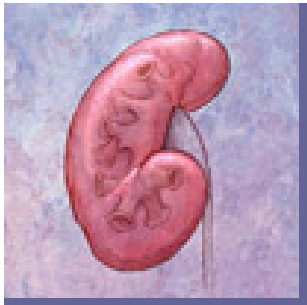
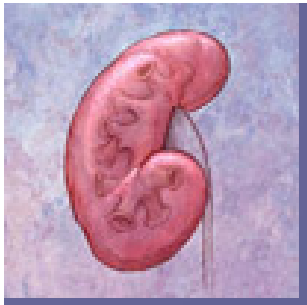


Chronic Kidney Disease (CKD)

Robert M. Centor, MD
Acting Associate Dean, Huntsville Campus
Associate Dean for CME
Professor and Director, Division of GIM
UAB



Patient Presentation

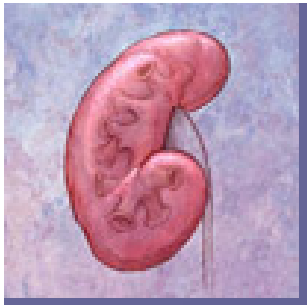
- WD is a 51 YOBM with long history of diabetes mellitus. He is admitted to the VA Hospital with left leg cellulitis. Review of his lab work including the following important labs:

Hemoglobin 10.3
Hematocrit 30.7

Calcium 7.7
Albumin 2.8

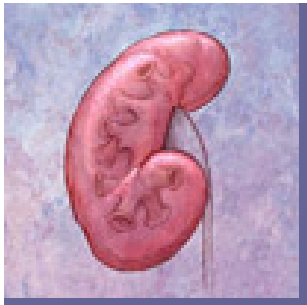
137	112	28
5.9	19	2.1

236



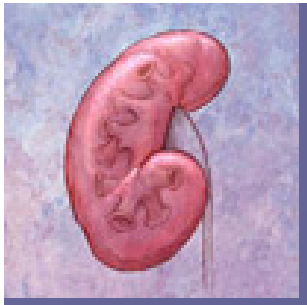
More clinical information

- Review of his laboratory data shows that they were similar to previous values
- 24 hour urine protein done one month prior to admission showed 2 grams of protein in 24 hours.
- Urine sodium 110 and urine potassium 22 with urine chloride of 156.
- PTH – 297



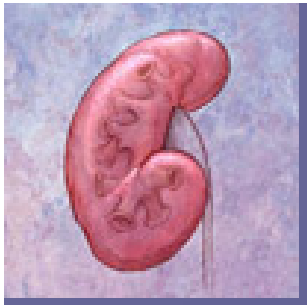
Goals of workshop

- Review some key management strategies for patients with CKD.
- Use recent articles to highlight recent guidelines for chronic kidney disease.
- Raise awareness of aggressive management of stage III CKD
- Develop strategies for improving care of stage III CKD and teaching about CKD



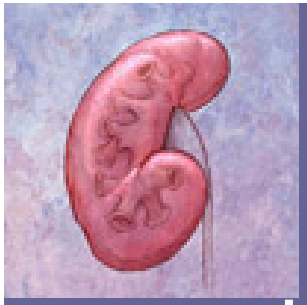
Determine estimated GFR.

- Using the GFR calculator that you can find on the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Page, we calculated and estimated his GFR = 40 cc/min
- www.kidney.org/professionals/kdoqi/index.cfm



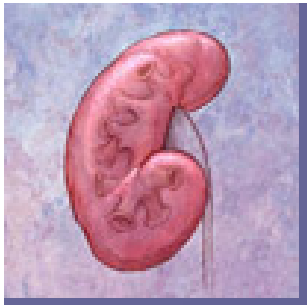
Chronic Kidney Disease Stages

- Using this GFR, we classified this patient as Stage III Chronic Kidney Disease
- The stages of CKD



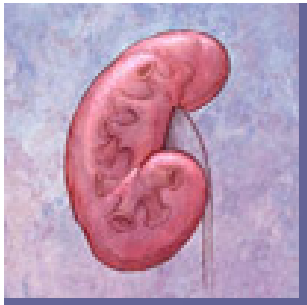
Stages of Chronic Kidney Disease: A clinical action plan

Stage	Description	GFR mL/min/1.73m)	Action*
	At increased risk	≥90 (with CKD RF's)	Screening, CKD risk reduction
1	Kidney damage w/ normal or increased GFR	≥90	Dx and Rx of comorbid dz, Slowing progression, CVD risk reduction
2	Kidney damage w/ mildly decreased GFR	60–89	Estimating progression
3	**Moderately decreased GFR**	**30–59**	**Evaluating and treating complications**
4	Severely decreased GFR	15–29	Preparation for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	Replacement (if uremia present)



Issues for our discussion

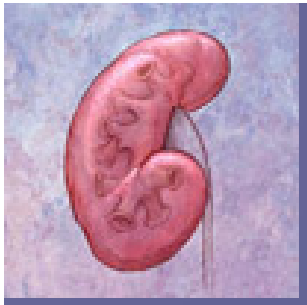
- Delaying progression of CKD
- Bone Disease
- Anemia
- Vascular Access
- Acidosis



Angiotensin-Receptor Blockade versus Converting-Enzyme Inhibition in Type 2 Diabetes and Nephropathy

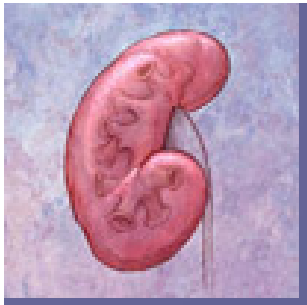
AH Barnett, SC Bain, P Bouter, B Karlberg, S Madsbad, J Jervell, J Mustonen, for the Diabetics Exposed to Telmisartan and Enalapril Study Group

NEJM 2004;351:1952-61



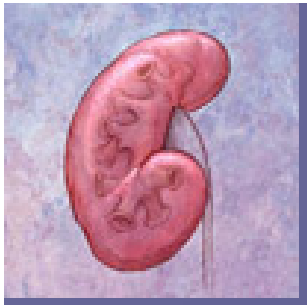
Importance of this Study

- Previous studies have documented independently that ACE inhibitors and ARB's can both decrease
  - proteinuria
  - the rate of progression of CKD in type II diabetes
- Prior to this study there was no head to head study comparing an ACE inhibitor and an ARB
- Editorials have asked for such a study



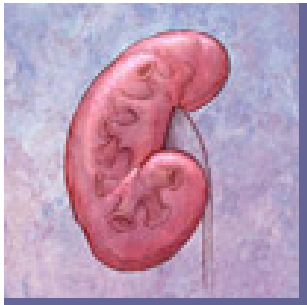
Study Design

- Perspective randomized double-blind, double-dummy parallel group study at 39 Centers in Northern Europe.
- Subjects
  - Age - 35-80
  - Race – white or Asian
  - Sex – Female or male
- Type II diabetes treated by diet or diet plus medications
- Mild to moderate hypertension with resting blood pressure of less than 180/95 on treatment
- Urine albumin excretion rate between 11 and 999 *µg*/min
- Glycosylated hemoglobin less than 12%
- Serum creatinine < 1.6 mg/dl



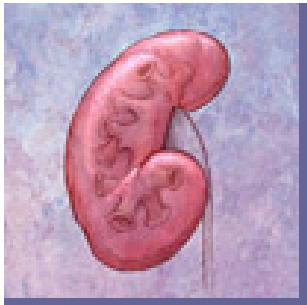
Baseline Characteristics of the Subjects

Variable	Telmisartan Group (N=120)	Enalapril Group (N=130)
Age – yr	61.2	60.0
Male sex – no of subjects (%)	87(72.5)	95 (73.1)
BMI	30.8	30.6
Diabetes duration	8.0	8.0
GFR – ml/min/1.73 m2	91.4	94.3
Serum creatinine – mg/dl	1.02	0.99
Urine albumin	46.2	60.0



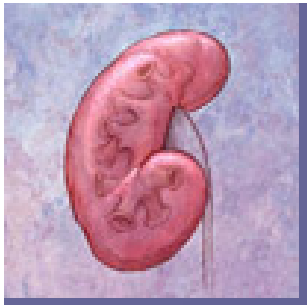
Secondary Renal End Points after Five Years of Treatment

End Point	Change from Baseline		Difference between Groups (95% CI)
	Telmisartan Group	Enalapril Group	
Serum creatinine (mg/dl)	0.10	0.10	0 (-0.66 to 0.65)
Urinary albumin excretion (ratio)	1.03	0.99	1.04 (0.71 to 1.51)



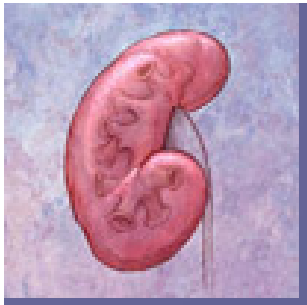
Discussion

- Both ARB's and ACE inhibitors have previously been shown to delay progression of renal dysfunction and chronic kidney disease.
- In this study no significant difference was found between ARB's and ACE inhibitors in preventing progression of kidney disease in patient with type II diabetes and early indications of chronic kidney disease



Guideline 13

- Interventions to slow the progression disease should be considered in all patients with chronic disease.
- Interventions that have proven to be effective include:
  1. Strict glucose control in diabetes
  2. Strict blood pressure control
  3. ACE inhibitors and/or ARBs

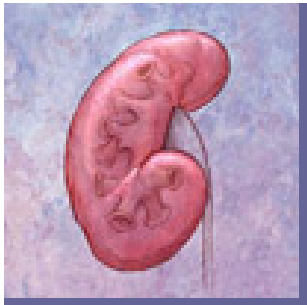


The nephrologist's role in the management of calcium phosphorous metabolism in patients with chronic kidney disease

