Maintenance Dialysis throughout the World in Years 1990 and 2010

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ABSTRACT
Rapidly rising global rates of chronic diseases portend a consequent rise in ESRD. Despite this, kidney disease is not included in the list of noncommunicable diseases (NCDs) targeted by the United Nations for 25% reduction by year 2025. In an effort to accurately report the trajectory and pattern of global growth of maintenance dialysis, we present the change in prevalence and incidence from 1990 to 2010. Data were extracted from the Global Burden of Disease 2010 epidemiologic database. The results are on the basis of an analysis of data from worldwide national and regional renal disease registries and detailed systematic literature review for years 1980–2010. Incidence and prevalence estimates of provision of maintenance dialysis from this database were updated using a negative binomial Bayesian meta-regression tool for 187 countries. Results indicate substantial growth in utilization of maintenance dialysis in almost all world regions. Changes in population structure, changes in aging, and the worldwide increase in diabetes mellitus and hypertension explain a significant portion, but not all, of the increase because increased dialysis provision also accounts for a portion of the rise. These findings argue for the importance of inclusion of kidney disease among NCD targets for reducing premature death throughout the world.

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There is growing emphasis throughout the world on understanding the effects of chronic diseases on population health. Recent advances in treating and preventing communicable diseases coupled with the dramatic rise in the prevalence of diabetes and hypertension have initiated a shift in focus to the relationship between NCDs and morbidity, most recently in developing regions of the world.1-4 This is exemplified by the United Nations 2012 Summit 2025 Initiative, which focuses on decreasing the burden of premature mortality to NCDs by 25% by year 2025.

The recent publication of the 2010 Global Burden of Disease Study (GBD) offers a systematic analysis of the contribution of disease and injury to morbidity and early mortality throughout the world.1 The 2010 GBD is the first edition to include CKD among the chronic diseases assessed and ranks it as the 18th most common cause of death, a substantial increase from its 27th ranking two decades before.1 These rankings illustrate the significant and increasing effect of CKD on global health.

The 2010 GBD makes it now possible for the first time to calculate the change in prevalence and incidence of provision of maintenance dialysis for 187 countries from 1990 to 2010. These estimates provide timely information and are highly relevant for countries striving to develop programs and strategies for addressing the needs of a quickly growing population of individuals that require the costly medical intervention of RRT.5,6
GLOBAL BURDEN OF MAINTENANCE DIALYSIS

In 2010, throughout the world, we have estimated 284 individuals per million population (pmp) to be undergoing maintenance dialysis (concise methods are included in Supplemental Appendix 1). In 2010, >60 countries provided universal access to maintenance dialysis (Supplemental Table 1). These countries accounted for 70% of prevalent maintenance dialysis and 60% of incident dialysis population worldwide (Figures 1 and 2, Tables 1 and 2).

Global Prevalence and Incidence

The global prevalence of maintenance dialysis has increased 1.7 times from 165 pmp patients in 1990 to 284 pmp in 2010. There was a 170% increase in prevalence of patients treated with maintenance dialysis in countries that provided universal access and approximately 250% among countries that provided universal access and approximately 180% among countries with partial access (Table 2).

The strongest contributor to a larger increase in incidence rate than prevalence is the continued expansion of programs that have recently granted universal or partial access to maintenance dialysis in low- and middle-income countries. In contrast, recent data for developed nations, such as the United States and Western Europe, actually demonstrate a stabilizing trajectory of dialysis initiation in recent years.7,8 Furthermore, in some countries, many patients are offered maintenance dialysis only as a bridge to kidney transplantation; this, in turn, could explain the higher increase in incidence rates when compared with the change in prevalence. Although mortality rates for patients undergoing maintenance dialysis have decreased, mortality is still significantly higher among dialysis patients when compared with the general population, which would also affect the prevalence over the incidence.7,9,10

Patterns of Change: Geography and Population Structure

Assessing patterns of change at a more granular geographic level allows for identification of regions where dramatic change has occurred and other parts of the world where provision of maintenance dialysis remains limited.

Figure 1. Age-standardized prevalence per million population of maintenance dialysis in year 2010 for 187 countries. ATG, Antigua and Barbuda; BRB, Barbados; COM, Comoros; DMA, Dominica; E. Med, Eastern Mediterranean; Fiji, Fiji; FSM, Federated States of Micronesia; GRD, Grenada and Trinidad; KIR, Kiribati; LCA, Saint Lucia; MDV, Maldives; MHL, Marshall Islands; MUS, Mauritius; SGP, Singapore; SLB, Solomon Islands; SYC, Seychelles; TLS, Timor-Leste; TTO, Trinidad and Tobago; TUN, Tunisia; VCT, Saint Vincent and Grenadines; VUT, Vanuatu; WSM, Samoa.
dialysis has remained stable during the last two decades. North America and Pacific Asian regions had the highest prevalence for maintenance dialysis in both 1990 and 2010, followed by world regions of Europe, Australasia, and portions of Latin America (Figure 1). The incidence of provision of maintenance dialysis has followed a similar geographic pattern over time (Figure 2). World regions with the consistently lowest estimates include Sub-Saharan Africa and South and Central Asia.

