Assessing Potential Glycemic Overtreatment in Persons at Hypoglycemic Risk

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IMPORTANCE Although serious hypoglycemia is a common adverse drug event in ambulatory care, current performance measures do not assess potential overtreatment.

OBJECTIVE To identify high-risk patients who had evidence of intensive glycemic management and thus were at risk for serious hypoglycemia.

DESIGN, SETTING, AND PARTICIPANTS Cross-sectional study of patients in the Veterans Health Administration receiving insulin and/or sulfonylureas in 2009.

MAIN OUTCOMES AND MEASURES Intensive control was defined as the last hemoglobin A1c (HbA1c) measured in 2009 that was less than 6.0%, less than 6.5%, or less than 7.0%. The primary outcome measure was an HbA1c less than 7.0% in patients who were aged 75 years or older who had a serum creatinine value greater than 2.0 mg/dL or had a diagnosis of cognitive impairment or dementia. We also assessed the rates in patients with other significant medical, neurologic, or mental comorbid illness. Variation in rates of possible glycemic overtreatment was evaluated among 139 Veterans Health Administration facilities grouped within 21 Veteran Integrated Service Networks.

RESULTS There were 652,378 patients who received insulin and/or a sulfonylurea with an HbA1c test result. Fifty percent received sulfonylurea therapy without insulin; the remainder received insulin therapy. We identified 205,857 patients (31.5%) as the denominator for the primary outcome measure; 11.3% had a last HbA1c value less than 6.0%, 28.6% less than 6.5%, and 50.0% less than 7.0%. Variation in rates by Veterans Integrated Service Network facility ranged 8.5% to 14.3%, 24.7% to 32.7%, and 46.2% to 53.4% for HbA1c less than 6.0%, less than 6.5%, and less than 7.0%, respectively. The magnitude of variation by facility was larger, with overtreatment rates ranging from 6.1% to 23.0%, 20.4% to 45.9%, and 39.7% to 65.0% for HbA1c less than 6.0%, less than 6.5%, and less than 7.0%, respectively. The maximum rate was nearly 4-fold compared with the minimum rates for HbA1c less than 6.0%, followed by 2.25-fold for HbA1c less than 6.5% and less than 2-fold for HbA1c less than 7.0%. When comorbid conditions were included, 430,178 patients (65.9%) were identified as high risk. Rates of overtreatment were 10.1% for HbA1c less than 6.0%, 25.2% for less than 6.5%, and 44.3% for less than 7.0%.

CONCLUSIONS AND RELEVANCE Patients with risk factors for serious hypoglycemia represent a large subset of individuals receiving hypoglycemic agents; approximately one-half had evidence of intensive treatment. A patient safety indicator derived from administrative data can identify high-risk patients for whom reevaluation of glycemic management may be appropriate, consistent with meaningful use criteria for electronic medical records.
Serious hypoglycemia, defined as requiring third-party assistance, is increasingly becoming recognized as a national public health issue that potentially affects the quality of life for millions of persons with diabetes mellitus. Among persons aged 65 years or older, hypoglycemic agents (sulfonylureas and insulin) are the second most common medications associated with emergency department visits or hospitalizations and adverse drug events reported to the US Food and Drug Administration, closely following warfarin. However, reliance on measurement of emergency department or hospital admissions or voluntary reporting underestimates overall adverse drug event frequency. These limitations notwithstanding, several such studies suggest that the problem may be increasing.

Approximately 75% of adverse drug events are managed in an ambulatory care setting. The annual rates of hypoglycemia requiring third-party assistance in the home or workplace among persons with diabetes who are receiving hypoglycemic agents are not known, although these rates have been reported to be as high as 59% for persons receiving insulin in a large health maintenance organization based on survey results. Such events are associated with depression and decreased quality of life as well as concerns such as daily debilitating worry and withdrawal from driving, exercise, sex, and going outside of the home to avoid hypoglycemia and its consequences. Moreover, based on post hoc analyses of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) and Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trials, serious hypoglycemia is also strongly associated with an increased risk of cardiovascular events, even in the absence of emergency department visits and hospitalization.

