

Clinical Approach to the Patient At-Risk for Kidney Disease: Rationale for Testing for Serum Creatinine and Albuminuria

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CKD Detection Program

USRDS

Disclosures

- Institutional research funding: NIH, CDC, National Kidney Foundation, Amgen, Baxter, Sigma Tau, NxStage, Genzyme, BMS, AMAG Pharmaceuticals
- Advisory boards in last year: WHO Advisory Panel on NCDs, Kidney Disease Improving Global Outcomes (KDIGO), International Federation of Kidney Foundations (IFKF), International CKD Detection Network
- Epidemiology consulting: NxStage, Amgen, Affymax

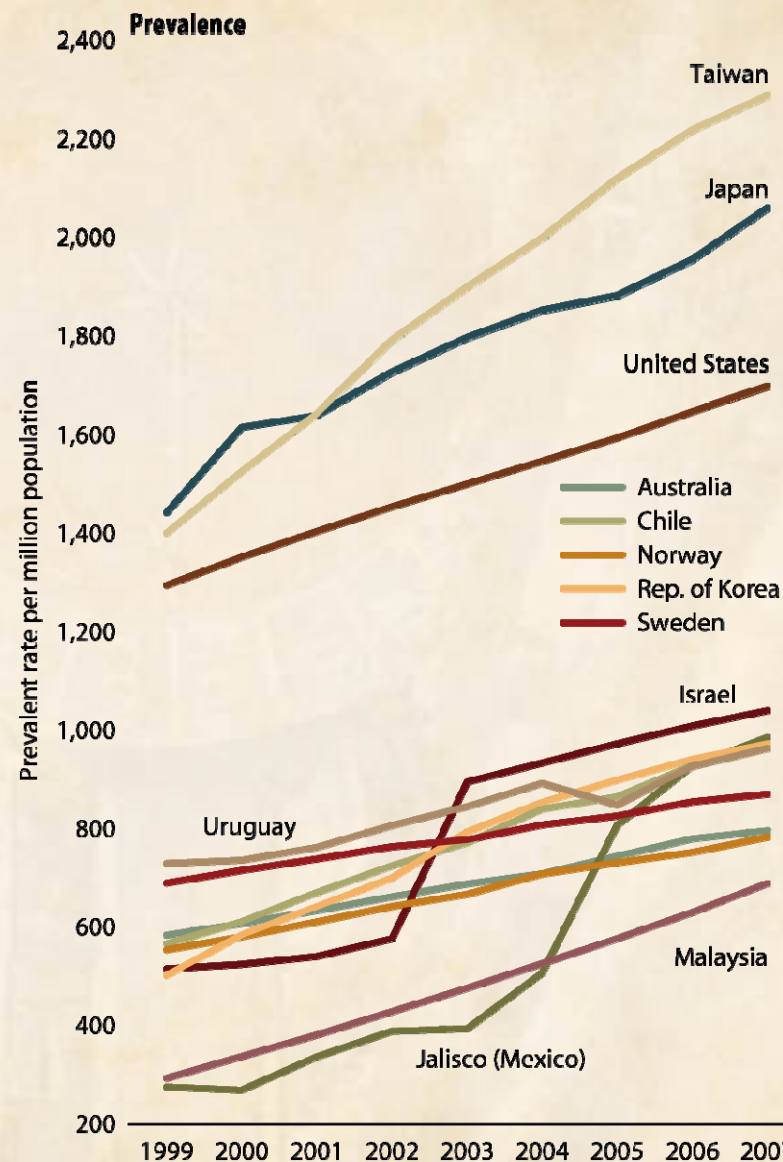
Why Should Kidney Disease be Assessed as a Major Chronic Disease?

- The ESRD population at less than 1% of the population may not justify a public health detection program for CKD
- However, on a health care cost basis ESRD is a very expensive disease costing up to \$75,000 US dollars/patient each year
 - ESRD is the most expensive chronic disease since the costs are continuing and ongoing until death
 - Hospitalization rates are the highest in the ESRD population
 - Not only is dialysis expensive but also the injectable medications to treat complications
 - The ESRD population is growing consuming an increasing part of the health care budget which is a major concern!
- Policy makers in High and Lower income countries have begun to question the ever increasing ESRD population costs when there is no concerted effort to prevent it.

Comparison of ESRD prevalence worldwide

Figure 12.1 (continued; Volume Two)

Data presented only for those countries from which relevant information was available; "." signifies data not reported. All rates are unadjusted. ^UK: England, Wales, & Northern Ireland (Scotland data reported separately). Data from Argentina, Czech Republic, Israel, Japan, Luxembourg, Shanghai, & Taiwan are dialysis only. *Latest data for Canada, Germany, Iran, Luxembourg, Pakistan, Russia, & Shanghai are for 2006. Data for France include 13 regions in 2005, 15 regions in 2006, & 18 regions in 2007.

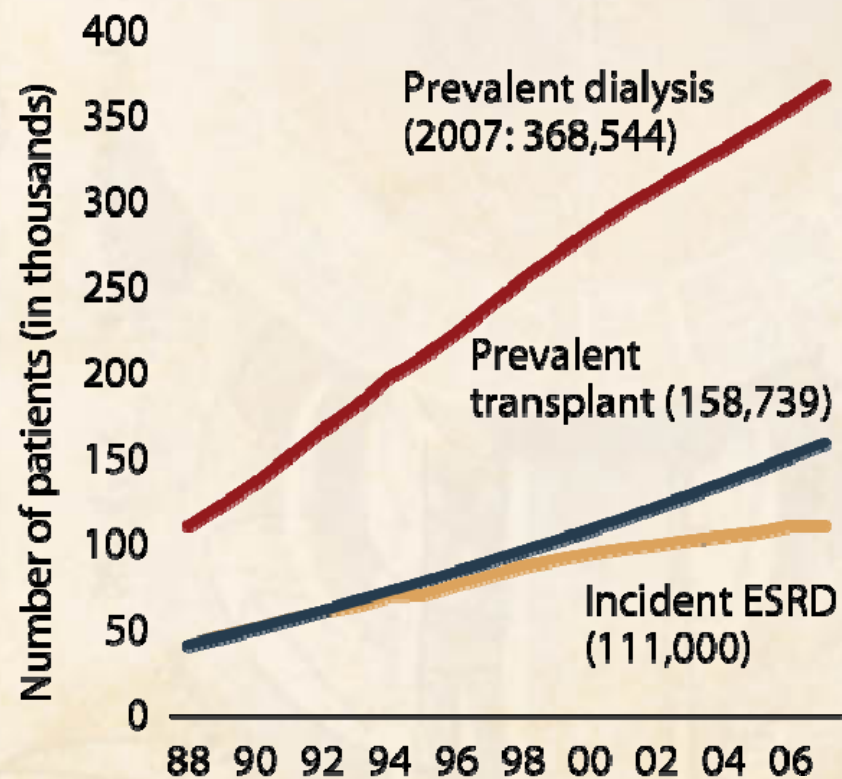


The growth of the ESRD population is being driven by improved survival and returning transplant patients!

