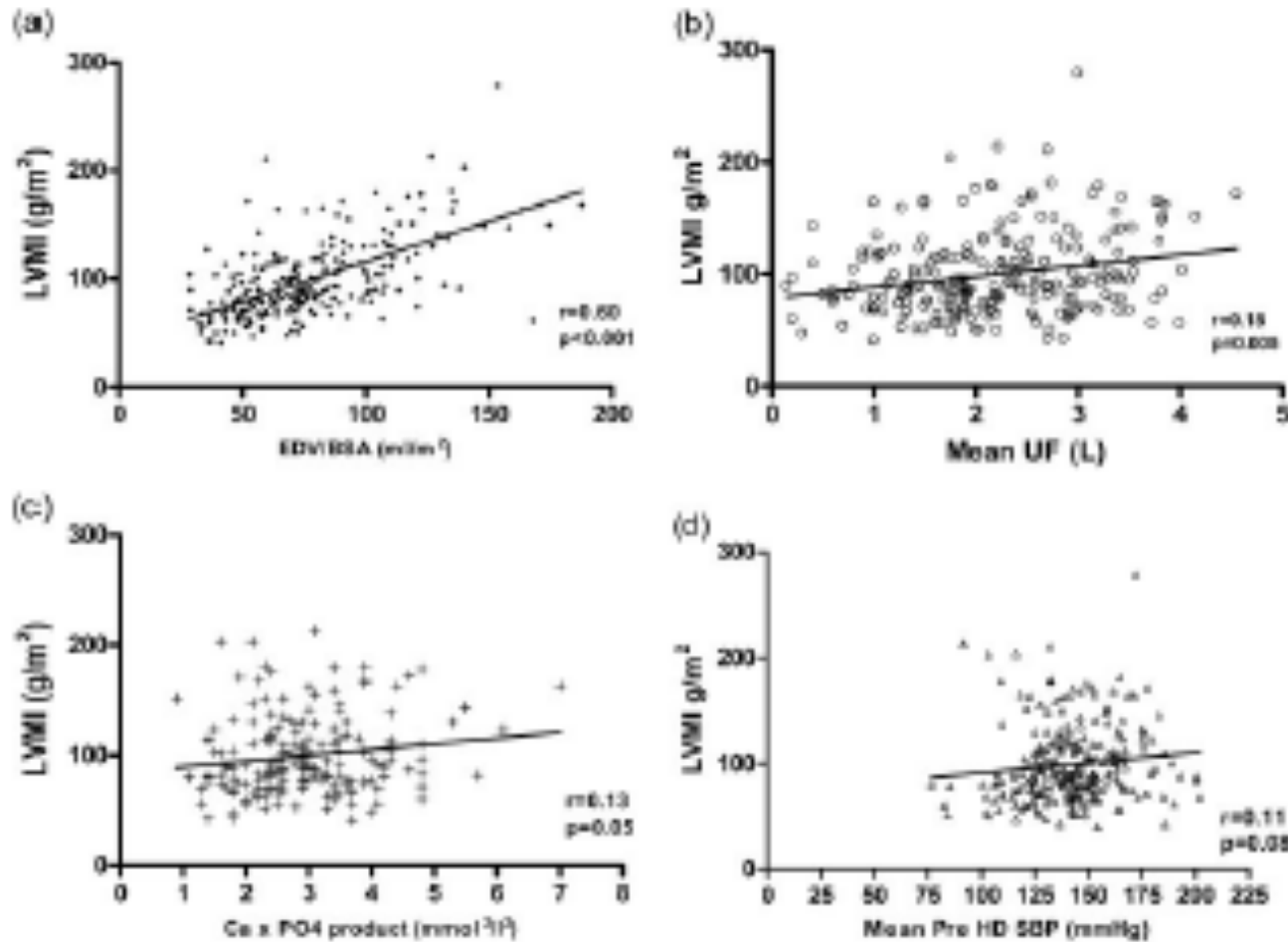
|  | B | β | P | 95% CI |
|---|---|---|---|---|
| Constant | −13.5 |  | 0.40 | −45.33 to 18.3 |
| EDV/BSA | 0.80 | 0.66 | <0.001 | 0.66 to 0.91 |
| Mean pre-HD SBP | 0.24 | 0.13 | 0.01 | 0.05 to 0.42 |
| Ca × PO4 product | 5.38 | 0.16 | 0.003 | 1.53 to 9.24 |

# Association between proteinuria and left ventricular mass index: a cardiac MRI study in patients with chronic kidney disease

Emily P. McQuarrie[1], Rajan K. Patel[1], Patrick B. Mark[1], Christian Delles[1], John Connell[1], Henry J. Dargie[1,2], Tracey Steedman[1,2] and Alan G. Jardine[1]

[1]BHF Cardiovascular Research Centre, Faculty of Medicine, 7 University of Glasgow. 126 University Place, Glasgow G12 8TA, UK and [2]Department of Cardiology, Western Infirmary, Dumbarton Rd, Glasgow, G11 6NT, UK

*Correspondence and offprint requests to*: Emily McQuarrie; E-mail: emilypf@hotmail.com

McQuarrie E et al., NDT 2011;26:933-38
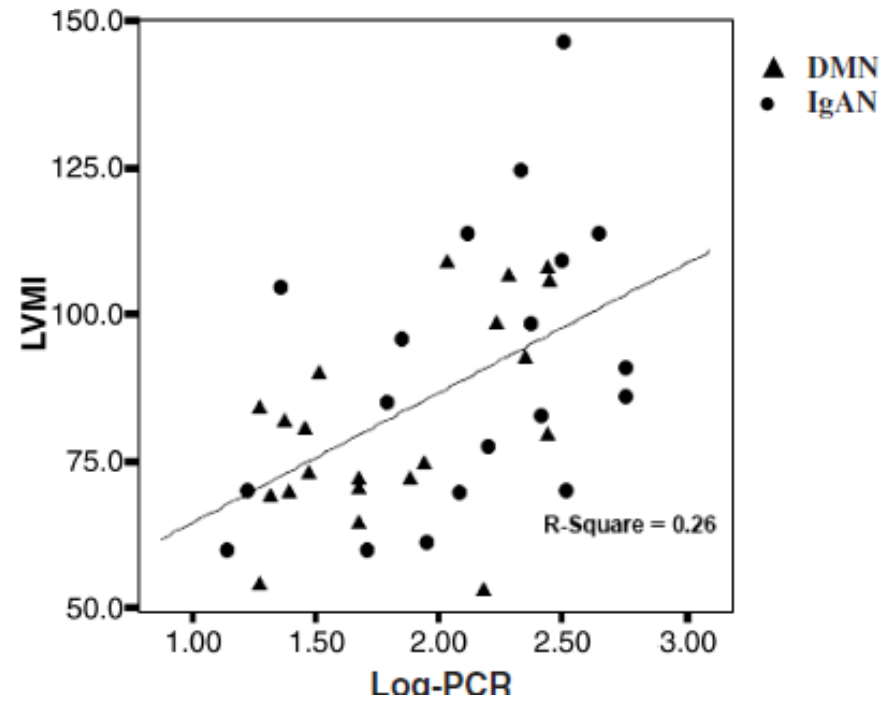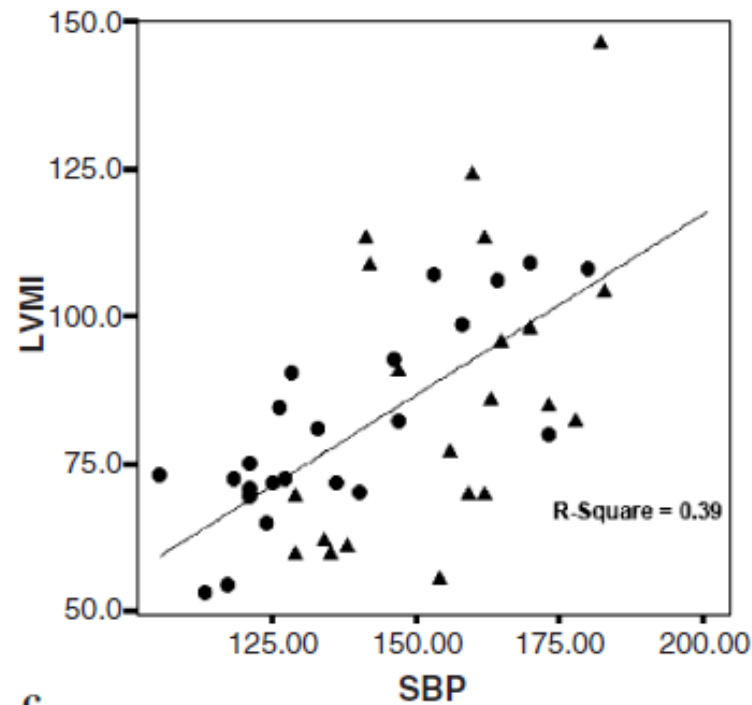
# Sodium & Aldosterone

# PLASMA RENIN AND EXCHANGEABLE SODIUM IN THE HYPERTENSION OF CHRONIC RENAL FAILURE
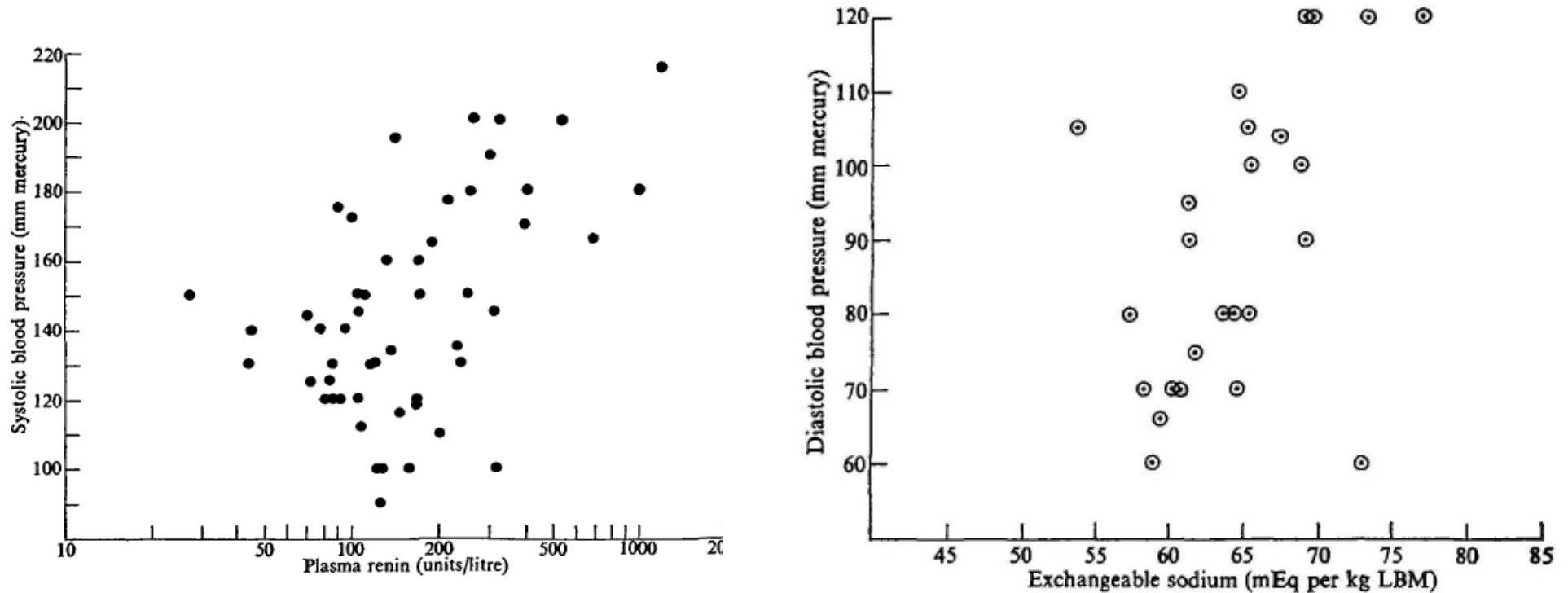
## The Effect of Bilateral Nephrectomy[1]

