Quale target pressorio nei pazienti nefropatici ?

Alberto Caiazza

Dipartimento di Medicina e Diagnostica
PO Borgo val di Taro (PR)
Azienda USL di Parma

Awareness of CKD by GPs

- The awarness of CKD by GPs was low with only ***3.9%*** of the overall study popolation and ***13.8%*** of patients with eGFR <60mL/min/1.73m having diagnosis of kidney disease

Ravera M.et *al. American J Kidney Dis 2011:57(1);71-77*

A feasible explanation for this low level of GP awareness could be the low rate of serum creatinine testing. Although serum creatinine measurement is more frequent in high-risk patients[18] with respect to the general population,[15-17] it still is too low because serum creatinine values were available for only 60% of the patients with hypertension in our cohort, thus suggesting that GPs did not correctly adhere to current guidelines recommending regular creatinine testing of the hypertensive population.[12]

Another explanation for the low GP awareness is that GPs adopt serum creatinine level instead of eGFR to identify patients with CKD.

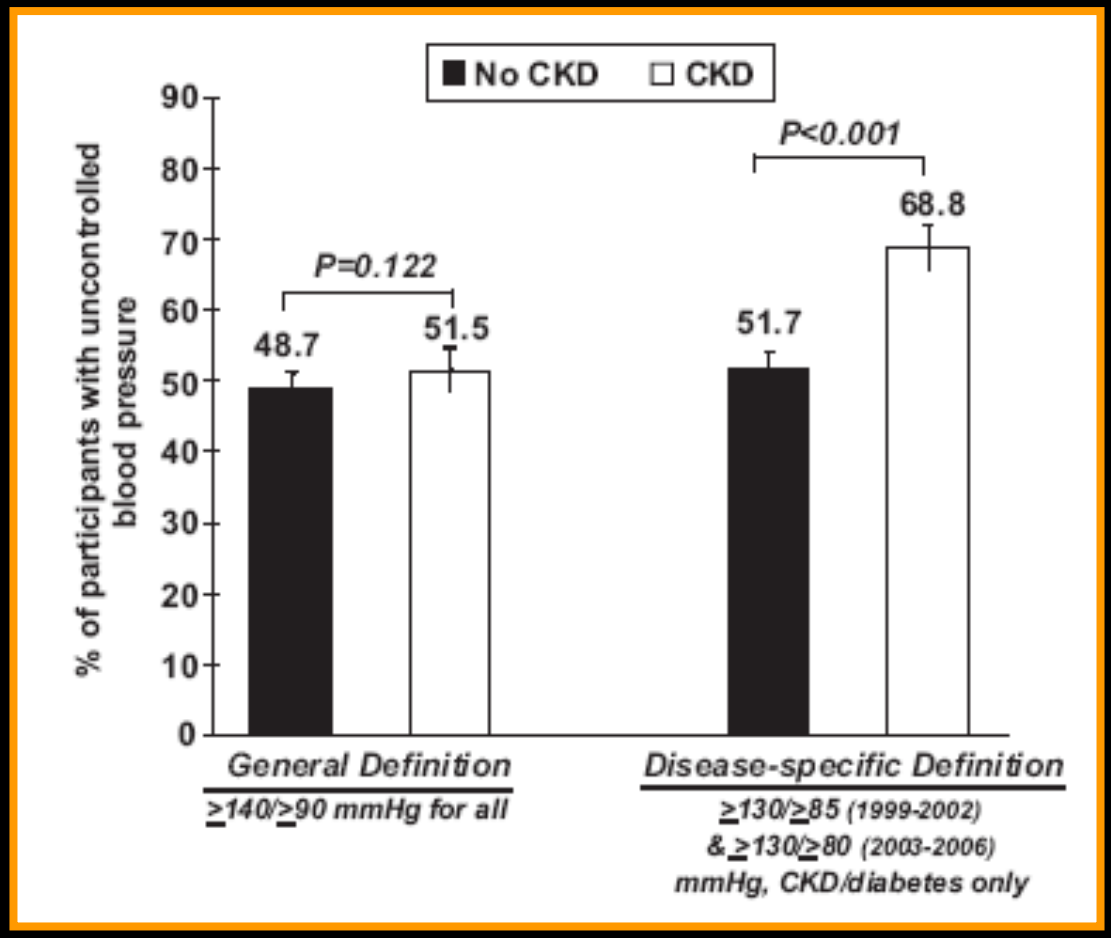
Ravera M.et *al.American J Kidney Dis 2011:57(1);71-77*

Kidney Early Evaluation Program (KEEP database)

- Rates of BP control in patients with stage 4 or 5 and stage 3 CKD were ***21%*** and ***20%*** respectively compared with ***13%*** and ***11%*** for patients with stages 2 and 1CKD respectively

