Longitudinal Incidence and Prevalence of Adverse Outcomes of Diabetes Mellitus in Elderly Patients

M. Angelyn Bethel, MD; Frank A. Sloan, PhD; Daniel Belsky, BA; Mark N. Feinglos, MD, CM

Background: The natural history of type 2 diabetes mellitus (DM) in the elderly has not been previously described in a national longitudinal sample.

Methods: This national longitudinal analysis (January 1, 1991, to December 31, 2004) examines mortality and morbidity rates in a representative sample of elderly patients newly diagnosed as having DM. Medicare beneficiaries diagnosed as having DM in 1994 (n=33 772) were compared with a control group (n=25 563) regarding death, lower extremity complications, nephropathy, retinopathy, cardiovascular complications, and cerebrovascular complications.

Results: The DM group had excess mortality of 9.2% by year 11 compared with the control group. By 2004, 91.8% of the DM group experienced an adverse complication compared with 72.0% of the control group. The DM group had a higher prevalence and incidence of microvascular and macrovascular complications at all time points compared with controls. Patients with DM were at increased risk for all lower extremity complications, particularly those requiring surgical intervention (gangrene, debridement, and amputation). Cardiovascular complications were a leading cause of morbidity, with 57.6% of the DM group diagnosed as having heart failure compared with 34.1% of the controls.

Conclusion: Elderly persons newly diagnosed as having DM experienced high rates of complications during 10-year follow-up, far in excess of elderly persons without this diagnosis, implying a substantial burden on the individual and on the health care system.

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The Global Incidence of type 2 diabetes mellitus (DM) continues to grow at an alarming rate. Current projections estimate that the number of people with DM will increase by 50.0% by 2010 and will nearly double by 2025. Although increasing age is a risk factor for the development of DM and for the development and progression of the microvascular and macrovascular complications of DM, little is known about the impact of DM in elderly populations. We used a nationally representative cohort of Medicare beneficiaries newly diagnosed as having DM to examine the incidence and prevalence of diabetic complications in those older than 65 years during an 11-year period.

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Methods

DATA

We conducted a national longitudinal study of US elderly persons diagnosed as having DM using a 5% sample of Medicare claims data and denominator files providing information on age, race/ethnicity, sex, and dates of death on the same individuals. These claims data, covering calendar years 1991 to 2004, came from inpatient, outpatient, Medicare Part B, and durable medical equipment files obtained from the Centers for Medicare and Medicaid Services. Medicare Part B claims did not include diagnostic information before 1991. The claims data contained dates of service, diagnosis (International Classification of Diseases, Ninth Revision, Clinical Modification), and procedures (Current Procedural Terminology). Healthcare Common Procedure Coding System codes were used in part to identify beneficiaries with low vision or blindness and end-stage renal disease (ESRD).

Sample Selection Process

Individuals were classified as having been diagnosed as having DM if they had at least 2 Medicare Part B claims or at least 1 inpatient claim that included a DM diagnosis code (International Classification of Diseases, Ninth Revision, Clinical Modification) and procedures (Current Procedural Terminology). We identified newly diagnosed cases of DM in 1994 by starting with 324,479 individuals with a diagnosis of DM in 1994 and excluding 278,107 persons with...
a diagnosis of DM before January 1, 1994 (Figure 1). The sample was further limited to beneficiaries 65 years or older at least 6 months before their first DM diagnosis in 1994 and not older than 95 years by December 31, 1994. These restrictions eliminated 11,551 persons. Finally, individuals who did not survive through July 1, 1994, and those who spent more than 6 months of 1994 in a Medicare risk plan (health maintenance organization) were excluded, leaving an analysis sample of 33,772 persons with incipient DM in 1994 (DM group).

To account for the fact that persons not diagnosed as having DM in 1994 could experience many of the same adverse health outcomes commonly associated with DM, we selected control groups (Figure 1). The first control group was created from a random sample of 75,000 persons with diagnoses associated with lower extremity adverse outcomes for each year, 1994 to 2004. For ease of presentation, only results for even-numbered years are given in the tables. To be included in the analysis in any given year the beneficiary had to be alive and not enrolled in a Medicare risk plan for 6 months or more during the year.

A Kaplan-Meier analysis using a statistical software program (SAS 9.0; SAS Institute Inc, Cary, NC) plotted the survival curves of beneficiaries in the DM group, control group 1, and death restrictions excluded an additional 7,388 persons.

