For many years the World Health Organization has stressed that the primary threat to public health in this century lies in four major chronic diseases: diabetes, cardiovascular disease, chronic lung disease, and cancer. These conditions now account for the majority of deaths not only in high-income countries but in the middle- and now the low-income nations as well.

By reducing alcohol and tobacco use, controlling salt and calorie intake, and combating a sedentary lifestyle, these diseases are largely preventable. In September, 2011, the United Nations held a summit on chronic diseases, looking at how member states can address their impact, and discussing the widespread problems of premature loss of life, loss of economic productivity, and financial stress on families, which can contribute to advancing poverty. For the first time, because of its impact on morbidity and mortality and its substantial cost to the healthcare system, chronic kidney disease was added to the list of major diseases.

All countries now recognize the substantial impact of an increasing population with kidney failure, people who face premature death if they do not receive dialysis or a kidney transplant. The reality is that many countries struggle with the costs of providing end-stage renal disease (ESRD) care, costs which place ministries of finance at odds with ministries of health. The demand for transplant organs has led to the emergence of transplant tourism, with the buying and selling of organs. Some have expressed that a regulated market system would help fill this demand. Others suggest that prevention is a more sustainable approach, for without it the need will continue to grow, outpacing the pool of potential donors and increasing the known risks of the exploitation of poor populations at the expense of the wealthy. While the Istanbul Declaration on organ trafficking and transplant tourism has denounced the practice, the large number of patients across the globe who have advancing kidney disease continues to fuel demand.

The growing number of ESRD patients thus needs to be addressed in terms not only of its public health disease burden, but of its costs to the healthcare system, and of the high demand for replacement organs. And the overall prevention of kidney disease needs to be viewed in context of competing demands for resources, particularly in the difficult economic times currently faced around the world.

As shown in the Venn diagrams on the next page, 9.3 and 8.5 percent of patients in the general population had diabetes and cardiovascular disease, respectively, in 2010, while 13.1 percent had CKD, defined by an estimated GFR less than 60 mL/min/1.73 m² or a urine albumin-to-creatinine ratio (ACR) of 30 mg/g or higher. Using only the eGFR, CKD prevalence was 6.3 percent; using only the ACR, it reached 9.2 percent — on a par with diabetes and cardiovascular disease. There is now substantial evidence that both eGFR and urine ACR are predictors of all-cause death, cardiovascular events, and ESRD (Lancet 2010).

With diabetes and hypertension known to be major risk factors for CKD, the awareness, treatment, and control of these conditions are crucial. NHANES data show that blood pressure control in the general population improved between 1988–1995 and 2005–2010, reaching almost 50 percent. LDL cholesterol control increased from 25 to 33 percent, while glycemic control rose from 31 to 48 percent overall, and from 37 to 58 percent in patients whose CKD is defined by an eGFR less than 60. These improvements in treatment and control may be contributing to the flat ESRD rate, despite the greater burden of diabetes in the general population.

While CKD has been characterized from population-level estimates in the NHANES data, much of the disease is silent and unrecognized, complicating any full assessment of its impact. We present data on CKD recognized through diagnosis codes reported on claims — an approach which clearly underestimates CKD
in the Medicare population, but has been shown to have high specificity, indicating individuals likely to have the disease. As identified from these codes within the 2010 prevalent population, CKD is recognized in 9.2 percent of older Medicare patients, and 1.4 percent of the younger employed population. When CKD patients newly identified during the year are included as well, CKD represents 11.9 percent of the Medicare population, and accounts for 27.5 percent of fee-for-service costs (see see Figure p.1 in the Volume Two Précis). When added to costs for ESRD patients, it appears that 35 percent of all Medicare expenditures are incurred by patients with a diagnosis of kidney disease.

