WHAT’S KNOWN ON THIS SUBJECT: In 2003, the US Food and Drug Administration issued warnings about hyperglycemia and diabetes with second-generation antipsychotics (SGAs). Since 2004, hyperglycemic and diabetes risk with SGAs has been stated in product labels, and published guidelines have recommended baseline metabolic screening.

WHAT THIS STUDY ADDS: Between 2006 and 2011, 11% of children 2 to 18 years starting an SGA had baseline glucose assessed. Youth at risk for diabetes may not be identified. Further, lack of screening impedes determining the contribution of SGAs to hyperglycemia.

OBJECTIVES: In 2003, the US Food and Drug Administration issued warnings about hyperglycemia and diabetes with second-generation antipsychotics (SGAs); guidelines have recommended metabolic screening since 2004. However, little is known of contemporary practices of glucose screening among youth initiating SGAs. Our objective was to evaluate baseline glucose assessment among youth in the Mini-Sentinel Distributed Database starting an SGA.

METHODS: The cohort included youth ages 2 through 18 newly initiating SGAs January 1, 2006, through December 31, 2011, across 10 sites. Baseline glucose was defined as fasting/random glucose or hemoglobin A1c (GLU) measurement occurring relative to first SGA dispensing. Differences in GLU assessment were evaluated with χ² tests and logistic regression.

RESULTS: The cohort included 16,304 youth; 60% boys; mean age 12.8 years. Risperidone was most commonly started (43%). Eleven percent (n = 1,858) had GLU assessed between 90 days before and 3 days after first dispensing. Assessment varied across SGAs (olanzapine highest), sites (integrated health care systems higher), ages (16–18 highest), years (2007 highest), and gender (female higher; all P < .001). GLU assessment among those starting olanzapine was more likely than among those starting quetiapine (odds ratio [OR]: 1.72 [95% confidence interval (CI): 1.37–2.18]), aripiprazole (OR: 1.49 [95% CI: 1.18–1.87]), or risperidone (OR: 1.61 [95% CI: 1.28–2.03]).

CONCLUSIONS: Few children and adolescents starting SGA have baseline glucose assessed. This is concerning because those at high diabetes risk may not be identified. Further, lack of screening impedes determining the contribution of SGAs to hyperglycemia development.

Adherence to Guidelines for Glucose Assessment in Starting Second-Generation Antipsychotics

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KEY WORDS antipsychotic agents, second-generation antipsychotic, olanzapine, risperidone, aripiprazole, quetiapine, child, adolescent, youth, glucose, hyperglycemia, glycosylated hemoglobin, monitoring, guideline adherence, retrospective studies

ABBREVIATIONS CI—confidence interval
FDA—US Food and Drug Administration
GLU—random glucose or fasting glucose or hemoglobin A1c
HbA1c—hemoglobin A1c
OR—odds ratio
SGA—second-generation antipsychotic

Dr Raebel designed the study, supervised the data analyses, interpreted the results, and drafted the initial manuscript; Dr Penfold participated in designing the study, participated in interpreting the results, and critically reviewed the manuscript; Dr McMahon participated in conceptualizing and designing the study, participated in interpreting the results, and critically reviewed the manuscript; Ms Shetterly carried out the analyses, participated in interpreting the results, and reviewed and revised the manuscript; Mr Goodrich carried out the analyses and participated in interpreting the results; Dr Andrade participated in designing the study, participated in interpreting the results, and critically reviewed the manuscript; Dr Reichman participated in conceptualizing and designing the study, participated in interpreting the results, and critically reviewed the manuscript; Ms Andrade participated in conceptualizing and designing the study, participated in interpreting the results, and critically reviewed the manuscript; Dr Gerhard conceptualized and designed the study, participated in interpreting the results, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

(Continued on last page)
Prescribing antipsychotic agents to children and adolescents has dramatically increased in recent years. Data from the National Ambulatory Medical Care Survey and US Census Bureau estimate that outpatient visits resulting in a prescription for an antipsychotic medication rose from 0.24 to 1.83 per 100 persons among individuals aged 0 through 13 years and from 0.78 to 3.76 per 100 persons among individuals aged 14 through 20 years between 1993 and 1998 and 2005 and 2009. Since the mid-2000s, essentially all prescriptions for antipsychotics in young patients are for the newer medications known as second-generation antipsychotic (SGAs) agents.