Access to Maintenance Dialysis in Developing Nations

The incidence and prevalence of maintenance dialysis are not equivalent to the burden of ESRD. In many countries in Africa and South Asia, chronic comorbidities contribute to the societal burden of ESRD as also infections such as malaria, schistosomiasis, HIV, and chronic hepatitis. Hence, there is likely a large, untreated burden of ESRD within these regions. These countries face the difficult task of allocating adequate resources for the care of this condition from the large economic strain likely to be imposed by universal provision of maintenance dialysis. The resultant rationing of maintenance dialysis often selects against the impoverished and socially marginalized groups, such as the elderly and chronically infirm, sections of society known to generally have higher rates of CKD. A study of >2000 patients with ESRD in South Africa between 1988 and 2003 revealed that more than half of these patients were not offered dialysis secondary to rationing of RRT. Factors that weighed into the decision to provide dialysis centered on patient access to transportation, degree of comorbidity, and social stability. Therefore, this continued depressed activity within these countries indicates continued limited regional ability to provide RRT rather than a lack of disease burden.

Population Structure

To assess the effect of changes in population structure over time on the burden of treated ESRD, we modeled projected estimates of the prevalence expected if all contributing factors aside from population growth and aging remained constant (Table 1). Within countries with universal dialysis access in 2010, population growth and aging should have contributed to a 41% increase in prevalent dialysis and a 55% increase among nations with limited dialysis access. Countries with universal access sustained a growth rate of 114% over and above the projected 41% increase, whereas countries with limited access sustained a growth rate of 99% over and above growth anticipated secondary to changes in population structure. These data indicate that although changes in population structure over time play an important role in explaining the dramatic increase in maintenance dialysis throughout the world, this is only a partial explanation.
Within low-income countries, general improved health conditions, such as prevalence of childhood malnutrition, water purity, sanitation, and improved treatment of infectious diseases (e.g., HIV), have contributed to more stable population growth and aging, as indicated by population-based ESRD estimates for these regions (Figure 3). The seemingly enormous growth rate in provision of maintenance dialysis above population estimates for these regions should be interpreted with caution (Figure 3). Regions in Sub-Saharan Africa likely experienced such a growth rate because maintenance dialysis in 1990 was largely nonexistent. In comparison, there has been measurable growth in Central Latin America and Eastern Europe over the last two decades by making significant progress toward increasing dialysis access to substantial portions of the population (Figure 4).

**Factors for Change: Population Burden of Diabetes Mellitus and Hypertension**

There is a robust literature evidencing the increase in diabetes mellitus and hypertension throughout the world, thought secondary to increasing life span, westernization of diet, and the rising tide of obesity and consequent metabolic syndrome. Because diabetes and hypertension are leading causes of ESRD, we determined the contribution of the global rise in these diseases to the rise in prevalence and incidence of maintenance dialysis (Figures 4 and 5). Results among countries providing partial versus universal dialysis were remarkably similar. We estimated an anticipated growth of approximately 50% in maintenance dialysis patients secondary to diabetes within the general population. Within countries providing universal dialysis access, there was a total increase of 184% and a 188% increase among countries providing partial dialysis access (Tables 3 and 4). A similar pattern emerged when assessing the increasing burden of hypertension among the general population relative to the growth in maintenance dialysis (Table 4). These percentages illustrate that even though the growth of diabetes mellitus and hypertension within the global population plays a large role in the increasing burden of maintenance dialysis, these drivers also do not explain the total rise in rates. The greatest contributor to markedly increased rates of dialysis provision remains the expansion of or governmental support for dialysis programs.

**Patterns of Growth: Sex Differences**

Sex imbalances in kidney transplantation are well described within the literature, where women are more often known to serve as living donors, whereas men are more likely to be in receipt of kidney transplants. Sex imbalances in the provision of maintenance dialysis are less well described. In limited-resource countries, the sex differences in provision of maintenance dialysis are similar to that for kidney transplantation, with a higher incidence in men than in women. Other factors that may play a role in sex imbalances within resource-limited settings may involve prioritization of men in patriarchal societies and family prioritization of men on the basis of earning potential.