BY R. WILKINSON, D. F. SCOTT, P. R. ULDALL, D. N. S. KERR, AND J. SWINNEY; WITH THE TECHNICAL ASSISTANCE OF VALERIE ROBSON

# Kidney

## Association Between Urinary Sodium, Creatinine, Albumin, and Long-Term Survival in Chronic Kidney Disease

Emily P. McQuarrie, Jamie P. Traynor, Alison H. Taylor, E. Marie Freel, Jonathan G. Fox,
Alan G. Jardine, Patrick B. Mark
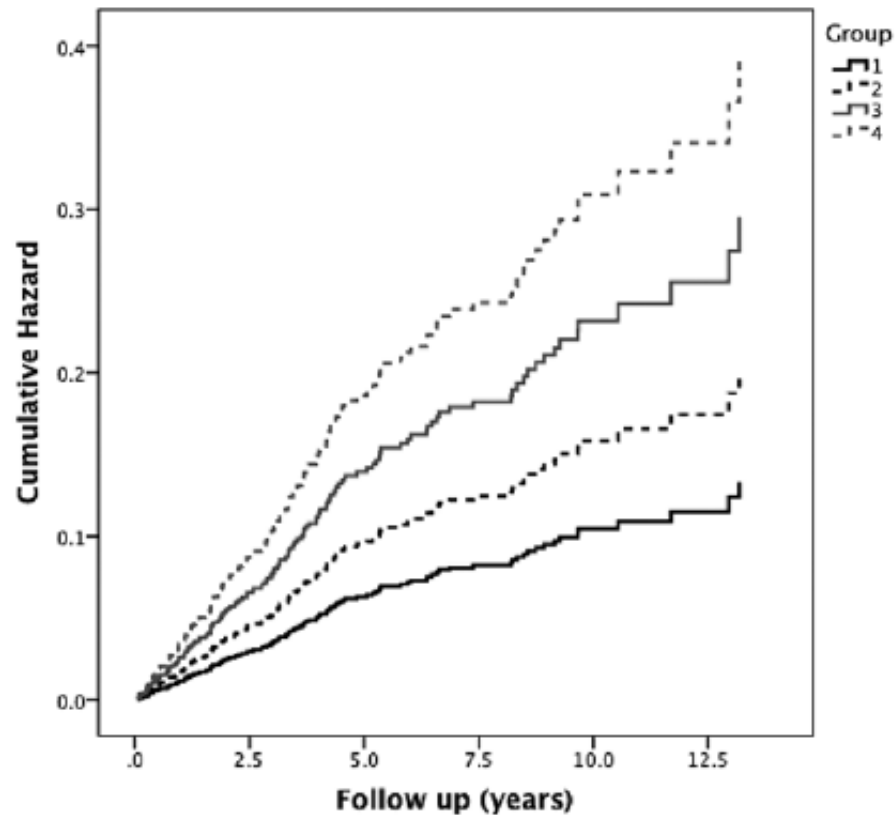
**Figure 3.** Hazard plot of risk of death or renal replacement therapy by combined urinary sodium to creatinine ratio (UNa:Cr) and albuminuria (1=low UNa:Cr, low urinary albumin to creatinine ratio [uACR]; 2=high UNa:Cr, low uACR; 3=low UNa:Cr, high uACR; 4=high UNa:Cr, high uACR) after adjusting for age, sex, estimated glomerular filtration rate (eGFR), proteinuria, mean arterial pressure (MAP), and diuretic or angiotensin-converting enzyme inhibitors (ACEi) usage. Variables included in the Cox regression model were age, eGFR, sex, MAP, $\log_{10}$ uACR, UNa:Cr, ACEi use, and diuretic use.

McQuarrie EP et al., Hypertension 2014:64:111-117

# Demonstration of Blood Pressure-Independent Noninfarct Myocardial Fibrosis in Primary Aldosteronism
## A Cardiac Magnetic Resonance Imaging Study

E. Marie Freel, BSc, MBChB, PhD; Patrick B. Mark, MBChB, PhD;
Robin A.P. Weir, MBChB, MD; Emily P. McQuarrie, MBChB; Karen Allan, BN;
Henry J. Dargie, MBChB, MD; John D. McClure, PhD; Alan G. Jardine, MBChB, MD;
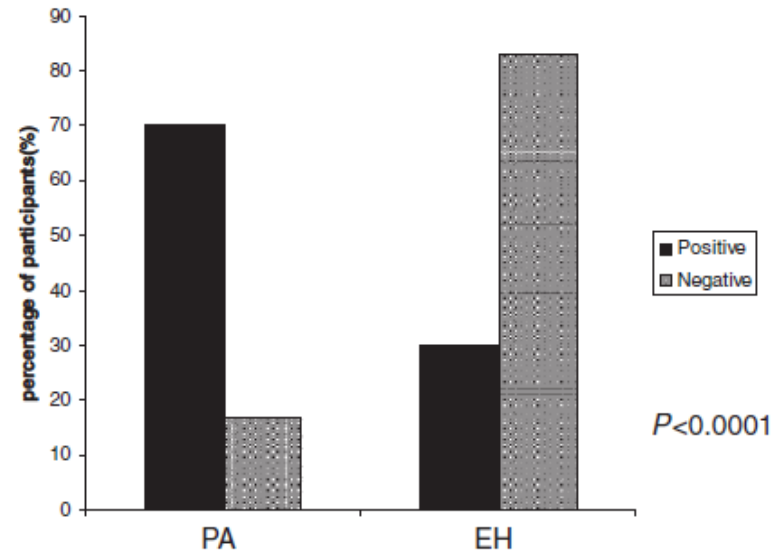Eleanor Davies, BSc, PhD; John M.C. Connell, MBChB, MD

**Figure 2.** Frequency of noninfarct late gadolinium enhancement in primary aldosterone (PA) vs essential hypertension (EH) patients. Frequencies compared using logistic regression (general estimating equations). Subjects with late gadolinium enhancement because of myocardial infarction were excluded.

# Urinary corticosteroid excretion predicts left ventricular mass and proteinuria in chronic kidney disease

Emily P. McQUARRIE[*][†], E. Marie FREEL[*], Patrick B. MARK[*][†], Robert FRASER[*],
Rajan K. PATEL[*][†], Henry G. DARGIE[‡], John M. C. CONNELL[§] and
Alan G. JARDINE[*][†]

[*]BHF Glasgow Cardiovascular Research Centre, University of Glasgow, 126 University Place, Glasgow G12 8TA, U.K.,
[†]Department of Renal Medicine, Western Infirmary, Dumbarton Road, Glasgow G11 6NT, U.K., [‡]Department of Cardiology,
Western Infirmary, Dumbarton Road, Glasgow G11 6NT, U.K., and [§]School of Medicine, University of Dundee, Dundee DD1
9SY, U.K.

McQuarrie EM et al., Clin Sci 2012;123:685-694
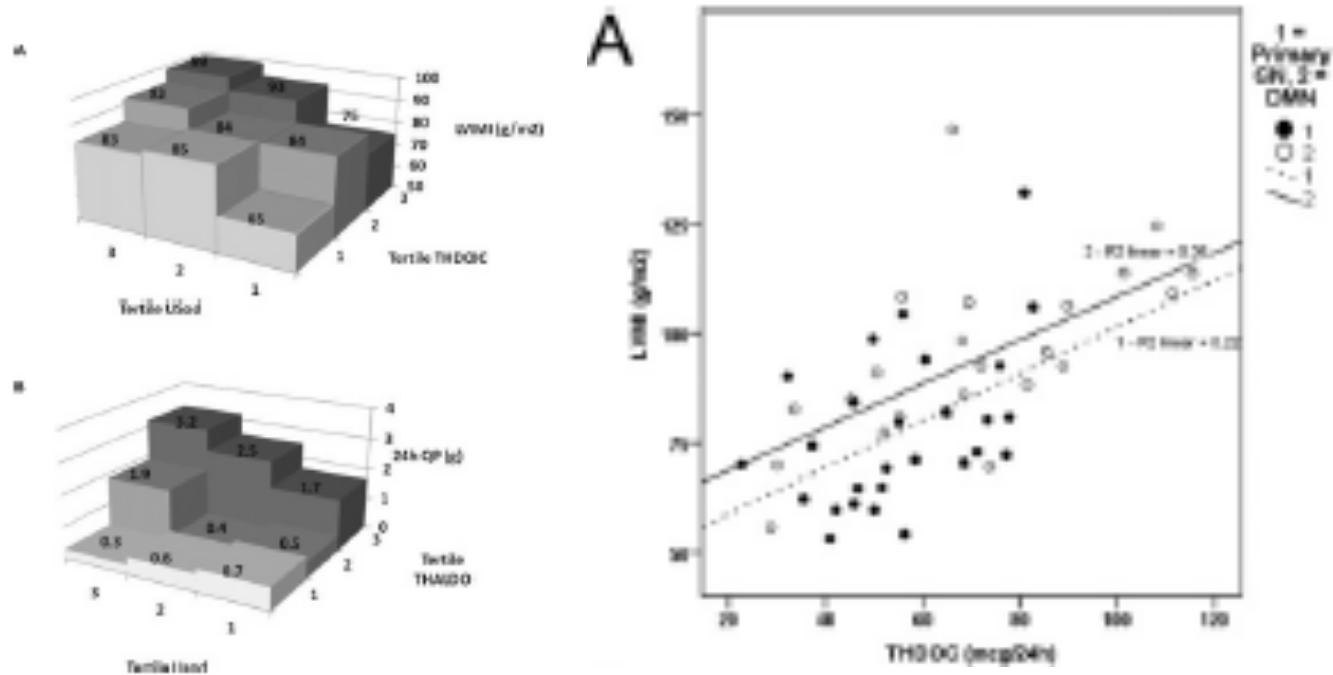
# Urinary sodium excretion is the main determinant of mineralocorticoid excretion rates in patients with chronic kidney disease