Table 1. Diagnoses and Outcomes Used to Identify Complications of Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Complications and Outcomes</th>
<th>ICD-9-CM and CPT Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic eye disease</td>
<td>369.xx, V26.00, V26.10, V26.15, 92392</td>
</tr>
<tr>
<td>Low vision or blindness*</td>
<td>369.xx, V26.00, V26.10, V26.15, 92392</td>
</tr>
<tr>
<td>Lower extremity complications</td>
<td>040.0, 250.7, 440.24, 785.4</td>
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<td>Gangrene</td>
<td>86.28, 11000, 11011, 11040-11042</td>
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<tr>
<td>Debridement</td>
<td>84.1x, 27290, 27295, 27590-27592, 27594-27596, 27598, 27880-27882, 27884, 27886, 27888, 28800, 28805, 28810, 28820, 28825</td>
</tr>
<tr>
<td>Amputation</td>
<td>402.91, 404.01, 404.11, 404.91</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>585, 586, 404.12, 404.13, 404.92, 404.93, 403.01, 403.11, 403.91</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>50340, 50360, 50365, V40.0, V56.0, V56.1, 39.27, 39.42, 39.43, 39.49, 39.50, 39.53, 39.93, 39.94, 90940, 90993, 90997, 90999, 93990</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>410.x, 412.x</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>428.0, 428.1, 428.9, 428.2x, 428.3x, 428.4x, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>585, 586, 404.12, 404.13, 404.92, 404.93, 403.01, 403.11, 403.91</td>
</tr>
<tr>
<td>Stroke</td>
<td>430.x-432.x, 436.x</td>
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</tbody>
</table>

*Low vision was identified using codes for medical devices such as magnifiers and high-magnification eyeglasses. Blindness was identified from the diagnosis codes shown.

OUTCOMES CLASSIFICATION

We selected adverse outcomes commonly, although not exclusively, associated with a diagnosis of DM using International Classification of Diseases, Ninth Revision, Clinical Modification, and Current Procedural Terminology codes in the claims data. We focused on myocardial infarction, congestive heart failure (CHF), stroke, chronic renal failure, ESRD, low vision or blindness, gangrene, debridement, and amputation (Table 1). Low vision was identified using codes for medical devices such as magnifiers and high-magnification eyeglasses. Blindness was identified using diagnosis codes. We also examined a variety of diagnoses associated with lower extremity adverse outcomes of DM.

ANALYSIS

We computed annual rates of incidence and prevalence of adverse outcomes for each year, 1994 to 2004. For ease of presentation, only results for even-numbered years are given in the tables. To be included in the analysis in any given year the beneficiary had to be alive and not enrolled in a Medicare risk plan for 6 months or more during the year.
and control group 2 though December 31, 2004. The survival analysis did not censor for enrollment in a Medicare risk plan. Unlike the claims files, which contained only information for persons not in risk plans, the denominator file contained information on all beneficiaries. Adverse outcomes were considered incident at the first service date at which the diagnosis or procedure first appeared, and they remained prevalent until death or to December 31, 2004. Because many beneficiaries died before the end of the observational period, we also computed rates of adverse outcomes for persons alive in 2004 or who died before 2004 and had the adverse outcome before death (cumulative incidence).

We used SAS 9.0 to perform a logit regression to determine the statistical significance of trends in incidence and prevalence and whether the trends differed for persons diagnosed as having DM. Explanatory variables were DM status (0-1), time trend (1-11 for analysis of prevalence; 1-10 for analysis of incidence), and an interaction term of the time trend and DM status. We used dates from 1994 to 2004 to compute trends in prevalence; however, because adverse outcomes sometimes occurred before DM was diagnosed, the analysis of trends in incidence excluded 1994.

Overall, demographic characteristics were similar among the 3 groups (Table 2). Age in control group 1 (mean, 75.1 years) was slightly higher than that in the DM group (mean, 74.4 years). Age in control group 2 was within 1 year of the mean age in the other 2 samples. Almost 60% of the patients in all the groups were women. Among persons with newly diagnosed DM in 1994, 11.4% were black. In control groups 1 and 2, 10.9% and 10.0% were black, respectively. Persons of Asian and Latino origin composed 2.2% or less of the 3 samples.

As expected in an elderly population, there was substantial attrition due to death in all the groups (Figure 2). However, Medicare beneficiaries in the DM group had excess mortality of 9.2% by 2004 relative to control group 2 (P<.001) and 11.8% relative to control group 1 (P<.001).

Being newly diagnosed as having DM translated into a loss of life expectancy of slightly more than 2 years.

Patterns of adverse outcomes differed substantially between patients with newly diagnosed DM in 1994 and the 2 control groups. Because patterns of events for both control groups were not significantly different, results for control group 1 will no longer be presented and control group 2 will be redefined as “the control group.”

