A randomized naturalistic study of an electronic hypoglycemia risk calculator in outpatient primary care

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ABSTRACT

Objective. Hypoglycemia (HG) occurs in up to 60% of patients with diabetes mellitus (DM) each year. Our objective was to assess a HG alert tool in an electronic health record system, and determine the tool's effect on clinical practice and outcomes.

Methods. The tool used a logistic-regression model to provide patient-specific information about HG risk. We randomized academic outpatient primary-care providers (PCPs) to see or not see the alerts. Adult patients were assigned to study group according to the first PCP seen during four months. We assessed five months' prescriptions, diagnostic testing, and HG. Categorical variables were compared by multinomial model, binary variables by logistic model, and continuous variables by linear model.

Results. A total of 3350 patients visited 123 intervention PCPs; 3395 patients visited 220 control PCPs. Intervention PCPs were shown 18,645 alerts. Patients' mean age was 55 years, with 61% female, 49% black, and 49% with Medicaid. Mean baseline A1c (8.7%) and body mass index (35.2 kg/m^2) were similar between groups. During follow-up, the number of A1c and glucose tests, and number of new, refilled, changed, or discontinued insulin prescriptions, were highest for patients with highest risk. Per 100 patients, the intervention group had significantly fewer sulfonylurea refills (6 vs. 8; $p<0.05$) and outpatient encounters (470 vs. 502; $p<0.05$). Frequency of A1c testing and HG events was unchanged.

Conclusions. Informing PCPs about risk of HG led to fewer sulfonylurea refills and visits. Longer-term studies are needed to assess the potential for long-term benefits of the alert.

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INTRODUCTION

Diabetes mellitus (DM) is one of the most common non-communicable diseases worldwide and is a major cause of morbidity and mortality. In 2010, DM was the seventh leading cause of death in the United States. In 2015, DM was present in more than 30 million Americans (9.4%) and about 25% of those 65 or more years of age (1). Hypoglycemia (HG) is recognized as the major limiting factor in optimal glycemic management for patients with both type 1 and type 2 diabetes (2-5). It has substantial negative effects on cardiovascular safety and quality of life (6-11). It also increases economic costs via healthcare utilization and lost productivity (12).

HG threatens safety and glycemic control (10, 13-16). The risk of HG increased substantially in landmark studies designed to show that intensive treatment to maintain near euglycemia (normoglycemia) significantly reduced long-term risks of vascular complications (16-18). In the Diabetes Control and Complications Trial (DCCT), patients with type 1 DM randomized to intensive therapy had about a three-fold higher risk of severe HG compared with their counterparts receiving conventional treatment (16). In the 4-T study of type 2 DM, the mean number of HG events per patient in individuals treated with insulin ranged from 2.3 to 12.0 per year, although less than 1 in 4 patients achieved A1C less than 6.5% (19). HG also occurs in approximately 20% to 60% of patients with type 2 DM who received oral medications according to some studies (10, 13-15, 20). A systematic review and meta-analysis of more than 500,000 patients showed that mild or moderate HG occurred in 45% of patients with type 2 diabetes on oral therapies or insulin, while severe HG occurred in 6% (20). In a recent survey of 1,984 adults with type 2 DM who received oral antihyperglycemic medications, 63% reported having at least one HG episode in the previous six months. Of these episodes, 46% were mild, 37% moderate, 13% severe, and 4% very severe (13). In a population more than 80 years of age with type 2 DM,

25% of hospital admissions associated with DM were due to severe HG (21). Newer drugs have led to somewhat lower risk. For example, a cohort study of more than 50,000 patients with type 2 DM showed a lower odds of severe HG in patients receiving a dipeptidyl peptidase 4 inhibitor (OR 0.51) or a glucagon-like peptide 1 agonist (OR 0.23) and significantly higher odds for patients receiving insulin (OR 2.77) or SU (OR 2.49) (22). When considering the prevalence of HG, the American Geriatrics Society recommends customizing glycemic control for older adults according to comorbidity, functional status, and life expectancy, noting that a target HbA1c of 7.5% to 8% is often appropriate for older patients with multiple comorbidities or impaired functional status (23).

Risk factors for HG in DM (24-32) include basal and bolus insulin (33, 34), SU drugs (5, 35, 36), chronic kidney disease (37), and certain combinations of medications for DM (38-40). Since clinicians should regularly assess the risk of HG in patients with DM (41, 42), an automated, point-of-care approach to estimating risk may help clinicians to save time and identify strategies to limit risk of HG among their patients. Based on a previously developed logistic regression model of HG, we created a computerized HG risk prediction tool that incorporates significant risk factors for HG [refer to companion article].

As adoption of electronic health record (EHR) systems increases (43), the need for EHR-based clinical tools that can improve decision-making and outcomes is growing. The objective of this study was to implement a HG alert tool in an EHR system, and determine its effect on clinical practice and outcomes. The hypothesis was that the intervention group of PCPs using the tool would have greater frequencies of DM-medication changes and counseling of patients about HG.

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METHODS

Trial design

To build a risk prediction model for HG, we first retrospectively studied risk factors identified in previously published articles and reports, to determine which were independently associated with HG in a local population. We targeted patients and outpatient primary care providers at Eskenazi Health on the campus of Indiana University-Purdue University Indianapolis. The retrospective study period was 2004 to 2013. Eligible patients were at least 21 years of age on 01 January 2004 and were prescribed or dispensed a drug for DM during the study period. The index date was defined as the first HG event for a patient during the study period. For patients who did not experience a HG event, their index date was a randomly selected visit date during the study period. The baseline period was defined as the two years prior to the index date. We excluded patients with a diagnosis of abnormal glucose tolerance complicating pregnancy or childbirth, and patients with fewer than two clinical encounters on separate dates during the baseline period. From the Indiana Network for Patient Care (44, 45), we extracted data about risk factors and demographics, from medical records of patients seen at the institution during the study period. Using this retrospective cohort, we conducted multivariable logistic regression analysis, with HG as the primary outcome. HG was defined as an outpatient plasma glucose value of less than 70 mg/dL (3.9 mmol/L), identified through laboratory reports, International Classification of Diseases diagnosis codes (46), or narrative text (e.g., notes from clinical encounters) that underwent natural language processing (NLP) to identify episodes of HG. Significance was defined by a p-value of less than or equal to 0.05. In logistic regression, positive risk factors included the following: eating disorder, infection within 30 days, insulin other than long-acting insulin, previous HG within 12 months, African-American, diabetic

neuropathy, Medicaid, alcohol, chronic heart failure, no antibiotics, antibiotics with a SU drug, dementia or falls, and A1C 6.5% or less. Negative risk factors included serum calcium, long-acting insulin plus a SU within 90 days, Hispanic, and age 75 or more years. The risk factors were then incorporated into a risk prediction tool that we designed and developed for clinicians. The tool was implemented over a four month period in 2016, for a random sample of outpatient primary care providers at Eskenazi Health. Outcomes were assessed during months five through nine, using an intention-to-treat analysis. The study was approved by the Institutional Review Board of Indiana University-Purdue University Indianapolis.

Setting and participants

The setting is Eskenazi Health, which is one of the five largest safety-net health institutions in the U.S. It is a tax-supported, urban healthcare system providing outpatient, inpatient, and community-based health services to residents of Marion County, Indiana. Sidney & Lois Eskenazi Hospital and a core of outpatient clinics are located on the campus of Indiana University-Purdue University Indianapolis. Additional community health centers providing primary care are located around the Indianapolis metropolitan area. In 2016, the institution reported 14,073 hospital admissions and 834,631 outpatient visits, including 236,945 visits to community health centers. The payer mix is 28% Medicaid, 20% Medicare, 11% commercial, and 24% uninsured. A special program of services is provided for many low-income patients who are not eligible for Medicaid benefits. Eskenazi Health has more than 1,000 physicians on its medical staff.

The Regenstrief G3 system is an advanced EHR system that includes computerized provider order entry (47). During the study period, G3 was Eskenazi's primary instrument for processing clinical data and monitoring clinical activity. The Indiana Network for Patient Care

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includes clinical data representing over 90 hospitals, the public health departments, local laboratories, imaging centers, and selected large-group practices. Participating institutions share a common file structure and term dictionary. The Network includes information about laboratory tests, demographics, encounters, diagnosis codes, and some information about prescribing and pharmacy. The study included clinicians who were scheduled to provide primary care at Eskenazi Health during the four-month intervention period at the beginning of 2016.