Emily P. McQuarrie[1,2],
Ellen Marie Freel[1],
Patrick B. Mark[1,2],
Robert Fraser[1],
John M.C. Connell[3]
and Alan G. Jardine[1,2]

[1] BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow G12 8TA, UK,
[2] Department of Renal Medicine, Western Infirmary, Glasgow G11 6NT, UK and
[3] School of Medicine, University of Dundee, Dundee, UK

McQuarrie E et al., NDT 2003;28:1526-32
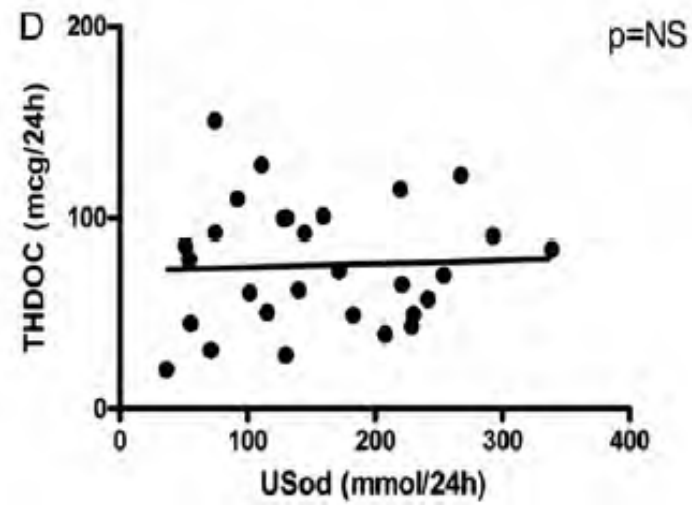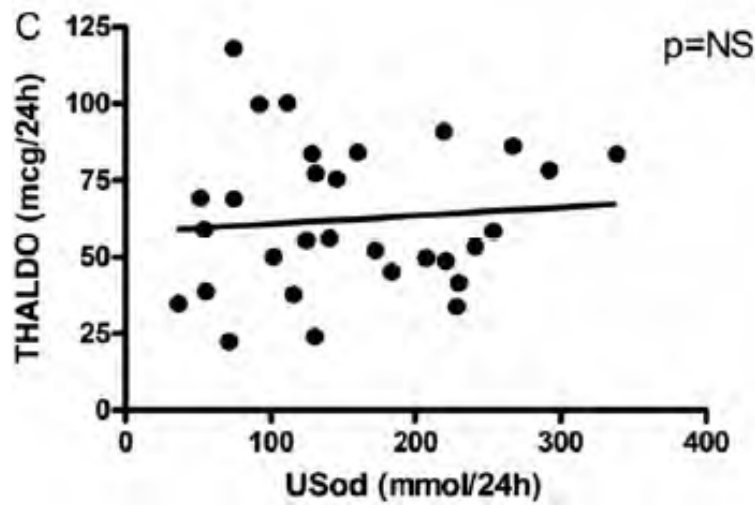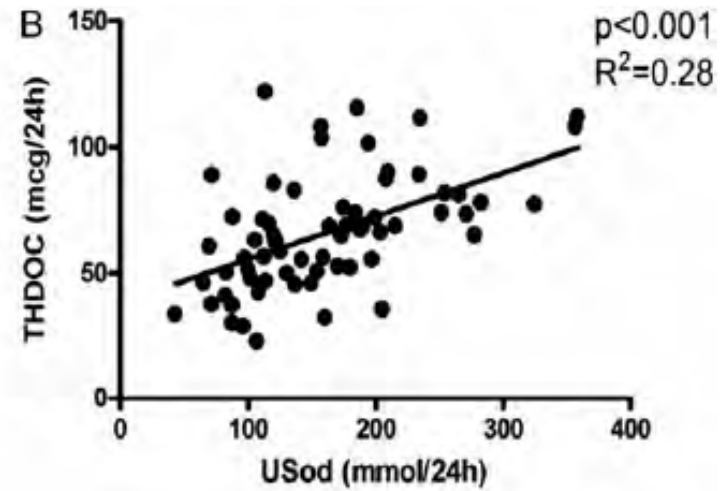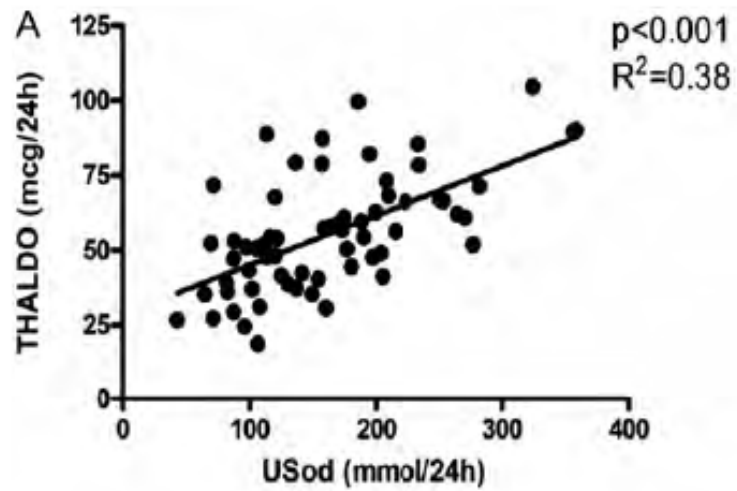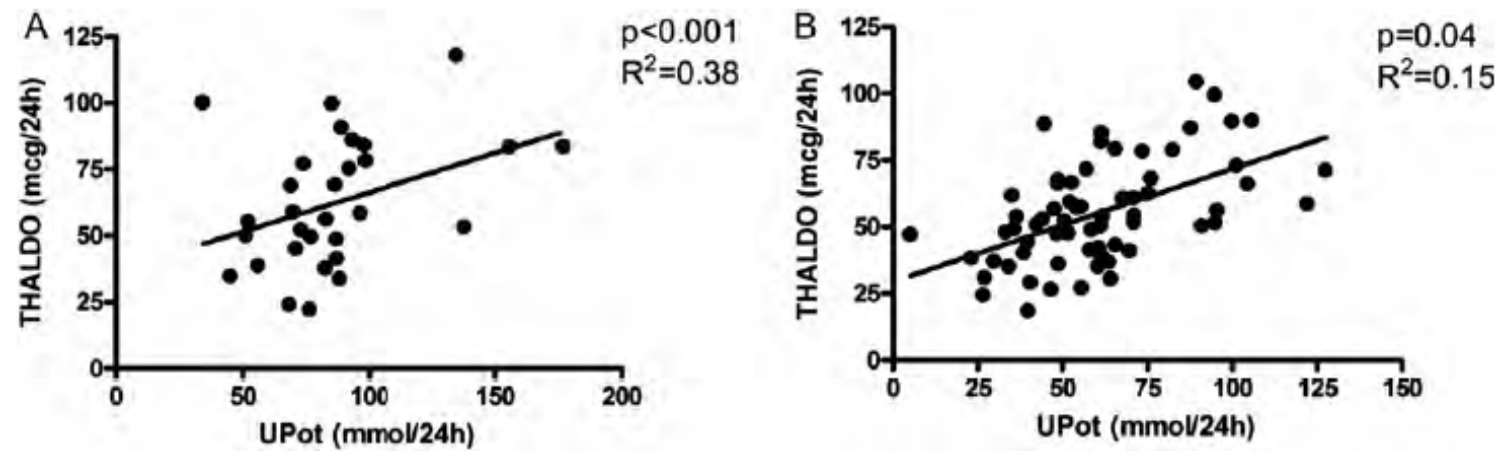
**FIGURE 3:** Scatterplot of THALDO versus urinary potassium excretion (mmol/24 h) with fitted linear regression line and an estimate of significance. A = EH patients; B = CKD patients.

McQuarrie E et al., NDT 2003;28:1526-32

# Long-Term Effects of Spironolactone in Peritoneal Dialysis Patients

Yasuhiko Ito,* Masashi Mizuno,* Yasuhiro Suzuki,* Hirofumi Tamai,[†] Takeyuki Hiramatsu,[‡] Hiroshige Ohashi,[§] Isao Ito,[‖] Hirotake Kasuga,[¶] Masanobu Horie,** Shoichi Maruyama,* Yukio Yuzawa,[††] Tatsuaki Matsubara,[‡‡] and Seiichi Matsuo,* on behalf of the Nagoya Spiro Study Group
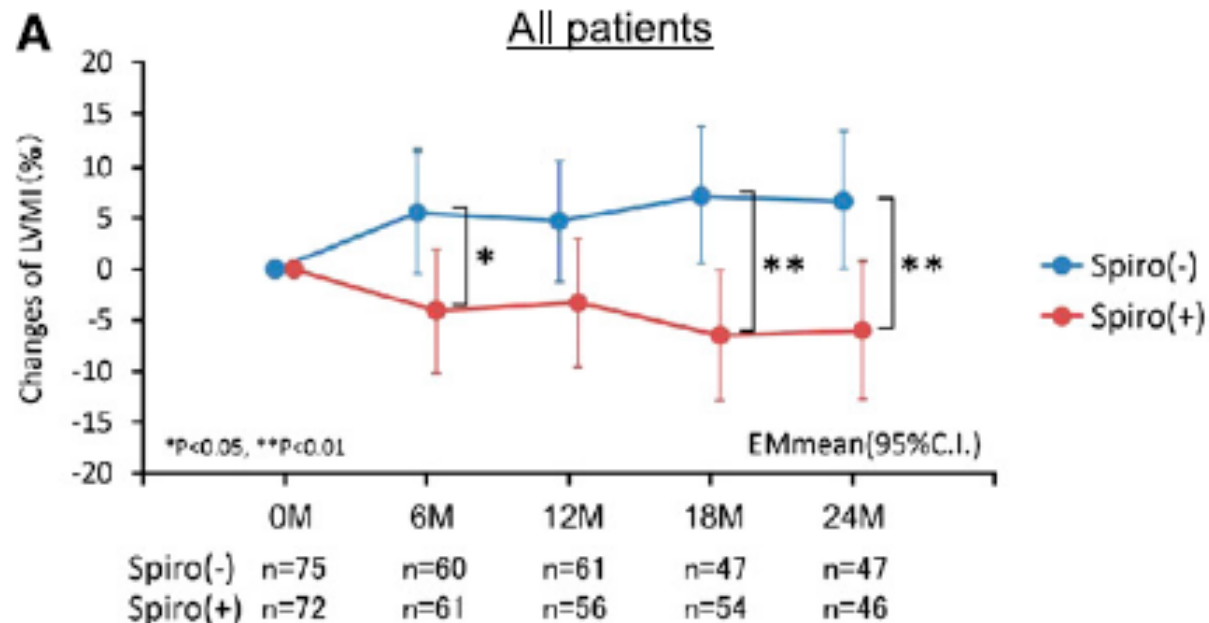
# Anti-albuminuric effect of the aldosterone blocker eplerenone in non-diabetic hypertensive patients with albuminuria: a double-blind, randomised, placebo-controlled trial

