Outline

- CKD background
  - End-stage renal disease (ESRD) epidemic
  - Tip of the iceberg vs. the base
- Pathophysiology
- CKD in the population
  - Stages of CKD – kidney function
    - kidney damage – persistent proteinuria even with normal of mildly reduced kidney function
  - Estimating kidney function (GFR = serum Cr + formula + calibration)
- Conditions associated with different stages of CKD (consequences)
  - [Diabetes], Hypertension, Anemia, Left ventricular geometry, Poor nutrition, bone disease
  - CVD [next lecture]
- Risk factors for ESRD & CKD progression
Global Kidney Disease 1

Evolving importance of kidney disease: from subspecialty to global health burden

Kai-Uwe Eckardt, Josef Coresh, Olivier Devuyst, Richard J Johnson, Anna Köttgen, Andrew S Levey, Adeera Levin

The Lancet; 382:158 - 169, 13 July 2013
## Definition and Classification of CKD: Clinical vs. Epidemiologic Context

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td><strong>Definition</strong></td>
<td><strong>Definition</strong></td>
</tr>
<tr>
<td>“Damage” Structure</td>
<td>Pathology Markers (urine, blood, imaging) Transplant</td>
<td>Urine alb/creat (ACR) &gt;30 mg/g</td>
</tr>
<tr>
<td><strong>Function</strong></td>
<td><strong>Function</strong></td>
<td><strong>Function</strong></td>
</tr>
<tr>
<td>GFR &lt;60 ml/min/1.73 m² (less than ½ the normal value in young adults)</td>
<td>eGFR &lt;60 ml/min/1.73 m²</td>
<td>eGFR &lt;60 ml/min/1.73 m²</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td><strong>Duration</strong></td>
<td><strong>Duration</strong></td>
</tr>
<tr>
<td>&gt;3 months</td>
<td>Single measurement</td>
<td>Single measurement</td>
</tr>
<tr>
<td><strong>Classification (Stage)</strong></td>
<td><strong>Classification (Stage)</strong></td>
<td><strong>Classification (Stage)</strong></td>
</tr>
<tr>
<td>Function</td>
<td>Function</td>
<td>Function</td>
</tr>
<tr>
<td>GFR &gt;90, 60-89, 30-59, 15-29, &lt;15</td>
<td>eGFR &gt;90, 60-89, 30-59, 15-29, &lt;15</td>
<td>eGFR &gt;90, 60-89, 30-59, 15-29, &lt;15</td>
</tr>
</tbody>
</table>
OPINION ARTICLE

Chronic Renal Confusion: Insufficiency, Failure, Dysfunction, or Disease

Chi-yuan Hsu, MD, and Glenn M. Chertow, MD

Table 3. Objective Findings Corresponding to Semiquantitative Descriptors: ASN Abstracts

