The Contribution of Increased Diabetes Prevalence and Improved Myocardial Infarction and Stroke Survival to the Increase in Treated End-Stage Renal Disease

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Abstract. This study examined the extent to which the greater than threefold increase in number of treated end-stage renal disease (ESRD) cases between 1978 and 1991 is explained by increases in the prevalence of diabetes, myocardial infarction (MI) and stroke survivors, and US population size. The change in number of persons in the United States with diabetes, a history of MI or stroke, and without these conditions was estimated for 1978 and 1991 using the Second and Third National Health and Nutrition Examination Surveys. The treated ESRD incidence rate and the increase in ESRD treatment attributable to each of these populations were calculated using these estimates and data from the United States Renal Data System. In the United States, there were an estimated 4.3 and 1.2 million more persons with diabetes and a history of MI or stroke, respectively, 22.7 million more persons without these conditions, and 36,881 more incident treated ESRD cases in 1991 compared with 1978. In 1991, treated ESRD incidence rates among persons with diabetes, a history of MI or stroke, and without these conditions were 2567, 1463, and 153 cases per million person-years, respectively. In 1991, 10,183 cases of the additional 36,881 treated ESRD cases (27.6%) resulted from the higher prevalence of diabetes; 1775 (4.8%) from increased MI and stroke survival; and 2904 (7.9%) resulted from growth of the US population without these conditions. The increasing number of treated ESRD cases in the United States is partly explained by the increase in diabetes prevalence and US population growth but only minimally by MI and stroke survival.

Population-based studies have found a large increase in the number of persons with diabetes (1,2) and a history of myocardial infarction (MI) (3,4) and stroke (5) in the US over the last several decades. Persons with diabetes (6,7) and those with a history of MI or stroke (8) have a higher risk of treated end-stage renal disease compared with persons of similar age without such co-morbidities. Also, upon initiation of dialysis treatment, a large proportion of incident end-stage renal disease cases has a history of diabetes, MI, and stroke; 49%, 14%, and 10%, respectively, in 1996 (9,10).

The incidence of treated end-stage renal disease has increased at an annual rate of 8% over the past 20 yr (Figure 1) (11). In 1978, fewer than 15,000 people initiated treatment for end-stage renal disease, in contrast to more than 50,000 in 1991 and 96,000 in 2000 (11). According to a recent USRDS forecast (12), more than 172,000 persons are expected to begin treatment in 2010 (Figure 1), making chronic kidney disease an important area to focus prevention efforts. However, the contribution of factors that may underlie the unabated increase in treated end-stage renal disease incidence are poorly understood (13).

We therefore conducted a study to estimate the proportion of the increase in treated end-stage renal disease incidence between 1978 and 1991 resulting from a higher prevalence of diabetes, improved MI and stroke survival, and growth of the US population without these conditions.

Materials and Methods

Using population-based data sources and epidemiologic methods, the increase in number of end-stage renal disease cases initiating treatment between 1978 and 1991 resulting from an increased number of persons with diabetes, more MI and stroke survivors, and overall US population growth were estimated. These estimates were calculated as the product of the change in the size of each respective population between 1978 and 1991 and the incidence rate of end-stage renal disease treatment among these populations in 1991 (Appendix A, panel 1). Data needed for this calculation were abstracted from four separate sources: the second and third National Health and Nutrition Examination Survey (NHANES II and III) (14,15), the United States Renal Data System (11), and the United States Census (16,17).

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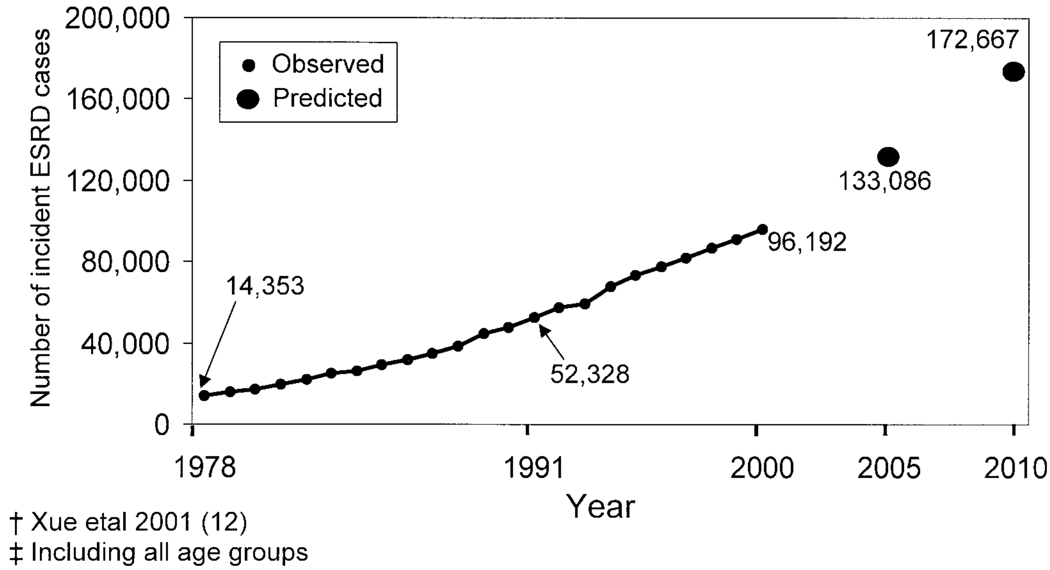

Figure 1. Actual (1978 to 2000) and predicted† (2005 and 2010) number of incident treated end-stage renal disease patients in the United States (9,11).