Our analysis indicates that at the global level, in both years 1990 and 2010, men were in greater receipt of maintenance dialysis than women, but dialysis rates for women increased more than men (Table 1). At the regional level, in 2010, men were in receipt of dialysis to a greater degree than women in all world regions except tropical Latin America, with most notable differences in regions of Australasia, South Asia, and

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**Table 1.** Decomposition analysis of the change in global dialysis prevalence rates and counts from 1990 to 2010 stratified by sex and provision

<table>
<thead>
<tr>
<th>Stratification According to Dialysis Provision</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global 1990 prevalence rate (pmp)</strong></td>
<td>180 (169, 191)</td>
<td>151 (143, 160)</td>
<td>165 (158, 172)</td>
</tr>
<tr>
<td><strong>Global 2010 prevalence rate (pmp)</strong></td>
<td>301 (293, 310)</td>
<td>269 (262, 276)</td>
<td>284 (279, 289)</td>
</tr>
<tr>
<td>Countries with universal maintenance dialysis access</td>
<td>254,593</td>
<td>236,213</td>
<td>490,806</td>
</tr>
<tr>
<td>No. of patients in 2010 expected secondary to population growth</td>
<td>295,018</td>
<td>271,522</td>
<td>566,577</td>
</tr>
<tr>
<td>No. of patients in 2010 expected secondary to population aging</td>
<td>367,291</td>
<td>327,809</td>
<td>692,991</td>
</tr>
<tr>
<td>Year 2010 prevalent patients</td>
<td>656,850</td>
<td>667,030</td>
<td>1,323,880</td>
</tr>
<tr>
<td>Percentage change between 1990 and 2010 because of Growth</td>
<td>16</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Aging</td>
<td>28</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Rate</td>
<td>114</td>
<td>144</td>
<td>129</td>
</tr>
<tr>
<td>Percentage total change, 1990–2010</td>
<td>158</td>
<td>182</td>
<td>170</td>
</tr>
<tr>
<td>Countries with partial maintenance dialysis access</td>
<td>112,569</td>
<td>100,050</td>
<td>212,619</td>
</tr>
<tr>
<td>No. of patients in 2010 expected secondary to population growth</td>
<td>135,138</td>
<td>118,675</td>
<td>253,761</td>
</tr>
<tr>
<td>No. of patients in 2010 expected secondary to population aging</td>
<td>175,418</td>
<td>155,014</td>
<td>330,396</td>
</tr>
<tr>
<td>Year 2010 prevalent patients</td>
<td>281,899</td>
<td>258,863</td>
<td>540,761</td>
</tr>
<tr>
<td>Percentage change between 1990 and 2010 because of Growth</td>
<td>20</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Aging</td>
<td>36</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Rate</td>
<td>95</td>
<td>104</td>
<td>99</td>
</tr>
<tr>
<td>Percentage total change, 1990–2010</td>
<td>150</td>
<td>159</td>
<td>154</td>
</tr>
</tbody>
</table>

All number sets in parentheses in indicate 95% uncertainty intervals.
Oceania (Figure 6). These results indicate that although social structures and limited resources likely play a role, there may also be a biologic explanation for sex disparities because there is a higher incidence of maintenance dialysis in men in nearly all societies.

Drivers of ESRD Burden: CKD Detection, Progression, and Death

Within the last decade, advances in detection of CKD through widespread implementation of creatinine and GFR measurements have enhanced our ability to detect kidney disease. Specifically, the conceptual model of CKD developed in 2002 by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative has aided our ability to quantify the burden of various stages of CKD and evaluate risk factors and outcomes for the CKD population. Such advances may have had a complex effect on ESRD burden. First, detecting earlier stage CKD allows for time to determine possible etiologies and factors contributing to CKD progression that has the potential to decrease the societal burden of ESRD. Alternatively, detecting later-stage CKD allows for time to prepare for initiation of maintenance dialysis before death. This increased ability to detect CKD at earlier stages and monitor disease progression (subsequently discussed) has possibly contributed to the growth in the ESRD population between 1990 and 2010.

CKD Progression
Understanding risk factors for CKD progression is pivotal to understanding drivers for perspective ESRD increase and for targeting ways in which risk factors for incidence and disease progression can be altered. Although certain determinants of CKD progression are unalterable, such as age, sex, race, and in some circumstances, CKD etiology, some interventions have the potential to affect the rate of progression. As previously stated, diabetes mellitus and hypertension have become the leading drivers for the growing ESRD population within high-, middle-, and low-income countries. Numerous studies indicate the benefit of glucose control and BP control on delaying progression of CKD. These facts highlight the importance of early CKD detection to allow for time to implement such disease-altering strategies.

Other contributors to CKD progression include episodes of AKI, which is hypothesized to initiate an inflammatory response that continues after the AKI episode has resolved. Causes of AKI vary geographically. The causes for AKI in the developed world regions include imagining contrast, surgery, toxicity from medications, critical illness, and complications to chronic diseases, such as cardiac and liver disease. Within developing world regions, causes can include toxicity from herbal treatments and complications during perinatal events. Again, the relationship between AKI episodes and CKD progression highlights the importance of early CKD detection to increase the likelihood of protecting remaining kidney function from such events.

