Development of a Tool to Assess Hypoglycemia Risk in Patients with Type 2 Diabetes

Katherine Brown PharmD

Follow this and additional works at: https://researchrepository.parkviewhealth.org/pharma

Part of the Pharmacy and Pharmaceutical Sciences Commons
Development of a Tool to Assess Hypoglycemia Risk in Patients with Type 2 Diabetes

Katherine Brown, PharmD
PGY1 Pharmacy Resident
Parkview Health | Fort Wayne, Indiana

Mentors: William Armstrong, PharmD, BCPS and Maryam Noureldin, PharmD, BCPS, BCACP

The speaker has no actual or potential conflict of interest in relation to this presentation.
Background

- More than 34 million US adults have diabetes (~1 in 10) and 90-95% have type 2
- In severe cases, can result in loss of consciousness, seizure, head injury, and other injuries to self or others
- Severe hypoglycemia: requiring assistance of another person to administer carbohydrate, glucagon, or other resuscitative actions
- Many risk factors for hypoglycemia

Risk Factors for Hypoglycemia

- Older age (> age 77)
- Medication-related
  - Insulin
  - Sulfonylurea
  - Beta blocker
  - Antidepressant
- Alcohol use
- Cognitive dysfunction
- Kidney dysfunction
- Untreated hypothyroidism
- Post-gastric bypass surgery
- Pregnancy
- Labile blood glucose
- Skipping meals
- Significant exercise

# Current Literature

## Hypoglycemia Associated With Hospitalization and Adverse Events in Older People

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Population-based cohort study over 4 year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Characteristics</strong></td>
<td>85,370 patients in cohort; 440 identified with severe hypoglycemia (0.5%)</td>
</tr>
<tr>
<td></td>
<td>Mean age 75, female 51%</td>
</tr>
<tr>
<td></td>
<td>93% had diagnosis of diabetes in severe hypoglycemia subgroup</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>Hospitalized hypoglycemia was independently associated with increased mortality (60% vs 19% mortality if no hypoglycemia)</td>
</tr>
<tr>
<td></td>
<td>Higher risk if more hypoglycemic episodes (P &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td>Hospitalized hypoglycemia independently associated with subsequent hospitalizations (P &lt; 0.001) and recurrent hypoglycemia (P &lt; 0.001)</td>
</tr>
<tr>
<td><strong>Conclusion</strong></td>
<td>Hypoglycemia severe enough for hospitalization put patients at substantially increased risk of morbidity and mortality</td>
</tr>
<tr>
<td></td>
<td>Older patients were even more at risk</td>
</tr>
</tbody>
</table>

# Development and Validation of a Tool to Identify Patients With Type 2 Diabetes at High Risk of Hypoglycemia-Related Emergency Department or Hospital Use

<table>
<thead>
<tr>
<th>Objective</th>
<th>Develop and validate a tool to categorize risk of hypoglycemic-related utilization in patients with T2D</th>
</tr>
</thead>
</table>
| Study Design | • Recursive partitioning, split-sample design  
• Classification tree of potential predictors  
• Validation using 3 sample patient groups |
| Inclusion/Exclusion | ICD-9: hypoglycemia  
ICD-9: SSTIs or osteomyelitis |
| Outcomes | Hypoglycemia-related ED or hospital use, 12 months follow-up |
| Baseline Characteristics | • 165,148 patients screened  
• Mean age 63.9 years, 47.6% female |

# Current Literature

## Development and Validation of a Tool to Identify Patients With Type 2 Diabetes at High Risk of Hypoglycemia-Related Emergency Department or Hospital Use

### Results

- Annual rate of 1+ hypoglycemia-related ED/hospital encounter: 0.49%
- Risk stratification: 6 patient-specific inputs
  - Prior hypoglycemia-related utilization
  - Insulin use
  - Sulfonylurea use
  - Prior year ED use
  - Chronic kidney disease stage
  - Age
- Internal validation sample categorized 2.0% high risk, 10.7% intermediate risk, and 87.3% low risk
- 12-month hypoglycemia-related utilization rates: 6.7%, 1.4%, and 0.2%

### Key Points

- Six inputs to categorize hypoglycemia risk
- Target interventions, reduce hypoglycemic risk, improve safety/QOL

---

Self Assessment Question #1

Which of the following factors may contribute to hypoglycemic risk?

a. Sedentary lifestyle
b. Use of long-acting insulin
c. History of severe hyperglycemia
d. Presence of severe lung disease
Self Assessment Question #1

Which of the following factors may contribute to hypoglycemic risk?

a. Sedentary lifestyle  
b. Use of long-acting insulin  
c. History of severe hyperglycemia  
d. Presence of severe lung disease
Self Assessment Question #2