NHANES II and III

NHANES II and III were designed to allow the estimation of the prevalence of common chronic conditions, including diabetes mellitus and a history of MI and stroke, for the civilian, non-institutionalized population of the United States. NHANES II data were collected between 1976 and 1980 (midpoint: July 1978) and NHANES III from 1988 to 1994 (midpoint: April 1991). In addition to demographic information (*i.e.*, age, race, sex), both NHANES surveys used in-home interviews to assess the presence of chronic health conditions including self-report of diabetes, MI, and stroke (Appendix B). Sampling weights to achieve US population estimates and variance estimators that account for the complex survey design employed in NHANES were applied in all calculations (18).

United States Renal Data System

Comprehensive data, including date of initiation of chronic outpatient therapy for end-stage renal disease, primary cause of end-stage renal disease and demographic characteristics are collected on every Medicare-eligible case of treated end-stage renal disease by the National Institutes of Diabetes and Digestive Kidney Diseases. Before 1996, data on comorbid conditions were not collected on all incident treated end-stage renal disease cases. However, in 1990, co-morbidity data were collected through medical chart review on a representative sample of treated end-stage renal disease cases from randomly selected dialysis centers in a special study (Case-Mix Adequacy Study). Therefore, for the current analysis, we assessed the prevalence of diabetes and a history of MI and stroke among the 1,903 Case-Mix Adequacy Study participants initiating end-stage renal disease treatment in 1990. The primary goal of the Case-Mix Adequacy Study were to evaluate the relationship of dialysis dose and dialyzer membrane on patient outcomes. Data collected as part of the Case-Mix Adequacy Study were abstracted from patient records kept at the dialysis facility where each patient received care. A copy of the abstraction form has been previously published.

Statistical Methods

The number of incident cases of treated ESRD was plotted by calendar year from 1978 through 1991. To investigate the increase in ESRD with the assigned cause of diabetes, incident counts were calculated by underlying cause of treated ESRD, diabetes or not diabetes, as assigned by the diagnosing physician. The difference in number of ESRD cases between 1978 and 1991 with an underlying cause of diabetes was divided by the overall increase in number of ESRD cases to estimate the impact of persons with an underlying diagnosis of diabetes on the incidence of ESRD.

Change in the number of persons in the US with diabetes, a history of MI or stroke, and without these conditions, between 1978 and 1991, was calculated as the difference in population estimates for each group using NHANES II and III (Appendix A; panel 2). Due to these conditions' strong associations with age, calculations were performed using five age groupings (30 to 44, 45 to 51, 55 to 64, 65 to 74, and $\geq$75 yr). NHANES II only included US citizens under age 75 yr; we therefore compared the prevalence of diabetes, MI, and stroke in 1978 and 1991 within each age category and imputed the average change to persons aged 75 yr and older for the 1978 estimate (Appendix A; panel 3).

The incidence rates of treated end-stage renal disease for persons with diabetes, with a history of MI or stroke, and without these conditions in 1991 were calculated as the number of incident cases of treated end-stage renal disease with each co-morbid condition divided by the number of people in the US population with the same condition (Appendix A; panel 4). The number of incident cases of treated end-stage renal disease with diabetes mellitus was estimated as the product of the total number of incident cases of treated end-stage renal disease in the US in 1991, obtained from the core United States Renal Data System data set, and the prevalence of diabetes among cases initiating end-stage renal disease therapy in 1990, as sampled in the Case-mix Adequacy Study (Appendix A; panel 5). Analogous methods were used to calculate the number of incident treated end-stage renal disease cases among persons with a history of MI or stroke and also for the population without diabetes, a history of MI, or stroke. Due to the low number of incident cases of treated end-stage renal disease between 18 and 29 yr old sampled in the Case-mix Adequacy Study (n = 82), we limited our data analysis to persons 30 yr and older.

Two sets of sensitivity analyses were performed. First, sensitivity analyses were performed by repeating all analyses stratified by race (White and Black), using four mutually exclusive categories (a history of MI/stroke only, diabetes mellitus only, both a history of diabetes mellitus and MI/stroke, and none of these conditions), and by both race stratification and use of mutually exclusive categories. Finally, analyses for diabetes were repeated capturing undiagnosed diabetes by defining diabetes as either a self-report of diabetes or a fasting plasma glucose ≥ 126 mg/dl.

Results

The number of cases of ESRD has been increasing exponenetially (Figure 1). For the overall US population, the total number of incident cases of ESRD was 14,353 in 1978, 52,328 in 1991, and 96,192 in 2000, respectively. There were 12,237 and 49,118 incident ESRD cases in 1978 and 1991 ≥ 30 yr of age, respectively (total increase $n = 36{,}881$). In 1978, 1281 (10%) of the incident cases of ESRD ≥ 30 yr of age were diagnosed with the assigned cause of diabetes compared with 18,218 (37%) in 1991. Overall, the increase in incident treated ESRD cases among the US population ≥ 30 yr of age with an assigned cause of diabetes ($n = 16{,}937$) is equivalent to 46% (16,937/36,881) of the overall increase in ESRD between 1978 and 1991.