Within the last decade, evidence for the relationship between CKD and cardiovascular (CV) events highlights the importance of treatment of modifiable CV risk factors within this population, such as lipid management and smoking cessation. Of concern are studies indicating that among patients with CKD, such targets are often not met. Foster et al. highlight suboptimal lipid control among patients with CKD in a cross-sectional National Health and Nutrition Examination Survey study of United States adults. The study illustrated the increased CV risk burden among patients with CKD.
Pre-ESRD CKD Mortality
Another contributor to rising ESRD rates is improved survival of patients with CKD. Individuals with pre-ESRD CKD are known to experience a significantly higher likelihood of all-cause mortality than the general population.61–63 The United States Renal Data System indicates that between 1995 and 2012, mortality for individuals >65 with and without CKD has decreased, but by 42% for those with CKD compared with 16% for those without. This decline in risk of death within the CKD population persists even when adjusting for demographic factors such as age, race, and sex.61 This success in mitigating premature death within the pre-ESRD CKD population within the last two decades may also have contributed to growth of the ESRD population because patients with CKD live long enough to progress to end stage.

Growing ESRD Population: Future Projections
Studies have projected growth of CKD and ESRD populations beyond year 2010. Within the United States, it is projected that by 2020 there will be 150,000 incident ESRD patients and 785,000 prevalent patients.7 Total Medicare spending for this 2020 ESRD population is estimated to approach $53.6 billion in comparison with expenditure in 2012 of $28.6 billion, which was 5.6% of total Medicare costs.7 Other countries have performed similar estimations of projected ESRD growth.64,65 By 2020, it is estimated that Greece’s ESRD prevalent population will grow to 15,147, with an annual incident increase of 2%.65 The projected growth of ESRD has also been modeled for Australia, which anticipates a 29% growth in the ESRD population by 2020. This growth is projected to require an average annual RRT per capita expenditure increase of 16%.64

Economic Effect of Provision of Maintenance Dialysis
Considering the economic implications of growth in the maintenance dialysis population throughout the world, we have modeled the percentage of total health care expenditure that would need to be allocated to the provision of maintenance dialysis for a portion of the national prevalent CKD stage 5 population under two different scenarios. The first considers 2010 costs for maintenance dialysis for the prevalent population using Thailand’s 2010 spending adjusted for national gross domestic product (Figure 7). The second considers the estimated annual per capita spending in the United States for hemodialysis patients in 2010 (Figure 8). When using the Thailand’s reimbursement rate for peritoneal dialysis, our results illustrate...
that of the 14 countries with >1% of the total health care expenditure allocated to maintenance dialysis, ten of these countries are located in Asia and North Africa/Middle East regions (Figures 7 and 8).

Applying Thailand’s peritoneal dialysis reimbursement rate, all countries ranged between 0.1% and 3.4% of total health care expenditure attributed to maintenance dialysis, except for Suriname with 47% (not shown in Figures 7 and 8). Using the per capita reimbursement for hemodialysis patients, world countries ranged from 0.2% to 4% of total health care expenditure in 2010 (Figure 8). The results of this analysis should be interpreted with caution because it assumes care delivery comparable with the referent country (i.e., United States, Thailand). What this analysis illustrates is that there are regional patterns, and regions with high prevalent ESRD burden and high rates of health care spending are most likely to be heavily affected financially by further increasing rates of treated ESRD.

Addressing the Burden: Dialysis Modalities, Transplant, and CKD Screening

Dialysis Modalities
Alleviating the expected increase in the global economic burden from the growth in the prevalent ESRD population will necessitate capitalizing on all forms of treatment beyond in-center hemodialysis. Within high- and middle-income countries, home-based RRTs, such as peritoneal dialysis and home hemodialysis, are feasible and defray the substantial costs of infrastructure maintenance and staffing and offer patient autonomy.66-69 Within the United States, there has been a 35% increase in home-based RRT between 2002 and 2012, most of which were peritoneal dialysis.7 Thailand has a universal health care structure meant to provide health coverage to individuals not covered by existing systems, such as social security. Maintenance dialysis was incorporated into universal coverage in 2007.70 This program prioritizes initiation with peritoneal dialysis and transition to hemodialysis for those deemed unsuitable for peritoneal dialysis.7 Thailand has a universal health care structure meant to provide health coverage to individuals not covered by existing systems, such as social security. Maintenance dialysis was incorporated into universal coverage in 2007.70 This program prioritizes initiation with peritoneal dialysis and transition to hemodialysis for those deemed unsuitable for peritoneal dialysis.70 Within developing countries, the financial gains of home-based therapies are less clear.71 Costs and supplies vary on the basis of regional production of solutions for peritoneal dialysis versus importation; therefore, home-based treatments, such as peritoneal dialysis, may not always be more cost-effective.71 Within such regions, country-level analyses are needed to determine unique barriers

