Chronic Kidney Disease Complications and Cardiovascular Risk Factors: Their Impact on Outcomes

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Disclosures

• Speakers Bureau
  – Boehringer-Ingelheim
  – Glaxo Smith Kline
  – Pfizer
  – Gilead

• Board of Directors
  – National Kidney Foundation – Louisiana Affiliate

• Board of Trustees
  – American Kidney Fund
Objectives

• At the end of this activity, the learner will be able to:
  – Discuss the risk factors for development of chronic kidney disease (CKD)
  – Implement cardiovascular disease risk reduction strategies for patients with chronic kidney disease
  – Discuss advances in the management of complications of CKD
Nephron

Kidney regulates:
- Water/fluid balance
- Acid-base balance
- Electrolytes
- Nitrogenous waste excretion
Kidney Disease by the Numbers

Population
- **26 million+** American adults have chronic kidney disease (CKD)
- **500,000+** Americans have irreversible kidney failure, or end-stage renal disease (ESRD), and require dialysis or kidney transplant to survive
- **385,000+** ESRD patients receive dialysis at least 3 times per week to replace kidney function
- **151,500** Americans with a functioning kidney transplant
- **80,000+** People die annually due to CKD, (ninth leading cause of death in the U.S.)
- **16,000+** Americans received a kidney transplant in 2008
- **75%** Of new dialysis patients have diabetes and/or hypertension as the underlying cause of irreversible kidney failure
- **80%** Of ESRD patients rely on Medicare for their primary health insurance
- **33%** Of ESRD patients are dually-eligible for Medicare and Medicaid

Cost
- **$20 Billion** Annual cost of the Medicare ESRD program
- **$42 Billion** Annual Medicare expenditures to treat people with CKD
- **$106,000** Cost of a kidney transplant per Medicare patient in the first year
- **$71,000** Medicare spending on a dialysis patient per-year
- **$17,000** Medicare spending per beneficiary for functioning transplant, per-year
- **$81,000** Medicare cost per patient for graft failure within the year
Chronic Kidney Disease in the U.S.

• **Over 26 million** Americans have chronic kidney disease\(^1\)
• In 2005, **485,012** of these Americans required renal replacement therapy\(^2\)
• **$20 Billion** – Annual cost of the Medicare ESRD program\(^3\)
• **$42 Billion** – Annual Medicare expenditures to treat people with CKD\(^3\)

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\(^3\)USRD.org website – 2009 Annual Data Report
The Kidney Disease Outcomes Quality Initiative or K/DOQI provides evidence-based clinical practice guidelines developed by volunteer physicians and health care providers for all stages of chronic kidney disease and related complications, from diagnosis to monitoring and management.

K/DOQI expands the Dialysis Outcomes Quality Initiative or DOQI, a project begun by the National Kidney Foundation in 1997 and recognized throughout the world for improving the care of dialysis patients.
Initial Scope of the Problem

• NHANES III – National Health and Nutrition Examination Survey
  – Sample of 15,625 non-institutional adults, age 20 years and older
  – Prevalence
    • CKD Stage 1 (normal kidney fxn) – 3.6 M
    • CKD Stage 2 (mildly decreased kidney fxn) – 6.5 M
    • CKD Stage 3 (moderately decr kidney fxn) – 15.5 M
    • CKD Stage 4 & 5 (severely decreased kidney fxn and kidney failure) 700,000 and 490,000, respectively

Coresh J. JAMA, 2007,
Prevalence of CKD

CKD Stage

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Millions of People</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90</td>
<td>3.60</td>
</tr>
<tr>
<td>60-89</td>
<td>6.50</td>
</tr>
<tr>
<td>30-59</td>
<td>15.50</td>
</tr>
<tr>
<td>15-29</td>
<td>1.70</td>
</tr>
<tr>
<td>&lt;15</td>
<td>0.49</td>
</tr>
</tbody>
</table>


Incidence of ESRD by Cause

Primary Diagnosis for Patients Who Start Dialysis

- Diabetes: 45% 
- Hypertension: 27% 
- Glomerulonephritis: 8% 
- Unknown/Missing: 5% 
- Other*: 15%

ESRD, end-stage renal disease.
*Includes cystic kidney disease, urologic disease, and other known causes of end-stage renal disease.