US Population Characteristics

Characteristics of the overall US population, persons with diabetes, persons with a history of MI or stroke, and incident cases of treated end-stage renal disease older than 30 yr of age in 1978 and 1991 are listed in Table 1. Compared with the general US population, in both years examined, persons with diabetes were older and more likely to be African-American, have a history of MI and stroke, and have hypertension. Additionally, those with a history of MI or stroke and incident cases of treated end-stage renal disease were older, and more likely to be male and have diabetes and hypertension. Overall, the US population grew by 26.7 million persons. As stated previously, the incident treated ESRD population increased by 36,881 cases from 1978 and 1991.

Estimating the Change in Population Size

The age-specific prevalence of diabetes in the US, for persons < 75 yr of age, increased an average of 59% between 1978 and 1991 (Table 2). This average change and a prevalence of diabetes of 13.2% in 1991 for the population ≥ 75 yr of age was used to estimate a diabetes prevalence of 8.3% for this population in 1978. Overall, between 1978 and 1991, the number of persons with diabetes mellitus in the US increased by 4.282 million.

On average, the age-specific prevalence of MI and stroke in the US, for persons < 75 yr of age, decreased by an average of 5% (Table 2). A prevalence of MI and stroke among the population ≥ 75 yr of age in 1978 of 23.8% was imputed from 22.6% in 1991. In 1991, there were 1.224 million more persons with a history of MI or stroke compared to 1978. Additionally, there were 22.261 million more persons in the US without diabetes or a history of MI or stroke.

Incidence of Treated End-Stage Renal Disease

Overall, 50% and 27% of incident cases of treated end-stage renal disease in 1990 in the Case-mix Adequacy Study had a

Table 1. Estimated number and composition of the overall United States population age 30 yr and older and sub-groups with self-reported diabetes mellitus, myocardial infarction or stroke survivors, and incident treated end-stage renal disease cases in 1978 and 1991

	US Population		Diabetes Mellitus[a]		History of Myocardial Infarction/ Stroke[a]		Incident End-Stage Renal Disease	
	1978	1991	1978	1991	1978	1991	1978	1991
Total (age ≥ 30 yr), thousands	113,200	139,900	5500	9600	8200	9400	12.2	49.1
Age, yr								
30 to 44, %	38[b]	45[b]	17	20	6	6	23	16
45 to 54, %	20[b]	18[b]	18	14	13	12	21	14
55 to 64, %	19[b]	15[b]	24	25	26	22	27	22
65 to 74, %	14[b]	13[b]	24	25	28	30	23	30
75+, %	9[b]	9[b]	17	17	28	30	7	18
African American, %	11[a]	9[a]	15	16	9	12	27	30
Male gender, %	47[a]	48[a]	41	43	62	65	55	54[c]
Diabetes mellitus, %	4.8[a]	6.9[a]	100	100	13	22	NA	50[c]
Hypertension, %	28[a]	26[a]	55	54	57	57	NA	86[c]
Myocardial infarction/stroke history, %	7.3[a]	6.8[a]	16	19	100	100	NA	25[c]

[a] Data estimated from self-reported medical history in the Second (1978) and Third (1991) National Health and Nutrition Examination Survey.
[b] Estimated from US Census Bureau data.
[c] Data is based on the 1990 United States Renal Data System's Case-Mix Adequacy Study.

Table 2. Census counts in millions, prevalence, and change in number of persons with diabetes mellitus, self-reported myocardial infarction and stroke, or neither condition in the United Stated for 1978 and 1991

Age Group (a)	1978				1991				Change (1978 to 1991)		
	Census Counts (b)	Prevalence (SE)[b]			Census Counts (f)	Prevalence (SE)[c]			Number in Millions (SE)[d]		
		Diabetes Mellitus (c)	MI/Stroke (d)	Neither (e)		Diabetes Mellitus (g)	MI/Stroke (h)	Neither (i)	Diabetes Mellitus (l)	MI/Stroke (m)	Neither (n)
30 to 44	43.195	0.014 (0.002)	0.011 (0.002)	0.975 (0.003)	61.420	0.030 (0.003)	0.009 (0.002)	0.963 (0.004)	1.218 (0.204)	0.046 (0.137)	17.057 (0.238)
45 to 54	22.800	0.044 (0.005)	0.042 (0.004)	0.920 (0.006)	25.743	0.052 (0.007)	0.043 (0.005)	0.908 (0.008)	0.333 (0.207)	0.141 (0.170)	2.411 (0.236)
55 to 64	21.703	0.066 (0.007)	0.098 (0.007)	0.847 (0.010)	21.006	0.112 (0.008)	0.095 (0.008)	0.819 (0.010)	0.905 (0.228)	−0.132 (0.213)	−1.186 (0.250)
65 to 74	15.581	0.093 (0.004)	0.145 (0.007)	0.786 (0.007)	18.274	0.128 (0.010)	0.151 (0.011)	0.764 (0.012)	0.875 (0.187)	0.494 (0.221)	1.711 (0.192)
75+	9.969	0.083[a] (0.007)	0.238[a] (0.009)	0.703[a] (0.011)	13.489	0.132 (0.007)	0.226 (0.009)	0.688 (0.010)	0.949 (0.116)	0.674 (0.159)	2.273 (0.118)
Overall	113.200	0.048 (0.012)	0.073 (0.014)	0.889 (0.017)	139.900	0.069 (0.016)	0.068 (0.017)	0.879 (0.021)	4.282 (0.430)	1.224 (0.409)	22.261 (5.971)

