Projecting ESRD Incidence and Prevalence in the United States through 2030

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ABSTRACT

Background Population rates of obesity, hypertension, diabetes, age, and race can be used in simulation models to develop projections of ESRD incidence and prevalence. Such projections can inform long-range planning for ESRD resources needs.

Methods We used an open compartmental simulation model to estimate the incidence and prevalence of ESRD in the United States through 2030 on the basis of wide-ranging projections of population obesity and ESRD death rates. Population trends in age, race, hypertension, and diabetes were on the basis of data from the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey and the US Census.

Results The increase in ESRD incidence rates within age and race groups has leveled off and/or declined in recent years, but our model indicates that population changes in age and race distribution, obesity and diabetes prevalence, and ESRD survival will result in a 11%–18% increase in the crude incidence rate from 2015 to 2030. This incidence trend along with reductions in ESRD mortality will increase the number of patients with ESRD by 29%–68% during the same period to between 971,000 and 1,259,000 in 2030.

Conclusions The burden of ESRD will increase in the United States population through 2030 due to demographic, clinical, and lifestyle shifts in the population and improvements in RRT. Planning for ESRD resource allocation should allow for substantial continued growth in the population of patients with ESRD. Future interventions should be directed to preventing the progression of CKD to kidney failure.

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At the end of 2015, there were 687,093 people with ESRD in the United States, defined in the US Renal Data System (USRDS) and in this study as patients formally registered to receive maintenance dialysis or transplantation as RRTs.[1] In 2013, 79% of patients with ESRD had Medicare as either the primary (416,808 patients) or secondary (57,677 patients) payer. Patients with ESRD represent 1% of the Medicare population but account for 7% of Medicare's expenditures.[2] It is important to estimate future trends in this large population with substantial costs to properly allocate the resources needed for their care.

Although the crude (overall) ESRD incidence rate has been increasing, the age-, sex-, and race-adjusted incidence of ESRD has leveled off and declined since 2009.[3] However, US Census[4]

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projections on the basis of declining death rates in the general population and changes in the racial demographics of the country indicate an aging, more racially diverse general population, which forms a growing at-risk pool of potential patients with ESRD.

We are using a simulation model that incorporates contemporary trends in population demographics, obesity, diabetes, and hypertension to project ESRD incidence and prevalence. This work incorporates more specific diagnosis data within age and race groups in an effort to improve and update the estimates currently in the literature on ESRD prediction and projection.

Significance Statement

Although ESRD incidence rates in the United States increased dramatically through the 1980s and 1990s, the incidence of ESRD adjusted for age, sex, and race leveled off and declined after 2009, prompting speculation that the upward trend may have stabilized in the 2000s. Using a simulation model, the authors show that, despite a decrease in incidence rates within age and race groups, the aging population and changes in the racial distribution of the population will result in increasing crude ESRD incidence rates and annual numbers of new patients. These findings along with decreasing ESRD death rates will result in a substantial increase in the prevalent ESRD population by 2030. This finding has important implications for dialysis infrastructure planning and Medicare and Medicaid budgeting.

METHODS

Simulation Modeling Approach

To project incidence and prevalence of ESRD in the United States between 2013 and 2030, we developed a compartmental model to simulate the incidence and prevalence of certain conditions, such as diabetes and ESRD. This model is described in detail in Supplemental Appendix 1. There were two primary simulation models: a model of diabetes prevalence, primarily on the basis of population size and obesity, and a model of ESRD prevalence. The diabetes prevalence results were used as inputs in a separate simulation model of the ESRD population. Additional inputs for the ESRD model included US Census counts and projections of the number of people in each race and age group in the general population, National Health and Nutrition Examination Survey (NHANES) data on hypertension prevalence and "other" (*i.e.*, nonhypertension and nondiabetes) diagnosis ESRD incidence rates, and ESRD death rates. Transition rates between compartments were modeled as changing from year to year using a restricted cubic spline estimate with knots in 1988 and 1999. Parameters for these spline estimates were determined using Nelder–Mead optimization[5] (*via* the "optim" function in R[6]) on the sum of squared error in diabetes prevalence on the basis of the NHANES data for the diabetes model and the USRDS data on ESRD incidence rates for the ESRD model. Prevalence was modeled using incidence and death as the primary means of entry and exit from the prevalent population as shown in Supplemental Figure 1. The simulation model was then used with US Census projections, extrapolated "other" diagnosis ESRD incidence rates, and hypothetical obesity and ESRD death rate projections to project ESRD incidence and prevalence through 2030. Uncertainty in projected ESRD incidence and prevalence was calculated using ranges of projected inputs instead of through confidence intervals, which produced unrealistically narrow estimates (Supplemental Appendix 2). Programming for the simulation model was performed using the R v. 2.15.0 statistical package.[6]

Demographic Categories

There are many population factors that may influence trends in ESRD incidence and prevalence, but age, race, hypertension, and diabetes are consistent and strong predictors of ESRD. Some other factors identified as important in the literature include sex, ethnicity, and body mass index (Supplemental Appendix 3). Our simulation model projections incorporate age and race group trends in hypertension and diabetes separately and combine the results for estimates of overall ESRD incidence and prevalence. The ESRD data come from the Centers for Medicare & Medicaid Services data as briefly described in Supplemental Appendix 4.

General Population Size Estimation and Projections

Census data for our analyses used US Census Statistical Abstracts of the United States,[7] and projections beyond 2010 were taken from US Census projections.[8,9] These counts were smoothed to reduce the effect of changes in question format and/or sampling methods in 2000.

Obesity Prevalence and Projections

The prevalence of obesity, defined as a body mass index of 30 kg/m^2 or more, may have started to level off,[10] or it may continue to increase.[11] There is an established progression of obesity to diabetes to kidney disease that makes obesity trends of particular interest when making predictions about the ESRD population (Supplemental Appendix 5).

For the simulation models, past obesity prevalence data were obtained from the NHANES for each age and race group.[12] The two dashed lines in Figure 1 projecting the prevalence of obesity for the overall population are not intended to be specific predictions of future obesity prevalence. These projections deliberately represent an extreme range of plausible trends in the prevalence of obesity to estimate the maximum influence that changes in obesity prevalence might have on the ESRD population. We expect that the actual trend in obesity prevalence will be between these two projections. The linear and quadratic regressions used for these projections both had an R^2 above 0.95 for observed trends between 1989 and 2013. These projections were performed and used separately within each age and race group and then combined to estimate the effects of these extreme projections on the sizes of the diabetes and ESRD populations.

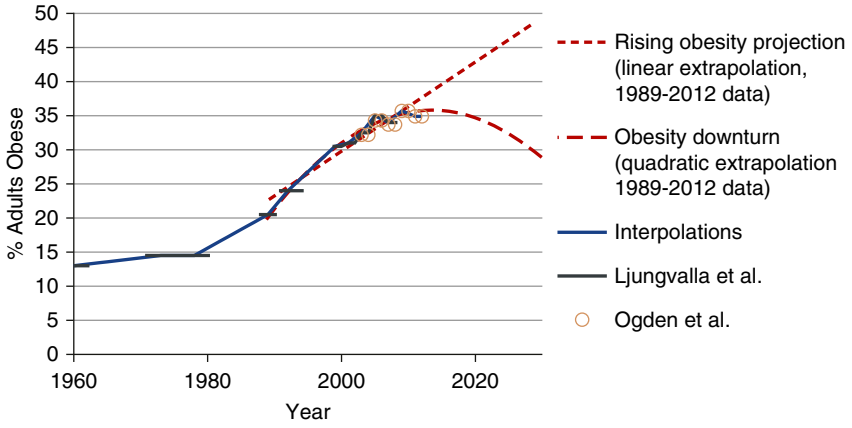

Figure 1. Obesity has risen, but the models cover a wide range of possible future trends. Estimated and projected trends in the prevalence of obesity (body mass index of 30+ kg/m^2; percentage) between 1960 and 2030 in the general United States population. Estimated obesity prevalence from Ljungvalla *et al.*[32] and Ogden *et al.*[10] using the National Health and Nutrition Examination Survey data.

ESRD Incidence Attributed to Diabetes or Hypertension

ESRD incidence was obtained from the USRDS Renal Data Extraction and Referencing (RenDER) system.[13] The incidence rates of ESRD for which the primary cause was attributed to diabetes or hypertension were estimated each year since 2012 separately for each age and race group. The model incorporates changes over time in the incidence of ESRD attributed to diabetes among the population with diabetes, but it does not distinguish the causes of these changes whether they are due to improved treatment of patients with diabetes or simply earlier diagnosis of diabetes, both of which could contribute to delayed onset of ESRD in this population. Additional detail on the diabetes data and modeling is available in Supplemental Figure 2 and Supplemental Appendix 5. In the simulation model, we used simulated estimates of diabetes prevalence in the general population on the basis of both linear and quadratic obesity assumptions. Similarly, we used observed hypertension prevalence data along with linear extrapolations constructed within each age and race group. Details on the hypertension data and results are available in Supplemental Appendix 6 and Supplemental Figure 3.

ESRD Death Projections

ESRD death rates were obtained from the USRDS RenDER system.[13] Deaths of patients with ESRD are required to be reported by their dialysis or transplant center; Supplemental Appendix 4 has more information. The death rate among patients with ESRD has decreased over the past two decades both overall and within specific age groups, but there are some signs that this decrease may have slowed in 2013.[14] We ran two models: first, assuming that the smoothened, pre-2015 downward trend continues unabated and second, assuming that the 2015 death rate remains constant through 2030. These observed trends and projections are illustrated in Figure 2, which shows both projections for each age group.

Population Movement and Loss to Follow-Up

Although data are supposed to be reported for all United States patients with ESRD, some (<1%) are lost to follow-up each year. In addition, patients are "lost" to one age group and "gained" by another age group as patients get older or die. The net gains and losses from each age/race group were projected using a linear model attenuating the slope by 10% of its value each year, a method that has proven successful in other research areas.[15]

This study was conducted as part of the USRDS Coordinating Center contract with the National Institutes of Health (the National Institute of Diabetes and Digestive and Kidney Diseases); research as part of the contract has been approved by the University of Michigan's Institutional Review Board (HUM0086162).

RESULTS

Diabetes Prevalence Projections

The use of obesity data to predict trends in diabetes prevalence seemed to produce results that were fairly consistent with observed results through 2016 for most age and race groups as shown in Supplemental Figure 2. On the basis of the linear and quadratic projected trends in obesity prevalence after 2015 (illustrated in Figure 1), diabetes prevalence in the total population is expected to be between 11% and 13% in 2030 compared with 11% in 2015 and 2016 on the basis of the NHANES data.

Diabetes prevalence is expected to increase for most age groups, although the obesity projections have more of an effect on the older age group projections, where diabetes is more common. Diabetes prevalence in 2030 is projected to be approximately 3% among adults under age 45 years old, 19%–22% (depending on obesity projections) for those 45–64 years old, 26%–32% for those 65–74 years old, and 18%–27% for those over age 75 years old.