Intervention

Working with technologists and software developers on our team, we developed and iteratively refined the risk prediction tool, which underwent user acceptance testing with a small group of test users. The tool was integrated into the EHR system. Based on a patient's characteristics, the tool was displayed at the edge of the computer display when a clinician logged into an eligible patient's electronic medical record. An example of the display is shown in **Figure 1** (initial collapsed form) and **Figure 2** (expanded). The tool displays the estimated two-year risk of HG, along with an indication of the presence of risk factors identified in the patient's medical record. The user can test hypothetical clinical variants, by modifying variables directly within the tool, to update the display of HG risk. For example, the user could determine how much the HG risk would change if the patient's age or related diagnoses changed. A feedback feature was included so that users could send comments to the project team.

Outcomes

For patients in intervention and control groups, we reported demographics and risk factors for HG, which was the primary outcome. We reported clinical practice measures, including laboratory testing for glucose and A1C, changes to prescribing of medications for DM,

and patient education related to HG, as assessed by NLP. We also assessed the number of clinical encounters. We reported outcomes stratified by quintile of HG risk.

In reporting drugs, insulin was categorized as long-acting, short-acting, or pre-mixed. Prescriptions were categorized as new, changed, refilled (with no changes), or discontinued, according to the type of order generated for the prescription. A change to a prescription was defined as a prescription for a drug when the most recent prescription for the same drug had different instructions. A refill was defined as a prescription for a drug when the most recent prescription for the same drug had the same instructions. If the prescription were a refill or change, but the preceding instructions were not available, then the prescription was considered to be "unknown whether refilled or changed". We included prescriptions for glucagon (4) and glucose tablets (48).

Sample size

We anticipated that 100 providers (physicians and resident housestaff) would be available for provider-level randomization at equal chance to receive or not receive access to the HG alert tool, and that a provider would, on average, see 150 patients during the four-month intervention period. With a total of approximately 15,000 patients and, assuming that the intra-cluster (physician) correlation is 0.05, cluster size 150 (patients), a coefficient of variation of cluster size no more than 0.23, and a 10% HG rate for the group without the access to the HG alert tool during the follow-up period, we would have 80% power to detect, at a two-sided significance level of 0.05, an absolute difference of at least 3.8% in the incidence rates of HG between the study groups.

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Randomization

We randomized primary care clinicians who provide outpatient care at Eskenazi Health, to see, or not see, the alert tool in outpatient clinical practice, for four months. For clinicians in the intervention group, the tool was displayed for all outpatients who were 21 or more years of age and were prescribed any of the following drugs for DM: acarbose, acetohexamide, alogliptin, canagliflozin, chlorpropamide, colesevelam, dapagliflozin, exenatide, glibenclamide, glimepiride, glipizide, glyburide, insulin, linagliptin, liraglutide, meglitol, metformin, nateglinide, pioglitazone, pramlintide, repaglinide, rosiglitazone, saxagliptin, sitagliptin, tolazamide, or voglibose. During the five-month follow-up period, we assessed patients' characteristics, prescriptions, diagnostic testing, and HG. Clinicians randomized to the control group did not see the computerized alert tool displayed for their patients while logged into the EHR.

Blinding

Clinicians in the intervention group did not receive specific training about the alert tool, because they are accustomed to seeing many different types of EHR-based alert tools without alert-specific training, and we sought to provide them with a typical experience in this regard, along with the availability of online documentation for those seeking details. Of course, the clinicians could not be blinded to the existence of the tool. Clinicians in the control group were not informed about the availability of the tool in the intervention group, but they might have learned about the tool through discussions with other healthcare personnel. The study team did not interact directly with the participating clinicians about the tool during the intervention period. The study design required the analyst to become aware of the group assignments during the analysis.

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Statistical methods

The index visit was defined as the first visit of an eligible patient to an outpatient primary care provider during the four-month intervention period. Intervention and control groups were analyzed with intention to treat, where the intervention was considered the treatment. Categorical variables with more than two levels were compared by a multinomial model, with fixed effect for the intervention group, and a random intercept for the primary care physician. Binary variables were compared by means of a logistic model, and continuous variables were compared by means of a linear model with similar independent variables. Similar methods were used to test for differences between quintiles of the predicted HG risk for intervention subjects. Analyses were conducted using SAS/STAT software, version 9.4 (SAS Institute, Inc., Cary, NC).

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RESULTS

The intervention period was 14 January 2016 to 30 April 2016. The follow-up period was 01 May 2016 to 30 September 2016. **Table 1** shows the demographic and clinical characteristics of each group, as well as outcomes. Intervention (N=3350) and control (N=3395) patients visited 220 PCPs. Patients' mean age was 55 years (SD 13), with 61% female, 49% black, 27% white, and 49% with Medicaid.

Outcomes by study group. Intervention PCPs (N=97) were shown 18,645 alerts about HG. Mean A1c (8.7%) and body mass index (35.2 kg/m^2) were similar at baseline between groups (**Table 1**). During the five-month follow-up period, the frequency of A1c testing and HG events was unchanged. The intervention group had 172 subjects who had a total of 218 episodes of HG; the control group had 168 subjects who had a total of 219 episodes. Per 100 patients, the intervention group had significantly fewer SU refills (6 vs. 8; $p<0.05$) and fewer outpatient encounters (470 vs. 502; $p<0.05$).

Outcomes by HG risk. We found numerous significant differences among quintiles of intervention patients by HG risk (**Table 2**). Patients with the highest risk of HG had more blood glucose tests, more A1c tests, and more new, refilled, changed, or discontinued insulin prescriptions. Although the mean A1c following the index date was about 8.5% at both extremes of HG risk, A1c before the index date was highest in the group with lowest HG risk.

Other measures. Few patients (N=13) had prescriptions for glucose tablets or glucagon, and few appeared to receive HG-specific education that was documented in the medical record. Clinicians' feedback about the alert tool indicated that the tool was useful, but the tool or its contents were not always prominent enough. Alert fatigue was mentioned as a potential barrier. In some cases, a greater understanding about the tool or its information was desired.

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Anecdotally, we also noted that several clinicians commented that the risk numbers reported by the tool appeared "too high" for action; in other words, the numbers were sometimes difficult to believe. No harms were identified as a result of the intervention.

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DISCUSSION

This study of 6,745 adult patients with diabetes who visited PCPs randomized to see or not see a HG alert tool showed that using the EHR to alert clinicians about the risk of HG was associated with 25% fewer SU refills and 6.4% fewer outpatient encounters over five months. These findings may be clinically and economically meaningful: the alert tool can have an impact in the management of DM. Because SU drugs have been associated with HG, "de-prescribing" or de-intensification of SU can be expected to help some patients with HG. In addition, fewer encounters may translate into cost savings. In the inpatient setting, clinical decision support has been shown to decrease the frequency of HG (49, 50), but the outpatient setting poses the additional challenges of more longitudinal care, less frequent contact with patients, and diversity of patients' settings.

Health information technologies are starting to prove useful in the management of DM. Mobile phones have been used (51, 52), including for dietary documentation (53). WellDoc™ provided patients with mobile phone-based software with real-time feedback about glucose levels and medications, and sent electronic logs to the patients' clinicians. This system led to a decrease in A1c (51). The use of secure messaging may help glycemic control, too (54). Virtual-reality tools have been described (55, 56). Huang *et al.* reported that a Web-based decision-support tool including an educational module, assessment of treatment preferences, personalized printout, and estimation of life expectancy and risk of complications was associated with decreased reports of HG over a one-month period (57). Tools based on robust analytics and requiring minimal training may be beneficial. Despite potential benefits, technologies require increased attention to the human factors involved in the interactions between person and machine. In Huang's study, which required training of patients and one hour of training of

clinicians, only 53% of physicians reported that their experience with the decision aid was acceptable. Our alert tool was clearly visible, but the feedback that we received indicated that the PCPs may not have always seen it. This phenomenon may have occurred due to the size or other aspects of the alert's design, or "competing" information on the screen. More comprehensive testing could be done to assess the alert's design-based characteristics and usability. Improving usability may directly increase users' responsiveness to alerts, thereby improving outcomes. Attending to usability among patients can also help. Wearable continuous glucose monitors can now alert patients about imminent HG, identify trends that inform important changes to self-management, and decrease duration (58, 59) and incidence (60) of HG, but today's devices are still invasive and are out of many patients' price range (61).

The number of HG events was similar between study groups. Several factors may account for this. First, though we thought that five months would be enough time to see a response to a change in clinical practice, the follow-up period may still be too short. Second, the capture of HG events might be insufficient: we did not have access to home-based glucometers, so the study might preferentially identify only the most severe cases of HG. Third, the EHR-based alert, though able to change clinical practice, might be insufficient to change the practices far beyond what PCPs are already doing; PCPs more frequently monitored glucose levels and changed insulin prescriptions in their high-risk patients. The alert tool may need to be coupled with greater education of both clinicians and patients regarding additional strategies to improve practice and self-management (62, 63). Our setting's high prevalence of low-income patients can pose a special challenge for self-management strategies, especially those that require resources such as glucometry supplies and adequate sources of nutrition. Timelier sharing of glucometry data between patients and their clinicians might help with adjustments to lifestyle or treatment

that could decrease risk of HG (64). As we found in this study, the alert tool could also benefit from greater visual prominence, which might lead to larger changes in practice.