Katsuyuki Ando, Hiroshi Ohtsu, Shunya Uchida, Shinya Kaname, Yoshihiro Arakawa, Toshiro Fujita, for the EVALUATE Study Group*



Ando K et al., Lancet Diab Endo 2014:2:944-53
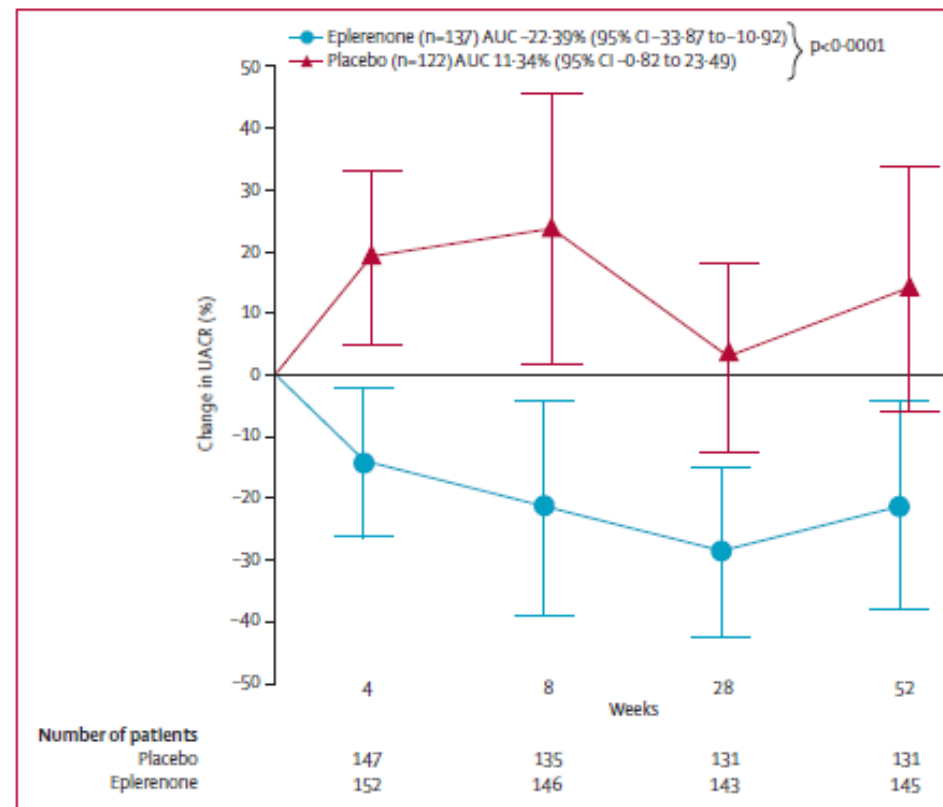
# Effect of mineralocorticoid receptor antagonists on proteinuria and progression of chronic kidney disease: a systematic review and meta-analysis

Gemma Currie[1*†], Alison H. M. Taylor[1†], Toshiro Fujita[2], Hiroshi Ohtsu[3], Morten Lindhardt[4], Peter Rossing[4,5,6], Lene Boesby[7], Nicola C. Edwards[8], Charles J. Ferro[8], Jonathan N. Townend[8], Anton H. van den Meiracker[9], Mohammad G. Saklayen[10], Sonia Oveisi[11], Alan G. Jardine[1], Christian Delles[1], David J. Preiss[12] and Patrick B. Mark[1]
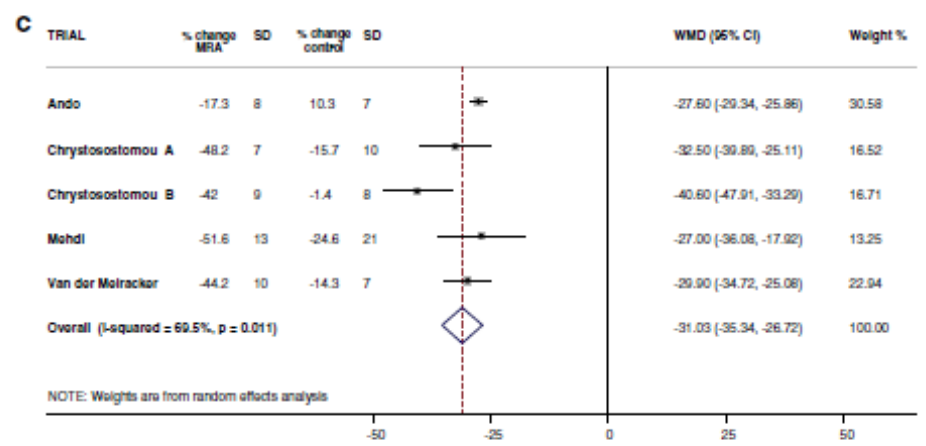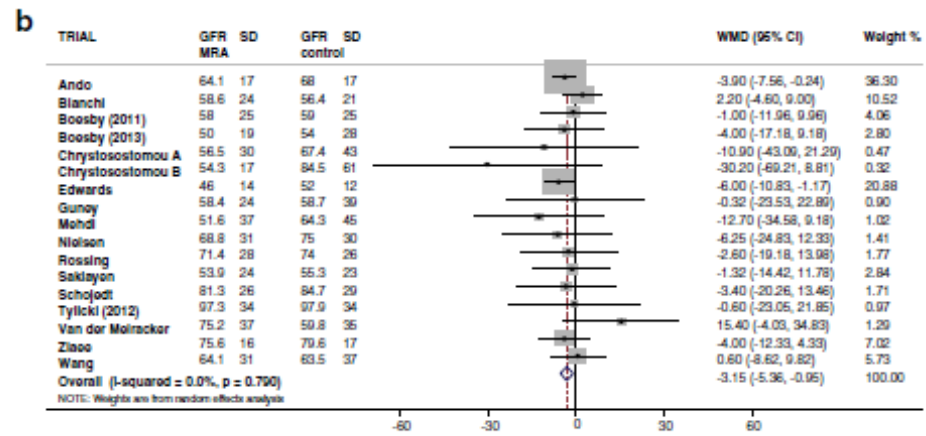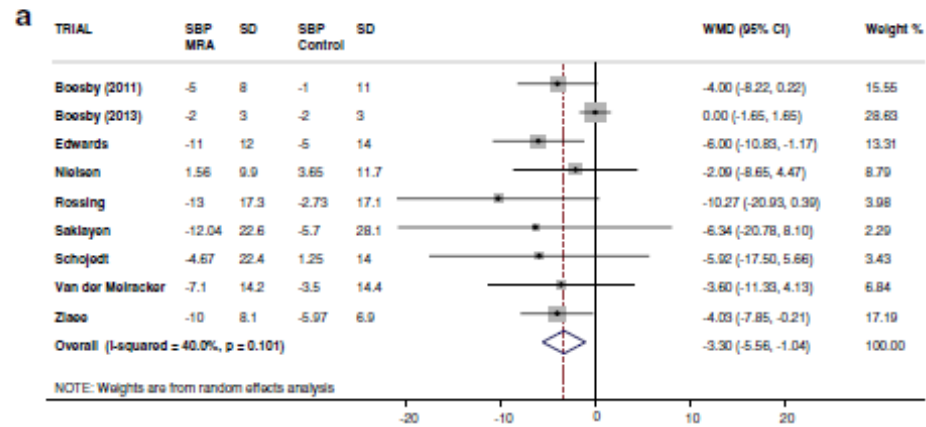
Fig. 2 (See legend on next page.)