Despite this high disease burden, the rate of progression to ESRD has been relatively stable over the last several years, suggesting that CKD patients are dying at a higher rate before they reach ESRD or that they are progressing to ESRD at a slower rate. The continuing decline in rates of death from cardiovascular disease (the major cause of mortality in the CKD population), along with improved treatment and control of hypertension and increased use of ACEIs/ARBs/renin inhibitors, suggest that progression of CKD to ESRD may indeed have slowed.

Care of CKD patients after diagnosis is challenging to assess. In the Medicare CKD population (age 65 and older), it appears that 93 percent see a primary care physician within a year of diagnosis, while 64 percent visit a cardiologist; only 31 percent, however, see a nephrologist. When restricted to patients with CKD of Stages 3–5 (based on diagnosis codes), these rates reach 93, 65, and 60 percent. Similar data are reported for the employed population. And as we show in Chapter Two, only one-third of patients with diabetes, and 5 percent of those with hypertension, receive a urine albumin test within a year, despite the fact that these measurements are recommended by the American Diabetes Association and the American Heart Association.

Rates of hospitalization, and of rehospitalization within 30 days, are progressively higher with advancing CKD. The issue of rehospitalization has received more attention for patients in the general population than for those with CKD, despite the fact that the rate for CKD patients is almost 40 percent higher. The rate accelerates as patients approach ESRD, reaching 43 percent in the month prior to ESRD initiation. These data show the substantial burden of disease and needed care in the CKD population, burdens illustrated as well in our data on mortality and cardiovascular disease in CKD patients.

New figures show that, when compared to the general population, Medicare Part D prescription drug use for those with CKD is dominated by diuretics, statins, beta blockers, ACEIs, and calcium channel blockers. Interestingly, thyroid replacement therapy is very common in the CKD population, a fact which has received little attention.

This year we again highlight data on acute kidney injury (AKI). In both the Medicare and employed populations, rates of AKI rise with age. Recurrent hospitalizations for AKI are common, with rates reaching 28 percent for patients whose original AKI did not require dialysis, and 33 percent for those dialyzed during the original hospitalization; these numbers rise to 34 and 49 percent for blacks/African Americans. The rate of outpatient follow-up with a nephrologist in the year following AKI, however, is barely 20 percent.

Drug treatment changes considerably after an AKI event. The use of ACEIs/ARBs, for example, declines in the three months after discharge, but returns to the pre-AKI rate. It does not, however, exceed this initial rate, despite that fact that CKD has progressed. » Figure 1.1; see page 140 for analytical methods. NHANES participants 2005–2010, age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin creatinine ratio (ACR).
Between 1988–1994 and 2005–2010, the overall prevalence estimate for CKD — defined by an eGFR <60 ml/min/1.73 m² or an ACR ≥30 mg/g — rose from 12.3 to 14.0 percent. The largest relative increase, from 25.4 to 40.8 percent, was seen in those with cardiovascular disease. For eGFR <60, prevalence rose from 4.9 to 6.7 percent, with the largest increase in those age 40–59; for ACR ≥30 mg/g, the estimate rose from 8.8 to 9.4. » Table 1.a; see page 140 for analytical methods. NHANES III (1988–1994) & 2005–2010 participants age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin creatinine ratio (ACR).

Here we look at several subgroups of NHANES 2005–2010 participants, showing the percentage in each population with an eGFR <60 ml/min/1.73 m² and an ACR ≥30 mg/g. Nearly 28 percent of participants with cardiovascular disease (CVD) had an eGFR less than 60, compared to 19.3, 12.9, and 7.4 percent of those with diabetes, hypertension, and a high body mass index, respectively. Participants with diabetes were the most likely to have an ACR ≥30 mg/g, at 29.9 percent, compared to 24.3, 14.8, and 11.7 percent among those with CVD, hypertension, and a high BMI.