PCPs sometimes underestimate the incidence of HG. In our study, several clinicians reported that the displayed HG risk appeared “too high to believe”. Many other studies have demonstrated the high incidence of HG in a variety of populations. In our population, we had verified the plausibility of our estimates: indeed, more than 5% of subjects had documented HG even during our short follow-up period. In addition, the expected risk of HG was correlated with the observed incidence. These results underscore our finding that the actual incidence of HG is often higher than clinicians appreciate or would guess, and suggests that clinicians could benefit from greater education about HG and how to work with their patients to improve safety. Cox *et al.* reported significant variation in physicians' knowledge about patients' symptoms and awareness of HG (65). In our study, although patients at the greatest risk of HG saw the most glucose and A1c testing, and the most changes to insulin prescriptions—and some degree of HG risk might not be readily modifiable—additional, more tailored changes to managing these patients appear warranted, including counseling and glucagon prescriptions. For some patients, tailored management might entail de-intensifying drug therapy, using drugs associated with a lower risk of HG (66), or pursuing other strategies to narrow the range of blood glucose levels, to avoid both low and high extremes.

This study has limitations. Since the unit of randomization was the physician and not the patient, there could be imbalances in patient characteristics between groups. The use of both diagnosis codes and NLP to detect HG could be expected to detect most, but not all, of the HG events that came to the clinicians' attention. Mild to moderately severe cases may be under-represented. Patient-identified and self-treated HG events are out of scope for this study. If the

text of a prescription's instructions changed, but the prescription's dose, route, and frequency did not actually change, the prescription would be classified as changed instead of refilled. Patients represented in this study come from an urban safety net and have a high prevalence of minorities, low income, and low education. Other types of patients might yield different outcomes. We have no reason to believe that the clinicians studied would treat DM and HG differently for different populations, or that other clinicians would treat HG in a significantly different way, but the study did not assess that.

In summary, displaying patients' risk of HG to PCPs led to 25% fewer SU refills and 6.4% fewer outpatient encounters. Improving long-term incidence of HG and other outcomes may require greater attention to technical usability, more education of both PCPs and patients, and additional changes to clinical practice.

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TRANSPARENCY

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Authors' contributions. MW, XL, SE, SR, AC, and LR designed the study. JC provided computer programming related to the intervention. SO, ET, and XL conducted the analysis. All authors interpreted the findings. MW drafted the manuscript. All authors reviewed or revised the manuscript, approved the manuscript, and accepted accountability for the work.

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TABLES

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
Age (years)			
21-44	664 (20)	791 (23)	0.3231
45-64	1954 (58)	1967 (58)	
65-74	532 (16)	471 (14)	
75-84	173 (5)	152 (4)	
≥ 85	27 (1)	14 (0.4)	
Gender			
Female	2063 (62)	2060 (61)	0.4736
Male	1287 (38)	1335 (39)	
Race			
Black	1590 (47)	1685 (50)	0.0805
White	986 (29)	852 (25)	
Spanish	163 (5)	180 (5)	
Native American	8 (0.2)	4 (0.1)	
Other	481 (14)	534 (16)	
Unknown	122 (4)	140 (4)	
Insurance			
Medicaid within 90 days of index date	1569 (47)	1666 (49)	0.0599
Insured without Medicaid	1617 (48)	1656 (49)	
Uninsured	164 (5)	73 (2)	
Body mass index (kg/m^2)			
N	3323	3392	
Mean ± SD	35.24 ± 9.19	35.18 ± 9.20	0.8703
Hypoglycemia			
Within 12 months preceding study period: n subjects	448 (13)	436 (13)	0.9934
During study period	175 (5)	173 (5)	0.9921
Pre-existing medical conditions			
Alcohol	290 (9)	310 (9)	0.4240
Autonomic failure	152 (4)	157 (5)	0.8635
Cancer	1479 (44)	1530 (45)	0.1633
Chronic heart failure	179 (5)	175 (5)	0.7343
Coronary artery disease	545 (16)	512 (15)	0.9148
Dementia	386 (12)	361 (11)	0.3822
Diabetic neuropathy	659 (20)	688 (20)	0.5054
Infection within 30 days of index date	201 (6)	214 (6)	0.5566
Last hospital discharge before index date, among those who were hospitalized			
1-30 days before index date	117 (12)	183 (19)	0.3940
31-365 days	371 (39)	333 (35)	
> 365 days	474 (49)	424 (45)	

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Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
A1c			
Last prior to index date			
N	3181	3239	
Mean ± SD	8.63 ±12.80	8.73 ±12.89	0.2478
≤ 6.5%	870 (27)	940 (29)	0.8143
> 6.5%, < 7%	364 (11)	323 (10)	
≥ 7%, < 8%	644 (20)	650 (20)	
≥ 8%, < 9%	423 (13)	409 (13)	
≥ 9%	880 (28)	917 (28)	
Missing	169	156	
After index date			
N	1946	2020	
Mean ± SD	8.28 ± 5.96	8.06 ± 3.55	
Serum calcium (mg/dL) prior to index date			
N	2969	2943	
Mean ± SD	8.93 ± 0.51	8.91 ± 0.50	0.4115
Encounters before index date			
Number of subjects with hospital admission in prior year	492 (15)	517 (15)	0.9963
Number of hospital admissions, mean per patient			
Mean ± SD	0.30 ± 1.02	0.33 ± 1.20	0.8451
Number of outpatient encounters, total, in year prior			
Mean ± SD	10.07 ± 8.39	10.37 ± 8.54	0.2666
Non-emergency outpatient, in year prior			
Mean ± SD	9.29 ± 7.83	9.54 ± 7.80	0.3262
Emergency department, in year prior			
Mean ± SD	0.78 ± 1.60	0.83 ± 1.62	0.2442
Encounters in 5 months after index			
Number of subjects with hospital admission	230 (7)	231 (7)	0.8765
Number of hospital admissions, mean per patient			
Mean ± SD	0.10 ± 0.50	0.10 ± 0.57	0.4566
Number of outpatient encounters, total			
Mean ± SD	4.70 ± 4.54	5.02 ± 4.48	0.0178
Non-emergency outpatient			
Mean ± SD	4.39 ± 4.26	4.68 ± 4.18	0.0247
Emergency department			
Mean ± SD	0.31 ± 0.78	0.34 ± 0.85	0.2000
Any insulin in 5 months after index date, N (%)	537 (16)	482 (14)	0.2118
Long-acting insulin in 5 months after index date			

Hypoglycemia alert

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
Subjects with at least 1 Prescription			
N (%)	303 (9)	265 (8)	0.3755
Number of Prescriptions			
Mean ± SD	2.20 ± 1.84	2.44 ± 2.91	
New			
Mean ± SD	0.04 ± 0.27	0.04 ± 0.28	0.8856
Refilled			
Mean ± SD	0.03 ± 0.21	0.02 ± 0.20	0.4993
Changed			
Mean ± SD	0.04 ± 0.30	0.05 ± 0.51	0.2540
Discontinued			
Mean ± SD	0.03 ± 0.20	0.03 ± 0.20	0.7792
Unknown whether refilled or changed			
Mean ± SD	0.06 ± 0.23	0.04 ± 0.21	0.1276
Short-acting insulin in 5 months after index date			
Subjects with at least 1 Prescription			
N (%)	169 (5)	183 (5)	0.4656
Number of Prescriptions			
Mean ± SD	1.72 ± 1.00	1.76 ± 1.57	
New			
Mean ± SD	0.03 ± 0.18	0.03 ± 0.20	0.5934
Refilled			
Mean ± SD	0.01 ± 0.11	0.01 ± 0.13	0.3056
Changed			
Mean ± SD	0.01 ± 0.15	0.01 ± 0.20	0.9087
Discontinued			
Mean ± SD	0.02 ± 0.12	0.02 ± 0.14	0.2753
Unknown whether refilled or changed			
Mean ± SD	0.02 ± 0.16	0.02 ± 0.15	0.6598
Pre-mixed insulin(e.g., 70/30 or 75/25) in 5 months after index date			
Subjects with at least 1 Prescription			
N (%)	149 (4)	115 (3)	0.1015
Number of Prescriptions			
Mean ± SD	2.00 ± 1.72	2.04 ± 1.58	
New			
Mean ± SD	0.01 ± 0.14	0.01 ± 0.12	0.5492
Refilled			
Mean ± SD	0.01 ± 0.17	0.01 ± 0.16	0.6967
Changed			
Mean ± SD	0.02 ± 0.17	0.01 ± 0.14	0.2611
Discontinued			
Mean ± SD	0.01 ± 0.12	0.01 ± 0.12	0.7599