Incidence of Kidney Failure

*(per million population)*

Per person per year total Medicare ESRD expenditures

Figure p.31

Period prevalent ESRD patients with Medicare as primary payer.
United States Renal Data Systems (USRDS)

www.usrds.org
Compiles information on ESRD patients primarily and limited information on CKD
Medicare oversight of data and trends
Definitions
  Incident patients: New to dialysis
  Prevalent patients: Currently on dialysis
ESRD networks

Figure 2.39

Network 1 Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
Network 2 New York
Network 3 New Jersey, Puerto Rico, Virgin Islands
Network 4 Delaware, Pennsylvania
Network 5 Maryland, Virginia, Washington D.C., West Virginia
Network 6 Georgia, North Carolina, South Carolina
Network 7 Florida
Network 8 Alabama, Mississippi, Tennessee
Network 9 Indiana, Kentucky, Ohio
Network 10 Illinois
Network 11 Michigan, Minnesota, North Dakota, South Dakota, Wisconsin
Network 12 Iowa, Kansas, Missouri, Nebraska
Network 13 Arkansas, Louisiana, Oklahoma
Network 14 Texas
Network 15 Arizona, Colorado, Nevada, New Mexico, Utah, Wyoming
Network 16 Alaska, Idaho, Montana, Oregon, Washington
Network 17 American Samoa, northern California, Guam, Hawaii
Network 18 Southern California
Kidney Disease: Improving Global Outcomes (KDIGO)

• Mission Statement
  – Improve the care and outcomes of kidney disease patients worldwide through promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines.

• Implications
  – Kidney disease has become a pandemic problem, therefore CKD education has become a hot topic world-wide
KDIGO

• Global Effort
• Multidisciplinary approach
• Resource sharing
• Long-term goal: Optimize outcomes

• Pandemic ESRD world-wide
  – Currently 1 million on dialysis
  – In 10 years the number will double

• Guidelines
  – K/DOQI – world-wide usage
  – Translated into 12 languages
  – Standard of Care: US, UK, Canada, Most EU, Australia, NZ, Austria
Figure 80.1 Incidence of end-stage renal disease (ESRD) per million population in 2003. Data presented only for those countries from which relevant information was available. All rates are unadjusted. Data from Israel, Jalisco (Mexico), Japan, Luxembourg, the Philippines, and Taiwan represent dialysis only.

(Data supplied by the United States Renal Data System. The interpretation and reporting of these data are the responsibility of the author and in no way should be seen as an official policy or interpretation of the U.S. government.)
What is Chronic Kidney Disease?
Chronic Kidney Disease

1. Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney with or without decreased GFR, manifest by either;
   • Pathological abnormalities, or
   • Markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests

2. GFR < 60 mL/min/1.73 m² for ≥ 3 months, with or without kidney damage

Enknoyan G and Levin NW. AJKD 2002;39(2):S1-S266.
Figure 69.3 Average rate of glomerular filtration rate (GFR) decline due to aging. This average rate (top curve) is compared to hypothetical patients each with the onset of a progressive kidney disease at age 25 years but with different rates of GFR decline. Note that small differences in GFR decline can result in large differences in time to onset of end-stage renal disease (ESRD).

Figure 69.1 Pathogenetic steps in natural progression of kidney disease. The mechanisms of natural progression are arbitrarily categorized as those induced by decreased glomerular filtration rate (GFR), proteinuria, and systemic hypertension.

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Clinical Manifestations and Markers of Kidney Disease

• Clinical manifestations
  – Often asymptomatic
  – High blood pressure
  – Edema of hands and feet

• Markers
  – Protein and/or blood in the urine
  – Elevated serum creatinine and/or BUN
  – Decreased glomerular filtration rate (GFR)
  – Anemia
Measuring Proteinuria

• Urinalysis gives a qualitative measure
  – Results are negative, trace, +1, +2
  – Easy, but cannot follow changes over time

• Spot urine protein:creatinine ratio gives a quantitative measure\(^1\)
  – Easy to collect sample in office
  – Reliable
  – Can use to follow changes over time

• 24-hour urine collection is also quantitative
  – Difficult to implement

Urine Protein: Creatinine Ratio

- Calculate from lab results, making sure that both values are in g or mg.