Nearly 11 percent of participants with CVD had both an eGFR <60 and an ACR ≥30, compared to 8.6 percent of those with diabetes and 4.1 and 2.1 percent, respectively, of those with hypertension and a high BMI. » Figure 1.11; see page 140 for analytical methods. NHANES III (1988–1994) & 2005–2010 participants age 20 & older; eGFR calculated using CKD-EPI equation; urine albumin creatinine ratio (ACR).
Among 2010 point prevalent general Medicare patients age 65 and older, diabetes was reported in 24 percent, and CKD in 9.2 percent. In the younger MarketScan population (with a mean age of 56.7), these rates were 10.1 and 1.4 percent. Figure 2.1; see page 141 for analytical methods. Point prevalent general (fee-for-service) Medicare patients age 65 & older; point prevalent MarketScan patients age 50–64. Diabetes, CKD, CHF, & CVA determined from claims.

Among Medicare patients, claims data identify 13.7 percent of blacks/African Americans, and 8.8 percent of whites, as having prevalent CKD in 2010, compared to 11.5 and 7.0 percent identified using only the combined 585 codes. The most commonly reported stage-specific code in the prevalent CKD population is 585.3 (Stage 3), at 3.4 and 5.2 percent for white and black/African American Medicare patients, respectively. Figure 2.2; see page 141 for analytical methods. Prevalent Medicare patients surviving cohort year, without ESRD, age 65 & older.
Fourteen percent of NHANES participants have CKD. The likelihood of CKD increases with age, is recognized in women more often than in men, and occurs in 14.3 percent of whites and 16 percent of blacks/African Americans. Among Medicare patients age 65 and older, a CKD diagnosis code is more likely in older patients, men, and blacks/African Americans, and in patients with cardiovascular disease (CVD), at 23.1 percent compared to 10.3 and 15.8 percent in patients with diabetes or hypertension. In MarketScan patients age 55–59 and 60–64, the odds of a CKD diagnosis code are 18 and 43 percent higher compared to patients age 50–64, are lower in women compared to men, and are three times higher in patients with diabetes, hypertension, or cardiovascular disease than in patients without these conditions. » Table 2.d; see page 141 for analytical methods.

Patients alive & eligible all of 2009. CKD diagnosis represents date of first CKD claim during 2009; physician claims searched during 12 months following that date.
In both CKD and non-CKD populations age 66 and older, adjusted rates of hospitalization increase with greater comorbidity. In 2010, for example, admissions for Stage 4–5 CKD patients with both diabetes and cardiovascular disease reached 882 per 1,000 patient years — more than twice the rate among patients with neither diagnosis. » Figure 3.2; see page 142 for analytical methods. January 1, 2010 point prevalent Medicare patients, age 66 & older on December 31, 2009. Adj: age/gender/race/prior hospitalization/comorbidity; rates by one factor are adjusted for the others. Ref: Medicare patients age 66 & older, 2010.

In both CKD and non-CKD populations age 66 and older, adjusted rates of hospitalization increase with greater comorbidity. In 2010, for example, admissions for Stage 4–5 CKD patients with both diabetes and cardiovascular disease reached 882 per 1,000 patient years — more than twice the rate among patients with neither diagnosis. » Figure 3.2; see page 142 for analytical methods. January 1, 2010 point prevalent Medicare patients, age 66 & older on December 31, 2009. Adj: age/gender/race/prior hospitalization/comorbidity; rates by one factor are adjusted for the others. Ref: Medicare patients age 66 & older, 2010.

Thirty-four percent of hemodialysis patients are rehospitalized within 30 days, compared to 24 percent of patients with CKD and 18 percent in the general Medicare population. » Figure 1.1; see page 142 for analytical methods. January 1, 2010 point prevalent Medicare patients, age 66 & older on December 31, 2009, unadjusted. Includes live hospital discharges from January 1 to December 1, 2010.
The thirty-day all-cause rehospitalization rate among patients with CKD of Stages 4–5 was 26 percent in 2010, compared to 23 percent in those with Stage 1–2 CKD; rates for death or rehospitalization were 33 and 28 percent, respectively. The rehospitalization rate among CKD patients (24 percent) exceeded the rate of the combined end-point of death or rehospitalization in non-CKD patients, at 22 percent.