Use of SGAs is associated with hyperglycemia and other metabolic abnormalities such as weight gain and abnormal lipid profiles. In adults, weight gain, lipid, and glucose abnormalities differ across individual SGAs. The risk of weight gain and early cardiometabolic abnormalities with SGAs appears to be enhanced in youth, in part related to the fact that young patients are often receiving an SGA for the first time. Andrade et al reported an increased rate of diabetes among 5 to 18 year olds exposed to SGAs; however, findings were inconsistent and depended on the comparison group. Margari et al found a nonsignificant increase in blood glucose in a small study of antipsychotic-naive children and adolescents starting risperidone. There is little comparative data on the risk of hyperglycemia and type 2 diabetes mellitus in youth treated with various SGAs.

Because of rising concerns about potential longer term risks of type 2 diabetes mellitus, cardiovascular disease, and premature death in the severely mentally ill exposed to SGAs, in 2003, the US Food and Drug Administration (FDA) issued warnings about hyperglycemia and diabetes risks with SGAs. Since 2004, these potential risks have been included in all SGA product labels, and published national and international guidelines have recommended obtaining metabolic screening (eg, obtaining a fasting glucose) before initiation of any SGA. Glucose screening before SGA initiation is important to guide considerations regarding treatment alternatives and choice of antipsychotic agent and to provide a baseline value that can enable informed interpretation of future, on-therapy glucose monitoring.

An epidemiologic study by Haupt et al employing laboratory claims data from patients of all ages up to 65 years treated with SGAs between 2000 and 2006 demonstrated that metabolic monitoring was not conducted as recommended. They documented cardiometabolic monitoring practices had not changed substantially since the FDA warnings. SGA product label revisions, and national monitoring guidelines issuance. Mitchell et al recently conducted a systematic review and meta-analysis of international studies of metabolic monitoring, including studies published before and after formal monitoring guidelines were available. They too found that suboptimal metabolic monitoring among patients prescribed SGAs continued after guidelines were published. However, little is known about actual practices of baseline blood glucose assessment specifically among children and adolescents starting therapy with an SGA in the United States; there has not been a large study examining metabolic monitoring across multiple geographic regions, and data more recent than 2006 are not available. We sought to examine baseline glucose monitoring in youth prescribed SGAs in the United States by using data from the Mini-Sentinel project, a pilot program funded by the FDA to develop national capacity to rapidly conduct postmarket active medical product safety surveillance and to demonstrate the usefulness of this information to the FDA.

METHODS

This retrospective cohort study was conducted by using the Mini-Sentinel Distributed Database, a national distributed electronic health care database network built to provide an efficient tool for public health medical product safety surveillance queries and epidemiologic assessments. One of the current Mini-Sentinel activities is an assessment of diabetes risk in youth newly initiating an SGA and, as part of assessing diabetes risk, we explored the feasibility of using blood glucose data available from these youth for baseline confounding adjustment. The population for this overall Mini-Sentinel assessment of diabetes risk in youth initiating an SGA has been previously described. In brief, the children and adolescents for whom baseline laboratory results data availability were assessed for the current study included those aged 2 through 18 years who were newly initiated an SGA for any indication between January 1, 2006, and December 31, 2011. Newly initiating an SGA was defined as having at least 180 days before the first SGA with no dispensing of any antipsychotic agent. These youth must have had both medical and prescription drug coverage for at least the 180 days preceding the date of the first dispensing of the SGA. Youth with preexisting diabetes were excluded from the study cohort.

One foundational element of the Mini-Sentinel Distributed Database is that network data partners periodically extract, transform, and load source data into the Mini-Sentinel common data model format to facilitate use of shared programming code across sites. Other foundational principles of the Mini-Sentinel Distributed Database include that only the minimum necessary amount of data leave any SGA. Glucose screening before SGA initiation is important to guide considerations regarding treatment alternatives and choice of antipsychotic agent and to provide a baseline value that can enable informed interpretation of future, on-therapy glucose monitoring.