<table>
<thead>
<tr>
<th>Value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td>&lt;0.3</td>
<td>Non-nephrotic</td>
</tr>
<tr>
<td>~1</td>
<td>Refer to nephrologist</td>
</tr>
<tr>
<td>10</td>
<td>Severely nephrotic</td>
</tr>
</tbody>
</table>
Kidney Disease

- Increasing in frequency and incidence
- Multiple co-morbid conditions
  - Anemia
  - Cardiovascular disease
    - Heart failure
    - Heart Attacks
    - Peripheral vascular disease
    - Cerebrovascular disease
      - Stroke or TIA
  - Bone Disease
  - Electrolyte disorders
- Disproportionately affects minority populations
Figure 71.4 Risk factors for cardiovascular disease. Schematic overview of traditional (i.e., Framingham) risk factors (green), “novel” risk factors (orange), and more or less “uremia-specific” risk factors (blue).

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Causes of Chronic Kidney Disease

• Diabetes Mellitus
• Hypertension
• Congenital anomalies and obstructive uropathy
• Tubulointerstitial Disorders
• Infections (Chronic Urinary Tract, Post-streptococcal, HIV, Hepatitis C, others)
• Kidney stones (Nephrolithiasis)
• Lupus and other vasculitic diseases
• Obesity (FSGS)
• Drugs (Heroin, Cocaine, NSAIDS, etc.)
• Aging
• Others
Number and Percentage of U.S. Population with Diagnosed Diabetes

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

Obesity (BMI ≥30 kg/m²)

1994

2000

2007

Diabetes

1994

2000

2007

No Data <14.0% 14.0-17.9% 18.0-21.9% 22.0-25.9% >26.0%

No Data <4.5% 4.5-5.9% 6.0-7.4% 7.5-8.9% >9.0%

Obesity Trends* Among U.S. Adults

BRFSS, 2008

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Leading Causes of ESRD

• Diabetes and hypertension are the most common causes of ESRD\(^1\)

• Hypertension increases the risk of microalbuminuria and ESRD\(^1\)
  – Microalbuminuria is an early warning sign of kidney disease\(^2\)
  – Up to 40% of patients with hypertension have microalbuminuria (UAE rate of 30-300 mg/24 h)\(^2\)
  – Microalbuminuria identifies patients who need more intensive therapy\(^2\)

ESRD, end-stage renal disease; UAE, urinary albumin excretion.

\(^1\)United States Renal Data System. *USRDS 2002-2008 Annual Data Report*.
Patients With Type 2 Diabetes

- 63% have hypertension\(^1\)*
- 40% have uncontrolled hypertension\(^1\)
  - Hypertension in patients with diabetes is 1.5 to 3 times more prevalent than in age-matched patients without diabetes\(^2\)
  - Patients with hypertension and diabetes have 5 to 6 times greater risk of ESRD compared to those with hypertension and without diabetes\(^3\)
- 28.2% have microalbuminuria (UAER between 30 and 300 mg/24 h)\(^1\)
- 7.6% have proteinuria (UAER >300 mg/24 h)\(^1\)
- 52.9% take >3 prescription medications\(^1\)
- At least 58% have uncontrolled diabetes (A1C >7.0%)\(^1\)

ESRD, end-stage renal disease; UAER, urinary albumin excretion rate.

*Hypertension defined as BP $\geq$140/90 mm Hg or treatment with antihypertensive medications.

\(^1\)Harris MI. Diabetes Care. 2000;23:754-758.


Major Risk Factors for Diabetic Nephropathy

- Being African-American, Mexican-American or Pima Indian
- Genetic susceptibility, as evidenced by diabetic nephropathy in a sibling
- Hypertension
- Increased glomerular filtration rate
- Less optimal glycemic control (uncontrolled diabetes)
- Increased plasma pro-renin activity
- Increased red cell sodium-lithium countertransport
Progression of Type 2 Diabetic Renal Disease

Interventions

Slows Progression

Protection

<table>
<thead>
<tr>
<th>Microalbuminuria</th>
<th>Proteinuria</th>
<th>ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early-stage</td>
<td>Late-stage</td>
<td>End-stage</td>
</tr>
<tr>
<td>CKD 1-2</td>
<td>CKD 3-4</td>
<td>CKD 5</td>
</tr>
</tbody>
</table>

Kidney Disease

CV morbidity and mortality

ESRD, end-stage renal disease.