These studies have led to a consensus among major American and European diabetes professional societies to recommend individualized target goals for persons with diabetes who are older or who have significant acute or chronic medical, neurologic, or mental comorbid conditions that put them at higher risk for hypoglycemia. These recommendations are consistent with long-standing recommendations from the American Geriatrics Society and the Veterans Affairs–Department of Defense.

The Institute of Medicine has long proposed that prevention of adverse drug events should be a national patient safety goal. However, there are no quality measures available that address prevention of hypoglycemia in ambulatory care settings. Although the cause of hypoglycemic events is often behavioral and preventable, rates of serious hypoglycemia are markedly higher in individuals receiving intensive glycemic control. A previously proposed quality improvement measure assesses possible overtreatment resulting from intentional or unintentional tight glycemic control in persons with diabetes with risk factors such as age and/or comorbid conditions. Such a measure could be used by health care systems or physician practices for clinical decision support, surveillance, or quality improvement. Taking advantage of the national integrated electronic health record system of the Veterans Health Administration (VHA), our objective in this study was to evaluate the rates of intensive glycemic control as a signal of potential overtreatment by age and comorbidity status, as well as variation at different organizational levels of the VHA.

Methods

Study Population

This study was approved by the Department of Veteran Affairs (VA)–New Jersey Health Care System Institutional Review Board. There was waiver of informed consent.

Diabetes mellitus was defined based on 2 or more International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for diabetes mellitus (250.xx,) associated with clinical face-to-face outpatient care on separate calendar days or any diabetes mellitus–specific medication prescription (insulin, sulfonylurea, biguanide, α-glucosidase inhibitor, meglitinide, or thiazolidinedione). Data sources included the VHA National Patient Clinical Data Set (Austin, Texas; to obtain ICD-9-CM and diagnostic codes) and the Decision Support System (to obtain laboratory data and medication information). To approximate National Committee of Quality Assurance criteria for continuous enrollment, individuals with diabetes mellitus were eligible for the study if they had received care within the VHA health care system in fiscal year (FY) 2009 (October 1, 2008, to September 30, 2009). Because veterans may obtain care from more than one facility, we determined a patient’s parent facility based on where they received most of their ambulatory care. Multiple facilities are administered by regional Veterans Integrated Service Networks (VISNs).

The study population included veteran patients receiving insulin and/or a sulfonylurea who had at least 1 hemoglobin A1c (HbA1c) value documented in FY 2009. For our primary outcome measure, we identified the study population as having at least 1 of the following additional criteria: age 75 years or older, last serum creatinine measurement greater than 2.0 mg/dL (to convert to micromoles per liter, multiply by 88.4), or an ICD-9-CM diagnosis of cognitive impairment or dementia in ambulatory care. From a population health perspective, individuals aged 75 years or older have limited life expectancy and an increased comorbid illness burden and thus have decreased lifetime benefit and increased risk associated with intensive glycemic control. Impaired renal function affects the metabolism of oral hypoglycemic agents and insulin. In the ACCORD trial, participants with serum creatinine levels between 1.0 and 1.3 mg/dL had greater risk of serious hypoglycemia than did those with normal creatinine levels (<1.0 mg/dL); participants with creatinine level greater than 1.3 mg/dL had an even higher risk. To be conservative, we restricted our measure to even worse renal function. As a sensitivity analysis, we evaluated patients older than 70 years or those with a serum creatinine level of 1.7 mg/dL or greater. Cognitive impairment may adversely affect patients’ ability to self-manage their diabetes and was associated with increased risk of serious hypoglycemia in both the control and intensive treatment arms of the ACCORD trial.
As a secondary analysis, we identified individuals with advanced complications of diabetes, limited life expectancy, cardiovascular or ischemic vascular disease, and major medical, neurologic, and mental health conditions that would decrease benefit or increase risk of tight control using previously developed ICD-9-CM taxonomies (Supplement [eTable 1]). We used one ICD-9-CM code for each condition, consistent with industry standards for glycemic control measures. We defined potential overtreatment in these patients based on their last HbA1c value in FY 2009, again consistent with industry standards, using 3 different thresholds (<7.0%, <6.5%, and <6.0%); to convert to a proportion of total Hb, multiply by 0.01), which reflect increasingly tight glycemic control.