<table>
<thead>
<tr>
<th>Abstract No.</th>
<th>Descriptor</th>
<th>Range of Renal Function</th>
</tr>
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<tbody>
<tr>
<td>1998</td>
<td></td>
<td></td>
</tr>
<tr>
<td>712*</td>
<td>&quot;Mild&quot;</td>
<td>Serum creatinine 1.5-3.0 mg/dL</td>
</tr>
<tr>
<td>746*</td>
<td>&quot;Mild&quot;</td>
<td>Serum creatinine 1.54-3.0 mg/dL in men, 1.36-3.0 mg/dL in women</td>
</tr>
<tr>
<td>760</td>
<td>&quot;Moderate or advanced&quot;</td>
<td>Several categories of serum creatinine, all &gt;1.4 mg/dL</td>
</tr>
<tr>
<td>767*</td>
<td>&quot;Severe&quot;</td>
<td>Creatinine clearance &lt;25 mL/min with and without hemodialysis</td>
</tr>
<tr>
<td>771</td>
<td>&quot;Moderate&quot;</td>
<td>Creatinine clearance 20-60 mL/min</td>
</tr>
<tr>
<td>774*</td>
<td>&quot;Severe&quot;</td>
<td>GFR 2-10 mL/min or on dialysis</td>
</tr>
<tr>
<td>823*</td>
<td>&quot;Severe&quot;</td>
<td>&quot;Renal clearance&quot; &lt;30 mL/min</td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td></td>
</tr>
<tr>
<td>783*</td>
<td>&quot;Mild&quot;</td>
<td>Serum creatinine 1.0-1.4, 1.5-2.5 mg/dL, or MDRD estimated GFR 50-70, and &lt;50 mL/min</td>
</tr>
<tr>
<td>801*</td>
<td>&quot;Mild&quot;</td>
<td>Serum creatinine &gt;96 μmol/L (&gt;1.1 mg/dL)</td>
</tr>
<tr>
<td>828</td>
<td>&quot;Moderate&quot;</td>
<td>Serum creatinine 300-500 μmol/L (3.4-5.6 mg/dL)</td>
</tr>
<tr>
<td>829</td>
<td>&quot;Advanced&quot;</td>
<td>Serum creatinine ≥500 μmol/L (5.6 mg/dL)</td>
</tr>
<tr>
<td>860*</td>
<td>&quot;Moderate&quot;</td>
<td>Creatinine clearance &lt;60 mL/min</td>
</tr>
<tr>
<td>903*</td>
<td>&quot;Mild&quot;</td>
<td>Serum creatinine 1.5-3.0 mg/dL</td>
</tr>
</tbody>
</table>

* Denotes in abstract 4/1.
ESRD Incidence Internationally

Taiwan
USA
Mexico
Japan

Lancet 2013; 382: 260–72
ESRD Prevalence

Taiwan

Japan – longer life expectancy on dialysis

USA

Mexico

Lancet 2013; 382: 260–72
Reported Causes of ESRD

Diabetes
Hypertension
CGN

Taiwan
USA
Japan

Proportion (%)
Relationship of Prevalence of ESRD to Gross National Income (GNI) Per Person

Taiwan

Japan

USA

Lancet 2013; 382: 260–72
Incident counts & adjusted rates of ESRD, by race
Figure 1.5 (Volume 2)

- ESRD Prevalence in 2010: 594,374 patients (415,000 Dialysis, 179,000 transplant)
  - 61% White
  - 32% African-American
  - 1.4% Native American
  - 5.5% Asian, Pacific-Islander
- Gender: 57% male
- Physician designed “Cause”
  - 37.8% Diabetes
  - 24.8% Hypertension
  - 14.6% Glomerulonephritis
  - 4.8% Cystic disease
- Total costs: $47.5 B ($29 B medicare)
Adjusted incident rates of ESRD & annual percent change
Figure 1.2 (Volume 2)

Adjusted prevalent rates of ESRD & annual percent change

Figure 1.10 (Volume 2)

December 31 point prevalent ESRD patients.
Adj: age/gender/race; ref: 2005 ESRD patients.
Incident counts & adjusted rates of ESRD, by race
Figure 1.6 (Volume 2)

- Incidence counts still increasing
- Adjusted incidence rates have plateaued in all groups

Geographic variations in adjusted incident rates (per million population), by HSA, 1998

Incident ESRD patients, by HSA; rates adjusted for age, gender, & race. Excludes patients residing in Puerto Rico & the Territories.
Geographic variations in adjusted incident rates (per million population), by HSA, 2003
Figure p.7 (continued; Volume 2)

Incident ESRD patients, by HSA; rates adjusted for age, gender, & race. Excludes patients residing in Puerto Rico & the Territories.
Geographic variations in adjusted incident rates (per million population), by HSA, 2008
Figure p.7 (continued; Volume 2)

Incident ESRD patients, by HSA; rates adjusted for age, gender, & race. Excludes patients residing in Puerto Rico & the Territories.
Distribution Medicare Patients & Costs for CKD, CHF, diabetes, & ESRD, 2000 & 2010

- High cost growing population
  HOWEVER –
- Under-diagnosis of CKD has decreased over time explaining some of the marked increase in "diagnosed" CKD

- Distinguish – costs “with” vs. costs “for” CKD/ESRD
Total Medicare ESRD expenditures, by modality
Figure 11.6 (Volume 2)

Period prevalent ESRD patients, patients with Medicare as secondary payor are excluded.