ESRD Incidence Projections

Figure 3 shows the annual ESRD incidence rate from 1980 to 2030 by age. The ESRD incidence rate increased appreciably between 1985 and 2005 for adults age 65 years old and older. The temporal trend was projected to be rather flat for those under age 45 years old: from 77 per million per year in 2015 to 72–77 per million per year in 2030. The incidence rate is projected to increase for those ages 45–64 years old from 561 per

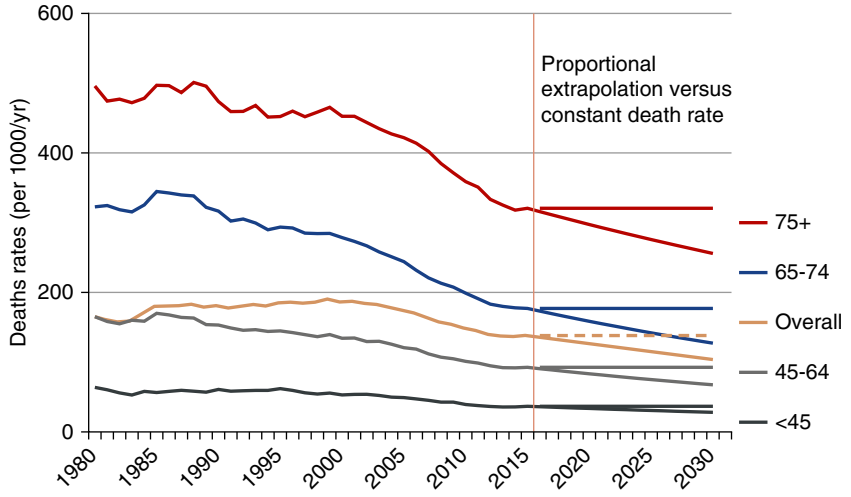

Figure 2. Death rates among ESRD patients have fallen. Age-specific ESRD death rates (per 1000/year) by year (1980–2030), with two projections after 2012 (proportional decrease and constant death rate). The 1980–2013 data from the US Renal Data System RenDER[13] with extrapolations after 2012 on the basis of proportional decrease in death rates and constant death rates.

million per year in 2015 to 604–620 per million per year in 2030. There was a decline in the projected incidence for those aged 65–74 years old from 1142 per million per year in 2015 to 1019–1116 per million per year in 2030. The rate among those age 75 years old and over was more variable; the simulation model (solid curves in Figure 3) did not predict the sudden decrease observed among patients in that age group between 2010 and 2013 from 1518 to 1391 per million per year (dashed curves in Figure 3). Thus, the incidence rate projected between 2015 and 2030 was fairly flat: from 1473 per million per year in 2015 to 1419–1500 per million per year in 2030.

ESRD Prevalence Projections

ESRD death rate projections (as illustrated in Figure 2) and ESRD incidence projections (Figure 3) were used to estimate the trends in ESRD prevalence (Supplemental Appendix 1). The increasing incidence rate along with the constant or decreasing ESRD death rates mean that the prevalence of ESRD (per million) is projected to continue to increase after 2015 as shown in Figure 4 and separately by race in Supplemental Figure 4. Each panel in Figure 4 shows simulated and projected results from one of four scenarios representing different assumptions about obesity trends and ESRD death rate trends after 2015. For adults under 45 years old, the prevalence is expected to vary between a 15-year proportional decrease of 2% to an increase of 7%. The prevalence of ESRD is expected to rise 19%–39% for adults 45–64 years old, 23%–75% for those 65–74 years old, and 4%–51% for adults over 74 years old.

Figure 5 summarizes the results of the different projections (2015–2030) of proportional increases in the annual incidence count and rate and the annual prevalence count and proportion. The ranges shown in the vertical bars in Figure 5 represent results from the different assumptions of future trends in obesity prevalence and ESRD death rates. The projected number of patients with prevalent ESRD is expected to increase more than the prevalence (proportion), because US Census projections indicate that the size of the United States population (the denominator) will increase. The differing obesity projections changed the 2030 prevalence count by 28,000–33,000 patients, whereas the differing death rate projections changed the 2030 prevalence count by 255,000–260,000 patients.

As sensitivity analyses, we used data on population diabetes prevalence from the Centers for Disease Control and Prevention (CDC) National Health Interview Survey instead of the NHANES; we used two race groups (white and nonwhite) instead of three, and we used different smoothing methods across the age and race group estimates of population obesity. Results from all three sensitivity analyses supported continued growth in ESRD incidence and prevalence as in the main analyses (Supplemental Figure 5 and Supplemental Appendix 7). The two-race simulations exhibited less instability. They also generally predicted smaller growth, as did using the lower CDC diabetes prevalence estimates. The variation stemming from using different smoothing methods on the obesity estimates within each age and race group was negligible (results not shown).

DISCUSSION

Population obesity, hypertension, diabetes, age, and race can be used to model ESRD incidence and prevalence. On the basis of these inter-relationships, we project that the annual number of incident patients, the annual number of prevalent patients, and the crude incidence rate and prevalence of ESRD will increase in the United States through 2030. There will likely be steady or decreasing age-specific incidence rates of ESRD during this period, possibly due to improvements in care, but these will be offset by increases in the older and the nonwhite United States population, even if obesity prevalence is controlled.

Some prior work developing projections of ESRD incidence and prevalence has used methods insensitive to underlying changes in population and specific causes of incidence. Port et al.[16] successfully bracketed the actual 2000 ESRD prevalence by plotting both linear and exponential growth curves on data through 1997. A stepwise autoregressive method with exponential smoothing came within 10% of the 2010 prevalence on the basis of 1982–1997 data.[17]

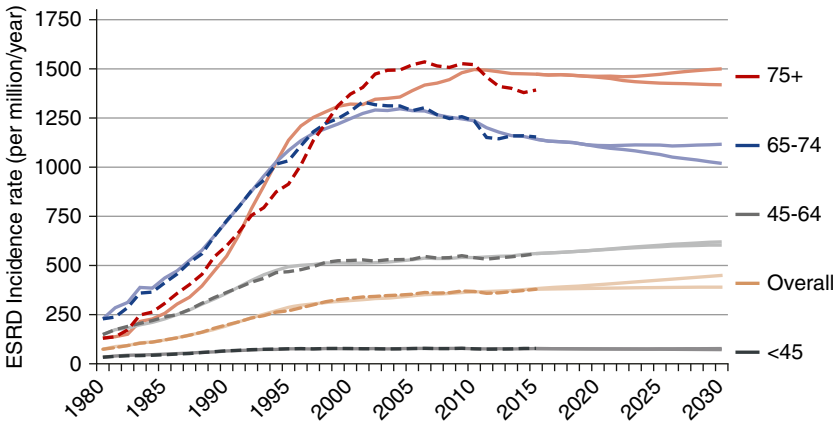

Figure 3. Age-specific incidence rates have leveled off. Annual ESRD incidence rate (per million per year) from 1980 to 2030 by age, with two assumptions about the projected trend in obesity prevalence after 2012. Dashed lines represent reported data, and solid lines represent simulated data. Incident counts are from the US Renal Data System RenDER system[13] (accessed January 2016). Population counts are from smoothed Centers for Disease Control and Prevention–bridged US Census data. Simulation results are on the basis of increasing obesity trend versus decreasing obesity projections.

The simulation model by Gilbertson *et al.*[18] used linear projections of the diabetic and nondiabetic populations to project ESRD incidence and prevalence in a compartmental model. Their compartments were defined by incidence, prevalence, diabetes status, and mortality over seven age groups, three race groups, and two diagnosis groups (diabetic and nondiabetic). Their results were generally within 10% of the USRDS-reported ESRD incidence and prevalence in 2015.

Our simulations use more recent data, include more population data, and separate hypertension from other causes of ESRD. These results indicate that the overall incidence rate will continue to increase between 11% (rising to 428 per million per year in 2030 versus 386 per million per year in 2013) and 18% (rising to 453 per million per year in 2030) depending on obesity trends. Incidence counts are expected to increase to 154,000–163,000 per year, a 27%–34% increase over the 2015 incidence count of 121,542. ESRD prevalence is expected to increase to between 2700 and 3500 per million, an increase of 29%–68% over the 2015 prevalence of 2087 per million. The increasing size of the United States population will also affect the ESRD population size. The number of patients with prevalent ESRD is projected to continue to increase to between 971,000 and 1,259,000 patients by 2030, an increase of 41%–83% over the 2015 prevalence count of 687,093 patients with ESRD. The differing obesity projections varied the 2030 prevalence count by 28,000–33,000 patients, a difference in the ESRD prevalence proportion of 79–92 per million. The differing death rate projections had a larger effect than the differing obesity projections, and they varied the 2030 prevalence count by 255,000–260,000 patients or a difference in the ESRD prevalence proportion of 710–723 per million. Constant death rate projections yielded lower prevalence than decreasing death rate projections; in other words, if new or existing treatments decrease ESRD death rates, we can expect a substantially larger ESRD population.

The United States population is expected to continue to age both through the baby boomer effect and through generally increased lifespans. Because age is strongly associated with ESRD incidence, the aging population will offset the decreasing age-specific incidence rates shown in Figure 3, resulting in an increasing crude incidence rate of ESRD.[19] This is not new; the age-, sex-, and race-adjusted incidence rate of ESRD has been decreasing since 2006,[20] but the aging population has resulted in an increasing overall crude incidence rate and count. Similar trends have been seen in Japan.[21]

Another consequence of the aging United States population is an aging ESRD population. In 2013, approximately 40% of all patients with ESRD were older than 65 years old. In 2030, we project that this proportion will increase to 55%–61% depending mainly on whether the death rate in the ESRD population continues to remain constant (55%–56%) or decline (61%) (Supplemental Figure 6). The aging ESRD population will likely affect the types of care provided to the dialysis population, resulting in increases in the resources required for the dialysis population beyond the quantitative increases projected in these analyses. Although the patient count is expected to increase up to 88% by 2030, the cost to Medicare, already exceeding $30 billion/year, may grow well beyond this percentage increase due to the complications associated with caring for an increasingly older population, unless costs per patient are somehow reduced (*e.g.*, through increasing use of more economical treatment modalities for ESRD, such as peritoneal dialysis and home hemodialysis, both of which are cheaper than in-center hemodialysis).[22,23]

Our findings indicate an increase in ESRD prevalence through 2030. It is imperative to develop new treatment and prevention options that will ameliorate this projected trend. The best long-term approach is to prevent patients from reaching ESRD in the first place, perhaps through better obesity, diabetes, and hypertension prevention and management programs. If genetic markers, such as APOL1, are causal risk factors in the etiology of ESRD[24], then treatments that address these factors could result in lower ESRD incidence overall and substantially reduced racial disparities in ESRD incidence. A number of studies of sodium-glucose cotransporter 2 inhibitors among patients who are diabetic and patients who are not diabetic have shown slowed progression to kidney disease end points, preventing albuminuria and/or substantial reduction in kidney function as measured by the eGFR.[25] These