Currie G et al., BMC Nephrology 2016;17:127
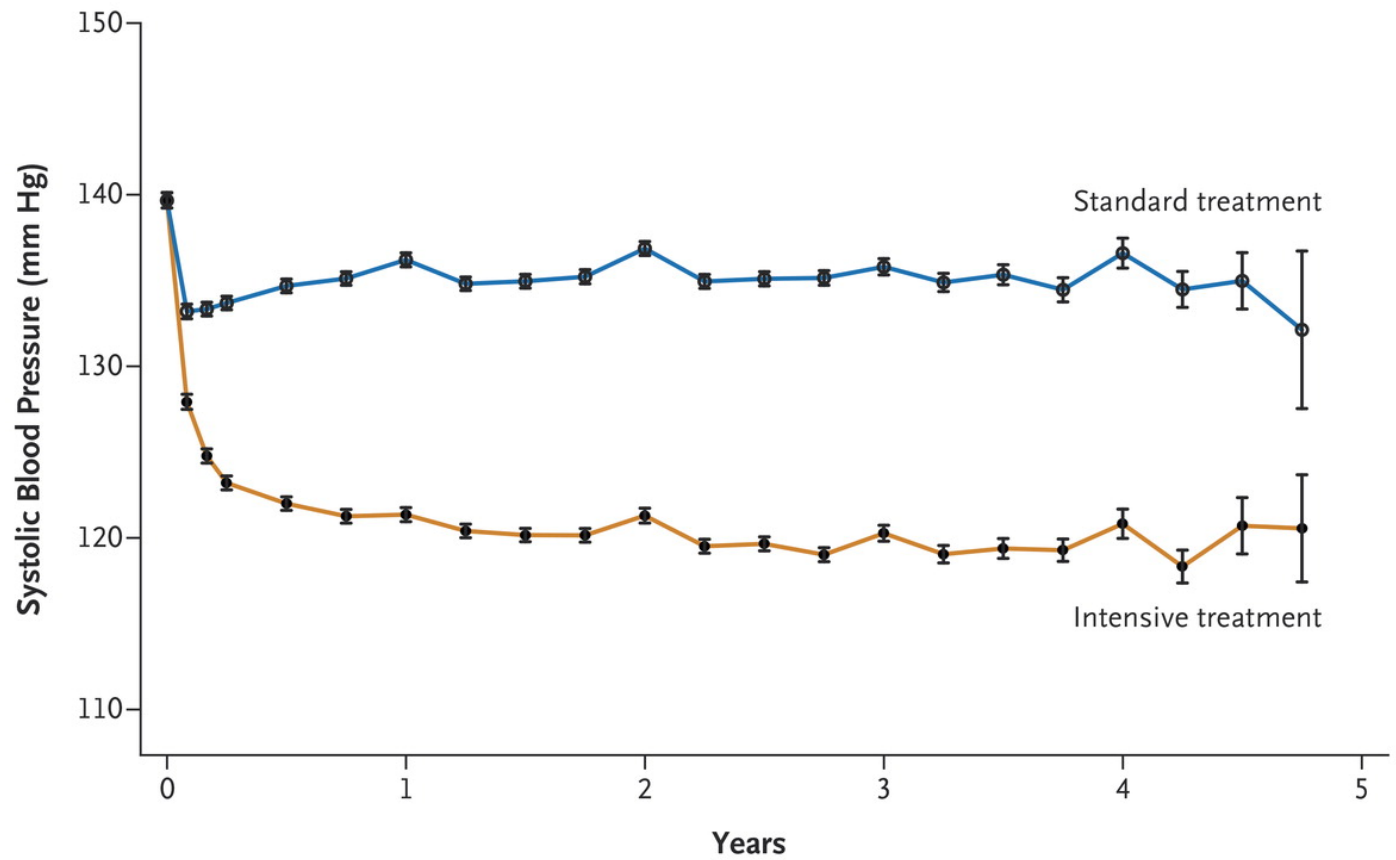
| No. with Data | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Standard treatment | 4683 | 4345 | 4222 | 4092 | 3997 | 3904 | 3115 | 1974 | 1000 | 274 |
| Intensive treatment | 4678 | 4375 | 4231 | 4091 | 4029 | 3920 | 3204 | 2035 | 1048 | 286 |
| | | | | | | | | | | |
| **Mean No. of Medications** | | | | | | | | | | |
| Standard treatment | 1.9 | 1.8 | 1.8 | 1.8 | 1.8 | 1.8 | 1.8 | 1.8 | 1.8 | 1.9 |
| Intensive treatment | 2.3 | 2.7 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 3.0 |

SPRINT  NEJM 2015;373:2103-2116

## A Primary Outcome

Hazard ratio with intensive treatment, 0.75 (95% CI, 0.64–0.89)

Standard treatment

Intensive treatment

Cumulative Hazard

Years
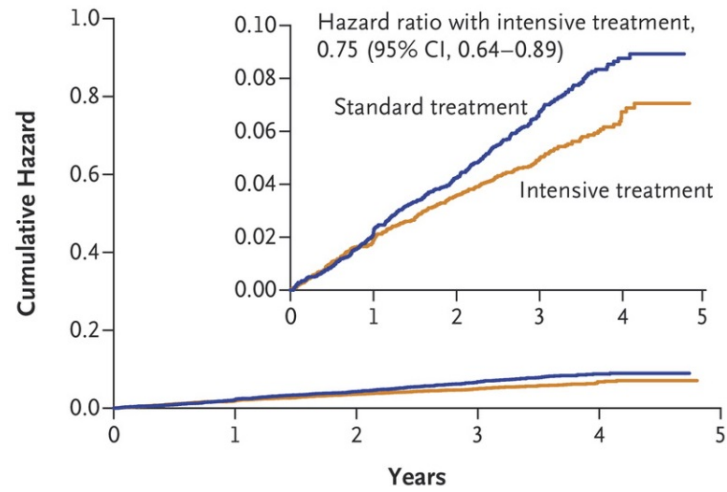
No. at Risk

| | | | | | |
|---|---|---|---|---|---|
| Standard treatment | 4683 | 4437 | 4228 | 2829 | 721 |
| Intensive treatment | 4678 | 4436 | 4256 | 2900 | 779 |

## B Death from Any Cause

Hazard ratio with intensive treatment, 0.73 (95% CI, 0.60–0.90)

Standard treatment

Intensive treatment

Cumulative Hazard

Years
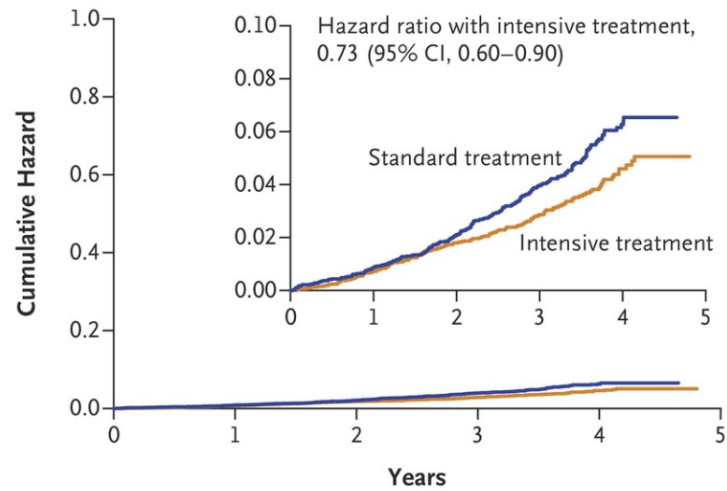
No. at Risk

| | | | | | |
|---|---|---|---|---|---|
| Standard treatment | 4683 | 4528 | 4383 | 2998 | 789 |
| Intensive treatment | 4678 | 4516 | 4390 | 3016 | 807 |

SPRINT  NEJM 2015;373:2103-2116

| Subgroup | Intensive Treatment | Standard Treatment | Hazard Ratio (95% CI) | Hazard Ratio (95% CI) | P Value for Interaction |
|---|---|---|---|---|---|
| | *no. of patients with primary outcome/total no. (%)* | | | | |
| Overall | 243/4678 (5.2) | 319/4683 (6.8) | | 0.75 (0.64–0.89) | |
| Previous CKD | | | | | 0.36 |
| No | 135/3348 (4.0) | 193/3367 (5.7) | | 0.70 (0.56–0.87) | |
| Yes | 108/1330 (8.1) | 126/1316 (9.6) | | 0.82 (0.63–1.07) | |
| Age | | | | | 0.32 |
| <75 yr | 142/3361 (4.2) | 175/3364 (5.2) | | 0.80 (0.64–1.00) | |
| ≥75 yr | 101/1317 (7.7) | 144/1319 (10.9) | | 0.67 (0.51–0.86) | |
| Sex | | | | | 0.45 |
| Female | 77/1684 (4.6) | 89/1648 (5.4) | | 0.84 (0.62–1.14) | |
| Male | 166/2994 (5.5) | 230/3035 (7.6) | | 0.72 (0.59–0.88) | |
| Race | | | | | 0.83 |
| Black | 62/1454 (4.3) | 85/1493 (5.7) | | 0.77 (0.55–1.06) | |
| Nonblack | 181/3224 (5.6) | 234/3190 (7.3) | | 0.74 (0.61–0.90) | |
| Previous cardiovascular disease | | | | | 0.39 |
| No | 149/3738 (4.0) | 208/3746 (5.6) | | 0.71 (0.57–0.88) | |
| Yes | 94/940 (10.0) | 111/937 (11.8) | | 0.83 (0.62–1.09) | |
| Systolic blood pressure | | | | | 0.77 |
| ≤132 mm Hg | 71/1583 (4.5) | 98/1553 (6.3) | | 0.70 (0.51–0.95) | |
| >132 to <145 mm Hg | 77/1489 (5.2) | 106/1549 (6.8) | | 0.77 (0.57–1.03) | |
| ≥145 mm Hg | 95/1606 (5.9) | 115/1581 (7.3) | | 0.83 (0.63–1.09) | |

0.50   0.75   1.00   1.20

Intensive Treatment Better    Standard Treatment Better

SPRINT  NEJM 2015;373:2103-2116

**Table 2. Primary and Secondary Outcomes and Renal Outcomes.***

| Outcome | Intensive Treatment | | Standard Treatment | | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|---|---|
| | *no. of patients (%)* | *% per year* | *no. of patients (%)* | *% per year* | | |
| **All participants** | (N = 4678) | | (N = 4683) | | | |
| Primary outcome† | 243 (5.2) | 1.65 | 319 (6.8) | 2.19 | 0.75 (0.64–0.89) | <0.001 |
| Secondary outcomes | | | | | | |
|   Myocardial infarction | 97 (2.1) | 0.65 | 116 (2.5) | 0.78 | 0.83 (0.64–1.09) | 0.19 |
|   Acute coronary syndrome | 40 (0.9) | 0.27 | 40 (0.9) | 0.27 | 1.00 (0.64–1.55) | 0.99 |
|   Stroke | 62 (1.3) | 0.41 | 70 (1.5) | 0.47 | 0.89 (0.63–1.25) | 0.50 |
|   Heart failure | 62 (1.3) | 0.41 | 100 (2.1) | 0.67 | 0.62 (0.45–0.84) | 0.002 |
|   Death from cardiovascular causes | 37 (0.8) | 0.25 | 65 (1.4) | 0.43 | 0.57 (0.38–0.85) | 0.005 |
|   Death from any cause | 155 (3.3) | 1.03 | 210 (4.5) | 1.40 | 0.73 (0.60–0.90) | 0.003 |
|   Primary outcome or death | 332 (7.1) | 2.25 | 423 (9.0) | 2.90 | 0.78 (0.67–0.90) | <0.001 |
| **Participants with CKD at baseline** | (N = 1330) | | (N = 1316) | | | |
| Composite renal outcome‡ | 14 (1.1) | 0.33 | 15 (1.1) | 0.36 | 0.89 (0.42–1.87) | 0.76 |
| ≥50% reduction in estimated GFR§ | 10 (0.8) | 0.23 | 11 (0.8) | 0.26 | 0.87 (0.36–2.07) | 0.75 |
| Long-term dialysis | 6 (0.5) | 0.14 | 10 (0.8) | 0.24 | 0.57 (0.19–1.54) | 0.27 |
| Kidney transplantation | 0 | | 0 | | | |
| Incident albuminuria¶ | 49/526 (9.3) | 3.02 | 59/500 (11.8) | 3.90 | 0.72 (0.48–1.07) | 0.11 |
| **Participants without CKD at baseline‖** | (N = 3332) | | (N = 3345) | | | |
| ≥30% reduction in estimated GFR to <60 ml/min/1.73 m²§ | 127 (3.8) | 1.21 | 37 (1.1) | 0.35 | 3.49 (2.44–5.10) | <0.001 |
| Incident albuminuria¶ | 110/1769 (6.2) | 2.00 | 135/1831 (7.4) | 2.41 | 0.81 (0.63–1.04) | 0.10 |

\* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
¶ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
‖ No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.