Wolfgang C. Winkelmayer, Raisa Levin, and Jerry Avorn

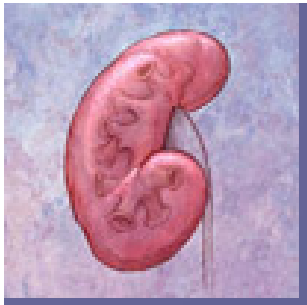
Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

Kidney International 2003;63:1836-1842



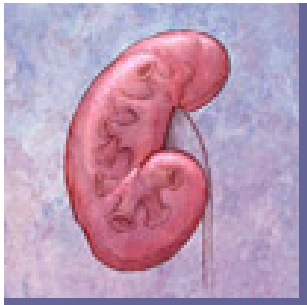
Methods

- In this cohort study, 314 patients with chronic kidney disease were evaluated for indicators of calcium phosphorus metabolism management prior to renal replacement therapy
  - PTH measurement
  - Vitamin D metabolites
  - Receipt of calcitriol or calcium containing phosphate binders



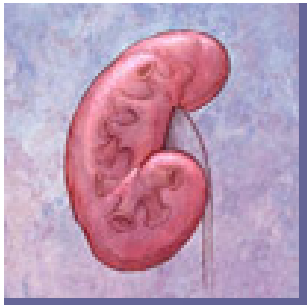
Methods

- Pharmaceutical records were searched for the year prior to the onset of RRT.
- Patients who had appropriate testing were compared with those who did not have testing.
- Variables included demographic variables and visits with nephrologists.



Measured parameters

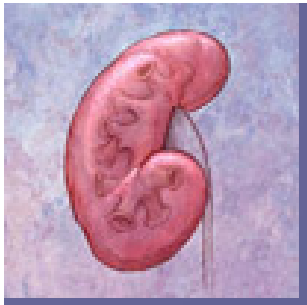
- PTH Testing
  - Tested patients were 68% more likely to see a nephrologist than controls.
- Calcitriol
  - Recipients were 6 times as likely to see a nephrologists than non-recipients.
- Calcium Containing Binder Prescriptions
  - Recipients were 6.5 times more likely to see a nephrologist.



Effect of management of calcium-phosphate metabolism on 1-year mortality

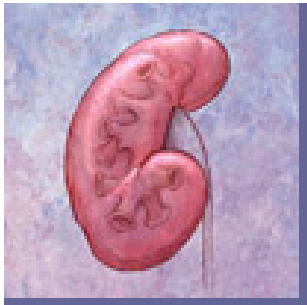
Multivariate Analyses

Model	Odds ratio	95% Confidence interval	P value
Late vs. early referral	1.22	1.00-1.48	0.05
Presence of any calcium-phosphate care measure prior to first RRT	0.65	0.51-0.84	<0.001



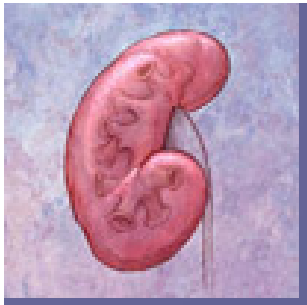
Summary

- Generalist physicians are less likely than nephrologists to manage calcium phosphorous metabolism in CKD
- We have long known that managing calcium and phosphorous is important for bone disease
- These data suggest that it may decrease cardiovascular disease.



Guideline #10

- Bone Disease and disorders of calcium phosphorous metabolism develop during the course of chronic disease and are associated with adverse outcomes.
  - Patients with GFR less than 60 should be evaluated for bone disease and disorders of calcium and phosphorous metabolism
  - Patients with either bone disease or disorders of calcium phosphorous metabolism should be evaluated and treated.

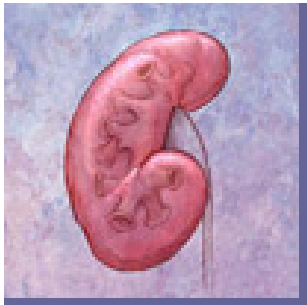


Association of Hematocrit value with cardiovascular morbidity and mortality in incident hemodialysis patients

Suying Li and Allan J. Collins

Nephrology Analytical Services, Minneapolis Medical Research Foundation and University of Minnesota, Minneapolis, Minnesota

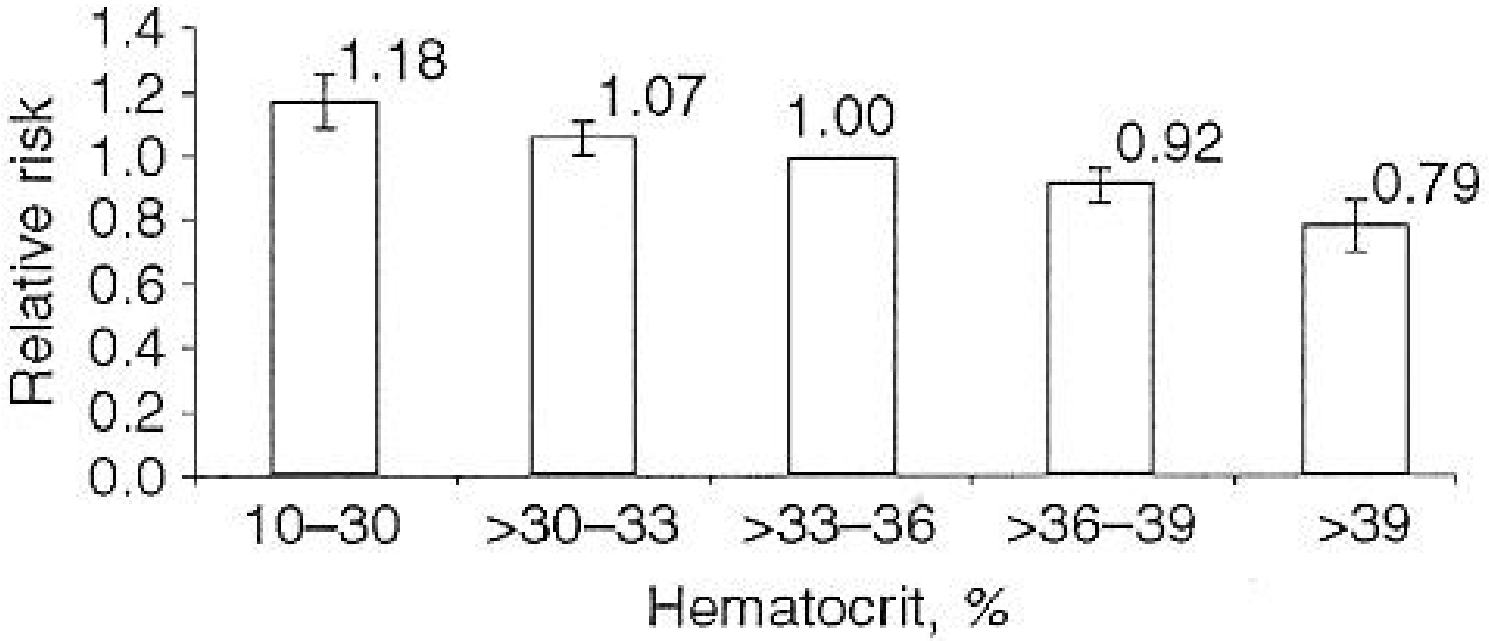
Kidney International 2004;65:626-633

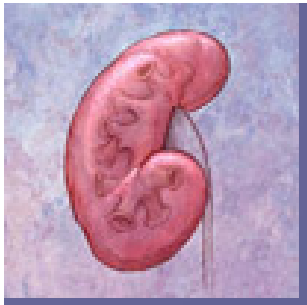


Methods

- Analysis of incident hemodialysis patients.
- Patients divided into groups on the basis of initial hct at hemodialysis initiation.
- Outcome measures include hospitalization (up to 2.5 years) and mortality (up to 3 years)

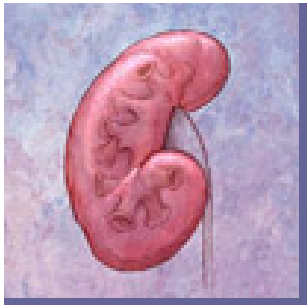
Adjusted relative risk of first hospitalization due to any cardiac cause, according to hematocrit value





Summary

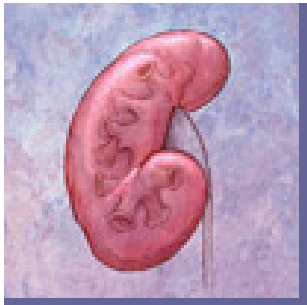
- This analysis supports previous analyses which shows that pre-dialysis hematocrit is related to cardiovascular morbidity and mortality.
- Currently nephrologists have switched primarily to using hemoglobin rather than hematocrit as a better and more reliable predictor of outcomes.
- The correct hemoglobin/hematocrit targets for treating anemia in chronic kidney disease remain controversial.