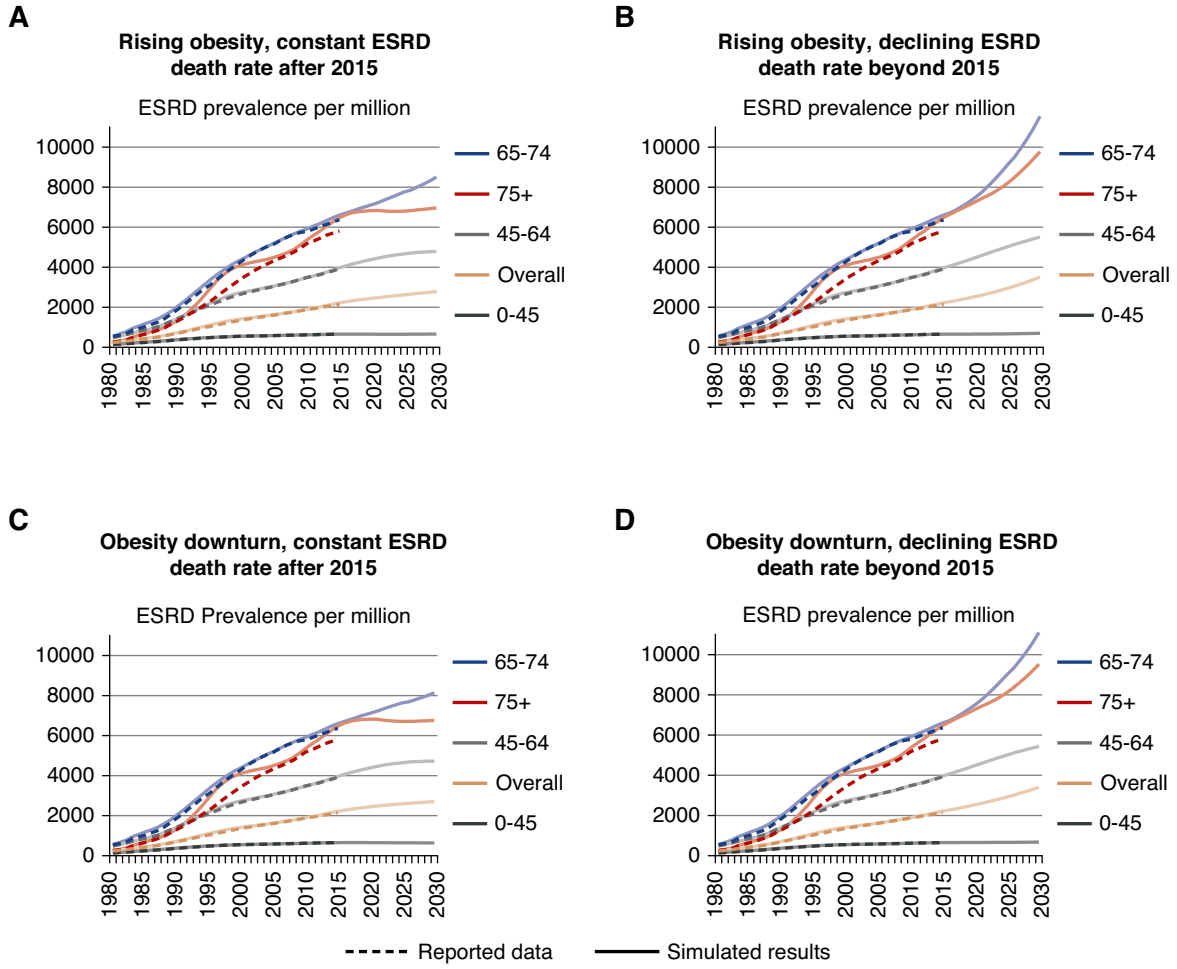

Figure 4. ESRD prevalence is increasing. (A–D) ESRD prevalence proportion (per million) by assumptions of obesity and ESRD death rate trends after 2012, age group (color coded), and year (observed [dashed curves] and simulated through 2012; projected after 2012 [solid curves]). The 1980–2012 ESRD prevalent counts are from the US Renal Data System RenDER.[13] Population data are from smoothed Centers for Disease Control and Prevention–bridged US Census data. Simulation results are on the basis of increasing obesity trend versus decreasing obesity projections and constant ESRD death rate versus continued proportional decrease.

treatments and other new treatments could continue or accelerate current trends in decreasing age-specific ESRD incidence.

We expect that we will also need alternative treatments that will both improve patient outcomes and reduce the resources needed for the ESRD population. In-center dialysis is one of the more expensive options for ESRD care in the long term.[26] Patient survival and other outcomes are generally better with a transplant compared with dialysis,[27] and increasing use of these options would reduce the overall resources needed to care for this population. Recent improvements in transplantation allocation have helped reduce racial disparities and are likely to produce better results for the people who receive kidney transplants.[28,29] Work is progressing on alternatives to dialysis and donated organ transplantation, including artificial kidneys.[30] We need to continue to develop innovative, patient-centered approaches that provide more options to continue providing the needed care for these patients.

The projections in this study assume that recent trends in the population and in the process of transitioning to ESRD will continue and that death rates among patients with ESRD will stay within the wide range assumed in our analysis. Although we attempted to portray the effects of reasonably wide ranges of future trends in obesity and ESRD care, new disruptive changes in the treatment among any of these populations will have cascading effects through the entire system that will not be reflected in these analyses. These effects may lag the introduction of the treatment, especially if the treatment is "upstream" in the causal chain, such as with the SGLT2 or APOL1 studies. Alternatively, large increases in transplantation instead of dialysis, through technological advancements or legislative changes, would reduce the overall death rate of ESRD, resulting in larger ESRD population sizes than we have projected. Any effects of these new developments, however, would have to be extreme to substantially affect the ESRD population by 2030.

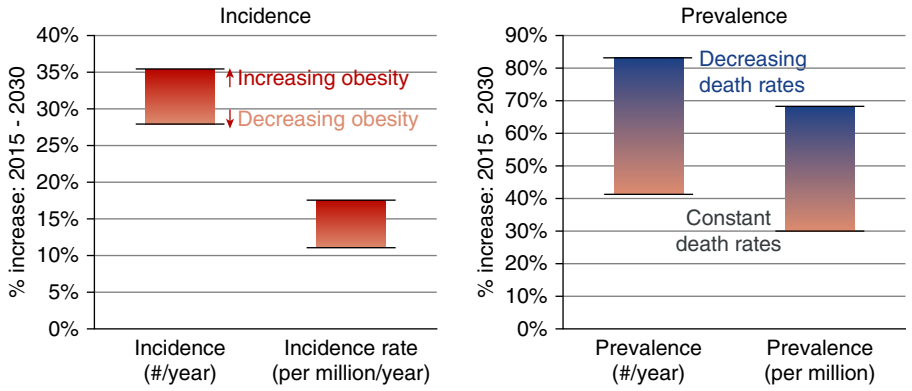

Figure 5. ESRD incidence and prevalence should rise by 2030. Ranges of projected increases in incidence/prevalence. Each bar represents the range of results across four sets of simulations, each with a different set of assumptions. The range of projected incidence and incidence rates are shown on the basis of the increasing obesity versus decreasing obesity assumptions. Separate bars are shown for the prevalence under differing assumptions about the ESRD death rates (constant versus decreasing death rates); the obesity assumptions made smaller differences in ESRD prevalence.

An alternative treatment for people with ESRD is conservative management (*i.e.*, managing symptoms without RRT [dialysis or transplantation]). This option was not included in our projections. Frail, elderly patients may be choosing conservative management more frequently over time instead of dialysis or transplantation.[31] If this is true, then the incidence of RRT and early death rates among those patients may be lower than our projections.

The aging population; the increasing proportion of blacks in the United States population; the rising prevalence of comorbid conditions, such as diabetes and hypertension; and decreasing ESRD death rates (*e.g.*, due to improved treatment of patients with ESRD) have made an increasing prevalence of ESRD in the United States population very likely, even with future improvements in slowing CKD progression to ESRD.

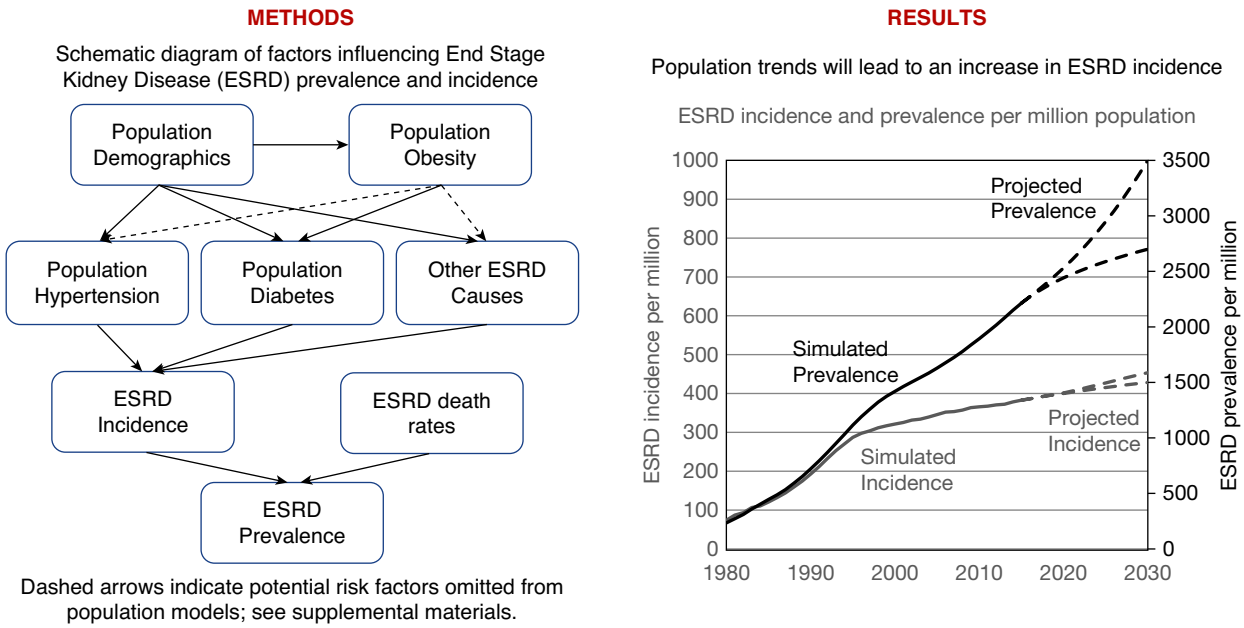

Figure 6. Visual abstract of factors incorporated into the simulation as influencing ESRD incidence and prevalence. Causal relationships between obesity and hypertension or other ESRD causes and additional losses (*e.g.*, lost to follow-up) were handled as described in Supplemental Appendix 1.