[a] Data not available in NHANES II. Values were imputed based on average change in prevalence in all of the other age groups (Appendix A, panel 3).
[b] Estimated using the Second National Health and Nutrition Examination Survey (1976 to 1980).
[c] Estimated using the Third National Health and Nutrition Examination Survey (1988 to 1994).
[d] Column (l) = Increase in number of persons with diabetes mellitus from 1978 to 1991; [column (f) × column (g)] minus number of persons with diabetes in 1978 [column (b) × column (c)]. Column (m) = Increase in number of persons with history of MI/Stroke from 1978 to 1991; [column (f) × column (h)] minus number with MI/Stroke in 1978 [column (b) × column (d)]. Column (n) = (f) × (i)–(b) × (e) = Increase in number of persons with neither comorbidity from 1978 to 1991; [column (f) × column (h)] minus number with neither comorbidity in 1978 [column (b) × column (e)].

history of diabetes and history of MI or stroke, respectively (Table 3, column c). In contrast, 39% of this population had none of these conditions. The prevalence of these co-morbidities varied by age. The overall and age-specific incidence rates of treated end-stage renal disease was higher among persons with diabetes mellitus and persons with a history of MI or stroke when compared with the general US population (Figure 2 and columns f and g of Table 3). In contrast, the incidence was lower among persons without diabetes mellitus or a history of MI or stroke.

Cases of Treated End-Stage Renal Disease Attributable to the Factors Studied

In 1991, there were 36,881 more incident cases of treated end-stage renal disease, older than age 30 yr, compared with 1978 (Figure 3). The increase in the population with diabetes mellitus accounted for 10,183 incident cases of treated end-stage renal disease in 1991 (Table 4 and Figure 3). This represents 27.6% (10,183/36,881) of the increase in treated end-stage renal disease between 1978 and 1991. In contrast, 4.8% (1,775/36,881) of the overall increase in treated end-stage renal disease incidence between 1978 and 1991 was attributable to the increased number of MI and stroke survivors (Table 4 and Figure 3). The increase in the size and growth of the US population older than 30 yr of age without a history of MI or stroke accounted for 2904 incident cases of treated end-stage renal disease in 1991. This is equivalent to 7.9% of the increase in treated ESRD cases between 1978 and 1991. In sum, 40% (95% CI, 33 to 48%) of the increase in treated end-stage renal disease in the US population could be attributed to an increased prevalence of diabetes mellitus, more MI and stroke survivors, and growth of the US population without these conditions.

Sensitivity Analyses

Performing all of the analyses separately for White and Black patients and pooling the results, 10,094 (27.3%), 2,592 (7.0%), and 3,332 (9%) cases of treated ESRD could be attributed to a higher prevalence of diabetes mellitus, more MI and stroke survivors, and US population growth respectively. Additionally, in re-analyzing the data using four mutually exclusive categories (a history of MI/stroke only, a history of diabetes mellitus only, both a history of MI/stroke and diabetes, and none of these conditions), 12,279 cases (standard error 1618) corresponding to 33% of the 36,881 additional cases of treated ESRD between 1991 compared to 1978 could be attributed to the factors explored. Finally, in race-specific analyses, these four mutually exclusive categories accounted for 35% of the increase in incident treated ESRD cases (data not shown).

Additional sensitivity analyses were performed defining diabetes as either self-report of a previous diagnosis or fasting plasma glucose ≥126 mg/dl. Using this definition of diabetes, there were 5.6 million more persons in the US population with diabetes in 1991 compared with 1978 (compared with 4.3 million using self-report). However, compared with the incidence of treated ESRD among persons with self-reported dia-

Table 3. Calculation of treated end-stage renal disease incidence rates among individuals with diabetes (top third of table), a history of myocardial infarction or stroke (middle third of table) and none of these conditions in 1991 (bottom third of table)