USRDS 2011 ADR
Total Medicare ESRD expenditures per person per year, by modality

Figure 11.7 (Volume 2)
Total Medicare spending for injectables
Figure 11.9 (Volume 2)

Period prevalent dialysis patients.
Total PPPY outpatient expenditures, by dialysis modality & race, 2009

Figure 11.19 (Volume 2)

Period prevalent dialysis patients, 2009.
Overall expenditures for CKD in the Medicare population
Figure 6.5 (Volume 1)


NKF CKD Guidelines – Standardized definition and staging
Increasing Rates Plateau Later at Older Ages (suggests improved access/acceptance of treatment)
Incident patients; adjusted for age, gender, race, & primary diagnosis. 1996, used as reference cohort.
“Good news, Mr. Herndon. We worked out the budget, and we have a kidney.”
Stages of Chronic Kidney Disease

- **Stage 1**: Kidney Damage with Normal Filtration
  - Glomerular Filtration Rate: 60-89 ml/min/1.73m²

- **Stage 2**: Kidney Damage with Mildly Decreased Filtration
  - Glomerular Filtration Rate: 30-59 ml/min/1.73m²

- **Stage 3**: Moderately Decreased Filtration
  - Glomerular Filtration Rate: 15-29 ml/min/1.73m²

- **Stage 4**: Severely Decreased Filtration
  - Glomerular Filtration Rate: < 15 ml/min/1.73m²

- **Stage 5**: Kidney Failure
  - Glomerular Filtration Rate: Treated ESRD

- **Normal**: ~ 120 ml/min/1.73m²
“It’s got to come out, of course, but that doesn’t address the deeper problem.”
Prevalence of CKD - Methodology

- Estimating GFR
  - *Equations using serum creatinine* vs. iothalamate GFR
  - Using serum creatinine alone wastes lots of information

- Calibration of serum creatinine
  - Precision (Good), Bias (currently Terrible)

- Standardization is important; <60 for defining CKD is conservative (compared to <80-90 which is ~2 SD below normal for young adults) allowing for some imprecision in calibration

- Precision of GFR estimates based on equations
  - Better at lower GFR

- Estimating progression of CKD
  - Slope vs. time to event
  - Rise in serum creatinine vs. change in GFR estimate
MDRD study equation

\[ R^2 = 90.3\% \]
No bias
Better precision

91% within 30% of GFR

24-hour creatinine clearance

\[ R^2 = 86.6\% \]

Biased if “true” creatinine is measured

Levey et al Ann Intern Med 1999
Phases in Model Development and Selection

Development
- Develop multiple models; Compare complex to simpler models using 2/3 of data

Internal Validation
- Select best models for external validation; Validate and compare within base models using 1/3 of data

External Validation
- Identify best fitting and most generalizable models; Comparison among base models

Final Model
- Ease of use in clinical practice

Category 1 (10 studies)
- Development 5,504
- Internal validation 2,571

Category 2 (20 studies)
- 4,870

Matrix:
1 & 2
## Quantifying Bias, Precision & Accuracy of Estimated GFR (eGFR) for Measured GFR (mGFR)

| Criteria   | Metric                      | Definition                                                                 |
|------------|                            |                                                                           |
| Bias       | Median difference          | Median (mGFR-eGFR)                                                       |
|            | Median percent difference  | Median (mGFR-eGFR)/mGFR*100                                             |
|            | difference                 |                                                                           |
| Precision  | IQR difference             | Interquartile range of (mGFR-eGFR)                                       |
|            | IQR % difference           | Interquartile range of (mGFR-eGFR)/mGFR*100                              |
|            | P₃₀                         | Percent of eGFR within 30% of mGFR                                       |
| Accuracy   | Median absolute difference | Median |mGFR-eGFR|               |
|            | RMSE*                       | Square root of mean (log mGFR - log eGFR)²                               |

mGFR = Measured GFR, eGFR = Estimated GFR

* RMSE measures precision when bias is 0 (development datasets)
MDRD Study Equation – Creatinine Calibration