Progression of Kidney Disease

- Microalbuminurina
- Proteinuria
- Doubling of Serum Creatinine Levels
- End-Stage Renal Disease

CV Events

Death
Black Americans Have Higher Rates of Risk Factors

- Black Americans are 1.8 times as likely to have diabetes mellitus than age-adjusted White Americans\(^1\)
- \(~43\%\) of Black Americans over age 20 have hypertension\(^2\)
  - Compared with White Americans, hypertension develops earlier and blood pressures are higher
- Black Americans have the highest observed rate of Hepatitis C (3.2\%)\(^3\)
- Black Americans have the highest rates of obesity
  - (40\% BM, 50\% BF)

\(^1\)www.diabetes.org/uedocuments/NationalDiabetesFactSheetRev.pdf.
\(^2\)www.americanheart.org/presenter.jhtml?identifier=3000927.
## Stages of Chronic Kidney Disease and Clinical Action Plans

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mg/dl/1.73 m²)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>&gt;90</td>
<td>Dx and Tx, slow progression, CVD risk factor reduction</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mildly decreased GFR</td>
<td>60-90</td>
<td>Estimating progression</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased GFR</td>
<td>30-59</td>
<td>Evaluating and treating complications</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased GFR</td>
<td>15-29</td>
<td>Preparation for kidney replacement therapy</td>
</tr>
<tr>
<td>5</td>
<td>Kidney Failure</td>
<td>&lt;15</td>
<td>Kidney replacement therapy (if patient uremic and interested)</td>
</tr>
</tbody>
</table>
# K/DOQI Optimal CKD Care
(Early Detection of CKD)

<table>
<thead>
<tr>
<th>Interventions that delay progression</th>
<th>Prevention of uremic complications</th>
<th>Modification of Co morbidity</th>
<th>Preparation for renal replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitors or ARBs</td>
<td>Malnutrition</td>
<td>Cardiac Disease (CAD, CHF)</td>
<td>Education</td>
</tr>
<tr>
<td>BP control</td>
<td>Anemia</td>
<td>Vascular Disease (PAD, PVD)</td>
<td>Information on renal replacement options</td>
</tr>
<tr>
<td>Glycemic control</td>
<td>Osteodystrophy</td>
<td>Neuropathy (DM)</td>
<td>Timely access placement</td>
</tr>
<tr>
<td>Protein restriction?</td>
<td>Acidosis</td>
<td>Retinopathy (DM)</td>
<td>Timely initiation of dialysis</td>
</tr>
</tbody>
</table>
Multidisciplinary Team Required in CKD Management

Physicians (PCP)  Nephrologists  Nutritionists  Other Specialists  Nurse Practitioners  Social Services

Multidisciplinary Approach to the Continuum of CKD

Kidney Function

- >90 mL/min: Kidney damage but normal function
- 89-60 mL/min: Mild decline in function
- 59-30 mL/min: Moderate decline in function
- 29-15 mL/min: Severe decline in function
- <15 mL/min: End stage kidney failure

Stage 1
- Blood pressure control (<125/75)

Stage 2
- Blood sugar control (60-120 mg/dL, HbA1C <6.5)
- Urine protein reduction
- Lipid profile (LDL <100 mg/dL)

Stage 3
- Anemia management (Hb 11-12 g/dL)
- Mineral management (calcium <9.5, phosphorus<5.0 mg/dL)
- Discuss kidney replacement options/access
- Establish dialysis access
- Evaluate for transplantation

Stage 4
- Initiate dialysis
- Plan for transplant
- Medical mngt CKD5

Stage 5

Associated Conditions and Goals
- Advanced practitioner
- Anemia mgt nurse
- Nurse educator
- Dietitian
- Social worker
- Clinical pharmacist
CKD Complications

- Hypertension
- Anemia
- Metabolic
  - Hyperkalemia
  - Acidosis
- Renal Osteodystrophy
- Malnutrition
Awareness, Treatment, and Control of Hypertension in the United States