Statistical Analysis
We calculated the overall rates of overtreatment (HbA1c <6.0%, <6.5%, and <7.0%) for the primary and additional high-risk subpopulations. As a sensitivity analysis, we also assessed the incremental increase in the overtreatment rate by including HbA1c values of 7.0% to 7.4%, which would be within the 95% confidence range of a 6.9% HbA1c value from a high-quality clinical laboratory. We evaluated the variation of rates at the VISN and facility levels.

Identification of Positive Deviants
Positive deviants are defined as high-performing facilities (ie, low overtreatment rates in lower-performing environments [VISNs]). In this study, we used the following strategy for each HbA1c threshold. First, we compared the rate of an individual facility with the VISN average (excluding that facility) to identify potential positive deviants (statistical outliers) for each of the 21 VISNs using a statistical test recommended by the National Committee of Quality Assurance. We constructed a 99% CI for the rate difference between a facility and its corresponding VISN using the following formula:

\[
(\text{Facility Rate} - \text{VISN Rate}) \pm 2.576 \times \sqrt{\left(\frac{\text{Facility standard error}}{\text{VISN rate}}\right)^2 + \left(\frac{\text{VISN standard error}}{\text{VISN rate}}\right)^2},
\]

in which the VISN Rate is the average rate in a VISN minus the comparison facility, and Facility and VISN are the standard errors for the VISN and facility rates, respectively. Thus, 99% CIs for each of the 139 facilities were calculated at each of the 3 HbA1c thresholds. Facilities with 99% CIs not containing zero were statistical outliers: potential positive deviants (the facility rate being lower than the VISN rate) or potential negative deviants (the facility rate being greater than the VISN rate).

Second, we graphed a scatterplot of facilities based on their 5 values (VISN Rate – Facility Rate) and outlier status. Among the statistical positive outliers, we identified the most extreme outliers based on their proximity to less extreme outliers. These were considered positive deviants, recognizing that the threshold for choosing is arbitrary.

Results
We identified 1 104 230 patients with diabetes, which constituted approximately 20.0% of the total VHA patients in FY 2009. We then identified 652 378 patients who received a sulfonylurea and/or insulin during the year and had an HbA1c value determined during that year. The characteristics of the study population are reported in Table 1; approximately half were taking sulfonylureas alone and approximately half were taking insulin with or without sulfonylureas. Among patients younger than 55 years and those aged 75 years or older, serum creatinine values of 2.0 mg/dL or greater were present in 3.6% and 9.2%, respectively; for the same age groups, 5.2% and 17.7% of individuals, respectively, had a serum creatinine value of 1.7 mg/dL or greater. Cognitive impairment or dementia was present in 2.7% and 14.6% of these participants, and cardiovascular disease was identified in 15.8% and 48.4%. The overall rate of HbA1c less than 7.0% was 41.6%, with a range from 29.6% among individuals younger than 55 years to 51.2% for those aged 75 years or older. Patients meeting 2 or more criteria for high risk had a slightly higher (3%-5%) rate at each threshold compared with those with only 1 condition for high risk (data not shown).

As presented in Table 2, 205 857 patients of the study population (31.5%) were 75 years or older, had a serum creatinine value of 2.0 mg/dL or greater, or had a diagnosis of cognitive impairment or dementia (group A). The addition of advanced diabetes complications, diminished life expectancy, and major neurologic disorders increased the proportion of high-risk patients to 42.9% (group D); the inclusion of cardiovascular disease, ischemic vascular disease increased the proportion to 60.6% (group E). When mental conditions or substance abuse were included, 430 178 patients (65.9%) were considered as high risk (group G). In the sensitivity analysis with more inclusive criteria of age and serum creatinine (age >70 years and serum creatinine ≥1.7 mg/dL), we identified an additional 79 619 patients (12.2% of the study population) compared with those in group A, resulting in 285 476 patients (43.7% of the study population), and an additional 33 170 patients (5.1% of the study population) compared with those in group A, resulting in 463 348 patients (71.0% of the study population), respectively (data not shown).