An epidemiologic study by Haupt et al employing laboratory claims data from patients of all ages up to 65 years treated with SGAs between 2000 and 2006 demonstrated that metabolic monitoring was not conducted as recommended. They documented cardiometabolic monitoring practices had not changed substantially since the FDA warnings. SGA product label revisions, and national monitoring guidelines issuance. Mitchell et al recently conducted a systematic review and meta-analysis of international studies of metabolic monitoring, including studies published before and after formal monitoring guidelines were available. They too found that suboptimal metabolic monitoring among patients prescribed SGAs continued after guidelines were published. However, little is known about actual practices of baseline blood glucose assessment specifically among children and adolescents starting therapy with an SGA in the United States; there has not been a large study examining metabolic monitoring across multiple geographic regions, and data more recent than 2006 are not available. We sought to examine baseline glucose monitoring in youth prescribed SGAs in the United States by using data from the Mini-Sentinel project, a pilot program funded by the FDA to develop national capacity to rapidly conduct postmarket active medical product safety surveillance and to demonstrate the usefulness of this information to the FDA.
Because claims data for laboratory procedures (ie, Current Procedural Terminology codes, including codes for individual glucose tests and for glucose tests that are part of comprehensive metabolic panels) only indicate that a laboratory test was completed and do not contain clinical results values, laboratory claims are of limited use when assessing safety outcomes associated with medication use. Therefore, laboratory results data from data partners’ electronic health records and clinical laboratory systems were employed to develop and implement the Mini-Sentinel Distributed Database clinical laboratory results data table. We used this Mini-Sentinel Distributed Database clinical laboratory results data table for the current exploration of baseline glucose assessment before or at initiation of SGA. Ten Mini-Sentinel data partners that had incorporated clinical laboratory results data into the Mini-Sentinel Distributed Database laboratory results table participated in this evaluation. Participating data partners included Aetna Informatics (national), Group Health Research Institute (Washington), Humana: Comprehensive Health Insights, Inc (national), Marshfield Clinic Research Foundation (Wisconsin), Meyers Primary Care Institute (Massachusetts), and the Kaiser Permanente Center for Effectiveness and Safety Research sites in Hawaii, the Northwest (Oregon and Washington), Colorado, Mid-Atlantic States (Maryland, Virginia, and Washington, DC), and Georgia.

In this study, baseline (ie, screening) blood glucose assessment was considered to include either fasting or random glucose or hemoglobin A1c (hereafter referred to as GLU) measurement occurring relative to the first SGA dispensing date. GLU result measurements were identified from individual test results and from panels of laboratory test results (eg, comprehensive metabolic panels). The primary baseline GLU measurement relative time window was defined as 90 days before (−90) through 3 days after (+3) the first dispensing date. Narrower time windows (eg, 14 days before through 3 days after) and a broader time window (ie, 90 days before through 30 days after) were also assessed. Although the study team primary definition of baseline or screening GLU testing included up to 3 days after the date of the first SGA dispensing, including an analysis that allowed up to 30 days after initial SGA dispensing accounts for scenarios where a physician visit occurred on day 0 during which both the SGA and the GLU laboratory testing were ordered, and the baseline laboratory testing was completed more than 3 days later as a result of that order.

Descriptive analyses were conducted overall, within age categories, by gender, by calendar year of cohort entry, by individual data partners, by specific SGA, and according to whether the blood GLU test was a random glucose, fasting glucose, or hemoglobin A1c (HbA1c). Differences in GLU assessments were evaluated with \( \chi^2 \) tests. The likelihood of GLU testing was assessed by using logistic regression models adjusted for specific SGA, age, data partner site, and gender. All analyses were conducted by using SAS version 9.2 (SAS Institute, Inc, Cary, NC).

The Director of the Department of Health and Human Services Office for Human Research Protections has determined that the Common Rule does not apply to activities conducted as part of the Sentinel Initiative. Mini-Sentinel activities are public health surveillance, and public health surveillance activities are not under the purview of institutional review boards. Health Insurance Portability and Accountability Act regulations for public health surveillance do apply. Personally identifiable health information is not transmitted to either the Mini-Sentinel Operations Center or to the FDA.