- **ESRD incident rates growth have begun to slow and in some cases actually decline in some countries of the World**
- **Death rates have declined which drives up the prevalent population**
- **The lack of improvement in the transplant graft survival rates after the first year has led to an increasing number of patients returning to dialysis thereby contributing to the expensive growth of the dialysis population.**

Patient counts, by modality

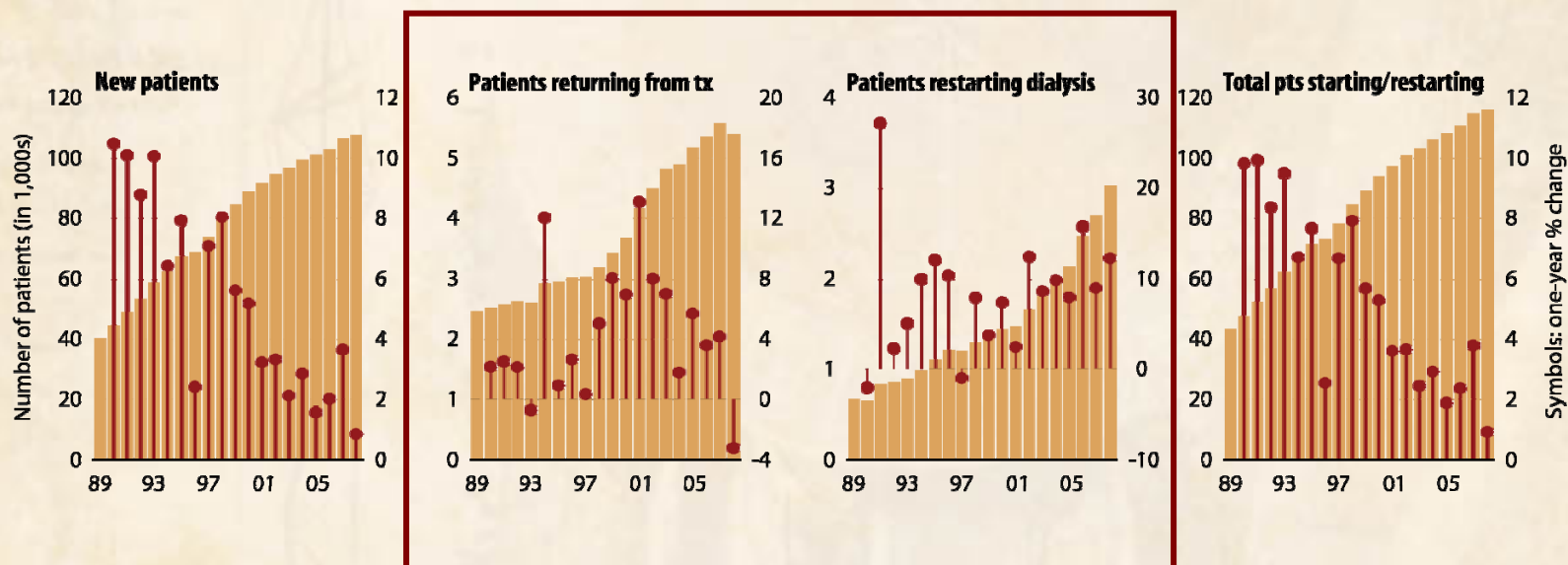
Figure p.3 (Volume 2)



Incident & December
31 point prevalent
patients.

Counts of new & returning dialysis patients

Figure p.2 (Volume 2)



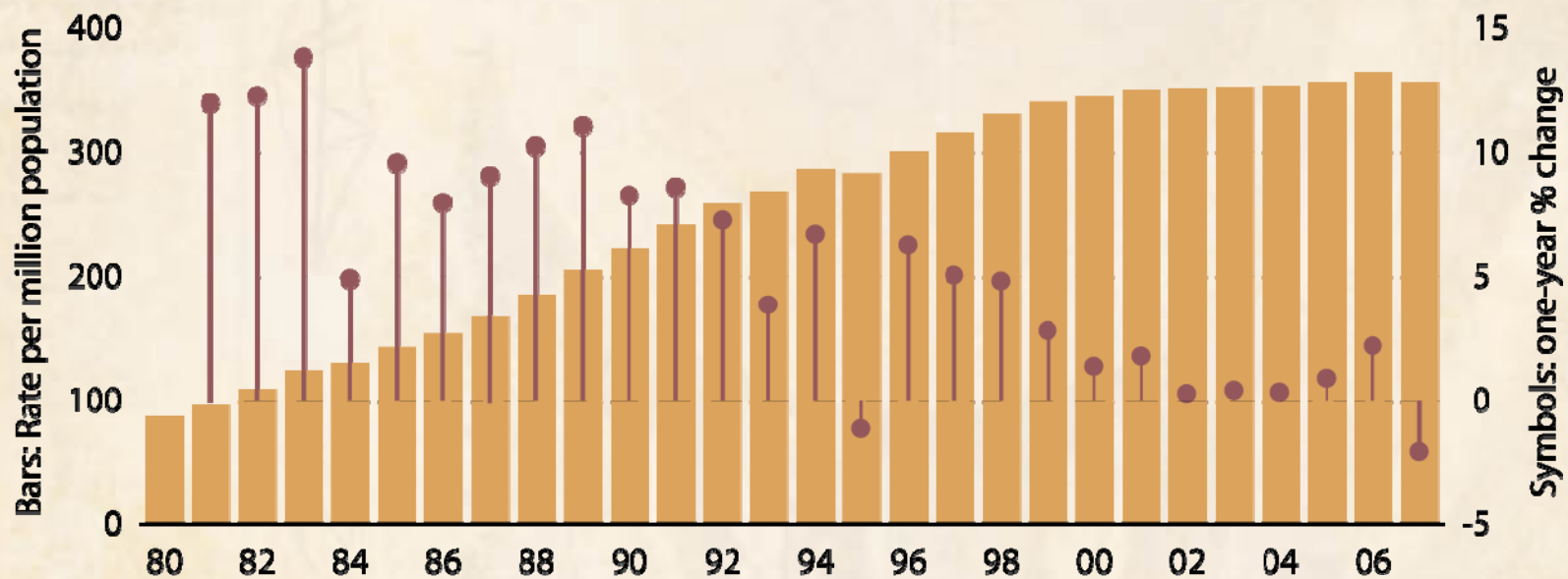
CMS Annual Facility Survey.

USRDS 2009 ADR



Adjusted incident rates & annual percent change

Figure 2.3 (Volume 2)



Incident ESRD patients; rates adjusted for age, gender, & race.

USRDS 2009 ADR

USRDS

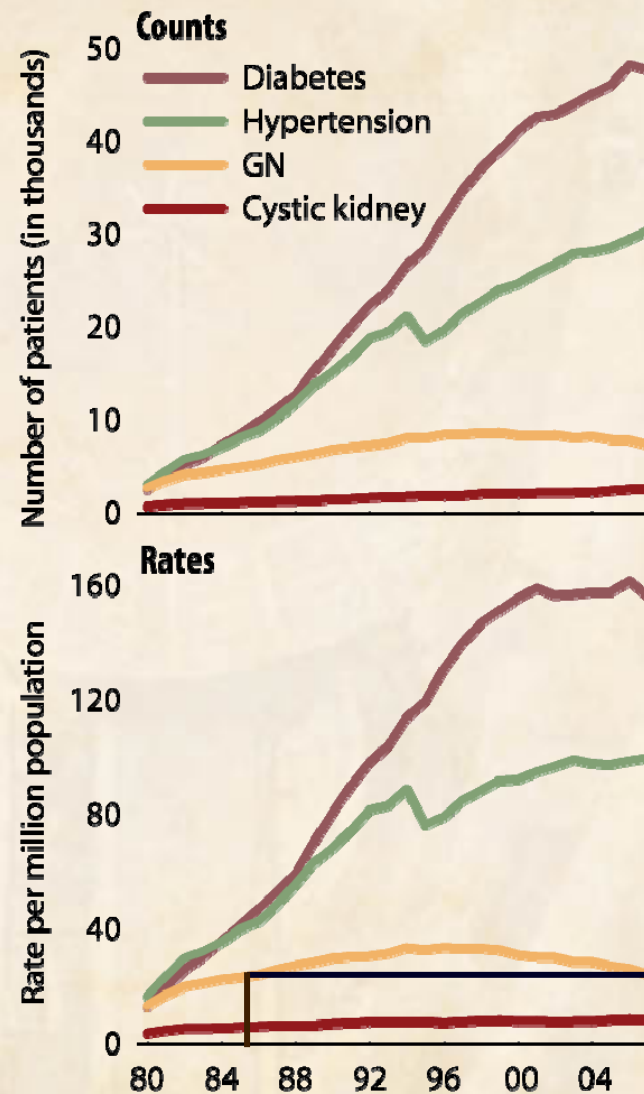
Incident counts & adjusted rates, by primary diagnosis

Figure 2.8 (Volume 2)

ESRD rates from GN have fallen to levels in the 1980s!