Age group (a)	Incident End-Stage Renal Disease in 1991			US Population (1991), in Millions	End-Stage Renal Disease Incidence Rates (SE) in 1991, per 1,000,000	
	Total Number of Cases[a] (b)	**Diabetes** Prevalence % (SE),[b] (c)	Number (SE) with **Diabetes Mellitus**[c] (d)	Number (SE) with **Diabetes Mellitus**[d] (e)	Among Persons with **diabetes**[e] (f)	Overall US Population[f] (g)
30 to 44	7599	39 (3)	2956 (231)	1.824 (0.184)	1620 (207)	119
45 to 54	6776	62 (3)	4192 (224)	1.336 (0.172)	3137 (439)	247
55 to 64	10,655	61 (2)	6446 (263)	2.346 (0.169)	2747 (228)	466
65 to 74	14,874	53 (2)	7839 (303)	2.329 (0.176)	3364 (286)	733
75+	9214	35 (3)	3243 (252)	1.776 (0.093)	1826 (172)	621
Overall	49,118	50 (6)	24,767 (584)	9.613 (0.364)	2567 (631)	203
Age group	Total Number of Cases	**Myocardial Infarction/Stroke** Prevalence % (SE)	Number (SE) with a **History of Myocardial Infarction or Stroke**	Number (SE) with a **History of Myocardial Infarction or Stroke**	Among **Myocardial Infarction or Stroke Survivors**	Overall US Population
30 to 44	7599	6 (2)	473 (118)	0.520 (0.194)	908 (294)	119
45 to 54	6776	20 (3)	1321 (190)	1.106 (0.166)	1195 (228)	247
55 to 64	10,655	28 (2)	2964 (251)	1.996 (0.197)	1485 (172)	466
65 to 74	14,874	38 (2)	5704 (310)	2.750 (0.160)	2074 (186)	733
75+	9214	36 (3)	3323 (264)	3.049 (0.160)	1090 (98)	621
Overall	49,118	27 (5)	13,786 (528)	9.421 (0.332)	1463 (461)	203
Age group	Total Number of Cases	**Neither Condition** Prevalence % (SE)	Number (SE) with **Neither Condition**	Number (SE) with **Neither Condition**	Among Persons **Without** Diabetes, History of Stroke or Myocardial Infarction	Overall US Population
30 to 44	7599	59 (3)	4494 (233)	59.172 (0.207)	75 (4)	119
45 to 54	6776	34 (3)	2300 (219)	23.382 (0.196)	98 (9)	247
55 to 64	10,655	29 (2)	3126 (245)	17.197 (0.177)	182 (14)	466
65 to 74	14,874	33 (2)	4883 (285)	13.953 (0.173)	350 (21)	733
75+	9214	44 (3)	4031 (262)	9.277 (0.094)	435 (29)	621
Overall	49,118	39 (6)	18,835 (556)	122.982 (0.389)	153 (40)	203

[a] Column (b) was abstracted from the United States Renal Data System.
[b] Column (c) was abstracted from the 1990 Case-Mix Adequacy Study only for incident cases of treated ESRD in 1990 (17).
[c] Column (d) = column (b) × column (c); numbers may differ slightly due to rounding.
[d] Column (e) was calculated using data from NHANES III.
[e] Column (f) = column (d) ÷ column (e); numbers may differ slightly due to rounding.
[f] Column (g) was abstracted from the United States Renal Data System Annual Report.

betes, the incidence of treated ESRD within each age group was lower among those with either self-reported or undiagnosed diabetes. The larger increase in number of persons with diabetes but lower incidence rate of treated ESRD associated with this broader definition of diabetes offset one another, and the overall increase in incident treated ESRD cases was similar (n = 10,673) to the analyses that relied on self-report to define diabetes (Table 4, n = 10,183).

Discussion

Both a higher prevalence of diabetes mellitus and improved MI and stroke survival have been proposed as explanations for the increase in treated end-stage renal disease incidence (13). However, the factors examined in the current study explained only a minority of the increase in treatment for end-stage renal disease incidence between 1978 and 1991. In our study, among the population between 30 and 74 yr of age, the age-specific self-reported prevalence of diabetes mellitus increased by 59% between 1978 and 1991. Overall, diabetes mellitus was present in 50% of incident treated end-stage renal disease cases in 1990. According to our calculations, the increase in diabetes accounted for nearly 28% of the increase in incident end-stage renal disease treatment.

On the basis of these reports, we expected a large percentage of the increase in treated end-stage renal disease incidence to be due to an increased number of MI and stroke survivors. In the current study, the age-specific risk of treated end-stage renal disease was much higher for persons with a history of MI or stroke compared with the overall population. However, in each age group, the change in MI and stroke prevalence was