Estimated GFR, ml/min/1.73m²

Under-estimation
mGFR>eGFR

Over-estimation
mGFR>eGFR

(mGFR-eGFR)/mGFR*100, %

Calibrated
Uncalibrated

Performance of the Equations in External Validation

CKD-EPI A. ME SL

MDRD Study equation

Under-estimation mGFR>eGFR

Over-estimation mGFR>eGFR

Estimated GFR, ml/min/1.73m²

Measured GFR, ml/min/1.73m²
Performance of the MDRD Study equation and new CKD-EPI equation by CKD Status in the Category 2 dataset (20 studies)
Distribution of GFR: MDRD, CKD-EPI, early estimate of “true” GFR – NHANES III

MDRD eGFR
CKD-EPI eGFR

Indirect Regression Estimate of Distribution of True GFR
[Caution – limited by Assumptions & lack Of unselected Population based data]

GFR (ml/min/1.73m²)
“Normal” GFR vs. Age

Prevalence of Chronic Kidney Disease in the United States


*Coresh et al. JAMA. 2007;298(17):2038-2047*
Distribution of Albumin to Creatinine Ratio

Albumin to Creatinine Ratio, mg/g

Percentage

1988-1994
1999-2004

0
0.5
1
1.5

Albumin to Creatinine Ratio, mg/g
Estimated GFR Distribution

Estimated GFR, ml/min/1.73 m²

Percent

1988-1994
1999-2004
1988-1994 Conservative Trends Analysis (+0.04 ml/dl)

US Trends in the Prevalence of CKD by Age and Stage

Coresh et al, JAMA in press 2007
<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1.18</td>
</tr>
<tr>
<td>Adjusted for age</td>
<td>1.15</td>
</tr>
<tr>
<td>+ sex and race</td>
<td>1.12</td>
</tr>
<tr>
<td>+ diagnosed diabetes and hypertension</td>
<td>1.06</td>
</tr>
<tr>
<td>+ body mass index</td>
<td>1.03</td>
</tr>
<tr>
<td>Estimated GFR &lt; 60 ml/min/1.73m² in 1999-2004 vs. 1988-1994</td>
<td>OR</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1.47</td>
</tr>
<tr>
<td>Adjusted for age</td>
<td>1.50</td>
</tr>
<tr>
<td>+ sex and race</td>
<td>1.53</td>
</tr>
<tr>
<td>+ diagnosed diabetes and hypertension</td>
<td>1.45</td>
</tr>
<tr>
<td>+ body mass index</td>
<td>1.43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Estimated GFR&lt; 60 ml/min/1.73m² in 1999-2004 vs. 1988-1994</th>
<th>Conservative Trends Analysis*</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td></td>
<td>1.17</td>
<td>1.02-1.34</td>
<td>0.03</td>
</tr>
<tr>
<td>Adjusted for age</td>
<td></td>
<td>1.13</td>
<td>0.99-1.30</td>
<td>0.07</td>
</tr>
<tr>
<td>+ sex and race</td>
<td></td>
<td>1.15</td>
<td>1.00-1.32</td>
<td>0.05</td>
</tr>
<tr>
<td>+ diagnosed diabetes and hypertension</td>
<td></td>
<td>1.10</td>
<td>0.96-1.26</td>
<td>0.17</td>
</tr>
<tr>
<td>+ body mass index</td>
<td></td>
<td>1.08</td>
<td>0.94-1.24</td>
<td>0.29</td>
</tr>
</tbody>
</table>
Distribution of NHANES participants with diabetes, congestive heart failure, & markers of CKD, with GFR estimated by the CKD-EPI equation

Figure 1.1 (continued; Volume 1)

NHANES participants age 20 & older.