Table 3. Decomposition analysis of the change in global dialysis prevalence rates and counts for patients receiving dialysis secondary to diabetes mellitus from 1990 to 2010 stratified by sex

<table>
<thead>
<tr>
<th>Stratification Based on Dialysis Provision</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countries with universal maintenance dialysis access</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1990 maintenance dialysis patients secondary to DM</td>
<td>80,453</td>
<td>86,392</td>
<td>166,846</td>
</tr>
<tr>
<td>Patients expected in 2010 secondary to increase of DM in general population</td>
<td>125,457</td>
<td>119,261</td>
<td>244,718</td>
</tr>
<tr>
<td>Year 2010 maintenance dialysis patients secondary to DM</td>
<td>222,782</td>
<td>250,886</td>
<td>473,668</td>
</tr>
<tr>
<td>Percentage of dialysis prevalence increase because of increase of DM prevalence in the population</td>
<td>56</td>
<td>38</td>
<td>47</td>
</tr>
<tr>
<td>Percentage total change</td>
<td>177</td>
<td>190</td>
<td>184</td>
</tr>
<tr>
<td>Countries with partial maintenance dialysis access</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1990 maintenance dialysis patients secondary to DM</td>
<td>18,878</td>
<td>19,018</td>
<td>37,896</td>
</tr>
<tr>
<td>Patients expected in 2010 secondary to increase of DM in general population</td>
<td>30,712</td>
<td>29,212</td>
<td>59,924</td>
</tr>
<tr>
<td>Year 2010 maintenance dialysis patients secondary to DM</td>
<td>53,138</td>
<td>56,022</td>
<td>109,160</td>
</tr>
<tr>
<td>Percentage of dialysis prevalence increase because of increase of DM prevalence in the population</td>
<td>63</td>
<td>54</td>
<td>58</td>
</tr>
<tr>
<td>Percentage total change</td>
<td>181</td>
<td>195</td>
<td>188</td>
</tr>
</tbody>
</table>

DM, diabetes mellitus.
for broad-based provision of RRT for the largest segment of the population at the lowest cost.

Renal Transplantation
Renal transplantation offers clear benefits in terms of quality of life and survival and societal economic benefit. Within the last two decades, advances in immunosuppression have led to improved allograft and patient survival. Within high-income countries, advances in ability to transplant across blood groups, paired kidney donation programs, and preemptive renal transplants have collectively increased rates of renal transplantations. However, resource scarcity limits this treatment modality in both high- and low-income regions. Low-income countries experience added limitations of infrastructure and shortages of surgical expertise. Resultant transplant tourism and organ trafficking that occur in such settings to address deceased donor organ shortages often target the most impoverished members of such populations. Further, financial constraints secondary to lack of governmental financial support for transplant programs lead to early discontinuation of immunosuppressive therapy, leading to premature graft loss.

Population-level CKD Screening
The most effective prevention against further ESRD growth is CKD prevention. Systematic population-based CKD screening should be considered by societies around the world to determine the portion of the population at risk versus those affected by CKD. Currently, few societies implement systematic screening for adults unless they have risk factors, such as diabetes mellitus or advanced age. Considering that early- to moderate stage CKD is relatively asymptomatic, screening has multiple advantages. First, screening identifies individuals with CKD that might not be diagnosed until late stage when symptoms manifest, but when options for retarding progression are few. Second, screening for CKD may facilitate detection of undiagnosed diabetes, hypertension, and CV disease.

Long-reaching Effect: ESRD and the Global Burden of NCDs
The recent 2012 United Nations Summit held to address the global burden of NCDs concluded with the formation of the 2025 Initiative. This initiative resolves to decrease the global burden of NCDs by 25% by 2025. Although an important initiative that focuses global attention on the leading causes of premature mortality, the initiative focuses specifically on diabetes, cancer, CV disease, respiratory diseases, and neurologic disease. In light of the rising burden of both pre-ESRD CKD and ESRD, omission of CKD as an independent cause of premature life loss will inevitably detract from the overall success of the initiative. Furthermore, with success in decreasing the burden of these specifically targeted NCDs, the consequent increased survival may potentially cause a further increase in the prevalence of CKD globally. As noted, our estimates illustrate such a continued rise in both CKD and ESRD, as survival within the CKD population also improves, and countries expand their ability to provide RRT to the ESRD population.