All trends in prevalence for the diabetic and nondiabetic cohorts were statistically significant at P<.001 (Table 3). More than half the patients in the DM group experienced at least 1 adverse outcome in the first year. Approximately one quarter of the control group had an adverse outcome in 1994. After 10 years of follow-up, among those who survived to December 31, 2004, 7 of 10 persons in the DM group experienced an adverse outcome compared with 4 of 10 in the control group. Considering those who died and those who survived (cumulative incidence), 92% of the DM group experienced an adverse outcome compared with 72% of the control group.

The highest rates of complications in the DM and control groups were for the lower extremities (835 and 592 per 1000, respectively) (Table 3). This 11-year prevalence was driven primarily by high rates of pain in the feet, claudication, and cellulitis. Nearly half of the DM group (cumulative incidence) experienced pain in the feet compared with approximately a third of the control group; claudication occurred in 35% of the DM group vs approximately 19% of the control group. Cellulitis was diagnosed in 30% of the DM group compared with 19% of the control group. Differences were most apparent for the more severe adverse outcomes, typically requiring surgical intervention. Gangrene occurred in 19% of the DM group and in just more than 1% of the control group. As a result, amputation was also rare in the control group (3% in the DM group and 0.5% in the control group).
The second most prevalent complications were for cardiovascular disease, affecting nearly 7 of 10 persons in the DM group compared with 4 of 10 in the control group. The major contributor to cardiovascular complications was CHF, with 58% of persons in the DM group being diagnosed as having CHF by 2004 or before death compared with 34% of the controls. Of persons still alive in the DM group in 2004, 51% were diagnosed as having CHF, almost double the rate in the controls (28%). Almost half of the DM group experienced a cerebrovascular outcome vs 3 of 10 persons in the control group.

Nephropathy and retinopathy complications were less common than cardiovascular complications. However, the prevalence of nephropathy increased markedly from 1994 in the DM group by a factor of 6 for those who survived and by almost a factor of 5 when considering survivors and decedents (cumulative incidence). The increase in prevalence was driven primarily by chronic renal failure. The increase in the prevalence of retinopathy complications in the DM group was similar to that of nephropathy. By the end of the study, 5% to 6% of persons in the DM group had low vision or blindness.

**Table 3. Prevalence of Complications, 1994-2004**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
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<tbody>
<tr>
<td>Any adverse outcome†</td>
<td>535</td>
<td>544</td>
<td>605</td>
<td>642</td>
<td>685</td>
<td>706</td>
<td>918</td>
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<tr>
<td>Cardiovascular</td>
<td>296</td>
<td>423</td>
<td>516</td>
<td>575</td>
<td>617</td>
<td>655</td>
<td>679</td>
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<tr>
<td>Myocardial infarction</td>
<td>73</td>
<td>127</td>
<td>175</td>
<td>212</td>
<td>241</td>
<td>266</td>
<td>265</td>
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<tr>
<td>Congestive heart failure</td>
<td>216</td>
<td>306</td>
<td>383</td>
<td>435</td>
<td>472</td>
<td>511</td>
<td>576</td>
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<tr>
<td>Cerebrovascular</td>
<td>131</td>
<td>232</td>
<td>312</td>
<td>378</td>
<td>437</td>
<td>488</td>
<td>463</td>
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<tr>
<td>Stroke</td>
<td>88</td>
<td>143</td>
<td>191</td>
<td>226</td>
<td>253</td>
<td>279</td>
<td>313</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>54</td>
<td>92</td>
<td>143</td>
<td>196</td>
<td>253</td>
<td>308</td>
<td>284</td>
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<tr>
<td>Chronic renal failure</td>
<td>41</td>
<td>60</td>
<td>88</td>
<td>119</td>
<td>160</td>
<td>201</td>
<td>212</td>
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<td>ESRD</td>
<td>12</td>
<td>16</td>
<td>24</td>
<td>31</td>
<td>38</td>
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<tr>
<td>Diabetic retinopathy</td>
<td>47</td>
<td>107</td>
<td>163</td>
<td>214</td>
<td>261</td>
<td>312</td>
<td>220</td>
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<tr>
<td>Low vision or blindness</td>
<td>9</td>
<td>22</td>
<td>33</td>
<td>43</td>
<td>52</td>
<td>64</td>
<td>53</td>
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<tr>
<td>LECs</td>
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<td>472</td>
<td>612</td>
<td>710</td>
<td>778</td>
<td>835</td>
<td>728</td>
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<tr>
<td>LEC neuropathy§</td>
<td>49</td>
<td>113</td>
<td>174</td>
<td>233</td>
<td>291</td>
<td>349</td>
<td>253</td>
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<tr>
<td>Claudication</td>
<td>89</td>
<td>168</td>
<td>236</td>
<td>294</td>
<td>340</td>
<td>390</td>
<td>350</td>
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<tr>
<td>Pain in feet</td>
<td>88</td>
<td>213</td>
<td>330</td>
<td>444</td>
<td>535</td>
<td>617</td>
<td>466</td>
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<tr>
<td>Cellulitis</td>
<td>67</td>
<td>144</td>
<td>209</td>
<td>268</td>
<td>313</td>
<td>365</td>
<td>305</td>
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<tr>
<td>Ulcer</td>
<td>43</td>
<td>82</td>
<td>116</td>
<td>148</td>
<td>177</td>
<td>207</td>
<td>200</td>
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<tr>
<td>Gangrene</td>
<td>39</td>
<td>75</td>
<td>111</td>
<td>143</td>
<td>174</td>
<td>207</td>
<td>188</td>
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<tr>
<td>Debridement</td>
<td>35</td>
<td>68</td>
<td>96</td>
<td>123</td>
<td>145</td>
<td>167</td>
<td>155</td>
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<tr>
<td>Amputation</td>
<td>7</td>
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<td>16</td>
<td>18</td>
<td>22</td>
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<td>33</td>
</tr>
<tr>
<td>Sample, No.</td>
<td>33 772</td>
<td>27 543</td>
<td>22 338</td>
<td>18 604</td>
<td>16 085</td>
<td>13 305</td>
<td>33 772</td>
</tr>
</tbody>
</table>