Sarafidis P.A et al. ***Am J Med 2008;21:332-340***

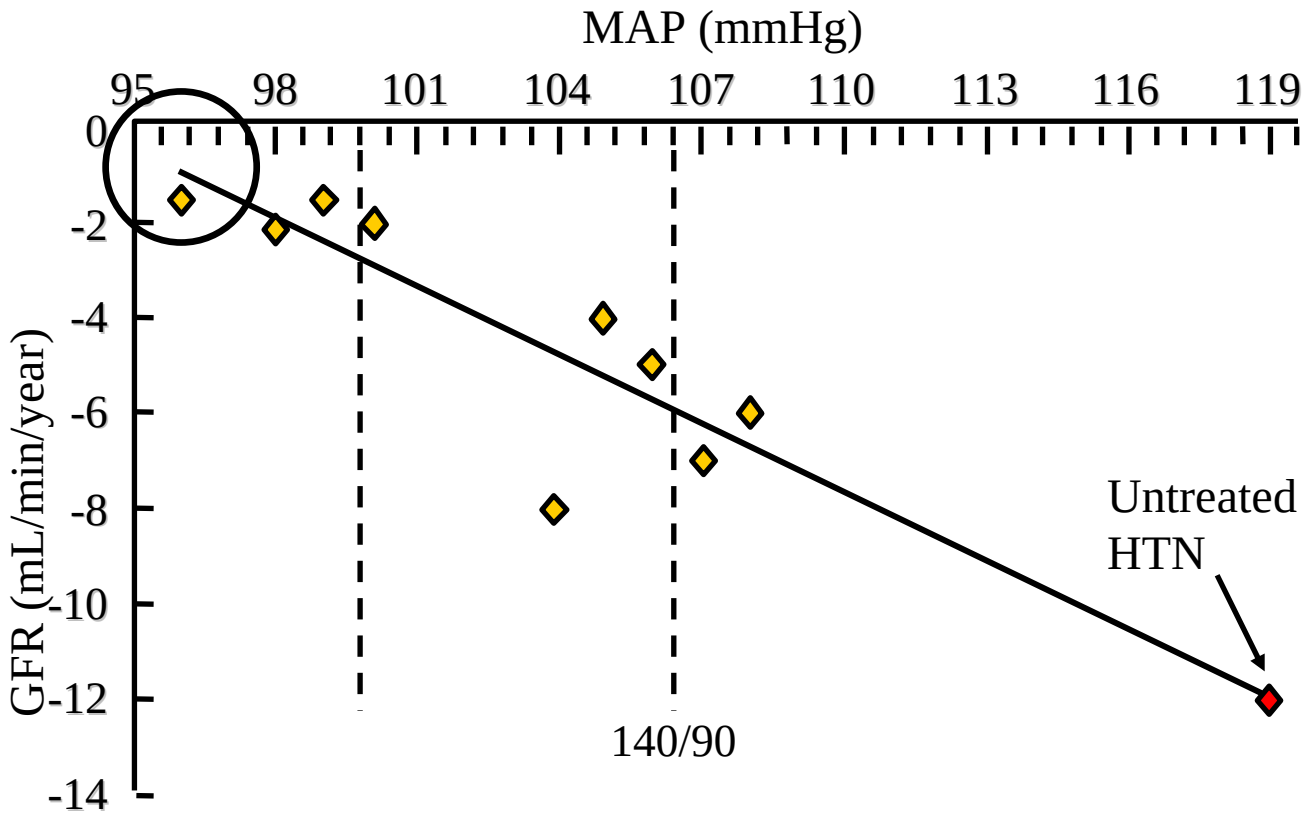
Percentage of NHANES 1999-2006 partecipants with hypertension with uncontrolled BP by CKD status



Plantinga L.C. et al. *Hypertension 2009; 54:47-56*

Protection against progression of renal dysfunction has two main requirements:
a) strict blood pressure control (<130/80 mmHg and even lower if proteinuria is >1 g/day)
b) lowering proteinuria to values as near to normal as possible

Meta-analysis: lower SBP results in slower rates of decline in GFR
in patients with and diabetes



Bakris GL, Am J Kidney Dis 2000; 36:646

SPECIAL ARTICLE www.jasn.org

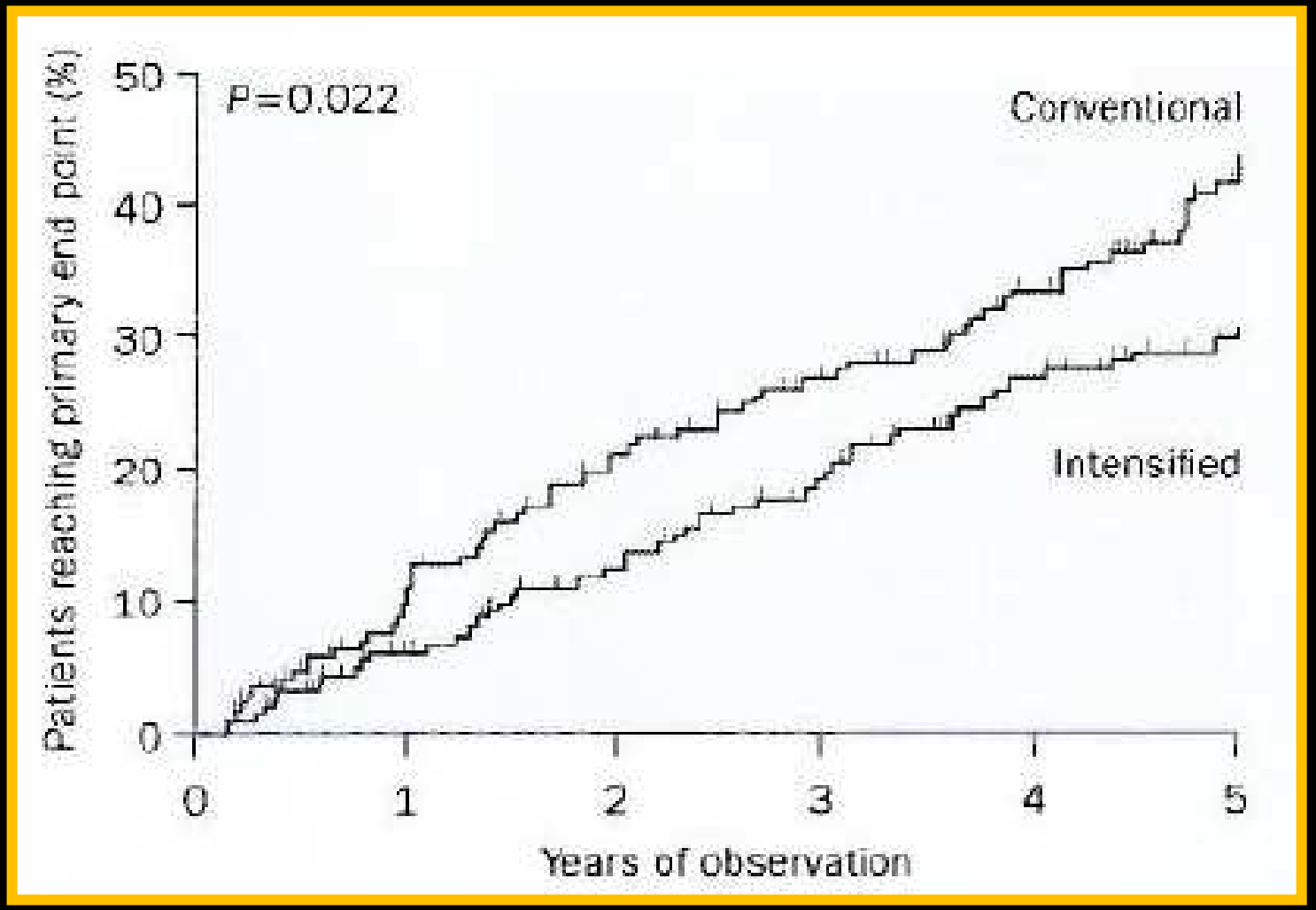
Blood Pressure Control in Chronic Kidney Disease: Is Less Really More?