Rates of rehospitalization increase with the severity of CKD, and are highest among males and blacks/African Americans within all groups except patients with CKD of Stages 4–5; rates in these patients are similar by gender and highest in races other than white or black/African American. » Figure 3.9; see page 142 for analytical methods. January 1, 2010 point prevalent Medicare patients, age 66 & older on December 31, 2009; unadjusted. Includes live hospital discharges from January 1 to December 1, 2010
The highest rehospitalization rates during the transition to ESRD are observed following an index hospitalization for infection, with 44 percent of discharges followed by a rehospitalization within 30 days during the first quarter before ESRD initiation. In the quarter following ESRD initiation, 44 percent of discharges from hospitalizations for infection are followed by death or rehospitalization within 30 days. » Figure 3.13; see page 142 for analytical methods. Incident ESRD patients, January 1 to October 1, 2010; age 67 or older, unadjusted.

Among non-CKD patients age 66 and older, adjusted mortality rates are 15 percent higher than unadjusted rates. For CKD patients, rates adjusted for patient characteristics, hospitalizations, and comorbidities are 41–50 percent lower. Adjusted mortality reaches 115 deaths per 1,000 patient years for patients with Stage 4–5 CKD. » Figure 3.15; see page 143 for analytical methods. January 1, 2010 point prevalent patients age 66 & older. Adj: age/gender/race/prior hosp./comorbidities. Ref: 2010 all patients.

There has been little change by CKD status in the percentage of patients receiving stress tests, nor has the use of coronary angiography changed appreciably, despite recognition of CKD as a risk factor for both coronary events and increased mortality. The use of echocardiography in CKD patients with CHF, in contrast, has grown, from 42 percent in 2000 to 48 percent in 2010. » Figure 4.2; see page 144 for analytical methods. January 1 point prevalent Medicare patients age 66 & older. CKD stages not available from claims data in 2000.
There is a graded increased risk of mortality with advancing CKD; the two-year mortality rate after MI, for example, at 44 percent in patients with no CKD, rises to 58 and 68 percent for those with Stage 3 and 4–5 CKD. Similar trends occur for death following CVA/TIA, CHF diagnosis, and coronary revascularization. Although the probability of death is lower in patients with advanced CKD who have CABG surgery compared to PCI, these are observational data and there may be confounding by indication. » Figures 4.4–7; see page 143 for analytical methods. January 1 point prevalent Medicare patients age 66 & older. CKD stages not available from claims data in 2000.
<table>
<thead>
<tr>
<th>Year</th>
<th>Beta blocker</th>
<th>Clopidogrel</th>
<th>Warfarin</th>
<th>Statin</th>
<th>Amiodarone</th>
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<tbody>
<tr>
<td>2007</td>
<td>59,922</td>
<td>53.8</td>
<td>52.2</td>
<td>14.2</td>
<td>21.2</td>
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<tr>
<td>All CKD</td>
<td>12,611</td>
<td>47.4</td>
<td>56.4</td>
<td>18.3</td>
<td>19.0</td>
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<tr>
<td>Stages 1–2</td>
<td>650</td>
<td>50.5</td>
<td>54.2</td>
<td>19.2</td>
<td>18.9</td>
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<tr>
<td>Stage 3</td>
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<td>52.6</td>
<td>60.6</td>
<td>19.6</td>
<td>19.7</td>
</tr>
<tr>
<td>Stages 4–5</td>
<td>2,129</td>
<td>42.4</td>
<td>62.0</td>
<td>19.7</td>
<td>16.8</td>
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</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Beta blocker</th>
<th>Clopidogrel</th>
<th>Warfarin</th>
<th>Statin</th>
<th>Amiodarone</th>
</tr>
</thead>
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<tr>
<td>2010</td>
<td>50,894</td>
<td>57.2</td>
<td>60.3</td>
<td>16.0</td>
<td>24.3</td>
</tr>
<tr>
<td>All CKD</td>
<td>16,348</td>
<td>52.2</td>
<td>66.4</td>
<td>20.3</td>
<td>23.2</td>
</tr>
<tr>
<td>Stages 1–2</td>
<td>666</td>
<td>57.1</td>
<td>64.3</td>
<td>21.3</td>
<td>19.2</td>
</tr>
<tr>
<td>Stage 3</td>
<td>4,505</td>
<td>55.0</td>
<td>68.2</td>
<td>21.4</td>
<td>24.8</td>
</tr>
<tr>
<td>Stages 4–5</td>
<td>3,316</td>
<td>44.4</td>
<td>69.9</td>
<td>21.4</td>
<td>21.3</td>
</tr>
</tbody>
</table>