Which of the following patients would likely have the highest risk of severe hypoglycemia?

a. 82 year-old female with type 2 diabetes, cognitive disease, hypothyroidism, 3 hospitalizations in previous year, and use of basal insulin, bolus insulin, and a sulfonylurea

b. 24 year-old pregnant female currently taking propranolol for migraine prophylaxis

c. 45 year-old male with type 2 diabetes and hypertension taking metformin, long acting insulin and lisinopril

d. 68 year-old male with type 2 diabetes and alcoholism, hospitalized once in previous year, and currently noncompliant with medications
Self Assessment Question #2

Which of the following patients would likely have the highest risk of severe hypoglycemia?

a. 82 year-old female with type 2 diabetes, cognitive disease, hypothyroidism, 3 hospitalizations in previous year, and use of basal insulin, bolus insulin, and a sulfonylurea

b. 24 year-old pregnant female currently taking propranolol for migraine prophylaxis

c. 45 year-old male with type 2 diabetes and hypertension taking metformin, long acting insulin and lisinopril

d. 68 year-old male with type 2 diabetes and alcoholism, hospitalized once in previous year, and currently noncompliant with medications
Setting

- Parkview Health
  - 10 hospital health system
  - Close to 800,000 patients
  - Northeast Indiana and Northwest Ohio
- More than 100 PPG locations
Study Purpose

• Known risk factors for hypoglycemia
• Can we use patient-specific information to predict individual hypoglycemic risk?
• Can we create a screening tool to identify patients and help guide clinical therapy?
Study Design

• Retrospective, single center study
• Time frame: 1/1/2019 to 12/31/2020
  • 1/1/2019 to 12/31/2019: baseline period
  • 1/1/2020 to 12/31/2020: analysis period
Study Design

**Inclusion**
- Type 2 diabetes
- 18 years or older
- “Active” patient of Parkview Health

**Exclusion**
- Type 1 diabetes
- Gestational diabetes
- Latent or dormant diabetes
- Active pregnancy diagnosis in the study period
- Deceased prior to 1/1/2021
Baseline Characteristics

41,425 patients
Mean age: 64 years
49.4% female
Predictive Model

- Created in partnership with Business Intelligence
- Data extraction and deidentification
- Ensemble forest model
- “Machine learning”
  - Model training, correction, repeat
Features (Risk Factors)

- Demographics
- Most Recent Labs
- Diagnoses
- Utilization
# Features (Risk Factors)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Most Recent Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>HbA1c</td>
</tr>
<tr>
<td>Gender</td>
<td>Blood glucose</td>
</tr>
<tr>
<td>Height</td>
<td>Serum creatinine</td>
</tr>
<tr>
<td>Most recent weight</td>
<td>BUN</td>
</tr>
<tr>
<td>Most recent BMI</td>
<td>Estimated GFR</td>
</tr>
</tbody>
</table>

This table lists the demographic and laboratory features that are considered risk factors.
Features (Risk Factors)

**Diagnoses**
- Cognitive disease (Alzheimer’s, dementia)
- Hypothyroidism
- Gastric bypass surgery
- Pregnancy
- Current alcohol use (any amount)

**Utilization**
- Number of previous ED/hospital-related hypoglycemic episodes
- Number of previous ED encounters for any reason
- Walk-in clinic encounters for any reason
Outcomes of the Model

• Model has potential to predict 5 outcomes:
  • Hypoglycemia-related ED encounter
  • Hypoglycemia-related hospital admission
  • All-cause ED encounter
  • All-cause hospital admission
  • Hypoglycemic event during ED encounter or hospital admission (<70 mg/dL)
Results: Influential Variables

- Top influential variables for each model outcome
- **Red** = positive influence
- **Blue** = negative influence
- **Purple** = variable influence
## Results: Influential Variables