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Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
Unknown whether refilled or changed			
Mean ± SD	0.04 ± 0.19	0.02 ± 0.15	0.0294
Sulfonylurea in 5 months after index date			
N Subjects with at least 1 Prescription (%)	724 (22)	827 (24)	0.0931
Number of Prescriptions			
Mean ± SD	1.50 ± 0.88	1.55 ± 0.84	0.2286
New			
Mean ± SD	0.06 ± 0.27	0.07 ± 0.26	0.0584
Refilled			
Mean ± SD	0.06 ± 0.27	0.08 ± 0.33	0.0143
Changed			
Mean ± SD	0.02 ± 0.16	0.02 ± 0.18	0.2788
Discontinued			
Mean ± SD	0.04 ± 0.22	0.05 ± 0.22	0.6878
Unknown whether refilled or changed			
Mean ± SD	0.15 ± 0.36	0.16 ± 0.37	0.2991
Glucose tablets in 5 months after index date			
New:	2	7	
Discontinued:	0	3	
Unknown whether refilled or changed	1	1	
Glucagon injection in 5 months after index date			
New	7	6	
Refilled	0	1	
Discontinued	0	1	
Unknown whether refilled or changed	1	1	
Antibiotics in 5 months after index date			
Number of Subjects with at least 1 Prescription			
Mean ± SD	0.20 ± 0.40	0.19 ± 0.39	0.5669
Number of Prescriptions			
Mean ± SD	0.39 ± 1.12	0.37 ± 1.01	0.6572
New			
Mean ± SD	0.17 ± 0.54	0.15 ± 0.48	0.3345
Refilled			
Mean ± SD	0.03 ± 0.24	0.03 ± 0.20	0.6583
Changed			
Mean ± SD	0.01 ± 0.14	0.02 ± 0.17	0.1464
Discontinued			
Mean ± SD	0.15 ± 0.45	0.15 ± 0.45	0.9649

Hypoglycemia alert

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
Unknown whether refilled or changed			
Mean ± SD	0.03 ± 0.17	0.02 ± 0.14	0.3832
Number of diagnostic tests in 5 months after index date			
A1C			
Mean ± SD	0.72 ± 0.72	0.74 ± 0.72	0.0728
Glucose level			
Mean ± SD	1.55 ± 3.57	1.63 ± 3.91	0.4920
Creatinine			
Mean ± SD	1.20 ± 3.08	1.22 ± 3.20	0.6280
Glomerular filtration rate, estimated (mL/min/1.73m^2), baseline period			
N	2888	2853	
Mean ± SD	103.16 ±40.07	104.39 ±38.47	0.8177
Patient education related to hypoglycemia	2	8	

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
HG Risk Score						
N	670	670	670	670	670	
Mean ± SD	0.14 ± 0.05	0.26 ± 0.03	0.36 ± 0.03	0.48 ± 0.04	0.72 ± 0.11	<.0001
Median (Min, Max)	0.15 (0.02, 0.21)	0.26 (0.21, 0.31)	0.36 (0.31, 0.42)	0.48 (0.42, 0.57)	0.70 (0.57, 0.99)	
Subjects (%) with HG						
In 12 months preceding study period	50 (8)	50 (8)	72 (11)	85 (13)	191 (29)	<.0001
During study period	23 (3)	19 (3)	31 (5)	32 (5)	70 (10)	<.0001
Age						
Mean ± SD	50.1 ±12.8	53.6 ±12.3	55.1 ±12.7	57.6 ±12.7	59.2 ±11.5	<.0001
Median (Min, Max)	51 (21, 92)	54 (22, 90)	56 (21, 89)	58.5 (21, 90)	60 (24, 90)	
Gender						<.0001
Female	380 (57)	415 (62)	450 (67)	385 (57)	433 (65)	
Male	290 (43)	255 (38)	220 (33)	285 (42)	237 (35)	
Race						<.0001
White	196 (29)	229 (34)	212 (32)	183 (27)	166 (25)	
Black	146 (22)	227 (34)	335 (50)	408 (6)	474 (71)	
Hispanic	85 (13)	38 (6)	21 (3)	16 (2)	3 (0.4)	
Native American	2 (0.3)	4 (1)	1 (0.1)	1 (0.1)	0 (0.0)	
Other	199 (30)	134 (20)	81 (12)	48 (7)	19 (3)	
Unknown	42 (6)	38 (6)	20 (3)	14 (2)	8 (1)	
Insurance						
Insured without Medicaid	362 (54)	370 (55)	337 (50)	281 (42)	219 (33)	<.0001
Medicaid	261 (39)	269 (40)	288 (43)	368 (55)	431 (64)	

Hypoglycemia alert

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
Uninsured	47 (7)	31 (5)	45 (7)	21 (3)	20 (3)	
Body Mass Index (kg/m^2)						
N	663	666	663	664	667	
Mean ± SD	35.87 ± 9.83	36.00 ± 9.22	35.75 ± 9.25	34.16 ± 8.30	34.43 ± 9.13	<.0001
Median (Min, Max)	34 (14, 80)	35 (15, 82)	34 (14, 78)	33 (12, 89)	33 (12, 71)	
Prior medical conditions						
Alcohol	32 (5)	43 (6)	51 (8)	71 (11)	93 (14)	<.0001
Autonomic failure	43 (6)	22 (3)	18 (3)	30 (4)	39 (6)	0.0032
Cancer	229 (34)	252 (38)	299 (45)	313 (47)	386 (58)	<.0001
Chronic heart failure	8 (1)	8 (1)	14 (2)	43 (6)	106 (16)	<.0001
Coronary artery disease	51 (8)	60 (9)	77 (12)	141 (21)	216 (32)	<.0001
Dementia	36 (5)	52 (8)	78 (12)	87 (13)	133 (20)	<.0001
Diabetic neuropathy	107 (16)	86 (13)	82 (12)	149 (22)	235 (35)	<.0001
Infection within 30 days of index date	32 (5)	37 (6)	39 (6)	40 (6)	53 (8)	0.1692
Last hospital discharge before index date						
N	565	570	514	435	304	
1-30 days	10 (9)	4 (4)	8 (5)	29 (12)	66 (18)	<.0001
31-365 days	31 (30)	41 (41)	56 (36)	81 (34)	162 (44)	
> 365 days	64 (61)	55 (55)	92 (59)	125 (53)	138 (38)	
Last A1C prior to index date						
N	599	643	639	645	655	
Mean ± SD	10.01 ±23.73	8.68 ±10.58	8.12 ± 4.18	8.35 ±12.23	8.09 ± 2.23	0.0145
Missing	71	27	31	25	15	
≤ 6.5%	123 (21)	170 (26)	191 (30)	204 (32)	182 (28)	<.0001

Hypoglycemia alert

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
> 6.5% to < 7%	59 (10)	86 (13)	76 (12)	72 (11)	71 (11)	
≥ 7% to < 8%	133 (22)	119 (19)	131 (20)	124 (19)	137 (21)	
≥ 8% to < 9%	84 (14)	92 (14)	81 (13)	91 (14)	75 (11)	
≤ 9%	200 (33)	176 (27)	160 (25)	154 (24)	190 (29)	
A1C after index date						
N	375	363	372	404	432	
Mean ± SD	8.50 ± 8.01	8.52 ± 6.44	7.79 ± 1.90	8.00 ± 2.09	8.54 ± 7.89	
A1C change						
N	349	356	360	396	426	
Mean ± SD	-2.53 ± 31.72	-0.70 ± 15.26	-0.18 ± 1.58	-0.74 ± 15.15	0.44 ± 7.97	0.1860
Number of subjects with any insulin in 5 months after index date	78 (12)	84 (13)	88 (13)	114 (17)	173 (26)	<.0001
Long-acting insulin prescriptions in 5 months after index date						
Number of Subjects with at least one Prescription (%)	48 (7)	45 (7)	44 (7)	64 (10)	102 (15)	<.0001
Number of Prescriptions						
Mean ± SD	2.29 ± 2.00	1.96 ± 1.46	2.00 ± 1.35	2.16 ± 1.83	2.37 ± 2.09	<.0001
Median (Min, Max)	2 (1, 12)	1 (1, 7)	2 (1, 8)	2 (1, 11)	2 (1, 12)	
New						
Mean ± SD	0.04 ± 0.23	0.02 ± 0.17	0.03 ± 0.20	0.04 ± 0.25	0.10 ± 0.43	<.0001
Median (Min, Max)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 3)	0 (0, 5)	
Refilled						
Mean ± SD	0.03 ± 0.23	0.02 ± 0.21	0.02 ± 0.21	0.03 ± 0.23	0.03 ± 0.18	0.8658