On the basis of our findings, any plans for ESRD resource allocation should allow for substantial continued growth in the size of the population of patients with prevalent ESRD through 2030 through increasing ESRD incidence and possibly, also through decreasing ESRD death rates. This has strong implications for planning of dialysis infrastructure (dialysis facilities, provisions for home hemodialysis, increased peritoneal dialysis use, *etc*.) and Medicare and Medicaid budgeting. We need to continue developing innovative approaches to prevent ESRD and care for patients with ESRD to address this growing need.

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The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the US Government. The funder had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

DISCLOSURES

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SUPPLEMENTAL MATERIAL

Supplemental Appendix 1. Simulation modeling approach.

Supplemental Appendix 2. Discussion of confidence intervals around population estimates.

Supplemental Appendix 3. ESRD demographics.

Supplemental Appendix 4. CMS ESRD reporting requirements.

Supplemental Appendix 5. Diabetes.

Supplemental Appendix 6. Hypertension and other ESRD causes.

Supplemental Appendix 7. Sensitivity to racial categories, source of diabetes information.

Supplemental Figure 1. Compartmental model.

Supplemental Figure 2. Annual diabetes prevalence from 1980 to 2013 by age group for racial groups used in simulation: (A) white, (B) black, and (C) other.

Supplemental Figure 3. Prevalence of hypertension by year, age, and race group on the basis of NHANES data.

Supplemental Figure 4. (A–D) ESRD prevalence proportion (per million) by assumptions of obesity and ESRD death rate trends after 2012, age/race group (color coded), and year (observed [dashed curves] and simulated through 2012; projected after 2012 [solid curves]).

Supplemental Figure 5. ESRD projections based on different data sources and race groups.

Supplemental Figure 6. Age distribution of prevalent ESRD patients, by obesity assumption and death rate assumption.

REFERENCES

1. United States Renal Data System: Medicare expenditures for persons with ESRD. In: *2017 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2017. Available at: http://www.usrds.org. Accessed February 8, 2018
2. United States Renal Data System: Medicare expenditures for persons with ESRD. In: *2015 USRDS Annual Data Report: Epidemiology of kidney disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2015. Available at: http://www.usrds.org. Accessed February 8, 2018
3. United States Renal Data System: Incidence, prevalence, patient characteristics, and treatment modalities. In: *2015 USRDS Annual Data Report: Epidemiology of kidney disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2015. Available at: http://www.usrds.org. Accessed February 8, 2018
4. United States Census Bureau: Older People Projected to Outnumber Children for First Time in U.S. History, 2018. Available at: https://www.census.gov/newsroom/press-releases/2018/cb18-41-population-projections.html. Accessed May 1, 2018
5. Nelder JA, Mead R: A simplex method for function minimization. *Comput J* 7: 308–313, 1965
6. R Core Team: R: A Language and Environment for Statistical Computing, 2015. Available at: http://www.R-project.org/. Accessed September 1, 2015
7. U.S. Census Bureau: Statistical Abstract Series. Available at: https://www.census.gov/library/publications/time-series/statistical_abstracts.html. Accessed January 8, 2016
8. U.S. Census Bureau: 2000 National Population Projections: Detailed Data Files (Total Population by Age, Sex, Race, and Hispanic Origin). Available at: http://www.census.gov/population/projections/data/national/np-d1.html. Accessed January 8, 2016
9. U.S. Census Bureau: 2014 National Projections: Summary Tables. Table 1. Available at: http://www.census.gov/population/projections/data/national/2014/summarytables.html. Accessed January 8, 2016

10. Ogden CL, Carroll MD, Kit BK, Flegal KM: Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA* 311: 806–814, 2014
11. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL: Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007-2008 to 2015-2016. *JAMA* 319: 1723–1725, 2018
12. Centers for Disease Control and Prevention (CDC): National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Available at: http://www.cdc.gov/nchs/hdi.htm. Accessed February 8, 2016
13. USRDS Renal Data Extraction and Referencing (RenDER) System: Version 3.0. Available at: http://www.usrds.org/render/xrender_home.asp. Accessed May 1, 2018
14. United States Renal Data System: Mortality. In: 2017 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2017. Available at: http://www.usrds.org. Accessed February 8, 2018
15. Møller B, Fekjaer H, Hakulinen T, Sigvaldason H, Storm HH, Talbäck M, et al.: Prediction of cancer incidence in the Nordic countries: Empirical comparison of different approaches. *Stat Med* 22: 2751–2766, 2003
16. Port FK: End-stage renal disease: Magnitude of the problem, prognosis of future trends and possible solutions. *Kidney Int Suppl* 50[Suppl]: S3–S6, 1995
17. Xue JL, Ma JZ, Louis TA, Collins AJ: Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. *J Am Soc Nephrol* 12: 2753–2758, 2001
18. Gilbertson DT, Liu J, Xue JL, Louis TA, Solid CA, Ebben JP, et al.: Projecting the number of patients with end-stage renal disease in the United States to the year 2015. *J Am Soc Nephrol* 16: 3736–3741, 2005
19. United States Renal Data System: Incidence, prevalence, patient characteristics, and treatment modalities. In: 2016 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2016. Available at: http://www.usrds.org. Accessed February 8, 2018
20. United States Renal Data System: Incidence, prevalence, patient characteristics, and treatment modalities. In: 2017 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2017. Available at: http://www.usrds.org. Accessed February 8, 2018
21. Wakasugi M, Kazama JJ, Narita I: Anticipated increase in the number of patients who require dialysis treatment among the aging population of Japan. *Ther Apher Dial* 19: 201–206, 2015
22. McFarlane PA, Pierratos A, Redelmeier DA: Cost savings of home nocturnal versus conventional in-center hemodialysis. *Kidney Int* 62: 2216–2222, 2002
23. Sinnakirouchenan R, Holley JL: Peritoneal dialysis versus hemodialysis: Risks, benefits, and access issues. *Adv Chronic Kidney Dis* 18: 428–432, 2011
24. Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, Freedman BI, et al.: Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science* 329: 841–845, 2010
25. Pecoits-Filho R, Perkovic V: Are SGLT2 inhibitors ready for prime time for CKD? *Clin J Am Soc Nephrol* 13: 318–320, 2017
26. Held PJ, McCormick F, Ojo A, Roberts JP: A cost-benefit analysis of government compensation of kidney donors. *Am J Transplant* 16: 877–885, 2016
27. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LYC, et al.: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 341: 1725–1730, 1999
28. Melanson TA, Hockenberry JM, Plantinga L, Basu M, Pastan S, Mohan S, et al.: New kidney allocation system associated with increased rates of transplants among black and Hispanic patients. *Health Aff (Millwood)* 36: 1078–1085, 2017
29. The Organ Procurement and Transplantation Network: The New Kidney Allocation System (KAS) Frequently Asked Questions, 2015. Available at: https://optn.transplant.hrsa.gov/media/1235/kas_faqs.pdf. Accessed September 25, 2017
30. NIH National Institute of Biomedical Imaging and Bioengineering: Artificial Kidney Development Advances, Thanks to Collaboration by NIBIB Quantum Grantees. Science Highlight, 2018. Available at: https://www.nibib.nih.gov/news-events/newsroom/artificial-kidney-development-advances-thanks-collaboration-nibib-quantum. Accessed February 8, 2018
31. Noble HR, Agus A, Brazil K, Burns A, Goodfellow NA, Guiney M, et al.: PAlliative Care in chronic Kidney diSease: The PACKS study--quality of life, decision making, costs and impact on carers in people managed without dialysis. *BMC Nephrol* 16: 104, 2015
32. Ljungvalla Å, Zimmerman FJ.: Bigger bodies: long-term trends and disparities in obesity and body-mass index among US adults, 1960–2008. *Social science & medicine* 75: 109–119, 2012

See related editorial, "Growth of the ESKD Population: Progress or Peril?," on pages 3–4.

Supplemental materials

Table of Contents

Supplemental Appendix 1: *Simulation modeling approach*

ESRD incidence was modeled in separately depending on whether it was diagnosed as caused by diabetes, hypertension, or other causes. Within each diagnosis group, the models were calculated separately within each age and race category. The results were combined for overall estimates and for race- and age-specific reporting.

Figure 3 shows the annual ESRD incidence rate from 1980 to 2013 by age group. The ESRD incidence rate was greater for older adults, especially after the late 1980s. The simulated temporal trend was rather flat after the year 2000 for those under age 45, remaining within a range of 74-80 per million per year in the reported data or the simulation model's estimates. For

people aged 45-64 the trend was rising slightly, from 514 to 543 per million per year (simulation model's estimate) and 525 to 537 per million per year (reported data) between 2000 and 2013. There was a decline in the incidence for those aged 65-74, from 1237 to 1149 per million per year (simulation model's estimate) and 1281 to 1151 per million/year in 2013. The rate among those aged 75 and over was more variable, and the simulation model did not capture the observed drop between 2010-2013 from 1518 to 1391 per million/year.

The incidence rates by age and by race obtained through simulation modeling seem to be ranked among the demographic groups and diagnoses in a manner consistent with the relative rates reported in the published literature. The simulations matched data from other sources that show higher incidence for blacks and greater increases in ESRD incidence since 1980 in the older population.[1]

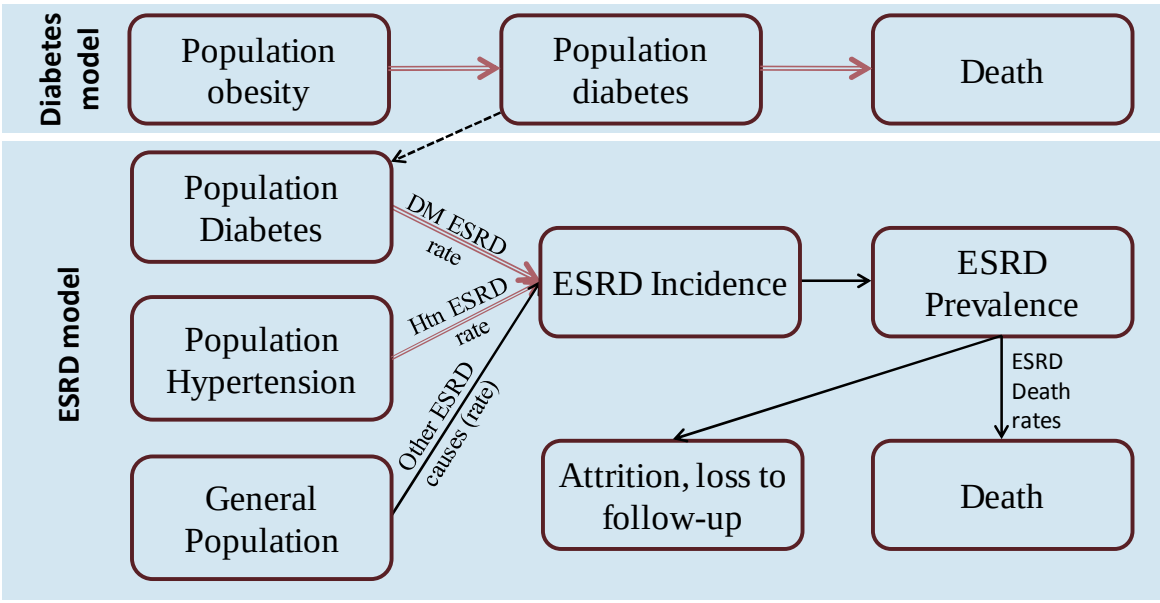
Attempts at validation using earlier periods to predict known 2015 data tend to over-estimate current incidence for much the same reason as the Gilbertson et al. simulation model did: the earlier data do not adequately reflect the downturn in diabetes incidence. We used data through the year 2000 to estimate incidence in 2013 and showed a result of roughly 144,000 incident patients/year, which was higher than the Gilbertson et al. result of 136,000. The actual incidence rate in 2013 was 118,160.[2] We acknowledge that substantial changes to the treatment of ESRD patients would render the current projections inaccurate as well.