**RESULTS**

The cohort included 16 304 children and adolescents, comprising 40% (\( n = 6526 \)) girls and 60% (\( n = 9778 \)) boys, mean age 12.8 years (SD 4.0). Risperidone was the SGA most commonly started (43%; \( n = 6956 \)), followed by aripiprazole (31%; \( n = 5035 \)), quetiapine (20%; \( n = 3245 \)), olanzapine (4%; \( n = 659 \)), and other agents (2%; \( n = 409 \)). The cohort age distribution included 2% (\( n = 364 \)) ages 2 to 4 years, 22% (\( n = 3508 \)) ages 5 to 9, 17% (\( n = 2738 \)) ages 10 to 12, 26% (\( n = 4282 \)) ages 13 to 15, and 33% (\( n = 5412 \)) ages 16 to 18. The proportion entering the cohort each year included 5% entering in 2006, 5% in 2007, 20% in 2008, 28% in 2009, 23% in 2010, and 19% in 2011.

Detailed results of baseline GLU assessment data availability for 14 days before through 3 days after, 90 days before through 3 days after, and 90 days before through 30 days after starting an SGA are shown in Tables 1 and 2. Eleven percent (\( n = 1858 \)) of youth had GLU assessed between 90 before and 3 days after the first SGA dispensing date. The cohort proportion with GLU assessed varied across SGAs (10% for risperidone to 18% for olanzapine; \( P < .001 \); Table 1), data partner sites (mean 19% at integrated health care delivery systems versus 8% at medical practices affiliated with large national health insurance plans; \( P < .001 \)), age (7% for ages 2–4 years to 14% for ages 16–18 years, \( P < .001 \); Table 2), and cohort entry year (ranging from a high of 17% in 2007 to a low of 9% in 2008; \( P < .001 \); Fig 1). Thirteen percent of girls had GLU assessed versus 16% of boys (\( P < .001 \)). Random glucose was most often measured, followed by fasting glucose, and HbA1c (Table 1). Differences in the cohort proportion with GLU assessed were observed regardless
of whether the relative time window assessed was 90 days before through 3 days after, 14 days before through 3 days after, or 90 days before through 30 days after the first dispensing date (Tables 1 and 2).

In adjusted analyses, youth starting olanzapine were more likely to have GLU assessed between 90 days before and 3 days after the first dispensing date compared to youth starting quetiapine (odds ratio (OR): 1.72 [95% confidence interval (CI): 1.37–2.18]), aripiprazole (OR: 1.49 [95% CI: 1.18–1.87]), or risperidone (OR: 1.61 [95% CI: 1.28–2.03]).

**DISCUSSION**

We found only 11% of children and adolescents in this large US cohort had GLU assessed between 90 days before and 3 days after starting an SGA. Expanding the time frame to include the 30 days after starting an SGA only increased the proportion of youth with any GLU assessment to 15%. Importantly, this study included 6 years (2006 through 2011) subsequent to the publication of guidelines and product labeling recommending metabolic screening before initiating any SGA. Infrequent baseline GLU assessment was consistently observed across years, age groups, gender, and specific SGAs. The rate of baseline GLU screening did not exceed 17% in any year; there was no consistent increase or decrease in the rate of baseline GLU screening.

### Table 1: Baseline Blood Glucose Assessment Among 16,304 Children and Adolescents Starting a SGA Agent by Specific Agent