Hypoglycemia alert

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
Changed						
Mean ± SD	0.03 ± 0.28	0.02 ± 0.23	0.02 ± 0.18	0.04 ± 0.30	0.08 ± 0.43	0.0008
Discontinued						
Mean ± SD	0.03 ± 0.21	0.01 ± 0.13	0.02 ± 0.13	0.03 ± 0.21	0.05 ± 0.28	0.0026
Short-acting insulin prescriptions in 5 months after index date						
N subjects with at least one prescription (%)	20 (3.0)	28 (4.2)	32 (4.8)	32 (4.8)	57 (8.5)	0.0001
Number of Prescriptions						
Mean ± SD	2.05 ± 1.15	1.64 ± 0.99	1.62 ± 1.01	1.62 ± 0.94	1.74 ± 0.96	
New						
Mean ± SD	0.02 ± 0.15	0.02 ± 0.18	0.02 ± 0.13	0.02 ± 0.15	0.05 ± 0.25	0.0090
Refilled						
Mean ± SD	0.004 ± 0.086	0.004 ± 0.067	0.01 ± 0.10	0.01 ± 0.13	0.02 ± 0.15	0.4168
Changed						
Mean ± SD	0.02 ± 0.16	0.01 ± 0.14	0.02 ± 0.19	0.01 ± 0.11	0.02 ± 0.13	0.6999
Discontinued						
Mean ± SD	0.01 ± 0.10	0.01 ± 0.13	0.01 ± 0.09	0.01 ± 0.09	0.03 ± 0.18	0.0010
Pre-mixed insulin prescriptions in 5 months after index date						
N subjects with at least one prescription (%)	22 (3)	24 (4)	24 (4)	31 (5)	48 (7)	0.0032
Number of Prescriptions						
Mean ± SD	1.86 ± 1.32	1.29 ± 0.55	2.08 ± 1.72	1.71 ± 1.13	2.56 ± 2.33	
Median (Min, Max)	1 (1, 6)	1 (1, 3)	1 (1, 7)	1 (1, 6)	2 (1, 12)	
New						
Mean ± SD	0.003 ± 0.055	0.004 ± 0.067	0.02 ± 0.15	0.01 ± 0.10	0.03 ± 0.24	0.0137

Hypoglycemia alert

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
Refilled						
Mean ± SD	0.004 ± 0.086	0.01 ± 0.10	0.01 ± 0.09	0.02 ± 0.18	0.04 ± 0.29	0.0034
Changed						
Mean ± SD	0.02 ± 0.17	0.001 ± 0.039	0.01 ± 0.10	0.01 ± 0.14	0.03 ± 0.29	0.0098
Discontinued						
Mean ± SD	0.01 ± 0.12	0.01 ± 0.08	0.01 ± 0.13	0.01 ± 0.08	0.03 ± 0.18	0.0066
Sulfonylurea prescriptions in 5 months after index date						
N subjects with at least one prescription (%)	167 (25)	148 (22)	158 (24)	144 (21)	107 (16)	0.0003
Number of Prescriptions						
Mean ± SD	1.44 ± 0.69	1.49 ± 0.82	1.38 ± 0.82	1.62 ± 1.04	1.60 ± 1.01	
New						
Mean ± SD	0.07 ± 0.26	0.06 ± 0.27	0.05 ± 0.24	0.05 ± 0.30	0.05 ± 0.26	0.5691
Refilled						
Mean ± SD	0.07 ± 0.29	0.05 ± 0.24	0.04 ± 0.22	0.07 ± 0.32	0.05 ± 0.28	0.1355
Changed						
Mean ± SD	0.02 ± 0.13	0.03 ± 0.20	0.02 ± 0.20	0.02 ± 0.17	0.004 ± 0.086	0.1123
Discontinued						
Mean ± SD	0.05 ± 0.23	0.04 ± 0.22	0.04 ± 0.22	0.05 ± 0.23	0.04 ± 0.20	0.8869
A1c tests in 5 months after index date						
Subjects with at least 1 test						
N	375	363	372	404	432	

Hypoglycemia alert

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)						
	HG Risk Quintile					
Characteristic	**1**	**2**	**3**	**4**	**5**	**p-value**
Mean ± SD	1.20 ± 0.48	1.20 ± 0.45	1.20 ± 0.44	1.22 ± 0.46	1.35 ± 0.63	
All subjects						
N	670	670	670	670	670	
Mean ± SD	0.67 ± 0.70	0.65 ± 0.68	0.67 ± 0.68	0.73 ± 0.70	0.87 ± 0.82	<.0001

FIGURE LEGENDS

Figure 1. Alert tool in initial collapsed form. The alert shows the two-year risk of hypoglycemia. It provides a link ("Learn more and see options") to expand the display to show more information (see **Figure 2**).

Figure 2. Alert tool in expanded form. Patients' characteristics that contribute to risk of hypoglycemia are shown. The user can modify these to test hypothetical scenarios.

Hypoglycemia alert

FIGURES

Figure 1. Alert tool in initial collapsed form.

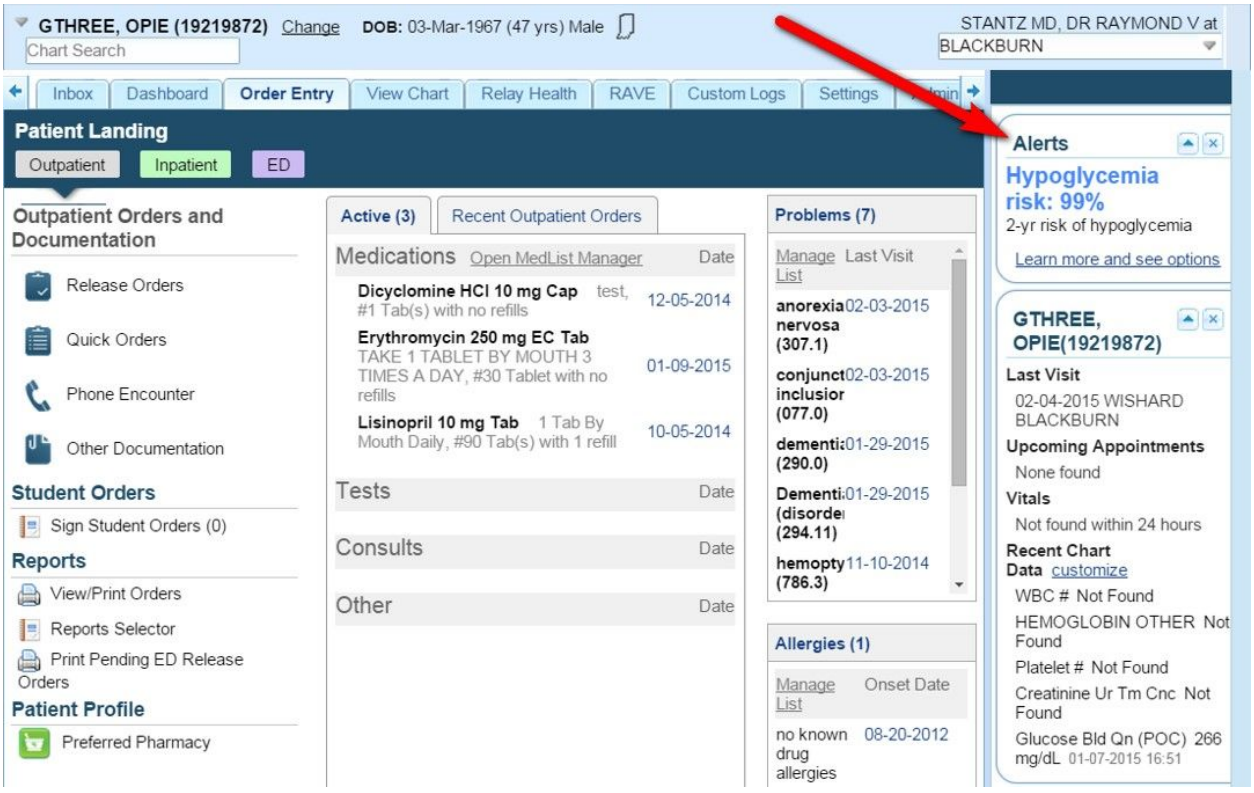

Figure 2. Alert tool in expanded form.