Treating Anemia early in renal failure patients slows the decline of renal function: A randomized controlled trial

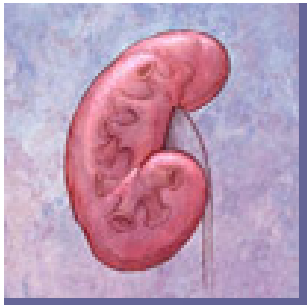
Chariclia Gouva, Petros Nikolopoulos, John Ioannidis, and Kostas Siamopoulos

Kidney International 2004; 66:753-760



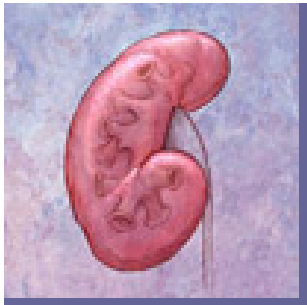
Methods

- Randomized control trial comparing subcutaneous erythropoietin vs. placebo for treating anemia in CKD



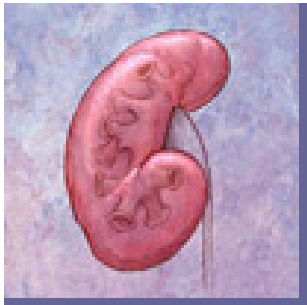
Eligibility Criteria

- Chronic kidney disease not caused by diabetes mellitus.
- Serum creatinine 2-6 mg/dL
- Hemoglobin 9-11.6 g/dL
- Absence of a variety of contraindications to this study



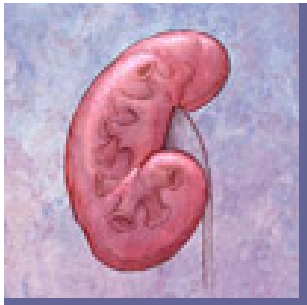
Endpoints

- Progression of chronic kidney disease – defined as a doubling of creatinine, a creatinine > 8, or initiation of renal replacement therapy - or death from any cause
- Secondary endpoints: hemoglobin, serum creatinine, and creatinine clearance at 12 months



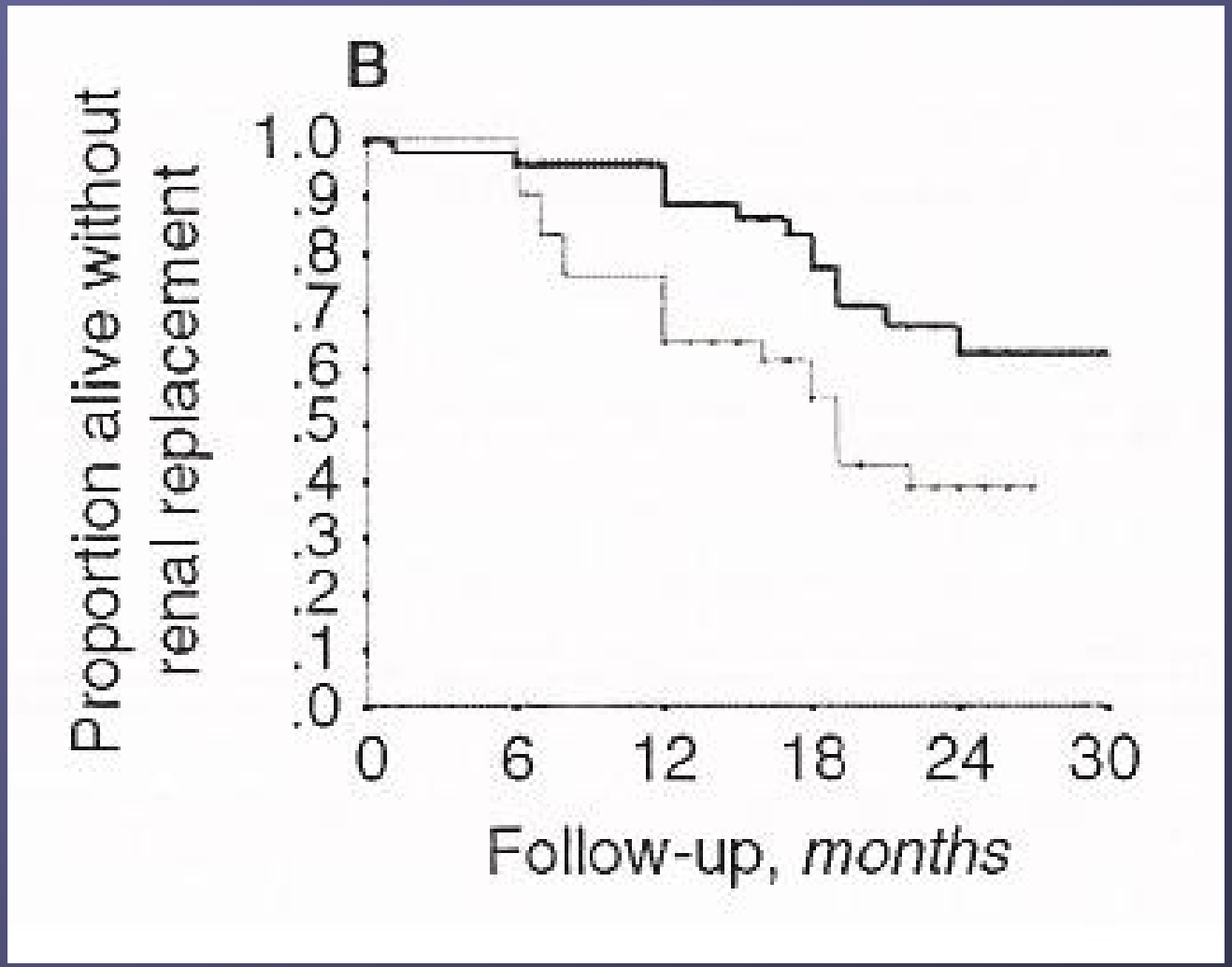
Baseline Characteristics

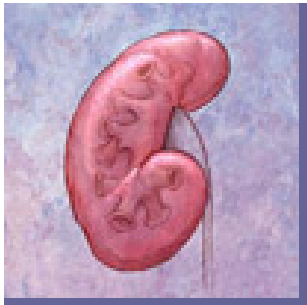
	Early arm N = 45	Deferred arm N = 43	P value
Female/male	20/25	18/25	0.98
Age, mean (SD), years	66.7 (10.4)	64.2 (12.2)	0.44
Hemoglobin, mean (SD), *g/dL*	10.1 (0.5)	10.1 (0.6)	0.72
Serum creatinine, mean (SD), *mg/dL*	3.27 (0.99)	3.39 (0.82)	0.27
Creatinine clearance, mean (SD), *mL/min*	25.7 (9.1)	22.3 (6.0)	0.14



Hematologic and renal parameters at 12 months

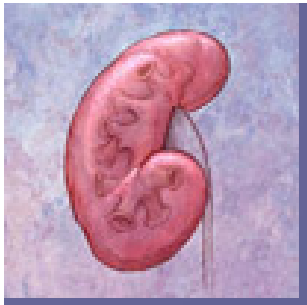
	Early arm	Deferred arm	P value
Hemoglobin, mean (SD), *g/dL*	12.9 (0.4)	10.3 (1.0)	<0.001
Hematocrit, mean (SD), %	38.4 (1.5)	31.4 (2.6)	<0.001
Serum creatinine, mean (SD), *mg/dL*	3.81 (1.43)	5.07 (2.39)	<0.001
Creatinine clearance, mean (SD), *mL/min*	21.9 (9.4)	16.1 (6.3)	<0.001


B
Proportion alive without renal replacement
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
.0
0
6
12
18
24
30
Follow-up, *months*



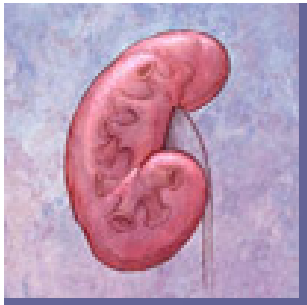
Implications

- This RCT suggests that erythropoietin may decrease the progression of CKD in anemic patients
- Thus we must consider adding erythropoietin treatment to blood pressure control and treating proteinuria as methods to delay progression of kidney disease
- This study is not a definitive study but rather a small study of CKD patients



Guideline 8

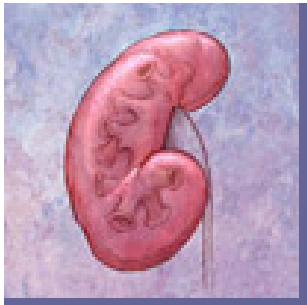
- Anemia usually develops during the course of CKD and may be associated with adverse outcomes
  - Patients with GFR less than 60 should be evaluated for anemia by measuring hemoglobin.
  - Anemia in CKD should be treated
  - The guideline for treating anemia states that the current target for hemoglobin is 11-12
  - This target refers to erthryopoietin therapy and does not imply an indication for blood transfusion.



Delayed nephrologist referral and inadequate vascular access in patients with advanced chronic kidney failure

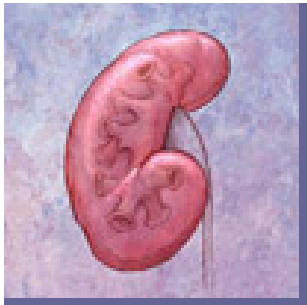
Jerry Avorn, Wolfgang C. Winkelmayer, Rhonda L. Bohn, Raisa Levin, Robert J. Glynn, Elliot Levy, William Owen, Jr.

Journal of Clinical Epidemiology 55(2002) 711-716



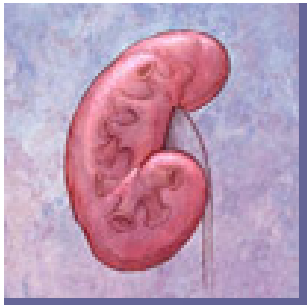
Study Design

- This epidemiological study used Medicare and Medicaid databases to exam patients who had been seen for at least 12 months prior to initiating dialysis.
- Patients had to have at least 1 month of dialysis following the index procedure and regular continuing claims for dialysis.



