Disrupting the “Norm” in Chronic Kidney Disease

James A. Sloand, MD, FACP
Senior Medical Director
Baxter Healthcare Corporation
McGaw Park, IL

Adjunct Professor of Medicine
University of Rochester
Nephrology Division
Rochester, NY
Disrupting the “Norm”

- Current state of CKD/ESRD
- What places patients at risk for CKD/ESRD
- What we can and should we do to resolve
Disrupting the “Norm”

- Current state of CKD/ESRD
- What places patients at risk for CKD/ESRD
- What we can and should we do to resolve
Background:

What is the natural course of kidney function?
What is Chronic Kidney Disease (CKD)?
Natural Loss of Kidney Function with Age

Rate kidney function decline in normal and in hypothetical patients with onset of progressive renal disease at age 25:

**Progression at Different Rates:**

*Influence of Endogenous and Exogenous Factors*

<table>
<thead>
<tr>
<th>Rate</th>
<th>ml/min/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Starting at age 45</td>
</tr>
<tr>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>5.0</td>
<td></td>
</tr>
</tbody>
</table>

GFR, ml/min/1.73m²
What is Chronic Kidney Disease (CKD)?

- < 60 % of normal kidney function (i.e. < 60mL/min)
- Persistent abnormalities of the kidney demonstrated by imaging studies or by abnormalities in the urine (albumin, blood), irrespective of “ % of kidney function”

% Function = how well washing the blood of waste
### NKF CKD Stages

#### Table 12. Definition and Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73 m²)</th>
<th>With Kidney Damage*</th>
<th>Without Kidney Damage*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With HBP**</td>
<td>Without HBP**</td>
</tr>
<tr>
<td>≥90</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>60–89</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>30–59</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>15–29</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>&lt;15 (or dialysis)</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Shaded area represents chronic kidney disease; numbers designate stage of chronic kidney disease.

* Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

** High blood pressure is defined as ≥140/90 in adults and >90th percentile for height and gender in children.

* May be normal in infants and in the elderly.

K-DOQI. *AJKD* 2002
Levels of Kidney Function in a Cross Sectional of the US Population
Levels of Kidney Function

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73m²)</th>
<th>N (19,500)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90</td>
<td>5,900 30%</td>
</tr>
<tr>
<td>60-89</td>
<td>5,300 27%</td>
</tr>
<tr>
<td>30-59</td>
<td>7,600 39%</td>
</tr>
<tr>
<td>15-29</td>
<td>400 2%</td>
</tr>
<tr>
<td>&lt;15</td>
<td>300 1.5%</td>
</tr>
</tbody>
</table>

JASN 2002; 13:1338-1349
Where did they go?

GFR (mL/min/1.73m²) | N (19,500)
--- | ---
>90 | 30%
60-89 | 27%
30-59 | 39%
15-29 | 2%
<15 | ~2% (25 x reduction)

JASN 2002; 13:1338-1349
Longitudinal Follow-up of CKD: Decreased Kidney Function is Associated with Cardiovascular Disease, 1996-2000

Table 2. Adjusted Hazard Ratio for Death from Any Cause, Cardiovascular Events, and Hospitalization among 1,120,295 Ambulatory Adults, According to the Estimated GFR. *

<table>
<thead>
<tr>
<th>Estimated GFR</th>
<th>Death from Any Cause</th>
<th>Any Cardiovascular Event</th>
<th>Any Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60 ml/min/1.73 m²†</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>45–59 ml/min/1.73 m²</td>
<td>1.2 (1.1–1.2)</td>
<td>1.4 (1.4–1.5)</td>
<td>1.1 (1.1–1.1)</td>
</tr>
<tr>
<td>30–44 ml/min/1.73 m²</td>
<td>1.8 (1.7–1.9)</td>
<td>2.0 (1.9–2.1)</td>
<td>1.5 (1.5–1.5)</td>
</tr>
<tr>
<td>15–29 ml/min/1.73 m²</td>
<td>3.2 (3.1–3.4)</td>
<td>2.8 (2.6–2.9)</td>
<td>2.1 (2.0–2.2)</td>
</tr>
<tr>
<td>&lt;15 ml/min/1.73 m²</td>
<td>5.9 (5.4–6.5)</td>
<td>3.4 (3.1–3.8)</td>
<td>3.1 (3.0–3.3)</td>
</tr>
</tbody>
</table>

* The analyses were adjusted for age, sex, income, education, use or nonuse of dialysis, and the presence or absence of prior coronary heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.
† This group served as the reference group.