Detail on the compartmental model

ESRD death-rate estimates were combined with ESRD incidence estimates (as shown in Supplemental Figure s1) to estimate trends in ESRD prevalence. The increasing incidence rate

along with the increasing size of the United States population and the generally decreasing age-specific ESRD death rates mean that the number of prevalent ESRD cases generally increased throughout the simulation period.

Supplemental Figure s1: Compartmental model



Diabetes model output used (⇢) with census data for diabetes input in ESRD model. DM/Htn/Other ESRD rate refers to ESRD where the primary cause was diabetes, hypertension, or other causes. Each arrow (transition rate) is expected to differ by age/race group and year

→ Estimated and extrapolated separately using available data

⇒ Estimated as latent variable in simulation

Equations for compartmental model

Each "compartment" in the compartmental model shown in figure 2 is a relevant population group, e.g., people with diabetes or people who have died. Populations can enter and leave these compartments. "Sources" in a compartmental model are special compartments from which the relevant population originates. The size of a source influences the incidence, or 'flow' into the next compartment. For example, if the population of people with obesity is larger, then it is expected that more people develop diabetes in a given year. Usually there are no flows into a source. "Sinks" are special compartments that the population cannot leave (i.e., "death"). Compartments, sources, and sinks used in the simulation model were defined as follows.

General population (Gp) for a given year and demographic (age-race) group (DG) (source) = Gp(year, DG)

- Based on US Census data, with smoothing to handle changes in racial prevalences produced by changes in the methods (e.g. sampling) and the question format.

Population obesity (source) = P_{Ob} (year, DG) = Gp(year, DG) * Obesity prevalence (DG)

- Obesity prevalence (DG) from NHANES obesity data with linear interpolations
- See "Obesity prevalence"

Population diabetes (compartment) = P_{dm}(year, DG) = P_{dm}(year-1) + P_{ob}(year-1)*(1-exp(-λ_{DM}(DG))) – P_{dm}(year-1)*(1-exp(-$\lambda_{DM\text{-}dth}$(DG)-$\lambda_{DM\text{-}dth\text{-}change}$(DG)*((year>1991)*.1*(year-1991)*(year<2002)+(year>2001))))

- λ_{DM} (DG)= Rate, transition from obesity to diabetes per year for each DG
- $\lambda_{DM\text{-}dth}$(DG)= Rate, transition from diabetes to death per year for each DG
- $\lambda_{DM\text{-}dth\text{-}change}$(DG): Allows for change in $\lambda_{DM\text{-}dth}$(DG), to account for indications that the death rate for people with diabetes may have improved.[3]
- See "Diabetes prevalence"

Population Hypertension compartment) = $P_{Hypertension}$ (year, DG) = Gp(year) * hypertension(DG) prevalence data

- Hypertension(DG) prevalence data used from published sources for each DG
- See "Hypertension prevalence"

ESRD(year, DG) (compartment) = ESRD(year-1, DG) + (Source({cause} , year-1, DG)*(1-exp(-$\lambda_{RCS\text{-}ESRD\{diabetes,\ hypertension\}}$(DG) - $\gamma_{ESRD\{other\}}$(DG))) – ESRD(year-1)*(1-exp(-γ_{Dth}(DG))))*(exp(-0.5*γ_{Dth}(DG))) - ESRD(year-1, DG)*(1-exp(-γ_{Dth}(DG))) - $\gamma_{emigration}$(DG)*ESRD(year-1,DG)

- {Cause} categorized as diabetes, hypertension, other
- Source{cause} = source population of cause: population with diabetes, population hypertension, or whole population. Incidence for each diagnosis is added to the ESRD compartment. The death rate among incident patients, assumed to have

an average of half of a year of follow-up, is applied across the sum of all incident patients (thus the exp(-0.5*γ_{Dth}(DG)) term).

- $\lambda_{RCS\text{-}ESRD\{diabetes,\ hypertension\}}$ (DG): Represents terms used in restricted cubic spline (RCS) for the rate of transition from source{cause} to ESRD per year
- $\gamma_{ESRD\{other\}}$(DG) = Other cause (non-hypertension, non-diabetes) transition rate
- γ_{Dth}(DG) = Transition from ESRD to death. Note that death rates are not calculated for each individual cause.
- $\gamma_{emigration}$(DG) = Transition from ESRD to loss of follow-up or emigration (e.g. emigration from the United States) as a percentage of previous prevalent population

Death (sink): not tracked separately, used for illustrative purposes

Attrition(sink): not tracked separately, used for illustrative purposes. This includes actual emigration from the United States as well as loss to follow-up for other reasons.

Legend: "Year" indicates the calendar year, and "DG" indicates the demographic group (age-race category). Each rate labeled with the Greek letter lambda λ is estimated using the Nelder-Mead optimization to minimize the sum of the squared differences between actual and simulated ESRD incidence. Other transition rates indicated with the Greek letter gamma γ are taken from actual rates. Flows are modeled as being strongly influenced by the size of each source population; however, this model does not assume that patients explicitly move from one compartment to another. Patients are not tracked individually, and the overall size of a population generally increases as calendar time increases.

The compartmental model has been used successfully in the past for chronic disease.[4] In this simulation, the compartments and flows (transition rates) used in each of the simulation models are diagrammed in Supplemental Figure s1. After diabetes prevalence was estimated using obesity and demographic data in the diabetes simulation model (see Supplemental Appendix 5: *Diabetes*), the results were used in the ESRD simulation model as inputs, along with general population size, hypertension prevalence, 'other' diagnosis ESRD incidence rates, and the remaining ESRD data. The outputs of the ESRD simulation model include ESRD incidence, prevalence, and deaths for each year for each demographic and diagnosis group of patients.

Transition rates to ESRD were allowed to change from year to year. Nelder-Mead optimization[5] (via the "optim" function in R[6]) was used on the sum of squared error in the incidence rates to obtain the estimated rates and their trends over time via restricted cubic splines. Knots at 1988 and 1999 were chosen based on the fit of the overall simulation model. Simulations for the obesity-to-diabetes transition in the population were constructed separately, and the results used for ESRD incidence with the primary causes identified as diabetes. Each of these simulations was modeled separately by age-race group, with separate rates calculated within each group. Incidence due to diabetes, hypertension, and other causes were each handled separately for each age and race group. The rates were generally small, so we did not separately model the reduction in the 'at risk' population due to (for example) the proportion of patients developing ESRD.

Supplemental appendix 2: Discussion of confidence intervals around population estimates

The current analyses do not present confidence intervals for data within individual years or for the projections. Confidence intervals are used to estimate the probable range of results from identical samples drawn from a single source population, not for estimates of the population as a whole. While the USRDS probably misses some cases of ESRD, the fact that ESRD patients are required by law to be registered so Medicare payment can be arranged means that relatively few patients are omitted. Confidence intervals for the estimated projections based on the simulation models containing over two million patients with incident ESRD over the years are unrealistically narrow, and the use of the entire US ESRD population means that statistical techniques based on sampling are not valid. We feel that the range of estimates based on the

varying input assumptions shows the accuracy or uncertainty of these projections in a way that is much more theoretically and practically justifiable.

Supplemental appendix 3: *ESRD demographics*

Some factors identified as important in previous literature include age (adjusted hazard ratio [HR] of ESRD incidence = 1.60 {1.21-2.10} for age 55+ v. age <55 years), race (adjusted HR = 2.47 {1.17-5.21} for black v. white), sex (adj. HR = 1.49 {1.10-2.01} for male v. female), comorbid conditions such as hypertension (adj. HR = 1.44 {1.31-1.59} per 19 mmHg higher systolic blood pressure) and diabetes (adj. HR = 6.10 {4.57-8.13} versus people without diabetes), BMI (adj. HR = 1.13 {1.00-1.29} per 1 kg/m^2 increase), and ethnicity (historically, adjusted incidence rates among Hispanics have been 1.35-1.95 times higher than among non-Hispanics). [7,8]

While ideally we would consider all individual risk factors for ESRD, including race, ethnicity, sex, more specific diagnosis categories (e.g. tracking specific glomerular diseases separately), genetic predictors, and various comorbid conditions, the estimates within individual categories of specific demographic, diagnostic, comorbid, and genetic factors for this analysis would be extremely unstable (if data were available at all), and definitions for some of the racial and ethnic categories have changed over time.

Supplemental Appendix 4: *CMS ESRD reporting requirements*

Whenever a patient starts treatment for ESRD, CMS requires that their information be reported on the Medical Evidence Form (CMS Form 2728) for them to receive Medicare benefits. The current (as of 2018) version of this form includes patient factors such as sex,

ethnicity (Hispanic/Latino), race (White, Asian, Black/African American, Native Hawaiian or Other Pacific Islander, American Indian/Alaska Native), the primary cause of ESRD identified by the treating physician, and several other factors. Many of the fields on the form have undergone revisions over the years; for example, in 2015 the cause of ESRD field was updated to use ICD-10-CM codes. Since 1995, this form has been required for all patients, not just Medicare-eligible patients. Patients with acute kidney failure who recover without a 2728 form being submitted are excluded from these analyses. Patients who recover permanently or who were lost to follow-up due to emigration were handled by a parameter estimated as a proportion (usually quite low) of the group being simulated, which was allowed to change over time.