Incident ESRD patients; rates adjusted for age, gender, & race.

USRDS 2009 ADR



Adjusted incident rates of ESRD due to diabetes, by age, race, & ethnicity

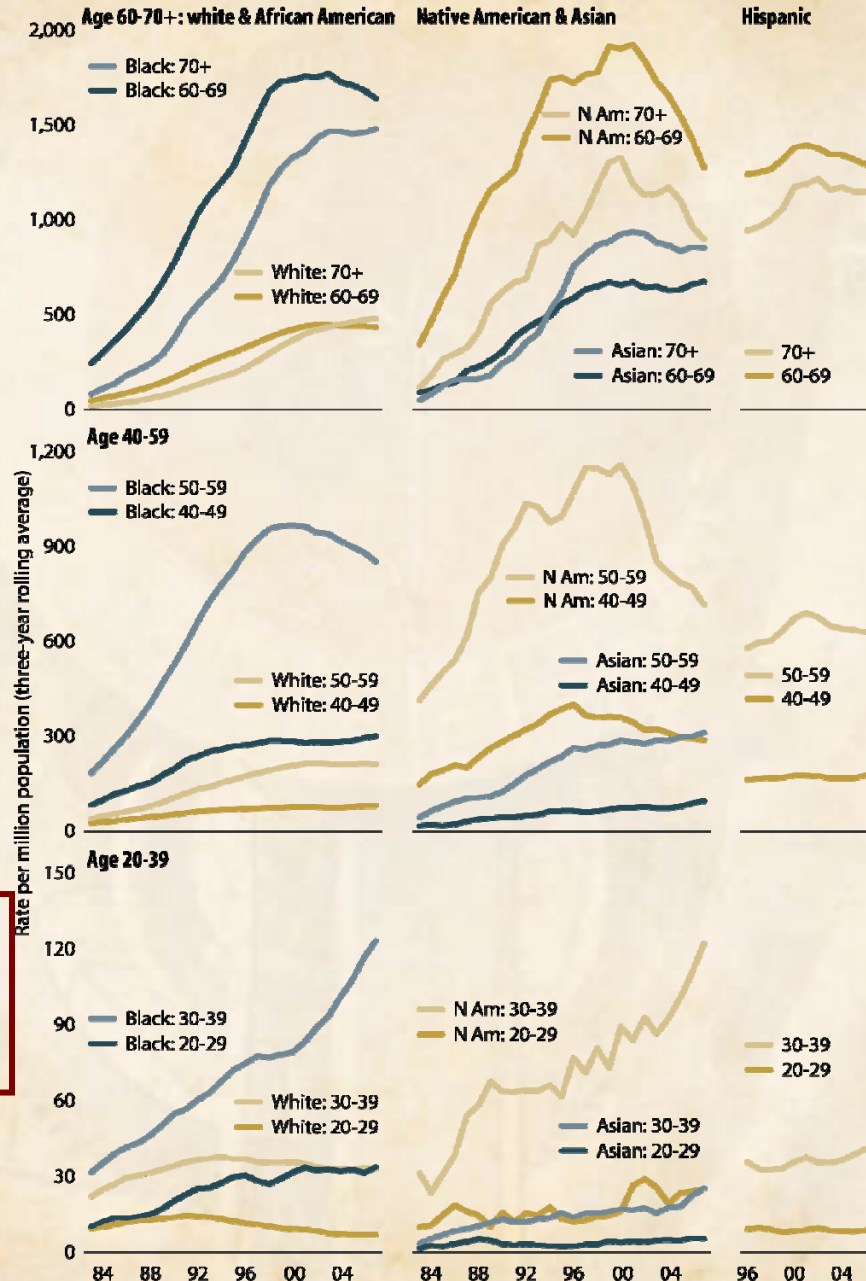
Figure 1.21 (Volume 2)

ESRD rates due to Diabetes have fall for minorities over age 40!

Younger minority Populations have increasing ESRD rates due to Diabetes!

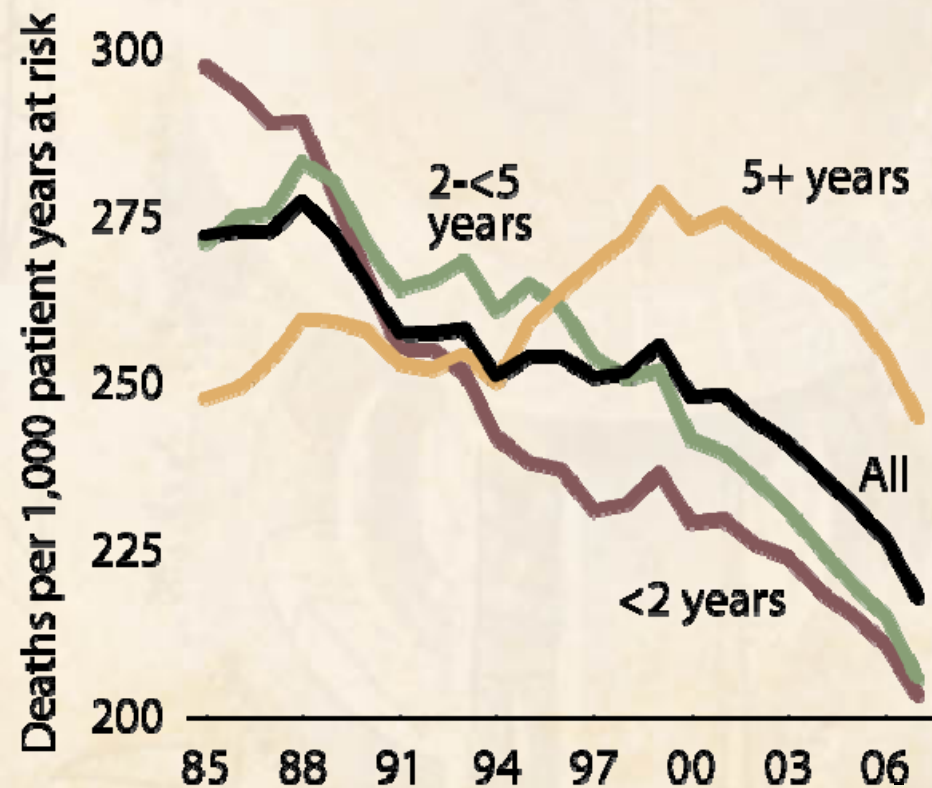
Incident ESRD patients.