USRDS 2010 ADR
Distribution of NHANES participants with diabetes, congestive heart failure, & markers of CKD, 2005–2010

Figure 1.1 (volume 1)

NHANES participants 2005–2010, age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin creatinine ratio (ACR).
CKD: Associated Conditions & Consequences of Under-diagnosis & Inaction
Association of Complications with level of GFR in Adults

- Hypertension #7
- Anemia #8
- Nutrition #9
- Abnormalities of bone, calcium & phosphorus #10
- Neurological changes #11
- Functioning and Well Being #12

Am J Kid Dis 39:S1-S266, 2002
Hemoglobin Levels, Women
Median and 5th and 95th Percentiles, adjusted to age 60 years

Estimating GFR

- eGFR
- True GFR
- Endogenous Filtration Marker Blood Concentration: Creatinine, Cystatin, Blood urea nitrogen
- Kidney non-GFR: secretion, reabsorption: Tubular secretion, Metabolism, Tubular reabsorption
- Non-kidney: generation, degradation: Muscle mass age, sex, race frailty (-), Steroids, inflammation, Diet, protein metabolism, catabolism
Risk Factors for ESRD & CKD
MULTIPLE RISK FACTOR INTERVENTION TRIAL (MRFIT)

• Randomized trial to test effect of a multifactor program to prevent CHD
• 361,662 men screened from 11/73-11/75
• Screening took place in 18 U.S. cities
• 12,866 high risk men, 35-57 years, entered into trial
MRFIT SCREENEES (N=361,662) DATA COLLECTED

- Age, race*, sex
- History of MI
- Prescribed medication for diabetes*
- Blood Pressure*
- Serum cholesterol-
- Cigarette smoking-
- Zip code

Red indicates published ESRD risk factors
* Indicates ESRD relationship is STRONGER than for CHD; - indicates WEAKER
METHODS

Outcome
- ESRD incidence (treated or death from renal disease) ascertained from the National Death Index (1979 to 1990) and the Social Security Administration (1973 to 1990)

Analysis
- Survival analysis using Kaplan-Meier and Cox proportional hazards analysis
### NUMBER OF ESRD CASES IN MRFIT SCREENEE MEN THROUGH DECEMBER, 1990

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>No. Men</th>
<th>Treated</th>
<th>Deaths</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>317,908</td>
<td>553</td>
<td>128</td>
<td>681</td>
</tr>
<tr>
<td>Black</td>
<td>23,490</td>
<td>117</td>
<td>38</td>
<td>155</td>
</tr>
<tr>
<td>Other</td>
<td>12,618</td>
<td>38</td>
<td>13</td>
<td>51</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>353,337</td>
<td>708</td>
<td>179</td>
<td>887</td>
</tr>
</tbody>
</table>
## RELATIVE RISK OF ESRD IN 20,222 AFRICAN AMERICAN MEN COMPARED WITH 332,544 WHITE MEN SCREENED FOR MRFIT, 1973-90

<table>
<thead>
<tr>
<th>Adjusted for</th>
<th>All-Cause ESRD</th>
<th>Hypertensive ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age only</td>
<td>3.20 (2.62-3.91)</td>
<td>5.16 (3.64-7.31)</td>
</tr>
<tr>
<td>Age, systolic blood pressure</td>
<td>2.56 (2.09-3.13)</td>
<td>3.84 (2.68-5.48)</td>
</tr>
<tr>
<td>Age, serum cholesterol</td>
<td>3.25 (2.66-3.98)</td>
<td>5.21 (3.68-7.40)</td>
</tr>
<tr>
<td>Age, cigarettes/d</td>
<td>3.26 (2.67-3.98)</td>
<td>5.35 (3.77-7.59)</td>
</tr>
<tr>
<td>Age, median income</td>
<td>2.32 (1.82-2.95)</td>
<td>2.83 (1.80-4.45)</td>
</tr>
<tr>
<td>Age, diabetes</td>
<td>2.73 (2.23-3.34)</td>
<td>4.83 (3.40-6.86)</td>
</tr>
<tr>
<td>Age, previous myocardial infarction</td>
<td>3.20 (2.62-3.91)</td>
<td>5.19 (3.66-7.35)</td>
</tr>
<tr>
<td>All of the above</td>
<td>1.87 (1.47-2.39)</td>
<td>2.42 (1.52-3.84)</td>
</tr>
</tbody>
</table>