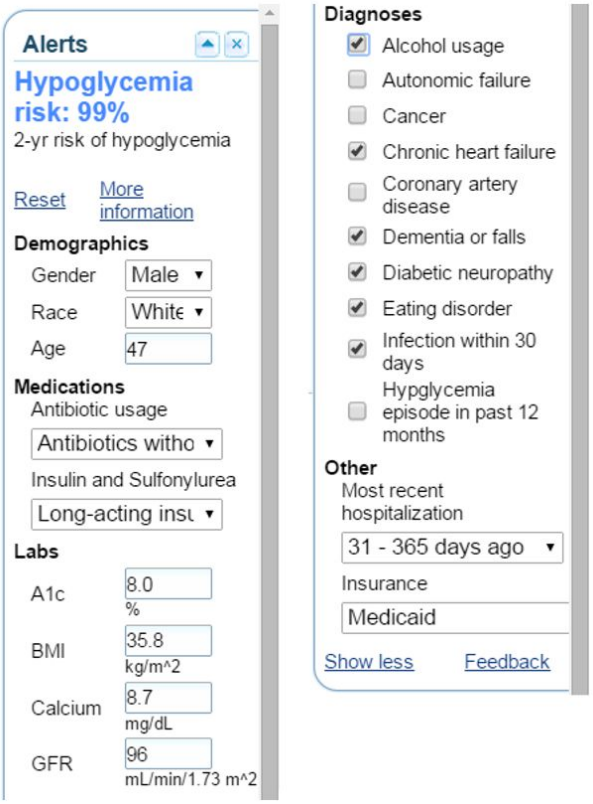

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
Age (years)			
21-44	664 (20)	791 (23)	0.3231
45-64	1954 (58)	1967 (58)	
65-74	532 (16)	471 (14)	
75-84	173 (5)	152 (4)	
≥ 85	27 (1)	14 (0.4)	
Gender			
Female	2063 (62)	2060 (61)	0.4736
Male	1287 (38)	1335 (39)	
Race			
Black	1590 (47)	1685 (50)	0.0805
White	986 (29)	852 (25)	
Spanish	163 (5)	180 (5)	
Native American	8 (0.2)	4 (0.1)	
Other	481 (14)	534 (16)	
Unknown	122 (4)	140 (4)	
Insurance			
Medicaid within 90 days of index date	1569 (47)	1666 (49)	0.0599
Insured without Medicaid	1617 (48)	1656 (49)	
Uninsured	164 (5)	73 (2)	
Body mass index (kg/m^2)			
N	3323	3392	
Mean ± SD	35.24 ± 9.19	35.18 ± 9.20	0.8703
Hypoglycemia			
Within 12 months preceding study period: n subjects	448 (13)	436 (13)	0.9934
During study period	175 (5)	173 (5)	0.9921
Pre-existing medical conditions			
Alcohol	290 (9)	310 (9)	0.4240
Autonomic failure	152 (4)	157 (5)	0.8635
Cancer	1479 (44)	1530 (45)	0.1633
Chronic heart failure	179 (5)	175 (5)	0.7343
Coronary artery disease	545 (16)	512 (15)	0.9148
Dementia	386 (12)	361 (11)	0.3822
Diabetic neuropathy	659 (20)	688 (20)	0.5054
Infection within 30 days of index date	201 (6)	214 (6)	0.5566
Last hospital discharge before index date, among those who were hospitalized			
1-30 days before index date	117 (12)	183 (19)	0.3940
31-365 days	371 (39)	333 (35)	
> 365 days	474 (49)	424 (45)	
A1c			
Last prior to index date			
N	3181	3239	
Mean ± SD	8.63 ±12.80	8.73 ±12.89	0.2478

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
≤ 6.5%	870 (27)	940 (29)	0.8143
> 6.5%, < 7%	364 (11)	323 (10)	
≥ 7%, < 8%	644 (20)	650 (20)	
≥ 8%, < 9%	423 (13)	409 (13)	
≥ 9%	880 (28)	917 (28)	
Missing	169	156	
After index date			
N	1946	2020	
Mean ± SD	8.28 ± 5.96	8.06 ± 3.55	
Serum calcium (mg/dL) prior to index date			
N	2969	2943	
Mean ± SD	8.93 ± 0.51	8.91 ± 0.50	0.4115
Encounters before index date			
Number of subjects with hospital admission in prior year	492 (15)	517 (15)	0.9963
Number of hospital admissions, mean per patient			
Mean ± SD	0.30 ± 1.02	0.33 ± 1.20	0.8451
Number of outpatient encounters, total, in year prior			
Mean ± SD	10.07 ± 8.39	10.37 ± 8.54	0.2666
Non-emergency outpatient, in year prior			
Mean ± SD	9.29 ± 7.83	9.54 ± 7.80	0.3262
Emergency department, in year prior			
Mean ± SD	0.78 ± 1.60	0.83 ± 1.62	0.2442
Encounters in 5 months after index			
Number of subjects with hospital admission	230 (7)	231 (7)	0.8765
Number of hospital admissions, mean per patient			
Mean ± SD	0.10 ± 0.50	0.10 ± 0.57	0.4566
Number of outpatient encounters, total			
Mean ± SD	4.70 ± 4.54	5.02 ± 4.48	0.0178
Non-emergency outpatient			
Mean ± SD	4.39 ± 4.26	4.68 ± 4.18	0.0247
Emergency department			
Mean ± SD	0.31 ± 0.78	0.34 ± 0.85	0.2000
Any insulin in 5 months after index date, N (%)	537 (16)	482 (14)	0.2118
Long-acting insulin in 5 months after index date			
Subjects with at least 1 Prescription			
N (%)	303 (9)	265 (8)	0.3755
Number of Prescriptions			
Mean ± SD	2.20 ± 1.84	2.44 ± 2.91	

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
New			
Mean ± SD	0.04 ± 0.27	0.04 ± 0.28	0.8856
Refilled			
Mean ± SD	0.03 ± 0.21	0.02 ± 0.20	0.4993
Changed			
Mean ± SD	0.04 ± 0.30	0.05 ± 0.51	0.2540
Discontinued			
Mean ± SD	0.03 ± 0.20	0.03 ± 0.20	0.7792
Unknown whether refilled or changed			
Mean ± SD	0.06 ± 0.23	0.04 ± 0.21	0.1276
Short-acting insulin in 5 months after index date			
Subjects with at least 1 Prescription			
N (%)	169 (5)	183 (5)	0.4656
Number of Prescriptions			
Mean ± SD	1.72 ± 1.00	1.76 ± 1.57	
New			
Mean ± SD	0.03 ± 0.18	0.03 ± 0.20	0.5934
Refilled			
Mean ± SD	0.01 ± 0.11	0.01 ± 0.13	0.3056
Changed			
Mean ± SD	0.01 ± 0.15	0.01 ± 0.20	0.9087
Discontinued			
Mean ± SD	0.02 ± 0.12	0.02 ± 0.14	0.2753
Unknown whether refilled or changed			
Mean ± SD	0.02 ± 0.16	0.02 ± 0.15	0.6598
Pre-mixed insulin(e.g., 70/30 or 75/25) in 5 months after index date			
Subjects with at least 1 Prescription			
N (%)	149 (4)	115 (3)	0.1015
Number of Prescriptions			
Mean ± SD	2.00 ± 1.72	2.04 ± 1.58	
New			
Mean ± SD	0.01 ± 0.14	0.01 ± 0.12	0.5492
Refilled			
Mean ± SD	0.01 ± 0.17	0.01 ± 0.16	0.6967
Changed			
Mean ± SD	0.02 ± 0.17	0.01 ± 0.14	0.2611
Discontinued			
Mean ± SD	0.01 ± 0.12	0.01 ± 0.12	0.7599
Unknown whether refilled or changed			
Mean ± SD	0.04 ± 0.19	0.02 ± 0.15	0.0294
Sulfonylurea in 5 months after index date			

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
N Subjects with at least 1 Prescription (%)	724 (22)	827 (24)	0.0931
Number of Prescriptions			
Mean ± SD	1.50 ± 0.88	1.55 ± 0.84	0.2286
New			
Mean ± SD	0.06 ± 0.27	0.07 ± 0.26	0.0584
Refilled			
Mean ± SD	0.06 ± 0.27	0.08 ± 0.33	0.0143
Changed			
Mean ± SD	0.02 ± 0.16	0.02 ± 0.18	0.2788
Discontinued			
Mean ± SD	0.04 ± 0.22	0.05 ± 0.22	0.6878
Unknown whether refilled or changed			
Mean ± SD	0.15 ± 0.36	0.16 ± 0.37	0.2991
Glucose tablets in 5 months after index date			
New:	2	7	
Discontinued:	0	3	
Unknown whether refilled or changed	1	1	
Glucagon injection in 5 months after index date			
New	7	6	
Refilled	0	1	
Discontinued	0	1	
Unknown whether refilled or changed	1	1	
Antibiotics in 5 months after index date			
Number of Subjects with at least 1 Prescription			
Mean ± SD	0.20 ± 0.40	0.19 ± 0.39	0.5669
Number of Prescriptions			
Mean ± SD	0.39 ± 1.12	0.37 ± 1.01	0.6572
New			
Mean ± SD	0.17 ± 0.54	0.15 ± 0.48	0.3345
Refilled			
Mean ± SD	0.03 ± 0.24	0.03 ± 0.20	0.6583
Changed			
Mean ± SD	0.01 ± 0.14	0.02 ± 0.17	0.1464
Discontinued			
Mean ± SD	0.15 ± 0.45	0.15 ± 0.45	0.9649
Unknown whether refilled or changed			
Mean ± SD	0.03 ± 0.17	0.02 ± 0.14	0.3832
Number of diagnostic tests in 5 months after index date			
A1C			