USRDS 2009 ADR



Adjusted mortality rates, by vintage

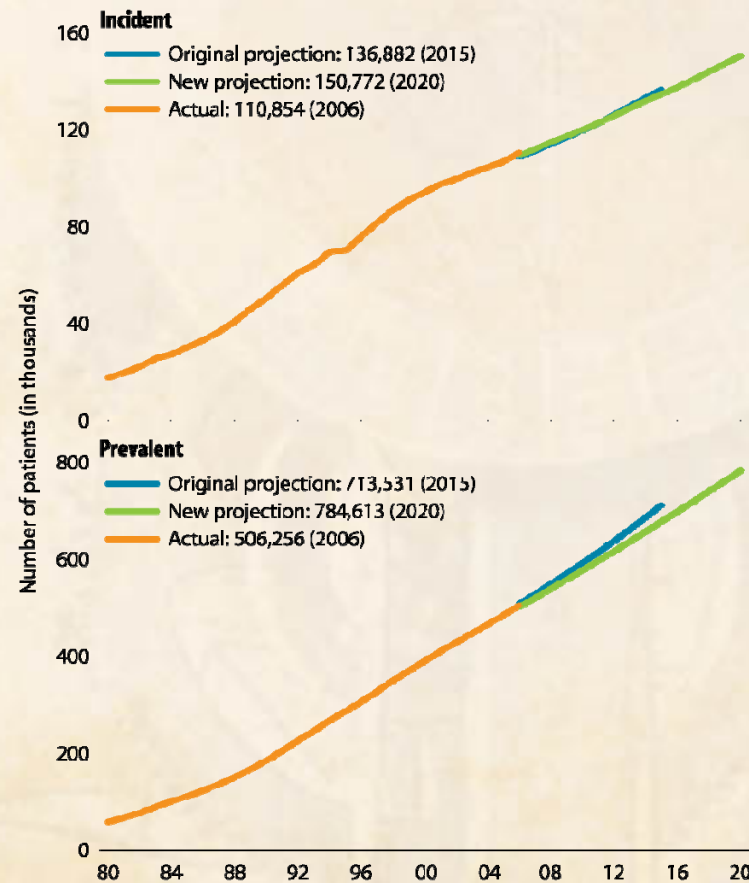
Figure 6.7 (Volume 2)



Period prevalent dialysis patients; adjusted for age, gender, race, & primary diagnosis. Dialysis patients, 2005, used as reference cohort.

Projected counts of incident & prevalent ESRD patients through 2020

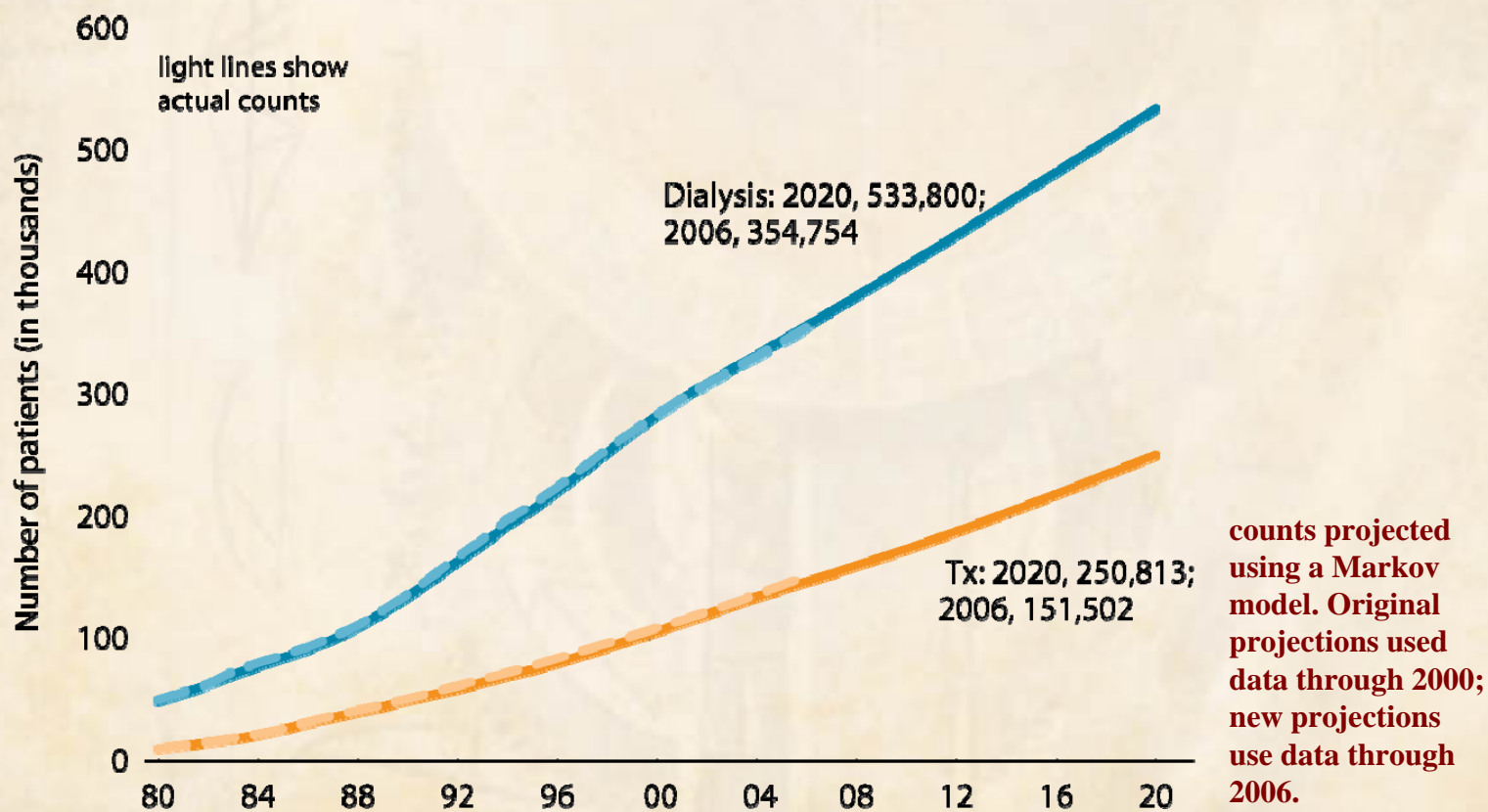
Figure 2.1 (Volume 2) USRDS 2008 ADR



counts projected using a Markov model. Original projections used data through 2000; new projections use data through 2006.

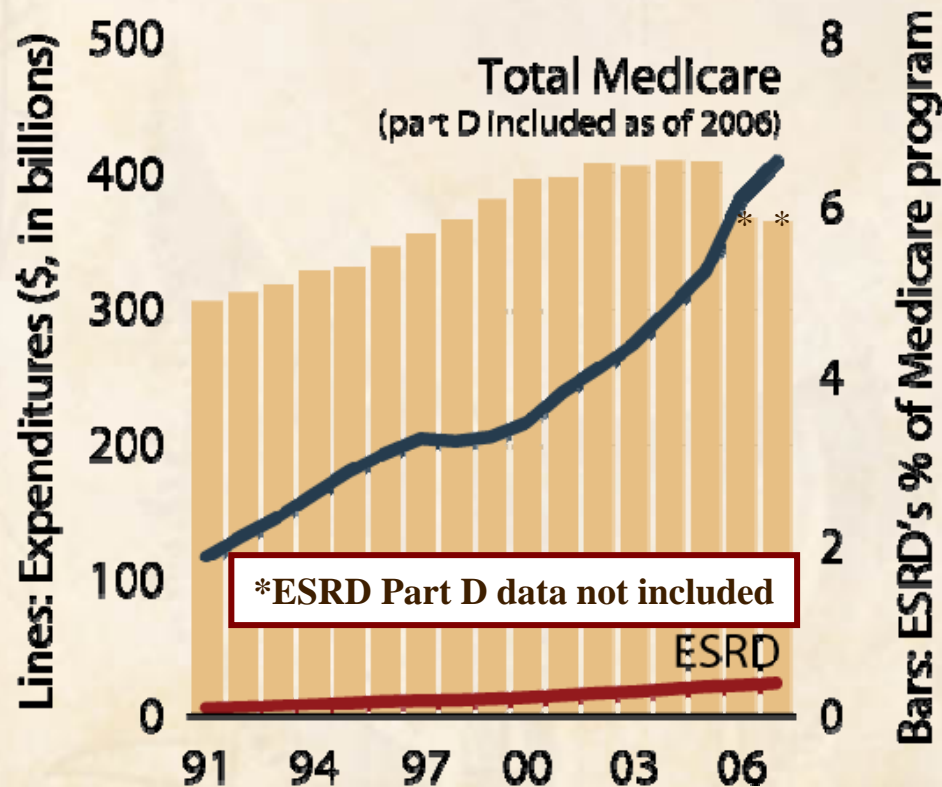
Projected growth of prevalent dialysis & transplants populations

Figure 2.2 (Volume 2) USRDS 2008 ADR



Costs of the Medicare & ESRD programs

Figure 11.2 (Volume 2)



Total ESRD expenditures are from paid claims (Table K.2) as well as estimated costs for HMO & organ acquisition. ESRD costs in 2007 are inflated by 2 percent to account for costs incurred but not reported. Total Medicare expenditures obtained from the CMS Office of Financial Management, Division of Budget. Data for 2006 & 2007 include Part D amounts for total Medicare, but no Part D amounts for ESRD.