Go A et al. Chronic Kidney Disease and the Risk of Death, Cardiovascular Events, and Hospitalization. NEJM 2004;351:1296-305
What happens to those who survive to levels of kidney function $< 15\%$ (or mL/min)?

[Graph showing the progression of kidney function decline over age with lines indicating different rates of decline (1 ml/min/yr, 1.0 ml/min/yr, 2.0 ml/min/yr, 3.0 ml/min/yr, 5.0 ml/min/yr).]
End Stage Renal Disease (ESRD)
56% Forecasted Growth of *Dialysis* Population by 2020

U.S. Renal Data System. USRDS 2008 Annual Data Report. Figure 2.2. National Institutes of Health. Bethesda, MD.
CKD/ESRD

Who are they?

What got them here (ESRD)?
Incident rates of reported ESRD per million population, by age, gender, *race, & ethnicity* & primary diagnosis (adjusted)

Incident ESRD patients; unknowns dropped. Rates by age adjusted for gender & race, rates by gender adjusted for age & race, rates by race & ethnicity adjusted for age & gender, & rates by primary diagnosis adjusted for age, gender, & race. *Values for cells with ten or fewer patients are suppressed.*
Who are they?

What got them here (ESRD)?
Main Causes of CKD/ESRD: *Diabetes* and *Hypertension*

Incident counts & adjusted rates, by primary diagnosis

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

USRDS 2009
Figure 2.8 (Volume 2)
Who is the “face” of ESRD

- ~70% of new cases of ESRD are caused by Diabetes and Hypertension
- Among new patients with ESRD due to diabetes, almost 1/3 (31%) are African-American
- Among new patients with ESRD due to “hypertension”, more than ½ (51%) are African-Americans.

NKDEP
From USRDS 2005
Disrupting the “Norm”

- Current state of CKD/ESRD
- *What places patients at risk for CKD/ESRD*
- What we can and should we do to resolve
What places patients at risk for CKD/ESRD

- Patient Susceptibility: *Nature and Nurture*
What places patients at risk for CKD/ESRD

- Susceptibilities: Nature
  - Genetic predisposition
    - salt sensitivity
    - ACE gene polymorphism \(^1\)
      i.e. D/D vs I/D vs I/I
    - MYH9 gene polymorphism \(^2\)
      - (60% of African-Americans have a *risk* haplotype) \(^3\)
  - Medication intolerances

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ACE Inhibition Protects Renal Function In Non-diabetic African Americans with CKD

Follow-up (Months)

Percent With Events

Ramipril vs Amlodipine: RR = 0.69, $P < 0.05$  
Ramipril vs Metoprolol: RR = 0.80, $P < 0.05$

Relative Risk of CEI-Induced Cough is significantly higher in Blacks in multivariate regression analysis in 892 patients receiving first ever CEI Dose

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk</th>
<th>Cumulative Risk</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First yr of CEI Rx</td>
<td>1.03</td>
<td>0.87-1.15</td>
<td>0.11</td>
</tr>
<tr>
<td>Female</td>
<td>1.09</td>
<td>1.002-1.16</td>
<td>0.049</td>
</tr>
<tr>
<td>Black Race</td>
<td>2.58</td>
<td>1.21-4.65</td>
<td>0.01</td>
</tr>
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CEIs may protect residual kidney function (RKF), but can all patients adhere to therapy?