SPRINT  NEJM 2015;373:2103-2116

# Anything new?

# Effect of lowering blood pressure on cardiovascular events and mortality in patients on dialysis: a systematic review and meta-analysis of randomised controlled trials

Hiddo J Lambers Heerspink, Toshiharu Ninomiya, Sophia Zoungas, Dick de Zeeuw, Diederick E Grobbee, Meg J Jardine, Martin Gallagher, Matthew A Roberts, Alan Cass, Bruce Neal, Vlado Perkovic
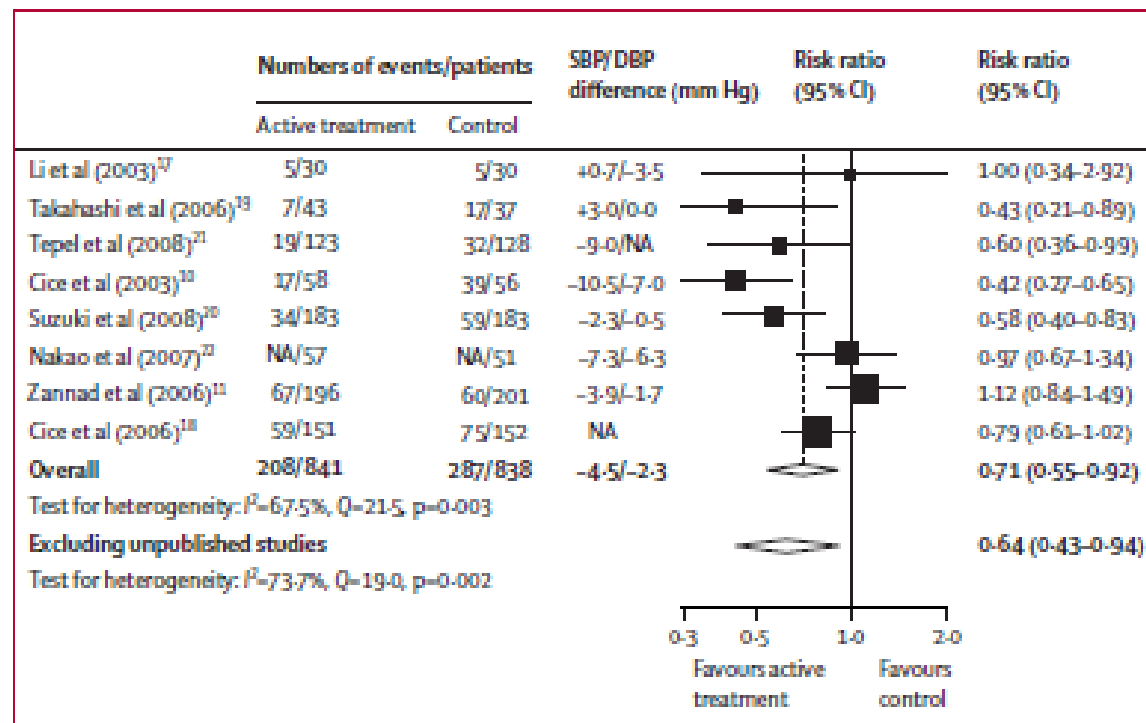
Figure 2: Risk of cardiovascular events for blood pressure lowering treatment versus control regimens
DBP=diastolic blood pressure. SBP=systolic blood pressure. NA=not applicable. The overall mean difference in systolic and diastolic blood pressure in the active treatment group compared with the control group is also shown. Negative values indicate lower mean follow-up blood pressure in the active treatment group.

Lancet Feb 2009

Relation of MACE with baseline Serum Phosphate and Haemoglobin
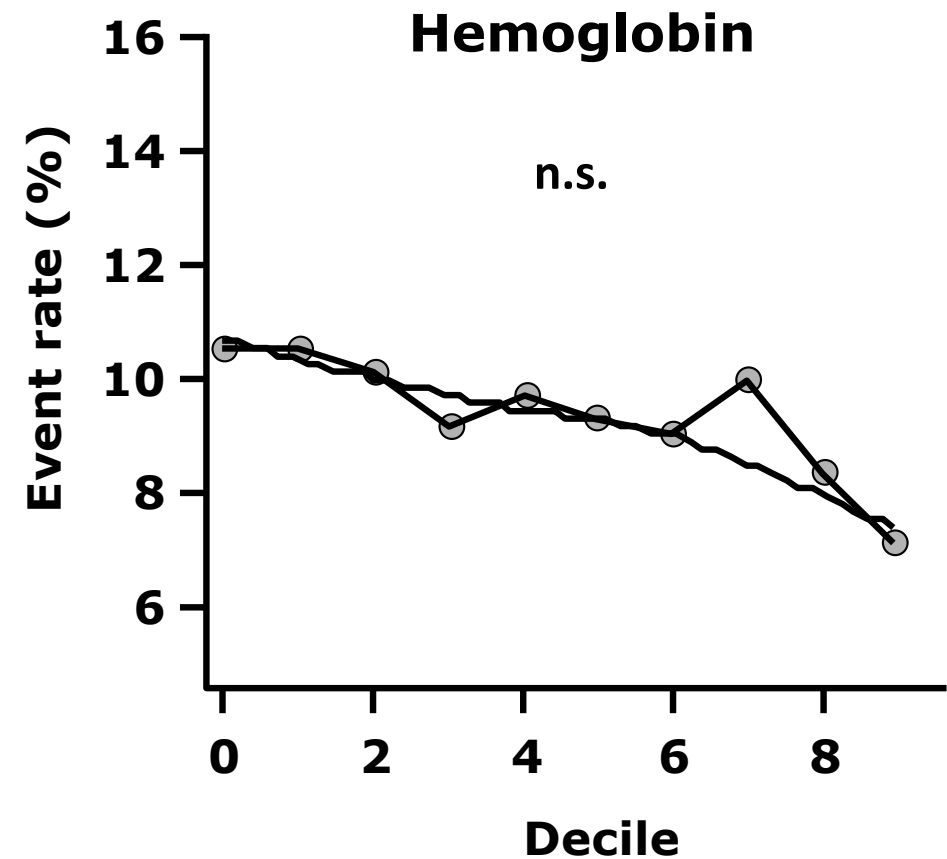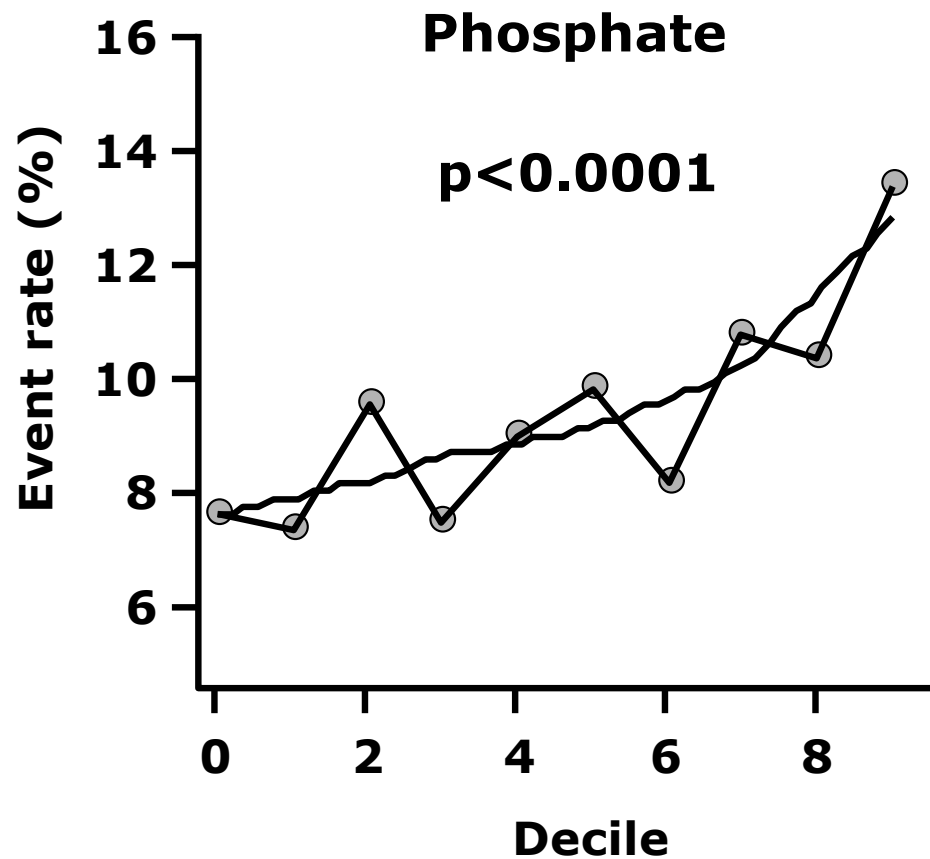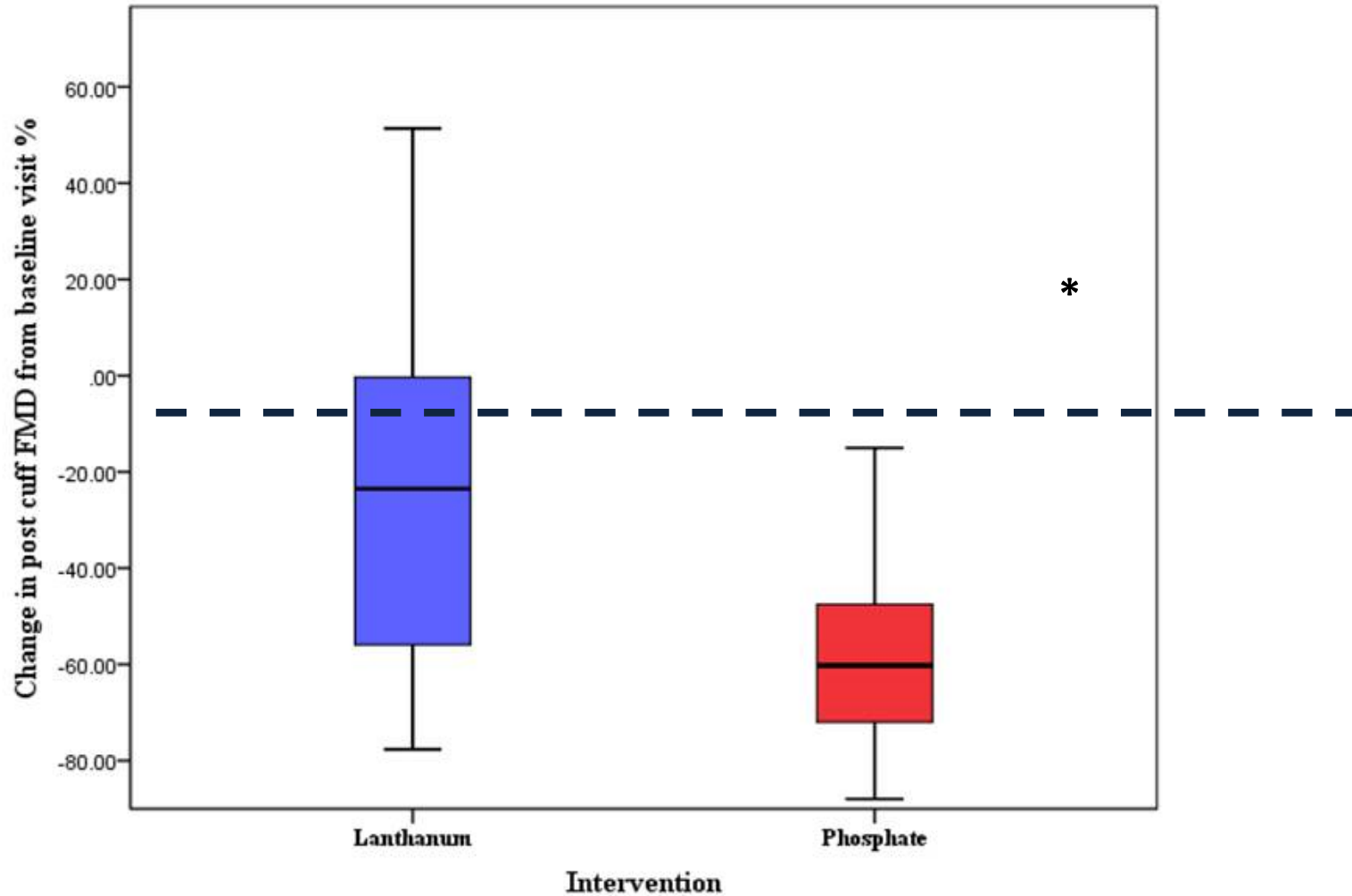
# Phosphate – direct effects on vascular function
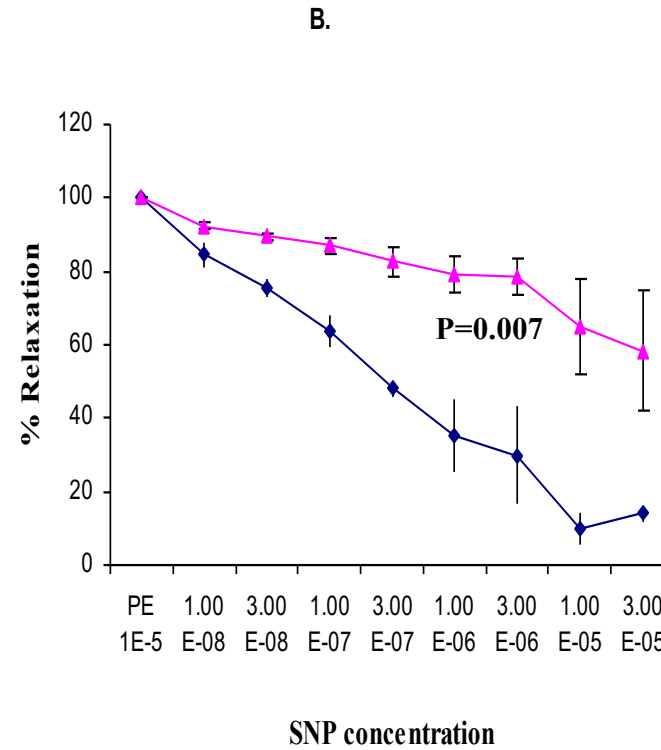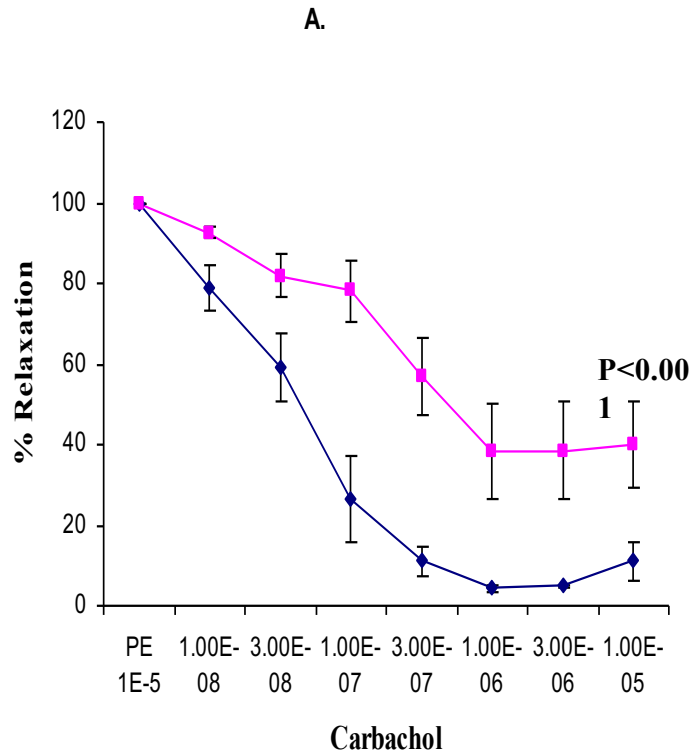