The Cost of Inaction is too high to just let the ESRD program just grow!

- **High income countries are facing the increasing costs of the ESRD program**
 - **Japan ESRD costs 4.5% of their total Health Care Budget!**
 - **In Taiwan, which has the high incidence and prevalence rates, ESRD consumes 8.5% of their total Health Care Budget**
- **Low and middle income countries are struggling just to create primary care system and beginning to address chronic diseases such as Diabetes and heart Disease such that they simply cannot afford to treat all the ESRD patient**
- **The only rational answer is to address prevention but HOW?**

Principle of designing a detection program for kidney disease-1

- **Public Health detection programs are, by their nature, crude methods to find the most individuals with a potential disease while minimizing the number of false positives**
- **Once an individual goes through a detection program, referral to the medical system is intended to lead to greater precision in the diagnosis thereby farther reducing the false positives before more detailed evaluations are made which add cost and potential risk**

Principle of designing a detection program for kidney disease-2

- **Detection programs should use simple tests that are easily available in routine medical practice thereby reducing the complexity of the detection effort**
- **The message must be directed at educating not just the professionals but the general public about the disease! (It is not just about the doctors!) (WKD: Common, Harmful and Treatable)**
- **Detection programs are population tools that are intended to find the greatest number of possible cases to address awareness, treatment and control of risk factors to reduce morbidity and mortality**

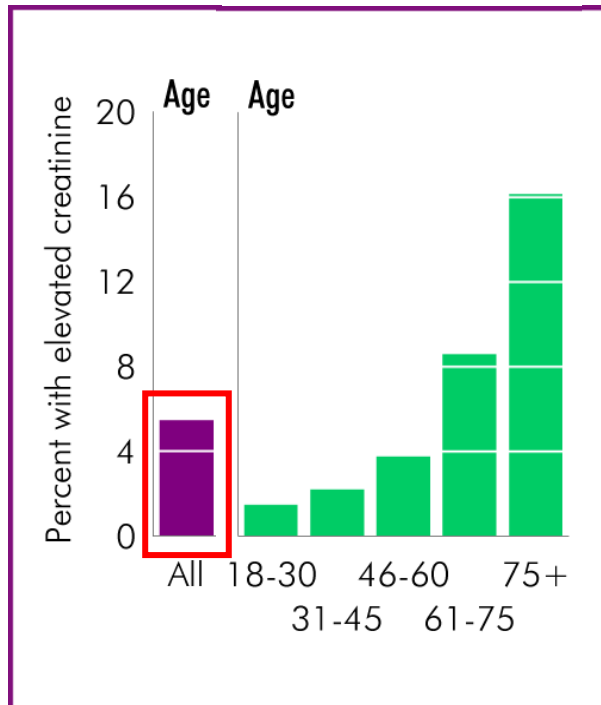
Approach to defining the target CKD population

- Use the ESRD population major diseases to target the general population at risk
 - United States Kidney Early Evaluation Program
 - Started in 1997
 - Targeted populations with Diabetes, Hypertension, a family history of the diseases or of kidney disease (Diabetes and hypertension account for 71% of the ESRD cases)
 - No specific age group
 - Targets families with genetic diseases such as diabetes and hypertension
- Population level specificity, sensitivity and decision tree analyses: Classic risk factor analysis
- Both need cost effectiveness studies

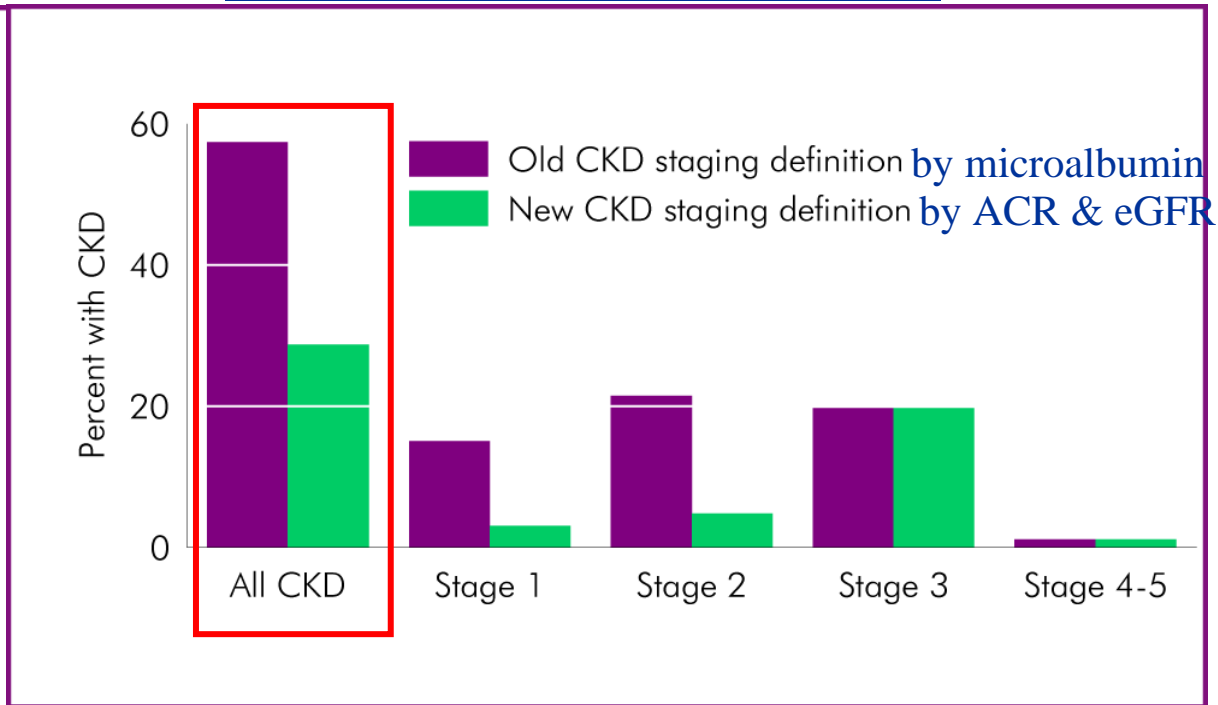
Figures 5.1 & 5.3 KEEP ADR 2007

Elevated serum creatinine levels and CKD by staging in KEEP participants

CKD by Creatinine



CKD by staging system



KEEP N = 52,892.