There is also requirement that patients with ESRD who die will have the CMS form 2746 filled out by the dialysis or transplant provider within 30 days of death. This form identifies 90% of the ESRD population deaths. To supplement this information, the USRDS uses additional death information as detailed in the ESRD analytical methods section of their annual data report.[9]

Supplemental Appendix 5: *Diabetes*

Supplemental Figure s2 shows the annual point prevalence of diabetes on December 31 of each year from 1980 to 2013, by each age group within each race category, as a percentage of the population, as well as the curves simulated using population obesity data. The use of obesity data to predict trends in the empirical data seemed to result in trends that match observed data and parameter estimates that match published literature reasonably well.

The simulation model produced estimates for a rate parameter defining the diabetes incidence based on the obese population for each age and race group. These estimates varied widely, from 0.03 for whites under age 45 to 0.39 for blacks over age 75 years. Older patients

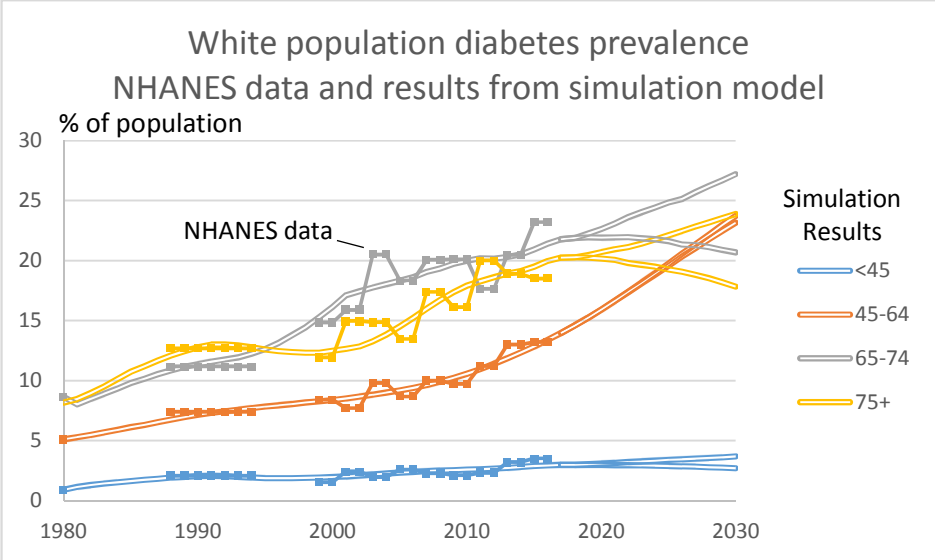
had higher incidence rates, as did black patients. These results matched CDC findings comparing relative diabetes incidence among different age groups and races,[10,11] and simulations based on the CDC results reached similar conclusions to those based on the NHANES data. While incidence rates for specific demographic categories are difficult to find in the literature, the overall rate of 0.016 is similar to the rates reported elsewhere. For example, Fox et al. found that 65/593 obese participants aged 40-55 in samples taken during the 1980s and 1990s progressed to diabetes over 8 years, which corresponds to an average incidence rate of 0.015/year.[12] This result indicates that our rate is not outside reasonable bounds of diabetes incidence rates among obese populations.

The death rates and departure rates among diabetic patients were allowed to change over time, since published data has shown that these rates may be decreasing, and the death rates arrived at by the Nelder-Mead optimization were similar to those found in these sources.[13]

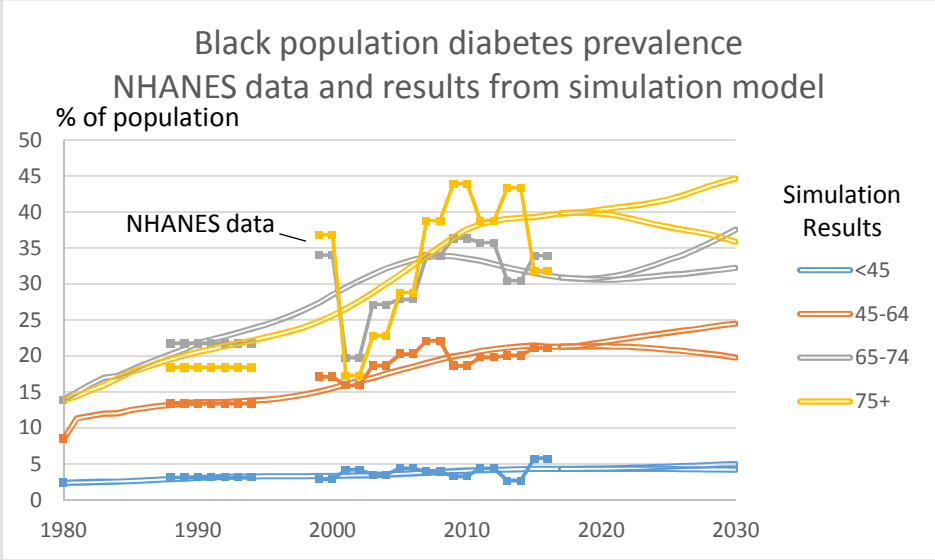
The NHANES data in Figure s2 illustrate the dilemma when attempting to use estimates based on the most specific group possible; even with the large samples available and sophisticated sampling methodology, the NHANES estimates of diabetes prevalence vary quite a bit within age/race groups from survey to survey. See Supplemental appendix 7: Smoothed population estimates for more discussion on how this was dealt with in the modeling process.

Supplemental Figure s2: Annual diabetes prevalence from 1980 to 2013 by age group, for racial groups used in simulation: (a) White, (b) Black, and (c) Other.

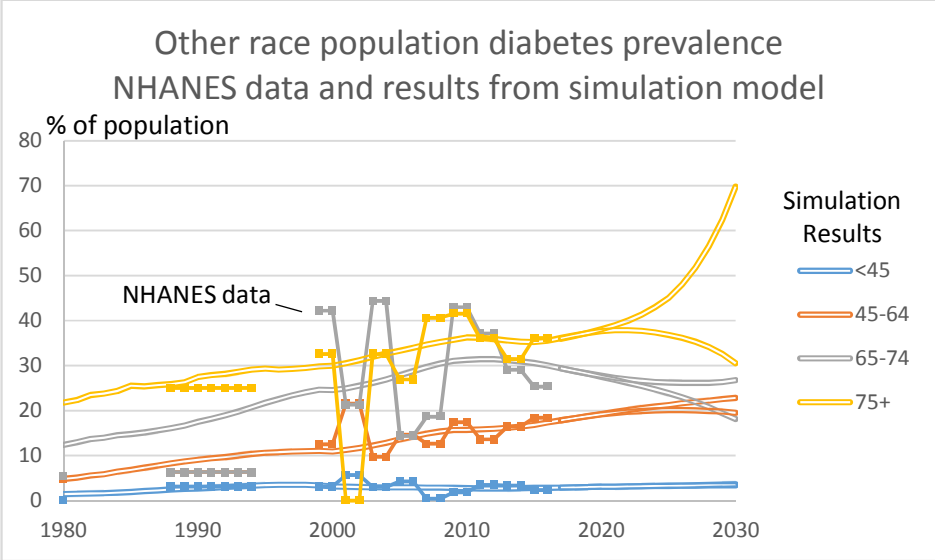
(a) White



(b) Black



(c) Other



Diabetes prevalence and projections

Our approach for modeling diabetes prevalence focused on predicting diabetes using the obese population. Obesity is a recognized risk factor for type 2 diabetes, is the most prevalent form of diabetes among adults.[14,15] Eighty percent of the adult population with diabetes is overweight or obese.[16] We used both CDC National Health And Nutrition Examination Survey (NHANES) and National Health Interview Survey (NHIS) data on the self-aware (i.e. diagnosed) diabetic population in separate runs to describe the population at most risk of ESRD with diabetes identified as the primary cause. Both sets of runs projected similar increases in the diabetes and ESRD population.

The transitions from obesity to diabetes and from diabetes to death were modeled as latent transition rate variables. The diabetes death rate was allowed to smoothly change over a period between 1991 and 2002 to reflect possible improvements in diabetes care; improvements

on the death rates among people with diabetes around this period have been reported in the literature.[17] Projections were calculated based on simulated incidence and post-1996 death rates.

When using NHANES data, the obesity and diabetes prevalence for people over the age of 75 who were neither white nor black was 0% in the 2000-01 dataset. We used instead interpolated rates based on the adjacent NHANES datasets. Similarly, data for patients over the age of 75 were missing from the 1976-1980 NHANES data; we used values that were proportional to the 65-74 year-old values, based on proportions calculated using the 1988-2000 data.

The prevalence of diabetes per million population is expected to increase to 11-13% of the population, compared to 9% in 2016, but due to the increase in population, the prevalence count of people with diabetes is expected to increase by 46%-67% between 2015 and 2030; this range agrees reasonably well with estimates found in other literature, such as 54% in Rowley et al.[18]

Currently, fewer than 10% of U.S. patients in the early stages are aware of their kidney disease; furthermore, even among patients with a CKD diagnosis, diabetes, or hypertension, only 43%-48% had received urine albumin testing.[19] Programs that increase awareness may lead to earlier detection and, through preventive interventions, reduced ESRD incidence.

Supplemental Appendix 6: *Hypertension and other ESRD causes*

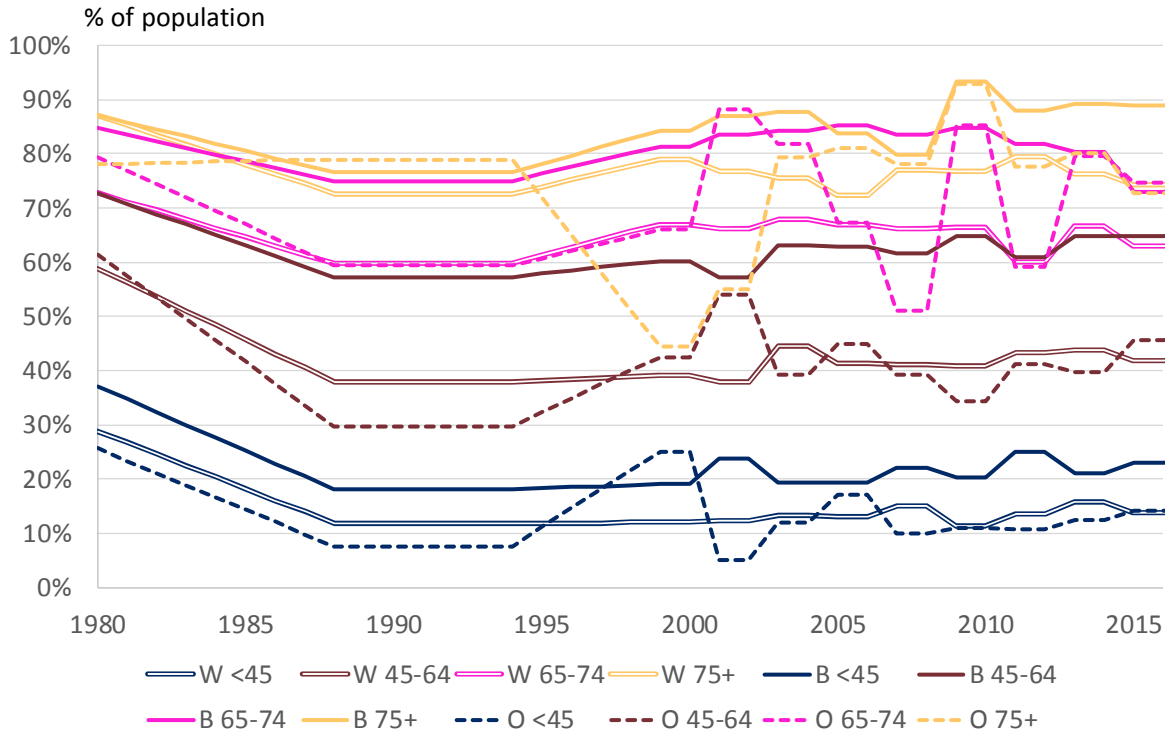
Hypertension prevalence and projections

Hypertension in NHANES was defined as having any of the following indicators: a systolic blood pressure (SBP) of 140 mmHg or greater, a diastolic blood pressure (DBP) of 90

mmHg or greater, or subject responses indicating that they were taking antihypertensive medicine, or had been diagnosed as having hypertension at least twice.