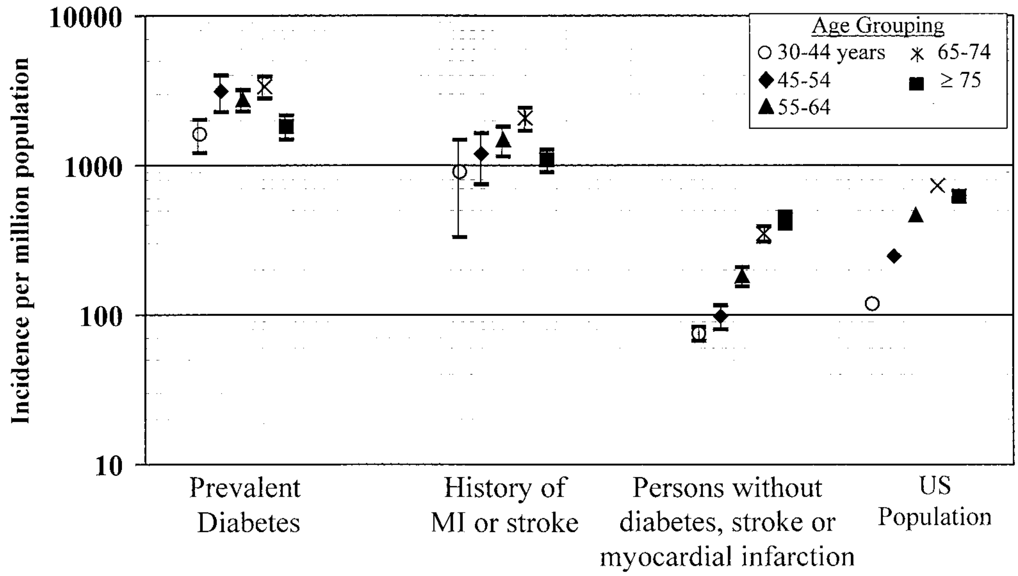

Figure 2. Age-specific treated end-stage renal disease treated incidence rates (95% CI) in 1991 among persons with prevalent diabetes mellitus, a history of myocardial infarction (MI) or stroke, without these conditions, and for the overall US population.

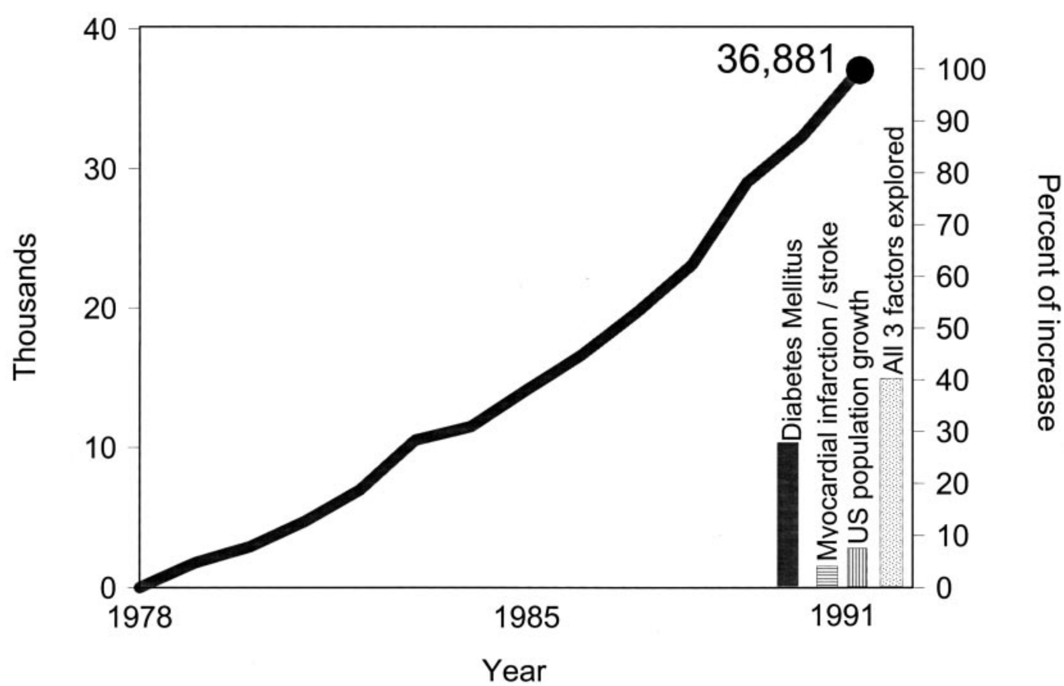

Figure 3. Increase in number of incident treated end-stage renal disease cases ≥ 30 years of age from 1978 to 1991 (line) and number/percentage of total increase in ESRD attributable to improved myocardial infarction and stroke survival, increased prevalence of diabetes, and a larger US population in 1991 (bars).

small, and the associated standard error for this change was large, indicating that the prevalence of MI or stroke may not have changed substantially between 1978 and 1991. This may explain our finding that this population is responsible for only a small percentage of the increase in treated end-stage renal disease incidence.

Although the effect of a lower MI and stroke case-fatality rate on treated ESRD incidence was directly analyzed in the current study, the impact of primary prevention of MI and stroke was not. It is possible that the successful efforts aimed at preventing MI and stroke has resulted in a longer life expectancy and, as such, more time at risk for developing ESRD requiring treatment. Unfortunately, the current analysis did not have data available to assess such secondary effects. In contrast, this reasoning seems incongruous with the purported renoprotective effects of statins (19) and certain anti-hyperten-

Table 4. Overall change in treated end-stage renal disease cases in 1991, compared with 1978, and the estimated number of cases resulting from the change in the number of individuals with diabetes mellitus, myocardial infarction and stroke survivors, and the number of people with neither condition

Age Group, yr	Overall Actual Change[a]	Estimated increase (SE) in Treated ESRD Attributed to: Increased Diabetes Mellitus Prevalence[b]	Increased Number of Myocardial Infarction/ Stroke Survivors[c]	Increased Population without Diabetes, Myocardial Infarction or Stroke[d]
30 to 44	4847	1976 (415)	41 (203)	1296 (67)
45 to 54	4153	1044 (665)	169 (168)	237 (23)
55 to 64	7387	2487 (659)	−194 (291)	−216 (17)
65 to 74	12,079	2943 (678)	1024 (493)	598 (36)
75+	8415	1733 (268)	735 (186)	988 (65)
Total[e]	**36,881**	**10,183 (1257)**	**1775 (642)**	**2904 (104)**