Klag et al.  JAMA, 1997
BP & Risk of ESRD
Mid-Atlantic ESRD Case-Control Study

- **Investigators**: Perneger TV (Phd thesis), Klag MJ, Whelton PK
- **Objective**: To systematically study risk factors for ESRD
- **Design**: Case-control study.
- **Setting**: Population-based study in Maryland, Virginia, West Virginia, and Washington, D.C.
- **Participants**:
  - 716 newly treated patients with kidney failure aged 20 to 64 years identified using ESRD registry records
  - 361 controls selected by random digit dialing and frequency age-matched
- **Measurements**: Self-reported history by telephone interview
Risk Factors for ESRD in Mid-Atlantic Case Control Study

- h/o hypertension (presence & duration)
- h/o diabetes (not only for diabetic kidney disease)
- African-American race
- Low income
- Poor access to care (number of missing teeth)
- Analgesic use (acetaminophen)
- Alcohol consumption (>2 drinks/day)
- Family history of ESRD
- h/o MI or stroke
- Recreational drug use
- Smoking (abstract only)
Summary

• In adults Chronic Kidney Disease (CKD) is far more common than ESRD
  – 15 million (8%) adults with CKD stage 3-5
    (GFR<60 ml/min/1.73 m²)
  – ~10 million (5%) other adults with kidney damage
    (persistent proteinuria)

• CKD is associated a number of treatable conditions
Key Points

• ESRD is treated kidney failure which reflects both treatment (good) and failure (bad)

• CKD & CVD share many risk factors and mechanisms (endothelial damage, inflammation…)

• Trends in CKD (increasing→flat) differ from trends in CVD (most risk factors except obesity, DM are decreasing)

• CKD patients have additional risk factors for CVD (including anemia and volume overload) which play a smaller role in the general population
Co-Management of Pts with CKD

At increased risk
Kidney damage
120

Mild ↓Kidney function
90

Moderate ↓Kidney function
60

Severe ↓Kidney function
30

Kidney failure
15

Primary Care Physician
Kidney Doctor
Co-Management of Pts with CKD

At increased risk
Kidney damage
Primary Care Physician
Mild ↓Kidney function
Moderate ↓Kidney function
Severe ↓Kidney function
Kidney failure