Potential overtreatment rates, also reported in Table 2, were 11.3%, 28.6%, and 50.0% for the thresholds of HbA1c less than 6.0%, less than 6.5%, and less than 7.0%, respectively, for our primary denominator. We observed similar rates in the subpopulations added with additional inclusion criteria as well as in our sensitivity analysis using lower age and serum creatinine levels (data not shown). An additional 18.1% of individuals had HbA1c values between 7.0% and 7.4%.

Figure 1 shows that rates by VISN ranged from 8.5% to 14.3%, 24.7% to 32.7%, and 46.2% to 53.4% for HbA1c less than 6.0%, less than 6.5%, and less than 7.0%, respectively. Figure 2 shows variation by individual facility stratified by VISN. The magnitude of variation by facility was larger, with overtreatment rates for Hba1c ranging from 6.1% to 23.0%, 20.4% to 45.9%, and 39.7% to 65.0% for HbA1c less than 6.0%, less than 6.5%, and less than 7.0%, respectively (Figure 2). The maximum rate was nearly 4-fold that of the minimum rates for HbA1c less than 6.0%, followed by 2.25-fold for HbA1c less than 6.5% and less than 2-fold for HbA1c less than 7.0%.
Table 1. Characteristics of the Study Population*

<table>
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<tr>
<th>Characteristic</th>
<th>Study Population</th>
<th>&lt;55</th>
<th>55-64</th>
<th>65-74</th>
<th>≥75</th>
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<tr>
<td>Overall No. (%)</td>
<td>652 738 (100)</td>
<td>77 192</td>
<td>237 360</td>
<td>162 798</td>
<td>175 388</td>
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<td>Age, mean (SD), y</td>
<td>66.55 (11.00)</td>
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<td>60.27</td>
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<td>Sex</td>
<td>17 046 (2.6)</td>
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<td>Antiglycemic agents</td>
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<td>Sulfonylureas only</td>
<td>329 917 (50.5)</td>
<td>33 067</td>
<td>11 062</td>
<td>82 819</td>
<td>103 408</td>
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<td>114 604 (17.6)</td>
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<td>47 883</td>
<td>28 534</td>
<td>23 618</td>
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<td>Insulin only</td>
<td>208 217 (31.9)</td>
<td>29 556</td>
<td>78 854</td>
<td>51 445</td>
<td>48 362</td>
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<td>Serum creatinine available, mg/dL</td>
<td>581 533 (89.1)</td>
<td>68 812</td>
<td>213 284</td>
<td>144 900</td>
<td>154 537</td>
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<td>1.7-1.9</td>
<td>32 366 (5.0)</td>
<td>12 546</td>
<td>74 19 (3.1)</td>
<td>8725 (5.4)</td>
<td>14 968 (8.5)</td>
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<tr>
<td>2.0-2.4</td>
<td>19 016 (2.9)</td>
<td>77 100</td>
<td>44 700</td>
<td>49 700</td>
<td>8790</td>
</tr>
<tr>
<td>2.5-2.9</td>
<td>68 02 (1.0)</td>
<td>36 40</td>
<td>180 80</td>
<td>177 70</td>
<td>2855</td>
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<tr>
<td>≥3.0</td>
<td>16 777 (2.6)</td>
<td>16 41</td>
<td>62 0 0</td>
<td>44 08</td>
<td>4528</td>
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<td>Comorbidities</td>
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<tr>
<td>Diminished life expectancy</td>
<td>71 097 (10.9)</td>
<td>2947</td>
<td>20 060</td>
<td>20 603</td>
<td>27 487</td>
</tr>
<tr>
<td>End-stage hepatic disease</td>
<td>2890 (0.4)</td>
<td>486</td>
<td>1675</td>
<td>503</td>
<td>224</td>
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<tr>
<td>Cancer</td>
<td>68 682 (10.5)</td>
<td>2512</td>
<td>18 637</td>
<td>20 213</td>
<td>27 320</td>
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<td>Advanced diabetic complications</td>
<td>50 852 (7.8)</td>
<td>3858</td>
<td>16 856</td>
<td>13 780</td>
<td>16 358</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>205 92 (3.0)</td>
<td>243</td>
<td>958</td>
<td>500</td>
<td>358</td>
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<tr>