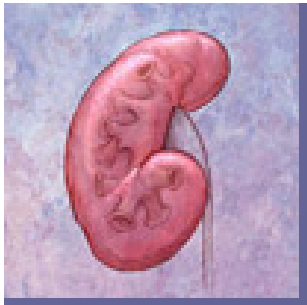
Covariate Analysis

- Covariates include:
  - Demographics: age, gender, race, SES
  - Frequency of visits with a nephrologist
  - Co-morbid conditions



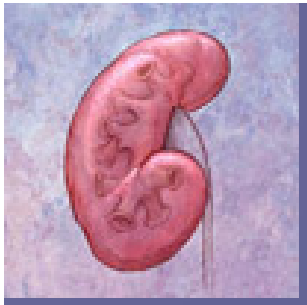
Referral Patterns

- Later referral – patient having a first nephrologist encounter less than 90 days prior to initiation of maintenance dialysis
- Frequency of nephrologist care – dichotomized as to greater than or less than 3 visits in the previous year



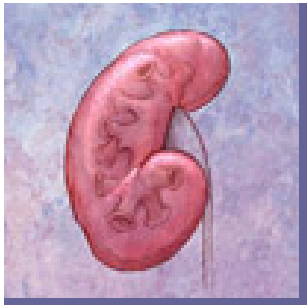
Results

- Early referral to a nephrologist was strongly predictive of starting dialysis with permanent vascular access
- Similarly frequent nephrology visits also predicted this
- Unexpectedly, African-Americans were more likely to have permanent vascular access placed prior to dialysis
- All of these associations remained after controlling for co-morbidity and renal diagnoses



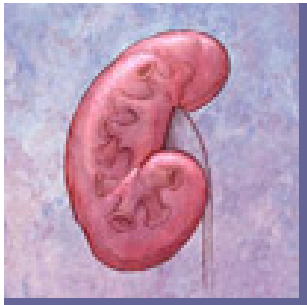
Context

- Since we know that patients who have adequate vascular access do much better initially with dialysis - requiring shorter hospitalizations and less health care expenditures - this study strongly reinforces the need for early nephrology referral in patients who are progressing toward ESRD



Guideline

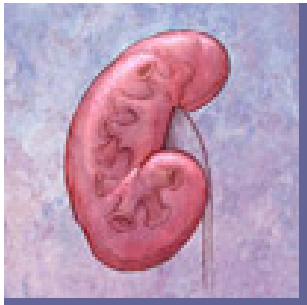
- Timing of access placement
  - Patients with CKD should be referred to construct primary AV fistula when their clearance increases below 25cc/min, their serum creatinine is greater 4mg/dl, or within 1 year of the anticipated need of dialysis



Prevalence of Acidosis and inflammation and their association with low serum albumin in chronic kidney disease

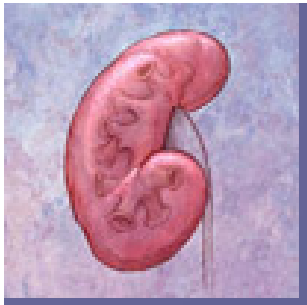
Joseph A. Eustace, Brad Astor, Paul M. Muntner, T. Alp Ikizler, and Josef Coresh

Kidney International 2004; 65: 1031-1040



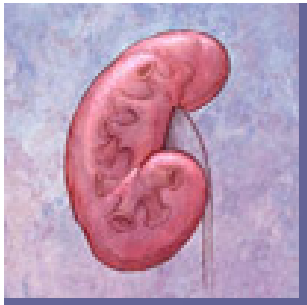
Study Design

- This is an analysis of NHANES III (National Health and Nutrition Examination Survey)
- This study evaluated the relationship between markers of inflammation, serum bicarbonate and serum albumin levels



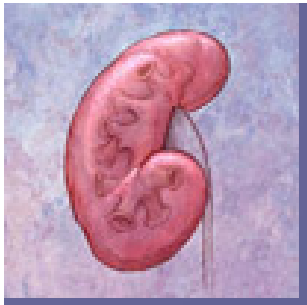
Multivariate analysis

- Multivariate analysis showed strong relationship between serum bicarbonate levels and serum albumin levels as well as between CRP levels and albumin levels



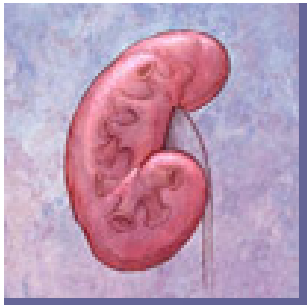
Context

- Hypoalbuminemia in CKD can reflect nutritional status.
- As kidney disease progresses, nutritional status can worsen
- Experimental data suggests that acidosis may lead to malnutrition
- We do not have a study that looks at the potential benefits of treating acidosis in chronic kidney disease patients



Guideline on metabolic acidosis

- In chronic kidney disease patients staged III, IV and V, the serum levels of bicarbonate should be maintained at 22 mEq/L



Patient Presentation

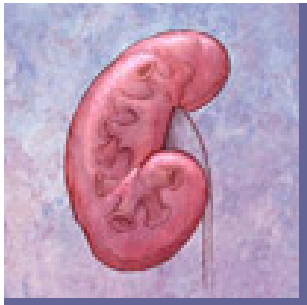
- WD is a 51 YOBM with long history of diabetes mellitus. He is admitted to the VA Hospital with left leg cellulitis. Review of his lab work including the following important labs:

Hemoglobin 10.3
Hematocrit 30.7

Calcium 7.7
Albumin 2.8

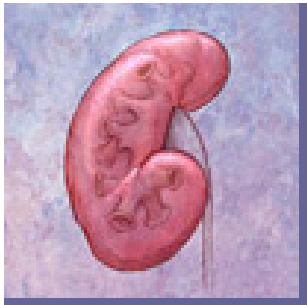
137	112	28
5.9	19	2.1

236



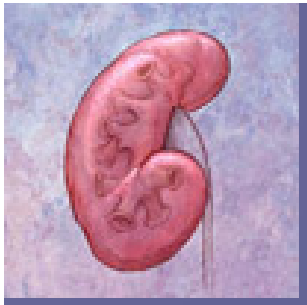
More clinical information

- Review of his laboratory data shows that they were similar to previous values
- 24 hour urine protein done one month prior to admission showed 2 grams of protein in 24 hours.
- Urine sodium 110 and urine potassium 22 with urine chloride of 156.
- PTH – 297



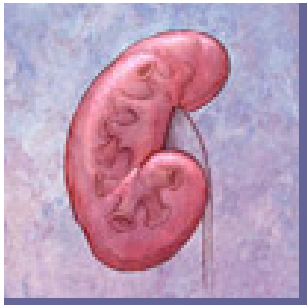
Issues Covered

- Delaying progression of chronic kidney disease
- Bone Disease
- Anemia
- Vascular Access
- Acidosis



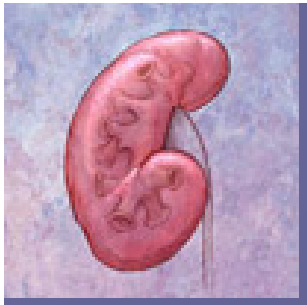
Omissions

- Cardiovascular risk factors
- Hypertension control
- Diabetes management



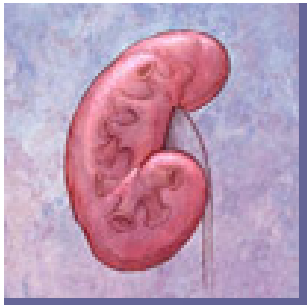
Summary

- Most physicians do not treat all the potential complications of CKD
- The early diagnosis of Stage III CKD presents us with an opportunity to modify subsequent morbidity
- Primary care physicians should develop a “checklist” for managing these patients, including timely nephrology referral



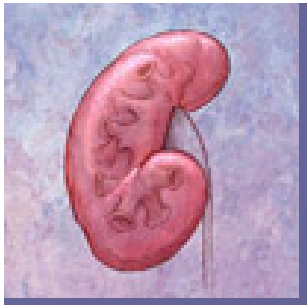
My Stage III CKD checklist

- Determine GFR
  - Use either Cockcroft-Gault or MDRD
  - If data available – plot progression
- Proteinuria
  - Check for proteinuria
  - If present use ACE inhibitors and ARBs to decrease



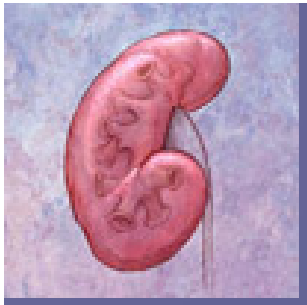
Checklist 2

- Anemia
  - Follow hemoglobin
  - If less than 12 refer to nephrology for possible EPO
- Mineral metabolism
  - Check calcium, phosphate and PTH levels
  - If abnormal, either start calcium replacement (either calcium carbonate or calcium acetate), or refer to nephrology for management



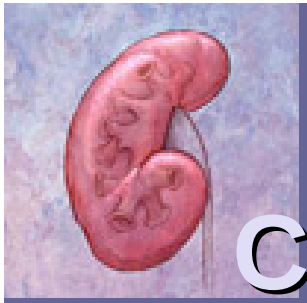
Checklist 3

- Acidosis
  - If bicarbonate < 22, then start either calcium carbonate (when needed for mineral metabolism) or Shohl's or bicitra solution with goal bicarbonate of 22
- Access
  - Refer to nephrology when ESRD expected in 1 year or less (either from progression plot or low GFR)



Checklist 4

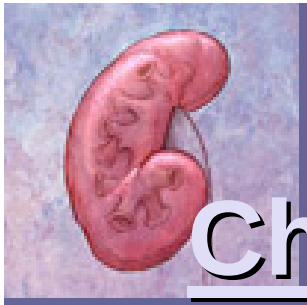
- Hypertension
  - Treat aggressively – goal BP 120/80
- Lipids
  - Treat aggressively – goal LDL 70
- Diabetes
  - Work to achieve excellent HgbA1C