Elevated serum creatinine

Male > 1.5 mg/dl
Female > 1.3 mg/dl

CKD Stages

Stage 1: eGFR \geq 90, ACR \geq 30 mg/g
Stage 2: eGFR 60–89, ACR \geq 30 mg/g
Stage 3: eGFR 30–59
Stage 4: eGFR 1–29
Stage 5: eGFR < 15 or patient on dialysis

+ Microalbuminuria
> 20 mg/l



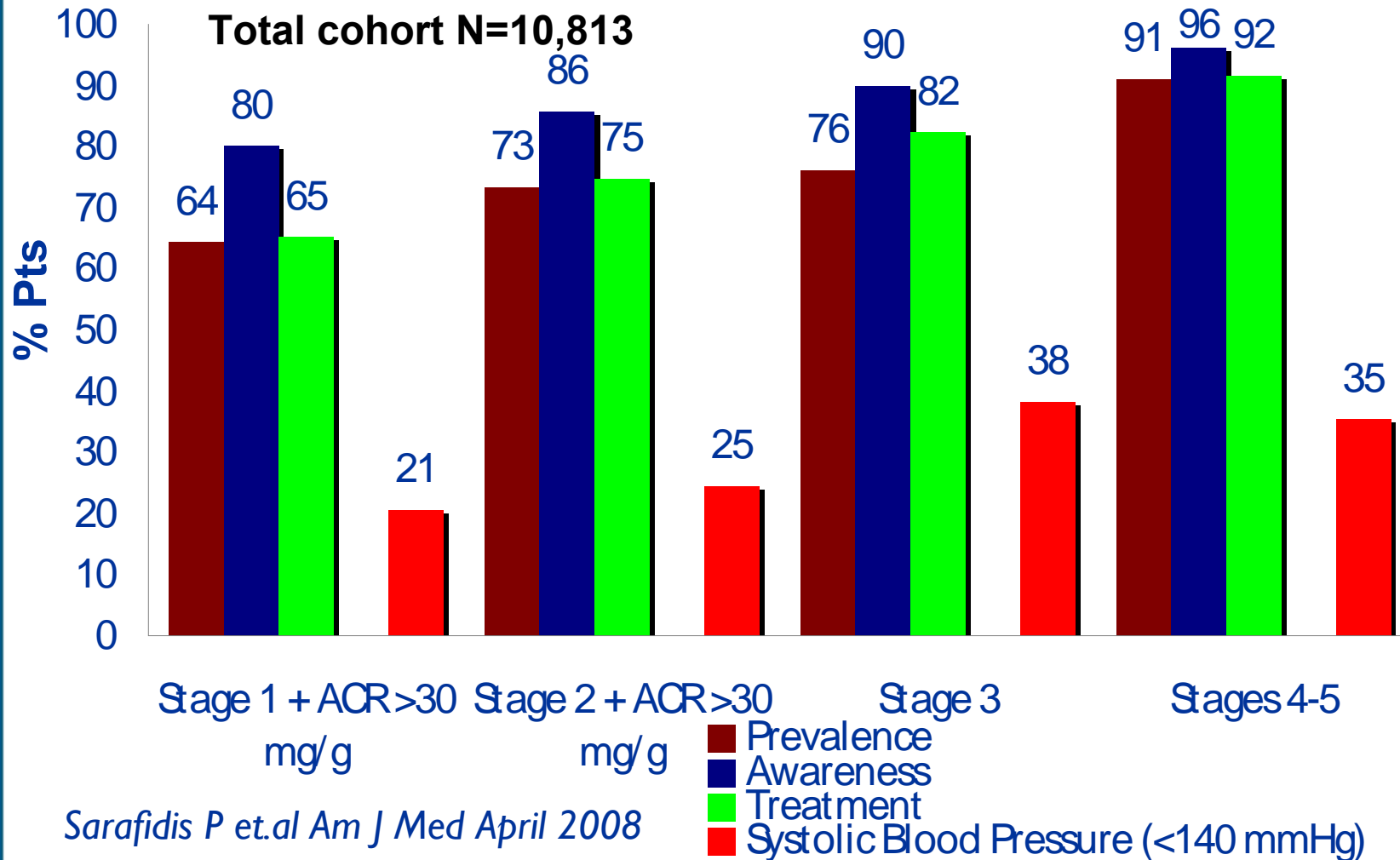
Hypertension Awareness, Treatment, and Control in Chronic Kidney Disease*

Pantelis A. Sarafidis, MD, PhD, Suying Li, PhD, Shu-Cheng Chen, MS, Allan J. Collins, MD, Wendy W. Brown, MD, MPH, Michael J. Klag, MD, MPH, George L. Bakris, MD

- **Hypertension prevalence, awareness, treatment, and blood pressure control rates in the population with chronic kidney disease are limited**
- **The objective of this study was to determine the state of blood pressure control in patients with chronic kidney disease.**
- **Study cohort from the NKF KEEP system**

***Sarafidis P et.al Am J Med 2008**

Prevalence, Awareness, Treatment, and Control of HTN in KEEP Cohort by CKD stage with <140/90 mmHg as goal



Participants in detection programs follow-up with their doctors!

- **Participants are given educational materials and encouraged to see their doctors**
- **Doctors receive CKD practice guidelines for care**
- **Follow-up increases with increasing evidence of CKD**
- **Participant see their doctors about BP and kidney tests results**

Likelihood of KEEP participants seeing their Doctor in follow-up based on eGFR*

eGFR	Odds Ratio (CI)	P-Value
• < 30	3.81 (2.29-6.31)	< 0.0001
• 30-< 40	1.58 (1.23-2.04)	0.0004
• 40-< 50	1.65 (1.39-1.96)	< 0.0001
• 50-< 60	1.37 (1.21-1.56)	< 0.0001
• 60-< 70	1.04 (0.94-1.16)	0.4534
• 70-< 80	1.05 (0.94-1.16)	0.4029
• 80-< 90	0.93 (0.83-1.04)	0.1901
• ≥ 90	1.00 REF.	