Table 1. Characteristics of patients			
Characteristic	**Intervention N (%) (N=3350)**	**Control N (%) (N= 3395)**	**p-value**
Mean ± SD	0.72 ± 0.72	0.74 ± 0.72	0.0728
Glucose level			
Mean ± SD	1.55 ± 3.57	1.63 ± 3.91	0.4920
Creatinine			
Mean ± SD	1.20 ± 3.08	1.22 ± 3.20	0.6280
Glomerular filtration rate, estimated (mL/min/1.73m^2), baseline period			
N	2888	2853	
Mean ± SD	103.16 ±40.07	104.39 ±38.47	0.8177
Patient education related to hypoglycemia	2	8	

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
HG Risk Score						
N	670	670	670	670	670	
Mean ± SD	0.14 ± 0.05	0.26 ± 0.03	0.36 ± 0.03	0.48 ± 0.04	0.72 ± 0.11	<.0001
Median (Min, Max)	0.15 (0.02, 0.21)	0.26 (0.21, 0.31)	0.36 (0.31, 0.42)	0.48 (0.42, 0.57)	0.70 (0.57, 0.99)	
Subjects (%) with HG						
In 12 months preceding study period	50 (8)	50 (8)	72 (11)	85 (13)	191 (29)	<.0001
During study period	23 (3)	19 (3)	31 (5)	32 (5)	70 (10)	<.0001
Age						
Mean ± SD	50.1 ±12.8	53.6 ±12.3	55.1 ±12.7	57.6 ±12.7	59.2 ±11.5	<.0001
Median (Min, Max)	51 (21, 92)	54 (22, 90)	56 (21, 89)	58.5 (21, 90)	60 (24, 90)	
Gender						<.0001
Female	380 (57)	415 (62)	450 (67)	385 (57)	433 (65)	
Male	290 (43)	255 (38)	220 (33)	285 (42)	237 (35)	
Race						<.0001
White	196 (29)	229 (34)	212 (32)	183 (27)	166 (25)	
Black	146 (22)	227 (34)	335 (50)	408 (6)	474 (71)	
Hispanic	85 (13)	38 (6)	21 (3)	16 (2)	3 (0.4)	
Native American	2 (0.3)	4 (1)	1 (0.1)	1 (0.1)	0 (0.0)	
Other	199 (30)	134 (20)	81 (12)	48 (7)	19 (3)	
Unknown	42 (6)	38 (6)	20 (3)	14 (2)	8 (1)	
Insurance						
Insured without Medicaid	362 (54)	370 (55)	337 (50)	281 (42)	219 (33)	<.0001
Medicaid	261 (39)	269 (40)	288 (43)	368 (55)	431 (64)	
Uninsured	47 (7)	31 (5)	45 (7)	21 (3)	20 (3)	

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
Body Mass Index (kg/m^2)						
N	663	666	663	664	667	
Mean ± SD	35.87 ± 9.83	36.00 ± 9.22	35.75 ± 9.25	34.16 ± 8.30	34.43 ± 9.13	<.0001
Median (Min, Max)	34 (14, 80)	35 (15, 82)	34 (14, 78)	33 (12, 89)	33 (12, 71)	
Prior medical conditions						
Alcohol	32 (5)	43 (6)	51 (8)	71 (11)	93 (14)	<.0001
Autonomic failure	43 (6)	22 (3)	18 (3)	30 (4)	39 (6)	0.0032
Cancer	229 (34)	252 (38)	299 (45)	313 (47)	386 (58)	<.0001
Chronic heart failure	8 (1)	8 (1)	14 (2)	43 (6)	106 (16)	<.0001
Coronary artery disease	51 (8)	60 (9)	77 (12)	141 (21)	216 (32)	<.0001
Dementia	36 (5)	52 (8)	78 (12)	87 (13)	133 (20)	<.0001
Diabetic neuropathy	107 (16)	86 (13)	82 (12)	149 (22)	235 (35)	<.0001
Infection within 30 days of index date	32 (5)	37 (6)	39 (6)	40 (6)	53 (8)	0.1692
Last hospital discharge before index date						
N	565	570	514	435	304	
1-30 days	10 (9)	4 (4)	8 (5)	29 (12)	66 (18)	<.0001
31-365 days	31 (30)	41 (41)	56 (36)	81 (34)	162 (44)	
> 365 days	64 (61)	55 (55)	92 (59)	125 (53)	138 (38)	
Last A1C prior to index date						
N	599	643	639	645	655	
Mean ± SD	10.01 ±23.73	8.68 ±10.58	8.12 ± 4.18	8.35 ±12.23	8.09 ± 2.23	0.0145
Missing	71	27	31	25	15	
≤ 6.5%	123 (21)	170 (26)	191 (30)	204 (32)	182 (28)	<.0001
> 6.5% to < 7%	59 (10)	86 (13)	76 (12)	72 (11)	71 (11)	

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
≥ 7% to < 8%	133 (22)	119 (19)	131 (20)	124 (19)	137 (21)	
≥ 8% to < 9%	84 (14)	92 (14)	81 (13)	91 (14)	75 (11)	
≤ 9%	200 (33)	176 (27)	160 (25)	154 (24)	190 (29)	
A1C after index date						
N	375	363	372	404	432	
Mean ± SD	8.50 ± 8.01	8.52 ± 6.44	7.79 ± 1.90	8.00 ± 2.09	8.54 ± 7.89	
A1C change						
N	349	356	360	396	426	
Mean ± SD	-2.53 ± 31.72	-0.70 ± 15.26	-0.18 ± 1.58	-0.74 ± 15.15	0.44 ± 7.97	0.1860
Number of subjects with any insulin in 5 months after index date	78 (12)	84 (13)	88 (13)	114 (17)	173 (26)	<.0001
Long-acting insulin prescriptions in 5 months after index date						
Number of Subjects with at least one Prescription (%)	48 (7)	45 (7)	44 (7)	64 (10)	102 (15)	<.0001
Number of Prescriptions						
Mean ± SD	2.29 ± 2.00	1.96 ± 1.46	2.00 ± 1.35	2.16 ± 1.83	2.37 ± 2.09	<.0001
Median (Min, Max)	2 (1, 12)	1 (1, 7)	2 (1, 8)	2 (1, 11)	2 (1, 12)	
New						
Mean ± SD	0.04 ± 0.23	0.02 ± 0.17	0.03 ± 0.20	0.04 ± 0.25	0.10 ± 0.43	<.0001
Median (Min, Max)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 3)	0 (0, 5)	
Refilled						
Mean ± SD	0.03 ± 0.23	0.02 ± 0.21	0.02 ± 0.21	0.03 ± 0.23	0.03 ± 0.18	0.8658

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
Changed						
Mean ± SD	0.03 ± 0.28	0.02 ± 0.23	0.02 ± 0.18	0.04 ± 0.30	0.08 ± 0.43	0.0008
Discontinued						
Mean ± SD	0.03 ± 0.21	0.01 ± 0.13	0.02 ± 0.13	0.03 ± 0.21	0.05 ± 0.28	0.0026
Short-acting insulin prescriptions in 5 months after index date						
N subjects with at least one prescription (%)	20 (3.0)	28 (4.2)	32 (4.8)	32 (4.8)	57 (8.5)	0.0001
Number of Prescriptions						
Mean ± SD	2.05 ± 1.15	1.64 ± 0.99	1.62 ± 1.01	1.62 ± 0.94	1.74 ± 0.96	
New						
Mean ± SD	0.02 ± 0.15	0.02 ± 0.18	0.02 ± 0.13	0.02 ± 0.15	0.05 ± 0.25	0.0090
Refilled						
Mean ± SD	0.004 ± 0.086	0.004 ± 0.067	0.01 ± 0.10	0.01 ± 0.13	0.02 ± 0.15	0.4168
Changed						
Mean ± SD	0.02 ± 0.16	0.01 ± 0.14	0.02 ± 0.19	0.01 ± 0.11	0.02 ± 0.13	0.6999
Discontinued						
Mean ± SD	0.01 ± 0.10	0.01 ± 0.13	0.01 ± 0.09	0.01 ± 0.09	0.03 ± 0.18	0.0010
Pre-mixed insulin prescriptions in 5 months after index date						
N subjects with at least one prescription (%)	22 (3)	24 (4)	24 (4)	31 (5)	48 (7)	0.0032
Number of Prescriptions						
Mean ± SD	1.86 ± 1.32	1.29 ± 0.55	2.08 ± 1.72	1.71 ± 1.13	2.56 ± 2.33	
Median (Min, Max)	1 (1, 6)	1 (1, 3)	1 (1, 7)	1 (1, 6)	2 (1, 12)	
New						
Mean ± SD	0.003 ± 0.055	0.004 ± 0.067	0.02 ± 0.15	0.01 ± 0.10	0.03 ± 0.24	0.0137