What places patients at risk for CKD/ESRD

- Susceptibilities: Nurture/ Environment
  - Environmental Lead Exposure \(^1,^2\)
  - Diet

Making Choices of Diets High in Fat, Sodium, and Calories

485+400 calories
21.5g + 17.5g of fat
1040mg + 309mg sodium
Choices have consequences...
“Diabetes”* in School-Aged Kids > 20%


*F Kaufman

Students who were > 95th percentile for body mass index, by age and sex, based on reference data.
Obesity Contributes to Kidney Disease

Metabolic Syndrome
- Obesity
- Insulin resistance
- Hyperinsulinemia
- Dyslipidemia

Abnormal Fetal Environment

Chronic Kidney Disease

HTN

PPAR

Weight Control Cytokines (Leptin, TNFα, IL-6)

DM2

Are the “choices” voluntary?
What Food “Choices” are *really* available?
Access to healthy foods worse in poor areas

Anne Harding
Wed Jan 21, 2009 2:00pm EST

NEW YORK (Reuters Health) - People who live in poorer neighborhoods in the U.S. are less likely to have easy access to supermarkets carrying a wide variety of fresh produce and other healthy food, an analysis of 54 studies confirms.
Three studies found a reduced risk of obesity among people with more supermarkets in their neighborhood;

two of these studies found a link between easier access to convenience stores and increased obesity risk.
What else places patients at risk for CKD/ESRD

• Susceptibilities: Nurture/ Environment
  • Environmental Lead Exposure
  • Diet
    + Genetics
Low 25-OH Vitamin D levels are associated with ESRD/Death

Spline shows the continuous association between 25(OH)D levels and the development of dialysis or death with underlying kidney disease among 13,328 participants of NHANES III

Incident Rate Ratio of Developing ESRD < 15ng/mL
2.64 (1-7.05) Adjusted 1
2.88 (1.10-7.55) Adjusted 2

Distribution of 25(OH)D levels by race/ethnicity in the NHANES III

Why the disparity?

Vitamin D Metabolism

Sun / UVB

7-dehydrocholesterol

Diet (Dairy):

Ergocalciferol (D2)

cholecalciferol (D3)

Hydroxylation

25-OH Vitamin D

Banks M, Sprague SM. Vitamin D and PD. PDI 2008; 28: S33-37.
Vitamin D Metabolism

- Sun / UVB
  - skin
  - 7-dehydrocholesterol
  - 25-OH Vitamin D

- Diet (Dairy):
  - ergocalciferol (D2)
  - cholecalciferol (D3)
  - hydroxylation

Banks M, Sprague SM. Vitamin D and PD. PDI 2008; 28: S33-37.
What places patients at risk for CKD/ESRD

- Susceptibilities (Nature and Nurture)
- Access to care
What places patients at risk for CKD/ESRD

- Susceptibilities
- Access to care
  - Routine Medical Care
    - Identify, educate, prevent and treat CKD
What places patients at risk for CKD/ESRD

- Susceptibilities
- Access to care
  - Routine Medical Care
  - Effective Health Care Providers and System
What places patients at risk for CKD/ESRD

- Susceptibilities
- Access to care
  - Routine Medical Care
  - Effective Health Care Providers and System
    - Sensitive to
      - Social, Culture and Linguistic
      - Biologic Differences
        - Awareness of side effects of drugs that potentially influences adherence
          i.e. ACE-inhibitor-induced cough
Relative Risk of Cough in multivariate regression analysis in 892 patients receiving first ever CEI Dose

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Availability of generic Losartan!

What places patients at risk for CKD/ESRD

- Susceptibilities
- **Access to care**
  - Routine Medical Care
  - Effective Health Care Providers and System (sensitivity)
  - **Self-imposed limitation to access**
What places patients at risk for CKD/ESRD

- Susceptibilities
- **Access to care**
  - Routine Medical Care
  - Effective Health Care Providers and System (sensitivity)
- **Self-imposed limitation to access**
  - Lack of trust of the “system” or provider: good reasons!
  - Misinformation about the facts
    - “normal for ethnic minorities to have a higher BP”
  - Sense of hopelessness for the future
Disrupting the “Norm”

- Current state of CKD/ ESRD
- What places patients at risk for CKD/ESRD
- *What we can and should do to resolve*
What we can and should do to resolve

- Public Health Initiatives
  - Health Care Plans to provide universal coverage and easy accessibility

- NIH funded research
  - i.e. biological factors that increase risk
    - translational research re: MYH9 polymorphism
What we can and **should** do to resolve