Julia B. Lewis

Division of Nephrology and Hypertension, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee

J Am Soc Nephrol 2010;21:1086-1092

Effect of strict BP control on renal survival (ESCAPE Trial)



Wuhl E. et al. *N Engl J. Med 2009;361:1639-1650*

Hot Topics in Nephrology: A Debate

American Journal of Nephrology

Am J Nephrol 2010;32:370–373
DOI: 10.1159/000319636

Published online: September 3, 2010

Debate: PRO Position

People with Chronic Kidney Disease Should Have a Blood Pressure Lower than 130/80 mm Hg

Robert D. Toto

University of Texas Southwestern Medical Center Dallas, Dallas, Tex., USA

Hot Topics in Nephrology: A Debate

American Journal of Nephrology

Am J Nephrol 2010;32:374–376
DOI: 10.1159/000319637

Published online: September 3, 2010

Debate: CON Position

People with Chronic Kidney Disease Should Have a Blood Pressure Lower than 130/80 mm Hg

Rajiv Agarwal

Indiana University School of Medicine and Richard L. Roudebush Veterans Administration Medical Center, Indianapolis, Ind., USA

Blood pressure goal in chronic kidney disease: what is the evidence?

Rajiv Agarwal

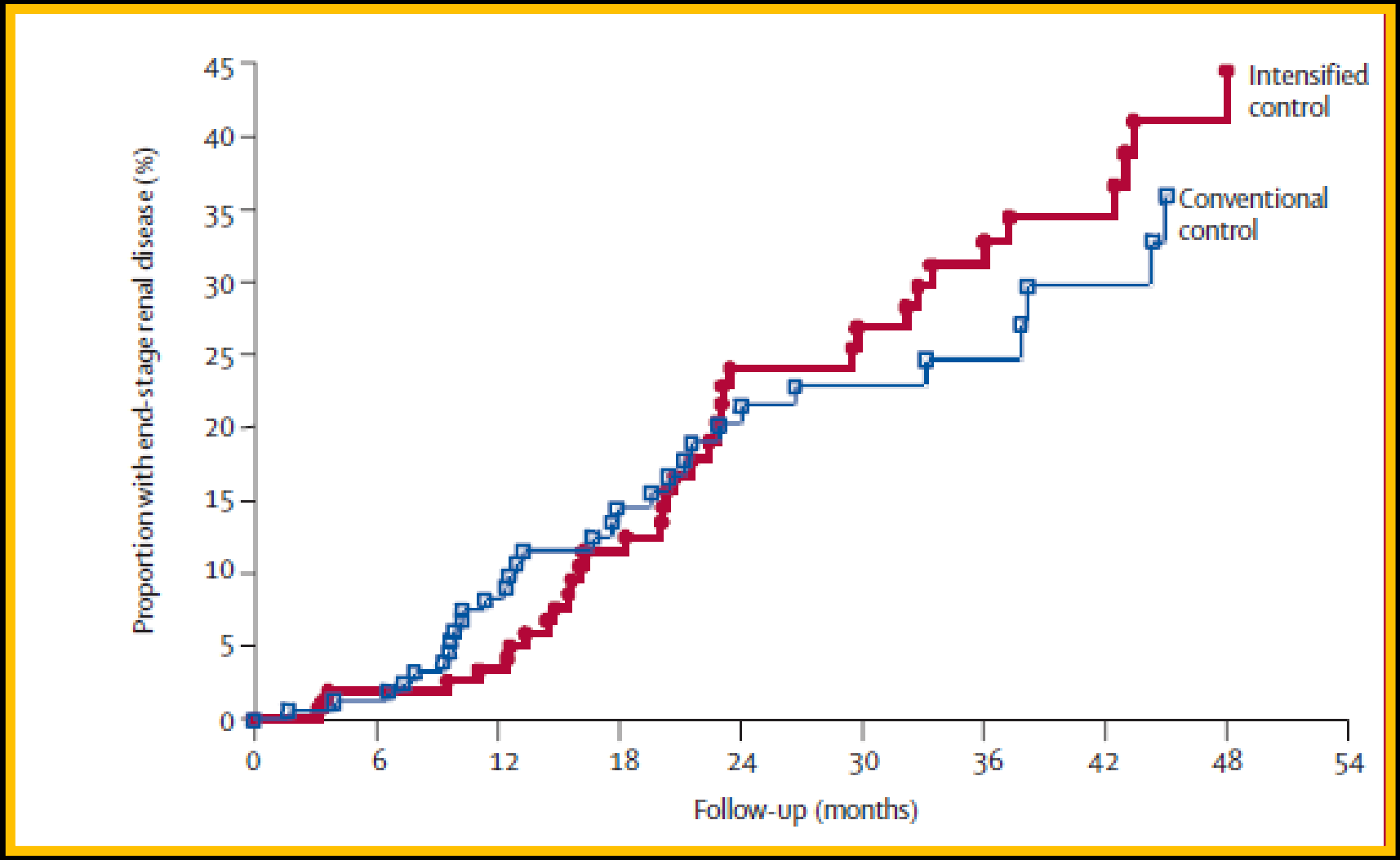
Curr Opin Nephrol Hypertens 2011;20:229-232

Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial

*Piero Ruggenenti, Annalisa Perna, Giacomina Loriga, Maria Ganeva, Bogdan Ene-Iordache, Marta Turturro, Maria Lesti, Elena Perticucci, Ivan Nediyalkov Chakarski, Daniela Leonardis, Giovanni Garini, Adalberto Sessa, Carlo Basile, Mirella Alpa, Renzo Scanziani, Gianbattista Sorba, Carmine Zoccali, Giuseppe Remuzzi, for the REIN-2 Study Group**