The prevalence of hypertension has not been increasing nearly as much as has the prevalence of obesity. Whites and blacks generally had a 2-5% increase in hypertension between 1988-94 and 2007-2012,[20] but this may have been due to aging. White median age increased from 32 in 1980 to 39 in 2000, and black median age increased from 25 to 30 over the same period.[21] While the prevalence of hypertension differs a great deal by age and race, Figure s3 below indicates that it has not varied a great deal over time within these groups.

Supplemental figure s3: Prevalence of hypertension by year, age, and race group based on NHANES data.



As a result, we lacked observational data that indicated the population-level influence of obesity on hypertension levels, and while obesity is a recognized risk factor for individual patient hypertension, this causal factor was omitted from the simulations of population data. Projections

used linear regressions on recent past hypertension prevalence, resulting in a small increase of 2% overall, due more to demographic shifts (e.g. the aging population) than to progression within age/race groups.

ESRD incidence attributed to other causes

In 2013, the USRDS attributed 73% percent of all ESRD incidence to diabetes or hypertension as the primary cause.[22] The remaining ESRD subtypes were 'other' (9%), glomerulonephritis (8%), unknown/missing (7%), cystic kidney disease (2%), and other urologic diseases (1%). Linear regressions on the combined "other-cause" subtype of ESRD were used to project trends through 2030. The R^2 values for linear regression models were 0.96 for most ESRD subtypes based on 1985-2013 data and for the glomerulonephritis and "other/missing" subtypes based on 1999-2013 data. In other linear models, the R^2 value was 0.84 for the cystic-kidney–disease subtype and 0.67 for urologic-disease subtype. While obesity can exacerbate or be a causal factor in some of these other conditions, this mechanism was treated as ignorable in these simulations.

Supplemental figure s4: ***ESRD prevalence proportion (per million) by assumptions of obesity and ESRD death-rate trends after 2015 (a-d), age/race group (color coded), and year (observed [dashed curves] and simulated through 2015; projected after 2015 [solid curves])***

The figures provided in the report show ESRD prevalence by age and separately by race in order to simplify the display. The following figures show ESRD prevalence by race and, within each race category, by age group as well.

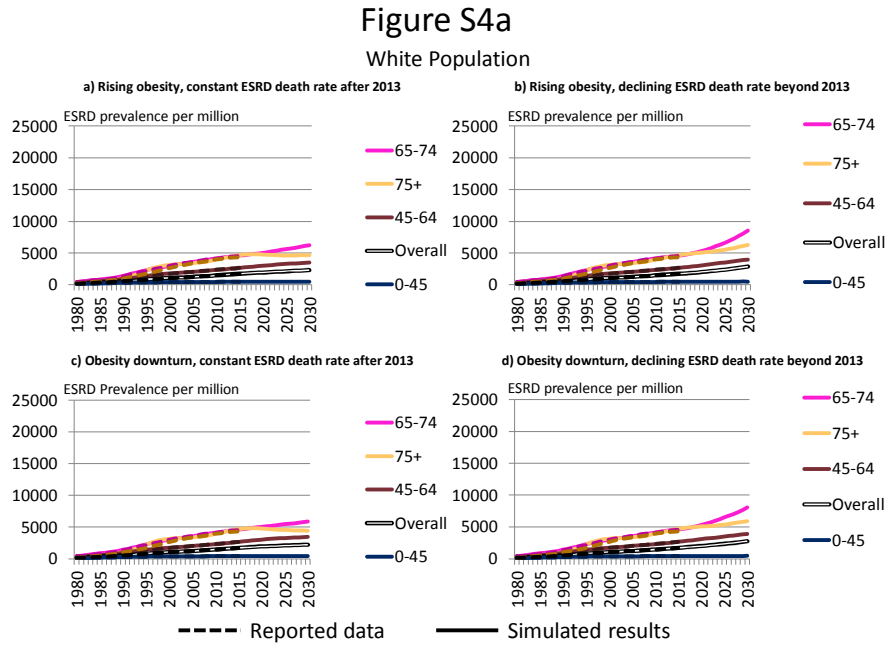


Figure S4b

Black Population

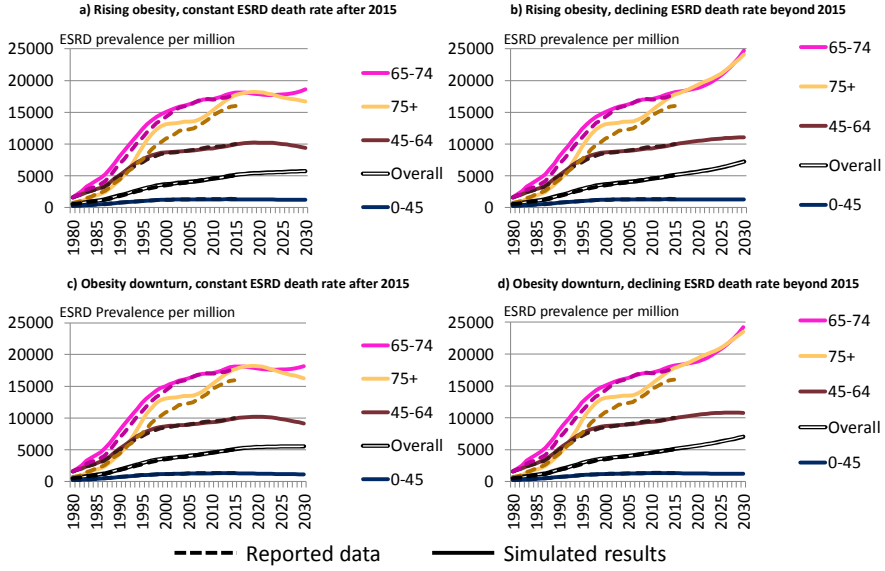
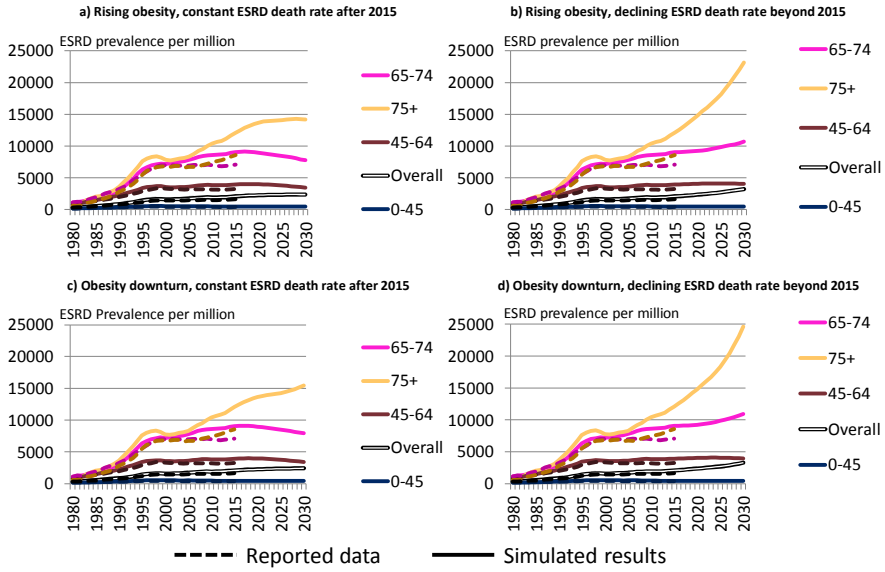


Figure S4c

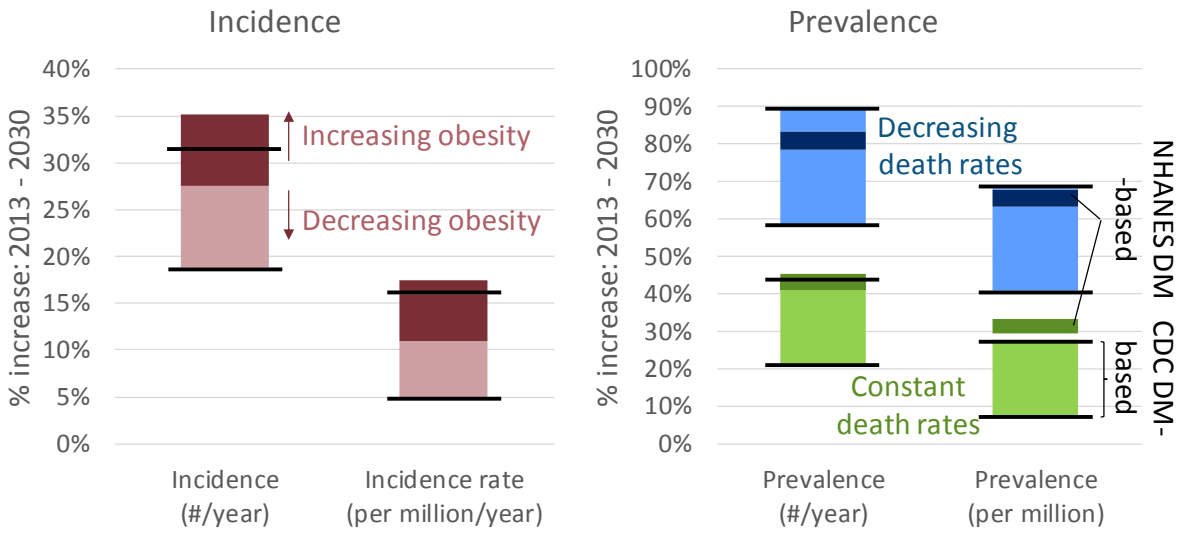
Other Race Population



Supplemental appendix 7: ***Sensitivity to racial categories, source of diabetes information***