- **Public Health Initiatives**
  - **Health Care Plans** to provide universal coverage and easy accessibility
  - **NIH funded research**
- **Changing Publicly–Funded School Lunch Programs**
  - **Low fat**
  - **Low sodium**
  - **Dairy** (lactose-free equivalent)
  - **Higher potassium**
Zoning and tax incentives to spur the development of full-service grocery stores that devote a certain amount of space to fresh produce, meats, dairy and other perishables.
What we can and **should** do to resolve

- Public Health Initiatives
- *Education*
What we can and **should** do to resolve

- **Public Health Initiatives**
- **Education**
  - **Public Service Messaging: Racial, Cultural, and language appropriate about CKD risks and treatment**

http://www.cdc.gov/

**REACH U.S.**-supports programs and interventions
Education and Public Service Messaging

CKD needs a face
that those at risk can identify with!
What we can and **should** do to resolve

- Public Health Initiatives
- **Education**
  - **Public Service Messaging:** Racial, Cultural, language considerations
  - **Use the new** CKD Education Benefit (**H.R. 6331**)
H.R. 6331: Changes in Reimbursement: Education Benefit

Payment for up to 6 CKD Educational Sessions for Patients with Stage 4 CKD (15-30% of kidney function)

• Goals
  • Managing co-morbidities to delay onset of ESRD
  • Prevention of uremic complications
  • Educate about modality options to ensure informed choice
• Education provided by Physicians (PCPs, Nephrologists, etc), NP, PA, CNS
1) Enable information to be *Integrated* into Lifestyle Change

2) Patient empowerment to actively seek means to achieve desired outcome (BP goals, Vitamin D, Phosphate Control, etc.)

**Improving Outcomes**
Education: Kidney Replacement Options
Education: Kidney Replacement Options

In-center HD

Home Dialysis: PD + HHD
Education:

**Significant Survival Advantages to having a role in choice**

In-center HD

Home Dialysis: PD + HHD

---


Knowledge of Kidney Replacement Options: Significant Early Survival Advantages to PD

In-center HD


Home Dialysis: PD + HHD

USRDS 2008: 5.1% of black prevalent dialysis patients were treated with PD
What we can and **should** do to resolve

- Public Health Initiatives
- Education
- **HCP Awareness of and Appropriate Adjustment to Patient Differences**
What we can and should do to resolve

- Public Health Initiatives
- Education
- Health Care Professional (HCPS) Awareness of and Adaptation to Patient Differences
  - Engaging patients in ways that facilitate communication
What we can and **should** do to resolve

- Public Health Initiatives
- Education
- HCP Awareness of and Appropriate Adaptation to Differences
- *Community-Based Interventions*
What we can and **should** do to resolve

- Public Health Initiatives
- Education
- HCP Awareness of and Appropriate Adaptation to Differences
- **Community-Based Interventions**
  - Communications that support and disseminate scientifically-derived measures to achieve best health
What we can and should do to resolve

- Public Health Initiatives
- Education
- HCP Awareness of and Appropriate Adjustment to Differences
- Community-Based Interventions
  - Communications that support and disseminate scientifically-derived measures to achieve best health
  - *Improve health education and individual empowerment*

“I control my fate; it doesn’t control me”
Summary and Conclusions

The Current “Norm”

- CKD and ESRD are occurring in increasing numbers across the population, creating poor health and fiscal outcomes.
- Disparities exist in kidney-related outcomes.
- The contributors to these kidney-related disparities are complex, involving physiologic, environmental, cultural, and infrastructural causes.
Summary and Conclusions

**Disrupting the “Norm” in Chronic Kidney Disease**

- Will require an open-minded, multifaceted approach involving public health, educational, and community initiatives
Accomplishments on national, community and individual levels

K/DOQI CKD Stages
GFR mL/min/1.73m²

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (mL/min)</th>
</tr>
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<tbody>
<tr>
<td>&lt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>60–89</td>
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</tr>
<tr>
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<td>15–29</td>
<td>15–29</td>
</tr>
<tr>
<td>&lt;15 (or dialysis)</td>
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H.R. 6331: CKD Education Benefit

...but...
Systematic Diagnosis and Treatment of Disparities

H.R. 6331, Medicare Improvements for Patients and Provider Act
The “Long Walk” to improve outcomes for all patients with CKD will require that...