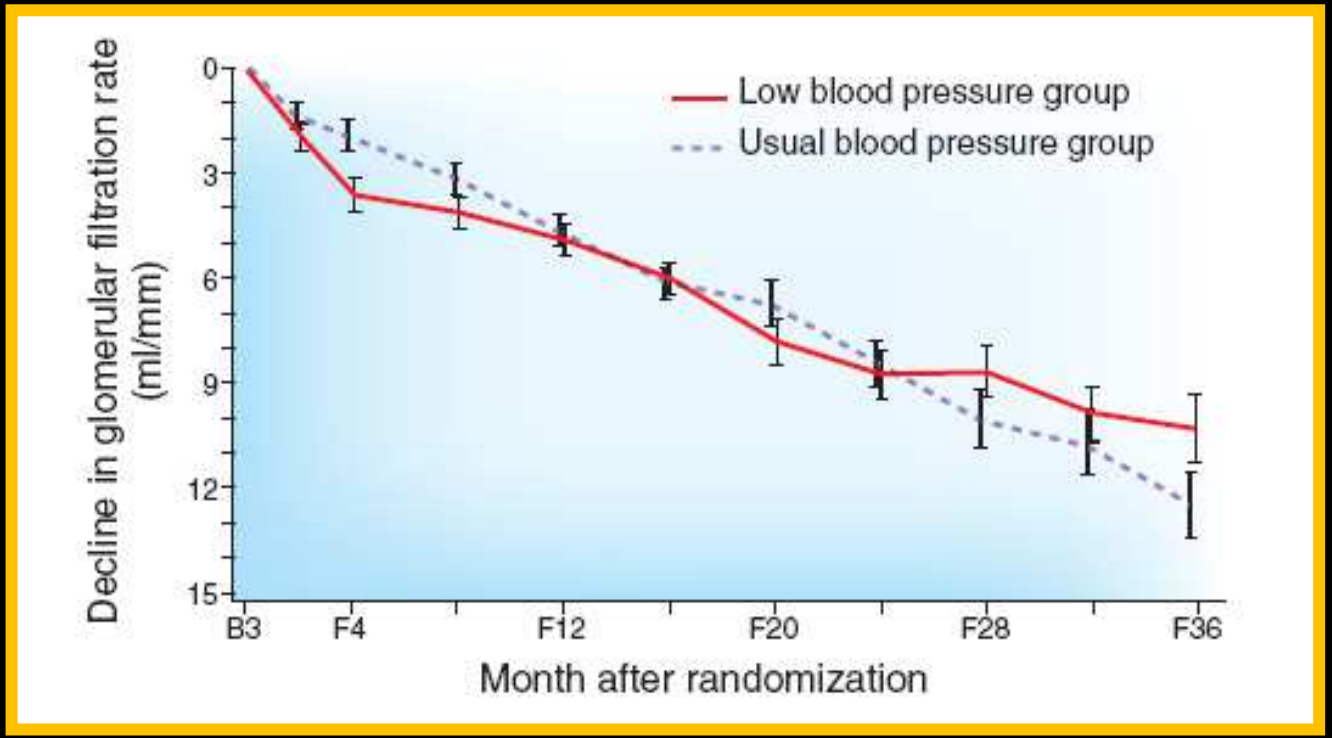
Lancet 2005; 365: 939-946

Proportion of Patients with ESRD in each study arm



Ruggenenti P. et al. *Lancet 2005;365:939-946*

Estimate decline in the GFR from baseline to selected follow-up times in MDRD



Lewis J B. *J Am Soc Nephrol 2010;21:1086-1092*

The NEW ENGLAND JOURNAL of MEDICINE

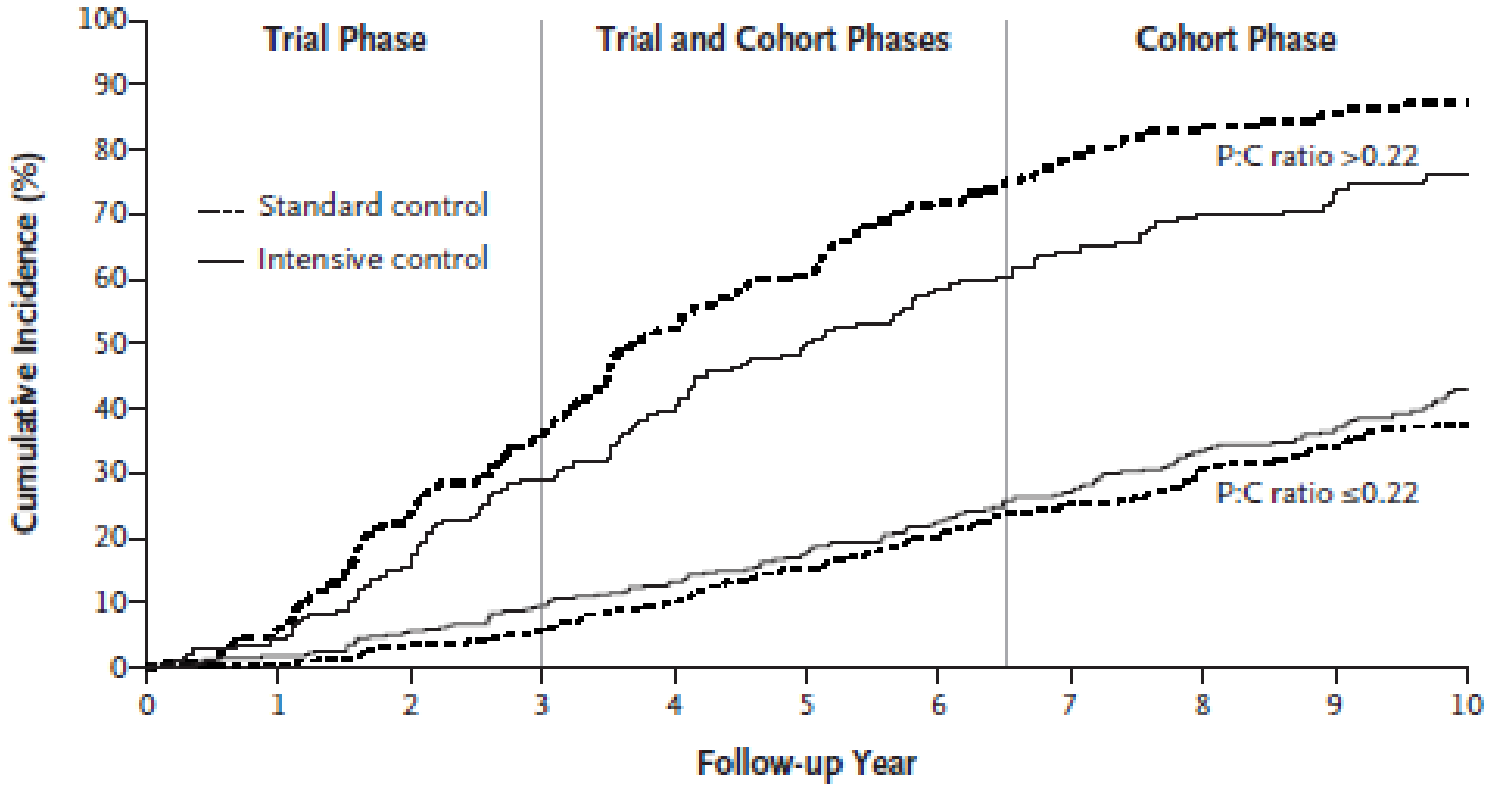
ORIGINAL ARTICLE

Intensive Blood-Pressure Control in Hypertensive Chronic Kidney Disease

Lawrence J. Appel, M.D., M.P.H., Jackson T. Wright, Jr., M.D., Ph.D., Tom Greene, Ph.D., Lawrence Y. Agodoa, M.D., Brad C. Astor, M.P.H., Ph.D., George L. Bakris, M.D., William H. Cleveland, M.D., Jeanne Charleston, R.N., Gabriel Contreras, M.D., M.P.H., Marquetta L. Faulkner, M.D., Francis B. Gabbai, M.D., Jennifer J. Gassman, Ph.D., Lee A. Hebert, M.D., Kenneth A. Jamerson, M.D., Joel D. Kopple, M.D., M.P.H., John W. Kusek, Ph.D., James P. Lash, M.D., Janice P. Lea, M.D., Julia B. Lewis, M.D., Michael S. Lipkowitz, M.D., Shaul G. Massry, M.D., Edgar R. Miller, Ph.D., M.D., Keith Norris, M.D., Robert A. Phillips, M.D., Ph.D., Velvie A. Pogue, M.D., Otelio S. Randall, M.D., Stephen G. Rostand, M.D., Miroslaw J. Smogorzewski, M.D., Robert D. Toto, M.D., and Xuelei Wang, M.S., for the AASK Collaborative Research Group*

N Engl J Med 2010;363:918-929