**Table 4.b**: see page 143 for analytical methods. *January 1 point prevalent Medicare patients with Medicare Parts A, B, & D enrollment.*
Sixty percent of general Medicare patients, and 58 percent of patients with CKD, were enrolled in Part D in 2010, as were 69 percent of patients with ESRD. The proportion of patients with other creditable coverage is similar among CKD and Medicare patients, at about 13 percent, but a higher proportion of CKD patients have retiree drug subsidy coverage, at 21 compared to 15 percent. Eight percent of CKD patients have no known source of drug coverage — a level lower than the 13 percent seen in the general Medicare population. 

In terms of frequency of use, the top 15 drugs covered by Medicare Part D are similar in the general Medicare and CKD populations. Simvastatin, for example, is the most frequently used drug in the general Medicare population, and second on the list for CKD patients. Three drugs — metoprolol, metformin and hydrochlorothiazide — appear in the top 15 for general Medicare patients, but not for CKD patients, in whom furosemide (a loop diuretic) has a more potent diuretic effect, and metformin is contra-indicated secondary to the increased risk of lactic acidosis. Carvedilol, allopurinol, and hydrocodone, in contrast, make the list only for CKD patients. Interestingly, potassium chloride is one of the most frequently used medications in the CKD population, which may indicate a more aggressive use of diuretics in these patients. 

PPPY total costs for Part D-covered medications in 2010 were 3.3–3.9 times greater for LIS patients than for those without LIS. Costs in LIS and non-LIS patients vary from $3,985 and $1,010 PPPY, respectively, in the general Medicare population to $5,997 and $1,733 among patients with CKD, and to $7,243 and $2,114 among those on dialysis. 

In general, Medicare totals include Part D claims for all patients in the Medicare 5 percent sample enrolled in Part D. CKD total includes Medicare CKD patients, as determined from claims. ESRD totals include all Part D claims for Medicare ESRD patients enrolled in Part D.
Data here show the rising incidence of AKI. While in isolation there appears to be an epidemic, it is likely that a proportion of this change is the result of code creep. Superimposed on this figure is the proportion of reported AKI patients requiring dialysis. While the threshold for defining AKI has changed over time, the threshold for when to initiate dialysis has likely remained fairly stable. In contrast to the incidence of AKI, the incidence of AKI requiring dialysis has been declining, further supporting the notion of code creep for AKI diagnoses.

» Figure 6.1; see page 145 for analytical methods. Medicare patients age 66 & older.

Acute kidney injury is highly associated with age. Among Medicare patients age 66–69, for example, the rate of AKI in 2010 was 13.6 per 1,000 patient years, and increased to 18.1, 24.9, 34.2, and 46.9, respectively, with increasing ages of 70–74, 75–79, 80–84, and 85 and older. Similar patterns are seen in both the MarketScan and Ingenix i3 populations.

» Figure 6.3; see page 145 for analytical methods. Medicare AKI patients age 66 & older, & MarketScan & Ingenix i3 patients age 20–64.