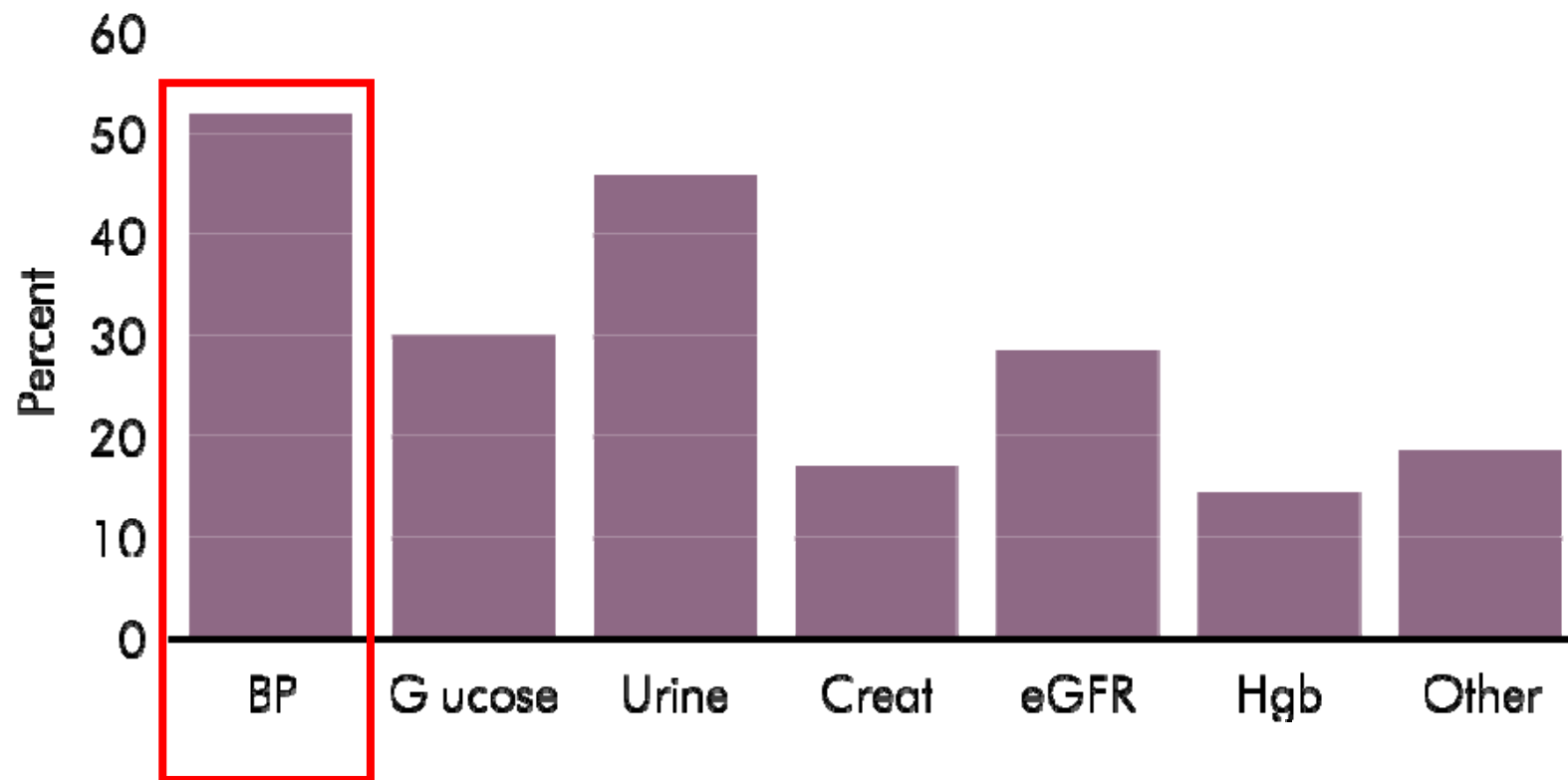
N=17,853

Collins et al AJKD Vol 51, pages S69-S76 2008

•Estimated glomerular filtration rate, mL/min per 1.73 m²

Figure s.22

KEEP participants who return their follow-up forms & reasons for seeing a doctor about their test results



CKD Public health detection programs throughout the year

- **The Kidney Early Evaluation Program KEEP is now routinely operating in Japan, Mexico, United States, and the United Kingdom**
- **The Australian Kidney Evaluation for You (KEY) is modeled after the KEEP program with similar findings**
- **The International CKD detection network is developing with at least 10 countries meeting in Geneva in September 2009**
- **CKD and Public health was presented at the World Congress of Nephrology in Milan**
 - **There have been at least three specific public health forums on CKD in Australia, Brazil and Turkey this May with Ministries of Health**
- **The United States requested WHO add CKD to the non-Communicable Disease agenda thru an official letter to WHO Secretary General Margaret Chan, MD in December 2008**

Public Health approach to defining the CKD population

- **Determine prevalence of disease**
- **Determine predictors of the disease**
- **Develop appropriate targets of risk for death**
- **Develop decision tree analyses when the disease is highly interactive and colinear with other chronic diseases**

Odds of CKD, by risk factor: Classic independent risk factor approach

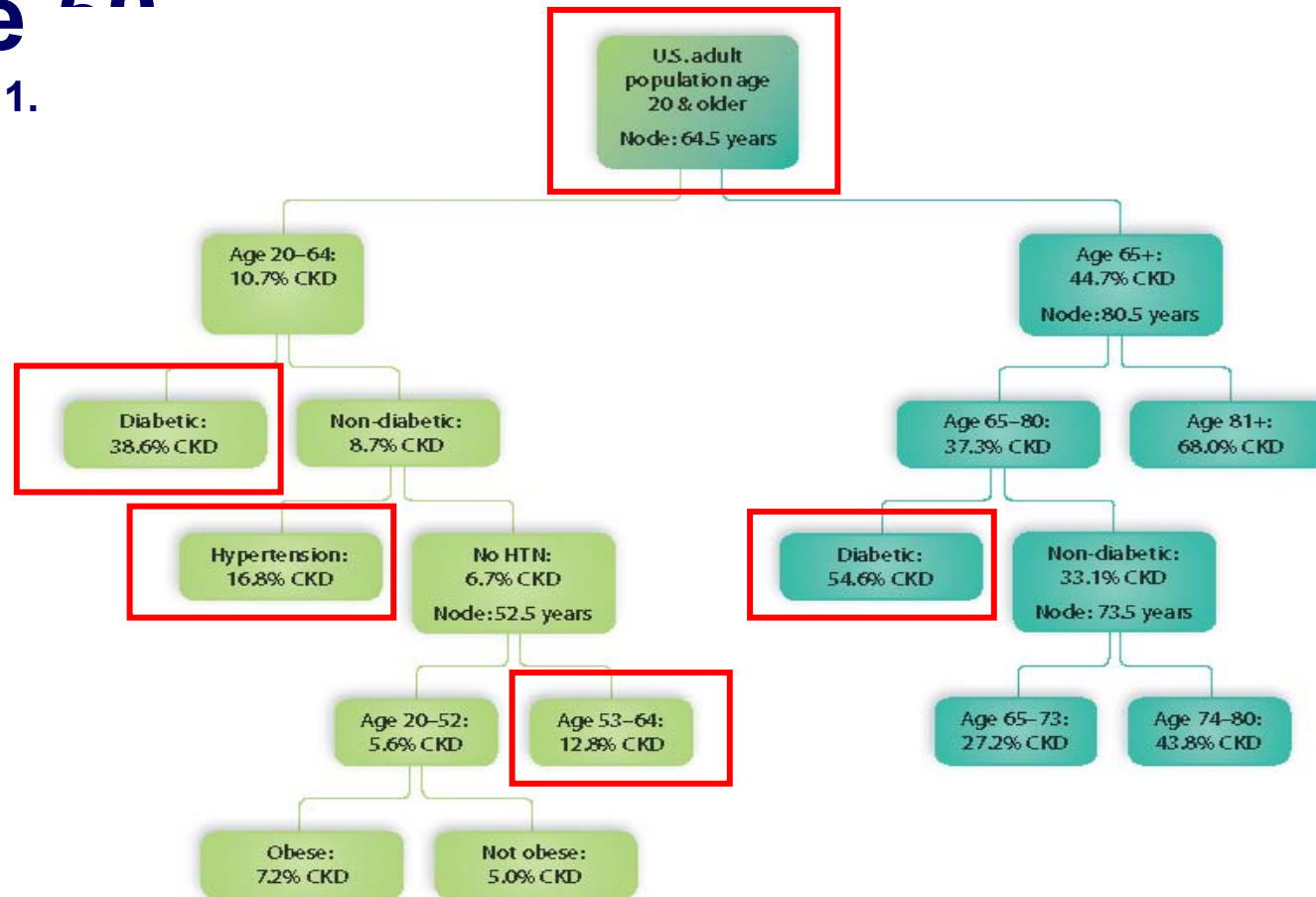
Table 1.b (Volume 1) **USRDS 2008 ADR**

	OR	CI	p-value
Age			
20-39	ref		p<0.001
40-59	1.61	1.35 - 1.92	
60+	5.89	5.01 - 6.93	
Gender			
Male	ref		p<0.001
Female	1.44	1.31 - 1.58	
Race/ethnicity			
Non-Hispanic white	ref		0.0055
Non-Hispanic black	1.06	0.95 - 1.19	
Other	1.24	1.08 - 1.42	
Self-reported diabetes			
Yes	2.5	2.07 - 3.02	p<0.001
No	ref		
Self-reported hypertension			
Yes	1.77	1.59 - 1.97	p<0.001
No	ref		
Self-reported CVD			
Yes	1.92	1.65 - 2.24	p<0.001
No	ref		
Current smoker			
Yes	1.11	0.95 - 1.29	0.1791
No	ref		
Obesity status			
Obese (BMI ≥ 30)	1.08	0.95 - 1.22	0.2183
Not obese	ref		

NHANES 1999–2006,
participants age 20 & older.

Classification tree, with significant interactions: DM, HTN, age

Figure 1.