*Adults with hypertension aged 18 to 74 years.
†Controlled: BP <140/90 mm Hg.
‡Data for 1999-2000 were computed (M. Wolz unpublished data, 2003) from the National Heart, Lung, and Blood Institute, and data for the National Health and Nutrition Examination Surveys (NHANES) II and III, phases 1 and 2, are from JNC VI.
### JNC 7: Classification of Blood Pressure

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>$\leq 120^*$</td>
<td>$\leq 80^*$</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>121-139</td>
<td>81 - 89</td>
</tr>
<tr>
<td>Hypertension, Stage 1</td>
<td>140-159</td>
<td>90 – 99</td>
</tr>
<tr>
<td>Hypertension, Stage 2</td>
<td>$\geq 160$</td>
<td>$\geq 100$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Goal BP, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated hypertension(^1)</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>African American(^1)</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>Senior(^1)</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>High CAD risk(^2,(*)</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Chronic kidney disease(^1,(*)</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Diabetic(^1,(*)</td>
<td>&lt;130/80</td>
</tr>
</tbody>
</table>

\(*) Represents revised target BP goal.
## JNC 7 Compelling Indications

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diuretic</th>
<th>BB</th>
<th>ACEI</th>
<th>ARB</th>
<th>CCB</th>
<th>AA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Post-MI</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>High CAD risk</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Diabetes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Recurrent stroke prevention</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

# Delaying the Progression of Nondiabetic Kidney Disease

<table>
<thead>
<tr>
<th>Clinical Assessment</th>
<th>Target Blood Pressure</th>
<th>Preferred Agents for CKD</th>
<th>Additional Agents to Reduce CVD Risk and Reach Target Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure &gt;130/80 mmHg and spot urine total protein-to-creatinine ratio &gt;200 mg/g</td>
<td>&lt;130/80 mmHg</td>
<td>A</td>
<td>ACE inhibitor or ARB</td>
</tr>
<tr>
<td>Blood pressure &gt;130/80 mmHg and spot urine total protein-to-creatinine ratio &lt;200 mg/g</td>
<td>&lt;130/80 mmHg</td>
<td>B</td>
<td>None preferred</td>
</tr>
<tr>
<td>Blood pressure &lt;130/80 mmHg and spot urine total protein-to-creatinine ratio &gt;200 mg/g</td>
<td></td>
<td>C</td>
<td>ACE inhibitor or ARB</td>
</tr>
<tr>
<td>Blood pressure &lt;130/80 mmHg and spot urine total protein-to-creatinine ratio &lt;200 mg/g</td>
<td></td>
<td>None preferred</td>
<td></td>
</tr>
</tbody>
</table>

Lifestyle Modifications for Prevention and Management of Hypertension

- Reduce weight
- Increase physical activity
- Moderate consumption of:
  - alcohol
  - sodium
  - saturated fat
  - cholesterol
- Maintain adequate intake of dietary:
  - potassium
  - calcium
  - magnesium
- Avoid tobacco

# Lifestyle Modification Recommendations

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Avg systolic reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight: (body mass index = 18.5-24.9 kg/m²)</td>
<td>5 – 20 mmHg / 10 kg weight loss</td>
</tr>
<tr>
<td>DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and lowfat dairy products with reduced content of saturated and total fat</td>
<td>8 -14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to 2.4 grams of sodium or 6 grams of sodium chloride a day</td>
<td>2 – 8 mmHg</td>
</tr>
<tr>
<td>Aerobic physical activity</td>
<td>Engage in regular aerobic physical activity at least 30 minutes a day, most days of the week</td>
<td>4 – 9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>Men: limit to ≤ 2 drinks* per day. Women and lighter persons: limit to ≤ 1 drink per day</td>
<td>2 – 4 mmHg</td>
</tr>
</tbody>
</table>

Multiple Antihypertensive Agents Often Needed to Achieve Target BP

<table>
<thead>
<tr>
<th>Trial</th>
<th>Target BP (mm Hg)</th>
<th>No. of antihypertensive agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKPDS¹</td>
<td>DBP &lt;85</td>
<td>1</td>
</tr>
<tr>
<td>ABCD²</td>
<td>DBP &lt;75</td>
<td>2</td>
</tr>
<tr>
<td>MDRD³</td>
<td>MAP ≤92</td>
<td>3</td>
</tr>
<tr>
<td>HOT⁴</td>
<td>DBP ≤80</td>
<td>4</td>
</tr>
<tr>
<td>AASK⁵</td>
<td>MAP ≤92</td>
<td></td>
</tr>
<tr>
<td>IDNT⁶</td>
<td>SBP ≤135/DBP ≤85</td>
<td></td>
</tr>
<tr>
<td>ALLHAT⁷</td>
<td>SBP ≤140/DBP ≤90</td>
<td></td>
</tr>
</tbody>
</table>

DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

2. Estacio RO et al. *Am J Cardiol*. 1998;82:9R-14R.
Cardiovascular Disease Risk Factors

- Hypertension*
- Cigarette smoking
- Obesity* (BMI ≥ 30 kg/m²)
- Physical inactivity
- Dyslipidemia*
- Diabetes mellitus*
- Microalbuminuria or estimated GFR < 60 ml/min
- Age (older than 55 for men, 65 for women)
- Family history of premature CVD
  (men under age 55 or women under age 65)

*Components of the metabolic syndrome.
## Risk Factors for Cardiovascular Disease

### Traditional

- Older Age
- Male Gender
- White
- Hypertension
- Elevated LDL
- Decreased HDL
- Diabetes
- Tobacco Use
- Physical Inactivity
- Menopause
- Psychosocial stress
- Family history of CVD
- eGFR < 60 mL/min/1.73 m²

### CKD-Related (Nontraditional)

- Type (diagnosis) of CKD
- Decreased GFR
- Proteinuria
- Renin-angiotensin system activity
- Extra-cellular fluid volume overload
- Abnormal Ca & P metabolism
- Dyslipidemia
- Anemia
- Malnutrition
- Inflammation
- Infection
- Thrombogenic factors
- Oxidative stress
- Elevated homocysteine
- Uremic toxins

---

Cardiovascular Mortality

Cardiovascular mortality in the general population (NCHS) and in kidney failure treated by dialysis or transplant (USRDS)

Cardiovascular and Renal Disease Continuum

CHRONIC KIDNEY DISEASE

End Stage
ESRD

Progression
Chronic renal insufficiency (↓ GFR)
Albuminuria
Proteinuria

Initiation
Elderly, DM, ↑ BP

“At Risk”

CARDIOVASCULAR DISEASE

End Stage
CHF

Arteriosclerotic CVD events
CAD
LVH

At Risk
Elderly, DM, ↑ BP

BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; CVD = cardiovascular disease; DM = diabetes mellitus; ESRD = end-stage renal disease; GFR = glomerular filtration rate; LVH = left ventricular hypertrophy.
CKD Complications

• Hypertension
• Anemia
• Metabolic
  – Hyperkalemia
  – Acidosis
• Renal Osteodystrophy
• Malnutrition
Anemia

Hypertension and Anemia Are Associated with Progression to LVH

- Anemia and hypertension—risk factors for CVD—are associated with progression to LVH, which is highly prevalent in patients with CKD\(^1\)
- Levin et al conducted a prospective, multicenter study to assess left ventricular growth in a Canadian cohort, including 446 predialysis patients with mild-to-moderate renal impairment\(^2\)
  - Echocardiograms were assessable in 246 patients at baseline and 12 months
  - Prevalence of LVH was shown to increase as kidney function decreases and as anemia develops\(^1\)

\(^1\)Levin A. *Nephrol Dial Transplant*. 2001;16(suppl 2):7-11.
Anemia Multiplies Mortality Risk in CKD¹

Likelihood of Death Before ESRD During a 2-Year Follow-up in Medicare Patients With CHF, CKD, DM, Anemia, or a Combination of these Comorbidities

<table>
<thead>
<tr>
<th>Secondary effects of anemia correction on the cardiovascular system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in high cardiac output</td>
</tr>
<tr>
<td>Reduced stroke volume</td>
</tr>
<tr>
<td>Reduced heart rate</td>
</tr>
<tr>
<td>Increase in peripheral vascular resistance</td>
</tr>
<tr>
<td>Reduction in anginal episodes</td>
</tr>
<tr>
<td>Reduction in myocardial ischemia</td>
</tr>
<tr>
<td>Regression of left ventricular hypertrophy</td>
</tr>
<tr>
<td>Stabilization of left ventricular dilation</td>
</tr>
<tr>
<td>Increase in whole blood viscosity</td>
</tr>
</tbody>
</table>