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)

Characteristic	HG Risk Quintile 1	2	3	4	5	p-value
Refilled						
Mean ± SD	0.004 ± 0.086	0.01 ± 0.10	0.01 ± 0.09	0.02 ± 0.18	0.04 ± 0.29	0.0034
Changed						
Mean ± SD	0.02 ± 0.17	0.001 ± 0.039	0.01 ± 0.10	0.01 ± 0.14	0.03 ± 0.29	0.0098
Discontinued						
Mean ± SD	0.01 ± 0.12	0.01 ± 0.08	0.01 ± 0.13	0.01 ± 0.08	0.03 ± 0.18	0.0066
Sulfonylurea prescriptions in 5 months after index date						
N subjects with at least one prescription (%)	167 (25)	148 (22)	158 (24)	144 (21)	107 (16)	0.0003
Number of Prescriptions						
Mean ± SD	1.44 ± 0.69	1.49 ± 0.82	1.38 ± 0.82	1.62 ± 1.04	1.60 ± 1.01	
New						
Mean ± SD	0.07 ± 0.26	0.06 ± 0.27	0.05 ± 0.24	0.05 ± 0.30	0.05 ± 0.26	0.5691
Refilled						
Mean ± SD	0.07 ± 0.29	0.05 ± 0.24	0.04 ± 0.22	0.07 ± 0.32	0.05 ± 0.28	0.1355
Changed						
Mean ± SD	0.02 ± 0.13	0.03 ± 0.20	0.02 ± 0.20	0.02 ± 0.17	0.004 ± 0.086	0.1123
Discontinued						
Mean ± SD	0.05 ± 0.23	0.04 ± 0.22	0.04 ± 0.22	0.05 ± 0.23	0.04 ± 0.20	0.8869
A1c tests in 5 months after index date						
Subjects with at least 1 test						
N	375	363	372	404	432	

Table 2. Characteristics of intervention patients, by quintile of estimated risk of hypoglycemia (HG)						
	HG Risk Quintile					
Characteristic	**1**	**2**	**3**	**4**	**5**	**p-value**
Mean ± SD	1.20 ± 0.48	1.20 ± 0.45	1.20 ± 0.44	1.22 ± 0.46	1.35 ± 0.63	
All subjects						
N	670	670	670	670	670	
Mean ± SD	0.67 ± 0.70	0.65 ± 0.68	0.67 ± 0.68	0.73 ± 0.70	0.87 ± 0.82	<.0001

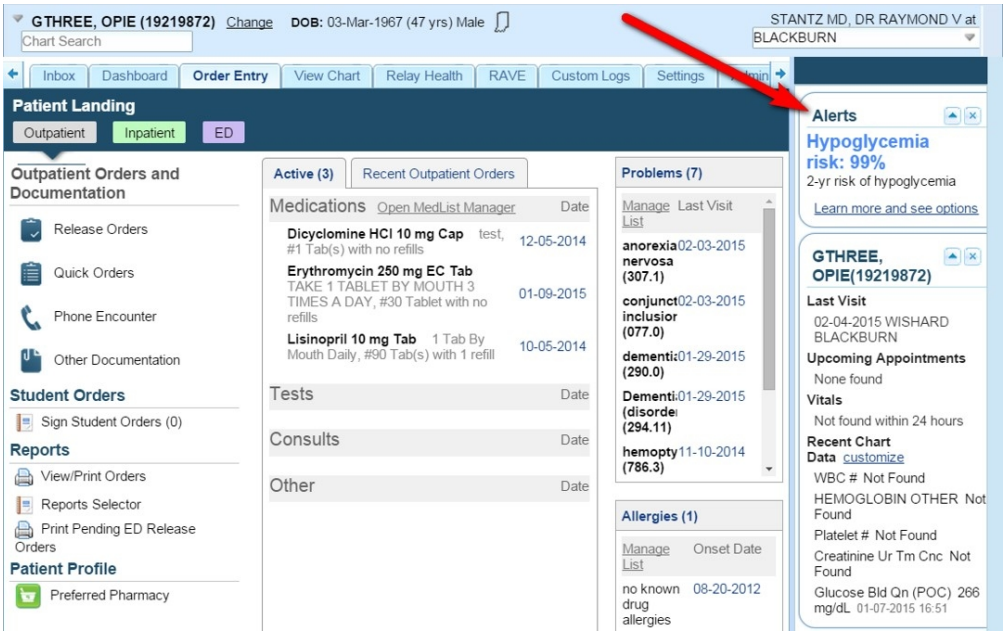

Figure 1. Alert tool in initial collapsed form. The alert shows the two-year risk of hypoglycemia. It provides a link ("Learn more and see options") to expand the display to show more information (see Figure 2).

228x143mm (120 x 120 DPI)

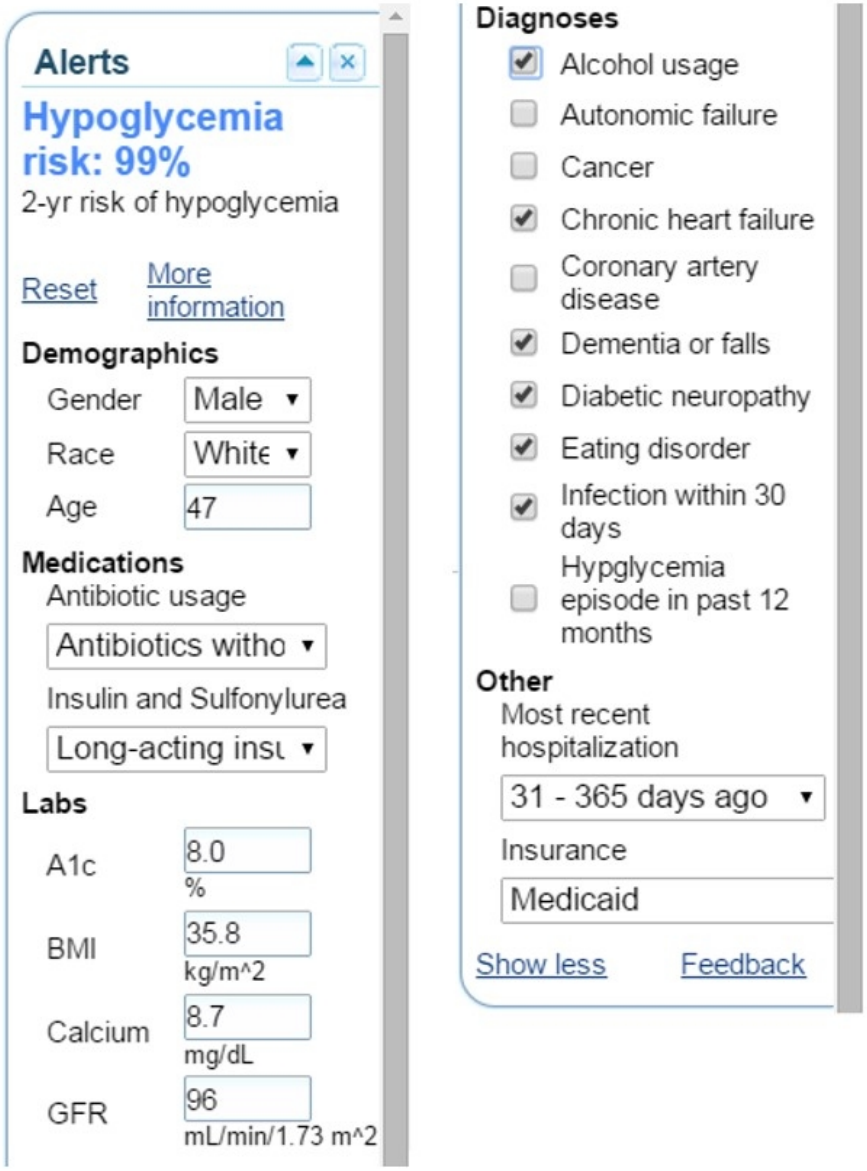

Figure 2. Alert tool in expanded form. Patients' characteristics that contribute to risk of hypoglycemia are shown. The user can modify these to test hypothetical scenarios.

129x175mm (120 x 120 DPI)