Following hospital discharge for an AKI hospitalization, the probability of one recurrent hospitalization event is 0.29 overall and 0.28 and 0.36, respectively, in whites and blacks/African Americans. The probability of having more than one AKI event is highest in black/African Americans compared to whites — at 0.15 versus 0.09 for two events and 0.07 versus 0.03 for three.

» Figure 6.9; see page 145 for analytical methods. Medicare AKI patients age 66 & older. 2009–2010.
Following an AKI hospitalization, 75 percent of patients see a primary physician within three months of discharge, while 38 and 13.2 percent, respectively, see a cardiologist or nephrologist.

Surprisingly, fewer than half of the patients with a recurrent AKI see a primary care physician within three months of their second discharge, while 24.4 percent see a cardiologist and 18.1 and 12.2 percent, respectively, see a nephrologist (any or outpatient).

Outpatient visits to a nephrologist following an initial or recurrent AKI event are more likely in patients with CKD than in those without. » Figures 6.13–14; see page 145 for analytical methods. Medicare AKI patients age 66 & older, 2009–2010.

Among individuals suffering an AKI event, the probability of serum creatinine and urine protein testing is higher, regardless of race, in those seeing a nephrologist than in those who do not. » Figures 6.16–17; see page 145 for analytical methods. Medicare AKI patients, age 66 & older, 2009.
When comparing cardiovascular medication use in patients prior to, in the first three months after, and at one year following an AKI or recurrent AKI event, the greatest increases in medication use occur in patients who had dihydropyridine calcium channel blockers, loop diuretics, or beta blockers prescribed within the three months prior to their AKI event. Patients using thiazide diuretics or an ACEI/ARB/renin inhibitor, in contrast, are likely to use less of these medications at three months post-AKI, but generally return to their pre-AKI use levels by twelve months. » Figure 6.18; see page 145 for analytical methods. AKI patients with Part D coverage, 2009.

**Figure 6.18**

Drug therapy prior to & after hospitalization for AKI in patients with Medicare Part D coverage, for initial & recurrent AKI

**Initial AKI**
- Within 3 months prior
- Within 3 months after
- Cumulative 12 months

**Recurrent AKI (in 2009)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial AKI</th>
<th>Recurrent AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Blocker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dihydropyridine CCB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loop diuretic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI/ARB/renin inhib</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazide diuretic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CKD status changes significantly following an AKI hospitalization. Among those with CKD of Stages 1–2 prior to the hospitalization, for example, 43 percent are classified as having Stage 3–5 CKD. And of those with Stage 3–5 CKD pre-hospitalization, 12.6 reach ESRD. Among patients with an AKI hospitalization requiring dialysis, of those classified as Stage 1–2 CKD, 41.4 percent are reclassified as having CKD of Stages 3–5 after their hospitalization; among patients with Stage 3–5 CKD pre-hospitalization, 62 percent reach ESRD. » Figures 6.21 & 6.23; see page 145 for analytical methods. Medicare AKI patients age 66 & older, 2010. Figure 6.23: data limited to AKI events with dialysis.

**Figure 6.21**

Changes to CKD status following hospitalization for AKI in Medicare patients, 2010

**Figure 6.23**

Changes to CKD status following a hospitalization for AKI with dialysis in Medicare patients, 2010
Congestive heart failure affects 9.5 percent of patients in the fee-for-service Medicare population, and accounts for nearly 22 percent of expenditures. Nearly 34 percent of expenditures go toward the 23.4 percent of patients with diabetes. And patients with CKD, who represent 8.4 percent of the point prevalent population, account for 17.0 percent of total expenditures. » Figure 7.7; see page 146 for analytical methods. Populations estimated from the 5 percent Medicare sample using a point prevalent model (see appendix for details). Population further restricted to patients age 65 & older, without ESRD. Diabetes, CHF, & CKD determined from claims; costs are for calendar year 2010.