Figure 72.4 Secondary effects of anemia correction on the cardiovascular system.
### Other secondary effects of anemia correction

<table>
<thead>
<tr>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced blood transfusions</td>
</tr>
<tr>
<td>Increased quality of life</td>
</tr>
<tr>
<td>Increased exercise capacity</td>
</tr>
<tr>
<td>Improved cognitive function</td>
</tr>
<tr>
<td>Improved sleep patterns</td>
</tr>
<tr>
<td>Improved immune function</td>
</tr>
<tr>
<td>Improved muscle function</td>
</tr>
<tr>
<td>Improved depression</td>
</tr>
<tr>
<td>Improved nutrition</td>
</tr>
<tr>
<td>Improved platelet function</td>
</tr>
<tr>
<td>(Hypertension)</td>
</tr>
<tr>
<td>(Vascular access thrombosis)</td>
</tr>
</tbody>
</table>

**Figure 72.5** Other secondary effects of anemia correction. Parentheses indicate negative and adverse effects.

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## Optimal CKD Care
### (Early Detection of CKD)

<table>
<thead>
<tr>
<th>Interventions that delay progression</th>
<th>Prevention of uremic complications</th>
<th>Modification of Co morbidity</th>
<th>Preparation for renal replacement therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitors or ARBs</td>
<td>Malnutrition</td>
<td>Cardiac Disease (CAD, CHF)</td>
<td>Education</td>
</tr>
<tr>
<td>BP control</td>
<td>Anemia</td>
<td>Vascular Disease (PAD, PVD)</td>
<td>Information on renal replacement options</td>
</tr>
<tr>
<td>Glycemic control</td>
<td>Osteodystrophy</td>
<td>Neuropathy (DM)</td>
<td>Timely access placement</td>
</tr>
<tr>
<td>Protein restriction?</td>
<td>Acidosis</td>
<td>Retinopathy (DM)</td>
<td>Timely initiation of dialysis</td>
</tr>
</tbody>
</table>
CKD Complications

• Hypertension
• Anemia
• Metabolic
  – Hyperkalemia
  – Acidosis
• Renal Osteodystrophy
• Malnutrition
# Laboratory Tests

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Normal Value</th>
<th>CKD Stage 1-2</th>
<th>CKD Stage 3-4</th>
<th>CKD Stage 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine Clearance (24 hr urine or estimated)</td>
<td>100 ml/min/1.73 m²</td>
<td>&gt; 60 ml/min/1.73 m²</td>
<td>Stage 3 (30-59 ml/min/1.73 m²)</td>
<td>&lt; 15 ml/min/1.73 m²</td>
</tr>
<tr>
<td>Potassium (K+)</td>
<td>3.6 – 5.4 mg/dl</td>
<td>3.6 – 5.4 mg/dl</td>
<td>3.6 – 5.4 mg/dl</td>
<td>3.6 – 5.4 mg/dl</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.5 – 10.5 mg/dl</td>
<td>8.5 – 10.5 mg/dl</td>
<td>8.5 – 10.5 mg/dl</td>
<td>8.5 – 10.5 mg/dl</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.5 – 5.5 mg/dl</td>
<td>3.5 – 5.5 mg/dl</td>
<td>3.5 – 5.5 mg/dl</td>
<td>3.5 – 5.5 mg/dl</td>
</tr>
<tr>
<td>Parathyroid Hormone (PTH)</td>
<td>35 – 60</td>
<td>35 – 60</td>
<td>60 – 150</td>
<td>150 – 300</td>
</tr>
<tr>
<td>Ca x P (calcium-phosphorus product)</td>
<td>&lt; 40</td>
<td>&lt; 40</td>
<td>40 – 50</td>
<td>&lt; 55</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt; 3.6 mg/dl</td>
<td>&gt; 3.6 mg/dl</td>
<td>&gt; 3.6 mg/dl</td>
<td>&gt; 3.6 mg/dl</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>12 – 14 gm</td>
<td>12 – 14 gm</td>
<td>12 – 14 gm</td>
<td>11 – 12 gm</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>36 – 45%</td>
<td>36 – 45%</td>
<td>36 – 45%</td>
<td>33 – 42%</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>&gt; 60 ng/dl</td>
<td>&gt; 60 ng/dl</td>
<td>&gt; 60 ng/dl</td>
<td>&gt; 60 ng/dl</td>
</tr>
<tr>
<td>25-hydroxy</td>
<td>&gt; 30 ng/dl</td>
<td>&gt; 30 ng/dl</td>
<td>&gt; 30 ng/dl</td>
<td>&gt; 30 ng/dl</td>
</tr>
<tr>
<td>1,25-dihydroxy</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Secondary Hyperparathyroidism (SHPT)