<table>
<thead>
<tr>
<th>Hypoglycemia-related ED Encounter</th>
<th>Hypoglycemia-Related Hospital Admission</th>
<th>All-Cause ED Encounters</th>
<th>All-Cause Hospital Admission</th>
<th>Hypoglycemia During Encounter</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c</td>
<td>Previous ED enc</td>
<td>Previous ED enc</td>
<td>Previous ED enc</td>
<td>SCr</td>
</tr>
<tr>
<td>Glucose</td>
<td>A1c</td>
<td>BUN</td>
<td>Age</td>
<td>Previous ED enc</td>
</tr>
<tr>
<td>SCr</td>
<td>Glucose</td>
<td>SCr</td>
<td>SCr</td>
<td>BMI</td>
</tr>
<tr>
<td>Previous ED enc</td>
<td>SCr</td>
<td>Glucose</td>
<td>Previous hosp adm</td>
<td>Glucose</td>
</tr>
<tr>
<td>BUN</td>
<td>BMI</td>
<td>A1c</td>
<td>BUN</td>
<td>A1c</td>
</tr>
<tr>
<td>Age</td>
<td>Long-acting insulin</td>
<td>Age</td>
<td>Glucose</td>
<td>Age</td>
</tr>
<tr>
<td>BMI</td>
<td>Age</td>
<td>BMI</td>
<td>A1c</td>
<td>Long-acting insulin</td>
</tr>
<tr>
<td>Long-acting insulin</td>
<td>Metformin</td>
<td>Previous hosp adm</td>
<td>Metformin</td>
<td>BUN</td>
</tr>
<tr>
<td>DPP-4</td>
<td>Previous hosp adm</td>
<td>Female</td>
<td>BMI</td>
<td>Metformin</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>BUN</td>
<td>Metformin</td>
<td>Long-acting insulin</td>
<td>Previous hosp adm</td>
</tr>
</tbody>
</table>

**variables sorted in order of highest influence to lowest influence for each outcome**
## Results: Non-Influential Variables

<table>
<thead>
<tr>
<th></th>
<th>Hypoglycemia-Related ED Encounter</th>
<th>Hypoglycemia-Related Hospital Admission</th>
<th>All-Cause ED Encounters</th>
<th>All-Cause Hospital Admission</th>
<th>Hypoglycemia During Encounter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
</tr>
<tr>
<td>Sex</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
</tr>
<tr>
<td>Previous hypoglycemia-related ED enc.</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
</tr>
<tr>
<td>Previous hypoglycemia during admission</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
</tr>
<tr>
<td>Gastric bypass surgery</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
</tr>
<tr>
<td>SGLT-2</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
</tr>
<tr>
<td>TZD</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
</tr>
<tr>
<td>TCA</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
</tr>
<tr>
<td>Cognitive disease</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>White</td>
<td>Green</td>
<td>White</td>
<td>Green</td>
<td>White</td>
</tr>
</tbody>
</table>
Model Performance: AUC

• Area under the curve
• Healthcare models: > 0.8 is desirable
• Previous hypoglycemic risk models: 0.83
• At Parkview:
  • All-cause ED encounters or all-cause hospital admissions: 0.75
  • ED or hospital encounters for hypoglycemia: 0.82
Model Performance: Precision and Recall

- **Precision**: What proportion of positive identifications was actually correct?
- **Recall**: What proportion of actual positives was identified correctly?

<table>
<thead>
<tr>
<th></th>
<th>All-Cause Encounters</th>
<th>Hypoglycemia-Related Encounters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ED Encounters</td>
<td>Hospital Admissions</td>
</tr>
<tr>
<td>Precision</td>
<td>0.49</td>
<td>0.21</td>
</tr>
<tr>
<td>Recall</td>
<td>0.54</td>
<td>0.54</td>
</tr>
</tbody>
</table>
Discussion/Limitations

• ED and hospital encounters as a PROXY
  • Ideally prevent all hypoglycemic events, not just in “measurable locations”
• Limited by numbers
• Data from 2019 and 2020
  • Final version would be “real-time” data
Future Directions

Implementation into Parkview Health EHR

Guide for physicians

Interventions

• Continuous glucose monitor
• Hypoglycemia education
• Medication modification
  • Glucagon prescription
• Referral
  • Dietician
  • Diabetes education
  • Endocrinology
  • Ambulatory Care Pharmacist
Conclusion

- Many known hypoglycemia risk factors
- Factors are unique to each patient
- Predictive model helps determine unique AND specific risk—helps guide therapy
Acknowledgements

- William Armstrong, PharmD, BCPS
- Maryam Nour Eldin, PharmD, BCPS, BCACP
- Elizabeth Meisberger, PharmD, BCPS, BCCP
- Karen Dunkelberger, RPh, MSHI, CPPS
- Jamie Gaul, PharmD, BCPS
- Sarah Ferrell, PharmD, BCPPS
- Kelly Etnier
- Kayla McGee
- David Franks
- Chad Shirar, MBA
- Emily Schroeder, MD, PhD
References


• True BL, Perry PJ, Burns EA. Profound hypoglycemia with the addition of a tricyclic antidepressant to maintenance sulfonylurea therapy. Am J Psychiatry. 1987 Sep;144(9):1220-1221.


Development of a Tool to Assess Hypoglycemia Risk in Patients with Type 2 Diabetes

Katherine Brown, PharmD
Katherine.brown1@parkview.com
PGY1 Pharmacy Resident
Parkview Health | Fort Wayne, Indiana

The speaker has no actual or potential conflict of interest in relation to this presentation.