CHRONIC KIDNEY DISEASE: RELATIONSHIP OF NEPHROLOGIST INVOLVEMENT AND DISEASE COURSE

Lori A. Orlando, MD
David B. Matchar, MD FACP

Duke University Center for Clinical Health Policy Research
& Durham VA, Durham NC

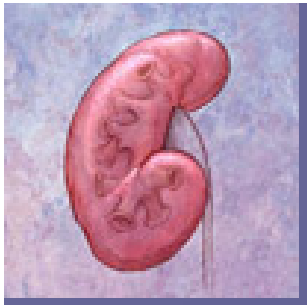


Chronic Kidney Disease (CKD)

- Population
  - CKD: 20 million patients (10% of US population)
  - ESRD: 430,000 patients in 2002
  - Incidence of both still increasing
- Economics
  - $17 billion per year in Medicare expenditures

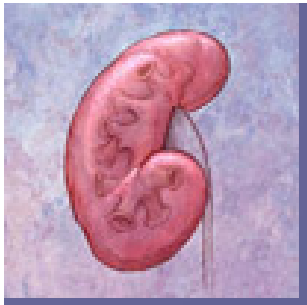
    $\Rightarrow$ Projected to be $40 billion per year by 2010

USRDS 2004 annual report at www.usrds.org, Coresh J. 41(1):1-12, Trivedi HS. AJKD 39(4):721-9



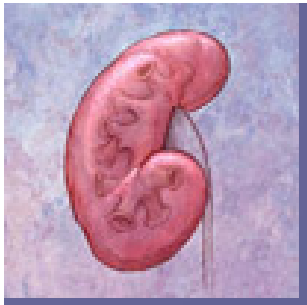
Management of CKD

- Improving management of CKD can:
  - Increase survival in CKD
  - Prolong development of ESRD
  - Improve morbidity and mortality of ESRD
- Early referral to nephrologist may improve outcomes
  - Retrospective studies of dialysis populations
  - Dichotomized referral time (1-6 months pre-dialysis)
- Nephrologists have limited capacity for pre-ESRD care



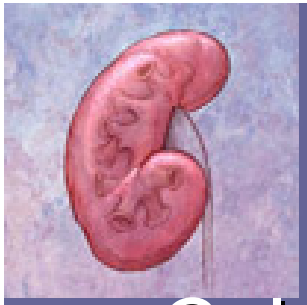
Objective

To examine the relationship between the stage of CKD at which a nephrologist becomes involved and disease progression or death



Methods

- Design: retrospective cohort study
- Setting: Durham VA database
- Inclusion Criteria:
  - Creatinine > 1.3 mg/dL on 2 occasions at least 3 weeks apart
  - Between January 1998 and December 1999
- Exclusion Criteria:
  - No primary care provider
  - Started dialysis within 3 months of entry into cohort

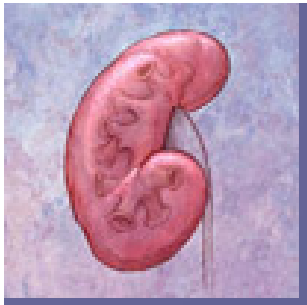


Definitions

- Calculated GFR
  - Serum creatinines through December 2003
  - Modified MDRD formula*
- CKD stage:
  - Stage 1: GFR > = 90 ml/min with proteinuria
  - Stage 2: GFR < 90 ml/min and > = 60 ml/min with proteinuria
  - Stage 3: GFR < 60 ml/min and > = 30 ml/min
  - Stage 4: GFR < 30 ml/min and > = 15 ml/min
  - Stage 5: GFR < 15 ml/min or on dialysis†

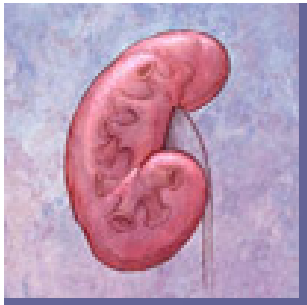
* Modified MDRD equation uses age, sex, race, and serum creatinine

† Dialysis identified by chart review of all patients with Stage > 3



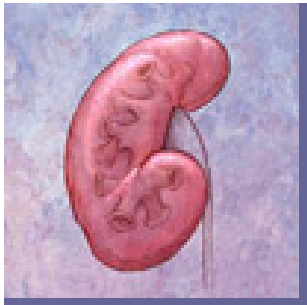
Data Sources

- GFR
  - Local DHCP laboratory database
- Demographics, comorbidities, death
  - Austin national inpatient database
  - Austin national benefits database
- Management
  - Medications: Local DHCP pharmacy database
  - Nephrologist care: Austin national outpatient database



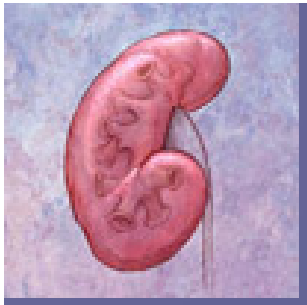
Data Sources

- CKD complications
  - Local DHCP laboratory database
    - Hypocalcemia (calcium < 8.5 mg/dL)
    - Hyperphosphatemia (phosphate > 4.5 mg/dL)
    - Anemia (hemoglobin < 12 mg/dL)
    - Hypoalbuminemia (albumin < 4.0 mg/dL)

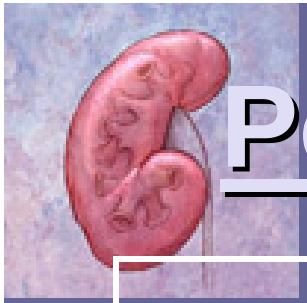


Analysis

- Created two groups: PCP-only and nephrology
- Cox proportional Hazards Analysis
  - Time spent in each stage
  - Time spent in early CKD (stages 1-3)
- Time calculated from first date reached a stage to first date reached higher stage or died
- Adjusted for comorbidity, demographics, medications, complications and propensity to see a nephrologist

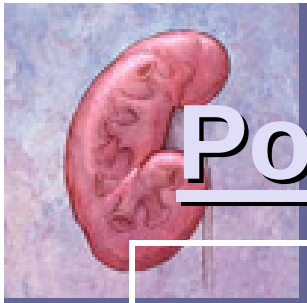


Results



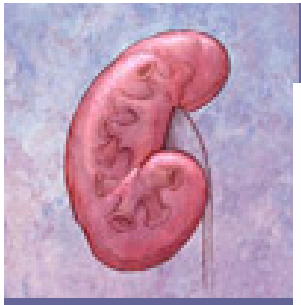
Population Characteristics

	Total	Nephrology	PCP-only	p-value
Number	1553	456	1097	
Days of follow-up (mean)	1296	1310	1285	0.3
Age (range)	70 (26-98)	68.7	70.3	0.01
Black race (%)	32%	33%	32%	0.77
Hospitalizations, mean (range)	2.6 (0-28)	2.8	2.5	0.03
Clinic visits, mean (range)	141 (7-1412)	170	129	0.0001
Lipid lowering agents (%)	39%	43%	38%	0.58
ACEIs (%)	52%	51%	52%	0.07