<td>Amputation</td>
<td>865 (0.1)</td>
<td>113</td>
<td>390</td>
<td>228</td>
<td>134</td>
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<tr>
<td>Advanced retinopathy</td>
<td>48 733 (7.5)</td>
<td>3610</td>
<td>15 899</td>
<td>13 259</td>
<td>15 967</td>
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<tr>
<td>Major neurologic conditions</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Cognitive impairment</td>
<td>23 879 (3.7)</td>
<td>1609</td>
<td>6658</td>
<td>5668</td>
<td>9944</td>
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<tr>
<td>Dementia</td>
<td>23 692 (3.6)</td>
<td>422</td>
<td>3006</td>
<td>4662</td>
<td>15 602</td>
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<tr>
<td>Other major neurologic conditions</td>
<td>24 822 (3.8)</td>
<td>2241</td>
<td>7989</td>
<td>6121</td>
<td>8471</td>
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<tr>
<td>Gastroparesis</td>
<td>2976 (0.50)</td>
<td>632</td>
<td>1320</td>
<td>623</td>
<td>401</td>
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<tr>
<td>Parkinson disease</td>
<td>5676 (0.90)</td>
<td>97</td>
<td>928</td>
<td>1466</td>
<td>3185</td>
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<tr>
<td>Aphasia</td>
<td>679 (0.10)</td>
<td>58</td>
<td>255</td>
<td>154</td>
<td>212</td>
</tr>
<tr>
<td>Dysphasia</td>
<td>152 (0.02)</td>
<td>2</td>
<td>50</td>
<td>36</td>
<td>64</td>
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<tr>
<td>Hemiplegia</td>
<td>5672 (0.90)</td>
<td>631</td>
<td>2241</td>
<td>1394</td>
<td>1406</td>
</tr>
<tr>
<td>Apraxia</td>
<td>73 (0.01)</td>
<td>6</td>
<td>33</td>
<td>19</td>
<td>15</td>
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<tr>
<td>Epilepsy</td>
<td>2294 (0.40)</td>
<td>399</td>
<td>959</td>
<td>469</td>
<td>467</td>
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<tr>
<td>Transient ischemic attack</td>
<td>8541 (1.30)</td>
<td>510</td>
<td>2629</td>
<td>2277</td>
<td>3125</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>242 207 (37.1)</td>
<td>12 186</td>
<td>77 140</td>
<td>68 019</td>
<td>84 862</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>16 737 (2.6)</td>
<td>1155</td>
<td>6193</td>
<td>4465</td>
<td>4924</td>
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<tr>
<td>Chronic heart failure</td>
<td>63 490 (9.7)</td>
<td>3348</td>
<td>18 995</td>
<td>17 089</td>
<td>24 058</td>
</tr>
<tr>
<td>Ischemic vascular disease</td>
<td>217 585 (33.3)</td>
<td>10 197</td>
<td>69 422</td>
<td>62 056</td>
<td>75 910</td>
</tr>
<tr>
<td>Major depression</td>
<td>37 313 (5.7)</td>
<td>830 2</td>
<td>19 914</td>
<td>5840</td>
<td>3257</td>
</tr>
<tr>
<td>Alcohol/substance abuse</td>
<td>37 054 (5.7)</td>
<td>11 623</td>
<td>19 724</td>
<td>4357</td>
<td>1350</td>
</tr>
<tr>
<td>HbA1c, mean (SD), %</td>
<td>7.51 (1.52)</td>
<td>8.25</td>
<td>7.67</td>
<td>7.36</td>
<td>7.10</td>
</tr>
<tr>
<td>HbA1c distribution, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;6.0</td>
<td>59 021 (9.0)</td>
<td>6010</td>
<td>20 453</td>
<td>14 096</td>
<td>18 462</td>
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<tr>
<td>6.0-&lt;6.5</td>
<td>92 062 (14.1)</td>
<td>7508</td>
<td>29 292</td>
<td>23 707</td>
<td>31 555</td>
</tr>
<tr>
<td>6.5-&lt;7.0</td>
<td>120 708 (18.5)</td>
<td>9316</td>
<td>39 148</td>
<td>32 442</td>
<td>39 802</td>
</tr>
<tr>
<td>7.0-&lt;7.5</td>
<td>110 608 (17.0)</td>
<td>9369</td>
<td>37 741</td>
<td>30 207</td>
<td>33 291</td>
</tr>
<tr>
<td>7.5-&lt;8.0</td>
<td>83 230 (12.8)</td>
<td>8453</td>
<td>30 657</td>
<td>22 206</td>
<td>21 914</td>
</tr>
<tr>
<td>8.0-&lt;8.5</td>
<td>56 873 (8.7)</td>
<td>7108</td>
<td>22 607</td>
<td>14 505</td>
<td>12 653</td>
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<tr>
<td>8.5-&lt;9.0</td>
<td>38 903 (6.0)</td>
<td>6113</td>
<td>16 512</td>
<td>9090</td>
<td>7188</td>
</tr>
<tr>
<td>≥9.0</td>
<td>91 333 (14.0)</td>
<td>23 315</td>
<td>40 950</td>
<td>16 545</td>
<td>10 523</td>
</tr>
</tbody>
</table>