Table 4. Decomposition analysis of the change in global dialysis prevalence and prevalent count for patients receiving dialysis secondary to hypertension from 1990 to 2010 stratified by sex

<table>
<thead>
<tr>
<th>Stratification Based on Dialysis Provision</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countries with universal maintenance dialysis access</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1990 maintenance dialysis patients secondary to hypertension</td>
<td>55,868</td>
<td>46,809</td>
<td>102,677</td>
</tr>
<tr>
<td>Patients expected in 2010 secondary to increase of hypertension in general population</td>
<td>74,930</td>
<td>59,072</td>
<td>134,002</td>
</tr>
<tr>
<td>Year 2010 maintenance dialysis patients secondary to hypertension</td>
<td>149,499</td>
<td>138,746</td>
<td>288,244</td>
</tr>
<tr>
<td>Percentage of dialysis prevalence increase because of increase of hypertension prevalence in the population</td>
<td>34</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>Percentage total change</td>
<td>168</td>
<td>196</td>
<td>181</td>
</tr>
<tr>
<td>Countries with partial maintenance dialysis access</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1990 maintenance dialysis patients secondary to hypertension</td>
<td>23,362</td>
<td>19,063</td>
<td>42,425</td>
</tr>
<tr>
<td>Patients expected in 2010 secondary to increase of hypertension in general population</td>
<td>36,835</td>
<td>28,909</td>
<td>65,744</td>
</tr>
<tr>
<td>Year 2010 maintenance dialysis patients secondary to hypertension</td>
<td>60,817</td>
<td>51,159</td>
<td>111,976</td>
</tr>
<tr>
<td>Percentage of dialysis prevalence increase because of increase of hypertension prevalence in the population</td>
<td>58</td>
<td>52</td>
<td>55</td>
</tr>
<tr>
<td>Percentage total change</td>
<td>160</td>
<td>168</td>
<td>164</td>
</tr>
</tbody>
</table>
Study Strengths and Limitations

The considerable strengths of the study involve its scope both in terms of geography and time course for comparison, methods applied to estimate provision of maintenance dialysis for countries for which no previous estimates exist, and ability to model how growth, aging, and prevalence of diabetes and hypertension account for the growth in the dialysis population over time. The limitations include an under-representation of data from countries of the world with limited registry information. When projecting estimates for country-years with limited information, the meta-regression tool borrows strength from data for other countries in the same region, or other regions in the same super-region, which relies on the assumption that similar countries have similar dialysis rates. The possible inaccuracy of this assumption is a limitation of this study and may also account for some of the differences from estimates in the literature. However, this report includes the results of an extensive literature review to detect all possible nationally representative data for countries for which no registry data exist to address such deficits. The results of our analysis also may not reflect the precise results of national registries for two reasons. First, in specific instances a national registry may have chosen a denominator population for a region that

Figure 6. Sex-stratified age-standardized maintenance dialysis incidence rate per million population for 21 world regions in year 2010.

Figure 7. Estimated percentage of country-specific total health expenditure allocated to prevalent maintenance dialysis using the Thailand dialysis reimbursement paradigm. ATG, Antigua and Barbuda; BRB, Barbados; COM, Comoros; DMA, Dominica; E. Med, Eastern Mediterranean; FJ, Fiji; FSM, Federated States of Micronesia; GRD, Grenada and Trinidad; KIR, Kiribati; LCA, Saint Lucia; MDV, Maldives; MHL, Marshall Islands; MUS, Mauritius; SGP, Singapore; SLB, Solomon Islands; SYC, Seychelles; TLS, Timor-Leste; TTO, Trinidad and Tobago; TUN, Tunisia; VCT, Saint Vincent and Grenadines; VUT, Vanuatu; WSM, Samoa.
differed from the national denominator used in this analysis. Second, our regression analysis estimates epidemiologic parameters for 1990 and 2010 on the basis of data gathered from available time points closest to those years.

SUMMARY

To our knowledge, this study is the first analysis of sufficient scope to describe the global prevalence and incidence of maintenance dialysis treatment for ESRD. Comparing 1990 and 2010, there has been a general trend of substantially increased provision of maintenance dialysis in both men and women above what was anticipated secondary to population growth, aging, and increase in prevalence of diabetes and hypertension, with most notable increases occurring in parts of Australasia, Asia, North America, and Western Europe. Oceania and portions of Sub-Saharan Africa have maintained a low prevalence of maintenance dialysis when compared with most of the world; however, growth in these regions has occurred. With the exception of tropical Latin America, men were more likely to receive dialysis than women; however, the global change in prevalence and incidence for treated women in the last two decades has surpassed that of men.

Maintenance dialysis is a costly treatment for ESRD with economic implications for both high- and low-income world regions. Within high-income regions of the world, efforts are needed to address drivers of increase in ESRD, such as obesity, diabetes mellitus, and hypertension. Research is needed to further evaluate reasons for sex differences within the ESRD population. Within regions of the world with emerging economies, expansion of dialysis to larger portions of the population is urgently needed, especially within Sub-Saharan Africa and Oceania, to save lives and deter the difficult task of patient selection when resources are limited.