CKD is a highly interactive disease with other chronic disease

- **The interrelationship between CKD, CVD, Diabetes and even COPD make it a very complex condition to address**
- **DM and CVD contribute to causing kidney disease and Kidney disease farther complicates DM and CVD disease**
- **Since there is no clear way to separate these conditions they must be addressed together until specific clinical trials tell us otherwise.**
- **Opinion: Progression of CKD at any stage is an obsession of nephrology even given the facts that ESRD is such a rare event!**
 - **Stage 4 CKD is a very important area with good intervention trial data for preventing progression to ESRD or death**
 - **Stage 4 CKD is the major transition zone for intensive intervention for CVD risk, death as well as planned transition to ESRD**
 - **Preemptive transplant, planned dialysis modality, vascular and peritoneal access placement and nutritional counseling are critically needed in stage 4!**

**CKD Health Examination Risk
Information Sharing: CHERISH**



State Level CKD Detection Program: Funded by the CDC

USRDS 2009 ADR

USRDS

CHERISH investigative Team and organizations

- **PI: Allan Collins, MD, FACP: University of Minnesota, CDRG**
- **Co-PI: Joseph Vassalotti, MD NKF**
- **CDC Project Officer:**
 - Desmond William, MD, PhD
 - Nilka Burrows, MPH
 - CDC Diabetes Translation group, CDC CVD group,
- **Co-Investigators, Collaborators and operations: CDRG and NKF**
 - David Gilbertson PhD, Jon Snyder PhD, Jiannong Liu PhD, Suying Li PhD, Tom Arneson MD, MPH, Robert Foley MB, MSc, Peter McCullough MD, Wendy St. Peter Pharm D, Alan Wang MS
 - Rebecca Seeman, RN, Field operations
 - Sarah Pederson, MS, Administrative authorization and oversight, IRB and project management
 - Monica Gannon
 - Shu Chen, MS
 - Frank Daniels, MS
- **IRB: Minneapolis Medical Research Foundation**

CHERISH CKD Pilot detection Criteria

- **Self reported**
 - Diabetes
 - Hypertension
 - Anyone age 50+ (liberal criteria for Pilot)
- **Medical Questionnaire**
 - DM, HTN, CVD, Stroke, CVD interventions, Insurance, education level, physician care
 - Ht, Wt, BP
 - Lab: Glucose, Urine microalbumin level, Urine albumin/creatinine ratio, serum creatinine, estimated GFR, HDL, LDL, HbA1c in DM,
 - Patient education materials and physician practice guidelines
 - Results for screening given to the participants
- **Follow-up**
 - within three months of first screening
 - At 12 months with repeat of initial questionnaire and data

CHERISH Sites: Pilot 4 states

- **Geographic locations**
 - California
 - Florida
 - Minnesota
 - New York
- **Sites: Selected based on age, gender and race distribution**
 - Two sites per state
 - Target participants: 100 per site
 - Total 800 from the four states
- **Started enrollment September 2008**
 - 890 screened in thru April 2009

CKD populations, primary care and nephrology: Opinion

- **CKD stages 1, 2 and 3 are the domain of primary care with nephrology providing guidance for detection and treatment**
- **Stage 4 CKD is the clinical domain of nephrology based on human resources, intervention trials and the complexity of hypertension, fluid overload, CHF/ISHD and other biochemical abnormalities (Ca, PO₄, PTH)**
- **There may be little progress in addressing CKD and ESRD without public awareness of the impact of the condition thereby motivating individuals to act.**

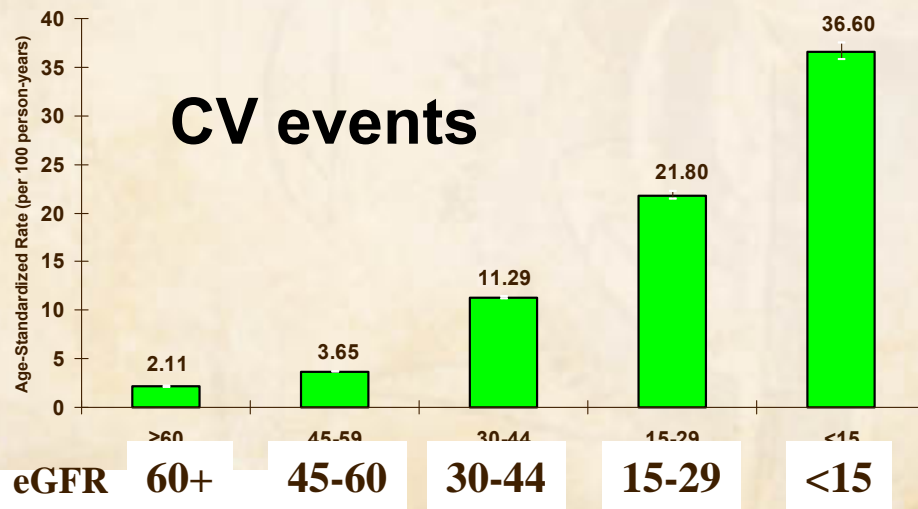
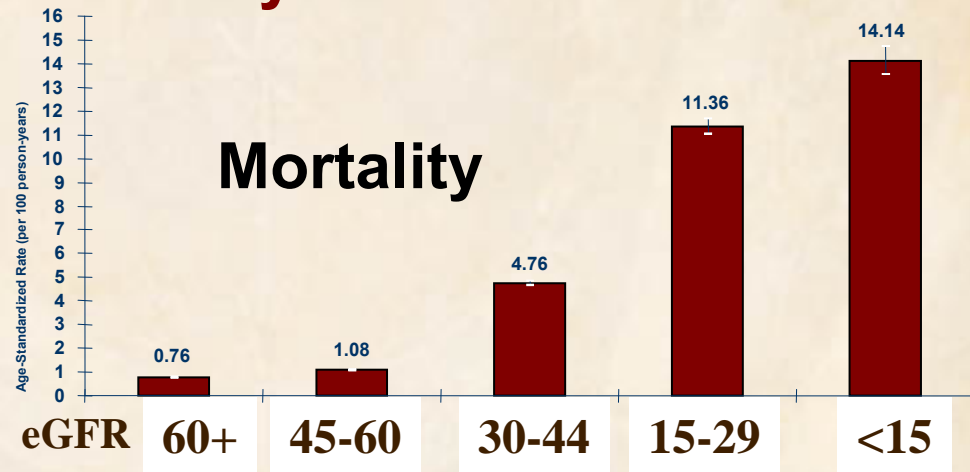
The approach to the patient at risk for kidney disease-1

- Target simple testing of the at-risk populations which include those with diabetes and hypertension
- Use simple tests to define the extent of the kidney damage or risk marker
 - Serum Creatinine
 - Estimate the Glomerular Filtration rate (MDRD or new CKD-EPI equation)
 - Repeat the measurement to ensure consistency (2 out of 3 tests below the risk level eGFR <60 ml/min/1.73 m² increased risk of death and adverse events)
 - Urine albumin to creatinine ratio
 - If greater than 30 mg/gm increased risk of death and adverse events

Age-Standardized Rates of All-Cause Mortality & Cardiovascular Events by eGFR Level

N=1,000,000 Kaiser Permanente with a Creatinine test

Go et al, NEJM 2004



**Risk of death:
16 times >
ESRD event**



The approach to the patient at risk for kidney disease-2

- **The main issue for the CKD patient is the risk of adverse cardiovascular events and death!**
- **ESRD is the rare event!!!**
- **“8” Cs of CKD treatment**
 - **Control weight and energy intake (avoid energy dense foods)**
 - **Control salt intake**
 - **Control blood pressure**
 - **Control lipids**
 - **Control and stop smoking**
 - **Continue to get exercise (30 minute walk/day)**
 - **Control progression of CKD**
 - **Consume some red wine (Dr. Ritz recommendation)**
- **Targets for CKD are different for BP (<130/80) and lipids (LDL <100mg/dl) than the general population**
- **Use of ACE-I/ARBs particularly in those with evidence of proteinuria**

The Approach to Chronic Kidney Disease

- **CKD is Common, Harmful and Treatable**
- **CKD is silent but DEADLY!**
- **CHERISH your Kidneys or Perish**
- **We can do more to address the human and societal cost of kidney disease**
- **What are you waiting for, Go do something about it!**