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.[3] 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.[3] Data for population prevalence used to calculate the etiology decomposition analysis (described below) were obtained from the GBD 2010 study.[7-9] "Hypertension" was defined as a systolic blood pressure ≥140mmHg as per Joint National Committee 7 criteria.[10]

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.

$$relative\ cost\ of\ dialysis_i = \left(\frac{CKD\ V\ prevalent\ cases_i}{2}\right)(Dialysis\ costs\ per\ patient_r)\left(\frac{GDP\ per\ capita_i}{GDP\ per\ capita_r}\right)\left(\frac{100}{THE_i}\right)$$

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).[11] Data was extracted on 1/15/2015. GDP for countries was obtained from the IHME GDP 2010 database, which was also 2005 PPP.[12] 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).[13] 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).[14]

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