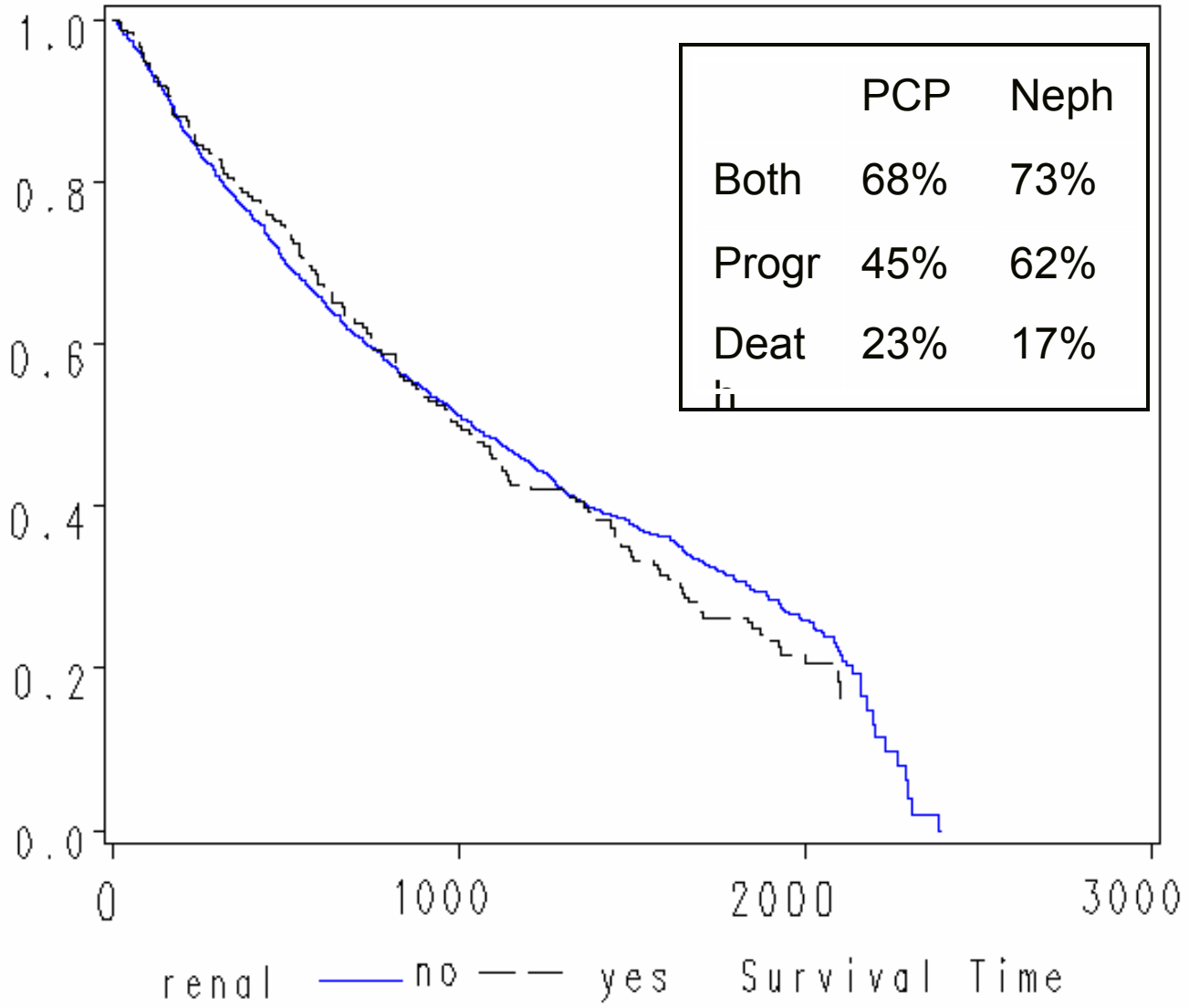


Population Characteristics cont

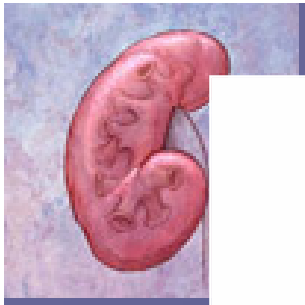
	Total	Nephrology	PCP-only	p-value
Diabetes (%)	52%	58%	49%	0.002
Hypertension (%)	92%	98%	90%	0.0001
Mean blood pressure <140/90(%)	37%	41%	36%	0.06
Proteinuria (%)	89%	75%	58%	0.0001
Tobacco use (%)	21%	21%	21%	1
Coronary Artery Disease (%)	49%	56%	57%	0.49
Hyperlipidemia (%)	24%	25%	24%	0.6
Hypocalcemia (%)	6%	6%	6%	0.82
Anemia (%)	9%	10%	9%	0.63
Hyperphosphatemia (%)	6%	9%	5%	0.006
Hypoalbuminemia (%)	50%	59%	49%	0.0002



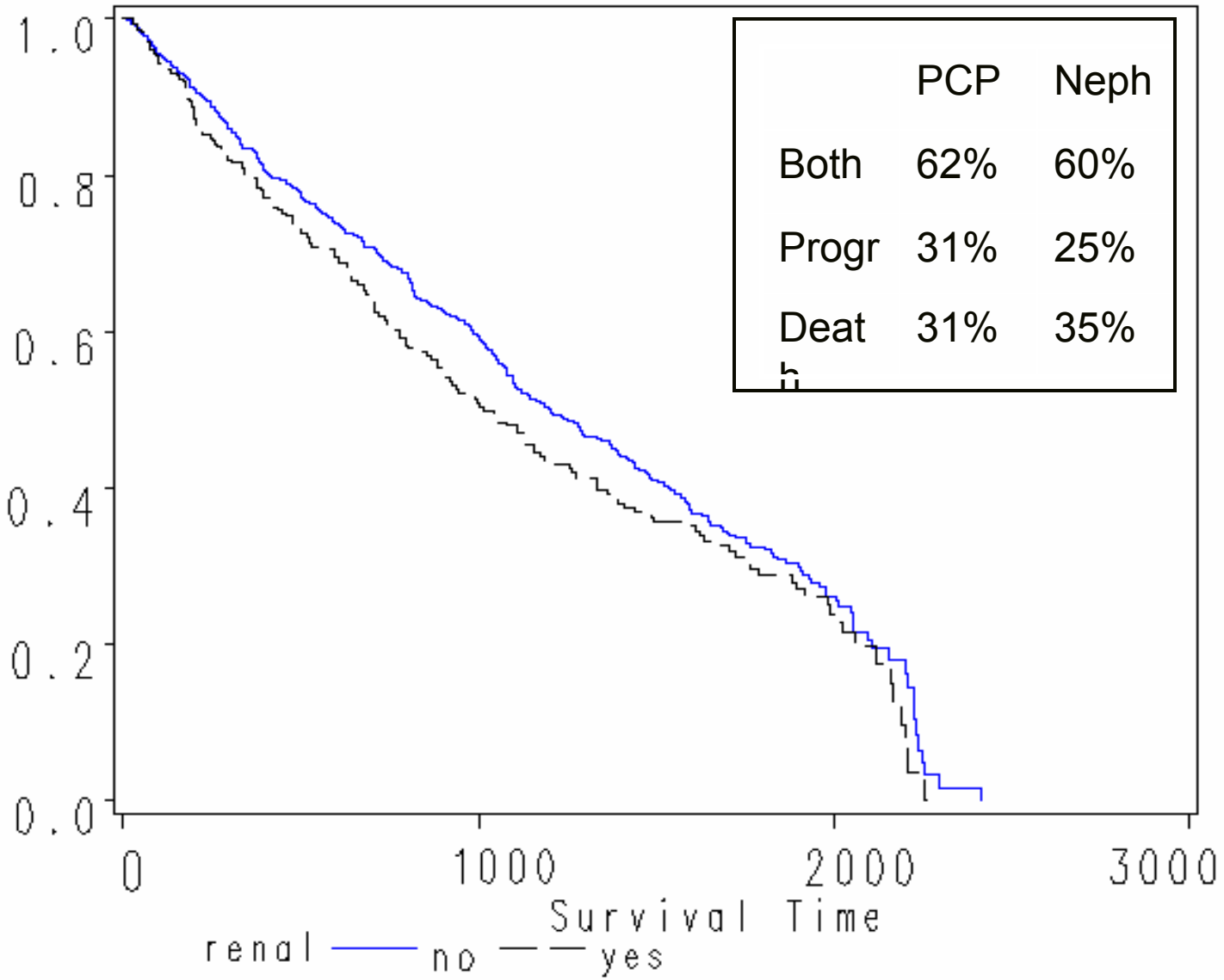
Survival Curve for Stage 1 to 2



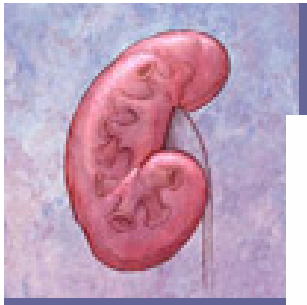
	PCP	Neph
Both	68%	73%
Progr	45%	62%
Deat	23%	17%



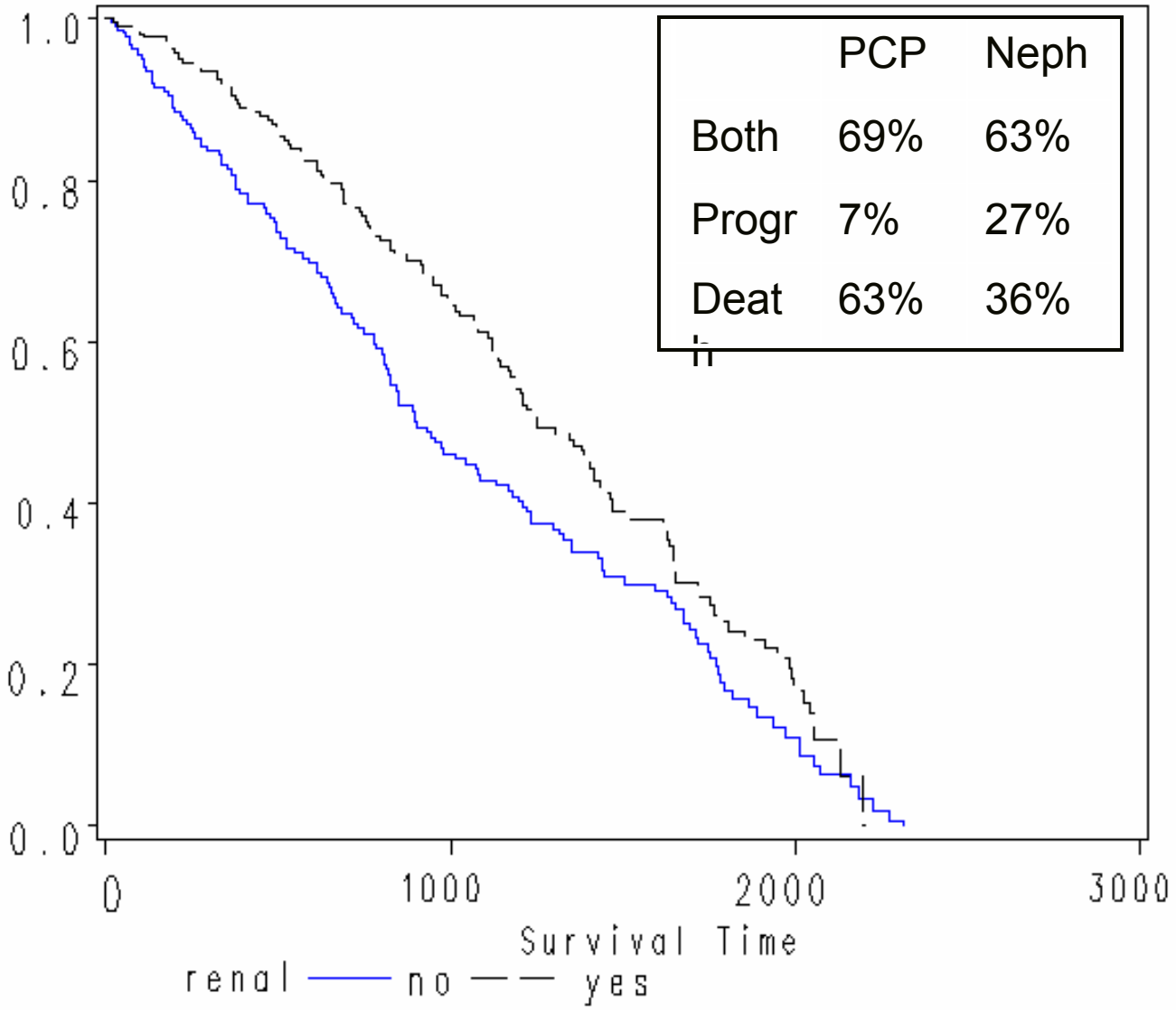
Survival Curve for Stage 2 to 3



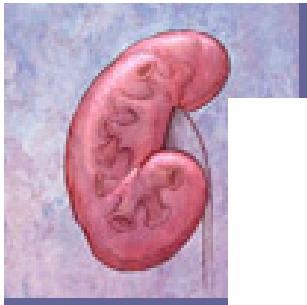
	PCP	Neph
Both	62%	60%
Progr	31%	25%
Death	31%	35%