Reduced Renal Mass

Decreased Serum 1,25(OH)₂D (active vitamin D calcitriol)

Increased Serum Phosphate

Hypocalcemia

Increased PTH Secretion

Increased Serum Phosphate

Decreased Vitamin D Receptors

Decreased Ca-Sensing Receptors

Parathyroid Glands

PTH = parathyroid hormone.
Effects of PTH on Bone in SHPT

$\uparrow$ PTH

Bone Formation (osteoblast activity)

$\uparrow$ Bone Resorption (osteoclast activity)
Prevalence of Elevated Intact Parathyroid Hormone (iPTH)

Patients With iPTH >65 pg/mL (%)


iPTH = intact parathyroid hormone

N = 1814

<table>
<thead>
<tr>
<th>eGFR Interval (mL/min/1.73 m²)</th>
<th>(n = 61)</th>
<th>(n = 117)</th>
<th>(n = 230)</th>
<th>(n = 396)</th>
<th>(n = 355)</th>
<th>(n = 358)</th>
<th>(n = 204)</th>
<th>(n = 93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;80</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>79-70</td>
<td>(n = 117)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>69-60</td>
<td>(n = 230)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>59-50</td>
<td>(n = 396)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49-40</td>
<td>(n = 355)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>39-30</td>
<td>(n = 358)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>29-20</td>
<td>(n = 204)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>(n = 93)</td>
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<td></td>
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</tr>
</tbody>
</table>
Prevalence of 1,25(OH)2D3 and 25(OH)D Deficiency/Insufficiency

# Recommended Goals for Hormone and Mineral Metabolism in CKD Stages 3 and 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPTH (pg/mL)</td>
<td>Stage 3: 35-70 (pg/mL); Stage 4: 70-110 (pg/mL); Stage 5: 150-300 (pg/mL)</td>
</tr>
<tr>
<td>Serum 25(OH) vitamin D (ng/mL)</td>
<td>&gt;30 (ng/mL)</td>
</tr>
<tr>
<td>P (mg/dL)</td>
<td>2.7 - 4.6 mg/dL</td>
</tr>
<tr>
<td>Ca (mg/dL)</td>
<td>Normal parameters for the lab</td>
</tr>
<tr>
<td>Ca x P product (mg²/dL²)</td>
<td>&lt;55 mg²/dL²</td>
</tr>
</tbody>
</table>

Figure 71.1 Causes of death in dialysis patients. CVD, cardiovascular disease; MI, myocardial infarction. (Data from USRDS, 2005).
Figure 71.2 Cardiovascular mortality in chronic kidney disease and end stage renal disease (ESRD). Cardiovascular mortality defined by death due to arrhythmias, cardiomyopathy, cardiac arrest, myocardial infarction, atherosclerotic heart disease, and pulmonary edema in the general population (GP) compared with those with ESRD treated by dialysis. Data stratified by age, race, and gender.

Summary

• Increasing prevalence of CKD in general population and especially among minority patients
• Patients with CKD have some of the highest risk for CVD
• Patients with CKD need aggressive CVD risk factor identification and management
• Management of CKD complications delays progression to ESRD
• Multidisciplinary approach often required to manage CKD patients to prevent CVD morbidity and mortality
Chronic Kidney Disease Stages

- **Stage 3**
eGFR 30-59
- **Stage 4**
eGFR 15-29
- **CKD Stage 5 (ESRD)**
eGFR < 15

**Moderate Kidney Disease**

**Severe Kidney Disease**

Kidney Failure
Hemodialysis
Peritoneal Dialysis
Transplantation