[a] Abstracted from the USRDS as number of incident cases of treated ESRD in 1991 minus number of incident cases of treated ESRD in 1978.
[b] Calculated as the product of Column (f) in top third (diabetes section) of Table 3 and column (l) in Table 2.
[c] Calculated as the product of Column (f) in middle third (MI/stroke section) of Table 3 and column (m) in Table 2.
[d] Calculated as the product of Column (f) in bottom third (neither diabetes or MI/stroke section) of Table 3 and column (n) in Table 2.
[e] Totals were calculated as the sum of the age-specific counts and standard errors using Taylor series approximations.

sive medications (20). However, it can be argued that the methodology used in the current study indirectly accounts for increased longevity in the "Neither MI/CVA or diabetes" group.

The results shown in Table 4 provide details of the impact of each of the risk factor investigated stratified by age. The increased prevalence of diabetes accounts for incident ESRD cases within each age group, while the higher number of MI/stroke survivors in 1991 primarily impacts the older age groups, and the increased population size without diabetes or a history of MI/stroke had a substantial impact on both the 30 to 44 yr olds and the ≥ 75 yr old group. Overall, these results appear to make intuitive sense. There was a large increase in diabetes prevalence among all age groups. In contrast, most persons with a history of MI/stroke were older than 65. Finally, the large increase in the US population 30 to 44 yr of age (22.3 million) may explain the increase in cases of ESRD in this age group and the moderate increased size of the US population ≥ 75 yr of age, a population with a high incidence of treated ESRD, explained a substantial proportion of the increase in treated ESRD among persons ≥ 75 yr of age.

The results of the current study should not be interpreted as suggesting that diabetes, MI, and stroke are not important risk factors for treated end-stage renal disease. In contrast, compared with the general population of similar age, as shown in Figure 2, the risk of treated end-stage renal disease is substantially higher among persons with diabetes and a history of MI or stroke. While the majority of the increase in treated end-stage renal disease incidence during the study period examined may not have resulted from an increased prevalence of these conditions, the high end-stage renal disease risk and large number of persons with diabetes, MI, and stroke in the US indicate that the overall impact of these conditions on end-stage renal disease incidence are substantial.

Reasons for a majority of the increase in treated end-stage renal disease incidence remain unresolved. However, broader access to dialysis therapy among persons with renal failure in the US has been reported and may explain a substantial proportion of the higher incidence of treated end-stage renal disease. For example, after initial Medicare entitlement for dialysis therapy, older adults may have had limited access to treatment. In 1978, 30% and 7% of incident treated end-stage renal disease patients were greater than 65 and 75 yr of age, respectively, compared with 50% and 19% in 1991. This secular trend may reflect more liberal access to dialysis therapy for older persons in the US. Furthermore, although 28% of the increase in ESRD was attributable to an increased prevalence of diabetes, the percentage of incident treated ESRD cases with an assigned cause of diabetes increased from 10% to 37%, an absolute increase of $n = 16{,}937$, between 1978 and 1991. Also, approximately 50% of incident ESRD cases in 1991 had diabetes. While the current study concluded that 10,183 of incident ESRD cases in 1991 were due to an increased prevalence of diabetes, less restrictive access to dialysis therapy or more severe diabetes may explain a substantial proportion of the increase in ESRD among persons with diabetes. However, the absence of barriers to end-stage renal disease therapy was noted in 1992, and the incidence of end-stage renal disease is still increasing (13).

Other potential reasons for the increase in ESRD may be higher usage rates of nephrotoxic agents such as analgesic medications. Although environmental exposure to lead at the population level has decreased dramatically, other environmental exposures may be related to the increase in ESRD. Unfortunately, data were not collected to permit the systematic analysis of these risk factors in the investigation of the increase in ESRD. Because the forecasted Medicare expenditures for ESRD are projected to increase to $28.3 billion by 2010, population-level research including the analysis of the USRDS may help better understand the increase in ESRD and avenues for prevention

This study has several strengths. First, it is a systematic study of the increase in treated end-stage renal disease incidence that occurred between 1978 and 1991. Understanding the secular changes that have impacted treated end-stage renal disease incidence is important in both defining the end-stage renal disease epidemic and may also be imperative in end-stage renal disease prevention. Second, the data used in the current study were derived from nationally representative samples of the US population. The second and third National Health and Nutrition Examination Surveys each include interview response from more than 14,000 participants 30 yr of age and older. Data were also used from the United States Renal Data System; a registry containing records for more than 90% of incident treated end-stage renal disease cases. Finally, because many MI and stroke survivors also have diabetes, we repeated all of the analyses using four mutually exclusive categories (a history of MI/stroke only, a history of diabetes mellitus only, a history of both diabetes mellitus and MI/stroke, and none of these factors) for the overall population and by race. Although the standard errors were larger, the results were similar using this alternate approach. Such consistency provides confidence in the robustness of our study results.