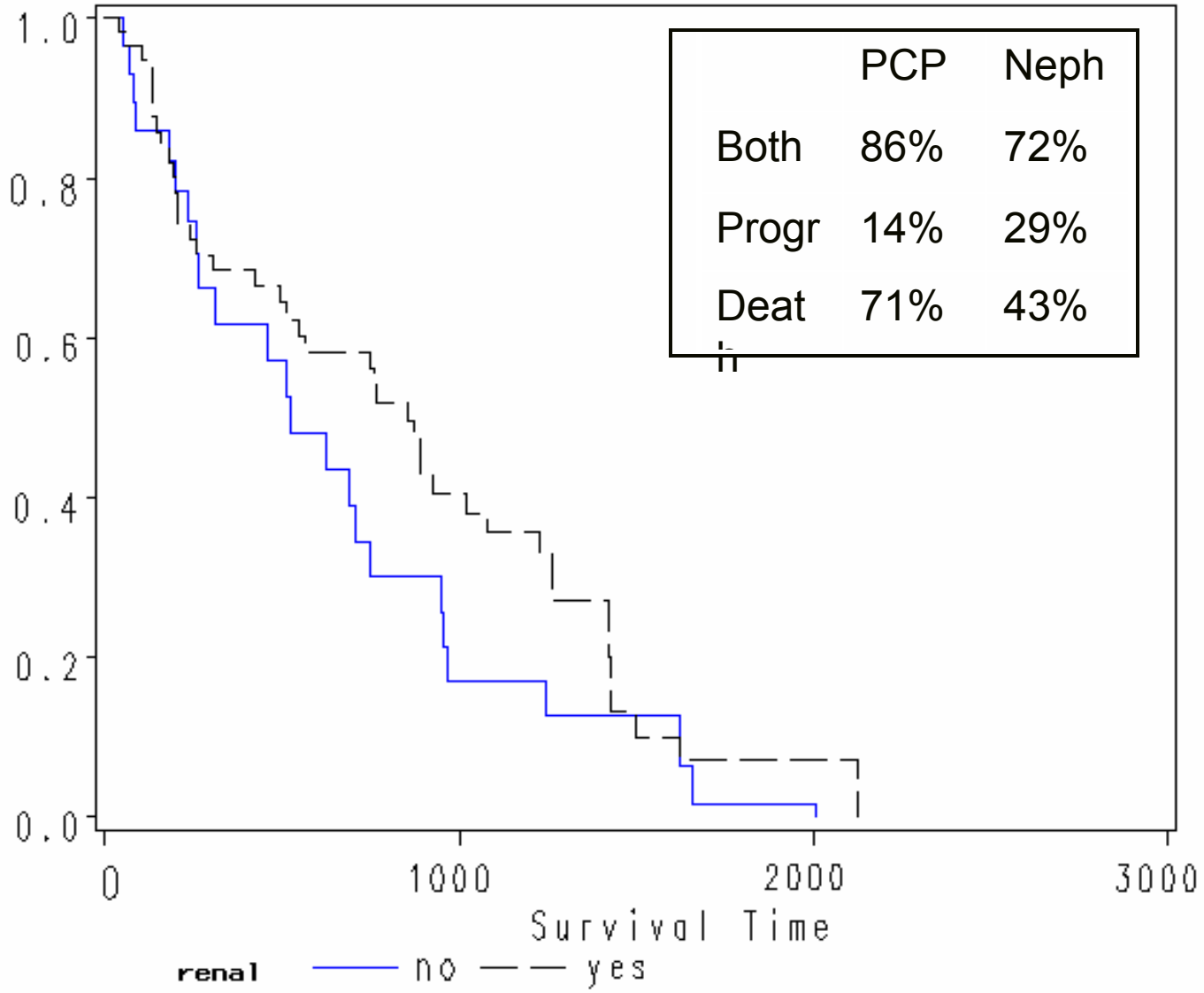
Survival Curve for Stage 3 to 4



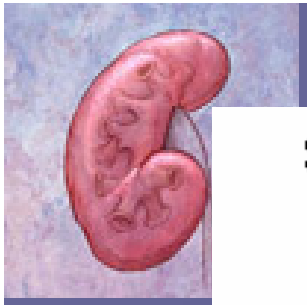
	PCP	Neph
Both	69%	63%
Progr	7%	27%
Death	63%	36%