Abbreviations: DM, type 2 diabetes mellitus; ESRD, end-stage renal disease; LEC, lower extremity complication.

*Prevalence rates per 1000 persons. Complications with prevalence rates less than 10 per 1000 persons in 2004 are not listed.
†First Diagnosed as Having DM in 1994
‡Includes a person only once if that individual has had any study complication in a given year.
§Includes mononeuropathy, polyneuropathy, and other diabetic complications with neurologic manifestations.

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vision or blindness vs approximately 4% in the control group.

The incidence of most adverse outcomes was much higher in the group with DM from the time of diagnosis through 10-year follow-up (1995-2004) (Figure 3). For example, the logit regression shows that the incidence of stroke was 62% higher ($P = .003$), of CHF was 65% higher ($P < .001$), of amputation was approximately 300% higher ($P < .001$), and of gangrene was 900% higher in the DM group than in controls (data not shown).

Trends in the incidence remained fairly stable during follow-up. Incidences of low vision or blindness, debridement, and amputation exhibited no statistically significant trend in either the DM group or the control group. There were significant increases in the incidence of chronic renal failure ($P < .001$) and ESRD ($P = .02$) between 1995 and 2004 but at the same rates in both groups. The incidence of gangrene increased in the DM group ($P < .001$) but decreased in the control group ($P = .001$). The incidences of myocardial infarction ($P < .001$) and stroke decreased ($P = .003$), and both groups decreased at the same rate. For heart failure, there was decreased incidence in both groups ($P < .001$), but the incidence in the DM group decreased more ($P < .001$).

**COMMENT**

This study provides the first nationally representative, decade-long examination of morbidity and mortality in elderly persons with newly diagnosed DM. Those diagnosed as having DM had substantially higher morbidity and mortality rates than controls. Increased cardiovascular and renal morbidity rates in patients with DM have
been well documented,\textsuperscript{3-5} but less information is available for other complications.\textsuperscript{6}

Although we began with 2 race/ethnicity–matched control samples, one including those without DM claims in 1994 and a second without DM claims for the duration of follow-up, we focus on the control group never developing DM for 2 reasons. First, the diagnostic criteria for DM changed in 1997,\textsuperscript{7} resulting in a lower threshold defining fasting hyperglycemia. Owing to this change, more individuals were diagnosed,\textsuperscript{8} and those diagnosed after 1997 were likely to be earlier in the course of their disease.\textsuperscript{9} Consequently, the control group without DM in 1994 plausibly included a different mix of individuals before and after 1997. Second, 24% of the initial control sample without DM in 1994 had documented DM by 2004, plausibly increasing the rates of adverse outcomes in this group.

The increased mortality risk during 10-year follow-up of the DM group is modest relative to the 2-fold increase attributed to DM reported elsewhere.\textsuperscript{10-12} Mortality risk for persons in the DM group increased with disease duration. Because the DM group consists of persons newly diagnosed, they are probably at an early stage in the disease process. Therefore, the differential in mortality rates was plausibly smaller than that seen in other studies. In addition, previous studies did not control for age. Persons with DM are often older than nondiabetic individuals drawn from the same population.\textsuperscript{6,13,14} In the present study, newly diagnosed persons were 8 months younger than controls, potentially moderating the effect of DM on mortality.