Cumulative Incidence of the Composite Primary Outcome According to Baseline Proteinuria Status



Appel L J. Et al. *N Engl J Med 2010;363:918-929 (AASK)*

Annals of Internal Medicine | REVIEW

Systematic Review: Blood Pressure Target in Chronic Kidney Disease and Proteinuria as an Effect Modifier

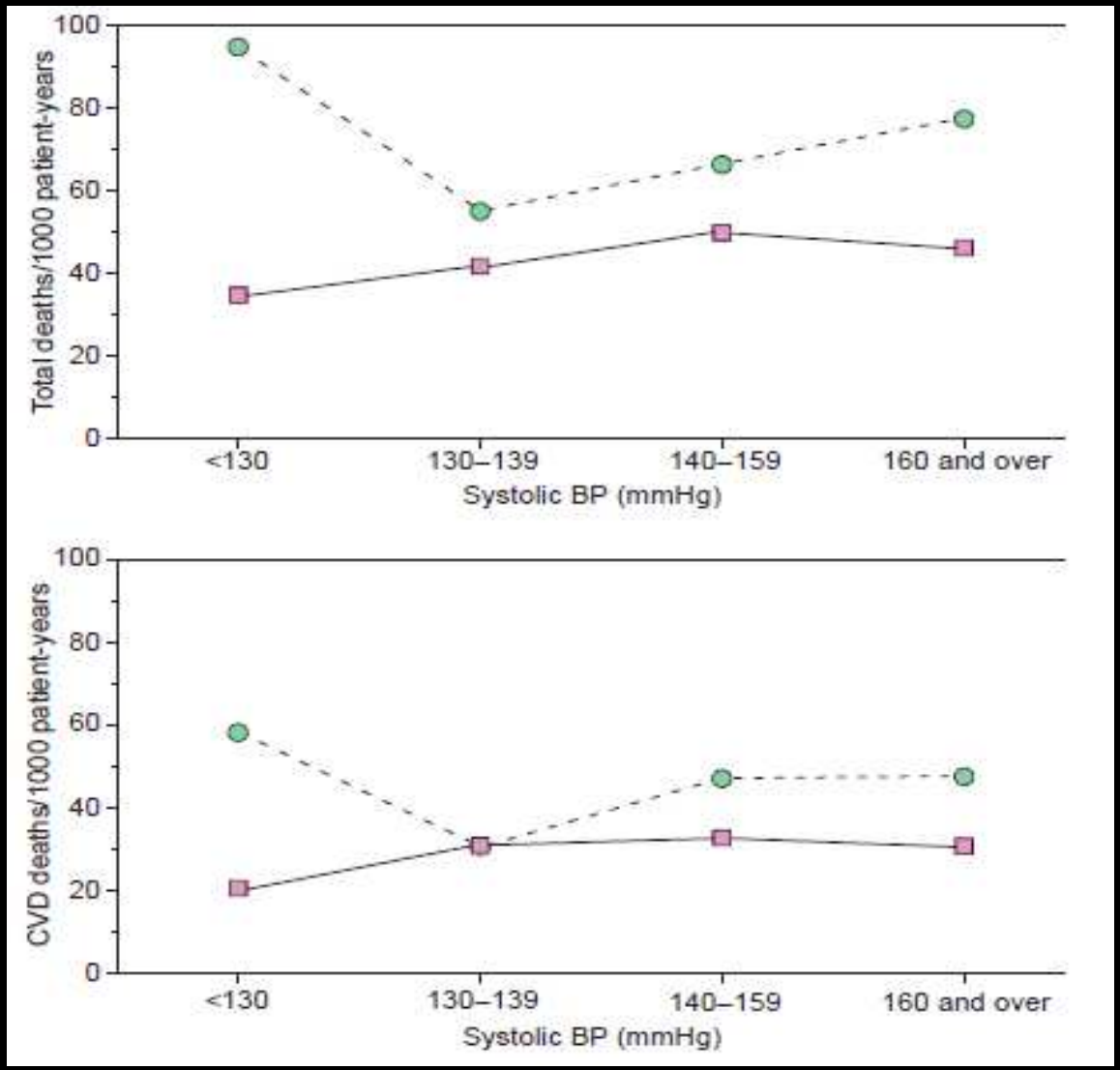
Ashish Upadhyay, MD; Amy Earley, BS; Shana M. Haynes, DHSc; and Katrin Uhlig, MD, MS

Ann Intern Med 2011;154:541-548

Outcome	MDRD Study		AASK Trial		REIN-2 Trial
	Trial	Observational Follow-up	Trial	Observational Follow-up	
≥50% (or ≥25 mL/min per 1.73 m^2) decrease in GFR, kidney failure, or death*	–	–	Risk reduction, 2% (95% CI, –22% to 21%); $P = 0.85$	HR, 0.91 (CI, 0.77 to 1.08); $P = 0.27$	–
Kidney failure				I, 0.71 to = 0.08	–
50% decrease failure‡				I, 0.78 to = 0.59	–
Kidney failure				–	23% vs. 20%; $P = 0.99$
Mortality, %	2 vs. 1; P = ND	10 vs. 6; P = ND	2 vs. 2; P = ND	–	2 vs. 1; P = ND
Cardiovascular mortality	–	–	HR, 0.98 (CI, 0.48 to 2.01); $P = 0.96$	–	1% vs. 1%; P = ND
CVD events	RR, 1.03§ (CI, 0.59 to 1.79)	–	2% vs. 3%; P = ND	–	–
Rate of annual GFR decline, *mL/min per 1.73 m^2*	Study A: 1.6‖ (CI, –0.8 to 3.9); $P = 0.18$ Study B: 0.5‖ (CI, –0.4 to 1.4); P =0.28	–	0.26‖ (CI, –0.21 to 0.64); $P = 0.25$	–	0.22 vs. 0.24; $P = 0.62$