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Supplemental Table 1. Countries listed by region providing universal maintenance dialysis access in 2010

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<td>Sub-Saharan Africa, East</td>
<td>Seychelles</td>
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Literature and internet search performed during July-August 2013 to create this table. Each of the 187 countries was searched by name in combination with “dialysis” “end-stage renal disease” “renal replacement therapy” “history of dialysis” using PubMed. If there were no PubMed article located, a general internet search using the same search terms was used. Only English hits were examined.
METHODS

Overview
The data for this analysis was extracted from the Global Burden of Disease 2010 (GBD 2010) database, the world’s largest composite database of disease and injury.1,3 The methods for the GBD 2010 are published in extensive detail.4,5 Below we will describe the analytic strategy specific to maintenance dialysis age- and gender-stratified incidence and prevalence estimation for the GBD 2010.

Study Design
This is a cross-sectional study evaluating the prevalence and incidence of maintenance dialysis in 1990 and 2010. This study also assesses the drivers of change in maintenance dialysis between these two years.

Setting
Maintenance dialysis prevalence and incidence data were collected through renal registries and extensive literature review for all countries for which such data were obtainable for the specified time periods of 1990 and 2010, or for the nearest year(s).

Participants
The eligibility criteria included data encompassing all ages and races from all countries included in the 2010 GBD analysis. Data points were excluded if in receipt of a kidney transplant or renal replacement therapy for acute kidney injury during those time periods.

The twenty-one geographic regions used in this analysis were defined using the structure outlined in the 2010 GBD analysis, employing the dual criteria of epidemiologic homogeneity and geographical contiguity.6 Exclusion criteria involved countries with populations smaller than 50,000 inhabitants, leaving a total of 187 included countries.

Variables
The primary outcomes of interest were prevalence and incidence rate of patients receiving maintenance dialysis who were not transplanted during the years of 1990 or 2010. Secondary variables of interest included gender and age.

Estimation Strategy
All data extracted encompassing 163 countries were modeled for 2010 GBD using the standard DisMod-MR (disease model metaregression) strategy using all epidemiological parameters available to estimate incidence and prevalence at the country level for all countries, age-groups, genders, and years.3,4

Data Source/Measurement
The data for this analysis of maintenance dialysis therapy were obtained from regional and national registry reports and literature review. Targeted searches for dialysis data in
countries/regions with no registries were conducted in an effort to address registry data gaps. Publications were accepted for inclusion if they were nationally representative of maintenance dialysis cases and within the desired timeframe. Remission rate in countries with a known lack of kidney transplantation, confirmed by targeted internet searches and expert consultation, were assumed to be zero. A total of 3,280 maintenance dialysis data points covering 163 countries were modeled for GBD 2010 using the DisMod-MR (Disease-Modeling-Meta-Regression) modeling strategy using all epidemiological parameters available as described in previous GBD publications, with a third stage of estimation cascade to produce consistent estimates at the country level from regionally consistent estimates of GBD 2010. For the remaining 24 countries for which country-level data were not available, reported estimates were derived from regional estimates using the methods outlined in previous GBD publications. Data for population prevalence used to calculate the etiology decomposition analysis (described below) were obtained from the GBD 2010 study. “Hypertension” was defined as a systolic blood pressure ≥140mmHg as per Joint National Committee 7 criteria.

**Study Size**

For nation-wide prevalence (e.g. total prevalent patients undergoing dialysis), the national population for that age/sex/year group was used as the effective sample size for registry data that cover the national population. Separate data for hemodialysis and peritoneal dialysis were combined when both were from the same source/age/sex/year/country in order to obtain overall estimates for prevalent provision of maintenance dialysis. Data with no measure of uncertainty (effective sample size, standard error, or 95% confidence interval) and duplicate data were dropped from the analysis. For countries with thousands of available data points for every sex/age, we kept only certain calendar years for analysis to maintain computational efficiency.

**Methods/ Quantitative Variables**

For the GBD 2010 study, we took advantage of the Bayesian structure of DisMod-MR and chose several priors to inform the parameter estimation. We assumed no remission (renal transplantation) occurs after age 80, prevalence is less than 9 per 1000 population, incidence is less than 3 per 1000 person-years, remission is less than 350 per 1000 patient-years, and excess mortality is less than 2 per patient-year. We chose these upper bounds to contain all available data and constrict the space in which DisMod could estimate the parameters. We also assumed decreasing remission over age after age 10, decreasing duration after age 20, and decreasing prevalence after age 80 in order to achieve a consistent age pattern across countries based on the age pattern seen in countries with reliable age-specific data. Remission was defined as kidney transplantation incidence divided by chronic dialysis prevalence for a given source/country/year/age/sex when data for both numerator and denominator were available. Age standardization was performed across regions and time based on standard weights obtained from the 2008 World Health Organization age standards.