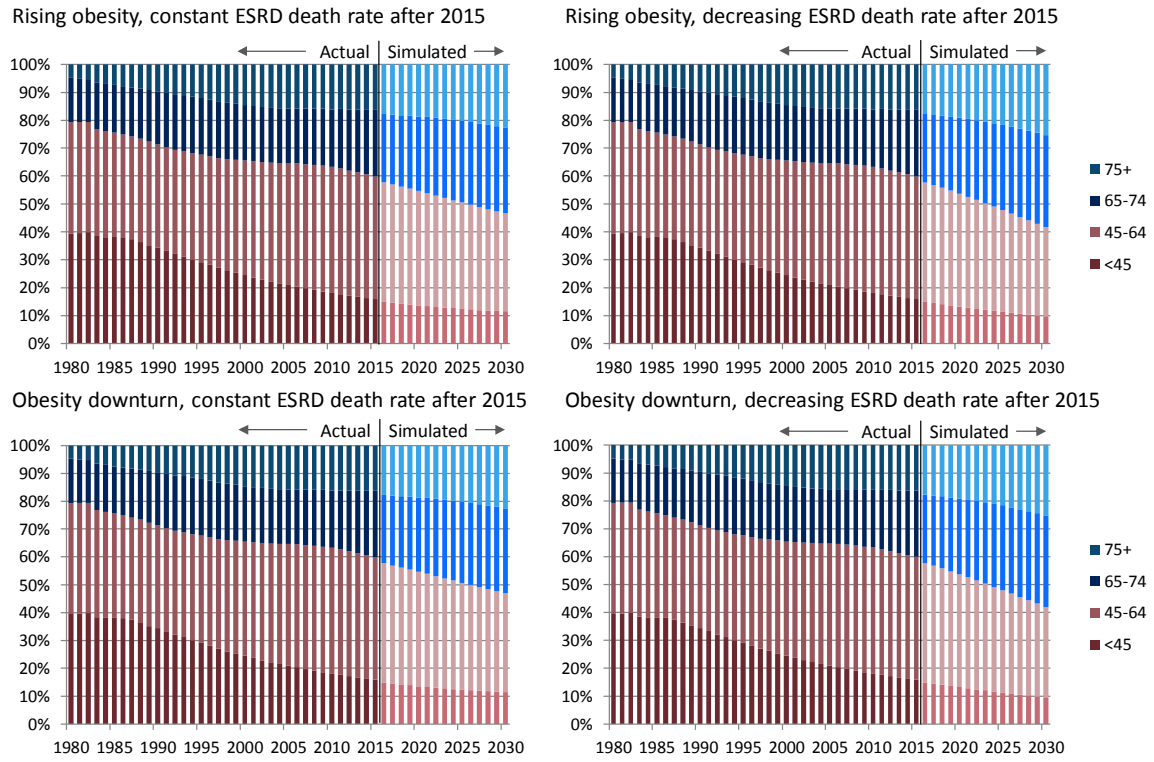
We ran the simulations using data from the CDC on age- and race-specific diabetes prevalence. This is based on self-reported diabetes, which has the disadvantage of not capturing undiagnosed diabetes and generally reports lower prevalence than diabetes based on NHANES data, which is what was presented in the manuscript. Using this data, we ran alternative models using either three racial groups (black, white, other) versus two (white, non-white). Figure s7 shows the range of projected increases in ESRD incidence and prevalence using these alternative data sources, compared with the projections used in the manuscript. In every run, there was substantial growth in the ESRD population. The runs based on CDC National Health Interview Survey diabetes prevalence and two racial groupings tended to have the lowest growth, followed by the runs using CDC diabetes prevalence and three racial groupings. The runs based on NHANES data using three racial groupings tended to have higher estimates; the fact that they were also based on more recent data (through 2015 instead of through 2013 for the runs based on CDC diabetes data) may have also contributed to this and to the narrower band of results. The three-race simulations generally exhibited more instability, especially when estimating trends in the smaller groups (e.g., 75+, other racial group). The larger estimates may represent improved accuracy due to including more specific patient categories in the simulation models; alternatively, they may reflect more unstable estimates due to smaller cell sizes. We believe that the three-racial group models using NHANES data provide the most accurate projections, and have focused the manuscript's results on these runs.

Supplemental figure s5: ESRD projections based on different data sources and race groups



Legend: Darker colors within each bar indicate range of estimates using NHANES diabetes data and three racial groups (black, white, other). Dark bars indicate range of estimates using CDC diabetes prevalence and either two (white, non-white) or three racial groups.

Supplemental Figure s6: Age distribution of prevalent ESRD patients, by obesity assumption and death rate assumption



Supplemental References

[1] United States Renal Data System. 2016 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016. Chapter 1: Incidence, Prevalence, Patient Characteristics, and Treatment Modalities.

[2] United States Renal Data System. 2017 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016. Reference table A1.

[3] Gregg, Edward W; Cheng, Yiling J; Saydah, Sharon; Cowie, Catherine; Garfield, Sanford; et al. Trends in Death Rates Among U.S. Adults With and Without Diabetes Between 1997 and 2006: Findings from the National Health Interview Survey. Diabetes Care35.6 (Jun 2012): 1252-7.

[4] Gilbertson, David T., Jiannong Liu, Jay L. Xue, Thomas A. Louis, Craig A. Solid, James P. Ebben, and Allan J. Collins. Projecting the Number of Patients with End-Stage Renal Disease in the United States to the Year 2015. J Am Soc Nephrol 16: 3736–3741, 2005.

[5] Nelder, J. A. and Mead, R. (1965) A simplex algorithm for function minimization. Computer Journal 7, 308–313.

[6] R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.

[7] Bash, Lori D., Brad C. Astor, and Josef Coresh.. 2009. Risk of Incident ESRD: A Comprehensive Look at Cardiovascular Risk Factors and 17 Years of Follow-up in the Atherosclerosis Risk in Communities (ARIC) Study. Am J Kidney Dis 55:31-41.

[8] United States Renal Data System. 2015 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2015. Reference table A.2(2). "Incidence of reported ESRD: per million population, by age, sex, race, ethnicity, & primary cause of ESRD: All patients, adjusted for age, sex, race, & ethnicity, U.S. with unknown age, race dropped."

[9] United States Renal Data System. 2017 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2017. "Volume 2: ESRD Analytical Methods."

[10] Centers for Disease Control and Prevention. Incidence of Diagnosed Diabetes per 1,000 Population Aged 18-79 Years, by Age, United States 1980-2014. https://www.cdc.gov/diabetes/statistics/incidence/fig3.htm. Accessed 3/2/2017.

[11] Centers for Disease Control and Prevention. Age-Adjusted Incidence of Diagnosed Diabetes per 1,000 Population Aged 18-79 Years, by Race/Ethnicity, United States, 1997-2014. https://www.cdc.gov/diabetes/statistics/incidence/fig6.htm. Accessed 3/2/2017.

[12] Fox, Caroline S., Michael J. Pencina, James B. Meigs, Ramachandran S. Vasan, Yamini S. Levitzky, Ralph B. D'Agostino. Trends in the Incidence of Type 2 Diabetes Mellitus From the 1970s to the 1990s: The Framingham Heart Study. Circulation. 2006; 113:2914-2918.

[13] Gregg, Edward W; Cheng, Yiling J; Saydah, Sharon; Cowie, Catherine; Garfield, Sanford; et al. Trends in Death Rates Among U.S. Adults With and Without Diabetes Between 1997 and 2006: Findings from the National Health Interview Survey. Diabetes Care35.6 (Jun 2012): 1252-7.

[14] Porth, Carol Mattson. Essentials of Pathophysiology. 2011. Wolters Kluwer Health | Lippincott Williams & Wilkins. P. 809.

[15] National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation. National Diabetes Statistics Report, 2014. CDC.

[16] National Institute of Diabetes and Digestive and Kidney Diseases. "Do you know some of the health risks of being overweight?" http://www.niddk.nih.gov/health-information/health-topics/weight-control/health_risks_being_overweight/Pages/health-risks-being-overweight.aspx

[17] Gregg, Edward W; Cheng, Yiling J; Saydah, Sharon; Cowie, Catherine; Garfield, Sanford; et al. Trends in Death Rates Among U.S. Adults With and Without Diabetes Between 1997 and

2006: Findings from the National Health Interview Survey. Diabetes Care35.6 (Jun 2012): 1252-7.

[18] Rowley, William R., Clement Bezold, Yasemin Arikan, Erin Byrne, and Shannon Krohe. Diabetes 2030: Insights from Yesterday, Today, and Future Trends. Popul Health Manag. 2017 Feb 1; 20(1): 6–12. Published online 2017 Feb 1. doi: 10.1089/pop.2015.0181.

[19] United States Renal Data System. 2016 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016. Volume 1, chapter 1: CKD in the General Population, p. 3.

[20] Mozaffarian, Dariush, Emelia J. Benjamin, Donna K. Arnett, Michael J. Blaha, Mary Cushman, Sarah de Ferranti, Jean-Pierre Després, Heather J. Fullerton, Virginia J. Howard, Mark D. Huffman, Suzanne E. Judd, Brett M. Kissela, Daniel T. Lackland, Judith H. Lichtman, Lynda D. Lisabeth, Simin Liu, MD, Rachel H. Mackey, David B. Matchar, Darren K. McGuire, Emile R. Mohler III, Claudia S. Moy, Paul Muntner, Michael E. Mussolino, Khurram Nasir, Robert W. Neumar, Graham Nichol, Latha Palaniappan, Dilip K. Pandey, Mathew J. Reeves, Carlos J. Rodriguez, Paul D. Sorlie, Joel Stein, Amytis Towfighi, Tanya N. Turan, Salim S. Virani, Joshua Z. Willey, Daniel Woo, Robert W. Yeh, Melanie B. Turner, on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics – 2015 Update: A Report From the American Heart Association. Circulation. 2015;131:e29-e322. DOI: 10.1161/CIR.0000000000000152.

[21] Hobbes, Frank, and Nicole Stoops. 2002. Demographic Trends in the 20th Century: Census 2000 Special Reports (censr-4). U.S. Department of Commerce, Economics and Statistics Administration, U.S. Census Bureau. Figure 3-20.

[22] United States Renal Data System. 2015 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2015. Reference table A.1.

SIGNIFICANCE STATEMENT

Although ESRD incidence rates in the United States increased dramatically through the 1980s and 1990s, the incidence of ESRD adjusted for age, sex, and race leveled off and declined after 2009, prompting speculation that the upward trend may have stabilized in the 2000s. Using a simulation model, the authors show that, despite a decrease in incidence rates within age and race groups, the aging population and changes in the racial distribution of the population will result in increasing crude ESRD incidence rates and annual numbers of new patients. These findings along with decreasing ESRD death rates will result in a substantial increase in the prevalent ESRD population by 2030. This finding has important implications for dialysis infrastructure planning and Medicare and Medicaid budgeting.