Evidence does not conclusively show that a currently recommended blood pressure target of less than 130/80 mmHg improves clinical outcomes more than a conventional target of less than 140/90 mmHg in adults with chronic kidney disease

Total and CVD mortality in patients with and without proteinuria for different SBP categories



Vepsalainen, J Internal Med 2012

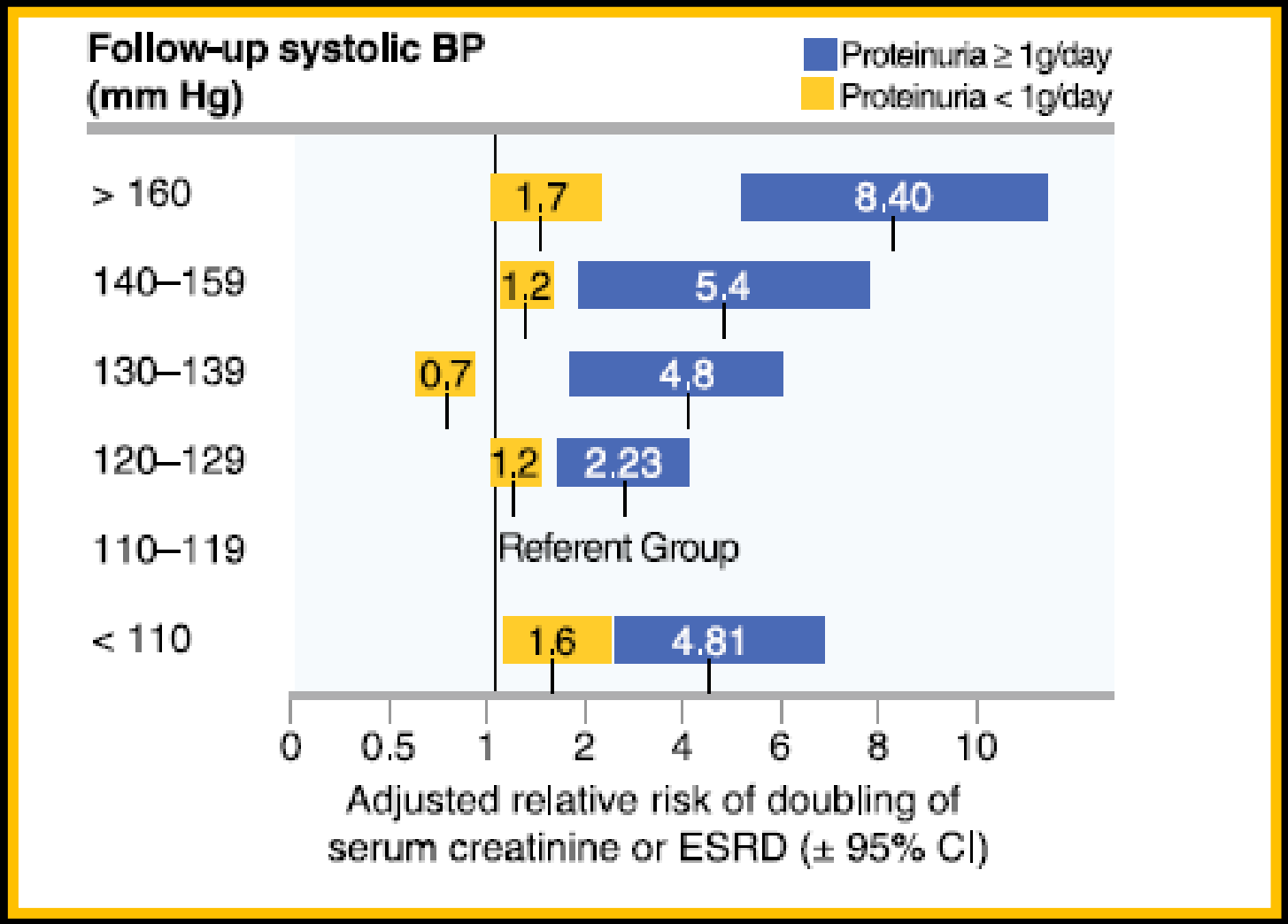
SPECIAL SITUATIONS IN THE MANAGEMENT OF HYPERTENSION (THEODORE KOTCHEN, SECTION EDITOR)