We updated the results of country-level prevalence and incidence of maintenance dialysis by
using the GBD 2010 country-level results as prior estimates in the DisMod-MR Bayesian framework and running new DisMod-MR models for each country-year separately in order to more accurately predict results at that level of detail in countries with data using only data in the year of interest or the closest year available and omitting all other years. Estimates in countries with no data depend on estimated super-region and region random effects within the model. For this update we relaxed the assumptions on the original model: excess mortality upper bound was widened to 10, the lack of remission after age 80 was removed, and country-level all-cause mortality was incorporated into the model rather than at the regional level.

Country-level Access to Maintenance Dialysis

For this analysis, we have listed the countries determined to have either universal access to maintenance dialysis or partial access, as determined through registry information and literature review (supplemental Table 1). Data presented include all ages of patients receiving maintenance dialysis for these countries. If a country was not indicated by literature review to provide universal access to maintenance dialysis to its population in 2010, it was categorized as providing partial access.

Decomposing changes in prevalence and incidence to changes in demographic, epidemiological, and prevalence of underlying diseases

To help understand the drivers of change in the number of prevalence and incidence cases from 1990 to 2010, the proportion of the change due to growth in total population, change in population age- and sex-structure, change in age- and sex-specific rates, and change attributable to population-level disease burden of diabetes mellitus and hypertension were estimated. Three counterfactual sets of prevalent and incident numbers were computed. First, the population growth scenario was computed as the expected number of prevalent/incident cases in 2010 if the total population numbers increased to the level of 2010 while both the population age/sex-structure and age/sex-specific rates remained the same as in 1990. Second, a population growth and population aging scenario was computed as the expected number of prevalent/incident cases in 2010 if both the total population numbers and age/sex-structure changed to 2010 levels while the age/sex-specific rates remained at 1990 levels. Third, a population disease burden scenario was computed for diabetes mellitus and hypertension respectively, based on disease burden of diabetes and untreated hypertension in the general population. The difference between 1990 case numbers and the population growth scenario is the change in prevalent/incident numbers due strictly to the growth in total population. The change from the population growth scenario to the population growth and aging scenario is the number of prevalent cases due to the aging of the population. The difference between 2010 prevalent/incident numbers and the population growth and aging scenario is the difference in prevalent numbers due to epidemiological change in age/sex-specific rates per person. The difference between expected dialysis cases due to population growth in diabetes mellitus and hypertension is the difference between the actual and expected number of dialysis cases secondary to each chronic disease. Each of these four differences is presented as the percentage change with reference to the 1990 prevalent/incident case numbers estimate.
Economic Analysis
To determine the cost associated with placing half of each country’s CKD stage V prevalent cases on dialysis, relative to each country’s total health expenditure, we use equation 1.

$$\text{relative cost of dialysis} = \left( \frac{\text{CKD V prevalent cases}}{2} \right) \left( \frac{\text{Dialysis costs per patient}}{\text{GDP per capita}} \right) \times \left( \frac{\text{GDP per capita}}{\text{THE}} \right)$$

Equation 1. % Total health expenditure calculation

“CKD V prevalence cases” is the estimated national prevalent count of CKD stage V cases among all ages in 2010 for country $i$; dialysis costs per patient are from reference country $r$ (the US or Thailand). “GDP” is gross domestic product; “THE” is total health expenditure for the country for which the calculation is being performed in 2010. We multiple by the GDP per capita ratio to adjust for prices differences between each country and the reference countries.

THE amounts at the country-level were obtained from the World Health Organization using year 2005 purchasing power parity (PPP). Data was extracted on 1/15/2015. GDP for countries was obtained from the IHME GDP 2010 database, which was also 2005 PPP. CKD stage V estimates were extracted from the GBD 2010 Study.

As many countries do not have national dialysis programs, using national prevalent dialysis counts to determine % THE expenditure would have led to falsely high rates for countries with no or low dialysis activity. Thus, we chose to use CKD Stage V estimates as a surrogate for the perspective maintenance dialysis population at the country level. As we assume less than 100% of the CKD stage V population will progress to ESRD, we used 50% of prevalent CKD V counts in this analysis (Equation 1).

We used two prospective per capita ESRD costs in this analysis. Since 2002, Thailand has had a governmentally-supported “PD first” policy, thus we used the Thailand per capita cost ($13,860) to estimate the % THE attributable to a national PD program for 2010 (Figure 7). Similarly, we performed the same analysis using the cost of total Medicare spending on hemodialysis per capita in the United States ($87,561) (Figure 8).
Sources