Despite the strengths of using national population-level data, there are some limitations to our methodology. First, the data components necessary for the current analysis were only available in 1978 and 1991. As new data become available, analysis of treated end-stage renal disease over a longer time period will be useful. Second, the assessment of co-morbidity differed across the data sets that we used. The United States Renal Data System relied on chart abstraction, and NHANES II and III relied on self-report. Patient recall can be inaccurate even for major events such as MI and stroke (21,22). While the methodology used provides confidence that the NHANES II and III estimates are comparable, using two separate data sources (NHANES and USRDS) may have produced a bias in the calculated incidence rate. Nonetheless, the National Center for Health Statistics surveys provides the best available estimates of morbidity prevalence for the US population. In addition, estimates of the relative risks of treated end-stage renal disease associated with diabetes and MI obtained in the general population using this methodology are similar to previously published relative risks from observational studies (6,8).

Our estimates of the proportion of treated end-stage renal disease attributable to a higher prevalence of diabetes and MI and stroke survival may be conservative because the lack of data on the presence of a history of MI or stroke at the time end-stage renal disease treatment was initiated in 1978. It is quite likely that persons with diabetes or a MI and stroke were less likely to receive end-stage renal disease treatment in 1978 compared with 1991. Therefore, these populations may explain a larger proportion of the increase in the incidence of end-stage renal disease treatment. For example, under the scenario that no MI or stroke survivors initiated end-stage renal disease therapy in 1978, the increase in treated end-stage renal disease attributed to this population would account for 37% (13,786/36,881) of the total increase in treated end-stage renal disease incidence between 1978 and 1991. Applying this scenario to persons with diabetes mellitus, 67% (24,676/36,881) of the increase in treated end-stage renal disease incidence could be attributed to this population. However, such attribution is misleading in that the increase in treated end-stage renal disease incidence could arguably be attributed to broader access to dialysis therapy among persons with co-morbid conditions rather than increased prevalence of these co-morbidities.

Although persons with diabetes, a history of MI, and a history of stroke are at very high risk for treated end-stage renal disease, the current analysis indicates that reasons other than a higher prevalence of diabetes, improved MI and stroke survival, and an increased US population size explain the majority of the increase in treated end-stage renal disease incidence between 1978 and 1991. Given the results of the current study, it remains possible that more liberal access to therapy or greater severity of kidney disease in these populations may explain a majority of the increase in ESRD therapy. Costs for ESRD treatment have increased to over $15 billion and abatement of these costs and the incidence of treatment for ESRD are not expected anytime soon. To stem the tide of rising ESRD incidence and costs, it is first necessary to determine reasons for the increase in treated ESRD. Therefore, the continued study of explanations for the increase in ESRD incidence in the US is necessary.

Appendix

Panel 1

Increase in number of ESRD cases initiating treatment between 1978 and 1991 resulting from increased number of persons with diabetes

= Increase in number of persons with diabetes between 1978 and 1991 (Panel 2) * Incident rate of ESRD treatment among persons with diabetes in 1991 (Panel 3)

Panel 2

Increase in number of persons with diabetes between 1978 and 1991

= Number of persons in US with diabetes in 1991 (estimated from NHANES III) **minus** number of persons in US with diabetes in 1978 (estimated from NHANES II)

Panel 3

Prevalence of diabetes among persons ≥ 75 years of age in 1978

$$\left(1/\left(1+\frac{\sum_{\text{Each age group}}\left(\frac{\text{(Age-specific DM prevalence in 1991 minus 1978)}}{\text{Age-specific diabetes prevalence in 1978}}\right)}{\sum_{\text{Each age group}}(1)}\right)\right) * \text{Diabetes prevalence among} \geq 75 \text{ years of age in 1991}$$

Panel 4

Incident rate of ESRD treatment among persons with diabetes in 1991

$$= \frac{\text{Number of incident cases of treated ESRD with diabetes in the US in 1991 (Panel 4)}}{\text{Number of persons in the US with diabetes in 1991 (estimated from NHANES III)}}$$

Panel 5

Number of incident cases of treated ESRD with diabetes in the US in 1991

= Number of incident treated ESRD cases in 1991 in the United States (abstracted from the United States Renal Data System) * Percentage of incident cases of treated ESRD with diabetes (abstracted from the 1990 Case-Mix Adequacy Study)

Appendix A. Derivation of data elements used in the formula to calculate the increase in number of ESRD cases initiating treatment between 1978 and 1991 resulting from increased number of persons with diabetes. Analogous formulae were used in calculating the increase in treated ESRD cases associated with a history of MI or stroke and none of these conditions.

	Survey	
	NHANES II	NHANES III
Diabetes	Do you have diabetes or sugar diabetes? (and) Did a doctor tell you that you had it?	Have you ever been told by a doctor that you have diabetes or sugar diabetes?
Heart Attack	Has a doctor ever told you that have had any of the following conditions? Heart Attack?	Has a doctor ever told you that you had a heart attack?
Stroke	Have you ever had a stroke? (and) Did a doctor tell you this?	Has a doctor ever told you that you had a stroke?

Appendix B. Second and Third National Health and Nutrition Examination Survey (NHANES II and III, respectively) questions relevant to the current study.

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