Blood Pressure Targets for Patients with Diabetes or Kidney Disease

Colleen Flynn · George L. Bakris

Curr Hypertens Rep 2011

Relative Risk of CKD Progression in RT



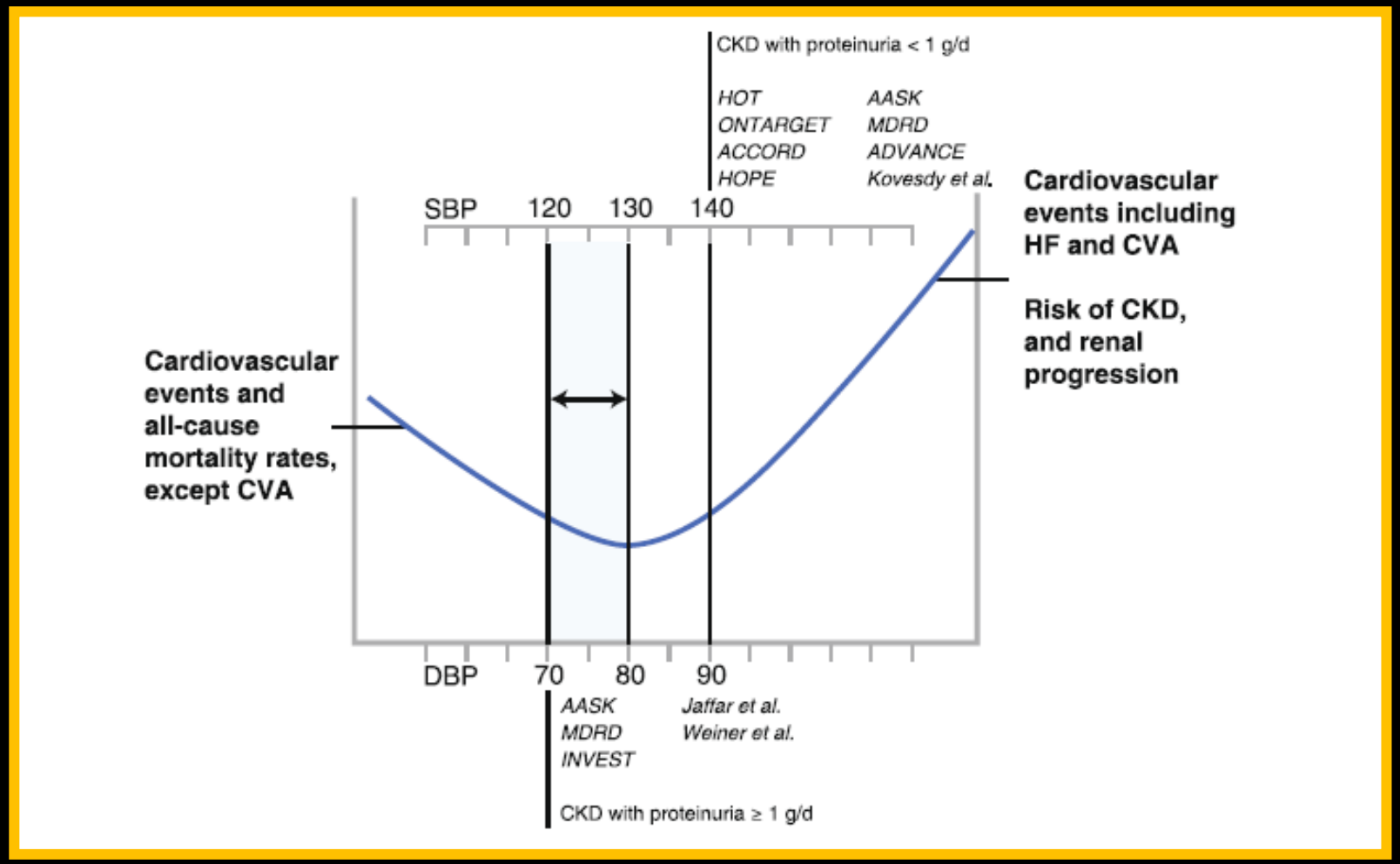
C.Flynn and G.Bakris *Curr Hypertens Rep 2011*

What is the Ideal Blood Pressure Goal for Patients with Stage III or Higher Chronic Kidney Disease?

Yazan Khouri · Susan P. Steigerwalt ·
Mershed Alsamara · Peter A. McCullough

Curr Card Rep Sept 2011

Cardiorenal outcomes according to achieved BP from clinical trials



Khouri Y. Et al. *Curr Cardiol Rep 2011*

ORIGINAL INVESTIGATION

LESS IS MORE

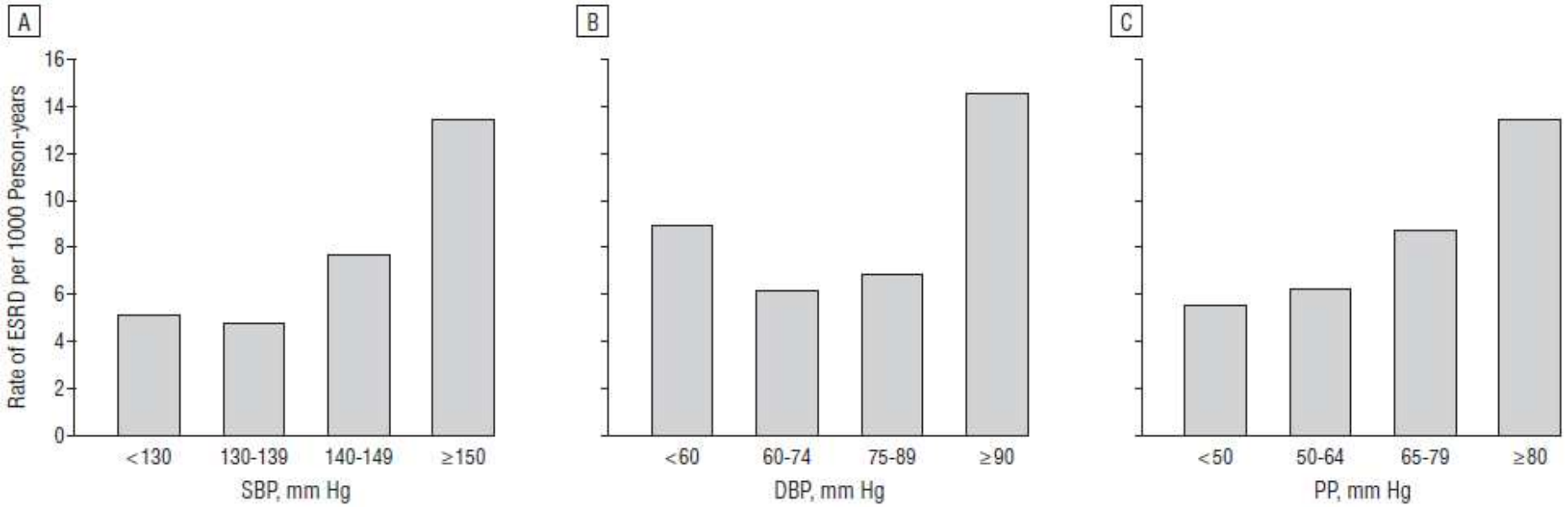
Blood Pressure Components and End-stage Renal Disease in Persons With Chronic Kidney Disease

The Kidney Early Evaluation Program (KEEP)

Carmen A. Peralta, MD; Keith C. Norris, MD; Suying Li, PhD; Tara I. Chang, MD; Manjula K. Tamura, MD; Stacey E. Jolly, MD; George Bakris, MD; Peter A. McCullough, MD; Michael Shlipak, MD; for the KEEP Investigators

Arch Intern Med 2012 ; 172(1): 41-47

Rates of ESRD according to SBP,DBP,PP levels



Peralta CA et al for the KEEP Investigators *Arch Intern Med 2012 ; 172(1): 41-47*