Stevens KK et al., NDT 2016 (ePub)

Stevens KK et al., Lancet 2015;385:S10

# Oral phosphate loading reduced flow mediated dilatation by over 50% in normal human subjects.



Stevens KK et al., NDT 2016 (ePub)

Stevens KK et al., Lancet 2015;385:S10

*p<0.001
compared with baseline measures

*Clinical Study*

# Fibroblast Growth Factor 23 Predicts Left Ventricular Mass and Induces Cell Adhesion Molecule Formation

Kathryn K. Stevens,[1,2] Emily P. McQuarrie,[1,2] William Sands,[1] Dianne Z. Hillyard,[1] Rajan K. Patel,[1,2] Patrick B. Mark,[1,2] and Alan G. Jardine[1,2]

[1] Renal Research Group, ICAMS, University of Glasgow, 126 University Place, Glasgow G12 8TA, UK
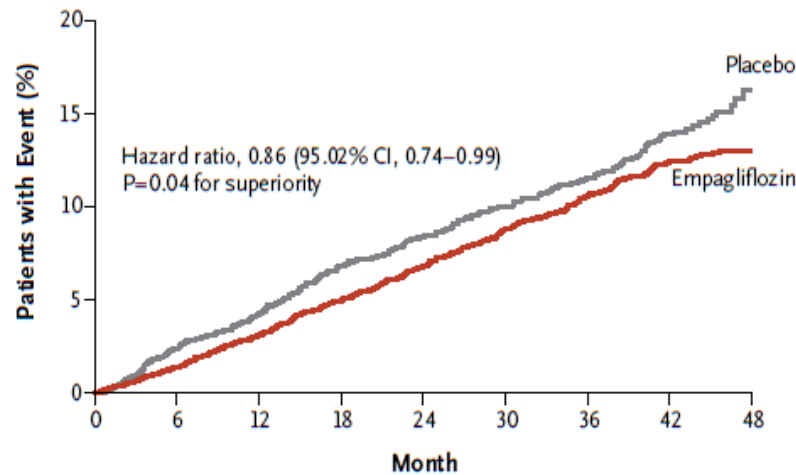[2] Renal Unit, Western Infirmary, Glasgow G11 6NT, UK
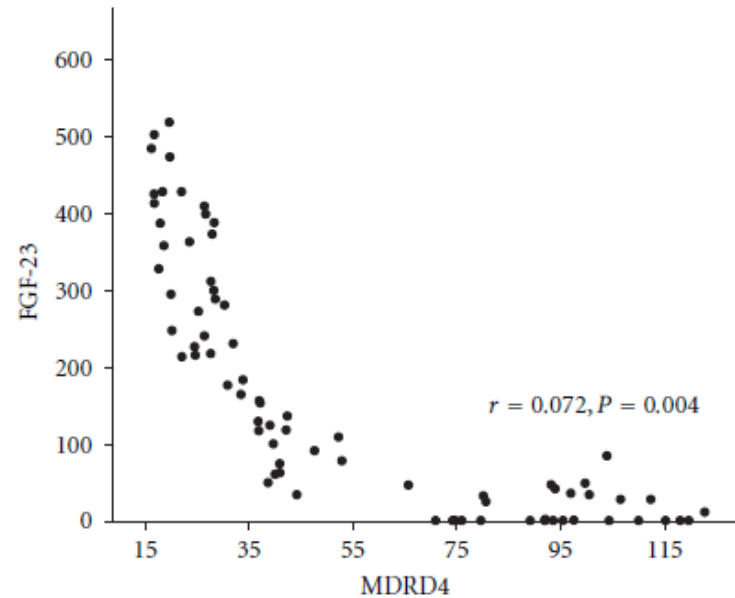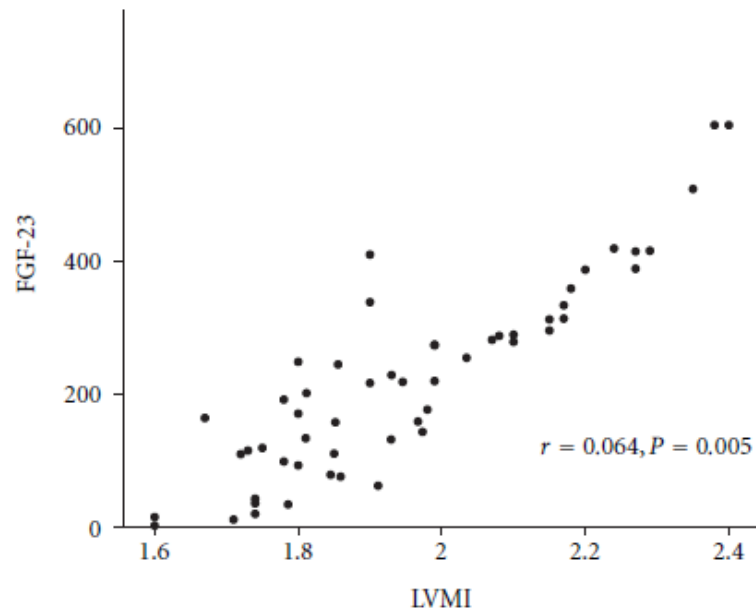
Stevens KK et al., Int J Nephrol (2011)

| | Exp $\beta$ | Confidence interval | | P value |
|---|---|---|---|---|
| | | Lower | Upper | |
| FGF-23 | 4.9 | 1.2 | 20.3 | 0.027 |
| Systolic BP | 1.08 | 1.03 | 1.14 | 0.003 |
| Ur PCR | 1.87 | 1.54 | 2.23 | 0.005 |

# Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D.,
David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D.,
Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H.,
Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D.,
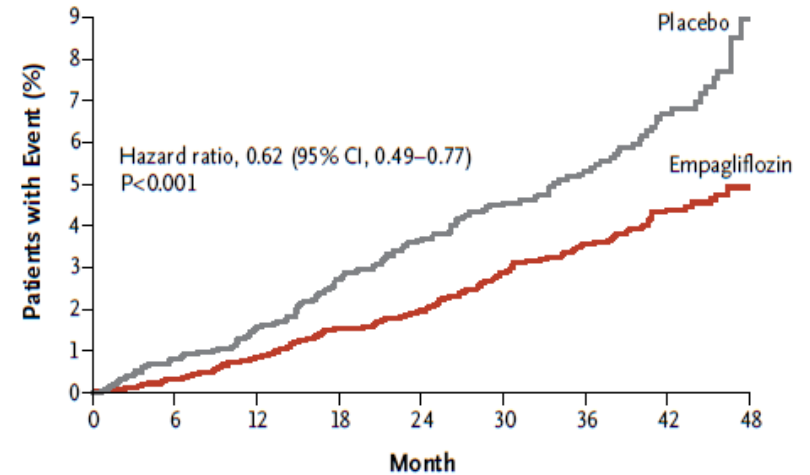and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

Zinman B et al., NEJM 2015;373:2117-28

# Effects of dapagliflozin on blood pressure in hypertensive diabetic patients on renin–angiotensin system blockade

Michael A. Weber, Traci A. Mansfield, Federica Alessi, Nayyar Iqbal, Shamik Parikh & Agata Ptaszynska
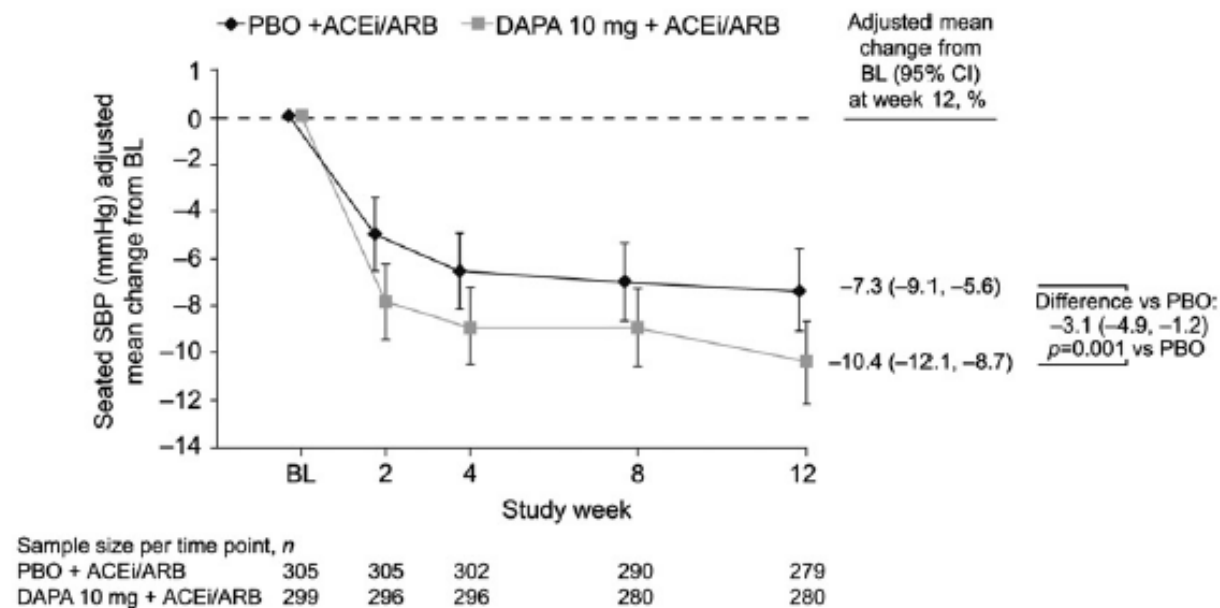
# Patiromer induces rapid and sustained potassium lowering in patients with chronic kidney disease and hyperkalemia

David A. Bushinsky[1], Gordon H. Williams[2], Bertram Pitt[3], Matthew R. Weir[4], Mason W. Freeman[5], Dahlia Garza[6], Yuri Stasiv[6], Elizabeth Li[7], Lance Berman[6] and George L. Bakris[8]
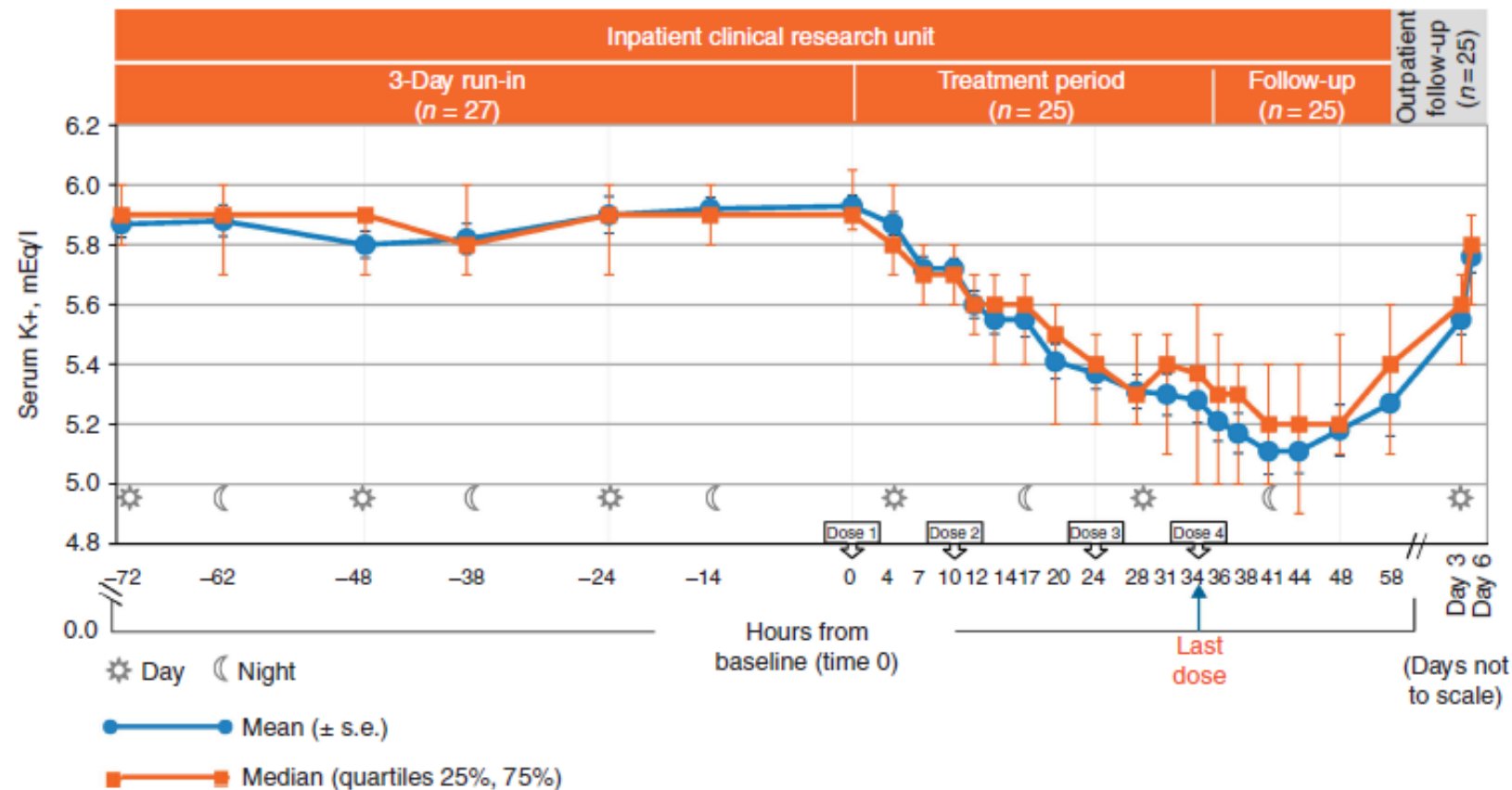
Bushinsky DA et al., KI 2015;88:1427-33

# Treatment with patiromer decreases aldosterone in patients with chronic kidney disease and hyperkalemia on renin-angiotensin system inhibitors

Matthew R. Weir[1], George L. Bakris[2], Coleman Gross[3], Martha R. Mayo[3], Dahlia Garza[3], Yuri Stasiv[3], Jinwei Yuan[3], Lance Berman[3] and Gordon H. Williams[4]



Weir MR et al., KI 2016;90:696-704

**a** Systolic blood pressure

Mean (±SE) Blood Pressure (mm Hg)

| No. at Risk | Baseline | Day 3 | Week 1 | Week 2 | Week 3 | Week 4 |
|---|---|---|---|---|---|---|
| Systolic Blood Pressure: | 242 | 216 | 236 | 223 | 218 | 218 |

Study Visit

**b** Diastolic blood pressure

Mean (±SE) Blood Pressure (mm Hg)

| No. at Risk | Baseline | Day 3 | Week 1 | Week 2 | Week 3 | Week 4 |
|---|---|---|---|---|---|---|
| Diastolic Blood Pressure: | 242 | 216 | 236 | 223 | 218 | 218 |

Study Visit

Weir MR et al., KI 2016;90:696-704