<table>
<thead>
<tr>
<th>Time Elapsed Relative to Starting SGA</th>
<th>Blood Glucose Laboratory Test Type</th>
<th>Any GLU</th>
<th>Aripiprazole</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
<th>Other Agents, Total, n = 16,304</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 d before through 3 d after</td>
<td>Any GLU</td>
<td>277 (6)</td>
<td>54 (8)</td>
<td>155 (5)</td>
<td>401 (6)</td>
<td>17 (4)</td>
<td>904 (6)</td>
<td>.006</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>42 (&lt;1)</td>
<td>10 (&lt;1)</td>
<td>44 (&lt;1)</td>
<td>99 (&lt;1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasting</td>
<td>77 (2)</td>
<td>37 (1)</td>
<td>148 (2)</td>
<td>269 (2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Random</td>
<td>158 (3)</td>
<td>108 (3)</td>
<td>211 (3)</td>
<td>535 (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No glucose</td>
<td>4758 (85)</td>
<td>605 (82)</td>
<td>3090 (95)</td>
<td>6555 (94)</td>
<td>392 (98)</td>
<td>15,400 (95)</td>
<td></td>
</tr>
<tr>
<td>90 d before through 30 d after</td>
<td>Any GLU</td>
<td>611 (12)</td>
<td>118 (18)</td>
<td>389 (11)</td>
<td>717 (10)</td>
<td>45 (11)</td>
<td>1858 (11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>78 (2)</td>
<td>6 (1)</td>
<td>72 (1)</td>
<td>182 (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasting</td>
<td>131 (3)</td>
<td>15 (2)</td>
<td>211 (3)</td>
<td>433 (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Random</td>
<td>402 (8)</td>
<td>97 (15)</td>
<td>434 (6)</td>
<td>1237 (8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No glucose</td>
<td>4424 (88)</td>
<td>541 (82)</td>
<td>2876 (89)</td>
<td>6239 (90)</td>
<td>366 (90)</td>
<td>14,446 (89)</td>
<td></td>
</tr>
<tr>
<td>90 d before through 30 d after</td>
<td>Any GLU</td>
<td>764 (15)</td>
<td>139 (21)</td>
<td>476 (15)</td>
<td>940 (14)</td>
<td>56 (14)</td>
<td>2375 (15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>89 (2)</td>
<td>8 (1)</td>
<td>104 (2)</td>
<td>244 (2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasting</td>
<td>188 (4)</td>
<td>24 (4)</td>
<td>306 (4)</td>
<td>634 (4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Random</td>
<td>487 (10)</td>
<td>107 (16)</td>
<td>530 (8)</td>
<td>1497 (9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No glucose</td>
<td>4271 (85)</td>
<td>520 (79)</td>
<td>2769 (85)</td>
<td>6016 (87)</td>
<td>353 (86)</td>
<td>13,929 (85)</td>
<td></td>
</tr>
</tbody>
</table>

* Other agents includes asenapine, ziprasidone, paliperidone, iloperidone, and lurasidone.

### Table 2: Baseline Blood Glucose Assessment Among 16,304 Children and Adolescents Starting a SGA Agent by Age Group

<table>
<thead>
<tr>
<th>Time Elapsed Relative to Starting SGA</th>
<th>Blood Glucose Laboratory Test Type</th>
<th>Age Group in Years</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 d before through 3 d after</td>
<td>Any GLU</td>
<td>2–4, n = 564 (20%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>17 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasting</td>
<td>55 (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Random</td>
<td>91 (3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No glucose</td>
<td>351 (96)</td>
<td></td>
</tr>
<tr>
<td>90 d before through 30 d after</td>
<td>Any GLU</td>
<td>27 (7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>28 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasting</td>
<td>79 (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Random</td>
<td>178 (5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No glucose</td>
<td>337 (93)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>90 d before through 30 d after</td>
<td>Any GLU</td>
<td>36 (10)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>40 (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fasting</td>
<td>113 (5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Random</td>
<td>222 (6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No glucose</td>
<td>328 (90)</td>
<td></td>
</tr>
</tbody>
</table>

* χ² test comparing any GLU assessment among the age groups.