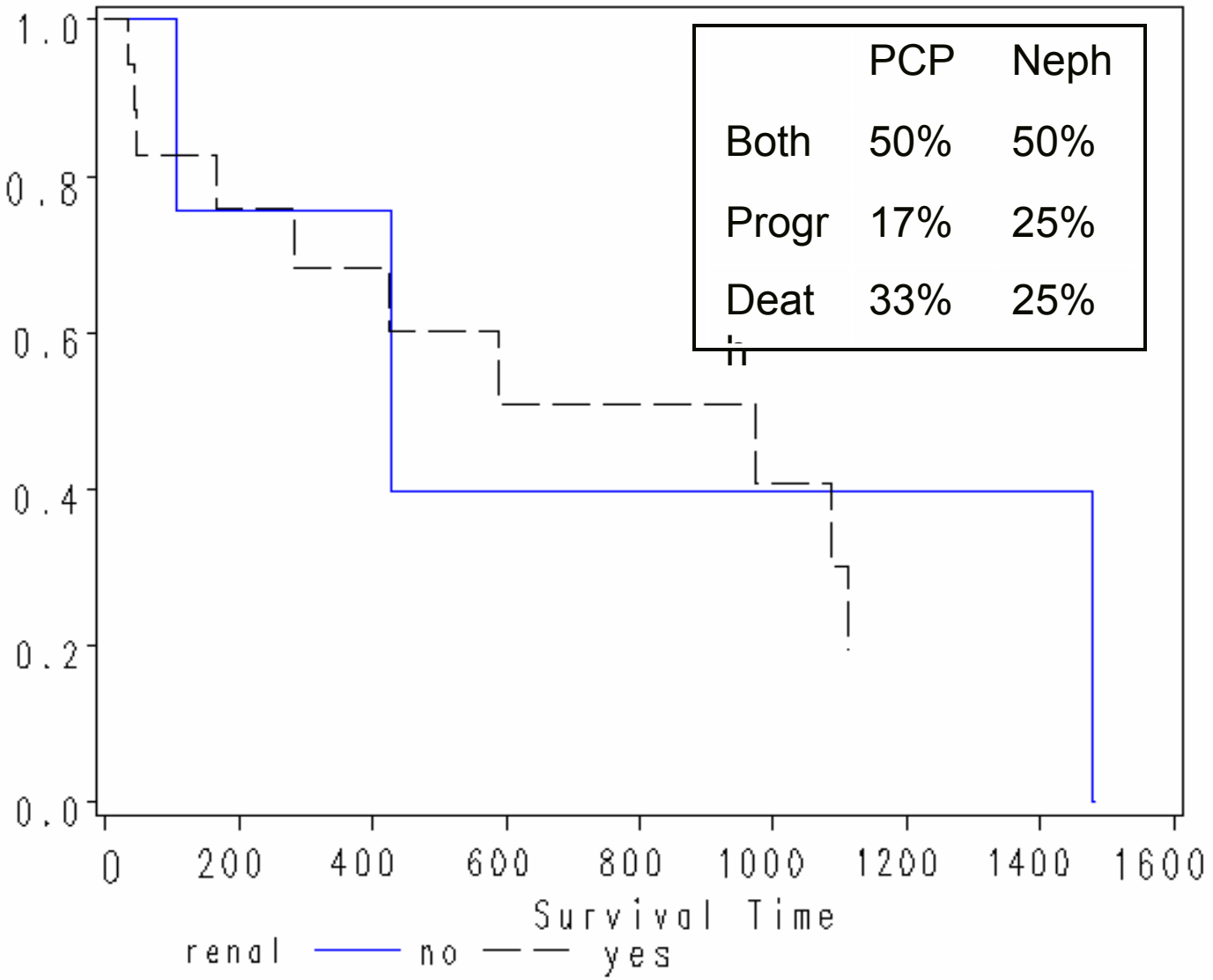
Survival Curve for Stage 4 to 5



	PCP	Neph
Both	86%	72%
Progr	14%	29%
Deat h	71%	43%

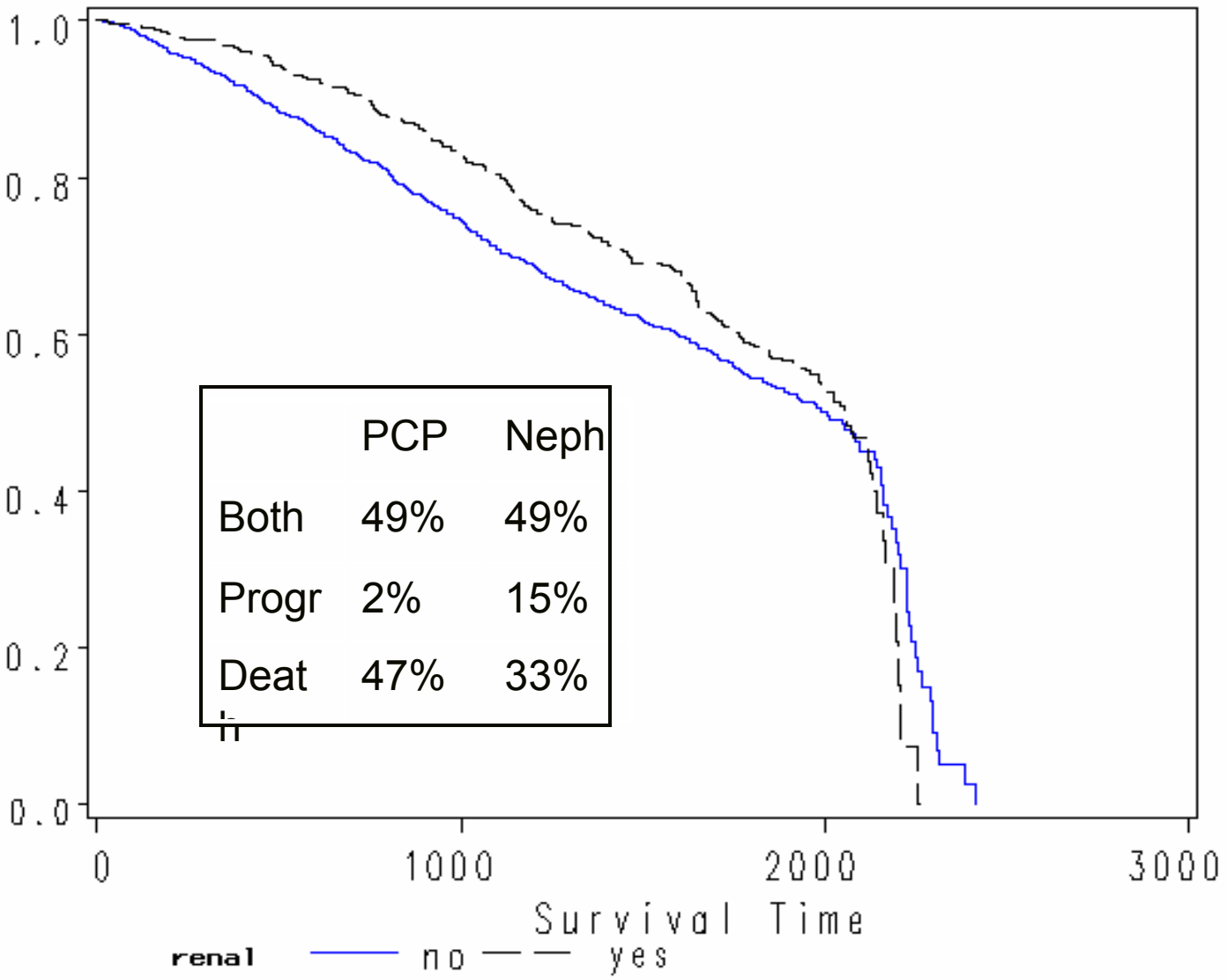


Survival Curve for Stage 5 to Dialysis

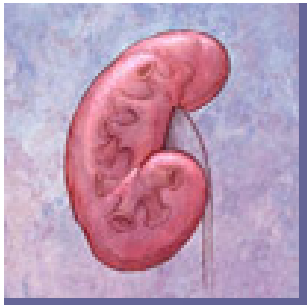


	PCP	Neph
Both	50%	50%
Progr	17%	25%
Death	33%	25%

urvival Curve for Early CKD to Advanced CKD



	PCP	Neph
Both	49%	49%
Progr	2%	15%
Death	47%	33%

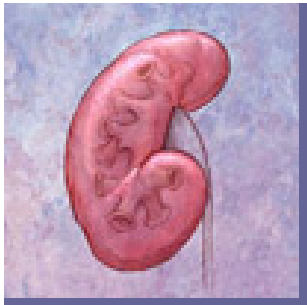


Summary

- Those followed by a nephrologist at CKD stages ≥3 had less disease progression and fewer deaths

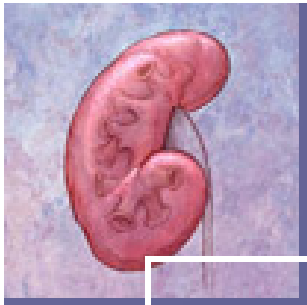
  ⇒ Supports guideline recommendations for early referral

- Mortality is profound
  - At CKD stages ≥ 2 more people died than progressed



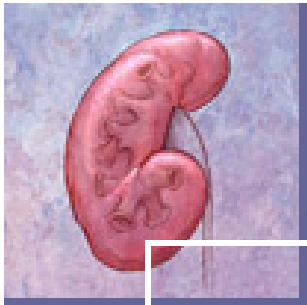
Limitations

- Retrospective study design
  - Reliance on ICD-9 codes for comorbidities
  - Loss of patients as they leave the system
- Creatinine rather than GFR used to identify cohort
- Unable to account for unmeasured bias in referral to nephrologists



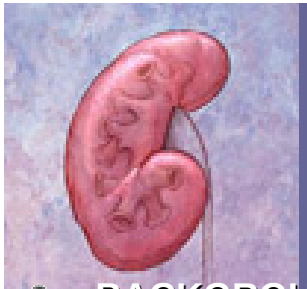
Survival Analysis

	Stage 1 to 2	Stage 2 to 3	Stage 3 to 4	Stage 4 to 5	Stage 5 to ESRD
Unadjusted median days to endpoint	1149	1206	1158	794	709
PCP-only vs Nephrology p-value	0.41	0.32	<0.0001	0.03	NA
Number PCP-only group	995	624	209	28	6
No. with CKD progression	445	156	14	4	1
No. died	231	217	131	20	2
No. with composite endpoint (%)	676 (68%)	376 (60%)	145 (69%)	24 (86%)	3 (50%)
Number Nephrology group	222	263	207	58	20
No. with CKD progression	138	120	56	17	5
No. died	24	53	74	25	5
No. with composite endpoint (%)	162 (73%)	173 (65%)	130 (63%)	42 (72%)	10 (50%)



Survival Analysis Hazard Ratios

	Stage 1 to 2	Stage 2 to 3	Stage 3 to 4	Stage 4 to 5	Pre-ACKD to ACKD
Age	1	1.01	1	1.02	1
Race	0.71*	0.89	1.11	1.24	0.82*
ACEI	1.1	0.62*	0.68*	0.96	0.53
ACEI started during stage	0.73*	1.13	1.03	2.14	NA
Anti-lipid medications	0.64*	0.57*	0.54*	0.71	0.46*
Diabetes	1.32*	1.18	1.13	NA	1.31*
Hypertension	0.8	0.9	0.9	NA	0.85
Tobacco use	1	0.79	0.92	NA	0.89
Vascular Disease	1.35*	1.52*	0.86	NA	1.54*
High HgA1c	1.14	1.28*	1.53*	NA	1.33*
Positive Urine Protein	1	1	1.12	NA	1.46*



- **BACKGROUND:** Chronic kidney disease (CKD) affects 11% of the U.S. population, about 20 million people. Improving the management of CKD increases survival in those with CKD, prolongs development of end-stage renal disease (ESRD), and improves morbidity and mortality once ESRD develops. Slowing progression and delaying ESRD are now more important than ever as the incidence of CKD is increasing, in large part due to an increasing prevalence of CKD risk factors such as age, hypertension, and diabetes. These concerns have lead investigators to retrospectively evaluate the timing of nephrology referral on the morbidity and mortality of dialysis populations. Based upon the results of these preliminary studies, experts have recommended early referral to nephrology specialists. However, widespread implementation has been limited by the capacity of currently practicing nephrologists. To better evaluate the exact role and timing of nephrology intervention we examined the relationship between the severity of CKD, the presence of subspecialty care, and progression in a pre-ESRD population.
- **METHODS:** We retrospectively identified a cohort of veterans with primary care providers at the Durham, NC VA hospital who had CKD, defined as two abnormal outpatient serum creatinines (> 1.3 mg/dL) at least 3 weeks apart between January 1, 1998 and December 31, 1999. We gathered data from cohort inception until December 31, 2004 on disease course, CKD-related complications, medications, comorbidities, and mortality. Disease course, the time spent in each CKD stage, was evaluated using a Cox proportional hazards model adjusted for demographics, comorbidites, medications, and a propensity score for two groups: those followed by a primary care provider only and those followed by a nephrologist. We used the propensity score to adjust for bias in patients referred to nephrologists.
- **RESULTS:** We found 1,553 veterans with CKD, a prevalence of 13%. The mean age was 70 years, all were male, 33% were African-American, >90% had hypertension and >50% had diabetes and coronary artery disease. 50% used angiotensin converting enzyme inhibitors (ACEI) and less than 3% used erythropoietin. The median number of days spent in each CKD stage was as follows: stage 1 -1,149, stage 2 -1,206, stage 3 -1,158, stage 4 -794, and stage 5 -709. There was no difference in survival between the two groups during stage 1 or 2; but during stages 3 through 5 individuals in the nephrology group spent an average of 152 days more in each stage. ACEIs and statins slowed progression while HgbA1c values>7.0% and vascular disease accelerated it.
- **CONCLUSIONS:** These data suggest that an appropriate time for referral to a nephrologist for patients with CKD may be around stage 3. Prospective studies are needed to further clarify the role and timing of nephrologists in the early stages of CKD.