Cardiovascular and cerebrovascular disease are major causes of morbidity in the DM group. Previous data have established that DM is a cardiovascular disease risk equivalent,\textsuperscript{15} and patients with DM have higher rates of CHF, myocardial infarction, and stroke. The present data confirm an excess cardiovascular risk in the DM group; however, neither cardiovascular nor cerebrovascular incidence decreases appreciably after time of diagnosis. In fact, the incidences of chronic renal failure, ESRD, and gangrene increase. With 1 cohort it is not possible to determine whether the trends observed for these complications imply that preventive measures are not used or are ineffective or whether the methods for detecting disease have improved, resulting in an apparent increase in incidence across time. However, it is known that for patients with DM in the United States, fewer than 7% meet the treatment goals for lipids, blood pressure, and glycated hemoglobin.\textsuperscript{16,17}

The morbidity related to lower extremity complications in this cohort is substantial and occurred in those with and without DM. Fifty-two percent of the sample never diagnosed as having DM had lower extremity complications in the base year or during follow-up compared with 73% of the DM cohort. Although usually not fatal, lower extremity complications are chronic and debilitating and are likely to result in substantial long-term use of medical resources. The most common causes of morbidity in both groups were pain in the feet (which might also include pain related to arthritis or another nonvascular etiology), claudication, and cellulitis. Gangrene was also common among those with DM, but not in the control group. Although rates of amputation were low in both groups, the cumulative incidence was 7 times higher in the DM group.

Gregg et al\textsuperscript{6} examined the prevalence of lower extremity disease in the 1999-2000 National Health and Nutrition Examination Survey population. The mean age of that population was 57 years, and 10% reported having DM. Among those with DM, the prevalence of any lower extremity disease was 30.2%, approximately twice that in the population without DM (17.6%). The present data, derived from a cohort nearly 20 years older, reveal a larger burden of disease.

Bertoni et al\textsuperscript{13} also demonstrated that lower extremity complications, including gangrene, amputation, and lower extremity infection (cellulitis and lymphangitis), caused significant morbidity among patients with DM in a 5% sample of Medicare for 1994 to 1996. The present analysis extends both observations across 10 years of follow-up: nearly 30% of the DM group had cellulitis compared with 19% of the control population. However, amputation occurred in only 3.5% of the present population, a much smaller proportion than that seen by Bertoni et al.\textsuperscript{13}

The present study has several strengths. It examines a large, nationally representative sample of elderly patients. The data set allowed us to define temporal variations in incidence for 10 years after the base year and prevalence across an 11-year period. The design includes a method shown to identify persons with DM in Medicare claims data sets with a sensitivity of 63% and a specificity of 98%.\textsuperscript{18} We account for the time of exposure to DM by including only those diabetic patients first diagnosed in 1994, allowing us to track the early effects of the disease on morbidity and mortality rates.

We acknowledge several study limitations. First, the incipient cohort follows individuals with DM only from their first diagnosis. We cannot ascertain actual onset of disease. Similarly, the diagnosis of DM may create an ascertainment bias for the adverse outcomes measured in this study: once DM is present, surveillance for known macrovascular and microvascular complications increases, perhaps causing patients with DM to be diagnosed more frequently and possibly earlier in the course of disease.

Second, this analysis excluded individuals enrolled in health maintenance organizations for more than 6 months of a given year from that year’s data. As a result, we eliminated 2% to 12% of the sample each year. Individuals may enter and leave health maintenance organizations for reasons related to their health, affecting the composition of the sample.

Third, claims data tend to be less accurate than clinical reports in identifying patients with specific conditions. Although the use of claims data for billing purposes theoretically leads to a tendency to overdiagnose, some studies suggest that underdiagnosis may be more common.\textsuperscript{19,20}

Between 1994 and 2004 there was an enhanced emphasis on earlier diagnosis and treatment of DM, and thresholds for glucose, lipid, and blood pressure control have been lowered, all in an effort to further reduce the incidence of complications. The present findings demonstrate that for several complications, including myocardial infarction, CHF, and stroke, the incidence decreased after the date of diagnosis of DM. However, for
other important complications, in particular chronic renal failure and ESRD, the incidence increased. Although the present data provide no insight into the cause of these patterns, the burden of DM complications, on the individual and on the health care system, is enormous. Continued longitudinal surveillance may define whether the increasing emphasis on prevention and improved treatment options will provide reductions in morbidity and mortality in the ever-growing population of elderly patients with DM.

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REFERENCES