**Note:** Any GLU is the sum of any HbA1c, fasting, or random blood glucose.

Detail not shown because some cell sizes are < 6.
assessed over time. Younger children appeared to even less often have GLU screening before starting an SGA than did teenagers. Baseline GLU assessment was possibly selective given that olanzapine, a drug more likely associated with metabolic abnormalities,4,13 had a statistically significantly higher likelihood of assessment than quetiapine, aripiprazole, or risperidone. Although GLU assessment when initiating olanzapine was statistically significantly more frequent than when initiating aripiprazole (which appears to have the lowest D2 binding), some SGA (eg, quetiapine has the lowest D2 binding). Some SGA (eg, risperidone) also bind to muscarinic and histamine receptors. Although the exact mechanism is not clear, the SGAs contribute to weight gain, likely through blockade of serotonin receptors, and antihistaminic and antimuscarinic effects in the central nervous system that result in appetite stimulation and reduced satiety. Weight gain is the most common and important adverse effect of SGAs in children and adolescents.8,7,28–30 The extent to which SGAs adversely affect GLU levels independent of drug-induced weight gain is unclear. Nevertheless, because studies have revealed worsening glucose control and new-onset diabetes during treatment with SGAs including olanzapine and risperidone,29,31,32 obtaining a baseline glucose level to establish whether glucose control is normal or impaired at the time of initiating SGA therapy is prudent. This frequency of 11% of baseline glucose testing for children and adolescents ages 2 through 18 prescribed SGAs is similar to that reported by Haupt et al among commercially insured SGA users aged <65 years between 2000 and 2006. In their entire cohort, baseline glucose monitoring, pooled across the 2 periods of July 2000 through September 2003 and March 2004 through November 2006, occurred in 17.3% to 21.8%, but monitoring was lower in those aged 12 to 17 (13%–16%) and even lower in those aged younger than 12 years (7%–11%). Although Morrato et al found 31.6% of 5370 Medicaid youth taking SGAs had glucose monitoring, this monitoring percentage included the first 6 months after SGA initiation, thereby being inflated by on-therapy monitoring.

A strength of our work is that the patient clinical and administrative data that comprise the Mini-Sentinel Distributed Database, including those data in the clinical laboratory results table employed in this study, were obtained during routine health care treatment, payment, and operations at usual care settings across the United States, in both fee-for-service and integrated (eg, health maintenance organization) health care delivery settings. Therefore, these findings, covering a time frame through 2011, are likely applicable to ambulatory health care delivery across insured populations of children and adolescents in the United States.

This work also has limitations. The large national insurance plans participating as Mini-Sentinel data partners only have access to laboratory results data from a subset (not all) of their enrollees. Thus, baseline GLU laboratory testing was likely completed for some youth, but the results were not captured in the Mini-Sentinel Distributed Database. Although this potentially contributed to the low cohort proportion with GLU measurement at those data partner sites, GLU measurement among this cohort was also low (19%) at data partner sites that were group or staff model integrated health care delivery systems with electronic health records considered to have complete laboratory results data capture.

To our knowledge, this is the largest cohort of children and adolescents starting SGAs studied and the first SGA-glucose/HbA1c evaluation to employ a clinical laboratory test results database rather than laboratory claims data. Taken together, these data are clearly concerning, in that medical practice in the United States lags behind evidence and guidelines and in that vulnerable youth who receive medications that can have documented adverse cardiometabolic effects are not screened sufficiently. Further work is needed to better understand the underlying reasons for the low levels of GLU baseline screening despite the evidence. For example, Morrato et al investigated factors associated with glucose testing (baseline or on-therapy monitoring between 30 days before and 180 days after starting an SGA) in youth ages 6 through 19 years in a Medicaid population. They found that preexisting diabetes and

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**FIGURE 1**
Percentages of 16,304 children and adolescents from 2006 to 2011 with any blood glucose result available from 90 days before through 3 days after starting a SGA agent.
dyslipidemia, more frequent health care utilization, and having a severe mental illness diagnosis were directly associated with increased likelihood of glucose testing. In future work, it will be important to clarify whether these (and other) factors are associated separately with glucose screening at baseline.

CONCLUSIONS

We conclude that, despite FDA warnings about hyperglycemia and diabetes and published recommendations to screen for diabetes and prediabetes, few children and adolescents starting an SGA have baseline blood glucose assessed. This finding is very concerning because it suggests that youth at high risk of diabetes may not be identified or adequately assessed for treatment alternatives. Further, lack of baseline screening impedes determination of the contribution of SGAs to hyperglycemia and diabetes outcomes.

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