Abbreviation: HbA1c, hemoglobin A1c.

Conversion factors: To convert serum creatinine to micromoles per liter, multiply by 88.4; HbA1c to a proportion of total Hb, multiply by 0.01.

* Data are given as number (percentage) of patients. The Study population included patients with diabetes who were receiving insulin or sulfonylureas and had an HbA1c value available in fiscal year 2009.

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We identified positive deviants as the extreme outliers based on a significant statistical difference at the \( P < .01 \) level and proximity to the nearest less-extreme outlier. Figure 3 is a scatterplot of the differences between facilities and their respective VISNs. Separate plots were made for each outlier status (high, nonoutlier, and low) at each of the 3 threshold HbA1c levels. Although there were 32, 31, and 31 facilities with rates statistically significantly lower than the mean rates for the remainder of the VISN (potential positive deviants) at HbA1c thresholds of less than 6.0\%, less than 6.5\%, and less than 7.0\%, respectively, only 3 were considered positive deviants after inspecting their \( \delta \) values. Facility (A) was identified by both the HbA1c less than 6.0\% and less than 6.5\% thresholds, facility (B) was identified by both the HbA1c less than 6.5\% and less than 7.0\% thresholds, and facility (C) was identified by only the HbA1c less than 7.0\% threshold. We also marked these positive deviants as the extreme outliers based on a significant statistical difference at the \( P < .01 \) level and proximity to the nearest less-extreme outlier.
Discussion

Our results indicate that a substantial proportion of largely elderly veteran patients with significant comorbid conditions who are receiving hypoglycemic agents have evidence of intensive glycemic control and therefore are potentially being overtreated based on the most recent professional society and federal agency guidelines. Of individuals who were either 75 years or older or had renal insufficiency and/or cognitive impairment, 1 in 10 patients had a last HbA1c value below 6.0% and approximately half had values below 7.0%. The rates of possible overtreatment were only slightly less for the most inclusive population that included individuals with advanced diabetes-related complications, serious comorbid conditions, and cardiovascular or ischemic disease. By including HbA1c criteria from 7.0% to 7.4%, which takes into account measurement error as well as the fact that targets closer to 8% or even higher may be appropriate for most higher-risk patients, we identified close to 20% additional individuals who may benefit from a reevaluation of therapy.