120
90
60
30
15

Primary Care Physician
Kidney Doctor
EXTRA SLIDES
<table>
<thead>
<tr>
<th>Chronic kidney disease</th>
<th>Acute kidney injury</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Functional criteria</strong></td>
<td>Increase in serum creatinine by 50% within 7 days; increase in serum creatinine by</td>
</tr>
<tr>
<td>GFR &lt; 60 mL/min per 1.73 m² for &gt; 3 months</td>
<td>26.5 μmol/L (0.3 mg/dL) within 2 days; or oliguria</td>
</tr>
<tr>
<td><strong>Structural criteria</strong></td>
<td>None</td>
</tr>
<tr>
<td>Kidney damage for &gt; 3 months (albuminuria is the most common</td>
<td>Stages based on serum creatinine or urine output; stage 1: serum creatinine ≥ 1.5-1.9</td>
</tr>
<tr>
<td>marker of kidney damage and is also associated with rapid</td>
<td>1.9 times baseline, ≥ 26.5 μmol/L increase, or urine output &lt; 0.5 mL/kg per h for</td>
</tr>
<tr>
<td>progression)</td>
<td>6–12 h; stage 2: serum creatinine ≥ 2.0–2.9 times baseline or urine output &lt; 0.5 mL/</td>
</tr>
<tr>
<td></td>
<td>kg per h for ≥ 12 h; stage 3: serum creatinine ≥ 3.0 times baseline, ≥ 353.6 μmol/L</td>
</tr>
<tr>
<td></td>
<td>(≥ 4 mg/dL), renal replacement therapy, or (in patients &lt; 18 years) a decrease in</td>
</tr>
<tr>
<td></td>
<td>estimated GFR to &lt; 35 mL/min per 1.73 m², urine output &lt; 0.3 mL/kg per h for ≥ 24 h,</td>
</tr>
<tr>
<td></td>
<td>or anuria for ≥ 12 h</td>
</tr>
<tr>
<td><strong>Staging</strong></td>
<td></td>
</tr>
<tr>
<td>GFR categories (mL/min per 1.73 m²) and related terms: G1 ≥ 90</td>
<td></td>
</tr>
<tr>
<td>(normal or high); G2 60–89 (mildly decreased); G3a 45–59</td>
<td></td>
</tr>
<tr>
<td>(mildly to moderately decreased); G3b 30–44 (moderately to</td>
<td></td>
</tr>
<tr>
<td>severely decreased); G4 15–29 (severely decreased); G5 &lt; 15</td>
<td></td>
</tr>
<tr>
<td>(kidney failure)</td>
<td></td>
</tr>
<tr>
<td>Albuminuria categories, approximate equivalent for AER (mg per</td>
<td></td>
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<tr>
<td>day) and ACR (mg/g) and related terms: A1 &lt; 30 (normal to</td>
<td></td>
</tr>
<tr>
<td>mildly increased); A2 30–300 (moderately increased); A3 &gt; 300</td>
<td></td>
</tr>
<tr>
<td>(severely increased)</td>
<td></td>
</tr>
<tr>
<td><strong>Burden</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Prevalence</strong></td>
<td></td>
</tr>
<tr>
<td>~10% of adults (from 4% at 20–39 years to 47% at ≥ 70 years in</td>
<td></td>
</tr>
<tr>
<td>the USA)</td>
<td></td>
</tr>
<tr>
<td><strong>Annual incidence</strong></td>
<td>Acute kidney injury requiring hospital admission in Alberta, Canada for patients</td>
</tr>
<tr>
<td>~1% in middle age; twice as frequent in black compared with</td>
<td>without chronic kidney disease 0.1% (0.01% requiring dialysis); for patients with</td>
</tr>
<tr>
<td>white populations</td>
<td>stage 3 disease 0.5–7.1% (0.03–0.17%); for patients with stage 4 disease 7.0–11.7%</td>
</tr>
<tr>
<td></td>
<td>(0.5–2.5%); and 34.8% for acute kidney injury of any severity in chronic kidney</td>
</tr>
<tr>
<td></td>
<td>disease stage ≥ 4</td>
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<tr>
<td></td>
<td>For patients already admitted to hospital, rates are ~10–20% for any acute kidney</td>
</tr>
<tr>
<td></td>
<td>injury with 0.3% requiring dialysis (highest with sepsis, cancer</td>
</tr>
<tr>
<td></td>
<td>and surgery)</td>
</tr>
<tr>
<td><strong>Lifetime cumulative incidence</strong></td>
<td></td>
</tr>
<tr>
<td>~50% for chronic kidney disease and ~2% in white and ~7% in</td>
<td></td>
</tr>
<tr>
<td>black populations for end-stage renal disease</td>
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</tr>
</tbody>
</table>

GFR=glomerular filtration rate. AER=albumin excretion rate. ACR=albumin-to-creatinine ratio. *Varies by age and risk factor distribution. † In the absence of evidence of kidney damage, GFR category G1 or G2 do not fulfill the criteria for chronic kidney disease. ‡ Terms for categories G2 and A2 are relative to young adult levels; category A3 includes nephrotic syndrome (albumin excretion usually >2200 mg/day [ACR >2220 mg/g]).

Table 1: Definitions, stages, and burden of chronic kidney disease and acute kidney injury