European Heart Journal
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Authors/Task Force Members: Giuseppe Mancia (Chairperson) (Italy)*, Robert Fagard (Chairperson) (Belgium)*, Krzysztof Narkiewicz (Section co-ordinator) (Poland), Josep Redon (Section co-ordinator) (Spain), Alberto Zanchetti (Section co-ordinator) (Italy), Michael Böhm (Germany), Thierry Christiaens (Belgium), Renata Cifkova (Czech Republic), Guy De Backer (Belgium), Anna Dominiczak (UK), Maurizio Galderisi (Italy), Diederick E. Grobbee (Netherlands), Tiny Jaarsma (Sweden), Paulus Kirchhof (Germany/UK), Sverre E. Kjeldsen (Norway), Stéphane Laurent (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Luis Miguel Ruilope (Spain), Roland E. Schmieder (Germany), Per Anton Sirnes (Norway), Peter Sleight (UK), Margus Viigimaa (Estonia), Bernard Waeber (Switzerland), Faiez Zannad (France)

Mancia, Eur Heart J 2013

Recommendations	Class [a]	Level [b]	Ref. [c]
Lowering SBP to <140 mmHg should be considered.	IIa	B	303, 313
When overt proteinuria is present, SBP values <130 mmHg may be considered, provided that changes in eGFR are monitored.	IIb	B	307, 308, 313
RAS blockers are more effective in reducing albuminuria than other antihypertensive agents, and are indicated in hypertensive patients in the presence of microalbuminuria or overt proteinuria.	I	A	513, 537
Reaching BP goals usually requires combination therapy, and it is recommended to combine RAS blockers with other antihypertensive agents.	I	A	446
Combination of two RAS blockers, though potentially more effective in reducing proteinuria, is not recommended.	III	A	331, 433, 463
Aldosterone antagonists cannot be recommended in CKD, especially in combination with a RAS blocker, because of the risk of excessive reduction in renal function and of hyperkalaemia.	III	C	-

Mancia, Eur Heart J 2013

Summary of KDIGO guideline. What do we really know about management of blood pressure in patients with chronic kidney disease?

David C. Wheeler[1] and Gavin J. Becker[2]

[1]Centre for Nephrology, University College London Medical School, London, UK and [2]Department of Nephrology, Royal Melbourne Hospital, Parkville, Victoria, Australia

Wheeler, Kidney Int 2013

Summary of recommendations for management of BP In adult CKD patients with and without Diabetes

Albuminuria (mg/day)[a]	BP Target mm Hg	Preferred agent
< 30	⩽ 140/90 mm Hg	None
30–300	⩽ 130/80 mm Hg	ACE-I or ARB
> 300	⩽ 130/80 mm Hg	ACE-I or ARB

Wheeler, Kidney Int 2013

Take home messages 1

- Awareness of hypertension among individuals with CKD remains suboptimal and rates of BP control remain poor.

- There is evidence for an additional nephroprotective advantage of tight BP control towards the low-normal range in young patients and in patients with proteinuria

Take home messages 2

- Evidence does not conclusively support BP targets less than 130/80 vs a conventional target of less than 140/90 In adults with CKD.

- Lower BP targets may be beneficial in subjects with proteinuria of 300 - 1000 mg/d

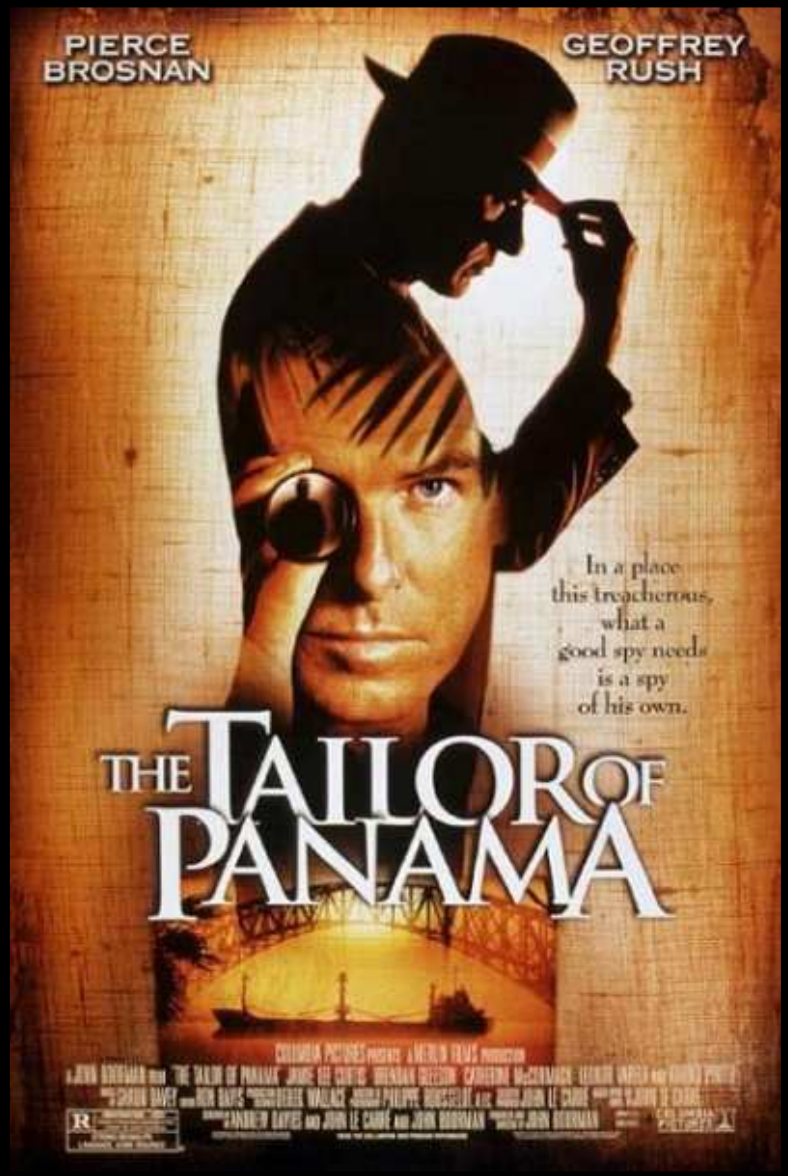
……. *and the future ?*

HALT-PKD (Progression of Polycystic Kidney Disease)
compares BP targets of 95/60 to 110/75 mmHg vs 120/70 to 130/80

SPRINT (Systol ic Blood Pressure Intervention Trial)
compares SBP targets of less than 120 mmHg vs less than 140mmHg in 9000 patients with CKD and CV disease

……. and waiting for the next trials?

Remember ……



The good tailor knows very well that one size does not fit all