While being 75 years or older does not necessarily contraindicate tight control, for most persons the marginal lifetime benefit compared with 8.0% HbA1c is minimal, and the harms (known and unknown) of medications are potentially greater. Indeed, the current National Committee for Quality Assurance–Health Effectiveness Information Data Set HbA1c less than 7.0% measure relevant to the time period of the data and still active excludes individuals aged 65 years or older as well as those with advanced diabetes complications, dementia, and cardiovascular or ischemic disease. Our primary inclusion criteria, cognitive impairment and chronic kidney disease, are common among persons with diabetes, especially the elderly. The most recent NHANES (National Health and Nutrition Examination Survey) (2005-2008) found a national prevalence of estimated glomerular filtration rate of less than 60 mL/min/1.73 m² of 6.0% for the diabetes population younger than 65 years and 37.4% of those older than 65 years. Similarly, based on a nationally representative sample, the prevalence of dementia in individuals aged 71 to 79 years was 5%, increasing...
to 24% for those aged 80 to 89 years; rates in persons with diabetes are not known but may be higher because of an increased incidence of vascular disease in diabetes. Our reliance on an HbA1c target of less than 7.0% was also conservative. Indeed, the American Geriatrics Society recommendation for the Choosing Wisely campaign stated that the use of medications other than metformin to lower HbA1c to less than 7.5% in persons older than 65 years is not warranted because of the potential for harm relative to benefit. Higher values of HbA1c, from 8.0% to 8.5% or 9.0%, are recommended for patients with major comorbid conditions or limited life expectancy.

Although our primary denominator for potential overtreatment was limited to 2 conditions, there are compelling justifications to include additional significant comorbid illnesses, as recommended by all major guidelines. First, the ACCORD trials and ADVANCE trials demonstrated an association between chronic medical conditions and serious hypoglycemia events as well as with serious cardiovascular events. Although there was an increased risk of cardiovascular mortality with higher HbA1c levels in both the control and intensive treatment arms of ACCORD, this relationship was not observed in ADVANCE. A recent observational study suggested that the risk of self-reported hypoglycemia was greatest in persons with either near-normal or poor glycemic control. However, the generalizability of these post hoc analyses is limited because persons with advanced diabetes complications, serious mental illness or substance use, and advanced medical or neurologic conditions, as well as those taking sedatives or pain medications, are excluded from clinical trials. Such comorbidity conditions could result in sudden changes in food intake and symptoms, such as confusion and disorientation, that are often antecedent to serious hypoglycemia. Although the rates of specific conditions in the US population with diabetes are not known, 45% of that population self-reported their health status as poor or fair in a nationally representative population.
Our findings of marked variation among VHA facilities are not surprising. Prior studies have documented similar variation in undertreatment (defined as HbA1c >9.0%) for veterans with and without mental health conditions stratified by insulin use. Similarly, use of antihyperglycemic agents varies markedly among VHA facilities. Elucidation of the causes of this variation may lead to targeted interventions to reduce hypo- glycemia risk. In fact, the identification of positive deviants (ie, facilities that achieve good performance that contrasts sharply with the performance of other facilities in its network) suggests that there are practical solutions in the field waiting to be identified, evaluated, and perhaps disseminated.

Our findings suggest the need for greater efforts to promote individualized targets, especially for elderly patients with chronic conditions. Individual physicians need to examine their practice and their assumptions about goals for patients that may differ considerably from those of the patients and the influences that underlie those assumptions. Implications for population health and relevant policy, as well as the financial costs of treatment of preventable hypoglycemia, are also important.