‘...after climbing a great hill, one only finds that there are many more hills to climb....[we] can rest only for a moment....for [our] long walk is not yet ended.’

Nelson Mandela
Humanitarian
Nobel Peace Prize 1993
1918-
Thank You

“\textit{I am the master of my fate: I am the captain of my soul.}”

William Ernest Henley
English Poet
1849–1903
Disrupting the “Norm” in Chronic Kidney Disease:

A national, community, & individual responsibility

“I am the master of my fate: I am the captain of my soul.”

William Ernest Henley
English Poet
1849–1903
Median age of incident patients, by race/ethnicity

Figure 2.10

For Hispanic patients we present data beginning in 1996, the first full year after the April 1995 introduction of the revised Medical Evidence form, which contains more specific questions on race & ethnicity.
I have made missteps along the way. But I have discovered the secret that after climbing a great hill, one only finds that there are many more hills to climb. I have taken a moment here to rest, to steal a view of the glorious vista that surrounds me, to look back on the distance I have come. But I can rest only for a moment, for with freedom comes responsibilities, and I dare not linger, for my long walk is not yet ended.
Figure 2
High-Poverty Areas of DC Are Underserved by Supermarkets

Source: USDA's Economic Research Service, Geographic Information Systems Unit, from 2000 FNS administrative data and 1990 census data on
Summary

The current norm and Conclusion

- CKD and ESRD are increasing population and fiscal problems
- Disparities exist in kidney-related outcomes
- The contributors to these kidney-related disparities is complex, involving physiologic, environmental, cultural, and infrastructural causes.
- Resolution will require an open-minded, multifaceted approach involving public health, educational, and community initiatives
Incident rates of reported ESRD per million population, by gender (adjusted)

Incident ESRD patients; unknowns dropped. Rates by age adjusted for gender & race, rates by gender adjusted for age & race, rates by race & ethnicity adjusted for age & gender, & rates by primary diagnosis adjusted for age, gender, & race. *Values for cells with ten or fewer patients are suppressed.
Disrupting the “Norm” in Chronic Kidney Disease

“A journey of a thousand miles must begin with a single step.”

Lao Tzu
Chinese Philosopher
“Tao Te Ching” (“The Book of the Way”).
600 BC-531 BC
Prevalence of CKD Stages

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*JASN* 2002; 13:1338-1349

25 x reduction
What we can and should do to resolve

- Public Health Initiatives
- Education
- HCP Awareness of and Appropriate Adjustment to Patient Differences
  - Learnings via medical education, NKF, ASN, RPA
  - Application of culturally-sensitive prevention and treatment strategies
  - Earning the trust of all patients
‘...after climbing a great hill, one only finds that there are many more hills to climb.... look back on the distance [we] have come....[we] can rest only for a moment....for [our] long walk is not yet ended.’

Nelson Mandela
Humanitarian
Nobel Peace Prize 1993
1918-
What we can and **should** do to resolve

- Public Health Initiatives
- Education
- HCP Awareness of and Appropriate Adjustment to Differences
- Community-Based Interventions
  - community, family, individuals need to “own” the problem to help work toward resolution
  - **Work to develop greater trust in medical intentions**
What places patients at risk for CKD/ESRD

- Susceptibilities
- Access to care
  - Prenatal care and pre-maturity
    - Fewer glomeruli at birth

---

What places patients at risk for CKD/ESRD

- Susceptibilities
- **Access to care**
  - Routine Medical Care
  - Health Care Providers and System sensitive to
    - Culture: motivational interviewing and interaction
    - Biologic Differences
      - side effects of drugs potentially influencing **adherence**
        i.e. ACE-inhibitor-induced cough

Limits effective care
Based on these issues, is it any surprise to see
Racial Differences In Prevalence of HTN?

Adult Population With Hypertension* by Age, Gender, and Race, U.S., 1999–2004

* Systolic blood pressure \( \geq \) 140 mm Hg, diastolic blood pressure \( \geq \) 90 mm Hg, on antihypertensive medication.
**Non-Hispanic.
Source: NHANES, NCHS.