A recent systematic review involving 44 guidelines, 17 quality metrics, and 8 pay-for-performance programs found that clinical standards did not substantively incorporate evidence about increased risk for hypoglycemia in vulnerable populations. Similarly, based on a review of the National Quality Measures Clearinghouse, there are no measures either in the United States or internationally that address systematic monitoring of hypoglycemia as a potential unintended consequence of intensive glycemic control in patients at high risk. However, current guidelines now promote individualized target values, the Choosing Wisely Campaign has made overtreatment of diabetes in the elderly a focus, and the Department of Veterans Affairs has emphasized the importance of chronic comorbid conditions and is developing a national action plan to reduce adverse drug events that would include hypoglycemic safety.

Nonetheless, it may still be difficult to overcome currently held beliefs. The magnitude of potential overtreatment in our study occurred even though the VHA did not endorse the less than 7.0% glycemic measures and has recommended individualized target goals of greater than 8.0% for persons of advanced age with major comorbid conditions since 1997. We suggest that the results of overtreatment found in the present study are more likely to be attributable to the general acceptance of tight control for most persons that was advised by other guidelines and experts during this period and marketed by other governmental agencies, professional societies, and industry. In contrast to the extensive research focusing on clinical inertia around the issue of intensification of therapy (implementation of practice change), there is little research on lowering intensification of treatment. Moreover, such lowered intensification will have to take place in an environment that promotes performance measurement and pay for performance and one in which drug and device companies sponsor approximately one-third of Accreditation Council for Continuing Medical Education courses.

In contrast to implementation of a new practice that may involve addition or substitution for an old practice, implementation involves practice reversal and, in addition to learning, requires deliberate “unlearning.” Unlearning requires a change in one’s knowledge and, in the case of a health care practice, a change in the beliefs about consequences. Key to a national de-implementation strategy is the development of a patient safety indicator for electronic medical records that can address potential overtreatment at both the physician practice and health system levels. This indicator can support clinical decision support, population health surveillance, and internal quality improvement. These functions are consistent with federal policies to establish meaningful use criteria to simultaneously improve quality, safety, and efficiency for national high-priority conditions.

Our study has several limitations. We relied on administrative codes, although this is the industry standard for indicators and measures. Second, the population was limited to patients receiving care in the VA system, although many of them would be eligible for Medicare. We addressed potential or possible overtreatment; however, there may be reasons why a given individual might appropriately receive tight glycemic control. There are social factors associated with hypoglycemia not ascertainable in our data, specifically social support, decreased health literacy, and health numeracy. Individuals may have had additional laboratory tests and medication refills outside the VA system. We did not determine the relationship of medication adherence and persistence with HbA1c values. Finally, we did not correlate the risk of hypoglycemia with the rates of potential overtreatment because of limitations in coding or otherwise capturing the most severe hypoglycemic events, including those resulting in paramedic or emergency department visits, or hospitalizations. Additionally, studies have indicated that such patients experience other events that can be attributed to hypoglycemia, including accidental falls and automobile accidents.

We also acknowledge that the clinical impact of this approach cannot be ascertained. The annualized rate of hypoglycemic episodes per 100 patient-years varied among the 3 major trials: 3.1% (HbA1c 7.5%) vs 1.0% (HbA1c 6.4%) from ADVANCE, 2.7% (HbA1c 7.3%) vs 1.5% (HbA1c 6.5%) from ACCORD, and 15.7% (HbA1c 6.9%) vs 4.3% (HbA1c 8.4%) from the VA Diabetes Trial. Although findings from the studies cannot be generalized, the marked difference between treatment arms suggests that less stringent control in the elderly will reduce hypoglycemic events in practice.

In conclusion, there has been increasing evidence from both randomized clinical studies and observational studies of the magnitude and risk of serious hypoglycemia. Our study provides confirmation that intensive glycemic control, representing possible overtreatment, is common among older veterans receiving care in the VHA. Our approach using administrative data and laboratory values is a feasible tool for proactive surveillance of patients at high risk and is thus consistent with evolving national policy for meaningful use criteria for electronic health records as a foundation for patient safety efforts. Finally, our approach is consistent with the duties of our profession as defined more than 2 millennia ago: “As to diseases, make a habit of two things: to help, or to at least do no harm.”
Glycemic Overtreatment Safety Indicator

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REFERENCES


